Chapter 7

SURGERY

Whenever physicians have failed in their drug treatment of patients, they have turned to the surgeon for further help. "Those diseases which medicines do not cure, iron (the Knife) cures; those which iron cannot cure, fire cures, and those which fire cannot cure, are to be reckoned wholly incurable" (Hippocrates). Epilepsy is no exception to this rule, and a wide variety of procedures have been carried out for the relief of seizures in the past. We will limit ourselves here to reviewing only those operations that were directed towards the cranium of the patient, leaving aside such remedies as oophorectomies or cervical sympathectomy and the like.

In August of 1890, Sir Victor Horsley gave a report on surgery of the central nervous system before the Combined Sections of Surgery and Neurology at the International Medical Congress in Berlin. Part of his presentation dealt with surgery for focal epilepsy, and it is of interest to review the state of the art at that time. The most relevant excerpts from his speech are as follows: "The first deliberate operation to relieve a case of focal epilepsy in which no gross lesion was discoverable was performed by myself, and I am therefore naturally anxious that the question of such active interference should be thoroughly tested. Moreover, a most important practical conclusion will indirectly result from a free decision on the point, for I need hardly remind you that by leading to earlier operation it will inevitably secure the discovery of small but gross lesions, of which the existence, from the absence of optic neuritis, etc., may have remained undetected. . . . it is easy to denote the instances in which the operation

should be performed, namely, in all those where an initial spasm of one segment or part of the body can be detected. The foci of the representation of movement of individual segments as they exist in the cortex are now fairly well known, and I have indicated on this photograph of one of Professor Cunningham's beautiful casts the position of these foci, as I have found them in man, from observation of the effects of direct application, for diagnostic purposes, of the electrical excitation of the cortex. This arrangement of the foci, suggested by observation on the orang, and the methods I employ for correctly localising the sulci on the exterior of the head, I shall, with my colleague, Dr. Beevor, describe at the next meeting of this Section. The procedure to be adopted in these cases is, I venture to suggest, as follows: The correct examination of the case, the observation of attacks by trained nurses and attendants, will, in some cases of epilepsy, enable a positive opinion to be expressed regarding the seat of the epileptogenous disturbance. Exploration of this spot should therefore, in my opinion, be undertaken, after a few months' trial with bromides, douches, etc. If no gross lesion is observable when the cortex is exposed, it should be stimulated with the induced current, preferably of a Du Bois-Reymond coil, furnished with one Daniell or chloride of silver cell, and with aseptic electrodes of platinum two millimeters apart. Careful observation will soon show movement of each segment.

"The locality giving rise to the initial spasm should then be excised. Owing to the fact that the focus alone of the representation of one segment is thus removed, only slight and temporary paresis follows.

"This determination for diagnostic purposes of points by electrical excitation was suggested and employed by me in 1883 in a case of encephalocele, but I did not apply it to the purpose of differentiating cortical foci, until 1885. The case I then operated upon (No. 1 in the table), and which I regarded as hopeless, has since improved and developed in a most remarkable way, demonstrating very strikingly the chief point to be noted in all these cases, namely, the immediate and progressive improvement in the mental condition. Of course this observation holds good for all successful operations for epilepsy whether depend-

ent on gross lesions or not, and it is evident, therefore, that from two distinct points of view, the excision of an epileptogenous focus, is beneficial.

"So far few cases have offered themselves as suitable for this line of treatment, but I have tabulated those known to me, and no doubt this list will soon be supplemented.

"Upon the results of this operation as a relief of epilepsy and traumatic epilepsy, which are evidently distinctly favourable considering the hopeless nature of the cases, I wish to add a few words. Personally, I do not think that a final answer can be given on the permanency of the freedom from epilepsy until each case has been observed for about five years, but if the attacks are only mitigated in severity, and not absolutely cured, a notable relief is afforded, of which the improvement in the mental condition is at once the clearest evidence and the most desirable result."

Table 3 of the paper gives the essential information about his cases and is reproduced here as Table 19. We can see the emphasis on electrical stimulation of the cortex, excellent wound healing, and good postoperative results. Looking at the results in more detail, we find that three of the patients were regarded as having had "epilepsy arrested" with follow-up periods of three weeks, six months, and two years respectively. Two patients were regarded as improved as far as their seizures were concerned, and only one continued to have attacks after a brief three months' remission. One-half of the patients were, therefore, regarded as seizure-free and five-sixths as definitely benefited.

Probably as a result of this report by Horsley, the 1890's became a period of rather intense neurosurgical activity and Matthiolius reviewed the literature on surgical treatment of epilepsy in 1899. A number of different neurosurgical procedures had been carried out, among which were simple trephination, splitting of the dura, excision of cerebromeningeal scars, and/or excision of portions of the motor areas which were identified by electrical stimulation. He collected from the literature 221 posttraumatic cases and found that, as a result of these mentioned procedures, forty-nine patients (22.2%) were "cured," forty-one patients (18.5%) were improved, the operations were unsuccessful in 119 patients (53.8%), and there was a mortality of twelve patients

(5.4%). He contrasted this with a group of 110 nontraumatic cases of which fourteen were cured (12.7%), twelve improved (10.9%), the operation was unsuccessful in fifty-six (50.9%), and there was a mortality of twenty-eight patients (25.5%). The difference in the results between these two groups is at least in part attributable to the inclusion of an unknown number of brain tumors in the nontraumatic category. The body of Matthiolius' paper contains a detailed description of four of his own cases and adequate summaries of 160 patients that had been collected from the literature. From these 164 patients, I have selected all those nontumor cases that had been followed for at least one year after operation. Thirty-eight patients met these criteria. Of these, thirteen were reported as "cured" (34%); thirteen were improved (34%), and twelve had derived no appreciable benefit from the operation (31%). Inasmuch as surgeons might have been inclined to report mainly their successful cases rather than their failures, these figures could be favorably biased. They are given here mostly because of historical interest.

In 1910, Clusz reviewed the long-term results of operative treatment of traumatic Jacksonian epilepsy. He collected all cases from the literature that were seizure-free for three years postoperatively. He found twenty-one such cases and stated that this figure is regrettably low when one considers the great number of operations that have been reported for this condition. He felt that a good prognosis could be given to patients who were younger at the time of operation, and in whom overt local changes could be found in the brain at time of surgery. He also felt that it was not necessary to remove cortical brain tissue in order to have a good result, and that postoperative paralysis after excision of brain tissue usually disappeared for the most part soon after operation. Immediate postoperative seizures could disappear subsequently. Occasionally seizures stopped even several months or years after surgery.

Tilmann reported on twenty patients of his own who were operated on for traumatic epilepsy prior to 1910. He found that twelve patients were "cured" (60%), one was improved (5%), four were unchanged (20%), two were still under treatment (10%), and the operative mortality was one (5%). The "cure"

TABLE 19

SIR VICTOR HORSLEY'S TABLE SHOWING SURGICAL RESULTS FOR TREATMENT OF EPILEPSY IN 1890*

Case	*Date of Operation*	*Sex and Age*	*Duration of Disease*	*Nature of Disease*	*Segment or Segments, seat of Initial Spasm*	*Operation*	*Healing of Wound*	*Result*	*Surgeon and Physician*	*Place of Publication*
O.H.	19 x.1886	M. 10	4 yrs.	Severe generalized fits, principally nocturnal, uncontrollable and destructive	Left angle of mouth (frequently bilateral)	Exposure of facial area in R hemisphere. Determination by excitation. Excision of focus	Immediate union	Diminution of fits. Perfect mental recovery. Education complete vii, 1890	Horsley Ferrier	*Journal, 23,* iv, 1887
W.B.	30 v.1888	M. 20	7 yrs.	Severe generalized fits. Morose and despondent	Left fingers and wrist	Exposure of upper limb area in R hemisphere. Determination by excitation. Excision of focus	Immediate union	Diminution in number and severity of attacks. Improvement in mental condition	Keen	*International Journal of Medical Science, xi,* 1888.
C.R.	4 x.1888	M. 27	18 yrs.	Severe right-sided fits, becoming generalized	Thumb	Exploration of Left hemisphere. Determination of thumb focus. Excision of same	Immediate union, delayed a little by accumulation of wound secretion	Arrest of the epilepsy. Report ceased three weeks after operation	Nancrede	*Medical News, 24, xi,* 1888, *p.* 586.

J.G.	12 vi.1888	M. 35	14 yrs.	Severe generalized fits	Left fingers and wrist	Exposure of upper limb area in R hemisphere. Determination by excitation. Excision of focus	Primary union delayed	Arrest of epilepsy	Deaver Lloyd	*International Journal of Medical Science, xi,* 1888, p. 477.
R.L.	23 i.1890	M. 39	17 yrs.	(a) Severe generalized fits. (b) Attacks of petit mal	Left Shoulder (when first seen)	Exploration of cortex, slight evidence of fibroid change in arachnoid. Determination of shoulder and other upper limb foci by excitation. Excision of shoulder focus	Immediate union	Marked mental improvement. Temporary arrest of the severe fits. Return of epilepsy as before three months later	Crichton-Browne Horsley	Unpublished
G.C.	16 i.1890	M. 41	25 yrs.	Generalized fits. No petit mal	Fingers and wrist	Exploration. Exposure of genu of fissure of Rolando. Dura little adherent. Cortex yellowish. Removal of fingers and wrist foci	Immediate union	Complete arrest of the epilepsy, vii, 1890	Horsley Jackson	Unpublished

*Printed with permission from the *British Medical Journal:* "Remarks on the Surgery of the Central Nervous System" by Sir Victor Horsley, which appeared in the British Medical Journal, 1890, Vol. 2, 1286–1292.

had lasted, in four cases, more than three years; in three, more than two years; in three, more than one year, and in two, more than one-half year.

Pussep, who reviewed in 1922 twenty years of experience with surgical treatment of epilepsy, was markedly less impressed. His material is of special interest because it covers 318 patients who had been operated upon by Pussep himself. Forty-nine patients had idiopathic epilepsy; twenty-eight had generalized posttraumatic epilepsy by history, but no objective evidence of trauma was found at time of operation; forty-six had generalized posttraumatic epilepsy and objective evidence of trauma; forty-three had focal posttraumatic epilepsy; ninety-seven had generalized epilepsy with focal onset; twenty-three had Jacksonian seizures; thirteen had generalized epilepsy associated with inflammatory or degenerative disease (postencephalitis, meningitis, multiple sclerosis), and nineteen had generalized epilepsy and associated dementia. The operative procedure consisted in general of trephination, removal of bone and dura, and placement of a Kocher valve. In cases of focal seizures, the responsible area of cortex was in addition excised. Whenever larger areas of cortex were removed, a layer of adipose tissue was inserted to avoid the development of adhesions. All patients had been treated preoperatively for several years with bromides. Only when this method was unsuccessful and the patients had more than two severe seizures per week was an operation considered. Postoperatively, bromide therapy was reinstituted, and it was repeatedly found that the dosage could be reduced by a considerable extent. He regarded as "definitive cure" freedom from seizures for more than five years. This occurred in thirteen patients (4%); in twenty-nine cases (14%) seizures recurred after three years, and seventy-one patients (28%) were seizure-free for one year. If one were to use arrest of seizures for at least one year as a criterion in regard to the success of the operation (which is still frequently done in today's studies), one finds that 113 of Pussep's cases qualified. This represents 35 per cent of the total group and is therefore essentially the same as the rate calculated on basis of Matthiolius' figures from the literature. It is likely, therefore, that Matthiolius' figures are not as biased as one might have assumed,

but were representative of the results obtained around the turn of the century and no change in surgical technique had occurred within the subsequent two decades. Improvement, but not cessation of seizures, had occurred in 106 (33%) of Pussep's patients and ninety-six patients were unchanged (30%). Once again these are the same results as obtained through Matthiolius' literature review. Pussep's mortality rate was 0.9 per cent. He was not impressed with the success of his efforts, and concluded that the surgical results were as unsatisfactory as those with medical treatment. The reason for his disappointment lay in the observation that short-term success frequently vanished if one had the opportunity to follow the patient long enough. Looking at the variety of his patients operated upon, it is not too surprising that long-term remissions occurred only infrequently. It would have been interesting to see a comparison of remission rates among the patients who had clearly focal, questionably focal, and clearly non-focal seizures, but this was not done in his paper.

Penfield and Jasper's surgical results up to 1949 are listed in Table 20. The figures were obtained by combining Tables XVIII-1 and XVIII-2 of their book *Epilepsy and the Functional Anatomy of the Human Brain* (1954). Follow-up duration varied usually between one to seven, or ten years. Craniotomy without excision did not lead to major improvement in the patient's condition. Complete freedom from attacks was accomplished in one-fifth to one-quarter of all patients.

The 1940's brought a major change in operative technique. The electroencephalograph had become standard equipment in the workup of epileptic patients, and the finding that a number of patients had focal spike or sharp wave activity suggested that these abnormalities serve as a trigger for the patient's seizures. It was hoped that removal of this area of electrical abnormality could therefore lead to complete seizure cessation. EEG machines were introduced into the operating room, and the focus of seizure activity was delineated further by direct recordings from the brain, in the resting state as well as after stimulation with electricity or drugs. The most important change in thinking that resulted from this advance in technique was the observation that seizures which had been regarded as "petit mal" in the adult

TABLE 20

SURGICAL RESULTS AT MONTREAL NEUROLOGICAL INSTITUTE UP TO 1949 ACCORDING TO PENFIELD AND JASPER, 1954*

	Complete Freedom From Attacks (%)	*75% Improved or Better* (%)	*50% Improved* (%)	*Slight Improvement* (%)	*No Change* (%)	*Worse* (%)	*No. of Patients Involved in Study*
1929–1939 Series:							
Meningocerebral Cicatrix Excision	22.5	22.5	32	10	11	2	62
Cerebral Cicatrix Excision	19	21	19	9	30	2	53
1939–1944 Series:							
Cortical Excision	25.3	30.5	13.6	12	18.6	0	59
Craniotomy Without Excision	0	0	32	14	54	0	16

**Epilepsy and the Functional Anatomy of the Human Brain* by Wilder Penfield and Herbert Jasper. Published by Little, Brown and Company, Boston, 1954.

or "epileptic equivalents" frequently originated in the anterior portions of one temporal lobe. These structures can be removed unilaterally without producing a serious neurological deficit, and a new field for surgery was opened by this technological advance.

