THE PROGNOSIS OF PATIENTS WITH EPILEPSY

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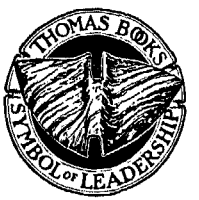

CHARLES C THOMAS • PUBLISHER

Springfield • Illinois • U.S.A.

Published and Distributed Throughout the World by
CHARLES C THOMAS • PUBLISHER
BANNERSTONE HOUSE
301-327 East Lawrence Avenue, Springfield, Illinois, U.S.A.
NATCHEZ PLANTATION HOUSE
735 North Atlantic Boulevard, Fort Lauderdale, Florida, U.S.A.

Library of Congress Catalog Card Number: 68-29685

Printed in the United States of America
BB-14

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FOREWORD

When I was asked to write this book, I had initially considerable doubts whether the topic would indeed merit extended discussion. My misgivings were based, in part, on the currently accepted view that epilepsy is not a disease but a symptom of a variety of different illnesses. They were also related to the feeling that seizure control should no longer be a great problem in the majority of patients, if they receive expert medical management.

If epilepsy is only a symptom, the prognosis would obviously depend upon the course of the basic illness, and to write a book on the prognosis of a symptom would be anachronistic to say the least. In regard to treatment, new anticonvulsants are steadily produced, and one gains the feeling that any results that are reported may soon be hopelessly outdated.

The reason for accepting the task, in spite of these considerations, lay in the opportunity to review the actual progress that has been made in the medical and surgical treatment of seizure patients and to delineate the characteristics of patients who respond to treatment as opposed to those in whom treatment results are, at present, unsatisfactory. The third, and possibly most important aspect was the hope that one might find some clues about pathophysiologic mechanisms underlying this disorder. Prognosis obviously means prediction. If we can predict accurately the course of a given patient's illness and the factors that will influence it, we may be a step closer in the understanding of the condition. The book presents, therefore, a statement of where we stand today in our concepts about this ancient disorder, the achievements that have been accomplished during the

past six to eight decades, and it also points out the areas where progress has been lacking.

The personal investigations that are reported here mark a departure from classic scientific methodology. Traditionally one forms a hypothesis on the basis of existing data and subsequently puts it to the test. I have purposely refrained from making any hypotheses in order to proceed in as unbiased a fashion as possible. The various steps in the data collection and workup resulted primarily from statistical considerations, rather than from the intention to prove or disprove a given point. The statistically significant results of each step of the investigations dictated the further course of data workup, Although these studies dealt only with seizure patients, the methodology can, of course, be applied to any other condition one may wish to study and is likely to become increasingly useful for medical research in the future.

In contrast to other publications which emphasize that epilepsy is the "hopeful disease," this book will concentrate on those areas where current results are unsatisfactory. This is not due to an inherent pessimism of the author but results from the conviction that a realistic rather than an optimistic outlook is called for. Baseless optimism can seriously hinder future medical research because the problem that is to be investigated does not attract its proper attention as a result of wishful thinking. Hope has always and will always be with us, and a paragraph such as the following reads strangely modern: ". . . and the present generation has witnessed an advance in the treatment of these diseases equalled in perhaps no other branch of therapeutics. Thanks to the influence of one drug and its combinations, hundreds of epileptics have been cured, and thousands are leading useful lives who would otherwise have been incapacitated by the disease. Although the condition of many sufferers is still gloomy enough, it is not without hope, and to them also, we may surely trust, the progress of the recent past is the dawn of a brighter day."

The "drug and its combination" is not Dilantin,® but salts of bromide, and the words were written by Gowers around 1880. All of us who have been treating chronic seizure patients in the

1960's will be aware of cases whose condition "is still gloomy enough." By pointing out the areas where our efforts have not been very successful, it is hoped that more interest may be stimulated in regard to this fascinating disorder of the central nervous system and that this will eventually lead to the eradication of the condition. As has been mentioned previously, the results of the studies presented here may soon be obsolete, but if some of the ideas and suggestions that are contained in the following pages can contribute to their obsolescence this book will have served its purpose.

ACKNOWLEDGMENTS

A book of this type is obviously not the work of one person, and I am indebted to a number of people for their continued help.

For the statistical procedures I am grateful to Doctor J. Grisell, head of the Computing Laboratory of the Lafayette Clinic, and his able assistants: Mr. R. Gudobba, Mrs. P. Levin, Mrs. R. Bendiner, Miss K. Lennox, and Mr. J. Porzak. They have worked with me step by step and I am most happy to gratefully acknowledge their efforts. I would also like to express my thanks to the staff of the Neurology Division of the Lafayette Clinic, especially nurses and attendants. They have made it possible to take care of some severely regressed—and sometimes psychotic —patients who had been living for years behind closed doors in various state hospitals. These patients had to be integrated on an open ward with other patients from the community who had a variety of different neurological illnesses. This was a major accomplishment for which the staff deserves full credit. Special thanks are also due to my EEG technicians, Mrs. E. Davenport and Mrs. B. Brown, who have been exceedingly helpful by obtaining top quality records from some very severely disturbed patients, and who were always willing to schedule an extra patient at a moment's notice whenever I felt that a special study would be helpful at that particular time.

The manuscript itself, however, could not have come about without the unceasing efforts of the staff of the Michigan Epilepsy Center under the direction of Doctor R. D. Dennerll, and its office manager, Miss J. A. Cheek. The librarians, Mrs. M. Hagstrom and Mrs. C. Perliss, kept procuring literature from

numerous sources; the EEG technicians, Mrs. P. Scerpella and Mrs. B. Pachucki, were not only instrumental in recording the patients involved in the follow-up studies and the VRA Project, but also helped in collation of EEG data. A special vote of thanks is due to Miss J. Smith who worked long and hard in typing, retyping, and typing again the manuscript, assembling the bibliography and proofreading part of the material with other members of the staff. For typing the major portions of the final copy, I am grateful to Mrs. E. Lessnau. The final proofreading was accomplished with the dedicated help of Mrs. M. M. Bryan and Mrs. C. Perliss.

I would also like to thank Mr. A. E. Hearron, Jr., of the Health Statistics and Evaluation Center of the Michigan Department of Public Health, for sending me the data on the patients who had died. Doctor W. Dickerson, Superintendent of Caro State Hospital (now retired), was most cooperative in arranging transfers of his patients to the Lafayette Clinic, and it was a pleasure to have had the opportunity to work with him. To Doctor V. Samuel, I am grateful for his help in arranging the transfer of patients from Pontiac State Hospital, and to Doctor C. Chen, for sending us some of his patients from Northville State Hospital.

It is also a pleasure to thank Doctor J. Gottlieb, Director of the Lafayette Clinic, for allowing me complete freedom of action in the pursuit of these investigations. Doctor R. D. Dennerll, Director of the Michigan Epilepsy Center, has been most helpful in sponsoring the follow-up projects and by putting all the resources of the Center at my disposal in the preparation of the manuscript. I am grateful to him also for reviewing the manuscript, and making valuable suggestions. Doctor J. Grisell, and my wife, Doctor M. Rodin, were likewise drafted into the process of manuscript review and I am happy to acknowledge their help.

While numerous people collaborated in data collection, data workup, presentation of results, and preparation of the manuscript, the fact that this book was written at all is due to the initiative of one person only, Mr. Payne Thomas of Charles C Thomas, Publisher. He suggested that I consider writing a de-

tailed exposition of the problem after I had presented some of the data of the follow-up studies at the Pan-American Medical Society meeting in May, 1965. It was indeed a pleasure having had the opportunity of working with him and his staff.

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PART ONE
REVIEW OF THE LITERATURE

Chapter 1

RESULTS OF FOLLOW-UP STUDIES AND GENERAL PROGNOSTIC CRITERIA

A statement that is frequently quoted to the lay public as well as to the medical profession is as follows: "With current medical therapy approximately 80 to 85 per cent of all cases can be controlled" (Forster, 1960), or "Treatment of epilepsy with anticonvulsants results in control of seizures in approximately 80 per cent of the cases" (Fabing and Barrow, 1954). This would suggest that seizure control is a problem in only a small minority of patients. It is apparent, however, that the statements contain nothing in regard to what constitutes "control" of seizures. When one reviews the literature and stipulates that a minimum of one year must have elapsed without the occurrence of a seizure before the patient is placed in the "controlled" group, one obtains a somewhat different impression. Results of studies spanning more than sixty years are shown in Table 1. Only those studies were included where patients had been followed for at least one year. It can be seen that the highest percentage of complete freedom from seizures for a two-year period prior to last examination of the patient was obtained by Trolle, 1961, and it is only 37 per cent. It is apparent, therefore, that approximately two-thirds of all patients with epilepsy are likely to have a chronic seizure disorder in spite of modern medical treatment. Surprisingly enough one can also see that modern drugs have not brought about a substantial change in long-term remission rates. Turner, with bromide medication in 1907, achieved seizure control for a two-year period in 33 per cent of his patients. If one were to doubt Turner's figures as to the efficacy of bromide medication, we can

point to Stone and Arieff, who reported in 1940 that they brought about remissions as a result of bromide treatment in 78 per cent of ninety-eight patients treated at the Epilepsy Clinic of Northwestern University School of Medicine. Attacks were stopped from the beginning of treatment in 38 per cent of patients and remissions ranged from six months to eight years. A remission of at least six months prior to last visit occurred in 48 per cent of their patients. By 1951, Arieff reported even higher six-month

TABLE 1

PERCENTAGES OF TERMINAL REMISSIONS GIVEN IN THE LITERATURE FOR ADULTS WITH EPILEPSY

	Minimum Duration of Terminal Remission (in years)	*Percentages of Patients Remitted*	*Number of Patients Examined*
Habermaas, 1901	2	10.3	937
Turner, 1907	2	32.0*	87
		33.6**	125
Grosz, 1930	10	10.99	91
Kirstein, 1942	3	21.8	174
Alstroem, 1950	5	22.0*** (approximately)	897
Kiorboe *et al.* 1958 (Short duration, onset after age 17 years)	4	32	130
Strobos, 1959	1	38	228
Probst, 1960	2	31	83
Trolle, 1961	2	37	799
Juul-Jensen, 1963	2	32.1	969
Lorgé, 1964	2	34	177

* Positive family history for epilepsy

** Negative family history for epilepsy

*** Group U 29.2%, Group P 22.7%, Group K 14.2%

Note: Studies containing follow-up of less than 1 year were omitted.

remission rates; 83 per cent of 140 patients treated only with bromides, and 80 per cent of ninety-one patients treated by phenobarbital only. Total remission rate, regardless of drug used, was given as 68 per cent. These figures are presented merely to point out the problem one is confronted with when evaluating the effectiveness of new anticonvulsant medications; length of follow-up of the patient is the all-important variable.

But let us return to the quotation that "80 to 85 per cent of all patients with epilepsy can be controlled." Where did these figures originate? They are probably taken from a paper published in 1952 by Yahr *et al.* who stated in their summary that "The use of diphenylhydantoin (Dilantin) sodium and phenobarbital in this group of 319 patients resulted in 79 per cent control or improvement of seizures regardless of causation. The addition of other anticonvulsants added 6 per cent, giving an overall rate of 85 per cent improvement or control." The attentive reader will note immediately that there is an important qualification in this statement. The authors did not talk about control only, but also about improvement. When we examine the breakdown of the 85 per cent figure, we find 48 per cent completely controlled and 37 per cent improved. When we look for the duration of complete control we find the criterion "complete absence of seizures for periods varying from less than six months to five and one-half years." The paper does not contain a breakdown in regard to the number of patients who were seizure-free for less than six months as opposed to the number of patients who were free from seizures for several years. Inasmuch as the group apparently contains a number of patients whose follow-up period was relatively short, an overall figure of 48 per cent control is not surprising. It agrees, as a matter of fact, with Stone and Arieff's bromide treatment results.

The fact that control of seizures is inversely related to the period of follow-up is important to remember and can be demonstrated whenever follow-up data spanning several years are available. One of the clearest demonstrations of this phenomenon is recorded by Bridge, 1949, and his figures are reproduced in Table 2.

Long-term follow-up studies are quite difficult to perform, especially in the United States due to the mobility of its population, but Alstroem (1950) had the opportunity to examine 897 epileptic patients during the years of 1945 to 1950 who had been originally diagnosed during the period of 1925 to 1940. He divided the total group into three subgroups, depending on presumed etiology of seizures. One group, U, consisted of patients where the etiology of seizures was unknown; in the second group,

TABLE 2

DURATION OF THE PERIOD FREE FROM SEIZURES AT TIME OF FOLLOW-UP STUDY ON 472 EPILEPTIC CHILDREN AS GIVEN BY BRIDGE, 1949*

Period of Freedom	*Number of Cases*		*Per cent*	
5 years or more	81		17	
4 years or more	101		21	
3 years or more	134		28	
2 years or more	161		34	
1 year or more	187		40	
6 months or more	218		46	
1 month or more	264	264	56	56
All others living		147		31
Dead		45		10
Unknown		16		3
Total		472		100

* From *Epilepsy and Convulsive Disorders in Children* by E. M. Bridge. Copyright McGraw-Hill Book Company, Inc., New York, 1949. Used by permission of McGraw-Hill Book Company, Inc.

P, etiology was probably known, and in group three, K, etiology was known. Percentages of recovery were calculated separately for males and females in these groups. A +3 result referred to freedom from seizures for five years or more; and a +2, freedom from seizures for at least three years or an appreciable decrease in the frequency or severity of seizures. Patients who had not changed or who had shown only slight improvement or deterioration were placed in a ± category, while patients who had shown a considerable and distinct exacerbation of seizures were classified as −2 or −3. Table 3 is a reproduction of Alstroem's Table 6. If we concentrate on the +3 group (i.e. freedom from seizures for five years) and calculate the percentage for the total group, we arrive at a figure of approximately 22 per cent.

Alstroem proceeded, subsequently, to calculate the probability of an epileptic becoming seizure-free at varying intervals after the manifestation of the disease. He found considerable differences between patients who showed mental changes and those who were mentally unaffected. He observed that within five years after the onset of the illness approximately 20 per cent of the mentally healthy patients had recovered. The correspond-

TABLE 3

PERCENTUAL DISTRIBUTION OF FOLLOW-UP RESULTS BY ALSTROEM, 1950*

		U (unknown)			*P (probable)*			*K (known)*		
	Seizure Prognosis	M	F	M + F	M	F	M + F	M	F	M + F
+3	Freedom from seizures for five years or more	29.7	28.7	29.2	25.0	19.0	22.7	9.6	23.4	14.2
+2	Freedom from seizures for at least three years	18.3	19.7	19.0	18.5	20.7	19.3	9.6	6.4	8.5
±1	Some improvement or exacerbation	49.3	49.0	49.2	48.9	55.2	51.3	64.9	55.3	61.7
−2 and −3	Considerable and distinct exacerbation in respect of the nature or frequency of seizures	2.6	2.7	2.6	7.6	5.2	6.7	16.0	14.9	15.6

* Reprinted with permission from Alstroem, Carl H.: A study of epilepsy in its clinical, social and genetic aspects. *Acta Psychiatrica et Neurologica, Supplementum 63*, 1950.

ing figure after ten years was almost 30 per cent. The incidence of recovery thereafter fell rapidly and did not reach 35 per cent even after several decades of observation. The mentally unaffected group had, according to Alstroem, the best prognosis; nevertheless, it is clear from his figures that two-thirds of this group had remained chronic seizure patients. For the mentally affected patients the prognosis was poorer still. Even after twenty years of observation the incidence of recovery did not reach 10 per cent. If we take the liberty of combining the two groups of Alstroem (the mentally healthy and the mentally affected) to form one large group of all epileptics, we can see that the incidence of recovery from seizures after twenty years of observation would be only 20 per cent. In other words, 80 per cent of all patients with epilepsy are likely to have a chronic seizure disorder. This does not rule out short-term remissions or changes in seizure patterns, it merely reemphasizes that epilepsy should be regarded as a chronic condition with remissions and exacerbations.

From the data presented so far we can now formulate the next question, Are there any criteria that would reliably differentiate the patient who is likely to show a complete recovery from one who will continue to go on with seizure activity in spite of adequate therapeutic efforts? A review of the literature showed that this is not possible at the present time, but there are certain indices which lend themselves to a better general prognosis, while others tend to be associated with an unfavorable course. Let us now go through a number of variables that have been investigated in the past and examine the various opinions given.

Sex has not been shown to affect prognosis appreciably although Gowers (1885) felt that males had a slightly better prognosis than females, but this view could not be confirmed by others (Turner, Guttmann (1929), Alstroem, Kirstein (1942), Trolle, Strobos (1959)).

As far as age of onset is concerned there is considerable evidence that the earlier the condition manifests itself, the more refractory it tends to be to treatment. It becomes, however, quite difficult at times to decide what one should regard as the age of onset of epilepsy because a number of children may have one or

several febrile or nonfebrile seizures during the first few years of life, but the chronic seizure disorder may not make its appearance until puberty or even later. The question whether the first convulsive seizure should be taken as age of onset, or the time at which recurrent seizures developed remains unanswered. Most studies reported in the literature do not make this distinction. Nevertheless, the general consensus is that seizure disorders starting in childhood or adolescence have less frequent permanent remissions than those starting after age twenty (Grinker *et al.* (1960), Guttmann, Himler, and Raphael (1945), Merritt (1963), Brain (1951), Turner, Selbach (1953), Lempp (1964)). One opinion to the contrary comes from the distant past: "those cases of epilepsy which come on before puberty may undergo a change, but those which come on after twenty-five years of age for the most part terminate in death" (Hippocrates). Habermaas (1901), as well as Grosz (1930), did not feel that age of onset allowed any statement about prognosis. While onset in childhood has been stated to carry a relatively unfavorable prognosis, those cases which start during the first year of life tend to have the poorest prognosis of all (Kiørboe (1961), Hedenstroem and Schorsch (1963), Strobos). This aspect of the problem will be dealt with further in Chapter 2.

While early onset tends to have a poorer prognosis, there are several papers available that deal specifically with "late onset epilepsy," but again the definitions of "late onset" vary. Furthermore, there is frequently no way of knowing whether or not patients who start with seizures for the first time in adult life have had febrile or nonfebrile convulsions in infancy. Hyllested and Pakkenberg (1963) defined late onset seizures as starting after the age of forty-five and found the prognosis to have been quite good unless the disorder was caused by a brain tumor. A follow-up of four to fourteen years showed that nineteen of fifty-nine patients had died, but of the remaining forty individuals, thirty-five had no, or only rare, seizures. Woodcock and Cosgrove (1964), studying patients at the Montreal Neurological Institute in cases where seizures came on after the age of fifty, commented that "in many of the nontumor group, the seizures are chiefly nocturnal, easily controlled by anticonvulsants and not a major

problem to the patient." The relatively good prognosis of patients with late onset epilepsy is also probably a factor in the prognosis of posttraumatic seizures which will, however, be discussed separately. Serafetinides and Dominian (1963) defined late onset as starting after twenty-five years of age, and 70 per cent of their cases started having seizures under the age of forty. Their data can, therefore, not be directly compared with the previous two studies. With a minimum follow-up of four years, they found that 56 per cent were improved, but only 37 per cent seizure-free for at least one year. This figure is, therefore, similar to the other figures listed in Table 1.

In regard to duration of the illness, prior to start of therapy and its relation to prognosis, we have the same difficulty that was mentioned under age of onset. What definition should we use: the very first seizure, or time of onset of recurrent attacks? A definition is even more important here than in the previous paragraphs because it is well known through family histories that individuals may have one or two seizures which never recur. The inclusion of these patients in a drug treatment group will undoubtedly raise the percentage of cases that are "completely controlled by medication" when in fact the patients would not have had further seizures anyway. Nevertheless, the literature shows remarkable unanimity on this point. Practically all studies point out that the shorter the duration of the illness prior to treatment, the better the prognosis. Gowers found that with less than one year duration, 83 per cent of patients could have their seizures arrested. If the illness had lasted ten years or longer, only 24 per cent had their seizures arrested. Similar opinions were voiced by Turner, Alstroem, Habermaas, Oppenheim (1908), Brain, Muskens (1928), Kiørboe, and Trolle.

Somewhat related to duration of illness is the number of seizures the individual has experienced prior to treatment, and it likewise tends to show a direct relationship to prognosis. The fewer seizures the individual has had, the better the chances for remission (Grinker *et al.*, Gowers, Turner, Frantzen (1961), Juul-Jensen (1963), Merritt, Perkins, and Laufer (1947), Probst). Strobos did not find this relationship in regard to major seizures, but noted it to hold true for minor attacks.

The severity of the illness as expressed by the frequency of occurrence of seizures also shows a definite relationship to results of anticonvulsant treatment. The milder the disorder, the easier it is influenced by medication (Gowers, Lennox (1960), Frantzen, Lorgé). Yahr *et al.*, as well as Ranheim *et al.* (1965), did not find such a relationship. A history of recurrent status epilepticus was regarded as an unfavorable prognostic sign by Grosz and by Lennox.

As one might expect, the relationship of seizure types to prognosis has been investigated intensively. The general conclusion seems to be that grand mal, if uncomplicated by other seizures, has the best prognosis; and psychomotor seizures, especially when present in addition to grand mal, have the poorest outcome in regard to complete arrest of attacks (Gowers, Turner, Grinker *et al.*, Arieff, Frantzen, Juul-Jensen (1963), Kiørboe, Hedenstroem and Schorsch (1963), Strobos, Muskens, Probst). A comparison of the percentages of remissions obtained by various authors in grand mal seizures and psychomotor seizures is shown in Table 4. The duration of follow-up varies considerably among authors; nevertheless, the findings do not differ appreciably. It is obvious that in all instances patients with psychomotor seizures enjoyed fewer remissions than those with grand mal. Lennox pointed out that patients who have amnesia for their psychomotor attacks have a poorer prognosis than those in whom this is not the case.

In regard to these series of psychomotor patients one should remember, however, that all of the series probably contain a number of individuals who not only have psychomotor attacks

TABLE 4

COMPARISON OF REMISSION RATES OF PATIENTS WITH PURE GRAND MAL VERSUS PATIENTS WITH PSYCHOMOTOR SEIZURES

	Grand Mal Only		*Psychomotor Seizures*	
	%	N	%	N
Yahr and Merritt, 1959	59	290	20	85
Frantzen, 1961	55	165	34	76
Kiørboe, 1961	58	64	21	28
Trolle, 1961	56	147	35	159
Juul-Jensen, 1963	63	318	20	44

but also, on occasion, grand mal seizures; they suffer therefore from two different seizure types. A combination of different seizures, regardless of specific types, represents a prognostically poorer outlook, as we will see later. This may affect the statistics adversely, and one would theoretically have to treat the data from the patients with pure psychomotor seizures separately. Although this is theoretically desirable, it is frequently impossible to do because patients who have only psychomotor attacks without ever having had a grand mal seizure are relatively infrequent, and it is therefore difficult to get a large enough sample for statistical purposes. A further point of interest with respect to the difference in prognosis for psychomotor versus grand mal seizures is that even Gowers, as well as Turner and Muskens, commented that grand mal seizures are more responsive to treatment than minor seizures and "equivalents."

The opinions concerning petit mal are divided and will be taken up in a separate chapter. Infantile myoclonic seizures will also be discussed later. The prognosis of adult patients with other seizure types tends to fall somewhere between the two extremes of grand mal and psychomotor seizures, except for akinetic and/or myoclonic seizures which are quite difficult to control by medication (Yahr and Merritt, 1959).

It has already been mentioned that the presence of more than one distinct seizure type in the same patient carries an unfavorable prognosis as to complete cessation of all attacks. This has been pointed out by Turner, Arieff, Juul-Jensen (1963), Lempp, Lorgé, Selbach, Strobos and Yahr *et al.* The usual course of events in these cases seems to be that the major seizures tend to show a decrease in frequency and intensity, but minor seizures are likely to continue (Juul-Jensen (1963), Lorgé, and Yahr *et al.*).

Hedenstroem and Schorsch in 1963 reported a study that dealt specifically with the question of why some institutionalized patients respond to anticonvulsant medication, while others remained refractory in spite of maximal efforts. There could be no question about optimal medical treatment for their patients. It was again observed that even in the hospital situation the therapy refractory cases contained significantly less grand mal (25%) and significantly more psychomotor seizure patients (54%).

The conclusion seems inescapable that our drug armamentarium is still quite inadequate for minor seizures even under optimal circumstances.

The relationship of seizures to the sleep-waking cycle was also investigated, in regard to ultimate seizure cessation, by a number of authors. Gowers felt that the prognosis was better when seizures occur in one state only (either waking or sleeping) than if they occur in both of these states. Turner, on the other hand, felt that attacks occurring only during daytime (which included the early morning awakening seizures) had a better prognosis than seizures which occurred during sleep. A poorer prognosis for nocturnal seizures was also reported by Probst. Although they tend to improve in time, their complete cessation occurs rarely. Kiørboe reported that seizures occurring mostly in sleep in children have a good prognosis. No relationship between wakefulness versus sleep and prognosis was noted by Hedenstroem and Schorsch (1963) as well as Strobos. Janz (1962) has recently prepared an extensive review of clinical and electroencephalographic differences between patients whose seizures occurred during sleep only, during the waking state only, and in both states. As it is a cross-sectional study, it does not cover prognosis, but it should be consulted by anyone who is interested in the cyclic manifestation of the epilepsies. As far as menstrual cycle is concerned, no difference in seizure prognosis was found by Strobos.

In regard to etiology of epilepsy and its relationship to prognosis, the literature is far from unanimous. This is, in a way, not surprising because the ultimate cause of epilepsy is unknown and all of the causes that are listed in the literature are in all probability contributory elements rather than the primary etiology. Alstroem's work has already been commented upon, but it bears repeating that he found epilepsy of unknown etiology to have the best prognosis; cases with probably known etiology stood in the middle, and those with definitely known etiology fared the worst. Other authors who have tried to group their seizure patients into *symptomatic* and *idiopathic* did not find this relationship (Arieff, Kiørboe, Trolle, Kirstein, Yahr *et al.*).

Although Juul-Jensen (1963) found the best prognosis in pa-

tients with epilepsy of unknown cause, he qualified his statement by saying, "if cases who had temporal lobe epilepsy were excluded." In view of our previous discussion, this is obviously an important qualification. When he subdivided his material of symptomatic epilepsies into "cerebrovascular disease, head injury, infantile encephalopathy, meningoencephalitis, oxycephaly, multiple sclerosis, etc.," he found the best results in cerebrovascular disease and meningoencephalitis, the poorest in head injuries. The poor result in posttraumatic epilepsy is at variance with other reports, but inasmuch as there is such extensive literature available on this topic it will be taken up in a separate chapter. The view that patients who had an organic etiology for their seizures did worse than those in whom no such etiology was present was also put forth by Habermaas, Lennox, and by Strobos.

As far as the influence of a positive family history of epilepsy on the prognosis of the condition is concerned, Gowers felt that positive heredity histories "lead to easier cessation of seizures but also to a greater chance of relapse and therefore a permanent cure is not easily achieved." Turner did not find a difference as far as arrest of seizures was concerned between hereditary and nonhereditary cases. Lorgé observed that patients with a positive family history did poorer than did those with symptomatic epilepsies, and Hedenstroem and Schorsch (1963) noted in their institutionalized sample that there was also a tendency for hereditary cases to be more resistant to treatment, but the finding did not reach statistical significance.

While etiology presents considerable classification difficulties, no such problems are encountered when one relates seizure prognosis to neurological examination, mental state, and intelligence of the patient. There is considerable agreement between authors that an abnormal neurological examination, an abnormal mental state, and/or low intelligence, carries a poor prognosis with respect to long-term outcome; while patients who have a normal neurological examination, no psychiatric difficulties, and average or above average intelligence tend to do well in general (Gowers, Habermaas, Oppenheim, Muskens, Brain, Arieff, Himler and Raphael, Alstroem, Lorgé, Strobos). Again, one is re-

minded of one of Hippocrates' aphorisms: "in every disease it is a good sign when the patient's intellect is sound." Apparently, however, there are important exceptions to this general rule as far as the intactness of the neurological examination is concerned. Hedenstroem and Schorsch (1963) found this an unimportant variable in their institutionalized patients concerning seizure control, and a similar observation will be commented upon in Chapter 6. On the other hand, dementia was found, even in Hedenstroem and Schorsch's (1963) sample, significantly more frequently in patients who were refractory to treatment. In regard to cerebral atrophy, as demonstrated by pneumoencephalography, no difference was found between this variable and the course of the illness by Hedenstroem and Schorsch (1963), and also by Kiørboe. Juul-Jensen (1963) observed that slight cortical or ventricular atrophy had no influence on clinical prognosis and 51.4 per cent of patients were completely or nearly seizure-free, while this was the case in only 33.6 per cent of patients who had considerable ventricular or cortical atrophy.

The laboratory examination that would appear the most closely related to the epileptic state is, of course, the electroencephalogram and one might expect that it would be a good indicator of a patient's prognosis.

One of the earliest papers on the relationship between the electroencephalogram and treatment results was by Hoefer *et al.* (1947). Ninety-six patients were investigated and it was noted that "In adequately treated cases the EEG becomes more normal. Incidence and duration of paroxysmal bursts are diminished first in the basic run and eventually also during overventilation. Furthermore, the basic activity tends to approach that in normals of the same age group. However, abnormal activity does not fully disappear in most instances." Out of forty patients whose seizures were abolished by treatment (length of time not specified) the EEG became normal in nine; in the other thirty-one, some paroxysmal activity persisted and became even worse in four instances. The opposite phenomenon (namely, EEG improvement in face of persistent seizures) was noted in three cases. Perkins and Laufer found that 53 per cent of thirty-four patients who had a normal EEG by the time of discharge from an army hospital

had no further seizures. The EEG was normal in 21.7 per cent of forty-six patients whose seizures continued subsequently. Follow-up evaluations ranged between four and nineteen months. Toman (1949), in discussing the neuropharmacology of anticonvulsant medication, stated his opinion as follows: "The correlation between clinical and EEG improvement varies widely from patient to patient. At one extreme are the frequent cases of complete suppression by trimethadione of spike and wave discharges with concomitant freedom from seizures. An intermediate group is found in which a diffuse dysrhythmia disappears under diphenylhydantoin treatment, leaving a focal dysrhythmia which may previously have gone unnoticed. Finally, there are the occasional cases in which the focal or diffuse EEG signs continue unabated while the patient enjoys complete freedom from seizures. The latter effects, like changes in severity of seizures, probably represent the ability of anticonvulsant drugs to prevent convulsive activation of normal areas by a primary focus."

Ever since electroencephalography became a clinical tool, investigators have been confronted by the problem that a number of patients with known epilepsy have normal EEGs. The percentages given vary widely between authors, mostly because of differences of opinion as to what is a normal EEG, but regardless of the actual numbers involved the fact remains that normal EEGs are observed in patients with known seizure disorders. For this reason Abbott and Schwab (1948) investigated the meaning of the normal EEG in a patient who has epilepsy. From a total material of 193 cases the authors selected forty patients with normal EEGs who were then matched for age with a group of thirty-eight patients who had abnormal EEGs. Comparing the two groups it was found that the normal EEG group had a later age of onset of the disorder, fewer different kinds of seizures, less frequent seizures, a greater response to medication, more remissions while off medication, more frequent seizures during sleep rather than during the waking state, and a greater ability to work. Patients with abnormal records were found to have had spells during infancy, head injuries or other encephalopathy, and a positive family history of epilepsy. For these reasons it was felt that patients with a normal EEG have a better prognosis.

The papers mentioned so far cover, in essence, experiences that were accumulated subsequently. Most authors now subscribe to the feeling that an EEG which is initially normal, or has become normal as a result of treatment, is significantly more frequently encountered in patients whose seizures cease for some time than in those where they persist (Frantzen, Hedenstroem and Schorsch (1958), Juul-Jensen (1963), Kiørboe *et al.* (1958), Landolt (1957), Messina and Ragonese (1965), Serafetinides and Dominian). The comment is also frequently made that clinical improvement precedes EEG improvements sometimes by several years. While normalization of the EEG tends to herald a good prognosis, the opposite (namely, continuing EEG abnormality) is not necessarily an indication that seizures will remain uncontrolled (Juul-Jensen, 1963). A lack of correlation between EEG and seizure outcome was especially evident in patients with grand mal, according to Frantzen.

Greenstein (1953) found that patients with a family history of epilepsy rarely showed a normal EEG, and that an earlier onset of seizures was associated with more abnormal EEGs. No relationship was found concerning time of day of seizures, frequency of attacks, or duration of the illness.

Probst limited himself to a comparison of patients who had a normal versus a nonspecifically abnormal EEG. No statement was found in the paper whether or not the patients were on anticonvulsant medication at the time of the EEG recording. Probst found no overall difference in regard to prognosis between the two groups. A statistically significant difference was observed, however, when the seizure type was taken into account. Patients with focal seizures and a normal EEG had a poorer prognosis than patients with a normal record and centrencephalic seizures. In contrast to this a nonspecific dysrhythmic record in a focal seizure patient was associated with a better prognosis than when it occurred in a patient with centrencephalic epilepsy.

Juul-Jensen's (1963) series is one of the largest follow-up studies, covering 720 patients. He concluded that abnormal background rhythms in the initial pretreatment EEG suggested a poorer prognosis, but paroxysmal activity in the initial EEG

did not seem to predict a poorer outcome. Improvement of the EEG during treatment was related to a better prognosis, but no definite relationship could be established between deterioration of the EEG and prognosis. Most important for future prognosis was the appearance of the EEG background during treatment. Patients who had "nearly no seizures" showed normal background rhythms in 59.7 per cent, while this was the case in only 14.3 per cent of patients with severe epilepsy. Bilaterally synchronous paroxysms occurring during treatment were not significantly related to prognosis. The group of focal symptomatic epilepsies could be subdivided into mild and severe groups. The mild group did better as far as seizure control was concerned when there was no EEG focus. The presence or absence of an EEG focus was of no importance in the severe group. No relationship was found between the various types of EEG foci and prognosis.

In regard to the likelihood of recurrences of seizures after medication withdrawal, Juul-Jensen (1964) noted that the presence of slow wave foci or bilateral paroxysms increased the risk of recurrence. Landolt also observed that the EEG does not allow definitive conclusions as to the time when anticonvulsant treatment can be reduced. He felt that anticonvulsant treatment should be continued as long as the patient showed seizure discharges in his electroencephalogram, but he also knew of several cases where the patient had become seizure-free, had gone off anticonvulsant medication, and continued to show focal seizure activity in his recording. Furthermore, he noted that, in some instances, patients who had a normal EEG would show immediate recurrence of seizures if the medication was reduced even slightly. In this connection one might point to Hedenstroem and Schorsch's (1958) observation on four patients who had been seizure-free for a considerable period of time, but showed a relapse soon after an electroencephalographic examination. The tracings had not shown any indication of the impending recurrence of seizures in these cases. Kiørboe *et al.* emphasized the point that the initial EEG is not as important for prognosis as the changes that occur while the patient is undergoing treatment. In a group of patients who had no seizures

during the year immediately prior to reexamination, significantly more normal EEGs were encountered than in the group of patients with seizures in the year in question. As far as specific EEG abnormalities are concerned, it was noted that patients with independent bitemporal foci hardly ever became seizure-free for at least one year. Messina and Ragonese felt that age was an important variable in the relationship between EEG and the prognosis of epilepsy. The agreement between electroencephalographic and clinical improvement was found to have been poorer in younger individuals.

Wakana *et al.* (1964) followed one hundred patients for three years after an initial pretherapy EEG. It was found that the EEG can provide prognostic criteria if one looks at specific features of the tracings rather than at a global rating of abnormality. Three groups were formed, namely, normal EEGs, dysrhythmic EEGs, and slow EEGs. As far as the normal EEG was concerned, patients whose seizures started before age fifteen had a poor outcome, while those who had a normal EEG and started after the age of fifteen years did well. In the dysrhythmic group the opposite was the case: patients with early onset did better than those who had started after age fifteen. In the group with predominantly slow activity there was no relationship between age at time of onset of seizures and outcome.

The studies mentioned so far mostly contain heterogeneous groups of seizure patients as far as seizure types are concerned. Ulrich (1961) made a specific effort to deal only with patients who had clinically focal motor or sensory seizures. He found that EEG foci were encountered relatively infrequently in these patients, and for practical purposes all types of EEG findings could be elicited. It was also observed that definitive prognostic statements could not be made on basis of the appearance of the electroencephalogram.

It is apparent, therefore, that the relationships between the clinical seizures and the interictal EEG are, for the most part, indirect. Precise prognostic statements cannot be made on basis of the electroencephalogram alone, in the majority of cases. The exceptions to this general rule will be taken up later.

At this point we may now address ourselves to the problem:

How long should a patient, who is completely controlled on anticonvulsants, remain under this treatment, and what are the chances of recurrence of seizures if treatment is stopped, either on the patient's own account or as a result of the physician's recommendation? It is remarkable that there is not much information available on this obviously important question. Yahr *et al.* decreased anticonvulsant medications gradually in twenty-six patients who had been seizure-free for two years or more. Complete withdrawal of medications without recurrence of seizures could be accomplished in five patients only. Nine had a "significant reduction of medication without recurrences of seizures," and twelve had recurrences during the period of medication reduction. No correlation with type, frequency, or causation of seizures and success of withdrawal of medication could be found. The length of follow-up after complete withdrawal was accomplished was not mentioned in the paper. Strobos reported that forty-one out of eighty-six completely controlled patients attempted gradual reduction of medication; nineteen of these experienced a recurrence; sixteen were still proceeding with gradual reduction while his paper was written; the remaining six tolerated discontinuation of anticonvulsant medications well. Again, the length of follow-up was not stated. He commented that patients who had bilateral synchronous abnormalities in the EEG, which became normal during drug treatment, seemed to tolerate withdrawal better. Juul-Jensen (1964) studied the recurrence of seizures in two hundred patients who had been seizure-free for at least two years and 35 per cent showed a recurrence of seizures within two years after anticonvulsant drugs were discontinued. The recurrences occurred in 50 per cent in close relation to the attempted discontinuation of medication; 33 per cent showed recurrence during the first year and the rest during the second year. It was found that the length of the period during which medication withdrawal took place (ranging between one month and three months) had no influence on the frequency of recurrence. Clear criteria for patients in whom withdrawal did not result in a recurrence of seizures could not be found, but the presence of slow wave foci and bilateral paroxysms in the electroencephalogram increased

the risk of recurrence. The risk increased with higher age at time of onset, and epilepsy of known pathogenesis also had a slightly increased risk of recurrence. Type of seizure, its severity, and the presence of atrophy in the pneumoencephalogram were of no importance. It was also pointed out that when seizures recurred after withdrawal of drugs, they could usually be brought under control again by reinstitution of medications and the patients were subsequently not more difficult to treat.

Reviewing this material the reader will probably be left with a sense of bewilderment. There is agreement in the literature on some points and considerable disagreement on others. It may be best, therefore, to summarize those findings on which the majority of authors agree:

1. Approximately one-third of all epileptic patients are likely to achieve a terminal remission of at least two years.

2. The percentage rises to between 50 and 60 if one considers only those patients who have grand mal seizures without associated minor attacks.

3. It drops to approximately 20 to 30 per cent if one deals with patients who have psychomotor seizures.

4. The percentages of patients who are regarded in terminal remission stand in marked indirect relationship to the length of follow-up.

5. The longer the illness has lasted, the less likely will control be achieved.

6. The more seizures the patient has experienced prior to his first visit to the physician, the less likely will be complete control.

7. The more different seizure types a given patient has experienced, the less likely control.

8. The more abnormal the neurological examination, mental status examination, and the lower the IQ, the more difficult will it be to control the patient.

9. The younger the patient at the time of onset of the illness, the less likely will complete control be achieved; but there are some authors who feel that age at time of onset is not a good prognostic indicator.

10. The initial EEG is of limited value for prognosis, but a

persistently abnormal EEG during treatment tends to be associated with poor seizure control.

Opinions are more divided between authors on the importance of heredity, other etiological factors, nocturnal versus diurnal seizures, and sex.

In regard to the question of drug withdrawal after seizure control has been established for a number of years, the literature contains only a few studies and further investigations of this important area are needed.

Chapter 2

CHILDHOOD EPILEPSY

The majority of patients with epilepsy have their first seizure before ten years of age, and a considerable amount of literature exists that deals specifically with childhood epilepsy and its prognosis.

Let us first consider some general statements that have been made about epilepsy starting in childhood, which would allow a comparison with those made about adult epileptics.

Livingston wrote in 1961: "The medical treatment for epilepsy today is effective in the control of seizures in about 60 per cent of cases. The number of seizures in another 25 per cent can be cut down until they are hardly a handicap. In the remaining 15 per cent, the seizures are refractory to all of the available forms of therapy." Breg and Yannet stated in 1962, ". . . a satisfactory degree of seizure control and social adjustment can be achieved in at least 85 to 90 per cent of mentally normal children. But only 50 per cent can be expected to become completely seizure-free with anticonvulsant therapy during childhood." It is important to point out the qualification that was contained in the statement, namely, "mentally normal" children. We can note again that the meaning of the word "control" is not defined. Remission rates obtained through actual follow-up studies conducted by various authors are shown in Table 5; they range between 16 and 55 per cent. Monrad's two series are of interest because the 1932 report contains nearly twice as many patients in the seizure-free group as the 1923 report. It is not quite clear why this marked change in figures has occurred except, possibly, that the patients in the 1923 report had been treated, for

TABLE 5

PERCENTAGES OF TERMINAL REMISSIONS GIVEN IN THE LITERATURE FOR CHILDREN WITH EPILEPSY

	Minimum Duration of Terminal Remission (in years)	*Percentages of Patients Remitted*	*Number of Patients Examined*
Monrad, 1928	3	28	43
Monrad, 1932	3	50	84
Clemmesen and Moltke, 1935	2	33	76
Faxén, 1935	3	15	95
Wilkins, 1937	1	23	200
Keith, 1937 (Ketogenic diet)	1	36	160
Keith, 1947 (Ketogenic diet)	4	35	190
Bridge, 1949	5	17	472
Lennox, 1951	1½	24	680
Hess, 1958	3	16	228
Kiørboe, 1961	1	41	136
Lundervold and Jabbour, 1962	1	32	100
Fukuyama *et al.* 1963	"complete control" (length of time not specified)	30	801
Lundervold, 1964	2	55	78

the most part, with bromides and borax while the patients mentioned in the 1932 report had also received phenobarbital. A similar phenomenon of marked increase in the number of patients who are controlled, when reported by the same author, can be seen in Lundervold and Jabbour's (1962) data. In 1962, 32 per cent of patients were reported seizure-free for *one* or more years, while in Lundervold's study in 1964, 55 per cent were free from seizures for *two* years or more. The patient populations were different in these two studies; one being conducted in the United States of America, the other in Norway, but this is not likely to account for the discrepancy. The reasons may lie, at least in part, in the fact that the Minnesota sample was drawn from an outpatient clinic, while the patients in the Oslo series were returned from the community for study five or more years after their initial evaluation. The possible importance of

such differences in methodology will be amplified later on. It is, of course, interesting to note that Lundervold's 1964 figure, which is the highest in the table, does not differ appreciably from Monrad's 1932 figure of 50 per cent. This is even more obvious when one considers the fact that Lundervold's remission rate was based on seizure freedom for at least two years, and Monrad's on freedom from seizures for at least three years. We can see again that there has not been the long-awaited breakthrough as a result of new drugs in the past thirty years. Keith's figures, as far as treatment with the ketogenic diet is concerned, have remained constant over a ten-year period; 36 per cent of patients were regarded as seizure-free in 1937, and 35 per cent in 1947. The 1947 report deals with remission rates spanning four to twenty-two years of follow-up.

In 1934 Clemmesen and Moltke reported on seventy-six children treated for epilepsy, twenty-five of whom were regarded as cured, which meant freedom from seizures for two years. This would amount to 33 per cent, as listed in the table. However, the series includes one case of narcolepsy and six cases of isolated seizures, and when these are removed, the remission rate would drop to 26 per cent. One of the lowest figures in the table, namely, 16 per cent remissions reported by Hess (1958), requires further comment. He noted that maximum efforts had been made in this group of 228 patients, but he pointed out that his material probably contained a negative selection because seizure-free patients frequently did not come for control observations and could therefore not be followed. This explanation would, however, not apply to Faxén's (1935) study which was a questionnaire type of follow-up study of patients who had been seen at least three years earlier.

The paper by Fukuyama *et al.* published in 1963 presents a rather typical example of potentially misleading information. The paper is entitled "Medical Treatment of Epilepsies in Childhood: A Long-Term Survey of 801 Patients," and it is stated in the summary: "The authors have reviewed their therapeutic results in 801 epileptic children, all of whom were followed up for a long period. Complete or nearly complete control of seizures was obtained in about 55 per cent of patients, while a smaller

proportion (12%) of the patients demonstrated intractable resistance to medication." From the title and the summary one would gain the impression that the authors want to emphasize that they had a large number of patients available who had been followed for a long period of time and that their results are therefore authoritative. When the paper is examined in detail, one finds the following: out of 1,800 cases of infants and children suffering from chronic recurrent epileptic attacks, 801 were selected who have attended the clinic regularly for a period of *over half a year* at least. Complete control of seizures was obtained in 243 patients (30%), suppression of over 90 per cent of seizures in 182 (23%), 50 to 89 per cent suppression of seizures in 180 (23%), 10 to 49 per cent suppression in 103 (13%), and no significant change or aggravation of the condition was observed in 93 (12%). The authors concluded that ". . . medical therapy was more or less effective in 708 cases (88%) in total; whereas no significant changes or even some aggravation of symptoms were observed only in 93 cases (12%)." If we look at the length of follow-up one finds the following statements: "Patients were followed by the authors during various periods which were distributed in the following manner: 203 cases (25%) for seven to twelve months, 259 cases (32%) for one to two years, 159 cases (20%) for two to three years, 71 cases (9%) for three to four years, 58 cases (7%) for four to five years, and 51 cases (6%) for over five years." As mentioned before, a genuine long-term survey would mean a follow-up of at least three years and hopefully five years, but 77 per cent of the authors' patients were followed for a period of time less than three years, and only 6 per cent of the cases were followed for more than five years. There is also no statement in the paper regarding the length of time the patients had to be completely seizure-free in order to qualify for inclusion in the completely controlled group. But even if we assume that this means a remission rate of at least one year, the 30 per cent figure is not particularly high.

Wilkins found in 1937 that forty-six out of two hundred children (23%) were seizure-free for at least one year. Trying to find criteria which would allow a prediction of good outcome, he

noted that a better chance for remission existed in those patients who had seizures less frequently than one a month. Remissions were also more frequent in patients who had a fewer total number of seizures spaced at long intervals. If the illness started after the age of four years, chronological age was not important for outcome. There was, however, only one child out of the forty-six with freedom from seizures who was under four years of age at the time of initial evaluation. This would suggest that children whose seizures start under age of four are not likely to have long remissions. As far as duration of illness was concerned, most remissions were encountered in patients who had had attacks for less than five years. Patients with normal intelligence and/or normal neurological examination also had a better outcome. Spontaneous remissions, without the children ever having been treated, were also noted but usually in milder cases. However, this was occasionally seen in severe disorders.

Bridge (1949) found the following variables *unrelated* to seizure remission: heredity, personality maladjustment, environmental strain, and duration of illness. Comparing eighty-one cases who had been seizure-free for five years or more with the rest of the sample, he found no differences in regard to age of onset, seizure type, single or multiple seizure types, duration of illness, or intensity of illness. In regard to seizure type there was only one exception: he found akinetic seizures particularly difficult to control and these were not represented in the sample of eighty-one seizure-free patients. Brain injured children were also significantly less common in this sample than in the rest of the group. Investigating the circumstances around cessation of seizure activity in these eighty-one children, he found that in about one-half of the group no reason for cessation could be found; for the other half the reasons were varied, but medication such as bromides, phenobarbital or ketogenic diet accounted for seizure arrest in only 27 per cent of the group.

Lennox (1960) reported the remission rate for more than five years as only 6 per cent of his patients. Probably we have here the same problem that was discussed in regard to Hess's figure in Table 5, when one is forced to calculate the percentages from current outpatient files. Lennox further states: "If a patient, as a

result either of treatment or the kindness of nature, has a reduction to 5 per cent or less of his former attacks (from twenty to one a day, or from once a week to twice a year), he has experienced arrest or approximate cure of his illness. . . . Whether the cause or the result of epilepsy, structural abnormality of the brain is a definite hurdle in the path of full recovery. . . . Presumably the more widespread the lesion, the higher the hurdle—for example, a diffuse encephalitis versus a localized cicatrix . . . petit mal, . . . has by far the best prognosis. . . . Control of generalized convulsions follows control of petit mal at a distance, and is followed in turn by control of focal convulsions and of attacks of temporal epilepsy. Recurrence of status epilepticus is especially foreboding. Frequency of convulsions or psychomotor seizures, particularly if the patient has amnesia for them, clouds the prognosis. . . . Even if all the factors named are in the patient's favor, attacks may persist. On the other hand, if chances of relief seem against him, seizures may greatly diminish or even vanish." With all the experience that Lennox had accumulated in a lifelong effort to understand the nature of epilepsy, the last sentences strike one as particularly sad. They had to be written because they correspond to the facts, but they are also testimony to our abysmal ignorance in regard to the true nature of the disorder.

Yannet (1949) approached the problem of prognosis from a somewhat different aspect and he stated: "While there has been much written on the subject of prognosis in epilepsy, it is difficult to evaluate adequately. The primary reason for this is that the surveys, as a rule, were concerned almost exclusively with the effect of treatment on the incidence of seizures alone. Unfortunately, this fails to take into consideration the many other factors that determine whether an epileptic child is living a relatively normal life in his community. It is conceivable that an emotionally well adjusted child having three to five spells a year is infinitely better off than the child having only one spell a year but seriously handicapped by personality deviations resulting from untreated tensions in the home directly related to the epileptic state."

Yannet reported subsequently on a follow-up study, carried

out at New Haven, on children who were seen at least one year after therapy was instituted and in whom accurate records of seizures, school progress, adjustment at home and community, as well as adequate clinical studies were available. A good result was defined as ". . . less than five spells per year (grand mal); completely satisfactory adjustment in school according to the mental ability of the child; relatively normal community life in line with the age of the child, and satisfaction on the part of the parents as regards to the epileptic state." A poor result was defined as ". . . relatively serious behavior and personality disorders including home, school, and community; seizures occurring five or more times per year, and relative disappointment on the part of the parents as to the progress of the child in reference to the epileptic state." Ninety-nine cases with grand mal seizures were studied and with these criteria in mind the following observations were made. Eighty-three per cent of idiopathic cases had a good result; all cases with positive family history had a good result as compared to only three-quarters of the cases with a negative family history; children with congenital cerebral defects had a good result only in 30 per cent; most of these children were also mentally retarded; about 64 per cent of the birth trauma group had a good result. Little difference was found between the response of those children whose spells began prior to one year of age as compared to those whose spells started later (80% versus 88% good results), and a good response was obtained in 87 per cent of children in whom treatment was started within one year after the onset of spells as compared to 71 per cent good response when treatment was started more than one year after onset. Yannet felt that this difference was probably not significant.

The statement that idiopathic epilepsy responds better to treatment than symptomatic seizures was also made by Fukuyama *et al.* Chao (1958) too, felt that ". . . epilepsy of genetic etiology has a better prognosis for mental and motor development than epilepsy of symptomatic cause. Of the idiopathic group, petit mal absence carries the best prognosis. Most of the patients outgrow their seizures before adolescence and maintain normal to superior intelligence. The majority of patients with

grand mal seizures of idiopathic origin outgrow their seizures in early adult life. The prognosis is less favorable, with respect to complete seizure control and mental development, for mixed seizures of the idiopathic type with either two or three types of petit mal or with petit mal and grand mal seizures. The prognosis is extremely variable in patients with symptomatic epilepsy, varying from extremely good in children with seizures of unifocal origin to extremely grave in cases of multifocal or diffuse encephalopathy. Multifocal and generalized seizures are usually less responsive to treatment than are unifocal seizures . . . prognosis in all cases is further darkened if there are persistent and prolonged seizures, particularly generalized seizures with cyanosis, because of the possibility of the seizures themselves adding insult to injury and causing further deterioration."

Frequently one finds in the literature "idiopathic epilepsy" being equated with "genetic epilepsy." This is unfortunate because in a considerable number of instances of "idiopathic epilepsy" no evidence for a positive family history of epilepsy can be elicited. On the other hand, one can sometimes find a family history of epilepsy in cases with clearly "symptomatic" seizure disorders. This confusion between terms probably beclouds the issue further whether true genetic epilepsy has a good or a bad prognosis, or whether heredity makes no difference at all in regard to seizure control.

No difference in the incidence of family history of epilepsy in regard to seizure control was obtained by Bridge, and by Lundervold and Jabbour, but Craig and MacKinnon (1965) stated that the prognosis of patients with a family history of epilepsy is better than that of those whose seizures are probably related to undisclosed organic lesions. A study group reporting to the World Health Organization on Juvenile Epilepsy in 1957 also expressed the opinion that ". . . except for the babies dying in early infancy, the prognosis of the types of epilepsy in which genetic factors predominate is better than the other types as regards the number of fits, their responsiveness to treatment, and the infrequency of undesirable psychological changes."

In regard to age of onset, Monrad found it not to be significant. This was also the opinion of Lundervold and Jabbour. On

the other hand, Fukuyama *et al.* stated that the younger the age of onset, the worse the result of treatment. Complete control or suppression of over 90 per cent of seizures was obtained in 46 per cent of patients whose seizures started under one year and in 75 per cent of cases who started between twelve and fourteen years. Hess found terminal remissions infrequently in patients whose seizures started between birth to four years (17%). The most frequent terminal remissions occurred in patients whose seizures started between five to nine years (30%), and they were the least frequent when seizures started between ages ten to fifteen (5%). The complete disagreement between Fukuyama *et al.* and Hess in regard to the outcome of patients who started with seizures after ten years of age should be noted. Wilkins' observation on the rarity of remissions when seizures start before four years of age has already been mentioned, but it is repeated here because it agrees with the findings of Hess.

As far as focal seizures are concerned, Hess observed that if these started early in life there are significantly more frequent remissions than in centrencephalic seizures. The later the onset of the illness, the worse the prognosis for focal seizures, and if they started after nine years of age there were no remissions.

Craig and MacKinnon (1965) felt that seizures in babies occurring between the ages of one and six months are usually due to brain damage and carry a poor prognosis. Keith (1964) noted that out of fifty-six children who had convulsions during the first month of life, eighteen had died (32%) and of the survivors 68 per cent became seizure-free. In regard to neonatal convulsions, Burke (1954) found that out of forty-eight cases who had seizures during the first fifteen days of life, eighteen (37.5%) died within a few days. Twenty-seven of the survivors could be followed for periods of time ranging between six months and four and one-half years; five were severely retarded mentally (18%), but only two had had further convulsions (7%). There was close agreement in the mortality rates of Keith and Burke. The disagreement between the number of patients becoming seizure-free may be due to the longer follow-up (10 to 14 years) in Keith's cases. These figures are also of theoretical importance. If epilepsy is caused by birth injury and symptomatic epilepsy

has a bad prognosis, one would expect that children who convulsed within a few days after birth would show a very serious and intractable form of epilepsy. The data on hand do not confirm this concept; they show, on the contrary, that only one-third of the survivors have a chronic seizure disorder. This would suggest, therefore, that the differentiation between symptomatic and idiopathic, as far as birth injury is concerned, is not very fruitful for prognosis in regard to seizure control.

As far as some other prognostic characteristics are concerned, Bergemann (1936) found herself in agreement with Muskens (1928) as well as Grosz (1930) that personality changes in the beginning of the illness represent an unfavorable prognostic sign, but Bridge felt that personality maladjustment made no difference in seizure control. Lundervold and Jabbour reported that no significant differences were found in regard to the incidence of mental retardation, prenatal insults, abnormal birth, birth presentations, birth weight, or postnatal cranial injuries, and the response to treatment. Histories of infection of the central nervous system, including viral and bacterial meningoencephalitis were, however, obtained in 30 per cent of their unimproved group in contrast to 15 per cent of those clinically free from seizures. A combination of low IQ, abnormality of speech, behavioral disturbances, and developmental retardation was observed twice as frequently in the unimproved group as in the other two groups. Cases with more frequent seizures were more difficult to control. In his 1964 study Lundervold found no significant correlation between frequency of attacks and clinical outcome, but cases with more severe and long-lasting seizures were found to be more difficult to control. Faxén noted that among epilepsies with organic etiology, cerebral malformations and birth trauma had the poorest prognosis.

In regard to specific seizure types, there tends to be agreement that grand mal seizures are the easiest to influence by treatment (Chao; Craig and MacKinnon; Fukuyama *et al.;* Hess; Keith). Monrad, on the other hand, found the prognosis to have been the same for grand mal, petit mal, and mixed seizures, but a part of this contradiction appears to reside in what constitutes petit mal, and this will be taken up subsequently in further detail.

There is virtually unanimous agreement that infantile myoclonic seizures have the worst prognosis, but this will also be discussed in greater detail later on. Psychomotor seizures also tend to be somewhat more resistant to treatment as reported by Fukuyama *et al.;* Hess; Livingston and Petersen (1956); and Lundervold and Jabbour. The observation that a combination of different seizure types has a poorer prognosis was reported by Chao and by Keith, but Bridge did not find this to be the case in his sample.

The critical reader will note that criteria which have been implicated as being of good or of poor prognostic significance in childhood epilepsy also have been advocated for the prognosis of the adult patient. Although remission rates for children (as shown in Table 5) are slightly higher than those shown in Table 1 for adults, this is possibly offset by the shorter follow-up in most instances.

Two other conditions peculiar to childhood also should be mentioned briefly. Seizures characterized predominantly by tonic manifestations are often refractory to treatment according to Gastaut *et al.* (1963). The other condition is "acute infantile hemiplegia of obscure origin" (Ford). This is not infrequently encountered although precise figures are lacking. Children, usually under the age of three years, suddenly develop a severe convulsive seizure or status epilepticus which has focal features. This is followed by hemiplegia. The hemiplegia, although improving later on to some extent, tends to remain permanent and some deformity contracture of the extremities, especially of the hand, is usually present later on. The children nearly always show on follow-up some mental retardation and frequently have behavioral difficulties as well as epilepsy. Prognosis as to recovery from the acute condition is good, but quite poor for all the sequelae that have been mentioned. A considerable proportion of these children tend to become inmates of state hospitals. Although the clinical course of the condition is usually quite similar, the etiologies may be diverse. Vascular causes (i.e. venous sinus thrombosis) are listed as most prominent in the literature, but infections and toxic processes also have been assumed, and precise information about the nature of the condition is still not

available. A classic description of this illness is contained in Gowers's book (1885), and he also noted that hemiplegia is more frequently found on the left than on the right side. Gastaut *et al.* (1960) recently have restudied this condition in great detail and have suggested the term H.H.E. syndrome (i.e. Hemiconvulsions-Hemiplegia-Epilepsy). The initial episode was followed by further convulsions within one year in 82.6 per cent of 150 cases. Psychomotor seizures appeared after more than three years in one-half of the patients.

To what extent can the EEG help in the prognosis of childhood seizures? Livingston (1954), although usually on the optimistic side, paints a rather gloomy picture in this regard. "There is no definite relationship, in many cases, between the degree of abnormality in the electroencephalogram and the severity of the epileptic state. Some patients who present marked electroencephalographic abnormalities have fewer and milder seizures than those who have minimal changes in their brain wave patterns. There is also no specific correlation between the clinical course of a patient's seizure and the pattern of subsequent electroencephalograms. In some patients, repeat electroencephalograms present more numerous abnormalities in spite of the fact that the clinical seizures have been controlled with anticonvulsant medication. In other patients the seizures will become more frequent and more severe, and a repeat electroencephalogram will show a marked improvement in the brain wave pattern. . . . The only type of electroencephalographic abnormalities which disappear, in most cases, from the electroencephalogram concurrent with clinical improvement attained by medical therapy are (1) the three per second spike and wave forms such as are seen in the electroencephalograms of patients with petit mal . . . and (2) the petit mal variant forms such as are seen in the electroencephalograms of patients with minor motor epilepsy who are treated with the ketogenic diet."

Chao *et al.* (1958) had a considerably better opinion about the prognostic capabilities of the EEG than Livingston. Inasmuch as they provide a great deal of specific information, their statements will be quoted extensively.

"The original electrographic findings have prognostic signifi-

cance in terms of the outcome for the patient in relation to the number of seizures, in the ease with which such seizures may be controlled, and in the evaluation and differentiation of nonprogressive from progressive pathology. In children, the possibility of predicting future mental and motor development will be greatly influenced by the original and subsequent electrographic findings. The following may be considered reliable factors of prognostic evaluation in these terms: (1) A normal electroencephalogram in the patient, whether child or adult, with known convulsions or epileptic symptoms may be considered a good prognostic sign, in that, statistically, patients presenting with normal electroencephalograms show less in the way of neurological deficit, generally show a better response to medication, and rarely show progressive deterioration or deficit. (2) Demonstration of the classic three per second spike and wave pattern against a normal background in a patient with the classic absence seizures may be considered a good prognostic sign, in that such findings rule against the presence of palpable cerebral pathology. The outlook for mental and motor development is generally good. While the control of seizures may be difficult initially, there is a strong chance for spontaneous remission as the child reaches his teens or early adulthood. (3) Demonstration of slow-spike and wave diffuse patterns is a prognostically poorer sign, both in terms of control of seizures and in terms of motor and mental development. (4) If interpretation and evaluation are based largely upon the natural history of such cases, the fourteen and six per second positive spike pattern may be considered to have a relatively good prognostic significance. It has been demonstrated that, although such patients are sometimes refractory to drug therapy and require considerable experimentation in order to find an effective agent for the control of attacks, if this is their sole electrographic abnormality they usually do not have evidence of other neurological abnormality and do not develop any. When this pattern is present in children, both the pattern and the clinical symptoms generally will disappear before adolescence or in the adolescent period. (5) In infants and young children, the demonstration of hypsarhythmia is a poor prognostic feature in that it is almost inevitable that there will

be some degree of mental and motor retardation; however, the spontaneous remission of seizures in later childhood is not uncommon in this group. (6) Circumscribed focal abnormalities in otherwise normal electroencephalograms have a better prognostic significance than all other forms of electroencephalographic abnormalities, with the exception of fourteen and six per second positive spikes and the classic three per second spike and wave pattern. Indeed, in children, the demonstration of a focal slow-spike abnormality in the midtemporal region may constitute the most benign, in terms of its natural history, of any symptomatic finding known. In these children, the seizures are generally easy to control, and the abnormality and seizures usually disappear in late childhood or early adulthood; the incidence of temporary or persisting neurological deficit is relatively low. (7) Focal abnormality existing against a background which is diffusely abnormal is a poorer prognostic finding than the purely focal record and is often a sign of both diffuse and focal involvement of the brain. However, it is possible in certain instances for the focal discharge to disrupt the total activity of the brain so that when and if the focal discharge is curbed through the use of surgery or medication the generalized disturbance will subside, thus indicating that the essential abnormality was primarily focal. (8) Paroxysmal slow activity against a normal background may be a relatively good prognostic electrographic finding; however, this evaluation is much less assured than that given above for the other types of abnormality.

"Perhaps the greatest error of electrographic evaluation is the one of trying to equate the dramatic character of an electrographic abnormality with the severity of the patient's symptoms. Thus, a monorhythmic dysrhythmia—by which we mean, for example, an electroencephalogram consisting of little except low voltage five to six per second rhythmic waves—may have a much greater significance in terms of clinical abnormality and underlying pathology than does a record in which there is a dramatic demonstration of numerous high voltage three per second spike and wave bursts. This is because such a finding may be a sign of deterioration and, therefore, in spite of its undramatic character, a sign of a diffuse encephalopathy of severe degree. Thus, it is

almost impossible to equate the degree of (nonspecific) dysrhythmia as such with the severity of the epilepsy or even of an underlying encephalopathy."

Several points deserve to be emphasized—while a normal EEG tends to be associated with a good prognosis a summary statement that an "abnormal" EEG is prognostically poorer would be a gross oversimplification. The distinctions made by Chao *et al.* between focal abnormalities, appearance of background rhythm, and presence of paroxysms are important because they represent different, and in part, independent phenomena with different prognostic value. Focal abnormalities in form of spikes and/or sharp waves carry different significance in children. They do not necessarily represent the fixed atrophic lesions that we are used to finding in adults with these patterns. Extensive work on this problem has been carried out by Gibbs *et al.*, who reported in 1954 on the disappearance and migration of epileptic foci in childhood. Follow-up studies were obtained on forty-five children above the age of nine who had shown, prior to that time, an occipital focus of seizure activity: 40 per cent of them had normal tracings on follow-up and were seizure-free; 23 per cent had an occipital focus and about one-quarter were seizure-free; in 18 per cent the occipital focus had disappeared and was replaced by a temporal occipital focus and about one-quarter were seizure-free; in 14 per cent the focus had shifted to the midtemporal area, and about one-third were seizure-free; 5 per cent had fourteen and six per second positive spikes, and approximately one-third were seizure-free. Recalculating all figures, one finds approximately twenty-six children seizure-free, that is, about 57 per cent. Ninety-eight patients who had a midtemporal focus were restudied after the age of fifteen: 53 per cent had normal EEGs and all were seizure-free; in 15 per cent the focus had shifted to the anterior temporal area and none were seizure-free; 23 per cent had fourteen and six per second positive spikes, and one-half of them were seizure-free—when the figures are recalculated there are approximately sixty-five patients seizure-free (66%). Gibbs *et al.* concluded that ". . . the evidence indicates that the discharging lesion and the structural lesion are distinct and independent. Unlike the structural lesion, the dis-

charging lesion can migrate, and it commonly heals completely. Healing of the discharging lesion appears to depend on some as yet unknown processes that are intimately related with growth and development. Experience with the present group of cases suggests that when a focus has disappeared and the electroencephalogram has remained normal for one year it is safe to discontinue medication."—No figures were given to support this opinion—"However, when phenobarbital or other barbiturates are employed, they should be discontinued gradually over a period of two weeks to avoid flare-up that sometimes occurs as a result of sudden barbiturate withdrawal. . . . Present experience suggests that it is wise to continue anticonvulsant medication until one year after the last seizure in cases in which a previously abnormal EEG has become normal awake and asleep. Normalization of the EEG is evidence of a recovery process that probably has carried the patient out of danger of further seizures. In order to play doubly safe, however, medication can be continued for another year; a second normal electroencephalogram awake and asleep at the end of that time indicates that no relapse has occurred and gives added assurance that medication can be discontinued without a recurrence of seizures." No statement was made in regard to the length of follow-up of these children in this paper.

