Of the 28 patients originally recruited, 25 completed the two parts of the trial, and filled in the diary cards successfully. Two of the three patients that dropped out did so because of severe cramps during the placebo period. The order in which the treatments were given played an important part in the results (Table 1). Patients who started with quinine, and then went over to placebo, experienced more nights with cramp during the placebo period (65%) than those who started with placebo (37%). The test for carry over is significant (Mann Whitney W=247.5, $P<0.05$). However, the difference between the two treatments in the first period alone is not significant.

Table 1. Overall percentage of nights in each period in which cramp was experienced by the 25 patients.

	% of nights with cramp		
Treatment	1st period ($n=750$)	2nd period ($n=750$)	Both periods ($n=1500$)
Quinine	*27*	*14*	*20*
Placebo	*37*	*65*	*51*

n = total number of nights.

Although the trial appears to have shown that quinine is beneficial overall, in that there is a significant difference between the proportion of nights with cramp while on quinine and placebo (20% versus 51%, confidence interval 0.185 to 0.395, $P<0.01$), the carry over effect renders the cross over design of the trial invalid. This carry over effect suggests that withdrawal of quinine induces cramps. This is totally unexpected, and has not been reported before. Such an effect is difficult to explain. The lack of significant difference between the two treatments during the first period, suggests that quinine is not an effective treatment for cramps, in the dosage used. It has been suggested that quinine is more effective for night cramps at a higher dose,[2] but this runs the risk of more side effects. Apart from the unusual effect reported here, there would also be the risk of cinchonism. This can, in severe cases, lead to deafness, optic atrophy and cardiac dysrhythmias. Furthermore, the half life of quinine has been variously reported as seven, 11 and 19 hours,[2,4,5] so it is possible that it can accumulate, if taken every night. Fortunately, there were no side effects recorded in this study.

N R DUNN

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Defusing the explanation of epilepsy

Sir,

Doctors may experience difficulty when describing the nature of seizure disorders, as anxious patients seldom grasp the neurological details on which doctors base their explanations. The resultant confusion may increase the patient's concerns instead, leading to non-compliance and dissatisfaction. While working at a national centre for children with epilepsy, I came to realize that a helpful comparison was needed to explain seizure disorders successfully. This would involve a familiar, recognizable household object, particularly something which could be seen and touched, and which would lend itself to a description of epileptic seizures. Over time, I found a standard electrical plug to be the most suitable comparison. This concept is echoed by Oliver Sacks in *The man who mistook his wife for a hat,* in which he talks of a mechanistic neurology with similarities to capacitors and fuses.[1]

A simple comparison can be drawn between seizure activity in the brain and the conduction of current through an electric plug, thus providing an analogy which is readily comprehensible to patients and straightforward for the doctor to explain. The main power supply (central nervous system) may suddenly generate an excessive burst of electrical current (neuronal discharge) which is then conducted to the plug in the wall socket (lobe or cortex) (Figure 1). Here, it exceeds the capacity of the fuse (seizure threshold) which leads to an alteration in the flow of current (seizure) and a subsequent malfunction or cessation in the action of the appliance (motor, sensory or cognitive function). The fuse is clearly the weakest portion of the circuit and is thus especially sensitive to any excessive bursts of electrical current. This correlates closely with our understanding of low seizure thresholds, and how individuals may be predisposed to having seizures.

Patients often have queries about the aetiology of epileptic seizures, the determinants of their severity and the role of medication in their treatment. The aetiology of seizure disorders can be clarified by demonstrating to patients how they may have been born with a weaker fuse leading to an innate predisposition to epilepsy, or how they may have started life with an appropriate fuse which was later weakened by pathological processes. The analogy can also be expanded to

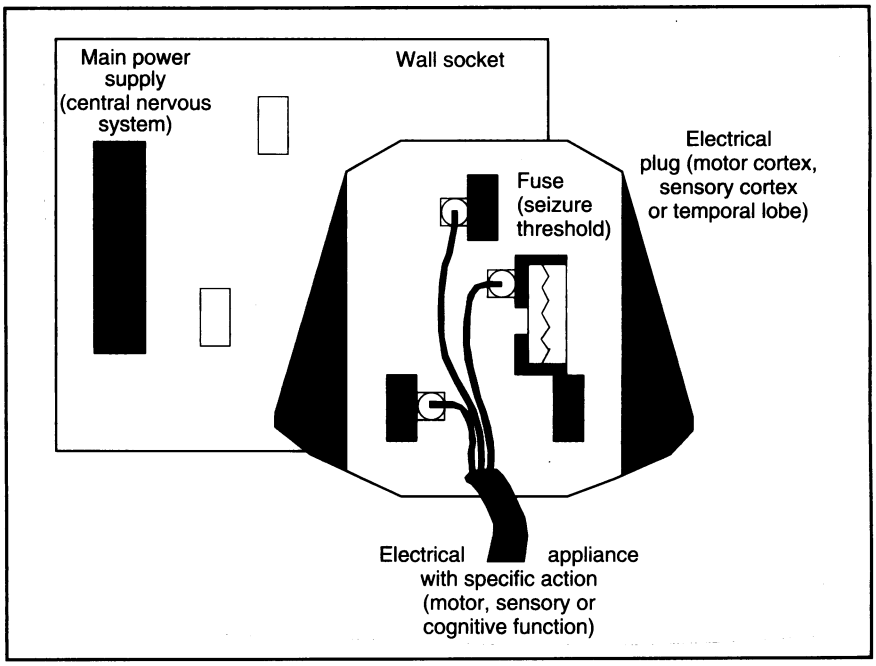

Figure 1. *Diagram comparing seizure activity in the brain and the conduction of current through an electrical plug.*