Before discussing the results of temporal lobectomies, one should mention Russell Meyers' (1954) critical review of the concepts underlying surgery for focal epilepsy. Electroencephalography had been used extensively to delineate the epileptogenic focus at time of surgery, and his series of eighty-one patients could be taken as representative in regard to the progress that had been achieved in the thirty years after Pussep. Although Meyers made no reference to Pussep's paper, the entire tone of his report is quite similar. His insistence on adequate length of follow-up ("The follow-up period should appreciably exceed the longest known preoperative remission.") and his emphasis on providing clear criteria which would allow classifying a patient as "seizure free," "improved," et cetera has led him to conclude that ". . . one cannot but be disappointed in the results." Actually his results were better than Pussep's. With a follow-up of at least five years, nine patients (11.1%) were seizure-free; nineteen (23.5%) improved, and forty-three (53%) were unimproved. Ten had died (12.3%); five of these were operative mortality and five had died subsequent to discharge from the hospital. The percentage of cases remaining seizure-free for five years had increased from Pussep's 4 per cent to 11 per cent by 1954. Meyers' results would in all probability have looked much better had he not insisted on admirably strict follow-up criteria. A patient was regarded ". . . as 'seizure free' only if followed for five or more years, at least the last three of which have been without benefit of anticonvulsant medication. Similarly, cases have been designated as 'improved' only if after five or more years the reported frequency of seizures has been *less than half* of that experienced preoperatively. Due allowance was made in each case for the duration of periods of 'spontaneous' remission recorded in the preoperative protocols. In addition, to be classified as 'improved' a patient must have either discontinued all drugs or remained on an anticonvulsant regimen *equivalent to or quantitatively less than* that of the preoperative period of observa-

tion." Meyers, just as Pussep and Horsley, insisted on a follow-up of at least five years or longer before a patient could be called seizure-free, but this is not usually the case with other reports in the literature. Although Meyers' paper was very clearly written and contained a number of specific suggestions, it does not seem to have made an appreciable impact in regard to the way follow-up results are reported.

This becomes obvious when one examines the steady stream of publications that deal with results of surgery for temporal lobe seizures. Follow-up periods are usually less than five years. Frequently, no statements are made of how follow-up was achieved (i.e., by letter or by personal examination), and in some instances one could even wonder about such a clear criterion, namely, "freedom from seizures." There should obviously be no doubt about the meaning of this term, but one can find in relatively recent reports such statements as this: "Sensory auras without motor component or disturbance of consciousness were not considered attacks for purposes of these follow-up analyses" (Rasmussen and Jasper, 1958), or "Some of these patients reported an occasional aura and/or rare momentary lapses of memory, so fleeting that they remained unnoticed by others in the patient's company, and occurring at most four to five times during the year." (Simmel and Counts, 1958). While these patients are undoubtedly markedly improved in regard to their preoperative state, it is not quite clear whether they should be placed in a "completely seizure-free" group. I am mentioning this merely because such different criteria could make comparisons between statistics of various authors somewhat difficult. Table 21 gives a general impression about some of the results that have been reported in regard to freedom from seizures after temporal lobe surgery.

Whenever Penfield and Steelman's (1947) classification was used by various authors, groups four and three were combined, because this seemed to be the general practice, and the figures reported from Montreal are then more closely similar to those of other authors reporting "seizure freedom." This is, of course, considerably different from Meyers' stringent criteria and the results reported in the table are bound to be inflated for this

reason. In evaluating the figures shown in Table 21, we should also remember that the time listed under length of follow-up is not necessarily synonymous with length of time for which the patients have been seizure-free. The progress report of Bailey *et al.*, published in 1953, is not included in the table because the presentation of the material did not lend itself to this type of tabulation. In general, we can see that seizure freedom for varying periods of time has been reported for 11 to 58 per cent of patients undergoing anterior temporal lobectomy. It is clear that

TABLE 21

RESULTS OF SURGERY FOR TEMPORAL LOBE EPILEPSY
(COMPLETE FREEDOM FROM SEIZURES)

	Length of Follow-up	*Percentages of Patients Remitted*	*Number of Patients Involved in Studies*
Penfield and Flanigin, 1950	1 year to 10 years	52.9	51
Bailey and Gibbs, 1951	6 to 40 months	48	25
Green *et al.*, 1951	6 to 30 months	52	23
Guillaume *et al.*, 1953	6 months to 4 years	57	110
Petit-Dutaillis *et al.*, 1953	More than 6 months	56	16
Woringer *et al.*, 1955	5 months to 2½ years	50	22
Penfield and Paine, 1955	1 to 7 years	45	203
Picaza and Gumá, 1956	8 to 48 months	58	34
Morris, 1956	4 to 9 years	41.7	36
Gibbs *et al.*, 1958	At least 1 year	35	63
Ajmone-Marsan and Baldwin, 1958	8 months to more than 3 years	38	50
Falconer *et al.*, 1958	1 to 6 years	50	50
Paillas, 1958	1 to 9 years	40	50
Simmel and Counts, 1958	5 years	27	40
Green *et al.*, 1958	17 months to 8½ years	40	38
Northfield, 1958	3 months to 5 years "good results"	40	30
Fenyes *et al.*, 1961	2 to 5 years	23	34
Feuersten *et al.*, 1961	2 to 8 years	32	28
Rasmussen and Branch, 1962	1 to 25 years	43	389
Falconer and Serafetinides, 1963	2 to 10 years	53	100
Green and Scheetz, 1964	2 to 15 years	11.7	60

with such a wide range of results, different criteria must have been applied by various authors in regard to "seizure freedom."

In order to overcome the problem of varying lengths of follow-up, I have selected from the literature the cases which had been followed for at least five years and have tabulated them in regard to freedom from seizures. This is shown in Table 22. We find a rather respectable remission rate of 41 per cent. This is even more impressive when one considers that for the most part patients were selected for operation only after they had proven refractory to drug treatment. In contrast to medical treatment, the surgical results of temporal lobectomies do not seem to deteriorate markedly with the passage of time.

TABLE 22

RESULTS OF TEMPORAL LOBECTOMIES WHEN ONLY PATIENTS ARE CONSIDERED WHO HAD BEEN FOLLOWED FOR AT LEAST FIVE YEARS

	Number of Patients Seizure Free	*Number of Patients Operated upon*
Paillas, 1958	10	26
Rasmussen and Jasper, 1958	21	57
Fenyes *et al.*, 1961	2	12
Fegersten *et al.*, 1961	1	5
Northfield, 1958	1	1
Falconer and Serafetinides, 1963	28	52
Total	63	153

Percentage of patients seizure free who had been followed for at least five years, 41.1%.

Rasmussen and Branch (1962) stated: "Two-thirds of the patients who did not have attacks during the first year after operation remained seizure-free during the subsequent follow-up period. Two-thirds of the remainder have had only rare attacks separated by long intervals. Thus, at the end of a seizure-free first year after operation, a patient has about a 90 per cent chance of achieving a good result as far as the long-range prognosis is concerned.

"Three-fourths of the patients who did not have attacks during the first two years after operation remained seizure-free subsequently, and three-fourths of the remainder have had only rare

attacks separated by long intervals. Thus, a patient who is seizure-free at the end of the second year after operation has a 95 per cent chance of achieving a good long-term result. By the end of the third or fourth postoperative year, most of these patients discontinued all anticonvulsant medication. Some continue to take small doses because of persistence of occasional faint warnings of an attack or because some persistent electroencephalographic abnormality indicates that there is a small residual seizure tendency and that continuation of some anticonvulsant medication seems a worthwhile precaution."

The review of the literature showed that complications are generally regarded as rather rare, and mortality ranges from zero to 1.6 per cent (Rasmussen and Branch). These figures are representative for the rest of the literature.

The criteria which are applied to make a patient eligible for surgery vary somewhat among different centers. In general, patients are considered for operation if they have psychomotor seizures which have proven refractory to medical treatment, and if the EEG shows on serial tracings a persistent clear-cut focus of spike or sharp wave activity in one temporal area. Some surgeons will also operate if there are bilateral EEG abnormalities present, and on occasion, patients will be operated upon even if the seizures are not a major handicap but if their behavior is of such a nature as to render them a burden to themselves and/or society.

Having demonstrated that anterior temporal lobectomy can indeed be very useful, it would seem that there should be a considerable number of the total epileptic population who would be eligible for this type of treatment. Unfortunately, this does not appear to be the case. Green and Scheetz (1964) had by 1961 operated on seventy-eight patients, "From a total in excess of 2,500 patients who were examined because of epilepsy at the Arizona State Hospital, Seizure Clinic of St. Joseph's Hospital, and on the private service as inpatients or outpatients. . . ." Only 3.1 per cent of all epileptics had, therefore, become eligible for temporal lobe surgery in a center where there was a great deal of interest in this type of procedure. Woringer *et al.* (1955) had selected twenty-two patients out of 1,300 epileptics for operations

(1.6%). At the Montreal Neurological Institute, which probably has the largest series of temporal lobectomies in the world, 389 patients were operated on for temporal lobe epilepsy between 1928 and 1960 (Rasmussen and Branch).

The reason for these relatively small numbers lies in the fact that the great majority of patients with psychomotor seizures have bilateral EEG abnormalities. The assumption underlying temporal lobe surgery is, of course, that there exists one focus of pathological cerebral activity which may be removed either in totality or at least to a major extent.

Some patients who have bilateral foci have, however, been operated upon, and on general grounds, it would seem that patients who did have bilateral disturbances would do worse after operation than those who had a clear unilateral focus. Jasper *et al.* (1951) found, indeed, that when the EEG abnormality was unilateral, 67 per cent of the patients fell into the "success" group, which is a combination of Penfield and Steelman's groups three and four; but ". . . when there seemed to be a shifting focus, excision resulted in placing only 21 per cent of the cases in the success groups." By 1960 the Montreal group reported of the bitemporal group: ". . . complete or nearly complete relief of seizures in 24 per cent; whereas in patients with unilateral temporal EEG abnormality two patients out of three received similar benefit" (Bloom *et al.*, 1959/1960). Similar opinions about better results in clearly unilateral cases were expressed by Bailey *et al.;* Picaza and Gumá (1956); Gibbs *et al.* (1958); Falconer *et al.* (1958); Paillas (1958); and Falconer and Serafetinides (1963). There are, however, some dissenting voices. Ajmone-Marsan and Baldwin (1958) felt that patients with bilateral abnormalities did no worse than unilateral cases; but it should, of course, be remembered that although the patients had bilateral EEG abnormalities, one side was consistently more active, otherwise the patient would not have been operated on at all.

Fenyes *et al.* (1961) found likewise: "The preoperative EEG cannot be relied upon in forecasting the outcome of surgery . . ." They felt also that "The good results produced by surgery are not always reflected truly by the postoperative EEG tracings,

either. The same applies to the bad results. For this reason, in judging the postoperative condition of the patient both the EEG and the clinical data should be taken in account.

"From all this it follows that the EEG pattern suggesting poor prognosis does not necessarily represent a contraindication to surgery for temporal epilepsy. In a considerable percentage of such cases, good, or even excellent, results may be achieved by operation."

Jasper *et al.* (1961), dealing with a larger case material, also noted that the postoperative EEG did not always reflect the final outcome, but it tended to do so in the majority of seventy-one cases. The EEG prognosis was regarded as quite satisfactory in at least two out of three cases, and was not extremely in error in any case.

At present there seem to be no reliable preoperative criteria which will allow the physician to give an accurate prognosis in regard to the likelihood of rendering the patient seizure-free by operation. Denis Hill suggested in 1958 that a good outcome can be expected in the presence of (1) mesial temporal sclerosis as evidenced by reduced barbiturate fast activity beneath the temporal lobe; (2) unilateral sphenoidal spike focus; (3) normal or aggressive personality, and (4) concordance of EEG, clinical, pneumoencephalographic, and psychological data. The paper by Kennedy and Denis Hill (1958) gives a detailed report on the relationship between good surgical results and reduced barbiturate fast activity from recordings between the sphenoidal electrode and the ipsilateral ear. Fergersten *et al.* (1961) found that patients with a good outcome had (1) an onset of seizures after fifteen years of age; (2) a mid- to anterior temporal spike focus, and (3) few and mild psychic symptoms. They did not have (1) bilateral cerebral atrophy; (2) generalized dysrhythmia in the electroencephalogram, or (3) etiological evidence of diffuse cerebral damage. In general, it is felt that patients who are found at operation to have a small discrete lesion tend to have a better prognosis than when the removed tissue appears normal histologically (Paillas; Green and Scheetz; Falconer and Serafetinides). The guidelines suggest, therefore, that a good outcome can be expected when there is a small but definite lesion

that can be removed surgically. If there is a suspicion that more than one area of the brain has potential epileptogenic properties, the prognosis becomes more doubtful.

Apart from temporal lobectomies, one should mention some other neurosurgical procedures that have been carried out in the hope of rendering patients seizure-fee. Turner (1963) tried unilateral or bilateral temporal lobotomies (cutting tracts in the temporal lobes rather than removing tissue) in thirty-eight patients. Reduction of grand mal and psychomotor seizures was noted and the psychiatric state of the patients was usually improved. The symptoms of aggression and bad temper were most benefited; paranoid ideation responded the least. The work record of the patients was unsatisfactory after operation. Those who had been unemployed remained unemployed. Patients who had been employed preoperatively tended to gravitate towards less arduous work. It was emphasized that the operation can be performed either unilaterally or bilaterally without producing demonstrable intellectual deficit.

Rasmussen (1963), reviewing the results of frontal lobe excisions, found that 250 patients had been operated on during the years 1929 to 1960 at the Montreal Neurological Institute. Of 183 patients with nonneoplastic lesions, 168 were available for follow-up. The duration of follow-up ranged from one to thirty-one years with a median period of eight years. Twenty-seven patients had had no attacks since discharge from the hospital (16%); another twenty-eight patients had had a few attacks in the early postoperative months or years, but became seizure-free subsequently (17%); fifty-three patients showed a marked reduction in seizure tendency (30%); and sixty patients had an unsatisfactory result (36%). These results are therefore not quite as good as those for temporal lobectomies. Rasmussen also made the point that it has become apparent that "Discrete and restricted epileptogenic foci seem to be rare and most patients exhibit larger epileptogenic areas with varying thresholds of epileptogenicity . . .". This is in keeping with the opinion in 1958 expressed by Gibbs *et al.*: "Both electrocorticography and nonoperative electroencephalography show that severe epileptic disorders are usually associated with widespread seizure activity,

which is not confined to a single cortical area, but involves numerous cortical areas and may involve an entire system or more than one system. Thus, the disease is not punctuate but, like an infectious process, is diffuse or systemic. The surgeon is faced with the difficult task of removing large parts of the brain in order to eliminate the areas of present and potential primary discharge."

