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Editorial

Epilepsy after first seizures: risks and implications

All patients who develop epilepsy experience a first seizure, but for some a first seizure is an isolated event. The dilemma for the clinician, be that a general practitioner, casualty officer, or hospital based physician, lies in determining whether a recent event was the first of several or a single seizure. There are now several studies that have given estimates of the risk of recurrence after a first or single seizure but they have produced conflicting results.[1–11] Estimates of recurrence rates have varied from 27% by three years up to 84% after a variable length of follow up.[1 2] Two further recently published studies, one British,[12] one American,[13] explore this area in different ways and comparisons help clarify some of the problems, even though the estimates of recurrence rates for first seizures by three years are 78% and 29% respectively.

Few epidemiological or prognostic subjects are so bedevilled by selection bias as the estimation of risk of recurrence following a first seizure. Factors that may influence recurrence rates include the case definitions used for ascertainment, diagnostic uncertainty, referral patterns within the population studied, the timing of assessment for inclusion in the study, and the prevalence of a variety of potential risk factors within the population studied.

The National General Practitioner Study of Epilepsy (NGPSE)[12] has attempted to be as comprehensive and sensitive in its case ascertainment as possible. Notifications were taken from 275 general practitioners between June 1984 and October 1987 for every person with suspected seizures or epilepsy. The great virtue of the NGPSE survey is its attempt at comprehensive case ascertainment which makes it as independent as possible of influence from referral patterns. The different systems of health care on the two sides of the Atlantic may potentially have enormous effects on referral patterns which can influence recurrence rates in studies of specialist origin. The NGPSE study included any possible seizures including febrile convulsions and seizures associated with acute illness (acute symptomatic seizures). Case review revealed 564 patients with at least one definite epileptic seizure in a population of 1091 notifications. The decision about whether a seizure was "definite" was taken six months after entry, the length of time possibly increasing certainty. When analysis of recurrence is undertaken for first seizures, including those for patients who were only notified to the study after a second or subsequent event had raised the suspicion of epilepsy, the estimated recurrence rate was 78% (95% CL 78–81) by three years. Estimated recurrence rates, however were only 46% (95% CL 39–53) at three years for the group of subjects who were notified at the time when they had had only a single seizure. A single episode is less likely to be diagnosed definitely as a seizure than are recurrent episodes. Inclusion of patients for analysis after a second episode will increase recurrence rates.

Hauser *et al*[13] adopted a much more specific and restrictive definition of a first seizure. Subjects were recruited from hospital based practice including hospital admissions, EEG referrals and neurology and epilepsy clinic referrals at a University Hospital. Of those with newly identified unprovoked seizures 74% had had previous seizures before the first contact. They included in the report only those who had a definite unprovoked seizure, documented by an eye witness, and who, on extensive review of the past history, had not experienced a previous unprovoked seizure. Consent forms were signed within 24 hours of the first seizure and an exhaustive protocol was completed within 30 days of the index seizure. All acute symptomatic and febrile seizures were excluded from this analysis. Clearly this study excluded a great many patients who would have been included in the NGPSE.[12] Hauser *et al*[13] argue that their interviewing techniques reduce the possibility of inclusion of patients as having a first seizure who have in fact experienced previous seizure episodes, perhaps in the form of partial seizures of one kind or another. Seizure recurrence among those with two or more unprovoked seizures is two to three times higher than those with single seizures[14] which may explain some of the discrepancy. However, the estimated risk of recurrence at three years was only 29% in the series by Hauser *et al* compared with 46% for the comparable group in the NGPSE.

The influence of antiepileptic drugs may confound estimates of seizure recurrence. Some studies have suggested that this influence is negligible when they have compared patients within their population who were treated with those who did not receive treatment.[5 13] The NGPSE[12] survey suggests that treatment may be effective in preventing recurrence though again patients were not randomised to treatment or no treatment. A randomised study of antiepileptic drugs versus no treatment has been started in Italy and initial data from this show a large reduction in the risk of recurrence[15] (a halving of risk). As 80% of patients in the study of Hauser *et al*[13] were treated, compared with only 15% in the NGPSE survey, this influence may go a considerable way to explaining differences in recurrence rates on each side of the Atlantic. Certainly assessment of risk from any study should take into account the proportion of patients who receive antiepileptic drug treatment, though there must always be uncertainty about the compliance of patients treated after a first seizure.

The period that elapsed following a first seizure is another important influence on the continuing risk. This

was clearly identified as a factor influencing recurrence rates by Hopkins *et al.*[5] The NGPSE survey allows the calculation of hazard rates at different times following a first seizure that clearly demonstrate this phenomenon. The rate of recurrence fell from 0·033 per week in the first six months to 0·004 per week in the one to three year period following a first seizure.

Different case mixes within populations with differing risk factors will influence recurrence rates. The British and American studies have agreed in identifying certain risk factors.

Previously it had proved difficult to identify prognostic factors for recurrence after a first seizure. In the NGPSE,[13] recurrence rates were influenced by aetiology, seizure type, and age, as well as the time elapsed from the first attack. Thus acute symptomatic seizures carried a 46% (95% CL 34–57) three year risk of recurrence compared with an 85% (95% CL 77–92) and 81% (95% CL 77–86) three year recurrence for remote symptomatic and idiopathic seizures. Partial seizures had a 94% (95% CL 90–99) recurrence rate by three years compared with a 72% (95% CL 67–77) recurrence rate for tonic-clonic seizures. Recurrence rates were highest in the first 15 years of life and over the age of 60 (83%). The NGPSE survey does not address the role of the EEG in predicting a recurrence.

