EPILEPSY AND THE CONVULSIVE STATES

BY

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DEFINITION

Epilepsy is the expression of occasional, sudden, rapid, excessive local discharge in the grey matter (Jackson, 1932). A convulsion is the involuntary tonic and clonic muscular movements to which this gives rise; the other clinical manifestations being an impairment of consciousness or other psychic function and a disturbance of the Autonomic Nervous System (Lennox, 1949a). In epilepsy, any of these clinical features or combinations of them may predominate, so the term covers a wide diversity of conditions.

HISTORY

Epilepsy was known to early Greek and Latin writers as “The Falling Sickness” and “The Sacred Disease”, and it was Hippocrates who first expressed disbelief in this latter description. “It appears to me to be no wise more sacred than other diseases, but has a natural cause from which it originates like other affections” (Adams, 1843). Many famous people are said to have suffered from it, including Julius Caesar, Napoleon, Alexander the Great, Mary Queen of Scots, and Swedenborg.

CLASSIFICATION

The epilepsies are best studied in terms of the neuronal discharge which gives rise to them, and four aspects of this discharge will be considered: (1) the site of origin of the discharge; (2) the nature of the discharge (as reflected by E.E.G. readings); (3) the pathology which appears to be associated with the discharge; (4) the clinical manifestation of the discharge.

(1) The site of origin of the discharge.

The discharge may arise in a symmetrical and generalized manner from the central grey matter, or may originate in one specific portion of the cortex or grey matter. In the latter group, the discharge may remain localized, or spread and become generalized (Symonds, 1955).

The former group is known as generalized epilepsy (Gastaut, 1954a) (central epilepsy of Symonds, 1955), and includes two distinct types. The major seizures (grand mal) consist of generalized convulsions and unconsciousness. The minor seizures (petit mal) manifest themselves either as brief lapses of consciousness, myoclonic jerks, or loss of muscular tone, resulting in a fall. Patients describe them as blanks, jerks, and falls.

Those seizures which arise in a limited system of brain matter, often called focal, local, or Jacksonian epilepsy in the past, are now referred to as partial epilepsy (Gastaut, 1954b). They are usually associated with a demonstrable pathology, and the initial symptoms and signs in an attack are related to the site of origin of the discharge, although generalized convulsions may follow.

(2) The nature of the discharge.

The normal electroencephalogram, taken from a resting adult subject with his eyes closed, shows an alpha wave formation of 8–13 cycles per second. In a generalized convulsion, a quite different wave formation is seen. It consists of an increase in speed and amplitude of the wave pattern up to 30 cycles per second (Gibbs and Gibbs, 1941) and is the same whether the fit is part of a grand mal attack, occurs during anaesthesia, or is eclamptic in origin.

During a minor seizure of central origin, the typical wave complex consists of a rapid spike followed by a slow wave, these complexes occurring about three times per second. The myoclonic type of minor seizure more commonly shows a series of two to five rapid spikes, sometimes with an associated slow wave (Grinker et al., 1938).
Cases of partial epilepsy typically show a slow wave activity related to the site of the discharge. For example, in cases of psychomotor epilepsy, who have episodes of compulsive, aggressive behaviour, the discharge can be demonstrated arising in one or both temporal lobes (Walton and Osselton, 1951a).

(3) Associated pathology.

Only in about 25 per cent of patients suffering from epilepsy can any related pathology be found and Lennox (1949b) divides such findings into four groups:

(a) Congenital defects in the central nervous system, e.g. cerebral diplasia, cerebromacular degeneration, mental defectiveness.
(b) Acquired changes in the brain, e.g. birth trauma, tumours, cysts, haemorrhage, atherosclerosis, meningitis and encephalitis, abscess, general paresis, and tubercle.
(c) General conditions and diseases. Toxaemia of pregnancy, uraemia, malaria, infective fevers, asphyxia, oxygen intoxication, carbon monoxide poisoning, tetany, hyperventilation, hypoglycaemia, alcoholism, migraine, anaesthetic drugs, electric shock, and cerebral oedema.
(d) Convulsant drugs. Local anaesthetics, picrotoxin, leptazol, absinth, ergot, lead, caffeine, nicotine, camphor, and magnesium sulphate.

Most of the above-named conditions are only occasionally accompanied by fits, but their relationship to them is too frequent to be fortuitous, and it seems probable that in a small proportion of the population, who are "convulsion prone", these lesions can act as precipitating factors.

