with troxidone. This does not necessitate withdrawal of the drug but requires added caution and more frequent blood-cell counts. The appearance of signs of kidney dysfunction requires immediate withdrawal of the drug.

Paramethadione ("Paradione").—Paramethadione is a close analogue of troxidone. Its dosage schedule and toxicity are similar. Toxic manifestations are less frequent, and intolerance to troxidone does not necessarily mean intolerance to paramethadione. Its use is indicated in those patients with petit-mal seizures who are refractory to treatment or develop toxic reactions to troxidone. Occasionally the combination of both drugs gives better results than either one alone. The same precautions that were detailed for troxidone apply to the use of paramethadione.

Phensuximide ("Milontin").—This is indicated for the treatment of petit mal when troxidone and paramethadione, administered either alone or in combination, have proved ineffective. The starting dose is 0.5 g. three times a day, with gradual increases of 0.5 g. Therapeutic effect is usually obtained in the range of 2 to 3 g. a day. The limiting side-effects are nausea, vomiting, dizziness, drowsiness, and dreamlike states. These disappear with adjustment of dosage or withdrawal of the drug. Transient microscopic haematuria has been reported during its administration, but all investigations are not in agreement regarding occurrence or significance. It would seem wise to do urinalyses and blood-cell counts at stated intervals for patients receiving the drug for long periods until more is known about its toxic manifestations.

Causes of Failures of Therapy

The success in the use of anticonvulsant drugs is related to the degree of skill used by the physician in administering the available drugs. Failure to obtain the optimum results in therapy are related to a number of factors: failure to recognize a progressive neurological disease, particularly brain tumours; failure to use proper drugs; failure to administer proper dosage; premature withdrawal of drugs; frequent shifting of drugs; poor indoctrination of patient in regard to the therapy; and lack of recognition of social and economic needs of patient.

The largest number of failures are related to failure to administer the proper amount of the drug and failure to use two or more drugs in combination. There is no established dosage of any of the anticonvulsant drugs. The guiding rule should be to start with a small or moderate dose of the drug which is considered to be suitable for the patient, with gradual increase of dosage at suitable intervals until the seizures are controlled or the appearance of minor toxic symptoms make further additions inadvisable. If serious toxic symptoms develop, the drug should be withdrawn and another substituted. If the drug used initially is well tolerated but is not capable of controlling the seizures, another compound should be added. Usually large doses of each drug are needed when two or more drugs are used.

Success of Anticonvulsant Therapy

The results of treatment in 319 cases of epilepsy were: controlled, 154 (48%); improved, 118 (37%); and uncontrolled, 47 (15%) (Yahr *et al.*, 1952). These results are good when compared with those which could be obtained 25 years ago, but they are still inadequate. New compounds are being tested regularly, and it is quite probable that a more effective therapy will be available in the near future.

The question arises of when it is advisable to withdraw medication in patients who have been under therapy and have had no seizures for many months or years. Some children and young adults may have a few seizures in the course of a year or two and then have a complete remission. Spontaneous remissions may also occur in patients who have had seizures for many years. It is also possible that a remission may be induced by the treatment. It is our rule to administer anticonvulsants to patients with any type of seizure except petit mal for a period of at least three years

after all seizures have disappeared. At this time the dose of the drug can be reduced every four to six months by one-third to one-fifth of the amount required to control the seizures. If seizures recur the drug should be readministered in full dosage. The results (see Table) obtained in

Results of Reduction and Elimination of Medication in Various Types of Seizures

	Total No.	Seizure-Free		Recurrences	
		Off Medication	On Reduced Dosage	Off Medication	On Reduced Dosage
Petit mal	14	12	2	—	—
Grand mal and other	71	17	19	9	30

the attempt to discontinue anticonvulsant therapy in patients who had been seizure-free for a prolonged period have been disappointing, except for those with petit mal attacks (Yahr and Merritt, 1956).

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PITFALLS AND SUCCESS IN SURGICAL TREATMENT OF FOCAL EPILEPSY*

BY

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In the earliest days of the specialty of neurosurgery, excision of cortex was tried, but soon fell into disrepute, as a method of treating epileptic seizures. Recently, however, the method has slowly returned to respectability, thanks to growing understanding and better methods.

