# II: Treatment and prognosis


## Abstract

**Treatment and prognosis were studied in 122 patients with non-febrile seizures in a population of 6000. Phenytoin and phenobarbitone were the most commonly prescribed drugs, although the popularity of phenobarbitone had declined over time. The average duration of treatment was relatively short, and most patients received single drug treatment. Treatment patterns were erratic, and the surveillance and audit of treatment generally poor. Recurrence after a first attack was found in four fifths of the patients. Generally the total number of seizures suffered by each patient was small, the period of active epilepsy short, and remission when it occurred was usually permanent. The cumulative probability of continuing activity fell and the proportion of patients in remission rose over time. Patients with partial or mixed seizure types had a poorer overall prognosis.**

**The course of the epilepsy in the early years of treatment proved to be a useful guide to the long term prognosis, and the possibility that effective treatment might influence long term prognosis is raised.**


## Patients and methods

Treatment and prognosis was studied in the patients described in the preceding article. Data were gathered both from a review of each case record and from personal interview. Patients with single seizures were included, and epilepsy (two or more seizures) was classified as either active (a seizure within 24 months of the survey date) or inactive (no seizures within 24 months of the survey date).

## Results

### TREATMENT

The number and type of anticonvulsant medication received by each patient (*a*) throughout the course of the epilepsy (from the onset of seizures to the time of the survey) and (*b*) at the time of the survey was recorded, as was the duration of treatment (tables I and II).

TABLE I—*Details of treatment received by patients with epilepsy (n=122) since diagnosis*

| | No | | No |
|---|---|---|---|
| Treatment prescribed: | | Carbamazepine | 5 |
| Monotherapy throughout | 74 | Ethosuximide | 5 |
| Polytherapy at some time | 22 | Others* | 5 |
| No drugs at any time | 26 | | |
| | | Duration of treatment (n = 96): | |
| Drugs used (n = 96): | | ≤5 years | 55 |
| Phenobarbitone | 63 | 6-10 years | 14 |
| Phenytoin | 49 | 11-15 years | 13 |
| Valproate | 18 | ≥16 years | 14 |
| Primidone | 9 | | |

*Each of the following used in single patient: troxidone, dexamphetamine, sulthiame, clonazepam, acetazolamide.

TABLE II—*Details of treatment received at time of survey*

| Treatment state (n = 122) | No | Drugs used (n = 47) | No |
|---|---|---|---|
| Receiving anticonvulsant treatment: | | Phenytoin | 24 |
| Monotherapy | 32 | Phenobarbitone | 15 |
| Polytherapy | 15 | Valproate | 8 |
| Total | 47 | Primidone | 4 |
| Anticonvulsants discontinued | 49 | Carbamazepine | 2 |
| No drugs prescribed | 26 | Ethosuximide | 1 |

### NUMBER AND PATTERN OF SEIZURES

Table III shows the total number and type of seizures experienced by each patient from the onset of epilepsy to the time of the survey and the pattern of seizures over time in the 114 patients whose attacks started three or more years before the survey date (to allow time for a pattern to be ascertained). Seizure pattern was classified into four categories. Remission is defined as a seizure free interval of 24 or more months.

*Burst*—Repeated attacks occurring with no remission, followed by a remission continuing to the time of the survey (55 patients).

*Intermittent*—Repeated attacks occurring with at least one period of remission interposed (13 patients).

*Continuous*—Repeated attacks continuing with no remission up to the time of the survey (25 patients).

*Single*—A single attack with no recurrence (20 patients).

Those with partial and mixed seizures types were significantly more likely to have had more than 50 attacks and to be in the continuous category than those with other seizure types ($p < 0.05$ and $p < 0.001$ respectively), but no other relations were found. In those with the "burst pattern" (n = 55) the duration of active epilepsy (the time from the first to the last seizure) was less than one month in 10, less than 12 months in 26, and less than five years in 37 and less than 10 years in 45.

### RELAPSE OF SEIZURES AND REMISSION

Figure 1 shows the cumulative probability of a patient continuing to have active epilepsy, calculated using life table methods[1] (for all patients whose attacks began 24 or more months before the survey date). Figure 2 shows the proportion of patients in or entering a period of remission (more than two or four years) at successive years after the onset of seizures (by definition, this calculation includes only those whose follow up exceeds two and four years respectively). No significant differences were found when the probability rates for active epilepsy and the proportion of patients in remission were calculated separately for males and females, age of onset above or below 30, or idiopathic and symptomatic epilepsy.

