CLINICAL AND SOCIAL PROBLEMS OF EPILEPSY*

BY

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LECTURE I

In his Lumleian Lectures in 1890 Hughlings Jackson set forth his mature views "On Convulsive Seizures." Among his more important conclusions was his placing of the seat of the epileptic disturbance in the cells of the cortex. Paralysis was due to "destroying lesions," convulsions to "discharging lesions." Epilepsy was the name for "occasional, sudden, excessive, rapid, and local discharges of grey matter." These discharges occurred "because the cells have by some pathological process become highly unstable" (Jackson, 1931).

Jackson held that the study of unilateral convulsions unaccompanied by loss of consciousness was the key to the understanding of convulsions in general. Such convulsions, he said further, "tell us nothing of the pathological processes by which the local instability results." In this statement he warns against an error still prevalent at the present day, that focal convulsions necessarily indicate gross or expanding lesions such as tumour.

Jackson was not the first to describe unilateral convulsions, now known universally by his name. He himself gave the credit to Bravais, though in fact they had been observed from the days of antiquity, and Bright and Wilks both noted such disturbances and attributed them to lesions in the cortex of the brain (Temkin, 1945). In Gowers's (1901) words Jackson showed a "mode of investigation" rather than a new type of epileptic attack. He brought convulsions into line with his conception of physiological levels in the nervous system. Local convulsions he called "epileptiform" to distinguish them from "epileptic" convulsions or "genuine" epilepsy. The former referred to discharges at a relatively low physiological level—the middle level or sensorimotor cortex—the latter to discharges at a higher level, which he thought to be in the prefrontal region.

These conclusions received powerful support from the subsequent discovery by Fritsch and Hitzig, and shortly after by Ferrier, of the excitability of parts of the cortex to electrical stimuli. To these researches Jackson expressed his great indebtedness, for they showed that stimulation of the cortex could produce not only isolated movements but local and general convulsions. Great physiologists thereafter confirmed and expanded these observations in the laboratory, and neurological surgeons demonstrated them on the exposed cortex of human subjects.

So the matter stood until Berger (1929) announced his discovery of the recording, through the unopened skull, of the spontaneous electrical activity of the brain. Later he (Berger, 1932) showed that epileptic attacks were accompanied by large electrical discharges. Amplified several million times, the record of the brain waves forms the

electro-encephalogram. The new method has opened broad avenues of research, of which the problems of epilepsy are but one. Gibbs, Lennox, and Mrs. Gibbs, of Boston (1936, 1938), were the first to associate distinctive changes in the electro-encephalogram with different types of epileptic attack: after two and a half years' experience they formulated the view that epilepsy is a paroxysmal cerebral dysrhythmia. The electro-encephalogram shows the brain to be the seat of constant rhythmic activity. The rhythm varies under physiological conditions—for example, in waking from sleep there is an increase in the rate of the discharges. This is a time at which epileptic attacks are especially prone to occur. According to this view seizures are due to sudden and excessive changes of rhythm either to the fast or to the slow side. Grand mal is characterized by extreme acceleration of the electrical activity of the cortex; psychomotor attacks by extreme slowing of this activity; and petit mal by alternation of fast and slow activity. The same types of dysrhythmia (though shorter in duration and of lower voltage) may be present between attacks.

Thus the discharges of grey matter conceived by Hughlings Jackson, as a result of his clinical observations, to be the basis of epilepsy have passed from the realm of hypothesis. The electro-encephalogram records their presence though it fails to reveal their pathogenesis.

The Significance of Local Epilepsy

The phenomena of local epilepsy continue to afford valuable aid, first in the understanding of epilepsy in general, and secondly in clinical diagnosis, provided that within this term are included discharges arising in any excitable area of the cortex and not only the motor cortex. In local epilepsy we can recognize both positive and negative phenomena and learn something of factors which may excite or suppress abnormal cortical activity (Holmes, 1927).

In *local motor epilepsy* the positive element consists of movements, usually clonic. When these cease the affected part is commonly left partly or completely paralysed (Todd's paralysis); this weakness may last for a few minutes or for much longer, occasionally for several days even in the absence of any progressive lesion (Feiling, 1942). It is usually attributed to exhaustion of the cortical neurones, but it may be due to a positive inhibitory action of the discharge, as sometimes an attack is represented solely by loss of movement. When in a local epileptic attack the speech centres are involved the effect is always purely inhibitory—namely, a loss of speech.

