Some types of Disseminated Sclerosis.

A Thesis for the degree of M.D.

by

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It is only within comparatively recent years that Disseminated or Multiple Cerebrospinal Sclerosis has been recognised as an important disease, distinct in its clinical history and pathological anatomy from all other chronic diseases of the nervous system. As far back as 1840 lesions in the brain and spinal cord which are now recognised as being characteristic of this disease, were figured by Cruveilhier[1] and Carswell,[2] but these were looked upon merely as a pathological curiosity, and their clinical significance was not recognised till much later. Various observations upon the disease were published from time to time by Turck, Rokitansky, Frerichs and others, principally from the anatomical point of view, but the effort to isolate it clinically was not attended with much success. An important contribution to the literature of the subject was added in 1863 by Rindfleisch, who described minutely the pathological changes which he had observed in a case of this kind, and argued from these that the morbid process began as a chronic inflammation in the walls of the smaller arterioles, followed by a local increase in the adjacent connective tissue, and a consequent atrophy of the nerve elements.[1] Between the years/

1. Anatomie Pathologique 1835-1842.
2. Illustrations of the Elementary Forms of Disease 1838.

1. Histologisches Detail Zu der Grauen Degeneration von Gehern und Ruckenmark. Virchow's Archiv 1863 Bd. XXVI.

years 1862-1866 a thorough investigation of the whole subject was undertaken at the Salpetriere, Paris by Vulpian, Charcot and others, and as the result of these researches the disease was finally isolated both clinically and pathologically. Charcot's classical description was delivered as a lecture in 1868, and is to be found in his work on Diseases of the Nervous System[1]. After this, observations and verifications went on apace, especially in France, but it is curious to note how slowly the recognition of the disease by the medical profession of this country progressed. As late as the year 1875, the late Dr. Moxom, demonstrating a series of eight cases, introduced the lecture by the following remarks:- "The recognition of this disease by English Physicians will appear singularly slow at the time (which must soon come) when its characters are more generally known. Some disorders have received universal credit though they are only identified by symptoms without any certain morbid anatomy; such as Paralysis Agitans etc. Other disorders are equally generally allowed, although they have only a constant morbid anatomy without any certain symptoms; such as cerebral abscess etc. It must then appear strange that a singular and definite disease, of which I am about to relate a few cases/

1. Charcot, Diseases of the Nervous System. New Sydenham Society, 1877. Vol. I.

cases, has not yet been admitted by the profession of this country, when we know that it not only has constant and characteristic symptoms, but also a quite peculiar and very remarkable morbid anatomy. Although the two cases under my own care, of which I shall give the post-mortem appearances, are, as far as I know, the only ones in which the diagnosis has been made sure, by inspection after death, on this side of the Channel, yet cases of Insular Sclerosis (Sclerose en plaques, inselformige Sclerose) have been recognised and verified in France and Germany in many instances."[1]

Later writers have devoted their attention particularly to the atypical varieties of the disease, which are by no means rare. The name of Dr. Buzzard, in this country, is intimately associated with this investigation, and more especially with what he himself has termed the Hysterical variety. In a small work written in 1891 entitled "On the simulation of Hysteria by Organic Diseases of the Nervous System" he discusses this subject at some length, emphasizing especially the frequency with which such cases are wrongly diagnosed as pure Hysteria. In 1893, in association with Dr. Head he published the results of a series of researches regarding/

1. Guy's Hospital reports Series III. Vol. XX. 1875.

regarding the occular and ophthalmic phenomena as an important aid to diagnosis, more especially in the Hysterical type of the disease[2].

But even now, as formerly, it is from the continent that the more important contributions to our knowledge of the subject are forthcoming. Valuable work has been done by Oppenheim. The investigations of Uhthoff and Parinaud from the Ophthalmic aspect have led to important results. Dr. Pierre Marie's name is especially associated with his theory regarding the infectious nature of the disease, a theory which, at the time of its promulgation, was received with considerable incredulity, but which, as the evidence in its favour accumulates, is becoming more generally accepted.[1] The subject of the Aetiology of the disease is exhaustively discussed in an article by Oppenheim published in 1896, where in addition to the ordinary infectious diseases, he includes Influenza and Malaria amongst the causative factors, and lays considerable stress upon the influence of metallic poisons and other chemicals in a certain proportion of the cases[1][2].

2. British Medical Journal, Vol. II. 1893, p.788.
1. Lectures on Diseases of the Spinal Cord. Marie. New Sydenham Society 1895. p.133
1. Berliner Klinische Wochenschrift. Berlin. March 2nd.1896
2. For the early part of this history, I am largely indebted to the work of Dr. T. K. Monro. "A History of the Chronic Degenerative Diseases of the Central Nervous System."

Glasgow, 1897.

In its typical form Disseminated Sclerosis presents a clinical picture which is highly characteristic, and in which the symptoms are of a very striking order. It is, however, met with under the most diverse forms, and in the following pages I shall record and comment upon a few cases which have come under my own observation, and which form an excellent illustration of the many different phases which the disease may assume. A brief consideration of the morbid Anatomy and Pathology will serve to demonstrate how readily such diversities may arise.

Scattered throughout the Brain and Spinal Cord of a patient who is the subject of this disease, there are islets of Sclerosis varying in size from a millet seed to a florin. Each islet is isolated, although it occasionally happens that two or more may run together. Any part of the nerve tissue may be involved, but the morbid process shows a special affinity for the white matter, and in consequence the areas of sclerosis are most frequently met with on the surface of the spinal cord, medulla oblongata, pons Varolii and Crura Cerebri. In the Cerebral Hemispheres they are located principally in the white matter of the Centrum Ovale, in the Corpus Callosum and in the walls of the ventrieles. The basal ganglia are not infrequently invaded. The cranial nerves are often affected, the Sclerosis involving the whole thickness/

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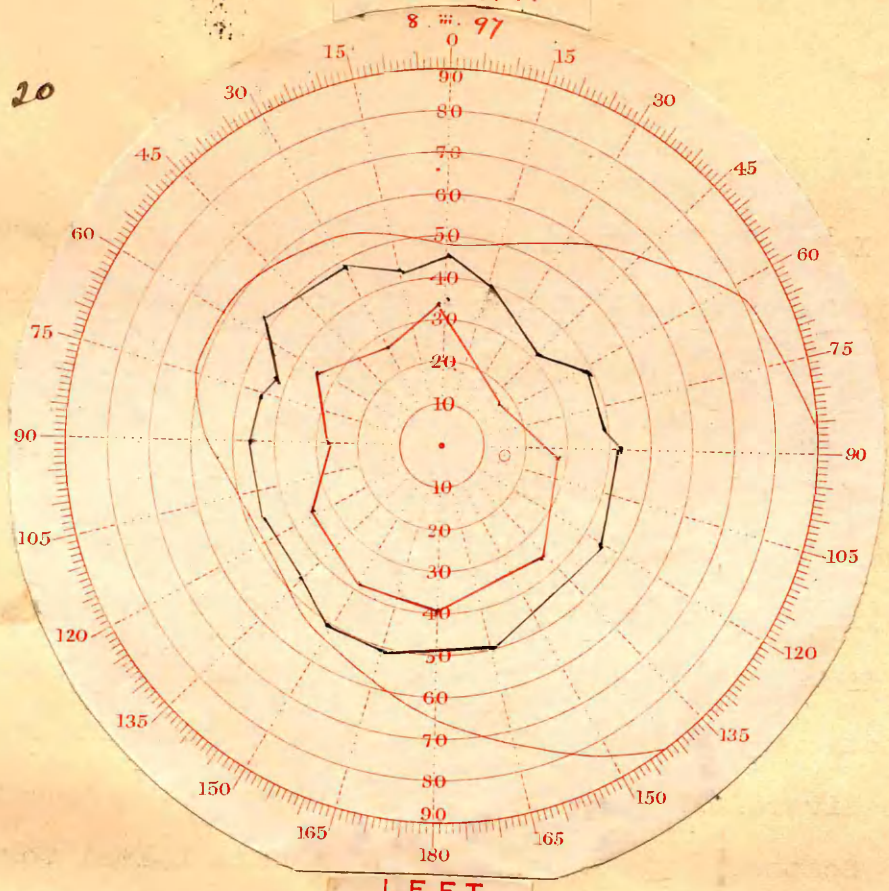

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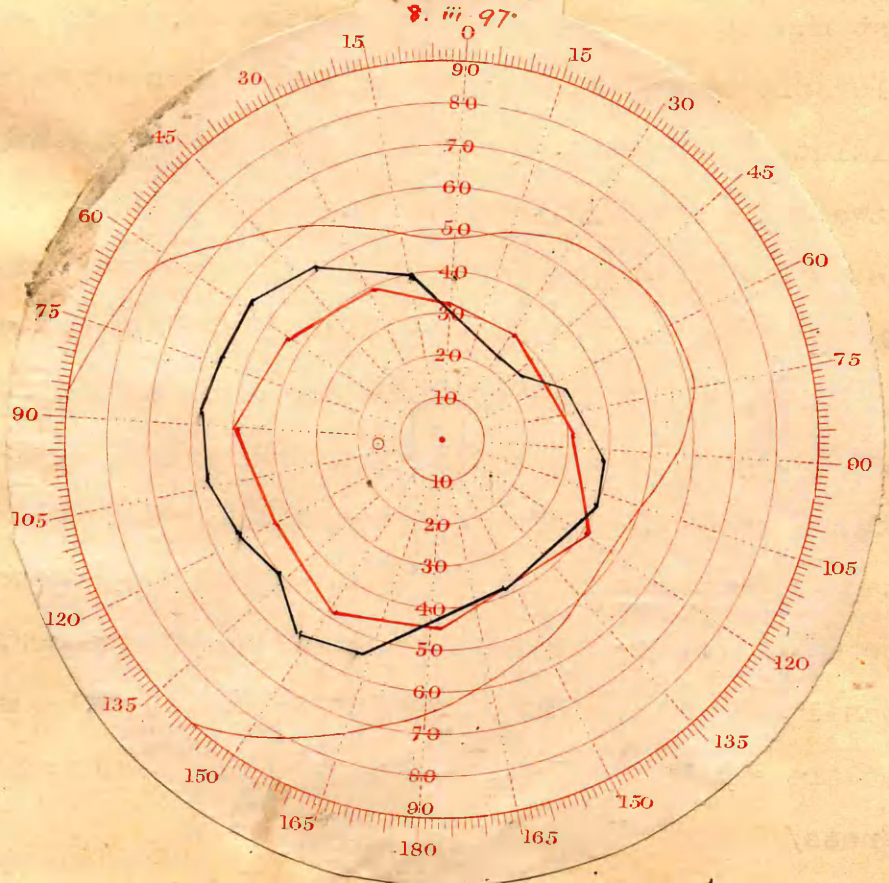


thickness of the nerve near its root, or only a part. The roots of the spinal nerves are less frequent seats. The grey matter of the spinal cord is not exempt from invasion, indeed there is no portion of the cerebrospinal axis which may not be implicated.

The lesion consists essentially in an overgrowth of the neuroglia element of the nerve structures, which is associated probably secondarily, with degenerative changes in the nerve fibres themselves. Examining microscopically a single islet, we find that the morbid process is farthest advanced in the centre and passing outwards to the periphery there is a gradual transition to healthy tissue. At the periphery we may observe a relative increase in the interstitial neuroglia, while there may not be any appreciable alteration in the nerve fibres. Towards the centre various stages in the destruction and absorption of the myelin sheath will be seen, while at the centre itself this structure may be entirely absent, the axis cylinders then lying naked, surrounded by a great excess of neuroglia. The axis cylinders themselves are somewhat altered from the normal. Some are enormously enlarged while a few are atrophied, but for the most part they will be found to be larger rather than smaller than in their normal physiological condition. It is especially noteworthy that the nerve fibres are not destroyed/

destroyed. Their continuity is not broken, and therefore secondary degeneration does not follow. Herein lies the important distinction between this disease and the ordinary system degenerations of the Brain and Spinal Cord. In these, for instance in Tabes, increase of the connective tissue element is secondary to degenerative changes in the essential nerve structures. The axis cylinder is destroyed, and secondary degeneration then follows along the whole course of the individual nerve fibre. It is a very essential difference, and serves to explain much of the peculiar pathology and clinical history of Disseminated Sclerosis. For instance rapid and almost complete recovery, after more or less profound paralysis, is of fairly common occurrence. When such a phenomenon occurs, it is supposed that the inflammatory process has been a somewhat acute one, and has seriously interfered with the function of the axis cylinders. Not being destroyed, however, they are capable of resuming their function when the inflammatory lesion subsides. Cases are also on record in which certain of the more commonly recognised symptoms of the disease, after having been present for a short time, have entirely disappeared. In such a case the morbid products of inflammation may have been absorbed, and the structures in consequence have resumed their normal physiological condition.

Charcot/

Charcot himself has expressed the opinion that in some cases the white substance is restored to the axis cylinders which have been denuded. This subject will be further discussed at a later stage. The most striking symptom of a typical case of Disseminated Sclerosis is undoubtedly the characteristic Intentional or Volitional tremor. To account for this peculiar phenomenon it is usually explained that the white substance normally acts as an insulator. Hence in those fibres which have been deprived of their myelin sheath, the nerve impulses are liable to be diffused into the surrounding tissue, just as an uninsulated wire will allow an electric current passing through it to escape into whatever substance it may be in contact with. Under normal physiological circumstances a voluntary impulse, starting from a higher centre, passes through unimpaired axis cylinders, and, reaching a muscle, sets up a proportionate degree of contraction in each of its fibres. It is evident, however, that the same impulse, passing through fibres which vary greatly in their degree of insulation, will reach the muscle in a very irregular condition, and will therefore set up contractions which are correspondingly irregular. This view of the pathology was first suggested by Charcot, and is generally taught. It is not however considered an adequate explanation by all writers (Erb. etc) and other theories

have/

have been suggested. These mostly demand that a particular situation, e.g. the Optic Thalamus, should be invaded by sclerosis before the tremor will follow. This view of the case is supported by the fact that in certain of the atypical forms of Disseminated Sclerosis tremor may be absent.

When we consider the multiplicity of the lesions, and their indiscriminate localisation, we are not surprised at the variety of the symptoms which may be met with. There is more cause for surprise in the fact that it should be at all possible to indicate any special group of symptoms as the usual clinical features of the disease. It is common to divide the disease into three types, (1) The Spinal, (2) The Cerebral, (3) The Cerebro-spinal. The first two are less common than the last, and are only found during the early stages of the disease. It is however principally in connection with these that difficulties in diagnosis arise. For instance a lesion may develope in the lateral columns of the cord, giving rise to symptoms identical with those of Primary Spastic Paraplegia, so that a differential diagnosis may be for a long time impossible. In an exactly similar manner the disease may simulate Locomotor Ataxia, so as to render the differential diagnosis exceedingly difficult or even impossible, until the developement of some new symptom indicating the true nature of the disease.