(4) Clinical types.

The distinguishing features of minor seizures (petit mal) and partial epilepsy have already been mentioned; it remains to describe a major epileptic attack.

Motor, sensory, or psychic symptoms may precede the seizure by hours or days, and immediately before the actual fit about half the patients experience a more acute premonition of the event, the so-called aura. The nature of this aura varies as widely as do the prodromal symptoms.

The convulsion may begin with a loud cry, and, as consciousness is lost, the patient falls to the floor in a state of tonic muscular spasm, lasting about half a minute and accompanied by increasing cyanosis. This stage is followed by a series of increasingly severe tonic spasms lasting about one minute and usually accompanied by copious salivation, and loss of sphincter control. As the paroxysms abate, the patient falls into a profound sleep, on recovering from which he may perform acts of which he has no final memory. The social disadvantages of this postepileptic automatism may be serious.

Status epilepticus represents the disorder at its maximum, the sleep following one fit being interrupted by the next attack. A case is reported of a thirteen-year-old girl who recovered perfectly after having 3,231 major fits in 17 days (McDougall, 1919).

AETIOLOGY

Normal functioning of the human brain depends on its ability to limit afferent impulses to the appropriate neuronal channels, in circumstances where spread of the discharge into a host of other channels is theoretically possible. Failure to limit this neuronal release is the essential defect in epilepsy. The liability to such failure differs widely in a random group of patients and is reflected in the variable dosage of convulsant drugs required to produce fits in such a group.

Cure et al. (1948) demonstrated this variation using leptazol and showed that the minimum dosage in terms of body weight was regularly less in epileptic patients than in normal controls.

In the experimental animal, the main methods used to produce convulsions are electrical stimulation, convulsant drugs, and the production of epileptogenic lesions by chemicals and freezing.

The following metabolic changes have been shown to increase the liability of some patients to fits: fall in blood oxygen, abnormally high blood oxygen, alkalosis, decrease in blood calcium concentration, increase in blood chloride concentration, increase in tissue permeability, and fall in blood sugar. The reverse conditions diminish the tendency of these same patients to fits.

The occurrence of convulsions during anaesthesia has been related to: lack or excess of morphia, oxygen and carbon dioxide, impure agents, pyrexia, excessive dosage of atropine, calcium deficiency, surgical stimulation, sepsis, disturbed renal function and a specific convulsant organism (Kemp, 1944).
It seems that in the presence of one or more of these predisposing factors, a sufficiently strong stimulus may evoke a convulsion and that both the initial factor and the final stimulus may vary in different cases (Pask, 1942).

Kemp (1944) postulates that the essential mechanism is hypoxia of the cerebral tissue, thus correlating many of the predisposing factors. Oxygen requirements are raised by pyrexia and atropine, and oxygen dissociation decreased by alkalosis. This alkalosis is caused by hyperventilation which, in turn, may be due to light ether anaesthesia, pyrexia and surgical stimulation.

Brenner and Merritt (1942) suggest that a disturbance of acetylcholine metabolism may be concerned in the aetiology or mechanism of convulsions. They showed its convulsant properties when applied locally to the cortex of cats, an effect potentiated by neostigmine methyl sulphate. Fiamberti (1937) has used intracisternal acetylcholine to produce convulsions in the treatment of dementia praecox. Certainly, it is the only chemical normally present in the cortex which has been shown to have this effect.

During electroencephalographic examination of patients, certain methods are used to precipitate epileptic-like electrical changes. These changes persist for any length of time only in known epileptics and in a proportion of apparently normal patients who are presumably "convulsion prone". The main methods employed to induce these changes are: over-hydration, drug-induced sleep, intravenous leptazol, and audio- and photic-stimulation.

This predisposition of some patients to convulsions, even though they are not known epileptics, is borne out by the work of Williams and Sweet (1944). They followed up 42 patients who had had convulsions during anaesthesia, and out of 22 of them on whom e.e.g.s were performed 73 per cent showed abnormalities similar to those seen in idiopathic epilepsy, as opposed to 12 per cent in a normal control group. In a further series, 75 per cent of idiopathic epileptic cases showed similar changes.

Rosenbaum and Maltby (1943) studied 20 cases who had had toxaemia of pregnancy and 20 further patients in whom the condition had progressed to convulsions. When examined, 65 per cent of the latter group had abnormal e.e.g. readings, and 60 per cent a family history of fits. Of the "toxaemia only" series, 10 per cent showed abnormal e.e.g.s and 10 per cent gave a family history of fits.