During the stage of paralysis the tendon reflexes are usually increased as compared with the normal side, and if the lower limb is involved the plantar reflex is extensor. The involuntary movements may remain localized to the part first affected or may spread in a manner corresponding to the representation of movements in the cortex. Walshe (1943) emphasizes that the motor cortex is not a mosaic of points but an area of graded

*The Lumleian Lectures, delivered to the Royal College of Physicians, April 13 and 15, 1948. (Abridged.)

representation of movement. For example, in the hand area the movements represented are predominantly but not exclusively those of the hand. Thus a stimulating lesion tends to release a widespread convulsion. The most complex movements have the widest field of representation, and these have the lowest convulsive threshold. Such movements are those of the thumb and index finger, angle of mouth, and great toe, in one of which the convulsive movements of a motor Jacksonian attack almost always start.

In *local sensory epilepsy* there are analogous sensory phenomena described as numbness, tingling, or deadness, limited to one area, as the hand or foot, or "marching" as in the motor attack. Sensory loss may follow, usually in the form of astereognosis, but sometimes including also impairment of pain and temperature sense.

Local visual epilepsy consists of crude visual sensations described usually as flashes of light appearing on one side of the body and attributable to discharges in the opposite occipital cortex; these are usually followed by transient impairment of vision in the affected half-field.

The "*uncinate fit*," due to discharges in the region of the uncinate gyrus of the temporal lobe, is unique by reason of the associated psychical symptoms. A subjective smell, unpleasant and nauseating, is the usual local sign, and with it occurs the "dreamy state" described by Jackson, or more elaborate disturbances of memory. It is a common experience that smells have a special power of reviving memories, and it is evident that such associations implicate mechanisms in the temporal lobe, for in temporal epilepsy these seem to be released. The result varies: a familiarity state, meaning a strong sense that everything going on has happened before; a sense of strangeness in which surrounding objects or people are recognized but seem unreal; or a vision of a definite picture which recurs with each attack.

Auditory epilepsy consists of subjective ringing or other sounds occurring in the episodic manner of epilepsy and referred to the ear opposite to the side of the discharge in the temporal lobe. It is rare as an isolated phenomenon and is not followed by deafness, since hearing has a bilateral cortical representation and is not affected by unilateral lesions.

In all these types of local epilepsy peripheral stimuli may influence the attack in the direction either of facilitation or of inhibition. Thus, occasionally, continued use of a part may start an attack there, or repeated sensory stimuli may set off a sensory attack. Bright lights may incite visual epilepsy, and a noise, even a special musical note (Holmes, 1927), may precipitate auditory attacks in those subject to them. More frequently an attack just beginning may be arrested by peripheral stimuli, as by rubbing or grasping an affected limb.

The Question of Consciousness.—These phenomena of local epilepsy are important in clinical diagnosis because they point clearly to the situation of the discharging lesion, except that the uncinate seizure does not of itself tell us whether the disturbance is in the right or the left temporal lobe. A local discharging lesion may: (a) remain localized; (b) spread locally as through the motor or sensory area; (c) spread locally and thence by association fibres to the opposite side of the brain. When this occurs consciousness is lost: it may indeed be clouded just before this occurs if the local spread is rapid (Walshe, 1943). The spread can only be by association fibres; when local convulsions are produced experimentally, section of the corpus callosum prevents spread to the opposite side and general convulsions and unconsciousness do not occur (Penfield and Erickson, 1941).

Major Seizures (Grand Mal)

Gowers's accounts of the major convulsive seizure, which is much commoner than the Jacksonian attack, have never been improved upon. There is great variation in its mode of onset, but the picture of the developed attack is fairly uniform. It may begin with local manifestations known as

the aura, which indicate the site of the initial discharge—motor, sensory, visual, etc. The usual pattern of the later stages is subject to modifications which may cause difficulty in diagnosis. The characteristic phases may not be distinguishable: only tonic rigidity or only clonic movements may be observed. As in local epilepsy, a major attack may occasionally be precipitated by peripheral stimuli, as by handling a limb, by a sudden noise, by the hearing of music (Critchley, 1937), or by a sudden emotional disturbance.