The study was continued further by Gibbs and Gibbs, and in 1960 they reported on the good prognosis of midtemporal epilepsy. Seven hundred and thirty-nine persons who had midtemporal spikes but no other seizure activity were investigated. It was found that these foci were increasingly common up to the age of eight years. Their occurrence fell rapidly between eight and fifteen years, and thereafter a pure midtemporal spike focus was rare. A follow-up study of ". . . 120 children whose seizures began after the age of five and who had a spike focus in the midtemporal region and no seizure activity elsewhere revealed that by the age of eighteen years, 85 per cent of such children had no symptoms clearly identifiable as epileptic. In 55 per cent of the eighteen-year-olds the electroencephalogram had normalized and all epileptic symptoms had ceased. Thirty per cent developed fourteen and six per second positive spikes by the age of

eighteen; half of these were asymptomatic and half complained of headaches, dizzy spells, paresthesia, or visceral and vegetative symptoms. Ten per cent developed a negative spike focus in the anterior temporal region, and 5 per cent continued to have negative spikes in the midtemporal region. All patients with negative spikes continued to have convulsions or, in the case of patients with an anterior temporal spike focus, trance-like attacks or confusional episodes. Only this last mentioned group (the 10% with an anterior temporal spike focus) had a residual, seriously handicapping disorder, which can be considered more or less permanent."

Gibbs summarized his feelings about the prognostic importance of certain EEG features in 1954 as follows: Infantile spasms —hypsarhythmia (commonest, ages one to three years) has a bad prognosis. Petit mal variant (commonest in ages two to five years) is only slightly less malignant than infantile spasms. Petit mal (commonest in ages six to twelve years) has a relatively good prognosis; it tends to subside in late adolescence and it is rarely associated with brain damage or intellectual impairment. Occipital focus (commonest in ages three to five years): by nine years of age, 48 per cent of patients cease to have seizures. Midtemporal focus (commonest in ages between seven and ten years): 50 per cent of patients when restudied after age fifteen had normal EEGs and were seizure-free. Fourteen and six per second positive spikes (commonest in late adolescence and young adults) is a relatively benign type of epilepsy; it is easily controlled by drugs and tends to subside with increasing age. Anterior temporal lobe focus—psychomotor epilepsy (commonest in adults): it is less likely to clear up with increasing age and is commonly resistant to medication.

Hess likewise found that EEG foci in children are inconstant, but focal clinical features tend to remain constant. It was also observed that, in general, normalization of the EEG occurred only several years after clinical freedom from attacks. In a subsequent study, Isler and Hess (1960) pointed out that in about one-third of epileptogenic foci, regardless of location, the EEG became normal or nonspecifically abnormal later on. In another third the focus persisted in the same area but showed occasion-

ally more spread into adjacent regions and in the rest of the patients the focus was replaced by generalized abnormalities. No significant correlations between location of EEG focus and seizure outcome were noted. It was felt that the topographic localization of the epileptogenic focus does not seem to be important prognostically in regard to cessation of seizures, persistence of attacks or change to generalized seizures. These results are, of course, contrary to those of Gibbs and Gibbs, but it is conceivable that the length of follow-up might have been important. Approximately two-thirds of Isler and Hess's cases had been followed for two to five years and the rest for more than five years. The length of follow-up in the Gibbs' series is not specified in the 1954 paper and reported as ranging between two and sixteen years in the 1960 study. There was no breakdown provided which would allow one to calculate the average length of follow-up of the Gibbs' cases. Hess also found that patients with normal EEG or nonspecific abnormalities had the strongest tendency towards remission, those with typical spike and wave patterns the least.

Lundervold and Jabbour reported that patients with a normal or nonspecific abnormal EEG had the best prognosis. In his second series Lundervold noted the same phenomenon but added that improvement of a previously markedly abnormal EEG is likewise indication of a good prognosis. Fukuyama *et al.* stated that the outcome was better in patients who had no spikes in their initial EEG than those who did, but no further details were given.

Courjon and Cotte (1958) felt that children under three years of age who have an abnormal EEG several days or several months after the first seizure manifestation have a poorer prognosis than those with a normal tracing.

Yannet *et al.*, using the classification described previously, found no difference in regard to good or poor outcome whether the EEG was normal or abnormal.

Lamontagne and Fischgold (1965) noted considerable correspondence between EEG and clinical improvement but they also stated that they did not know the degree of probability of a permanent cure if the EEG had normalized and they also did

not know the probability of recurrence of seizures in a patient whose EEG had remained abnormal.

The importance of the EEG as a prognostic tool after the very first convulsive seizure was stressed by Aass *et al.* (1956) ". . . an abnormal EEG . . . indicates far greater possibility for recurrent seizures." Of thirty-nine children with a normal EEG after the first seizure, five (13%) had recurrent convulsions within two to five years, but this was the case in forty-six of sixty-one children (75%) who had an abnormal tracing.

As far as the prognosis of children with neonatal convulsions and the electroencephalogram is concerned, Harris and Tizard (1960) followed thirty-one babies for at least one year. Birth weight, age at time of onset of seizures, age at cessation of seizures, clinical diagnosis and type of seizures, as well as rhythmic slow wave activity, focal sharp waves or spikes, repeated stereotyped sharp waves or wave complexes, gross asymmetry, small amplitude, sharp waves during episodic sleep activity, fast activity, and type of EEG pattern during the seizure did not show any definite relationship to the findings at follow-up. The only statistically significant finding was that out of seven children with unilateral EEG abnormalities other than "simple flattening," six were clinically normal and only one abnormal at age of one year or more. Out of twelve children with bilateral abnormalities, two were clinically normal at age one, eight were abnormal, and two had died. The authors pointed out that even more important for prognosis was the duration of the seizures in the neonatal period. Of ten children who convulsed for less than two days, nine were normal and one abnormal at follow-up; while out of ten who convulsed for more than two days, only two were normal and eight abnormal.

One of the most recent reviews of this problem is by Tibbles and Prichard (1965). Of 135 children recorded during the first month of life, 126 were traced; of these, 106 were alive at time of follow-up. Seventy-five of the survivors were examined in the department of pediatrics and the rest followed through the mail. The length of follow-up is not stated in the paper. It was found that 70 per cent of children with normal EEGs had at follow-up normal intellect and no handicap; while in the abnormal EEG

group, 33 per cent had normal intellect and no handicap. The previous suggestion of Harris and Tizard about the prognostic differences between unilateral and bilateral abnormalities was not commented upon by Tibbles and Prichard.

Although not dealing with prognosis, the study of Passouant and Cadilhac (1962) should be mentioned because it demonstrates the pleomorphism of clinical and EEG features that result from different stages of cerebral maturation. The paper points out the difficulties one can encounter when one tries to relate clinical to electroencephalographic features in infancy and early childhood.

A specific investigation regarding discontinuation of anticonvulsant medication when children had been controlled for some time was performed by Zenker *et al.* in 1957. Out of 117 children who had become seizure-free for periods ranging between one-half and nine years, twenty-five showed relapse after anticonvulsants were either decreased or discontinued. Relapse was more common in children who had intellectual defects or personality changes. It was also more frequently seen around puberty regardless of age of onset of the illness and in children who had had infrequent seizures while on medication. Duration of seizure freedom prior to discontinuation of medications seemed unrelated to relapse rate. Hereditary factors were also unimportant in this respect. As far as the EEG was concerned, relapses were not observed when the EEG had markedly improved or become normal under treatment. When the EEG had remained abnormal in spite of anticonvulsant treatment, relapses occurred in twelve out of thirty-three patients; when the EEG had shown moderate improvement, relapses were noted in three out of sixteen patients.

Having given a general review of the problem we can now proceed to examine in detail three conditions that are peculiar to childhood, namely, febrile convulsions, petit mal, and infantile spasms—hypsarhythmia. Breathholding spells will not be discussed because they are clearly nonepileptic. Those episodic conditions that present with headaches, abdominal pain, dizziness, or other manifestations, and that are variously diagnosed as "epileptic equivalents" or "borderland of epilepsy" will also be

omitted because I am not sure that the diagnostic criteria of different authors are uniform enough to allow for meaningful comparisons.

To summarize the information that has been presented in this chapter, we may state that the percentages for terminal remissions in children have been reported to range between a low of 15 per cent and a high of 55 per cent. Similar to the situation in the adult, there exists agreement that patients who have only grand mal seizures tend to respond best to medication while those with psychomotor seizures fare poorer in this respect. There is less agreement in the literature on other prognostic factors. The importance of heredity, other etiological factors, age at time of onset of the illness, and personality adjustment are controversial. As far as the EEG is concerned, there tends to be agreement that patients who have a normal tracing, or those whose EEG normalized during treatment, are likely to have a better outcome. It needs to be emphasized, however, that the term "abnormal EEG" is a gross oversimplification, and different types of EEG abnormalities tend to carry different prognostic information. Reviewing the material one also gains the feeling that there is less agreement on firm prognostic criteria when it comes to children than when one is dealing with adults.

Chapter 3

FEBRILE CONVULSIONS

Accurate information about the incidence of febrile convulsions is not available at the present time, but the following observations may serve as guidelines. Patrick and Levy (1924) found that 4.2 per cent of 752 unselected infants and children who were seen at "better baby conferences" had suffered from convulsions at one time or another. Thom (1942) reported that 6.7 per cent of 3,461 children coming from a "fairly typical cross section representing the working class" of the city of Boston had convulsions. Cooper reported in 1965 that out of 4,779 children born in 1946 and subsequently kept under observation, 107 had experienced convulsive seizures by two years of age (2.2%). These figures, however, refer to all forms of convulsions and not to febrile seizures only. W. Lennox (1960) estimated that ". . . something like 2 per cent of children in the community have one or more febrile convulsions in their first five years, or perhaps 2.5 per cent at any age." Friderichsen and Melchior (1954) found that out of 1,507 children admitted to the pediatric department of Sundby Hospital with fever over 37.6 degrees centigrade, 171 had febrile convulsions (11.3%).

Being confronted with a child who has just had a febrile seizure and assuming that the patient does not suffer from an overt infection of the central nervous system, one would like to know the answers to several questions. These could be listed as follows:

1. Will the patient develop further febrile convulsions?
2. If he does, will this lead to brain damage?
3. Is this convulsion the first indication of future epilepsy?

4. Can anything be done to prevent further recurrences?

In regard to the first question, Table 6 lists some recurrence rates that have been given in the literature. They range from a low of 22 per cent (Frantzen *et al.*, 1964) to a high of 71 per cent (Peterman, 1941). Frantzen's figure was based on a preliminary report of a short follow-up period and may therefore be unduly low. According to Herlitz's (1941) calculations the risk of recurrence of febrile convulsions after the first seizure is 34.9 per cent ± 2.5 per cent, after the second seizure 46.5 per cent ± 4.4 per cent, and after the third, 60.0 per cent ± 6.3 per

TABLE 6

RECURRENCE RATES OF FEBRILE AND AFEBRILE SEIZURES AFTER INITIAL FEBRILE CONVULSIONS

	Febrile Seizures (%)	*Isolated Afebrile Seizures* (%)
Herlitz, 1941	see text	
Ekholm and Niemineva, 1950	15	
Peterman, 1952	71	
Melin, 1954		10.4
Livingston, 1954	52	
Millichap *et al.* 1960	54	17.0
Frantzen *et al.* 1964	22	3.4

cent. If there was a history of seizures in childhood in one of the parents, the risk for recurrence after the first seizure increased to 62.5 per cent.

The second question, whether brain damage is likely to result, is very difficult to answer because appropriate studies are not available. Zimmerman (1938) as well as Fowler (1957) have demonstrated anoxic changes in the brains of children which they regarded as having been caused by the seizures. The results of these studies are somewhat difficult to apply to the clinical situation because we do not know what the state of the brain was before the seizures occurred. The children reported in these two studies were of course all severely ill, and in most instances the convulsions were merely an added complication rather than

the sole cause of the condition. This problem could be studied much better in the animal. From a clinical point of view Ekholm and Niemineva (1950) observed in their follow-up study of sixty-six children with "infectious convulsion" that forty-seven (71%) were normal in all respects after seven to twenty-nine years. Mental development was "more or less retarded" in four (6%). Friderichsen and Melchior had five children in their series of 282 (1.7%)who were found to be mentally defective or retarded at follow-up. Margaret Lennox (1949), comparing the mental development of epileptic children with those who had only febrile seizures, found no difference between the groups in this respect. There were 21.6 per cent abnormal patients in the febrile convulsion group and 22 per cent in the group of epilepsies. These figures are also difficult to evaluate. One cannot say with certainty whether some retardation had been present prior to the onset of febrile seizures, or if it was brought on as a result of the convulsion. Fukuyama (1963) felt that "minor syndromes such as behavior disorders, speech disorders, et cetera, could be frequently encountered." Marked "psycholability" was also encountered in many of Zellweger's patients (1948). Again, we do not know if convulsions in these instances were merely an incidental added complication or if they were causally related. Therefore, we have at the present time no definitive data that would allow a firm conclusion in this respect. On general grounds, we could probably say that the seizures are obviously of no benefit to the subsequent mental and emotional development of the child; but the extent to which they are harmful remains as yet to be determined. One could easily expect considerable individual variation depending upon several different features of past history, as well as frequency and intensity of the convulsive episodes.

As far as the third question is concerned, in regard to the chances for epilepsy to develop, we are on somewhat firmer ground. Table 7 gives some figures from the literature. As one can see, the percentages reported are quite low. The authors that are listed in this table have all carried out longitudinal studies of febrile convulsive patients. The numbers, therefore, are not artificially inflated like those obtained if one tries to deter-

mine how many epileptics have had febrile convulsions in infancy or childhood. Herlitz felt that a definite statement about the risk of future epilepsy cannot be given because of short follow-up periods, but it should in all probability not exceed a small per cent. In order to get this low incidence, one has to be careful in the diagnosis and must differentiate between "simple febrile convulsions" and "epilepsy triggered by fever." The clear-

TABLE 7

INCIDENCE OF EPILEPSY AFTER FEBRILE CONVULSIONS

	Duration of Follow-up	*Percentages of Patients who Developed Epilepsy*	*Number of Patients Examined with Febrile Convulsions*
Frantzen *et al.* 1964	Several months to 2 years	1.9	206
Horstmann and Schinnerling, 1963	Few months to 12 years	9	108
Millichap *et al.* 1960	Six months to 2 years	4	107
Friderichsen and Melchior, 1954	1 year to 15 years	2.4	282
Faxén, 1935	More than 3 years	5	238
Herlitz, 1941	More than 3 years	2.5	424
Zellweger, 1948	More than 4 years	14.3	105
Ekholm and Niemineva, 1950	7 to 28 years	6	66
Livingston, 1954	More than 10 years	2.9	201

Note: Arranged by length of followup.

est demonstration of this difference was given by Livingston (1954). Out of 498 children, who were followed for at least ten years after an initial febrile seizure, 282 (56.5%) subsequently developed epilepsy. When the groups were divided into 201 patients with typical febrile convulsions and 297 patients with atypical febrile seizures, it was found that six (3%) of the first, and 276 (93%) of the second group had developed epilepsy. These striking differences point to the importance of accurate diagnosis at the time of the first seizure.

Twelve criteria, which have been cited by various authors as being important for the differential diagnosis, are rank ordered

in Table 8. The order was based on the number of different authors who felt a particular criterion to be important.

Ad-1: A focal convulsion always argues for the occurrence of future epilepsy, while a benign febrile convulsion has to be generalized and symmetrical (Friderichsen and Melchior; Fukuyama; Horstmann and Schinnerling (1963); M. Lennox; Patrick and Levy; Prichard and McGreal (1958); Peterman; Livingston; W. Lennox; Chao *et al.* (1958); Jennings (1954); Melin (1954); Zellweger (1958)).

TABLE 8

CRITERIA GIVEN IN THE LITERATURE FOR DIFFERENTIATING BENIGN FEBRILE CONVULSIONS FROM EPILEPSY TRIGGERED BY FEVER

1. Type of seizure nonfocal versus focal
2. Age at time of first febrile convulsion
3. Normal versus abnormal EEG
4. Duration of the actual seizure in minutes
5. Family history of benign febrile convulsions versus family history of epilepsy.
6. Number of recurrences of febrile convulsions
7. Absence or presence of preexisting external causes
8. Type of findings during postictal state
9. Absence or presence of neurological deficit either preexisting or after the seizure
10. Intelligence
11. Sex
12. Responsiveness of the convulsion to medication

Note: Arranged by frequency with which finding is cited by various authors.

Ad-2: In regard to age of onset, benign febrile convulsions tend to occur mostly between six months and preschool age. Patrick and Levy felt that the six-month to eighteen-month period is the most common for benign febrile convulsions, but most other authors extend the upper limit to four, five, or six years (Friderichsen and Melchior; Fukuyama; Horstmann and Schinnerling; M. Lennox; Prichard and McGreal; Chao *et al.*). Onset under one year of age was felt to favor future epilepsy by Pache (1954); Melin, and Hrbek (1957).

Ad-3: A normal EEG several days after the seizure argues for benign febrile convulsions; an abnormal EEG for epilepsy (Friderichsen and Melchior; Fukuyama; Horstmann and Schinnerling; M. Lennox; Prichard and McGreal; Peterman; Livingston;

W. Lennox; Chao *et al.;* Jennings). This area is, however, not too clearly delineated in regard to specific features such as type of EEG abnormality and—even more important—the speed with which a record should become normal after a febrile convulsion. Doose *et al.* (1966) felt that a combination of focal and centrencephalic abnormalities had an especially poor prognosis in regard to the development of future epilepsy.

Ad-4: A long seizure argues for epilepsy; a brief one is in favor of benign febrile convulsions. Different authors disagree in regard to how long is "long," but most of them regard the maximum duration of a benign febrile convulsion as thirty minutes (Friderichsen and Melchior; Patrick and Levy; Prichard and McGreal; Peterman; Jennings). Hrbek allows fifteen minutes and Fukuyama gives twenty minutes; but Livingston and Horstmann and Schinnerling allow up to one hour for benign febrile convulsions. These are obviously vast differences and more data will have to be obtained to settle this question.

Ad-5: A family history of benign febrile convulsions is favorable; a family history of epilepsy is unfavorable (Friderichsen and Melchior; Fukuyama; Horstmann and Schinnerling; M. Lennox; Patrick and Levy; Peterman; Livingston; Jennings).

Ad-6: Frequent recurrence of seizures (more than six, Livingston; more than three, Horstmann and Schinnerling) or a series of seizures in a short period of time favor epilepsy (Horstmann and Schinnerling; M. Lennox; Jennings; Hrbek; Zellweger).

Ad-7: Preexisting external causes, like birth injury, have been regarded as favoring subsequent epilepsy (Fukuyama; Horstmann and Schinnerling; M. Lennox; Patrick and Levy; Hrbek).

Ad-8: Sustained postictal coma or Todd's paralysis suggests future epilepsy (Fukuyama; Patrick and Levy; W. Lennox; Jennings).

Ad-9: A neurological deficit, either preexisting or after the seizure, is in favor of subsequent epilepsy (Doose *et al.;* Fukuyama; Prichard and McGreal; Chao *et al.*).

Ad-10: Normal IQ is in favor of benign febrile convulsions; low IQ favors epilepsy (Fukuyama; Horstmann and Schinnerling).

Ad-11: Female sex favors epilepsy (Horstmann and Schinnerling; M. Lennox).

Ad-12: Failure of the individual seizure to respond to adequate medication favors epilepsy (Friderichsen and Melchior).

As far as height of fever is concerned, Prichard and McGreal accept a temperature of over 100 degrees Fahrenheit for benign febrile convulsions, while Chao *et al.* and Jennings require 103 degrees or more.

Reviewing these criteria we can see that they actually boil down to the assumption that a brief self-limited, but generalized, seizure in a child with an otherwise healthy central nervous system, occurring no sooner than six months and no later than six years of age, is not likely to be followed by a chronic seizure disorder. The literature also emphasizes that the likelihood of future epilepsy increases in proportion to the number of unfavorable prognostic indices that are present in a given case. It is, of course, interesting to note that most of the criteria that are given for distinguishing benign febrile convulsions from epilepsy have also been advocated to distinguish between epileptic patients who have a good prognosis as against those who have a poor one. This would strengthen the belief that benign febrile convulsions represent one of the mildest forms of epilepsy rather than being a completely separate entity. One could therefore visualize a continuum of intensity of seizure activity in childhood with benign febrile convulsions on the one extreme and infantile spasms—hypsarhythmia on the other. The other forms of childhood epilepsy would fall prognostically somewhere in between.

This brings us to the fourth question, To what extent can further seizures be prevented after the initial episode? Apart from fever reduction, two courses of action have been advocated. One consists of the continuous treatment of the child with regular anticonvulsant medication to the same extent as if the patient had proven epilepsy (M. Lennox; Peterman); the other of intermittent treatment with phenobarbital at the time of a febrile illness only (Prichard and McGreal). If the first seizure was a typical benign febrile convulsion, Chao *et al.* recommend continued anticonvulsant medication after the second seizure; Jennings after the third; and Livingston *et al.* (1947) after more than four seizures per year. All authors agree that patients with atypical febrile seizures should go on regular anticonvulsant medication immediately. As far as duration of treatment is con-

cerned, it is usually given as one to two years after the last seizure and after the EEG has normalized. It should be pointed out at this time that all these recommendations are based purely on clinical intuition; nevertheless, they are at times propounded in a rather evangelistic manner. Shanks (1951) stated, for instance, in a paragraph entitled Epilepsy as a Preventable Condition: "It cannot be too strongly emphasized, however, that there is a very real possibility that epilepsy under favorable conditions may be preventable. There can be no doubt that convulsions beget convulsions and that uncontrolled convulsions lead in themselves to progressive mental impairment. It follows that no child or adult should be allowed to have repeated fits without the most energetic attempts to control them in the shortest possible time. It is better to use phenobarbitone unnecessarily than to await until repeated fits have confirmed the diagnosis. A confirmed epileptic is an incurable epileptic." The last sentence of the paragraph is especially impressive because it takes care of over 2,000 years of "medical progress" representing a delayed echo of Hippocrates. In his treatise on the sacred disease one can find ". . . it is curable no less than the others, unless, when, from length of time, it is confirmed, and has become stronger than the remedies applied." Addressing oneself to the other parts of the paragraph one would assume that there ought to be an abundance of data by now, showing that epilepsy can indeed be prevented. It is therefore astonishing to find that there is a remarkable lack of controlled studies which deal with actual attempts to find out whether either of the two courses of prophylactic treatment that have been advocated is of any value.

Livingston *et al.* treated sixty-three children with daily doses of anticonvulsants after the first febrile seizure. Attacks recurred in thirty-three (52%). Of thirty-one patients who received no or irregular treatment, fifteen had further seizures (49%). Treatment with anticonvulsants was therefore of no help in preventing further febrile seizures in this group of patients. Millichap *et al.* (1960) compared the results of continuous versus intermittent treatment with phenobarbital in nineteen and twenty-one patients respectively. Seizures recurred in 43 per cent of the continuously treated, and in 53 per cent of the intermittently treated group. Although the numbers of patients involved in these two

studies are relatively small, the results are in essential agreement.

The most extensive investigation to answer the question of preventability of seizures by continuous anticonvulsant medication is being conducted at the present time by Frantzen *et al.* in Denmark. Only a preliminary report is available so far, but even these results are of considerable interest. I am indebted to Doctor Frantzen for the translation of the manuscript into English. Two hundred and twenty children, admitted to the pediatric department of Copenhagen County Hospital after their first febrile convulsion, were extensively studied from the neurological and general medical point of view. All children were under seven years of age and none had had afebrile attacks before. The temperature had been higher than 37.5 degrees centigrade during the febrile illness in all instances; EEGs were obtained twice, on the third or fourth day after admission and on the tenth day. Prior to being discharged from the hospital, the children were divided into two groups, one group comprising children born on odd days, and another containing children born on even days. The group born on odd days was placed on Dilantin (5 mg/kg). The children were then followed as outpatients initially at three months, six months, twelve months, and then once a year. General medical and EEG examinations were made at each follow-up visit. Follow-up information was available on 206 children. Approximately one-half had been followed for one to two years, one-fourth for more than two years; the rest were presumably followed for less than one year, although this is not specifically mentioned in the paper. Out of these 206 children, thirty-eight had developed further febrile convulsions (18%), seven children had one or several afebrile attacks (3%), but only four developed recurrent afebrile seizures, i.e. epilepsy (1.9%). These percentages differ slightly from those given by Frantzen *et al.* in their summary because I based them on the 206 patients that were followed rather than on the original group of 220. As far as recurrence rate of febrile seizures was concerned, it was found to have been 20 per cent for the treated and 23 per cent for the untreated group. A major point of interest was the observation that, of the seven children who had developed afebrile seizures, only one belonged to the treatment group; the other six were

found in the control nontreated group. In contrast to other reports in the literature, family history, birth pathology, and nature as well as duration of the initial seizure, were of no prognostic value in regard to the occurrence of subsequent nonfebrile convulsions. These latter findings agree with the most recent observations by Doose *et al.* (1966).

Taking the three studies of Livingston *et al.*, Millichap *et al.*, and Frantzen *et al.* together, the evidence seems to indicate that there is no reason for the belief that continued, or intermittent, administration of anticonvulsant medication can prevent the occurrence of further febrile seizures. Although this negative result is regrettable, the observation by Frantzen *et al.* that the treated group did, for the most part, not develop nonfebrile seizures is of importance. If this result can be substantiated on a larger sample of patients with a longer follow-up, it might yet show that long-term chronic epilepsy can be avoided in a number of cases.

In summary we may say that the incidence of febrile convulsions in the general population is not known at the present time, but it is estimated to lie around 5 per cent. Recurrence rates of febrile seizures after the first convulsion have been reported to range from a low of 22 per cent to a high of 71 per cent. Occurrence of isolated afebrile seizures after the first febrile convulsion has been given between 3 and 17 per cent. Chronic epilepsy occurred between 2 and 14 per cent of patients who had initially a febrile convulsion.

Criteria were given to differentiate between "benign febrile convulsions" and "epilepsy triggered by fever." These criteria resemble markedly the ones that have been advocated to differentiate between epileptic patients with a good versus poor prognosis. This would seem to lend strength to the belief that febrile convulsions are one of the mildest forms of epilepsy.

There is no evidence to date that continued or intermittent treatment with anticonvulsant medication can prevent the recurrence of further febrile seizures, but there is preliminary suggestive information that it may prevent the occurrence of afebrile seizures or chronic epilepsy. Further controlled studies in this important area are urgently needed.

Chapter 4

PETIT MAL

In regard to the prognosis of petit mal, one cannot readily compare the old literature with present day follow-up studies, because the term has acquired a very specific meaning as a result of EEG studies. At present, it is limited to attacks which are characterized electroencephalographically by diffuse, high voltage, bilaterally symmetrical and synchronous three cycles per second spike wave activity lasting several seconds. The clinical expression of this electrical disturbance is either pure unresponsiveness and staring on the part of the patient, or additional blinking of eyelids, or minimal jerking of the arms or head, or very slight automatic movements of the tongue, lips, or extremities. A history of "staring spells" may sometimes be noted in patients with psychomotor seizures, and this can cloud the diagnostic classification, but an EEG examination during the seizure will usually clarify the picture. We will initially limit ourselves to the discussion of the pure form of petit mal and leave the other two members of Lennox's (1960) "petit mal triad," namely, myoclonic and akinetic seizures, until later. However, we have to mention one other term which overlaps the present day use of petit mal and that is "pyknolepsy." Friedmann (1906) has been given credit for the earliest description of this condition (Adie, 1924; Pohlisch, 1923). When one reviews Friedmann's paper, one finds that the cases which were reported in detail do not form a well-defined group from the present day point of view. Five patients were adults, the attacks had started during adult life, and they lasted up to several minutes. The four reported children do correspond to today's concept of petit

mal. Friedmann regarded the condition not as epilepsy but as narcolepsy, and tried to differentiate it from epileptic petit mal by the following features:

1. The disturbance in consciousness is only a partial one.
2. It is easily provoked and easily suppressed.
3. The individual attacks come about as a result of sudden excitement, certain situations, or momentary stimuli.
4. Mental concentration or other external stimuli when properly timed may inhibit the onset or terminate the existing attack.
5. Apart from prolonged bed rest, they are uninfluenced by drug treatment.
6. The entire abnormality represents a relatively mild defect, is compatible with an otherwise healthy nervous system, and does not result in damage to the mental development even if it occurs in childhood.

Although Friedmann is being credited with describing the condition, the term "pyknolepsy" was coined by Schroeder and appeared for the first time in a paper by Sauer in 1916. The paper contains a very detailed description of eight children with a variety of different seizure phenomena. Seven of the patients were regarded as having suffered from pyknolepsy. It is of historical interest to review these cases because they should, of course, be the prototype for this diagnosis.

CASE 1. Sixteen-year-old boy, head injury at age eleven, unconscious for five minutes. A few days later became dizzy, stated it got dark before his eyes, raised both hands, and fell. Attacks recurred for three to four weeks about five times a week, duration two to three minutes. In addition, milder seizures consisting only of momentary dizziness. Subsequently, some remissions and exacerbations in the condition. Description of attacks as seen in hospital: sits up in bed, kicks with hands and feet, twitching of facial musculature, duration approximately thirty seconds. Occurred during day and night, on one occasion during the night did not awaken with seizure, snored, grabbed the nightstand, threw it over, face was cyanosed. Psychiatrically: became increasingly irritable, aggravated other patients and nursing personnel, used vile language. Attacks improved, patient was discharged, no follow-up.

CASE 2. Seven-year-old female, age two and one-half onset of seizures, got up from chair, went down to floor, and crawled around in a circle, duration of seizure not quite a minute, up to twenty-five attacks daily. Stopped after three months. Four years later different seizure type. Twitching of right hand, runs to mother and hangs on to her. Takes a deep breath. Afterwards tired and yawns. Three to four attacks per day and similar frequency during the night. Once a major seizure, the patient fell to the ground was unconscious and twitched. Description of attack witnessed in hospital: jumps up, becomes red in face, grabs mother with hands and feet. Releases mother after about fifteen seconds, moves hand over head and face, sits down in chair again as if nothing had happened. During the attack, while hanging on to mother, rhythmic to-and-fro movements of head and trunk. Three years later second visit to hospital. Attacks had remitted after initial hospital visit but had returned three months before second visit. Seizures seen in hospital: child gives a frightened shout, grabs mother with arms around the waist, makes restless movements of the trunk, encircles the mother's legs with her own, proceeds to climb up on mother and hangs there. Duration fifteen to twenty seconds. Does not respond immediately afterwards, then becomes tearful and says, "Just had one." School performance good. Child was still having seizures at the time paper was published.

CASE 3. Six-year-old female. Minor seizures since age two, since age three falls and has frequently injured herself but gets up immediately afterwards as if nothing had happened. Seizure observed in hospital: duration ten to fifteen seconds, eyelids close slowly. With longer attacks some twitching of eyelids, eyes deviated upwards, arms limp. Generally does not fall, keeps objects in hand and continues playing immediately afterwards, four to six attacks per hour. Occasionally some swaying and knees become limp. Falls at times but gets up again right away. Still having seizures when discharged from hospital.

CASE 4. Eleven-year-old male. Three months prior to visit onset of seizures, head drops, stares straight ahead, "funny expression of eyes." Duration few seconds, initially one to two per day. Attacks observed in hospital: patient stares vacantly, face expressionless, slight drooping of eyelids, no motor manifestations. Does not drop objects he holds in his hand. Duration one to two seconds. Immediately afterwards says, "It happened again." Thirty to forty attacks per day, normal Binet IQ. Readmitted one year later, attacks only one to two per day, no personality or intellectual change. No further follow-up.

CASE 5. Nine-year-old male. Onset of seizures, age eight. Stops playing, drops objects, stares vacantly, arms tremble somewhat, resumes playing after a few moments as if nothing had happened. Sei-

zures as seen in hospital: patient runs away as if trying to hide at onset of seizure, stands slightly bent forward, head drops, eyes deviate upwards. Duration approximately twelve to fifteen seconds, occasional loss of bladder control, up to one hundred or more attacks a day. At last contact still having seizures but less frequent.

CASE 6. Seven-year-old male. Age three fell from couch, three days later first seizure, becomes completely red in face as if he couldn't get air, then shakes head, duration momentary only. Has never fallen, did not even stumble or stop while running upstairs during attacks. In beginning was supposed to have had them every minute. This lasted seven weeks, then complete freedom from attacks for three years. Seizures returned at age seven. Observation in hospital: sits up in bed, cries out, kicks bystanders with arms and legs, grinds teeth, pupils unreactive during seizure, reacts defensively to pinpricks. After the seizure deep sleep, hardly can be awakened. Attacks repeat every fifteen minutes. Attacks disappeared after patient was placed in isolation. Initial diagnosis: hysteria. Readmission two years later, up to 104 attacks counted per day in the hospital. During seizure face shows furious expression, patient is irritable, talks in angry tone of voice, in beginning of seizures does not answer but later on swears to himself. Towards the end of the seizure answers in irritated tone of voice and later on does not remember what he had said, no amnesia for attacks. Behavior pleasant when not having attacks. Other attacks on different admissions: pulls blanket in front of face, turns onto stomach, goes into knee-elbow position, subsequently kneels in bed, throws himself forward then turns with throwing and kicking movements onto back, lies rigidly for approximately one minute. At last contact still having seizures.

CASE 7. Twelve-year-old male. Age six starts yelling during onset of sleep, can hardly be aroused. When awakened does not know that he had cried. During daytime, momentary attacks of initially few absences, later on started dropping objects, head and body turns to right, eyes deviate upwards and to the right, sometimes smacking movements of the lips, up to forty attacks per day. Every three to four weeks there is one day when the attacks are innumerable. Follow-up: attacks frequent but occur in cyclic fashion with maximum every four weeks. Patient has then hundreds of attacks per day, every few seconds and attacks last several seconds; has only short clear moments, may be incontinent of feces during that day, is completely incompetent mentally that day. This state improves on the second day. Patient is completely well on the third day. Attacks themselves are always exceedingly brief, momentary loss of consciousness, slight turning of the head, and then attack is over. At last contact was still having daily seizures but the "bad days" much less frequently. Able to attend high school.

Sauer concluded that patients should be regarded as having pyknolepsy when there is no evidence of mental or intellectual deterioration in spite of exceedingly frequent attacks which show periodic remissions and exacerbations, and which probably cease around puberty. It was also felt that the most pronounced difficulty in making the diagnosis remains in a definitive separation of this group from the group of epilepsies.

There are several rather interesting features in this paper. From today's point of view we would probably regard cases 1, 2, and 6 as having suffered from psychomotor seizures and cases 3, 4, 5, and 7 as pure petit mal absences. Case 3 also had akinetic attacks and case 7 contains a typical description of petit mal status. Of considerable interest is the statement in regard to probable cessation of attacks around puberty. All of Sauer's cases still had seizures at the time of last hospital visit, and the paper mentions cessation of seizures more as a hope than as a fact. Nevertheless, as we shall see in the subsequent literature review, this particular feature became one of the main characteristics for diagnosis of pyknolepsy.

Pohlisch reviewed the concept and established the following criteria which differentiated pyknolepsy from "genuine" epilepsy: disappearance of the attacks without the production of epileptic personality change; uselessness of anticonvulsant drugs; frequent seizures from the start; duration, in general, from early school age to puberty; only rarely interrupted by short pauses; monotony of seizure type; absence of generalized convulsions and epileptic equivalents. He found pyknolepsy to be rather rare. He subsequently reported thirty-two personal cases of whom he regarded twenty-six as pyknolepsy; the others, as epilepsy or questionable epilepsy. He regarded as characteristic the frequency of seizures from the very first day: five to ten attacks per day are regularly found, and a smaller number should lead one to consider "genuine" epilepsy. Attacks are more frequent immediately after arising and in the forenoon than in the evening. Of seventeen children treated with phenobarbital, temporary improvement was seen in six. He felt that the condition was separable from epilepsy and was not narcolepsy.

In 1923, Adie gave a report to the section of neurology of the Royal Society of Medicine and characterized the condition as: "A disease with an explosive onset between the ages of four and twelve years, of frequent short, very slight, monotonous minor epileptiform seizures of uniform severity, which recur almost daily for weeks, months or years, are uninfluenced by antiepileptic remedies, do not impede normal mental and psychical development, and ultimately cease spontaneously never to return. At most, the eyeballs may roll upwards, the lids may flicker, and the arms may be raised by a feeble tonic spasm. Clonic movements, however slight, obvious vasomotor disturbances, palpitations, and lassitude or confusion after the attacks, are equivocal symptoms strongly suggestive of oncoming grave epilepsy, and for the present they should be considered as foreign to the more favorable disease." He did regard it as a form of epilepsy in children, but felt that it is distinguishable by its clinical features and the prognosis is always good. During the ensuing discussion he admitted, however, that major attacks have occurred in some of the cases ". . . in fact there seemed to be every gradation from pyknolepsy to ordinary epilepsy."

Rosenthal (1935) gave a review of the literature and history of the condition up to 1935. He concluded from his own cases, as well as those from the literature, that pyknolepsy represents an intermediate condition which contains the elements of two groups of diseases without being identical with either one of them. He regarded it as an intermediate between a specific autonomic disturbance on the one hand and epilepsy on the other. He rejected the opinion that the condition was narcolepsy, but

	Cured	*Changed to Epilepsy*	*Chronic Cases*
44 pure cases which had few symptoms associated with the attack	56.5%	30.0%	13.5%
33 atypical cases, those which had a greater variety of symptoms during the attack	40.0%	40.0%	20.0%
25 mixed cases, which had features combining pure as well as atypical features	20.0%	32.0%	48.0%

he emphasized that some cases changed to grand mal epilepsy in the second or third decade. He felt that females had a somewhat poorer prognosis for seizure cessation than males. When he compared the outcome of the illness after several decades, he distinguished the three groups shown on page 59.

If one considers these three different subgroups as one total group, 102 cases are obtained, and when percentages are calculated one finds that 42.1 per cent were regarded as cured, 33.3 per cent had changed to epilepsy, and 24.5 per cent had continued with minor seizures. These figures can be compared with one of the most recent reports by Kuhlo (1965) on seventy-six patients, thirty-one (40%) of whom had enjoyed a terminal remission of at least two years; twenty-seven patients (35%) had changed to grand mal epilepsy, and petit mal persisted in eighteen (24%). The close correspondence of these figures is, of course, striking.

The concept of pyknolepsy being a separate disease entity was again reviewed by Janz in 1955. He concluded that pyknolepsy constitutes a form of petit mal epilepsy. He investigated ninety-eight cases, eighty-eight of whom had started with pyknolepsy and ten who developed pyknolepsy after the first major seizure. This represented 7.7 per cent of all patients with epilepsy seen in nine years (total number 1,272). Studying the outcome of 163 cases he found that spontaneous cure (i.e. seizure freedom for at least two years, ten to fourteen years after onset of the illness and with the patient not on medication) had occurred in only 16 per cent. Thirty-one per cent were still pyknoleptic and 53 per cent had developed major seizures. The few spontaneous remissions occurred on the average after four years but were also seen as late as ten years after onset of the illness. Transition into grand mal usually occurred after five years, but could be seen as late as twenty-two years. He concluded that spontaneous arrest is therefore not the rule but the exception and pyknolepsy appears to be a prelude of later grand mal epilepsy.

American authors have never been impressed with pyknolepsy being anything else than petit mal, and Bridge (1949) does not even mention the term. The reason for the existence of the term

was its supposedly good prognosis. It was, therefore, essentially a retrospective diagnosis. As Lennox (1960) pointed out, a ". . . classification that permits diagnosis only in retrospect is hardly a useful one. . . . The term is welcomed by parents because it connotes something different from epilepsy. However, physicians should not allow paths of thought to be confused by mislabeled signboards." Lennox also pointed out that the first description of classical petit mal he had come across in the literature was contained in a book by Tissot, the observations being dated September, 1769. The beautiful description of the case in Lennox's book is well worth reading.

Inasmuch as the term pyknolepsy was based on a misconception in the first place, it serves no purpose to continue its use. The subject was dealt with in some detail here to point out that it should be regarded as a historical curiosity rather than as a distinct disease entity. Inasmuch as pyknolepsy is petit mal, I will, in the subsequent discussion of the literature, use this term only.

Bridge found that petit mal epilepsy ". . . runs a course with less fluctuations than the predominantly convulsive form. Daily seizures continue to recur year after year with some variation in frequency but rarely with intervals of freedom. After adolescence, seizures that have been frequent for several years may gradually diminish and disappear spontaneously. . . . While the outlook for cessation of seizures may be uncertain, the outlook for essentially normal living is good. . . . Seizures themselves fade in importance both to him and to others of his associates." As far as incidence is concerned, he found that petit mal, either alone or in combination with other forms, comprised approximately 12 per cent of the cases seen at the Epilepsy Clinic.

As to the likelihood of patients with petit mal developing grand mal, Lennox (1960) noted that the older the individual at the time of onset of petit mal, the greater the likelihood that some other seizure type besides petit mal will develop. He found from his patient material that if petit mal began during the first five years of life, 42 per cent had major attacks later on; if it developed between five and nine years, major seizures

occurred in 50 per cent; and if petit mal started at ten years of age or later, 76 per cent of the patients developed other forms of seizures, usually grand mal. In total, out of 404 patients 54 per cent later developed grand mal or psychomotor seizures.

Paal (1957) who followed thirty-nine cases with typical petit mal for periods ranging between six and seventeen years found that they could be divided into three groups: 36 per cent were completely free from seizures for at least two years; 32 per cent had developed grand mal seizures in addition, and another 32 per cent continued to have petit mal only. The group of patients in whom grand mal appeared along with petit mal was predominantly male, those in whom petit mal persisted unchanged tended to be predominantly female, and the group in whom petit mal disappeared was also predominantly female. It was impossible to arrive at specific prognostic criteria in regard to the three courses from the clinical picture or from the electroencephalogram. Heredity had no influence on the course of the illness and patients with organic cerebral damage, or increased incidence of seizures in the early hours of the morning, did not have a more unfavorable prognosis. However, all patients who had an aura later developed major seizures. A greater frequency and spontaneous occurrence of petit mal in the EEG was not an unfavorable prognostic sign. In the clinically seizure-free group the EEG did not show typical three cycles per second spike waves at the time of remission, but it was not always normal. Atypical spike wave bursts could still be seen up to seventeen years after cessation of petit mal.

Holowach *et al.* (1962) reviewed the histories of eighty-eight children with petit mal and, like others, found the condition to be uncommon. Out of 1,054 patients at the seizure clinic of St. Louis Children's Hospital only sixty patients had petit mal. Twenty-eight cases were supplied from private practice. Family history of epilepsy was present in 42.6 per cent, and ten per cent had brain damage of recognized etiology. The overall incidence of brain damage and mental retardation was 24 per cent. Fifty-four children (61%) had additional seizures other than petit mal, 37 per cent had them prior to, 16 per cent during, and 46 per cent after, the onset of the petit mal. Eight children were

completely controlled on phenobarbital. This point is emphasized here because there is a tendency in the neurological literature to regard phenobarbital and/or Dilantin as useless in this condition, and the drugs of choice are usually the succinimides and diones. Of seventy-two patients who had kept follow-up appointments, forty-five (62.5%) were completely controlled for at least one year. Twelve children (16.6%) were improved, and eleven (15.2%) unimproved. In four children, attacks disappeared after treatment efforts had essentially been abandoned. Anticonvulsants were discontinued in sixteen children following four years of treatment after the last seizure; this constituted 22.2 per cent of the total group. It was concluded by the authors: "The review suggests that petit mal is not entirely benign and unaccompanied by cerebral pathologic changes with effect on mentality or personality, nor spontaneously cured at puberty. The high incidence of grand mal and other seizures in these children is emphasized and prophylactic therapy suggested."

Lees and Liversedge (1962) also discussed the prognosis of petit mal. It was found that of twenty-three patients with classical petit mal and three cycles per second spike wave activity in the EEG only three were known to have ceased having attacks (one was taking anticonvulsant medication). Of nineteen patients with classical petit mal who did not show three cycles per second spike and wave activity at the time of the EEG only four had ceased to have attacks. Of thirty-two patients with classical petit mal who had, in addition, grand mal seizures, only three had ceased to have attacks. Freedom from seizures had lasted for at least one year. The authors felt also that the older the patient at the time of onset of petit mal, the greater the likelihood for the appearance of an additional seizure type. It was noted that a few patients with petit mal do cease to have attacks, some before puberty and some after, but the number in whom the disease can be considered arrested is small. The authors commented further: "If children under the care of pediatricians ceased to have attacks, then they would not attend adult clinic. This would overload the adult group with those not in remission, and would produce a falsely low arrest-rate. On the

other hand, pediatricians may have the impression of a favorable outcome if a child is relatively free from attacks at puberty; but even if he is completely free from them, a few years' follow-up into adult life may be long enough for further attacks of petit mal, or for other forms of epilepsy to appear. Very long follow-up studies from childhood to adult life are required to produce more data on prognosis." Lees and Liversedge continued: "Another point which emerged in our study was that many patients gradually learn to live with petit mal and to disregard their attacks very largely. This disregard and eventual cessation of visits to doctors or hospital may add to the general impression of a high natural arrest-rate in the disease. This impression may also be created when petit mal becomes mixed epilepsy, often in late childhood or adult life, and the 'category' of the epilepsy changes. These patients are often thought of not as cases of petit mal (with a bad prognosis) but as grand mal, despite the onset as petit mal. The exclusion of such cases from studies of petit mal weighs in favour of a good prognosis for the disease. One is scarcely justified in regarding a change from petit mal to grand mal as a good prognostic factor." If one calculates the total remission rate of Lees and Liversedge's patients, one finds forty-two patients with pure petit mal; ten of these could not be traced by the authors; seven (21%) had shown terminal remissions of seizures.

Doose and Scheffner's report on the therapy and prognosis of petit mal absences appeared also in 1962. Ninety-nine children were included, half of whom had been seen for one to five years and the other half for six to fourteen years. Fifty-nine children became free from seizures and forty continued to have attacks (no statement was made in regard to the duration of time for which the patients had been seizure-free). It was found that in 80 per cent of the children who had become seizure-free, therapy was started relatively early in the course of the illness. In the forty children who had not become seizure-free, only 30 per cent were treated regularly, another 30 per cent were treated for a short period of time only, and medication was regarded as having been inadequate in 40 per cent. As far as grand mal was concerned, fifty-one patients had had grand mal seizures at some

time during the illness. Petit mal preceded the major seizures, at times by several years, in twenty-nine cases. In eighteen cases, grand mal preceded petit mal, and in four instances the two seizure types occurred nearly simultaneously. Of thirty-four who had pure petit mal at the beginning of treatment, only one developed subsequent grand mal. The authors attributed this to the effect of adequate anticonvulsant medication. The risk for subsequent grand mal also seemed to be somewhat higher for boys than for girls. This is similar to Paal's conclusion. The authors also stated it had been claimed by Christian that absences, with some features of automatisms like chewing, smacking and picking movements, were more difficult to influence therapeutically than absences without these symptoms. In their own material forty-seven children had such symptoms, but they were no different as far as therapeutic results were concerned from those which did not have this symptomatology. A family history of epilepsy had no influence on the therapeutic results. It was concluded that under optimal therapy 95 per cent of patients with pure absences can achieve freedom from seizures. The reasons for this conclusion are not immediately apparent from the statistics that were presented in this particular paper.

In 1963, Currier *et al.* reported on the prognosis of pure petit mal. Thirty-nine patients were studied and strict criteria were employed for the definition of petit mal. Furthermore, the patients had visited the hospital with the primary difficulty of petit mal rather than grand mal seizures. It was found on follow-up examination that three of the patients had had infantile convulsions. Thirty-two cases could be followed, but follow-up EEGs were obtained only in eleven. The average length of time of follow-up was eighteen years. Thirteen patients continued to have petit mal (40%); two had grand mal only (6%); five had grand mal and petit mal (15%); and twelve had no seizures for two years or more (37%). A total of twelve patients had experienced grand mal seizures after the onset of petit mal, and in five of these it had ceased spontaneously or was under complete control with medications. Psychomotor seizures did not develop in any of the patients. It was noted that if the patient reached the age of twenty-one and still had petit mal seizures, the sei-

zures would continue indefinitely within the limits of the follow-up. It was also stated that in all but one in whom petit mal persisted the frequency of attacks had greatly decreased to an average of one or less a day. When petit mal attacks continued they were in general not bothersome to the patient and did not interfere with his activities to any extent. If the patient had not experienced grand mal by the age of eighteen, it did not develop later. It was difficult to predict whether a patient would continue to have petit mal or would experience grand mal seizures, but favorable prognostic signs were listed as follows: early onset (between three and ten years), more than ten petit mal spells a day when at the most frequent, positive family history, normal mentality, and a normal neurological examination. Favorable electroencephalographic findings relative to nonoccurrence of grand mal appeared to be the posterior emphasis of the spike wave discharges and single rather than multiple spike discharges. Unfavorable electroencephalographic findings in regard to future grand mal appeared to be a slow basic pattern, and slow two or three per second spike wave bursts. There was no evidence of progressive physical or mental deterioration in any of the patients except one who developed multiple sclerosis. The authors concluded that ". . . 'Pure' petit mal appears to be a relatively benign disorder which occurs twice as often in girls as in boys, is associated with a family history of grand mal seizures in half the cases, occurs usually between the ages of three and thirteen, more often than not continues into adult life, usually does not bring on grand mal seizures, is not transformed into psychomotor seizures, and is not associated with mental or neurologic deficits or degeneration."

Hertoft reviewed the literature in 1963 and also reported on fifty patients who had been followed for an average of just under thirteen years after the first attack. EEG criteria were used for diagnosis; however, the EEG was not necessarily taken at the onset of the illness but at some time during its course. Twenty-four patients (48%) had no seizures at follow-up; fifteen still had petit mal; eleven had petit mal and/or grand mal. Only six patients (12%) had a completely normal EEG; 54 per cent still had spike wave formations in the record at the time of

follow-up, and of these, four continued to have regular generalized spike wave paroxysms. The oldest of these patients was thirty-six years of age. Twenty-three patients (46%) received no antiepileptic drugs at time of follow-up; of these, nineteen were seizure-free. Ten patients (20%) were below average in regard to intelligence (IQ below 90), but only nineteen of these patients were actually tested by a psychologist; thirty-one were estimated clinically. Ten patients were unable to manage for themselves socially; seven received public allowances. The prognosis was identical for females and males and was found to be independent of the age of patient at the first seizure and independent of possible etiologic factors.

In 1965, Bergamini *et al.* studied the late development of grand mal epilepsy in patients with "pure" petit mal. Seventy-eight cases were followed from five to fourteen years. Forty-two did not develop grand mal; thirty-six did. Of the forty-six patients who were treated early and adequately, 30 per cent developed late grand mal; and of thirty-two treated later and/or inadequately, 68 per cent developed late grand mal. The majority of patients without late grand mal had an age of onset between four and six years, while the late grand mal group had an age of onset mostly between eight and ten years. There was no difference in regard to family history of epilepsy. A clinical cure (an interval of more than one year without petit mal and an additional two years without grand mal) occurred in 70 per cent of patients with petit mal treated early and adequately, and only in 18 per cent treated late and/or inadequately. Of the clinically cured patients, 57.8 per cent had EEGs that were free of abnormalities.

One of the most recent reports on the prognosis of patients with petit mal comes from Livingston *et al.* (1965). The authors also felt that it is a relatively rare type of epileptic seizure, and out of 15,102 epileptic patients only 364 (2.3%) had "true" petit mal. One hundred and seventeen patients had been followed regularly for at least five years, and the duration of follow-up ranged between five and twenty-eight years. At the time of first visit 94.9 per cent were found to have been neurologically and intellectually normal; 5.1 per cent had evidence of

mental retardation and brain damage. The cerebral pathology was present in these patients before the onset of their petit mal seizure disorder. Seventeen (14.5%) of the 117 patients had other types of seizures prior to the onset of petit mal. Four had simple febrile convulsions, and thirteen had major epileptic seizures. Patients were regarded as controlled when there was no recurrence of petit mal during the entire observation period, after freedom from seizures had been obtained and the EEG showed absence of typical diffuse bilaterally synchronous spike and wave forms. Ninety-two (78.6%) of the 117 patients were controlled of their petit mal spells. Twenty-five (21.4%) were uncontrolled. One hundred of the 117 began with petit mal; of these one hundred, fifty-nine were treated with a major motor anticonvulsant regime such as phenobarbital or Dilantin in addition to a specific petit mal anticonvulsant. Twenty-one of the fifty-nine (35.6%) who were treated with the combined therapy developed grand mal seizures; whereas thirty-three (80.5%) of the forty-one patients who were treated with a specific petit mal anticonvulsant alone subsequently developed grand mal seizures. It was also felt that the later petit mal seizures started, the more likely they were to be followed by other seizure types. Of eighty-one patients in whom seizures started between two and one-half and ten years of age, thirty-six subsequently developed major seizures, but this was the case in eighteen out of nineteen patients who started with petit mal between the ages of eleven and fifteen years. No statement was made in the paper about the controllability of the grand mal seizures in these fifty-four patients. Of the 117 patients, eleven suffered with attacks of petit mal status, and six of these manifested evidence of brain damage at the termination of the investigation. It was felt this indicated that petit mal status should be considered as a serious disorder and one which is commonly associated with the development of brain damage.

Kuhlo's (1965) report represents an extension of the material published by Paal. Seventy-six patients with typical petit mal absences and three cycles per second spike wave activity in the EEG, but without associated grand mal seizures, had been followed for at least six years. Twenty-seven (35%) had changed

to grand mal; eighteen (24%) continued to have petit mal; thirty-one (40%) had had a terminal remission of at least two years. Transition to grand mal occurred somewhat more often in male patients. Persistence of petit mal or cessation of petit mal seizures tended to occur more frequently in females. Persistent focal EEG abnormalities and appearance of petit mal status showed a tendency to be associated with future grand mal. If absences had been present for two years, hydantoins or phenobarbital were found to have been ineffective in preventing grand mal seizures.

Gibberd (1966) concluded on the basis of 139 cases that had been seen since 1949 at The London Hospital that a tendency for petit mal to cease existed at any age and not just at puberty. Sex, family history, psychological state, and electroencephalographic findings did not influence the prognosis for petit mal in his sample. Prognosis was better if grand mal did not occur in addition to petit mal. The presence of frequent myoclonus was regarded as being possibly a poor prognostic sign. The tendency to develop grand mal was associated with a poorer prognosis for petit mal, an abnormal psychological state, a poor response of petit mal to treatment, and an abnormal background activity in the EEG.

Eighty-two of the 139 patients (59%) had associated grand mal. Grand mal developed after the onset of petit mal in seventy patients (50%). The total number of patients who had shown complete remissions could not be extracted from the material presented in the paper. If one limits oneself to the fifty-nine cases on whom two EEGs were available, one finds thirty-four patients (57%) in whom petit mal was regarded to have ceased clinically (no episode of petit mal for five years). Of these thirty-four patients, fourteen (41%) still had spike wave activity in their EEGs. Gibberd's paper did not distinguish between classical three per second spike waves and brief bursts of atypical spike wave activity, but this distinction is essential when one talks about cessation of petit mal. It is not clear, therefore, even from this subgroup, how many patients had actually ceased to have petit mal seizures. It is also remarkable that a paper dealing with the prognosis of petit mal written in 1966 bases its

case material on clinical description of the attacks rather than on EEG criteria. While the EEG leaves much to be desired in its relationships to other forms of epilepsy, the three cycles per second spike wave pattern lasting several seconds is so pathognomonic that its presence in the EEG should be required before accepting a final diagnosis of petit mal. It happens rather frequently that the clinical description suggests petit mal, but the electroencephalogram demonstrates the presence of a temporal lobe focus. Incorrect classifications therefore are bound to occur when one has to rely only on clinical histories.

Having listed various authors and opinions, what is one to conclude about the prognosis of "pure" petit mal? To facilitate a comparison of the various findings, two tables have been constructed listing the observations of several authors. Table 9 gives remission rates for petit mal, and Table 10 the incidence of occurrence of grand mal after the onset of petit mal. The material of Livingston *et al.* is not included in Table 9 because remission rates are given for petit mal only and not for associated grand mal. Therefore, we do not know how many patients enjoyed freedom from all types of seizures. It should also be pointed out that Table 9 shows only minimum length of follow-up which is

TABLE 9

COMPLETE REMISSION OF PETIT MAL

	Minimum Duration of Follow-up (in years)	*Percentages of Patients Remitted*	*Number of Patients Examined*
Doose and Scheffner, 1962	1	59	99
Holowach *et al.* 1962	1	62	72
Lees and Liversedge, 1962	1	21	32**
Pohlisch, 1923	2	46	26
Rosenthal, 1935	2	27	36
Paal, 1957	6	36	38
Kuhlo, 1965	6	40	76
Hertoft, 1963	8	48	50
Janz, 1955*	10	16	163
Currier *et al.* 1963	15	37	32

* No seizures of any type and seizure free without medication for at least two years.

** Untraced cases omitted.

Note: No seizures of any type; arranged by minimum duration of follow-up.

TABLE 10

DEVELOPMENT OF GRAND MAL AFTER ONSET OF ILLNESS AS PETIT MAL

	Percentages of Patients Developing Grand Mal	*Number of Patients Examined with Petit Mal*
Janz, 1955	53	163
Paal, 1957	31	38
Lennox, 1960	54	404
Holowach *et al.* 1962	46	88
Currier *et al.* 1963	37	32
Bergamini *et al.* 1965*	46	78
Kuhlo, 1965	38	76
Livingston *et al.* 1965**	54	100
Gibberd, 1966	50	139

* 30% of patients who were treated early and adequately.
68% of patients treated later and/or inadequately.
** 36% of patients having combined therapy.
80% of patients who had received petit mal therapy only.

not necessarily identical with duration of remission. The length of time of freedom from seizures prior to follow-up was not specified in the majority of cases reported. The figures might also differ if EEGs had been obtained on all patients at time of follow-up, because they might have shown classical three cycles per second spike wave activity in a number of cases that were regarded from the clinical point of view as seizure-free.

In general, it would seem that the weight of the evidence shows the following:

1. The condition is relatively rare and the stricter the criteria employed the more infrequently it is found.
2. Although numerous seizures tend to occur per day for several years in childhood, they tend to decrease in number and intensity during adolescence and adulthood so that they do not form a major handicap for the patient later on.
3. Approximately one-third to one-half of all patients who start with petit mal will develop grand mal seizures later in life. There is suggestive evidence that this might be prevented to some extent by giving phenobarbital or

Dilantin in addition to specific petit mal drugs at the beginning of treatment.

4. Petit mal starting after the age of eight to ten years seems to carry a higher risk for the development of future grand mal than its occurrence prior to that age.

5. Mental deterioration is unlikely.

As far as petit mal status and its relation to subsequent brain damage is concerned, this condition is so rare that more work has to be done before a definitive conclusion can be reached.

Chapter 5

INFANTILE SPASMS—HYPSARHYTHMIA; AKINETIC AND MYOCLONIC SEIZURES

Lennox (1960) had tried to include "pure" petit mal absences, as defined in the previous chapter, with akinetic and myoclonic seizures into a petit mal triad, but this suggestion generally was not well received by other authors. This probably resulted from the fact that the prognosis and etiologies differ markedly between these conditions. Akinetic or astatic attacks are usually regarded as being associated with brain damage and are, for practical purposes, resistant to treatment at the present time. The electroencephalographic expression has been reported as consisting of a slow spike wave discharge repeating at one and one-half to two cycles per second instead of three cycles per second (Petit Mal Variant—Gibbs and Gibbs, 1952), but hypsarhythmia or other EEG abnormalities can also be observed.

Myoclonic jerks and myoclonic seizures—characterized electroencephalographically by multiple spikes followed by a wave—are not limited to childhood and can be the expression of a variety of different conditions. If they occur in infancy or early childhood, they tend to carry an exceedingly serious prognosis. In contrast to "pyknolepsy," this condition has been regarded as a form of epilepsy for more than one hundred years. The names that have been applied have varied considerably, as did the presumed etiologies, but its relative refractoriness to treatment has stayed essentially constant. The most widely used term to describe the condition at the present time is "infantile spasms" and/or "hypsarhythmia." Neither of these terms is completely satisfactory because "infantile spasms" do not occur only in in-

fancy but also in early childhood, and the word "spasm" does not emphasize the epileptic nature of the attacks strongly enough. Furthermore, the term does not convey the severity of the clinical condition. Hypsarhythmia, on the other hand, a term used by Gibbs and Gibbs to describe the EEG picture that is frequently found in these children, pertains to the EEG only, and is not necessarily present in all patients with "infantile spasms." Other names that have been applied include the terms: massive myoclonic jerks of infancy, lightning seizures, minor motor seizures, salaam seizures, drop seizures, epilepsia nutans, secousses, flexion spasms, BNS (Blitz-Nick-Salaam seizures), propulsive petit mal and the West syndrome. The latter term is used as tribute to Doctor West, who had described the condition in a letter to the editor of *The Lancet*, dated January, 1841, in order to obtain help for his son who had developed this illness. His description is so vivid and concise, covering all the essential clinical features, that the main portions of his letter will be reproduced here.

"Sir: I beg, through your valuable and extensively circulating Journal, to call the attention of the medical profession to a very rare and singular species of convulsion peculiar to young children.

"As the only case I have witnessed is in my own child, I shall be very grateful to any member of the profession who can give me any information on the subject, either privately or through your excellent Publication.

"The child is now near a year old; was a remarkably fine, healthy child when born, and continued to thrive till he was four months old. It was at this time that I first observed slight *bobbings* of the head forward, which I then regarded as a trick, but were, in fact, the first indications of disease; for these *bobbings* increased in frequency, and at length became so frequent and powerful, as to cause a complete heaving of the head forward towards his knees, and then immediately relaxing into the upright position, something similar to the attacks of emprosthotonos; these bowings and relaxings would be repeated alternately at intervals of a few seconds, and repeated from ten to twenty or more times at each attack, which attack would not continue more than two or three minutes; he sometimes has two,

three, or more attacks in the day; they come on whether sitting or lying; just before they come on he is all alive and in motion, making a strange noise, and then all of a sudden down goes his head and upwards his knees; he then appears frightened and screams out; at one time he lost flesh, looked pale and exhausted, but latterly he has regained his good looks, and, independent of this affection, is a fine grown child, but he neither possesses the intellectual vivacity or the power of moving his limbs, of a child of his age; he never cries at the time of the attacks, or smiles or takes any notice, but looks placid and pitiful, yet his hearing and vision are good; he has no power of holding himself upright or using his limbs, and his head falls without support."

West goes on saying that he had tried all known remedies, without success, and had subsequently taken the child to ". . . Sir Charles Clarke and Dr. Locock, both of whom recognized the complaint; the former, in all of his extensive practice, had only seen four cases, and, from the peculiar bowing of the head, called it the 'salaam convulsion'; . . . . Sir C. Clarke knows the result of only two of his cases: one perfectly recovered; the other became paralytic and idiotic; lived several years in that state, and died at the age of seventeen years. I have heard of two other cases, which lived one to the age of seventeen, the other nineteen years, idiotic, and then died. . . . Although this may be a very rare and singular affection, and only noticed by two of our most eminent physicians, I am, from all I have learnt, convinced that it is a disease (*sui generis*) which, from its infrequency, has escaped the attention of the profession. I therefore hope you will give it the fullest publicity, as this paper might rather be extended than curtailed."

In a postscript Dr. West gave a brief progress note: "In my own child's case, the bowing convulsions continued every day, without intermission, for seven months; he had then an interval of three days free; but, on the fourth day, the convulsions returned, with this difference, instead of bowing, he stretched out his arms, looked wild, seem to lose all animation, and appeared quite exhausted."

For further historical review of the condition the reader is referred to the paper by Bower and Jeavons (1959), and the

chapter on astatic epilepsy in Lennox's book. There is still some controversy in the literature whether these attacks are predominantly due to an inhibitory mechanism or whether the falls result from massive myoclonic jerks. The myoclonic jerks are readily observable in a number of children, but others merely seem to lose posture and crumple to the floor, while still others may have both seizure types on different occasions. Inasmuch as it has not been demonstrated that the prognosis differs substantially between these various forms and there is so much overlap even in a given patient, no attempt will be made to enter into this controversy here.

Chao *et al.* (1957) noted that the prognosis was good in regard to eventual cessation of massive spasms. "However, over 15 per cent of patients have other types of seizures (focal, generalized, or akinetic) or develop them after the massive spasms cease. The severe mental deterioration represents a most serious aspect with respect to prognosis. Intellectual ability may improve after spasms cease entirely but it seldom returns completely to normal. . . . A more favorable prognosis with respect to mental development exists when seizures continue only for short periods. . . . Patients whose massive spasms occur singly rather than in series also tend to carry a better prognosis."

Livingston *et al.* reported in 1958 on 698 children with what he called "minor motor epilepsy"; the earliest age of onset was found to have been eight days, and the latest five and one-half years. These constituted approximately 9 per cent of all children studied at the Epilepsy Clinic of Johns Hopkins Hospital out of a total of 7,832 children. The condition is, therefore, somewhat more common than pure petit mal absences. IQ at one year of age was estimated to have been normal in fourteen children; twenty-one were slightly retarded; 248 moderately retarded, and 388 severely retarded. Hypsarhythmia was found to have been present in the electroencephalogram in 511 out of 594 EEGs (86%). The etiological conditions were quite diverse. The authors noted that these spells are exceedingly difficult to control with anticonvulsant drugs and felt that the ketogenic diet was the most effective therapy. Seizures rarely recurred after five or six years of age. With the ketogenic diet, complete control of

spells was obtained in 91 of 186 patients who had been on this form of therapy (49%). The most serious aspect of minor motor epilepsy was, however, the associated mental retardation. Bower and Jeavon's writing in 1959 on infantile spasms and hypsarhythmia stated: "All workers agree that most patients remain mentally defective although the spasms diminish in frequency or disappear. A few die within a few years of the onset of spasms." They went on to say that of their twenty-two patients, two had died, nineteen remained mentally retarded, and one child recovered completely in all respects.

