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CLASSIFICATION OF THE EPILEPSIES*

BY

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No lecture on epilepsy can begin without reference to Hughlings Jackson, who almost a century ago defined epileptic seizures as the expression of occasional, sudden, excessive, rapid, local discharge in the grey matter. This definition needs hardly any qualification to-day. Yet within the last fifteen years our knowledge of epilepsy has greatly expanded owing to the introduction of the electroencephalogram, a method by which the discharge, which was for Jackson hypothetical, can now be seen and recorded in many seizures. The knowledge thus gained is still in process of assimilation, and what we believe to-day may no longer be true in a year's time. I am not perturbed by this reflection. It is necessary for clear thinking to have beliefs. It is equally important that we should be prepared to change them, which is not so easy. I would commend to you in this connexion Sir Thomas Browne's saying that "to purchase a clear and warrantable body of truth, we must forget, and part with, much of what we know."

If we are to think clearly about epilepsy we must begin by arranging our observations in some kind of order. The classification of seizures in terms of medical science is in itself a problem which has exercised many minds in recent years. I shall put before you the method of classification which I have proposed myself and believe at present to be the most satisfactory. It requires tabulation of the data under separate headings, and the most convenient arrangement is in parallel vertical columns.

The first heading is Clinical. A seizure is a clinical event, and the symptoms observed, or elicited by questioning the patient, must be classified in terms of clinical usage. What these terms should be I will discuss later. It will suffice for the moment if I say that under the Clinical heading we shall record clinical phenomena only—for example, loss of consciousness, convulsive movements, odd behaviour, and abnormal sensations. The heading for the second column is Anatomical. If we accept Hughlings Jackson's definition—and there is no reason to doubt it—the discharge must begin somewhere in the brain. It will be our aim under this heading to indicate the site of origin of the discharge. The third heading is Physiological. Seizures may be accompanied by observed disorder of function in the neurones. Of this the only example at present known is the physical disturbance recorded by the E.E.G.

The fourth column is Pathological. The terms of classification in this column will be those to which we

are all accustomed, inflammation, trauma, new growth, and so on. Finally, I think it useful for practical purposes to have a column in which to record any specific response of seizures to particular drugs or other forms of treatment. A convenient heading will be Therapeutic. In this column we shall make such entries as dione-responsive, primidone ("mysoline")-responsive, and so on. Our object, of course, will be to establish correlations between groups of data in the different columns.

Clinical Patterns of Seizure

I will now go back to consider the classification of seizures in clinical terms. The simplest method is to make use of the plan followed in recording a neurological examination. We begin with the mental state and record loss or clouding of consciousness, disordered behaviour, disturbance of thought, hallucinations, and illusions. Next comes speech, which may be arrested or disorganized in a seizure. After this we take the special senses, any of which may be involved in an attack. Then we have the motor system to consider, which will include a large part of our clinical data—convulsive movement, tonic or clonic, generalized or localized. Sensation will also include many data provided by the patient's account of numbness, tingling, and other somatic sensory experience in attacks. Finally, there is the important heading for visceral symptoms, which may be motor—for example, vasoconstriction, salivation, or involuntary micturition—or sensory—for example, the well-known epigastric aura. The visceral symptoms are commonly both motor and sensory.

I shall not attempt to describe the great variety of symptoms or combinations of symptoms that may be observed in epileptic seizures. The point I wish to make now is that it has been possible to relate certain clinical patterns of seizure to certain anatomical sites of discharge, so that we can speak of pre-central or post-central seizures, temporal-lobe seizures, occipital-lobe seizures, and so on.

In this process of clinico-anatomical correlation the E.E.G. has proved very useful, for when the epileptic discharge arises near the surface of the brain it is associated with a localized electrical disturbance which can often be recorded, either in association with seizures or in the intervals between them. This is a more delicate, and often a more certain, method of establishing the site of the discharging lesion than any other, and has made us more confident of the relationship between clinical pattern and anatomical site than when we had to depend upon the evidence provided by pathological lesions. Sometimes the E.E.G. will indicate the site of discharge when the clinical pattern is of doubtful value. On the other hand, the clinical pattern may sometimes be distinctive when the E.E.G. fails to reveal any localized discharge, probably because the discharge is arising deeply and is therefore not picked up by the scalp electrodes.

*A clinical lecture delivered at Guy's Hospital.

Contribution of the E.E.G.