Meyers had expressed the problem, in 1954, by saying: "The above observations suggest one of two alternatives: either recurring spikes at a particular region do not in themselves constitute a reliable index of the site from which seizures are initiated, in which case excision of the region is obviously pointless; or they constitute reliable indicators, in which case multiple foci rather than a single focus must be supposed to exist in cortical and subcortical structures. The technical problem of excising all such 'points' would appear to be a rather formidable task. An impressive body of evidence is gradually accumulating to indicate the role played by brain structures other than the cortex in initiating certain grand and petit mal seizures and to suggest that multiple foci—or what appear to be such—are more frequently at play than has generally been supposed." This sentence brings to mind the statement by Pussep that only when the illness has lasted no more than a year can one expect a complete cure. The prognosis becomes less favorable with a longer duration. A longer illness apparently produces special changes in the brain which lead to an increase in its irritability. If one were to exchange the words "increased irritability" with "multiple foci of epileptogenic activity," we would be using the language of the 1960's.

Among other procedures which should be mentioned are pallidotomy, pallidoamygdalotomy, and pallidoansotomy, which have been performed mostly by Spiegel *et al.* (1958). Twelve patients were involved; follow-up ranged from six months to three years; seizures were controlled or markedly diminished in frequency in seven of the patients (53.8%). This procedure is still in its experimental stage. The same applies to splitting of the corpus callosum, and only isolated patients have been subjected to this procedure.

In children with severe intractable seizures, hemiplegia, mental retardation, and associated behavior problems, removal of the entire hemisphere has been carried out on occasion. French *et al.* (1961) reported on eight such cases that were followed for six to ten years. Seven had excellent results in regard to seizure improvement. Goldensohn *et al.* (1961) reported on eleven patients and seizures were abolished in six. Other reports give similar good results: Cobb and Pampiglione (1953); Obrador and Larramendi (1953); Ransohoff and Carter (1954); Goodall (1957); Matera and Castro (1963), and Rasmussen. Wylie McKissock had performed, by the time of this writing, over sixty hemispherectomies at The National Hospital, Queen Square, London. The long-term results so far have not been published, but he indicated in a personal communication: ". . . there are quite a number of patients who lead reasonable lives and some of whom are working." If one considers the severity of the basic disorder and the magnitude of the operation, it is remarkable that some patients are able to function in the community when otherwise they would probably be inmates of a state hospital. The procedure is obviously applicable only to a small number of patients who have a nonfunctioning hemisphere to start out with; but it seems that a considerable proportion of these patients can be significantly improved in regard to behavior, as well as seizures, through this operation.

What can therefore be concluded about the results of surgical treatment as they have been presented in the literature? The main points may be summarized as follows:

1. If a structural lesion—either gross or microscopic—can be identified and removed, the patient can expect a good outcome.
2. A number of patients with temporal lobe epilepsy have structural lesions which are discovered only as a result of temporal lobectomies and could not be suspected on clinical grounds.
3. Operative results for temporal lobe epilepsy seem to be definitely superior to medical treatment.

4. Results appear to be somewhat poorer when one deals with epileptogenic foci in other parts of the brain, unless a structural lesion can be demonstrated.

5. Hemispherectomy appears to be of value in certain patients with infantile hemiplegia, intractable convulsive seizures, and behavior disturbances; but more long-term follow-up studies about the postoperative social adjustment would be of interest.

6. The vast majority of epileptic patients do not have single removable lesions, but seem to suffer from a more diffuse process. Operative intervention can therefore be expected to benefit only a small segment of the total group.

7. Reporting of surgical results could be improved. Instead of giving ranges or average duration of follow-up, it would be advisable to have statements about actual length of complete freedom from seizures prior to last examination.

8. In evaluating the final results of surgery, it would be helpful if patients were reexamined by a physician and had a repeat EEG evaluation five years after the operation. Follow-up studies conducted through the mail or by telephone may give a higher success rate than might be warranted by the facts.

Chapter 8

INTELLIGENCE

A review of the literature up to 1900 is included in Turner's book, and up to 1960 in the book by Lennox. The proportion of epileptic patients who were mentally afflicted was reported at the turn of the century to be between a high of 87 per cent and a low of 47 per cent, depending on different studies, and whether or not institutionalized patients were examined. These figures include all degrees of mental abnormality. If one limits oneself to marked dementia, one finds figures ranging between 14 and 22 per cent. If one takes ability to work as a criterion, one finds inability to do any kind of work, even under supervision, in approximately 50 per cent of cases at the turn of the century. It should be emphasized again that most of the figures reported come from studies carried out in institutions. Turner tried to establish some criteria that could be related to mental deterioration. In order to do this he grouped cases reported in the literature into four classes, depending upon the intensity of mental impairment, and related these to sex, heredity, duration of the illness, age of the patient at onset of the disease, character, type and combination of seizures, frequency of seizures, facies epileptica, and stigmata of degeneration. Turner's four classes were as follows:

> Class A. In this division are included all those epileptic individuals in whom no mental impairment can be detected. They may be regarded as differing in no way from normal persons in the same social sphere and with similar educational advantages. The memory is good; they are bright, active, and intelligent, and are capable of

earning their own living; only in rare instances do they show the epileptic face. Their physical condition is good, and for all practical purposes may be regarded as normal.

Class B. This class, to which the majority of epileptics belong, includes those who exhibit the first degree of mental enfeeblement, which is characterised mainly by some defect of memory, more especially a forgetfulness of recent events. In other respects their mental condition is good; they have fair intelligence and capacity for work. They are able to earn their living and to attend to their several duties. Their physical condition varies. A considerable proportion show the epileptic face.

In Class C are found those cases which present the second degree of mental impairment. In addition to an impaired memory, there is defective power of initiation and capacity for work, which, however, may be well done under direction and supervision. They are slow in comprehension, and are often lazy. Many of them are irritable, eccentric, and passionate. About 50 per cent show the epileptic face.

Class D contains those who show the third or most pronounced degree of dementia. They present the typical features of epileptic dementia, *viz.*, a defective memory, confusion of ideas, poor capacity for work even under direction, absence of initiative, and a slow and dull comprehension. Although not legally insane, they require supervision. Their physical condition is as a rule good, they eat heartily and sleep well. The majority have the epileptic face.

Table 22 of Turner's book is reproduced as Table 23. It gives the percentages of males and females in the various mental classes that were observed in a colony for epileptics. It can be seen that approximately 14 per cent were regarded as mentally normal and 29 per cent as markedly demented. It deserves to be emphasized that marked dementia was therefore not the rule, even in an institutional setting at that time. Turner commented also: "It should, however, be pointed out that the above percentages do not faithfully depict the mental state of epileptics

TABLE 23

TOTAL NUMBER OF MALES AND FEMALES WITH THEIR PERCENTAGE FREQUENCY IN THE FOUR SUBDIVISIONS OF MENTAL FAILURE, FROM 161 CASES OF EPILEPSY AT THE CHALFONT COLONY, TURNER, 1907*

Mental Class	*Males*	*Females*	*Total*	*Percentages*
A	9 (8.8%)	13 (22.0%)	22	13.6
B	35 (34.3%)	16 (27.2%)	51	31.6
C	29 (28.4%)	12 (20.3%)	41	25.4
D	29 (28.4%)	18 (30.5%)	47	29.1
Totals	102	59	161	99.7

*From *Epilepsy—A Study of the Idiopathic Disease* by William A. Turner. The Macmillan Company, New York, 1907.

in general, as it is obvious that those cases which seek treatment at a colony for epileptics do so on account of some mental disability which prevents their earning a living under ordinary conditions."

In regard to heredity he concluded that ". . . a family tendency to either epilepsy or insanity, although offering no obstacle to the arrest of the seizures in favourable cases, materially increases the probability of the disease becoming confirmed and the supervention of dementia."

His conclusions in regard to the other variables are as follows: ". . . although the duration of epilepsy from the commencement of the seizures is a potent factor in determining the subsequent mental condition, it is not the only influence in the production of dementia.

". . . under five years' duration there is a considerably greater percentage of cases with no mental impairment, or merely some interference with the memory than of those with well-marked mental deficiency . . . if the convulsions have lasted over ten or eleven years only a trifling percentage are found in Class A, the majority showing the mental characteristics of Classes C and D. It should, however, be especially pointed out that in a very few cases the disease may have lasted for periods of thirty or more years without any obvious mental impairment."

In regard to age at time of onset of the illness: "Those epileptics in whom the disease commences in early childhood show

only a small percentage with normal mental health and a high percentage with profound mental impairment.

"From the first quinquennial period onwards the percentage of cases showing no obvious mental deficiency progressively increases, until in the fourth quinquennium (16 to 20 years) a greater percentage is found with normal mental health than with marked mental disability." He concluded that: ". . . epilepsy commencing in infancy and childhood is least favourable for arrest of the fits and most favourable for the production of confirmed cases. It is also found that the common type of epilepsy—that commencing during the period of puberty—is most suitable for arrest of the seizures and least likely to be associated with mental infirmity."

In regard to type of seizures, he stated that "(a) Mental deterioration is found in association with both types of seizure" (i.e. major as well as minor), "but is less frequent in those cases in which the major fit is the main expression of the disease; (b) freedom from mental impairment is also found in both types, but to a small extent only in those cases characterised by the minor fit, whether alone or in conjunction with the major fit; (c) the mind is more frequently affected to a slight extent in those cases in which the minor seizures occur alone; (d) the mind attains its most universal and profound impairment when the disease is manifested by a combination of the major and minor attacks."

In regard to frequency of seizures, he reported: ". . . a definite relation between the frequency of the seizures and the mental state, to such an extent that when the fits are of very frequent recurrence (daily) none of the patients was without obvious mental impairment, over 50 per cent of them exhibiting the deepest degree of dementia. On the other hand, if the seizures are so infrequent as to be counted by the quarter or the year, over 50 per cent were found to be mentally normal, or merely with defect of memory. Between these extremes there are various gradations, so that the general statement may be made that there is a direct relationship between the frequency of the seizures and the degree of mental impairment—the more frequent the attacks the more common and profound the associated dementia." He

emphasized subsequently that patients whose seizures occur in series have an especially poor prognosis in regard to mentality. A few of his patients (7.6%) whose seizures tended to occur in series were found in Class A and 46.1 per cent in Class D, but these percentages were obtained on a sample of thirteen patients only. He also noted: ". . . that even when the fits are arrested, there is not necessarily an unimpaired mental state." Some of his patients (16.6%) were found in Class D and 50 per cent in Class A, but the sample was limited to six patients in this instance.

The term "facies epileptica" is no longer in use, but Turner commented as follows: "The close relation which exists between mental disability and facial expression is nowhere more readily seen, and studied, than in cases of confirmed epilepsy. So characteristic indeed is the facial appearance of many epileptics that the term 'facies epileptica' has been applied to it. Although difficult to define, it is readily discerned by those who are in the habit of treating large numbers of epileptics. It may, in general terms, be described as an expression of dullness and heaviness, with an absence of emotional mobility of the features. It differs from that of the ordinary dement by a particular expression, which stamps the individual as an epileptic. . . . Its presence was noted in those with mental integrity as well as in those showing the several degrees of dementia; but its percentage frequency showed a progressive accession as the degrees of dementia increased, so much so that amongst the most demented, 72.3 per cent showed the characteristic expression. It is more frequently seen in male than in female epileptics, for of the seventy-three cases only nineteen were women."

In regard to stigmata of degeneration, which were not defined further, he found that out of nine patients in Class A only two had stigmata, while out of twenty-nine patients in Class D, stigmata were found in twenty-seven. He concluded ". . . the more pronounced the mental enfeeblement, the more frequent the evidence of structural degeneration."

Muskens (1928) stated his views as follows: "Each new case of epilepsy coming under the care of a physician should be considered from the standpoint of the patient's inherent men-

tality. Is he a case where the mental endowment is such that he can collaborate with the physician in his own treatment, or is he too poorly endowed mentally? Where the patient belongs to the first group where the mental endowment is good, the prognosis is certainly hopeful. . . . The question may be asked, Does psychical deterioration form an inseparable part of the malady? . . . The answer to such a question is that mental deterioration may form a part of epilepsy in the same way that infectious processes and furunculosis may be symptoms in a case of diabetes. There is no necessity for psychical deterioration to be a symptom in epilepsy except under special circumstances. Where the patient starts life poorly endowed mentally, probably there may be a history of hereditary mental disease; or where severe encephalitis has occurred early in life, mental or psychical deterioration is almost certain to be a prominent symptom in the disease. Where, on the other hand, the patient starts with good mental endowment, then, in my opinion, any psychical deterioration is due to the fits. This point is of great importance, and I would emphasize my opinion that there is no need for any intelligent patient suffering from epilepsy to develop psychical deterioration if he in the beginning is properly treated and the malady be arrested. Where, however, the treatment is neglected or inadequate, the psychical changes inevitably follow." Muskens provided no figures of his own to support his views.

Turner's findings are actually of greater value because they can be compared with reports published in the 1960's. Lorgé (1964), whose paper has already been mentioned in a previous chapter, gives quite explicit figures. Out of 142 patients who had been seen either as outpatients or inpatients at a Swiss institution for epileptics, 48.5 per cent were found mentally normal at time of follow-up, while 25.4 per cent had shown symptoms of dementia. When the material was subdivided into outpatients and inpatients, it was found that 77 per cent of the outpatient population were mentally normal and 11.3 per cent were demented, while only 27.6 per cent of inpatients were mentally normal and 37.6 per cent had shown dementia. There has been, therefore, no appreciable change in regard to the presence of dementia in patients with epilepsy during the past half century. Lorgé noted

also a relationship between arrest of seizures and mentality. The vast majority of patients whose seizures were arrested showed no mental changes, but in some instances dementia did occur in spite of the fact that the seizures were controlled. He concluded that mental changes are more rare, but by no means impossible, in patients who respond to therapy; while they are more frequent, but by no means the rule, in patients who do not respond to treatment. Mental changes, but not necessarily dementia, were found more frequently in hereditary epilepsies than in the symptomatic forms. Severity of epilepsy as expressed by frequency of seizures was found definitely related to personality changes as well as dementia. As far as the EEG is concerned, patients who had temporal foci showed mental changes in 62.6 per cent (N 85); but patients who had diffuse EEG changes or normal EEGs showed mental changes only in 29.4 per cent (N 160).

The percentages of patients who show mental changes will obviously depend upon the type of patient population one is working with. Juul-Jensen's figures (1963), derived from patients seen at a University Hospital, were considerably better than Lorgé's. Out of 967 patients, 646 (66%) were regarded as mentally normal, while 128 (13%) showed "severe mental deviation." Arnold (1954), who reported on observations made at the seizure clinic of The University Hospital in Vienna, did not give incidence figures for dementia and/or personality changes, but he found a correlation coefficient of .36 between duration of illness and personality changes. No significant correlation was noted between personality changes and severity of the seizure disorder. Among patients whose illness had lasted less than five years, 30 per cent did not show evidence of dementia or personality changes, but this was the case in only 12.8 per cent of patients whose illness had lasted more than seventeen years.