It can be argued, that these e.e.g. changes have, in fact, been caused by the convulsions, and were not present before them, but such changes are seen in up to 25 per cent of people who have never convulsed (Williams, 1941) and are absent in 25 per cent of those who have (Walton and Osselton, 1951b).

In terms of neuronal stability, the population falls into three groups: the large majority who will convulse only under markedly abnormal conditions; the known epileptics whose fits occur where no obvious or precipitating factors are present; and a third group, intermediate between the two, and not known epileptics, who will convulse if presented with one or more of the predisposing factors previously listed and then with an adequate stimulus. The patients who convulsed under anaesthesia and during pregnancy, referred to in the preceding studies, would presumably be of this last group (Williams and Sweet, 1944; Rosenbaum and Maltby, 1943).

**TREATMENT**

Where possible, this is directed against the associated pathology, the excision of localized lesions being sometimes possible. Recently, cases of psychomotor epilepsy have been successfully treated by excision of one or both temporal lobes (Penfield and Flanigin, 1950).

Treatment of idiopathic epilepsy is devoted to the suppression of attacks, the treatment of the fits when they occur, and the sensible but not excessive regulation of the patient's life to his condition.

**Suppression of attacks.**

Major epileptic seizures can sometimes be prevented and almost always diminished in frequency and severity by drug therapy. Derivatives of three main groups are used; those of barbituric acid, hydantoin, and acyl urea. Examples of each of these groups are: phenyl ethyl malonyl urea (phenobarbitone Luminal, Gardenal); sodium diphenyl hydantoinate (Dilantin sodium, Solantyl, phenytoin sodium); and phenacetyl urea (phenurone, Epielase).
**Petit mal** attacks respond better to derivatives of oxazolidine 2-4 dione, the main one being trimethyloxazolidone dione (epidione, tridione).

The anticonvulsive action of these drugs depends on the grouping:

\[ R \text{C} \xrightarrow{\text{CO}} N \quad R \]

Therapy must be continued for at least three years after the last fit has taken place, and toxic manifestations are an indication to change the drug and not to stop therapy. Recently, a drug of low toxicity of the dione group, primidone (Mysoline), has been introduced and found of value in both major seizures and petit mal (Handley and Stewart, 1952; Smith and McNaughton, 1953).

The seizure threshold can be further elevated by improving the general health, a ketogenic diet and low water intake, though these last two methods may demand considerable fortitude from the patient.

Care during a convulsion consists of preventing injury, especially tongue biting, and clearing the airway.

**Status epilepticus** is treated by the intravenous injection of phenobarbitone (5 grains (300 mg) for an adult) and tridione (15 grains (900 mg)). Other methods of treatment are the use of magnesium sulphate, bromides, and, as a last resort, rectal bromethol (80 mg/kg). The withdrawal of cerebrospinal fluid sometimes ends an attack, but lumbar puncture in these cases is technically difficult.

The factors predisposing to convulsions during anaesthesia, already listed, should be avoided as far as possible, but if anaesthesia has to be undertaken in their presence, barbiturate premedication, a small atropine dosage, keeping the patient cool and adequately oxygenated through a free airway, will render fits less likely.

When such convulsions occur, the administration of anaesthetic agents should be stopped, intubation performed if possible, and the lungs forcibly inflated with oxygen. An intravenous injection of a 2½ per cent solution of thiopentone sodium is then given slowly until muscle movements cease. Even when allowance is made for the slowing of the circulation time which accompanies the fit, apnoea from the thiopentone can easily result and the patient must then at once be inflated with oxygen. The muscle paroxysms can alternatively be controlled by giving a short-acting relaxant such as suxamethonium chloride, which has the merit of allowing easy intubation and inflation, and avoids further circulatory depression. However, during the convulsions, considerable assistance is required to hold a limb steady enough for intravenous injection of any sort.

Most cases of toxaemia of pregnancy do not proceed to convulsions if placed on a strict régime of bed rest and reduced fluid intake. But if fits develop, three avenues of treatment are available: heavy morphinization, rectal bromethol or paraldehyde, and continuous spinal or epidural anaesthesia, the effectiveness of the latter procedure being related to its hypotensive effect.

### REFERENCES