The main point of this commentary, however, is to review the ethical decision to use chewing gum containing sucrose for the children in the control group. There are several reasons why an ethics committee based in the United Kingdom might have taken a different view from that reached in Finland.

Firstly, the use of chewing gum containing sucrose was not without risk to the dental health of children susceptible to caries in the control group. The previous study on xylitol that used a sucrose chewing gum in a control group was in older children (average age 10.2 years) and did not test the effect on the primary dentition which may be at greater risk.⁵ Admittedly this risk was small considering the very limited time of the experiment.

Secondly, the researchers seemed to be aware of the risk and therefore excluded children in whom caries was "noticed" when they took the first nasopharyngeal samples. They did not employ a dentally trained person to undertake this baseline examination, however, and may well have missed several children already suffering from the disease. This can be inferred from the observations of the dental nurse who, four months after the end of the trial, noted 44 children with dental decay. It is extremely unlikely that a fifth of the children developed new carious lesions in the six months in question, particularly when 21 children in the study group received xylitol chewing gum for the first two months.

The precise nature of this examination by the dental nurse is not stated but probably did not include the use of dental radiographs. Without these further lesions may have been missed specifically on the proximal surfaces of the molar teeth, surfaces particularly at risk from sucrose in the diet.

Thirdly, children in the control group already suffering from caries would have been subjected to increased risk of new or extended carious lesions. Such a risk would be considered by many too great to justify the possible benefits likely to accrue from the clinical trial. Furthermore, it seems to take little account of the guidance that "parents and guardians of minors cannot give consent on their behalf to any procedures which are of no particular benefit to them and which may carry some risk of harm."⁶

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Long term use of lamotrigine and vigabatrin in severe refractory epilepsy: audit of outcome

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New antiepileptic drugs have a pivotal role in the successful treatment of the 20-30% of patients with epilepsy that is resistant to drug treatment. They are considered to be effective in such patients if they reduce the frequency of seizures by 50% or more because few patients are rendered seizure free.¹ Despite these drugs' apparent success with this outcome measure,^{2,3} the question still remains whether new antiepileptic drugs affect the long term prognosis of refractory epilepsy as measured by mortality and freedom from seizures.¹ We report our follow up audit of patients recruited from 1987 to 1989 into two uncontrolled open label clinical studies of lamotrigine and vigabatrin.^{2,3}

Patients, methods, and results

The two open label trials in 128 patients (vigabatrin) and 125 patients (lamotrigine) were both described in detail in 1990.^{2,3} All patients had confirmed severe medically refractory epilepsy and were evaluated as inpatients or outpatients at the Chalfont Centre for Epilepsy or the National Hospital for Neurology and Neurosurgery. After the trials the patients could continue the trial drugs, which were licensed in 1989 (vigabatrin) and 1991 (lamotrigine). By using hospital records and by contacting general practitioners, referring physicians, and the patients directly, we determined (a) how many patients were free of seizures, (b) how many were still taking the trial drug, and (c) how many had died. When appropriate the data on lamotrigine and vigabatrin were compared with the χ^2 test.

We successfully followed up 120 (96%) and 124 (97%) of the patients in the vigabatrin and lamotrigine trials respectively. Four of the five lost to follow up in the lamotrigine group and two of the four lost to follow up

Table 1—Long term outcome in patients with refractory epilepsy entered into open label studies of vigabatrin and lamotrigine as additional treatment

Outcome	Lamotrigine (n = 125)	Vigabatrin (n = 128)
Responded to treatment*	26	41
Lost to follow up	5	4
Seizure free	1	2
Continuing to take trial drugs	11	9
Stopped but restarted trial drugs	3	4
No longer taking trial drugs	89	96
Died	16	13

*50% or greater reduction in frequency of seizures.

in the vigabatrin group were no longer taking their respective trial drug. Table 1 shows details of the patients. A total of 16 (13%) of the lamotrigine group and 13 (10%) of the vigabatrin group had died in about 850 patient years. Of those living, 89 (86%) of the lamotrigine group and 96 (86%) of the vigabatrin group were no longer taking their respective trial drug, although 26 (21%) of the lamotrigine group and 41 (31%) of the vigabatrin group had responded to treatment. One patient was seizure free while taking lamotrigine and two were seizure free while taking vigabatrin. There were no significant differences at $P < 0.05$ between the lamotrigine and vigabatrin groups.