The statements mentioned so far deal with a total assessment of a patient's mental functions rather than with individual test results. Personality or emotional dysfunctions are frequently treated together with intellectual deficits leading to a final conclusion about mentality of the patient. The German language literature, especially, contains numerous references to "personality change associated with epilepsy" (epileptische Wesensvera-

enderung), but no measures have been devised to demonstrate or quantify this phenomenon. The English language literature tends to insist that these mental and/or emotional changes are not specific for epilepsy, but there is, likewise, no objective material available to prove this point. Rather than enter into a controversy that cannot be settled on basis of existing data, I will limit myself to reviewing statements about intellectual abilities of epileptic patients.

Although IQ tests are far from perfect at the present time, they have proven to produce consistent results which can be subjected to statistical analysis. Tests of this type have been in use for more than fifty years. It is, therefore, surprising that the literature does not seem to contain too many references in regard to serial studies of intelligence in epileptic patients. Most reports give mean values for a group of patients. There is usually no homogeneity in the samples, and the groups contain patients in various stages of their illness. Repeat tests on the same patient after several years of effective or ineffective treatment are only infrequently reported. Before entering into these specific studies, a few more general reports should be mentioned.

Bridge (1949) found that 38 per cent of epileptic children were severely handicapped by mental retardation, while seizures were a severe handicap in only 21 per cent (N 472). He felt that frequency, severity, and duration of the convulsions were roughly proportional to the degree of mental impairment. Lennox also noted a stepwise increase in the percentage of patients who showed retardation depending on number of major seizures. Nine per cent of patients with less than ten convulsions were found to have been retarded as opposed to 54 per cent of those who had more than 1,000 convulsions. Patients who had more than one different seizure type had a poorer prognosis for mentality than those with one seizure type only. Patients with petit mal had the best prognosis in this regard, in Lennox's as well as Bridge's group. In contrast to this opinion, Janz (quoted by Bamberger and Matthes, 1959) felt that the mental development of children with petit mal was not as good as might be expected. The child who is regarded as exceptionally bright in preschool age shows inability to concentrate, flightiness and nervousness

later on. This leads to impaired performance in school or on th job. Occasionally there is, in addition, progressive intellectu loss.

The point that private patients have better intelligence tha patients seen at hospitals or at a clinic was made by Collins ar Lennox in 1947. It was reported that the private patients ha better than average intelligence and patients with genetic ep lepsy did better than patients who had a symptomatic seizu disorder. The Stanford-Binet IQ of the younger age grou ranged from 52 to 153 with an average of 104.2; the adult grou ranged from 47 to 139 with an average of 111.4 (Wechsle Bellevue); the average for all the three hundred patients w 109. An onset of seizures early in life, but not a long history epilepsy, was noted to have been deleterious. Intelligence qu tients were found to have been highest in petit mal and lowest patients who had psychomotor and grand mal seizures combin The highest scores were seen in patients with normal or nea normal EEGs or those patients who had only petit mal c charges in their recordings. The lowest scores were seen in tients who had a slow basic EEG or had petit mal variant for tions in their tracings. Verbal and Block Design tests were h performed, and tasks involving rote memory and concentrat were done the worst. By 1951, Collins had expanded the st to four hundred patients; the mean Wechsler-Bellevue IQ sc was 108 for the group as a whole. She found little evidence deterioration except in organic cases. She regarded as the m definite and probably most significant finding the superiorit intelligence of the constitutional group over those subjects wh disorder was due to brain damage. As far as subtests of Wechsler scales were concerned, it was found that sixty-e patients had a ten point higher Verbal IQ, and sixty-four tients a ten point higher Performance IQ. When Digit Span Arithmetic were taken as a separate scale for measuring cor tration, it was found that the verbal abilities were slightly hi than the performance, with concentration showing the lo scores. Rank ordering the subtests from highest to lowest, (prehension was on top, and Digit Span on the bottom of the Age of onset showed a significant correlation with IQ (.25

level of statistical significance), but duration of illness was not significantly related (—.06).

Zimmerman *et al.* (1951) examined one hundred children and adolescents, as well as two hundred adults, who had been seen at the Neurological Institute of the Columbia-Presbyterian Medical Center of New York. The children achieved a mean IQ of 92.60 on the Stanford-Binet test. The authors felt: "While falling within the average range . . . the quotient is considerably lower than is expected of children in general . . ." A comparison of full scale to performance IQs for various seizure categories is shown in Table 24.

TABLE 24

INTELLIGENCE QUOTIENTS FOR DIFFERENT SEIZURE TYPES ACCORDING TO ZIMMERMAN *et al.*, 1951*

	Average Full Scale IQ	*Average Performance IQ*
Entire group	92.60	89
Idiopathic petit mal	105.50	110
Idiopathic petit mal and grand mal	91.50	88
Idiopathic grand mal	91.25	84
Symptomatic epilepsy	89.00	78
Traumatic epilepsy	89.00	73

*From "*Intellectual and Emotional Makeup of the Epileptic*" by F. T. Zimmerman et al., which appeared in *Archives of Neurology and Psychiatry*, 1951, Vol. 65, 545.

It is apparent that, with exception of idiopathic petit mal, the performance IQ scores were lower in all groups. As far as the IQs of the two hundred adults were concerned, the entire group had a value of 100.35; idiopathic petit mal, 108.70; idiopathic petit mal and grand mal, 103.54; idiopathic grand mal, 98.50; symptomatic epilepsy, 98.13; traumatic epilepsy, 98.52. Zimmerman *et al.* also commented that the IQ is higher among children if the onset of the grand mal appears late than if it appears early in the child's life.

A similar difference in IQ scores between children and adults was noted by Dennerll *et al.* in 1964. One hundred children undergoing diagnostic evaluation at the Michigan Epilepsy Center received a mean Full Scale IQ of 89 on the Wechsler Intelli-

gence Scale for Children (WISC). The mean Full Scale IQ for one hundred adults was found to have been 96.9. Both groups had slightly higher Verbal than Performance abilities. Comprehension ranked relatively high while Digit Span and Digit Symbol were relatively low.

Henderson reported in 1953 on a survey conducted by the Ministry of Education in London of certain representative school districts in England and Wales. All children who were known to be epileptic were examined by the school medical officers in order to find out how many were in need of treatment and education in special schools, and what effect epilepsy had on children living in the community. A total of 365 children were examined. Of these, 59 per cent were of average intelligence; 31 per cent were below average, and only 10 per cent were above average at the time of the examination. IQ scores, as obtained through the Revised Terman-Merril Forms L or M, were as follows: less than 70 (15%), 70 to 84 (16%), 85 to 114 (59%), and 115 or over (10%). Forty-two per cent of patients who had seizures at least once a month had an IQ below 85 compared with 27 per cent of those who had seizures at longer intervals.

Folsom (1953), reviewing the literature on cognitive functions in epileptics, concluded that there is no cognitive deficit which is characteristic of all epileptics (i.e. of seizures), and that there is no clear cut evidence of an impairment which differentiates deterioration in epilepsy from deterioration in other disorders. In order to detect specific differences between patients with nonfocal grand mal epilepsy and those suffering from psychomotor seizures, Folsom Quadfasel and Pruyser (1955) compared two groups of nineteen patients each on subtests of the Wechsler-Bellevue Intelligence Scale and on the Wechsler Memory Scale. The groups were matched for Full Scale IQ. There was also close correspondence in regard to age, education, age of onset, and duration of the seizure disorder. The grand mal group did not differ significantly on these tests from the norm, but the psychomotor group showed a trend to impairment on tests of verbal intelligence, of memory, and of verbal memory. The differences between the grand mal and the psychomotor group were significant beyond the two per cent level of confidence. The majority of

the psychomotor patients had either bilateral or left-sided EEG abnormalities; only one patient had a unilateral right-sided focus. All but two of the psychomotor patients had grand mal seizures. The study dealt, therefore, not only with differences between psychomotor and grand mal epilepsy, but also with differences between a group of patients who have one seizure type only, versus a group who has two different seizure types.

Halstead (1957) compared the Stanford-Binet IQs of fifty-six epileptic children drawn from schools in Birmingham (twenty-eight from normal schools, twenty-eight from a special residential school) against those of fifty-four children matched for age, sex, and socioeconomic level. The mean IQ of the control group was 99.8 and that of the epileptic group 87.5 (79.2 for residential school children, 95.9 for epileptic children from the normal schools). Children who had only grand mal seizures had, on the average, the highest IQs (92.0); those with petit mal took an intermediate position (83.6), and patients with grand mal and petit mal had the lowest scores (82.7). The term petit mal included akinetic seizures and was not limited to "pure absences." Children with a positive family history of epilepsy had higher IQ scores than those without. Lower scores were found in association with earlier onset and a longer duration of the illness. Patients with frequent grand mal seizures did poorer than those with infrequent attacks, but the reverse was the case in the petit mal patients. The epileptic children seemed to be especially handicapped by slowness in thinking, difficulties in immediate memory, and manual dexterity. As a group the epileptic patients were found to have been more heterogeneous than the control group, with about 60 per cent more "scatter" in all tests. Brain injured children had, as one would expect, the lowest scores of all.

Delaveleye and Sauveur (1964) reported the results of the Binet-Simon test given to three hundred epileptic children between ages four and fourteen years. The mean IQ was 80.8, but the standard deviation of 22.6 indicated the marked heterogeneity of the sample. The following factors were found to have adversely influenced the IQ: (1) the presence of major seizures, (2) the frequency of major seizures, (3) the severity of major

seizures, (4) onset of seizures before four years of age, (5) external etiology leading to significant cerebral disturbance. The authors state: "The mean IQ is little or hardly altered in cases of petit mal or its equivalents, if the major attacks are not very frequent and without serious complications, if the exogenous etiology has occurred after four years and has had slight initial consequences."

Keith *et al.* (1955) examined the records of children, who had been diagnosed at the Mayo Clinic as convulsive disorders during the years 1950 and 1951, with special regard to the mental status. It was found similar to Bridge that 37 per cent were mentally retarded, 14 per cent dull-normal, and 48 per cent of average or better than average intelligence. The percentage of retardation was greater in cases diagnosed as symptomatic (73%) than in those classified as idiopathic (22%). Keith *et al.* found, like others, that the incidence of retardation was greater among the patients who had more frequent convulsive attacks than among those who had less frequent seizures.

In connection with these foregoing statements, Livingston's comment (1961) would seem somewhat contradictory. He stated: "We have not observed a statistically significant relationship between epilepsy and mental retardation. . . . We have followed thousands of patients for many years and can definitely state that the vast majority of them maintained normal intellectual capacities." Part of the problem here seems to lie in the definition of mental retardation and "normal intellectual capacities." The terms have obviously two meanings, a colloquial versus a technical one. Using the technical language of the Wechsler Intelligence Scale, an IQ range between 90 and 109 is regarded as normal, while an IQ level of 69 or below is regarded as defective. Between these scores lie the dull-normal and the borderline defective patients. It is technically true that the majority of epileptic patients have normal intellect as defined above, but they tend to cluster towards the lower end of the normal range rather than at the center. It appears that the normal IQ curve is shifted somewhat to the left of center in the epileptic population, but not quite far enough to place the peak into the dull-normal or borderline range. The fact that a patient has nor-

mal intelligence at time of testing does not preclude the possibility that he could have achieved a bright-normal or even superior test score on basis of his native genetic endowment had it not been for the conditions related to his epilepsy. These considerations will be more fully dealt with when our own data are presented. They are merely mentioned at this time to point out that some of the contradictions in the literature may be more apparent than real.

An example that the persistence of epileptic seizures could have a deleterious influence on intelligence is also provided by Walker and Jablon's findings (1961) on posttraumatic epilepsy. Table 167 of their book is reprinted here as Table 25.

TABLE 25

RELATION OF WECHSLER-BELLEVUE INTELLIGENCE TEST TO PATIENTS SEIZURE-FREE (GROUP 1) AND PATIENTS CONTINUING TO HAVE SEIZURES (GROUP 2) ACCORDING TO WALKER AND JABLON, 1961**

	*Group 1**		*Group 2**	
Wechsler-Bellevue test	*Number*	*Percent*	*Number*	*Percent*
≤89	5	8.9	25	21.4
90–119	39	69.6	78	66.7
≥120	12	21.4	14	12.0
Total	56	100.0	117	100.0
Unknown	2	—	9	—

* The difference between the two groups is statistically significant ($P < .05$).

**From *A Follow-up Study of Head Wounds in World War II*, a V.A. Medical Monograph by A. Earl Walker and Seymour Jablon. Copyright U. S. Government Printing Office, Washington, D.C., 1961.

It shows that, as far as the IQ range between 90 and 119 is concerned, there is no appreciable difference between the group that had become seizure-free as opposed to the group who continued to have attacks. Approximately two-thirds of all patients fell into this IQ bracket. The differences were at the higher and lower ends of the scale. Less than 10 per cent of the seizure-free group had an IQ below 89, but this was the case in more than 20 per cent of patients who were still having attacks; this group

was correspondingly less represented in the above 120 IQ bracket.

While these observations suggest that seizures can have a deleterious influence on intelligence, Lennox emphasized that his findings on monozygotic twins demonstrated that ". . . seizures in and of themselves do not weaken the intelligence." Of thirteen pairs in which one member had chronic epilepsy, the mean IQ was 103.2 in the unaffected and 100.7 in the affected twin. In his book, Lennox did not give details about the seizure types and frequency of occurrence of the seizures in this group of monozygotic twins. In the earlier report by Lennox and Collins (1945) there were six twin pairs with only one of the co-twins having seizures and where the epileptic twin had no evidence of serious brain injury. The spread between the two IQ scores was five points, with the healthy twins having at times the lower score. The authors stated: "In three of the six cases, contrary to what might be expected, the epileptic co-twin has the higher score and the average score for the six nonepileptic co-twins is 92 and for the six epileptic co-twins it is 91, a difference of only one point. However, in each of these six twins, the seizures of the affected co-twin were either few, or of the relatively innocuous petit mal (pykno-epilepsy) variety." The last sentence is obviously important for a final conclusion whether repeated generalized seizures do or do not affect intelligence.