Unfortunately in the majority of cases the clinical features of the major convulsive seizure provide no indication of the site of the discharging lesion. An aura as a first distinct stage of the fit is present in about three-fifths of cases (Gowers, 1901; Lennox and Cobb, 1933), but in only a minority of these has it a clear "local sign"; in the rest it consists of indefinite epigastric or cephalic sensations. These may be of practical value to the patient as warnings enabling him to sit or lie down before he becomes unconscious, but the neural localization of the sensations is unknown. Analogy with local epilepsy becoming generalized suggests that seizures without detectable local onset may begin with a focal discharge in a "silent" area. Jackson, as already noted, thought that the seat of discharge must be in the prefrontal region. Later investigations have neither proved nor disproved this hypothesis. Electrical stimulation of the prefrontal region produces no movements beyond conjugate movement of the eyes and turning of the head to the opposite side. Most electro-encephalographic studies do not point to a single focus as the origin of generalized seizures. Golla, Graham, and Walter (1937), however, found abnormally slow waves which they called " δ " waves present between attacks in a considerable proportion of cases of major epilepsy: these were localized, and it appeared possible that they corresponded to epileptogenic areas in "silent" parts of the cortex.

Inhibition in Epileptic Attacks

Grand mal is mainly a manifestation of excitation not usually accompanied or followed by inhibitory phenomena except sleep. But, as in local epilepsy, diffuse epileptic discharges may be mainly or wholly inhibitory in their effects. Certain attacks occur which are characterized by sudden unconsciousness with slumping or falling but no convulsion: the patient may get up immediately or lie unconscious for several minutes. They have been called "static seizures" (Hunt, 1922): Kinnier Wilson spoke of somewhat similar attacks as "akinetic," and Lennox (1945a) has defined them clearly under this term. Clinically they seem more akin to major epilepsy than to petit mal, both in their relative severity and in their prognosis; but as regards the electro-encephalogram and also their response to remedies they are nearer to petit mal.

Petit Mal

The petit mal is almost pure inhibition. The term is much misused, often being applied to any attack of short duration. It should be restricted to attacks of loss of consciousness lasting usually only a few seconds, without warning and without sequel. An occasional fall would not exclude the diagnosis, but frequent falls are inconsistent with a diagnosis of petit mal. During the attack the expression is blank, speech ceases, the eyes may turn upwards, the eyelids flicker, and there may be a little jerking of the head, occasionally of the arms, but no cyanosis or convulsion. The attacks are less likely to occur when the patient is occupied by physical or mental activity, but if they occur while he is walking he may continue without colliding with others and without dropping anything held in his hand.

As is well known, petit mal attacks frequently coexist with major seizures: about two-thirds of children beginning with petit mal develop grand mal. If, however, such children remain free of major seizures the attacks may cease entirely after a few years, with no impairment of mentality even after many thousands of attacks. This pure form was described by Adie (1924) and others as "pyknolepsy." Lennox (1945a) prefers the name "pykno-epilepsy" to emphasize that they are not something different from epilepsy. Since they are now recognized as identical with petit mal there is no need to retain either of these additional names.

The nature of the petit mal is especially obscure. An epileptic discharge in an area of complex activity such as a speech area causes, as already noted, a loss of function—not the production of words but speechlessness. Pure loss of consciousness seems to indicate an inhibitory discharge in the highest level of integration in the nervous system. The electrical changes both during and between petit mal seizures are the most constant and characteristic of all types of epileptic discharge, and they arise symmetrically and synchronously over a wide area of the cortex, but chiefly in the frontal lobes. Penfield (Penfield and Erickson, 1941) argues, however, that there can be no final re-representation of sensorimotor functions in the frontal lobes, since the removal of large parts of these does not abolish conscious processes in man, and he suggests that the level of final integration lies in the region of the hypothalamus.

Release Phenomena in Epilepsy

After a major epileptic attack the patient may for a time exhibit co-ordinated activity, which is, however, obviously uncontrolled, or unconscious in the sense that the patient has no awareness of what he is doing. Similarly, certain attacks occur which are characterized solely by abnormal behaviour except that at the onset there may be champing movements of the jaws, grimacing or muttering, occasionally a writhing or turning movement of the trunk. Such attacks, which are not uncommon, have in the past usually been explained as post-epileptic automatism, the assumption being that they were sequels of a brief petit mal seizure. It is doubtful, however, whether there is any unconsciousness, though there is an alteration of consciousness indicated by complete amnesia for the whole episode. The term "psychomotor attack" or "psychic equivalent" is now usually used for them: their clinical distinction from other types of seizures is supported by distinctive electroencephalographic tracings.