Comment

Of those successfully followed up 6-8 years after recruitment into open label trials for vigabatrin and lamotrigine, three patients were rendered seizure free. Indeed, 86% of those still living were no longer taking

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the trial drugs; this was probably due to inefficacy or intolerance. However, there may be confounding factors such as withdrawal of the treatment after successful surgery for epilepsy or after entry of patients into other drug trials.

The high death rates that we observed of about 15 per 1000 patient years for vigabatrin and 19 per 1000 patient years for lamotrigine are comparable with the high mortality of 13–33 per 1000 patient years in this population.^{4,5}

Thus the addition of either vigabatrin or lamotrigine to the treatment of a particularly refractory type of epilepsy has only marginal benefit in terms of mortality and freedom from seizures. These drugs may be more beneficial in less refractory epilepsy or in different patient groups, and they may prove to have fewer adverse effects than older antiepileptic drugs. However, new antiepileptic drugs are developed to improve the prognosis of severe refractory epilepsy, and we should

not deceive ourselves that this task has been accomplished.

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Do authors know who refereed their paper? A questionnaire survey

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The process of peer review of medical research before publication has come under considerable scrutiny,¹ although it would be fair to say that no better system has yet been devised. Much attention has been given to the question of whether or not referees produce better quality reports when blinded to the identity of the authors of the papers they are asked to review—the answer being a qualified yes.^{2,3} Another frequently asked question is whether or not referees should sign their opinions.⁴ However, to our knowledge no one has asked a simpler question: can authors guess the identity of the reviewer anyway?

Methods and results

Psychological Medicine is a leading international academic journal of psychiatry. For a five month period all those who submitted a manuscript to the journal were asked if they could guess the identity of the referees assigned to their paper (usually two or three), drawn from the pool of 580 available to the editors. All authors were sent a simple form asking them to write down the presumed identity of each referee and to indicate their degree of certainty on a four point scale, ranging from very uncertain (1) to certain (4). Alternatively the author could say that he or she had no idea of each referee's identity. The single page questionnaire was sent at the same time as the author was given the final decision about acceptance or rejection of the manuscript. Proportions were compared using the χ^2 test without Yates's correction.

A total of 135 forms were sent out and 94 received back (70%). As expected,⁵ non-responders were more likely than responders to have had their paper rejected (44.0% v 7.8%, $\chi^2 = 19.9$, $df = 1$, $P < 0.001$). The total number of referees' reports for the 94 papers for which we received responses was 252. Of these 252 referees 15 were correctly identified (5.9%), 36 were incorrectly identified (14.3%), and in 201 (79.7%) the author had no idea of the referee's identity. Nearly all papers were reviewed by more than one referee (usually three) in

four instances the author indicated the correct referee but against the wrong report. In two instances there were reasons to believe this was because of a misreading of the reference number and that the identity had been correctly guessed. If all those who had identified a referee of their paper but for the wrong report were given the benefit of the doubt then the correct number of guesses rose to 19 (7.5%).

The mean level of certainty for those who correctly identified the referee was 2.5 (lying between uncertain and fairly certain), compared with 1.8 for inaccurate guesses (between very uncertain and uncertain) ($t = 2.55$, $df = 46$, $P = 0.014$).

Using authors rather than referees as the denominator we found that those who correctly identified one or more referee were more likely to have had their paper accepted ($\chi^2 = 4.61$, $df = 1$, $P = 0.03$).

Comment

Anyone who has ever submitted a scientific paper will no doubt be familiar with the elaborate process of intuition and detection that goes into attempting to deduce the identity of the anonymous referee who has praised or damned the paper. This study suggests that even for a specialty journal such efforts are largely unrewarding and that most referees remain anonymous.

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