ON THE EXTREMES IN MUTABILITY OF SYMPTOMS IN DISSEMINATE SCLEROSIS.

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It is many years since Dr. Buzzard directed attention to the fact that of all organic diseases of the nervous system disseminate sclerosis is the most likely to be mistaken for hysteria; since then this axiom has received ample corroboration. Although not limited to the early stages of the disease, the difficulties in the way of diagnosis may then be especially perplexing; frequently the indications are vague and only seem to hint at the presence of some indefinite disorder of the nervous system. Absence of characteristic indications, however, by no means constitutes the only difficulty; well-defined symptoms may appear, but they may be abrupt in their onset, erratic in their course, and transient in their duration. They may replace each other with bewildering inconstancy, and after a time may subside and give rise to the impression that manifestations so evanescent are inconsistent with the presence of organic disease. It is with the object of illustrating, on the one hand, the extraordinarily rapid permutations which may occur in the course of distinct indications of organic disease; and on the other, the persistence of such indications for years, followed by their entire subsidence, that I venture to relate in detail the symptoms of two typical cases. In both of them the early appearance of several cardinal symptoms removed any difficulty as to diagnosis.

CASE I.

A married woman, M. T., aged 28, enjoyed good health up to February, 1908, when, in consequence of eating some fish called "hake," which was probably not fresh, she was attacked the same night with severe vomiting and purging which continued through the following day. She was confined to her bed for a week, and on getting up found that she could not walk, and could barely stand. Some days afterwards she had double vision, and a few days subsequently it was seen that her left eye squinted (external strabismus), a condition which lasted about three weeks. She then recovered the use of her legs, and the squinting ceased. For about four months she could walk "on and off" for one, or even two miles, but for some weeks she has been unable to walk at all. About the middle of July she had difficulty in passing water, and on two occasions she passed faeces involuntarily.

I am indebted to Dr. E. T. Larkam for the details of this history, and at his request I took the patient into hospital on August 6th, 1908.

State on Admission.

The patient is a healthy, well-nourished, cheerful woman. She has had no previous illness. There is no history nor indication of syphilis. She speaks perfectly well, without any trace of hesitancy or of syllabic utterance. She moves her arms without difficulty; there is no intention tremor. She can move her legs slightly when in bed, but she can neither stand nor walk. The vision is single, and there is no strabismus. There is no nystagmus even on extreme lateral deflection of the eyeballs. The pupils are moderately dilated and of equal size; they react normally both to light and to accommodation. There is no defect of colour vision, but the patient says that she cannot see as distinctly as formerly. On ophthalmoscopic examination, the discs are found to be pale, but not atrophic. The legs are slightly spastic. The knee-jerk is excessively exaggerated on both sides. A lively and continuous ankle clonus can be induced on both sides by slight pressure with the fingertip on the ball of the foot. Patellar clonus is easily obtained on both sides. The Babinski response is of the extensor type, and can also be easily obtained on both sides. The umbilical reflex is absent. Sensation to touch is defective: the patient feels the point of a pin, but below the knees the perception is blunted, whilst above the knees to the upper part of the thighs the pin-point is felt almost normally. Perception is again blunted over the lower part of the abdomen, especially on the left side; above the umbilicus it is normal. A firm pin-prick on either hip produced involuntary movements of the corresponding leg. The sensation to heat and cold is quite normal. Sensation in the arms to any form of stimulus is not diminished. The muscular sense is unimpaired.

After-History.

August 12th, ankle clonus was less easily produced; there were slight indications of nystagmus. On the 15th the sensory disturbances had almost disappeared; nystagmus was very obvious. On the 17th sensation was quite normal. The knee-jerk was exaggerated, but neither patellar nor ankle clonus could be obtained. The Babinski reaction was flexor on both sides. Nystagmus was very pronounced. On August 23rd diplopia reappeared without perceptible deviation of the eye-

ball; it ceased when one eye was closed. On the 24th the patient complained of slight numbness on the left side of the face, which she said "felt drawn." On August 26th the diplopia had disappeared. On the 29th there was slight ankle clonus, on firm pressure, on the right side only. On August 31st both pupils were dilated, and they reacted sluggishly to light and accommodation; the left pupil was rather irregular in shape. Diplopia is again present, and the patient says that she feels sleepy when double vision is present. Nystagmus is still very pronounced. Ankle clonus could be obtained on the left, but not on the right side. The Babinski reaction was extensor on the left side and flexor on the right.

