*Chronic Encephalitis.**

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CLINICAL and pathological experience has shown that encephalitis lethargica, like neuro-syphilis and disseminated sclerosis, is essentially a chronic disease. For whether it declares itself acutely or insidiously, and however complete the recovery from the initial phase may appear to be, in a large proportion of cases the infection, which has evidently lain dormant for weeks, months or years, again becomes active and gives rise to the grave disabilities with which we are familiar. The distressing result is that we never know when the patient is cured. At present we are at a prognostic *impasse*.

The disease commonly begins as an acute illness, with the symptoms and signs of which we are not here concerned. Suffice it to say that it may be severe, with high fever and general constitutional disturbance; or subacute, with or without distinctive features, such as lethargy and diplopia; or so slight that it is looked upon as a trivial event. The mortality-rate has been differently estimated, but it probably lies between 20% and 30%. Of the survivors, some are left with residual troubles, that may in time disappear, or become stationary, or get worse. Others remain well for so long that we hope that the cure is complete. But there is always the danger of relapse and the development of late manifestations.

An important group of cases is that in which the disease seems to be chronic from the beginning. Of course there is the possibility that the initial attack has been missed, or passed over as either influenza or a common cold. But with that in mind cases are not infrequently met with in which the most searching inquiries fail to reveal the history of a suspicious illness.

Clinical Forms of the Disease.

Although the virus of encephalitis lethargica has a predilection for the brain-stem and corpus striatum, no part of the nervous system is immune. It has to be remembered also that the disease is a general infection with a special affinity for the neuraxis, but attacks other structures as well, notably the ductless glands. The variability of its clinical manifestations is, therefore, not surprising. At the same time there is the danger, when dealing

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with a new disease where our knowledge is far from complete, of overstressing its polymorphism and of using it as a harbour for our diagnostic difficulties. The clinician with his mind attuned to new possibilities requires the constant check of pathological investigation. Nevertheless, chronic encephalitis lethargica is already stamped by the occurrence of many distinctive disorders of function, and others, doubtless, will yet come to light.

It is useful to separate various clinical pictures or syndromes from the diverse manifestations of the disease. With a wide-spread infection of this sort a classification on rigid anatomical or physiological lines is impracticable. More convenient, if less scientific, is one that is based on common groupings of symptoms and signs which more or less indicate the main anatomical incidence of the lesion, although different physiological units may be involved. But here again the liability to recurrences may so alter the clinical picture throughout the course of the complaint that classification on any basis becomes complicated and inadequate.

In the time at my disposal I will not attempt more than a brief outline of some of the physical disorders of function presented by the disease in its late stages. The mental changes which are so important, especially in children, are dealt with by Dr. Marshall.

The Parkinsonian Syndrome.

In adults this is the most common disability of a general kind resulting from encephalitis lethargica. It occurred, for example, in 70 out of 129 cases studied by Mme. Lévy (5). It may appear rapidly during the acute illness when there is some hope of improvement. But more often its evolution is slow and progressive from the outset, although in its course there may be stationary periods.

The clinical picture of the disorder in its fully developed form is now so familiar that to describe it afresh would be unnecessary. It would be more profitable to consider some of the features which indicate the mild Parkinsonian state. These are often slight, but, as a rule, so alter the patient's appearance and behaviour that they at once arrest attention. He, too, is always aware that something is wrong, and his constant complaint is of a sense of weariness and reduction in vigour. These symptoms will be discussed later in more detail, since they may be present in extreme form without gross physical signs. With them, but not invariably, there is lethargy or insomnia, which may last continuously for many months, or disappear for a time and recur. The sleeplessness is particularly resistant to treatment. Such disorders of sleep are, of course, not peculiar to the Parkinsonian state, but may form part of any of the clinical pictures of chronic encephalitis lethargica.

