rates if commercial intrusion is to be successfully countered and if the provision of medicolegal services for the profession is to remain within its own control.

The Medical Protection Society has identified two areas of clinical practice which are extremely, and disproportionately, costly in litigation terms and which, in its opinion, place an unfair financial burden on its membership, irrespective of specialty. These are neonatal brain damage—perhaps better, and less emotively, described as idiopathic encephalopathy of the newborn—and circumstances in which junior doctors in training posts are held totally, or in part, liable for damages.

Causation in neonatal brain damage may never be satisfactorily established to a scientific standard of probability.[3-6] However, a defence against claims for compensation in respect of infants allegedly harmed by medical negligence leading to hypoxic-ischaemic encephalopathy may fail on the lower standard of proof required by the law in civil, as opposed to criminal, cases—that is, on the balance of probabilities. To deny an infant compensation may be considered to be an injustice, yet to award compensation against the doctor or midwife in circumstances where causation is not clearly established may replace one injustice with another. Nor should it be overlooked that the brain damaged infant who cannot establish causation will not recover compensation under existing no fault compensation schemes.

Almost by definition doctors in training are more liable to make mistakes than are their trained senior colleagues (who pays for the training?). The Medical Protection Society held a meeting in December 1988 at which these and other relevant issues were discussed. A considerable amount of essential factual information was provided. Invitations to attend were sent to the profession's negotiators, but, regrettably, in many instances these invitations were declined. The society hoped that the information thus made available would be of help in the conduct of negotiations with the government. The proceedings of the meeting will be published shortly and circulated widely within the profession with the aim of providing best information on the issues. It then is the responsibility of the profession's negotiators to develop such policies as are deemed to be in the best interests of the profession against an informed background.

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2 Beecham L. From the council. *Br Med J* 1989;**298**:122-3. (14 January.)
3 Anonymous. Birth and origins of cerebral palsy. *N Engl J Med* 1986;**315**:124.
4 Nelson Karin B, Ellenberg JH. Antecedents of cerebral palsy: multivariate analysis of risk. *N Engl J Med* 1986;**298**:81-6.
5 Blain E, Stanley FJ. Intrapartum asphyxia: a rare cause of cerebral palsy. *J Pediatr* 1988;**112**:515-9.
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Disciplining doctors

SIR,—In Miss Wendy Savage's letter regarding the unsatisfactory nature of current disciplinary procedures for doctors she refers to a recent case in which a suspended doctor "successfully used the High Court to force his health authority to lift his suspension."[1] I believe that the case referred to is one that arose in this region and that Miss Savage was quoting a report in a national newspaper. The report was erroneous, and this has been drawn to the attention of the editor.

The facts are that the doctor was suspended after serious allegations were made against him, pending their independent review. After the review it was decided that the case against him did not warrant continued suspension, and he was reinstated without delay. The doctor had appealed to the High Court for an injunction, but the decision to reinstate him was made before the court had come to any conclusion. His appeal made no difference to either the decision to reinstate or its timing. The total period of the suspension was two months, and in the circumstances, which included the coinciding summer holiday period, Yorkshire Regional Health Authority acted with commendable expedition.

Counsel's opinion has been sought as to whether the court would have had jurisdiction in the matter, as this remains unclear.

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1 Savage W. Disciplining doctors. *Br Med J* 1988;**297**:1047. (26 November.)

Merit awards

SIR,—I resent the opinion expressed by Dr B A Evans that the merit award system is corrupt.[1] It may seem unfair and unjust, but it is not corrupt.

In Wales the system works well. Local holders of awards meet each year in each district and discuss possible names. Two of the local holders then attend a national meeting, where each district puts forward its candidates and speaks on their behalf. Opinions from central organisations and royal colleges are evaluated, and opinions from chairmen of district health authorities are also heard.

Depending on the number of awards that may be made available and taking into account a fair representation of all specialties, two lists are prepared for the meeting later in the year with the chairman of the advisory committee and his advisers. This meeting is attended by all the district representatives, who have strongly to support their candidates and show reason for preference against colleagues from other districts. The chairman himself has already obtained opinions on the candidates on the two lists and is well informed about each consultant. In Wales if individuals are considered meritorious in the eyes of their colleagues they will receive an award.

Obviously the system is not ideal and some truly capable people will be missed. I can assure you, however, that all the representatives in the merit award system work honourably, with fairness and honesty.

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1 Evans BA. Merit awards. *Br Med J* 1989;**298**:52. (7 January.)

Children of "the troubles"

SIR,—We found the personal view of Dr Moira Connolly[1] a very moving cry from the heart but are even more upset when we reflect on the implications of the article for our country.