September 3rd, no nystagmus nor spontaneous diplopia, but when the eyes are directed to the left as far as possible the patient experiences double vision. When the object on the extreme left, at which she is looking, is very slowly moved towards the median line, her eyes following the movement, the double vision persists, but if the object is rapidly moved towards the median line the vision at once becomes single. When the movement is slow the left eyeball is seen to lag behind its fellow. The patient complains of "pins and needles" in both hands, most strongly in the right. There are slight indications of ankle clonus on both sides. The patient says that she has a peculiar smarting sensation in the mouth, with a "cold feeling like peppermint" on drawing in the breath. Both smarting and buccal anaesthesia are chiefly towards the left side. Sensation to a pin-point is duller on the skin of the left cheek than on the right. The sense of taste is unaltered on either side of the tongue. The reflex of the soft palate is absent, and the voice is somewhat nasal. On September 5th diplopia was present only when the eyes were directed to the extreme left. Evanescent ankle clonus could be produced on both sides, and the Babinski reaction is again extensor on both sides. On September 7th the buccal anaesthesia is the same as on the 3rd; slight nystagmus, but no diplopia is present. Feeble ankle clonus could be obtained on the right side, but none on the left. On September 10th the nystagmus is more pronounced; the buccal anaesthesia is much less and is limited to the left side. On the 12th the nystagmus is absent; the patient can walk about the ward unaided. On the 21st the nystagmus is very slight; ankle clonus is absent, and the Babinski reaction is flexor on both sides; the knee-jerk is still exaggerated. On September 23rd there was a faint flicker of nystagmus; the buccal anaesthesia is quite gone. The patient progressively improved during the ensuing ten days; at their expiration the only physical sign present was the knee-jerk, which continued to be much exaggerated. On October 3rd the patient left the hospital; she was able to walk with ease, and she said that she felt quite well.

On January 25th, 1909, the patient came to the hospital, and said that she felt weak on the left side. She was depressed by the fear of a return of her trouble. The knee-jerk was much exaggerated. Patellar clonus and fugitive indications of ankle clonus could be obtained on both sides. The response to the Babinski reaction was extensor on both sides. The patient could walk fairly well, without spasticity or ataxia.

On February 1st the patient was readmitted. She was very emotional and depressed. The knee-jerk was excessive; patellar clonus, but no ankle clonus nor Babinski response could be obtained. There was no intention tremor nor abnormal speech. On the 6th a lively and continuous ankle clonus was obtained on the left side; on the right it was feeble and transient. The Babinski response was extensor on both sides, but was more pronounced on the left. The patient says that she cannot see any one approaching her on the left side until they are close up to her; on being tested, there was no hemianopsia. The optic discs as previously, were pale. Slight nystagmus was present. After this date all the symptoms gradually subsided, and the patient regained her natural cheerfulness. She left the hospital on March 3rd, 1909, feeling quite well.

CASE II.

P. C. is an unmarried woman, aged 24, who, after undergoing some family trouble, began to have sensations of "pins and needles" in the knees in January, 1904. The legs then became numb, the sensation of numbness slowly spreading upwards as high as the body. Soon afterwards the legs gradually lost power, until in February the patient was unable to get about without help. She then was confined to bed and on two occasions had incontinence of faeces but not of urine. Her condition continued unchanged until August 9th, 1904, when she was admitted into hospital.

State on Admission.