These attacks of elaborate but purposeless activity, whether they constitute the whole attack or follow a recognizable epileptic incident, must be due to release of lower mechanisms from conscious control. The highest centres, whatever may be their neural site, are either inactivated directly by an epileptic discharge or exhausted by such a discharge, as a limb may be paralysed after a local motor seizure.

The type of activity shown in automatism is of great variety, but tends to repeat itself in successive attacks in the same patient. Usually harmless, it may include violence or indecent exposure and thereby assume serious social or medico-legal significance.

Epileptic Myoclonus

Many patients subject to major epilepsy exhibit between attacks sudden sharp myoclonic jerks, usually limited to flexor movements of the upper limbs, and commonly described by patients or relatives as "the jumps." They occur chiefly and often exclusively in the early morning hours, so that the patient may knock over the breakfast cups, but in a few patients they are very frequent throughout the day.

Rarely, an attack may jerk the patient suddenly to one side and bring him to the ground. Of considerable value in diagnosis, and occasionally the sole manifestation of an epileptic tendency, they are difficult to explain, for they are usually bilateral and associated with bilateral cortical discharges in the electro-encephalogram and yet are unaccompanied by any loss of consciousness.

Status Epilepticus

In this condition the patient has attacks of major epilepsy recurring for hours or days without recovery of consciousness. Isolated attacks, however frequent, with recovery between attacks, are not status epilepticus.

ESSENTIAL MECHANISMS

Irritation (positive discharge), inhibition (negative discharge), and release—these seem to be the essential mechanisms in epilepsy: they are seen most clearly in local epilepsy, but are also detectable in generalized attacks. Conceived and elaborated by the philosophical mind of Hughlings Jackson, they are not invalidated by later researches, and remain sound hypotheses which help in the interpretation of clinical phenomena.

Diagnosis of Epilepsy

The separation of epilepsy from other paroxysmal disorders is a common clinical problem. Gowers (1907) included within "the borderland of epilepsy" fainting or syncope, vasovagal attacks, vertigo, migraine, and certain disturbances of sleep, including narcolepsy; he was, however, careful to say that these troubles seem to be "near epilepsy, but not of it." Twenty years ago, in his Lumleian Lectures, Collier (1928) went further, feeling that these disorders, as well as tetany, were closely related to epilepsy and that some metabolic dyscrasia might underlie them all. However, such biochemical changes as have been found in epilepsy cannot be regarded as primary or causative.

Purdon Martin (1945) has expanded Jackson's theory of the discharging lesion, applying it to a wide variety of paroxysmal disorders as well as to some conditions of continuing irritation such as the thalamic syndrome. He does not suggest that any of these is epileptic. Gibbs and Lennox (1938), however, suggest that a disturbance which is essentially epileptic—involving abnormal rhythmic activity—may start in any portion of the nervous system. In clinical epilepsy this is in the cortex; but this conception extends to chorea, Parkinsonism, neuralgia, etc.

There seems a danger here of theory outrunning experience. There may well be many types of discharging lesion, but it does not follow that all these phenomena are epileptic. Williams (1944) sees a similar danger in the presence of electro-encephalographic disturbances of an epileptic kind in many conditions not usually considered epileptic—for example, faints and toxic convulsions. If all these electrical changes are to be regarded as epileptic "the limits of epilepsy will become so wide as to make the term meaningless."

In the uncertain state of knowledge of these various disturbances of nervous function, classification should rest on clinical distinction. Viewed in this light the resemblances between migraine, faints, etc., and epilepsy become less impressive than the differences between them. For a clinician a diagnosis of epilepsy carries certain implications: it means that there may be serious intracranial disease, and involves the possibility of progressive mental deterioration and always of certain social consequences, complications which do not arise in other paroxysmal disorders.