Being confronted with such a hopeless outlook, Stamps *et al.* (1959) were impressed by the exhibit of Sorel and Dusaucy-Bauloye in 1958 on the results of treatment of these patients with ACTH and they tried this compound subsequently in sixty of their patients. Their report presents an example of how the investigator's hopes can at times exceed factual data. The summary and conclusions state: "Before the introduction by Sorel of ACTH for the treatment of hypsarhythmia, the prognosis for patients with this condition was extremely poor; 85 per cent became mentally retarded and 10 per cent died. Electroencephalographic and clinical studies on sixty consecutive patients with infantile spasms with hypsarhythmia, some of whom have been followed up for over a year, indicate that ACTH therapy results in a dramatic improvement in at least 30 per cent of such cases. When a good response to ACTH is obtained, the electroencephalogram normalizes, a great clinical improvement occurs, the spasms cease, and further retardation is prevented." The attentive reader will note that "some" of the patients were followed "for over a year." The body of the paper gives no indication about the length of follow-up of any of the children and it is therefore difficult to see how the conclusion that "further retardation is prevented" can be justified. A further point of interest emerges from the study of the paper, namely, a statement: "Although the seizures tend to subside by the fourth year of life even without treatment, retardation is permanent." This points out the fact that the stopping of seizures is not necessarily equivalent to significant improvement in mentality. If one examines the table that accompanies the paper, one finds that seizures were

eliminated (time unspecified) in eighteen (30 per cent), decreased in thirteen (22 per cent), and unchanged in twenty-nine (48%). As far as "motor performance and alertness" was concerned, six (10%) became normal, eighteen (30%) were improved, and thirty-six (60%) were unimproved, while nine (15%)patients showed a relapse after improvement. If we subtract the nine patients who had shown a relapse, we find that fifteen out of sixty patients (25%) had shown normalization or improvement in "motor performance and alertness." To turn this figure around, 75 per cent remained mentally retarded, which is not too strikingly different from the 85 per cent quoted in the introductory paragraph of the paper.

Fukuyama *et al.* (1960) reported "excellent results" from ACTH injections, in the summary of their paper, but in the paragraph on results, one finds: "Among forty-eight cases, twelve cases (25%) became entirely free from seizures, and in seventeen cases (35.4%) seizures diminished remarkably." In the discussion one reads: "Our global result was inferior to that of abovementioned authors because complete control of both clinical seizures and electroencephalographic abnormalities was attained in only eight among thirty-four cases (23.5%), while other authors reported the effectiveness in 70 to 100 per cent of patients."

Trojaborg and Plum (1960) found that 25 per cent of all children between birth to two years admitted for the first time because of convulsions to the Paediatric Clinic of Copenhagen University Hospital had infantile spasms. Hypsarhythmia was found in 80 per cent. Definite clinical effects were found in regard to reduction or cessation of the attacks in seven of twenty-two children treated with ACTH (32%). No definite effect upon the mental state was found. Pauli *et al.* (1960) reported poor success with ACTH treatment in fourteen children; only four showed improvement in regard to seizures, and in no instance was there significant improvement in the mental state.

A decreasing incidence of treatment effect in relation to length of follow-up was noted by Dumermuth in 1961. Thirty-eight patients were treated with ACTH or hydrocortisone. Initially, 68 per cent of this group showed a good result. Twenty-six patients were followed for more than one year; of these twenty-six pa-

tients, sixteen had had a good result initially (61%), but after one year only six of them (37%) still had a good outcome. If the percentage of patients with good outcome is calculated for the total group of twenty-six patients who were followed, regardless of initial success, one finds definite improvement in only 23 per cent. The clinical findings gave no indication why some patients had a good result while others did not.

Noting these varying statements about the effectiveness of steroid treatment, Jeavons and Bower (1961) subsequently decided to study the natural history of infantile spasms in order to have definitive figures against which the effects of the treatment could be measured. Their summary is quoted in its entirety because of its obvious importance: "Thirty infants with the syndrome of infantile spasms and mental retardation occurring before the age of one year have been followed by clinical and EEG examination for periods of two to six years. None were treated with corticotrophin or steroids. There was a steady reduction in the number still having spasms, and at three years over half the patients were free of them. Focal or major fits occurred in one-third of the total and did not show the same tendency to disappear with age. The EEGs became more organized and at three to three and one-half years more than one-third were normal. Hypsarhythmia was rare by this age but was found even at six years. Mental improvement was much rarer and only two patients became mentally normal. The mortality rate was 13 per cent by three and one-half years. There was little difference between the symptomatic and cryptogenic groups with regard to the rate of disappearance of spasms and EEG improvement. Mental retardation, however, was less severe in the cryptogenic group even at one year and this group showed a slight but definite general improvement later; whereas none occurred in the symptomatic group."

Bower and Jeavons (1961) compared these results with the outcome in twenty-three children who had been treated with corticotrophin and/or prednisolone. It was found: "Spasms ceased during treatment in eighteen patients but recurred in thirteen after treatment. Some EEG improvement occurred in all patients except one, and a non-epileptic record was achieved

in nine, though relapse occurred in five of those whose spasms recurred. Eight were given a second course of treatment but seven again relapsed. At the end of an average follow-up period of eight months, eleven patients had no spasms" (48%). "The effect of corticotrophin was similar to that of prednisolone; although, with the doses employed, corticotrophin appears preferable. No immediate mental improvement occurred, and only two cases eventually achieved a development quotient of eighty or more. Although the drugs had a temporary beneficial effect in both the symptomatic and cryptogenic groups, better results were achieved in the latter group. A comparison is made with a group of patients not treated with hormones and it is concluded that on the whole these drugs have a long-term beneficial effect on the spasms; whereas their effect on mentality is doubtful. It is possible that under hormonal treatment there is an acceleration of the natural changes which occur with age."

The observation that "idiopathic" cases of infantile spasms have a better prognosis, regardless of type of treatment, was also made by Matthes (1954). The symptomatic group contained 30 per cent of ninety patients, half of these had died by the time of follow-up which ranged up to thirty-three years; the other half, with exception of one case, was profoundly retarded mentally. As far as the idiopathic group was concerned 80 per cent were alive at time of follow-up and one-quarter had shown normal physical and mental development.

Stolecke and Pache (1962) made the point that children who were treated prior to age nine months had a better outcome than those who received their first treatment after that age. Of eleven children who were treated with ACTH prior to nine months of age, four had a complete remission with subsequent normal physical and mental development. This was the case in three out of seventeen children only, who were treated after the ninth month. The length of follow-up was not stated in their paper.

Bray reported in 1963 a four-year follow-up study of the ten patients who had been originally reported by Low in 1958. Although the number of patients is small, it is the only report dealing with long-term results of corticotrophin and cortisone therapy. Bray concluded from his study: "No correlation was

found between the infants' initial clinical and electroencephalographic response to therapy and their follow-up intelligence quotients. The similar initial electroencephalographic findings, contrasted with the marked follow-up differences in levels of intellectual functioning, illustrate the limited prognostic value of the electroencephalogram in this syndrome. Similarly, no correlation was noted in the patients' initial response to therapy, and the presence or absence of microcephaly or focal neurological deficit. In the absence of any other rational treatment, and despite the dismal prospect suggested by this report and those of others, renewed efforts to treat patients earlier and more intensively with cortisone and corticotropin could be undertaken. However, in the light of four years' experience, such an approach might be a reflection more of therapeutic desperation than of rational expectation of good results."

Schmidt (1964) reported on the effects of ACTH and prednisone in a group of thirty-two children with infantile myoclonic seizures. Four children were regarded as cured after treatment (12%); sixteen improved, and twelve had not changed. Seizures and EEG were more easily influenced than psychomotor development. It was felt that success can be expected only with high dosages and long-term administration of the compounds. It was also felt that the shorter the period of time between onset of the condition and treatment, the better the ultimate success. The follow-up duration ranged from three months to three years.

Another study appearing in 1963 was by Doose who reported on eighty-one children with this condition. He pointed to the discrepancies in the literature regarding treatment results but felt that these were due to different dosages used, different compounds, and different length of treatment. As far as his own series was concerned, out of thirty-six adequately treated children thirty became initially seizure-free (83%); three improved, and three remained unchanged. In regard to final result of follow-up ranging between three months and two and one-half years, twenty-four children were seizure-free (77%); three improved; four were unchanged, and five patients had died. He listed the following factors as being important for the success of treatment:

1. Children who are severely damaged frequently respond quite slowly, temporarily, or not at all, but strict correlations between type and extent of preexisting damage and response to treatment were not present, because occasionally, even severely damaged patients showed a good response.
2. Seizures were more easily influenced in infancy than in older children and treatment results were better with a shorter duration of illness.

He found, as have others, that the influence of hormonal treatment on mental development was more difficult to assess. The majority of children had marked mental retardation prior to treatment. A positive effect of therapy on mental development was seen rarely in such cases. In less damaged children improvement in development could be seen more frequently. In some children a marked discrepancy between physical and mental development could be observed. Some children regained their motor functions soon after cessation of seizures without at the same time showing definite progress in their mental development. He concluded that treatment with ACTH or corticosteroids can bring about a rapid cessation of seizure activity in the majority of cases (70%). Children who have not been already damaged can be saved from mental and physical deterioration. In children who are retarded a progression of this damage can be prevented, and the physical and mental development can be beneficially influenced on occasion. In general, he felt that there are quite narrow limits to the success of hormonal therapy, because in the majority of patients the condition is due to marked cerebral damage. Nevertheless, the treatment results can be improved if the children are treated immediately after the onset of seizures. Start of treatment within the first weeks was regarded as even more important in infantile myoclonic seizures than in other forms of epilepsy. We will return to this point in more detail later.

In 1964 Harris reported on seventy-five children suffering from infantile spasms and treated with ACTH. She found: "Only six have apparently recovered at a follow-up of one or two years, though temporary favourable clinical and EEG response had been seen in many more cases. None of the patients who did not

show EEG improvement in relation to the first course of ACTH eventually recovered." One of the most recent reports at the time of this writing was by Danielsen in 1965, who treated twenty-three children with corticosteroids. The attacks ceased during treatment in fourteen (60%) and improved in one. Seventeen patients had hypsarhythmia, which disappeared in twelve during treatment but recurred afterwards in one. Seizure freedom had dropped to eight cases (34%) by the time of follow-up, which ranged between six months and four and one-half years. Mental retardation was found to be unaffected by steroid treatment. Danielsen concluded: "Although the effect on the mental development is doubtful, the effect on the incidence of attacks and on the EEG pattern is considerable. Steroid treatment of patients with infantile spasms and hypsarhythmia must therefore be regarded as the best treatment available at present, and treatment should be instituted as soon after the commencement of the attacks as possible."

This brings us to the crux of the problem. Although Sorel and Dusaucy-Bauloye's paper is widely quoted in references, its main message does not seem to have reached subsequent investigators. Their report was based on twenty-one children with hypsarhythmia, seventeen of whom were followed for one month to six and one-half years. Seven of these seventeen received ACTH treatment. In five of the seven cases the EEG normalized completely within several days, and in one the tracing improved markedly but a left temporal focus remained. The EEG was not influenced in the last case. From a clinical point of view the epileptic attacks disappeared immediately in six cases. The patient whose EEG did not respond also showed no clinical improvement. The main point of the paper is contained in the sentences: In two of these cases treatment could be instituted during the first week. Motor and mental status returned to normal, and physical and intellectual development subsequently proceeded in a normal manner, with a follow-up of two years in one case and nine months in the other. In the other two cases where treatment was instituted after three to four months, the seizures had disappeared but the intellectual state had not normalized completely. In the two cases where treatment could not

be instituted until quite late the dementia was total. This treatment, therefore, completely modifies the prognosis of this serious condition of infancy, but it should be instituted with the greatest possible speed.

If we were to summarize the relevant points of the paper, one would say that out of seven patients treated with ACTH, six had complete freedom from seizures during the limited follow-up period, but only two subsequently continued with normal mental and physical development. These two patients had been treated within the *first week* of the onset of the illness. Gastaut *et al.*, reporting on four cases in 1959, also emphasized this point. They stated that if the illness has been present only for several days or weeks before treatment is started and before signs of mental regression are noted, recovery is rapid and total. If, on the other hand, treatment is started only after several months or several years, the intellectual deficit cannot be overcome and the status quo remains.

The conditions under which one could expect an improvement in mentality were, therefore, quite clearly spelled out in these two papers. With the literature having reached considerable proportion in the subsequent years, one might have expected that this point would have been considered and that we would by now have definitive figures that would allow us to compare the effects of treatment instituted within the first one or two weeks after the onset of the illness, against the results achieved if treatment is started after one to two months, or even later. If one reviews the literature from this specific point of view, one finds a remarkable paucity of material. The majority of authors either do not give definite data as to the time of initiation of treatment in relation to the first appearance of symptoms, or they create larger groups with treatment starting within the first three months or first six months after onset of illness. It is impossible from their tables or figures to select those cases that were treated within the first month or weeks. Gastaut *et al.* had only one case out of the four that was treated within one month after the onset of the illness, and this child recovered completely. Bower and Jeavons had one case of cryptogenic infantile spasms that was treated within three weeks after onset of the illness. The developmental

quotient before and after treatment was low but ". . . this child subsequently reached eighty-three." There was also one case in their symptomatic group that was treated within four days, but no effect on mentality occurred. Dummermuth's Case 1 was treated within a few days, and immediate cessation of seizures was noted with subsequent normal psychomotor development. The developmental quotient two years later was 117. Harris' Case 2 was treated ". . . very soon after the onset of infantile spasms. The EEG improvement occurred very rapidly and no further spasms occurred, but he was moderately retarded at follow-up." Koch and Gruetzner's (1960) Case 1 was treated six weeks after onset. The EEG normalized; seizures stopped, and normal physical and mental development occurred. Their Case 2, also treated six weeks after onset, showed initial improvement but subsequent relapse. At follow-up, three months later, there were occasional infrequent seizures. Mental development had progressed but was retarded in contrast to his unaffected twin brother. Pauli *et al.* (1960): Cases 8 and 11 were treated one month after the onset of the illness, but both children were already definitely retarded; there was no effect on the condition. Schmidt noted among the patients who could be treated "immediately" that there were three of the four patients who showed subsequent normal development. What is meant by the term "immediately" cannot be reconstructed from his figures, because the table combines patients treated within one to three months. Stolecke and Pache's Cases 7 and 26 were treated after two weeks of illness. One showed completely normal physical and mental development; the other improved in regard to seizures but remained retarded mentally.

We are therefore confronted with the fact that on this apparently most important variable we still have quite inadequate information. I am especially emphasizing this point because we are dealing with a condition which represents a human catastrophe. If there is any hope that permanent mental retardation is avoidable, even in a segment of the various conditions that can cause the clinical and EEG picture of infantile spasms, it should certainly be pursued most energetically. It would be most interesting to see whether the long-term results in regard to the

mentality of a large number of children, treated within the first two to three weeks after onset of the condition, do in fact differ from those who are treated later or not at all. This answer is not available at the present time. It could only become available if pediatricians and general practitioners were informed that the symptom of infantile spasms and/or hypsarhythmia represents a medical emergency, as acute as ileus for instance, and immediate vigorous steroid treatment is indicated. EEGs obtained at weekly intervals would give an indication about the effectiveness of treatment. Dosages could be adjusted in an upward or downward direction depending upon the EEG picture rather than relying on clinical observation only. A program like this would, within a few years, tell to what extent the steroids are effective, and one could then define the subgroups in which success can be anticipated. It is obvious that if a severe congenital malformation of the brain exists, steroids are not likely to be of much help, but at the beginning of the illness one may not be absolutely certain about the presence or absence of congenital malformations. It would seem better at this point in time to treat the total group of patients regardless of presumed etiologies and to evaluate later who is responding and why. The results of such a program might prove a complete failure in the long run, but this should certainly not deter us from the attempt.*

* Since this chapter was written, some evidence has appeared that high doses of Valium® can be beneficial in this condition. The Valium analogue Mogadon® appears to be even more effective. It is not yet approved by the Food and Drug Administration in this country, but reports from Europe and selected investigators in the United States are encouraging. While these drugs may be as effective as the steroids—or even more so—they will probably not change in the least the relationship between time of onset of treatment and long-term mental state. The studies suggested above will have to be carried out regardless of the type of treatment that is "most modern" at any given point in time.

Chapter 6

POSTTRAUMATIC EPILEPSY

As far as the evaluation of prognostic factors in posttraumatic epilepsy is concerned, we are not only confronted by the problem as to what constitutes epilepsy (i.e. single seizure versus recurrent attacks), but also by the difficulties in deciding when a head injury is serious enough to be regarded as a cause of seizures. An additional difficulty lies in the technique of follow-up. Results based merely on correspondence are likely to be different from those obtained through personal interviews. The combination of these factors, as well as the variability in the length of follow-up of patients, is bound to reflect itself in diversified opinions not only in regard to the incidence of epilepsy after a blow to the head, but also in regard to control of seizures once they have become established. The majority of statistics regard the occurrence of even a single seizure at any time after trauma as posttraumatic epilepsy. This will obviously bias medication results in a favorable direction because one will never know whether the patient would have had further spontaneous attacks or not. On the other hand, it is equally possible that a number of patients may develop seizures after a relatively minor insult to the cranium, and the etiology of the disorder is not at all related to the injury, but resides in the large pool of "cryptogenic" epilepsy, and seizures would have made their appearance regardless of the intervening trauma. These are difficult diagnostic problems which can only be solved by careful study of the individual patient and his family. These investigations are quite time-consuming and may even necessitate in certain instances electroencephalographic recordings from the parents and siblings of the

patient in order to avoid improper classifications. These points are emphasized here because it has been claimed that true posttraumatic epilepsy tends to have a good prognosis. However, before we address ourselves to this aspect we should return to more basic questions. They could be formulated as follows:

1. What is the incidence of epilepsy after head trauma?
2. What are the characteristics of the injury or of the individual that will favor the subsequent development of epilepsy?
3. Once epilepsy has developed, what are its chances for remission?
4. What are the characteristics of the patient with established posttraumatic epilepsy who will enjoy a complete remission?

As far as incidence is concerned, Table 11 provides some findings of investigators spanning nearly fifty years. Reviewing the table we can see that the figures range from a low of 4 per cent to a high of 43 per cent. It is clear that these figures are quite meaningless as far as any prediction is concerned because they are bound to be contaminated by the problems mentioned in the first paragraph of this chapter. However, the picture changes considerably if we limit our survey to statistics dealing only with penetrating head injuries. As shown in Table 12 the spread is considerably narrower, with the majority of studies showing incidence figures around 40 to 50 per cent. Dural penetration per se is, of course, not the most severe injury that can be survived, and the various series that are listed in the table still contain different degrees of cerebral injuries.

We may now ask ourselves how long after injury the patient is liable to experience the first seizure. Table 13 provides some figures from the literature and shows, in essence, that the vast majority of patients who develop posttraumatic epilepsy have their first seizure within one to two years after injury. The literature points out that most patients actually have the first attack within a few months, but there is no absolute end point in time at which the patient can be definitely reassured that epilepsy will not occur. Baumm (1930) reported an onset as late

as twelve years, and Ascroft (1941) even between sixteen and twenty years after injury.

This brings us to the second question, What characteristics of the wound or of the patient favor the appearance of seizures after an injury? It has been shown rather conclusively by sev-

TABLE 11

INCIDENCE OF POSTTRAUMATIC EPILEPSY

	Type of Sample	*Percentages of Patients with Posttraumatic Epilepsy*	*Number of Head Injured Patients Involved in Study*
Sargent, 1921	WW I	4.5	18,000
Rawling, 1923	WW I gunshot wounds	25	452
Alajouanine *et al.* 1928	WW I	23	602
Wagstaffe, 1928	WW I gunshot wounds	10	377
Baumm, 1930	WW I	24	1,040
Credner, 1930	WW I	38	1,990
Ascroft, 1941	WW I gunshot wounds	34	317
Denny-Brown, 1942	WW II	8	630
Gliddon, 1943	WW I gunshot wounds	10	500
Watson, 1952	WW II penetrating head injuries only	42	286
Russell and Whitty, 1952	WW II penetrating head injuries only	43	820
Phillips, 1954	WW II closed head injuries	6	500
Brun, 1955	Civilian	8	1,648
Walker and Jablon, 1961	WW II	28	739
Caveness and Liss, 1961	Korean Campaign	24	407
Evans, 1962*	Korean Campaign	20	422
Jennett, 1965	Civilian, blunt head injuries	10	1,000

* Selected sample, onset of illness no sooner than one month after injury.

eral authors on large series of cases that the degree of cerebral damage resulting from an injury stands in direct relationship to the incidence of future epilepsy (Ascroft; Baumm; Caveness and Liss (1961); Credner (1930); Evans (1962); Gliddon (1943); Rawling (1922); Wagstaffe (1928); Walker and Jablon

TABLE 12

INCIDENCE OF POSTTRAUMATIC EPILEPSY WHEN ONLY PENETRATING HEAD INJURIES ARE CONSIDERED

	Percentages of Patients with Posttraumatic Epilepsy	*Number of Head Injured Patients Involved in Study*
Rawling, 1923	35	206
Wagstaffe, 1928	19	176
Baumm, 1930	44	562
Credner, 1930	49	1,234
Ascroft, 1941	45	129
Gliddon, 1943	19	137
Watson, 1952	42	286
Russell and Whitty, 1952	43	820
Caveness and Liss, 1961*	51	73
Walker and Jablon, 1961**	51	133
Evans, 1962	42	137

* Dura and brain penetration of profound degree.

** Recalculated by Caveness and Liss according to their criteria.

(1961). Representative figures contrasting the incidence of epilepsy after simple closed head injuries and penetrating head injury are shown in Table 14. Although percentages vary among different investigators, all series demonstrate the substantially higher risk of epilepsy with increasing severity of the injury. Linear skull fractures do not seem to increase the risk for future epilepsy over that for simple closed head injuries with scalp lacerations. Comparing the figures given by Evans, both of these groups yielded 8 per cent of epileptic patients. Depressed frac-

TABLE 13

TIME BETWEEN INJURY AND ONSET OF POSTTRAUMATIC EPILEPSY

Denny-Brown, 1942	Within 1 year	86%
Russell and Whitty, 1952	Within 1 year	73%
Caveness and Liss, 1961	Within 1 year	75%
Baumm, 1930	Within 2 years	66%
Credner, 1930	Within 2 years	72%
Ascroft, 1941	Within 2 years	78%
Phillips, 1954	Within 2 years	86%
Walker and Jablon, 1961	Within 2 years	75%

TABLE 14

COMPARISON OF INCIDENCE OF EPILEPSY AFTER SIMPLE CLOSED HEAD INJURIES AND PENETRATING INJURIES

	Simple Closed Head Injuries		*Penetrating Injuries*	
	%	N	%	N
Rawling, 1923	11	47	35	206
Wagstaffe, 1928	3	60	19	176
Credner, 1930	20	244	49	1,234
Ascroft, 1941	24	66	45	129
Gliddon, 1943	4	130	19	137
Walker and Jablon, 1961	18	50	36	472
Caveness and Liss, 1961	12	117	51	73
Evans, 1962	8	136	42	138

tures are, of course, more epileptogenic, and the figures reported merge with those given for dural penetration.

Another method of estimating the degree of cerebral injury as a result of a blow to the head is provided by the length of unconsciousness and the length of posttraumatic amnesia. The duration of unconsciousness has been shown to stand in direct relationship to the frequency of occurrence of posttraumatic epilepsy by Walker and Jablon as well as by Evans. Some figures demonstrating the relationship between length of posttraumatic amnesia and occurrence of seizures are shown in Table 15. It is

TABLE 15

RELATIONSHIP OF DURATION OF POSTTRAUMATIC AMNESIA TO INCIDENCE OF POSTTRAUMATIC EPILEPSY

Denny-Brown, 1944	Posttraumatic amnesia	Less than 24 hours	10.9%
		1 to 7 days	4.6%
		More than 7 days	3.4%
Phillips, 1954		Less than 24 hours	4.6%
		More than 24 hours	11.5%
Jennett and Lewin, 1960	Early epilepsy	Less than 24 hours	3.0%
		More than 24 hours	12.0%
	Late epilepsy	Less than 24 hours	6.7%
		More than 24 hours	14.2%
Evans, 1962		Less than 24 hours	13.8%
		More than 24 hours	36.2%

again apparent that the longer the period of posttraumatic amnesia, the more likely the occurrence of seizures. Only Denny-Brown's report (1944) differed from these trends. He felt that local rather than generalized brain damage was the most important factor in the production of epilepsy.

Apart from intensity of injury, what are some of the other potential etiological factors that have been investigated? Walker and Jablon examined the following variables and found them unrelated to the development of seizures: age at time of injury, difficulties during delivery of the patient, birth order, previous systemic illness, alcohol consumption, previous head injury, postinjury EEG, and frequency of nervous disorders in the immediate family. As far as family history of epilepsy is concerned, it was felt that this might have played some role in a subgroup of patients whose seizures were not of the focal type. A constitutional factor on which epileptics with focal seizure types differed significantly from the nonepileptic sample was peculiarly enough a more frequent history of constipation in the epileptic patient. Other features that did play a role in the production of epilepsy were increase in dimensions of the wound in all planes (both diameter of defect and depth of wound), duration of unconsciousness after the injury, amount of neurological impairment (but no evidence that any one type of impairment was a more potent determinant than another), presence of intracranial foreign bodies, and all factors tending to delay healing of the wound. Location of the wound was not of major importance in their series.

Although Walker and Jablon's findings are, in general, quite representative of the literature, a few points should be elaborated upon. As far as wound healing is concerned, Ascroft found that if healing took place within fifteen days the incidence of seizures was 22 per cent; but if healing was delayed beyond sixty days it rose to 45 per cent.

Location of the wound in relation to posttraumatic seizures has been extensively investigated and some representative figures are shown in Table 16. Baumm's figures did not lend themselves to this type of tabulation, but they point out likewise that lesions in the Rolandic area are most epileptogenic while occipi-

tal lesions show this propensity the least. Russell and Whitty (1952) noted also that wounds situated within five centimeters of the sagittal line resulted in a significantly lower incidence of seizures than those that were farther down on the convexity. This observation stands by itself, since I have not found it mentioned in other reports.

Reviewing the figures in Table 16, one should remember that the locations mentioned are mostly approximations. What one author may call frontal or parietal might be included under Rolandic by another. It would seem that the general trend of the

TABLE 16

RELATIONSHIP OF SITE OF LESION TO INCIDENCE OF POSTTRAUMATIC EPILEPSY

	Frontal (%)	*Rolandic* (%)	*Parietal* (%)	*Temporal* (%)	*Occipital* (%)
Credner, 1930	45		47.3	36.7	32.3
Ascroft, 1941					
Total group	26.5	46	38.5	42.5	27.5
Subgroup with dural penetration	31	54	52	59	41
Gliddon, 1943	6.1	22.9	11.4	12.9	5.7
Watson, 1947	26.7	50.7		35	33.3
Russell and Whitty, 1952	39	55	65	38	38
Walker and Jablon, 1961	33.7		36	32.5	23.9
Evans, 1962					
Missile injuries only	24	39	42	35	17

figures is more valuable than their absolute level. The tendency appears to be for wounds in the general vicinity of the Rolandic region to have the highest incidence of seizure disorders. The figures in Table 16 are also of some theoretical interest in regard to the primary cause of epilepsy. A widely held assumption is that the most important cause of epilepsy resides in injury to the central nervous system. This could occur *in utero*, at birth, or postnatally, and manifest itself in a seizure disorder at some later stage of life. If cerebral trauma were indeed the necessary *and sufficient* cause then we should obtain in the overwhelming majority of patients a positive history of such trauma and—even more importantly—the incidence of posttraumatic epilepsy

after penetrating head injuries should not be only approximately 45 per cent, if all studies are combined, but should be around 90 per cent. Even if we take into account the location of the lesion, the highest percentage that has been reported is that by Russell and Whitty, namely, 65 per cent for penetrating injuries in the parietal area. If we combine Russell and Whitty's figures with those of Credner, in regard to penetrating parietal injuries, we still arrive at only 56 per cent. We are therefore confronted with the problem why only approximately one out of two severely brain injured individuals, with approximately the same amount of injury in approximately the same area, will develop seizures while the other will be spared this additional complication. These observations are merely mentioned in order to point out that, although cerebral trauma is a potent epileptogenic factor, it does seem to need an additional, as yet unknown, process in order to trigger a seizure disorder.

As far as foreign bodies remaining in the brain are concerned, Redlich (1919) observed that in 34 per cent of patients with epilepsy, foreign bodies were present in the brain, but this was the case in only 22 per cent of nonepileptics. He felt, however, that this difference was too small to be of major importance. He found no differences between bone and metal fragments in regard to their epileptogenicity. Baumm also found only a 3 per cent difference (12% versus 9%) in the epileptic versus nonepileptic sample in regard to foreign bodies and felt that this was clearly too small to be significant. This finding agrees with the observations of Watson (1947). Ascroft felt that foreign bodies were not important in the production of future epilepsy if they consisted of metal. Evans agreed with this observation but thought that remaining bone fragments were epileptogenic. Gliddon concluded that retained foreign bodies were epileptogenic, and bone fragments more so than metal.

The problem of heredity is also somewhat controversial. No evidence for hereditary predisposition was found by Watson, and by Phillips (1954), but Evans found a somewhat greater incidence of positive family history of epilepsy in the sample of Korean War veterans who developed seizures than those who did not.

These observations dealt with the problem of whether or not seizures will develop at all. We can now address ourselves to the third question, What can be expected in regard to the course of the illness once a seizure has made its appearance? Several authors feel that it is prognostically important to distinguish between "early" and "late" epilepsy. Unfortunately, different workers apply different criteria to what constitutes early epilepsy and the results are therefore not directly comparable. Ascroft felt that ". . . in about one-third of the patients having fits after gunshot wound of the head, epilepsy may be of a more or less transient character. The earlier the fits begin the less likely are they to become persistent. In the first week after injury, . . . the risk of a man having fits is about 5 per cent (15 of 317 cases), but the risk of the fits becoming persistent is only one in five. Fits starting in the second week stand an equal chance of being temporary or of becoming persistent. As the weeks pass the odds against the fits being of a temporary character rapidly increase. From the sixth month to the end of the second year the risk of developing epilepsy is about 10 per cent, but the odds favor the epilepsy becoming persistent as five to one. If the onset of fits is delayed beyond two years, the epilepsy will be persistent." He commented further that seizures soon after injury are of little prognostic significance for the occurrence of late epilepsy.

Jennett (1965) defined early epilepsy as occurring within one week of the injury, and felt the real significance of early epilepsy is that it increases by about four times the chance of epilepsy developing later. This applies even if there has been only a single seizure in the first week, no matter how severe or trivial the injury. He pointed out that there is one exception in "immediate" epilepsy when a generalized convulsion occurs within a minute of an injury, usually a trivial one. Such an episode, according to him, does not seem to predispose to later epilepsy. He found the highest risk for late epilepsy in patients who have had a combination of prolonged posttraumatic amnesia and a depressed skull fracture; 47 per cent of these patients developed late epilepsy.

Credner defined early epilepsy as occurring during treatment of the wound and late epilepsy as occurring after wound

healing was accomplished and the scar had been formed. With this definition in mind, she examined 330 patients with open head injuries and found that forty-one patients (12%) fell into the group of early epilepsy. Of these forty-one patients, sixteen (39%) had seizures only during the time of wound treatment, while the seizure disorder persisted in the remaining cases.

Denny-Brown (1942), although giving no figures of his own, stated that epilepsy occurring within the first four weeks after injury has an excellent prognosis. Evans who defined early epilepsy as seizures occurring within the first month after injury, noted that patients with early seizures were likely to develop late epilepsy, except for those having seizures within twenty-four hours after injury. The type of seizure was found to be of no value in forecasting the appearance of late epilepsy. Of 105 patients with epilepsy, thirty-seven had their first seizure within eighteen days of the injury, and this period stood out because it was followed by a gap of two weeks in which no initial seizure occurred; therefore, this figure expressed the number of initial seizures in the first month after injury. Ascroft noted that all patients who experienced seizures within the first month after injury had their first attack within the first fourteen days. Maki (1964) observed that 58 per cent of early epileptics were also late epileptics, and this was based on a sample of 125 cases. Masquin and Courjon (1963) found seven cases of early posttraumatic epilepsy (occurring within three weeks after injury) in a series of sixty-two patients. All except one had subsequent seizures within one year. It is important to point out here that some of these studies (Jennett; Masquin and Courjon; Maki) dealt with civilian head injuries only. There may well be a difference whether one deals with a sample of war head injuries or those that occur in everyday life. It would seem that a war injury sample is more likely to contain a much larger selection of true posttraumatic epilepsy cases; while a civilian sample with mostly mild head injuries will tend to contain a larger representation of the "cryptogenic" cases which are not necessarily related to the trauma. These possible differences will have to be kept in mind when one compares results of different authors.

Walker and Jablon felt that their data supported the concept

of a more favorable prognosis for the early epilepsies. When they plotted the course of epilepsies occurring within the first week, and compared it with similar plots containing patients whose seizures started between the first week and three months, as well as patients whose seizures started after three months, it was found that the early epilepsies had a definitely lower incidence each year than the later developing cases. They concluded that an onset less than one week after the injury carries the best prognosis, and an onset more than three months after injury the poorest. A decreasing incidence of future attacks, depending on the time of occurrence of the first siezure, was also noted by Baumm, and his figures are shown in Table 17. These

TABLE 17

RELATIONSHIP OF TERMINAL REMISSIONS TO TIME OF ONSET AT FIRST SEIZURE AFTER INJURY ACCORDING TO BAUMM, 1930

(N = 562)

First Seizure Occurring	*Terminal Remission (%)*
Up to 1 week after injury	55
Up to 1 month after injury	41
Up to 3 months after injury	31
Up to 6 months after injury	24
Up to 1 year after injury	25
Two to 3 years after injury	8.7
More than 3 years after injury	2.9

figures are of importance because they come from the bromide-phenobarbital treatment era. They are also similar to those of Ascroft which also date from that period. In Russell and Whitty's series, 35 per cent of patients with convulsions during the first month had no further seizures.

Symonds (1935) and Wagstaffe have been quoted in the literature as saying that early posttraumatic epilepsy has an excellent prognosis, but this is not borne out by a review of their original papers. Symonds wrote: "Although it is probably true that the early fits frequently do not recur, their occurrence indicates an increased risk of future epilepsy." Wagstaffe actually stated that the number of early fits observed in his cases that

could be traced was too small for definite conclusions to be drawn.

While these are examples of positive relationship between early onset and good outcome, Caveness (1963) in his series of Korean War veterans found no relationship between time of first seizure and subsequent cessation of attacks.

Walker and Jablon's findings that patients with early onset of seizures had a better prognosis was not borne out by Evans' study, when only those cases were considered that had their first seizure at least one month after onset of injury. No relationship between time of onset and subsequent course of epilepsy was noted, either in regard to duration of the subsequent seizure disorder or change in frequency of attacks. Ascroft had mentioned that seizures starting two years after the injury were always persistent, but this was not confirmed by Evans. Nevertheless, there seems to be a group of patients who start with seizures more than two years after injury and who carry a poor prognosis. Phillips pointed out that 15 per cent of 190 cases fell into this category. He felt that this group contained severe posttraumatic epilepsies; the seizures were mainly generalized and started, in several instances, with status epilepticus. He thought that these formed a most interesting group and would require a more detailed survey than was possible in his study.

It seems, therefore, that the majority of reports point out that seizures occurring within the first week or two may be followed by a chronic seizure disorder, but this is not nearly as common as it is when seizures start later. The tendency seems to be that the later the seizure disorder starts after injury, the more likely it is to become chronic.

If we disregard time of onset for the moment, what tends to be the usual course after seizures have made their appearance? Symonds felt that "All observers agree that the liability to the attacks once established tends to persist, that the fits become more frequent and more severe, and their repetition is often accompanied by slight progressive dementia of the kind observed in idiopathic epilepsy. Therefore, as a late complication of head injury, traumatic epilepsy is likely to be a cause of total disability for both the manual and the mental worker." He also

stated that the prognosis of traumatic epilepsy is much the same as that of the idiopathic variety as far as major seizures are concerned, but patients with minor seizures might have a better prognosis. This rather pessimistic statement can be contrasted with the opinion by Walker (1957) that ". . . posttraumatic seizures . . . do not have the same prognosis or implications as so-called idiopathic epilepsy." Walker (1962) commented further: "The fact that permanent disability is not a result of posttraumatic epilepsy is emphasized in addition to the need to reassure patients of this favorable prognosis." Table 18 gives some results of remission rates cited in the literature. Again we are handicapped by the fact that a number of authors give terms like "cure" without mentioning for what period of time seizures have been absent prior to the last follow-up examination. The table shows considerable spread: 4 per cent as the lowest rate for remissions having lasted at least six years, and 53 per cent as the

TABLE 18

PERCENTAGES OF TERMINAL REMISSIONS GIVEN IN THE LITERATURE FOR POSTTRAUMATIC EPILEPSY

	Duration of Seizure Freedom	*Percentages of Patients Remitted*	*Number of Patients Involved in Study*
Alajouanine *et al.*, 1948*	At least 6 years	4.1	143
Baumm, 1930	"observed for at least 7 years"	15	247
Credner, 1930	No time given	6	339
Ascroft, 1941	"for some years prior to last examination"	31	96
Watson, 1952	At least 1 year	17	126
Brun, 1955	No time given "cured"	53	92
Walker and Jablon, 1961	At least 2 years At least 5 years	34 21	207
Evans, 1962	2 years or more	39	81
Caveness, 1963	2 years or more	53	109

* Selected series, all patients had cranial surgery after injury.

highest for a period lasting at least two years. When we remember that a number of these series contain patients who have had only one or two seizures altogether, the figures shown are not markedly different from those seen in "idiopathic" epilepsy. Although there is probably not much difference in this particular respect, there may be some in the frequency of occurrence of seizures in the patients who continue to have posttraumatic epilepsy. Redlich pointed out in 1919 that patients with gunshot wounds tend to have infrequent seizures. This observation agrees with Walker and Jablon's findings reported in 1961. They mentioned that, as far as major seizures are concerned, ". . . only 30 per cent of the men who ever had major fits have had such attacks more than twice a year, and 45 per cent had none for two years." Evans found that only eighteen out of seventy-five patients had more than one seizure a year in the two years prior to follow-up carried out seven to eleven years after injury. This agreement between authors is of importance because in Redlich's time only phenobarbital and bromides were available as anticonvulsant medications, and the infrequent occurrence of major seizures can therefore not be credited to modern anticonvulsant medications.

Masquin and Courjon emphasized also the good prognosis of posttraumatic epilepsy, and stated that well and regularly applied medication in patients not suffering from alcoholism leads to recovery within one to five years in 75 per cent of cases. They noted also that the majority of patients showed relatively few seizures (one to two convulsive attacks). This is, of course, an obvious problem in regard to definition of epilepsy. If we insist on a definition that epilepsy means recurrent seizures, the majority of Masquin and Courjon's patients might not have qualified for inclusion in the series, and the final opinion of the authors regarding the good prognosis of posttraumatic epilepsy might have been considerably different.

Watson's series (1952) is of interest because he deliberately excluded patients in whom epilepsy developed within the first four weeks unless seizures persisted subsequently; fifty-three patients were followed for a three-year period, all had penetrating head injuries. He found that only nine (17%) of the patients were

free from seizures for one year or longer, while forty-four (83%) continued to have seizures. Of these forty-four patients, twenty (37.8%) had shown some improvement in their seizure disorder, nine (17%) were unchanged, while fifteen (28.2%) had become worse.

In regard to seizure types that can result from trauma, it is generally agreed that nearly all the forms of epilepsy occurring spontaneously can also be seen after injury, but it is important to point out that Walker and Jablon have not found classical three cycles per second spike wave activity and associated petit mal in any of their patients. Although the older literature frequently gives accounts of "petit mal" in some posttraumatic cases, a review of the actual case reports indicates that one is dealing with temporal lobe type seizures and other abortive seizure manifestations rather than true petit mal.

In regard to mental deterioration, Stevenson (1931) felt that it is more rapid in traumatic than in idiopathic epilepsy and is related mainly to the frequency of the seizures. When seizures are infrequent, however, deterioration is more rapid and marked in severe wounds of the head than in idiopathic epilepsy with a similar frequency of seizures.

One might assume that the electroencephalogram could be a useful tool in the prognosis of patients with posttraumatic epilepsy, but this does not appear to be the case. Marshall and Walker (1961) compared EEGs that were obtained within six months after injury with those taken five or more years later, and correlated these with cessation of attacks for at least two years versus continuance of seizures. No statistically significant correlation could be found between these factors and normalcy or abnormalcy of the electroencephalograms. It was concluded that the EEG is not a sufficiently sensitive indicator to foretell the course of posttraumatic epilepsy. Masquin and Courjon agreed that it is remarkably difficult to predict posttraumatic epilepsy from the electroencephalogram. Their study was based on sixty-two seizure patients who had been followed since their initial injury. Unfortunately, their study suffers from a serious handicap, inasmuch as the authors did not report on control patients who had received head injuries without developing

epilepsy. This limitation has to be kept in mind when one evaluates their conclusions. They stated that while ". . . normalization of the EEG is not a definitely favourable prognostic sign, the finding of a focus of slow spikes and waves, spikes, or subclinical seizures is of unmistakable unfavourable prognostic significance . . . the gradual disappearance of localized changes as a rule carries a good prognosis; whereas persistence, exacerbation, and bilateralization of the changes spell a protracted epileptic aftermath, particularly when focal irritative changes are concerned."

Phillips stated that he had only insufficient electroencephalographic information on his patients, but found that in nearly 30 per cent of cases the EEG was quite normal. Walker commented further in 1962: "Serial recordings do not enable an accurate prognosis, for although episodic discharges may precede the convulsion, they may also resolve without overt seizures. Perhaps the only valid conclusions to be drawn from the electroencephalogram is that a normal record after a head injury indicates little brain damage and hence a slight chance of epilepsy developing, whereas an abnormal tracing is usually associated with more severe cerebral injury and hence a greater chance of seizures. However, even the most disorganized electroencephalogram does not mean that seizures will invariably occur in the future. . . . Once epilepsy has been established, the EEG does not distinguish the cases that have a good versus a bad prognosis."

In the early days of electroencephalography, Williams (1944) had thought that "When changes that have been described as larval attacks are seen at an interval after injury, epilepsy is virtually certain to supervene." He regarded as "larval attacks" EEG changes that consisted of "characteristic epileptic outbursts." It is fair to assume that these changes are similar to what Walker called "episodic discharges," which can resolve without overt seizures. The disappearance of electroencephalographic seizure discharges without the development of overt clinical epileptic manifestations has also been seen by ourselves in a sample of severe head injured patients who had a fatal outcome (Rodin *et al.*, 1965).

The question still remains why some patients stop having seizures after a period of time, but others continue with the disorder indefinitely. Walker and Jablon made a detailed study and found that location of the wound, depth of wound, time of debridement, wound complications, neurological deficit, handedness, and type of attacks showed no difference in regard to whether seizures persisted or ceased. There were only two differences found: the seizure-free group had a lower incidence of posttraumatic syndrome and a higher intelligence quotient than the group where seizures persisted. It was pointed out, however, that both of these phenomena may have been the *result* of seizures, rather than being related to their *cause.*

Caveness (1963) reported on the material of Korean War veterans and defined cessation of attacks as a terminal remission of at least two years prior to last follow-up. Fifty-eight out of 109 patients fell into this group. Comparing these fifty-eight patients against the others, no statistically significant differences were found in regard to missile versus nonmissile injury, time of onset of seizures in relation to injury, attack pattern, site of injury, severity of injury and whether or not the patient had ever been placed on medication. The only finding that showed statistically significant differences between Caveness's two groups was in regard to frequency of seizures. Eighty-five per cent of patients who had suffered one to three seizures had a terminal remission, but this was the case only in 53.1 per cent of patients with four to thirty seizures, and 21 per cent of "multiple" seizures which "defied accurate count." Seizures ceased in 42 per cent of the patients who had been placed on continued anticonvulsant medication and in 56 per cent of men who had never received such treatment. This is obviously an important piece of information because it points out that in a number of cases the natural course of the illness is apparently self-limiting. Another important point that emerges from Walker's, as well as Caveness's studies, seems to be that although a more severe injury tends to favor the initial appearance of epilepsy, it subsequently plays no role in its persistence. This should again provide considerable food for thought about the real causes of chronic seizure disorders.

Finally, we come to the question of mortality in patients with posttraumatic epilepsy. This is a difficult problem and not too much information is available. Credner noted that out of fifty patients who died, forty-one (82%) had suffered from seizures. Limiting herself only to patients with penetrating head injuries, it was noted that forty-seven of the fifty patients who died had had penetrating head injuries; 81 per cent of this group had epilepsy. The overall incidence of epilepsy in patients with penetrating head injuries was, however, only 49 per cent; there was, therefore, an excess of mortality for patients with epilepsy in this group. Walker referred to the problem in 1957 and stated that over a period of ten years the risk to life is increased at least two to three times by posttraumatic epilepsy, but: "How much of this increased risk is due to the cerebral wound, the neurological deficit, or the epilepsy is not easy to determine." Wagstaffe gave somewhat contradictory statements. He said in the paragraph dealing with mortality that the onset of seizures has no marked effect on the mortality. He went on to say that epileptic patients had a mortality of 16 per cent; whereas the mortality rate of all head injury cases was 10 per cent. This, he felt, was not a sufficient difference to justify any conclusions, but in the summary of his paper he stated that "the mortality in cases which have developed traumatic epilepsy is rather higher than in other cases of gunshot wounds of the head."

Reviewing these opinions, it is probably fair to assume that patients who suffer from chronic posttraumatic epilepsy carry a slightly higher mortality risk than those head injured patients in whom this complication is absent.

In summary, one could conclude in regard to the four questions that were initially posed:

1. The incidence of epilepsy after head trauma stands in direct relationship to the severity of the injury, ranging from approximately 12 per cent in simple closed head injuries to approximately 37 per cent for penetrating head injuries. These figures are approximations only, and represent the averages of the studies listed in Tables 11 and 12.

2. In regard to the characteristics of the injury or of the individual that would favor the subsequent development of epilepsy, it is apparent that factors which increase the severity of the injury or interfere with wound healing are most important. Also, central-parietal wounds seem to be most epileptogenic. The role of hereditary predisposition is controversial at the present time.

3. In regard to frequency of terminal remissions, there does not seem to be too much difference between posttraumatic and "cryptogenic" epileptic patients. A two-year terminal remission appears to occur in about one-third of the posttraumatic group. There is, however, a suggestion that patients with posttraumatic epilepsy tend to have relatively infrequent seizures.

4. In regard to characteristics of the patient with established posttraumatic epilepsy who will enjoy a complete remission, the literature fails to provide convincing criteria that would allow accurate prognostication. The only exception might be that patients who have very frequent seizures tend to have a poorer chance for remission than patients whose seizures are spaced by long intervals.

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 Scienee, 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
Fegersten *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 l 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 wl 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 lc scores. Rank ordering the subtests from highest to lowest, (prehension was on top, and Digit Span on the bottom of th 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	39.6
	Symptomatic cases only	31.3
Krohn, 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.

Chapter 11

PROGNOSIS FOR SEIZURE CONTROL

By the end of 1959, the Michigan Epilepsy Center had files of over 1,000 patients who had been seen by a team of specialists including neurologists, psychiatrists, electroencephalographers, psychologists, pediatricians, and social workers over the previous ten years. The case records were exceedingly detailed and could form a solid basis for statistical treatment of the data. The Center is, however, a consulting facility only. It makes recommendations to the treating physician and does not engage in continued day-to-day patient management. It works through the referring physician rather than taking over patient care entirely. This can obviously affect the results of follow-up investigations. Treatment recommendations may not have been carried out to the fullest extent either by the physician in charge or by the patient, and continued medical supervision by a specialist might have improved the outcome in a number of cases. The results of the follow-up studies of patients seen at the Center therefore do not necessarily reflect what could have been accomplished under ideal circumstances, but what is actually happening in a large metropolitan area of the United States. There is no reason to believe that the level of general medical care is inferior in Detroit to that in other large cities of this country and the results can probably be taken as being representative for the country at large.

There is, of course, always the problem of patient selection. One may assume that only the most inveterate cases would be referred to a special facility as an epilepsy center, and one would therefore obtain a negative selection that would *a priori* bias the

results. This is fortunately not the case. Patients are at times referred after their very first seizure; others come because the diagnosis is in doubt; others have no particular problem in regard to seizure control but present psychiatric or intellectual difficulties as the prime handicap, and there are, of course, also some patients who have made the rounds and tried most other facilities with the Michigan Epilepsy Center being just another stop on the road in search of seizure control. For all practical purposes, the Center sees probably a rather typical cross section of patients with known or suspected epilepsy.

It became apparent that the fullest use of the detailed workup of the patients could only be made by having most of the information in a form that would allow statistical manipulation of the data. For this reason code sheets were constructed that covered the neurological history, neurological examination, psychiatric evaluation, psychological test results, laboratory examinations, and EEG findings. By the end of 1959 these sheets were ready for use with a clinical population. We simply wanted to know whether there were any features in all of the material that was so meticulously accumulated that would bear a definitive relationship to the prognosis for epileptic children in regard to the previously mentioned areas. It was also decided to proceed with the workup of the data in as unbiased a fashion as possible. There was no hypothesis that was to be confirmed or rejected. The data were handled as if we knew nothing whatsoever about epilepsy, letting the results of the statistical findings dictate the subsequent steps of data workup rather than guiding it by preconceived assumptions.

FIRST FOLLOW-UP STUDY

In order not to be confounded by temporary short-term remissions it was decided to select only those patients who had fulfilled the following criteria: (1) had been seen at the Center at least five years earlier; (2) had received the complete workup as previously stated; (3) lived in the greater Detroit metropolitan area; (4) had been ten years old or younger at the time of

initial evaluation, and (5) had received a definitive diagnosis of epilepsy.

The last consideration involved a problem of definition. Does a patient who has had only one seizure merit a final diagnosis of epilepsy, or should one require the presence of recurrent seizures for the diagnosis? In order to avoid the uncertainties of the isolated seizure in childhood, the rule was adopted that the patient must have had at least three seizures that could be diagnosed as clearly epileptic on the basis of the clinical history. Attacks of abdominal pain, headache, or syncope were excluded and so were breathholding spells and febrile convulsions. This policy led, therefore, to a definitely epileptic sample but may have excluded some patients with the mildest forms of the illness. When all the restrictions were applied, our supply of potential cases had dwindled considerably. After being unable to locate some, getting refusals to cooperate with reexaminations by others, we ended up with thirty-two patients who could be reexamined. Five (15.6%) of these had been institutionalized in the meantime at Caro State Hospital for Epileptics, and these patients were transferred for purposes of reevaluation to the Lafayette Clinic. All patients had a repeat electroencephalogram, and information in regard to seizures, behavior, and school achievement was obtained at that time. The patients were reexamined during the first half of 1960. They had been seen initially between 1950 and 1954 inclusive.

Description of Sample

The average duration of follow-up was seven years and the distribution is shown in Table 27. The mean age at initial evaluaton was 6.2 years, and the breakdown is listed in Table 28. There were nineteen boys and thirteen girls in the group. The mean duration of the illness prior to initial evaluation was 2.9

TABLE 27

FOLLOW-UP SPAN

Years	5	6	7	8	9
Patients	9	10	5	7	1

TABLE 28

AGE AT INITIAL EVALUATION

Years	1	2	3	4	5	6	7	8	9	10
Patients	2	1	1	4	7	2	2	4	3	6

years, and the distribution is detailed in Table 29. The seizure types are shown in Table 30. Nine patients had more than one seizure type. In order to avoid duplication, further description of the initial findings will be shown in relation to the follow-up results. Of the twenty-seven patients living in the community all

TABLE 29

DURATION OF ILLNESS

Years	1 or less	2	3	4	5	6	7	8	9
Patients	9	9	3	5	2	2	1	0	1

but five were still taking anticonvulsant medications (81.5%). Four of these five patients had been seizure free for five years or more; the fifth patient was still having seizures, but the mother claimed to have lost the prescription.

From the total group living in the community, fifteen (55.6%) were still having seizures; three (11.1%) had remitted for one year prior to follow-up; one (3.7%) for two years; two (7.4%) for five years; three (11.1%) for six years; two (7.4%) for eight years, and one (3.7%) for nine years.

A terminal remission of two years or more had therefore oc-

TABLE 30

SEIZURE TYPES

Major seizures with focal features	11
Major seizures without focal features	9
Psychomotor seizures	7
Minor focal motor seizures	4
Absence	4
Minor nonfocal motor seizures	3
Akinetic	2
Myoclonic jerks	1

curred in nine (33.3%) patients, and a terminal remission of five years or more in eight (29.6%) patients.

Electroencephalogram

The initial EEG had been normal in eight (25.8%); borderline in one (3.1%); mildly abnormal in two (6.3%); moderately abnormal in six (18.8%), and markedly abnormal in fourteen (43.8%). One record was technically poor and had to be disregarded. It should be pointed out that the patients were, for the most part, already on some anticonvulsant regime which was not discontinued for the test. A comparison of the initial EEG with the follow-up EEG is shown in Table 31. The EEG had stayed

TABLE 31

AMOUNT OF EEG ABNORMALITY

	Initial EEG	*Follow-up EEG*
Normal	8	10
Borderline	1	3
Mildly abnormal	2	4
Moderately abnormal	6	3
Markedly abnormal	14	10
Technically poor	1	2

the same in eight cases (25.0%); improved in eleven cases (34.4%); deteriorated in seven (21.9%). It was normal on both evaluations in three (9.4%) and three patients could not be compared because of technical difficulties. This refers to an overall evaluation of EEG abnormalities. Table 32 shows a com-

TABLE 32

SEIZURE PATTERNS

	Initial EEG	*Follow-up EEG*
No seizure patterns	9	16
Questionable	3	3
Mild	3	2
Moderate	6	4
Marked	10	5
Technically poor	1	2

parison in regard to seizure patterns in the initial and follow-up EEG. The amount of seizure patterns had remained the same in two patients; it had decreased in sixteen; increased in five; no seizure patterns had been present on either occasion in six, and no comparison was possible in three patients. In regard to focal abnormalities the results are presented in Table 33. The amount

TABLE 33

FOCAL ABNORMALITIES

	Initial EEG	*Follow-up EEG*
None	21	26
Mild	4	3
Moderate	3	0
Marked	3	1
Technically poor	1	2

of focal abnormalities had not remained the same in any of the patients; it was less in ten, more in three; focal patterns were not seen in either recording in sixteen, and no comparison was possible in three cases.

The tendency of the electroencephalogram was, therefore, towards improvement, especially in regard to the presence of seizure patterns and focal abnormalities.

Of the five patients whose seizure patterns had become worse, four were still having seizures (one state-hospitalized), and one was controlled for at least two years; however, his rating had gone only from "none" in the initial EEG to "questionable" in the follow-up EEG.

Of the three patients whose focal disturbance had become more pronounced, one was controlled (the rating went from "none" to "mild") and two were still having seizures.

Of the sixteen patients whose seizure patterns had improved, five had shown clinically a terminal remission of at least two years; the others were still having seizures. Seizure patterns which had been present in the initial EEG disappeared from the recordings in ten patients; but only three of these had clinically remitted, while the others were still having seizures.

An investigation into EEG background activity showed that

the general tendency was towards an increase in amount of alpha rhythm, decrease in theta activity, and decrease in amplitude by the time of follow-up. This agrees with what one would expect to occur as a result of maturation. The improvement of the background activity was not related to a change in the seizure state. Only two patients showed deterioration in background frequencies, both were still uncontrolled by medication although one of the two patients had shown some improvement in his seizure disorder.

The five institutionalized patients had the following seizure patterns: infantile spasms-hypsarhythmia in two, focal minor motor seizures in two, focal major seizures in one. The age at time of onset of the illness was since birth in one, seven weeks in one, eleven months in one, eighteen months in one, and two years in one.

Seizures had started before the age of two in ten additional patients. Eight of these were still having seizures at follow-up and two had remitted; both of the latter were mentally slow. One was in regular school but a D student with a moderate behavior problem, and the other presented no behavioral difficulties but was in an ungraded class.

Intercorrelation of Findings

As had been mentioned before, the main reason for this preliminary study was the opportunity to study a large number of relationships between variables. All the information that was contained on the code sheets was punched onto IBM cards and a frequency distribution was obtained for all the variables. Variables which had appeared less than five times in the entire sample (e.g. severe head injury, hypsarhythmia, cesarean section) were eliminated and 137 variables were intercorrelated on an IBM 704 computer. A "missing data" intercorrelation program was used, which computes the product-moment correlation (Pearson r) between all pairs of variables based on only those data common to each pair of variables. The variables used are shown in the Appendix. It was hoped that this procedure would demonstrate all the variables that were significantly correlated with

"seizure state at the time of follow-up"; it would likewise show the significant correlates with behavior and/or school problems at the time of follow-up; in addition it could produce a host of relationships which are not necessarily related to prognosis but deal with more general problems in epilepsy (e.g. relationship between psychological test results and seizure frequency; family history of epilepsy and seizure type or EEG patterns). The statistically significant correlations that were obtained with the variable "seizure state at time of follow-up" are shown in Table 34.

TABLE 34

SIGNIFICANT CORRELATIONS WITH SEIZURE STATE AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for academic achievement	.487	1%
Amount of theta activity in EEG	.444	2%
Vocalization at onset of major seizure	.417	2%
Amount of physical illnesses	.401	5%
Duration of seizure disorder prior to evaluation	.362	5%
Seizures occurring mostly within two hours after awakening	.420	5%
Etiological factors present in history	.394	5%
Mental retardation present	.383	5%
Family history of psychiatric hospitalization	.412	5%
Seizures started during first year of life	.302	10%
Highest degree of fever attained	.498	10%
Amount of abnormality in EEG, Evaluation II	.347	10%
Amount of fast activity in EEG, Evaluation II	−.330	10%

In order to understand this and the subsequent tables, a few explanations have to be given in regard to the coding. A full description of the coding system has been published previously, Rodin *et al.* (1962). If a phenomenon was either present or absent such as specific seizure type, it was coded as 1, meaning absent, and 2, meaning present. If a phenomenon could be graded in regard to its intensity, this was done on a 9-point scale with 1 meaning "phenomenon absent" and 9, "phenomenon present to maximum extent." On occasion the normal phenomenon was placed in the middle of the scale and the two extremes on either end. Whenever a time element was involved (such as for

duration of seizure disorder or age at time of sitting up), the sequence was from the lowest to highest. Figures 1 through 3 show an example for each of the types of scales used.

At the time of coding the charts, a prognosis was given to each

CURRENT SEIZURES PRESENT SINCE

[0] Not recorded
[1] Less than 1 month
[2] 1–2 months
[3] 3–6 months
[4] 7–11 months
[5] 1–3 years
[6] 4–6 years
[7] 7–9 years
[8] 10–15 years
[9] More than 15 years

FIGURE 1. Example of scale used in MEC follow-up projects

ACTIVITY DURING FIRST YEAR OF LIFE

[0] Not recorded
[1] Almost none
[2]
[3] Moderately underactive
[4]
[5] Normally active
[6]
[7] Moderately overactive
[8]
[9] Hyperactive

FIGURE 2. Example of scale used in MEC follow-up projects

FEEDING PROBLEMS IN INFANCY

[0] Not recorded
[1] None
[2]
[3] Mild
[4]
[5] Moderate
[6]
[7] Marked
[8]
[9] Severe

FIGURE 3. Example of scale used in MEC follow-up projects

patient for result of treatment in regard to seizures, behavior, and academic achievement. These prognoses were pure speculations to be confirmed or disproven at time of actual follow-up. They were based on traditional neurological criteria. Prognosis was coded from 1, meaning excellent, to 9, meaning extremely poor outcome expected. The variables listed above the broken line in Table 34 are correlated to a statistically significant degree; the correlates below the broken line show a tendency towards statistical significance. The different levels of significance with equally high or higher correlation coefficients result from unequal numbers in the separate calculations. Unless specifically stated as "Evaluation II" all variables refer to the state of the patient at time of initial examination.

Reviewing Table 34 one finds, in essence, that a good or poor outcome in regard to seizures was related to the duration of the illness, the presence or absence of possible etiological factors, mental retardation, and amount of background slowing in the electroencephalogram. These findings confirm what has been reported in the literature. There was also a suggestion that patients who had a greater number of physical illnesses did not achieve seizure control, and that patients whose seizures occurred mostly within two hours after awaking in the morning did poorly. The variable vocalization at onset of major seizure refers to the "epileptic cry" and the study suggested that this phenomenon may also carry a poor prognosis when it occurs in children.

The highest correlation coefficient was obtained—interestingly enough—with prognosis for academic achievement. This prognosis was based on the following criteria: The preschool child with normal landmarks of development, absence of mental retardation at time of examination, and absence of hyperkinetic behavior was given a good prognosis. The degree of presence of any of these criteria led to the prediction of poorer scholastic achievement. The same criteria were also applied to the school age child, but in addition, the previous school achievement was taken into account. This is, of course, a clinical way of estimating intelligence especially in the preschool child where formal testing is difficult. A point of interest in this respect is that the prognosis for seizure state received a correlation coefficient of

only .12 with the actual outcome, and this of course was not significant. I had tried to predict seizure outcome intuitively using the conventional criteria at the disposal of the clinical neurologist, and this resulted in complete failure. The data would suggest in retrospect that one might have done better in predicting seizure outcome by using the criteria for prognosis in regard to school performance. It is, however, important to point out at this time that none of the correlations shown in Table 34 as well as the subsequent tables dealing with this investigation can be taken at full face value. We must remember that we are dealing with a large number of variables and a small number of patients. This will inevitably affect the outcome of the calculations, and chance correlations are undoubtedly present. It is impossible to say which significant correlations are indeed reproducible on the basis of one sample alone. Therefore, before attaching too much weight to any given correlation, one might be better off at present to look for patterns that ring true on the basis of past experience, than to conclude firmly that a newly found correlate is indeed important.

Factor Analysis

Inasmuch as correlation coefficients give only the strength of relationship between two variables, it was of interest to see whether groups of symptoms and/or signs could be demonstrated which would show mutual relationships. It was hoped that the statistical technique of factor analysis might demonstrate syndromes that exist within a group of childhood epilepsies which might have a bearing on prognosis. The computer program available to us at that time was able to manipulate only 50 variables for factor analysis. The variables that were selected are shown in the Appendix. With principal axis solution and Varimax rotation, eight factors were obtained. Four of these were of relevance in regard to follow-up findings. Factor I deals with school achievement and will be presented later. Factor II, Table 35, points out that the EEG is likely to remain abnormal in regard to background rhythms and seizure patterns when the children were underactive during the first six months of life,

and it also suggests that the patients whose seizures start early in life continue to show EEG abnormalities. However, for the most part the factor shows that the EEG tends to behave as an independent variable. The absence of relationship to clinical sei-

TABLE 35

FACTOR II

.95	Child underactive during first year of life
.85	Abnormal EEG, Evaluation II
.84	Little alpha rhythm in EEG, Evaluation II
.81	Marked amount of theta activity in EEG, Evaluation II
.70	Seizure pattern in EEG, Evaluation II
.54	Marked theta activity in EEG, Evaluation I
.45	Early onset of convulsive disorder
.40	Seizure disorder started during first year of life
.38	Behavior problem at time of follow-up
.37	Poor alpha rhythm in EEG, Evaluation I
.33	Focal disturbance in EEG, Evaluation II
.31	Objective findings on neurological examination, Evaluation I

zure state at time of follow-up is especially notable. Factor III, Table 36, presents some of the characteristics of the patient who is likely to become institutionalized as a result of his illness. An interesting aspect of this factor is that it deals essentially with seizure intensity and it is shown here standing by itself unrelated

TABLE 36

FACTOR III

.85	Combination of seizures
.78	History of status epilepticus
.54	Long duration of individual attacks
.41	Institutionalized
.36	Minor focal motor seizures
.33	Early onset of convulsive disorder
.32	No evidence of social factors contributing to illness

to the EEG or presumed etiologies. Factor VI, Table 37, is the only one that showed some relationship to seizure state at time of follow-up. Even here the relationship is not very strong, the variable appearing quite low on the factor. Nevertheless, the factor suggests that excessively high fevers are associated with evidence

of brain damage and intellectual loss and these patients may not be controllable by medication.

To summarize some of the results of the factor analysis in regard to prognosis one could say that (1) the electroencephalogram behaves for the most part as an independent variable, but there is a suggestion that it is likely to remain abnormal in children whose seizures started in the first year of life (2) if a child has a history of repeated status epilepticus, a combination of different seizure types, and the individual attacks last a long period of time, the prognosis for making a satisfactory adjustment in the community is poor. Seizures may or may not stop after the

TABLE 37
FACTOR VI

.94	High fever
.82	Poor academic prognosis
.58	Poor behavior prognosis
.54	Low IQ
.54	Academic school problem at time of follow-up
.50	Objective findings on initial neurological examination
.49	Poor seizure prognosis
.47	Seizures same or worse
.42	Behavior problem at time of follow-up
.42	Marked theta activity in EEG, Evaluation I

patient is institutionalized, and (3) children with marked mental retardation and abnormal findings on neurological examination are likely to remain uncontrolled in regard to seizures and to present chronic behavior problems.

These conclusions have emphasized the poor outcome of patients, but the results of the factor analysis can of course also be read from the opposite point of view: (1) the EEG is likely to improve if the seizure disorder did not start in infancy; (2) a child who has only one seizure type, no history of status epilepticus, and whose major seizures are of brief duration is not likely to deteriorate to a level that will require institutionalization. The factor does not apply to patients with infantile spasms because this seizure type was not represented in the factor analysis, and (3) children who have no evidence of mental retardation

and a normal neurological examination are likely to show improvement in their seizures, and are not likely to become chronic behavior problems.

Before entering into further speculations, we have to remind ourselves that these results are merely to be taken as suggestions for future study and not as final conclusions. It has been pointed out repeatedly that we were forced to work with a small sample and this is always undesirable.

SECOND FOLLOW-UP STUDY

After we had established that the coding system could give meaningful findings, it was apparent that a larger sample of patients was needed. It was therefore decided to conduct a second follow-up study on all patients regardless of age, who fulfilled essentially the same criteria as the group of children in the first study. The age limitation was dropped in order to get as large a sample as possible. Patients qualified for inclusion in the second follow-up study by fulfilling the following criteria: (1) definite diagnosis of epilepsy as defined in the first follow-up study; (2) residence in the greater Detroit metropolitan area; (3) complete workup at the Center prior to January, 1956;— The second follow-up study was conducted between 1961 and 1962. The five-year minimum between original evaluation and follow-up was therefore maintained—, and (4) no participation in the first follow-up study.

Using these criteria, 222 patients became eligible for the study.

Eighty-six (38.7%) patients could not be reached either by mail or telephone. Of the remaining 136 patients, thirteen (9.6%) had died; thirty-three (24.3%) refused to return to the Center for reexamination. Eighty-three (61.0%) were reexamined at the Center, seven (5.1%) were found to have been institutionalized at Caro State Hospital, and these patients were transferred to the Lafayette Clinic for reevaluation. The main body of the data that will be presented subsequently deals with the results of follow-up of these ninety patients.