All of the reports mentioned so far dealt only with cross-sectional data. The earliest study of serial intelligence tests in a group of epileptic children that I have found in the literature was by Tylor Fox (1924). A total of 130 children attending the Lingfield Epileptic Colony were tested in two successive years by means of the Binet test. The results were as follows: "Gained over ten points . . . 1, gained from six to ten points . . . 9, gained from three to five points . . . 19, stationary or showing a gain or loss of not more than two points . . . 53, losing three to five points . . . 25, losing six to ten points . . . 12, losing over ten points . . . 11." The main body of the paper dealt with test results on the Binet-Simon scale, a reasoning test, Porteus Maze tests and tests for reading, spelling, and arithmetic. These tests had been given to 150 children. It was found that the epi-

leptic children had most difficulty with tasks that involved immediate memory, written language, and abstract thinking.

Patterson and Fonner (1928) obtained two or more IQs (Binet-Simon) of ninety-eight institutionalized epileptic children attending the colony school. A deviation of two points in either direction from the original figure was attributed to possible experimental error, and any subsequent result which approximated by two points or less the original finding was regarded as showing no change in the IQ. When the amount of the difference between the two quotients exceeded two, the result was interpreted as an increase or decrease depending upon whether the subsequently derived IQ exceeded or fell short of the original figure. In fifty-one boys tested, the IQ ranged from 38 to 114 at the time of the first examination and from 45 to 113 at that of the second. Thirteen boys showed no change in the IQ as previously defined upon retesting, while twenty showed a decrease with lapse of time and eighteen showed an increase. The maximum loss was seventeen points and maximum gain was eighteen points. The time interval elapsing between the two tests varied from one year and four months to three years and seven months. The IQ of the forty-seven girls varied from 47 to 109 at the first examination, and from 42 to 109 at the second. The interval between tests was from one year to three years and ten months. Eighteen patients showed no change; sixteen showed an increase, and thirteen showed a decrease in the score. The maximum gain was twenty-six points; the maximum loss, nine points. Of the total group only eight children had a normal IQ. Of these eight, three showed no change in IQ; two showed an increase, and three showed a decrease. Of the three children who had shown a decrease, seizures had become more frequent in two, while there had been no increase in the number of seizures in one. Of the two children who had shown an increase in IQ, one had infrequent seizures while the other continued to have frequent attacks.

On the basis of the total sample they concluded: "Not only is the IQ not constant but it varies in a rather unusual fashion, i.e. it sometimes declines and sometimes increases. Moreover the rise does not always correspond with a decrease in seizures or with

the administration of luminal—although it may sometimes—nor does the fall necessarily appear with increase in seizures or without the administration of luminal. It may coincide with any of these factors but in the main it manifests its pecularities independently of their influence."

Their final conclusions were as follows:

1. The IQ varies considerably in the epileptic.
2. This variation may involve either a rise or decline in score.
3. This variation in the epileptic may occur at any mental level.
4. The variation in the IQ seems in the main to be independent of seizure frequency or severity or of medication.
5. The rate and extent of deterioration in epilepsy as determined by the IQ seems to show great individual variation.
6. The subject of the IQ in epilepsy invites further investigation.

Dawson and Conn reported in 1929 on the IQs of forty-nine epileptic children seen at the Royal Hospital for Sick Children in Glasgow. The ages of the children varied from four to twelve years. The mean IQ at the time of the first test was 80.65 (Binet). This was significantly below that of the hospital children in general who had a mean IQ of 90.57. When patients suffering from endocrine and cerebral disease were excluded, the mean IQ of the nonepileptic patients was 91.76.

In twenty instances a healthy sibling was given the Binet also. The mean IQ of the patients whose siblings were tested was 80.60; that of the healthy siblings was 91.20. Twenty-one patients were retested at intervals varying from eight months to four years and eight months. The mean IQ at the time of the first test was 82.09, and 66.52 at the time of the second test. This difference was statistically significant. In ten cases there was little difference between the results of the two tests, but the general tendency was towards deterioration which was very serious in some cases. The final conclusions of the authors were as follows: "(1) The average intelligence of epileptic children is appreciably

below the normal. (2) There is definite evidence of deterioration that is due directly to epilepsy. (3) All epileptic children do not deteriorate equally; some appear to show no deterioration; some lapse into a state of complete imbecility." No significant correlation was found between severity or frequency of the convulsions at time of admission to the hospital and subsequent improvement in general condition or mental progress, but a significant correlation existed between improvement in general condition and mental progress. It was also felt that epileptic patients come from a stock which appears to be normal as far as intelligence is concerned.

Fetterman and Barnes (1934) examined outpatients attending the Epileptic Clinic of the Lakeside Hospital Dispensary of Cleveland by means of the Stanford-Binet test. A total of 105 patients were tested regardless of age; the only criterion of selection was command of the English language. Forty-six were retested at intervals from one to two years. The average intelligence quotient for the 105 patients studied was 74, with a range from 34 to 133. On retest, nineteen patients showed a slight increase in the intelligence quotient; twenty-three showed a moderate loss, and in the remainder the quotient was unchanged. It was felt that the average of these changes was not larger than the difference which one may obtain between tests and retests on normal persons.

Twenty-five patients were tested three or more times. The authors regarded as the most interesting feature of these serial studies the fluctuation of the intelligence quotient from one test to another. "What may look like a significant change one year may be entirely offset the next year by a change of equal magnitude in the opposite direction. Only two patients showed a decline in the intelligence quotient from both the first to the second test and the second to the third test." It was also concluded: "Sedative medication, even when long continued, did not produce deterioration in the intelligence as measured by the Binet test."

A study by Sullivan and Gahagan (1935) involved 103 epileptic children admitted to the Children's Hospital, Los Angeles, California. The Stanford-Binet test was used in most cases. IQs

were found to have ranged from 11 to 141 with a mean of 88 and a median of 92.4. In a previous study on school children in the Los Angeles school system involving 63,147 cases, the median IQ was established at 105, and a group of forty-five children admitted to Los Angeles Children's Hospital for allergies showed a median IQ of 103. Forty-four children were retested at intervals of one month to four years and eleven months. The average interval was fourteen months. The median IQ at time of first test was 95.0; at time of second test, 91.6. The Pearson Product Moment correlation between IQs on first and second test was .897. Twenty patients changed in a positive direction; twenty-two in a negative direction, and two showed no change. Twenty-two cases of idiopathic epilepsy were then selected from the material and treated by separate statistics. The mean IQ at time of first test was 87.2, and on second test it was 85.8. This difference in the means was not statistically significant, but it was in agreement with the general downward trend. It was concluded that the mean IQ of epileptic children was appreciably and significantly below that of other hospital children examined. These further conclusions were reached by Sullivan and Gahagan (1935):

1. The epileptic group shows greater variation on retests than is reported in studies of unselected school children.

2. There is shown mental deterioration of the group as a whole on retests.

3. Our group does not show as great a deterioration on retests as is shown by Dawson and Conn, Fox, and others. . . .

4. Our results show no large changes that would change the diagnostic classification in 65.6 per cent of the group. Changes of ten points or more occur in 34.4 per cent of the cases retested. These changes are in both directions (improving and deteriorating).

5. Large changes in a positive direction or a negative direction occurred most frequently in cases of average or superior intelligence.

6. No change in a positive direction occurred in an

amount great enough to result in a child classified as feebleminded on a first examination, later to be classified as not feebleminded.

7. In only one case did a child classified as normal on a first examination deteriorate so rapidly as to be classified as feebleminded on a later test.

Kugelmass *et al.* (1938) studied 129 institutionalized epileptic children and ninety-one children from private practice selected from hospitals and special schools. The authors stated: "The condition was classified as primary if idiopathic epilepsy was the sole disturbance and as secondary if, besides epilepsy, a constant cerebrogenic factor was superimposed on the mental status. The children were considered improved if either or both the number and the intensity of the seizures diminished and unimproved if either or both the number and the intensity of the attacks did not diminish because of treatment or nontreatment. The mental tests involved a variety of appropriate scales, a weighed average of all results constituting the final rating for each child."

The institutionalized group was mentally retarded and no significant difference between primary and secondary epilepsy was seen in these children. The IQ of children who had responded to treatment was slightly higher than those who had not (median for primary improved 56, unimproved 49). The median IQ for the improved private patients was 99 and for the unimproved 90. In order to detect mental growth the children were retested at intervals of three months to three years. The correlation coefficient between the first and final test was .90. It was found that the ". . . improved and unimproved children were limited alike in their ability to raise their mental status, the unimproved as a group dropped twice as low at the 75 percentile of the distribution."

Yacorzynski and Arieff published two papers in 1942, one demonstrating the absence of deterioration in patients with nonorganic epilepsy, while the other emphasized deterioration of patients with organic epilepsy. As far as the first paper is concerned (Yacorzynski and Arieff, 1942), sixty-three outpatients with nonorganic epilepsy were tested with the Stanford-Binet test at intervals of one to three years. Each patient was tested

two to four times. They stated: "Eight patients showed significant increases of the intelligence quotients between the first and final tests, and seven patients significant decreases. Some of these changes must be accounted for on the basis of chance fluctuations which are characteristic of the epileptic patients. If only progressive changes of the intelligence quotient are taken as indicating a real trend in the direction of improvement or deterioration then only one patient, or 1.6 per cent, improved, and three patients, or 4.8 per cent, deteriorated. . . . There appears to be no relationship between the reduction in the number or severity of seizures and the changes of the intelligence quotients."

In the second paper (Arieff and Yacorzynski, 1942), twenty-seven patients were reported: posttraumatic epilepsy was present in eight, inflammatory disease of the central nervous system in eight, brain tumors in five, vascular disease in four, and chronic alcoholism in two. The intervals between tests ranged between one and ten years. Separate Stanford-Binet IQs were obtained from two to five times on each patient. The average IQ on the first test was 74.3. The sixty-three patients in the non-organic group had had an IQ of 85.1. The average IQ shift in the organic group was a loss of six points. A significant increase of IQ was found in 11 per cent and a significant decrease in 37 per cent. Four of the fifteen patients who were tested more than twice showed a progressive trend towards deterioration (26.6%). No difference as to the degree of deterioration was found in regard to the various organic etiological factors.

Tenny (1955), reporting on IQs of children at White Special School for Epileptics in Detroit, noted a median IQ of 84 (N 690) with a range from 52 to over 130. A total of 284 children were retested, and changes were observed ranging from a decline of thirty-five points to an increase of over fifteen points. The median IQ on retests was 80, an average decline of three points for the group retested. The time between tests and retests was not mentioned in the paper. The negative change in IQ was noted to have been somewhat more marked in pupils whose seizures had increased than for those whose seizures were unchanged, decreased, or controlled.

While serial studies of the same patient are obviously prefera-

ble over cross-sectional data, they, of course, are not always obtainable. Cross-sectional data can be used to advantage, however, when one has a control group against which the deteriorated group can be compared. This was done by Chaudhry and Pond (1961), who reported on a comparison of twenty-eight epileptic children with brain damage and associated intellectual and social deterioration against an equal number of patients matched for age and sex with epilepsy and brain damage but no deterioration. No difference was found in regard to age of onset of brain damage, age of onset of seizures, site and extent of brain damage, amount and duration of anticonvulsant treatment, presence of behavior disorder, or family history of epilepsy. Significant differences were observed in regard to the frequency of seizures, response to anticonvulsant medication, and focal as well as generalized EEG abnormalities. The deteriorated patients fared poorer in all these respects. The authors commented also: "Attention is drawn to certain cases which improve after long periods of apparent deterioration and a hypothesis is put forward that some form of 'subclinical' epilepsy may be partly responsible for deterioration which is not a true dementia."

A similar point was made by Michaux (1964), who stated that intellectual decrease in epileptic children may be temporary due to an "obtunded state" which clears up after several weeks or months, and the child definitely should not be excluded from school because he shows marked decrease in memory, inattention, and loss of interest. IQ tests may confirm dementia, but Michaux emphasized that this is a temporary state which can disappear.

Illingworth (1955) and Dekaban (1960) addressed themselves to the problem of mental deterioration in previously healthy infants who developed epilepsy, and although Illingworth thought that he had ". . . not found a reference in the literature to this type of case," he subsequently went on describing patients who had for the most part infantile spasms, which we have discussed extensively in a previous chapter. Dekaban's cases are likewise those of infantile spasms of unknown cause.

As had been pointed out in the beginning of this chapter, Turner had emphasized that "stigmata of degeneration" or "evi-

dence of structural degeneration" was found more commonly in patients who had shown mental deterioration.

A specific study in regard to constitutional differences between deteriorated and nondeteriorated patients with epilepsy was carried out by Paskind and Brown and reported in 1939. Fifty deteriorated and thirty-nine nondeteriorated epileptic patients were subjected to anthropometric studies. Eighty measurements were recorded for each patient. In addition, fifty-seven indices were calculated for each patient to show the relation in size between a given part of the body and other parts. It was found that the deteriorated patients could be distinguished from the nondeteriorated on the following measures: heavier per unit of height on all indices relating weight to height, wider trunks per unit of height, narrower faces per unit of face height. Values of unusual size in head, hand and foot measurements, and unusual indices occurred more often in the deteriorated patients, while unusually large measurements and indices of exceptional size in regard to trunk and entire body measurements were more common in the nondeteriorated group. The nondeteriorated group came from a stock with less neuropathy; the age of onset was later; they had fewer seizures and more and longer remissions.

Two more studies might be mentioned, although they do not deal directly with intelligence. Serafetinides *et al.* (1963) studied the psychiatric and social findings in patients with late onset epilepsy. Twenty-three patients were regarded as normal prior to the onset of their seizure disorder. Seven of these showed "epileptic deterioration"; four others had a psychoneurotic illness; two had personality changes; two had a psychotic illness, and eight had remained normal. It was found that the outlook for the psychiatric illness was relatively poor compared with the prognosis for seizures. There was a downward trend in social class after the onset of epilepsy and an increasing restriction of social activities. This group is not representative for a group of epilepsies, because it came from the Maudsley Hospital and the patients were initially referred because of suspected psychiatric difficulties.

Glithero and Slater (1963) performed an interesting follow-up study on a subgroup of epileptic patients, namely, those who

present in addition to epilepsy a symptom picture that closely resembles a schizophrenic psychosis. Sixty-four patients were involved and the follow-up was accomplished seven to eight years after the onset of the psychosis. It was found that "the state of the patients had by no means stabilized then, as readmission to hospital with improvement and discharge was continuing to occur." The main conclusions were the following:

"Of the sixty-four patients followed up, thirty were living entirely at home, sixteen mainly at home with periodic readmission to hospital, nine mainly in hospital, and nine entirely in hospital.

"Social interests were mainly impaired, with one patient participating actively, thirteen with moderate interest, the remainder needing encouragement or being without interest.

"Personal relationships were at a better level, nine patients having well-preserved personalities, twenty-four being socially adequate, the remainder moderately or severely impaired.

"Work records were surprisingly good; twenty-five patients were in full-time work, and four more were in part-time work, i.e. 45 per cent having some paid employment.