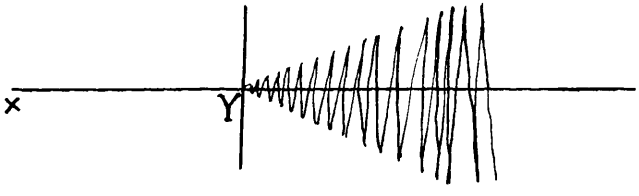
In/

In other cases the most clamant symptoms may be of cerebral origin. Amongst these may be mentioned Vertigo, impairment of speech, a peculiar mental attitude, manifestations of associated Hysteria, etc. Where these are the most prominent symptoms, the case is equally liable to be misunderstood. The difficulty of determining whether such a patient is merely hysterical, or is really the subject of serious organic disease is sometimes very great, a difficulty which is further increased by the fact that purely hysterical symptoms are liable to be associated with the early stages of Disseminated Sclerosis, more especially in young women.

In the great majority of cases, and in almost all that are past the early stages, both spinal and cerebral symptoms will be observed, and the nature of the disease will then as a rule be readily recognised.

There are three cardinal symptoms which occupy a prominent position in the classical description of the disease. These are (1) Tremor on voluntary movement, (2) A peculiarity of Speech which is described as Syllabic or Scanning, (3) Nystagmus ~~Tremor~~ Tremor. The peculiar character of this phenomenon gives to it a position of great importance amongst the diagnostic symptoms of the disease. It is only educed by voluntary effort, the patient lying perfectly still/

still while the muscles are in repose. Hence have arisen the terms Volitional or Intentional which are commonly employed to denote these peculiarities. At the commencement of any voluntary act the amplitude of movement is slight, but as the effort continues the range becomes rapidly increased. For instance in the test experiment of causing the patient to drink water from a glass, the tremor is at first comparatively slight, but increasing rapidly as the glass approaches the lips, the oscillations may finally reach an amplitude of six or seven inches. This has been diagrammatically represented by Charcot.



During the period X Y, the muscles are at rest. A muscular contraction is attempted which results in the onset of tremors, the amplitude of which is at first small but increases rapidly.

The movements are very jerky in character, and are not truly rhythmical. They increase in proportion to the amount of muscular exertion employed. If attention is drawn to them, or if an effort is made on the part of the patient to control them, they become correspondingly more violent. In an advanced stage of the disease all the muscles of the body will/

will be involved, and those muscles which control the widest range of movement will produce the most striking effects. Thus at the end of the action already referred to, when the glass of water is close to the lips of the patient, the wide range of movement in the hands is due to muscles controlling the shoulder and elbow joints, while the rhythmical movements of the head and upper part of the body are the result of coarse tremor in the large muscles of the neck and trunk. It is this same feature of the disease, combined as a rule, with an element of Spasticity, that gives rise to the peculiarity of gait commonly met with.

Impairment of Speech.- When present in a well-marked degree, this symptom is highly characteristic. Its description is contained in the four adjectives, Slow, Monotonous, Scanning and Spasmodic. The articulation of each syllable is attended with an undue amount of effort, and the utterance is slow and very deliberate. Sometimes the delivery is abrupt or "explosive," the speech having then a "staccato" quality. There is an absence of the normal modulations of tone, and every syllable is spoken with equal emphasis. In addition it is frequently noted that the voice has a peculiar high-pitched intonation, and is curiously monotonous. The importance of these symptoms has been variously estimated. Buzzard has expressed the opinion/

opinion that they have been allowed to rank too high, being less frequently present than is commonly supposed. He says:- "A laboured articulation is useful for purposes of diagnosis, but in my experience it is not often present."[1] In none of the cases to be afterwards described was this symptom at all typical, and in the majority the articulation was not notably impaired.

Nystagmus is a symptom of great importance, more especially in the exclusion of a possible functional basis. It is present in a considerable variety of the other chronic diseases of the nervous system, notably in Cerebellar disease and Friedreich's ataxia, and its pathology is obscure. Its detection in cases of Disseminated Sclerosis will often go far to confirm a doubtful diagnosis. Uhthoff has described two varieties (1) True Nystagmus, or spontaneous oscillations of the eyeballs occurring quite apart from any voluntary effort on the part of the patient, and therefore not requiring any artifice on the part of the observer for its demonstration. Only a very small proportion of cases present this symptom. Out of 100 instances of the disease examined by Uhthoff, it was observed in 12. Nystagmus of this type indicates some definite intra-cranial lesion. (2) Nystagmoid Oscillations. These are only brought out when the patient is made to look far to the right or left, and/

1. Lancet 1895 Vol. 1. p.77.

and will in very many cases be found to be associated with, and may possibly depend upon, paresis of certain of the occular muscles. Uhthoff's statistics bear out that 58% of cases present this form. Marie, however, considers this figure too small, and would raise the percentage to 70 or 80. The oscillations are in almost all cases lateral, but occasionally vertical, and even rotatory nystagmus has been observed.

There is a certain mental attitude which is described as characteristic of Disseminated Sclerosis. It takes the form of undue complacency and contentment. While fully realising in many cases the gravity of his condition, this does not appear to depress him as one would expect, and he rarely seems unhappy in consequence. While there is not the undue hopefulness of ultimate recovery, which one finds, for instance, in an advanced case of Phthisis, the subjects of Disseminated Sclerosis are liable to seize upon any temporary improvement in their symptoms and to exaggerate their importance. They are very keen that every method of treatment should be adopted, and are always hopeful as to the effects of these. It is not common to find any marked impairment in the mental acuity, but slight weakness of intelligence is not unfrequently observed. Only in very exceptional cases does one find any considerable degree of/

of mental alteration, but occasionally it does happen that these patients sink into a condition of chronic Dementia.

There is a certain peculiarity of facial expression which is common to a great many of these patients. Charcot has described it as a "vague expression." It gives an impression of mental weakness, which may not be confirmed by conversation with the patient. This peculiarity of physiognomy is often enhanced by its association with certain occular defects, notably paresis of some of the Occular muscles.

Many of the mental phenomena of the disease are to be explained by the close association of Hysteria with certain forms of Disseminated Sclerosis, which has already been indicated. Among these may be included the attacks of spasmodic laughter which are sometimes observed, and which the patient is quite unable to control, so much so that in a few cases they constitute quite a distressing feature of the illness.

These then are some of the more important phenomena associated with Disseminated Sclerosis. It will not be necessary at the present stage to pursue further the symptomatology of the disease. Other symptoms will be considered as they arise in connection with the cases to be afterwards described. Those which have been mentioned more especially the/

the first three, (Intentional Tremors, Nystagmus and The Scanning Speech), are the evidences of the disease upon which it is customary to depend largely in forming a diagnosis. Nevertheless there is abundant reason to believe that the disease may exist, and yet not include any of these among its symptoms. After having demonstrated a case which presented the following symptoms; Characteristic tremors on voluntary movement, loss of power in various limbs, Exaggerated knee jerks, nystagmus, slow and peculiar speech, pallor of both optic discs and certain bulbar symptoms, Dr. Buzzard remarked:- "I believe that for one typical case like this, there may be very many indeed, the symptoms of which are so widely divergent, that the idea of Insular Sclerosis may easily fail to present itself to anyone familiar only with the classical form of the disease."[1]

From amongst these atypical varieties I shall first select for consideration that type which is associated with the name of this author, namely the Hysterical Type, and I shall again quote his own words:- "There is a form of Disseminated Sclerosis of supreme importance from the fact that the patient is regarded perhaps for years as an example of Hysteria, and the serious organic disease, underlying the nervous symptoms, is very frequently indeed overlooked. In this/

1. Lancet 1895. Vol. I. p.77.

this, which usually but not invariably, affects the female sex, there is often a history of moral or physical shock, followed by loss of power in one or more limbs, aphonia, convulsive seizures and alteration of manner of the kind which is termed Hysteria."[1] A patient came under his observation with a history of fainting following the discovery of a compromising letter. This was associated with a condition of nervous dread from which she afterwards recovered. Two years later she was attacked with vomiting and cramp in the Sciatic districts, refused food, and was said to be dying. She suddenly recovered in twenty-four hours, and was completely well in six months. Two years later she had loss of power in both legs and diplopia. Recovered in three months. Three years later more vomiting and loss of power, which again subsided, and she remained well till four years afterwards. Then on the death of her husband, loss of vision and vomiting occurred, and paralysis of the right arm slowly developed. "We found definite limitation in the field of vision, and well marked atrophy of both discs. There was no distinct tremor of the limbs, but the knee jerks were exaggerated, and there was ankle clonus." Again he says:-

"Looking back I can remember a number of cases in which this/

1. British Medical Journal, Vol. II. 1893. p.780.

this recovery from more or less powerlessness for a time, to be followed by a return of trouble in the same or another limb, led me into a temporary error of diagnosis, until the sequel, by displaying the typical symptoms of Insular Sclerosis, cleared up the obscurity. When the remissions occurred in young females, I used to fancy that the term Hysteria could be satisfactorily applied to the case, whilst, if the patient belonged to the other sex, not a little suspicion of malingering would sometimes cross my mind. Subsequent experience, extending over many years, has pretty well convinced me that the view still widely held, that a shifting loss of power, from one limb to another, is characteristic of Hysteria, is an error which has arisen from cases of Insular Sclerosis being diagnosed as Hysteria."[1]

The following case belongs, I believe, to this type, although it presents some unusual features.

Case A. M.P. Aet. 12. Occupation Schoolgirl.

Admitted to the Glasgow Royal Infirmary for the first time on March 2nd. 1897, complaining of loss of power in the lower limbs. Five weeks prior to her admission she had taken ill somewhat suddenly, the onset being associated with shivering, vomiting and general malaise, which persisted throughout the day. On the following day she complained of prinkling/

1. Lancet Vol. 1. 1895. p.79.

prinkling sensations in the right arm. Two days later the right leg became affected similarly, and on the following day she became conscious of loss of power in these limbs, affecting first the arm, and later, the leg. The paralysis in a short time became so profound that she was unable to lift either limb off the bed, and this continued for about ten days. Then improvement took place equally rapidly, so that at the end of the fortnight she was able to walk without assistance, and she continued to do so for about a week. Then a relapse occurred. She complained of severe paroxysmal pains in the ankles, knees and thighs, and shortly afterwards paralysis set in affecting first the left leg and later the right.

There was no evidence of a neurotic taint either in the personal or family history. She had never been considered a robust girl, but, with the exception of measles, which she had as an infant, and occasional attacks of so-called Influenza, she had had no other illness of importance. There was no history of Scarlet Fever, Rheumatism or Chorea. When admitted she was found to be considerably emaciated, but atrophy was not localised to any special group of muscles. The lower limbs were very powerless, and she was quite unable to walk. The left leg was weaker than the right. As she lay in bed the feet occupied the position of Talipes Equinus/

Equinus, and there was a flail-like movement at the ankles. The knee jerks were only slightly obtained, but ankle clonus was elicited. The plantar reflexes were abolished. In the lower limbs the tactile, painful and Thermic senses were found to be impaired, but elsewhere they were normal. The grasp of the hands was exceedingly feeble, but equal on the two sides. When held out the hands presented a fine tremor. There was slight left facial paralysis. Pupillary phenomena were normal. A distinct contraction of the field of vision was observed, both for white and for coloured objects. see p. 6 No Ophthalmoscopic changes were discovered.

Physical examination of the internal organs failed to reveal anything abnormal, beyond the presence of a V.S. murmur at the base. An electrical examination of the muscles was conducted by the hospital electrician Dr. George Macintyre, who made the following notes:-

Electric sensation felt in right arm and leg distinctly at 8½ cm.

Right leg - Muscles supplied by the ext. pop. nerve contract at 8½ c.m.

Tibialis anticus,	faradic gives	C. at 6½ cm.
	galvanic "	K.C.C. & A.C.C. at 6 m.a.
Peroneus longus,	faradic "	C. at 7 cm.
	galvanic "	A.C.C., no K.C.C. at 3 m.a No opening contraction
Soleus,	faradic "	C. at 7¾ cm.
	galvanic "	K.C.C. and A.C.C. at 5 m.a.

Left/

Left leg -

Ext. pop. nerve,	faradic gives	C. at 7½ c.m.
	galvanic "	no K.C.C., marked A.C.C. at 4 m.a.
Tibialis anticus,	faradic "	C. at 7 cm.
	galvanic "	K.C.C. and A.C.C. at 6 m.a.
Soleus,	faradic "	C. at 7½ cm.
	galvanic "	slight K.C.C., marked A.C.C. at 9 m.a.

A rapid improvement took place, so much so, that within a fortnight of her admission she was walking about the ward without assistance. The impairment of sensation disappeared entirely. The left facial paresis noted on admission was found to be gone a few days later, but almost immediately afterwards slight paralysis was detected affecting the right side of the face. This was also of short duration, but a fortnight later while she was in other respects remarkably well, right facial paralysis recurred, and was this time complete, involving even the muscles of the forehead. For a fortnight this symptom continued, and its disappearance was gradual, commencing first in the upper facial muscles. She was dismissed greatly improved on April 30th., and the case was indexed in the ward journal as Hysterical Paralysis.

She was readmitted on July 19th., 1898. In the interval she had enjoyed fairly good health, and had for a considerable period been employed as a message girl. There had been no return/

return of any paralytic phenomena. Five weeks prior to her readmission, she was seized with severe paroxysmal pains in the left temple, and on the following morning she had an attack of vomiting, associated with violent retching, which continued for some hours. Then she complained of prinkling sensations on the left side of the face and mouth, and for three weeks this was her only symptom. Another attack of vomiting, similar to the first, preceded the onset of prinkling sensations on the right side of the face and mouth. This passed off, and after a few days a similar attack was followed by the same sensations affecting all the limbs. During this time she did not attempt to walk "being afraid she would stagger." She did not, however, make any complaint of giddiness. A week later the prinkling sensations disappeared from the left side, and she became conscious of loss of power affecting that side only, but involving both the arm and leg.

On admission, she was found to be greatly emaciated, and very feeble. Her mental condition was peculiar. She was quite bright and inclined to talk a great deal, but at times she was rather incoherent. There was no impairment of speech, but her voice was peculiarly high pitched. The pupils were widely dilated, and reacted feebly. There was no nystagmus. The power of convergence was imperfect, due apparently/

apparently to paresis of the right Internal Rectus. The muscles in both arms were feeble, but those of the left were especially so. Triceps and Biceps jerks were obtained on both sides, but were rather exaggerated in the left arm. No tremor was observed. The left leg was paralysed, and the muscular power of the right was very feeble. Both lay in the position of Talipes Equinus. There was an appreciable degree of Adductor spasm in both legs. Both knee jerks, but especially the left, were abnormally active, and ankle clonus was obtained on the left side. Plantar reflex was absent on the left side, and very feeble on the right. Abdominal reflexes were absent. Common sensation, the sense of pain and the thermic sense were all rather impaired everywhere. The Heart was as before.

On the evening of the 22nd. July, three days after admission, quite suddenly, she fell into a curious condition of collapse. The face was flushed, with the exception of well defined white rings encircling the eyes and mouth. The skin was covered with a clammy sweat. The extremities were cold. The pulse was extremely rapid and very feeble, the respirations irregular and shallow, but never Cheyne-Stokes. She never actually lost consciousness, nor had she any convulsions or twitchings. She was extremely restless and moaned a great deal, complaining of a feeling of tightness

across/

across the foot of the sternum. The pupils were unequal, the left being larger than the right, but both reacted normally. There was well marked lateral nystagmus. Tache cerebrale was readily obtained. She was very sick and vomited a good deal. She also had some difficulty in swallowing. Urine and Faeces were discharged involuntarily. A specimen of urine was found to contain a distinct quantity of sugar.