The patient is a well-developed, healthy-looking young woman. She can barely stand and then only very unsteadily; she is quite unable to walk. The ataxia is not increased when the patient closes her eyes. The legs are spastic. There is some lateral nystagmus. There is no intention tremor nor any abnormality of speech. The knee-jerk is greatly exaggerated on both sides. Ankle clonus can be produced on the left side but not on the right. The Babinski reaction is of the extensor type on the right side; it cannot be satisfactorily obtained on the left side. The umbilical reflex is absent. Sensation to the pin-point is dulled on both legs, the dullness extending upwards nearly as far as the sternum; on the arms sensation is normal. Sensation to heat and cold is unimpaired both as regards the legs and the body generally. The pupils react to light and to accommodation. The optic discs are pale; on the left side the pallor is more pronounced on the temporal half of the disc.

After-History.

In this case the reflexes varied but little during her five months' stay in hospital, except that on one or two occasions the Babinski response was of the flexor type. The nystagmus varied in degree; sometimes it was very pronounced, whilst at others it could only be developed by extreme deflection of the eyeball. The discs showed no further change. The sensory symptoms varied but slightly. There was never any intention tremor, nor syllabic speech. On one occasion involuntary evacuation of faeces occurred; micturition was sometimes hasty, but there was no incontinence of urine. Broadly speaking, the condition of the patient was unchanged during her stay in hospital. When she left she could neither walk nor stand. She left the hospital on January 21st, 1905, and remained at home in bed until August, 1907, when she began to have power of movement in the toes of both feet. The use of the legs gradually returned, until, in November, 1907, she could walk with aid of support from chairs and other articles of furniture. In March, 1908, she could walk unaided, and has done so since.

She visited the hospital on August 15th, 1908, when she walked without any difficulty, and said that she does not notice anything wrong with her. The articulation was distinct, and there was no intention tremor; nor was there any nystagmus. The knee-jerk was very lively on both sides. There were still some indications of ankle clonus on the right side, but none on the left. The Babinski response was of the flexor type on both sides.

From the clinical standpoint these cases are suggestive: the first of them as regards diagnosis, and the second as regards prognosis. In a doubtful case alternations of symptoms and reflexes, similar to those encountered in the case of M. T., might easily lead to error if the diagnosis were founded on the results of a single examination made at a time when the critical indications are in abeyance and the Babinski response is flexor. The second case warns against dogmatic pronouncement of an unfavourable prognosis without admitting the possibility that the symptoms may subside for a time, even after prolonged paralysis; and it is to be remembered that the remission may last for a considerable period. In both of these cases experience teaches that sooner or later the disease will return.

Instances in which remissions and variations of the symptoms have occurred in the early stage of disseminate sclerosis, followed by their partial or complete disappearance for months or years, are by no means uncommon; but I have not been able to find any record of equally rapid and repeated interchange of many of the cardinal symptoms of the disease, such as occurred in the first of the preceding cases. Seeing that the physical signs which characterize the disease are determined by the occurrence of multiple sclerotic patches dispersed over the central nervous system, it is difficult to explain the erratic disappearances and returns of indications thus produced. *Post-mortem* investigation of the morbid anatomy of disseminate sclerosis is seldom obtained in any but advanced cases, when the symptoms have been progressive and continuous for a considerable time; under such conditions the anatomical changes are usually distinctive and well marked. In the primal stages of the disease, the nature of any focal changes are little more than conjectural.

The pathogeny of disseminate sclerosis is obscure. The antecedent conditions which have been suggested as possibly causal are so numerous and so diverse as to discredit their direct etiological relationship. In many instances it is quite possible that the alleged causal factor has exercised an influence on the development of the disease by depressing the systemic powers, and thus favouring the onset of symptoms previously quiescent and unnoticed, although the morbid processes were probably latently in progress. The patient, M. T., attributed her illness to the fish she had eaten, which doubtless produced a sharp attack of gastro-enteritis; but there is no convincing evidence to show any direct relationship between the poisoning and the sclerosis. P. C. attributed her illness to severe mental strain caused by family trouble. This again, would only act as a developing agency.