"The follow-up showed that the epilepsy had tended to get less troublesome with time; ten patients (five of them after lobectomy) had had no fits in the past year, and in a further thirty-five patients fits constituted no problem medically or socially.

"Schizophrenic symptomatology was closely related to social capacity and freedom. One-third of the patients had had a remission of schizophrenic-like symptoms, and a further third had experienced improvement in this respect. A few of these patients, however, are known subsequently to have relapsed for a time. The evidence suggests that the schizophrenic-like symptoms, which have manifested at one stage in the life-history of the epilepsy, tend to settle down at a later stage.

"Psycho-organic sequelae in the form of personality changes such as perseverativeness, dullness, retardation, circumstantiality, impairment of memory, etc., were present in twenty-nine cases. Paranoid and schizophrenic-like symptoms constituted a source of disability in thirty-four cases. These two forms of aftereffect appeared to be independent of one another.

". . . It does not appear that the lobectomized patients had done any better than other patients not operated on, except in their reduced liability to fits.

"The total impression gained from the follow-up study is that these patients have an illness which runs a stormy course towards an end-state of general impairment. This impairment is of an organic type, affecting both intellectual functions and affective aspects of the personality, and is of a kind commonly seen in late stages of chronic epilepsy."

As far as the EEG is concerned, Livingston (1954) made a strong statement that it is of no value in predicting a patient's mental state. "Some physicians seem to have the impression that the electroencephalogram, in addition to its diagnostic value in epilepsy, is also a measure of a patient's intelligence. This definitely is not true. *The electroencephalogram is by no means an indicator of the mental state of a patient.* The majority of children who present evidence of mental retardation, but do not have epileptic seizures, have normal electroencephalograms." These views require some comment. It is true that convincing relationships between IQ and features of the EEG so far have not been demonstrated in the normal population. It is equally true that a number of severely retarded nonepileptic patients have normal EEGs. It is not correct, however, to assume that the EEG does not reflect, in some cases, severe impairment of an epileptic patient's mental state. The reason for these discrepancies lies in the fact that the EEG is sensitive to brain injury and most of the patients with epilepsy and intellectual difficulties have suffered some form of damage to the brain. It is therefore not unreasonable to expect that the EEG can reflect at times the patient's mental state.

Probst's paper (1960), to which I have previously alluded, could be taken as an argument for Livingston's views, and against the thesis suggested above. He had compared thirty-nine epileptic patients with normal EEGs against forty-four with generalized nonspecific abnormalities. No significant difference was found between these two groups in regard to mental or intellectual changes. It should be pointed out that Probst's study dealt with only two subgroups of the epileptic population and

did not cover the entire spectrum of the illness. Furthermore, a record of an epileptic patient may be normal on one occasion and abnormal on another. The borders between the groups are therefore not fixed, but fluid. Probst might have come up with different results had he compared patients with normal EEGs and strong 9 to 11 cycles per second alpha rhythms against patients with slow or disorganized background activity. In regard to the normal EEG, we have to remember also that some low voltage desynchronized records will be called normal because they occur in a number of normal individuals, but they may also result from neuronal loss or they may represent the phenomenon which Landolt (1957) has called "forced normalization." This occurs mostly in patients with psychomotor seizures. The patients usually show focal seizure patterns in their EEG recordings which disappear as the attacks are temporarily brought under medical control. The patient's mental state at that time is, however, characterized by psychotic thinking. This disappears with change in medication regime and the previously seen EEG seizure patterns reemerge, as do the clinical attacks. Landolt emphasized that this "forced normalization" which is temporary has to be differentiated from normalization of the EEG in presence of persistent mental defect. This latter phenomenon is due to loss of cerebral tissue and a poor prognostic sign. The "typical epileptic personality change" appeared to correlate, according to Landolt, with generalized slowing of the EEG background rhythms. Gibbs and Gibbs (1941) have also stated that slowing of the background rhythms is characteristic of deteriorated epileptic patients.

Romano and Engel (1944) are usually given credit for having first described the EEG changes associated with delirium. Their definition of delirium encompassed all degrees of the organic mental syndrome ranging from a mild deficit of recent memory and difficulties on serial 7 subtractions to severe disorientation, somnolence, and stupor. Slowing of EEG background activity was the most consistent concomitant.

Stoller (1949) made a detailed investigation of the significance of slowing of the alpha rhythm of the EEG. Out of 2500 cases seen at the Maudsley Hospital and the National Hospital,

Queen Square, twenty showed slowing of the alpha rhythm. The dominant background frequency was 6 to 8 cycles per second in these cases. Twelve of the patients suffered from epilepsy. All twenty patients, with exception of one commercial artist, had shown obvious mental deterioration. When patients were selected for profound mental deterioration, no consistent EEG pattern was encountered. Stoller concluded that ". . . mental deterioration is not specifically associated with slowing of the dominant alpha-rhythm but, when the latter is present, mental deterioration is probable and, moreover, particularly so when the patient has suffered from fits. The important practical application of this is that when one encounters this phenomenon in the EEG of an epileptic one should consider the probability of mental deterioration."

Hill (1963) noted: "Many demented patients have normal records. On the other hand, others have a slow alpha rhythm (6 to 8 c/s) which blocks poorly to visual attention. The rhythms in these cases tend to be 'simplified,' show little spontaneous variability either of occurrence or of amplitude."

A specific study dealing with relationships between indices of intellectual impairment and slowing of EEG background rhythms was carried out by Jenkins in 1962. Although only nine of the fifty-seven patients were epileptic, the results are applicable to seizure patients. The total material was divided into four groups on the basis of amount of slow wave activity in the EEG. There was no difference in regard to age, education, and occupational status between the groups. Significant relationships were found between EEG slowing and lower scores on the Wechsler Adult Intelligence Scale Performance IQ (especially Digit Symbol, Block Design, Object Assembly, and Porteus Maze) as well as lower scores on the Benton Visual Retention Test and tests for weight discrimination. No relationship was found between EEG slowing and any test based on verbal input and verbal responses.

As far as seizure patterns are concerned, it has been pointed out by Gibbs and Gibbs (1952) that approximately 50 per cent of patients with a two cycle per second petit mal variant type of spike wave activity are mentally deficient. This is in marked contrast to the relative rarity of mental deficiency among patients

with the three cycle per second spike wave pattern. According to Lennox the three cycle per second spike wave group had a mean IQ of 109, and the two cycle per second group a mean IQ of 96. Lennox commented ". . . slow waves often match slow wits." As far as subtests were concerned, they were all below the average in the two cycle per second group. In the three cycle per second group they were above the average from Comprehension through Picture Completion. They were below in Object Assembly and Digit Span. The spread between the subtest scores of the two groups of spike wave discharges was highest for Comprehension, Similarities, and Block Design, and lowest for Digit Span. Lennox concluded: "The slow spike-and-wave formation does not represent simply an immature form of the three-per-second dart-and-dome pattern, but rather the confluence of three influences: extreme youth, heredity, and structural brain defect." The relationship between hypsarhythmia and mental deficiency has already been covered in detail in a previous chapter.

These findings refer of course mostly to children. In the adult, a combination of mildly slow background activity (7 cycles per second activity) with unilateral or bilateral temporal foci of sharp or slow wave activity, was found to carry a poor prognosis for mental and/or emotional functions (Rodin, 1957). The patient's symptoms may either reflect intellectual damage or may appear on clinical grounds to be purely psychiatric in nature. It is exceedingly rare that a patient with this type of EEG can hold employment in the community.

Patients with psychomotor seizures frequently have focal abnormalities in one or both temporal areas. Several studies are now available indicating that cognitive functions are selectively impaired, depending upon whether the right or left temporal region is involved. Dennerll (1964) reviewed this aspect of the literature and demonstrated also that regression weighted Wechsler scores allow the classification of psychomotor seizure patients into a right or left temporal group with considerable accuracy.

An EEG pattern that occurs only during sleep and correlates with psychosis in epileptic patients has been reported by Gibbs and Gibbs (1964) and was called "B Mittens." A total of 42 per

cent of psychotic epileptic patients showed "mitten" patterns in the Gibbs' series.

As a final point one might mention that there exist a number of patients who have episodic confusional or "clouded states" lasting for one or several days and sometimes weeks, which are due to nearly continuous seizure patterns in the EEG. It is only the electroencephalogram and no other test that can establish a definitive diagnosis of this condition. Names that have been applied are petit mal status, or spike wave status, but other types of seizure patterns can also be seen which are not necessarily of the spike wave variety, as will be shown in the section dealing with our results. These are the types of patients to whom Chaudhry and Pond, as well as Michaux, had referred.

If one were to summarize the views of the literature on intellectual and personality changes in the epileptic patient, one cannot help but conclude that more long-term interdisciplinary work between neurologists, psychiatrists, psychologists, and electroencephalographers is needed before firm conclusions can be reached. The data as they stand at present tend to show the following:

1. The group of epileptic patients can be divided into one of "pure epilepsy" and the other of "epilepsy associated with known brain damage of varying degrees." The "organic" group has lowered intelligence, but epilepsy is merely an added complication in these patients.
2. The "nonorganic" group has normal intelligence quotients, but there is a persistent suggestion that they tend to be shifted towards the low end of the normal range rather than being situated at the center.
3. Deterioration from a higher level appears to occur at times, but precise figures about the frequency of this phenomenon are not available due to the paucity of long-term longitudinal studies.
4. Follow-up studies which have been performed tend to show greater variability on test-retest measures than what would be expected from normal control groups.
5. The general trend for a group of patients tends to be in the downward direction, but the overall decrease in

IQ points is usually not marked. In the individual patient one may observe either a decrease or an increase in IQ on follow-up examinations. This cannot always be related to the patient's current seizure state. Although it is uncommon for the IQ to increase in the presence of uncontrolled seizures, arrest of seizures can, but does not have to be, associated with an increase in IQ. A decrease of the IQ on one retest cannot be taken as evidence for permanent deterioration, because it can be offset by an equal increase in IQ points on subsequent reevaluations.

6. There is a persistent suggestion that frequency of major seizures tends to be related to a decrease in intellectual function, and nearly all authors agree that an early onset of the illness is likely to be associated with decreased intelligence.

7. In regard to the "epileptic personality" no conclusions are possible at this time because of absence of reliably measured data.

8. There are certain EEG patterns which relate significantly to impaired intellectual or emotional functions, but a "normal" EEG in an epileptic patient does not automatically guarantee normal intellect and/or personality.

Chapter 9

MORTALITY

Livingston wrote in 1963: "As far as longevity is concerned, the patient should definitely understand that epilepsy per se rarely causes death and that there is no reason why an epileptic should not live as long as he would if he did not have epilepsy." Let us examine some of the opinions and statistics that have been presented during the past century and see to what extent the above quoted statement is upheld.

Although Gowers (1885) gave no figures of his own, the following excerpts from his book are appropriate because they can serve as a comparison for opinions expressed today. Gowers felt the danger to life in epilepsy was not great: "The chief danger of death in an attack is the liability to accidental asphyxia, in consequence of the occurrence of an attack during a meal, when food may get into the air passages, or of vomiting after an attack with the same result, or in consequence of the patient, in bed, after an attack, turning on to the face and being suffocated in the postepileptic insensibility. It is for this reason that the danger to life is much greater in the cases in which there exists this tendency to turn on to the face than in others. . . . But the commonest mode of accidental death in epilepsy is by drowning. The fit not only occasions the fall into the water, but effectually prevents any effort to escape, and often interferes with any attempt at rescue. Hence epileptics are sometimes drowned in a very small depth of water, as in a ditch. The danger of such accidental death is unquestionably greater than that of death from the direct severity of a fit. The latter is excessively rare, especially when the frequency of severe fits is taken into consideration.

Very rarely, however, epileptics pass into what is termed the 'status epilepticus' in which severe attacks recur very frequently, recovery from one being imperfect before another comes on. This state is one of considerable danger; it is, however, so rare, and the liability to it is so small, that it cannot be regarded as measurably increasing the risk of death in consequence of the disease." Gowers' opinions were derived on the basis of patient material seen mostly at the National Hospital for the Paralyzed and Epileptic. It did not deal to any great extent with institutionalized patients, and this may have been the reason why status epilepticus and death resulting from it occurred only infrequently in his sample. His statements point also to another interesting facet, namely, that status epilepticus has probably always occurred, for the most part, only in a certain segment of the epileptic population, namely, severely disabled patients who, in the majority, need institutionalization. Another possibility is that his material consisted mostly of adult patients and status appears to be more common in childhood.

Turner (1907), whose patient material was similar to that of Gowers, also gave no statistics of his own in regard to mortality but quoted the findings of Spratling from the Craig Colony for Epileptics in New York that sudden death as a result of a seizure occurred in 5 per cent of 150 cases. Death resulted from status epilepticus in 23 per cent, and from accidents during a fit in 12 per cent. The other patients died of conditions not necessarily related to epilepsy. The mean age at time of death was found by Spratling to have been 29.4 years. Other sources quoted by Turner gave mean ages of death as thirty-three years, thirty-nine years, forty years, and forty-eight years. These figures suggest that at the turn of the century the general life expectancy of patients with epilepsy was lower than what one would have expected had the illness not been present.

Munson's report, from the Craig Colony in 1910, is not only of historic interest but deserves more extensive review because it contains several practical points which are still of importance in today's management of patients. His findings dealt with 2,732 individuals, of whom 582 had died at the institution. The mean age at time of death was 30.08 years. The most common causes

of death were given as pulmonary conditions. Pneumonias occurred 142 times (24%); various other lung conditions including tuberculosis, 119 times (20%); sudden death, 99 times (17%); status epilepticus, 59 times (10%); series of seizures, 13 times (2%); mental disturbances with exhaustion, 13 times (2%). The cause of death was regarded as having been related to epilepsy in 174 instances (30%).

The group of "sudden death" is of special interest. Although it contained in Munson's cases a variety of conditions such as suffocation, accident, falling on railroad tracks, or suffering a fatal injury while in an automatic state, he also included cases where neither accident of any kind nor suffocation could be assigned as cause of death. These occurred mostly during the night and the patients were found dead in bed by the nurse. He presented several examples of this occurrence and suggested the use of hair pillows with a net covering rather than the usual soft pillows, but as more important he emphasized close and continuous observation: "Each patient must be seen every few minutes, for, as has been noted, these deaths occur very rapidly at times. Hearing cannot be depended on—seizures not infrequently take place silently. Patients sleeping in the same room or dormitory are not to be depended on as safeguards, as they not infrequently fail to appreciate the responsibility or are not awakened by the seizure. In this connection, single rooms may be mentioned in order to condemn them. They have apparent advantages, and no doubt add greatly to the comfort of the patient, but he is much safer sleeping in a room with others." His final conclusion in regard to mortality was this: "The duration of life after the onset of the disease may be several years, but as the onset is very common in the early years of life, the net result is the premature death of the epileptic as compared with normal people." Munson's statement about single rooms is most important. Sudden death from epilepsy, although infrequent, does occur at the present time. Modern hospitals place the emphasis on single or semiprivate rooms. It is impossible for the nursing personnel to check every patient in each room more frequently than every fifteen to twenty minutes. It takes, however, considerably less time for a patient to die. The only remedy would seem to

be that patients who are prone to have nocturnal seizures are placed together in an area that is under constant supervision of a night nurse or attendant. Patients who live at home should have their bedrooms adjacent to that of the parents and share their own room, whenever possible, with another sibling.