A slight degree of facial paralysis was observed at this time, affecting both sides of the face, but rather more marked on the right side.

For nearly a week she lay apparently moribund, but a gradual improvement took place. The temperature, which had been slightly febrile, the highest record being 100.8°, came down to normal. Pupils became equal, but the nystagmus persisted. Tache Cerebrale disappeared. Sugar disappeared from the urine. The knee jerks, which, during the attack had been difficult to elicit, returned, and again became exaggerated. Superficial reflexes also returned. Incontinuance of Urine and faeces continued to be troublesome for some time afterwards. Complete control of the bladder did not return for more than a month.

During her convalescence other phenomena were noted. Tremor of the hands and arms became well marked, being brought/

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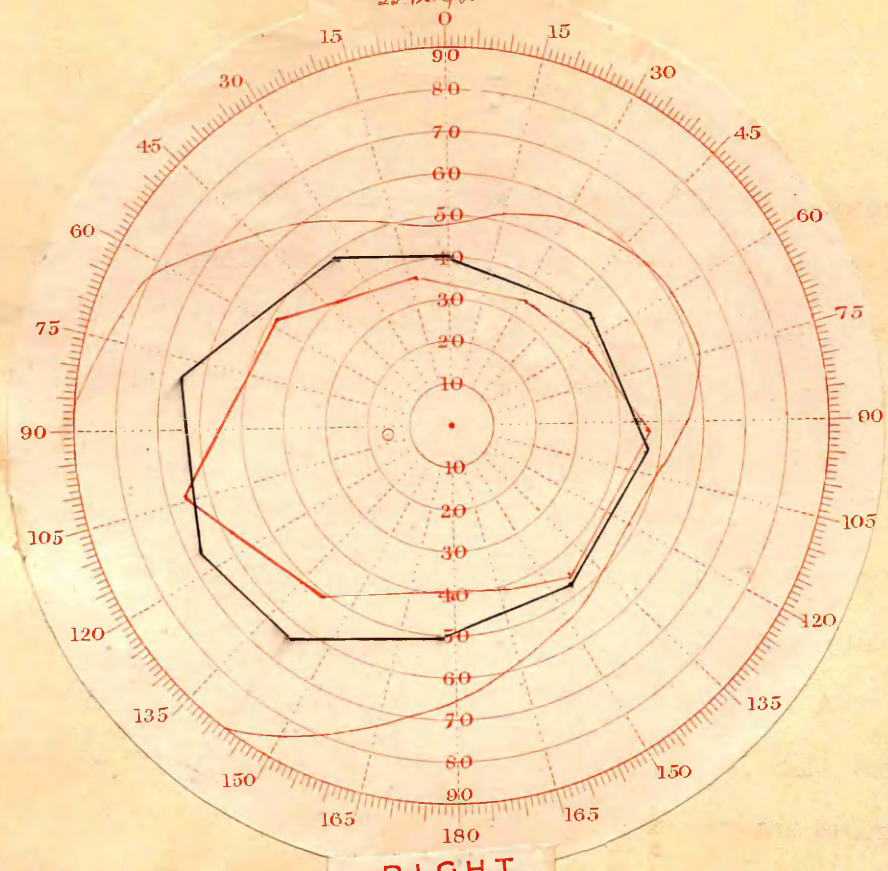

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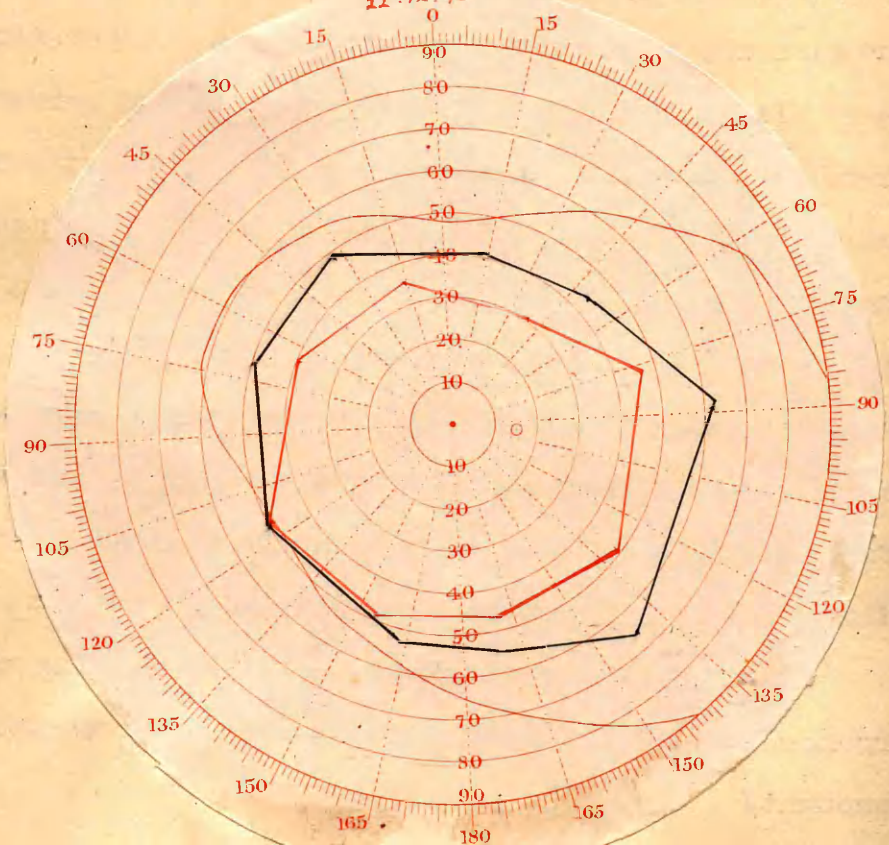


brought out especially when she attempted any delicate voluntary movement. Paresis of the left external Rectus muscle was detected, in addition to that of the right Internal Rectus which had already been noticed. Occasionally she complained of diplopia.

On the 7th. of September she was sufficiently well to walk a few steps unassisted, and after this improvement was rapid. The facial paralysis passed off very gradually, disappearing first from the right side and later from the left.

An examination of the eyes about this time revealed some contraction of the field of vision both for white and for colours. The Optic discs were considered to be rather unduly pale. There was no appreciable visual defect. The pupils continued to be much dilated, and to respond very feeble both to light and in accommodation. An electrical examination of the muscles, on September 22nd., gave the following reactions:-

"The external popliteal nerve responds slightly to 2 m.a. and very distinctly to 4 m.a. on both sides; with this current there is a prolonged contraction, broken by some clonus. The tibialis anticus and the extensor communis digitorum on both sides respond markedly to 8 m.a. with the constant and 7 cm. with the induced current, but not to a weaker/

weaker current. This is the case with a short current, but when a current of long duration is passed there appears a slowly produced spasm which continues during the passage of the current, and disappears slowly after the current is stopped. The induced current gets response at once, but seems comparatively weak. The left gastrocnemius gives the same slow spasm with a strong continued current, and very little response to a quick current of galvanism. The spasm is an over-extension of the foot, with over-extension of the toes, as though the current went to the front of the leg; it takes almost five seconds to disappear."

"The right leg with the same current seems to give no contraction (?) of the gastrocnemius, but there is great spasmodic over-extension of the toes and flexion of the foot. The induced at 7 m.a. gives contraction on the left, but none on the right. The right gastrocnemius, therefore, does not respond to the current. The left gastrocnemius with a strong current gives slight immediate contraction, and then a slow, strong spasm."

On her dismissal, November 11th., emaciation was still a striking feature of her condition, but she was walking easily without assistance. The knee jerks were very active, and there was a trace of ankle clonus. Nystagmus was still demonstrable.

This case, then, in the first place, is an excellent illustration of the extreme difficulty with which we are sometimes confronted, of differentiating between a case of pure Hysteria, and one which is dependent upon organic disease of the nervous system.

During her first residence in the Infirmary a diagnosis of Hysteria was favoured. The fleeting nature of her paralytic symptoms, especially, were looked upon as indicating a functional basis, but as I have already pointed out, certain modern neurologists, notably Buzzard in this country, and Oppeheimer on the Continent, have succeeded in gathering evidence to show that these symptoms point rather in the opposite direction, and in favour of Disseminated Sclerosis. The organic lesions, they argue, are capable of giving rise to symptoms of an hysterical nature, and these may be prominent before any evidences of the more serious malady have appeared. Then when phenomena, which might have been suspected of having an organic basis, present themselves, they are associated in the mind of the physician with the symptoms of Hysteria which he has previously observed, and he accordingly treats them merely as manifestations of the same disease. An aid to diagnosis is said to exist in the order in which the paralytic phenomena present themselves. In our case the illness commenced with a hemiplegia (a rare phenomenon/

phenomenon in Hysteria) affecting the right side, first the arm and later the leg. Improvement took place rapidly so that at the end of a fortnight she could walk without assistance. For a week she continued to have voluntary control of all her limbs. Then the left leg became paralysed, later the right again lost power, and she became paraplegic. "The hysterical woman, who has lost all power of her legs, will, it is true, very often later on (while still paraplegic) lose the power of one arm (usually the left), but in my experience she is not prone to lose the power of a limb, then recover it, and then lose it in the other."[1] Our case is of this type, and therefore confirms in so far the experience of Dr. Buzzard.

Marie, quoting from Miss Blanche Edwards, states that hemiplegia is not an uncommon symptom in this form of Disseminated Sclerosis; that, as a rule, it is associated at its commencement with an apoplectiform seizure; that it is usually a transient symptom and may completely disappear. The initial symptoms in our patient could hardly be called apoplectiform, although they probably had a cerebral origin. She was suddenly seized with violent vomiting, and this was followed next day by prinkling sensations in the right arm. Two/

1. Quain's Dictionary of Medicine. Article on Disseminated Sclerosis by Dr. Buzzard,

Two days later the leg became affected similarly, and on the following day there was loss of power in both. In other respects the character of this hemiplegiac seizure corresponds with the observations of Miss Blanche Edwards.

The Electrical reactions of the muscles are not likely to yield any information of importance in the differential diagnosis, as neither in the paralysis of Hysteria, nor in that of Disseminated Sclerosis (except in exceptional cases) are the nerve filaments supplying the muscle cut off from their Trophie centres. In our case, it is difficult to account for the disturbance in the polar reactions observed during her first residence. The degree of alteration from the normal was slight, and perhaps the disuse of the muscles, associated with the general wasting, may be sufficient to explain it.

The presence of ankle clonus, although but slightly developed, pointed strongly in favour of organic disease. This symptom is rarely if ever present in pure Hysteria, although it is not uncommon to find the deep reflexes exaggerated. In Disseminated Sclerosis, on the other hand, even at an early period of the disease, not only are the deep reflexes greatly increased, but, as a general rule, typical ankle/

ankle clonus will be readily elicited. The detection of this latter symptom in any case where previously all the phenomena observed have indicated a purely hysterical basis, ought to raise in the mind of the physician grave doubts as to the correctness of his diagnosis.

On the other hand the detection of Sensory disorders rather favoured the diagnosis of Hysteria. Such disorders are not common in Disseminated Sclerosis, and their occasional presence is looked upon merely as a clinical curiosity. Their occurrence in the Hysterical type of the disease may be explained on the ground that this particular symptom has a functional basis. Freund of Breslau has investigated this subject and has found that sensory disorders when they do occur in uncomplicated cases of Disseminated Sclerosis, are seated mostly in the extremities of the limbs, namely in the fingers and toes, that they are but slightly pronounced, of temporary duration and liable to change. It is a physiological fact that it requires a greater amount of damage to destroy the function of a sensory than of a motor nerve fibre, and herein doubtless lies the explanation of the infrequency of sensory disturbances in Disseminated Sclerosis. The axis cylinders, being intact, are able to continue their function in spite of the absence of their myelin sheaths.

It is at this stage of the disease when the diagnosis is still doubtful and the possibility of a purely hysterical basis cannot be excluded, that, according to the observations of Buzzard and Head, a careful and minute investigation of the occular phenomena and visual functions is likely to be of great value. This subject has received much attention of recent years from these observers, and from Uhthoff and Parinaud on the Continent. These authorities claim for it a position of supreme importance in the diagnosis of such cases as we have at present under consideration.

In this particular case however they did not materially assist in the differential diagnosis, at least during her first residence, when their aid would have been most valuable.

Nystagmus was absent, nor was there paresis of any of the occular muscles. The importance of these symptoms have already been alluded to.

The pupillary phenomena were practically normal. Marie mentions three ways in which these may be altered:- (1) Myosis, (2) Inequality of the Pupils, (3) A diminution in their action under the influence of light or convergence. In our case, the tendency, at this stage, at least, was rather to mydriasis than to myosis, otherwise they were perfectly normal.

Ophthalmoscopic examination revealed a normal fundus.

Degenerative/

Degenerative changes in the optic disc should always be looked for in any case where the existence of this disease is suspected. Even at a comparatively early stage of the disease, these may manifest themselves, and when sufficiently advanced to be appreciable, they constitute a most important diagnostic sign. It is only within very recent years that the frequency with which atrophic changes accompany Disseminated Sclerosis, has been fully realised. It is not very many years since it was generally believed and taught that Optic Nerve Atrophy belonged peculiarly to Tabes, and that its occurrence in other diseases of the nervous system was unusual. Recent investigations however have proved this to be erroneous. In Tabes Atrophy is said to occur in 15% of cases (Gowers), while out of 100 instances of Disseminated Sclerosis, examined by Uhthoff, the fundus was normal in only 48, while in 5 of the remainder there were visual defects unassociated with any appreciable ophthalmic change. The results obtained by Dr. Buzzard are very similar. Out of 100 cases of Disseminated Sclerosis, of the Hysterical type, examined by him, he found "undue pallor of the disc" in 46%, and, in other types of the disease, changes were found in 37.5%.

Uhthoff asserts that "with the exception of Cerebral Tumours and Tubercular Meningitis, there is no disease of the/

the nervous system (even including Tabes) which is so often accompanied by ophthalmic changes as Disseminated Sclerosis." Every degree of alteration in the disc may be observed from complete decolouration of the whole papilla, to a slight pallor in its temporal aspect. In the great majority of cases, the change is a very slight one, and it is doubtless the ability or inability of individual observers to appreciate these slighter alterations that has caused so much discrepancy in statistics as to their relative frequency. The pathological changes in the optic nerve are precisely similar to the lesions which are found elsewhere throughout the nervous system. An islet of sclerosis developes in some portion of the optic nerve or tract, which, here as elsewhere, leaves the axis cylinders more or less intact and functionally active. An extensive lesion may thus exist, and yet give rise to neither signs nor symptoms. Where, however, ophthalmoscopic changes are present these must depend upon secondary degenerative changes in the nerve fibres. Nevertheless very manifest alteration in the disc may be visible, and yet the patient be unconscious of any very serious visual defects. The difference between the optic atrophy of Disseminated Sclerosis and of Tabes is therefore a very essential one. In the latter there is first of all optic neuritis, which is followed by progressive destruction/

destruction of the nerve fibres, culminating within a comparatively short time in complete blindness. It is doubtful whether true Optic Neuritis ever does occur in Disseminated Sclerosis. A condition closely resembling it is occasionally seen, when a sclerotic lesion attacks the optic nerve just at its entrance to the globe of the eye. Uhthoff describes this condition as true Optic Neuritis, but Buzzard objects to this term, and prefers to call it a state of intense hyperaemia.