Apart from its localizing value, the E.E.G. may sometimes provide data for use in the pathological column. For example, replacement of the normal alpha rhythm by localized very slow wave activity indicates an active or recent destructive lesion. Generalized slow-wave activity is met with in the presence of increased intracranial pressure.

But the main contribution of the E.E.G. to the study of epilepsy has arisen from the discovery that there is a large group of seizures associated with a particular *pattern* of electrical disturbance. In this instance the data belong to the physiological column. The distinctive feature of this pattern of discharge is that it is bilateral, synchronous, and symmetrical. Now, taking the physiological column as our point of departure, we may proceed to see what correlations can be established with data in the other columns. The clinical pattern of seizures associated with this type of E.E.G. is quite simply described, but at this point we must digress for a moment to define terms commonly, and sometimes loosely, used in the clinical description of seizures—major or grand mal, and minor or petit mal. It is generally accepted that a major seizure is one in which there is loss of consciousness and generalized convulsive movement. Any other kind of seizure is usually described as minor epilepsy. This division is, I think, unsatisfactory, for there is a great variation, not only in the pattern but in the duration of seizures which would thus be included in the minor category. I can see no completely satisfactory solution for this difficulty, but if we take as our measure the *duration* of the attack we shall find that there is a large group in which the seizure is over in less than a minute. As a term of clinical usage *petit mal* was often in the past employed to describe these very brief seizures, but, as I shall later explain, *petit mal* has now lost its purely clinical meaning. It is convenient to have a term for these little attacks, and minimal seizure is, I think, appropriate, provided that we remember that the word “minimal” refers only to the duration of the seizure.

Now, when we examine the clinical features of attacks associated with the bilateral, synchronous, and symmetrical discharge we find that they are either minimal seizures of a particular kind or major seizures which from the moment of onset are attended by loss of consciousness and generalized convulsion. I must reiterate that these major seizures are not preceded by any other symptoms. As we shall observe later, an epileptic discharge arising in any part of the brain can spread to involve the whole of it and will then be attended by loss of consciousness and generalized convulsion. In such attacks—focal or partial seizures—there is nearly always some initial symptom corresponding with the site of the initial discharge, and if the onset of an attack can be recorded by the E.E.G. localized discharge will be apparent, preceding the general spread. But in the seizures of the group which we are now discussing both the convulsive movements and the electrical discharge are symmetrical and generalized from the first.

Minimal Seizures

The minimal seizures of this group are of two kinds, each as a rule well defined. The most frequent form is the “lapse” or “absence.” There is a sudden, brief suspension of mental function with loss of consciousness. The whole episode lasts from 5 to 15 seconds, and may easily pass unnoticed. During the attack the patient has a fixed stare and is motionless, but there is sometimes twitching of the eyelids and occasionally of the arms, and the eyeballs may turn upwards. The seizure ends as abruptly as it began, and the patient will continue with what he was previously doing or saying as if there had been no interruption. Sometimes the lapse may be longer and last up to a minute, but it is probable that in such cases there has been a very rapid succession of brief attacks. Occasionally the lapse may be incomplete—that is to say,

consciousness is not lost, but clouded, and the patient may be able to describe a momentary state in which he is dimly aware of what is going on around him but unable to initiate thought or action. But where consciousness is lost—and this is the general rule—he has no memory of the time during which the seizure occurred, being aware of the interruption only when it is over.

The other form of minimal seizure observed in patients of this group is the myoclonic attack. This consists of involuntary jerks of the muscles without loss of consciousness. These jerks are usually bilateral and symmetrical, but vary in their extent and distribution. They are often confined to the upper limbs. The duration of the jerks is very brief, not more than a fraction of a second, but there may be a succession or volley of jerks. If the jerk is of large extent whatever is held in the hand may be flung into the air, or if the trunk and lower limbs are involved the patient may be thrown to the ground. Occasionally there may be loss or clouding of consciousness in a myoclonic seizure, but as a rule the patient is aware of all that is happening.

A third variety of minimal seizure has been described as belonging to the group under consideration—the so-called “akinetic” attack in which the patient falls, without loss of consciousness and without myoclonus. Doubt has been cast upon this interpretation, the alternative explanation being that the fall is due to a brief single myoclonus involving the lower limbs. Of this it is difficult to be certain, but I believe from my own observation that true akinetic seizures do occur, and this belief is supported by accounts given by intelligent patients who describe their minimal seizures as of three separate kinds—“blanks,” “jerks,” and “falls.”