The early signs of Parkinsonism are found more in the upper part of the body, especially the face, than elsewhere. The face is greasy, the expression tends to be fixed, the eyes staring, the mouth often a little open, and a pool of saliva may be seen between the lower lip and the teeth. The palpebral fissures may be wide or narrow, but blinking is infrequent, and quivering of the lids, when an attempt is made to open or shut the eyes, is a constant sign. Diplopia, squint and nystagmus are less commonly found than in the acute stage of the disease, but defects in ocular movement or pupillary reaction are never absent. The external ocular palsies are supranuclear in origin, and consist of defective conjugate movement, especially on convergence. A striking abnormality that is sometimes observed is intermittent spasm of the elevators of the eyes. The pupils are not usually altered in size or shape, but are often unequal, and almost always show some disturbance of reflex action to light or of accommodation or both. They may be fixed. Impairment of the pupillary accommodation reflex and of conjugate convergence of the eyes go together. Although there may be no definite diplopia, mistiness of vision from defective muscle balance or ciliary paralysis is often complained of, and may be a persistent defect.

A characteristic feature of the Parkinsonian state is the relative immobility of the affected parts even in the apparent absence of rigidity, at all events to the ordinary clinical tests. In its minimal development this is evident in slight fixity of the facial expression and of the eyes, a tendency to hold the head still, a reduction of the associated swinging movement of the arm in walking, and a diminution in the natural fidgetiness of the healthy individual.

Along with the face, one upper limb is usually slightly affected in the mild cases of Parkinsonism, and when there is any rigidity its cog-wheel character can best be detected at the wrist. Of the other slight signs of the Parkinsonian syndrome, two only will be mentioned, namely, excess of saliva in the mouth, the result of diminished activity of the swallowing reflex, and micrographia. Even slight involvement of the right hand is apt to be portrayed in the handwriting, which becomes smaller, the reduction in size of the letters being progressively evident towards the end of each line, as the script goes on. In addition, the lines forming the letters are slightly wavy, although tremor of the hand may not be seen.

Involuntary Movements.

Involuntary movements of many different kinds are amongst the common manifestations of chronic encephalitis lethargica. The

time of their appearance in relation to the onset of the disease, their duration, and the constancy of any one form show great variation. More than one variety may be seen in the same patient, and they may change during the course of the illness. Some are slight and almost insignificant, others are large and arresting, and, in a severe case, the body may be in an almost constant riot of movement.

Involuntary movements rarely, if ever, occur as the sole manifestations of the disease. Mental or physical derangements of some sort are also present, but may be so slight as to be easily missed by the casual observer. Emotional instability and restlessness, especially at night, lapses in behaviour, minor pyramidal or extra-pyramidal signs and oculo-motor defects are perhaps the most frequent slighter accompaniments of involuntary movements, but any of the dramatic respiratory disorders may be found.

Mme. Lévy (5) has grouped the involuntary movements of encephalitis lethargica as follows: (1) Choreiform movements, (2) bradykinesia, (3) myoclonic movements, and (4) tremors. But there are many others—for example, innumerable tics, shuffling and stamping movements of the feet, ocular or glossal spasm complex automatic actions of the whole body, and the "imitative" movements described by Babinski and Klebs (1). Brief mention only will be made of some of these abnormal reactions.

Bradykinesia is the term used by Marie to denote slow, regular, rhythmic movements, often of great amplitude. Such are torsion of the trunk, athetoid movements of the limbs, spasmodic torticollis and grimacing. They are not often encountered.

Myoclonic movements are well known in the acute phases of the disease. But they may also appear as late manifestations in any part of the body and persist for months, accompanied by pain and cutaneous tenderness, radicular in distribution. The pain is often severe and continuous, and may last long after the shock-like muscular contractions have gone. The contractions are rhythmical, at a rate which varies, and may reach forty a minute, and involve part of a muscle, a whole muscle, or a muscle group. Usually they are of insufficient strength to displace a limb segment. When they are localized, the upper abdominal wall or the diaphragm is most often the part affected, and in the latter case the objective manifestation of the contractions is recurrent hiccup.

Tremor of different parts of the body occurs chiefly as a complication of the Parkinsonian syndrome. Froment and Delore (4) have rightly insisted that, unlike the tremor of paralysis agitans, it occurs only during voluntary movement or the maintenance of an active posture. In addition to the limbs it is found elsewhere, giving rise, for example, to shaking of the head, clicking of the teeth,

to-and-fro movements of the tongue, and a rhythmical sucking action of the lips.

All involuntary movements are aggravated by emotional disturbance and fatigue, and, so far as I know, disappear during sleep.