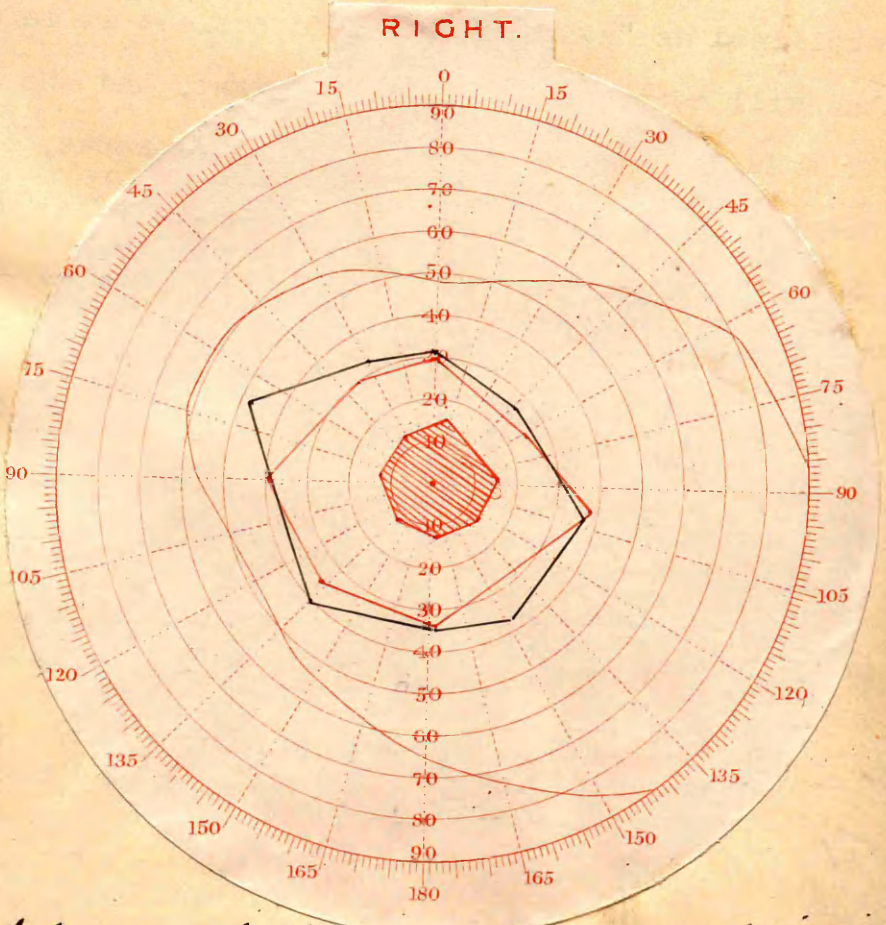
The occurrence of sudden and transitory blindness in Disseminated Sclerosis is a symptom of considerable interest and importance. It is no doubt homologous in its pathology with the sudden onset of paralysis in one or more limbs, a symptom which we have already considered. It depends upon the fact that the sclerosis is the result of an inflammatory process which may be more or less acute at the outset, but gradually subsides. The acuteness of the inflammation interferes with the normal function of the essential nerve elements in the vicinity, rendering them temporarily inactive, but not destroying them. On the subsidence of the inflammation they resume their function, but a chronic inflammatory process continues which results in the formation of an islet of sclerosis. The patient can now see, and may himself be unconscious of any visual defect, nevertheless in/

in a considerable proportion of cases it will be possible to demonstrate that such exists. This may take the form of contraction of the field of vision, inability to appreciate differences in the intensity of light, etc. The initial defect of vision need not amount to actual blindness. Various degrees of transitory amblyopia are met with. The symptom as a rule affects one eye at a time, and is likely to be unassociated with any appreciable ophthalmoscopic change. One can readily understand that such a case, presenting no evidence or organic disease, and occurring perhaps in a young woman who is undoubtedly hysterical, is extremely likely to be diagnosed as Hysteria. Buzzard says:- "The visual troubles are very frequently themselves a fertile source of error. A girl is brought to an Ophthalmologist, because she has more or less suddenly lost the sight of one eye. It is probable that the ophthalmoscope fails to detect the slightest sign of any change in the fundus. The girl, on inquiry, is said to be emotional, and on some previous occasion to have partially lost the power of a limb, which, however, had been absolutely recovered Or there may be a history of numbness or deadness in the limb. These are all symptoms which, it is notorious, have been looked upon as characteristic of Hysteria. I do not know whether such is the case; indeed I have grave doubts upon/

upon the point; but, I am sure, from observation, often extending over many years, of a large number of cases, that they are symptoms of a stage of Disseminated Sclerosis. I venture to urge this more particularly, because it is quite possible that the patient when seen by the Ophthalmologist, may present as little objective symptoms in her body generally as she does in the eyes. The reflexes may be found, perhaps, somewhat exaggerated, as they usually are in Hysteria, and nothing else may be noticeable. The unilateral blindness, in these circumstances, is very likely to be explained as "hysterical"; the patient is informed that she will certainly recover her sight, and she and her friends go away rejoicing. In a few weeks, or possibly months, the sight gradually returns. After an uncertain period, a similar condition may recur either in the same or the other eye. Again no decolouration of the disc is perceptible, and the diagnosis of "hysteria" appears to be confirmed. Let the cases be followed up, and it will be found that gradually very unmistakable symptoms of Disseminated Sclerosis will appear, and one or both of the optic discs will be found to be atrophic."[1]

In the same article this writer expresses the view that a/

1. British Medical Journal, Vol. ii, 1893. p.783.



within the shaded area red upon a white base is distinguished. Between the two red outlines it is seen as black

a careful examination of the field of vision in doubtful cases will afford material aid to a diagnosis. He then records the researches of himself and Dr. Head which may be briefly mentioned.

Contraction of the field of vision has long been known to occur in this disease and the fact was first pointed out by Charcot himself. It is however equally well recognised as a symptom of Hysteria, and therefore would be of little value in the differential diagnosis of the two diseases. Buzzard and Head, however, believe they have discovered in the contracted field and dyschromatopsia of Disseminated Sclerosis a certain peculiarity, the detection of which should bias the physician strongly in favour of organic disease.

The outer segment of the retina is physiologically colour-blind. A coloured object striking this portion will give no impression of colour whatever. Move it gradually inwards, and a point will be reached when its colour can be appreciated. In both diseases this limit will be found unduly near the centre of the disc, but in Disseminated Sclerosis, Buzzard and Head have detected a transitional stage, or neutral zone, where a red or blue object upon a white base will appear as black, until it becomes sufficiently near the centre to be recognised, and similarly

a/

a green or yellow object upon a black base will appear as white.

In our patient an examination of this sort might have been of value, but it is obvious that in carrying out an investigation of this kind, the observer is very much at the mercy of the patient, whose intelligence must be equal to the task, and when the patient is an hysterical girl it is extremely doubtful how far her replies may be depended upon.

The perimetric tracings obtained were therefore of no great value. Indeed the peculiar irregularity in the field, which was demonstrated during her first residence, was considered rather to be indicative of Hysteria, because in this disease, the contraction, having merely a functional basis, due to exhaustion of the retina, is not a constant quantity, and its degree is continually changing.

I have now reviewed and discussed the main features of the case as they appeared during her first residence. While the diagnosis of Hysteria was made provisionally, several of the phenomena observed, as has been shown, indicated a possible organic basis, and the subsequent history of the illness proved this to be the case.

Her more or less complete recovery, followed by a period of comparatively good health, extending over nearly fourteen months/

months, is quite compatible with what we know of Disseminated Sclerosis. The disease however, was still present though temporarily quiescent. The onset of her second illness is not unlike that of her first. A violent attack of vomiting precedes each onset of subjective symptoms, which are referred successively to the left side of the face and mouth, the right side of the face and mouth, and then to the limbs. In the case of the left arm and leg, these are followed by loss of power. When admitted the left arm and leg were found to be paralysed while those of the right side were extremely feeble. The spastic character of the paralysis was more evident then in her previous illness. The Adductors were rigid, the knee jerks exaggerated and ankle clonus was obtained on the left side. The condition of the superficial reflexes, and the impairment of sensation, were practically as before, the latter now involving the whole body. Three days after admission there occurred the incident of the illness, which removed it once and for all from the domain of functional diseases. The very serious symptoms from which she suffered at this time, when, for a period of nearly a week, she was considered to be moribund, must have originated from some serious intracranial mischief giving rise to pressure on the brain.

It is quite possible that this attack was really of the nature/

nature of the so-called "Congestive Seizures" which are common in general Paralysis of the Insane, and which are also known to occur occasionally in Disseminated Sclerosis, as was first pointed out by Charcot himself. Pyrexia commonly accompanies these attacks, and in our patient the temperature fluctuated about 100°, the highest record being 100.8°. Usually it is higher, reaching 102° or even 104°. The inequality of the pupils and the well-marked Nystagmus, as also, though to a less extent the Tache Cerebrale, indicated a cerebral origin. The occurrence of double facial paralysis was probably the result of some lesion about the pones. Difficulty in swallowing and temporary glycosuria may have arisen from some disturbance in the region of the medulla, and the serious interference with Cardiac and respiratory functions may have had the same source.

As these symptoms passed off, and the patient began to recover, a few of the ordinary evidences of Disseminated Sclerosis became more prominent, and helped to confirm the diagnosis. The nystagmus persisted, and even at the time of her dismissal this symptom could still be elicited. The importance of this phenomenón has already been considered. Gowers says:- "Nystagmus may safely be accepted as evidence/

evidence of more than Hysteria, and this (Disseminated Sclerosis) is one of the many maladies in which the symptom is of great diagnostic value."

Paresis of certain of the occular muscles, affecting in this case the right and the left external recti, is very common. The external rectus is the muscle most frequently affected, and Parinaud has observed that when the paresis involves any of the others, it is usually those which are associated with one another in certain movements of the eyeball. Thus in our patient the muscles affected were those which are concerned in carrying the eyeballs to the left side. She occasionally suffered from diplopia, a symptom which depends directly upon the paresis. For if the power of any muscle is diminished, while its fellow in any particular movement is unaffected, the attempt to effect that movement will carry the eyes into different axes.

The occurrence of tremor in the hands and arms was an additional diagnostic symptom of doubtful importance, for it was not characteristic, although only brought out by voluntary movement. Probably it was to be accounted for by the weakness of the muscles.

The failure to elicit the knee jerks, while the cerebral attack lasted, may have been due to the spastic condition of the Hamstring muscles being sufficient to mask their presence/

presence. Later on they returned, became greatly exaggerated and were associated with ankle clonus.

Loss of control of the bladder and rectum is usually looked upon as a late phenomenon in this disease, and in the typical varieties it is so, but in a considerable proportion of the atypical forms that have been recorded, interference with these functions has been present even at an early stage.

The Optic discs were considered to be unduly pale, but this was unassociated with any appreciable visual defect, with the exception of a slight degree of contraction of the field of vision both for white and coloured objects.

Finally I would remark that the age of our patient is not against the diagnosis of Disseminated Sclerosis. In a recent Cyclopaedia of Diseases of Children (Keating) there is a record of sixty cases, the disease developing in one instance in an infant. Oppenheim, indeed, expresses the opinion that many of the cases of this disease, observed in adults, really date from childhood, but do not give rise to any overt signs until adult life is reached.

Case B. The following case I record as one of Disseminated Sclerosis, but with certain misgivings, for although a careful examination of the symptoms has led to the adoption of this diagnosis, the whole aspect of the case is very different from any of the more ordinary forms of the disease.

A marked feature of the illness has been the curious variations which the nervous phenomena have presented from time to time, in consequence of which, I have been unable to epitomize the report, which is therefore given in full.

S.M. "at home" aet 16.

Admitted to the Glasgow Royal Infirmary 11th. January 1899, complaining of loss of power in the lower limbs. The following report was sent by her own medical attendant:-

"On Monday, 9th. December 1898 I was called to see the above patient, whom I found in bed, complaining of intense headache, photophobia, pains all over and sore throat. She had complained of giddiness for a few days before. I treated the case as one of Influenza, and with antipyretics the temperature, which was 103°, came down and the pains ceased. The headache however, although greatly relieved, still remained, and did not leave entirely until the third or fourth day. It was only then that I noticed slight internal squint and dilatation of the pupil of the left eye. There was only slight contraction of the pupil on stimulus of light. She then complained of a peculiar feeling all over the/

left side of the face and the inside of the mouth, and that she could not chewwith the left side. There was no facial paralysis to any great extent manifest, although the saliva ran slightly from the left side of the mouth. At this time, viz. about a week after the initial attack, her temperature was normal. No paralysis of arms or legs. Knee jerks normal. No ankle clonus. Later she complained of numbness and prickling in the right arm, but no loss of power was perceptible. This passed off, and the next thing that happened was paresis of the right leg. This latter symptom still remains, and has existed for about three weeks. The left leg is now beginning to show slight paresis with perhaps a very slightly exaggerated knee reflex, and she cannot now stand at all, and is even unable to sit up in bed. The paralysis of the external rectus muscle is much improved, and the pupil is now acting almost normally. If anything it contracts a little more than the right pupil. Photophobia still exists, although to a less extent, and only since Wednesday last, 4th. January has the power (grip) of the right hand become less. All through her illness, since the feverishness disappeared, her appetite has been good. Bowels a little constipated."

Patient is one of a family of ten, of whom nine are now alive. The other died in infancy. No evidence of a neurotic/

neurotic taint is obtainable. She has not had any previous illness of importance. On admission the following note was made. 11th. January. Patient presents a considerable degree of anaemia. She is rather thin. Her face has a vacant drowsy look, and it is evident from her behaviour that there is some mental enfeeblement, although her replies to questions are prompt and intelligent. She keeps the left eye half closed, and complains of being troubled when exposed to a bright light. This intolerance of light is only present in the left eye. A slight degree of lateral nystagmus is brought out when she attempts to look far to the right or left side, and when she does so it is noticed that she cannot carry either eye to its extreme distance in an outward direction, but this does not cause diplopia. The pupils, which, in a medium light, appear to be equal, show a difference in their size when exposed to the light of a lighted taper. Both are rather sluggish in their response to light, but the right contracts more than does the left. A rough examination of the field of vision, which alone is possible in her utterly helpless condition, does not bring out any defect. Ophthalmoscopic examination shows some undue fulness of the veins. The discs are pale and clearly cut. (Some days later the eyes were examined by Dr. Rowan, who expressed the opinion that there was a slight/

slight degree of atrophy). There appears to be a slight degree of paralysis all over the right side of the face, affecting even the Occipito-frontalis. The tongue when protruded occupies the middle line. It presents a fine tremor. There is some loss of power in the right arm. The fingers are kept partially flexed, and she is unable to fully extend them. There is also some degree of wrist drop. No rigidity is at present demonstrable. Her grasp with the right hand is very feeble. There is no paralysis of the left arm.

She lies with the legs drawn up, and states that she is unable to extend them. They can readily be forcibly extended, and this causes her no pain. The movement of extension is resisted, and it is difficult to say whether the resistance is voluntary or involuntary. There appears to be some adductor spasm, but the degree of this varies from time to time. When the legs have been extended, she is unable to draw them up voluntarily, but when a sharp point is applied to the sole they are quickly flexed.