Before going into these results, the thirty-three patients who refused to return for reexamination should be discussed some-

what further. It might be assumed that these patients had, in the majority, enjoyed a long remission and by concentrating on patients who in fact returned for reexamination one would *a priori* deal with a negative selection. All of these thirty-three patients had been contacted by telephone and reasons for not wanting to be reexamined were given as follows:

1. Seizures had stopped—nine (27.3%)
2. Are working and do not want to take time off from work—eight (24.2%)
3. Various excuses, for instance, has a bad heart; does not want to come in; cannot get transportation; does not want any more examinations—seven (21.2%)
4. Are being treated elsewhere and see no point in further examinations—five (15.2%)
5. Agreed to return for reevaluation, but failed to keep appointments—four (12.1%)

In the group of nine patients who had stated that they had achieved complete seizure control, the length of remission was given as ten years in two, seven years in three, and five years in one. Three patients merely stated they "don't have spells anymore."

On basis of this admittedly meager information we could say that six patients had shown a terminal remission of at least five years' duration. This would amount to 18.1 per cent of the group who were not formally reexamined. This number is presented here only in order to allow some comparison later on with the group that was, in fact, reexamined.

As far as the thirteen patients who had died were concerned, three (23.1%) had been institutionalized and had died at Caro State Hospital. Table 38 lists the causes of death as given on the death certificates, the age at time of death, and the age at time of onset of the seizure disorder for all thirteen patients.

If we exclude the three patients with brain tumors, we find the mean age at time of death to have been 18.5 years. The mean duration of the seizure disorder was nine years. As far as the three patients with brain tumor are concerned the diagnosis had clearly been missed in the seventy-year-old patient. In the other two cases, epilepsy had preceded the detection of the tumor by

fifteen and nine years. Both of these patients had started with seizures during adolescence, which is a rather common age of onset for epilepsy of unknown cause. This reemphasizes the need for continued medical supervision, even of relatively long-standing cases of seizure disorders.

As far as the institutionalized group is concerned, it has been mentioned that it amounted to only 5 per cent of this sample. This is smaller than the 18 per cent observed in the first follow-up study. The finding is explainable by the fact that the second

TABLE 38

CAUSE OF DEATH

		Age at Time of	
		Death	*Onset*
M.D.	Brain tumor—died 8 days postoperatively	70	69
D.L.	Brain tumor—did not survive operation	32	17
E.W.	Brain tumor—did not survive operation	22	13
I.F.	Acute pulmonary embolism	60	39
T.B.	Diabetes—hypoglycemic shock	10	4
M.V.	Epilepsy (aspiration pneumonia)	19	13
R.J.	Epilepsy (aspiration of gastric contents)	10	7 months
P.S.	Epilepsy (adrenal insufficiency)	9	2
M.P.	Epilepsy (autopsy refused by parents)	1	5 weeks
C.H.	Status epilepticus	20	17
A.M.	Drowning	35	10
J.R.	Drowning	17	12
R.K.	Drowning	14	7

study dealt predominantly with older patients. If we limit ourselves to the twenty-seven patients who were ten years old or younger when first seen at the Center, we find that six (22.2%) of them had become institutionalized. This percentage is quite similar to that obtained from the sample in the first follow-up study.

Turning our attention now to the ninety patients who were reexamined either at the Center or the Lafayette Clinic, it should be mentioned that prior to reexamination of each patient the initial history was coded in the same manner as for the first follow-up study and a prognosis was assigned to each patient on

basis of this information. The patient was then seen in neurological evaluation; an interval history was obtained, and specific historical information about birth and early development, which had on occasion been lacking in the patient's chart, was supplemented. The mental status of the patient was evaluated and coded, all patients had another electroencephalogram; but most of them did not go to sleep during the tracings. The patients who were on anticonvulsant medication were not taken off their drugs prior to the EEG. Eighty-five (94.4%) patients were given a Bender-Gestalt test; the WAIS was administered to fifty-four (60.0%) patients, and the WISC was given in fourteen (15.5%) instances. All this material was recorded on the coding forms and transferred onto IBM cards.

Description of Sample

The duration of follow-up is shown in Table 39. There were forty-nine males and forty-one females in the group. Table 40

TABLE 39

DURATION OF FOLLOW-UP

Years	12	11	10	9	8	7	6	5
Patients	2	5	7	14	9	14	20	19

contains the seizure types that had been present at time of initial evaluation. Forty-two (46.6%) patients had one seizure type only; two (2.2%) had major seizures and intermittently only auras; thirty-nine (43.3%) had two distinct seizure types; six (6.7%) had three seizure types, and one had four different types

TABLE 40

SEIZURE TYPES

Nonfocal grand mal	41
Focal grand mal	30
Psychomotor seizures	21
Absence	20
Focal minor motor seizures	12
Myoclonic jerks, myoclonic seizures or akinetic seizures	12
Nonfocal minor motor seizures	5
Psychic or sensory seizures	3

of attacks. The term "absence" refers to the clinical description of the attack and is not necessarily synonymous with 3 cycles per second spike wave activity in the EEG, or "pure petit mal."

As far as etiology was concerned, none could be ascertained in fifty-one cases (56.6%); various degrees of birth injuries were reported in twenty-nine (32.2%); postnatal head injuries that could have been of etiological importance were noted in eight (8.8%); cerebral infections in eleven (12.2%); a positive family history of epilepsy was present in thirty-five (38.8%), and thirteen (14.4%) patients had evidence for a family history of epilepsy as well as some added insult to the central nervous system. These figures do not add up to ninety because some patients had evidence of more than one type of insult to the central nervous system. All the patients except four had been on anticonvulsant medication prior to their first visit to the Center. The anticonvulsant regime was judged adequate in terms of type of drug and dosage for the particular seizure type in sixty-one (67.7%), and inadequate in twenty-five (27.7%) patients. Nine (10.0%) patients had suffered from grand mal status epilepticus. In order to avoid duplication, the description of the sample in terms of age when first seen, age at time of onset of seizures, intelligence, et cetera, will be shown in relation to follow-up results and will therefore be omitted here.

Results

Twenty-nine patients (32.2%) had become seizure free for two years or more prior to reevaluation; twenty-seven (30.0%) had shown some improvement in regard to frequency of occurrence or severity of seizures, and thirty-four (37.7%) had remained essentially unchanged or become somewhat worse. Seizure freedom for five years or more had been achieved in fifteen patients of the total group (16.7%), and one patient had been seizure free for ten years (7.1% of fourteen patients who had been followed for ten years or more). It is interesting to note here that a two-year terminal remission had occurred in the same proportion of cases in this study as in the first one (32.2% versus 33.0%). The five-year remission rate was lower in this second

group than in the first (16.7% versus 29.0%). Ten patients had stopped taking anticonvulsant medication; eight of these had been seizure free for three to seven years; two were still having seizures but drug treatment was discontinued by the parents. One of these patients was profoundly retarded mentally, had myoclonic jerks and myoclonic seizures for which drug treatment had been totally ineffective. The patient's mother had therefore stopped buying medications. The other patient had clear-cut evidence of petit mal during the follow-up electroencephalogram, but the mother had felt that the patient's seizures had improved to an extent that treatment was no longer needed.

TABLE 41

MAJOR SEIZURES

	Frequency of Maximal Occurrence	*Frequency at Evaluation I*	*Frequency at Evaluation II*
Less than once a year	0	7	30
About once a year	4	6	3
2 to 3 seizures per year	5	7	6
4 to 6 seizures per year	1	6	7
7 to 12 seizures per year	3	6	8
About once a month	6	11	2
2 to 3 a month	9	6	10
Once a week	3	3	2
More than once a week	40	19	3

As far as major seizures were concerned, forty patients (44.4%) had at one time experienced more than one seizure per week and only nine (10.0%) had had less than three seizures per year. Table 41 shows the tendency for improvement of major seizures. We can see that by the time the patients were initially seen at the Center, seizures for the most part had already decreased in frequency from their maximum and they had further decreased by the time of second evaluation. The same phenomenon can be observed for minor seizures, shown in Table 42.

As far as the EEG is concerned the initial tracings could be evaluated in seventy-eight cases. In twelve instances the record was either technically poor or the tracings had been obtained at a local hospital and only the EEG report was available in the

TABLE 42

MINOR SEIZURES

	Frequency of Maximal Occurrence	*Frequency at Evaluation I*	*Frequency at Evaluation II*
Less than once a year	0	0	24
About once a year	0	0	1
2 to 3 seizures per year	1	2	2
4 to 6 seizures per year	2	5	2
7 to 12 seizures per year	2	4	1
About once a month	2	1	0
2 to 3 a month	1	1	6
Once a week	1	4	1
More than once a week	39	31	11

chart. These seventy-eight tracings were then compared with the ones obtained at follow-up. The results in regard to overall EEG abnormality, seizure patterns, and focal abnormalities are shown in Tables 43, 44, and 45.

TABLE 43

AMOUNT OF EEG ABNORMALITY

	Initial EEG	*Follow-up EEG*
Normal	18	11
Borderline	12	7
Mildly abnormal	10	15
Moderately abnormal	24	23
Markedly abnormal	14	22

The EEG had stayed the same in twenty-seven patients, deteriorated in twenty-four, and improved in twenty-two. It had been normal on both evaluations in five patients.

TABLE 44

SEIZURE PATTERNS

	Initial EEG	*Follow-up EEG*
No seizure patterns	30	34
Questionable	9	7
Mild	14	13
Moderate	18	17
Marked	7	7

TABLE 45
FOCAL ABNORMALITIES

	Initial EEG	*Follow-up EEG*
None	54	44
Mild	8	15
Moderate	10	11
Marked	4	6

Twenty-two patients had had no seizure patterns in their tracings at either evaluation; twenty had remained the same in regard to the amount of seizure activity; eighteen had improved, and eighteen had deteriorated.

Thirty-three patients had had no focal findings in either recording; twenty-three had deteriorated; eleven improved, and nine had stayed the same in this respect. In two instances no comparison was possible because information was missing on the first trace.

Reviewing these tables we find that in contrast to the clinical picture the EEG had in general not shown appreciable improvement; it had actually deteriorated somewhat. This deterioration was not due to an increase in seizure patterns but to an increase in focal abnormalities. These findings are therefore in contrast to the observations of the first follow-up study. The question arises again whether the age difference between these two groups was the decisive factor for the different results. The information summarized in Tables 46, 47, and 48 was applicable to a study limited to twenty-five children who were age ten or younger at initial evaluation and who had two satisfactory EEGs.

TABLE 46
AMOUNT OF EEG ABNORMALITY
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
Normal	7	4
Borderline	4	4
Mildly abnormal	1	2
Moderately abnormal	3	7
Markedly abnormal	10	8

The EEG had improved in regard to overall amount of abnormality in six patients; it had deteriorated in seven; it had remained the same in nine; it had been normal on both occasions in three. EEG seizure patterns had improved in four patients, deteriorated in five, had remained the same in seven, and nine

TABLE 47
SEIZURE PATTERNS
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
No seizure patterns	12	12
Questionable	1	3
Mild	1	2
Moderate	6	4
Marked	5	4

patients had not had seizure patterns on either occasion. Focal disturbances had improved in four, deteriorated in four, and sixteen patients had not had focal abnormalities on either occasion. Focal abnormalities could not be adequately evaluated in the first tracing of one patient and the comparison was therefore based on 24 individuals.

TABLE 48
FOCAL ABNORMALITIES
AGE 10 OR YOUNGER

	Initial EEG	*Follow-up EEG*
None	20	20
Mild	3	2
Moderate	0	2
Marked	1	0

The tendency towards improvement of the EEG was therefore not borne out in this particular sample and this reemphasizes the caution one has to use when one compares percentage figures based on small samples. It also points out the necessity of using tests for statistical significance of the data.

Intercorrelation of Findings

As mentioned before, the main goal of this investigation had been to find prognostic criteria especially in regard to seizure control. To accomplish this, frequency distributions were obtained for the entire material, and 155 variables were then selected for intercorrelation. They are shown in the Appendix. The rule was adopted that each variable had to have been present in at least ten individuals; but this rule unfortunately prevented the inclusion of the variable "state hospitalized at time of follow-up" because only seven individuals had fallen into this category. An exception was made for grand mal status epilepticus. Although it had occurred in only nine individuals, its omission from computations would have been regrettable.

Correlations with Seizure Outcome

Table 49 lists the statistically significant correlations with the variable seizure state at time of follow-up with data obtained at the time of the initial evaluation.

TABLE 49

SIGNIFICANT CORRELATIONS BETWEEN FINDINGS FROM INITIAL EVALUATION AND SEIZURE-STATE AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Psychomotor seizures	.323	1
Combination of different seizure types	.294	1
Prognosis for seizure control	.277	1
Duration of seizure disorder	.276	2
Seizure patterns in EEG	.205	5
Grand mal status epilepticus	.203	5
Psychiatric diagnosis in addition to diagnosis of epilepsy	.255	5
Spike wave activity in EEG	.230	10
Amount of abnormality in EEG	.200	10
Female sex	.198	10
Prognosis for behavior	.188	10

Reviewing Table 49 we find that a poor outcome in regard to seizure control seemed to depend mostly upon (1) psychomotor seizures, (2) presence of more than one seizure type, (3) long duration of the illness, (4) history of grand mal status epilepticus, and (5) marked seizure patterns in the initial EEG. Female patients showed a tendency towards poorer outcome, but this did not reach statistical significance. It is of interest that prognosis for seizure control was significantly correlated (although the correlation coefficient was still quite low) with seizure outcome in this particular sample. This suggests that prognostication may be easier in a predominantly adolescent and adult population than in children.

Table 50 lists the variables that had shown significant correlates with seizure state; but were obtained at the time of re-evaluation.

One can note that patients whose seizures persisted tended to have either psychiatric difficulties and/or organic mental

TABLE 50

SIGNIFICANT CORRELATES BETWEEN FINDINGS OBTAINED AT FOLLOW-UP EXAMINATION AND SEIZURE-STATE AT FOLLOW-UP

	r	*Significance Level* (%)
Behavior problem	.417	1
Seizure patterns in EEG	.393	1
Proverb interpretation concrete	.391	1
Amount of abnormality in EEG	.372	1
Response to adequate amounts of anticonvulsant medication	−.365	2
Combination of different seizure types	.308	5
Psychomotor seizures	.280	2
Focal sharp waves in EEG	.277	2
Amount of theta activity in EEG	.272	2
History of depression	.263	5
Organic mental changes	.240	5
Personality disorder	.244	5
Amount of focal disturbance in EEG	.228	5
Amount of alpha activity in EEG	−.211	10
Academic school problem	.352	10
Spike wave activity in EEG	.209	10

changes. The EEG tended to be abnormal, showing diffuse or focal seizure patterns and/or marked theta activity. If we now compare Table 34 from the first follow-up study with Tables 49 and 50 from the second study, we find that we have not made any discovery that has not been mentioned some place in the literature. Practically each one of these findings has been reported in the past to be associated with a poor outcome if present, and a good outcome if absent. What is more interesting, and also discouraging, is the fact that there is hardly any overlap between the results of the two studies. What was statistically significant in one failed to show statistical significance in the other. Although we could blame the age difference again, it is important to point out that repetition of findings in regard to seizure outcome is not easy, and this is probably the major reason for the divergent opinions in the literature. The only finding that showed significant correlation with seizure state at time of follow-up in both studies was duration of seizure disorder prior to initial evaluation. We will return to this particular aspect later in more detail.

FACTOR ANALYSIS

As mentioned at the time of discussion of the first follow-up results, one is not only interested in relationships between a pair of variables, but one would like to know which of these symptoms and signs form a group that would relate to prognosis. Therefore, a factor analysis was again performed. The ninety variables that were included in the factor analysis are shown in the Appendix. Principal axis solution and Varimax rotation were used and fourteen factors were extracted. The first factor is shown in Table 51. It demonstrates the characteristics of the chronic epileptic patient with brain damage. The seizures express themselves clinically most consistently in the form of focal minor motor attacks. If we view the factor from the opposite side we find that patients with normal IQ, normal Bender-Gestalt test performance, normal landmarks of development, and normal neurological examination tend to have a good prognosis for seizures and employment. This expresses in factorial form the opinions that have been stated

TABLE 51

FACTOR I

.96	Low Full Scale IQ, Evaluation II
.96	Low Full Scale IQ, Evaluation I
.91	Low Verbal IQ, Evaluation II
.91	Low Verbal IQ, Evaluation I
.86	Low Performance IQ, Evaluation I
.85	Low Performance IQ, Evaluation II
.78	Bender test rated "organic", Evaluation I
.77	Present seizure-state same or worse, Evaluation II
.68	Organic mental syndrome, Evaluation II
.48	Late onset of talking age
.46	Received special schooling
.44	Immaturity on psychological testing, Evaluation I
.43	Objective neurological findings, Evaluation I
.38	Symptom present during first year of life
.36	Focal minor motor seizures, Evaluation I
.34	Not employed, Evaluation II

in the literature. The factor as presented in Table 51 could be called "epilepsy associated with cerebral damage." The damage tends to occur most frequently in infancy and early childhood, but it should be pointed out that the factor loadings for the variables dealing with age relationships begin at .48 and are not high on the list. This suggests that onset in childhood, although common, is not a necessary prerequisite.

The second factor, Table 52, deals almost exclusively with

TABLE 52

FACTOR II

.89	Seizure patterns in EEG, Evaluation I
.85	EEG abnormal, Evaluation I
.72	Seizure patterns in EEG, Evaluation II
.70	EEG abnormal, Evaluation II
.57	Marked amount of theta activity, Evaluation II
.57	Generalized paroxysmal activity, Evaluation II
.53	Generalized paroxysmal activity, Evaluation I
.52	Spike wave activity, Evaluation I
.48	Spike wave activity, Evaluation II
.39	Absence—myoclonic jerks, myoclonic seizures and/or akinetic seizures, Evaluation I
.33	Poor alpha rhythm, Evaluation II
.31	Present seizure-state same or worse, Evaluation II

EEG characteristics. It suggests that a tracing which contains seizure patterns when the patient is already on some anticonvulsant medication is not likely to become completely normal later. Seizure patterns tend to persist and the EEG background tends to slow down to the theta frequency range. Clinically, one finds most commonly a member of Lennox's petit mal triad. It has been mentioned in the literature review that these various clinical conditions do not necessarily represent a homogeneous sample, but they were placed into one group for the intercorrelations and factor analysis in order to increase the number of patients with which one is dealing. Pure petit mal absences had occurred in six patients only, and it would not have been possible to perform adequate statistical studies. Classical three cycle per second spike wave activity was not included for the same reason. The factor expresses the observation reported in the literature that seizure activity in the EEG is related to the overt clinical seizure state only to a relatively minor degree. The factor might be called "EEG seizure activity." The next seven factors did not deal with prognostic information and will not be presented here.

Factor IX, Table 53, represents what might be called "mixed psychomotor epilepsy." It shows the characteristics of a segment of the epileptic population that tends to be resistant to our current anticonvulsant drug regime. It is the only factor where seizure outcome heads the list of variables. It also shows that the organic mental syndrome is usually not too pronounced in this

TABLE 53

FACTOR IX

.70	Present seizure-state same or worse
.61	Behavior problem at follow-up
.50	Psychomotor seizures, Evaluation I
.49	Personality problem, Evaluation II
.39	Proverb interpretation concrete, Evaluation II
.38	Verbal less than Performance IQ, Evaluation I
.37	Psychiatric diagnosis made in addition to diagnosis of epilepsy, Evaluation I
.34	Social factors contributing to illness
.33	Combination of seizures, Evaluation II
.30	Little personal relationships during adolescence
.30	Not employed, Evaluation II

group of patients because it appears on the factor only as concrete proverb interpretations. Furthermore, the factor points out that psychomotor epilepsy and behavioral difficulties are indeed fairly commonly related.

Factor X is shown in Table 54 because it points to the existence of what might be called the "specific seizure propensity" of the individual. It is somewhat akin to Factor III of the first study. It shows essentially that frequency of recurrence of seizures is unrelated to presumed etiology as well as neurologic, psychiatric, psychologic, and electroencephalographic observations. This factor can therefore be regarded as the nucleus of the epilepsy problem. Until we find variables that relate to this factor we are likely to remain in the dark about the real cause of the disorder. The term "seizure propensity" rather than "seizure threshold"

TABLE 54

FACTOR X

.77	Frequent grand mal seizures at time of Evaluation I
.69	History of frequent grand mal seizures prior to Evaluation I
.52	History of clusters of seizures per day, Evaluation I
.38	No, or, brief remission of major seizures prior to Evaluation I

was chosen because the latter has acquired a very specific meaning in regard to the ease with which seizures can be induced in normals or epileptics by means of drugs or electricity. As will be shown later, the "seizure threshold" of the individual (i.e. amount of drug needed to induce an epileptic attack) is *not* related to his "seizure propensity" (i.e. the tendency of the individual towards *recurrent* seizures). This latter tendency is a totally separate phenomenon and constitutes the core of the epilepsy problem.

To summarize the results of this factor analysis we could say (1) patients who show an organic mental syndrome and low IQ are likely to have an uncontrolled seizure disorder and an illness that dates to early childhood; (2) the EEG behaves for the most part as an independent factor of its own, but diffuse paroxysmal activity is frequently linked to one of the forms of Lennox's petit mal triad; (3) a considerable number of chronic epileptic pa-

tients are likely to show evidence of temporal lobe seizures, personality difficulties, and organic mental changes, and (4) there exists a factor of specific "seizure propensity" which is essentially unrelated to the information that is currently obtained in the workup of our patients. This factor represents the core of the epilepsy problem.

Analysis of Variance

Data analysis up to this point had led to interesting observations but it had not provided firm criteria upon which prognosis for seizure control could be based. A source of disappointment was the fact that only one correlate had appeared in both follow-up studies as significantly related to seizure outcome. This was the variable "duration of illness." The two studies had been in much better agreement in regard to criteria for behavior and school achievement, as will be shown later; but unless we can find significant relationships to seizure control, with findings that can be obtained at the first examination of the patient, we cannot realistically say that we have accomplished very much in regard to prognosticating the course of epilepsy.

The results presented so far have been based on a correlational analysis. Of equal interest are any mean differences in the variables between our various groups of patients. To study these differences, an analysis of variance was used.

The ninety patients were divided into three groups: (1) completely controlled for at least two years, twenty-nine patients; (2) improved but still having seizures, twenty-seven patients, and (3) essentially no change since initial evaluation or deterioration, thirty-four patients. Variables that showed a continuous distribution such as age, number of seizure types, amount of EEG abnormality were subjected to the F test. For variables that had been coded as dichotomies such as sex, seizure type, seizures present during first year of life, the Chi Square test was used. Altogether 190 variables were then selected from the initial evaluation and examined in this manner. The list of variables used is included in the Appendix. Inasmuch as we are concerned about prognosis, data obtained on follow-up examination were not in-

cluded except for summary statements dealing with behavior, school achievement, employment, and overall condition of the patient. Table 55 shows the statistically significant results of the F tests, and Table 56, the statistically significant results of the Chi Square tests. Variables that had previously shown statistically significant correlation coefficients are marked by an asterisk. It was gratifying to see that all the variables that had shown significant relationships in the correlation matrix were represented in Tables 55 and 56, in spite of the different statistical methods. We are therefore dealing with correct observations that had occurred in this sample of patients and not with statistical artifact. The variables that do not carry an asterisk in Tables 55 and 56 had either not been included in the initial correlation matrix (the intercorrelation program had only allowed processing of 155 variables) or had shown a tendency towards statistical significance—for instance, amount of EEG abnormality. If we concentrate now on the findings obtained in the controlled group, we see the following important features:

1. The controlled group was the youngest.
2. More than one different seizure type was least common.
3. The seizure disorder was of shorter duration.
4. Injuries as a result of major seizures were infrequent.
5. The EEG recordings showed less seizure activity when the patients were first seen.
6. The EEG tracings showed also a lesser amount of overall abnormalities.
7. A tendency towards clusters of seizures over a few days with subsequent freedom from seizures for a few weeks was uncommon.
8. Psychomotor seizures were uncommon.
9. Psychiatric difficulties were not of major degree (i.e. no treatment recommended in most instances).
10. The patients' immediate response to anticonvulsant medication tended to be better.

The last point is in agreement with the observation by Lund (1966) that treatment results during the first three months cor-

TABLE 55

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS RELATED TO FOLLOW-UP STATE

	Controlled	*Improved*	*Unchanged or Worse*	*F*	*Significance Level (%)*
Frequency of injuries during major seizures	2.8	3.3	5.2	9.0	1
Combination of seizures*	1.4	2.6	2.5	7.7	1
Behavior problem at follow-up*	1.9	2.6	3.6	7.4	1
Age	13.6 years	24.1 years	19.3 years	6.8	1
Amount of seizure patterns in initial EEG*	2.8	3.8	5.2	5.1	1
Duration of seizure disorder* (major seizures)	5.6	7.2	7.1	4.9	1
Amount of EEG abnormalities	4.6	6.2	6.7	3.6	5
Duration of seizure disorder* (minor seizures)	5.5	7.1	6.8	3.3	5
Picture Arrangement (Wechsler IQ)	9.6	7.7	10.1	3.3	5
Prognosis for seizure control*	3.9	4.6	5.0	3.2	5
Object Assembly (Wechsler IQ)	9.7	8.4	11.0	3.2	5
Frequency of tongue biting during major seizures	3.2	4.4	5.3	2.9	10
Block Design (Wechsler IQ)	8.3	8.0	10.2	2.8	10
School truancy	2.8	1.4	2.3	2.7	10
Immaturity on psychological tests	5.6	6.8	6.2	2.6	10
Initial response to anticonvulsant medication	4.1	3.6	2.0	2.5	10
Performance IQ	94.1	87.9	99.3	2.5	10

TABLE 56

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS RELATED TO FOLLOW-UP STATE

		Controlled	*Improved*	*Unchanged or Worse*	X^2	*Significance Level* (%)
Clusters of major seizures for several days, freedom from seizures for several weeks						
	Absent	22	14	20	9.3	1
	Present	0	8	7		
Amount of diffuse delta activity in EEG						
	Absent	15	21	25	8.1	2
	Present	8	4	1		
History of severe infectious disease						
	Absent	18	25	24	7.2	5
	Present	11	2	10		
Psychiatric treatment recommended						
	Absent	28	24	25	7.0	5
	Present	1	3	9		
Psychomotor seizures*						
	Absent	27	18	24	6.5	5
	Present	2	9	10		
Cyanotic during major seizures						
	Absent	18	16	14	5.9	10
	Present	4	7	14		
Family history of meningitis						
	Absent	28	20	28	5.3	10
	Present	1	6	3		
Psychiatric diagnosis made in addition to diagnosis of epilepsy*						
	Absent	28	25	27	5.1	10
	Present	1	2	7		

related well with the course of the illness in the following year.

As far as grand mal status was concerned, the difference between the groups was not significant statistically, but the distribution was in the expected direction as shown in Table 57. In eighteen patients there was no definite information in the charts in this particular respect.

The interesting feature emerging from the analysis of variance is that presumed etiologies like birth injury, postnatal head injury, infection, or heredity were not relevant for seizure prognosis. Objective findings on neurological examination, poor school performance, and organic findings on psychological tests also did not preclude a terminal remission of at least two years.

The fact that age at time of initial evaluation was a significant variable in regard to seizure control is important because it

TABLE 57

	Controlled	*Improved*	*Same or worse*
Grand mal status			
Absent	21	21	21
Present	1	1	7

places the entire problem of prognosis into a different light. We can see that the group which had enjoyed a terminal remission of at least two years was the youngest with a mean age of 13.6 years, but the same or worse group—which one would regard as the worst off—stood in the middle, and the improved group contained the older patients. This was a somewhat unusual distribution, especially when we compare it with other findings such as frequency of injuries during major seizures, amount of seizure patterns, amount of EEG abnormality, or prognosis for seizure control where the improved group did indeed occupy an intermediate position. It was therefore important to look at the actual distribution of the follow-up results in regard to the age at which the patients were first seen at the Center.

Table 58 shows the relationships between seizure outcome and age at the time of initial visit arranged by decades. We can immediately see an interesting phenomenon. Children up to ten

TABLE 58

AGE AT TIME OF INITIAL EVALUATION AND SEIZURE-STATE AT FOLLOW-UP

Years	*0–10*	*11–20*	*21–30*	*31–40*	*41–52*	*Total*
In remission for at least 2 years	13	10	4	2	0	29
Improved	4	8	7	5	3	27
Unchanged or Worse	11	6	10	7	0	34
Total	28	24	21	14	3	90

years of age showed either a complete remission or remained essentially unchanged. Only four took the intermediate position of improvement. Patients seen in the second decade of life were, for the most part, either completely controlled or improved; but from the third decade on, complete control became markedly less common and the patients tended to fall either into the improved or unchanged/worse group.

Significant Differences among Groups Depending upon Age at which Patient is First Seen at a Specialized Center

The fact that age is an important variable for seizure prognosis having been established, it was of interest to see what the main differences are in a population of epileptic patients when they are divided on the basis of age at time of their first visit to a specialized center. The group of ninety patients was subdivided into twenty-eight patients ranging in ages between one and ten years, thirty-six patients in ages eleven to twenty-five years, and twenty-six patients from twenty-six to forty-four years. These three groups were compared on the same 190 variables that had been used in regard to seizure state at time of follow-up. The main results for the F tests and the Chi Square tests are shown in Tables 59 and 60.

The important features in regard to prognosis can be summarized as follows:

1. Adolescents and young adults tended to do best in regard to response to anticonvulsant medication, seizure state at follow-up (which does not necessarily imply com-

plete control), intellectual functions, neurological examination, and they had the least "organic" dysfunctions on psychological testing.

TABLE 59

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS DEPENDING UPON AGE AT INITIAL EVALUATION

	1–10 Years	*11–25 Years*	*26 years or older*	*F*	*Significance Level (%)*
Duration of seizure disorder (Major seizures)	5.3	6.0	8.6	28.8	1
Duration of seizure disorder (Minor seizures)	5.2	6.4	8.3	18.9	1
Organic pathology (Bender-Gestalt test)	5.8	2.4	4.3	11.1	1
Organic pathology suspected on other psychological tests	5.2	2.4	4.2	9.9	1
Frequency of injuries during major seizures	2.5	3.8	4.9	6.0	1
Object Assembly—Wechsler IQ	7.1	10.7	9.8	5.3	1
Psychotic tendencies on psychological tests	3.2	1.6	3.0	5.2	1
Overall condition of patient	3.8	3.2	4.6	4.5	5
Prognosis for seizure control	4.5	4.0	5.3	4.3	5
Clusters of grand mal seizures over several days, freedom from seizures for several weeks	1.1	1.5	2.3	4.0	5
Prognosis for behavior	4.6	3.7	5.0	3.9	5
Personality disturbances (Psychological tests)	5.6	6.2	7.4	3.9	5
Prognosis for intellectual functions	5.4	3.8	4.6	3.7	5
Grand mal status epilepticus	2.0	1.2	1.0	3.5	5
Comprehension—Wechsler IQ	7.3	10.1	8.8	3.5	5
Amount of fast activity—EEG	3.6	2.4	3.7	3.4	5
Objective findings on neurological examination	2.8	1.5	2.1	3.4	5
Amount of theta activity—EEG	5.0	4.0	3.7	3.3	5
Talking age	5.1	3.8	3.9	3.2	5
Seizure-state at follow-up	2.9	2.6	3.8	3.1	5
Response to anticonvulsant medication within first year of treatment	3.4	5.0	2.7	3.1	5

TABLE 60

SIGNIFICANT DIFFERENCES BETWEEN PATIENTS DEPENDING UPON AGE AT INITIAL EVALUATION

	1–10 Years	*11–25 Years*	*26 years or older*	X^2	*Significance Level* (%)
Family history of breathholding spells					
Absent	16	34	24	19.0	1
Present	10	2	0		
Seizure disorder started during first year of life					
Absent	10	29	22	13.6	1
Present	8	2	2		
Rotation of Bender-Gestalt figures					
Absent	4	29	15	13.3	1
Present	9	5	10		
Family history of chronic headache					
Absent	9	23	19	10.8	1
Present	17	13	5		
Seizures present during first year of life regardless of type and whether isolated or recurrent					
Absent	18	34	22	9.9	1
Present	10	2	4		
Anticonvulsant treatment discontinued by the time of follow-up					
No	19	33	26	9.9	1
Yes	7	3	0		

Diagnosis of psychiatric disorder made in addition to epilepsy						
	No	26	35	19		
	Yes	2	1	7	9.5	1
Emotional stress precipitating major seizures						
	No	17	24	13	8.9	5
	Yes	1	7	11		
Focal minor motor seizures						
	Absent	20	33	25	8.4	5
	Present	8	3	1		
EEG—left temporal focus						
	Absent	24	31	16	8.3	5
	Present	0	2	5		
Behavioral difficulties in school						
	Absent	20	32	25	7.2	5
	Present	8	4	1		
History of febrile convulsions						
	Absent	17	30	23	7.0	5
	Present	11	6	3		
Confusion after major seizures						
	Absent	18	22	17	6.7	5
	Present	0	9	7		
Fatigue after major seizures						
	Absent	15	18	11	6.1	5
	Present	3	13	13		

2. The group of children had the most recent onset of seizure disorders but also showed the most marked organic pathology, and grand mal status was most common in this age group.

3. The adult group had the longest duration of the seizure disorder. The patients likewise showed organic changes, and although doing better at follow-up in regard to seizure state than the children, they were the worst off in their overall functions mostly because of intellectual deficits and/or behavioral problems.

The finding that a left temporal EEG focus was age related, but not a right temporal focus, is of theoretical interest but would require validation on another sample. The significant differences in regard to the variables dealing with family history may merely reflect the possibility of obtaining more detailed historical information in the younger age group. The same applies to the personal history of febrile convulsions.

Significant Differences among Groups Depending upon Age at Time of Onset of Recurrent Seizures

The data having shown that chronological age at which the patient presents himself to a specialized center is of importance for his overall prognosis, and having shown also that duration of the seizure disorder prior to his first visit is another important consideration, it became imperative to investigate in detail the question of whether age at time of onset of the illness is important for the patient's seizure prognosis. This particular variable was originally not included in the coding forms, but it was available in the charts of the patients. The material could be divided into three approximately equal groups: onset within first three years of life, twenty-seven patients; between four and twelve years, thirty-one patients; and between thirteen to twenty-seven years, thirty patients.

Age of onset is, however, not as clear a variable as chronological age. The main problem is that a number of patients have one or two isolated febrile or afebrile seizures in infancy and have subsequently no difficulties until school age, puberty, or late

adolescence, at which time the chronic seizure disorder starts to develop. An arbitrary decision was made to regard as age of onset the time at which repeated attacks appeared, not the first isolated episode. The three groups were then compared on the previously mentioned 190 variables, and the statistically significant findings in regard to seizures are shown in Table 61. Significant findings in regard to intelligence will be presented later.

TABLE 61

SIGNIFICANT DIFFERENCES BETWEEN GROUPS DEPENDING UPON AGE AT TIME OF ONSET OF RECURRENT SEIZURES

	0–3 Years	*4–12 Years*	*13–27 Years*	*F*	*Significance Level (%)*
Amount of EEG abnormality	5.0	7.0	5.3	4.0	5
Seizure prognosis	5.3	4.0	4.3	3.8	5

		0–3 Years	*4–12 Years*	*13–27 Years*	X^2	*Significance Level (%)*
Emotional stress precipitating major seizure						
	Absent	19	20	15	11.3	1
	Present	3	2	13		
Family history of breathholding spells						
	Absent	17	26	29	9.2	1
	Present	7	5	0		
Postictal confusion after major seizures						
	Absent	20	19	17	7.8	5
	Present	2	3	11		
Family history of breech birth						
	Absent	22	25	29	6.5	5
	Present	2	6	0		
Absence						
	Absent	25	20	23	6.4	5
	Present	2	11	7		
Focal minor motor seizures						
	Absent	20	27	29	6.1	5
	Present	7	4	1		

It was interesting to see that although the youngest group was given the poorest prognosis for seizure control, the actual outcome did not differ between the three groups. As far as seizure patterns were concerned, the sample agreed with the literature that absences tend to start mostly between the ages of four and twelve, and during adolescence. A predominant seizure pattern of infancy and early childhood appears to be focal minor motor attacks. There was no significant difference in regard to focal or nonfocal major seizures, and in regard to psychomotor automatisms. The latter finding seems to be somewhat surprising because it is well known that psychomotor automatisms do not start in infancy. The explanation lies in the fact that they appeared, for the most part, as a second seizure type later in life and were then equally represented in all three groups.

The two variables dealing with family history of breech birth and breathholding spells are of potential interest but will have to be verified on another sample before one can attach clinical significance to the findings. The incidence of family history of epilepsy was not significantly different between the groups.

The EEG showed a somewhat unexpected behavior in this sample. The most marked amount of abnormality occurred in the group of patients that started with epilepsy between four and twelve years of age. The important feature of this aspect of the study was the negative observation that age of onset by itself was not significantly related to seizure outcome.

Duration of Illness

We still have to discuss the observation that duration of illness prior to first visit to the Center was the only finding that had been significantly related to seizure outcome in the first as well as the second follow-up study. A detailed breakdown of duration of illness in relation to terminal remissions revealed a somewhat surprising phenomenon as shown in Table 62.

Six of the seven patients who were seen within the first year of their illness had enjoyed complete remissions; but with those patients seen during the second year, the remission rate had

TABLE 62

RELATIONSHIP OF DURATION OF ILLNESS TO SEIZURE CONTROL

Initial Evaluation after Onset of Illness	*Number of Patients in Group*	*Number of Patients in Remission for at least two years*	*Percentages*
Within first year	7	6	85
Within second year	12	6	50
Within third year	9	3	33
Within fourth year	7	2	28
From 5 to 10 years	19	7	36
More than 10 years	36	5	13

dropped to one-half. With those seen between the third and fifth year, the rate had dropped approximately to one-third, and when patients were seen for the first time after ten years, a two-year terminal remission had occurred in only 13 per cent. While the overall trends are not surprising, the sharp decline in terminal remissions after the first year of illness is remarkable. It certainly suggests that vigorous anticonvulsant treatment at the onset can prevent chronic seizure disorders. An 85 per cent remission rate is, of course, impressive and one may well be inclined to credit our modern drugs with this result. A look at the literature casts some doubt on this opinion. Table 63, taken

TABLE 63

RELATIONSHIP OF DURATION OF ILLNESS TO SEIZURE CONTROL ACCORDING TO GOWERS, 1885*

	Cases		*Percentage*	
Duration	*Unimproved*	*Arrested*	*Unimproved*	*Arrested*
Less than 1 year	4	19	17	83
1 to 4 years	14	37	27	73
5 to 9 years	9	20	31	69
10 years and over	16	24	40	60
Total	43	100	30	70

*From *Epilepsy and Other Chronic Convulsive Diseases: Their Causes, Symptoms and Treatment* (unaltered republication of the work first published by William Wood and Company in 1885), Dover Publications, Inc., New York, 1964.

from Gowers' book, which was first published in 1885, likewise shows an 83 per cent remission rate for patients who were seen within the first year. The downhill trend thereafter is also observable. His results after the first year are actually better than ours, but Gowers did not define the length of time for which seizures had been "arrested" in his patients. Nevertheless, these results do bring to mind again Hippocrates' statement ". . . it is curable no less than others unless when from length of time it has become confirmed and stronger than the remedies applied." We are therefore dealing with an ancient observation which is very likely to be important for the pathophysiology of epilepsy. There are at least two possibilities that could account for this phenomenon. One is the problem of negative selection as suggested by Margaret Lennox (1967). The later the neurologist sees the patient, the greater the likelihood that the seizure disorder does not respond to the usual anticonvulsant regime. The other possibility is that seizures themselves set up a special condition in the brain which facilitates their recurrence and renders the patient more or less refractory to drug treatment. While the first possibility undoubtedly plays a significant role, this does not necessarily mean that the second possibility should be discarded. Its relative importance cannot be readily evaluated in this country because a vast majority of patients are receiving some treatment very soon after their seizure disorder starts. The problem could and should be studied in one of the underdeveloped nations where regular medical facilities are not uniformly available at the present time.

Lafayette Clinic Outpatient Results

A criticism that could be leveled against the material that has been presented so far is that the patients did not necessarily receive maximum benefit of modern anticonvulsant drugs. It has been mentioned before that the patients' treatment had been carried out by physicians in the community who were usually not specialists in neurology. In order to evaluate the extent to which a neurological training center with special interest in epilepsy can improve seizure patients, we investigated the results

that were achieved by the Neurology Outpatient Department of the Lafayette Clinic. This service was started in January, 1959, and by June, 1966, 123 patients were available who had been followed regularly for periods of time ranging between two and seven years. Patients who had been followed for less than two years were omitted from the study. The previously used criterion of at least three epileptic seizures was again required for a patient to be included in the series. The breakdown in terms of length of treatment is as follows: two years, twenty-seven patients; three years, eighteen patients; four years, twenty-two patients; five years, thirty-two patients; six years, seventeen patients; and seven years, seven patients. The results of treatment

TABLE 64

Last Seizure	Number of Patients
Within 1 month before last clinic visit	71
Within 1 to 3 months before last clinic visit	15
Within 4 to 6 months	5
Within 7 months to 1 year	8
Within 1 to 2 years	9
Within 2 to 3 years	3
Within 3 to 4 years	5
Within 4 to 5 years	3
More than 5 years	4

are listed in Table 64. Fifty-seven per cent of patients had had a seizure within one month of their last clinic visit, and remission of more than six months was accomplished in 32 patients only (26.0%). If we concentrate on the patients who had been seen for at least five years, we find that fifty-six patients qualified and their treatment results are shown in Table 65. Thirty-six patients (64.3%) had had a seizure within the last month of their clinic visit. A terminal remission of at least six months had occurred in eleven patients (19.6%), and a terminal remission of at least two years in only eight patients (14.3%). These are certainly not very encouraging figures, as they are markedly lower than those obtained in the previous follow-up studies at the Michigan Epilepsy Center. It may be argued that the Lafayette

Clinic patients were for the most part treated by resident physicians in training and not by Board certified specialists, which could have influenced the treatment results. This factor was proven not to be decisive, because for a period of one year (July, 1963 to June, 1964) I treated nearly all of these patients myself and was able to render seizure-free only two patients who had previously been uncontrolled.

There are two other arguments that can be advanced to explain the poor treatment results. One is that outpatients may or may not take their medications as prescribed, and the second is

TABLE 65

Last Seizure	Number of Patients
Within 1 month before last clinic visit	36
Within 1 to 3 months before last clinic visit	6
Within 4 to 6 months	3
Within 7 months to 1 year	2
Within 1 to 2 years	1
Within 2 to 3 years	1
Within 3 to 4 years	2
Within 4 to 5 years	1
More than 5 years	4

that we are dealing with a negative selection of patients. Since the Lafayette Clinic is known as a treatment center for epilepsy, the most inveterate cases are likely to come for help. As far as reliability of patients is concerned, seventy patients (56.9%) were judged as reliable, forty-one patients (33.3%) fairly reliable, and only twelve patients (9.8%) were definitely unreliable. This judgment was based on the progress notes which recorded whether patients kept their scheduled appointments and whether they were correct in stating the amount and type of medication that they were supposed to take. While reliability was therefore a problem to varying extents in approximately 43 per cent of the patients, the negative selection of inveterate cases was definitely of importance. Duration of illness and the relationship to terminal remissions are shown in Table 66. Only six patients were seen within one year after onset of the illness,

thirteen patients between two to five years, and thirty-seven patients had had seizures for more than five years. A terminal remission of at least two years had occurred in 21 per cent of the patients that were seen less than five years after onset of seizures, and in 10 per cent of patients who were seen for more than five years after the illness had been present. Although we can see again the relationship between duration of illness and treatment result, the remission rate noted in the group that was seen within the first five years is far from encouraging. A major reason for the poor results is probably the fact that the majority of patients

TABLE 66

Time when patients were first seen after onset of recurrent seizures	*Time of most recent seizure prior to last clinic visit*		
	Less than six months	*Six months to two years*	*More than two years*
1 year or less	3	2	1
2 years	3	0	0
3 years	2	1	1
4 years	2	0	1
5 years	2	0	1
6 to 10 years	11	0	1
11 to 20 years	12	0	2
More than 20 years	10	0	1

who keep attending an outpatient clinic regularly, do so because their seizures are not satisfactorily controlled. Outpatient surveys can therefore not be strictly compared with follow-up results where a group of patients is asked to return regardless of whether the patient appreciates a need for reevaluation or not.

Outpatient reviews really prove only that there still exists a reservoir of epileptic patients who are essentially refractory to our best therapeutic efforts. Although seizures may decrease somewhat in frequency of occurrence or intensity, long-term freedom from seizures is rarely achieved. The size of this reservoir in relation to the total epileptic population cannot be estimated at the present time. This could only be accomplished by a thorough epidemiological survey of a large community.

Lafayette Clinic Inpatient Review

The study on the Lafayette Clinic outpatients demonstrated the existence of this hard-core epilepsy population, but it did not lend itself towards defining the characteristics of the patient who is indeed refractory to treatment. The problem with outpatient evaluations is that one is confronted by two major uncertainties: (1) accuracy of the patient's report about the frequency of his seizures and (2) patient's adherence to his anticonvulsant regime. Both of these problems will inevitably contaminate the results of outpatient treatment. It happens fairly commonly that patients—especially ones with temporal lobe seizures—report that their attacks have stopped when in fact they have merely lost the aura and are no longer aware that seizures are taking place. Reports regarding cessation of petit mal have to be taken with equal caution. Even in regard to grand mal seizures some patients may not be aware of their occurrence, especially if they are predominantly nocturnal. As far as regularity of the patient's medication intake is concerned, one is of course even more at the mercy of the patient's report, which is a most undesirable state of affairs. Routine determinations of serum barbiturate and/or Dilantin levels at the time of each outpatient visit usually are not performed in this country. Both of these uncertainties can be resolved in a hospital situation. Medication intake is controlled by the nursing staff, and seizures are readily observable. We decided to review the charts of all epileptic patients who had been admitted to the inpatient neurology service of the Lafayette Clinic between January, 1959, and July, 1966. Criteria for inclusion in the study were (1) a definite diagnosis of epilepsy as defined previously and (2) a minimum of three weeks of hopitalization. A total of 245 patients became eligible: 132 had been referred from the community because of inadequate seizure control, thirty-one had been admitted from the community because of marked behavioral difficulties, and eighty-two had been referred from the state hospital system of the State of Michigan for research or teaching purposes (57 from Caro State Hospital for Epileptics, 25 from state hospitals for the mentally ill). The charts were abstracted, coded on specially

prepared forms, and the information transferred onto IBM cards. The main goal of the investigation was to define the characteristics of the patient whose seizures persist in the hospital in spite of maximum efforts towards seizure control. Medication regime had been carried out under my personal supervision in each of these cases and all newer anticonvulsants—including experimental drugs (except Tegretol® and Mogadon)—had been used in the treatment of refractory cases. The mean duration of hospitalization was 7.5 weeks. There were 129 males and 116 females in the sample. The mean age was 28.6 years with a range from five to sixty-four years. The mean duration of the illness was fifteen years with a range between one and fifty-two years. The seizure types are shown in Table 67.

TABLE 67

SEIZURE TYPES

Focal grand mal	115
Psychomotor seizures	60
Nonfocal grand mal	59
Focal minor motor seizures	35
Absence	34
Grand mal seizures but history inadequate to differentiate between focal and nonfocal	28
Nonfocal minor motor seizures	21
Focal grand mal variant seizures	15
Akinetic seizures	13
Myoclonic jerks	11
Nonfocal grand mal variant seizures	9
Absences with features of automatisms	8
Absences with some myoclonic activity	8

After obtaining frequency distributions for all variables and eliminating those which were inadequately represented in the sample, the total number of patients was divided into three subgroups: (1) no seizures in the hospital, 118 (48.1%); (2) one to three seizures in the hospital, 47 (19.1%), and (3) more than three seizures during hospitalization, 80 (32.6%).

A sample of the code sheets is contained in the Appendix. The variables that were used for statistical analysis are marked by asterisks. F tests were performed on the continuously distributed variables and Chi Square tests on phenomena that had been

TABLE 68

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures (N = 118)	*Group II 1–3 Seizures (N = 47)*	*Group III 4 or more Seizures (N = 80)*	*F*	*Significance Level (%)*
Frequency of occurrence of seizures just prior to hospitalization	5.2	7.0	8.1	39.1	1
Combination of seizures*	1.8	2.8	3.6	36.9	1
Frequency of maximal occurrence of seizures	6.7	8.3	8.8	29.0	1
Clusters of seizures in one day	1.7	2.0	2.8	26.7	1C
Frequency of injuries during seizures*	1.2	1.4	2.2	26.3	1C
Length of hospitalization in weeks	5.6	8.2	9.7	18.3	1
Seizure patterns in EEG*	1.7	2.3	2.7	14.2	1C
Amount of EEG abnormality*	3.1	3.6	4.0	12.5	1C
Age at onset of recurrent seizures in months	212.0	143.9	117.4	11.2	1
Age at onset of first seizure in months	189.3	124.6	103.3	8.5	1
Amount of abnormality in sleep EEG	2.5	3.1	4.2	8.0	1C
Amount of abortive spike wave activity in EEG	1.1	1.4	1.5	7.5	1C
Amount of schooling	3.7	3.4	2.9	6.0	1

Clusters of seizures over several days, freedom from seizures for several weeks*	1.2	1.3	1.7	6.0	1C
Amount of theta activity in EEG	2.8	2.9	3.3	5.9	1C
Amount of diffuse paroxysmal activity in EEG (not spike wave)	1.0	1.3	1.0	5.8	1C
Age in years	31.4	27.7	25.5	4.8	1
Amplitude of background voltage in EEG	3.4	4.0	3.9	4.8	1
Neurological findings suggesting cerebral pathology	1.6	1.8	2.1	4.5	5C
Duration of main seizure type	7.2	7.7	7.8	4.3	5
Evidence of bilateral cerebral disease	1.8	2.0	2.2	4.2	5
Amount of diffuse delta activity in EEG	1.1	1.1	1.3	4.2	5C
Status epilepticus	1.1	1.2	1.4	4.0	5
Number of admissions	1.2	1.4	1.6	4.0	5
Amount of focal EEG abnormality	1.6	1.6	2.0	3.5	5C
Abortive paroxysmal activity in EEG	1.1	1.2	1.4	3.5	5C
Amount of photic driving response at flash rates of 13 c/s and higher	1.4	1.4	1.1	3.4	5C
Neurotic tendencies on psychological tests	2.5	2.3	2.0	3.2	5C
Immaturity on psychological tests	2.7	3.3	2.1	3.1	5C
Spike wave activity in EEG	1.1	1.2	1.3	3.1	5C
Full Scale IQ	80.8	77.8	72.6	3.0	5

C indicates scales that have been condensed from nine points to four or five points between MEC study (1961) and LC study (1966).

graded as present or absent. Table 68 shows the statistically significant differences between the groups for the F tests and Table 69 for the Chi Square tests. The variables that are marked by asterisks had shown significant differences between the controlled and uncontrolled groups in the second follow-up study conducted at the Michigan Epilepsy Center. The mean values for some of the scales cannot be directly compared with those shown on Table 55 dealing with the results of follow-up at the Michigan Epilepsy Center because by the time of the Lafayette Clinic inpatient review—summer, 1966—we had condensed a number of the nine-point scales to four or five-point scales. The condensed scales are marked by a C on the extreme right hand side of the table. In order to get an approximate comparison between the findings in Table 55 and Table 68, the mean values of the condensed scales would have to be multiplied by two.

Reviewing Tables 68 and 69, we can notice that we are indeed dealing with a continuum of seizure intensity, with Group II standing clearly in the middle on most variables. Patients who had no seizures in the hospital had had, on the average prior to admission, seizures approximately every six weeks; patients with four or more seizures had on the outside approximately one a week. Maximal frequency of seizures in Group I (no seizures in the hospital) was between one and two a month, and in Group III (four or more seizures in the hospital) more than one per week. The Group III patients had more commonly a combination of seizure types; more frequently clusters of seizures in one given day, and clusters of seizures for several days with subsequent freedom from seizures for several weeks; more frequent injuries as a result of seizures; more frequent status epilepticus; were hospitalized longer in an attempt towards better seizure control, and were more frequently readmitted because of poor control after having been discharged from the hospital. They were younger at the time of onset of the recurrent seizure disorder (mean age 9.7 years versus 17.6 years), and younger at the time of first seizure (mean age 8.6 years versus 15.7 years). They had received less schooling, had lower IQs (72.6 versus 80.8), and had more evidence of bilateral cerebral involvement on neurological examination and on the EEG. The electroencephalo-

TABLE 69

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Nonfocal minor motor seizures					
Absent	117	46	61	34.9	1
Present	1	1	19		
Special schooling					
Absent	92	24	36	27.0	1
Present	19	19	39		
Nonfocal grand mal variant seizures					
Absent	118	47	71	19.2	1
Present	0	0	9		
Theta rhythm present in EEG with eyes open					
Absent	113	44	63	15.9	1
Present	5	3	17		
Akinetic seizures					
Absent	116	46	70	12.2	1
Present	2	1	10		
Psychomotor seizures*					
Absent	100	33	52	10.9	1
Present	18	14	28		
Focal grand mal variant seizure induced by Megimide					
Absent	84	39	52	9.7	1
Present	3	4	12		
Focal response to Megimide in left anterior temporal area					
Absent	89	38	51	9.3	1
Present	3	2	10		
Focal slow wave discharges in resting EEG					
Absent	110	41	64	8.9	5
Present	7	6	16		
Right midtemporal focus in resting EEG					
Absent	114	39	72	8.8	5
Present	4	8	8		

TABLE 69 (Continued)

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Psychotic symptoms in history					
Absent	84	39	71	8.8	5
Present	33	8	9		
Petit mal absence with myoclonic components					
Absent	118	43	76	8.8	5
Present	0	4	4		
Grand mal but history inadequate to differentiate between focal and nonfocal					
Absent	98	42	77	8.2	5
Present	20	5	3		
Family history of twins on paternal side					
Absent	101	38	69	8.1	5
Present	2	6	4		
Family history of more than one stillbirth					
Absent	99	40	76	7.8	5
Present	6	5	0		
Family history of febrile convulsions on the maternal side					
Absent	98	39	68	7.2	5
Present	2	6	6		
Focal response to Megimide in right midtemporal area					
Absent	85	31	57	7.2	5
Present	8	9	4		
Neurotic symptoms in past history					
Absent	108	39	77	7.0	5
Present	9	8	3		
Family history of early infantile deaths on maternal side					
Absent	97	36	70	6.7	5
Present	8	9	5		

TABLE 69 (Continued)

SIGNIFICANT DIFFERENCES RELATED TO SEIZURE FREQUENCY DURING INPATIENT TREATMENT

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level* (%)
Family history of neurological disease other than epilepsy on paternal side					
Absent	96	35	67	6.5	5
Present	8	10	8		
Family history of diabetes on paternal side					
Absent	97	37	67	6.3	5
Present	5	8	9		
Family history of psychiatric disorders on maternal side					
Absent	82	26	58	6.3	5
Present	25	19	18		
Focal minor motor seizures					
Absent	108	38	64	6.2	5
Present	10	9	16		
Family history of febrile convulsions in males					
Absent	97	37	68	6.1	5
Present	4	7	6		
Sleep recording less abnormal than waking record					
Absent	25	8	18	6.0	5
Present	12	5	1		

gram was more abnormal in regard to amount of seizure patterns, general abnormality, amount of theta and delta activity, certain types of paroxysmal discharges and focal abnormalities. The Group III patients also had less of a photic driving response at high flash rates and the sleep recordings were more abnormal. The important negative findings are again: no significant differences in regard to any of the presumed etiological factors. The Chi Square tests demonstrated the seizure types that were the most difficult to control: focal and nonfocal minor motor seizures, nonfocal grand mal variant seizures (major seizures characterized

either by tonic phase only or prolonged clonic without tonic phase —Rodin, 1964), akinetic seizures, psychomotor seizures and petit mal absences with myoclonic features. The seizure type called "grand mal but history inadequate to differentiate between focal and nonfocal" refers mostly to patients with nocturnal seizures. These patients did relatively well in the hospital. The finding that the psychiatric variables of psychotic and neurotic symptoms occurred less frequently in the most severe seizure group does not necessarily indicate an inverse relationship between seizures and these symptoms, but may merely reflect the fact that patients with psychiatric difficulties were admitted on account of this symptomatology rather than because of the intensity of their seizure disorder. The variables dealing with family history are listed in the table because they did show statistically significant differences, but they do not appear to be clinically meaningful at this time and do not form a recognizable pattern. The important feature, as far as family history is concerned, is that family history of epilepsy did not differentiate the groups.

Megimide® activation had been carried out under EEG control in 194 patients, and the induced seizures were photographed in 134 patients. The methodology and preliminary findings have been published previously (Rodin, 1964). The results of Megimide activation were, for the most part, not of importance in regard to the question at hand, except for the fact that focal grand mal variant seizures were more commonly induced in Group III patients, a right midtemporal EEG focus occurred more commonly in Group II, and a left anterior temporal focus was found more commonly in Group III. It is important to point out that although the mean Megimide threshold for seizure induction was the lowest in Group III, the finding did not reach statistical significance. The means were 201 mg for Group I, 203 mg for Group II, and 174 mg for Group III. The standard deviations were 115, 95, and 117 mg respectively. The Megimide threshold does, therefore, not reflect the individual's propensity towards spontaneously recurring seizures, and the drug cannot be used to establish a diagnosis of epilepsy on the basis of the dosage needed to induce a clinical seizure. This finding has also considerable theoretical significance in regard to anticonvulsant

drugs. The pharmaceutical industry depends in its determination of whether a compound has anticonvulsant properties or not, to a large extent, upon changes in threshold to Metrazol® or electrical stimulation. This practice has led to the discovery of important anticonvulsant agents but may not yield the drug which will permanently eradicate the patient's "seizure propensity." Inasmuch as seizure threshold and seizure propensity are different phenomena, different mechanisms are in all probability operative which may well require a different pharmacological attack.

Another important observation from this initial data analysis was that a number of variables which had been found to be of importance in the follow-up study conducted at the Michigan Epilepsy Center—dealing with long-term seizure control—turned out to be important also for the success or failure of short-term anticonvulsant treatment in the hospital.

In this initial data analysis of the Lafayette Clinic inpatient group we had purposely included all epileptic patients, regardless of referring source and regardless of presenting complaint, in order to get the full spectrum of epilepsy. This ranged from mild cases, whose main problem consisted of behavioral difficulties with seizures being more or less incidental, through patients whose seizures could not be adequately controlled on an outpatient basis, to patients who had to reside in an institution for epileptics. It may be argued, however, that by including the institutionalized group we have biased our results and they are therefore not directly applicable to the majority of epileptic patients who reside in the community. Subsequently, in order to meet this criticism, we concentrated in the data analysis on the 132 patients who had been referred from the community because their seizures had not been adequately controlled. The specific question we wanted to answer was— Who is the epileptic patient residing in the community who will continue to have seizures in the hospital even with maximal treatment efforts? The group of 132 patients was therefore split again into three subgroups: one containing sixty patients (45.5%) who did not have any seizures during their entire hospitalization, another containing thirty-four patients (25.7%) who had between one and three

seizures in the hospital, and the third consisting of thirty-eight patients (28.8%) who had four or more seizures while hospitalized. These percentage figures are, of course, of interest by themselves because they indicate that nearly every other patient who is uncontrolled in the community can be brought under temporary control in the hospital environment. This refers however to short-term control only, because it is not justifiable to keep a patient in the hospital for any length of time if he has no seizures. Nevertheless, it is important to point out that a significant short-term improvement can be accomplished in approximately half of the patients who are uncontrolled in their home situation. The thirty-eight patients who had four or more seizures in the hospital are definitely a part of the hard-core group that is essentially resistant to our present day treatment program. F tests and Chi Square tests were again performed in order to find the variables that would distinguish between the three groups. The results of the F tests are listed in Table 70 and the Chi Square results in Table 71. The variables that differentiated the remitted from the unremitted group in the second follow-up study, conducted at the Michigan Epilepsy Center, are marked by an asterisk. The previously mentioned continuum in the severity of seizure disorders is again reflected in the results of treatment. Nearly all variables show an orderly increase in amount of abnormality between the group having no seizures in the hospital and the group having more than four seizures, with the intermediate group standing indeed in the middle. Only amount of paroxysmal activity (not necessarily spike wave) and background voltage of the EEG did not follow this trend. It is again remarkable that none of the supposed etiological factors bears any relationship to result of treatment in the hospital.

If we omit now all those variables that had shown statistically significant differences between groups in one study only, and concentrate on those that had shown statistically significant differences in more than one study, then we find that the prognostic criteria for seizure control which we had set out to develop can be summarized in essentially eight questions:

1. How long has the patient had seizures? The longer

TABLE 70

COMPARISON OF PATIENTS REFERRED FROM THE COMMUNITY FOR SEIZURE CONTROL

	Group I No Seizures (N = 60)	*Group II 1–3 Seizures (N = 34)*	*Group III 4 or more Seizures (N = 38)*	*F*	*Significance Level (%)*
Combination of seizures*	1.8	2.8	3.3	17.0	1
Number of admissions to hospital	1.2	1.2	2.0	12.5	1
Frequency of injuries during seizures*	1.1	1.4	1.9	11.5	1C
Amount of EEG abnormality*	2.9	3.7	4.0	10.4	1C
Length of hospitalization in weeks	4.6	7.8	8.3	9.6	1
Frequency of maximal occurrence of seizures	7.3	8.1	8.8	9.3	1
Frequency of occurrence of seizures just prior to hospitalization	6.7	7.1	8.3	7.6	1
Clusters of seizures over several days, freedom from seizures for several weeks*	1.3	1.4	2.2	7.2	1C
Amount of diffuse paroxysmal activity in EEG (not spike wave)	1.0	1.4	1.0	6.9	1C
Clnsters of seizures in one day	1.9	2.0	2.8	6.8	1C
Amount of focal EEG abnormality	1.5	1.6	2.2	6.4	1C
Seizure patterns in EEG*	1.7	2.4	2.7	6.3	1C
Amplitude of background voltage in EEG	3.5	4.3	4.1	4.7	1
Neurological findings suggesting cerebral pathology	1.3	1.6	1.8	4.5	5C
Background amplitude on the left in EEG	3.6	4.3	3.9	4.0	5
Abortive spike wave activity in EEG	1.1	1.4	1.4	3.3	5C
Amount of theta activity in EEG	2.5	2.9	3.1	3.2	5C

C indicates scales that have been condensed from nine points to four or five points between MEC study (1961) and LC study (1966).

TABLE 71

COMPARISON OF PATIENTS REFERRED FROM THE COMMUNITY FOR SEIZURE CONTROL

	Group I No Seizures	*Group II 1–3 Seizures*	*Group III 4 or more Seizures*	X^2	*Significance Level (%)*
Special schooling					
Absent	47	18	20	11.3	1
Present	9	13	17		
Focal slow wave discharges in EEG					
Absent	57	29	27	10.8	1
Present	3	5	11		
Psychomotor seizures*					
Absent	51	24	21	10.4	1
Present	9	10	17		
Nonfocal grand mal variant seizure					
Absent	60	34	34	10.2	1
Present	0	0	4		
Right anterior temporal focus induced by Megimide activation					
Absent	43	28	23	9.8	1
Present	1	0	5		
Right anterior temporal focus in resting EEG					
Absent	55	33	30	6.8	5
Present	5	1	8		
Family history of psychiatric disorder on maternal side of family					
Absent	42	18	26	6.3	5
Present	10	14	8		

the duration of the disorder, the poorer the results of treatment.

2. Is there one seizure type or more than one? The more different seizure types, the less likely it becomes that the patient will be controlled even in a hospital setting.

3. Are psychomotor seizures present? If yes, chances for medical control are immediately markedly reduced.

4. How frequent are the seizures? If they occur several times a month while the patient is on some anticonvulsant medication, chances for complete control are slim.

5. Does the patient have clusters of seizures over a few days and subsequently no seizures for several weeks? The more frequently this phenomenon occurs, the less likely is control achievable.

6. Does the patient injure himself during the seizures? The more frequently this happens, the less likely will he be controlled.

7. What is the degree of abnormality of the EEG while the patient is on some anticonvulsant regime? The more abnormal the EEG, the more likely will be poor control.

8. Are there seizure patterns in the EEG while the patient is on some anticonvulsant medication? The more seizure patterns, the less likely control.

While the presence of one adverse criterion does not rule against success of drug treatment, a combination of a number of these criteria make long-term seizure control unlikely.

Discriminant Function Analysis

After we had established these eight criteria, one could proceed to the next step, namely, determining the precise weights which each of these variables carries in relation to seizure prognosis. The goal of the investigation was to present the physician with a formula, on basis of which he could give a reasonably accurate prediction, whether the seizures are likely to become completely controllable or not. In order to accomplish this aim, a discriminant function analysis was carried out. This is a statistical way of classifying individuals into certain groups and provides the probability of the individual's being a member of any of the groups. The computer program used was an adaptation of the one developed by the University of California (W. J. Dixon, 1965). Up to eleven variables could be used, but the program required complete information on each of the variables. One hundred eight-one Lafayette Clinic inpatients had complete data on all the previously mentioned eight variables. Two subgroups were formed from this material: one consisting of eighty-one patients who had not had any seizures in the hospital while on anticonvulsant medication; the other consisting of one hundred patients who had at least one seizure in spite of adequate

drug treatment. A comparison between the mean values of the two groups on these variables is shown in Table 72. The multiple discriminant function program classified correctly sixty-two (76%) of the patients who did not have seizures in the hospital, and eighty-one (81%) of those who continued to have attacks. The total correct classification was therefore 78 per cent. By chance one would expect a 50 per cent correct classification. Table 73 shows the probabilities supplied by the computer classification in relation to the actual findings at time of hospitaliza-

TABLE 72

	*Group I**	*Group II***
Amount of EEG abnormality	3.1	3.9
Seizure patterns in EEG	1.7	2.6
Psychomotor seizures	1.1	1.3
Combination of seizures	1.8	3.4
Duration of illness	7.2	7.8
Frequency of seizures at present	4.9	7.7
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.6
Injuries during seizures	1.3	1.9

* No seizures in hospital

** At least 1 seizure in hospital

tion. It can be seen that if the formula provided a probability of classification that was less than .75, it was not very useful for prognostication. If on the other hand, the probability was .90 or higher, a false classification was encountered only very rarely.