In 1922 I began to make brain wounds experimentally and to study the healing process. In 1927 I operated for the first time (one case) to remove an area of scarred brain, in the hope of curing the patient of his "traumatic epilepsy." That was in the Presbyterian Hospital, New York City. Rumour reached me then that Otfried Foerster was operating on such patients in Breslau. So I spent six months in his clinic in 1928. Here was something better than the useless methods in vogue at the time, covering the scars with various substances. Fortunately for me, his surgical specimens had not yet been studied, and so I set to work to cut microscopical sections of the material he had removed radically from the brain of some 12 sufferers. He allowed me to join him in the publication of those first cases (Foerster and Penfield, 1930a, 1930b). On leaving Germany I made my home in Montreal, and have since spent an increasing amount of time in operating-room and laboratory, working on this problem.

Clinical electroencephalography made its appearance about 1936, after the pioneer observations of Berger, Adrian, and others. This served to enlarge the field, and, slowly by means of medical team-work, a rational system of radical therapy has come into existence, replacing the previous hit-or-miss surgical procedures.

To-day, my associate Theodore Rasmussen and I have splendid help and guidance in electroencephalography

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from Herbert Jasper, in neuroradiology from Donald McRae, and in neurology and medical therapy from Francis McNaughton and many other neurologists.

Brain wounds and tumours now constitute a small proportion of the lesions to be excised. Atrophied convolutions in the cerebral cortex, resulting from a large variety of causes, are more frequent and have proved to be more favourable to success.

The days of "idiopathic" and "cryptogenic" epilepsy are passing and temporal-lobe epilepsy forms the largest single group among what Kinnier Wilson called "the epilepsies."

It is not my purpose to make an accounting of the results of surgical therapy. I have done this, in the past, on three successive occasions for cases from the Montreal Neurological Institute, with follow-up analyses. The last survey was made with the help of Kenneth Paine (Penfield and Paine, 1955) and described the results in 234 cases operated upon during a five-year period. Patients whose seizures were due to brain tumour were not included. In general it may be said that, in that series, the attacks were stopped in 41% of the cases, and the result was regarded as satisfactory in an additional 35%. The case mortality has remained in the vicinity of 1.5% in the total series of 470 patients that have been analysed.

My purpose here is to deal, somewhat at random, with the pitfalls that wait for neurosurgeons in this field. Most neurosurgeons have learned to live dangerously. They seem to like it. But the surgery of atrophic epileptogenic lesions has a special set of hazards that might merit discussion.

1. Adhesions

Contrary to an earlier conception, simple adhesions between dura and arachnoid are not to be considered a cause of seizures unless the cortex has been lacerated so that dural arteries enter the brain, through the adhesions, to anastomose with intracerebral arteries. Nevertheless, it must be our aim to decrease post-operative adhesions as much as possible so that secondary procedures are more easily carried out. Furthermore, the methods of avoiding adhesion formation, so far as one can tell, are also the methods of preventing brain oedema, a condition to which I refer later.

If the surface of the brain is exposed for any length of time it becomes injected, with the rapid appearance of small new vessels, and adhesions will form even if the surface is kept moist with the most perfectly balanced irrigation fluid of the Ringer-Locke variety. To avoid this injection the surface should be covered with an inert impermeable membrane, such as plicofilm, as soon as the dura is turned back, and only exposed as necessary. My own conclusion is that the pia becomes inflamed as the result of an exchange between brain and air that can occur through fluid but not through dura mater or membrane, as though the exchange were gaseous. The obvious injection of the pia disappears within a few minutes after plicofilm is laid upon it, if it has not been present too long.

2. Post-operative Neuroparalytic Oedema

During the first two weeks after operation there are usually local transient disturbances of the brain that reach their maximum during the first five days. These consist of one or more of the following symptoms: headache, contralateral paresis, focal seizures due to neighbourhood discharge, aphasia, etc. The severity of these symptoms depends a good deal on the duration of final operative exposure of cortex. Cortical stimulation and cortical excision, if properly carried out, should produce, of themselves, little reaction in the surrounding brain. This

statement is borne out by the fact that when the dura remains closed, except over the area to be excised, the symptoms may not appear at all unless there is a post-operative blood clot.

In cases of secondary excision, carried out some years after a first excision, there are apt to be troublesome adhesions between the dura and pia-arachnoid. Consequently we have sometimes substituted electrical stimulation of the cortex through the unopened dura for the purposes of localization. The electrocorticogram was also carried out, in part at least, upon the outer surface of the dura. If the dura was then opened only in the area required for the cortical excision, the post-operative course usually proved to be remarkably smooth.

It has been a habit to attribute the paralytic and irritative symptoms to oedema of the brain. But it is probably more accurate to attribute both the symptoms and the oedema to a common cause such as circulatory change in the remaining cortex or to alterations of ganglion-cell chemistry produced directly during the brain exposure.