She is quite unable to stand, her legs giving way helplessly beneath her. She is also unable to assume or maintain the sitting posture.

There appears to be considerable deficiency in the sense of touch, as well as in the sense of pain, the latter being/

being markedly defective in the hands. Her replies however are very unreliable. The sense of heat and cold is also greatly impaired. It is most acute in the left arm and left side of the trunk, but elsewhere her replies are as often wrong as right.

In the arms the sense of position is accurate. She is however unable to tell in which position her legs are lying, or in which direction her toes are pointing.

With the hands she is unable to feel the shapes of various articles placed in the palm.

There is a good deal of tenderness over the Mammary regions, but none in the Ovarian.

She complains of numbness in the right arm and hand, and of a prinkling sensation in the right side of the face. The senses of taste and smell are both impaired, but more especially the latter. She did not recognise the small of peppermint, of lemon nor of brandy.

Patellar reflexes are slightly exaggerated, and on the right side ankle clonus is obtained. There is no increase in the deep reflexes of the arm.

Plantar reflexes are distinctly exaggerated, but the epigastric is not obtained.

Tache cerebrale is present.

There is no pain or tenderness in the spine.

Pulmonary/

Pulmonary physical signs seem normal. There is a basal V.S. murmur, but otherwise the heart is normal. Temperature is normal.

Urine (1018) does not contain albumen.

13th. January. Since admission urine was passed in bed on one occasion. This has not occurred prior to admission. The bowels also moved involuntarily, although she was conscious of the desire and gave warning.

16th. January. Knee jerks could not be obtained to-day. Ankle clonus is elicited on the right side.

18th. January. The left eye is now kept widely open, and there is no longer photophobia.

21st. January. A rise of temperature occurred on the 19th. inst., reaching 102.6° at midnight. Subsequently it fell gradually, and it is now normal. It was accompanied by sore throat.

The skin about the sacral region is rather red, so a waterbed has been ordered. She is passing evacuations in bed.

27th./

27th. January. The facial paralysis has become rather more evident, and still extends to the Occipito-frontalis and Corrugator Supercilii. The paralysis is not complete. The tongue deviates slightly to the right.

The condition of the eyes is not much altered. The difference in the pupils is not now so obvious. They continue to be unduly dilated, and are sluggish in their responses. At the present time there is a considerable degree of contracture of the right arm, and she resents its being manipulated as it causes some discomfort in the shoulder joint. There is also some rigidity in the left arm, but it is probably largely voluntary. She can stretch out the left arm to its full extent, and in doing so no tremor is observed. The right arm is not much moved voluntarily. She is however able to move any of the joints, and the degree of apparent paralysis varies very considerably from time to time. She nearly always lies with the legs drawn up, and at present she resents their extension, although she does not complain of any localised pain.

To-night the patellar reflex on the left side is active, perhaps a little exaggerated, and there is a tendency to clonus. In the right leg, on the other hand, no reflex is obtained, and there is no suggestion of clonus. Plantar reflexes/

reflexes are active. Common sensation is evidently much impaired everywhere. Her replies however are quite untrustworthy. On testing the same area more than once her replies vary. She frequently states she is touched when she is not, and vice versa. Sense of pain is dulled especially in the legs. In the arms, and in the upper part of the trunk, she usually distinguishes between the sharp and the blunt end of a pin, and she is also able to do so all over the scalp. There is a slight improvement in the bladder and rectal conditions, but for the most part evacuations are still passed in bed.

28th. January. This morning there is noted a marked tremor of the upper lip, especially on the right side.

February 6th. Right facial paralysis is still slightly present. Sensation in the face seems almost normal.

There is some rigidity of the right arm. She is unable to fully extend the fingers when the wrist is in extension. She is unable to perform any delicate movements with the hands, for instance, she cannot place the tip of the thumb on the tip of each finger in order. The movements of pronation and supination are very imperfect. She is unable to raise the right arm to the head. Once or twice she/

she has managed to turn herself in bed, but as a rule she requires assistance.

Pupils respond very sluggishly to light and make hardly any response in accommodation.

Nystagmus is not now present.

Sense of Smell was again tested, and appeared much impaired.

In other respects there is no material alteration in her condition.

13th. February. Since yesterday patient's temperature has been somewhat elevated. In the evening it rose to 101.2°, and to-night it is 102°. Yesterday she was complaining of frontal headache, but to-day this is gone, and her complaint now is of her throat which is congested.

There is scarcely any evidence now of facial paralysis. There is also more power in the right hand than there was. Her grasp is stronger, although she is still unable to move the dynamometer at all. The muscles of the right arm are distinctly lacking in tone, compared with those of the left, and this is more evident in the upper arm than in the fore-arm. There is still great impairment in the sense of touch in the legs. In the abdomen the tactile sense and sense of pain are less active on the right side than on the left. This difference is even more evident in the arms, while in the/

the face the same difference cannot be demonstrated.

Patellar reflexes are still absent. There is no improvement in the power of voluntary movement in the legs. She is complaining of pain in them to-night and resents their manipulation.

All evacuations are passed in bed.

26th. February. She is, if anything, rather better. For a few days she has been able voluntarily to move the toes, and makes an attempt to flex the knees and thighs. She is still unable to state in what position her legs are lying.

There is quite a well-marked degree of atrophy of the muscles of the right upper arm. In the forearm and hand the same difference is not evident, but the muscles seem to be lacking in tone compared with those of the left side. Facial paralysis has now disappeared entirely.

She still passes urine in bed, but sometimes gives warning when her bowels are going to be moved.

5th. March. She is growing distinctly more anaemic. The pulse is very shabby, and just now its rate is 116 per minute. A loud basal V.S. murmur is now present.

The improvement noted in last entry continues to be manifest. She moves the legs and the feet when asked to do/

do so, but it is still a feeble attempt.

There is a marked improvement in sensation. Her replies when a light touch was employed all over the legs were to-day quite accurate, and she always distinguished between the sharp and the blunt end of a pin. The sense of posture is still very defective. The right patellar reflex is obtained to-day, but not the left.

The power of the right upper arm muscles is very feeble while in the forearm it is fairly good. Atrophy of the upper arm muscles is becoming more manifest. Measuring six inches above the tip of the olecranon process, the circumference on the right side is $7\frac{1}{2}$ inches, while at the same level on the left arm it is $8\frac{1}{4}$ inches. One inch below the olecranon process (the arm being in the semiflexed position) the circumference on the two sides is found to be $7\frac{3}{4}$ inches.

The temperatures have been oscillating recently, frequently reaching 100^{0} in the evening, and last night reaching its highest register 100.8^{0}.

Urine contains a trace of albumen, but no tube casts are detected in the deposit.

12th. March. Patient is becoming extremely anaemic in appearance. An examination of the blood shows 65% of haemoglobin and/

and 85% of corpuscles.

There is not much alteration in the nervous phenomena. Very well marked ankle clonus is present on both sides. The patellar reflex is present on the right side, but absent on the left. There is no patellar clonus.

Common sensation and the sense of pain are somewhat defective in the legs, but are active elsewhere throughout the body.

Large tremors are observed in the arms when she is carrying anything to the mouth. When she attempts to touch anything which is some distance from her, these are brought out.

She usually gives warning now before passing evacuations.

16th. March. For a day or two patient has been complaining of discomfort about the throat, associated with difficulty in swallowing. There has been some congestion of the tonsils and a little mucus exudation, but hardly sufficient to account for her evident discomfort. To-night she is complaining very much but seems unable to locate the situation of her uneasiness or pain. On the chest being examined she winces when the hand is placed over the praecordial area. The heart is very tumultuous, and something like a thrill is felt accompanying its movements.

On/

On auscultation especially about the third interspace close to the sternum, very superficial murmurs are heard of a grating quality and having a triple rhythm. There is no increase in the area of cardiac dulness.

She looks feverish and her temperature is 101.8°F.

17th. March. There is an increase in the area of cardiac dulness reaching to about an inch beyond the left nipple line and to the right border of the sternum. The murmurs are less grating but are still well marked.

She is rather better this morning.

18th. March. Patient is evidently better to-day. The temperature is down, and is at present 99.6°. Pulse continues to be very rapid and very shabby, the average rate being 150 per minute.

A still greater increase is noted in the area of cardiac dulness, giving a transverse measurement of $5\frac{3}{4}$ inches. The left border lies fully 2 inches outside the nipple line, while the right border is slightly beyond the right sternal margin. The dulness reaches as high up as the second rib and has a conical outline. The double murmur is still well marked all over the praecordial area. To-day it is loudest in the 5th. interspace close to the sternum.

23rd. March. A change for the worse is very evident. She is now markedly emaciated, and lies very prostrate. She is pretty acute mentally, replying intelligently when addressed, but when left alone she is liable to talk incoherently. She is also rather irritable and emotional.

The Cardiac dulness is found to be much the same as in the last note. There is a diffuse heaving all over the Cardiac area. At the mitral area a V.S. murmur is heard which is carried up into the axilla. A double murmur evidently pericardial is heard towards the sternum.

Respirations are rapid and somewhat gasping this morning, 35 per minute. Temperature continues to oscillate - the highest register since last note being 101°.

Measuring the arms at the levels mentioned in a previous note, the circumference of the right arm is $6\frac{3}{4}$ inches, and the left $7\frac{1}{4}$ inches.

There is considerable rigidity in the legs. Ankle clonus is still very well marked in both. On neither side is the knee jerk obtained, but perhaps the rigidity of the hamstring muscles prevents this. The tactile sense is still much impaired. While ankle clonus is being elicited she is conscious of the shaking, but is unable to state in which leg it is being produced. Listening in the lateral portion of the chest abundant subcrepitant rales are/

are heard on the left side. They are much less abundant on the right side. She is too ill to be disturbed for further examination.

30th. March. She looks very much exhausted, and is becoming much more emaciated. For some time her mental condition has been showing considerable impairment. To-night this is very manifest, and she is wandering in her talk. The upper border of Cardiac dulness comes unduly high up, but the right border has returned to its normal situation. The outer border comes rather more than an inch outside the nipple line. The apex beat is in the 4th. interspace, and is felt for nearly an inch outside the nipple line. Another pulsation is felt in the second interspace, which seems to be synchronous with the apex beat. A loud V.S. murmur is audible, apparently mitral regurgitant. No murmur of pericardial origin is now heard. There is little new to note in regard to the nervous phenomena. The eyes were examined with the Ophthalmoscope to-night, and the optic nerve atrophy was found to be more advanced than on admission. The veins are considerably distended, while the arteries are small. The pupils are widely dilated, and make very little response either to light or in accommodation. The left pupil is larger than the right and responds more sluggishly/

sluggishly. Indeed it scarcely reacts at all.

Visual Acuteness L $\frac{4}{6}$ R $\frac{3}{6}$

When the face is in repose, there seems to be a slight droop in the left angle of the mouth, but test movements do not bring out any impairment of muscular power.

The constant flexure of the legs at the knees seems to have given rise to a structural shortening, for the legs cannot be fully extended, even when a considerable degree of force is employed. The patellar reflexes are not obtained. Ankle Clonus is still present.

Tactile sense seems sharper than it was, but she has difficulty in locating the part on which she is touched.

She apparently has paraesthesiae, as she insists that her shoes and stockings are on. Evacuations are all passed in bed.

9th. April.- Patient is becoming more and more emaciated. Measuring the arms at the same level as formerly, the right side is found to be $5\frac{3}{4}$ inches and the left $6\frac{1}{2}$. The legs are much swollen with oedema, this feature being quite new within the last few days. Another new feature is the developement of bedsores about the ankles. There is one on the internal aspect of each leg, which may be due to pressure from the way she lies. Another on the outer aspect of the right/

right ankle can scarcely be the result of pressure, and looks quite like a trophic sore.

Since last note the temperature has on several occasions been elevated, reaching about 102° or over. During the last two occasions, to-day and on the 7th. inst., this has been accompanied by a rigor.

The Cardiac physical signs are practically as they were. The V.S. murmur is very loud and blowing at the apex, and seems to be certainly of organic origin. No recurrence of pericardial friction has been noted.

To-day and yesterday she has had retention of urine requiring the use of the catheter. Urine 1012 acid, Turbid, trace of albumen.

Deposit contains pus cells and a few granular tube casts.

Ankle clonus is very well marked. It is present even as she lies without employing any means to elicit it. The knee jerk is obtained.

A very slight degree of left facial paralysis is found, affecting only the elevators of the angle of the mouth.

May 3rd. Patient's mental condition is improved. She is brighter, and less inclined to talk nonsense. For the most part she is very good-humoured, but at times she is irritable and/

and peevish. Lately she has taken to singing a good deal to herself.

Slight lateral nystagmus is obtained to-night. The pupils are equal, and respond better to light than they did, but it is noticed that when they are exposed suddenly to a bright light, a moderately active contraction results which is almost immediately followed by a recoil to a condition of wide dilation. There is almost no contraction in either pupil on convergence.

Lip tremor during speech is to-night very evident. Her articulation is fairly good, but inclined to be rather stuttering. It is not slow or scanning.

The atrophy of the right upper arm is not so appreciable now as it was, in consequence of the emaciation having lessened the circumference of the left arm. On applying the Faradic current, however, it was easily demonstrated that the muscles of the right arm responded less actively than those of the left. The same remark applies to the muscles of the hands, which, on the right side, are distinctly atrophied as compared with the left. In the forearms this difference was not so readily appreciated, but it does seem to be present to a slight extent.

On testing the knee jerks to-night no reflex was obtained at first, but, on arranging so as, as far as possible,/

possible, to get rid of the flexor spasm, it was elicited on both sides. Ankle clonus is still very easily elicited in either foot. The voluntary power of the lower limbs is manifestly improved, but she cannot yet extend the knees. She is still unable to maintain the sitting posture, when the heels are on the bed. To-night she was made to sit up with her legs hanging over the side. During this proceeding, large tremors were observed in the trunk and head. By various means, tremors quite of the intentional type were elicited in the arms. She has no longer retention, but the urine trickles constantly away. It is ammoniacal, and contains pus. There is absolute rectal incontinence. Bedsores have developed about the hips. Oedema of feet and legs is entirely gone.

This illness commenced apparently as an attack of Influenza. It occurred at a time when this disease was rife, and at the outset presented its ordinary features. The frequency with which Disseminated Sclerosis follows acute diseases is now commonly recognised. Marie in particular has drawn attention to this subject. He says:- "This is what usually occurs: a person of between 20 and 30 years of age contracts an infectious disease, (it will presently be seen in the enumeration which I shall make how different the nature of the infectious diseases may be), and either/

either in the course of the disease, or during the period of convalescence which follows it, or perhaps some months later, the first symptoms of the nervous affection occur. In some cases these symptoms improve, and may completely disappear, the morbid process not having then produced sclerosis, but having been definitely arrested. In other cases the symptoms which have occurred become aggravated either progressively, or by sudden exacerbations, and before long the whole clinical aspect of Insular Sclerosis presents itself."[1]

In the enumeration which follows no mention is made of Influenza, but other writers within recent years (Oppenheim etc.) have recorded cases in which the onset of Disseminated Sclerosis has apparently been closely connected with that disease. The subject will be further discussed when the Aetiology comes to be considered.

Taking up individual symptoms we find a considerable similarity between those presented in this case and those which we have already considered in connection with Case A. For instance we find Transient Paralytic phenomena,
spasticity and Ankle Clonus
Occular and Ophthalmic changes including
Nystagmus
Tremors.