The charts of the three patients whose classifications were grossly in error were then reviewed to ascertain the reasons for the incorrect classification. The patient who did not have seizures in the hospital, in spite of the fact that the formula had predicted with .93 probability that seizures would occur, had been drinking alcohol excessively prior to hospitalization and had neglected her medication regime. The hospital environment provided stability, but after discharge the patient returned to her old ways and the seizure disorder became again uncontrolled. Equally interesting were the two patients who should not have had a seizure in the hospital according to the formula, with a

probability of .93 and .94 respectively, but each one had in fact experienced one seizure while on anticonvulsant medication. In both instances, the seizure occurred in the afternoon of a day when the patients had received an intravenous drug administration in the morning. One patient had received Megimide in an attempt to reproduce his seizure pattern in the EEG laboratory. He had reacted with a marked confusional state which corresponded to his spontaneous attacks, but he did not enter into a generalized seizure. The seizure did occur, as has been

TABLE 73

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	16	14
.75 to .89	15	4
.90 to .98	31	1
*Group II***		
Less than .75	27	13
.75 to .89	25	4
.90 to .99	29	2

* No seizures in hospital

** At least 1 seizure in hospital

mentioned, later that afternoon. The other patient had participated in an investigation involving the psychotomimetic properties of Sernyl (1-phenylcyclohexyl piperidine monohydrochloride) in the EEG laboratory during the morning and a generalized seizure occurred on the ward later that afternoon. It is reasonable to assume that seizures would probably not have occurred in these two patients had they not participated in the investigative studies earlier in the day.

Cross Validation

Inasmuch as the variables that had been used for the discriminant function analysis had also shown significant differences between the three groups in the follow-up study at the Michigan

Epilepsy Center (remission for at least two years, seizures improved, seizures same or worse), it was of interest to see what success could be achieved if the formula were to be applied to this independent sample of patients. Fifty-nine patients were available who had complete information on all the eight variables. Nineteen had been seizure free for at least two years, and forty continued to have some seizures. Wherever scales had been changed between the two investigations, the original nine-point scales were condensed to the appropriate Lafayette Clinic scales. The mean values for these two groups of patients on the comparable scales are shown in Table 74. Applying the weights ob-

TABLE 74

	*Group I**	*Group II***
Amount of EEG abnormality	2.8	3.7
Seizure patterns in EEG	1.8	2.8
Psychomotor seizures	1.0	1.3
Combination of seizures	1.6	2.9
Duration of illness	5.6	7.4
Frequency of seizures at present	6.2	7.9
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.7
Injuries during seizures	1.8	2.7

* No seizures for at least 2 years

** Seizures within the last 2 years prior to follow-up

tained from the Lafayette Clinic inpatient sample to these fifty-nine patients, it was found that fourteen (73%) of the seizure free and thirty-six (90%) of the other patients were correctly classified. This gave an overall success rate of 84 per cent. The cross validation demonstrated therefore that the formula can be applied with success to another group of patients, and that the weights which predict short-term control can be utilized for prognostication in regard to long-term success of anticonvulsant treatment.

Use of Discriminant Function Formula

Table 75 shows next to each of the eight variables the coefficients for the discriminant functions of Group I and Group II,

as well as the constants that have to be subtracted from the results. In order to arrive at a prediction about the patient's seizure state, the following steps have to be taken:

1. The coefficient next to each variable has to be multiplied by the patient's coded finding on this particular item.

TABLE 75

DISCRIMINANT FUNCTION FOR PREDICTING SEIZURE CONTROL IN THE HOSPITAL

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Amount of EEG abnormality	1.57	1.78
Seizure patterns in EEG	0.09	0.21
Psychomotor seizures	6.08	6.25
Duration of illness	2.85	2.92
Frequency of seizures at present	0.56	1.02
Clusters of seizures over several days, freedom from seizures for several weeks	0.77	0.90
Combination of seizures	−0.39	0.06
Frequency of injuries during seizures	−0.41	−0.03
Constant	−17.43	−24.01

2. All eight coefficients are to be added and the constant 17.43 is subtracted. The obtained value represents the discriminant function for the patient's likelihood to fall into Group I (i.e. no seizures in the hospital while on anticonvulsant medication).

3. The original coded findings are then multiplied by the coefficients shown under Discriminant Function II and the constant 24.01 is subtracted from the result. This represents the discriminant function for Group II (i.e. at least some seizures will persist in the hospital in spite of adequate amounts of medication).

4. The patient can be classified in either of the two groups depending upon which discriminant function value is higher.

5. To establish the precise probability with which the patient is likely to fall into the assigned group, the differ-

ence between the two discriminant functions is obtained. If the difference were found to be zero, no prediction would be possible in this particular case. If it were 1.10, the probability for the patient to fall into the higher group would be .75, and if the difference were 4.60, the probability would reach .99. The estimated probabilities of correct classification for all the intermediate values are tabulated in the Appendix.

Two examples might illustrate the use of the formula. For simplicity's sake, those variables that carry a negative sign are grouped together with the constant, which also carries a negative sign, so that the subtotal can be easily subtracted from the values obtained from those variables carrying a positive sign.

EXAMPLE—POOR PROGNOSIS FOR SEIZURE CONTROL

Patient A, DISCRIMINANT FUNCTION 1:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*	
Amount of EEG abnormality	1.57 × 5	Marked	7.85	
Seizure patterns in EEG	0.09 × 4	Very likely but not diagnostic	0.36	
Psychomotor seizures	6.08 × 2	Present	12.16	
Duration of illness	2.85 × 9	More than 15 years	25.65	
Frequency of seizures at present	0.56 × 8	Once a week	4.48	
Clusters of seizures over several days, freedom from seizures for several weeks	0.77 × 3	Occasionally	2.31	
		SUBTOTAL	52.81	
Combination of seizures	−0.39 × 3	Two seizure types		− 1.17
Frequency of injuries during seizures	−0.41 × 4	Injures himself frequently		− 1.64
CONSTANT	−17.43			−17.43
		SUBTOTAL		−20.24
		TOTAL	32.57	

DISCRIMINANT FUNCTION 1 (52.81 minus 20.24 = 32.57)

Patient A, DISCRIMINANT FUNCTION II:

Amount of EEG abnormality	1.78	×	5 Marked	8.90	
Seizure patterns in EEG	0.21	×	4 Very likely but not diagnostic	0.84	
Psychomotor seizures	6.25	×	2 Present	12.50	
Combination of seizures	0.06	×	3 Two seizure types	0.18	
Duration of illness	2.92	×	9 More than 15 years	26.28	
Frequency of seizures at present	1.02	×	8 Once a week	8.16	
Clusters of seizures over several days, freedom from seizures for several weeks	0.90	×	3 Occasionally	2.70	
			SUBTOTAL	59.56	
Frequency of injuries during seizures	−0.03	×	4 Injures himself frequently		− 0.12
CONSTANT	−24.01				−24.01
			SUBTOTAL		−24.13
			TOTAL	35.43	

DISCRIMINANT FUNCTION II (59.56 minus 24.13 = 35.43)
Discriminant Function II (35.43) minus Discriminant Function I (32.57) = 2.86
The probability of the patient falling into Group II is .94.

The final value of 2.86 indicates that the probability of the patient falling into Group II (i.e. continue to have seizures while on adequate amounts of medication in the hospital) is .94. This would be an example for a patient who has a poor prognosis even in the hospital. An example of a patient having a good prognosis for seizure control might be as follows:

EXAMPLE—GOOD PROGNOSIS FOR SEIZURE CONTROL

Patient B, DISCRIMINANT FUNCTION I:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*
Amount of EEG abnormality	1.57 ×	1 EEG normal	1.57
Seizure patterns in EEG	0.09 ×	1 Absent	0.09
Psychomotor seizures	6.08 ×	1 Absent	6.08
Duration of illness	2.85 ×	4 Seven to 11 months	11.40

EXAMPLE—GOOD PROGNOSIS FOR SEIZURE CONTROL (*Continued*)

Frequency at present	0.56	×	3	Two to three a year	1.68	
Clusters of seizures over several days, freedom from seizures for several weeks	0.77	×	1	Never	0.77	
				SUBTOTAL	21.59	
Combination of seizures	−0.39	×	1	One type only		− 0.39
Injuries during seizures	−0.41	×	1	Never		− 0.41
CONSTANT	−17.43					−17.43
				SUBTOTAL		−18.23
				TOTAL	3.36	

DISCRIMINANT FUNCTION I (21.59 minus 18.23 = 3.36)

Patient B, DISCRIMINANT FUNCTION II:

Amount of EEG abnormality	1.78	×	1	EEG normal	1.78	
Seizure patterns in EEG	0.21	×	1	Absent	0.21	
Psychomotor seizures	6.25	×	1	Absent	6.25	
Combination of seizures	0.06	×	1	One seizure type only	0.06	
Duration of illness	2.92	×	4	Seven to 11 months	11.68	
Frequency of seizures at present	1.02	×	3	Two to three seizures a year	3.06	
Clusters of seizures over several days, freedom from seizures for several weeks	0.90	×	1	Never	0.90	
				SUBTOTAL	23.94	
Frequency of injuries	−0.03	×	1	Never		− 0.03
CONSTANT	−24.01					−24.01
				SUBTOTAL		−24.04
				TOTAL		− 0.10

DISCRIMINANT FUNCTION II (−24.04 minus 23.94 = −0.10)

Discriminant Function I (3.36) minus Discriminant Function II (−0.10) = 3.26

The probability of the patient falling into Group I (i.e. no seizures in the hospital while on anticonvulsant medication is .96.

To save oneself repeated multiplication, a table is included in the Appendix which lists the coefficients for each of the variables on the two discriminant functions in regard to any of the coded scores that can be encountered. It is, of course, obvious that the formula will work only if the same coding system is followed that was used in this study. Duplication of the results will depend not only on the use of the same scales but also on agreement between raters.

"Amount of EEG abnormality" refers to an overall global summary of the EEG findings while the patient is *on* anticonvulsant medication. Representative patterns showing various degrees of abnormalities can be seen in Figures 4–10. The variable called "seizure patterns in EEG" refers to the degree of certainty with which the presence of a seizure disorder can be suspected if the record is read blindly; that is, without access to any information about the patient's clinical condition. The coding of this variable could give rise to some discrepancies between raters who are not trained in the same laboratory.

The following guidelines were used for coding this particular variable. In order to question the presence of a convulsive disorder on reading an EEG blindly, the resting record during the

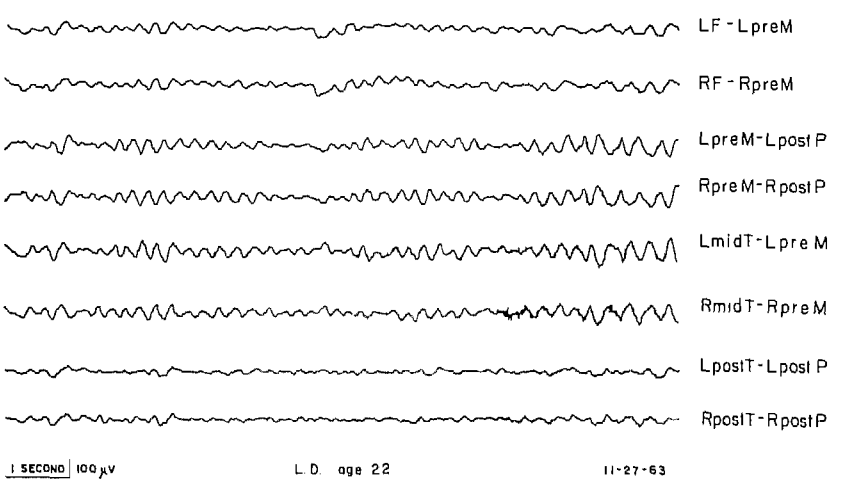


FIGURE 4. Rather stereotyped high voltage 5 c/s background rhythm. Markedly abnormal EEG (Code 5), no seizure patterns (Code 1), no focal abnormality (Code 1).

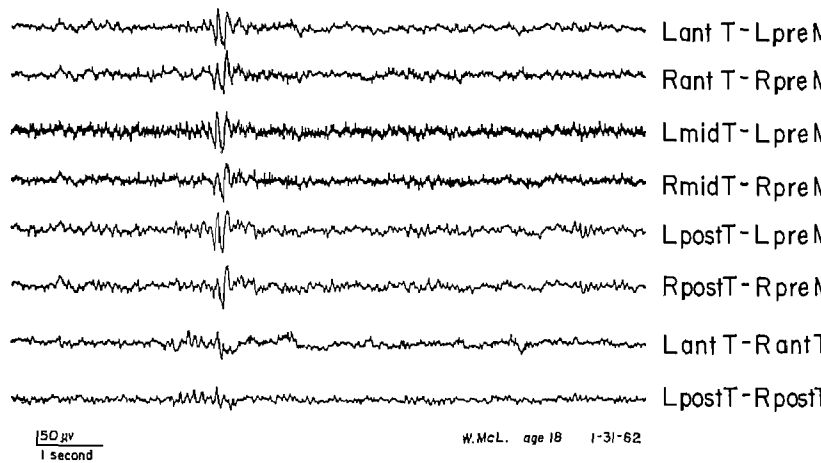


FIGURE 5. Somewhat disorganized background activity, occasional high voltage diffuse bursts but no spike components. Moderately abnormal EEG (Code 4), record raises the question of the presence of a seizure disorder (Code 2), no focal abnormality (Code 1).

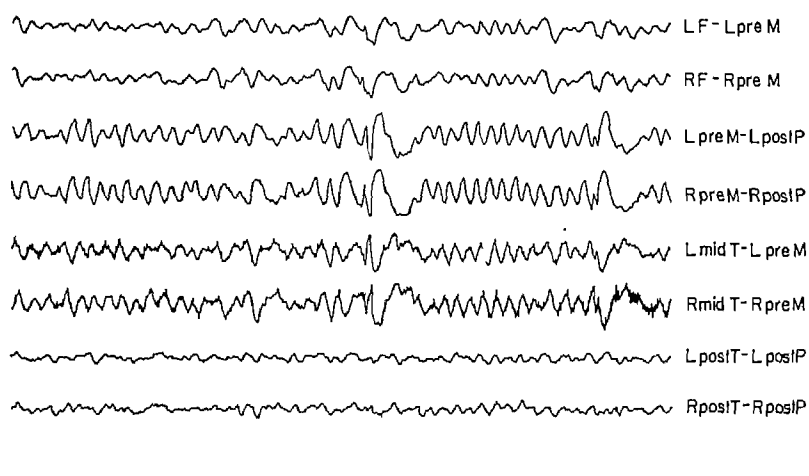


FIGURE 6. High voltage stereotyped 5-6 c/s background rhythm, occasional abortive spike wave activity. Markedly abnormal EEG (Code 5), presence of a seizure disorder is probable (Code 3), no focal abnormality (Code 1).

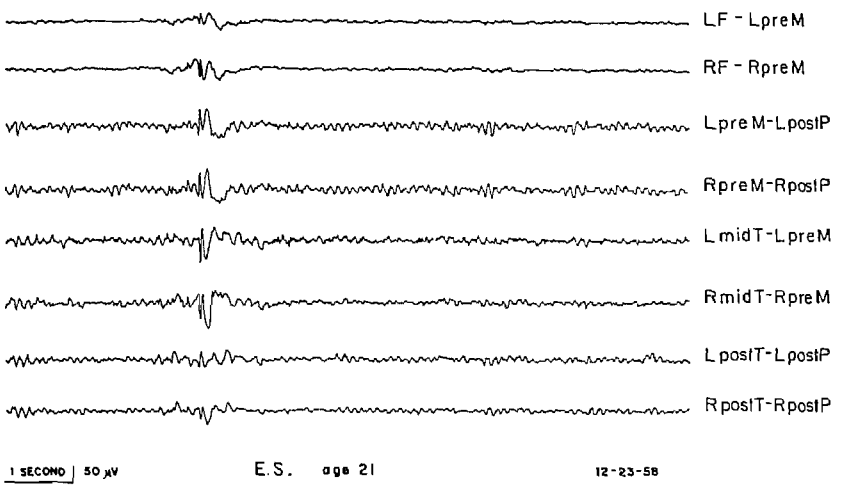


FIGURE 7. Normal background rhythms, occasional isolated spike wave discharges. Moderately abnormal EEG (Code 4), presence of a seizure disorder probable (Code 3), no focal abnormality (Code 1).

waking or sleeping state must have shown at least some diffuse paroxysmal activity with or without low voltage spike components or some focal sharp activity usually in one or both temporal areas. A seizure disorder was regarded as "probable" if there was definite but infrequent spike wave activity, or focal sharp wave or spike activity in any head location (except for occipital location in children where it was relegated to code number two, questionable). Code number four, "very likely but not diagnostic," referred to records which showed frequent brief spike wave bursts or focal sharp wave or spike activity that occurred in a periodic fashion building up in form of a crescendo over a few seconds and then decaying, the phenomenon repeating itself several times during the recording. The record was regarded as "diagnostic" of a convulsive disorder if it showed classical three per second spike wave activity lasting at least four seconds, or if some other clinical and electrographic seizure occurred during the recording period. "Petit mal status" or patterns like those in Figures 11 and 12 were also regarded as being diagnostic of a convulsive disorder. Hypsarhythmia did not occur in this sample of patients but would have been coded as either 4 or 5, de-

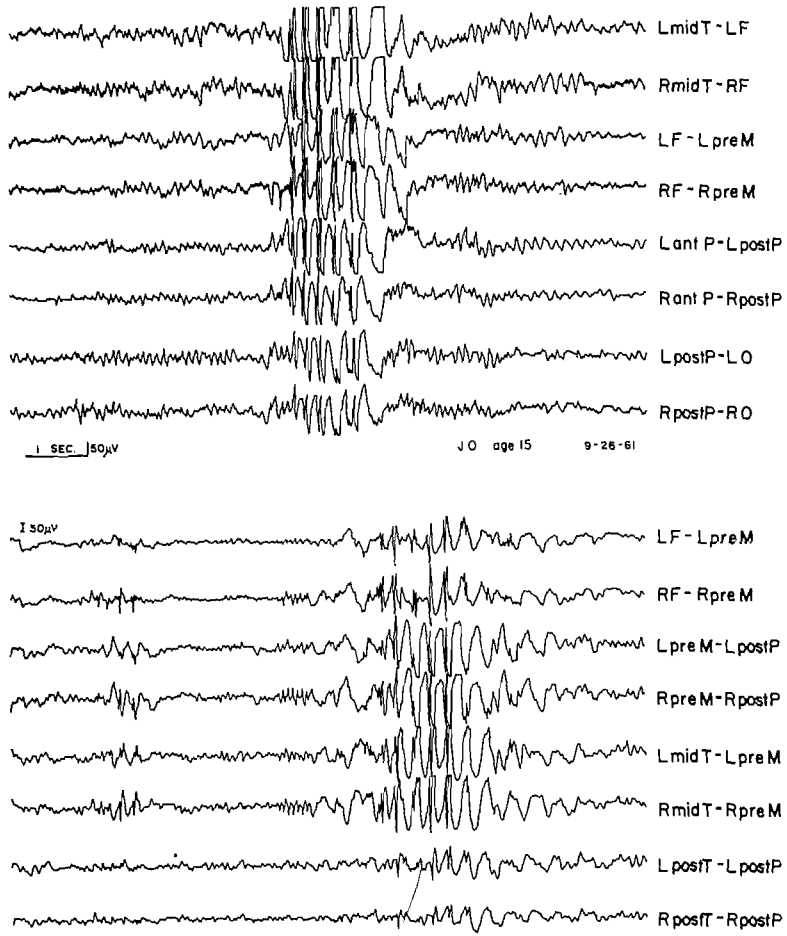


FIGURE 8. Normal background rhythms, high voltage diffuse spike wave discharges lasting 1-2 seconds. During sleep also suggestion of 14 and 6 c/s positive spike activity but the distribution atypical. Markedly abnormal EEG (Code 5), seizure disorder very likely but pattern not diagnostic (Code 4), no focal abnormality (Code 1).

pending on the intensity of the spike components. It should be noted here that the appearance of background activity did not enter into the classification for the variable dealing with seizure patterns. The appearance of the background was taken into account for the overall EEG rating. Likewise, 14 and 6 per second positive spikes were not entered into the "seizure

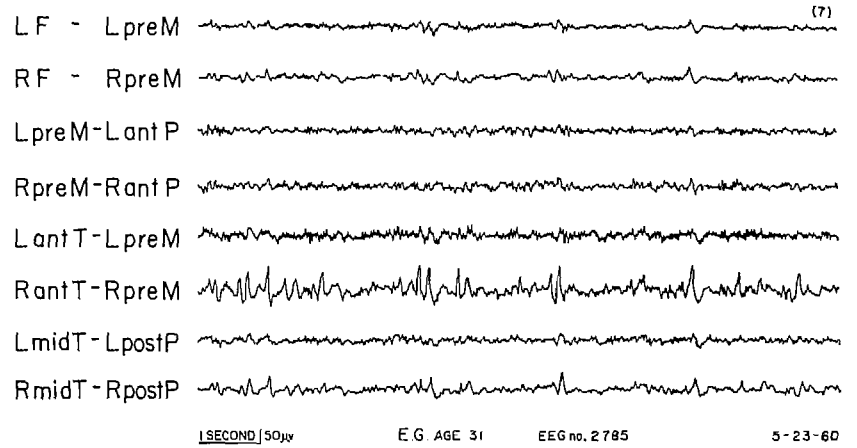


FIGURE 9. Background somewhat disorganized. Marked sharp wave activity in right anterior temporal area. Markedly abnormal EEG (Code 5), seizure disorder very likely but pattern not diagnostic (Code 4), focal abnormality marked (Code 5).

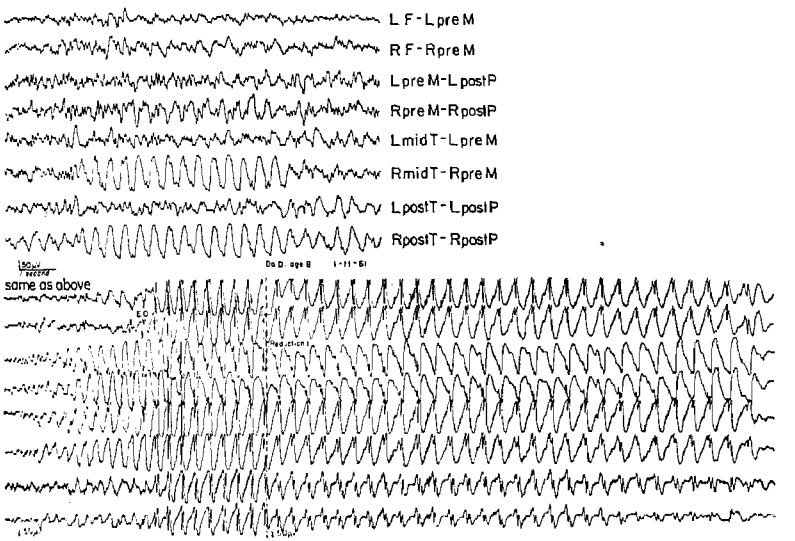


FIGURE 10. Background somewhat disorganized. High voltage rhythmic 2-3 c/s activity in right posterior temporal area spreading to midtemporal region, 3 c/s spike wave activity lasting more than 10 seconds. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), focal abnormality questionable (Code 2).

pattern" variable, but were taken up in the overall EEG diagnosis, and the record was rated either as borderline or mildly abnormal, depending upon the intensity of the phenomenon. Hyperventilation and photic stimulation had been carried out routinely in all instances. If classical 3 cycles per second spike wave activity lasting at least four seconds was induced with either of these methods, or some other recognized clinical and electrographic seizure, the record was classified as diagnostic for a convulsive disorder. If the resting record had not shown

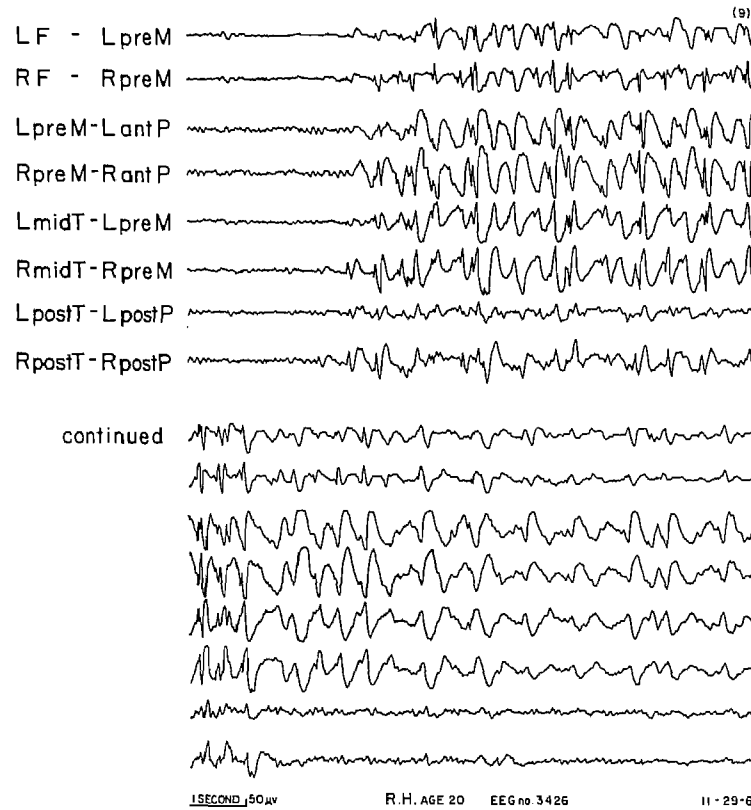


FIGURE 11. Background essentially normal, poorly formed 2-3 c/s spike wave activity lasting somewhat more than 10 seconds. Spike waves more pronounced on the right than on the left, especially in posterior temporal area. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), focal abnormality questionable (Code 2).

seizure patterns, but the patient responded to the flashing light with brief one to two second episodes of spike wave activity, the variable was coded as questionable or probable, depending upon the intensity of the phenomenon. If myoclonic jerking of the body or extremities accompanied spike wave bursts during photic stimulation, the record was rated either as "probable" or "very likely but not diagnostic," depending upon the intensity of the symptoms.

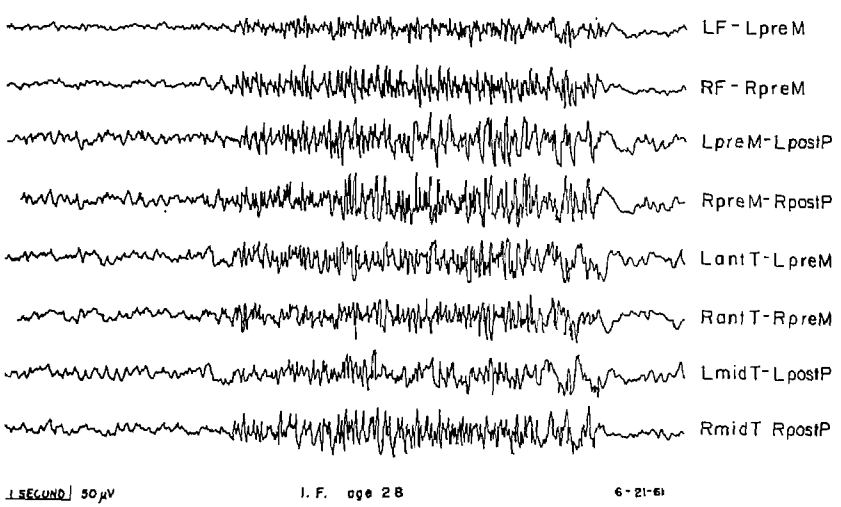


FIGURE 12. Background cannot be evaluated in this section of record because patient somewhat drowsy. Marked diffuse spike activity lasting 5-6 seconds. Example of what has been called grand mal seizure discharge by Gibbs. It should not be confused with barbiturate fast activity. Markedly abnormal EEG (Code 5), record diagnostic for seizure disorder (Code 5), no focal abnormality (Code 1).

It is obvious that there is some judgment involved in coding this particular variable, but differences between competent electroencephalographers are not likely to exceed more than two points. The coefficient for this particular variable is actually the lowest of all eight, and minor variations between raters are therefore not likely to interfere markedly with the predictive value of the total formula.

Psychomotor seizures were rated as either present or absent. "Combination of seizures" was coded on a 1 to 9 scale; 1 mean-

ing: only one seizure type present; 3: two distinct seizure types like grand mal and psychomotor or grand mal and absences; 5: three distinct seizures types, for instance grand mal, absences, and akinetic seizures; 7: four seizure types; and 9: more than four seizure types. The intermediate values (2, 4, 6, and 8) were coded when abortive seizures were also present. If the patient had, for instance, mainly focal grand mal seizures and at times only the aura, code 2 was given rather than 3 because the aura was not regarded as a separate seizure type. Myoclonic jerking, when present in addition to nonfocal grand mal seizures, was also rated as 2 rather than 3. However, if the patient had grand mal seizures and myoclonic seizures, and not merely isolated jerks of an extremity, a rating of 3 was given. A rating of 4 was given, for instance, to a patient who had focal grand mal seizures, intermittent auras and psychomotor seizures. The scale provided, therefore, a rough clinical estimate of epileptogenicity of a patient's brain tissue. Since all seizures have to originate in one restricted area of the brain before they spread to other regions, a variety of seizure patterns indicates that there is, in all probability, more than one cerebral system involved in the genesis of this particular patient's attacks, and one is dealing with a multiplicity of epileptogenic zones.

Duration of illness was coded from the onset of recurrent seizures as defined previously rather than from the very first isolated attacks. The scale went from 1 through 9, and is shown in Figure 13. The scale for frequency of seizures just prior to hospitalization is shown as Figure 14. The variable called "clus-

DURATION OF SEIZURE DISORDER

[0] Not Recorded
[1] Less than 1 month
[2] 1–2 months
[3] 3–6 months
[4] 7–11 months
[5] 1–3 years
[6] 4–6 years
[7] 7–9 years
[8] 10–15 years
[9] More than 15 years

FIGURE 13.

FREQUENCY OF SEIZURES AT PRESENT

[0] Not recorded
[1] Less than once a year
[2] About once a year
[3] 2–3 seizures a year
[4] 4–6 seizures a year
[5] 7–12 seizures a year
[6] Once a month
[7] 2–3 a month
[8] Once a week
[9] Several a week

FIGURE 14.

ters of seizures for several days, freedom from seizures for several weeks" is a rather interesting one. It was coded on a 1 through 5 scale, and the scale is reproduced as Figure 15. Female patients frequently state that this phenomenon occurs in connection with the menstrual period, but there are any number of male patients who also experience a cyclic occurrence of seizures, and it has been shown in these investigations that it carries a relatively poor prognosis. A detailed investigation of the pathophysiology of this symptom is definitely indicated because it might well shed considerable light on the genesis of epilepsy.

Frequency of injuries was coded on a 5-point scale which is reproduced as Figure 16. It also provides a clinical judgment of the severity of a given seizure. Some patients do not merely crumple and fall to the ground at the onset of the seizure, but pitch violently forward or backward which results in lacerations of supraorbital areas or scalp. The same applies to burn wounds occurring as a result of psychomotor seizures, especially in women working in the kitchen.

CLUSTERS OF SEIZURES OVER SEVERAL DAYS THEN FREEDOM FOR WEEKS

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

FIGURE 15.

If the patient had more than one seizure type, the highest values were used for duration of illness, frequency of occurrence, clusters of seizures, and frequencies of injuries, regardless of whether they referred all to the same seizure type or not. An example might clarify this point. Let us assume a patient had three or four grand mal seizures per year which started ten years ago. These never came in clusters but the patient did, on two occasions, suffer injuries as a result of the grand mal seizures. Five years ago the patient developed psychomotor seizures which occur now at the rate of two to three per month and frequently come in clusters, but the patient has not injured him-

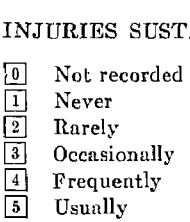


FIGURE 16.

self during these attacks. This particular patient would have received the following codes: psychomotor seizures, 2; combination of seizures, 3; duration of illness, 8; frequency at present, 7; clusters of seizures, 4; and injuries during seizures, 2. Therefore, the codes do not necessarily apply to a given seizure type only but to the patient's overall condition. The reason for doing so lies in the attempt to predict the course of a patient's epilepsy, rather than the course of only one of his seizure types.

Further Cross Validation

After we had demonstrated that the formula which was derived from an inpatient sample could be successfully applied to a group of Michigan Epilepsy Center outpatients followed over at least five years, it was of interest to see what the weights for the eight variables would be if they were developed on the basis of the Michigan Epilepsy Center second follow-up sample. A discriminant function analysis was therefore performed on the fifty-

nine patients who had complete data and the program classified correctly fifteen (79%) of the remitted and thirty-two (80%) of the unremitted patients. The breakdown in regard to probabilities and their accuracy of classification is shown in Table 76. We can see again that classifications involving a probability of less than .75 are not useful for prognostication, but probabilities of .90 or higher are not likely to be in error.

The chart of the patient who was classified by the formula as having had a remission for the past two years with a probability of .93 was reviewed. It was found that this patient was a sixteen-year-old girl at time of initial evaluation who had developed

TABLE 76

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	4	3
.75 to .89	2	1
.90 to .99	9	0
*Group II***		
Less than .75	5	6
.75 to .89	1	1
.90 to .99	26	1

* Seizure free for at least 2 years prior to follow-up

** Seizures have occurred within the past 2 years of follow-up

focal grand mal seizures as her only seizure type two years prior to her first visit to MEC. The seizures had occurred several times a week; they had never come in clusters; the patient had never injured herself, and the EEG was normal. She was taking Dilantin (100 mg twice a day) and phenobarbital (32 mg twice a day). After workup at the Center, an increase in her anticonvulsant dosage was recommended. At time of reevaluation the patient was twenty-six years old and continued to have focal grand mal seizures, and at times focal minor seizures several times a month. Her medication regime had never been changed in the past ten years and it still consisted of two capsules of Dilantin

and two 32 mg tablets of phenobarbital. This is obviously an inadequate drug regime and the computer classification is therefore not necessarily in error. This patient did have a good prognosis but her treatment had been neglected.

The coefficients and the constants for classifying patients into the remitted and unremitted group are shown in Table 77. When the weights from Table 77 were applied to the 181 Lafayette Clinic inpatients, one found that fifty-nine (73%) of Group I, and seventy-nine (79%) of the patients of Group II were correctly classified.

TABLE 77

DISCRIMINANT FUNCTION FOR PREDICTING OUT-PATIENT TREATMENT RESULTS

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Amount of EEG abnormality	2.46	2.20
Seizure patterns in EEG	0.40	1.36
Psychomotor seizures	9.48	11.37
Duration of illness	1.92	2.60
Frequency of seizures at present	1.35	1.66
Frequency of injuries during seizures	1.25	1.92
Clusters of seizures over several days, freedom from seizures for several weeks	−1.25	−1.57
Combination of seizures	−0.84	−0.27
Constant	−17.81	−30.28

The two samples of patients are of course not identical, and the predictions one is trying to make are therefore not necessarily the same. In the Michigan Epilepsy Center sample, one was trying to predict whether a patient is likely to achieve a terminal remission of his seizure disorder, which had lasted at least two years, after a minimum five-year follow-up. The Lafayette Clinic formula tried to predict whether a patient, when placed in a hospital environment and given adequate amount of anticonvulsant medication, is likely to have seizures during this period of time. One could, therefore, argue that some of the cases that have been classified incorrectly by the formula are not neces-

sarily wrong classifications, but the classification resulted from the different assumptions. It is conceivable, for instance, that a patient who is in the unremitted group, as far as the Michigan Epilepsy Center follow-up is concerned, could have been brought under control had he been hospitalized.

The two formulas together allow different prognostic statements about a given patient and open the way for an interesting experiment. In the future we can classify any epileptic patient by means of both formulas: using the Michigan Epilepsy Center weights to predict whether he is likely to achieve a complete remission with outpatient treatment within the next five years, and using the Lafayette Clinic formula to predict success of treatment in the hospital at this moment. A patient who falls into Group II, on basis of either formula, will probably remain a chronic seizure patient, but if a patient receives a classification of Group II, as far as the outpatient weights are concerned, and a classification of Group I in regard to hospital weights, it would seem that this patient should be hospitalized and short-term control could be achieved which might then lengthen into a long-term remission. This has potential practical importance. If one has a limited number of neurological beds available and a large number of patients on the waiting list, priorities can be established. Those patients who are doing poorly in the community but are classified as Group I on the basis of the Lafayette Clinic formula, could be given preference for admission over the cases that are rated as "poor success likely," even when treated in the hospital.

The results that have been presented so far indicate that the coding system did allow its originator to classify epileptic patients with reasonable accuracy into a potentially controllable or into an uncontrollable group. The question remained whether the system is simple enough that its use can be taught with ease to another physician who is careful in his observations and conscientious in the coding of the data. The material of the second follow-up study of the Michigan Epilepsy Center was coded by myself in conjunction with Doctor N. Velarde, who was at that time a second-year resident in neurology. The material of the Lafayette Clinic inpatients was initially coded by a

second-year medical student, Mr. Richard Robinson. Subsequently, he and I together checked each chart and code sheet for possible errors or differences in judgment. As far as the EEGs were concerned, I had interpreted and coded virtually all of the tracings. There was, therefore, a very definite potential bias in the way the coding forms had been filled out and it remained to be established whether or not another neurologist, using the system alone without interference by me, would come up with essentially similar results.

In 1964, the Michigan Epilepsy Center received a grant from the Division of Vocational Rehabilitation of the U.S. Public Health Service to study the factors that relate to employment problems of epileptic patients. By January, 1967, 236 patients had been seen, and coded, on essentially the same items that were used in the second follow-up study. The neurological evaluations, EEG interpretation, and the coding of the data, were performed by Dr. S. Gonzalez, who had finished his residency training in neurology, had spent one year studying electroencephalography at the same laboratory where my own training had been (Dr. R. G. Bickford, Mayo Clinic) and was on the staff of the Lafayette Clinic and the Michigan Epilepsy Center. This coded material being available, it was of considerable interest to see whether our findings in regard to seizure prognostication would be applicable to this particular group of patients. The sample consisted of adolescents and adults who had been referred to the Michigan Epilepsy Center from a variety of sources (private practitioners, neurologists, schools, social agencies, self-referrals) for this project. A group of 230 patients on whom complete data was available in regard to the eight variables involved in seizure prognosis was then subdivided. Group I consisted of thirty-eight patients who had had no seizures for at least two years; Group II, of 192 patients who had had seizures within the past two years. This was the grouping that had been used for the second follow-up study, except that in the second follow-up study the findings from initial evaluation had been used rather than the findings at follow-up. In the VRA sample only one evaluation was available and these findings had to be used. When the MEC weights that had been derived from the

second follow-up study were applied to the VRA patients, it was found that thirty-four patients of Group I (90%) and one hundred patients of Group II (48%) were correctly classified. The overall success rate was therefore only 58 per cent and not much better than chance. It was then thought that the Michigan Epilepsy Center weights, which had been derived from a relatively small sample of patients (i.e. 59), might not be stable enough to give reliable results. The Lafayette Clinic inpatient weights, which had been derived from a large group of patients were subsequently applied to the VRA sample. This resulted in a correct classification of all thirty-eight (100%) patients of the first group, and of eighty-four (42%) patients of the second group. The overall correct classification had now dropped to 53 per cent. These results presented, of course, a problem. They could be interpreted as follows: (1) The coding system is of no value because another neurologist cannot obtain similar results and (2) the incorrect classification is not really in error but is due to different premises.

Looking at the results in detail, we found it obvious that the distribution of incorrect classification was not one that could be ascribed to chance. The success rate for Group I was 90 and even 100 per cent, depending upon the weights used, but the success rate for Group II was low because too many patients were classified as controlled or controllable. Two possibilities could account for this finding: (1) Dr. Gonzalez had consistently coded the patients lower on the scale items than I had or (2) the VRA group consisted predominantly of patients whose seizure disorders were milder than either of those involved in the second follow-up sample or the Lafayette Clinic inpatient sample.

Looking at the means for the eight variables for Group I and II of the VRA sample, Table 78, we can see that they were indeed, for the most part, lower in the VRA sample than in the previous two groups, (Tables 72, 74). The question remained whether these lower mean values were due to the coding or the properties of the sample. Going over selected charts, we found it obvious that the VRA sample contained, in the great majority, milder cases. This can best be expressed by a comparison of the distribution in regard to frequency of occurrence of seizures

TABLE 78

	Group I	*Group II*
Amount of EEG abnormality	2.7	3.5
Seizure patterns in EEG	1.7	2.4
Psychomotor seizures	1.1	1.3
Combination of seizures	1.9	2.3
Duration of illness	7.5	7.4
Frequency of seizures at present	1.0	5.3
Clusters of seizures over several days, freedom from seizures for several weeks	1.3	1.5
Frequency of injuries during seizures	1.4	1.7

prior to evaluation as shown in Table 79. The incorrect classifications in Group II are therefore not necessarily in error, but they merely state that this particular patient might be brought under control in the hospital or that the patient is likely to have enjoyed a two-year remission five years from now. As a further check on this possibility, two more studies were performed.

Inasmuch as the problem centered around the correct classification of Group II, forty patients were selected from the VRA sample whose seizure frequency matched that of Group II of the second follow-up study. The weights from the second follow-up study were then applied to this group of patients. Thirty-one

TABLE 79

FREQUENCY OF SEIZURES PRIOR TO EVALUATION

Code Number and Description	*MEC 2nd Follow-up (N = 90)* (%)	*LC Inpatients (N = 245)* (%)	*VRA (N = 230)* (%)
1 Less than once a year	2.2	8.2	26.5
2 About once a year	4.4	.4	6.1
3 Two to three seizures a year	7.8	8.9	11.3
4 Four to six seizures a year	6.7	9.4	7.8
5 Seven to 12 seizures a year	11.1	4.1	6.5
6 Once a month	14.4	6.5	8.7
7 Two to three a month	7.8	15.1	10.0
8 Once a week	7.8	7.8	6.5
9 Several a week	37.8	39.6	16.5

(78%) patients were correctly classified as falling into Group II. This is, therefore, virtually the same success rate as had been achieved in the second follow-up project on which the weights had been developed initially (i.e. 80%). This result demonstrated, therefore, that the coding system is indeed useful and can be applied with success by someone else.

It remained to be determined whether the Lafayette Clinic inpatient weights would show a similar success rate when applied to a segment of the VRA population. The second project consisted, therefore, of creating two special subgroups from the total VRA sample: one consisting of sixty-one patients whose seizure frequency had been coded as 1 (i.e. less than once a year); the other of seventy-six patients whose seizure frequency had been coded as 7, 8, or 9 (i.e. between two to three per month to several a week). One would predict that a patient whose seizure frequency on the outside is less than once a year is not likely to have a seizure in the hospital. On the other hand, a patient who has at least two to three seizures per month, might well experience at least one seizure during a three-week period of hospitalization. When the weights from the Lafayette Clinic inpatient sample were applied to these two groups of VRA patients, it was found that sixty-one patients of Group I (100%) and sixty-eight patients from Group II (89%) were correctly classified. These results indicate that the formulas will allow prognostication in regard to a patient's treatment response with reasonable accuracy. They open the door to another practical application in patient management.

The occasion may arise that a patient claims he has not had seizures for the past year in order to obtain, for instance, a driver's license; but the physician has no way of knowing whether the patient's report is accurate or not. One could now compute the discriminant function using the Lafayette Clinic inpatient formula and predict the probability of the accuracy of the patient's statement. If the probability were to be .75 or higher for the patient to have seizures, even in the hospital, it might be advisable to admit this particular patient for observation to the hospital rather than simply accept his word as fact. As has been pointed out earlier, patients may not be aware themselves of

having seizures and underreporting should not automatically be equated with conscious distortion of information.

Two other important points have to be made in regard to the use of the formulas. One is that the weights were derived from a population that was predominantly in the adolescent and adult age bracket. They are, therefore, not necessarily applicable to children. At present we do not have available a sufficient sample of children on whom there is complete information in regard to the mentioned eight variables and who have been followed for a sufficient length of time. It is therefore not possible to determine to what extent the formulas would work in the pediatric age group. This requires further investigation. The second point is that virtually all of the patients had already been on some anticonvulsant regime prior to their being seen either at the Lafayette Clinic or Michigan Epilepsy Center, and the formulas cannot necessarily be successfully applied at this point to patients who have just experienced their first seizure. These aspects of the problem will also require specific investigations in the future.

Chapter 12

PROGNOSIS FOR BEHAVIOR

Having discussed the factors relating to seizure prognosis, we can now turn our attention to the second question that was asked initially, Will the patient's social behavior deteriorate? Here we are, however, on much looser ground than when one is talking about seizures because there are no hard lines that can be drawn. What is acceptable behavior in one family may be unacceptable in another, and there are no suitable quantitative tests that can be applied to a person's social competence. The findings that will be presented in the following pages should be taken as showing general directions, rather than providing specific answers. They are presented in the hope that they will stimulate further research in this area.

At the time of the first follow-up study at the Michigan Epilepsy Center in 1960, we had also inquired of the parents regarding the behavior of the child. For the children living in the community no behavioral difficulties were reported in seventeen instances (62.9%). Mild difficulties were present in five (18.5%), moderate difficulties in four (14.8%) and severe difficulties in one (3.7%). This was in marked contrast to reports of the parents at time of initial evaluation. Only five children (18.5%) had at that time no behavioral difficulties. Behavioral difficulties had been reported to be mild at initial evaluation in eight (29.4%), moderate in eleven (40.7%), and severe in three (11.1%).

Three explanations would seem possible for this phenomenon:

1. Behavior had indeed improved as a result of improvement in the seizure condition.

2. Behavior had improved as a result of normal maturational processes.

3. Behavior had not improved to such a marked extent as suggested by the figures, but the parents had become used to the problem and were able to tolerate more abnormality than they had been able to initially.

The first theory was the easiest to check. Table 80 shows the relationship between seizure state at time of follow-up and behavior. Remission refers to freedom from seizures for two years. It is apparent that reported improvement in the patient's behavior cannot be directly related to the remission of seizures. This leaves us with the other two alternatives, and both of these may well be operative together. The behavioral problems that had been reported initially consisted in the vast majority of

TABLE 80

RELATIONSHIP OF BEHAVIOR TO SEIZURE CONTROL

	Behavior Problem at Follow-up	
Remission	*Yes*	*No*
Yes	4	5
No	6	12

marked temper outbursts, hyperkinetic behavior, and inability to tolerate frustration. These are symptoms that one might well expect to improve with increasing age. Regardless of the causes for improvement in behavior, it was striking to see that only two children had shown deterioration. One had been sixteen months at time of initial evaluation and had developed severe personality difficulties by the time of follow-up. The other had changed from a rating of mild to one of moderate difficulty. The overall trend was quite clearly towards improvement for the majority of the cases.

Although one could expect improvement in most instances, it remained to be determined what type of patient is likely to show continued behavioral difficulties. For this reason it was of interest to look at the statistically significant correlations that were obtained with the variable "behavior at time of follow-up," as

shown in Table 81. Unless when specifically referred to as Evaluation II, the findings deal with observations on first evaluation.

Highest on the list appeared "psychotic tendencies on psychological testing," but it should be emphasized that this particular correlation was based on eight patients only and is undoubtedly inflated by this low number. The table points out that the chronic behavior problems tended to be related to aspects of brain damage and/or intellectual difficulties (e.g. excessively slow EEG background rhythms which persist up to the time of follow-up, excessively high fevers, poor marks in school, grade failure, no formal education, seizure disorder starting during the first year of life, some aspects of focal seizure activity).

The negative findings that are not represented on the table are also worthwhile to point out. One is the absence of a signifi-

TABLE 81

BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Psychotic tendencies on psychological testing	.945	1
Main background frequency in EEG	−.632	1
Average marks in school	−.619	1
Remission prior to first evaluation	.540	1
Left leg twitching during seizure	.469	1
No formal education	.469	1
Highest fever	.636	2
Grade failure at time of Evaluation II	.517	2
Academic school problem at time of Evaluation II	.478	2
Amount of theta activity in EEG	.407	5
Main background frequency in EEG, Evaluation II	−.403	5
Prognosis for academic achievement	.380	5
Seizures present since first year of life	.357	5
Sitting up age	−.442	10
IQ	−.362	10
Special schooling, Evaluation II	.345	10
Amount of theta activity in EEG, Evaluation II	.344	10
Amount of alpha activity in EEG, Evaluation II	−.321	10
Amount of alpha activity in EEG	−.319	10
Isolated nonfebrile convulsions prior to onset of chronic seizure disorder	.306	10

cant correlation between prognosis for behavior and the actual finding at follow-up. The correlation coefficient was .291. Although this was better than the relationship between seizure prognosis and seizure outcome (.125), it was too low to be of statistical significance. The reason for this finding may lie in the fact that in assigning a prognosis for future behavior I had relied mostly on the description of the child by the psychiatrist in the initial evaluation, and on the social milieu in which the patient was being brought up. These factors turned out to have been quite irrelevant in this sample of patients. The variable "social factors related to present illness" showed a correlation coefficient of .011 with the variable "behavior problem at follow-up" and the variable "psychiatric disorder diagnosed in addition to epilepsy" was correlated —.094 with behavior problems at follow-up. These findings would suggest that as far as epileptic children are concerned, behavior problems tend to persist mainly in the brain-damaged group. Behavioral difficulties as a result of poor social environment can be "outgrown," become internalized, or become tolerated by the parent to an extent that they are no longer reported to the physician. A potentially interesting observation in Table 81 is the finding that a remission in the seizure disorder prior to first evaluation was significantly correlated with subsequent long-standing behavioral problems. This variable refers to a group of children who had a few isolated seizures in infancy but started with chronic recurrent seizures at preschool or school age.

As was mentioned in Chapter 11, a factor analysis was performed on this material and Factor I, Table 82 shows the link

TABLE 82

FACTOR I

.92	Poor marks in school, Evaluation II
.86	Organic pathology suspected on psychological testing, Evaluation I
.57	Low IQ, Evaluation I
.55	Academic school problem at follow-up
.49	Behavior problem at follow-up
.47	Remission of seizures prior to Evaluation I
.39	Academic school problem at time of Evaluation I

between the areas of behavior and intelligence. If the factor is read from the positive side rather than the negative side, it suggests that epileptic children with normal intellect and no evidence of organic pathology on psychological tests, who have not had seizures in infancy (febrile or otherwise), tend to do well in school and are not likely to present chronic behavior problems later on. It should be remembered, however, that these conclusions are based on a small sample of children, and it will be necessary to study another group.

In the second follow-up study, involving ninety patients, we were dealing mostly with an adolescent and adult group of patients and the results will be influenced by this age factor. Sixteen patients (17.8%) had not had any behavioral difficulties at time of initial evaluation. Difficulties were regarded as having been mild in thirty-six (40.0%), moderate in thirty-one (34.4%) and severe in seven (7.8%). At the time of follow-up no behavioral difficulties were reported to have been present in thirty-seven patients (41.1%); problems were regarded as having been mild in twenty-five (27.8%), moderate in twenty-four (26.7%), and severe in four (4.4%). The rating for behavior had remained the same in forty-six patients (51.1%), had improved in forty (44.4%), and had become worse in four patients (4.4%) only. These results are in agreement with the findings obtained at the time of the first follow-up study. The fact that only four (4.4%) patients had shown deterioration in their social functions is reassuring. The changes that had taken place in these four patients were from a rating of mild to one of moderate difficulties. A change from no behavioral problems to one of definite problems had not occurred in this sample. The findings indicate that if an epileptic patient has no behavioral difficulties at the time of initial examination, it is very unlikely that he will develop them later on. The behavioral difficulties apparently tend to appear either prior to the onset of the seizure disorder or at about the same time as the seizures make their appearance. The subsequent course tends to be towards improvement for the majority of patients. Looking at the significant correlates that were obtained with the variable "behavior problem at time of follow-up" in the second MEC follow-up study, Table 83, we find that prognostica-

tion had been easier in this sample than in the group of children.

Social factors had become important now, and an initial diagnosis of psychiatric illness tended to carry a poor prognosis for subsequent behavior. In addition to environmental factors we see, as in the first study, some aspects of brain damage (abnormal neurological examination, abnormal Bender-Gestalt test). The negative signs for the correlations with special schooling and school grades are due to scale construction. Special schooling was coded as 1 (yes) and 2 (no). The scale for average grades went from 1, (unsatisfactory and grade failure) to 9 (superior or honor student). The correlates, although obtained on an adolescent and adult population, point out that the behavioral difficulties are of long standing, going back to school age and possibly in some instances to infancy.

Table 83 contains only those significant correlations that refer

TABLE 83

SIGNIFICANT CORRELATIONS OF FINDINGS OBTAINED AT INITIAL EXAMINATION WITH BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for behavior	.472	1
Prognosis for intellectual functions	.392	1
Social factors contributing to illness	.368	1
Behavioral difficulties in school	.340	1
Objective findings on neurological examination	.292	1
Feeding problems in infancy	.278	2
Attended special school	−.276	2
Amount of schooling	−.272	5
Diagnosis of psychiatric disorder in addition to diagnosis of epilepsy	.267	2
Average marks in school	−.247	5
Prognosis for seizure control	.244	5
"Organic" findings on Bender-Gestalt test	.235	5
Seizures related to menstrual period	.302	10
Frequency of grand mal seizures	.243	10
Grand mal status epilepticus	.224	10
Talking age	.222	10
Duration of pregnancy	.204	10
Spike wave activity in EEG	.200	10

to findings obtained on initial evaluation. The importance of brain damage for the behavior of the patient becomes even clearer if we look at the relationships obtained at follow-up examination, as shown on Table 84. For practical purposes organic mental changes head the list. Most of the other correlates are also associated with this particular problem (deterioration of Performance IQ, concrete proverb interpretations, organic Bender-Gestalt test, recent and remote memory loss, lower Ver-

TABLE 84

SIGNIFICANT CORRELATIONS OF FINDINGS OBTAINED AT FOLLOW-UP EXAMINATION WITH BEHAVIOR PROBLEM AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Academic school problem between Evaluation I and Evaluation II	.559	1
Organic mental changes	.542	1
Personality disorder	.430	1
Seizure state at follow-up	.417	1
Unemployed	.383	2
Performance IQ deteriorated between Evaluation I and Evaluation II	.381	5
Proverb interpretations concrete	.365	1
Full Scale IQ	−.363	1
"Organic" features on Bender-Gestalt test	.349	1
Remission for minor seizures	−.348	2
Amount of alpha activity in EEG	−.342	1
Recent memory impaired	.341	1
Response to adequate amount of anticonvulsant medication	−.331	5
Verbal IQ	−.324	2
Number of different seizure types has increased	.321	5
Combination of different seizure types	.316	5
Seizure patterns in EEG	.306	1
Remote memory impaired	.287	2
Serial 7 subtractions impaired	.278	5
Amount of photic driving response at medium flash rates	−.268	2
History of depression	.251	5
Amount of abnormality in EEG	.227	5
Spike wave activity in EEG	.221	5
Sociopathic or antisocial behavior	.221	10
Amount of theta activity in EEG	.204	10
Psychomotor seizures	.195	10

bal IQ, lower Full Scale IQ and difficulties with serial seven subtractions). As far as psychiatric symptoms are concerned, we find mostly personality disorders and depression; sociopathic and/or antisocial behavior are low on the list.

Of definite interest are the correlates with seizure activity, especially the observation of an increase in the number of different seizure types the individual has experienced. The poor response to medication is of course related to the previously mentioned variables, but we do not know what is cause and effect. Do the patients forget or ignore their anticonvulsant regime because of intellectual deficit and/or personality disorders, or do they suffer from a type of seizure disorder which is not responsive to medication? Both factors may be operative to different degrees in different patients. Psychomotor seizures tend to be refractory to medication, especially when they occur in combination with other seizure types. They appear on the table, but they are on the bottom of the list and the correlation does not reach statistical significance. This finding may seem in contradiction to the observations from the factor analysis that were presented in the chapter on prognosis for seizure control. A factor of intractable psychomotor seizures with associated behavioral problems and unemployment had been found. The factor merely states, however, that this group of patients exists and does not necessarily imply that the majority of patients with psychomotor seizures will have significant behavioral problems. It is a well-known clinical observation that a patient who has marked behavioral difficulties, especially if they are of psychotic proportions, is likely to suffer from psychomotor seizures. The converse is, however, not necessarily the case. The diagnosis of psychomotor seizures in a patient does not automatically imply a high degree of probability for the presence of behavioral problems.

Patients who are classified as suffering from psychomotor or temporal lobe seizures do not constitute a homogeneous group. Their seizures may originate in a variety of different structures within the limbic system (e.g. surface of temporal lobe, uncus, amygdala, hippocampus, island of Reil). One could therefore visualize several subgroups of psychomotor seizure patients, depending upon the locus of origin of the seizure discharge. While

a discharging lesion in the hippocampus might give rise to interictal memory loss and confusional states, this would not necessarily be expected from a lesion situated, for instance, in the island of Reil. Rather than taking the position that no statistically significant differences exist in regard to behavioral difficulties between psychomotor seizure patients and other epileptic patients, it would seem more profitable to clearly delineate that subgroup of psychomotor seizure patients in whom behavioral problems are quite prominent, and this aspect of the problem will require further study.

As far as the EEG is concerned, the amount of alpha rhythm at follow-up seems to be correlated best with behavior, a small amount being associated with behavioral difficulties and vice versa. The initial EEG appears to be of no prognostic value for the majority of cases as far as behavior is concerned, but it should be remembered that patterns like hypsarhythmia or petit mal variant were not included in the computations because they did not occur with sufficient frequency in the sample. On the whole we can say that the findings were in much better agreement with the first study than those that had dealt with seizure outcome.

As mentioned in the chapter on seizure prognosis, we were interested not only in intercorrelations but also in significant mean differences between groups. The material was therefore divided into two groups and analysis of variance between groups was carried out. Group I consisted of sixty-one patients with no or slight behavioral difficulties at time of follow-up, and Group II of twenty-eight patients who had shown moderate or marked problems in this respect. The data from one patient with mild behavioral difficulties had been accidentally omitted from the calculations. The 190 variables dealing with findings obtained at initial evaluation that had been used for seizure prognosis were again utilized. Table 85 contains the variables showing significant differences between groups on F tests, and Table 86 shows the Chi Square results. From the asterisks we can notice that all the variables that had shown significant correlations in the correlation matrix are represented in these tables. One of the correlates that had shown a tendency towards statistical significance

TABLE 85

SIGNIFICANT DIFFERENCES BETWEEN GROUPS HAVING BEHAVIORAL DIFFICULTIES AND NO BEHAVIORAL DIFFICULTIES

	No or Mild Behavioral Problem	*Moderate or Marked Behavioral Problem*	*F*	*Significance Level (%)*
Behavior prognosis*	3.8	5.6	19.1	1
Prognosis for intellectual functions*	4.0	5.9	14.5	1
Objective findings of cerebral pathology on neurological examination*	1.6	3.3	14.3	1
Organic findings on psychological tests	3.1	5.1	10.8	1
Seizure state at follow-up*	2.6	4.0	10.3	1
Similarities—Wechsler IQ	9.7	7.0	9.9	1
Average grades in school*	4.2	2.7	8.3	1
Amount of schooling*	4.2	3.2	7.1	1
Social factors contributing to illness*	4.0	5.5	6.7	5
Prognosis for seizure disorder*	4.2	5.2	6.5	5
"Organic" features on Bender-Gestalt test*	3.2	5.0	6.2	5
Talking age	3.9	5.3	6.1	5
Performance IQ	96.6	85.9	5.2	5
Picture Arrangement—Wechsler IQ	9.6	7.7	4.3	5
Duration of individual major seizure	3.5	4.2	4.3	5
Block Design—Wechsler IQ	9.5	7.5	4.2	5
Feeding problems in infancy*	1.5	2.3	4.2	5
Relation of menses to major seizures	3.4	5.6	4.1	10
Comprehension—Wechsler IQ	9.7	7.8	3.8	10
Digit Symbol—Wechsler IQ	8.4	7.0	3.8	10
Full Scale IQ	95.5	86.6	3.4	10
Clusters of minor seizures over several days, freedom from seizures for several weeks	1.6	2.7	3.0	10
Frequency of occurrence of loss of bladder control during major seizures	3.6	4.8	2.8	10

(10% level), namely, seizures occurring mainly around the menstrual period, is again represented as showing a tendency towards statistical significance. This finding might therefore become significant on a larger sample. The correspondence between correlation coefficients and the analysis of variance was again confirmed. Findings which appeared at the 10 per cent level of significance were, however, usually not duplicated by another

TABLE 86

SIGNIFICANT DIFFERENCES BETWEEN GROUPS HAVING BEHAVIORAL DIFFICULTIES AND NO BEHAVIORAL DIFFICULTIES

		No or Mild Behavioral Problem	*Moderate or Marked Behavioral Problem*	X^2	*Significance Level* (C_c)
Behavior problem in school*					
	Absent	57	19	10.0	1
	Present	4	9		
Employed*					
	Yes	18	2	5.8	5
	No	15	11		
Seizures present during first year of life					
	Absent	54	19	5.5	5
	Present	7	9		
Febrile convulsions					
	Absent	52	18	5.0	5
	Present	9	10		
Attended special school*					
	Yes	17	14	4.8	5
	No	42	12		
Postictal headaches					
	Absent	19	16	4.6	5
	Present	29	8		
Family history of excessive nervousness					
	Absent	41	18	4.0	5
	Present	17	14		
Family history of temper outbursts					
	Absent	50	19	3.0	10
	Present	8	8		
SPECIAL TEST FOR STATISTICAL SIGNIFICANCE OF SMALL NUMBERS (FISHER)					
Family history of breathholding spells					
	Absent	53	20		5
	Present	8	7		
Major seizures occurring mostly at night					
	Absent	38	23		5
	Present	10	1		

statistical method and should therefore not be taken too seriously.

In the first follow-up study it was noted that remission of the seizure disorder prior to first evaluation was significantly correlated with behavior problems at time of follow-up. A similar

observation exists in this material. Patients who had febrile convulsions in infancy or childhood showed significantly more behavioral difficulties at time of follow-up than those who did not have this condition. This is an interesting observation which invites further study.

As Tables 85 and 86 show, behavioral difficulties occurred for the most part in patients who had evidence for organic cerebral disease, and/or intellectual problems (objective findings on neurological examination, organic findings on psychological tests, poor school grades, lesser amount of schooling, late onset of talking). It is also of interest to note that the Performance IQ showed significant differences between the two groups, while the Verbal IQ did not. This will be discussed further when our material on intelligence is presented. Furthermore, it should be reemphasized that the behavioral difficulties tended to be of considerable duration going back to school age, and actually may have manifested themselves at times already in infancy in form of feeding problems.

As a next step in the data workup a discriminant function analysis was performed, as had been done in regard to seizure prognosis. Ten variables that had shown significant differences between the groups were selected. Twenty-two patients with no behavioral difficulties at time of follow-up and twenty patients with some problems in this regard had complete data on all the variables. The computer program classified correctly seventeen of the patients who did not have appreciable behavioral difficulties (77.3%), and seventeen who did have behavioral problems (85.0%). The overall correct classification was therefore 80.9 per cent. Table 87 shows the probabilities of the computer classification for Group I and Group II in relation to the actual findings. If the formula gave a .90 or higher probability for the patient to fall into the respective group, there were no incorrect classifications. The variables, with their weights and the constant that has to be subtracted, are shown in Table 88.

In regard to Performance IQ, the actual value was inserted in the formula. The variables "seizures during first year of life," "special schooling," and "behavioral difficulties in school" were rated as 1, meaning absent, and 2, meaning present. Special

TABLE 87

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	3	2
.75 to .89	10	3
.90 to .95	4	0
*Group II***		
Less than .75	5	0
.75 to .89	7	3
.90 to .99	5	0

* No or mild behavioral problem.

** Moderate or marked behavioral problem.

schooling had initially carried a negative sign in the coding system, but this was reversed for these computations in order to conform with all the other variables. The variables "organic pathology suspected from psychological tests," "feeding problems in infancy," "social factors contributing to illness," and "objective findings of cerebral pathology" had originally been coded as 1 through 9 scales, but the scales were condensed for

TABLE 88

DISCRIMINANT FUNCTIONS FOR PREDICTING BEHAVIOR

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Performance IQ	1.08	1.08
Organic pathology suspected from psychological tests	7.42	7.18
Seizures present during first year of life	19.85	21.27
Behavioral difficulties in school	29.66	33.16
Feeding problems in infancy	5.80	6.67
Talking age	0.08	−0.12
Special schooling	14.50	15.28
Average grades in school	5.91	6.81
Social factors contributing to illness	0.27	0.82
Objective findings of cerebral pathology on neurological examination	6.85	8.72
Constant	−110.17	−122.76

this purpose to 1 through 5 scales (1, meaning no problems; 2, mild difficulties; 3, moderate; 4, marked; and 5, severe difficulties). The scale for "average grades in school" was likewise condensed to a 5-point scale and is shown in Figure 17. The scale for "talking age" is reproduced as Figure 18 and was coded in

AVERAGE GRADES IN SCHOOL

0 Not recorded
1 Unsatisfactory and grade failure
2 Unsatisfactory but no grade failure
3 Average
4 Somewhat above average
5 Superior or honor student

FIGURE 17.

respect to time at which the child started to form the first sentences, rather than in regard to initial utterances like "mama" or "dada."

It is recognized that the weights for the discriminant functions were developed on a small sample, and so far we have not had the opportunity to cross-validate the results on another group of patients. They are presented here, as has been pointed out pre-

TALKING AGE (BEGINNING SENTENCES)

0 Not recorded
1 Under 12 months
2 12–14 months
3 15–17 months
4 18–20 months
5 21–24 months
6 25–28 months
7 29–32 months
8 33–36 months
9 Over 3 years

FIGURE 18.

viously, not as final conclusions but as a basis for further work. They do suggest, however, quite strongly that behavioral difficulties in the epileptic patient are for the most part not primarily due to rejection of the patient by his environment as a result of the seizures. Continued behavioral problems appear to be much more commonly related to aspects of cerebral damage and/or intellectual limitations.

Chapter 13

PROGNOSIS FOR INTELLECTUAL FUNCTIONS

The next question that we had wanted to answer was related to the probability of epileptic patients developing learning difficulties or intellectual deterioration. The average school grades of the twenty-seven children who were involved in the first follow-up project of the Michigan Epilepsy Center and who

TABLE 89

SCHOOL GRADES AT TIME OF FOLLOW-UP

	Number of Children	*Percentages*
Mostly A and B	8	29.6
Mostly C	6	22.2
Mostly D and E	4	14.8
Special education classes	7	25.8
Suspended from school	2	7.4

lived in the community are shown in Table 89. It can be seen that approximately half of the children did have considerable academic difficulties in school. The next table, Table 90, compares the average school grades against seizure state at time of

TABLE 90

SCHOOL GRADES VERSUS SEIZURE STATE

	A	*B*	*C*	*D and E*	*Special Education*	*Suspended*
Still having seizures	2	3	3	3	5	2
In remission	2	1	3	1	2	0

follow-up. No appreciable differences can be noted. Looking, however, at the seizure types of the five unremitted patients who were making A and B grades in school, one found that three had absences with some features of automatic activity as their only seizure type. One patient had psychomotor seizures only, and the other had monthly grand mal seizures.