### SINGLE SEIZURES, INACTIVE AND ACTIVE EPILEPSY

Table IV compares those with single seizures, active, and inactive epilepsy. Patients with single seizures were less likely to have partial seizures or to receive treatment than those with epilepsy, and active epilepsy was more common than inactive epilepsy in male patients and those with adult onset seizures.

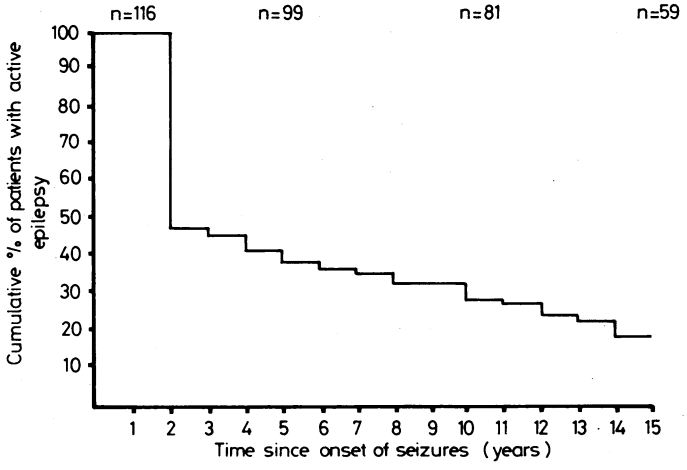


FIG 1—Cumulative probability of epilepsy remaining active in patient population at successive yearly intervals.

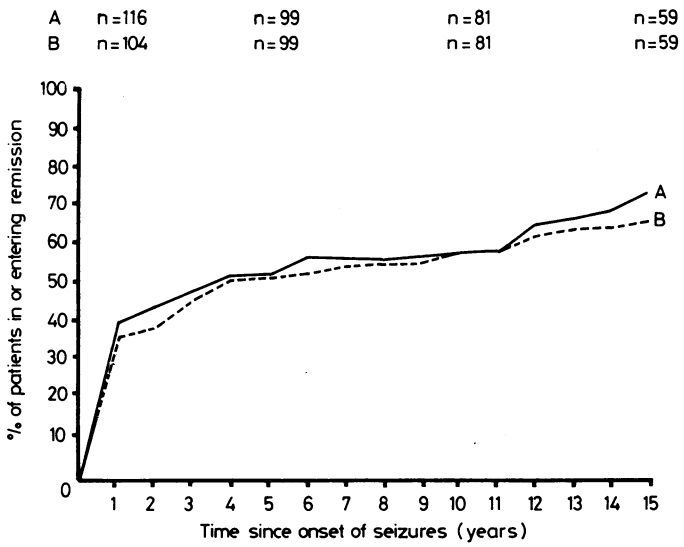


FIG 2—Proportion of patients in or entering a remission period (of at least two to four years) expressed as a percentage of the patients being followed up at successive yearly intervals. A=Remission of two or more years. B=Remission of four or more years.

patients were receiving a single drug.[5] It is a widely held misconception that anticonvulsant treatment is usually lifelong, although we are aware of no actual data confirming this. In the present study, in fact, treatment was often brief, and more than half the patients took anticonvulsants for less than five years, the withdrawal of treatment often being carried out of the patients' own accord. The surveillance and audit of treatment was generally poor, drug concentrations were rarely measured, and chronic toxic side effects rarely recorded. There was, in general, an insouciant attitude to many aspects of treatment.

Prognosis in epilepsy has been the subject of several hospital based surveys, which were extensively reviewed by Rodin.[6] He concluded that: "80% of 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 re-emphasises that epilepsy should be regarded as a chronic condition with remissions and exacerbations," and: "The percentage of patients who are regarded in terminal remission stand in marked indirect relationship to the length of follow up." These views are widely accepted; we emphasise them here, for although they might apply to the highly selected populations of chronic cases in specialist centres, we think that they are misleading for the general population of epileptic patients.

In this, the only community based study of prognosis in the United Kingdom, we have considered a number of different aspects. Firstly, the clinically important question of the chance of recurrence after a single fit. Seizures recurred in four out of five patients after the first fit in this survey and this is a higher proportion than is generally appreciated from hospital surveys.[7-9] Although this risk may be an overestimate, as single attacks may have been overlooked or concealed, it is evident that recurrence must be expected in a sizable majority of patients.