1. Lectures on Diseases of the Spinal Cord, p.133.

Yet in spite of these resemblances, there is a marked contrast between the two cases. One is accustomed to look upon Disseminated Sclerosis as a chronic disease, liable to sudden and acute exacerbations, alternating with periods of comparatively good health. Here however we have the symptoms arising out of an acute illness, and proceeding progressively with occasional intervals during which slight improvement was manifest, probably to a fatal issue, for with the functions of the bladder and rectum so seriously involved, and in the presence of cystitis and bedsores recovery cannot be looked for.

The multiplicity of the phenomena observed can only be accounted for by admitting the presence of numerous lesions throughout the central nervous system, and there can scarcely be any reasonable ground for doubt, when one considers the mode of onset, that these lesions were the direct result of the irritant which was the basis of her febrile attack. Whether or not this irritant was the toxin of Influenza cannot be more than conjectured, and a further confusion arises in the occurrence of Tonsillitis, Pericarditis and Endocarditis, a symptom group which is more than suggestive of the presence of the Rheumatic poison.

The irregularity of the paralytic phenomena was quite characteristic/

characteristic. First there are tingling sensations in the left side of the face and mouth, and this is followed by slight paresis there. Then similar sensations are complained of in the right arm. This passes off, and is not followed by any appreciable loss of power for some days afterwards. In the interval paresis of the right leg becomes manifest, and this is followed later by loss of power in the left leg. By the time she is admitted there is no evidence of paralysis on the left side of the face, but there is distinct paresis affecting all the muscles on the right side. This passes off, and some time afterwards slight paresis of the left side is again observed, which is of short duration.

On the other hand her paralytic symptoms presented some quite unusual features, notably the permanent flexor contracture, on account of which her legs were kept constantly flexed, so as actually to give rise finally to a structural shortening of the hamstring tendons. Involuntary flexion at the knee is not uncommon in this disease, just as it is a common symptom in Spastic Paraplegia, but it is usually transitory, and is associated with the pain of cramp. From the permanency of the symptom in our case and its long duration, one would infer some paralysis of the extensor muscles of the knee, but these were not specially lacking in tone, and were not atrophied out of proportion to the general emaciation./

emaciation.

The frequent failure to obtain the knee jerk, even though ankle clonus was well marked, was doubtless due to the spastic condition of the hamstring muscles, which prevented extension.

Tremor was never a prominent feature of the illness, but was now and again noted. It was not a fine tremor such as Case A presented, but the whole arm was involved, and its range was fairly wide.

The tremor seen in the upper lip during articulation was of the volitional type. This is a symptom of Disseminated Sclerosis, which, in certain cases, when combined with speech difficulties etc., may render the exclusion of General Paralysis a matter of considerable difficulty.

The condition of the arms may be described as one of spastic paresis, a symptom which is not uncommon in this disease.

Localised muscular atrophy is not infrequently met with. It results from the encroachment of an islet of sclerosis upon the anterior grey matter of the cord. Amy group of muscles may be affected, and occasionally the atrophy is pretty general, so that a difficulty may even arise in excluding Amyotrophic Lateral Sclerosis. Such a condition is one of great rarity, but various French writers have recorded cases.

When a limited group of muscles becomes atrophied, it is said to be most frequently those of the hand, and especially the Interossei. In our patient for many weeks atrophy of the right upper arm was alone detected, but latterly the muscles of the hand were found to be also involved.

The Faradic irritability was moderately active, although distinctly less so than on the left side, and one would infer from this, that only a certain number of the multipolar cells were destroyed, while the remainder were able to maintain the nutrition of their corresponding muscular fibres.

Loss of the sense of posture is the result of interference with the conduction of impressions from the muscles, and depends upon a lesion in the posterior column of the cord, or possibly in the direct cerebellar tract. It is a common symptom in Tabes, but its occurrence in this disease seems to be very rare, indeed I have not succeeded in finding any record of it. The cause of its rarity no doubt is to be found in the fact, already stated, that afferent nerves require a greater amount of damage to destroy their function than efferent nerves, and therefore lesions affecting the posterior column may not cause a sufficient amount of disturbance to produce this symptom. Islets in the posterior columns are by no means rare, giving rise to ataxia.

Therefore/

Therefore in all probability in a certain proportion of cases the sense of posture would also be found to be deficient if investigation were made.

The significance of involvement of the bladder and rectum, we have already considered. The complete paralysis of both in this case, on account of which the urine is constantly trickling away, and faeces are being discharged involuntarily and unconsciously, is the most serious symptom of her present condition. Minor degrees of bladder and rectal involvement are by no means infrequent, but so profound a condition of paralysis is most uncommon. It indicates a lesion involving the lumbar centres, and as we have already seen, when the morbid process attacks the grey matter it destroys the cells. Hence the condition is of very grave import.

The occurrence of bedsores is amongst the less common phenomena of the disease, and is usually a late manifestation.

The Ocular and Ophthalmic symptoms gave very important confirmatory evidence. Lateral Nystagmus was occasionally observed, but was never a well-marked symptom.

Paresis of the Occular muscles confined itself to the External/

External Recti, and was not associated with diplopia.

The variations in the pupillary phenomena were quite characteristic, as was also their inactivity on exposure to light, or in convergence. The inequality frequently observed especially when the eyes were exposed to a bright light, is also a symptom commonly found in Disseminated Sclerosis. In this case, even more than in Case A, the pupils were unusually dilated, thus differing from what, according to Marie is the more common condition, undue contraction.

The importance of Optic Atrophy as a diagnostic sign has been already fully discussed. In this case it was associated with very distinct visual defect. A careful examination of the field of vision was not possible. Neither her physical nor her mental condition would allow of it, and a rough examination was quite unsatisfactory.

It is rare to find so much mental enfeeblement as was present in this case especially in its later stages, but its occasional occurrence is recognised, and a final state of complete dementia is not unknown.

We are entitled then, I think, to assume that the illness was primarily of vascular origin; that the presence of an irritant in the blood has given rise to disseminated lesions/

lesions throughout the whole central nervous system. This is the pathology of Disseminated Sclerosis, and I am therefore inclined to look upon this case as an unusual form of that disease, in which the acuteness and progressiveness of the symptoms have been the result of the virulence and persistence of the toxin.

In dealing with the aetiology this subject will be further considered.

The following case, which is believed to be one of Disseminated Sclerosis in an early stage, presents some features of considerable interest.

Case C. P.W. Aet 57. Occupation Puddler.

Admitted to the Glasgow Royal Infirmary on September 23rd. 1898, complaining of pain in the right forearm on movement, and of trembling.

Twelve months previously, on waking one morning he found that his right forearm was quite benumbed and very painful. For the next four weeks, in consequence of these symptoms, he was unfit for any work. He then resumed his occupation and was irregularly at work until eight weeks ago, when he was obliged to give up altogether, on account of his being unable to use the right hand properly. He has not been conscious/

conscious of any improvement in his symptoms since their first commencement. So far as he is aware none of his other limbs have been affected. He gives no history of attacks of giddiness, nor has he been troubled with headache. He has not been conscious of any diminution in his visual acuteness.

His occupation has exposed him a good deal to cold draughts, and he is inclined to assign this circumstance as a cause of his illness. There is no evidence of his having had Syphilis.

Present Condition - He is well nourished, and well coloured. Apart from the nervous phenomena he appears to be healthy.

His main complaint is of pain in the right forearm of a shooting character, and only induced by movement, being as a rule quite absent when the limb is at rest. Sensations of numbness and prickling are also troublesome, and he thinks that his sense of touch with his fingers is not so acute as it was.

His grasp with the right hand is very poor. The right elbow jerk is not obtained, but the wrist jerk is present. The deep reflexes of the left arm are normal.

On attempting any voluntary movement with the right arm, a striking degree of tremor is brought out. On testing/

testing him with a glass of water, the oscillations present quite the character of the tremor of Disseminated Sclerosis. He however states that, sometimes, when the hand is lying on the bed quite at rest, he is conscious of slight tremor in it.

No impairment of the tactile, painful, or Thermic sense can be demonstrated. The muscular sense is accurate.

Muscular power in the legs is good.

There is no atrophy of the muscles anywhere. Those of the right forearm are quite of good tone.

The knee jerks are normally active. Pupils are rather small; the left is smaller than the right. Both react normally.

Nothing abnormal is discovered on Ophthalmoscopic examination.

There is no nystagmus.

There is no impairment of speech.

He has no bladder or rectal difficulty.

7th. October. The volitional tremors are less marked than they were, otherwise there is very little change manifest in the condition of the arm. The electric reactions of the muscles have been examined, and were found to be practically normal. Measuring the circumferences of the forearms at different levels, these are found to be equal on the two sides.

The legs are quite strong, and he has no difficulty in walking. The knee jerks are unduly active. No ankle clonus is obtained.

A slight difference in the appearance of the two sides of the face gives the impression of left facial paresis, but test movements do not confirm this. Trembling movements of the muscles of the left cheek have been observed from time to time.

The presence of lateral nystagmus has been noticed for some time. Inequality of the pupils remains as before. Patient is dismissed.

The case is interesting from several points of view. In the first place one is strongly prejudiced against the diagnosis of Disseminated Sclerosis by observing the age of the patient. Charcot in his account of Insular Sclerosis says:- "It rarely shows itself after thirty years. The age of forty seems, on the other hand, to be the outside limit to which patients attacked with Disseminated Sclerosis attain." Cases however have not infrequently been recorded of the disease occurring in patients who are over fifty. One such case, recorded by Dr. Bastian in which Disseminated Sclerosis was diagnosied, and was afterwards confirmed by post-mortem examination, occurred in a man who was over fifty years/

years of age when the first evidences of the disease appeared, and who lived to the age of sixty-two. Gowers refers to a case where the disease commenced as late as sixty.

The diagnosis in our patient depended, in the first instance, upon the tremor which was exceedingly characteristic Unilateral tremor is not common, although it not infrequently happens that one limb presents the symptom more characteristically than the other.

The age of the patient and the fact that, according to his own statement, tremor of the hand occurred even when the muscles were at rest, raised the question that he might possibly be the subject of Paralysis Agitans. For tremor apart from voluntary effort is an exceeding rare phenomenon in Disseminated Sclerosis, indeed Dr. Gowers is inclined to doubt its existence altogether. He says:- "It is said that in rare instances the movements have been known to continue during rest, but there is some doubt as to the nature of such exceptional cases."[1]

In our patient the evidence of its occurrence lies entirely upon his own assertion, as it was never actually observed.

The differential diagnosis of these two diseases should very/

1. Diseases of the Nervous System, Vol. ii. p.548.

very rarely give rise to any hesitation. The character of the tremors will of itself as a rule be quite sufficient to distinguish them. That of Paralysis Agitans is smaller, slower and more rhythmical and is especially localised in the fingers and wrists. It is rather diminished than increased by voluntary effort, or, if it is increased, it is only very slightly, not in the least like Disseminated Sclerosis. It is also a continuous tremor, the only cessation occurring when the patient is asleep. But apart altogether from these differences, the history of the case, the whole attitude of the patient, the facial expression and the peculiarities of gait are very different in the two diseases. Nevertheless cases are recorded (Herterich, Schultze) in which post-mortem examination has revealed the existence of Insular Sclerosis, although during life the symptoms were those of Paralysis Agitans. Prior to the isolation of Disseminated Sclerosis as a clinical entity, cases presenting these symptoms were all grouped under the name Paralysis Agitans. "Charcot, in inspiring the thesis of his pupil Ordenstein (1867), endeavoured to make plain the difference between the two. In his lecture he alludes to a case reported by Baerwinkel some ten years before. The patient during life was under Skoda's care, and the symptoms were carefully investigated and fully noted. In particular it/

it was observed that tremor only showed itself when voluntary movements were attempted. Paralysis Agitans was the diagnosis arrived at, but after death, patches of Sclerosis were found disseminated through all parts of the cerebro-spinal axis."[1]

The presence of pain in the forearm, as the most clamant symptom, suggested neuritis as a possible basis, and the manner in which the symptoms originated supported this view. The absence of any muscular atrophy, the presence of the deep reflexes, and the normal electric irritability of the muscles absolutely excluded this diagnosis. The lesion must therefore have been central. The developement or the recurrence of nystagmus under observation went far to confirm the diagnosis. The trembling movements of the left cheek were more like a twitching than a tremor, but so far as it went this symptom was more confirmatory than otherwise.

1. History of Chronic Nervous Diseases. Monro, p.80.

The next type of the disease which comes under consideration may be called the Spastic type.

Different degrees of spasticity in the lower extremities are amongst the commonest symptoms of Disseminated Sclerosis, and sometimes this symptom predominates to such an extent as to render a differential diagnosis between this disease and Primary Spastic Paraplegia a matter of some difficulty. Such an eventuality is only likely to arise in the earlier stages of the disease and in those cases in which the morbid process has attacked first the spinal cord in its lateral columns. In a few instances a diagnosis of Primary Spastic Paraplegia cannot but be made, in the absence of any evidence which would point to Insular Sclerosis. After describing such a case which had come under his own observation and which later developed gradually the characteristic symptoms of Disseminated Sclerosis, Dr. Byrom Bramwell remarks:- "Several other cases of the same kind have come under my notice, and in dealing with cases which appear to be Primary Lateral Sclerosis in young women, I always keep in view the possibility of their ultimately turning out to be cases of Disseminated Sclerosis."[1]

Certain writers have suggested that these cases are truly Primary Spastic Paraplegia to begin with, the lesions of/

1..Diseases of the Spinal Cord. Byrom Bramwell. p.521.

of Disseminated Sclerosis being superadded, and in a few instances the presence of both lesions has been proved. Probably however this has been a mere coincidence. The pathological process in the two diseases is quite distinct. In the former degenerative changes occur primarily in the essential nerve elements, and sclerosis is secondary, while in Disseminated Sclerosis, as we have seen, pathological changes occur first in the interstitial tissue.

The following is a good illustration of this type of the disease. It was recorded by Dr. Bloomfield in the British Medical Journal.[1]

Case D. The patient was admitted complaining of weakness and stiffness of the lower limbs.

The following note was made of his condition.

"He is a tall and well-developed man.. His appearance does not denote high mental developement; but he is particularly cheerful over his present condition and anticipates great results from any treatment suggested. The arms are well developed and their chief movements normal. The thigh and leg muscles are firm and well-developed. There is nothing approaching muscular wasting, but there is a distinct loss of power in the flexors. He cannot perfectly flex/

1. British Medical Journal 1889, Vol. ii. p.657.

flex the thighs on the pelvis, and completes the movement by catching hold of the thigh, and so bending it. There is some loss of power in the flexors of the knees and ankles. The knee jerk is excessive, short and sharp. There is no marked Rectus contraction as he lies in bed. Well marked ankle clonus. The legs are extended in bed, and the calf muscles particularly feel hard. There is some resistance in attempting to flex the leg at the knee. As he gets out of bed he pushes the extended limbs before him, and they are thrown into a condition of trembling until he gets the feet on the floor, and even then the trembling continues in the toes for a short time. In walking he supports himself by the bed or some other object, and as he walks with the upper part of the body bent forward, the legs drag behind him, and adhere closely to one another, so that each rubs forcibly against the knee of its fellow. The toes catch against the ground, the heel is some inches off the floor, and as he puts one leg before the other, the toes are seen to be dragged across the inside of the heel, and along the instep of the opposite foot.