describe the severity of epileptic seizures by using fuses of different strength to represent seizure threshold in mild, moderate and severe epilepsy. The role of medication in seizure disorders can then be explained in terms of strengthening the weaker fuses so that they approximate appropriate seizure thresholds more closely. However, increasing fuse resistance may impede other functions, which can be correlated with the potential side effects of anti-convulsant medication. The cause, severity and treatment of the patient's epilepsy can thus be demonstrated by selecting a fuse which best reflects their individual aetiology, seizure threshold and medication.

The comparison of an easily recognized household object with the often difficult to understand concept of seizure disorders, may help to defuse the explanation of epilepsy. This comparison may provide patients with a greater awareness of the need to find a suitable balance between adequate control of their seizures and the resultant side effects of medication. Analogies such as this may help to de-mystify epilepsy, and render seizure disorders more understandable to patients and their families.

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Reference

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Nephrotoxicity with non-steroidal anti-inflammatory drugs

Sir,

A 65 year old man in my practice was diagnosed as having cervical spondylosis. Because of increasing pain he was prescribed a variety of non-steroidal anti-inflammatory and analgesic drugs, including naproxen, diclofenac sodium, mefenamic acid, ketoprofen, and also the compound analgesic Tylex® (Cilag). These drugs were prescribed separately, not in combination, and in the doses recommended by the *British national formulary*, over a period of several months. He was referred for a consultant orthopaedic opinion. X-rays of the cervical spine and routine blood tests, including erythrocyte sedimentation rate, urea and electrolyte levels, and liver function tests, were carried out.

At this time he was developing further symptoms including loss of weight, anorexia, dyspepsia, night sweats, tiredness and general malaise. He consulted several times at the surgery with these continuing symptoms. He was also attending the orthopaedic outpatient clinic. Because of progression of his symptoms the blood results were obtained by telephone from the hospital. These showed that he was suffering from renal failure and he was immediately admitted to hospital. Sadly, his condition continued to deteriorate and he died following a cerebral haemorrhage.

At autopsy interstitial nephritis was found which was compatible with a nephrotoxic drug reaction, presumably caused by the treatment he had been receiving for his cervical spondylosis.

The case has been reported to the Committee on Safety of Medicines, but I am also writing this letter at the specific request of his family, who wish general practitioners to be fully aware of the risk of a nephrotoxic drug reaction with these widely used drugs, and to consider this possibility in the event of their patient developing unexplained symptoms which may indicate renal failure. The possibility of such a reaction is already recognized and is mentioned in the relevant data sheets, but it seems that the gastrointestinal side effects are more regularly considered.

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Disease register for patients with asthma

Sir,

With the current interest in asthma as a subject for disease management in general practice, it is becoming necessary for practices to maintain reliable registers of affected patients.

In my practice of 7672 patients, the computer listed 211 patients as having 'asthma' in 1992. In November 1992 a search for patients receiving repeat prescriptions for beta$_2$-agonist drugs or inhaled steroids in the past year produced 311 patients, 146 of whom were not recorded as having asthma. This latter group included nine patients who had repeat prescriptions for inhaled steroids only, and 71 who had received beta$_2$-agonists only. The remaining 66 patients had prescriptions for both types of drug.

Thus, 46 patients listed as having asthma did not receive repeat prescriptions for either class of asthma drugs during the year. Of these patients, 31 had these drugs prescribed acutely, and two had received repeat prescriptions for sodium cromoglycate. Thirteen of these patients had received no treatment for asthma at all: nine patients had received asthma treatment in the year before that studied, but one had not been prescribed asthma treatment for four years.

It would appear that a register of patients having asthma needs constant updating. Carrying out searches for patients receiving repeat prescriptions for beta$_2$-agonist and prophylactic drugs seems to be a reasonable way of identifying patients who are currently affected, but the period over which prescribing data should be collected must be specified. Many more patients would be identified if acute prescribing were also considered, but this could be associated with a risk of false diagnosis. There is also a need for policies to be made regarding patients listed as having asthma who are no longer receiving treatment. For example, if a patient, once diagnosed as having asthma, subsequently does not appear to be in need of treatment, should he or she be removed from the disease register?

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Audit and morbidity registers

Sir,

Liam Donaldson in his editorial in the *British Medical Journal* has drawn attention to the importance of morbidity registers for the assessment of resources.[1] He states that 'Disease registers restricted to general practice lists are more limited in their applicability in not having a natural population base'. Surely if such a base is to be found anywhere it is in a general practice population.

Morbidity registers have long been advocated for general practice,[2] primarily as a tool for research and teaching. Now an important new use has arisen, namely audit.[3] In the past it has been difficult to ensure that morbidity registers are complete and there have been problems in keeping them up to date.[4] This is usually because they have been too comprehensive, and it has been difficult to agree on definitions for some conditions.

As the implementation of the audit process gathers pace, it is becoming clear that certain chronic conditions are the most frequent subjects of clinical audit. The Isle of Wight medical audit advisory group has encouraged practices to establish