We may call the change in the brain "neuroparalytic oedema." The paralytic effect is usually most marked in the immediate vicinity of the cortical excision. Thus one may expect transient loss of cortical sensibility in the arm following removal of parietal convolutions just posterior to the post-central gyrus, and paralysis or paresis of the contralateral arm if the excision was located near the pre-central gyrus. When the anterior portion of one temporal lobe is excised there is usually transient weakness of movement of the opposite side of the face.

If the temporal excision is carried out on the dominant hemisphere there may well be aphasia which develops about the second day and continues for two or three weeks. This is no doubt due to exposure of Broca's frontal convolution above the fissure of Sylvius, or of the posterior speech area in the temporal lobe behind the frontier of removal. Since these excisions are carried out under local analgesia it is possible to demonstrate, immediately after excision, that these functional defects have not yet made their appearance.

On the other hand, there may be an irritative effect as well as a paralytic one. I have no idea what the cause of the appearance of these local seizures may be. We call them neighbourhood seizures and expect them perhaps once in five operations. They stop, after some increase in the phenobarbitone administration, in a few days. They sometimes make their appearance just before the paresis, affecting the same area, clears up.

On the other hand, if seizures that are of the same character as before operation persist in this post-operative period, and if the initial phenomenon of these seizures seems to the patient to be the same as the onset of his habitual attacks, the surgeon must assume that he has failed in his attempt. In most such cases it is best to reopen the craniotomy and make further excision with the help of electrocorticography and the safeguard of electrical stimulation. The earlier such a reopening is carried out the easier it is. After the third post-operative week bleeding is apt to be troublesome during the reopening.

3. Aseptic Meningitis

Craniotomies, like other operations, are normally followed by elevation of the patient's temperature for a few days. I will not discuss this reaction.

However, long-continued temperature elevation for a period of weeks means something more, and the surgeon thinks of infection or aseptic meningitis. This latter condition is much more frequent after cortical excision of atrophic lesions in the treatment of focal seizures than it is after craniotomies for other purposes (Finlayson and Penfield, 1941).*

*Aseptic meningitis is rare in brain-tumour surgery unless the ventricle is left open after very large excision, or unless the cisterna magna is widely open in the posterior fossa.

The cause of aseptic meningitis seems to be the entrance into the subarachnoid spaces of a product derived from blood that has clotted in the wound, and particularly if there is communication of fluid to the wound cavities outside the dura. According to the work of Ira Jackson (1949) at the Montreal Neurological Institute, the irritant substance is derived from haematin. He therefore suggested the name "aseptic haemogenic meningitis."

The signs and symptoms of the condition are as follows: headache, stiff neck, high fever usually at a maintained height, but sometimes showing daily drops in the elevation. Lumbar puncture reveals cerebrospinal fluid of amber colour, containing leucocytes, which may be increased to several hundred in the early stages. The pressure of spinal fluid is not greatly raised. The important feature in the identification of aseptic meningitis is that the spinal-fluid pressure is lower than it is in bacterial meningitis. The pressure, with the patient in the horizontal position, rarely rises above 250 mm. of water.

In order to prevent this reactive meningitis it has been my practice, at the time of operation, to close the ventricle if it has been opened. This can be done with two or three sutures of silk, placed in the ependyma, on either side of the opening, and tied very loosely over a square of "gelfoam."

When aseptic meningitis persists for a period of more than two or three weeks it may be wise to reopen the wound and close any fistula that may be present in dura or in ventricular wall. This usually puts an end to this exasperating complication quickly. In the operation of hemispherectomy, which I prefer to call hemicorticectomy, aseptic meningitis is a common complication.

4. The Lesion Left by Excision

If a surgeon who makes a removal were always to leave behind him a new cause of seizures, a new focus of epileptic discharge, the patient would have gained little by passing through this operative ordeal. The method of excision is therefore of great importance.

But first a word about the nature of an epileptogenic lesion: seizures of this type are not produced by scars, tumours, or cysts, nor by anything else that is extracerebral. The lesion that is epileptogenic consists of an abnormal area of living brain. In my experience the focus of discharge is always an area or zone of grey matter that has been altered by some pathological influence. It is seen, on inspection or during removal, to be more or less atrophic. But not all atrophic areas produce seizures; far from it. And therein lies a strange secret. The injured grey matter that is to become the chronic cause of seizures passes through a mysterious "ripening process" that requires months or years (Penfield, 1956).