Faints

Clinical differentiation is, however, sometimes very difficult. Much the commonest problem is to distinguish—

in doubtful cases, for in many the answer is obvious—between epilepsy and the fainting or syncopal attack. According to Lewis (1933), in a faint there are two distinct but simultaneous processes—namely, a slowing of the heart by increased vagal tone, and a fall of blood pressure by vascular relaxation, chiefly in the splanchnic area. These reactions are produced reflexly through a central nervous mechanism. The term vasovagal attack is therefore used by Lewis as an alternative to fainting or syncope, and such attacks are not epileptic, for they are not primarily neurogenic and they carry none of the implications of epilepsy. Between fainting and petit mal as formerly defined a careful history should distinguish, but between fainting and the akinetic type of epileptic attack, with loss of consciousness and falling but without convulsion, the resemblance is close. On the other hand, in a faint there may be clonic movements: they are usually slight in spontaneous faints, but are well known in cardiac syncope. Experience with blood donors has shown that they are sometimes marked (M.R.C. Report, 1944). In a recent paper dealing with attacks of unconsciousness in five hundred members of the Royal Air Force, Rook (1947) observes that “the occurrence of twitching or even major convulsions in association with loss of consciousness does not justify a diagnosis of epilepsy on these grounds alone.”

The one feature which is almost diagnostic is that a faint is a reactive phenomenon, a fit rarely so. The stimulus in the great majority of cases is emotional, though fatigue, recent blood loss, or other factors impairing the general health may facilitate the reaction. Difficulty arises because in persons predisposed to fainting the emotional stimulus may be a very slight one. Epileptic attacks are only rarely due to a direct emotional or reflex stimulus, but, as already noted, such a sequence does occur occasionally. Fox (1941) observes that as a generalization the statement that excitement causes fits is false: boredom, anxiety, and worry do, however, predispose in certain cases. He reported that when the patients under his care were subjected to frequent air raids there was no increase whatever in the frequency of their attacks. Shafar (1941) found this equally true of out-patients attending a London hospital throughout the war years.

The Syndrome of Gowers

Unfortunately the name “vasovagal” was given by Gowers (1907) to a syndrome of a different order which is certainly not a simple syncope, and whose relationship to epilepsy is also unconvincing. The picture in these attacks is not a uniform one, and this probably accounts for varied reports about their frequency. The features of a severe attack include extreme pallor, coldness, difficulty in breathing, pain of anginal distribution, and the *angor animi* or sense of impending death which Ryle (1939) stresses as the foremost feature. The attacks may last half an hour or more. In nearly all the patients there is a strong background of anxiety. Personally I have seen only a few cases in which the pattern of the attack corresponded closely to this severe type, but many in which a state of anxiety was associated with milder manifestations of the same order. Though there is no evidence of cortical disturbance and no unconsciousness or amnesia, they have been held to be epileptic variants in which autonomic disturbances dominate the picture instead of constituting only subsidiary features as in major epileptic attacks (Wilson, 1928). An occasional patient has also had epilepsy, and a family history of epilepsy, migraine, neurosis, or psychosis is quite frequent; but such evidence does not in my view place these attacks in the category of epilepsy, because they are clinically distinct and their prognosis and treatment are entirely different. Walshe (1941) points out that there is no consis-

tent evidence of either vasomotor change or vagal inhibition. The term vasovagal attack, if used at all, should therefore be employed in Lewis's sense as an alternative to syncope or fainting due to transient cerebral anaemia.

Laryngeal “Epilepsy” and Breath-holding Attacks

Also more closely allied to syncope than to epilepsy are attacks due to respiratory obstruction. One type is the so-called laryngeal epilepsy first described by Charcot as laryngeal vertigo. The attack follows coughing, and the subjects are usually of plethoric type with chronic laryngitis or bronchitis. In spite of an absence of previous or family history of epilepsy Whitty (1943) thinks that these attacks are primarily neurogenic—that is, caused by venous congestion in a predisposed person. Rook (1946) saw four cases in the Royal Air Force due to coughing or choking: in three electro-encephalograms were done and were normal. A predisposition must be admitted, since chronic coughs are so common and these attacks infrequent, but, as in predisposition to fainting, this is not a convincing argument for an epileptic basis.

Not so rare are the breath-holding spells of young children: in the North of England mothers call them “the kinks.” Bridge and others (1943) reported 83 cases from the Johns Hopkins Hospital, of whom 60% became unconscious and 40% had convulsions. Two of these children became epileptic and two probably did. But this is not epilepsy. It seems to me that great caution is needed in diagnosis, but if this is correct the treatment is of the psychological causes of the habit.