Respiratory Disorders.

A considerable literature has grown up concerning these striking and diverse abnormalities. At first they were often looked upon as hysterical—a not surprising mistake, for they can to some extent be controlled by voluntary effort, become aggravated by excitement, and are frequently associated with emotional instability and restlessness, especially at night. With some of the more severe respiratory disorders delusions and violence may develop, necessitating the patient's confinement in a mental hospital.

Turner and Critchley (6) have classified respiratory abnormalities into three groups: disorders of rate, disorders of rhythm, and respiratory tics.

Tachypnœa and bradypnœa are usually paroxysmal, the attacks varying in duration from a few minutes to several hours. With increase in the respiratory rate (60 to 100 a minute) breathing as a rule is shallow, not necessarily distressing, and there may be no accompanying tachycardia. Sometimes, however, breathing is deep as well as rapid, and, in prolonged attacks, tetany from over-ventilation of the lungs may then develop. Tachypnœa is followed by a period of either bradypnœa or apnœa before normal respiration is established. In bradypnœa the respiratory rate may fall as low as 6 per minute and the breathing is deep and often noisy and panting.

The term "dysrhythmia" is used to cover such abnormalities as sighing, apnœic pauses, breath-holding and the like. Breath-holding is a most dramatic performance, which may be often repeated, especially towards evening, and occur during sleep (Turner and Critchley (6)). After a few deep breaths the chest is held in full inspiration for as long as half a minute. The head is often thrown back, the limbs may perform various grotesque movements, the face may or may not be cyanosed, and, in the longer attacks, consciousness is sometimes lost for a short time. Noisy expiration follows and normal breathing is then established.

Respiratory tics.—Hiccup, yawning, spasmodic hard cough without expectoration, sniffling, hawking, sneezing, are all included under this heading. They are perhaps most often met with in young patients of school age, who, in addition, show changes in character and are subject to nocturnal excitement.

Spastic Paralysis and Muscular Atrophies.

Evidence of slight pyramidal disturbance is common enough as part of almost any syndrome of chronic encephalitis lethargica, but especially Parkinsonism; and, since Buzzard and Greenfield(2) described the first case, it has been recognized that hemiplegia, with or without an apoplectiform onset, may occur during an acute attack of the disease. So, also, rapidly developing paraplegia from myelitis has not been unknown in some of the epidemics. But paralysis of either cerebral or spinal origin may also develop insidiously and form the prominent part of the clinical picture. The diagnosis in such cases may be extremely difficult or remain uncertain, but, as a rule, distinctive phenomena are associated with the paralysis, or the history of the illness provides the clue. Thus, Wimmer (7) has described a case of hemiplegia in which the paralysis was gradually replaced by Parkinsonian features. These disorders may occur simultaneously and on different sides of the body, as in one patient I had under observation for several weeks. Another case where, however, the diagnosis is more doubtful, is that of a man of 53 who, three years after an acute attack of encephalitis lethargica, developed progressive paresis of one lower limb along with nystagmus and unilateral deafness. He was otherwise healthy.

Local muscular atrophies, with or without fibrillation, in different situations have been described by several observers. Thus, Wimmer (7) has recorded an example of wasting of the tongue, and I have at present under my care a patient with unilateral glossal atrophy with fibrillation. Sicard and Paraf, Froment and others have described amyotrophies in the limbs. These are often associated with pyramidal or sensory disorders, clearly pointing to spinal involvement. From histological and clinical evidence it would appear that muscular atrophies may be due to lesions either of the anterior horns or the roots, and, when radicular, there are often in addition severe root pains and cutaneous tenderness which may persist for months.

Endocrine Disorders.

Adiposity, with or without disturbance of the sexual functions, is fairly often met with. Duncan (3) found it in 7 out of 83 cases investigated at the London Hospital. One of my patients, a young girl, who became rapidly and grossly fat after an acute attack of the disease, had amenorrhœa lasting for many months. Later she developed exophthalmic goitre and her weight diminished, but did not fall to normal until she made an apparently complete recovery in eighteen months.

In another case, tachycardia, tremor, slight goitre and emotional instability appeared in a girl a few weeks after she seemed to have recovered from the acute phase of her illness, and persisted for many months.