The surgeon's problem is to remove the convolutions of the cortex without interrupting the circulation of the remaining convolutions. If he succeeds he does not produce a new epileptogenic lesion. The grey matter is thus left covered with pia. The white matter is left uncovered; but seizure discharge does not begin in white matter, and Hughlings Jackson's surmise in this regard has been amply verified. It is our custom to remove convolutions subpially, as first practised by Horsley, and not by cutting out rectangular blocks of tissue.

That the operative wound does not often ripen into a new epileptogenic lesion is borne out by the fact that when our patients are assessed for freedom from seizures in the first, the fifth, or the tenth years after operation, for example, the proportion of patients free of attacks does not decline.

On the other hand, many of our partial failures must be due to the fact that we fail to remove all of the epileptogenic grey matter. Sometimes, of course, complete removal is not possible, owing to multiplicity of foci or because the function of the area to be removed is too precious. More often, no doubt, the fault lies in the surgeon's ignorance or his desire to be done with a long operation. The removal of objectively normal convolutions is therapeutically useless; and craniotomy, when no removal is made, has not been

followed by success (with the exception of one case in 65 negative explorations derived from the total series—Case M.G.).

Herein is to be found the surgeon's major dilemma. He knows full well that he may fall into the pitfall of incomplete removal at any operation. Reliable pre-operative electroencephalographic study will keep him from operating on any patient whose focus of epileptic discharge lies in the brain stem, since conduction of rhythm potentials outward bilaterally along the centrencephalic system produces an easily recognized bilateral electrographic indication of central origin.

The surgeon's guide is, first, the clinical pattern of the seizures; secondly, the gross appearance of the brain; and, thirdly, the electrocorticogram. He usually orients himself by gentle electrical stimulation of cortex, and he may gain added help if he happens to reproduce the initial phenomenon in the patient's habitual seizure. He must discover atrophic tough gyri. They are usually narrow and slightly yellow. The removal of objectively normal gyri is useless, although it may be necessary, on occasion, to reach buried abnormal convolutions.

5. Incomplete Removal

When the surgeon has made his first excision, a second electrocorticogram may show increased activity of "spike" discharges in neighbouring abnormal gyri, and so he removes more, cautiously, with the help of his long-suffering partner the electroencephalographer. At last he may hear the welcome words "all clear, no spikes," and occasionally no slow waves that might point to injury or impaired circulation.

Sometimes the first post-operative electrogram, when off medication two weeks after operation, is nearly normal. Sometimes a patient who has been free of attacks may eventually come to have an electroencephalogram that is completely normal, in spite of, or rather I should say because of, the surgical removal.

6. Hemiplegia due to Interference with Lenticulostriate Arteries

This is a complication that we have encountered only in recent years after developing the surgery of temporal-lobe epilepsy. The anterior temporal lobe may be removed together with the uncus and hippocampal formation with impunity so long as the surgeon keeps the sucker, with which he makes these deep removals, within the pia that covers the mesial surface of the temporal lobe.

However, when further abnormal epileptogenic cortex is found to be present across the fissure of Sylvius (that is to say, within the insula or in the frontal and parietal opercula) removal brings a threat of sudden hemiplegia or hemiparesis. With the paralysis comes complete contralateral hemianopsia instead of the usual upper quadrantic hemianopsia that is apt to be associated with a generous anterior temporal lobectomy.

This is the most unsuspected pitfall of all. It is because I have fallen into it that I thought best to make this report, as a warning to my neurosurgical colleagues. My associate Richard Lende and I have collected and are analysing these cases in preparation for publication.

Our conclusion is that sudden paralysis may occur while grey matter is being removed from beneath the branching middle cerebral artery as it passes upward and outward over the insula and over the superior opercula. It seems most likely that some pulling or handling of the artery may cause occlusion of the perforating vessels that enter the perforated space which is situated just beyond. We have never seen objective evidence of vascular spasm, nor has there been uncontrolled haemorrhage. No ligations were made of these arteries, nor has the removal gone too deep so as to reach the capsule.

The warning is as follows: beware of badly scarred brain when it lies above the fissure of Sylvius; beware as you

approach the anterior perforated space. Some of the eight patients who have had this complication in my hands have recovered almost completely. All but three, or perhaps four, are better off in a general way than before operation. Nevertheless, it is well to recognize that this is the most dangerous of all areas for cortical removal.

In conclusion, this whole field of surgical therapy is opening slowly. The patients who are to be admitted to it are only those whose attacks are not controlled by the best medical therapy. But there are others, too, whose abnormal behaviour seems to depend upon the medication or upon the continuous effect of subictal discharge.