TABLE III—*Type, number, and pattern of seizures from onset of epilepsy to time of survey in 122 patients*

| Type | Number* | | | | | Pattern† | | | |
|---|---|---|---|---|---|---|---|---|---|
| | 1 | 2-10 | 11-49 | 50-99 | ≥100 | Single | Burst | Continuous | Intermittent |
| Partial‡ | 3 | 10 | 4 | 1 | 5 | 3 | 11 | 5 | 2 |
| Generalised§ | 15 | 43 | 7 | 0 | 6 | 13 | 38 | 9 | 10 |
| Mixed¶ | 0 | 0 | 4 | 1 | 10 | 0 | 2 | 11 | 1 |
| No details | 4 | 4 | 0 | 0 | 0 | 4 | 4 | 0 | 0 |
| Total | 22 (19%) | 57 (49%) | 15 (13%) | 2 (2%) | 21 (18%) | 20 (18%) | 55 (49%) | 25 (22%) | 13 (12%) |

*In five cases not known.
†In nine cases, onset of seizures too recent (less than three years) to categorise pattern.
‡Includes complex partial and complex partial evolving to secondary generalised seizures.
§Includes generalised absence, tonic clonic, and other "unspecified" generalised seizures.
¶Includes simple/complex partial and secondary generalised seizures, and generalised absence and tonic clonic seizures.

## Discussion

Treatment has received little attention in previous community surveys of epilepsy. Current drug treatment was recorded in two studies in the past 15 years, and only phenobarbitone and phenytoin were reported to have been used to any great extent.[2 3] Similar findings were obtained here, though the proportion of patients taking phenobarbitone had appreciably diminished over time (tables I and II). Valproate was the only other drug to have been used in more than 10% of patients and, perhaps because of its active marketing, appears to have been often chosen by the general practitioner as initial treatment in cases that might be considered inappropriate—for example, partial or symptomatic epilepsies. Treatment policy varied widely among the different hospital and practice doctors. After a single seizure, for instance, one in three patients received medication, and in one case phenobarbitone was prescribed unchanged for the next 30 years. Nearly half of those with active epilepsy at the time of the survey were not receiving anticonvulsant treatment, and a number of others were receiving inadequate or inappropriate treatment unchanged despite continuing fits. About one in 10 of all patients with epilepsy (two or more seizures) had never taken medication. The number of patients receiving more than one anticonvulsant drug (a subject of much recent interest[4]) was surprisingly small in this population. Of those treated, only 22 (23%) of 96 had received combination treatment at any point and 15 (32%) of 47 at the time of the survey. This is in sharp contrast to hospital practice; in the largest survey of 11 720 patients from clinics and institutions, for instance, the mean number of drugs per patient was 3·2, of which 84% were anticonvulsants, and less than 5% of the

TABLE IV—*Comparison of those with single seizures, active and inactive epilepsy*

| | Single seizures (n=22) | Inactive epilepsy* (n=68) | Active epilepsy† (n=32) |
|---|---|---|---|
| Sex: | | | |
| Male | 9 | 17 | 15 |
| Female | 13 | 51 | 17 |
| Age: | | | |
| Mean | 33 | 41 | 43 |
| Range | 6-72 | 1-83 | 4-78 |
| Age at onset (years): | | | |
| 1-20 | 13 | 42 | 13 |
| 21-60 | 6 | 20 | 15 |
| >60 | 3 | 6 | 4 |
| Seizure type: | | | |
| Generalised | 15 | 39 | 16 |
| Partial or mixed | 3 | 29 | 16 |
| No details | 4 | 5 | |
| Treatment at time of survey: | | | |
| No treatment | 15 | 6 | 5 |
| Drugs discontinued | 4 | 36 | 9 |
| Monotherapy | 3 | 20 | 9 |
| Polytherapy | 0 | 6 | 9 |
| Hospital follow up at time of survey | 2 | 13 | 7 |

*Inactive epilepsy: no attacks in the two years preceding the survey (in those with a history of two or more seizures).
†Active epilepsy: attacks in the two years preceding the survey (in those with a history of two or more seizures).