The view most in favour at the present time is that disseminate sclerosis is due to the action of an unknown, autogenous toxin. Although not universally accepted, it is probable that the toxin acts by setting up changes in the ultimate vascular supply of the parts affected. These changes comprise thickening of the vascular walls with the formation of thrombi in the minute vessels. In the first instance the nerve tissue of the parts affected undergoes softening, with fatty changes in the cells and destruction of the nerve sheaths. A marked peculiarity in

the morbid anatomy is then apparent; a considerable number of the axis cylinders persist and traverse the degenerated patches. The ganglion cells are frequently unaffected for a considerable time, though surrounded by partially-sclerosed tissue.

It is no easy matter to suggest a reasonable explanation of the way in which the ebb and flow of the symptoms in cases of disseminate sclerosis is produced. No single explanation will suffice to account for the inordinately variable duration of the abnormal reflexes—a duration that in some cases can be estimated by hours, whilst in others it involves months or even years. In the consideration of this question the anatomical changes in the brain and cord first claim attention. There is little doubt that many of the denuded axis cylinders continue to transmit impulses, although their conductive capacity is liable to fluctuations and interruptions of external causation. Temporary pressure from alterations in volume of the closely surrounding degenerating islets through which the nerve fibres pass is sufficient to impede or interrupt conduction; and as the alterations in volume are the result of recurrent evanescent changes in the walls of the minute vessels which supply the part, the degree of pressure will fluctuate. Again, many foci of degeneration are probably rapidly developed and are infinitely small in their inception, and yet they are capable of setting up temporary waves of disturbance through the surrounding areas, which for a time will derange the functional activity of the implicated nerve fibres. But inasmuch as the disturbance is not attended by any recognizable physical change, it will quickly pass away and function will be resumed. Subsequently, however, the areas thus affected may permanently succumb to the characteristic degenerative processes.

The rapid alternations in the Babinski response which occurred in the first case are scarcely to be explained on purely mechanical grounds. It is more probable that responses so immediately contradictory were due to the direct action of a toxin on the nerve cells. During adult life, and in the absence of certain special conditions, the extensor response to the Babinski test is generally accepted as affording evidence of organic disease of the nervous system. The exceptions comprise meningitis, post-epileptic stupor, certain stages of typhoid fever, some states of coma, and even ordinary sleep, in all of which the extensor response has occasionally been met with in individuals who otherwise yield the normal response. In addition to these conditions of internal relation, it has been found that the administration of certain narcotic drugs develops the extensor response in healthy subjects, whilst other narcotics fail to do so. The drug which produces the extensor response the most frequently is scopolamine. Volkmann¹ found that it almost invariably occurred in morphine-scopolamine narcosis. Kutner² observed it in 3 cases after the injection of 0.5 to 1 mg. of scopolamine. Link³ obtained it in 37 out of 43 patients who had received injections of scopolamine in doses varying from 0.4 to 1.2 mg. The extensor response was usually obtained in from fifteen minutes to one hour; in one instance it occurred two minutes after the injection was administered. The inverted response often persisted for several hours. In the narcosis produced by morphine or by ether the skin reflexes of the foot disappear. During the inhalation of chloroform the extensor response may sometimes be obtained at a certain stage of narcosis, after which it quickly disappears. Most frequently it is absent throughout the whole period of administration. Goldflam⁴ noticed that the extensor response produced by scopolamine quickly disappears when chloroform is administered.

Various theories have been propounded to explain the occurrence of the extensor response in scopolamine narcosis. Kutner⁵ is inclined to attribute it to temporary damage to the lateral paths of the pyramidal tract; or possibly to an intensification of a pre-existing weakness in these paths. Goldflam considers that the normal plantar reflex is a cortical reflex. If the reflex-arc is interfered with at any point beyond the posterior roots down to the origin of the anterior roots, or if the cortex is functionless, the plantar stimulus develops a purely spinal reflex by way of the posterior roots and collateral branches to the spinal centre for the extensors of the toes.