Joedicke (1914) reviewed life expectancy and causes of death on a material of 309 institutionalized patients in Germany and found that the peak incidence of death occurred between the ages of thirty and forty years; thirty-six died in status epilepticus (11.4%) and 117 (28%) succumbed as a result of pulmonary disorders acquired in ictal or postictal confusional states.

Gruhle (1924), reviewing the progress in the understanding of epilepsy during the years 1910 and 1920, quoted the work of Citronblatt dealing with the causes of death of 876 institutionalized epileptics in Switzerland during 1903 and 1907. Death occurred mostly between the twentieth and forty-ninth year of age. Ammann, in Switzerland, reported on 2,159 fatal cases and found the major proportion died between the ages of fifteen and fifty-five years, while the general population tended to die between fifty-five and eighty years (if infant mortality was excluded). Ammann concluded that the life expectancy of the epileptic is, on the average, shortened by one and one-half decades. The cause of death was related to epilepsy in 62 per cent, and 42 per cent died in a seizure. Two-fifths of patients dying in institutions as a result of epilepsy died from status epilepticus. Gruhle commented that these figures seemed surprisingly high to him. He also mentioned in his review the findings of Hahn, from a German state hospital, that during a twenty-year period 8 per cent of patients died in a seizure and 21 per cent in status epilepticus.

Musken's book, published in 1928, presented no statistics, but it was the feeling of the author that: "The immediate danger to life of an epileptic fit is not great. . . . At the same time, experience teaches that the life of an epileptic patient is comparatively shortened." Mortality is higher than normal and reaches its highest point between the ages of twenty-five and thirty years. A marked decrease in life expectancy for epileptic patients was also reported by Guttmann in 1929. In 1929

Ostmann reviewed 520 patients treated between 1900 and 1928 at a state institution in Germany. Twenty per cent of the patients died in a seizure and 12 per cent in status epilepticus. Grosz reported, in 1930, follow-up findings on patients with idiopathic epilepsy who had been seen at the University Clinic in Breslau during the years of 1906 and 1918. The fate of ninety-one patients could be ascertained; thirty-nine had died. Death was directly attributable to epilepsy in eleven; eight of these patients died during status epilepticus (20.5%); two died of injuries resulting from seizures, and one committed suicide during an episode of confusion.

The reviews covered so far have dealt for the most part with adults. The book by Bridge (1949) deals with children. Among 472 patients who had been followed for periods ranging from one to fourteen years, forty-five (9.53%) were found to have died. In twenty-eight of these (62.2%), the cause was directly attributable to epilepsy. Twenty-one had died of status epilepticus, that is 47.6 per cent of the total group who had died, and 75 per cent of the deaths that were attributed to epilepsy. Bridge also found that the longer the illness had lasted, the greater was the mortality. When the disease had continued from fifteen to twenty-one years, the death rate was nine times that of the group having had epilepsy less than three years. The likelihood for recovery appeared to be, however, unaffected by the duration of the disease.

Steinsiek (1950) reported on 502 autopsies of institutionalized patients who had died between 1933 and the first half of 1948. The mean age at time of death was 39.6 years. For patients with symptomatic seizure disorders he reported the mean age of death as 31.3 years. Compared with Munson's figure of 1910, approximately one decade had been added to the life span of the institutionalized epileptic during these thirty years. But the observation that patients with symptomatic seizure disorders still died at a mean age of 31.3 years suggests that this group had not derived as much benefit from the more modern treatment methods as the group of epileptics without overt cause. The autopsy results of Steinsiek subsequently dealt only with "genuine epilepsy," not with symptomatic cases. A definition of genu-

ine epilepsy was not given in his paper, but it is obvious from the autopsy findings that cases with overt cerebral disease had been excluded. He felt that 53 per cent of all deaths in his group were related to epilepsy. He listed these causes as follows: (1) abiotrophy with epilepsy ("Lebensinsuffizienz bei Epilepsie"), 140 cases (27.9%); (2) status epilepticus, forty-one cases (8.2%); (3) seizure, twenty cases (4%); (4) injury during seizure, twenty-three cases (4.6%); (5) suffocation during seizure, five cases (1%); (6) diseases of the respiratory system in connection with epilepsy, thirty-seven cases (7.5%). The main feature of the first group called abiotrophy was the absence of a definitive disease of any organ which could be regarded as a cause of death. Major disorders of internal organs could be excluded by autopsy, and for this reason Steinsiek assumed a central regulatory collapse, a premature wearing out ("Verbrauchtsein") of the brain. He felt that the process could be compared with debility of old age, but it occurred in these patients years, or decades, earlier and was limited to the brain. He separated the 140 cases called abiotrophy into acute and chronic. Of the 112 chronic cases, sixty-one (54.4%) had no demonstrable organic pathology; fifty-one (45.5%) had pathology which was regarded as incidental rather than etiologic. These were, for the most part, bronchopneumonias which *resulted* from the process of dying rather than being the primary *cause* of death. In the twenty-eight cases of acute abiotrophy no pathology was found in seven (25%) and incidental pathology in twenty-one (75%). The mean age of patients dying from abiotrophy was 40.3 years.

Epileptic seizures were the cause of death in eighty-nine (17.7%) cases (status, isolated seizure, injury or suffocation due to seizure); seventy-one (80%) of these died within the ages of ten and forty years. These patients were, therefore, younger than the previously mentioned group. In eighty-one patients (16.1%) disease of the respiratory system (excluding tuberculosis) was found to have been the cause of death. Approximately half of these forty-one were felt to have been related to the basic illness, and the diagnoses were listed as follows: aspiration gangrene, aspiration pneumonia, empyema after aspiration pneumonia, bronchopneumonia after status epilepticus. In the other forty

cases where death was not attributed to epilepsy, the diagnoses were these: lobar pneumonia, bronchopneumonia, and bronchiectasis with abscess. More than half (60.6%) of his total group of patients had died between the ages of ten and forty years.

Pigott *et al.* (1939), in a review of patients seen at the New Jersey State Village for Epileptics, noted that the average age at time of death was 38.8 years.

On the basis of his extensive follow-up study in Sweden, Alstroem (1950) concluded that a statistically significant excess mortality occurred in epileptic patients who had shown mental changes regardless of the etiology of the seizure disorder. However, patients who fell into the group of unknown etiology and who were mentally unaffected showed on the whole a mortality that was in agreement with that of the general population. Alstroem's findings are frequently referred to as evidence that "idiopathic epilepsy" has a good prognosis and shows no excess mortality. It is worthwhile emphasizing and repeating here that only those cases of epilepsy with unknown cause that *did not* have mental changes were found to have a good prognosis in this respect. When mental changes were present in the patient, the prognosis was poorer, regardless of presumed etiology of the condition. A lower age at time of death was also noted by Arieff (1951), who found that out of seventeen patients who had died, twelve were under the age of fifty years: ". . . which is rather young considering life expectancy."

Lennox (1960) felt: "A somewhat higher mortality for epileptics than for the general population is a reasonable expectation, but great variability exists. Factors increasing the chances of death are brain injuries that either antedate or are a consequence of seizures; severe grand mal that comes without warning, especially if interspersed with status epilepticus; abuse of alcohol or of driving privileges; low mentality; inadequate or ineffectual therapy, and disregard of sensible precautions, as in swimming alone in deep water." The causes of death of 118 patients seen by Lennox personally were given as follows: direct result of seizures (status epilepticus-10), twenty-nine cases (25%); result of complications from treatment, twenty-four cases (12%); accident (drowning-9), fourteen cases (12%); brain tumor, twelve cases

(10%); suicide, eleven cases (9%); cardiac or respiratory disorders, seventeen cases (14%); miscellaneous conditions, twenty-one cases (18%). Lennox added that many of these assignments were suppositional because most of the deaths occurred at a distance and autopsy was carried out in only a few instances. He did not give the ages at which death occurred in his patients.

Lennox's book also contains extensive references to mortality statistics which need not be repeated here but should be consulted by the interested reader. In my own opinion, the complexities involved in comparing census data from the general population against figures obtained from epileptic patients are such that the results which are obtained are of limited value only, and lend themselves to any interpretation that one might want to give. As an example of these difficulties, one might point to Schwade and Otto's study (1954), which is at times quoted as evidence that the epileptic patient has a mortality risk no greater than the average person. It was therefore of interest to examine this investigation in more detail. It is actually reported in the form of a letter to the editor of the *Journal of the American Medical Association*, and the conclusion quoted in its entirety reads: "The study and analysis made here support the thesis that the epileptic, under adequate medical control with patient and critical guidance and understanding of his problem, is substantially a mortality risk no greater than the average normal person." One can readily note that there are several qualifying phrases contained in this statement, the most important is "under adequate medical control." This is, of course, the heart of the problem; if the patient has no seizures because his condition is controlled by medication, he is not likely to die from epilepsy. Also, an implicit assumption is that control can be achieved in most instances; but as we have seen in the previous chapters, this is unfortunately not the case. Schwade and Otto's conclusions were based on a review of death certificates supplied by the Wisconsin State Board of Health for the year 1953. As far as the State of Wisconsin was concerned, seventy patients had died of epilepsy which constituted 0.2 per cent of the death total in the state during that year. Schwade and Otto reexamined the death certificates and eliminated forty-four cases as being inade-

quately documented. They found thereby that the death toll due to epilepsy itself was actually less than one per 1,000. Their study assumes, however, that the presence of epilepsy was known to all physicians who were responsible for signing the death certificates during the year 1953 in Wisconsin. It appears quite possible that a number of accidental deaths, especially drownings, might have been due to a seizure disorder which was unknown to the physician who had to sign the certificate, and for the forty-four patients that were subtracted by Schwade and Otto, there could be an equal number who might actually have to be added because they are contained in other categories. Therefore, it appears quite unlikely that completely accurate data will ever become available through the study of death certificates alone. Their letter contains also the interesting comment: "Accidental deaths, the result of falling from a relatively high place or of drowning, are noted here as unnecessary if the patient had been advised to avoid high places and swimming. When death occurs during the course of a seizure with resultant falling from a height or while swimming, the reporting of such a death makes it mandatory to include such incidents. We feel this small group could be removed from statistical data if patients were adequately advised." Although such advice is easy to give, it is exceedingly difficult for the patient to follow, and it should be reemphasized that drowning accidents especially are probably quite unavoidable in a number of instances. Gowers' warning bears repeating in this context, ". . . epileptics are sometimes drowned in a very small depth of water, as in a ditch." The ordidinary bathtub contains enough water in which a patient can drown. If one were to try to eliminate all the potential risks to life, one would have to seriously curtail quite a number of regular everyday activities, and appoint, in addition, a permanent twenty-four-hour guardian over the patient. This is obviously unreasonable and would bring only a life of misery, which the patient might want to end by suicide. A further point in their letter bears commenting upon: "When death resulted from the direct or accidental consequence of seizures, we feel it is probable either that no medical treatment was available or that treatment of the seizures was inadequate to control them." This

apparently assumes also that status epilepticus is avoidable and death from status is due to poor management of the patient.

Hunter published a detailed review on the problem of status epilepticus in 1959/1960, and noted that instead of having decreased as a result of anticonvulsant medications, it seems actually to be more common now than in the early nineteenth century. On the basis of death certificates obtained through the Registrar General's office for England and Wales, Hunter compared the incidence of status epilepticus for the years 1949 through 1956. In these years between 37.8 and 50.8 per cent of all patients, where epilepsy had been recorded on the death certificate, had died from status epilepticus. He pointed out, also, that about one-quarter of the total number of deaths from epilepsy, including status, occurred in institutionalized patients. He feels that this is important because ". . . most epileptics in institutions may be expected to be receiving supervised regular anticonvulsant medication which is not necessarily the case in epileptics treated as out-patients or those who do not report at all." Hunter's study would suggest that status and resultant death is not avoidable in all instances.

Pond *et al.* tried to make a further contribution to the problem of mortality of epileptic patients in 1960. Inasmuch as most studies that have been reported in the literature dealt either with institutionalized patients or with the experience of one investigator, the English group decided to study epileptic patients from fourteen general practices scattered over southeastern England. The purpose of the study was to estimate the prevalence of epilepsy within the general population and to assess the characteristics and problems of the epileptics so discovered. During the year of survey twelve out of 245 patients died. This represented a mortality rate of forty-nine per 1,000, which was regarded as more than four times as high as in the general population of England and Wales. Impressive as this may seem, the figure is actually of limited value because eight patients were over sixty years of age. Of these, four died of carcinoma, two of cerebral hemorrhage, one of cerebral abscess, and one of dementia. Of the four patients under sixty years, one died of heart failure, one of polyarteritis nodosa, and the other two died in epileptic seizures. Of these two

deaths, one was regarded as having definitely been due to a seizure; the other was not observed, but it was stated that the patient had choked on his food and died.