Differences in E.E.G. Wave Form

This, then, briefly is the clinical range of attacks associated with the bilateral, synchronous, symmetrical abnormality in the E.E.G.: major seizures of the generalized type, and two, or possibly three, species of minimal seizure. Corresponding with these different types of seizure there are differences in the wave form of the E.E.G. In the major seizure the normal alpha rhythm is replaced by waves of a much higher voltage, though of about the same rate—10 cycles per second—giving rise to a series of spikes, which continues unaltered throughout the tonic phase of the convulsion. In the clonic phase the series of spikes is interrupted by rhythmic slow waves corresponding with the intervals between the clonic spasms. In the form of minimal seizure represented clinically by a lapse of consciousness, the E.E.G. shows a regular sequence of alternating spikes and slow waves at a fairly constant rate of three spike-and-wave complexes per second. The myoclonic jerks are associated with isolated spikes or short runs of spikes which may be mixed up with an occasional slow wave. The akinetic seizure, whose existence is now doubted by some authorities, is accompanied by an E.E.G. of the same type as that seen in myoclonic seizures.

Anatomy and Pathology

We have now established in some detail correlations between physiological and clinical data for this group of seizures and must proceed to examine the data in the other columns. The anatomical site of discharge as determined by the E.E.G. would appear to be generalized, but it seems probable from animal experiments that bilateral, synchronous, symmetrical discharge in the cerebral cortex may represent the effect of an initial discharge arising in the central grey matter and propagated to the cortex. The evidence for this is strong enough to have given rise to the term “centrencephalic,” or more simply central epilepsy, for this group of seizures, so that we may provisionally enter the word central under the anatomical heading.

Under the pathological heading there are no positive data to record, for no one has ever been able to discover any histological basis for this group of seizures, which therefore remains idiopathic in the traditional sense of that word.

We may therefore enter the word idiopathic under the pathological heading. Incidentally it is in this group of seizures that heredity seems to be of more importance than in any other, so that we might perhaps add genetic in brackets under idiopathic.

Therapeutic Data

There now remains the therapeutic column, and in this we have important data to record, for the minimal seizures of this group often respond in dramatic fashion to the dione group of drugs, of which troxidone ("tridione") is that generally used. Dione-responsiveness appears to be specific for this particular type of seizure. It has no beneficial effect upon the major seizures of this group and may even increase their frequency. On the other hand, the drugs which are often effective in controlling the major seizures have usually no effect upon the minimal seizures.

To summarize the data we have now recorded for this group of seizures, they are as follows :

Clinical	Anatomical	Physiological	Pathological	Therapeutic
1. Major—generalized	Central	Bilateral, synchronous, symmetrical E.E.G. discharge	Idiopathic (genetic)	—
2. Minimal (a) lapses (b) jerks ..				Dione-responsive

"Central Epilepsy"

We now need a single descriptive term for this group of seizures. So far as the E.E.G. is a guide, the discharge being generalized, we might use the term "generalized epilepsy." Or we might speak of "central epilepsy" or of "idiopathic epilepsy," and in fact all these terms have been, and still are, used. This, I suppose, does not matter so long as we all understand what is meant. For myself, I prefer the term "central epilepsy," because it is a new one and therefore less liable to misinterpretation than terms which have been used in the past in other ways.

There are, however, some further problems of nomenclature which must be discussed if we are to understand what is being written about the epilepsies. You will find that petit mal is now generally used in a specific way to denote minimal seizures of the central type. Sometimes they are called true petit mal, with the implication that, although minimal seizures of similar clinical appearance may occur in association with other forms of E.E.G., it is only those minimal seizures having the bilateral synchronous patterns of E.E.G. that should truly be described as petit mal. The use of the name petit mal in this sense has been widely accepted, and I have no objection to it so long as it is remembered that it is a definition in terms of the E.E.G. and not a term of clinical description.

If we are going to call the minimal seizures of central epilepsy petit mal, it would seem quite logical to call the major seizures grand mal, again remembering that the E.E.G. is the criterion, and using grand mal only to describe major seizures of the central type. Having thus defined central epilepsy with its subdivision into petit mal and grand mal, I must deal very briefly with the natural history of the disease.