The variable "learning problems in school at time of follow-up" had been included in the intercorrelation matrix and the statistically significant correlates are shown in Table 91.

Reviewing the table we can see that prognostication had been a great deal easier for school achievement than for seizure con-

TABLE 91

SIGNIFICANT CORRELATIONS WITH LEARNING PROBLEMS IN SCHOOL AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Prognosis for academic achievement	.708	1
Organic factors suspected from psychological tests	.619	1
Immaturity on psychological tests	.618	1
Talking age	.603	1
IQ	−.602	1
Behavior problem at follow-up	.478	1
Highest degree of fever	.687	2
Left leg twitching during seizure	.468	2
Amount of theta activity in EEG	.449	2
Objective findings on neurological examination	.427	2
Activity during first year of life	−.743	5 (N = 6)
Personality disturbances on psychological tests	.569	5
Left arm or hand twitching	.415	5
Psychomotor seizures	−.391	5
Focal major seizures	.390	5
Left face twitching	.377	5
Vocalization prior to major seizure	.365	5
Cyanotic during major seizures	.365	5
Seizures present since first year of life	.365	5
Age at time of onset of seizure disorder	−.363	5
Background frequency of EEG	−.411	10
Amount of alpha activity in EEG	−.358	10
Amount of alpha activity in EEG, Evaluation II	−.340	10
Duration of illness	.330	10

trol or behavior. A reasonably accurate prognosis had been made even in the preschool child. We can see again, that similar to the behavior problems, the intellectual handicaps are related to brain damage as expressed by focal motor seizures, objective findings on the initial neurological examination, slow background in the EEG, and long-standing illness. They are not related to a family history of mental retardation. There are several other observations in the table that should be commented upon. Psychomotor seizures were found inversely related to school performance, suggesting that children with this seizure type ought to do well in school. This is, of course, contrary to expectation and may well be the result of the small sample. This question will have to be resolved on another group of patients, but at this point it would be advisable to keep an open mind about the pathological processes underlying psychomotor seizures in children, as these might differ from those of the adult type.

There is one other main problem one would like to have answered, Is the brain damage and resultant IQ loss due to the seizures, or are seizures merely the added complication of preexisting brain damage? Reviewing the table one does not find direct answers to this question, but there are some hints. The fact that the seizures are for the most part focal would argue that brain damage merely facilitated the occurrence of the seizure and was therefore preexisting. However, we also find in the table that cyanosis during the major seizures was significantly correlated with learning problems. One could therefore postulate that these children had suffered more cerebral anoxia during seizures, which had added insult to injury. The same applies to the observation that excessively high temperatures were found positively correlated with learning problems. Temperatures of 105 and 106 degrees Fahrenheit had been reported in some of these children during febrile illnesses and this could have resulted in some added damage to the brain. But we face again the problem that preexisting brain damage could have permitted much more intense seizure activity with resultant obvious cyanosis, and it could also have led to a faulty temperature regulating mechanism, which in turn allowed such excessively high temperatures to occur. A correlation which does not appear in

the table may also be of importance. If seizures per se were the main cause of the learning problems, one might assume that the more frequent the seizures, the more likely learning difficulties occur; but frequency of major seizures was not significantly correlated with this variable. On the other hand one could, of course, also argue that one or two severe seizures lasting one-half hour to one hour may do immeasurably more harm to the brain than any number of major seizures lasting only one to two minutes. These speculations are mentioned here to point out that retrospective studies may not allow final conclusions on this question and a prospective longitudinal approach may be needed. The factor analysis had placed school achievement

TABLE 92

FACTOR I

.92	Poor marks in school, Evaluation II
.86	Organic pathology suspected on psychological testing, Evaluation I
.57	Low IQ on initial psychological examination
.55	Academic school problem at follow-up
.49	Behavior problem at follow-up
.47	Remission of seizures prior to Evaluation I
.39	Academic school problem at time of Evaluation I

mainly in relation to intelligence and "organic" features on psychological tests. The factor did not contain any seizure variables except for a suggestion that some of these patients had isolated convulsions in infancy prior to the start of the recurrent seizure disorder. The factor is listed in Table 92.

SECOND MEC FOLLOW-UP STUDY

As had been mentioned previously, the material of the second follow-up study consisted for the most part of adolescent and adult patients, but the presence or absence of learning problems could be evaluated in twenty-nine patients. Six of the patients had no learning problems at time of follow-up. They were present to a mild degree in three, to a moderate degree in six, to a marked degree in six, and eight patients had experienced severe difficulties in this respect. The statistically significant findings of

the intercorrelation matrix relating learning problems at time of follow-up to findings obtained at initial examination are listed in Table 93. We can note that prognosis for academic achievement showed again a high correlation with actual outcome and that intelligence and aspects of brain damage are the most important variables. Focal seizure activity is represented in the table with only a tendency towards statistical significance (10% level). This suggests that focal seizure activity in the child may have more serious significance for intellectual development than it does when it occurs later in life. The significant correlates between learning problems at time of follow-up and other findings obtained at time of follow-up are shown in Table 94. The table

TABLE 93

SIGNIFICANT CORRELATIONS OF FINDINGS ON INITIAL EXAMINATION WITH LEARNING PROBLEMS IN SCHOOL AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Verbal IQ	−.834	1
Full Scale IQ	−.789	1
Prognosis for academic or intellectual achievement	.774	1
Performance IQ	−.677	1
"Organic" findings on Bender-Gestalt test	.614	2
Objective findings on neurological examination	.607	1
Talking age	.604	1
Prognosis for behavior	.599	1
Adequacy of medication regime	−.543	1
Seizures present during first year of life	.539	1
Immaturity on psychological tests	.537	1
Prognosis for seizure control	.528	1
Etiology of seizures unknown	−.463	1
Personality disturbances on psychological tests	.456	5
Attended special school	−.424	5
Duration of seizure disorder	.384	5
Spike wave activity in EEG	−.307	10
Grand mal status epilepticus	.373	10
Behavioral difficulties in school	.350	10
Walking age	.326	10
Focal minor motor seizures	.324	10
Condition of patient's head at birth	.321	10

TABLE 94

SIGNIFICANT CORRELATIONS OF FINDINGS AT FOLLOW-UP EXAMINATION WITH LEARNING PROBLEMS IN SCHOOL AT FOLLOW-UP

	r	*Significance Level* (%)
Amount of schooling	−.919	5
Proverb interpretation concrete	.841	1
Full Scale IQ	−.821	1
Verbal IQ	−.816	1
Organic mental changes	.800	1
Performance IQ	−.723	1
Average grades	−.698	1
"Organic" Bender-Gestalt test	.648	2
Remissions for major seizures	−.614	1
Amount of alpha activity in EEG	−.588	1
Serial 7 subtractions impaired	.577	2
Response to adequate amount of anticonvulsant medications	−.559	5
Behavior problem	.559	1
Remote memory impaired	.551	2
Combination of seizure types	.518	5
Remissions for minor seizures	−.497	5
Recent memory impaired	.475	5
Spike wave activity in EEG	.446	2
Amount of photic driving response at high flash rates in EEG	−.445	2
Amplitude of background rhythms in EEG	−.424	5
Amount of photic driving response at low flash rates in EEG	−.404	5
Sociopathic or antisocial behavior	.448	10
Amount of theta activity in EEG	.352	10
Focal minor motor seizures	.340	10
Seizure patterns in EEG	.312	10

reaffirms the findings in regard to intelligence and organic mental changes, but several additional points emerged that deserve to be mentioned. Verbal IQ seems to be more important for school success than Performance IQ. This is pointed out at this particular time because Performance IQ tends to suffer more in chronic seizure patients than Verbal IQ, as we have heard from Collins (1951), and we will note this to be the case when our IQ material is presented. Presence of seizures during first year of life appeared associated with poor school success in the first and the second follow-up studies, and we are therefore justified in re-

garding this as an important variable in the prognosis for school achievement. It should be emphasized that presence of seizures during first year of life did not correlate significantly with seizure state at follow-up. The importance of a seizure disorder starting during the first year of life lies, therefore, not in the fact that it will necessarily produce hard-core chronic epileptic patients, but that it signals future learning difficulties.

The negative relationship of learning problems with "etiology of seizures unknown" is encouraging because it points out that "idiopathic epilepsy" does not tend to give rise to major learning problems in school. The correlation with adequacy of medication regime carries a negative sign because of scale construction. The correlation states that the children with learning problems had been adequately treated with anticonvulsant medications prior to their first visit to the Center. Their response to anticonvulsants was, however, poor and they did not enjoy appreciable remissions for either major or minor seizures. Other aspects related to seizures were several seizure types in the same patient and spike wave activity in the EEG. The initial EEG showed no useful relationship in this sample; but the follow-up EEG tended to show seizure patterns, low voltage background rhythms, and/or marked theta activity. The correlation of learning problems with a poor photic driving response is of considerable theoretical interest and needs to be investigated further in the future.

Verbal, Performance and Full Scale IQ for Evaluation I, as well as for Evaluation II, had been included in the previously mentioned correlation matrix. The variables that were significantly related to Full Scale IQ on initial as well as follow-up examinations are shown with their correlation coefficients in Table 95. The differences in the magnitude of the correlation coefficients between the IQ at Evaluation I and Evaluation II have to be interpreted with some caution because there are three individuals in each group who had only one Wechsler IQ. The overall trends can nevertheless be discussed. Negative signs refer to low IQ. If we concentrate on the findings that were obtained on initial evaluation and which could have predictive value for IQ level at follow-up, we find mainly those that relate to developmental history, school performance, and findings of a cere-

TABLE 95

SIGNIFICANT CORRELATES WITH FULL SCALE IQ ON INITIAL EXAMINATION AND FOLLOW-UP EXAMINATION

Findings from Initial Examination	*r*	*Evaluation I Significance Level (%)*	*r*	*Evaluation II Significance Level (%)*
Verbal IQ	.934	1	.833	1
Performance IQ	.921	1	.757	1
Academic school problem	−.789	1	−.821	1
Prognosis for academic functions, poor	−.762	1	−.655	1
Bender-Gestalt Test "organic"	−.745	1	−.670	1
Amount of schooling, little	.718	1	.786	1
Average school grades	.556	1	.450	1
Talking age	−.517	1	−.343	2
No special schooling	.491	1	.420	1
Immaturity on psychological tests	−.423	1	−.404	1
Personality disturbances on psychological tests	−.405	1	−.504	1
Prognosis for seizure disorder, poor	−.392	1	−.372	1
Objective findings on neurological examination	−.363	1	−.499	1
Focal minor motor seizures	−.292	5	−.343	1
Birth weight	.289	5	.271	10
Psychotic tendencies on psychological tests	−.286	5	−.319	2
Seizures present during first year of life	−.282	5	−.406	1
Findings from Follow-up Examination				
Full Scale IQ	.858	1		
Verbal IQ	.825	1	.950	1
Performance IQ	.748	1	.913	1
Bender-Gestalt Test "organic"	−.666	1	−.749	1
Organic mental syndrome	−.577	1	−.727	1
Serial 7 subtractions, impaired	−.576	1	−.782	1
Difficulty concentrating	−.376	1	−.478	1
Unemployed	−.366	2	−.339	5
Focal minor motor seizures	−.354	1	−.353	1
Proverb interpretation, concrete	−.305	5	−.473	1
Spike wave activity in EEG	−.264	5	−.225	10

bral deficit on neurological examination and/or the Bender-Gestalt test. These are, of course, correlates that one expects on general grounds regardless of the presence or absence of epilepsy.

As far as specific correlates of Full Scale IQ at Evaluation I with epilepsy variables are concerned, these are quite meager: we find only focal minor motor seizures and presence of seizures during the first year of life. Seizure frequency, duration of the seizure disorder, and most important, seizure outcome at the time of follow-up, were not significantly correlated with initial IQ. The correlate with seizures during the first year of life is of interest from various points of view. It could be argued that seizures and the low IQ arise from a common denominator, namely prenatal or perinatal brain damage. Clinical experience indicates that this is certainly the case in a considerable number of instances, but it is of interest that the Full Scale IQ did not correlate significantly with the variable "etiological factors in neurological history." This suggests that the presence of known injuries to the central nervous system did not suppress the IQ too markedly in some cases and in other instances of markedly depressed IQ, no etiology was present by history. A detailed investigation was now required in regard to the relationship between age at time of onset of the seizure disorder and intellectual deficits. Before we go into this problem, there is other material that should be looked at. A number of significant correlations were present with the IQ as measured by the time of follow-up and not with initial IQ. These are listed in Table 96. The variables that were obtained on initial evaluation appear in the upper half and those that were obtained at follow-up, in the lower half of the table. Of interest is the fact that duration of seizure disorder at Evaluation I was correlated significantly with IQ at Evaluation II, but not with IQ at Evaluation I. This might suggest that a long-standing seizure disorder could have, by itself, a deteriorating effect on the IQ. Spike wave activity in the EEG also seems to carry a poorer prognosis for intellectual functions. The finding that isolated seizures in childhood tend to be associated with a poor prognosis, not only for behavior but also for intelligence, invites further study.

The intercorrelation matrix also had contained, in addition to Full Scale IQ, the Verbal and Performance IQ scores. It was thereby hoped to get a somewhat more detailed appraisal of relationships between clinical findings and cognitive functions.

A comparison of the correlation coefficients for Verbal, Performance, and Full Scale scores obtained at time of follow-up is presented in Table 97. Only those variables are shown that were found correlated to a statistically significant degree with either the Verbal or Performance scales. Variables that correlated with Full Scale IQ only, were omitted. All variables refer to findings obtained at initial evaluation. The variables are arranged from highest to lowest correlation coefficient for the Performance IQ.

TABLE 96

ADDITIONAL SIGNIFICANT CORRELATIONS OBTAINED WITH FULL SCALE IQ AT TIME OF FOLLOW-UP

Findings from Initial Examination	*r*	*Significance Level* (%)
Spike wave activity in EEG	−.388	1
Isolated infantile nonfebrile convulsions	−.327	1
Personal relationships during adolescence	.341	2
Prognosis for behavior	−.328	1
Duration of seizure disorder	−.292	5
History of bedwetting	.275	5
Etiology of seizure disorder unknown	.267	5
Findings from Follow-up Examination		
Remote memory	−.374	1
Behavior problem	−.363	1
Overall condition of patient	−.333	1
Amount of EEG abnormality	−.314	2
Amount of alpha activity in EEG	.263	5

It can be seen that the variables dealing with seizures (seizures present during first year of life, focal minor motor seizures, duration of seizure disorder, spike wave activity in EEG) were all correlated to a higher degree with Performance than with Verbal IQ. Findings on the neurological examination and the Bender-Gestalt test related also more to the Performance score than the Verbal, but school achievement was tied closer to the Verbal than the Performance areas.

The statistically significant correlations between the Verbal,

TABLE 97

SIGNIFICANT CORRELATIONS BETWEEN WECHSLER IQ VARIABLES AND FINDINGS OBTAINED ON INITIAL EXAMINATION

	Verbal	*SL** (%)	*Performance*	*SL** (%)	*Full Scale*	*SL** (%)
Performance IQ	.642	1	.779	1	.757	1
Full Scale IQ	.825	1	.748	1	.858	1
Bender-Gestalt Test "organic"	−.580	1	−.657	1	−.670	1
Amount of schooling	.813	1	.630	1	.786	1
Verbal IQ	.886	1	.609	1	.833	1
Prognosis for academic achievement	−.623	1	−.593	1	−.655	1
Objective findings on neurological examination	−.431	1	−.529	1	−.499	1
Personality disturbance on psychological tests	−.490	1	−.438	1	−.504	1
Seizures present during first year of life	−.356	1	−.416	1	−.406	1
Did not attend special school	.400	1	.398	1	.420	1
Spike wave activity in EEG	−.339	2	−.386	1	−.388	1
Personal relationships during adolescence	.284	5	.357	1	.341	2
Focal minor motor seizures	−.299	2	−.349	1	−.348	1
Immaturity on psychological tests	−.389	1	−.348	1	−.404	1
Prognosis for seizure disorder	−.370	1	−.320	2	−.372	1
Duration of seizure disorder	−.246	10	−.314	2	−.292	5
Isolated nonfebrile convulsions in infancy	−.304	2	−.305	2	−.327	1
Sitting up age			−.303	5	−.250	10
Birth weight			.302	5		
Average grades in school	.512	1	.290	5	.450	1
Talking age	−.349	2	−.287	5	−.343	2
Prognosis for behavior	−.321	2	−.285	5	−.328	1
Etiology of seizures unknown	.254	5	.244	10	.267	5
History of bedwetting	.268	5	.240	10	.275	5
Psychotic tendencies on psychological tests	−.344	1	−.224	10		
Family history of infantile nonfebrile convulsions	.255	5				

* Significance Level

Performance, and Full Scale IQ obtained at Evaluation II with clinical findings at time of follow-up are shown in Table 98. The variables are arranged from highest to lowest correlation co-

TABLE 98

SIGNIFICANT CORRELATIONS BETWEEN WECHSLER IQ VARIABLES AND FINDINGS OBTAINED ON FOLLOW-UP EXAMINATION

	Verbal	*SL** (%)	*Performance*	*SL** (%)	*Full Scale*	*SL** (%)
Bender-Gestalt Test "organic"	−.675	1	−.737	1	−.749	1
Academic school problems	−.816	1	−.723	1	−.821	1
Organic mental changes	−.658	1	−.695	1	−.727	1
Serial 7 Subtractions impaired	−.743	1	−.657	1	−.782	1
Difficulty concentrating	−.443	1	−.424	1	−.478	1
Proverb interpretation concrete	−.476	1	−.371	2	−.473	1
Amount of EEG abnormality	−.235	10	−.363	1	−.314	2
Behavior problem	−.324	2	−.361	1	−.363	1
Focal minor motor seizures	−.313	2	−.355	1	−.353	1
Amount of alpha activity in EEG			.297	2	.263	5
Amount of photic driving at high flash rates in EEG			.272	5		
Amount of photic driving at low flash rates in EEG			.268	5		
Overall condition of patient	−.350	1	−.262	5	−.333	1
Amount of fast activity in EEG			−.253	5	−.234	10
Remote memory impaired	−.421	1	−.240	10	−.374	1
Recent memory impaired			−.227	10	−.313	2

* Significance Level

efficient for the Performance IQ. These findings agree with those shown in the previous table but point out in addition that the EEG appears more closely related to the Performance than to the Verbal areas.

IQ Change in Relation to Seizure State

The results presented so far do not allow a direct differentiation between patients who had a low IQ possibly even before the onset of their seizure disorder and patients whose IQ had shown some decrease as a concomitant of the illness. A comparison of initial against follow-up Wechsler IQ scores was possible in 56 patients. Table 99 shows the mean values for the Full Scale,

TABLE 99

MEAN WECHSLER IQ LEVELS FOR INITIAL AND FOLLOW-UP EXAMINATION
(N = 56)

	Evaluation I	*Evaluation II*	*Difference*	*t*	*Significance Level (%)*
Verbal	94.50	93.67	− .82	0.72	NS
Performance	95.75	91.82	−3.92	2.75	1
Full Scale	94.96	92.41	−2.55	2.16	5
Information	8.19	8.58	+0.39	1.68	NS
Comprehension	9.40	9.33	−0.07	0.20	NS
Arithmetic	8.06	9.22	+1.16	2.96	1
Similarities	9.25	9.63	−0.38	1.01	NS
Digit Span	8.67	8.67	0.00	0.00	NS
Vocabulary	8.50	8.19	−0.30	1.09	NS
Digit Symbol	8.33	7.51	−0.82	2.60	5
Picture Completion	9.03	9.78	+0.75	2.20	5
Picture Arrangement	9.90	8.45	−1.45	3.39	1
Block Design	9.55	9.05	−0.50	1.58	NS
Object Assembly	9.98	8.12	−1.85	4.28	1

NS = not significant

Verbal, and Performance IQs as well as for subsections of the Wechsler tests on the patients involved in the second follow-up study. The differences between first and second evaluation, and the results of the t test for nonindependent means and levels of statistical significance are also shown. The IQ levels are somewhat biased towards the higher end because patients with marked mental retardation did not receive a Wechsler test on initial evaluation. We can see that at initial, as well as follow-up, examination the IQ was within the normal range, but by the

time of follow-up it had definitely shifted towards the low normal end. We can also note that the Verbal and the Performance IQ tended to show independent behavior. The Performance IQ dropped by nearly four points while the Verbal IQ showed a mean drop of less than one point. Within the verbal area an actual increase had taken place in the Arithmetic subsection. The Performance subtests which showed the most marked decrease were Object Assembly, Picture Arrangement, and Digit Symbol. One Performance subtest, namely, Picture Completion had shown some improvement. These observations indicate that there is indeed a slight but statistically significant overall decrease in intellectual functions present when patients are retested after a period of several years. The mean decrease is so slight that it would not be discovered by interview techniques and the patients remain within the "normal" range of intelligence. The fact that the performance items of the Wechsler test suffered the most is important to recognize, because deficits in these areas will surely be missed if one relies on one's judgment of the patient's intelligence on an interview only. With the verbal functions remaining intact, the patient may well be able to hide his performance deficit and the physician may remain unaware that some deterioration has taken place in the patient.

Analysis of Variance

Although the findings that have been reported indicated that intellectual deterioration does take place in a number of instances, they do not allow precise statements in regard to the question, Who is the epileptic patient whose IQ will deteriorate, as opposed to the patient whose IQ will stay intact or even increase? Theoretically it would be desirable to compare an equal number of patients, preferably fifty or more, whose IQ had increased by ten points or more, with an equal number whose IQ had remained within ten points in either the upward or downward direction, and an equal number of patients who had deteriorated ten points or more. This theoretical ideal could not be reached in our study because we had only fifty-six patients who had two Wechsler IQ tests. Patients who had received the

Stanford-Binet test during the initial evaluation could not be used for comparison. The Full Scale IQ had deteriorated ten or more points in eleven patients and had increased by ten or more points in five. Looking at the subtests, we find a decrease of ten or more points had occurred in the verbal area eight times and in the performance area, fourteen times. An increase of ten or more points had occurred in the verbal area also eight times and in the performance area five times. These observations show also that the performance area is more frequently involved in deterioration and is less likely to improve than the verbal skills.

We were confronted with the fact that a definitive conclusion about the clinical characteristics of the patient who will in all likelihood deteriorate in his intellectual functions may not be possible to accomplish in view of the small sample available; therefore, a compromise solution was attempted. The group of fifty-six patients who had had two Wechsler IQ tests was split into two subgroups. One consisted of patients whose Full Scale IQ had dropped by seven points or more, and the other consisted of patients who had either lost up to six points only, had remained the same, or had shown an increase by any number of points. Patients with initial IQs of 70 or below were excluded in order to avoid contamination of the sample with mental deficiency. This left twenty-two patients whose IQ had dropped seven points or more and eighteen patients who had shown less drop or an increase. The groups were then subjected to the same analysis of variance procedures that had been applied to seizure state and behavior. The variables which showed significant differences between the groups are listed in Table 100. The most important aspect of this table is the observation that seizures per se were indeed related to a deterioration of the IQ. The deterioration was unrelated to presumed etiology or the presence of damage to the central nervous sytem. It occurred more commonly in patients who had initially no or little evidence of organic dysfunction on the Bender-Gestalt test. The most surprising finding was that it occurred mostly in patients who had an initially higher IQ.

We have mentioned previously in the literature review that epileptic patients as a group tend to have a mean IQ that is

TABLE 100

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT CHANGE IN WECHSLER IQ SCORES

FULL SCALE IQ

	Decreased 7 or more points (N = 22)	*Decreased less, remained same, or increased* (N = 18)	*F*	*Significance Level* (%)
Performance IQ	108.3	99.2	11.5	1
Full Scale IQ	108.3	99.1	10.9	1
Present seizure state	4.0	2.2	9.3	1
Combination of seizures	2.7	1.7	9.3	1
Block Design—Wechsler IQ	11.8	9.6	8.5	1
Object Assembly—Wechsler IQ	12.2	10.3	7.6	1
Overall condition of patient	4.4	2.9	6.5	5
Relationship of time of day to minor seizures	1.3	3.7	6.2	5
Social factors contributing to illness	5.2	3.5	5.5	5
Frequency of occurrence of major seizures at initial evaluation	6.8	5.0	5.2	5
Organic features on Bender-Gestalt Test	1.5	2.6	4.7	5
Immaturity on psychological tests	5.1	6.3	4.5	5
Behavior problem on follow-up	3.1	1.9	4.5	5
Duration of seizure disorder (minor seizures)	7.0	5.2	4.3	5
Verbal IQ	105.8	98.8	4.3	5
Amplitude of background rhythms in EEG	5.1	6.3	4.1	5

within the "normal" range, but it is shifted towards the lower end of this range. The phenomenon demonstrated here would account for this observation. The higher IQ patients in the "bright normal" or "superior" range may suffer most from the influence of seizures and slip down into the "normal" group. Although they are now, technically speaking, normal, a real loss has taken place. It is conceivable that this loss in mental acuity is experienced by the patient and reacted to by various mental mechanisms leading to overt psychiatric symptoms, which differ between persons and depend, at least in part, upon the basic

personality structure of the individual. These symptoms could then express themselves clinically as personality disorders, depression, or withdrawal. This theory does not apply to epilepsy only; it could also be applied to other "degenerative" conditions of grey matter. It links the areas of psychiatry and neurology and suggests that, prior to the overt neurological disorder, a number of patients with beginning intellectual loss may have to move through the stage of "psychiatric illness' because their organic defect is too mild to be detected by everyday clinical practice.

To reemphasize this point it can be stated: The fact that a "normal" IQ is measured in a patient does not mean that it could not have been higher prior to the illness. There exists an electroencephalographic corollary to this theory. A low voltage desynchronized EEG does not necessarily mean that this particular tracing is normal for the patient; it could have changed from a dominant alpha pattern to the low voltage desynchronized type of activity. Low voltage desynchronized records have to be interpreted as normal because they occur quite commonly in normal individuals; however, these records may not represent the usual EEG of the person but a deterioration from a better organized alpha pattern. Our concepts of "normality" in the clinical, as well as the electroencephalographic field, will have to undergo a rather critical reassessment in the future.

Returning to epilepsy and the data on hand, we should emphasize that this deterioration from a higher level is not necessarily permanent, but reflects the state of affairs at a given moment in time. The work carried out on serial IQ tests in the 1930s and early 1940s becomes therefore most important because it emphasized the fluctuations that can occur in the IQ over relatively short periods and these fluctuations were not necessarily tied to the seizure state of the patient. The test-retest intervals reported in the literature were for the most part relatively short. One could conceive, however, of two processes being operative in the epileptic patient. One would consist of short-term, relatively marked fluctuations in IQ in upward or downward direction, depending in part upon the time relation to the patient's last seizure; the other, a long-term, less marked

downward course, if the illness persists unchecked for several decades. The short-term fluctuations are important to remember because they are quite likely to tie in with the emotional functions of the individual. The patient being deprived of a relatively stable internal environment, it is probably very difficult, if not impossible, for him to maintain a normal balance in his emotional life.

One other potentially important relationship to IQ deterioration mentioned in the table has still to be mentioned: the finding that adverse social factors were significantly more common in the deteriorating group. We are again confronted here with the problem of what is cause and what is effect. It could be theorized that a disrupted home life has a direct influence on the patient's intellectual functions. But it seems more likely that the relationship is indirect. A disturbed social environment is likely to lead to increased chronic stress on the patient, which leads to poor seizure control and subsequent intellectual loss. We are, however, at this point exceeding our data and should return to the facts as they were observed.

It was mentioned in the literature that the fluctuations in the patient's IQ could not be related to the current seizure state of the patient. The IQ may go up and the seizures become worse or vice versa. Let us look at our data in this respect. Three tables were prepared to allow easy comparison of the findings. Table 101 lists the patients whose Full Scale IQ had increased. The patients are arranged from most marked to least marked increase in Full Scale IQ points. Table 102 shows the patients whose Full Scale IQ had either shown no change or a mild decrease of up to and including six points. Table 103 shows the patients whose Full Scale IQ had dropped by seven or more points. The code for the numbers under seizure state at follow-up examination is shown in Table 104.

There was not a single patient in the entire sample whose seizure state had been rated as 9 at follow-up. The worst outcome was a rating of 8 which had been given to one case only. The tables demonstrate not only the relationship of seizure outcome to IQ change, but also the relative movement of Verbal versus Performance IQs, and the actual IQ values that were obtained on

the two evaluations. Looking at seizure state and IQ change first, we find an impressive correspondence if we concentrate on the group that had been seizure free for two years or more. Of the twenty patients whose IQs had increased, twelve were seizure free (60%). Of the fifteen patients whose IQs had shown no change or slight decrease, four (26.6%) were seizure free, and of the twenty-one patients whose IQs had decreased seven or

TABLE 101

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: IQ POINTS INCREASED

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
360	90	101	(+11)	93	119	(+26)	91	109	(+18)	3
332	57	75	(+18)	54	58	(+ 4)	51	66	(+15)	3
178	83	94	(+11)	69	76	(+ 7)	74	86	(+12)	1
340	91	101	(+10)	100	114	(+14)	95	107	(+12)	1
328	66	65	(− 1)	48	72	(+24)	54	65	(+11)	3
392	99	110	(+11)	99	104	(+ 5)	99	108	(+ 9)	1
283	119	139	(+20)	97	92	(− 5)	109	118	(+ 9)	1
48	103	107	(+ 4)	85	95	(+10)	94	102	(+ 8)	1
371	79	96	(+17)	92	86	(− 6)	83	91	(+ 8)	5
323	91	100	(+ 9)	97	103	(+ 6)	93	101	(+ 8)	1
242	76	76	(0)	59	65	(+ 6)	64	70	(+ 6)	1
318	76	81	(+ 5)	94	104	(+10)	84	90	(+ 6)	1
203	112	127	(+15)	124	117	(− 7)	119	124	(+ 5)	2
188	102	110	(+ 8)	104	101	(− 3)	103	106	(+ 3)	1
79	108	109	(+ 1)	98	110	(+ 2)	107	110	(+ 3)	7
276	91	91	(0)	93	97	(+ 4)	91	93	(+ 2)	1
351	71	64	(− 7)	53	62	(+ 9)	59	61	(+ 2)	2
104	89	92	(+ 3)	82	80	(− 2)	85	86	(+ 1)	5
194	94	99	(+ 5)	108	105	(− 3)	101	102	(+ 1)	1
238	70	67	(− 3)	76	80	(+ 4)	70	71	(+ 1)	1

Seizures controlled: 12 (60.0%), Improved: 5 (25.0%), Same or worse: 3 (15.0%)

more points, two were seizure free (9.5%). This correspondence is not nearly as pronounced if one looks at the improved or same/worse group. This finding reemphasizes, therefore, the value of long-term follow-up studies. It points out also that insistence on complete control of seizures (i.e. no seizures at all within the limits of the follow-up period, not just a decrease in frequency of occurrence) is not only theoretically desirable, but

of very practical importance. It would be advisable when follow-up results for epileptic patients are reported in the future, that the time interval between last seizure and follow-up date be clearly and explicitly stated. This has not been done in a considerable proportion of reported studies. Looking at the figures presented in Tables 101-103 in reverse, we find that out of eighteen patients who were seizure free for two years or more the IQ had increased in twelve (66.6%), stayed the same or decreased

TABLE 102

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: NO CHANGE IN IQ, OR MILD DECREASE UP TO SIX POINTS

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
236	95	96	(+ 1)	93	92	(− 2)	94	94	(0)	4
287	73	78	(+ 5)	90	84	(− 6)	80	80	(0)	8
395	85	89	(+ 4)	99	96	(− 3)	91	91	(0)	5
370	59	65	(+ 6)	103	95	(− 8)	78	77	(−1)	4
157	95	93	(− 2)	89	89	(0)	92	91	(−1)	4
225	94	87	(− 7)	73	73	(0)	82	80	(−2)	3
379	84	84	(0)	106	100	(− 6)	94	90	(−4)	4
347	69	69	(0)	77	69	(− 8)	71	67	(−4)	3
219	110	110	(0)	102	93	(− 9)	101	97	(−4)	4
77	82	84	(+ 2)	105	93	(−12)	92	87	(−5)	1
86	102	98	(− 4)	89	83	(− 6)	96	91	(−5)	1
139	121	114	(− 7)	114	115	(+ 1)	121	115	(−6)	1
150	101	95	(− 6)	104	98	(− 6)	103	97	(−6)	7
250	113	111	(− 2)	99	88	(−11)	107	101	(−6)	3
367	97	85	(−12)	90	92	(+ 2)	93	87	(−6)	1

Seizures controlled: 4 (26.6%), Improved: 8 (53.3%), Same or worse: 3 (20.0%)

slightly in four (27.7%), and decreased seven or more points in two (11.1%). When we look at the amount of increase or decrease in regard to the seizure state, we find that only one patient had deteriorated clinically and gained by three IQ points. There are two patients who were seizure free for two years, but lost eleven and eight points respectively. While freedom from seizures does not therefore guarantee an unchanged or improved IQ, a substantial increase in IQ in the presence of continued seizures appears quite unlikely.

TABLE 103

RELATIONSHIP OF IQ CHANGE TO SEIZURE STATE AT FOLLOW-UP: MODERATE TO MARKED DECREASE IN IQ POINTS

Patient Number	*Verbal*			*Performance*			*Full Scale*			*Seizure State*
	I	*II*		*I*	*II*		*I*	*II*		
338	101	95	(− 6)	121	115	(− 6)	111	104	(− 7)	7
266	87	79	(− 8)	89	82	(− 7)	87	80	(− 7)	2
100	96	90	(− 6)	110	106	(− 4)	104	97	(− 7)	4
118	110	108	(− 2)	99	90	(− 9)	107	100	(− 7)	4
177	110	106	(− 4)	102	95	(− 7)	109	102	(− 7)	3
322	73	67	(− 6)	80	69	(−11)	74	66	(− 8)	2
801	114	107	(− 7)	113	108	(− 5)	116	108	(− 8)	1
365	99	92	(− 7)	108	100	(− 8)	104	95	(− 9)	7
383	102	100	(− 2)	101	84	(−17)	102	93	(− 9)	7
277	101	93	(− 8)	92	80	(−12)	96	87	(− 9)	4
346	104	94	(−10)	108	102	(− 6)	107	97	(−10)	3
399	91	89	(− 2)	109	95	(−14)	101	91	(−10)	3
294	117	109	(− 8)	119	106	(−13)	119	108	(−11)	1
240	119	118	(− 1)	112	88	(−24)	117	105	(−12)	2
196	121	111	(−10)	118	108	(−10)	123	110	(−13)	3
168	84	72	(−12)	81	67	(−14)	81	68	(−13)	3
53	113	103	(−10)	118	108	(−10)	118	105	(−13)	7
381	103	95	(− 8)	112	96	(−16)	108	95	(−13)	4
145	122	104	(−18)	108	98	(−10)	118	102	(−16)	5
158	103	90	(−13)	104	77	(−24)	104	84	(−20)	4
285	84	71	(−13)	100	69	(−31)	91	68	(−23)	5

Seizures controlled: 2 (9.5%), Improved: 14 (66.6%), Same or worse: 5 (23.8%)

TABLE 104

CODE FOR THE NUMBERS UNDER SEIZURE STATE AT FOLLOW-UP EXAMINATION

1	Seizure free for 2 years or more
2	Practically seizure free except for occasional auras
3	Somewhat improved
4	Slightly improved
5	Same
6	Slightly worse
7	Somewhat worse
8	Moderately worse
9	Markedly worse

Concentrating on the actual IQ values, we can see that movement in the upward or downward direction can occur at any IQ level. The Verbal and Performance IQ tended to move for the most part in the same direction, but there were notable exceptions. In Case 283, the Verbal IQ increased by twenty points, but Performance IQ decreased by five points leading to a Full Scale increase of nine points. A similar situation occurred in Cases 371 and 203 and to a less marked extent in others. The opposite situation, a definite decrease in Verbal IQ coupled with a definitely increased Performance IQ, was observed only once (Case 351), although smaller fluctuations were seen in other cases (e.g. Cases 238 and 367).

We have stated before that the Performance IQ area tended to suffer more than the Verbal areas. It was therefore of interest to divide the patients on the basis of their Performance IQs in order to ascertain the characteristics of the individual whose Performance IQ is likely to deteriorate. It was hoped that this would bring the problem into sharper focus than exclusive reliance on Full Scale IQ. The fifty-six patients were divided into two groups: twenty-three patients whose Performance IQ had dropped by seven or more points, and thirty-three patients whose Performance IQ had decreased less, remained stable, or actually increased. The previously mentioned 190 variables were again used for analysis of variance and the statistically significant results for the F and Chi Square tests are shown in Tables 105 and 106. Duration of seizure disorder in regard to minor seizures heads the list. The group whose Performance IQ had dropped had, on the average, suffered from minor seizures for approximately ten years, while the other group had this condition for less than six years. Maximal frequency of major seizures as well as frequency at time of initial visit were significantly related to Performance IQ loss. The patients whose Performance IQ had decreased by seven or more points had, on the average, maximally one or more seizures per week and at time of initial evaluation, two to three per month. The other group had maximally two to three seizures per month and seven to twelve per year at time of first evaluation. The group that had lost Performance IQ points had also shown a poorer response to anticonvulsant treat-

ment, had more than one seizure type, and more frequently had clusters of major seizures over a few days. The patients were older on initial evaluation, had higher IQs to start with and less organic pathology on psychological testing. Unexpected were the observations that female patients more commonly tended to show loss of Performance IQ points, and so did patients whose seizures were classified as absences. It should be emphasized again that these patients did not necessarily suffer from "pure petit mal" with three cycles per second spike wave patterns in their EEGs, but that some of them had focal temporal EEG abnormalities, while the EEG was nonspecifically abnormal in others.

TABLE 105

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT PERFORMANCE IQ SCORES

	PERFORMANCE IQ			
	Decreased 7 or more points (N = 23)	*Decreased less or remained same* (N = 33)	*F*	*Significance Level* (%)
Duration of seizure disorder for minor seizures	7.8	5.7	12.3	1
Frequency of major seizures at initial evaluation	6.8	4.5	11.2	1
Object Assembly—Wechsler IQ	11.5	8.8	9.3	1
Maximum frequency of major seizures	8.3	6.4	9.1	1
Block Design—Wechsler IQ	11.0	8.5	8.3	1
Age	23	17	7.7	1
Organic pathology suspected from psychological tests	2.0	3.8	7.4	1
Performance IQ—Wechsler IQ	102.6	90.9	7.2	1
Clusters of major seizures over several days, freedom from seizures for several weeks	2.4	1.3	6.4	5
Combination of seizures	2.7	1.9	5.7	5
Response to anticonvulsant medication for period of three months to one year after onset of illness	2.6	5.1	5.7	5
Full Scale IQ	101.1	90.6	5.6	5
Picture Arrangement—Wechsler IQ	10.6	8.6	5.5	5
Response to anticonvulsants after the first year of treatment	4.4	6.3	4.1	5

Family history of epilepsy was not significantly related to Performance IQ changes. The positive relationship with family history of abortions would require confirmation on another sample before it can be definitely accepted. The observation that psychiatric treatment had been recommended much more frequently in patients whose Performance IQ had subsequently shown a decrease is of interest in regard to our previously mentioned hypothesis that IQ fluctuations are likely to manifest themselves in emotional disturbances. It is conceivable that these

TABLE 106

INITIAL EXAMINATION FINDINGS RELATED TO SUBSEQUENT PERFORMANCE IQ SCORES

		PERFORMANCE IQ			
		Decreased 7 or more points	*Decreased less or remained same*	X^2	*Significance Level (%)*
Psychiatric treatment suggested					
	Absent	14	31	7.4	1
	Present	9	2		
Family history of abortions					
	Absent	13	29	4.7	5
	Present	8	3		
Absence					
	Absent	13	28	4.1	5
	Present	10	5		
Male		9	23	3.9	5
Female		14	10		

patients had already experienced some IQ loss, even before initial evaluation which showed itself in behavioral symptomatology—which in turn was regarded as being of psychogenic origin. The total Performance IQ decrease may have been greater than is indicated by the two values that we obtained, because a pre-illness IQ was not available in these cases. A long-term study spanning at least ten years, starting at the time of the patient's first seizure with annual or biannual IQ tests, would be necessary to test this hypothesis.

Relationship of Intelligence to Age at Time of Onset of the Seizure Disorder

It has been mentioned in the chapter on seizure prognosis that a comparison was carried out between three groups of patients: those whose seizures had started between birth and three years of age, between four and twelve years of age, and thirteen to twenty-seven years of age. The statistically significant differences between these groups in regard to intellectual functions

TABLE 107

SIGNIFICANT DIFFERENCES IN INTELLECTUAL FUNCTIONS RELATED TO AGE AT ONSET OF THE SEIZURE DISORDER

	AGE AT ONSET				
	0–3 (N = 27)	*4–12* (N = 31)	*13–27* (N = 30)	*F*	*Significance Level* (%)
Object Assembly—Wechsler IQ	8.2	9.2	11.6	6.6	1
Talking age	5.4	4.2	3.4	5.2	1
Amount of schooling	2.8	4.0	4.3	5.2	1
Full Scale IQ	84.8	90.4	101.3	5.1	1
Verbal IQ	84.8	90.9	100.7	5.0	1
Digit Span—Wechsler IQ	6.4	8.0	9.6	3.9	5
Comprehension	7.6	9.1	10.4	3.3	5
Performance IQ	87.3	91.5	100.4	3.2	5
"Organic" Bender-Gestalt Test	5.0	3.7	2.9	3.1	5
				X^2	
Rotation of Bender Designs					
Absent	6	18	23	6.7	5
Present	8	10	5		

are shown in Table 107. It is immediately apparent that there are impressive relationships. The later the onset of the illness, the more normal the intellectual functions. One might assume that early onset also reflects longer duration of the illness, but this was not the case in this sample. Duration of illness prior to first evaluation was not different between the three groups. In contrast to what we have seen in the previous tables the Verbal areas rather than the Performance items (with exception of

Object Assembly) tended to be involved to a greater extent. We have seen before that deterioration as a result of the seizure disorder tended to affect the Performance area more than the Verbal tests. When it comes to intellectual development it would seem from this table that the Verbal areas are more afflicted than the Performance items. This particular aspect of the problem requires further study on another sample. The overall trend is, however, quite clear. The prognostic significance of a seizure disorder starting in early childhood lies in regard to the future intelligence of the patient, rather than in problems with seizure control. It could of course again be argued that children who develop seizures early in life are *a priori* brain damaged and the patient's IQ is lower, not because of seizures but because of underlying brain damage. While this is certainly the case in a number of instances, it is not the whole explanation because it was pointed out in a previous section that etiological factors did not show significant differences in regard to age at time of onset of the illness. Most clinicians will be familiar with cases of patients who developed normally until the seizure disorder made its appearance, but did not progress in a satisfactory manner thereafter. The cases of infantile spasms of unknown etiology present the most dramatic example. Doctor West's child is well worth remembering in this connection: "The child is now a year old, was a remarkably fine healthy child when born and continued to thrive until he was four months old. It was at this time that I first observed slight bobbings of the head forward . . . ."

This case is so important because the father, being a physician, would have been readily aware of birth injury, congenital malformation, or acute inflammatory disease of the central nervous system.

Discriminant Function Analysis

In spite of the fact that we had only a small sample of patients with two Wechsler IQ scores, an attempt was made to use discriminant function analysis in order to try to predict the patient whose IQ is likely to deteriorate. As had been mentioned in the chapter on seizure prognosis, complete data on each

variable was required for the computer program, and this led to a further decrease in the number of patients who became available for this aspect of the study. Group I consisted of nineteen patients whose IQs had dropped seven or more points, and Group II of twenty-nine patients whose IQs had dropped less, had remained essentially the same, or had increased by any number of points. Seven variables that had shown the largest differences between the two groups were chosen for the discriminant function analysis. Eighteen of the nineteen patients of Group I (i.e. had lost more than seven IQ points) were correctly classified by this procedure (95.0%), and so were twenty-

TABLE 108

DISCRIMINANT FUNCTION FOR PREDICTING LOSS OF 7 OR MORE IQ POINTS

Variables	WEIGHTS *Discriminant Function I*	*Discriminant Function II*
Combination of seizures	5.85	4.99
Frequency of major seizures at present	−1.60	−1.53
Clusters of seizures for several days, freedom from seizures for several weeks	3.01	2.19
EEG background amplitude	2.92	3.20
Organic pathology suspected from psychological tests	9.22	9.79
Social factors contributing to illness	4.01	3.42
Full Scale IQ	0.99	0.93
Constant	−79.22	−71.88

four patients of Group II (83.0%). The variables involved, as well as the weights and constants for the discriminant function, are shown in Table 108. Table 109 shows the probabilities indicated by the computer classification in relation to actual findings.

The coding of the variables "combination of seizures," "organic pathology suspected from psychological tests," and "social factors contributing to illness" has already been mentioned in previous chapters. EEG background was coded as shown in Figure 19 and for Full Scale IQ the actual score was inserted. Frequency of seizures refers to major seizures only. If the patient did not have major seizures, the variable was coded as 1

TABLE 109

PROBABILITIES FOR PATIENTS TO FALL INTO GROUP I OR GROUP II

	Correct Classification	*Incorrect Classification*
*Group I**		
Less than .75	4	0
.75 to .89	9	1
.90 to .95	5	0
*Group II***		
Less than .75	7	2
.75 to .89	7	3
.90 to .99	10	0

* IQ decreased 7 or more points.

** IQ decreased less than 7 points, remained the same, or increased.

BACKGROUND RHYTHMS VOLTAGE

0 Not recorded
1 0–10 μv
2 10–20
3 20–30
4 30–40
5 40–50
6 50–60
7 60–70
8 70–80
9 Above 80

FIGURE 19.

(frequency less than once a year) because a score of zero would have meant missing data and this was not acceptable for the computer program. An example of a patient who is likely to show loss of seven or more IQ points might be as follows:

EXAMPLE—POOR PROGNOSIS FOR INTELLECT

DISCRIMINANT FUNCTION 1:

VARIABLE NAME	*WEIGHT*	*CODE AND DEFINITION*	*RESULT*
Combination of seizures	5.85 × 3	Two seizure types	17.55
Clusters of seizures over a few days, freedom from seizures for several weeks	3.01 × 2	Rarely	6.02

EEG background amplitude	2.92 × 3 20–30 μv	8.70	
Organic pathology suspected from psychological tests	9.22 × 2 Mild	18.44	
Social factors contributing to illness	4.01 × 2 Mild	8.02	
IQ	0.99 × 118	116.82	
	SUBTOTAL	175.55	
Frequency of major seizures at present	−1.60 × 9 Several a week		−14.40
CONSTANT	−79.22		−79.22
	SUBTOTAL		−93.62
	TOTAL	81.93	

DISCRIMINANT FUNCTION I (175.55 minus 93.62 = 81.93)

DISCRIMINANT FUNCTION II:

Combination of seizures	4.99 × 3 Two seizure types	14.97	
Clusters of seizures over a few days, freedom from seizures for several weeks	2.19 × 2 Rarely	4.38	
EEG background amplitude	3.20 × 3 20–30 μv	9.60	
Organic pathology suspected from psychological tests	9.79 × 2 Mild	19.58	
Social factors contributing to illness	3.42 × 2 Rarely	6.84	
IQ	0.93 × 118	109.74	
	SUBTOTAL	165.11	
Frequency of major seizures at present	−1.53 × 9 Several a week		−13.77
CONSTANT	−71.88		−71.88
	SUBTOTAL		−85.65
	TOTAL	79.46	

DISCRIMINANT FUNCTION II (165.11 minus 85.65 = 79.46)

Discriminant Function I (81.93) minus Discriminant Function II (79.46) = 2.47

The probability of the patient falling into Group I (i.e. suffer loss of seven or more I.Q. points) is .92.

The results obtained by the discriminant function analysis suggest that prognostication in regard to intellectual deterioration may very well be possible, but the weights were developed on a small sample of patients, and the study should be repeated on a larger population. It should also be mentioned that these weights were derived from an adolescent and adult population and are therefore not necessarily applicable to children. Patients with childhood epilepsy present a special problem in this respect. In the child one could visualize the existence of two separate processes; both would result in progressively lower IQ scores, but they would have different origins. One process would be arrest or slowing of mental growth, and the other an actual loss of previously acquired material. It is conceivable that a number of children with epilepsy whose IQ scores decrease over the years do not, in fact, suffer at that time from a deteriorating process, as the progressively lower IQ scores would suggest; but their mental growth curve may be flattened and their abilities are being measured against increasing chronological age, leading to progressively lower scores. An example might illustrate this point.

A seven-year-old boy was recently seen at the Michigan Epilepsy Center for reevaluation. At the time of initial evaluation he had suffered from psychomotor seizures and his Full Scale IQ was reported as 90. Seizures had stopped thereafter, but he was returned to the Center for reevaluation because of a learning problem in school. His IQ two years later was measured as 73. Using the weights of the discriminant function analysis, the formula predicted that the patient would fall into Group II (i.e. loss of six points or less, or actual gain in IQ points), with .75 probability on the basis of the information obtained at inital evaluation. This was, of course, in contrast to the actual finding because the patient had "lost" seventeen points and he should have been placed into Group I (i.e. loss of seven or more points). On the basis of the previous assumption that one may be dealing in certain cases not with actual deterioration but with arrest or slowing of development, the patient's current achievement on the IQ test was rescaled. This time we did not use his actual chronological age of seven years, but his previous age of five

years. This resulted in an IQ level of 98, or an eight-point increase over his previous achievement. This finding indicates that if the patient had been an adult, the formula would have classified him correctly, and we are dealing here not with deterioration from a higher level to a lower level, but merely with a markedly slower growth curve. This aspect of prognosticating intellectual achievements in children will require further detailed study.

The formula also does not take into account those few cases of epileptic patients who suffer from what has been termed "petit mal status" or "spike wave status." An IQ obtained during a period of marked cerebral electrical abnormality may be spuriously low and increase by ten or more points within a few days if the patient's EEG clears up spontaneously or as a result of change in anticonvulsant medication. "Petit mal status" may not always be so pronounced that it can be easily diagnosed clinically, and the correct diagnosis rests entirely upon the electroencephalogram. Two examples might serve as illustrations:

Example 1. Patient P. M. was, at the time of initial evaluation, a ten-year old boy who had suffered from a febrile convulsion at ages three, five and seven respectively. Subsequently, he developed afebrile seizures recurring every six months until the age of nine. Grand mal seizures became exceedingly frequent thereafter; he had approximately one seizure a day, and he also had one episode of status epilepticus. He was placed on Dilantin and had no further major seizures, but numerous minor attacks occurred during which the eyes rolled up and the head jerked backwards. These occurred at the rate of approximately twelve a day. There was a family history of convulsive seizures, his seven-year-old brother had febrile convulsions, the paternal grandfather had suffered from epilepsy, and one paternal cousin also had seizures in childhood. On clinical examination the child was somewhat confused and slightly disoriented, but the rest of the neurological examination was normal. The Wechsler intelligence scales were as follows: Verbal, 75; Performance, 74; and Full Scale, 72. His electroencephalogram is shown in Figure 20. It shows repeated episodes of high voltage spike wave activity lasting four to five seconds at a time and recurring every ten to fifteen seconds. For practical purposes the EEG showed nearly continuous seizure activity, but there were no obvious clinical manifestations in the patient. After having tried several anticonvulsant drugs without success in the hospital, the patient received Librium®

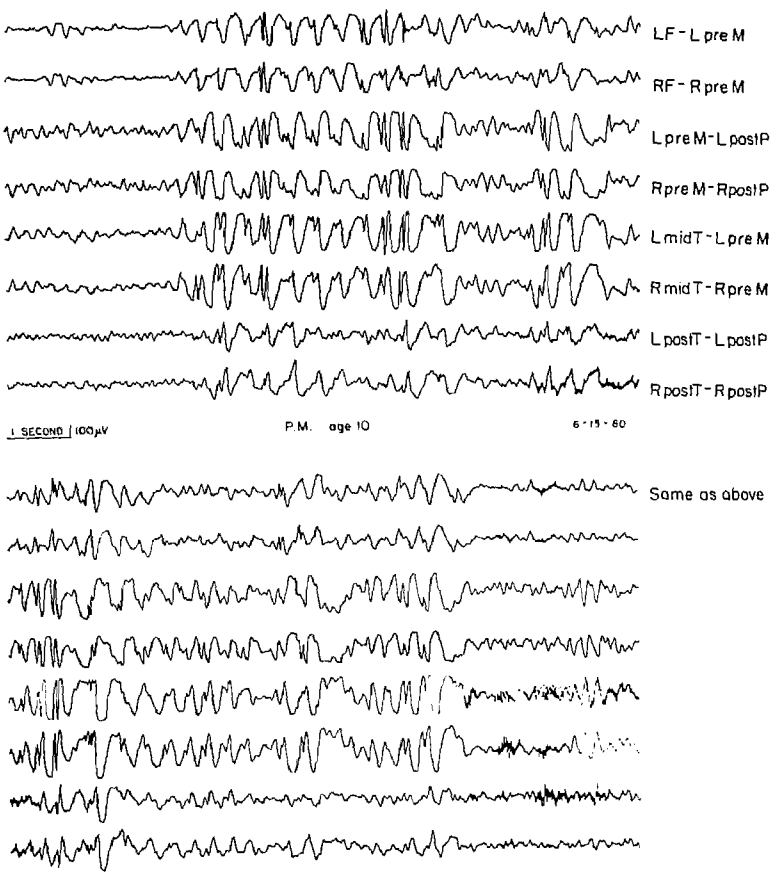


FIGURE 20. High voltage diffuse 2-3 c/s spike wave activity lasting several seconds, repeating every 10-15 seconds. Verbal IQ 75, Performance IQ 74, Full Scale IQ 72.

and this abolished the seizure activity in the EEG. The record showed a completely normal appearance during the waking state as shown in Figure 21, although there were still brief episodes of spike wave activity during sleep. The IQ, taken three days after the patient's EEG had shown marked improvement, was measured: Verbal, 90; Performance, 101; and Full Scale, 95. A reevaluation of the patient in 1966 showed the waking record still normal and during sleep there were some diffuse bursts but no appreciable spike components. The patient has not had any grand mal seizures in the meantime, although he did occasionally have some staring episodes. His Verbal IQ was 98; Performance IQ, 107; and Full Scale IQ, 102.

While this patient could have been regarded as a case of

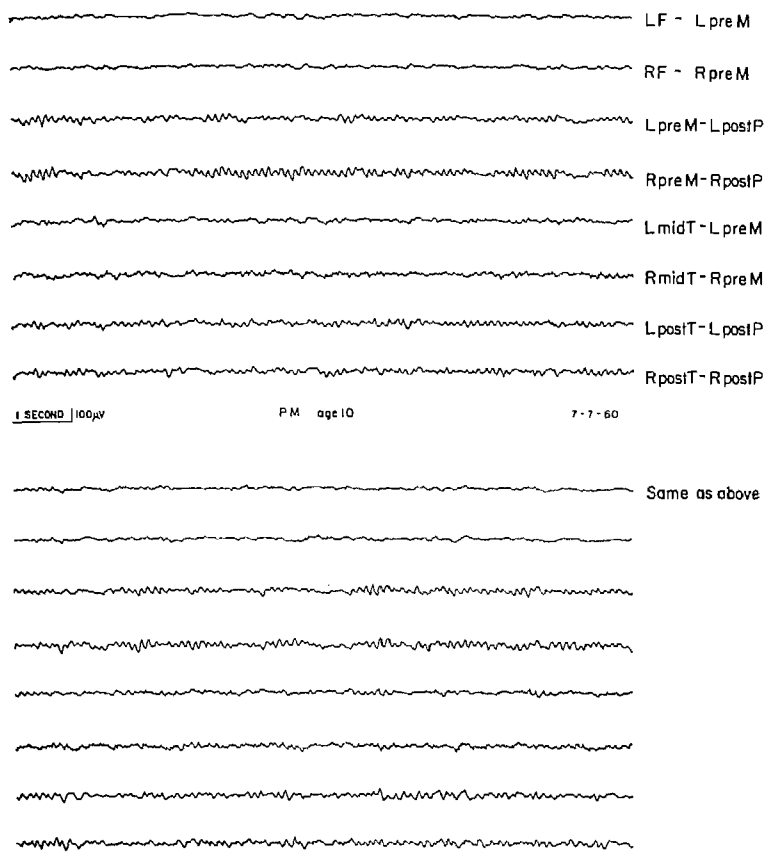


FIGURE 21. Record was obtained three weeks after that shown in Figure 20. Verbal IQ 90, Performance IQ 101, Full Scale IQ 95. Rather dramatic increase especially of Performance IQ.

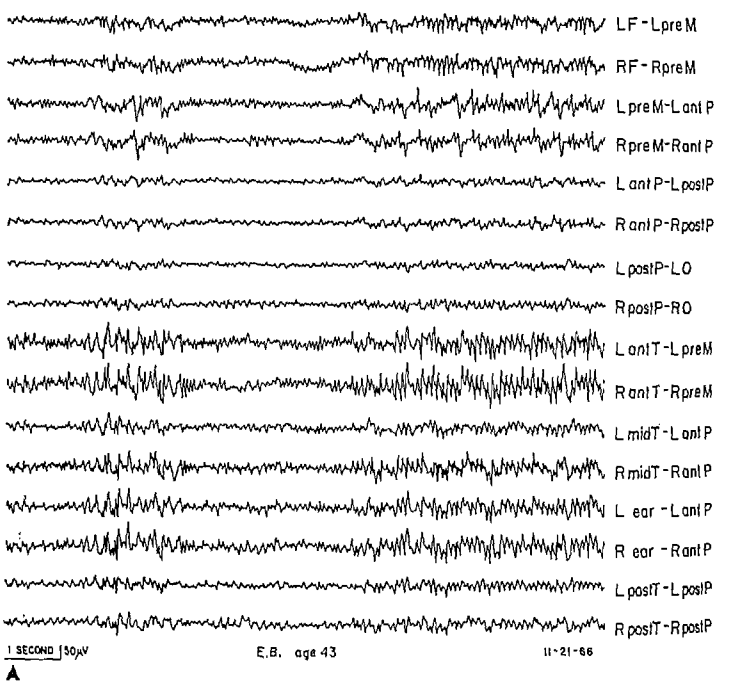
"petit mal status" or "spike wave status," patient E. B. presented a considerably different electroencephalographic picture but rather similar clinical findings.

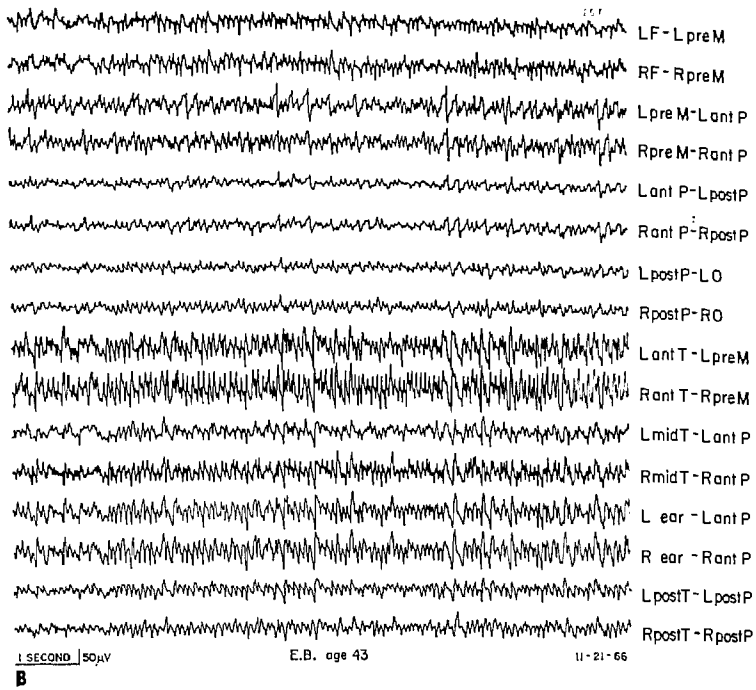
Example 2. Patient E. B. was a forty-three-year-old male, when seen in 1966, and since the age of two had suffered from nonfocal grand mal seizures which usually recurred once a year. From 1957 to 1965 he had a complete remission. Seizures recurred in 1965 after the death of his mother. He was then placed on Mesantoin® (200 mg four times a day) and had no major seizures thereafter, but he developed prolonged episodes lasting several days during which he is restless, confused, and unable to sleep. This state decreases after two or three days and the patient is mentally alert

without any difficulties for three or four days and then the cycle repeats again. An example of the patient's EEG is shown in Figures 22 A, B, C, D, and E. His IQ was obtained on a day when his electroencephalogram showed this marked disturbance, and it was recorded as a Verbal IQ of 98; Performance IQ, 71, and Full Scale IQ, 86. His IQ on a day when the electroencephalogram was essentially normal, as shown in Figures 23 A and B, was Verbal IQ, 104; Performance IQ, 84, and Full Scale IQ, 95.

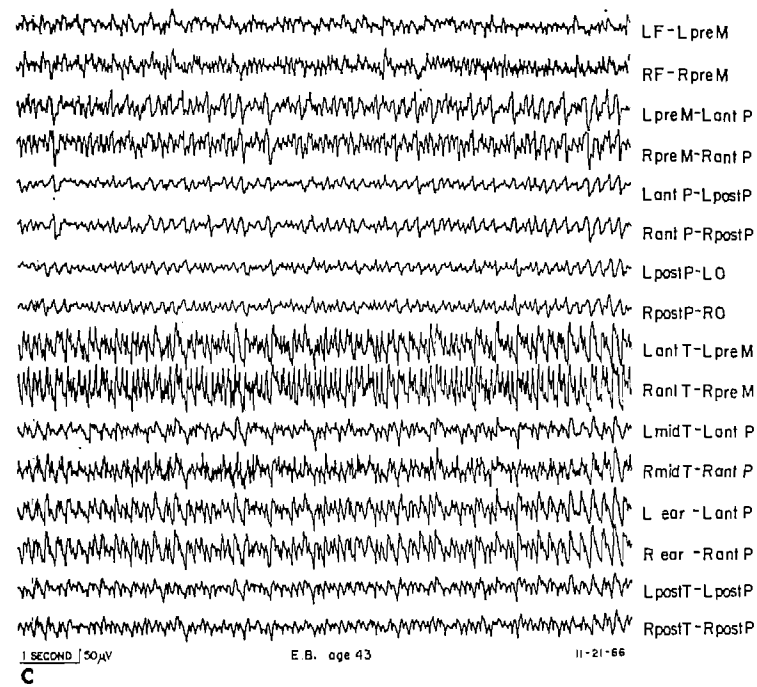
It was felt that this patient was on inordinate amounts of medication and it was decreased to Mesantoin® (100 mg four times a day), phenobarbital (65 mg three times a day), and Eskabarb® (100 mg at bedtime). This led to a marked improvement in the patient's condition. He had no major seizures and a marked decrease in frequency of occurrence as well as in length of the confusional states.

These cases clearly illustrate the value of the electroencephalogram in assessing the various causes of a patient's intellectual dysfunction. Due to the fluctuating nature of their disorder, epileptic patients lend themselves in a unique way to the study of mind-brain relationships, and the data that we have obtained so far are presented in the hope that they may stimulate further interdisciplinary investigations between psychologists, neurologists and electroencephalographers.




LF - L preM
RF - R preM
L preM - L ant P
R preM - R ant P
L ant P - L post P
R ant P - R post P
L postP - LO
R postP - RO
L ant T - L preM
R ant T - R preM
L midT - L ant P
R midT - R ant P
L ear - L ant P
R ear - R ant P
L postT - L post P
R postT - R post P
1 SECOND | 50μV
E.B. age 43
11-21-66

B


LF - L preM
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R ant P - R post P
L postP - LO
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L ant T - L preM
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R postT - R post P
1 SECOND | 50μV
E B. age 43
11-21-66

C

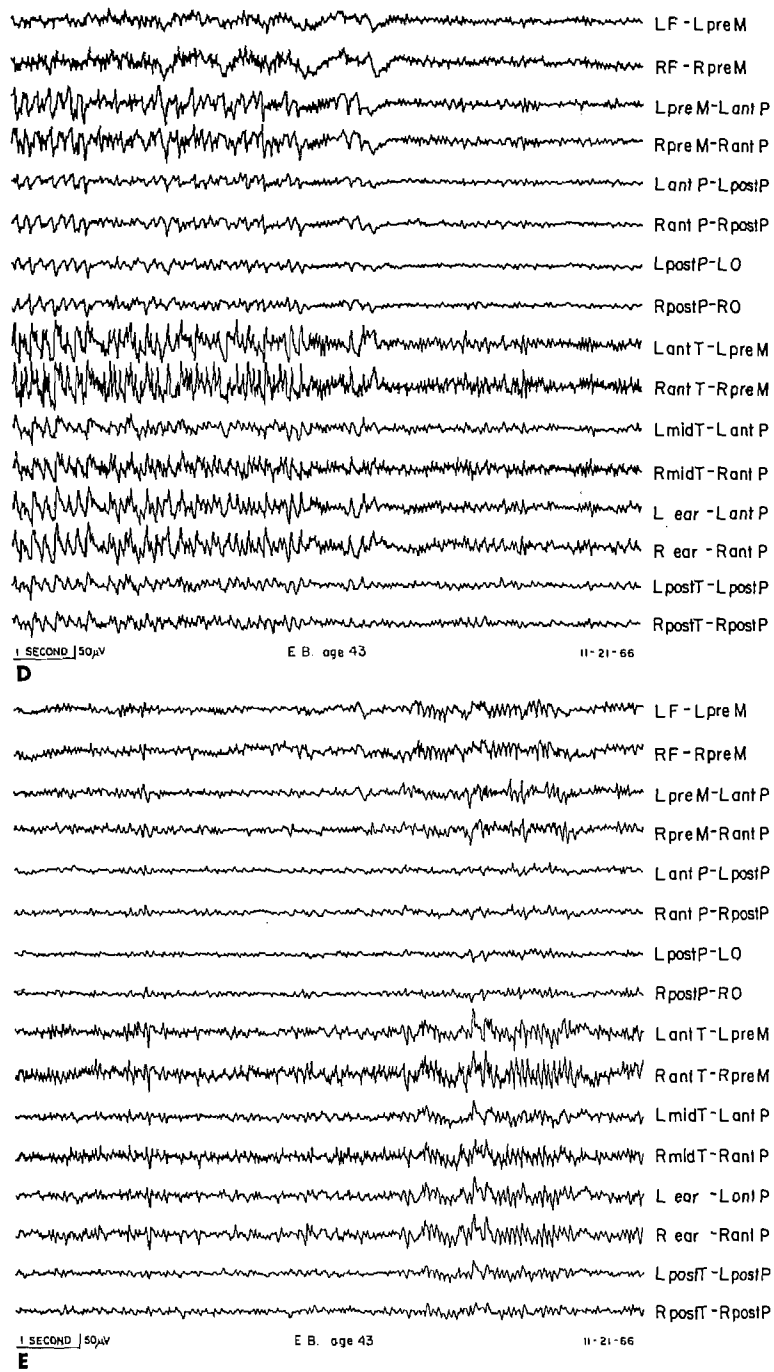

FIGURE 22. A-E represent 50 consecutive seconds of recording. Episodic high voltage diffuse spike activity most pronounced in anterior head regions lasting between 2 and 25 seconds, recurring every 5-15 seconds. Verbal IQ 98, Performance IQ 71, Full Scale IQ 86.