Narcolepsy and Cataplexy

Narcolepsy is theoretically nearer to epilepsy, as it is certainly a neurogenic disorder. Again some have sought to include this syndrome within the all-embracing concept of epilepsy, but we must separate it decisively on clinical grounds. Electro-encephalographic reports are contradictory, some showing an epileptic type of change (Cohn and Cruvant, 1944) and some only sleep changes. Narcolepsy means attacks of irresistible sleep or of a condition which resembles sleep (Nattrass, 1938). They are preceded by an intense feeling of fatigue, and can often be resisted for a time but seldom prevented: they last usually a few minutes, but it may be only a few seconds, and, exceptionally, if the patient is undisturbed he may continue to sleep. He is usually wakened easily and is alert at once. Frequency of attacks varies, but is usually fairly constant in each patient: there may be two or three daily or one every few minutes.

Cataplexy means attacks of loss of power and of tone induced by emotion of any kind, but especially hearty laughter. There is no loss of consciousness, but the patient sinks to the ground, unable to move or speak for perhaps half a minute. During the attack, as I have verified on several occasions, in striking contrast to inhibitory epilepsy, the tendon jerks are abolished and the plantar reflexes normal; the jerks return instantly when the attack is over. If a cataplectic attack is resisted it may pass into sleep.

The combination of narcolepsy and cataplexy which occurs in the majority of cases is unmistakable. If either type of attack occurs alone, confusion with epilepsy is possible. No case exhibiting the complete syndrome of sleep attacks plus cataplexy has been reported as developing epilepsy.

Other Types of Immobility

In cataplexy inhibition of postural tone is an essential feature. Certain other states of immobility occur in which tone is unaffected and posture maintained. This is seen in catalepsy, which in association with “waxy flexibility” of the limbs is one of the motor phenomena of schizophrenia.

Here the immobility is prolonged, but Rudolph (1946a, 1946b, 1947) has drawn attention to a condition which seems best explained as transient catalepsy, and which is known to nurses as "night nurses' paralysis." In an attack the individual becomes suddenly immobile in either a standing or a sitting position, unable to speak or move but fully conscious and able to see and hear. The attack may last for a few seconds or a few minutes. A similar fixity may result from intense fear; but fear and anxiety are not concerned in the attacks under discussion, nor are they apparently induced by fatigue. Rudolph has found that such attacks occur in others besides nurses, especially in people whose work keeps them stationary. As a rule of no serious significance, and not a condition for which medical advice is sought, it is occasionally dangerous, as in the case of a naval officer who had to be pushed aside on the bridge of a vessel because he was unable to move to prevent an imminent collision. Such a state might well be mistaken for petit mal, but there is absolutely no loss of consciousness.

"Sleep paralysis" is a condition of immobility occurring as a person awakes from sleep, or, less frequently, just before he falls asleep. It occurs in narcoleptic subjects and occasionally in normal people, and in the case of post-dormital paralysis is sometimes explained as a cataplectic state induced by a terrifying dream which wakens the subject but leaves him unable to move for perhaps several minutes.

Paroxysmal Vertigo

Labyrinthine vertigo is common, and is of much interest to physicians, as it comes to their notice in the first instance more often than to otologists. In the attack there is a powerful sensation of movement of surrounding objects, less frequently of the patient himself, usually rotatory, to right or left, sometimes vertical: the occurrence of vomiting, staggering, or falling is a measure of the severity of the attack. Difficulty in diagnosis may arise in various ways. First, some attacks are extremely sudden and brief: the patient is flung to the ground without warning, but picks himself up at once without sequel. Secondly, there may be no deafness or tinnitus: these may appear later in labyrinthine disease, or they may be absent because the lesion is not in the ear but in the central connexions of the labyrinth as in disseminated sclerosis and other brain-stem lesions. Thirdly, with the vertigo there may be transient loss of consciousness. I believe this to be very infrequent, and the absence of any unconsciousness or of any trace of convulsive movements distinguishes the great majority of these attacks from any type of epilepsy.

Migraine

Clinically a certain similarity between migraine and epilepsy is due to the occurrence of focal cortical disturbances in both. While typically such symptoms in migraine are precursors of headache, occasionally they occur independently of headache, and tend especially to do so in later life. However, they differ from local epilepsy markedly in several respects. The scotomata, hemianopia, and fortification spectra of migraine are quite different from the visual phenomena which occur in local occipital or temporal epilepsy or in the visual aura of generalized attacks, both in their character and in their duration. The pre-headache sensory symptoms of migraine differ from local sensory epilepsy in their much slower spread, usually lasting about twenty minutes, their predilection for the tongue, lips, and upper limb, with infrequent involvement of the leg, and most decisively, as Gowers (1907) pointed out, in that they may be felt bilaterally, as in both hands and all around the lips and tongue. Local convulsive movements do not occur in migraine, but the rare hemiplegia which accom-

panies a migraine attack is perhaps more difficult to distinguish from other cortical lesions. Those who are impressed by a close association between migraine and epilepsy seem to me to have overstressed the clinical resemblance between the two.