Petit mal seizures nearly always begin in childhood, and from the first occur with great frequency, up to 20 to 30 times a day. They are sometimes controlled by troxidone, but even if they are not they may cease about the age of puberty, never to recur. The lapses are so brief that they need not as a rule interfere with normal education, and the same is true of the jerks, unless they are so extensive as to cause falling. In a considerable proportion of the cases, however, the petit mal seizures are followed sooner or later by grand mal, and the liability to seizures of this type is likely to persist, with or without continuation of the petit mal. A series of myoclonic jerks during the first hour after waking in the morning is especially apt to conclude with a generalized convulsive seizure.

Grand mal seizures, with or without petit mal, may begin at any age, but rarely after 30. The drugs which have proved most effective in the treatment of grand mal are phenobarbitone and phenytoin sodium in combination, primidone, and methoin. The principles of treatment are simple. The drug or drugs chosen should be given first in moderate dosage. If the attacks continue, the dosage should be gradually increased up to the point at which either the attacks cease or intolerable toxic symptoms occur. In the latter case another drug or combination of drugs should be tried in the same way. Each therapeutic trial should be continued long enough for a just appraisal of the effect, having regard to the frequency of seizures before treatment was started. In this way the best medication can be determined, and in a considerable number of cases the seizures, even if they are not abolished, can be brought down to a frequency which is not incapacitating.

"Partial Epilepsy"

In all forms of epilepsy other than that which I have defined as central epilepsy, the clinical and E.E.G. data indicate a discharge arising in some part of the brain. It may be restricted to this part or spread to other parts, but the initial discharge is localized. This is what in the past has been called focal epilepsy, but Gastaut (1954), whose recent monograph, *The Epilepsies*, I would commend to you, prefers the term partial epilepsy for good reasons. It was for a long time supposed that focal epileptic seizures always arose from cells in the cortex and that there was a specific relationship between a particular cortical focus and a particular pattern of seizure. This no longer appears true, the fact being that the cortical neurones represent only one link in a circuit comprising at a deeper level neurones of the central grey matter. Cerebral function is represented not in a cortical mosaic but in sectors of brain which include cortex, optic thalamus (and other basal ganglia), and connecting neurones. The discharge responsible for a partial (as opposed to a generalized) seizure may arise either in the cortical or in the central grey matter. Partial epilepsy, proposed by Gastaut instead of focal epilepsy, is therefore a better term, and I think it should be adopted.

Of the symptoms of partial epilepsy there is an endless variety. I have been especially interested in the clinical patterns of seizures all my clinical life and continue to learn new ones. Hughlings Jackson penetrated to the core of the matter when he said 75 years ago that there were as many different epilepsies as there were sites of discharging lesions. Partial seizures may be of the major, minor, or minimal degree, depending upon the amount of spread of the discharge. In the major seizures there may be little or no clinical evidence of a localized onset, though careful questioning of the patient or a witness of the attack will often bring some important point to light, as, for example, twisting of the head and eyes to one side before the onset of generalized tonic spasm, or the memory of an unpleasant smell or visual hallucination before consciousness was lost. The minor or minimal seizures are much richer in clinical clues, for consciousness is often preserved, or is lost relatively late in the attack, and the patient is able to give an account of the initial symptom. Many partial seizures are thus easily identified—pre- and post-central from localized spasm or sensory disturbance, occipital from crude visual hallucinations, postero-inferior frontal from adverse movement of head and eyes, and some of the temporal lobe seizures from the occurrence of an olfactory aura, masticatory movements, or a dreamy state.

Murray Falconer (1954) has given an excellent account of the many seizure patterns that may result from discharge in different parts of the temporal lobe region. But discharge arising in this region or in the frontal lobe may begin and end with loss of consciousness. It may therefore be very difficult, sometimes I think impossible, to distinguish clinically between a minimal seizure arising from

the frontal or temporal regions and the lapse of petit mal, and here the E.E.G. may be of critical importance in arriving at a correct diagnosis.

You will have observed that I have attached a good deal of importance to the E.E.G. in distinguishing between central and partial seizures and in the localization of the site of discharge in the latter, but, as I have already indicated, the E.E.G. is by no means infallible. A positive E.E.G. depends first upon the chance of an epileptic discharge occurring while the record is being made. This chance may be a very small one, though various methods are now used to precipitate what are called subclinical seizures while the record is in progress. Nevertheless there are a great many cases in which we can be quite sure from the clinical evidence that the patient is suffering from epilepsy yet the E.E.G. is negative. This may be true for partial seizures even though the patient is having clinical attacks at the time the record is made. We recently had in the wards a man who was having partial seizures of pre-central origin with tonic and clonic convulsive spasm involving the left side of the face and adversion of head and eyes to the left. These occurred frequently during the period of the E.E.G. record, which showed no abnormality. It is probable in this case that the discharge was arising deeply.