Krohn (1963) noted the discrepancies that exist in the literature on the topic of mortality and reviewed all cases of death in epileptic patients that had come to his attention during a ten-year period. He recognized the problem that the mortality of institutionalized patients will differ considerably from the mortality of patients living in the community, and that one is not dealing with a pathological entity but a series of different diseases with different prognosis and mortality. His report was based on 107 patients whose diagnosis of epilepsy had been established beyond reasonable doubt. Krohn stated that some of the patients had died at the Norwegian State Hospital for Epileptics, some at the University Clinic in Oslo, and some in other hospitals. Some deaths were known only through reports from colleagues, from the families of the patients, or from newspaper announcements. No figures were provided to show the relative distribution of patients from the various sources. It was found that bronchopneumonia, thirty patients (28%); sudden death, fourteen patients (13%); and drowning, eleven patients (10%) comprised fifty-five cases, or more than one-half of the whole material. The other causes of death were listed as brain tumor, ten patients (9%); cardiovascular disease, seven patients (6%); status epilepticus, six patients (6%); degenerative CNS disorder, four patients (4%); accidents other than drowning, three patients (3%); suicide, three patients (3%); encephalitis, three patients (3%); agitation with collapse, two patients (2%); rupture of aneurysm, two patients (2%); cancer, tuberculosis, diabetes, five patients (5%); and unknown, seven patients (6%). Krohn thought that the group labeled bronchopneumonia consisted of patients ". . . who in reality can be said to have died from their epilepsy. They are patients with numerous and uncontrollable seizures, in poor general condition and with marked physical and psychical deterioration. The bronchopneumonia in itself is only the final stop, these patients do not die because of a bronchopneumonia, they get a bronchopneumonia because they are dying. The course is fulminant, and it does not respond to

treatment." Therefore, Krohn expressed independently essentially the same concept that had been postulated by Steinsiek. As far as mean age of death was concerned, it was found to have been 43.2 years in the patients who died from bronchopneumonia. Although death occurred in all age groups, few patients became really old, and more than half were under forty years at time of death. The mean duration of illness was 26.4 years. For the group of "sudden death" the mean age was 32.8 years and the mean duration of the illness was 16.7 years. The patients who drowned had a mean age of 20.5 years and a mean duration of illness of 13.8 years. The group of sudden death is of special interest because it points out that Munson's report of 1910 can still be read with great profit today. It is obvious that some patients with epilepsy die suddenly, and this eventuality has to be reckoned with. Autopsies of seven of the fourteen cases of sudden death were quite unrevealing. Krohn concluded that ". . . patients with a continuing heavy uncontrollable epilepsy die at a relatively early age . . . they show complications which are otherwise mostly found in senility." This is also the same concept as Steinsiek's, in regard to "epileptic abiotrophy," but was arrived at independently by Krohn (personal communication). Inasmuch as Krohn's data were obtained approximately half a century after those of Munson, a comparison could reflect the progress that has been achieved during that time. If we equate "bronchopneumonia" with the pneumonias of Munson, we find that they occurred in 28 per cent of Krohn's, and 24 per cent of Munson's sample. Sudden death occurred in 13 per cent of Krohn's patients, and in 17 per cent of Munson's patients. Fatal status epilepticus occurred in 5 per cent of Krohn's, and 10.1 per cent of Munson's population. The fact that bronchopneumonia in a relatively young population is listed as cause of death, in approximately the same proportion in 1910 as in 1963, reveals that antibiotics have not been of appreciable help for this condition. It strengthens the opinion that these bronchopneumonias are really terminal events rather than the cause of death.

A shortening of the life span of the patient with cryptogenic epilepsy also was noted by Peiffer (1963), who investigated autopsy results on 362 patients. The age at time of death showed

a sharp peak around thirty-five years, which is markedly lower than in the general population. The average duration of illness was found to have been 20.7 years. The duration of the illness showed some relationship to the frequency of occurrence of attacks. With daily seizures, the interval between first attack and death was 16 years; in cases of weekly attacks, it was twenty-three years; in cases of more infrequent attacks, twenty years.

The studies referred to so far have dealt, for the most part, with adult patients (with exception of those by Bridge and Lennox). Keith (1963) had the opportunity to follow 530 children who had been seen at the Mayo Clinic between 1922 and 1944. Thirty-four children had died (6.23%); causes of death were given as follows: unknown, thirteen (39.39%); accidents (drowning—4), seven (21.21%); status epilepticus, four (12.12%); diabetes, one (3.03%); brain tumor, one (3.03%); encephalitis, two (6.06%), and other unrelated disease, six (18.18%). Keith subsequently investigated children who had been under the age of three years at the time of first examination for convulsions, and who were seen at the Mayo Clinic between 1950 and 1954. Seventy-four children were personally reexamined and on 318 information was available through questionnaires. Of these 392 children, seventy had died (17.8%); in forty there were no reports on the cause of death. The causes were listed in the other thirty as: pneumonia, eight (26.6%); "died in convulsions," six (20%); strangulation or suffocation, three (10%); tuberous sclerosis, two (6.6%). The following conditions were listed as having occurred once: renal failure, ulcers of the colon, fever and dehydration, acute laryngitis, meningitis, influenza, "old brain injury," feeding, cardiac arrest and hypoplastic heart (phenylketonuria), brain tumor, and "degeneration of cerebrum and cerebellum." When Keith examined his material further, he found that of fifty-six children who started with convulsive seizures during the first month of life, eighteen had died (32.1%). With the exception of two patients all had demonstrable cerebral pathology. He concluded that one-fourth to one-third of the infants who have neonatal convulsions will die within a few months or years. Burke (1954) reported a detailed study on the prognostic significance of neonatal convulsions, and

found that out of forty-six children who had convulsions or muscular twitching in the neonatal period, eighteen (39%) died within the first thirteen days of life. The overwhelming majority of her children had convulsions on the first or second day of life, and only one child convulsed as late as nine days after delivery.

Farmer's textbook (1964), *Pediatric Neurology*, states that ". . . in spite of vigorous efforts to control seizures with anticonvulsant drugs, approximately 5 per cent of children in status epilepticus will die. In addition, occasional unexplained deaths in children with seizures may be the result of severe anoxia during a prolonged seizure."

The most recent contribution to the problem of mortality was made by Henriksen *et al.* in 1966. Their study, although reported so far in preliminary form only, is important because it deals with a relatively large number of patients who had not been institutionalized, were seen in a university setting, had received optimal treatment with all the modern anticonvulsants, and were, for the most part, personally examined by one of the authors. The material was representative for an epileptic population, but known brain tumors and vascular malformations had been excluded. Dealing with noninstitutionalized patients only, the most severe forms of epilepsy also were not represented. The sample was drawn from 3,325 patients who had been seen between 1950 to 1964. Compared with data from the Life and Reinsurance Company DANA, the ratio of observed to expected deaths was 293 per cent. The ratio was found to have been the highest during the second and third decade, 413 per cent and 558 per cent, respectively. Mortality was found to have been higher for men than for women (370% versus 216%). Alstroem's observation that only those patients who had mental changes died earlier was not borne out in this study. The ratio showed no marked difference when all mentally abnormal patients and all patients with symptomatic epilepsy were excluded (273%). Severity of epilepsy was found to have been important. Considering only cases who were mentally normal, who had no exogenous etiology, and relatively infrequent seizures, the ratio was found to have been 200 per cent. The lowest ratio was observed in patients with nonexogenous epilepsy, pure grand mal with no men-

tal changes and no, or very infrequent, seizures during treatment. This group was, however, too small to allow tests for statistical evaluation. Focal or paroxysmal EEG abnormalities showed no relationship to mortality. The causes of death were given on the death certificates as these: epilepsy, 26 per cent (including status and patients found dead after a seizure); suicide, 20 per cent; accidents, 11 per cent; brain tumor, 8 per cent (the neoplasms of these patients had escaped neurological detection during their lifetime), and other "normal causes of death," 36 per cent.

The average age at time of death was found to have been between thirty to forty-five years. The authors stated that the study will be continued on a larger group of patients with longer follow-up. Inasmuch as life expectancy is obviously an important question, not only on general principles but also for the specific reason of establishing equitable life insurance rates for epileptic patients, the Danish study deserves to be followed closely.

What should we then conclude about the life expectancy of patients with epileptic seizures? Table 26 provides a summary of some of the figures obtained for age at time of death. It appears to be quite obvious that the life expectancy of the epileptic in-

TABLE 26

PREDOMINANT AGE (IN YEARS) AT TIME OF DEATH AS GIVEN BY VARIOUS AUTHORS

Habermaas, 1901		25
Spratling*		29.4
Munson, 1910		30.08
Citronblatt, 1910**		20–49
Ammann, 1912**		15–55
Joedicke, 1913**		30–40
Muskens, 1928		25–30
Steinsiek, 1950	All cases	30.6
	Symptomatic cases only	31.3
Krolin, 1963	Cause of death:	
	Bronchopneumonia	43
	"sudden death"	32.8
	Drowning	20.5
Peiffer, 1963		35
Henriksen *et al.*, 1966		30–45

* Quoted by Turner, 1907

** Quoted by Gruhle, 1924

dividual does not reach that of the average person. It is also quite impressive that the figures have not shown a dramatic improvement during the past five decades. Although death as a direct result of a seizure is relatively rare, it does occur on occasion and is not preventable under all circumstances at the present time. However, it should be emphasized that in view of the variability of life expectancy, general statements covering all epileptics are likely to be an oversimplification. Life insurance companies might be well advised to take this variability into account. The question of whether or not a patient should receive life insurance and at what rate, should not depend simply upon the presence or absence of epilepsy, but rather upon the intensity of the condition in the particular patient who applies for insurance. It would be fair neither to patients nor to insurance companies if individuals who have one to two grand mal seizures per year and no other difficulties were to be regarded for insurance purposes the same way as patients who have had a history of several episodes of status epilepticus and who continue to have seizures several times a month in spite of adequate amounts of medication. More information on this question will become available soon, as a result of the Danish study.

PART TWO

PERSONAL INVESTIGATIONS

Chapter 10

INTRODUCTION

Having reviewed the literature, it became readily apparent that there are various opinions not only about the results that should be achieved with anticonvulsant medications, but also about good versus bad prognostic indices. The literature usually presents the data in form of percentage figures, and information in regard to the statistical significance of the observed findings is, with some notable exceptions, frequently lacking.

We know now from Tables 1 and 5 that approximately 30 per cent of all patients are likely to have a complete remission for at least two years. This percentage tends to rise to 50 per cent if one deals only with grand mal seizures uncomplicated by additional minor seizures. This still leaves considerable room for speculation. Why should approximately only every other patient with grand mal have a good result? Are there any features in the past history or examination of the patient that could give us clues for predicting who will in all probability have a good result as opposed to a mediocre or poor one? Hopefully, this prediction should be possible at the time of the first visit to the specialist. It should not be based on clinical intuition—which varies from observer to observer—but on a formula that is derived from statistical processing of actual follow-up results. Theoretically, one would like to be able to predict, at the time of the first visit, the result of treatment in regard to five different areas:

1. Will it be possible to stop the seizures?
2. Will the patient's social behavior deteriorate?
3. Will there be learning difficulties in school or intellectual deterioration later on?
4. Will the patient be able to earn a living for himself or will he remain dependent upon others?

5. Will the condition be of such malignancy that institutionalization is likely to become necessary in the future?

Satisfactory formulas for answering each of these five questions are not available at the present time. It was therefore decided to see whether computer technology could be of help in arriving at some of the missing answers.

The data that will be presented in the following sections of this book deal with efforts towards finding such formulas and cover a span of somewhat more than eight years. A considerable number of different studies were carried out and a vast amount of data was accumulated. The use of a computer was therefore essential. Although data reduction is the goal of utilizing computer technology, the path to this goal leads through an abundance of material and the investigator is frequently confronted with what Miller (1965) has aptly called "information input overload." To present the essential information from studies of this type in a logical, coherent, and nonredundant manner becomes a major problem. I will attempt to solve this by outlining first in historical perspective the various projects that were performed and their rationale but omitting the results. These will be taken up in separate chapters dealing with prognosis for seizure control, prognosis for behavior, and prognosis for intellectual functions. There will also be some data presented in regard to employment, factors leading to institutionalization, and some figures on mortality. The bulk of the material will, however, deal with prognosis for seizure control.

Seizures are of course the nuclear phenomenon of epilepsy. As far as prognosis about the condition is concerned, a reasonably accurate prediction of whether or not a patient is likely to be controllable by our current anticonvulsant drugs is the most important. If the seizures can be controlled by average (and not inordinate) amounts of medication, the patient's life is likely to follow much more normal channels than if he has to settle down to the existence of a "chronic epileptic" with its physical and social consequences.

The basic method employed in all the studies that will be reported consisted of the following:

1. Detailed coding of the patient's history, neurological

findings, psychiatric observations, EEG reports and psychological test results.

2. Obtaining the distributions for the frequency of occurrence of each variable that had been coded (over 1,000).

3. Subjecting those variables that had a sufficient frequency of occurrence in the sample to a variety of statistical procedures.

4. Whenever possible, cross-validating the results on another sample of patients.

The first study was performed in 1960, and dealt with a follow-up of thirty-two children seen at least five years earlier at the Michigan Epilepsy Center (MEC). Its purpose was to gather preliminary data that would allow a testing of the coding system, as well as our approach to data analysis. Having shown that the coding system and the data processing could give meaningful results, we found it necessary to check the results on a larger sample. The second project was therefore initiated in 1961 and dealt with ninety patients who were reexamined at least five years after their initial visit to MEC.

Inasmuch as one was dealing in both of these studies with outpatients who may or may not have received optimal treatment it was necessary to check these results against those that can be obtained on the basis of outpatient treatment by specialists. The treatment results of 123 patients who had regularly attended the neurology outpatient service of the Lafayette Clinic were therefore reviewed in 1966 (third project). If an outpatient does not achieve a good treatment result, the physician can never be certain whether the patient is taking his medication as prescribed and drug treatment is ineffective, or whether the patient is inconsistent in his medication habits in spite of his protestations to the contrary. For this reason, the fourth project was initiated in 1966. It consisted of a review of the treatment results of epileptic patients who had been admitted to the neurology inpatient service of the Lafayette Clinic. Two hundred forty-five patients were involved in this study.

In all of these studies, the coding of the patients' findings including their electroencephalograms was carried out either by

myself alone or in conjunction with residents or medical students. This raised the question of whether the results could be duplicated by another neurologist without interference by myself. By January, 1967, information was available on 230 patients who had been seen and coded by Doctor Salvador Gonzalez at the MEC as part of a project dealing with employability of epileptic patients. The application of the findings from this study to the previous findings from the MEC and Lafayette Clinic constituted the fifth project. The total number of patients seen in these five studies would theoretically amount to 720, but there is overlap, especially between the Lafayette Clinic inpatient and outpatient group, and there is some minor overlap between the Lafayette Clinic group and the patients seen by Doctor Gonzalez as part of the employment project. Nevertheless, one deals definitely with more than 500 individual patients who form the basis for the chapter on seizure prognosis.

The results in regard to prognosis for employment will not be gone into in considerable detail here because the material is still in partial process of data analysis and it will merit extended discussion of its own. These data will be presented only in regard to the major conclusions. The results in regard to behavior and intellectual functions are based only on patients seen as part of the second follow-up study (1961). They will show the trends that emerged from the study, but another sample of patients will be needed before definitive conclusions can be reached. The Michigan Epilepsy Center has recently received a grant from the U.S. Public Health Service to study cognitive functions in epileptic patients and more data should become available on this topic in the next three years. One could have chosen to omit the presentation of these preliminary results obtained at the follow-up studies but the reason for their publication is to demonstrate the complexity of the issue and to provide a stimulus for more research in this important area.