Aetiologically the relationship of migraine and epilepsy is puzzling. There is impressive evidence (Schumacher and Wolff, 1941; O'Sullivan, 1936) that the cortical phenomena of migraine are due to constriction of cerebral arteries, and that the subsequent headache results from dilatation and excessive pulsation, chiefly of branches of the external carotid. The occasional persistent hemianopia which follows a migraine attack (Adie, 1930) seems likely to be due to prolonged constriction. Vascular changes of this nature have no counterpart in epilepsy, and the pathogenesis of the two kinds of attack seems to be entirely different.

On the other hand there is undoubtedly a genetic relationship between the two disorders. The strongly hereditary character of migraine is not in doubt, but there is also a high incidence of migraine in the families of epileptics. Ely (1930) reported that of 171 persons suffering from epilepsy only 14% gave a family history of epilepsy but 60% gave a history of migraine in a former generation. There is, however, no special incidence of epilepsy in the families of sufferers from migraine. This seems to suggest that migraine is possibly the morbid ancestor of both migraine and epilepsy. Electro-encephalographic studies of migraine subjects have yielded varying results (Lennox, 1946; Dow and Whitty, 1947).

It is doubtful whether any practical deductions can be drawn from these observations connecting epilepsy and migraine. Migraine, though it causes an immense volume of suffering, is a much less serious disease than epilepsy. Lennox says that the two are emphatically not brothers but only some order of cousins. Nevertheless, in his admirable book *Science and Seizures* (Lennox, 1946) he calls migraine "headache seizures" and rather stresses a relationship to epilepsy because he feels this is encouraging for epileptics. No doubt this is true, but it is surely no less discouraging for the much more numerous migraine subjects to be given the idea that their headache attacks are akin to epilepsy. I do not think it is justifiable to speak of a "migraine-epilepsy syndrome."

The Practical Problem

In the present state of knowledge, even if electro-encephalographic records are available, the diagnosis of epilepsy is a clinical decision based on a summary of the evidence. It is therefore helpful to follow a simple plan, beginning by talking with the patient alone, and thereafter interviewing relatives or other observers separately. Children of school age can often give the necessary information as well as adults.

What can the patient tell us about an epileptic fit? Sometimes absolutely nothing, not even that he has fits. For example, the patient may be unaware that he is subject to convulsions in sleep or that he has petit mal during the daytime. In most cases he knows he has had an attack or seizure of some sort, or a series of attacks. He should be asked, "What is the first thing you notice when an attack occurs?" A minority of patients have no warning and become instantly unconscious. But in most cases this question is a vital one, for it brings out information regarding the aura or first stage of the major fit, and this may have precise localizing significance; while in local epilepsy the patient can describe the whole attack.

Secondly, the patient can tell us of his condition when he comes round. Some patients feel quite normal, but the majority have some form of discomfort after major

attacks; prominent among these are headache and a desire to sleep, signs of injury, tongue-biting, incontinence of urine, vomiting, and soreness of muscles.

Then we can hear from the patient of the time of attacks, in particular their relation to sleep and to menstruation. As to sleep, the attacks may (1) occur during sleep, which is virtually diagnostic—of these the patient usually knows by his condition on waking; (2) if diurnal, show a marked predilection for the early morning hours; (3) occasionally occur just as the patient falls asleep. Further, an account of morning myoclonus is common and helpful.

Finally, though the patient cannot tell us of his actions in a state of automatism, he is often aware of this condition through circumstantial evidence, such as finding he has wandered into some strange place. The second part of the history, from relatives, may be decisive, but is often singularly inconclusive.