As he stands upright the calf muscles are felt to be rigidly contracted. There is some weakness of the trunk muscles, and he complains of an aching pain in the lumbar spine. The Electric irritability of the muscles to the Faradic/

Faradic and Galvanic currents is normal. There is no loss of sensibility, and he is quite conscious as to the position and movements of his limbs; the closure of the eyes occasions no increased uncertainty of movement. The posterior columns of the cord are not affected. There is troublesome constipation and some incontinence of urine at night. The discs are pale but not atrophied. Pupils react to light. No Nystagmus. His speech is slow, with a peculiar emphasis on the last word of each sentence. At times it is merely thick."

Here then is a vivid picture of Spastic Paraplegia in a well advanced stage. There is very little indeed in the patient's condition to suggest that he is the subject of Disseminated Sclerosis. His previous history however leaves very little room for doubt as to the real nature of his disease.

There was a neurotic family history. A brother in America was said to be "all of a tremble," and probably was suffering from the same disease.

There was no history of syphilis.

Nearly 20 years previously, for over a period of two years, the nature of his occupation required him to work frequently in water, and he had caught severe chills on several occasions. He had no manifestation of the disease however for about three years afterwards. Then for a period/

period of three months he suffered from violent headaches and sleeplessness, and after a time these symptoms recurred. Then he had paresis of the legs affecting first the right and later the left also, associated with ankle clonus. About the same time there was loss of power in one arm.

During the following year he was in St. Thomas' Hospital under Dr. Murchison. His condition then was "Great muscular weakness, especially in the legs, and tremor on exertion. Speech slow; articulation peculiar; no anaesthesia; no ataxia; no affection of bladder or rectum." The case was then diagnosed as Disseminated Sclerosis.

Later he became worse and for some months was partially unconscious and helpless. There was also dysphagia. Epileptic fits occurred which were at first severe and of frequent occurrence, but later became less frequent. He continued to be subject to these attacks occasionally up till the time when the above report was written, over a period of twelve years. During this time spasticity in the lower limbs was all along a prominent symptom, and he was for long scarcely able to walk. At one period his arms were weak and trembling, and he was unable to feed himself, but this symptom only lasted a short time.

It is curious that at so late a stage of the disease, there should have been so little evidence of wide spread

lesions. It is a striking illustration of the remarkable degree of recovery of function which is possible in this disease, but which is usually more or less temporary.

It is far more common for this type of the disease to present itself at an early stage, and it is in these cases that the real difficulty in diagnosis is likely to arise, for there may be nothing either in the symptoms or in the history to lead one to suspect that the disease is other than Primary Lateral Sclerosis. This diagnosis will almost certainly be made, unless the sex of the patient, the personal or family history or some other circumstance should lead the physician to suspect its real nature, and to reserve judgment in view of possible developements which may indicate the true character of the disease.

Case E. For instance: A patient was admitted into the Royal Infirmary with a history and with symptoms quite typically those of Primary Lateral Sclerosis in a mild form of about two years duration. The only unusual symptom was a very marked degree of Nystagmus, which had appeared since the commencement of his illness. The eyes oscillated continuously quite apart from any voluntary movement of them by the patient. There was also paresis of both Internal Recti. Slight degrees of Nystagmus are not uncommonly found as a symptom of Primary Lateral Sclerosis, but so extreme a degree/

degree as was present in this case must be exceedingly rare, and was sufficient to raise a doubt as to the true diagnosis. The possibility of his being the subject of Disseminated Sclerosis cannot be excluded, but only prolonged observation by the detection of the occurrence or the continued absence of other of its more characteristic symptoms will make a definite decision possible.

Disseminated Sclerosis is frequently associated with a reeling or staggering gait. This symptom may have one of two sources. It may arise from a lesion of the cerebellum, or it may be due to involvement of the posterior columns of the cord. In the first of these, the loss is primarily in the sense of equilibrium, and the reeling gait, with legs straggling, and mostly wide apart, to which the term titubation is commonly applied, is the result of a voluntary effort on the part of the patient to keep from falling.

It is therefore quite different from the second, the ataxic/

ataxic form, in which the sense of equilibrium is normal and the defect lies in the power of co-ordination.

We have therefore here two types of the disease. (1) The Cerebellar type, (2) The Ataxic type. The Cerebellar form is usually associated with spasticity, and then gives rise to the Cerebello-spastic gait, which is probably the commonest form in Disseminated Sclerosis. Sometimes, but only rarely, this association does not exist, and then we have the purely cerebellar type, which, if it be associated with cerebral symptoms - nystagmus, giddiness, headache, etc. - may lead to a diagnosis of Cerebellar tumour. On the other hand cases of Cerebellar tumour may present symptoms closely analogous to those of Disseminated Sclerosis. Should the tumour be located in such a position as to press upon the motor path, this will give rise to spasticity, and may also initiate tremors more or less of the Intentional type.

It is only however in very exceptional instances that the differential diagnosis will present any real difficulty.

The course of the illness in cerebellar tumour is rapid and progressive. There will be a history of frequent vomiting of the cerebral type and of headache. Primary optic Neuritic rapidly progressing to blindness will also be met with in most cases. In Disseminated Sclerosis, on the/

the other hand, vomiting is not a feature of the disease; headache, though not uncommon, is rarely a prominent symptom; the Optic Atrophy is of quite a different character, very slow in its progress and rarely associated with any very serious interference with vision. Moreover the tremors resulting from the pressure of the tumour upon the motor nerve fibres will be associated with a degree of muscular weakness such as one is not likely to find in cases of Disseminated Sclerosis.

The Ataxic Type is the result of a lesion involving the posterior columns of the cord, and interfering with the passage of afferent impulses from the muscles. In Case B. we recognised the probable existence of such a lesion, giving rise to impairment of the muscular sense. In a few cases many of the symptoms bear a strong resemblance to those of Locomotor Ataxia, and as an example of this the following case is interesting:-

Case F. G.M. Aet. 36. Occupation Insurance Agent. Admitted to the Royal Infirmary for the first time in December/

December 1897, complaining of diminished power in the lower limbs of about three years' duration.

The first evidence of anything abnormal occurred towards the end of 1894 when he became conscious of a sensation of numbness in the lower limbs. He used to waken during the night to find the legs and thighs very cold and covered with a cold perspiration. His attention was next drawn to an increasing sense of weakness in the legs, associated with a tendency to stagger while walking, and he found that he could not walk any distance without feeling very tired. He had difficulty in getting out of the way of people in the street, and he would often have to stop when he met anyone walking quickly, being afraid lest they should collide. Such an accident, however never occurred. About the same time he began to feel the ground soft under his feet and he also complained of a feeling of tightness round the waist. These symptoms all passed off and between April 1895 and November 1896 he was in perfect health.

Then he had a relapse. He began to stagger while walking; had difficulty in walking in the dark; felt the ground soft under foot; had a sensation of tightness round the waist; had tingling and numb sensations in the legs and in the hands especially at night, and had paroxysmal pains in the legs also especially troublesome during the night./

night. These symptoms continued more or less up till the time of admission. He also had some visual difficulties. While reading the sight occasionally failed and everything became dim and misty for a short time. He did not have diplopia or squint. He had undue frequency of micturition, having to rise several times during the night for that purpose. He did not have incontinence, but he frequently felt that he could not retain the urine long after the desire to micturate came on. He had no rectal trouble. No gastric disturbance.

During this period of his illness he lost flesh, but his appetite was good and he felt well apart from the nervous phenomena. There was a history of Enteric Fever, when he was 22 years of age, and of haemoptysis when he was 28. There was no history of Syphilis.

There was no neuropathic element in the family history.

On admission the following note was made:-

He is thin but not anaemic.

Pupils are of medium size, the left being slightly larger than the right. They respond to light and in accommodation. No nystagmus is observed.

He can stand fairly well with feet together and eyes closed, but, after a few seconds, sways rather unduly. In walking he is unable to keep along a straight line. His gait is stiff and hesitating. He cannot be said to stamp the/

the heels, but he comes down more heavily upon the right heel than upon the left.

The knee jerks are exaggerated, and ankle clonus can readily be elicited on both sides.

Sensation is slightly impaired in the lower two-thirds of the legs. He can usually distinguish between the sharp and the blunt end of a pin.

There is a distinct deficiency in the thermic sense from the knees downwards.

He has a sensation of numbness in the hands. He can tie the neck-bands of his night-dress without much apparent difficulty, but is at times rather slow about it. He is conscious himself of being more clumsy with his fingers than he used to be.

Plantar reflexes are present, but not active.
Cremasteric and abdominal reflexes are not elicited.
Tache Cerebrale is obtained.
On percussing along the spinal column, he complains of some tenderness in the mid-dorsal region.

Examination of the lungs reveals some dulness at the right apex in front and behind, associated with prolongation of the expiratory murmur, but unaccompanied by rale.
Urine normal.

19th. January. Improvement is evident. He walks better.

There/

There is no tendency to stamp the heels, nor is there any dragging of the feet. Knee jerks are still exaggerated especially on the right side, and clonus is still well marked. The plantar reflex is brisker than it was, but neither abdominal, nor cremasteric reflexes can be elicited. The impairment of sensation cannot now be demonstrated. He is dismissed to-day.

This patient consults the physician on account of weakness in the legs. He asserts that he staggers when he walks, especially in the dark; that the ground feels soft under his feet; that his hands and feet feel benumbed; that he has a feeling of tightness round the waist, and that he sometimes has shooting pains in the legs. He presents Romberg's sign to a slight extent, and his gait has something of the tabetic character. The functions of the bladder have been slightly deranged. Investigation reveals an area of anaesthesia in the legs.

If the physician's attention is directed especially to this group of symptoms, he may hastily judge that the patient is the subject of Locomotor Ataxia. Further examination however reveals the absence of the Argyle-Robertson phenomenon, exaggeration of the knee jerks and the presence of ankle clonus. Inquiry into the history reveals/

reveals the fact that his present illness is a relapse, and that there was an interval of eighteen months between this illness and the previous one, during which time he enjoyed perfectly good health. Locomotor Ataxia is therefore excluded, and the whole aspect of the case points in favour of Disseminated Sclerosis even in the absence of intentional tremors, nystagmus or impairment of speech, and this diagnosis the subsequent history of the case proves to be correct.

He was re-admitted a year later, in January 1899 and the whole aspect of the case was now found to be altered. Improvement had continued for three or four months after dismissal. Then for a period of about a week he had retention of urine requiring the regular use of the catheter. This symptom passed off, but ever since then he has been growing gradually worse. His gait became very unsteady. Tremors of the hands and arms became troublesome so that he had great difficulty in writing. On admission he was found to present a pretty typical picture of Disseminated Sclerosis of the classical type.

"He is not very bright mentally, but there is no marked enfeeblement of intelligence. He appears for the most part very complacent, although the nurses consider him to be rather irritable and fault-finding.

There is no impairment of speech. The pupils are

unequal, the right being slightly larger than the left. They respond normally. Lateral nystagmus is brought out when he looks far to the right or left. There is no paresis of any of the Occular muscles. He still complains of the defect of vision which is described in the original report. After he has been reading for a certain time, the print seems to disappear, and he has to lay aside the book for a little while. On testing his visual acuteness, no impairment is manifest, nor does there appear to be any contraction of the field of vision. Ophthalmoscopic examination reveals a normal fundus. Volitional tremor is now a marked feature of the case, and is quite typical. It is entirely absent when the muscles are at rest. His writing is very shaky, but is legible.

His gait is exceedingly unsteady. It appears to be a combination of the spastic and the ataxic type. The whole sole of the foot is placed onthe floor, and it is liable to be brought down somewhat heavily more especially the left foot. There is very little flexion at the knee, and the feet are but slightly raised from the ground. There is a tendency to drag the right foot. His steps are unequal and are hesitating. He is quite unable to keep along a line. As he walks there is a good deal of large tremor evident all over the body, but especially in the upper segment.

The knee jerks are greatly exaggerated and there is well-marked ankle clonus on both sides. Patellar clonus is also obtained. The deep reflexes of the arm are perhaps a little increased. He no longer complains of the floor feeling soft under foot.

He has a feeling of numbness in the hands, but no loss in the tactile sense can be detected either there or anywhere else.

He has had some difficulty in swallowing, and is often afraid, while eating, that he may choke.

28th. February.- Patient considers himself much worse since admission. He is certainly walking very badly and is quite unable to walk across the ward without support. The tremor in the hands is not any greater than it was. On giving him a cup pretty full of water, he was able to carry it to the mouth and to drink without spilling any. Tremor however was very well marked both in the hands and in the head when the cup approached the lips.

He has some bladder difficulty, frequency of micturition being the most prominent symptom. He has not had incontinence. For some time the bowels have been moving involuntarily, and occasionally they have done so without his being aware of it. They are moved as a rule several times a day.

28th. March.- Patient is evidently becoming much worse. While examining him to-night the amount of tremor was extreme. On attempting to get out of bed the whole body trembled tumultuously. An attempt to put on his slippers, without assistance, failed on account of the tremor. While he tried to walk he had to be firmly supported, and large tremors were present throughout the whole body.

In the effort to drink a glass of water, much was spilt, but he succeeded to a slight extent. He himself states that he has never known the tremor to be so excessive before.

It is also observed to-night in the muscles of the right side of the face including those of the forehead. It is absent from the left side.

He has been complaining lately of cramps in the legs which cause him to draw them up involuntarily.

Frequency of micturition is still present. During the night he passes urine five or six times. Occasionally it has been passed in bed.

He still has a little diarrhoea. Involuntary defaecation is not infrequent. A further Ophthalmoscopic examination fails to reveal anything abnormal, nor does there appear to be any encroachment upon the field of vision. Nystagmus is only slightly marked.

He has no speech difficulties.

He/

He is dismissed to-day at his own desire.

Dr. Gowers mentions the fact that in a few instances inco-ordination of one or both hands hasbeen the first indication of the disease. The following case may be of this nature. It is difficult on any other basis to account for the symptoms.

Case G. R.S. Aet. 21. Occupation Labourer.

Admitted to the Glasgow Royal Infirmary, 11th. April 1899, complaining of loss of power in the hands of about three months duration.

About the end of January he began to be conscious of difficulty in performing certain movements with his hands, and this difficulty becoming gradually worse, he was obliged to give up work within a few weeks from the first onset of symptoms. He found that he was unable to perform any fine movements with his fingers, and since the beginning of February he has been unable to button his own clothes.

These sensations have been associated with a sense of numbness and with prickling sensations in the hands.

He has not been conscious of anything abnormal in regard to the movements or the sensations of his lower limbs. There has been no impairment in the functions of the bladder or rectum. He is not aware of any defect of vision. The nature of his employment (removing the rust from iron pipes) has exposed him a good deal to the fumes of an acid with which he is constantly working, and he himself mentions this as a probable cause of his illness.

Immediately prior to the onset of the present illness, he had been suffering for some time from pain in the back situated in the lower dorsal and upper lumbar regions, which was very troublesome, but which is now quite gone. He has had no previous illness of importance. A searching inquiry fails to elicit any evidence of a syphilitic taint. He has been pretty temperate in his use of alcohol.

He is married and his wife has had one child who is alive and well. She has had no miscarriages.