This is a field of therapy for epilepsy in which medical team-work is a prerequisite to success. And I can testify to the fact that there is no other field of medicine in which the gratitude of patients is more profound when success does crown the common effort.

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EPILEPSY AS A SOCIAL PROBLEM*

BY

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Recent years have witnessed dramatic advances in the diagnosis and treatment of the individual epileptic, and these have been vividly presented in the four masterly papers of this symposium. The social aspects of epilepsy are less spectacular than the clinical, and for this reason they have in the past been generally neglected, but interest in them has been initiated or reawakened and developed by the publication of the *Report of the Subcommittee on the Medical Care of Epileptics* (H.M.S.O., 1956), which discusses not only the appropriate arrangements in the National Health Service for the full diagnosis, treatment, and continued medical care of the epileptic, but also how he can play a useful and satisfying part in the community in which he lives, and what provision society now makes, and in the future should make, to enable and encourage the epileptic to lead as normal a personal, family, and social life as possible.

This presents a major problem. The incidence of epilepsy is between 2 and 4 per 1,000 of the population, so that in Great Britain there are between 100,000 and 200,000 epileptics. The label "epilepsy" embraces a wide range of disability, and covers fits varying widely in frequency, severity, and type in different patients and at different times in the same patient.

At one end of the scale is the epileptic with a history of infrequent attacks in the past, now free from attacks or with an occasional fit at long intervals, with or without treatment. In this group no special management is called for except periodic medical supervision and ensuring that the patients do not place their own or the public's lives in jeopardy if a fit occurs, so that, for example, the job of an engine-driver is barred.

At the other end of the scale we have the epileptic with (a) crippling motor disabilities, including paralysis

and involuntary movements, and/or (b) severe mental changes—dementia, depression, hallucinations, confusion, severe behaviour disorders, etc. In both these groups, although treatment must be directed to the accompanying fits, the major problems in management are likely to be those presented by the associated disorders, and in the vast majority of victims these are so severe that no social rehabilitation is possible.

There is one group of epileptics who have too often in the past been regarded as unemployable—namely, those who suffer from frequent daily major fits, often without warning, which appear to resist medical control. Experience shows that a large percentage of these benefit greatly from a full review—physical, psychological, and social, from standardization of treatment under expert supervision in a long-stay hospital, and from team-work in finding suitable employment.

The most pressing task of those who seek to ameliorate the lot of the epileptic is *educational*. The public have long cherished the belief that epilepsy is synonymous with mental deficiency and uncontrollable criminal impulses (a view fostered by some of our colleagues in criminal trials), and the epileptic is thus too often treated as a pariah. If progress is to be made these beliefs must be dispelled. They are the greatest obstacle to rehabilitation. The community must learn that 80% of epileptics (including those whose epilepsy follows a brain operation or injury) can, with appropriate care and encouragement, lead a normal life.

It is perhaps simplest to consider how this is to be achieved by discussing the problems which arise at different stages of life.

The Infant and Child Before School Age

This is the time at which the doctor (helped by the health visitor) can best explain to the parents the nature and implications of the child's attacks, and so restore a balanced outlook. It should be emphasized that not every fit in childhood means lifelong epilepsy: 75% of children who have had fits lose them in adult life. Moreover, even if the epilepsy persists it may not be of serious or crippling import, nor permanently incurable. The parents must not be over-anxious and full of the darkest forebodings, for this is certain to react on the child and make him feel different from other children. Again, parents must not be over-protective. Calculated risks must be accepted, but every precaution should be taken against avoidable accidents. For example, in the home fireguards should be used; sharp-edged and cornered furniture should so far as is possible be avoided; pans on a stove should have their handles pointing inward; teapots should be placed on the centre of the table; tablecloths should not be used or should be fixed.

Another unhappy outcome of the general ignorance and misrepresentation about epilepsy is the sense of guilt which it kindles in the parents, and which unless they are reassured may lead through mutual reproach to domestic strife, which reacts adversely on the child. Among the factors which may be wrongly regarded by the parents as having caused epilepsy in their child are the use of contraceptives and abortifacients, the practice of masturbation in pre-marital life, intercourse after over-indulgence in alcohol, and past venereal infection.

If at this age period there is need for medical care, this is readily available in most areas through the general practitioners and hospitals in the National Health Service. Where poverty or social embarrassment (for example, illegitimacy) renders it necessary that the child should be found a home the children's officer of local health and welfare authorities may be profitably consulted, and in this field voluntary bodies are most active and helpful—for example, the Invalid

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