One of the most interesting developments in recent years has been in our knowledge of the pathology of partial seizures, for which it seems possible that there is always an organic cause to be found—that is to say, a demonstrable histological lesion. The importance of scars, due to birth injury, neonatal anoxia, or encephalitis, has been increasingly revealed from the study of brain substance excised by neurosurgeons. Mr. Murray Falconer's lecture has told of what is now being done in the surgical treatment of partial epilepsy.

Conclusion

I will conclude with a brief account of the steps which should be taken in the investigation of a case of epilepsy. First and foremost there is the clinical history, including, of course, the family history, birth, neonatal symptoms, and past history, with special reference to any head injury, or encephalitis complicating one of the exanthemata, leading up to the description of the seizures, by patient and witness. Next comes the neurological and general examination. When this has been completed the distinction between central and partial epilepsy can very often be made on clinical grounds. It is, however, I think essential to have an E.E.G. in every case, for the combination of clinical and electrical data provides the surest basis for diagnosis and treatment. If the clinical and E.E.G. evidence agree in indicating the diagnosis of central epilepsy there is no need for radiographs of the skull, but in every case of partial epilepsy, or *when-ever there is any doubt*, radiographs should be taken. It is true that they will usually reveal nothing, but if this step is not taken the presence of a benign tumour may be missed, at a stage at which there are no symptoms of increased intracranial pressure or any abnormal physical signs—the stage, in fact, at which a benign tumour can be most safely removed. Many benign tumours of the kind which present with epileptic seizures contain areas of calcification; others may cause a shift of the calcified pineal, or erosion or thickening of bone. It has happened to me twice in the last three years to have encountered a patient in the early teens with seizures taking the form of attacks of unconsciousness, sometimes going on to generalized convulsive spasm, with no certain clue to the site of discharge, and without any other symptoms or signs, in which the radiograph revealed a calcified mass in the left temporal lobe. In each instance this proved to be a benign intraventricular tumour, which was successfully removed.

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A NEW TREATMENT OF BARBITURATE INTOXICATION

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The increasing popularity of barbiturates as suicidal agents has created a world-wide problem, and over the past decade the amount of barbiturate used on both sides of the Atlantic has more than trebled, while the incidence of barbiturate coma has increased fivefold (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954; Goldstein, 1947; Koppanyi and Fazekas, 1950, 1952, 1954; Møller, 1954; *Lancet*, 1951, 1953; Goodman and Gilman, 1947). Until recently the over-all death rate from barbiturate intoxication treated with central analeptics of different types has remained steady at about 10%, increasing to over 20% in serious cases (defined by Nilsson as "one which has been in coma for 24 hours or in which complications are present"). This figure has now been reduced as a result of improved medical care (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954) and possibly, although to a much less extent, the more judicious use of the newer central analeptics (Koppanyi and Fazekas, 1950, 1954; Eckenhoff *et al.*, 1949). We wish to discuss a new method of treatment incorporating the use of two new substances, $\beta\beta$ -methylethylglutarimide (NP13) and 2:4-diamino-5-phenylthiazole hydrobromide or hydrochloride (D.A.P.T.), which we feel should, when used in conjunction with good medical treatment, further reduce the death rate from this condition.

In our small series of 41 cases of pure barbiturate intoxication, of which nine were serious, there was one death, which we suggest was not due to the treatment, and we feel that the method has been promising enough to warrant further large-scale clinical trials.

The merit of the method lies in the fact that the more active agent, NP13, unlike the central analeptics in current use, appears to exert, in therapeutic doses at least, a direct antagonism to the offending barbiturate, and will readily restore the patient from a deep coma to a desired state of light anaesthesia—"the safe state"—from which spontaneous recovery to full consciousness usually occurs within eight hours. This removes the need for strict and prolonged medical and nursing care (Nilsson, 1951; Locket and Angus, 1952; Clemmesen, 1954; Møller, 1954) and virtually eliminates the risk of complications. The chemical structure of NP13 indicates a definite resemblance to the barbiturate ring system.

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