Diabetes insipidus and glycosuria are also occasional late results of the disease.

Asthenic Syndrome.

Lastly, there is a clinical picture of chronic encephalitis lethargica of which enfeeblement is the constant and main symptom, and in which the physical signs may be slight. Insufficient attention has been paid to this not uncommon syndrome.

The condition may follow an acute attack of the disease, either immediately or after a variable interval, or develop as a chronic state from the beginning. The patient's complaint is of a more or less persistent sense of fatigue, both mental and physical, not a mere inertia, but the discomfort of great weariness. There is diminished desire or power for effort, and physical exertion or mental exercise aggravates the sensation of weakness. The patient looks tired and lackadaisical, and his movements and speech are slow and without animation. For a considerable time he may, with difficulty, continue his work, but if the feebleness increases, as it usually does, he ultimately gives up the struggle and lies in bed or sits in a chair doing nothing. Unlike the weakness of myasthenia gravis, it is not as a rule much diminished by rest, and, unlike the neurasthenic, the patient does not tend to feel better as the day goes on. He may sleep well or be lethargic, but quite often insomnia is a serious complication. Especially when there are family responsibilities, the results of worry cloud the clinical picture, and depression, tearfulness and irritability lead to the common diagnostic error of anxiety neurosis.

This state of fatigue with the sense of general ill-health and weariness is common to most, if not all, Parkinsonians; but the point I wish to stress is that it quite frequently occurs as the sole or main disability. At the same time, in my experience, some of the patients who are afflicted in this way sooner or later develop the Parkinsonian syndrome, but with what frequency I cannot say, since the period of observation in many is as yet too short. In one case, a man of 40, the characteristic facies and bodily posture began to develop fifteen months after the onset of the illness.

Slight physical signs are almost always found, and of these, defective pupillary reactions and conjugate movements of the eyes, especially on convergence, are the most frequent. Sometimes there is a little weakness of voluntary movement of the face, tongue,

and palate; or again mild Parkinsonian signs or involuntary movements, such as tremor or facial tic, may be seen.

Recognition of this group of cases is important, not only from the point of view of the symptomatology of the disease as a whole, but also for their differentiation from psychogenic disorders, with which they are frequently confounded. In the literature occasional reference has been made to this clinical form of encephalitis lethargica as a " myasthenic " variety of the disease—a term which, in my opinion, should not be used; for between it and myasthenia gravis there are many essential clinical distinctions and complete pathological divergence.

The gaps in this brief outline of the clinical features of chronic encephalitis lethargica will be filled in by subsequent speakers. Our knowledge of the symptomatology of the disease, if yet imperfect, is steadily growing, but it must be admitted that in regard to prognosis and treatment we are at present profoundly ignorant. With nine years' experience now behind us, and a wealth of material at our disposal, much could be done by systematic investigation, especially at large hospitals, to throw more light on the nature of the disease in its various manifestations.

References.—(1) Babinski and Klebs, *Soc. de Neur.*, July 6th, 1922.—(2) Buzzard and Greenfield, *Brain*, 1919, xliii, p. 305.—(3) Duncan, *ibid.*, 1924, xlvii, p. 76.—(4) Froment and Delore, *Rev. Neur.*, No. 1, January, 1926.—(5) Lévy, *Les Manifestations Tradives de L'Encéphalite Épidémique*, Paris, Gaston Doin.—(6) Turner and Critchley, *Brain*, 1925, xlviii, p. 72.—(7) Wimmer, *Chronic Epidemic Encephalitis*, London, Heinemann.

(For discussion, *vide* p. 737.)

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*The Mental Aspects of Epidemic Encephalitis.** By ROBERT MACNAB MARSHALL, M.D.Glasg., Assistant Physician, Victoria Infirmary, Glasgow.

MY view of the nature of this disease coincides with that of Dr. Mackenzie. The disease encephalitis lethargica may be defined as an infection the toxic products of which have an affinity for the grey matter of the central nervous system, and so give rise to any of the syndromes of disease of that tissue or to any combination of such syndromes, and which runs a fickle course that may end in recovery, death, or the production of characteristic sequelæ.

In seeking to make a helpful contribution to a discussion of this protean disease it seems best not to try to give an epitome of the

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