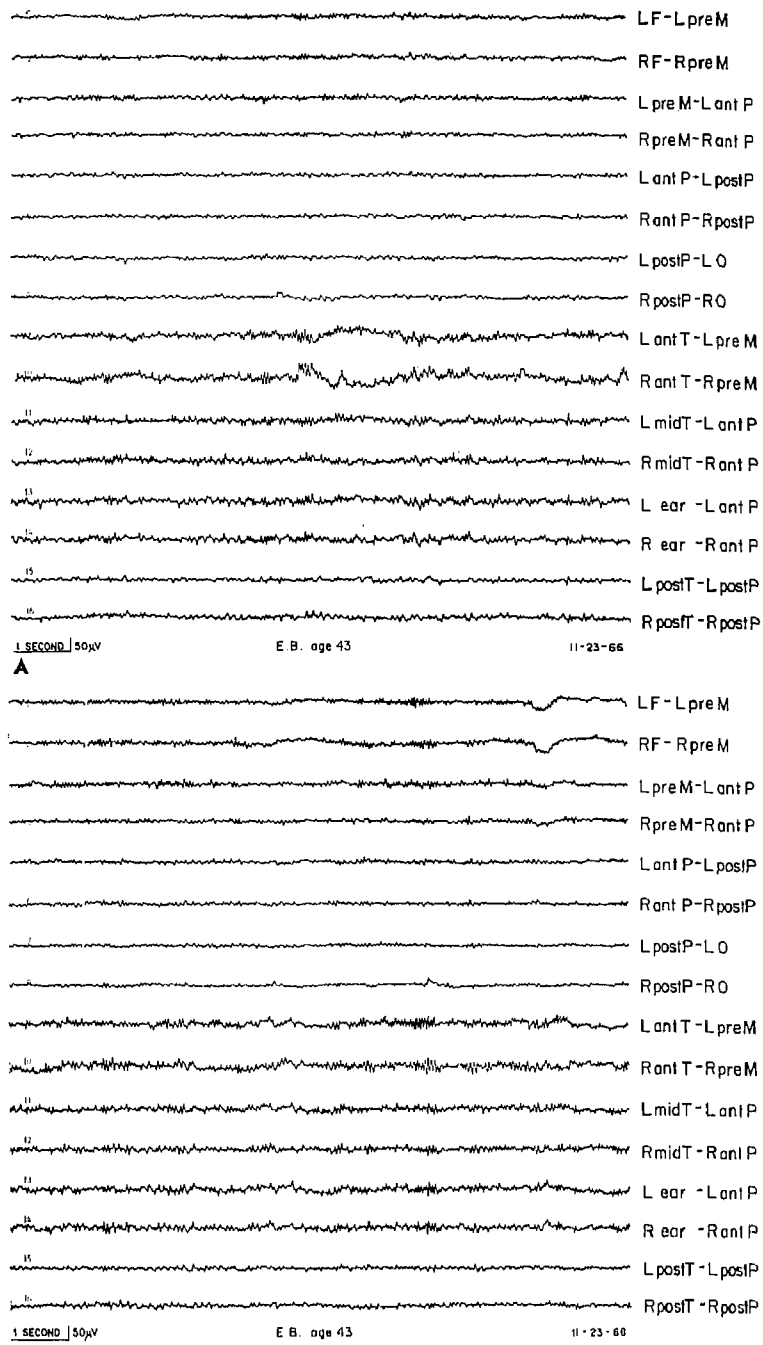

FIGURE 23. A and B represent 20 consecutive seconds of recording. Tracing was obtained two days after that shown in Figure 22. EEG somewhat disorganized but no seizure patterns. Verbal IQ 104, Performance IQ 84, Full Scale IQ 95. Further example that Performance IQ is more interefered with by seizure activity than Verbal IQ.

Chapter 14

PROGNOSIS FOR EMPLOYMENT

The fourth question that we had initially asked ourselves was, Will the patient be able to earn a living for himself or will he remain dependent upon others?

The second Michigan Epilepsy Center follow-up project provided preliminary information, in this regard, from forty-six patients. The other patients involved in the project were either still in some type of school situation or were housewives. Twenty patients were employed at time of follow-up, and twenty-six were unemployed. The statistically significant correlates, with findings obtained at the time of the initial examination in regard to employment state at follow-up, are shown in Table 110. The

TABLE 110

SIGNIFICANT CORRELATIONS OF FINDINGS ON INITIAL EXAMINATION WITH UNEMPLOYMENT AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Attended special school	−.388	2
Full Scale IQ	−.366	2
Average marks in school	−.359	2
Amount of theta activity in EEG	.341	5
Performance IQ	−.339	5
Verbal IQ	−.332	5
"Organic" findings on Bender-Gestalt Test	.331	5
Prognosis for intellectual functions	.315	5
Seizure activity in EEG	.310	10
Generalized paroxysmal activity in EEG	.308	10
Focal grand mal seizures	.292	10
Prognosis for behavior	.281	10

significant correlates between findings obtained at follow-up examination and employment state are listed in Table 111. The coding system had been constructed in such a manner that "presently employed" was marked as 1 and "unemployed" as 2; the high end of the scale therefore represents unemployment. It is apparent that unemployment was mostly related to lower intellect and/or organic mental changes on the initial as well as follow-up examination. There is also a significant correlation

TABLE 111

SIGNIFICANT CORRELATIONS OF FINDINGS ON FOLLOW-UP EXAMINATION WITH UNEMPLOYMENT AT TIME OF FOLLOW-UP

	r	*Significance Level* (%)
Organic mental changes	.477	1
Response to anticonvulsant medication	−.441	5
Serial 7 subtractions impaired	.415	1
Proverb interpretations concrete	.393	5
Recent memory impaired	.385	2
History of difficulty concentrating	.384	2
Behavior problems	.383	2
Verbal IQ	−.355	5
Full Scale IQ	−.339	5
Age	−.335	5
"Organic" findings on Bender-Gestalt test	.330	5
Remote memory impaired	.313	5
Amount of theta activity in EEG	.289	10
Nonparoxysmal diffuse hyperventilation buildup in EEG	.253	10

with behavioral difficulties. While this may not be surprising, it is, of course, of considerable interest that variables related to seizure types or seizure frequency did not show significant relationships. The only hint that seizures may interfere with employment is contained in the correlate which shows poor response to anticonvulsant medication. Unemployed patients, therefore, are not likely to be in complete remission. Analysis of variance between the employed and unemployed groups, utilizing the previously mentioned 190 variables, confirmed—as the asterisks show—the findings of the correlations matrix and placed them

in somewhat sharper focus. Behavioral problems head the list, these were probably of long standing, as we noted in the previous chapter, and so were intellectual difficulties. They manifested themselves probably during school age in the form of poor grades and also necessitated special education in approximately half of the unemployed patients. The six-year difference in mean age between the groups is important because it suggests that some of the patients may be getting a slow start on the employ-

TABLE 112

SIGNIFICANT DIFFERENCES BETWEEN EMPLOYED AND UNEMPLOYED GROUP

	Employed	*Unemployed*	*F*	*Significance Level (%)*
Behavior problem at follow-up*	1.9	3.4	7.5	1
History of school grades*	4.6	3.2	6.1	5
Age	26.5 yrs.	20.6 yrs.	6.1	5
"Organic" findings on Bender-Gestalt test*	2.5	4.3	5.1	5
Performance IQ*	101.9	88.3	5.1	5
Prognosis for intellectual functions*	3.6	5.1	4.8	5
Amount of theta activity in EEG*	3.6	4.8	4.8	5
Full Scale IQ*	101.3	88.5	4.6	5
Digit Symbol—Wechsler IQ	8.6	6.8	4.4	5
Paroxysmal activity in EEG	1.1	2.3	4.4	5
Clusters of minor seizures for several days, freedom from seizures for several weeks	2.7	1.3	4.2	5

ment market; but as they get older and their seizure disorder improves somewhat, they begin finding jobs. The hard-core unemployed epileptic individual is, in all probability, the patient with lower IQ, and/or organic mental changes with or without associated personality difficulty. The fact that seizures do not necessarily preclude employment is demonstrated by the observation that the variable "clusters of minor seizures for several days with freedom from seizures for several weeks" occurred significantly more frequently in the employed than in the unemployed group in this particular sample of patients. As had been pointed out in the chapter on seizure prognosis, patients who

TABLE 113

SIGNIFICANT DIFFERENCES BETWEEN EMPLOYED AND UNEMPLOYED GROUP

		Employed	*Unemployed*	X^2	*Significance Level* (C_t)
Postictal headaches					
	Absent	3	12	6.2	5
	Present	16	8		
Attended special school*					
	Yes	3	14	5.2	5
	No	16	12		
Majority of tests were not applicable due to small numbers in sample.					
Rotation of Bender designs					
	Absent	16	13	3.6	10
	Present	3	12		
Academic difficulties in school					
	Absent	15	11	3.6	10
	Present	5	15		
Postictal confusion (major seizures)					
	Absent	17	12	3.0	10
	Present	2	8		
Postictal fatigue (major seizures)					
	Absent	7	14	3.0	10
	Present	12	6		
Focal major seizures					
	Absent	8	18	2.8	10
	Present	12	8		

present this phenomenon are not likely to achieve a permanent remission. It also deserves to be repeated that the variable "present seizure state" did not show significant differences between the two groups.

It has been mentioned previously that the Michigan Epilepsy Center had received a grant from the U.S. Public Health Service, Division of Vocational Rehabilitation, to study the aspects that relate to employment problems of epileptic patients. The material from that study will not be presented here because it merits extensive discussion which is beyond the scope of this publication. It did, however, provide an opportunity to check the main findings that were mentioned here. In the material from the VRA project there was likewise no significant differ-

ence in regard to seizure frequency between employed and unemployed patients. The detailed breakdown for the VRA patients is shown in Table 114. Two important aspects emerge: (1) The patient who has seizures less than once a year is, for practical purposes, in remission and is employed in the majority of cases. This is of course what one would expect on general grounds and (2) the more interesting point is that on the bottom of the scale there is no difference between the groups. A considerable number of epileptic patients, therefore, are able to maintain employment in spite of having, on the average, several

TABLE 114

FREQUENCY OF OCCURRENCE OF SEIZURES AT PRESENT IN RELATION TO EMPLOYMENT STATUS

Code Number and Description	*Employed*	*Unemployed*
1 Less than once a year	32	12
2 *About once a year*	*6*	*5*
3 Two to three seizures a year	5	13
4 Four to six seizures a year	7	7
5 Seven to 12 seizures a year	4	6
6 Once a month	9	6
7 Two to three a month	11	9
8 Once a week	1	7
9 Several a week	13	19
Totals	88	84

seizures per week. The VRA study confirmed that seizures by themselves do not have to lead to unemployment. The major handicapping factors for the VRA group were likewise intellectual difficulties, organic mental changes, personality problems, and factors related to motivation.

The physician quite commonly hears the patient's complaint that he was fired because he had a seizure on the job, or he cannot find employment because "nobody will hire an epileptic." Although this may be the case in some instances, it has been my experience in virtually all cases where this was complained of by the patient, that subsequent mental status examination showed deficits which rendered the patient, for practical purposes, unemployable in a competitive work situation. The patient

may not be aware of these deficits, and it is much easier for him to blame his seizures for rejection by society, rather than organic mental changes, intellectual difficulties, or personality problems.

When the material from the VRA project is completely worked up, we should be able to provide formulas which will predict with reasonable accuracy the patient who is, in fact, unemployable in spite of all rehabilitative measures. More importantly, it should give the characteristics of those patients who are potentially employable, but for some reason or another have not succeeded in getting or maintaining a job. This would be the group towards which maximal rehabilitative efforts should be devoted.

Another interesting aspect of the findings is that they take the employment problems of the epileptic patient out of the strict realm of epilepsy (i.e. recurrent seizures) and place them in a more general framework. The factors that were found to be operative in the unemployed epileptic may well play a significant role in other hard-core unemployed individuals who tend to blame external circumstances rather than their own insufficiencies for their failure. It has been stated in the introduction to this book that the statistical methods used in this study to clarify aspects related to epilepsy could be applied without difficulty to any other condition one may want to investigate. Chronic unemployment is, in all probability, not only a sociological but, perhaps even more importantly, a medical problem in respect to the dimensions outlined above.

Chapter 15

INSTITUTIONALIZATION

A further question raised initially was in regard to the characteristics of patients who are likely to become permanent inmates of an institution for epileptics. The first follow-up study contained only five patients who had been institutionalized and the second study, seven patients. These numbers were too small for statistical purposes. We had, therefore, over the years transferred patients from Caro State Hospital for Epileptics to the Lafayette Clinic in order to get a clearer view of the problem. As previously mentioned in the chapter on seizure prognosis, fifty-seven of the Caro patients were included in the Lafayette Clinic inpatient review. These fifty-seven patients were contrasted against the 162 patients who had been referred from the community. Fortunately it turned out that there were no age or sex differences between the groups. The mean age was 26.6 years for patients from the community and 28.8 years for the Caro patients. There were eighty-six males and seventy-six females in Group I (patients from the community), and twenty-nine males and twenty-eight females in Group II (Caro State Hospital patients). Tables 115 and 116 show the variables that differed significantly between the two groups. The variables which are marked by an asterisk also showed significant differences in Tables 68 and 69 dealing with response to treatment in the hospital. The table containing the F tests demonstrates two main findings: (1) The Caro patients had an earlier onset and more intense seizure disorders than the patients referred from the community. There was a longer duration of illness, more frequent injuries during seizures, more different seizure types in

TABLE 115

SIGNIFICANT DIFFERENCES BETWEEN INSTITUTIONALIZED GROUP AND PATIENTS REFERRED FROM THE COMMUNITY

	Patients from Community	*Patients from Caro State Hospital*	*F*	*Significance Level (%)*
Duration of illness in years	12.2	22.7	45.8	1
Duration of main seizure type*	7.1	8.6	41.7	1
Amount of schooling*	3.8	2.4	41.0	1
Full Scale IQ*	83.6	64.0	36.8	1
Findings of cerebral pathology on neurological examination*	1.5	2.3	31.6	1
Frequency of injuries during seizures*	1.4	2.2	30.0	1
Focal atrophy on pneumoencephalography on the right	1.0	1.7	23.2	1
Age at time of onset of recurrent seizures in months*	170.7	84.1	21.7	1
Amount of alpha rhythm in EEG	2.8	2.0	19.9	1
Age at onset of first seizure in months*	151.6	65.3	19.5	1
Organic pathology suspected from psychological tests	2.5	3.1	17.3	1
Combination of seizures*	2.5	3.4	13.8	1
Evidence of bilateral cerebral disease*	1.9	2.3	12.8	1
Prenatal or perinatal injury suspected	1.4	1.9	12.5	1
Frequency of aura	2.6	1.8	10.7	1
Length of hospitalization in weeks*	6.8	9.2	8.8	1
Amount of theta activity in EEG*	2.8	3.3	8.5	1
Amplitude of background activity in EEG*	3.9	3.3	7.0	1
Amount of delta activity in EEG	1.1	1.3	6.9	1
Cerebral infection as etiological component	1.2	1.5	6.0	5
Frequency of maximal occurrence of seizures*	7.7	8.4	6.0	5
Neurotic tendencies on psychological testing	2.3	1.8	5.5	5
Clusters of seizures for several days, freedom from seizures for several weeks*	1.5	1.2	5.3	5
Amount of EEG abnormality*	3.4	3.8	4.9	5
Megimide induced seizure patterns, difficult to classify	2.8	3.7	4.8	5
Amount of fast activity in EEG	2.4	2.8	4.2	5
Evidence of left-sided cerebral disturbance from neurological examination and seizure patterns	1.4	1.8	4.0	5
Number of major seizures in hospital	3.1	6.6	6.4	5

TABLE 116

SIGNIFICANT DIFFERENCES BETWEEN INSTITUTIONALIZED GROUP AND PATIENTS REFERRED FROM THE COMMUNITY

		Patients from Community	*Patients from Caro State Hospital*	X^2	*Significance Level (%)*
Minor nonfocal motor seizures*					
	Absent	155	44	15.2	1
	Present	7	13		
Received regular schooling					
	Absent	9	14	14.7	1
	Present	144	39		
Focal grand mal seizures					
	Absent	92	19	9.2	1
	Present	70	38		
Theta rhythm present when patient has eyes opened*					
	Absent	151	46	5.9	1
	Present	11	11		
Focal grand mal variant seizure induced with Megimide*					
	Absent	121	37	5.4	5
	Present	8	9		
Received special schooling*					
	Absent	105	27	5.3	5
	Present	48	26		

the same individual, greater maximal frequency of seizures and more major seizures at the Lafayette Clinic. They also had more evidence of focal as well as diffuse cerebral pathology on clinical examination, pneumoencephalography, and psychological testing. The EEG mostly reflected cerebral damage with little alpha rhythm, more theta, delta and fast activity, and a greater amount of overall EEG abnormality. Amount of seizure patterns in the EEG, however, was not different between the groups, and (2) there were differences in regard to etiological factors. Prenatal and perinatal injuries, as well as cerebral infections, were significantly more common in the Caro group than in the group living in the community. A significant proportion of patients had been committed to the institution because of severe brain injury, making them unfit for life in the community, with epilepsy being superimposed.

We have repeatedly made the point before, that etiological factors did not seem to be of importance in regard to seizure control. The Caro State Hospital sample, however, showed that institutionalized patients had severe seizure disorders, and also more severe injuries to the central nervous system. The question arose, therefore, whether or not a greater intensity of the seizure disorder was a direct result of the more severe cerebral insults. To answer this question it was decided to divide the Caro State Hospital group into those patients in whom etiological factors had been present and into a group where no etiology could be demonstrated, and to compare the two groups on all variables. It should be mentioned at this time that the histories from Caro State Hospital were of excellent quality, containing very detailed information. In addition, we had in nearly all cases the opportunity to interview the parents after the patients had been transferred to the Lafayette Clinic. It was found that there were only twelve patients in whom absolutely no etiological factors could be implicated. When patients were included in whom one of the etiologies (prenatal or perinatal injury, postnatal head injury, cerebral infection, other significant external cause—e.g. cerebral malformation—, or family history of epilepsy) had been rated as questionably present, two groups could be formed. The first consisted of twenty-eight patients with no or questionable etiology; the other of twenty-seven patients with etiological factors. F tests and Chi Square tests were performed on the previously mentioned 190 variables. It was found that *no* statistically significant differences could be demonstrated between these two groups—apart from the variables dealing with etiology which had, of course, formed the basis of the separation into groups—except for the finding that a left-sided cerebral disturbance was found more commonly in the group in whom etiological factors were present (F 13.0, 1%). No significant differences were observed in regard to age at onset of illness, duration of illness, or to frequency, intensity or type of seizures. The IQ also was not significantly different (Full Scale 64 versus 61). This completely negative result was somewhat surprising and raised the question of whether we had contaminated our groups by including the cases of questionable etiology into those

with no discernible etiology, and by including family history of epilepsy as an etiological factor. It was therefore decided to take the twelve patients in whom no etiology had been present and contrast them with twelve patients who had had either definite cerebral infection or definite prenatal and/or perinatal injury. The major findings are shown in Table 117. Although we are dealing with a small sample, the trends are obvious. The patients with cerebral infection or perinatal injury were younger at the time of onset of their illness and younger in age at time of transfer to the Lafayette Clinic. This kept the duration of the illness essentially constant between the two groups. The group with known etiology also had an eleven-point lower mean IQ, but the intensity of the seizure disorder as expressed by remissions, frequency of maximal occurrence of seizures, frequency of seizures just prior to transfer to the Lafayette Clinic, frequency of seizures at the Lafayette Clinic, clusters of seizures in a given day, and occurrence of status epilepticus showed no differences between the groups. If there is a trend towards a difference at all, it would be that the group who had a definite etiology was actually slightly better off in respect to their seizure disorder. It is recognized that we are dealing with a very small sample of patients; nevertheless, there is no evidence that the intensity of the seizure disorder is related to the severity of cerebral injury.

Reviewing the patient material from Caro State Hospital, we noted that one is dealing essentially with three types of patients: (1) those who have an exceedingly intense seizure disorder, usually starting early in life, which does not yield to anticonvulsant treatment; (2) patients who have cerebral injuries, also usually acquired at an early age, leading to marked intellectual difficulties making them unfit for life in the community, and (3) a few patients with epilepsy whose main difficulty is not the intensity of the seizure disorder, or the severity of cerebral injury, but who show severe behavioral problems which cannot be tolerated by the environment.

The first group is the most interesting from the point of view of the epileptologist because it points to the existence of what one might call "malignant epilepsy." Fortunately this group is relatively small in size.

TABLE 117

COMPARISONS OF INSTITUTIONALIZED PATIENTS REGARDING THE INFLUENCE OF ETIOLOGICAL FACTORS

	No Etiology (N = 12)	*Definite Etiology* (N = 12)
Mean age at time of first seizure	7.8 years	3.1 years
Mean age at onset of recurrent seizures	10.4 years	5.9 years
Duration of illness	26.7 years	26.0 years
Number of patients who were in remission at time of transfer to Lafayette Clinic	0	2
Number of patients who had experienced remission in the past	2	2
Number of different seizure types in a given patient:		
One seizure type only	3	4
Two seizure types	5	4
Three or more seizure types	4	4
Main seizure types most difficult to treat:		
Grand mal focal	5	9
Grand mal nonfocal	3	1
Psychomotor seizures	4	1
Grand mal variant nonfocal	0	1
Grand mal variant focal	0	1
Number of patients whose seizures started during first year of life	2	5
Duration of seizure type most difficult to treat	more than ten years	more than ten years
Maximal frequency of occurrence of seizures	several per week	several per week
Frequency of seizures prior to transfer to Lafayette Clinic	2 to 3 a month	7 to 12 per year
Number of patients who had clusters of seizures in one day	9	10
Number of patients who had clusters of seizures over several days, with freedom from seizures for several weeks	3	1
Number of patients with status epilepticus	3	2
IQ	69.2	58.7
Number of major seizures during hospitalization at Lafayette Clinic	64	52
Number of minor seizures during hospitalization at Lafayette Clinic	66	39

Chapter 16

LIFE EXPECTANCY

In the second MEC follow-up study we had noted that out of 136 patients whose fate could be ascertained, thirteen (9.6%) had died. This is a rather high proportion if one considers the age group that one is dealing with. As had been stated in the chapter on seizure prognosis, the mean age of patients at the time of death was 18.5 years if one excluded the three patients who had suffered from brain tumors, and 24.5 years if they were included. These are, of course, unusually low ages and are probably, at least in part, due to the small sample. Nevertheless, the figures did agree with the literature that the average life span of patients with epilepsy is lower than that of the general population.

In order to get some more information on this topic, we had asked the Michigan Department of Health, Section of Vital Records, to send us a listing of all the patients whose death certificates had shown epilepsy, for the years 1960 through 1966. We also inquired about the total number of deaths, the mean age at time of death for all individuals, and the mean age at time of death of patients who had seizures. Table 118 lists the findings. Age at time of death was expressed by the median rather than the mean because of infant mortality and the open-end age beyond ninety years. The table indicates that the diagnosis of epilepsy had appeared on the death certificate in approximately 0.1 per cent of all cases. It also shows that the median age at time of death of the patients in whom epilepsy was noted on the death certificates was approximately two and one-half decades below that of the average resident of the State of Michigan.

TABLE 118

NUMBER AND MEDIAN AGE AT TIME OF DEATH DUE TO ALL CAUSES IN THE STATE OF MICHIGAN COMPARED WITH PATIENTS WHERE EPILEPSY WAS LISTED AS DIRECT OR CONTRIBUTING CAUSE OF DEATH*

Year	*Total Deaths*	*Median Age at Death*	*Epilepsy*	*Median Age at Death*
1960	67,912	68.3 years	81	35.2 years
1961	67,375	68.7 years	74	40.8 years
1962	70,049	69.1 years	95	41.8 years
1963	72,438	69.3 years	91	34.7 years
1964	72,129	69.2 years	97	36.5 years
1965	73,665	69.5 years	109	41.8 years
1966	74,596	69.5 years	119	43.5 years

* Courtesy Michigan Department of Public Health, Vital Records Section

It has been pointed out in the discussion of the literature that studies based on death certificates alone will give only general trends rather than completely accurate data. The problem is that the presence of epilepsy frequently is not reported on the death certificates. The total number of patients who have epilepsy undoubtedly exceeds that which is reported on the certificates. This is not merely an assumption, as I failed to find the name of one of my former epileptic patients on the list supplied by the Michigan Department of Health. When the specific death certificate was requested it was noted that the cause of death had been listed as drowning and the diagnosis of epilepsy had not appeared on the death certificate. The wording on the death certificates in regard to significant chronic illnesses is actually so ambiguous that there is no particular reason to include the diagnosis for the majority of cases. The most relevant section of the Michigan death certificate is represented in Figure 24. The emphasis is obviously on conditions that are regarded as having directly contributed to the death of the person. Unless the patient's death is actually witnessed, it is impossible to say whether a convulsive seizure had led to the patient's death or not. There is no space provided on the death certificates to list the chronic illnesses the patient may have suffered, regardless of whether or not they were considered by the physician as a contributory cause of death. These points are made here to demonstrate that

19. CAUSE OF DEATH Enter only one cause per line for (a), (b), and (c) * This does not mean the *mode of dying*, such as heart failure, asthenia, etc. It means the disease, injury or *complication which caused* death.	MEDICAL CERTIFICATION I. DISEASE OR CONDITION DIRECTLY LEADING TO DEATH*(a) _____ ANTECEDENT CAUSES Morbid conditions, if any, giving DUE TO (b) _____ rise to the above cause (a) stating *the* underlying cause last. DUE TO (c) _____ II. OTHER SIGNIFICANT CONDITIONS Conditions contributing to the death but not related to the disease or condition causing death.	Interval Between Onset and Death
19d. DATE OF OPERATION	19e. MAJOR FINDINGS OF OPERATION	20. AUTOPSY? Yes ☐ No ☐

21a. ACCIDENT (Specify) SUICIDE HOMICIDE	21b. PLACE OF INJURY (e.g., In or about home, farm, factory, street, office bldg., etc.)	21c. (CITY, VILLAGE, OR TOWNSHIP) (COUNTY) (STATE)
21d. TIME OF INJURY (Month) (Day) (Year) (Hour) m.	21e. INJURY OCCURRED While at Work ☐ Not While at Work ☐	21f. HOW DID INJURY OCCUR?

22. I hereby certify that I attended the deceased from _____, 19____, to _____, 19____, that I last saw the deceased alive on _____, 19____, and that death occurred at _____m., from the causes and on the date stated above.

23a. SIGNATURE (Degree or title)	23b. ADDRESS	23c. DATE SIGNED

FIGURE 24. Copy of medical section of death certificate.

the Vital Statistics Section of the Michigan Department of Health has, at present, no way of knowing what the median age at time of death is for all patients who have suffered from epilepsy. When data based on death certificates are published in the future, it would be advisable to describe the relevant sections of the death certificates so that the reviewer can form an opinion about the completeness of the sample.

The most reliable way of gathering information on this topic is, of course, through follow-up of large numbers of patients for a long period of time, as is currently being done in Denmark. Our results from the review of death certificates are given here to demonstrate methodological problems, and so that they can be compared with other data that are being collected through follow-up studies. In spite of the difficulties which one encounters in the interpretation of data from death certificates, it is interesting that the findings do agree with the current study by Henriksen *et al.*, who had noted that the majority of their patients had died between the ages of thirty and forty-five years.

Chapter 17

SUMMARY

SEIZURE PROGNOSIS

Review of the literature showed that there has been no substantial improvement in *long-term* remission rates of epileptic patients over the past sixty years. Statements that approximately 80 per cent of patients are controlled by anticonvulsant medications are usually due to short follow-up periods and the inclusion of "improved" patients in the "controlled" group. A direct relationship has been shown to exist between length of follow-up and the percentage of patients who are seizure free at any given time. In regard to characteristics of patients which are likely to influence prognosis, the literature showed consensus on the following features: Patients who are normal in all other respects, except for the seizure disorder, tend to have a good prognosis especially if they have only grand mal seizures. Patients whose EEG is normal or normalizes with treatment can likewise expect a good outcome. The prognosis becomes poor with long duration of illness, a combination of different seizure types, large total number of seizures, and early age of onset.

Opinions are somewhat divided in regard to the importance of frequency of occurrence of seizures, whether seizures occur in the waking or sleeping state, heredity or other etiological factors, and abnormal findings on neurological examination.

It is repeatedly pointed out in the literature that patients with psychomotor seizures have a poorer prognosis than patients who have grand mal seizures. It should be borne in mind, however, that psychomotor seizure patients usually also have additional grand mal seizures and, therefore, one tends to compare patients

who have more than one seizure type with those who have only one seizure type. This fact should be considered in future research dealing with psychomotor epilepsy. It is apparent that major seizures have always responded better to anticonvulsant treatment than minor attacks, and modern drugs have not changed this pattern appreciably. The electroencephalogram has been shown to relate only in part to seizure prognosis. The relationship tends to improve if one looks at specific features of the tracings rather than relying on a global rating of normal versus abnormal. It is important to recognize that focal seizure discharges in a child's electroencephalogram do not necessarily represent the fixed atrophic type of lesion that one is accustomed to find in the adult.

In regard to febrile convulsions, the literature review indicates that they can be roughly divided into two groups: (1) simple or "benign" febrile convulsions and (2) epilepsy triggered by fever. It is interesting to note that essentially all the criteria that are given for differentiating between these two conditions also have been listed as being of importance in distinguishing between cases of epilepsy with good or poor prognosis.

Pyknolepsy was extensively discussed and it was demonstrated that the condition originally described under this name does not represent a clinical entity, and it seems to serve no purpose to perpetuate the term.

The prognosis of petit mal is still somewhat controversial, but the majority of authors feel that the seizures gradually decrease in number and intensity during adolescence and adulthood so that they do not form a major handicap for the patient later on. Precise figures for actual complete remissions are not readily available because the follow-up examination would have to include EEG evaluations in all instances. Historical reports about cessation of petit mal are unreliable. Approximately one-third to one-half of all patients starting with petit mal develop grand mal seizures later on. There is suggestive evidence that subsequent development of grand mal can be prevented by combined prophylactic treatment. This aspect deserves more intensive investigation using matched groups.

Infantile spasms—hypsarhythmia represent the most severe

form of childhood epilepsy. The success and failure of steroid treatment was discussed and the point was made that immediate treatment seems to be imperative if one wants to avoid the profound mental decay accompanying the condition. It was suggested that infantile spasms—hypsarhythmia be regarded by the pediatrician and general practitioner as a medical emergency requiring immediate intensive treatment by specialists in the hope that permanent and severe loss of intellectual functions can be prevented.

In regard to posttraumatic epilepsy, there is still some controversy whether the patient's prognosis for long-term seizure remission differs from that of seizures due to other etiologies. Part of the difficulty resides in a problem of definition, namely, Does a single seizure after trauma constitute "epilepsy" or is the presence of several recurring seizures required for such a diagnosis? There tends to be agreement that the incidence of posttraumatic seizures stands in direct relationship to the severity of the cerebral injury. Penetrating wounds in the central-parietal regions appear to be most epileptogenic. The maximum incidence of posttraumatic epilepsy after wounds of this type was given in the literature as 65 per cent. This still leaves approximately one-third of patients who do not develop seizures after such injury. It seems therefore that cerebral damage, although a potent epileptogenic factor, cannot be sufficient cause for the development of a chronic seizure disorder. It is important to point out also that the probability for terminal remissions was shown, in two separate studies, to bear no relationship to the intensity of the injury. In general, the course of true posttraumatic epilepsy appears to be relatively mild with seizures spaced by fairly long intervals.

In contrast to medical treatment there has been definite progress in regard to surgical results. This is mostly attributable to the introduction of electroencephalography which demonstrated that patients with psychomotor seizures may have a single focal lesion in one temporal lobe. The surgical results do not seem to deteriorate in relation to length of follow-up as is the case with medical treatment. Operative intervention discloses, in a number of instances, previously unsuspected small but gross le-

sions which can be removed *in toto* with subsequent arrest of seizures. Unfortunately most patients with psychomotor seizures have multiple areas of pathological electrical activity, and only a relatively small number of patients become eligible for operation. Patients with focal discharges in areas other than the temporal regions tend to have a poorer surgical result. In severely disabled patients with infantile hemiplegias, uncontrolled seizures, and socially intolerable behavior, hemispherectomy appears to be of value. It was pointed out that neurosurgical follow-up criteria of patients have frequently been quite loose, and specific suggestions for improvements were made.

In order to determine long-term prognosis of seizure patients and the factors that are responsible for a good or poor outcome, two follow-up studies were conducted at the Michigan Epilepsy Center. The first was in the nature of a pilot study testing the data collection and data analysis procedures. Thirty-two children were involved who had been followed for at least five years after initial evaluation. A two-year terminal remission had occurred in 33.3 per cent, and a five-year terminal remission in 29.6 per cent. The second study dealt with ninety patients of all ages who had been followed for at least five years after initial evaluation. The two-year terminal remission rate was 32.2 per cent, and the five-year terminal remission rate was 16.7 per cent. These findings agree with the majority of studies published in the literature.

In order to arrive at prognostic indices for good versus poor outcome, the clinical and electroencephalographic findings were coded, punched on IBM cards, and subjected to the following statistical procedures: intercorrelation of findings, factor analysis, analysis of variance, and discriminant function analysis. Factor analysis produced four factors that were relevant for prognosis:

1. Epilepsy associated with cerebral damage.
2. EEG seizure activity.
3. Mixed psychomotor epilepsy.
4. Specific seizure propensity.

The following variables showed loadings on the various factors:

Ad 1. Patients with lowered IQ, "organic" features on psychological tests, abnormal findings on neurological examination, and slow landmarks of development showed

persistent seizures on follow-up and were unemployed.

Ad 2. The EEG was found to behave for the most part as an independent variable but was not likely to become normal if it showed seizure patterns at time of initial evaluation while the patient was already on some anticonvulsant medication. The factor loading in regard to seizure outcome was quite low.

Ad 3. Patients with psychomotor seizures in combination with other seizure types, in the presence of associated psychiatric difficulties, were found to have done poorly in regard to seizure outcome, behavior, and employment.

Ad 4. This factor dealt only with frequency of occurrence of seizures. This was shown to be unrelated to all other variables that were sampled, and this factor constitutes the core of the epilepsy problem.

Analysis of variance confirmed the findings obtained from the intercorrelation matrix. The most important variables that distinguished patients who had shown a two-year terminal remission from those who continued to have seizures were frequency of injuries during major seizures, number of different seizure types in the same patient, duration of seizure disorder, presence or absence of psychomotor seizures, presence or absence of clusters of seizures over several days followed by freedom from seizures for several weeks, degree of presence of seizure patterns in the initial EEG, and amount of overall EEG abnormalities.

Inasmuch as the patients in these samples had for the most part been treated by their family physicians rather than specialists in neurology, an attempt was made to compare these treatment results against findings obtained by the Neurology Outpatient Service of the Lafayette Clinic. One hundred twenty-three patients had been followed regularly for periods ranging between two and seven years. Seventy-four per cent of these patients had had a seizure within six months prior to their last clinic visit. In a subgroup of fifty-six patients who had been followed regularly for at least five years, a terminal remission of at least two years prior to last clinic visit had occurred in only 14.3 per cent of cases. It should be borne in mind, however, that the Lafayette Clinic Outpatient Service tends to see the more

difficult treatment problems, and patients who continue to attend outpatient clinics are likely to represent a negative selection. Findings from seizure clinics merely point to the existence of a group of hard-core, difficult to treat patients, but give no definite indication about the relative size of this group in comparison to the total epilepsy population.

Inasmuch as outpatients may or may not adhere to their prescribed drug regime, they do not readily lend themselves to a description of the characteristics of the patient whose seizure disorder is indeed resistant to anticonvulsant drugs. For these reasons, the results of treatment of 245 epileptic inpatients who had been hospitalized for at least three weeks on the Neurology Inpatient Service of the Lafayette Clinic were evaluated. One hundred thirty-two of these patients had been referred from the community because of uncontrolled seizures; eighty-two had been referred from the state hospital system of the State of Michigan for research and/or teaching purposes, and thirty-one had been admitted from the community because of marked behavioral difficulties. Of the 132 patients who had been referred from the community because of inadequate seizure control, 45.5 per cent did not have any seizures during hospitalization, 25.7 per cent had between one and three seizures, while 28.8 per cent had more than four seizures in spite of maximum treatment efforts. The subgroup of 132 patients, as well as the total group, were subjected to analysis of variance in order to delineate the characteristics of the patient who is unresponsive to maximum treatment efforts in the hospital. It was found that intensity of seizure disorder was the most important aspect in regard to treatment response. Presence or absence of presumed etiological factors was not of importance. The seven criteria that had differentiated between the remitted and the unremitted group in the long-term follow-up study of the Michigan Epilepsy Center also were found to have been important in the success or failure of short-term inpatient treatment. In addition, frequency of seizures immediately prior to hospitalization was important in regard to seizure control while hospitalized.

Discriminant function analysis based on these eight variables was performed. It classified correctly 76 per cent of the patients

who did not have seizures in the hospital and 81 per cent of those who had at least one seizure while on adequate medication. Cross-validation utilizing the sample of patients from the second follow-up study of the Michigan Epilepsy Center confirmed the results. The formulas for classifying the patients in regard to their likelihood of achieving seizure control, either in the hospital situation or as outpatients, were presented.

It was observed that the "seizure propensity" of the epileptic patient (i.e. tendency towards spontaneously recurring seizures) was not related to his "seizure threshold" as measured by the amount of Megimide needed to induce a clinical seizure. The implications of this finding were discussed from a theoretical as well as practical point of view.

Suggestions for the use of the discriminant function weights were made, especially in regard to selection of patients for inpatient treatment, and whether or not a patient's report about his current seizure frequency can be trusted. The weights were developed on predominantly adolescent and adult patients who already had been on some drug regime prior to their evaluation by a neurologist. Therefore, they will not necessarily be applicable to children or patients who have just experienced their first seizure.

The finding reported in the literature, that duration of seizure disorder prior to initial evaluation is important for prognosis, was confirmed. Eighty-five per cent of the patients seen in the first year had achieved a terminal remission of at least two years. If the patients were seen within the second year after the onset of their illness, the percentage of two-year terminal remissions had already dropped to 50 per cent, and if the illness had persisted for ten years or longer, the remission rate had dropped to 13 per cent. The possible implications for the pathophysiology of epilepsy were discussed and suggestions to study the phenomenon more intensively were made.

BEHAVIOR PROGNOSIS

As far as behavior is concerned, it was found in both follow-up studies that the tendency was towards improvement of ab-

normalities with the passage of time. Behavioral disturbances did not appear for the first time, in these samples, years after the seizure disorder had manifested itself; they either preceded the seizures or occurred at about the same time as seizures made their first appearance. Behavioral difficulties were most common and most persistent in the group of patients who had evidence of some form of cerebral damage. A discriminant function analysis was performed: 77.3 per cent of patients who did not have behavioral difficulties and 85.0 per cent of those who did were correctly identified. The variables related to the classification were Performance IQ, "organic" features on psychological tests, presence of seizures during the first year of life, history of behavioral difficulties in school, feeding problems in infancy, talking age, special schooling, average school grades, adverse social environmental factors, and objective findings of cerebral pathology on neurological examination. This aspect of the study represents preliminary data because it has not yet been cross-validated on another sample.

PROGNOSIS FOR INTELLECTUAL FUNCTIONS

The literature shows considerable controversy in this respect. There are only two points of definite agreement:

1. Epileptic patients can be subdivided into two groups. One might be called "epilepsy only," and the other, "epilepsy associated with brain damage of varying degrees." This latter group has definitely lowered intelligence as one might expect.
2. Epileptic patients show more fluctuation in upward or downward direction on test-retest measures than the normal population.

A further point upon which most authors are agreed is that patients whose seizures start in childhood have lower intelligence than those in whom the disorder manifests itself first in adolescence or adulthood. On the other points listed below there tends to be agreement between authors, but opinions to the contrary exist.

1. In cases of "epilepsy only," the intelligence level is

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1. In cases of "epilepsy only," the intelligence level is

within normal limits but shifted towards the lower end of the normal range.

2. Frequency of major seizures tends to be directly related to intellectual level.

3. A small but statistically significant decrease in intellectual functions can be seen on test-retest measures as far as group mean values are concerned.

4. The Performance areas of the Wechsler IQ scale appear to be more affected in epileptic patients than the Verbal areas.

The concept of "epileptic personality" was purposely omitted from consideration of the literature review because there exist only opinions and no reliably measured data.

The Michigan Epilepsy Center's second follow-up study contained fifty-six patients who had been tested twice on the Wechsler IQ scales with intervals ranging between five and nine years. On the initial tests, the mean Full Scale IQ was 94.5 with a Performance IQ of 95.7, and a Verbal IQ of 94.9. At the time of follow-up, the values were 93.6, 91.8, and 92.4. The decrease in Performance IQ was significant at the 1 per cent level of confidence, and that of the Verbal IQ at the 5 per cent level. A comparison of patients whose Full Scale IQ had decreased by seven or more points against those in whom the IQ had decreased less, remained stable or had increased, demonstrated that the patients with initially higher IQ levels tended to show decrease more commonly than patients in the lower intellectual range. This phenomenon could explain, in part, why there are proportionally fewer epileptic patients in the bright normal or superior range of intelligence than in the average population. The loss is usually not marked enough to place the patient into the dull-normal or borderline defective group. The point was made that a "normal" IQ score in the epileptic patient does not necessarily reflect his pre-illness intellectual level. The possible relations to emotional functions were discussed.

The Performance IQ was more affected by the seizure disorder than the Verbal IQ. It was demonstrated that seizures per se can lead to decrease in Performance IQ. The IQ tended to rise if the patient achieved a terminal remission of at least

two years. This was not the case if the seizure disorder was merely improved.

Discriminant function analysis was performed and criteria developed that would allow prediction as to whether a patient's IQ is likely to deteriorate. The formula classified correctly 95 per cent of patients whose IQ had dropped by seven or more points and 83 per cent of the others. The variables involved in the prediction were as follows: initial Full Scale IQ, number of different seizure types in the same patient, frequency of major seizures, clusters of seizures for several days—freedom from seizures for several weeks, "organic" features on psychological tests, presence of adverse social environmental factors, and EEG background amplitude. The formula has not been cross-validated as yet on another sample and will apply mostly to adolescents and adults rather than children.

Age at time of onset of the seizure disorder was not related to seizure outcome in this sample of patients. Definite relationships existed, however, between age of onset and intellectual functions. The mean Full Scale IQ of patients whose seizures started between birth and three years of age was 84.8, for the patients whose seizures started between four and twelve years it was 90.4, and for those who developed seizures between thirteen and twenty-seven years of age it was 101.3. A seizure disorder starting early in life, therefore, does not necessarily have a poor prognosis as far as seizure control is concerned but is likely to be associated with lowered intelligence, regardless of presumed etiology.

It is of considerable interest that modern statistical studies corroborated four of the points that were made by Turner in 1907 as being unfavorable in regard to intellectual functions:

1. Young age at time of onset of the illness.
2. Presence of major as well as minor seizures.
3. Frequent seizures.
4. Occurrence of the seizures in series.

EMPLOYMENT

Intercorrelation of findings on the patient sample from the second MEC follow-up study showed that employment problems

in the epileptic patients were related mainly to lower IQ, organic mental changes, and behavioral difficulties. It was surprising to note that seizure frequency was not related to the patient's employment state. This finding could be checked on another sample of 172 patients and was found to hold true, if patients whose seizure frequency was less than once a year were excluded.

INSTITUTIONALIZATION

The findings of fifty-seven patients from Caro State Hospital for Epileptics were contrasted against those of 162 patients referred to the Neurology Inpatient Service of the Lafayette Clinic from the community, in order to define the characteristics of patients who have to be institutionalized. It was found that the institutionalized patients tended to consist essentially of three groups: (1) patients with severe cerebral injuries, usually acquired early in childhood, (2) exceedingly intense seizure disorders, also usually starting early in life, and (3) some patients with epilepsy whose main difficulty is not the intensity of the seizure disorder or the severity of cerebral injury, but who show severe behavioral problems which cannot be tolerated by the community.

A comparison of institutionalized patients with known etiological factors against those in whom no recognizable etiology was present did not show appreciable differences between the groups. There was no evidence that the intensity of the seizure disorder was related to the intensity of cerebral injury.

LIFE EXPECTANCY

The literature review pointed out that the life expectancy of epileptic patients tends to be lower than that of the general population. Status epilepticus is still a significant cause of death, especially in patients who are institutionalized. There exists a group of patients with severe and uncontrollable seizures who die in early adulthood from generalized physical and mental deterioration. Death as a direct result from a seizure is quite

infrequent but does occur on occasion and is not preventable at all times. Inasmuch as patients with nocturnal seizures may roll over in bed and suffocate, the importance of supervised sleeping arrangements was stressed.

In order to check on the reports in the literature regarding life expectancy of epileptic patients, a survey of death certificates was carried out. The Michigan Department of Public Health calculated for us the annual median age at time of death for all persons who had died in the State of Michigan during the years 1960 through 1966, as well as that of persons where epilepsy was listed as primary or contributory cause of death on the death certificates. It was found that the median age at time of death from all causes ranged between 68.3 and 69.5 years. The median age at time of death for patients where epilepsy was mentioned on the death certificate ranged between 35.2 and 43.5 years. Surveys of this type have inherent methodological difficulties which were discussed and can only provide evidence for trends rather than leading to firm conclusions. Suggestions about improvements in the format of death certificates were made.

CONCLUSIONS

It has been mentioned in the Foreword that one of the main reasons for writing the book lay in the hope that some clues may be uncovered in regard to the pathophysiology of epilepsy. Reviewing the literature and my own investigations, it would seem clear that in the majority of instances epilepsy is *not merely* a symptom of a variety of other etiological conditions. By this I do not mean to deny the importance of the symptom of convulsive seizures in a patient who is developing a brain tumor, or in conditions such as tuberous sclerosis, Sturge-Weber syndrome, Unverricht's myoclonus epilepsy and the like. What is meant is that after a careful neurological evaluation has been performed, the majority of patients with chronic recurring seizures will not be found to have any other significant disease. Lest there be some misunderstanding on this point, I would like to reemphasize that a patient who starts with convulsive seizures at any age deserves the most careful neurological workup in order to eliminate the possibility of other neurological or metabolic illnesses; but the fact that convulsive seizures can be a symptom of a great variety of different illnesses affecting the central nervous system should not necessarily argue against the additional existence of a condition which I have called here "specific seizure propensity" of the individual. It is this aspect that deserves intensive study in the future. Although some type of injury to the central nervous system frequently can be demonstrated in patients with chronic seizure disorders, this is not a necessary nor sufficient cause for the disorder.

The difference between seizure threshold and propensity

towards spontaneously recurring seizures is likely to be of fundamental importance in the understanding of epilepsy. While a convulsive seizure is a symptom of a temporarily lowered threshold, it will remain isolated or infrequent unless the individual also has the necessary mechanisms for propensity towards spontaneously recurring attacks. The intensity of that latter factor is likely to make the difference between patients who have occasional seizures only and patients who are not controllable by current anticonvulsant treatment. It also may well make the difference between children who have what is now called "benign" febrile convulsions and "epilepsy triggered by fever."

Hughlings Jackson once pointed out that when confronted with an epileptic patient ". . . the first question in my mind is not 'Is it a case of epilepsy?' but 'Where is the lesion permitting occasional excessive discharge?'" This was indeed a giant step forward nearly one hundred years ago, but we should not continue merely to echo Jackson's thoughts. The great majority of neurophysiological and neurochemical investigations still deal with the "epileptogenic focus" or the properties of the "epileptogenic neuron." These are important studies, but they are likely to be insufficient in providing the final answer to the problem. In addition to Jackson's question, one should also ask one's self, What are the factors that are responsible for the spread of abnormal electrical activity in this particular patient? Even more important would be the question, How does the patient's condition differ on the five days of the week when he is seizure-free from that of the sixth day when he has an attack? The neurophysiological and neurochemical events that lead up to this sixth day of the overt seizure would deserve at least equal attention as that which is being paid to the epileptogenic focus. The focus, after all, tends to be a more constant event rather than an intermittent one. Studies which deal with the cerebral environment in which the epileptogenic focus finds itself on different days would certainly be most valuable and would deserve a high priority. It bears repeating that the main problem in chronic epilepsy is not only the epileptogenic focus or the paroxysmal discharge, but the abnormal spread of electrical activity to other parts of the brain and/or the periphery. The presence of a focus

or diffuse bursts tends to lower the seizure threshold, but those factors which allow for spread are the ones that are in all probability related to the seizure propensity of the individual. As a crude analogy, one might point to the development of a forest fire. A lighted cigarette carelessly thrown away in the woods during a hot and dry summer will result in a fire, the extent of which will depend on the preceding length of absence of rain. The same lighted cigarette thrown away in the same location during the rainy season will extinguish itself harmlessly. Let us therefore not remain obsessed only with the cigarette or focus, but consider in much greater detail the state of the rest of the cerebral forest. The investigations of focal epilepsy have brought about great improvements in our concepts about the disorder, but they remain incomplete. One has to see the entire spectrum of the condition, ranging from the mildest cases to severely demented individuals who still occupy state hospital beds, in order to fully appreciate the complexity of the issue.

The differentiation of epilepsy into *idiopathic* and *symptomatic* has not been very fruitful in the past and has not been shown to be of prognostic significance. One of the reasons for this is probably the fact that the terms do not designate homogeneous groups. The word "idiopathic" is frequently used synonymously with genetic and at other times it refers to patients in whom no etiology can be found by careful history. The fact that no etiology is discernible by history does not necessarily mean that the patient could not have a "small but gross" lesion in one temporal lobe, which is discovered only incidentally, as a result of temporal lobectomy for seizure control. The word "symptomatic" implies that the etiology lies in some form of injury to the central nervous system, yet in a number of instances this "injury" is only a relatively minor accident which may have nothing whatsoever to do with the appearance of the seizure disorder. In other instances a definite family history of epilepsy is available in clearly symptomatic cases where there also has been undeniable brain injury. It is an open question to what extent the two elements conspired to produce a seizure disorder which may or may not respond to treatment. While brain injury lowers seizure threshold, it has not been shown that it affects seizure

propensity. This would explain why the same amount of injury will produce only isolated seizures in one individual and a severe intractable disorder in another.

The "constitutional" factor in epilepsy has of course long been recognized but has recently been rather neglected. Although we have at present no way of knowing what this constitutional factor is, it serves no purpose to deny its existence because research efforts will then be thwarted. Part of the reason for omitting the constitutional element from consideration seems to have been that the word has been equated by some authors with "hereditary." This is unfortunate because it narrows the term and suggests a mechanism which so far has not been proven to be operative in the great majority of patients. There is definite evidence that certain EEG abnormalities are inherited in a dominant mode. There is also definite evidence that patients who have these EEG abnormalities are likely to have a lowered threshold for seizure induction, but—and this is the important point—there is no evidence that these patients also have a propensity towards spontaneously recurring seizures. Siblings of epileptic patients—especially of those who have spike wave activity in their EEGs—have a high incidence of EEG abnormalities but only a very low incidence of overt recurrent convulsive seizures. It is clear that some additional factor must be operative in the epileptic patient on which he differs from his siblings. If we accept the concept that the resting EEG is related to seizure threshold rather than seizure propensity, we could explain also the occasional paradox where under treatment the EEG actually may become worse but the patient better.

Classifications of epilepsy based on presumed pathophysiological mechanisms are not likely to be useful in the immediate future because of our ignorance in regard to the really important basic factors. Until the time comes that we do have the necessary understanding, we shall probably be well advised to stay on a purely descriptive level of the clinical condition. Although the term "epilepsy" has nothing to commend itself—except usage through the ages—it seems to serve little purpose to coin new words at this time which suggest knowledge that is not available.

A distinction between patients with "epilepsy only" and "epi-

lepsy associated with cerebral damage" of varying degrees may sound on the surface like a resurrection of the idiopathic versus symptomatic classification. This is, however, not the case. The term "epilepsy only" means that the patient is healthy in all other respects to the best of our knowledge. It does not imply the presence or absence of presumed etiological factors or any pathophysiological mechanism. The patient who is classified as having epilepsy associated with mild, moderate, or severe cerebral damage has obviously more than one handicap. The term does not indicate that cerebral damage caused the seizures; it could be a result of them, or it may actually be independent of the seizure disorder. Although a distinction of this type would not necessarily yield a prognosis for seizure cessation, it could be useful in forecasting the patient's overall life achievements.

It has been pointed out that the chances for a patient to achieve complete seizure freedom rest mainly on the intensity of his seizure disorder and its duration. There is possibly some relationship between these aspects. A severe seizure disorder tends to be refractory to treatment by the time the neurologist sees the patient. The question arises, however, whether the severity could have been influenced by more intensive treatment at the very onset of the illness. The finding that 85 per cent of patients who are seen by a specialist within the first year of their illness achieve a terminal remission of at least two years is most impressive. Even more important is the observation that the results drop to 50 per cent after the first year. Combining these findings with Lund's observations that treatment results of the first three months herald the future course of the disorder, a strong case could be made that a maximum effort should be exerted to control seizures at the very onset. The medication regime should be adequate for the age and weight of the patient and rearranged with each successive seizure. There would seem to be no room for complacency in this regard. Follow-up appointments should initially be closely spaced, and comparison EEGs should be obtained at each visit.

The problem is, however, that at the present time we have no way of knowing whether a seizure in a child or adult will remain isolated or whether it represents the beginning of a chronic sei-

zure disorder. A differentiation of these two conditions would certainly be most important and specific matched control studies dealing with the total evaluation of patients immediately after their first seizures are indicated. All of the currently used anticonvulsants tend to have some side effects in a significant number of patients when given in adequate dosages. Their indiscriminate use therefore is not to be advocated, but hesitation to use them is equally dangerous if they are indeed capable of preventing an individual from becoming a chronic epileptic patient. This is a dilemma the physician faces today, and it is regrettable that there are so far no rigorous studies available that could provide us with guidelines in this respect.

We must not be satisfied with treatment results that lead to "improvement" but not to cessation of seizures. The fact that intelligence tends to decrease if the illness persists unchecked has to be taken into account. This is even more important when we recognize that the patients with an initially bright normal or superior intelligence quotient are more likely to suffer loss of intellectual functions. A basically bright person confronted with the fact of decreasing intellectual functions cannot help becoming a problem to himself or to society. These aspects of the epilepsy issue tend to be glossed over at the present time when we hear of improvement in seizure control that is being achieved by modern drugs. We have to continue to search for better treatment, by drugs or other methods, that will lead to complete cessation of attacks. While intellectual decrease is a most serious event at any stage of life, it becomes a virtual catastrophe if it occurs in childhood. The physician has been trained to regard conditions as emergencies where the life of the patient hangs in the balance. We can now save lives but we are woefully inadequate in saving that which makes us specifically human—namely, the intellect. The saving of intellectual functions will have to assume greater urgency than it has been given in the past. While this applies to all patients, it could perhaps be most clearly seen in the cases of infantile spasms-hypsarhythmia. A delay of treatment of a few *days* might make the difference between a child who will become either an inmate of a state institution or a self-sustaining citizen. This condition would surely

qualify for emergency measures in spite of the fact that life itself is not at stake. Inasmuch as the specialist does not tend to see these children until later in the course of their illness, by which time irrevocable damage is likely to have occurred, it becomes imperative that general practitioners and pediatricians who represent the first line of medical defense become thoroughly familiar with the diagnosis and its potential implications. Treatment, complex as it is, may well be left in the hands of the specialist provided he is called to the scene immediately and can see the child within a matter of a few hours.

While these comments dealt with the duration of the illness and its relationship to treatment response, there also appears to be a relationship between age at time of onset and the severity of the disorder. We have not been able to demonstrate in our own studies that patients whose seizures start before the age of three years develop necessarily a chronic intractable disorder. This does not rule out, however, that a more indirect relationship might exist. It could be postulated that a severe seizure disorder is likely to manifest itself early in life, but not every instance of epilepsy starting in childhood has to be of this severity. The child, as a result of maturational factors, has *a priori* a lower seizure threshold than the adult. He may therefore respond with a seizure to less provocation than the older individual. A milder seizure tendency may bring on clinical seizures in the child which may promptly respond to anticonvulsant medication. The seizure tendency apparently decreases with increasing age, and this may well be the reason why patients with "late onset epilepsy" and posttraumatic epilepsy of adult life seem to have relatively infrequent seizures. This concept could explain why different authors come to different opinions about the prognostic importance of age at time of onset of the illness. It could also explain the observation of our own investigations that children are somewhat more likely to show either complete seizure cessation or chronic disorders rather than occupying a middle position of some improvement as time goes on.

With epilepsy being a condition of such diverse clinical manifestations and markedly varying intensity, it is apparent that any general rule about what epileptic patients can or cannot do is

bound to be unjust. Each patient deserves careful individual attention in regard to his assets as well as his liabilities. Restrictions that have to be applied should not hold across the board for all patients, but should deal only with a particular individual at a particular time. They should be reevaluated periodically in regard to their continued need, with the goal being maximal opportunity in the presence of minimal risk. In actual practice this means that some epileptic patients can be leading essentially normal lives, while others may not be able to operate motor vehicles and work around dangerous machinery, while still others may need more or less constant supervision by members of the family or in a hospital environment.

This book has emphasized, as mentioned in the Foreword, the areas where progress has been slower than one might have been led to believe. This was done in order to point out our deficiencies and pave the way for a more rapid pace of accomplishments, but it does present a potential danger. There has been over the past several decades a progressive liberalization of rules and laws in regard to epilepsy. Many dedicated persons have spent a great deal of effort to remove the stigma that is still attached to this diagnosis. These efforts are most important and are just beginning to bear fruit in a variety of ways. The findings reported in this book should not be used to undermine them. Baseless pessimism in regard to the condition is at least equally as dangerous as false optimism. As long as we are unable to cure the majority of our epileptic patients, we should at least try to make their lot as easy as humanly possible, while persisting in our efforts directed toward the permanent eradication of the disorder. At the present time, epilepsy still represents just as great a challenge as it has throughout the ages. By fully recognizing this challenge and bringing to bear on it, in addition to the most modern equipment, our best scientific minds, we should be able to find the way that will lead not only to the permanent cure of those patients who already suffer from the illness, but also to its prevention.

APPENDIX

VARIABLES USED IN FIRST MEC FOLLOW-UP PROJECT CORRELATION MATRIX

INITIAL FINDINGS

Age
Sex
Physical Health
*Duration of Labor
*Forceps Delivery
*Birth Difficulty
Feeding Problems in Infancy
Colic in Infancy
Crying During First Year of Life
Patient's Weight Gain Progress in Infancy
*Activity During First Year of Life
Sitting Up Age
Walking Age
Talking Age
*Delayed Maturation
*Seizures Present During First Year of Life
*Highest Degree of Fever Attained
*Febrile Convulsions
Nonfebrile Convulsions in Infancy
*Bedwetting
Usual Childhood Diseases without Delirium
*Behavior Difficulties in School
*Academic Difficulties in School
Personality Disorder
Family History
Infantile convulsions without fever
*Epilepsy
*Diabetes

*Temporary psychiatric hospitalization
*Chronic alcoholism
Seizure Type
*Nonfocal major
*Focal major
*Minor focal motor
*Psychomotor
***Combination of Seizures**
***Prognosis for Seizure Control**
***Prognosis for Behavior Control**
***Prognosis for Academic Achievement**
Major Seizures
Duration since onset
Present since first year of life
*Frequency of occurrence
*Remission in the past
Clusters of seizures in one day
*Status epilepticus
Relationship of time of day to seizures
Occurring within two hours after awakening
Frequency of occurrence of aura
Loss of bladder control
*Duration of one attack
State of Consciousness During Seizure
Dazed
Completely unconscious
Not altered
Posture During Seizure
Falls suddenly
No movements observed
Patient stiff
Twitching or shaking
Facial Color During Seizure
Pale
Cyanotic
Prominent Symptoms of Seizure
Blank stare

Head turns to right
Swallowing motions
Vocalization
Right arm or hand twitching
Left face twitching
Left arm or hand twitching
Left leg twitching
Postictal State
Confusion
Sleep
Unilateral muscle weakness
Nausea
Minor Seizure
Duration since onset
Frequency of occurrence
Remission in the past
Clusters of seizures in one day
Status epilepticus
Clusters of seizures over several days, freedom from seizures for several weeks
Relationship of time of day to seizures
Frequency of occurence of aura
Loss of bladder control
Duration of one attack
Dazed
No aftereffects
***Social Factors Contributing to Illness**
Etiological Factors in Neurological History
***Objective Findings of Cerebral Pathology on Neurological Examination**
***Psychological Test Results**
Intellectual level
Immaturity
Neurotic tendencies
Psychotic tendencies
Personality disturbances
*Organic pathology suspected

***Age at Onset of Convulsive Disorder**
Duration of Illness
***Highest Rise of GTT From Fasting**
EEG
*Amount of abnormality
*Amount of seizure patterns
*Amount of focal abnormalities
*Amount of alpha activity
*Amount of theta activity
*Amount of fast activity
Generalized paroxysmal activity
Intervals between paroxysms
Amplitude of background rhythms, Left
Amplitude of background rhythms, Right
Main background frequency
Adequate Effort but No EEG Change with Hyperventilation
Final Diagnosis
Convulsive disorder
Psychiatric disorder in addition to diagnosis of epilepsy
Mental retardation in addition to diagnosis of epilepsy

FOLLOW-UP FINDINGS

EEG
*Amount of abnormality
*Amount of seizure patterns
*Amount of focal abnormalities
*Amount of alpha activity
*Amount of theta activity
*Amount of fast activity
Generalized paroxysmal activity
Intervals between paroxysms
Amplitude of background rhythms, Left
Amplitude of background rhythms, Right
Main background frequency
Adequate Effort but No EEG Change with Hyperventilation
Patient On or Off Anticonvulsant Medication

*Present Seizure State
*Behavior Problem
*Academic School Problem
Attending or Attended Regular School
Attending or Attended Special School
No Formal Education
*Average Marks
Grade Failure
*Institutionalized

*The variables marked by asterisk were used in the factor analysis.

VARIABLES USED IN SECOND MEC FOLLOW-UP PROJECT CORRELATION MATRIX

INITIAL FINDINGS

*Sex
Physical Health
Difficulty During Pregnancy of the Mother
Duration of Pregnancy
Duration of Labor
*Birth Weight
*Condition of Child at Birth
Birth Cry
Condition of Patient's Head at Birth
*Birth Difficulty
Feeding Problems in Infancy
Colic in Infancy
Activity During First Year of Life
*Seizures Present During First Year of Life
*Sitting Up Age
Walking Age
*Talking Age
Toilet Training
Dry at Night
Highest Degree of Fever Attained
*Febrile Convulsions
Nonfebrile Convulsions in Infancy
*Bedwetting
*Behavior Difficulties in School
Amount of Schooling
*Attending or Attended Special School
Average Grades

***History of Personal Relations During Adolescence**
Family History
*Stillbirth
*Early infantile deaths
*Infantile convulsions with fever
*Infantile convulsions without fever
*Epilepsy
*Diabetes
*Chronic alcoholism
Seizure Type
*Nonfocal major
*Focal major
*Minor focal motor
*Psychomotor
*Absence
***Combination of Seizures**
Etiology of Seizures
*Unknown
*Birth injury
Postnatal head injury
*Cerebral infection
*Mixed hereditary and external cause
*Hereditary cause only
Prognosis for Seizure Control
Prognosis for Behavior Control
Prognosis for Academic Achievement
Adequacy of Medication Regime in the Past
Never Treated Before
***Patient's Initial Response to Adequate Amount of Anticonvulsants**
***Duration of Seizure Disorder**
Major Seizure
*Frequency of occurrence, Maximal
*Frequency of occurrence at present
*Remission in the past
*Clusters of seizures in one day
*Status epilepticus

Relation of menses to seizure
EEG
*Amount of abnormality
*Amount of seizure patterns
*Amount of focal abnormalities
Amount of alpha activity
Amount of theta activity
Amount of fast activity
Right temporal focus
Left temporal focus
Focus consists of theta discharge
Focus consists of complex discharge
*Focus consists of sharp wave or spike
*Generalized paroxysmal activity
*Amount of spike wave activity
*Amplitude of background rhythms, Left
Main background frequency
***Social Factors Contributing to Illness**
***Objective Findings of Cerebral Pathology in Neurological Examination**
Psychological Test Results
*Immaturity
*Neurotic tendencies
*Psychotic tendencies
*Personality disturbances
***Final Diagnosis Psychiatric Disorder in Addition to Diagnosis of Epilepsy**
***Organic Brain Pathology Suspected on Bender-Gestalt Test**
Rotation of 45 Degrees or More on Bender-Gestalt Test
***Verbal IQ Score**
***Performance IQ Score**
***Full Scale IQ Score**
***Difference Between Verbal and Performance Score**

FOLLOW-UP FINDINGS

***Age**
Seizure Type

Nonfocal Major
Focal Major
Minor Focal Motor
Psychomotor
Absence
Combination of Seizures
***Adequacy of Medication Regime in the Past**
Response to Adequate Amount of Anticonvulsant Medications
Change in Number of Seizure Types
Remission at Present for Major Seizures
***Remission in the Past for Major Seizures**
Remission at Present for Minor Seizures
Remission in the Past for Minor Seizures
***Remote Memory**
***Recent Memory**
***Serial 7 Subtractions**
***Proverb Interpretation**
Egocentric or Bizarre Interpretation
***Organic Mental Changes**
Difficulty Concentrating
***Personality Problem**
Sociopathic Behavior and/or Antisocial Behavior in P.I.
Depression
Destructive or Assaultive Behavior
EEG
*Amount of abnormality
*Amount of seizure patterns
*Amount of focal abnormalities
*Amount of alpha activity
*Amount of theta activity
*Amount of fast activity
*Right temporal focus
*Left temporal focus
Focus consists of theta discharge
*Focus consists of complex discharge
*Focus consists of sharp wave or spike
*Generalized paroxysmal activity

*Amount of spike wave activity
*Amplitude of background rhythms, Left
Amount of nonparoxysmal buildup, HV
Amount of paroxysmal buildup, HV
*Amount of photic driving at low flash rates
*Amount of photic driving at medium flash rates
*Amount of photic driving at high flash rates
Main background frequency
Abnormalities improved or deteriorated
*Organic Brain Pathology Suspected on Bender-Gestalt Test
Rotation of 45 Degrees or More on Bender-Gestalt Test
*Verbal IQ Score
*Performance IQ Score
*Full Scale IQ Score
*Difference Between Verbal and Performance Score
Verbal Scale Score Difference Between Evaluation I and II: Worse
Verbal Scale Score Difference Between Evaluation I and II: Better
Performance Scale Score Difference Between Evaluation I and II: Worse
Performance Scale Score Difference Between Evaluation I and II: Better
Interval Between Two Visits
Handedness
*Present Seizure State
Patient On or Off Anticonvulsant Medication
*Behavior Problem
Academic School Problem
Attending or Attended Special School
Average Marks in Regular School
*Gainfully Employed
Housewife Performing Duties Adequately
*Overall Condition of Patient

*Variables carrying asterisk were used for factor analysis.