Family history is good, and does not reveal any evidence of a neurotic tendency.

Present Condition. He is well nourished. His complexion is unhealthy, but he is not anaemic. His general condition is good.

There is nothing noteworthy about his mental state. He seems ordinarily intelligent. His speech is quite normal.

The/

The muscular system is of good tone all over the body. There is no atrophy anywhere. The grasp with both hands is fairly strong, although feebler than one would expect in a man of his muscular developement. There is a very manifest lack of the power of co-ordination in the muscles of the arms and hands. He can scarcely lift a pin from the bed, and is quite unable to button his nightdress. Carrying a cup of water to the mouth he used both hands, and the whole movement is very clumsy. When this is attempted with the eyes closed, the cup is not carried straight to the mouth, but often comes very wide of the mark. The same defect is brought out when he attempts to touch the point of his nose with each index finger. The degree of inco-ordination is not appreciably greater on one side than the other. When the hands are held widely apart and an effort is made, with the eyes closed, to clap them together, the palms rarely meet.

There is no tremor associated with any of these movements.

He is quite unable to distinguish the shapes of various objects placed in his hand.

The sense of posture is defective. He frequently makes mistakes as to the position in which his hands or forearms are lying, but he is more successful with the upper arm.

On trying his power of judging difference in weight, his replies are very inaccurate when the hands are tested, but are accurate when the test is applied to the feet. When the weights are placed in the hands, the fingers are closed upon them gently, and at the same time the forearm becomes gradually pronated. He is quite unconscious of these movements, and they are apparently beyond his control. There is no evidence of inco-ordination in the legs. He can stand with feet together and eyes closed without swaying unduly. His gait is quite normal. He can walk backwards with his eyes closed.

The deep reflexes all seem abnormally active. The knee jerk is exaggerated and there is a tendency to ankle clonus.

Superficial reflexes are normal. He complains of a sensation of numbness, and of "pins and needles" in the hands, and investigation reveals some deficiency in the tactile and painful senses over small areas, namely over the terminal palanges on their palmar surface; over the thenar eminences; along the outer aspect of the thumbs and lower third of forearm. These anaesthetic areas are practically symmetrical.

There is no area of tenderness in the spinal column.

Pupils are equal and respond normally to light and in accommodation.

Ophthalmoscopic examination reveals a normal fundus. There is no impairment in the visual acuteness, and no contraction of the field of vision. Lateral Nystagmus is present, but there is no paresis of any of the occular muscles.

Pulmonary and Cardiac physical signs are normal.

Urine contains a trace of albumen.

No sugar. No tube casts.

Inco-ordination of the movements of the arms and hands, exaggeration of the knee jerks, a tendency to ankle clonus, and nystagmus are then the main symptoms of this patient's condition. They certainly do not justify a diagnosis of Disseminated Sclerosis, but are quite sufficient to raise a suspicion that he may be the subject of this disease. One can scarcely conceive of a single lesion which could give rise to all.

The nature of his occupation is of interest, and his own impression that his illness was the result of frequent exposure to acid fumes is quite a feasible theory. In a recent/

recent paper by Oppenheim already referred to, he gives great importance to the influence of chemical poisons as an aetiological factor. Out of 28 cases observed by him, 11 of these, from the nature of their occupation, were exposed to the poisonous influence of lead, phosphorous and other metallic and chemical poisons.

Occasionally the subject of Disseminated Sclerosis presents a clinical picture closely resembling that of General Paralysis of the Insane, and in a few instances it may be very difficult to exclude the latter disease.

The following case, which I am disposed to look upon as one of Disseminated Sclerosis, was of this type.

Case H. W.G. Aet 33. Occupation Lorry maker.

Admitted to the Glasgow Royal Infirmary, 6th. February 1899, complaining of staggering, and of abnormal sensations in the feet and legs.

His illness is of about two years' duration. He gives an unsatisfactory account of it, being evidently rather enfeebled mentally. The staggering is what he lays most stress/

stress on, and apparently was the first symptom of which he was conscious. Prinkling sensations in the soles of the feet also annoy him, and have been present since the illness began. During the early part of this illness he was troubled with headaches, but he never vomited. His eyesight became impaired, so that about a year ago he went to the Eye Infirmary, and was ordered spectacles.

He has had no girdle sensation, and no shooting pains in the legs. He has had some difficulty in urination the act being usually delayed at the outset. There is no undue frequency. He has himself been conscious of impairment in his articulation during the past year.

Previous to the onset of this illness he enjoyed good health, and is not aware of having had any illness of importance. He has not had much to worry him. He is a total abstainer, and has been so all his life. There is no evidence of his having had Syphilis.

He is unmarried. He can give little information regarding his family history, and not much of importance. His mother is said to have died from alcoholism.

Present Condition. He is well nourished and well developed. His face has a silly, vacant expression, and he gives the impression that he is mentally weak. On talking to him his answers are for the most part intelligent, but he is liable to wander from the point.

His/

His speech has a peculiar drawl, and his articulation is rather thick and hesitating. The tongue when protruded presents large tremors, but there is no tremor of the lip.

The pupils are unduly contracted, but respond normally. There is well marked lateral nystagmus, but no paresis of any of the occular muscles. He is highly myopic. A good view of the fundus is exceedingly difficult to obtain. So far as can be made out, it is not abnormal. He is rather deaf, and this he says has developed within the last two years. There is no history of a discharge from the ears.

As he lies the feet are observed to occupy the position of Talipes Equinus, but the toes are greatly hyper-extended.

There is no Adductor Spasm, but there is some tendency to rigidity in the hamstring muscles.

The muscles are of good tone and there is no atrophy.

The knee jerks are greatly exaggerated. On the left side ankle clonus is very readily elicited, and it is also present, though less marked, on the right side. Patellar clonus is obtained on both sides.

Plantar reflexes are active but not exaggerated.

Tactile, painful and thermic senses are normal.

He is quite inable to stand with feet together and eyes closed. He staggers a good deal as he walks, and could not walk a line. The legs are kept stiff, and there is very little flexion at the knee. The feet are only lifted a very/

very short way from the ground.

There is no tenderness over the spine.

19th. March. In some respects patient is improved. Mentally, however, he is distinctly worse. He is exceedingly silly in his talk and behaviour, and on this account affords much amusement to the other patients. He is religiously inclined and frequently holds prayer meetings in the ward side room. On inquiry of his friends, this is found not to be a new feature, but that long before his illness commenced, this was his temperament.

His whole aspect and behaviour often suggest that he may be the subject of General Paralysis and the peculiar drawling character of his articulation rather supports that view. There is not however the same tendency to misplace and reduplicate the syllables of difficult words which is found in that disease, nor is the speech associated with any tremor of the lip.

There is no mental exaltation.

He walks better than he did, and is more successful in keeping to a straight line, but he is quite unable to walk 'heel and toe.' He was able to stand with feet together and eyes closed this morning without showing any tendency to fall.

Tremor is often observed in the limbs, and as he holds out/

out his hands at present this symptom is observed. It is of small range and rhythmical. Fascicular tremor was noticed in the right forearm. It has not previously been observed and is not found in any other muscles.

Exaggeration of the deep reflexes is still a marked feature of the case. Ankle and patellar clonus may both be elicited on either side, the latter much more readily than the former.

On the left side these signs are much more apparent than on the right. He makes no complaint of paraesthesiae. Nystagmus is still well marked.

28th. March. Patient dismissed to-day.
His condition remains practically unchanged. To-day ankle and patellar clonus were found to be more active on the right side than on the left.

On the whole I am disposed to look upon this case as one of Disseminated Sclerosis, in spite of the resemblance which it bore to General Paralysis. He was evidently a man who had led a quiet sober life, and had not been exposed to any of the influences which are usually recognised as the precursors of General Paralysis. The duration of his symptoms too was against this diagnosis. Two years after the/

the first onset of symptoms one would have expected the evidences of the disease to be further advanced. His age does not give much assistance, but if anything it favours the diagnosis of Disseminated Sclerosis, General Paralysis commencing as a rule somewhat later. The absence of any lip tremor was strongly against General Paralysis, while on the other hand the peculiar character of the tremor observed elsewhere was more of the character met with in that disease than in Disseminated Sclerosis.

It is uncommon to find this difficulty in the differential diagnosis occurring at so early a stage of the disease; far more commonly it arises during the late stages, when the patient is almost completely paralysed, and confined entirely to bed. In Disseminated Sclerosis intentional tremor of the face, lip and tongue may be present, giving rise to an apparently typical clinical picture of General Paralysis in an advanced stage. Further confusion may arise from the fact that in some cases a history of apoplectiform or Epileptiform seizures will be given, and these will immediately suggest the congestive attacks of General Paralysis. Moreover grandiose ideas are not unknown in Disseminated Sclerosis, a feature which may further complicate the diagnosis.

Nevertheless a careful inquiry into the early history of/

of the illness will almost certainly reveal the true nature of the disease.

AETIOLOGY.

The question of Aetiology is one of no small interest and importance, and has been the source of considerable diversity of opinion. Occasional reference has already been made to it in connection with individual cases, but a more detailed discussion is called for in view of the obscurity with which the subject is surrounded.

The disease most commonly manifests itself between the ages of 20 and 30. Its occasional existence in childhood, and the still greater rarity of its occurrence late in life has already been alluded to in connection with cases A and C. According to the experience of most writers the two sexes appear to be equally liable to the disease, although Charcot was of opinion that females were more frequently affected than males.

The more commonly assigned exciting causes are - exposure to cold and wet; mental shocks or anxiety, especially when the latter is associated with great fatigue; traumatism as,/

as, for instance, a fall or a blow on the head; and other depressing influences. In addition to these it has long been recognised that in a certain proportion of cases the disease emanates from an acute illness of an infectious nature. The frequency with which this relationship can be traced and the peculiar pathology of the disease have led many neurologists to adopt the view that Disseminated Sclerosis depends in every instance upon the presence of an irritant in the blood which sets up inflammatory processes in widely diffused areas throughout the central Nervous System involving especially the neuroglia element. The localisation of individual lesions is determined, not by any inherent property in the interstitial tissue, but by some peculiarity in the minute anatomy of the part. For instance undue tortuosity in a small arteriole may interfere sufficiently with the vascular stream to afford to the irritant circulating in the blood an opportunity of forming a coagulum. A thrombus is thus formed, and endarteritis results. The inflammatory process, thus started, then spreads outwards concentrically; the neuroglia cells are stimulated to proliferate, and this they do at the expense of the nerve fibres and especially of their myelin sheaths. The intimate microscopical changes in the blood vessels themselves support this view of the pathology. These will be found to be studded with nuclei, thickened and sclerosed

especially/

especially in their external coats, and these are structural changes which clearly indicate an inflammatory process. It is necessary, however, to state that certain observers do not admit this vascular origin. Gowers, for instance, insists that "the general history of this disease makes it impossible for us to ascribe it to the acquired influence of either organisms or their products, unless in occasional or exceptional instances (as after an acute disease) which perhaps approach, in nature, such forms of inflammation as that met with in the subjects of Syphilis. The common absence of distinct causation, the early adult age of the subjects and the frequent neuropathic heredity, all point to some inherent condition, some disseminated congenital tendency of the nutrition of the neuroglia." This view however is not generally held, and there is an increasing weight of evidence to show that a distinct relationship between Disseminated Sclerosis and Infectious Diseases is too frequently traceable to be passed over so lightly.

"Some disseminated congenital tendency of the nutrition of the neuroglia" may however explain the comparative rarity of the nervous affection as a sequel of acute diseases. The reference made by Dr. Gowers to "forms of inflammation met with in the subjects of syphilis" is to a condition which very closely resembles that of Insular Sclerosis, in which/

which disseminated lesions are present throughout the brain and spinal cord, scarcely distinguishable at times from those of Insular Sclerosis, but which agree with all syphilitic new formations in their tendency to caseate. These admittedly result from the presence of the specific toxine in the blood, and one can scarcely resist the conclusion, in view of other evidence at our disposal, that the process of their formation has been essentially similar, and that the difference depends upon the special properties of the syphilitic poison. The subject, however, is a very complex one, and still lies largely within the domain of conjecture.

We are at all events entitled to assert that a definite relationship exists between Disseminated Sclerosis and infectious diseases, and that there is much to be said in favour of the view that in all cases the lesions are the result of an irritant circulating in the blood. Marie goes much further: "I have little doubt, in fact," he says, "that in the employment of such a substance as the vaccine matter of Pasteur or lymph of Koch, the evolution of Insular Sclerosis will some day be rendered absolutely impossible." A great variety of acute diseases are credited with being capable of originating the disease. Marie enumerates the following: Enteric Fever (which heads the list in a decided manner), Pneumonia, Malaria, Measles, Scarlet Fever, Small-pox,/

pox, Diphtheria, Whooping Cough, Erysipelas, Dysentery, Cholera, and lastly he quotes a case of Charcot's where the disease appeared to follow Cerebral Rheumatism. In addition to these he adds 'unnamed infections':- "There are no special symptoms at the onset which indicate its existence; fever is known to have occurred, prolonged discomfort with or without gastro-intestinal symptoms, occasionally jaundice or pulmonary trouble, nothing else being known about the disease." Such indefinite illnesses, he believes, will account for those cases in which no other source of irritation can be discovered.

The nature and source of irritants capable of setting up the morbid processes are therefore very varied, and should the recent observations of Oppenheim in regard to chemical poisons as causative factors, be confirmed, these will afford further evidence in favour of the irritant theory, for it is clear that certain poisons may circulate in the blood capable of inducing these local changes, while at the same time giving rise to very little general disturbance.

Reviewing from this aspect the cases we have had under consideration, we find that in case B alone did the symptoms arise in the course of an acute illness; in case A there was a history of occasional indefinite febrile attacks - so-called Influenza; Cases C. and G. presented a possible source of infection in the nature of their employment. C. was a

puddler in an iron manufactory. In this process carbon, sulphur, silica and phosphorus are burned out of the iron. Oppenheim has traced the influence of the latter metal in certain instances. G's. occupation was the cleaning of rusted pipes. These are placed and left to steep in an acid bath, and are afterwards removed and cleaned. He is thus exposed to acid fumes, and his own spontaneous statement that he was disposed to look upon this circumstance as the cause of his illness, is of interest. In none of the others was any history obtained which could guide one to a probable source of infection. Case F had had Enteric Fever about eleven years prior to the first manifestations of nervous symptoms. One cannot place any importance upon this fact, but it is worth mentioning in view of the statement which is made by Oppenheim, that the morbid process may exist and yet give rise to no manifestations of its presence for many years after its first commencement. Indeed this author ventures the opinion that in many cases of the disease, apparently beginning at an adult age, the pathological condition had its starting point in childhood. He records an instance where a disturbance of sight, which occurred during the 14th. year, marked the commencement of the disease, and remained as the only symptom for 20 years. Had the optic tract therefore escaped, this patient would have/

have presented no evidence pointing to changes in the Central Nervous System for 20 years after their actual onset. On such a hypothesis almost any doubtful case could be explained, for there are few people who have not at one time in the course of their lives been the subject of an acute febrile disease.

I have said enough to show that the question of the aetiology of Disseminated Sclerosis is far from being a settled one, and that it is beset with peculiar difficulties. Further investigations are required and are fortunately in progress, for it is only by discovering the cause of the disease that we can hope to be ever in a position to successfully combat it.