Aids to Diagnosis

The Electro-encephalogram.—Only if attacks are induced artificially, or if the patient is having frequent attacks under observation, is it possible to observe the distinctive seizure patterns. Confirmation of a clinical diagnosis, or help in a doubtful case, therefore depends on any variations from the normal which may be found in the resting record. Certain paroxysmal discharges seen in this record are virtually diagnostic of epilepsy: clearly defined “larval” attacks—i.e., electro-encephalographic but not clinical attacks—were never found by Williams (1944) in non-epileptic subjects, and the only case in 8,000 in which a wave-and-spike outburst (the type associated chiefly with petit mal) was seen in a non-epileptic was the identical twin of an epileptic. The Harvard workers found this type of outburst in only 1 in 500 of non-epileptic subjects but in 77% of patients with a clinical diagnosis of petit mal. These observers (Gibbs, Gibbs, and Lennox, 1943) conclude that in about 48% of persons with a history of seizures a routine electro-encephalogram is of great value in diagnosis, and in about 42% it is of little or no value. The results depend largely on the frequency of examinations. They are of most value in the diagnosis of petit mal, in which class of case clinical diagnosis is most often in doubt. It must also be recognized that not infrequently successive records in the same patient are inconsistent—a fact which has disturbed a number of clinicians (Holmes, 1946; Rook, 1947). The interpretation of records is a specialized and skilled procedure, and the results must be evaluated only in conjunction with the clinical picture.

Induction of Fits.—Two methods may be used to induce fits for the purpose of diagnosis. The first is the production of alkalosis by overbreathing, the second to cause a positive water balance by forced ingestion of water and the administration of pitressin (Blyth, 1943). A couple of minutes' overbreathing may confirm a diagnosis of petit mal or bring out paroxysmal discharges in the electro-encephalogram. Otherwise these tests are formidable and have little place in ordinary practice.

The Clinical Decision.—Doubts and mistakes are inevitable even after the most painstaking analysis of the evidence. In civil practice, which is free from the complications in diagnosis encountered in the Services, the bias in a doubtful case should, in my view, be towards the diagnosis of epilepsy. If there is a history of recurrent attacks strongly suggestive of epilepsy, though certainty is lacking, the correct diagnosis is more likely to be epilepsy than anything else. Final judgment may be reserved, but appropriate treatment should be instituted.

[The Second Lecture, with the list of references, will appear in our next issue.]

ANTIHISTAMINE DRUG TREATMENT OF ACUTE NEPHRITIS

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This paper is a preliminary report on the use of “anthisan” in the treatment of acute nephritis in children. The number of cases so far treated is small, but the results have been so striking that we feel it is advisable to publish them at this stage in order to stimulate further work on the subject.

No specific treatment has yet been found which will abort acute nephritis or even appreciably modify its course. Treatment up till now has been directed towards providing rest both for the patient and, so far as this can be achieved by dietary restrictions, for his kidneys, in the hope that these organs have not already been irreparably damaged and will eventually recover spontaneously. If the response we have observed to treatment with anthisan can be confirmed over a larger series of cases a very material advance will have been made in the treatment of acute nephritis. In a centre such as this it will be some years before we see enough cases for the proper evaluation of the treatment with adequate controls. Therefore it is advisable that this work should also be undertaken at other and larger centres.

The well-known tendency for acute nephritis to occur at an interval of a week or two after an acute bacterial infection suggests that nephritis may be in the nature of an allergic response to bacterial toxins. The relationship which seems to exist between acute nephritis and some cases of anaphylactoid purpura lends further support to this theory. It would therefore appear reasonable to test the effect of the antihistamine drugs in this condition. So far as we are aware the only published work on this subject is that of Reubi (1946), who has claimed good results from treatment with “antistin” both in a few cases of experimentally induced nephritis in rabbits and in a small series of cases of acute nephritis in human beings. As might be expected, he found that antistin had no effect on chronic nephritis where the kidneys are already irreparably damaged.

We have now used anthisan in the treatment of eight successive cases of acute nephritis admitted to the Royal Aberdeen Hospital for Sick Children. The course of these cases has been compared with that of the nine consecutive cases of this condition admitted immediately preceding the institution of this treatment. Two cases of nephritis which were nephrotic in type from the outset have not been included, but, apart from them, all fresh cases of nephritis admitted to the hospital between October, 1946, and October, 1948, are included in either the anthisan or the control groups.

The groups differ in one important respect—i.e., they were not admitted during the same period of time—and it is of course possible that the later cases were suffering from a relatively benign form of nephritis. The two groups are, however, closely comparable as regards the duration of illness before admission and the clinical assessment of severity at the onset, based on albuminuria, haematuria,