This is especially so in those with partial seizures, but there were no correlations with other clinical factors. As noted by others,[8-11] we found that the second seizure occurred in most patients within 12 months of the first. We next looked at the total number and pattern of attacks in the population as a whole. In most patients the overall number of seizures experienced was small (between one and 10 attacks in 79 (68%)) and the "burst" pattern was the commonest pattern of seizure activity (55 (49%) patients) in which seizures occurred over a limited period followed by permanent remission (table III). The duration of activity in those with this pattern was often short (less than one year in 26 (47%)). An intermittent pattern (with remission and relapse) was seen in only 13 (12%) cases and in such cases there was often a clear provoking factor associated with relapse—for example, pregnancy, stress, or drug withdrawal—and a continuous pattern was found in 25 (22%) cases. The cumulative probability of a patient continuing to suffer seizures fell over time (fig 1) and the proportion of those in remission rose over time (fig 2), the rate of rise being greatest in the early years. Thus, for instance, 15 years after the onset of seizures only 19% of the patients had had a seizure in the previous two years, and these findings are similar to the only other comparable community survey carried out in Rochester, Minnesota.[12]

Taking an overall view of these results, in this general practice population about 2% of persons suffered at least one non-febrile seizure, and in most cases these recurred. Treatment was usually instituted at this stage, and most patients suffered a small number of attacks only (less than 10) over a short period (most less than one year). The epilepsy then remitted and remission was usually permanent (in three quarters of cases). In about one fifth the seizures continued relentlessly, and it is such patients presumably who form the bulk of "chronic epileptics" requiring continual medical care. Only about one in 10 patients experienced a remitting and relapsing course. The prognosis for control of seizures was worse in those with partial or mixed seizures. It is clear that the view that epilepsy is a chronic condition with a continuing liability to relapse is true for only a few cases, and this opinion reflects the selection bias of studies based on hospitals or institutions.

Finally, we would like to emphasise the importance of the temporal aspects of prognosis. We found that most patients entered remission early, the longer the epilepsy remained active the less likely was eventual remission, and relapse after remission was relatively rare. It follows that the long term prognosis for epilepsy in this population could have been largely predicted from its early course. At an arbitrary point of five years after the first seizure, for instance, of those whose epilepsy was still active, only 21% achieved subsequent terminal remission compared with 96% of those who were already in remission. Most patients who developed epilepsy were treated, and their condition then took a well circumscribed, short lived course, which suggests that treatment might be "curative." This is difficult to test in the absence of an untreated control group, and remarkably there is little information about the clinical course of untreated seizures. More than 100 years ago Gowers wrote: "The spontaneous cessation of the disease is an event too rare to be reasonably anticipated," and that effective treatment (with bromides) significantly improved this prognosis. He postulated that "each fit facilitates the occurrence of the next," and treatment, in suppressing seizures, might thus lessen the long term liability to relapse.[13] The effect of early treatment on long term prognosis in epilepsy is a crucial subject for future research, which the present study did not tackle. If Gowers's suggestion is correct there are important implications for our general management strategems.

We are grateful to the partners and staff of the general practice and to the patients for their help in this study and for the support provided by Parke-Davis & Co. We also thank Dr M Espir and Dr E H Reynolds for their helpful criticism of the papers.

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(*Accepted 24 May 1983*)

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CAPON WATER—"Take a Capon the guts being pulled out, cut in pieces, the fat being taken away, boiled in a sufficient quantity of spring-water in a close vessel, take of this broth three pounds. Borrage and Violet-water, of each a pound and a half; white Wine one pound, red rose leaves two drams and an half, the flowers of Borrage, Violets and Bugloss, of each one dram, pieces of bread, hot out of the oven, half a pound, Cinnamon bruised, half an ounce, distil it in a glass still according to art."

The simples are most of them appropriated to the heart, and in truth the composition greatly nourishes and strengthens such as are in consumptions, and restores lost strength, either by fevers or other sickness: It is a sovereign remedy for hectic fevers, and Marasmos, which is nothing else but a consumption coming from them. Let such as are subject to these diseases, hold it for a jewel. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)

SPIRIT AND WATER OF ANGELICA—"Take of the leaves of Angelica eight ounces, of Carduus Benedictus six ounces, of Bawm and Sage, of each four ounces, Angelica seeds six ounces; sweet Fennel seeds nine ounces. Let the herbs, being dryed, and the seeds be grossly bruised, to which add of the species called Aromaticum Rosarum, and of the species called Diamoschu Dulce, of each an ounce and a half, infuse them two days in thirty two pints of Spanish Wine, then distil them with a gentle fire, and with every pound mix two ounces of sugar dissolved in Rose-water.

Let the three first pounds be called by the name of Spirit, the rest by the name of water."

The chief end of composing this medicine, was to strengthen the heart and resist infection, and therefore is very wholesome in pestilential times, and for such as walk in stinking air. (Nicholas Culpeper (1616-54) *The Complete Herbal*, 1850.)