The view that the extensor response in scopolamine

narcosis is due to temporary exclusion of the cerebral cortex from the reflex circuit is difficult to reconcile with the absence of any such effect during the narcosis produced by many other drugs. Link suggests that this objection may be met on the hypothesis that some narcotic drugs possess specific properties in addition to their general narcotic action. Illustrative of this are Finkelenburg's⁶ observations that the injection of cocaine into the spinal canal leaves the reflexes unchanged; whilst if stovaine be injected, the deep reflexes first and subsequently the skin reflexes are abolished. Even in the rare instances of stovaine narcosis, in which the tendon reflexes are increased, the Babinski extensor response never occurs. The selective power of modifying the spinal reflexes thus shown to be inherent in some drugs affords a possible clue to the manner in which the variations in the symptoms were produced in the case first described. The drug produces very decided results, but they are limited to the effective period of each dose; when the influence of the drug passes off, the reflexes revert to the normal type. Assuming that an autogenous toxin is the causal agent by which disseminate sclerosis is developed, it may be further assumed that, in the early stages of the disease, the toxin is produced intermittently, and that it may derange the function of the implicated nerve structures before any recognizable anatomical changes are produced. Such disturbance of function would occur in waves corresponding to the intermittent evolution of the toxin; and being merely a "functional disorder," would subside as each batch of toxin was exhausted. Under such conditions, the rapid oscillations in the symptoms and reflexes would be accounted for.

The course of the symptoms in the second of the two cases is in marked contrast with that observed in the first. Instead of rapid interchanges between the symptoms and their entire subsidence in a few months, was comparative constancy and prolonged duration with paralysis extending over years. This is suggestive of physical changes, and yet the paralysis, along with the other symptoms, vanished. Cases of this kind point to the possibility of regenerative processes taking place in organically damaged areas. The lengthy persistence of the symptoms and abnormal reflexes with ultimate recovery is scarcely explicable on any other hypothesis. That the disease will eventually recur and be progressive is, unfortunately, more than probable; meanwhile, the symptoms have been in abeyance for upwards of twelve months.

REFERENCES.

- ¹ *Deut. med. Woch.*, 1903. ² *Ibid.*, 1904. ³ *Zeitschr. f. klin. Med.*, 1906. *Neurolog. Centralbl.*, 1903. ⁴ *Deut. med. Woch.*, 1904. ⁵ *Munch. med. Woch.*, 1906.

A CASE OF CONVULSIVE TIC.

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THE following case is perhaps of sufficient interest to warrant publication:

L. S., a boy, aged 11, had always been considered robust and healthy, and had no illness, except measles when he was a year old. His general characteristics were those of an unusually intelligent child of a somewhat serious disposition. His father and mother are healthy; they have two younger children, both healthy. There is no history of epilepsy nor insanity, nor of any grave nervous disorder in the family of either parent.

In May, 1907, he suffered from chicken-pox. During this illness the mother noticed that he occasionally jerked his head to one or other side, and sometimes also jerked his arms about. This was thought to be St. Vitus's dance, and little attention was paid to it, although it persisted.

Early in January, 1908, the boy came under observation suffering from acute otitis media. Examination of the ear was rendered difficult by the restlessness of the patient. The head was constantly and forcibly jerked towards either shoulder, generally the right, whilst the head was rotated with the chin towards the opposite shoulder. These movements were often accompanied by a sudden, loud hiccupping sound or a sharp, squeaking cry. The arms were frequently thrown outwards into the abducted position, or forcibly extended as though the patient were striking at something. More rarely the arms were folded across the chest. The power of speech was unaffected, and the patient could walk well, the leg muscles being unaffected.

On February 3rd, 1908, he developed a severe attack of scarlet fever complicated in its later stages by suppuration in several cervical glands. During the period of severe illness the spasmodic movements never entirely ceased but were not much in evidence.