VARIABLES USED IN SECOND MEC FOLLOW-UP PROJECT

F-TESTS

Age
Physical Health
Duration of Labor
Birth Weight
Condition of Child at Birth
Length of Time Till Mother Saw Child after Delivery
Feeding Problems in Infancy
Crying During First Year of Life
Activity During First Year of Life
Sitting Up Age
Walking Age
Talking Age
Toilet Training
Age at Which Dry at Night
Highest Degree of Fever Attained
Duration of Fever over 104 Degrees
Amount of Schooling
Average Grades
School Truancy
Personal Relationships During Adolescence
Etiology
Birth injury
Cerebral infection
Mixed hereditary and external cause
Hereditary cause only
Major Seizures
Duration since onset

Frequency of maximal occurrence
Frequency of occurrence at present
Remission in the past
Clusters of seizures in one day
Status epilepticus
Clusters of seizures over several days, freedom for several weeks
Relationship of time of day to seizures
Relation of menses to seizures
Frequency of occurrence of aura
Loss of bladder control
Tongue biting
Injuries sustained during attack
Duration of one attack

Minor Seizures

Duration since onset
Frequency of maximal occurrence
Frequency of occurrence at present
Remission in the past
Clusters of seizures in one day
Clusters of seizures over several days, freedom for several weeks
Relationship of time of day to seizures
Frequency of occurrence of aura
Duration of one attack

Combination of Seizures

Initial Response to Anticonvulsant Medications— 1-3 Months

Subsequent Response to Anticonvulsant Medications— 3 Months-1 Year

Subsequent Response to Anticonvulsant Medications— 1 Year and after

Seizure Pattern Change after Anticonvulsant Treatment

EEG

Amount of abnormality, waking record
Amount of abnormality, waking and sleep record
Amount of seizure patterns

Amount of focal abnormalities
Amount of alpha activity
Amount of theta activity
Amount of fast activity
Amount of diffuse delta activity
Amount of paroxysmal activity
Left background rhythms amplitude
Right background rhythms amplitude
Main background frequency
Wechsler IQ
Verbal Scale
Performance Scale
Full Scale
Information
Comprehension
Arithmetic
Similarities
Digit Span
Vocabulary
Digit Symbol
Picture Completion
Picture Arrangement
Block Design
Object Assembly
Organic Brain Pathology Suspected from Bender-Gestalt Test
Forty-five Degree or More Rotation of Bender-Gestalt Figures
Psychological Tests
Immaturity
Neurotic tendencies
Psychotic tendencies
Personality disturbances
Organic pathology suspected
Social Factors Contributing to Illness
Laboratory Findings Summary
Objective Findings of Cerebral Pathology on Neurological Examination
Etiological Factors Summary

Prognosis for Seizure Control
Prognosis for Behavior Control
Prognosis for Academic Functions
Follow-Up Results
Present seizure state
Behavior problem
Academic school problem
Average marks
Overall condition of patient

VARIABLES FROM SECOND MEC FOLLOW-UP PROJECT

CHI SQUARE TESTS

Sex
Pregnancy Complications
Marked nausea and vomiting
Labor Complications
Forceps delivery
Birth cry, induced versus spontaneous
Colic in Infancy
Attended Special School
Seizures Present During First Year of Life
Birth Difficulty
Febrile Convulsions
Bedwetting
Behavior Difficulties in School
Academic Difficulties in School
Severe Infectious Disease
Severe Head Injury with Unconsciousness
Neurotic Symptoms
Personality Disorder
Family History
Stillbirths
Breech deliveries
Multiple births
Early infantile deaths
Congenital defects
Mental retardation
Temper tantrums
Behavior problems

Academic school problems
Meningitis
Bedwetting
Breathholding spells
Infantile convulsions with fever
Infantile convulsions without fever
Epilepsy
Fainting spells
Severe chronic headache
Chorea
Diabetes
Excessive nervousness
Nervous breakdown
Temporary psychiatric hospitalization
State hospitalization
Chronic alcoholism
Abortions or miscarriages

Etiology Unknown

Seizure Type

Nonfocal major
Focal major
Minor focal motor
Psychomotor
Absence

Major Seizures

Present since first year of life
Occurring at night during sleep
Precipitating event—Nonspecific excitement
Precipitating event—Emotional stress
Precipitating event—Omission of anticonvulsant medications
Posture during attack—Slides gradually to ground
Posture during attack—Falls suddenly
Muscular action during attack—Classic tonic and clonic phase
Muscular action during attack—Patient stiff
Muscular action during attack—Twitching or shaking
Facial color during attack—Pale
Facial color during attack—Cyanotic

Eyes rolled up during attack
Postictal state—Fatigue
Postictal state—Headache
Postictal state—Confusion
Postictal state—Sleep
Postictal state—Nausea
Prominent feature of attack—Salivation
Prominent feature of attack—Vocalization
Prominent feature of attack—Right side twitching
Prominent feature of attack—Left side twitching
Minor Seizures
Occurring within 2 hours of awakening
Emotional stress as precipitating event
Consciousness during attack—Not altered
Consciousness during attack—Hears, but cannot respond
Consciousness during attack—Dazed
Consciousness during attack—Completely unconscious
Posture during attack—Not altered
Postictal state—No aftereffects
Postictal state—Sleep
Feature of attack—Random wandering around
Adequacy of Medication Regime in the Past
Reason for Referral—Emotional or behavior problems
Diagnosis of Psychiatric Disorder in Addition to Diagnosis of Epilepsy
Psychiatric Treatment Recommended
EEG
Right temporal focus
Left temporal focus
Type of discharge—Sharp wave or spike
Forty-five Degree Rotation in Any Figure on Bender-Gestalt Test
Follow-Up Results
Takes anticonvulsant medication
Attending regular school
Attending special school
Grade failure
Gainfully employed

ESTIMATED PROBABILITY OF CORRECT CLASSIFICATION (2 GROUPS)

DIFFERENCES BETWEEN DISCRIMINANT FUNCTIONS	PROBABILITY
.00	.50
.04	.51
.08	.52
.12	.53
.16	.54
.20	.55
.24	.56
.28	.57
.32	.58
.36	.59
.40	.60
.45	.61
.49	.62
.53	.63
.57	.64
.62	.65
.66	.66
.71	.67
.75	.68
.80	.69
.85	.70
.89	.71
.94	.72
.99	.73
1.04	.74
1.10	.75
1.15	.76
1.21	.77
1.26	.78
1.32	.79
1.39	.80
1.45	.81
1.52	.82
1.58	.83

1.66	.84
1.73	.85
1.81	.86
1.90	.87
1.99	.88
2.09	.89
2.20	.90
2.31	.91
2.44	.92
2.59	.93
2.75	.94
2.94	.95
3.18	.96
3.48	.97
3.89	.98
4.59	.99

CONSTANTS AND WEIGHTS FOR PREDICTING INPATIENT TREATMENT RESULTS

	Discriminate Function I								
	1	2	3	4	5	6	7	8	9
Constant	−17.48								
Injuries during seizures	−0.41	−0.82	−1.23	−1.64	−2.05	NA	NA	NA	NA
Combination of seizures	−0.39	−0.78	−1.17	−1.56	1.95	−2.34	−2.73	−3.12	−3.51
Psychomotor seizures	6.08	12.16	NA	NA	NA	NA	NA	NA	NA
Duration of seizure disorder	2.85	5.70	8.55	11.40	14.25	17.10	19.95	22.80	25.65
Frequency of occurrence of seizures at present	0.56	1.12	1.68	2.24	2.80	3.36	3.92	4.48	5.04
Cluster of seizures for several days, freedom from seizures for several weeks	0.77	1.54	2.31	3.08	3.85	NA	NA	NA	NA
Amount of EEG abnormality	1.57	3.14	4.71	6.28	7.85	NA	NA	NA	NA
Seizure patterns in EEG	0.09	0.18	0.27	0.36	0.45	NA	NA	NA	NA

	Discriminate Function II								
	1	2	3	4	5	6	7	8	9
Constant	−24.01								
Injuries during seizures	−0.02	−0.04	−0.06	−0.08	−0.10	NA	NA	NA	NA
Combination of seizures	0.06	0.12	0.18	0.24	0.30	0.36	0.42	0.48	0.54
Psychomotor seizures	6.25	12.50	NA	NA	NA	NA	NA	NA	NA
Duration of seizure disorder	2.92	5.84	8.76	11.68	14.60	17.52	20.44	23.36	26.28
Frequency of occurrence of seizures at present	1.02	2.04	3.06	4.08	5.10	6.12	7.14	8.16	9.18
Cluster of seizures for several days, freedom from seizures for several weeks	0.90	1.80	2.70	3.60	4.50	NA	NA	NA	NA
Amount of EEG abnormality	1.78	3.56	5.34	7.12	8.90	NA	NA	NA	NA
Seizure patterns in EEG	0.21	0.42	0.63	0.84	1.05	NA	NA	NA	NA

NA = Not Applicable

CONSTANTS AND WEIGHTS FOR PREDICTING OUTPATIENT TREATMENT RESULTS

	Discriminate Function I								
	1	2	3	4	5	6	7	8	9
Constant	−17.81								
Combination of seizures	−0.84	−1.68	−2.52	−3.36	−4.20	−5.04	−5.88	−6.72	−7.56
Clusters of seizures for several days, freedom from seizures for several weeks	−1.25	−2.50	−3.75	−5.00	−6.25	NA	NA	NA	NA
Injuries during seizures	1.25	2.50	3.75	5.00	6.25	NA	NA	NA	NA
Psychomotor seizures	9.48	18.96	NA	NA	NA	NA	NA	NA	NA
Duration of seizure disorder	1.92	3.84	5.76	7.68	9.60	11.52	13.44	15.36	17.28
Frequency of occurrence of seizures at present	1.35	2.70	4.05	5.40	6.75	8.10	9.45	10.80	12.15
Amount of EEG abnormality	2.46	4.92	7.38	9.84	12.30	NA	NA	NA	NA
Seizure patterns in EEG	0.40	0.80	1.20	1.60	2.00	NA	NA	NA	NA

	Discriminate Function II								
	1	2	3	4	5	6	7	8	9
Constant	−30.28								
Combination of seizures	−0.27	−0.54	−0.81	−1.08	−1.35	−1.62	−1.89	−2.16	−2.43
Clusters of seizures for several days, freedom from seizures for several weeks	−1.57	−3.14	−4.71	−6.28	−7.85	NA	NA	NA	NA
Injuries during seizures	1.92	3.84	5.76	7.68	9.60	NA	NA	NA	NA
Psychomotor seizures	11.37	22.74	NA	NA	NA	NA	NA	NA	NA
Duration of seizure disorder	2.60	5.20	7.80	10.40	13.00	15.60	18.20	20.80	23.40
Frequency of occurrence of seizures at present	1.66	3.32	4.98	6.64	8.30	9.96	11.62	13.28	14.94
Amount of EEG abnormality	2.20	4.40	6.60	8.80	11.00	NA	NA	NA	NA
Seizure patterns in EEG	1.36	2.72	4.08	5.44	6.80	NA	NA	NA	NA

NA = Not Applicable

DISTRIBUTION OF AGE AT DEATH FOR ALL INDIVIDUALS AND FOR THOSE WITH EPILEPSY MENTIONED ON DEATH CERTIFICATES*

	Total	*Infants*	*1–4*	*5–9*	*10–14*	*15–19*	*20–24*	*25–29*	*30–34*	*35–39*
1960 Total Deaths	67,912	4,702	716	389	302	475	524	529	760	1,110
Epilepsy Deaths	81	1	7	7	2	3	6	3	11	10
1961 Total Deaths	67,375	4,604	677	403	273	478	527	454	718	1,143
Epilepsy Deaths	74	—	4	3	4	3	5	6	5	5
1962 Total Deaths	70,049	4,367	609	372	319	450	521	483	700	1,084
Epilepsy Deaths	95	2	2	1	4	8	5	5	9	9
1963 Total Deaths	72,438	4,150	628	398	309	580	596	542	733	1,204
Epilepsy Deaths	91	—	5	2	5	7	5	14	8	9
1964 Total Deaths	72,129	4,043	615	408	340	652	691	544	790	1,161
Epilepsy Deaths	97	1	3	4	8	5	9	4	10	15
1965 Total Deaths	73,665	3,936	596	375	338	672	705	574	753	1,186
Epilepsy Deaths	109	1	1	4	7	3	6	10	6	14
1966 Total Deaths	74,596	3,751	629	418	403	760	766	631	710	1,142
Epilepsy Deaths	119	1	3	2	2	5	7	9	5	11

* Courtesy Michigan Department of Public Health, Vital Records Section

40–44	*45–49*	*50–54*	*55–59*	*60–64*	*65–69*	*70–74*	*75–79*	*80–84*	*85–89*	*90 and Over*	*Median Age At Death*
1,742	2,604	3,650	4,855	6,184	8,130	9,049	8,595	6,934	4,386	2,276	68.3
5	6	3	5	—	5	1	1	2	3	—	35.2
1,670	2,570	3,501	4,703	6,142	7,976	9,070	8,629	6,980	4,481	2,376	68.7
12	3	3	7	4	3	3	1	2	—	1	40.8
1,742	2,623	3,698	4,891	6,396	8,331	9,484	9,189	7,390	4,809	2,591	69.1
7	9	8	8	5	4	3	3	2	—	1	41.8
1,822	2,679	3,858	5,090	6,422	8,437	9,792	9,550	7,878	5,041	2,734	69.3
7	6	2	6	2	4	5	3	1	—	—	34.7
1,875	2,751	3,874	5,086	6,451	8,038	9,760	9,620	7,881	4,943	2,606	69.2
6	3	4	5	3	4	7	3	2	1	—	36.5
1,948	2,824	3,936	5,126	6,576	8,163	9,721	10,010	8,234	5,180	2,812	69.5
7	11	7	8	8	6	4	2	4	—	—	41.8
1,933	2,851	4,103	5,253	6,736	7,986	9,905	10,061	8,502	5,160	2,896	69.5
21	8	9	10	8	5	4	3	2	4	—	43.5

CONSTANTS AND WEIGHTS FOR PREDICTING INTELLECTUAL LOSS

	Discriminate Function I								
	1	2	3	4	5	6	7	8	9
Constant	−79.22								
Frequency of occurrence of seizures at present	−1.60	−3.20	−4.80	−6.40	−8.00	−9.60	−11.20	−12.80	−14.40
Combination of seizures	5.85	11.70	17.55	23.40	29.25	35.10	40.95	46.80	52.65
Clusters of seizures for several days, freedom from seizures for several weeks	3.01	6.02	9.03	12.04	15.05	NA	NA	NA	NA
EEG background amplitude	2.92	5.84	8.76	11.68	14.60	17.52	20.44	23.36	26.28
Organic pathology suspected from *psychological* tests	9.22	18.44	27.66	36.88	46.10	NA	NA	NA	NA
Social factors contributing to illness	4.01	8.02	12.03	16.04	20.05	NA	NA	NA	NA
Full Scale IQ	0.99	(Always Multiply by Actual Full Scale Figure)							

	Discriminate Function II								
	1	2	3	4	5	6	7	8	9
Constant	−71.88								
Frequency of occurrence of seizures at present	−1.53	−3.06	−4.59	−6.12	−7.65	−9.18	−10.71	−12.24	−13.77
Combination of seizures	4.99	9.98	14.97	19.96	24.95	29.94	34.93	39.92	44.91
Clusters of seizures for several days, freedom from seizures for several weeks	2.19	4.38	6.57	8.76	10.95	NA	NA	NA	NA
EEG background amplitude	3.20	6.40	9.60	12.80	16.00	19.20	22.40	25.60	28.80
Organic pathology suspected from psychological tests	9.79	19.58	29.37	39.16	48.95	NA	NA	NA	NA
Social factors contributing to illness	3.42	6.84	10.26	13.68	17.10	NA	NA	NA	NA
Full Scale IQ	0.93	(Always Multiply by Actual Full Scale Figure)							

NA = Not Applicable

NAME:_____

LAFAYETTE CLINIC INPATIENT EPILEPSY REVIEW—DR. RODIN

PROJECT 116
Coding Sheets

CARD 6

DATE OF EXAMINATION

1–2 ☐☐ Month
4–5 ☐☐ Day
7–8 ☐☐ Year

10 REFERRING SOURCE

0 Not recorded
1 Private M.D.
2 Agency other than State Hospital
3 Court or Police
4 Caro State Hospital
5 Northville State Hospital
6 Pontiac State Hospital
7 Ypsilanti State Hospital
8 Traverse City/Kalamazoo State Hospital
9 Lapeer/Plymouth State Hospital

12 RACE

0 Not recorded
1 White
2 Negro
3 American Indian
4 Mexican
5 Oriental
6
7
8
9

*14 BIRTH ORDER (*For 9 or more, Code as 9*)

☐

16 MAIN REASON FOR ADMISSION

0 Not recorded
1 Seizure control
2 Behavior control
3 Teaching or research purposes

* Asterisks indicate variables that were used in data analysis.

PATIENT'S GENERAL PAST MEDICAL AND PSYCHIATRIC HISTORY
(Check the boxes which are applicable. Code "0" for items on which no information.)

18 ☐ First born twin or other multiple birth
20 ☐ Second, third, or fourth multiple birth
*22 ☐ Delayed maturation
24 ☐ Breathholding spells
*26 ☐ Febrile convulsions (isolated episodes not directly related to current seizure disorder)
*28 ☐ Nonfebrile convulsions (isolated episodes not directly related to current seizure disorder)
30 ☐ Atypical spells: _____
*32 ☐ Bedwetting
*34 ☐ Neurotic symptoms: _____
*36 ☐ Psychotic symptoms: _____
*38 ☐ Personality disorder: _____
*40 ☐ Police record: _____

FAMILY HISTORY
(Check the boxes which are applicable. If no family history available, cross out entire section. Omit questionable data.)

STILLBIRTHS

*42 ☐ Male
*44 ☐ Female
46 ☐ Paternal side of family
*48 ☐ Maternal side of family
*50 ☐ More than one in family
*52 ☐ Sex unknown

State relationship to patient:

_____

EARLY INFANTILE DEATHS

*54 ☐ Male
*56 ☐ Female
*58 ☐ Paternal side of family
*60 ☐ Maternal side of family
*62 ☐ More than one in family
*64 ☐ Sex unknown

State relationship to patient:

_____

66–70 ☐☐☐☐☐ Lafayette Clinic inpatient number
71–78 Leave blank
79–80 [0][6] Card number

CARD 7 FAMILY HISTORY (*cont'd*)

TWINS

*2 ☐ Male
*4 ☐ Female
*6 ☐ Paternal side of family
*8 ☐ Maternal side of family
*10 ☐ More than one in family

State relationship to patient:

CONGENITAL MALFORMATIONS

12 ☐ Male
14 ☐ Female
16 ☐ Paternal side of family
18 ☐ Maternal side of family
20 ☐ More than one in family

State relationship to patient:

Type: ---

MENTAL RETARDATION

*22 ☐ Male
*24 ☐ Female
*26 ☐ Paternal side of family
*28 ☐ Maternal side of family
30 ☐ More than one in family

State relationship to patient:

BREATHHOLDING SPELLS

32 ☐ Male
34 ☐ Female
36 ☐ Paternal side of family
38 ☐ Maternal side of family
40 ☐ More than one in family

State relationship to patient:

INFANTILE FEBRILE CONVULSIONS

*42 ☐ Male
*44 ☐ Female
*46 ☐ Paternal side of family
*48 ☐ Maternal side of family
50 ☐ More than one in family

State relationship to patient:

EPILEPSY

*52 ☐ Male
*54 ☐ Female
*56 ☐ Paternal side of family
*58 ☐ Maternal side of family
*60 ☐ More than one in family
State relationship to patient:

_____

61–65 Leave blank
66–78 Duplicate these columns from original data on Card 6.
79–80 [0][7] Card number

CARD 8

OTHER NEUROLOGICAL DISEASES

*2 ☐ Male
*4 ☐ Female
*6 ☐ Paternal side of family
*8 ☐ Maternal side of family
*10 ☐ More than one in family
State relationship to patient:

_____

Specify type

_____

DIABETES

*12 ☐ Male
*14 ☐ Female
*16 ☐ Paternal side of family
*18 ☐ Maternal side of family
*20 ☐ More than one in family
State relationship to patient:

_____

PSYCHIATRIC DISORDERS

*22 ☐ Male
*24 ☐ Female
*26 ☐ Paternal side of family
*28 ☐ Maternal side of family
*30 ☐ More than one in family
State relationship to patient:

_____

Specify type

_____

SCHOOL HISTORY

*32 AMOUNT OF SCHOOLING

(Code only when education completed)

[0] Not recorded
[1] No formal schooling
[2] Attended grade school; did not complete 8th grade
[3] Attended grade school; graduated 8th grade
[4] Attended high school; not graduated
[5] Graduated from high school
[6] Attended college; not graduated
[7] Graduated from college; include in "college" any recognized formal post-high school
[8] Graduate school
[9] Doctoral degree

*34 ATTENDING OR ATTENDED SPECIAL SCHOOL

[0] Not recorded
[1] No
[2] Yes

*36 ATTENDING OR ATTENDED REGULAR SCHOOL

[0] Not recorded
[1] No
[2] Yes

*38 AVERAGE GRADES

[0] Not recorded
[1] Unsatisfactory and grade failure
[2] Unsatisfactory but no grade failure
[3] Average
[4] Somewhat above average
[5] Superior or honor student

*40 USE OF ALCOHOL BY PATIENT

[0] Not recorded
[1] Abstinent
[2] Social drinker
[3] One or more drinks per day
[4] Chronic alcoholism without DTs or Korsakoff's syndrome
[5] Chronic alcoholism with DTs or Korsakoff's syndrome

TYPE (S) OF CLINICAL SEIZURES PRESENT

*42 ☐ *Grand Mal Seizure, nonfocal:* No aura, loss of consciousness, falling, tonic phase, clonic phase, followed by sleep, some disorientation and memory loss.

*44 ☐ *Grand Mal Seizure, focal onset:* Either subjective aura, or head and neck turning to one side, or twitching of one side of the face or part of an extremity, loss of consciousness, tonic phase, clonic phase, sleep; on recovery possible weakness of one extremity or pronounced disorientation and memory loss.

*46 ☐ *Grand Mal Seizure* but history inadequate to differentiate between focal or nonfocal onset.

*48 ☐ *Grand Mal Variant Seizure—Nonfocal:* Loss of consciousness, falling, some twitching or shaking, no well-defined tonic and clonic phase like in classical grand mal, there may or may not be sleep afterward.

*50 ☐ *Grand Mal Variant—Focal onset:* Subjective aura, or head and neck turning to one side or twitching of one side of the face or twitching of one part of an extremity, loss of consciousness, falling, no tonic and clonic phase as in classical grand mal; some twitching or shaking, or merely generalized rigidity, there may or may not be sleep afterward.

*51 ☐ *Minor Motor Focal Seizure:* Consciousness may be retained or lost, no falling, patient feels weak and sits down or remains standing, twitching of one or more extremities, or twitching of the face, no Jacksonian march, may or may not sleep afterward.

*52 ☐ *Minor Motor Nonfocal Seizure:* Consciousness clouded, bilaterally symmetrical tonic extension or flexion of arms. There may be twitching but no definite jerking. May be confused afterwards, usually does not sleep. Retains posture or staggers.

53 ☐ *Minor Motor or Sensory Seizure with Jacksonian March:* Twitching and/or numbness starting in one discreet area (face, hand, leg) spreading in typical Jacksonian type of march.

*54 ☐ *Automatism (Psychomotor):* There may or may not be subjective aura, consciousness lost, posture retained, purposeless coordinated behavior which is inappropriate at that moment; when coming out of the seizure, patient is disoriented and may be belligerent, may or may not sleep, but sleep unlikely.

55 ☐ *Psychic or Sensory Seizure:* Subjective sensation on part of patient with no overt motor manifestations which occur suddenly and are not related to the situation the patient finds himself in; no loss of consciousness, no falling, no longer than about 15 minutes—usually only 1 to 2 minutes—usually no sleep afterward.

56 ☐ *Confusional State:* Confused and/or disoriented behavior lasting from several minutes to several hours, which is not preceded nor followed by a seizure.

*57 ☐ *Absence:* Consciousness lost, staring expression, posture unchanged, continues with activities as soon as seizure is over at precisely the point at which he had been interrupted as a result of the seizure, and no sleep after seizure.

*58 ☐ *Absence with features of slight automatism:* Some chewing or other slight repetitive activity.

*59 ☐ *Absence with features of mild myoclonic activity:* Blinking of eyelids, slight jerking of head or hands.

60 ☐ *Myoclonic Seizure:* Clouding of consciousness, posture may be retained, twitching of eyelids, back and fro movements of the head (nodding type), and bilaterally symmetrical jerking of arms and/or legs, no after-effects.

*61 ☐ *Myoclonic Jerks:* Isolated irregular jerks of one extremity with no change in consciousness and no loss of posture.

*62 ☐ *Akinetic Seizure:* Loss of consciousness and postural tone, patient gets up immediately after falling and has no other symptoms.

*63 ☐ *Temporal Lobe Components to Seizure Pattern:* (Check this box regardless how many other boxes have been checked if it is applicable—it serves as a summary column).

64 ☐ *Difficult to Classify*

65 Leave blank

66–78 Duplicate these columns from original data on Card 6.

79–80 [0][8] Card number

CARD 9 ONSET OF SEIZURES

AGE AT TIME OF FIRST SEIZURE

*1–3 ☐☐☐ Months

AGE AT ONSET OF RECURRENT SEIZURES

*5–7 ☐☐☐ Months

TOTAL DURATION OF ILLNESS PRIOR TO HOSPITALIZATION

*9–10 ☐☐ Years

REMISSION IN SEIZURE DISORDER

*12–13 ☐☐ Years

*15 COMBINATION OF SEIZURES

(The even numbers are to be checked if the patient has focal grand mal seizures and sometimes in addition auras only. The aura would then not represent a second seizure type. The scale would be marked on number 2. If there are focal grand mal seizures and psychomotor automatisms and auras only, the scale would be marked at 4, etc.)

[0] Not recorded
[1] 1 seizure type only
[2]
[3] 2 seizure types
[4]
[5] 3 seizure types
[6]
[7] 4 seizure types
[8]
[9] More than four seizure types

ETIOLOGY OF SEIZURES

*17 ☐ UNKNOWN (Check only if none of the other columns apply and adequate history available—place "0" in box if history inadequate.)

*10 PRENATAL OR PERINATAL INJURY

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely
[5] Definite

*21 POSTNATAL HEAD INJURY

[0] Not recorded
[1] Absent
[2] *Mild:* marked bruise or laceration, but no aftereffects.
[3] *Moderate:* marked bruise or laceration with or without skull fracture, no unconsciousness, but may have been momentarily dazed. Some aftereffects like vomiting or dizziness for a few days.
[4] *Marked:* injury associated with unconsciousness for a period of less than 5 minutes.
[5] *Severe:* injury associated with unconsciousness for more than 5 minutes.

*23 CEREBRAL INFECTION

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely
[5] Definite

*25 OTHER SIGNIFICANT EXTERNAL CAUSES

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely
[5] Definite. Specify: _____

*27 MIXED HEREDITARY AND EXTERNAL CAUSE

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely
[5] Definite

*29 HEREDITARY CAUSE ONLY

(A family includes 2nd cousins, great-aunts, and great-uncles, but not great-grandparents. If column 27 is checked this column becomes "0"—not recorded.)

[0] Not recorded
[1] *Absent:* no family history of infantile convulsions or epilepsy.
[2] *Questionable:* one other family member had isolated infantile convulsions.
[3] *Probable:* several other family members had infantile convulsions or one close relative had epilepsy.
[4] *Very likely:* several family members had infantile convulsions and one other had epilepsy.
[5] *Definite:* two or more family members had epilepsy.

SPECIFIC SEIZURE HISTORY

31 MOST DIFFICULT PROBLEM

[0] Not recorded
[1] Major seizures
[2] Minor seizures

TYPE OF SEIZURE

33–34 [ ][ ] (Indicate the type of seizure by noting the IBM column numbers which appear on Card 8, columns 42–62.)

CURRENT SEIZURE PRESENT SINCE FIRST YEAR OF LIFE

*36–38 [ ][ ][ ] Months

*40 DURATION OF THIS PARTICULAR SEIZURE TYPE

[0] Not recorded
[1] Less than 1 month
[2] 1–2 months
[3] 3–6 months
[4] 7–11 months
[5] 1–3 years
[6] 4–6 years
[7] 7–9 years
[8] 10–15 years
[9] More than 15 years

*42 FREQUENCY OF MAXIMAL OCCURRENCE OF SEIZURES

[0] Not recorded
[1] Less than once a year
[2] About once a year
[3] 2–3 seizures a year
[4] 4–6 seizures a year
[5] 7–12 seizures a year
[6] Once a month
[7] 2–3 a month
[8] Once a week
[9] Several a week

*44 FREQUENCY OF OCCURRENCE AT PRESENT

[0] Not recorded
[1] Less than once a year
[2] About once a year
[3] 2–3 seizures a year
[4] 4–6 seizures a year
[5] 7–12 seizures a year
[6] Once a month
[7] 2–3 a month
[8] Once a week
[9] Several a week

*46 IN REMISSION AT PRESENT

[0] Not recorded
[1] Absent
[2] Remission lasted 1 year
[3] Remission lasted 1–2 years
[4] Remission 2–3 years
[5] Remission 3–5 years
[6] Remission 5–7 years
[7] Remission 7–10 years
[8] Remission 10–15 years
[9] More than 15 years

*48 REMISSION IN THE PAST

[0] Not recorded
[1] Never
[2] Up to 1 year
[3] 1–2 years
[4] 3–5 years
[5] 6–8 years
[6] 9–11 years
[7] 12–14 years
[8] 15–20 years
[9] More than 20 years

*50 CLUSTERS OF SEIZURES IN ONE DAY

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

*52 STATUS EPILEPTICUS

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

*54 CLUSTERS OF SEIZURES OVER SEVERAL DAYS THEN FREEDOM FOR WEEKS

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

*56 FREQUENCY OF OCCURRENCE OF AURA

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

57–65 Leave blank

66–78 Duplicate these columns from original data on Card 6.

79–80 [0][9] Card number

CARD 10 TYPE OF AURA

2 ☐ Diffuse myoclonic jerks
4 ☐ Motor manifestations—right
6 ☐ Motor manifestations—left
8 ☐ Somatic sensory manifestations—right
10 ☐ Somatic sensory manifestations—left
12 ☐ Abdominal sensations
14 ☐ Vertigo
16 ☐ "Dizziness" other than vertigo
18 ☐ Déjà vue
20 ☐ Visual, auditory, or olfactory hallucinations
22 ☐ Fear
24 ☐ Difficulty speaking

*26 INJURIES SUSTAINED DURING ATTACK

[0] Not recorded
[1] Never
[2] Rarely
[3] Occasionally
[4] Frequently
[5] Usually

*28–29 LENGTH OF HOSPITALIZATION

☐☐ Weeks

*31 NUMBER OF ADMISSIONS

☐

*33–35 NUMBER OF MAJOR SEIZURES IN HOSPITAL WHILE ON MEDICATION

☐☐☐

*37–39 NUMBER OF MINOR SEIZURES WHILE ON MEDICATION

☐☐☐

41 SEIZURES RELATED TO MENSES WHILE IN HOSPITAL

[0] Not recorded
[1] No
[2] Suggestive
[3] Definitely

*43 SEIZURES RELATED TO LEAVE OF ABSENCE

[0] Not recorded
[1] No
[2] Suggestive
[3] Definitely

*45 SEIZURES RELATED TO TIME OF DAY

[0] Not recorded
[1] No
[2] Suggestive
[3] Definitely

47–48 IF RELATED TO TIME OF DAY, MOST COMMON TIME OF OCCURRENCE (Based on 24 hours)

☐☐

*50 SEIZURES OCCURRED IN WAKING HOURS ONLY

[0] Not recorded
[1] No
[2] Yes

*52 SEIZURES OCCURRED DURING SLEEP ONLY

[0] Not recorded
[1] No
[2] Yes

*54 SEIZURES OCCURRED DURING WAKING AND SLEEPING

[0] Not recorded
[1] No
[2] Yes

LATERALITY OF CEREBRAL DISTURBANCE

*56 RIGHT:

[0] Not recorded
[1] EEG only
[2] EEG and seizure pattern or neurological examination
[3] EEG, seizure pattern and neurological examination

*58 LEFT:

[0] Not recorded
[1] EEG only
[2] EEG and seizure pattern or neurological examination
[3] EEG, seizure patterns and neurological examination

*60 BILATERAL CEREBRAL INVOLVEMENT
(based on EEG, seizure patterns or neurological examination)

[0] Not recorded
[1] Absent
[2] Suggestively present
[3] Definitely present

*62 NO CEREBRAL DISTURBANCE (e.g. normal or Dys. 1 EEG, normal neurological, no focal seizure pattern)

[0] Not recorded
[1] Cerebral disturbance definitely present
[2] Cerebral disturbance suggestively present
[3] Cerebral disturbance definitely absent

*64 PNEUMOENCEPHALOGRAM DIFFUSE ATROPHY

[0] Not recorded
[1] Absent
[2] Suggestive dilatation of ventricles
[3] Definite ventricular dilatation

66-78 Duplicate these columns from original data on Card 6.
79-80 [1][0] Card number

CARD 11

PNEUMOENCEPHALOGRAM FOCAL ATROPHY

*2 RIGHT:

[0] Not recorded
[1] Absent
[2] Suggestively present
[3] Definitely present

*4 LEFT:

[0] Not recorded
[1] Absent
[2] Suggestively present
[3] Definitely present

*6 PNEUMOENCEPHALOGRAM CORTICAL ATROPHY

[0] Not recorded
[1] Absent
[2] Suggestively present
[3] Definitely present

8 ARTERIOGRAM FOCAL ABNORMALITY OF POSSIBLE ETIOLOGICAL SIGNIFICANCE

[0] Not recorded
[1] Absent
[2] Suggestively present
[3] Definitely present

10 LATERALIZATION ON ARTERIOGRAM

[0] Not recorded
[1] No lateralization
[2] Right side
[3] Left side

*12 OBJECTIVE FINDINGS OF CEREBRAL PATHOLOGY IN NEUROLOGICAL EXAMINATION (apart from organic mental syndrome)

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

PSYCHOLOGICAL TEST RESULTS

*14–16 VERBAL IQ

☐☐☐

*18–20 PERFORMANCE IQ

☐☐☐

*21–23 FULL SCALE IQ

☐☐☐

*25 IMMATURITY

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

*27 NEUROTIC TENDENCIES

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

*29 PSYCHOTIC TENDENCIES

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

*31 PERSONALITY DISTURBANCES

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

*33 ORGANIC PATHOLOGY SUSPECTED

[0] Not recorded
[1] None
[2] Mild
[3] Moderate
[4] Marked

SEIZURE PHOTOGRAPH ANALYSIS
INITIAL SYMPTOMS CONSIST OF:

35 ☐ Marked motor restlessness
37 ☐ Requests to stop test
39 ☐ Complains of dizziness
*41 ☐ Sits up
43 ☐ Isolated body or head jerks
45 ☐ Twitching of eyelids
47 ☐ Facial twitching unlocalized
49 ☐ Facial twitching, right
51 ☐ Facial twitching, left
53 ☐ Rhythmic blinking of eyelids
55 ☐ Rhythmic head nodding
57 ☐ Right arm twitching
59 ☐ Right leg twitching
61 ☐ Left arm twitching
63 ☐ Left leg twitching
64–65 Leave blank
66–78 Duplicate these columns from original data on Card 6.
79–80 [1][1] Card number

CARD 12 INITIAL SYMPTOMS CONSIST OF:

2 ☐ Verbalization
4 ☐ Vocalization
6 ☐ Looking around confused
8 ☐ Facial expression, bewildered
10 ☐ Facial expression, frightened
12 ☐ Facial expression, empty
14 ☐ Facial expression, angry

16	☐	Salivation
*18	☐	Chewing or swallowing or smacking
*20	☐	Head turns to right
*22	☐	Head turns to left
24	☐	Head swings to opposite side after initial turning
*26	☐	Head is retracted backwards
28	☐	Head is flexed towards chest
*30	☐	Eyes deviated to right
*32	☐	Eyes deviated to left
34	☐	Eyes swing to opposite side after initial turning
*36	☐	Eyes deviated upwards
38	☐	Eyes converge
40	☐	Extended right arm raised laterally
42	☐	Extended right arm raised anteriorly
44	☐	Extended right arm raised posteriorly
46	☐	Extended left arm raised laterally
48	☐	Extended left arm raised anteriorly
50	☐	Extended left arm raised posteriorly
*52	☐	Right arm flexed in elbow raised laterally
*54	☐	Right arm flexed in elbow raised anteriorly
56	☐	Right arm flexed in elbow raised posteriorly
*58	☐	Left arm flexed in elbow raised laterally
*60	☐	Left arm flexed in elbow raised anteriorly
62	☐	Left arm flexed in elbow raised posteriorly
*64	☐	Right arm held before face as if looking at head
66–78		Duplicate these columns from original data on Card 6.
79–80	☐1☐2	Card number

CARD 13 INITIAL SYMPTOMS CONSIST OF: (*cont'd*)

*2	☐	Left arm held before face as if looking at hand
4	☐	Right arm held above head as if touching back of head
6	☐	Left arm held above head as if touching back of head
8	☐	Right leg raised in extension
10	☐	Left leg raised in extension
*12	☐	Right leg raised while flexed in knee
*14	☐	Left leg raised while flexed in knee
16	☐	Right leg raised higher than left
18	☐	Left leg raised higher than right
*20	☐	Jackknifing
22	☐	Hyperextension of entire body
24	☐	Entire body rolls to the right
26	☐	Entire body rolls to the left
*28	☐	Legs diverge

TONIC PHASE

30 ☐ Tonic facial contraction, right
32 ☐ Tonic facial contraction, left
*34 ☐ Right arm extended in elbow and wrist
*36 ☐ Left arm extended in elbow and wrist
*38 ☐ Right arm extended in elbow, flexed in wrist
*40 ☐ Left arm extended in elbow, flexed in wrist
42 ☐ Right arm crosses over left
44 ☐ Left arm crosses over right
46 ☐ Arms diverge
*48 ☐ Fingers partially flexed, right hand
*50 ☐ Fingers partially flexed, left hand
*52 ☐ Fist, right
*54 ☐ Fist, left
*56 ☐ Right arm flexed in elbow
*58 ☐ Left arm flexed in elbow
59–65 Leave blank
66–78 Duplicate these columns from original data on Card 6.
79–80 [1][3] Card number

CARD 14—TONIC PHASE (*cont'd*)

*2 ☐ Right leg extended
*4 ☐ Left leg extended
6 ☐ Right leg flexed at knee
8 ☐ Left leg flexed at knee
10 ☐ Right leg crossed over left
12 ☐ Left leg crossed over right
14 ☐ Legs diverge
*16 ☐ Spontaneous Babinski's sign, right
*18 ☐ Spontaneous Babinski's sign, left

POSTICTAL STATE

20 ☐ Aphasia
22 ☐ Confused as to person
24 ☐ Confused as to place
26 ☐ Confused as to time
28 ☐ Random uncontrolled movements
30 ☐ Yelling
32 ☐ Aggressive behavior
34 ☐ Chewing, swallowing or smacking of lips
*36 ☐ Automatism
38 ☐ Sleep

ICTAL AUTOMATISM

40 DURATION

- [0] Not recorded
- [1] Less than 1 minute
- [2] Less than 1 to 2 minutes
- [3] Less than 2 to 3 minutes
- [4] Less than 3 to 5 minutes
- [5] Over 5 minutes

*42 [ ] Slight automatic acts, patient remains seated or lying.

*44 [ ] Marked rhythmic repetitive movements, patient remains seated or lying.

*46 [ ] Leaves chair, wanders about.

47–65 Leave blank

66–78 Duplicate these columns from original data on Card 6.

79–80 [1][4] Card number

MICHIGAN EPILEPSY CENTER AND LAFAYETTE CLINIC
ELECTROENCEPHALOGRAPHY

Coding Sheets
Department 3

☐☐☐☐☐ Patient number Name_____
☐☐☐☐☐ EEG number

PROJECT NAME_____
PHYSICIAN'S NAME_____

CARD 1

2-3 ☐☐ *Physician number*

RECORDING DATE

4-5 ☐☐ Month
6-7 ☐☐ Day
8-9 ☐☐ Year

AGE

10-11 ☐☐ Months
*12-13 ☐☐ Years

*14 SEX

[1] Male
[2] Female

15 HANDEDNESS

[0] Not recorded
[1] Right
[2] Left

16 PATIENT STATUS

[0] Not recorded
[1] Outpatient
[2] Inpatient
[3] Other—Describe:

_____

17 PLACE OF RESIDENCE

[0] Not recorded
[1] Greater Detroit
[2] Outside of Detroit

18 REFERRING PERSON OR AGENCY

- [0] Not recorded
- [1] Self
- [2] Spouse
- [3] Patient, sibling, or child
- [4] More distant relative or friend
- [5] Social agency
- [6] Physician or other hospital (except State Hospital transfer)
- [7] State Hospital transfer
- [8] Court or police
- [9] Other—Describe: _____

*19 LAST SEIZURE

- [0] Not recorded
- [1] Within one day
- [2] 1–3 days
- [3] 4–7 days
- [4] 8–14 days
- [5] More than 14 days

*20 ON ANTICONVULSANT MEDICATION

- [0] Not recorded
- [1] No
- [2] Yes

21-23 FAMILY NUMBER

□□□

24-28 NUMBER OF PROBAND

□□□□□

29 ANCESTRY

- [0] Not recorded
- [1] Father
- [2] Mother
- [3] Paternal grandfather
- [4] Paternal grandmother
- [5] Maternal grandfather
- [6] Maternal grandmother
- [7] Paternal aunt or uncle
- [8] Maternal aunt or uncle
- [9] Cousin

30 SIBLING ORDER

[0]
[1]
[2]
[3]
[4]
[5]
[6]
[7]
[8]
[9]

31 SIBLING TOTAL

[0]
[1]
[2]
[3]
[4]
[5]
[6]
[7]
[8]
[9]

32 CHILD

[0]
[1]
[2]
[3]
[4]
[5]
[6]
[7]
[9]

33 DRUG TREATMENT OF PATIENT OR RECENT ELECTRIC CONVULSIVE TREATMENT

[0] Not recorded
[1] None
[2] Drugs which do not affect EEG
[3] Drugs which could affect EEG, but patient received inadequate doses
[4] Tranquilizers in adequate amounts
[5] Barbiturates in adequate amounts
[6] Energizers or stimulants in adequate amounts
[7] Combination of drugs in adequate amounts
[8] Drugs which could affect EEG, adequate dose, but stopped for 48 hours
[9] Electric convulsive treatment within the last two months

*34 EEG DIAGNOSIS

[0] Not recorded
[1] Normal
[2] Borderline
[3] Mild abnormality
[4] Moderate abnormality
[5] Marked abnormality

*35 CONVULSIVE DISORDER SUSPECTED

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely, but not diagnostic
[5] Diagnostic

*36 FOCAL LESION SUSPECTED

[0] Not recorded
[1] Absent
[2] Questionable
[3] Probable
[4] Very likely but not diagnostic
[5] Diagnostic

ALPHA ACTIVITY

37 [ ] Present with eyes open (Score when not due to drowsiness)

*38 [0] Not recorded
[1] Absent
[2] Slight (less than 25% of recording time with eyes closed)
[3] Moderate (25–50% of recording time with eyes closed)
[4] Marked (50–75% of recording time with eyes closed)
[5] Excellent (75–100% of recording time with eyes closed)

THETA ACTIVITY

*39 [ ] Present with eyes open (Score when not due to drowsiness)

*40 [0] Not recorded
[1] Absent
[2] Slight (less than 25% of recording time)
[3] Moderate (25–50% of recording time)
[4] Marked (50–75% of recording time)
[5] Massive (75–100% of recording time)

FAST ACTIVITY

*41 [0] Not recorded
[1] Absent
[2] Slight (less than 25% of recording time)
[3] Moderate (25–50% of recording time)
[4] Marked (50–75% of recording time)
[5] Massive (75–100% of recording time)

42 [0] Not recorded
[1] Anterior head regions only
[2] Diffuse

*43 DIFFUSE DELTA ACTIVITY

[0] Not recorded
[1] Absent
[2] Slight (less than 25% of recording time)
[3] Moderate (25–50% of recording time)
[4] Marked (50–75% of recording time)
[5] Massive (75–100% of recording time)

DISCRETE RHYTHMIC SLOW WAVE FOCUS

44 [ ] Right frontal
45 [ ] Left frontal
46 [ ] Right motor
47 [ ] Left motor
48 [ ] Right parietal
49 [ ] Left parietal
50 [ ] Right occipital
51 [ ] Left occipital
*52 [ ] Right anterior temporal
*53 [ ] Left anterior temporal
*54 [ ] Right midtemporal
*55 [ ] Left midtemporal
56 [ ] Right posterior temporal
57 [ ] Left posterior temporal

58 ENTIRE RIGHT HEMISPHERE

[0] Not recorded
[1] Absent
[2] Present

*59 ENTIRE LEFT HEMISPHERE

[0] Not recorded
[1] Absent
[2] Present

TYPE OF FOCUS

*60 [ ] Theta
*61 [ ] Complex discharge
62 [ ] Sharp wave
63 [ ] Spike

64–65 Leave blank

66–70 [ ][ ][ ][ ][ ] Patient number
71–72 [ ][ ] Project number
73–74 [ ][ ] Deck number
75–76 [ ][ ] Evaluation number
77–78 [0][3] Department number
79–80 [0][1] Card number

CARD 2

MORE THAN ONE RHYTHMIC FOCUS

2 ☐ Shifting focus
3 ☐ Mirror focus
4 ☐ Independent foci

DISCRETE RANDOM SLOW WAVE FOCUS

5 ☐ Right frontal
6 ☐ Left frontal
7 ☐ Right motor
8 ☐ Left motor
9 ☐ Right parietal
10 ☐ Left parietal
11 ☐ Right occipital
12 ☐ Left occipital
13 ☐ Right anterior temporal
14 ☐ Left anterior temporal
15 ☐ Right midtemporal
16 ☐ Left midtemporal
17 ☐ Right posterior temporal
18 ☐ Left posterior temporal

19 ENTIRE RIGHT HEMISPHERE

[0] Not recorded
[1] Absent
[2] Present

20 ENTIRE LEFT HEMISPHERE

[0] Not recorded
[1] Absent
[2] Present

21 INDEPENDENT FOCI

[0] Not recorded
[1] Absent
[2] Present

GENERALIZED PAROXYSMAL ACTIVITY
(Express severity in frequency occurrence of bursts)

*22 ABORTIVE PAROXYSMS

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*23 DEFINITE PAROXYSMS BUT NOT SPIKE WAVE

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*24 ABORTIVE ATYPICAL SPIKE WAVES

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*25 ATYPICAL SPIKE WAVES

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*26 ATYPICAL SPIKE WAVES WITH MULTIPLE SPIKES

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

27 CLASSICAL SPIKE WAVES (3 c/s)

[0] Not recorded
[1] Absent
[2] Present

28 ATYPICAL SEIZURE PATTERNS

[0] Not recorded
[1] Absent
[2] Present

29 HYPSARHYTHMIA

[0] Not recorded
[1] Absent
[2] Present

BACKGROUND RHYTHMS VOLTAGE

*30 LEFT

[0] Not recorded
[1] 0–10 μv
[2] 10–20
[3] 20–30
[4] 30–40
[5] 40–50
[6] 50–60
[7] 60–70
[8] 70–80
[9] Above 80

*31 RIGHT

[0] Not recorded
[1] 0–10 μv
[2] 10–20
[3] 20–30
[4] 30–40
[5] 40–50
[6] 50–60
[7] 60–70
[8] 70–80
[9] Above 80

32 SYMMETRY

[0] Not recorded
[1] More than 60 μv lower on right
[2] 30–60 μv lower on right
[3] 10–30 μv lower on right
[4] Up to 10 μv lower on right
[5] Background symmetrical
[6] Up to 10 μv higher on right
[7] 10–30 μv higher on right
[8] 30–60 μv higher on right
[9] More than 60 μv higher on right

MAIN BACKGROUND FREQUENCY

*33–34 [ ][ ]

HYPERVENTILATION

*35 DIFFUSE NONPAROXYSMAL BUILDUP

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

36 [ ] Buildup persists for more than 1 minute

*37 DIFFUSE PAROXYSMAL BUILDUP

- [0] Not recorded
- [1] Absent
- [2] Slight
- [3] Moderate
- [4] Marked

38 [ ] Buildup persists for more than 1 minute

*39 FOCAL BUILDUP

- [0] Not recorded
- [1] Absent
- [2] Present in resting record but increased with hyperventilation
- [3] Not present, brought out by hyperventilation

AREA OF FOCUS

40 [ ] Right frontal
41 [ ] Left frontal
42 [ ] Right motor
43 [ ] Left motor
44 [ ] Right parietal
45 [ ] Left parietal
46 [ ] Right occipital
47 [ ] Left occipital
48 [ ] Right anterior temporal
49 [ ] Left anterior temporal
50 [ ] Right midtemporal
51 [ ] Left midtemporal
52 [ ] Right posterior temporal
53 [ ] Left posterior temporal

54 SPECIFIC EPILEPTIC CHANGES

- [0] Not recorded
- [1] Absent
- [2] Present in resting record but increased with hyperventilation
- [3] Not present, brought out by hyperventilation

PHOTIC DRIVING RESPONSE

LOW FLASH RATES 1–7 f/s

*55
- [0] Not recorded
- [1] None
- [2] Slight
- [3] Moderate
- [4] Marked

56
- [0] Not recorded
- [1] Mostly subharmonic
- [2] Mostly fundamental
- [3] Mostly harmonic

57 [0] Not recorded
[1] Occipital only
[2] Parieto-occipital
[3] Parieto-occipital-temporal
[4] Motor-parieto-occipital-temporal
[5] Diffuse

ALPHA RANGE 8–12 f/s

*58 [0] Not recorded
[1] None
[2] Slight
[3] Moderate
[4] Marked

59 [0] Not recorded
[1] Mostly subharmonic
[2] Mostly fundamental
[3] Mostly harmonic

60 [0] Not recorded
[1] Occipital only
[2] Parieto-occipital
[3] Parieto-occipital-temporal
[4] Motor-parieto-occipital-temporal
[5] Diffuse

HIGH FREQUENCIES 13 f/s AND ABOVE

*61 [0] Not recorded
[1] None
[2] Slight
[3] Moderate
[4] Marked

62 [0] Not recorded
[1] Mostly subharmonic
[2] Mostly fundamental
[3] Mostly harmonic

63 [0] Not recorded
[1] Occipital only
[2] Parieto-occipital
[3] Parieto-occipital-temporal
[4] Motor-parieto-occipital-temporal
[5] Diffuse

64–65 Leave blank

66–78 Duplicate these columns from original data on Card 1, Department 3.

79–80 [0][2] Card number

CARD 3

OTHER PHOTIC RESPONSES

2 ☐ Photomyoclonic response
3 ☐ Excessive, spikey appearing driving response
4 ☐ Abortive paroxysms
5 ☐ Spike wave paroxysms without clinical accompaniments
6 ☐ Spike wave paroxysms with clinical accompaniments
7 ☐ Grand mal type buildup

MISCELLANEOUS PHENOMENA

8 ☐ Anterior displacement of alpha
9 ☐ Posterior head regions slowing
10 ☐ Alpha notching
11 ☐ Lambda waves
12 ☐ Spikey appearing record
13 ☐ Other—Describe _____

SLEEP

*14
[0] Not recorded
[1] Normal
[2] Borderline
[3] Mildly abnormal
[4] Moderately abnormal
[5] Markedly abnormal

15
[0] Not recorded
[1] Induced
[2] Spontaneous

*16 SLEEP RECORD SHOWS MORE ABNORMALITY THAN WAKING RECORD
[0] Not recorded
[1] No
[2] Yes

*17 SLEEP RECORD SHOWS LESS ABNORMALITY THAN WAKING RECORD
[0] Not recorded
[1] No
[2] Yes

18 STAGES RECORDED
[0] Not recorded
[1] Drowsiness only
[2] V wave
[3] Spindles
[4] K complex spindles
[5] Delta

MAIN TYPE OF ABNORMALITY

19 ☐ Spikey V wave or K complex
20 ☐ Spindle *asymmetry*
21 ☐ 14 and 6 c/s positive spikes
*22 ☐ Focal sharp waves or spikes
23 ☐ Focal slow waves
24 ☐ Focal flattening
*25 ☐ Paroxysmal abnormalities
26 ☐ Atypical spike waves
27 ☐ Classical spike waves
28 ☐ Other—Describe: _____

AREA OF FOCAL ABNORMALITY

29 ☐ Right frontal
30 ☐ Left frontal
31 ☐ Right motor
32 ☐ Left motor
33 ☐ Right parietal
34 ☐ Left parietal
35 ☐ Right occipital
36 ☐ Left occipital
37 ☐ Right anterior temporal
38 ☐ Left anterior temporal
39 ☐ Right midtemporal
40 ☐ Left midtemporal
41 ☐ Right posterior temporal
42 ☐ Left posterior temporal

MEGIMIDE STUDY

QUANTITY GIVEN (cc)

*43-44 ☐☐

*45 GENERALIZED SLOWING

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*46 PAROXYSMAL RESPONSE

[0] Not recorded
[1] Absent
[2] Slight
[3] Moderate
[4] Marked

*47 FOCAL RESPONSE

[0] Not recorded
[1] Absent
[2] Present in resting record but increased with drug
[3] Not present, brought out by drug

AREA OF FOCAL RESPONSE

48 [ ] Right frontal
49 [ ] Left frontal
50 [ ] Right motor
51 [ ] Left motor
52 [ ] Right parietal
53 [ ] Left parietal
54 [ ] Right occipital
55 [ ] Left occipital
*56 [ ] Right anterior temporal
*57 [ ] Left anterior temporal
*58 [ ] Right midtemporal
*59 [ ] Left midtemporal
60 [ ] Right posterior temporal
61 [ ] Left posterior temporal

62 SEIZURE INDUCED

[0] Not recorded
[1] Absent
[2] EEG seizure only
[3] EEG and clinical seizure

63 ATTACK INDUCED WITHOUT EEG CHANGE

[0] Not recorded
[1] Absent
[2] Present

64–65 Leave blank
66–78 Duplicate these columns from original data on Card 1, Department 3.
79–80 [0][3] Card number

MICHIGAN EPILEPSY CENTER AND LAFAYETTE CLINIC
EEG SEIZURE PATTERNS

Department 3
Coding Sheets

☐☐☐☐☐ Patient number NAME_____
PROJECT NAME _____
PHYSICIAN NAME_____

CARD 4

CLASSICAL 3 c/s SPIKE WAVE

2 NUMBER OCCURRING IN RESTING RECORD

[0] Not applicable
[1] One
[2] Two
[3] Three
[4] Four
[5] Five
[6] Six
[7] Seven
[8] Eight
[9] Nine or more

3 AVERAGE DURATION

[0] Not applicable
[1] Less than 5 seconds
[2] 5–10 seconds
[3] 10–15 seconds
[4] 15–20 seconds
[5] 20–25 seconds
[6] 25–30 seconds
[7] 30–35 seconds
[8] 35–40 seconds
[9] More than 40 seconds

CLASSICAL 3 c/s SPIKE WAVE WITH MULTIPLE SPIKES

4 NUMBER OCCURRING IN RESTING RECORD

[0] Not applicable
[1] One
[2] Two
[3] Three
[4] Four
[5] Five
[6] Six
[7] Seven
[8] Eight
[9] Nine or more

5 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

CLASSICAL 3 c/s SPIKE WAVE WITH FOCAL ONSET

6 NUMBER OCCURRING IN RESTING RECORD

- [0] Not applicable
- [1] One
- [2] Two
- [3] Three
- [4] Four
- [5] Five
- [6] Six
- [7] Seven
- [8] Eight
- [9] Nine or more

7 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

AREAS INVOLVED

- 8 [ ] Left fronto-motor
- 9 [ ] Right fronto-motor
- 10 [ ] Left motor-parietal
- 11 [ ] Right motor-parietal
- 12 [ ] Left parieto-occipital
- 13 [ ] Right parieto-occipital
- 14 [ ] Left anterior-midtemporal
- 15 [ ] Right anterior-midtemporal
- 16 [ ] Left mid-posterior temporal
- 17 [ ] Right mid-posterior temporal

4 c/s SPIKE WAVE

18 NUMBER OCCURRING IN RESTING RECORD

- [0] Not applicable
- [1] One
- [2] Two
- [3] Three
- [4] Four
- [5] Five
- [6] Six
- [7] Seven
- [8] Eight
- [9] Nine or more

19 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

4 c/s SPIKE WAVE WITH MULTIPLE SPIKES

20 NUMBER OCCURRING IN RESTING RECORD

- [0] Not applicable
- [1] One
- [2] Two
- [3] Three
- [4] Four
- [5] Five
- [6] Six
- [7] Seven
- [8] Eight
- [9] Nine or more

21 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

4 c/s SPIKE WAVE WITH FOCAL ONSET

22 NUMBER OCCURRING IN RESTING RECORD

- [0] Not applicable
- [1] One
- [2] Two
- [3] Three
- [4] Four
- [5] Five
- [6] Six
- [7] Seven
- [8] Eight
- [9] Nine or more

23 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

AREAS INVOLVED

24 [ ] Left fronto-motor
25 [ ] Right fronto-motor
26 [ ] Left motor-parietal
27 [ ] Right motor-parietal
28 [ ] Left parieto-occipital
29 [ ] Right parieto-occipital
30 [ ] Left anterior-midtemporal
31 [ ] Right anterior-midtemporal
32 [ ] Left mid-posterior temporal
33 [ ] Right mid-posterior temporal

1–2 1/2 c/s SPIKE WAVE

34 NUMBER OCCURRING IN RESTING RECORD

- [0] Not applicable
- [1] One
- [2] Two
- [3] Three
- [4] Four
- [5] Five
- [6] Six
- [7] Seven
- [8] Eight
- [9] Nine or more

35 AVERAGE DURATION

[0] Not applicable
[1] Less than 5 seconds
[2] 5–10 seconds
[3] 10–15 seconds
[4] 15–20 seconds
[5] 20–25 seconds
[6] 25–30 seconds
[7] 30–35 seconds
[8] 35–40 seconds
[9] More than 40 seconds

1–2 1/2 c/s SPIKE WAVE WITH MULTIPLE SPIKES

36 NUMBER OCCURRING IN RESTING RECORD

[0] Not applicable
[1] One
[2] Two
[3] Three
[4] Four
[5] Five
[6] Six
[7] Seven
[8] Eight
[9] Nine or more

37 AVERAGE DURATION

[0] Not applicable
[1] Less than 5 seconds
[2] 5–10 seconds
[3] 10–15 seconds
[4] 15–20 seconds
[5] 20–25 seconds
[6] 25–30 seconds
[7] 30–35 seconds
[8] 35–40 seconds
[9] More than 40 seconds

1–2 1/2 c/s SPIKE WAVE WITH FOCAL ONSET

38 NUMBER OCCURRING IN RESTING RECORD

[0] Not applicable
[1] One
[2] Two
[3] Three
[4] Four
[5] Five
[6] Six
[7] Seven
[8] Eight
[9] Nine or more

39 AVERAGE DURATION

- [0] Not applicable
- [1] Less than 5 seconds
- [2] 5–10 seconds
- [3] 10–15 seconds
- [4] 15–20 seconds
- [5] 20–25 seconds
- [6] 25–30 seconds
- [7] 30–35 seconds
- [8] 35–40 seconds
- [9] More than 40 seconds

AREAS INVOLVED

- 40 [ ] Left fronto-motor
- 41 [ ] Right fronto-motor
- 42 [ ] Left motor-parietal
- 43 [ ] Right motor-parietal
- 44 [ ] Left parieto-occipital
- 45 [ ] Right parieto-occipital
- 46 [ ] Left anterior-midtemporal
- 47 [ ] Right anterior-midtemporal
- 48 [ ] Left midposterior temporal
- 49 [ ] Right midposterior temporal

FOCAL TEMPORAL SEIZURE (a) STARTS WITH GRADUAL BUILDUP OF DISCHARGES

AREA OF ONSET

- 50 [ ] Left anterior temporal
- 51 [ ] Left midtemporal
- 52 [ ] Left posterior temporal
- 53 [ ] Right anterior temporal
- 54 [ ] Right midtemporal
- 55 [ ] Right posterior temporal
- 56 [ ] Unclear

57 DURATION

- [0] Not applicable
- [1] Less than 30 seconds
- [2] 31–60 seconds
- [3] 1–3 minutes
- [4] 3–6 minutes
- [5] More than 6 minutes

FOCAL TEMPORAL SEIZURE (b) STARTS WITH DIFFUSE BURST

AREA MOST INVOLVED SUBSEQUENTLY

58 ☐ Left anterior temporal
59 ☐ Left midtemporal
60 ☐ Left posterior temporal
61 ☐ Right anterior temporal
62 ☐ Right midtemporal
63 ☐ Right posterior temporal
64 ☐ Unclear

65 DURATION

☐ Not applicable
☐ Less than 30 seconds
☐ 31–60 seconds
☐ 1–3 minutes
☐ 3–6 minutes
☐ More than 6 minutes

66–70 ☐☐☐☐☐ Patient number
71–72 ☐☐ Project number
73–74 ☐☐ Deck number
75–76 ☐☐ Evaluation number
77–78 0 3 Department number
79–80 0 4 Card number

CARD 5

FOCAL TEMPORAL SEIZURE (c) STARTS WITH SUPPRESSION OF ELECTRICAL ACTIVITY

AREA MOST INVOLVED SUBSEQUENTLY

2 ☐ Left anterior temporal
3 ☐ Left mid-temporal
4 ☐ Left posterior temporal
5 ☐ Right anterior temporal
6 ☐ Right mid-temporal
7 ☐ Right posterior temporal
8 ☐ Unclear

9 DURATION

☐ Not applicable
☐ Less than 30 seconds
☐ 31–60 seconds
☐ 1–3 minutes
☐ 3–6 minutes
☐ More than 6 minutes

FOCAL SEIZURE OTHER THAN TEMPORAL, STARTS WITH GRADUAL BUILDUP OF DISCHARGES

AREA OF ONSET

10 ☐ Left fronto-motor
11 ☐ Left motor-parietal
12 ☐ Left parieto-occipital
13 ☐ Right fronto-motor
14 ☐ Right motor-parietal
15 ☐ Right parieto-occipital

16 DURATION

[0] Not applicable
[1] Less than 30 seconds
[2] 31–60 seconds
[3] 1–3 minutes
[4] 3–9 minutes
[5] More than 9 minutes

FOCAL SEIZURE OTHER THAN TEMPORAL, STARTS WITH DIFFUSE BURST

AREA MOST INVOLVED SUBSEQUENTLY

17 ☐ Left fronto-motor
18 ☐ Left motor-parietal
19 ☐ Left parieto-occipital
20 ☐ Right fronto-motor
21 ☐ Right motor-parietal
22 ☐ Right parieto-occipital
23 ☐ Unclear

24 DURATION

[0] Not applicable
[1] Less than 30 seconds
[2] 31–60 seconds
[3] 1–3 minutes
[4] 3–9 minutes
[5] More than 9 minutes

GRAND MAL SEIZURE, STARTS WITH GRADUAL BUILDUP OF DISCHARGES

AREA OF ONSET

25 ☐ Left fronto-motor
26 ☐ Right fronto-motor
27 ☐ Left motor-parietal
28 ☐ Right motor-parietal
29 ☐ Left parieto-occipital
30 ☐ Right parieto-occipital
31 ☐ Left anterior-midtemporal
32 ☐ Right anterior-midtemporal
33 ☐ Left mid-posterior temporal
34 ☐ Right mid-posterior temporal
*35 ☐ Unclear

*36 ☐ GRAND MAL SEIZURE, STARTS WITH DIFFUSE BURST

SEIZURE DIFFICULT TO CLASSIFY ELECTROENCEPHALOGRAPHICALLY

*37 DURATION

[0] Not applicable
[1] Less than 10 seconds
[2] 11–30 seconds
[3] 31 seconds to 1 minute
[4] 1 minute to 3 minutes
[5] More than 3 minntes

POSTICTAL SLOW WAVE FOCUS

38 ☐ Left fronto-motor
39 ☐ Right fronto-motor
40 ☐ Left motor-parietal
41 ☐ Right motor-parietal
42 ☐ Left parieto-occipital
43 ☐ Right parieto-occipital
44 ☐ Left anterior-midtemporal
*45 ☐ Right anterior-midtemporal
46 ☐ Left mid-posterior temporal
*47 ☐ Right mid-posterior temporal
*48 ☐ Generalized slowing

CLINICAL TYPE OF RECORDED SEIZURE

*49	☐	Grand mal focal
*50	☐	Grand mal nonfocal
*51	☐	Major motor not typical grand mal focal
52	☐	Major motor not typical grand mal nonfocal
53	☐	Minor motor focal
54	☐	Minor motor nonfocal
55	☐	Absence with minimal myoclonic element
56	☐	Absence with marked myoclonic element
57	☐	Myoclonic jerks
*58	☐	Automatism
59	☐	Confusional state
60	☐	Psychic
61	☐	Sensory
62	☐	Akinetic
63	☐	Syncope
64	☐	Psychogenic
65	☐	Difficult to classify
66–78		Duplicate from Card 4, Department 3.
79–80	☐0☐5	Card number

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