Hauser *et al*[13] in their population of 208 patients undertook a statistically more sophisticated analysis of factors affecting recurrence rates than that which has so far been published by the NGPSE survey. Patients with a previous neurological insult and remote symptomatic seizures had 2·55 (95% CL 1·44–4·51) times the risk of recurrence of those with idiopathic seizures. In the remote symptomatic group the presence of Todd's paresis or previous acute symptomatic seizures relating to the original insult (for example, head injury or encephalitis) greatly increased the risk of recurrence. Among the cryptogenic group the presence of generalised spike-wave in the EEG increased the relative risk of recurrence by a factor of 2·69 (95% CL 1·28–5·67) and having a sibling affected increased the risk by 2·51 (95% CL 1·23–5·11).

It would be helpful to develop techniques that allow a more accurate individual prognosis for patients presenting with a first seizure. The data from both the NGPSE[12] survey and the study of Hauser *et al*[13] allow the application of multivariate proportional hazards analysis from which it may be possible to develop a prognostic index that could be used to predict risk of seizure recurrence on a more individual basis. This has already been undertaken in identifying risk of recurrence following the withdrawal of antiepileptic drugs[16] and a similar strategy could be developed for recurrence after a first seizure. The strength of such a model would inevitably be increased by data pooling and meta-analysis of the studies that exist, a step that should be actively considered by the groups working in the area. When the results of the Italian randomised study[15] of treatment of first seizures becomes available it should be possible to estimate the risks both on and off antiepileptic drug treatment, taking into account clinical factors such as aetiology, age, seizure type and time elapsed from the last attack.

What are the implications of these new data? The most important practical question is whether first seizures should be treated with antiepileptic drugs. The NGPSE survey suggests that the high risk of recurrence for other than acute symptomatic seizures does warrant serious consideration of treatment. A prognostic model would allow counselling of patients who inevitably will take the final decision about initiating treatment and complying with it. It must be recognised, however, that the diagnosis of a definite seizure from a single event is always difficult. Clinicians can have considerable difficulty differentiating between pseudo-seizures and epileptic seizures even when such seizures present in status epilepticus.[17] The potential for misdiagnosis when clinicians deal with a single event that may be imperfectly described to them is obvious. Another part of the decision making process that remains unclear is whether the early suppression of seizures prevents the development of chronic epilepsy. This has been suggested from circumstantial evidence[18] but answers to this will have to await large randomised studies with long term follow up of patients with first seizures and early epilepsy.

The second practical implication is the current licensing regulations applied by the Department of Transport. Most patients with a cryptogenic single seizure would currently be allowed to drive after 12 months though patients with a single seizure and some identified cerebral pathology such as a stroke will be treated as having epilepsy and barred from driving until they are seizure-free for two years. The NGPSE survey suggests that after a 12 month seizure-free interval following a first seizure the risk of a seizure in the next 12 months may still be in excess of 20%, which is the arbitrary cut-off point that is usually used to determine the suitability of an applicant to hold an ordinary driving licence. This in turn raises the question of whether single seizures deserve different treatment by the licensing authority or indeed by clincians. The NGPSE survey goes a long way to blurring the distinctions between a single seizure and epilepsy, and raises questions about the way in which we use the term. Traditionally a single seizure has not been considered to be epilepsy but it now seems that most single seizures are part of epilepsy though probably one that may be short lasting and characterised by only a few seizures over a relatively short period of time.[19] As a diagnosis of epilepsy is undoubtedly stigmatising,[20] Hart *et al*,[12] argue for a new term "pre-epilepsy" that would cover both single seizures and those with infrequent or few seizures who never experience a chronic and disabling epilepsy. Further complicating the issue with such a term, seems unhelpful. As first seizures become more closely identified with epilepsy we should rely not on new words but more on educating the patient and public about epilepsy to reduce the stigma.

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Neurological stamp

St Vitus (286–302)

According to legend St Vitus was accused of witchcraft and sorcery after miraculously curing the fits that afflicted the son of Emperor Diocletian. Just before being tortured St Vitus prayed that those who commemorated the day of his death should be protected from the dancing mania. St Vitus' dance was probably a form of mass hysteria with the participants dancing wildly until they fell to the ground exhausted. In Italy it was attributed to the bite of the venomous spider, the tarantula, and was thus called tarantarism. The tarantella, a rapid whirling Italian dance was once thought to be a cure for tarantarism. In Germany it was considered to be the work of the devil, curable only by the church until Paracelsus (1492–1541) attempted to prove that it was really a disease.

The illness, St Vitus' dance or chorea minor, was described by Sydenham in 1686 thus, "Chorea Sancti Viti is a sort of convulsion which chiefly invades boys and girls from 10 years of age to puberty; first, it shows itself by a certain lameness, or rather instability of one of the legs, which the patient drags after him like a fool; afterward it appears in the hand of the same side; which he that is affected by the disease, can by no means keep in the same posture for one moment, if it be brought to the breast, or any other position or place, by a certain convulsion, let the patient do what he can."

There have been a number of stamps honouring St Vitus including one in 1923 where he is shown as the patron saint of Fiume, now Rijeka. He is also the patron saint of dancers. The stamp shown here was issued by Czechoslovakia in 1970 (Stanley Gibbons 1893, Scott 1689).

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