In April, 1908, when he had got over his other troubles and was beginning to go about again, the spasmodic movements became more marked and certain new phenomena appeared. The facial muscles were affected by spasm, leading to various grimaces accompanying the other movements of the head. Extremely forcible sniffing movements of the nostrils, accompanied by a sharp and deep inspiration, were frequent. The trunk muscles were more generally affected, leading to various irregular, forcible twisting movements of the body. The legs were sometimes forcibly extended as though the boy were kicking at something. He could still walk, but often had a difficulty in starting, as spasms of the leg muscles caused a series of preliminary jumps and kicks.

In July, 1908, explosive utterances, both inarticulate and articulate, became prominent. Hiccupping sounds were the most common, but sounds imitative of dogs, cats and pigs were heard. Exclamations such as "dash!" "bosh!" "go on!" and "damn!" were shouted, often with wearisome persistency. These exclamations usually, but not always, accompanied the other muscular spasms. The power of co-ordinate movement was not interfered with, except at the actual moment of a spasm. The boy could dress himself, feed himself, write and practise the piano. He could drink from a full glass of water without spilling any, provided the glass was not upset by preliminary flourishes of the arm in the effort to grasp it. During sleep there were no unusual movements.

Since July, 1908, the condition has varied in severity from week to week, but on the whole has steadily got worse.

At the present time (February, 1909) the boy is in good physical condition, and is stouter and stronger than he was six months ago. There is no evidence of organic trouble in any of the systems, nor in the organs of special sense. The only abnormality noted has been a slight exaggeration of the superficial and tendon reflexes.

The spasmodic movements are extremely variable, very irregular in character, and of very constant occurrence, though occasionally the boy may be perfectly still for an hour or two. As instances of the force of the spasms, he has broken a fairly strong plate in two whilst holding it in his hands, and often tears his clothes or wrenches off buttons whilst dressing or undressing. He often bruises himself with his clenched fist.

His power of walking is now often interfered with, progression being made by a series of jumps. Sometimes, however, he can walk fairly well, except for an occasional kick with either leg. The worst feature is now the loud and incessant shouting, making life intolerable for the boy and his parents, and constituting a serious nuisance to neighbours.

His exclamations now include such words as "bloody" and "buggar." These occur not only as loud shouts accompanying spasms, but also in ordinary conversation interspersed with the other words. The boy says he does not want to use these words, but that they come to his tongue, and he must say them. He often repeats any observation made to him, in part or in whole. Generally one or two words are repeated several times, more rarely a whole sentence. When reading to himself, he may suddenly shout out a word or a part of a sentence.

He has frequently been heard to give involuntary expression to what is passing in his mind. For example, whilst thanking a comparative stranger for a small gift, he has suddenly shouted, much to his own confusion, "I don't think much of this, it's not much good."

The boy's moral character has also changed. Formerly particular about his personal appearance, he now takes no pride in being tidy, and says it is too much bother to wash and brush himself, and so forth.

He has become very irritable, especially with other children, and whilst previously very obedient, he is now ready to resent interference. If he be reprimanded about anything, the result is a severe attack of shouting and jumping, perhaps lasting for an hour or two. No mental obsessions have been apparent so far.

From the foregoing account it is evident that this case is an example of convulsive tic of the particular variety known as "Gilles de la Tourette's Disease." There are present:

1. The rapid, forcible, arrhythmic, and involuntary contractions of various muscles or groups of muscles, including those of phonation and respiration.
2. Explosive utterance, articulate and inarticulate.
3. The use of bad language—"Coprologia."
4. The repetition of words or phrases—"Echolalia."

The results of treatment have, so far, been unsatisfactory. Modified Weir Mitchell treatment produced no benefit. A prolonged change to a quiet country place was without good effect. Drugs of various kinds, including strychnine and arsenic, have been of no avail. Bromides produce a temporary improvement, and a small dose has been given nightly for some weeks past, as otherwise the boy gets almost no sleep, and there is consequently no rest for any other member of the household. An attempt has been made to keep the boy occupied, and to interest him in reading, drawing, music, physical exercises, etc. Whilst so occupied he is often comparatively quiet, but the period of quiescence is usually followed by a severe attack of spasms and shouting.