Its publication will only go further to fix in the minds of the population of mainland Britain the mass media view of life in Northern Ireland. Our upbringing was comfortably middle class, we admit, but we, like most of our countrymen, have little direct experience of terrorist or sectarian violence. Until this view is accepted in Britain there is little hope for reinvestment in Northern Ireland, and the large scale unemployment will continue to provide the best possible culture medium for terrorist recruitment. A decision to seek a career outside Northern Ireland as Dr Connolly has done is becoming increasingly common among those who "have had enough of the violence, bitterness, discrimination, and hatred." If all those of good will desert their country, however, then no one will be left to fight against the bigotry and hatred.

We are medical students in our final year and would hope to have gained some perspective on life in our homeland. Both of us intend to return to work in Northern Ireland (if we can get jobs) and hope that in some small way we can help to make one of the most beautiful countries in the world a place Dr Connolly will want to return to some day.

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1 Connolly M. A child of "the troubles." *Br Med J* 1988;**297**:1664-5. (24-31 December.)

Drug Points

Chronic active hepatitis associated with cimetidine

Drs P T BOYD, F LEPRE, and J D DICKEY (Princess Alexandra Hospital, Woolloongabba, Queensland 4102, Australia) write: We present a case with the typical pathological features of chronic active hepatitis associated with cimetidine.

A 32 year old Spanish woman presented in July 1985 with one week's history of jaundice, malaise, and mild right upper quadrant abdominal pain. She had been taking cimetidine 1000 mg/day for six months for peptic ulceration. She took no other drugs and drank little alcohol.

She was mildly feverish and deeply jaundiced. There was no hepatosplenomegaly and no signs of chronic liver disease. Serum bilirubin concentration was 99 μmol/l (normal <20), alkaline phosphatase 167 U/l (35-115), aspartate transaminase 1542 U/l (<30), lactate dehydrogenase 513 U/l (120-250), and γ-glutamyltransferase 363 U/l; serum albumin 41 g/l (35-50), total protein 64 g/l (63-80); prothrombin time 32 s (control 14 s); she was negative for hepatitis B surface antigen, hepatitis A IgM, and antismooth muscle antibody and positive for antinuclear antibody (hep-2 cell), speckled pattern 1/40. The liver and biliary tree were normal on ultrasonography. She was treated for acute hepatitis of undetermined cause. Cimetidine was stopped and liver function values returned to normal over 10 weeks.

Nine months later she suffered peptic ulceration again and cimetidine 1000 mg/day was restarted. One week later jaundice recurred. Liver function values were again deranged; prothrombin time was 19 s (control 14 s); she remained negative for hepatitis B surface antigen and hepatitis A IgM, and serum ceruloplasmin and α_1 antitrypsin values were normal. Liver biopsy showed features of chronic active hepatitis with partial effacement of architecture and regenerative nodules. Portal areas were expanded and linked and contained increased fibrous tissue and a moderately dense inflammatory infiltrate of lymphohistiocytic type. There was active piecemeal necrosis as well as lobular hepatitis with focal hepatocellular necrosis.

Prednisone 40 mg/day was started with the dose tapered to zero over two months, by which time results of liver function tests had returned to normal. A repeat biopsy specimen obtained eight months later was the same apart from showing less inflammation. Liver function values remained normal until August 1987, when the patient was lost to follow up.

There are few well documented reports of hepatitis due to cimetidine with confirmation by rechallenge.[1-5] When performed, liver biopsy has

shown abnormalities ranging from mild portal inflammation to centrizonal collapse with bridging. The course has been suggestive of a hypersensitivity reaction with a shorter period to development of abnormal liver function after re-exposure to the drug. Ours is the first case with typical pathological features of chronic active hepatitis. The evidence strongly implicated cimetidine. Inadvertent re-exposure to the drug caused rapid recurrence of jaundice and abnormal liver function values, and withdrawal of cimetidine and treatment with prednisone for two months returned these values to normal, although repeat biopsy still showed evidence of chronic active hepatitis. Pre-existing chronic active hepatitis exacerbated by cimetidine is unlikely in the absence of other recognised causes of chronic active hepatitis.

This case adds to the slowly accumulating evidence implicating cimetidine as a rare but definite hepatotoxin. The low incidence makes monitoring of liver function values unlikely to be cost effective, but when clinical hepatitis occurs cimetidine must be considered a potential villain.

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4 Ruiz Del Arbol L, Moreira V, Morena A, *et al*. Bridging hepatic necrosis associated with cimetidine. *Am J Gastroenterol* 1980;**74**:267-9.
5 Schwartz JT, Gyorkey F, Graham DY. Cimetidine hepatitis. *J Clin Gastroenterol* 1986;**8**:681-6.

Cardiotoxic effect with convulsions in terfenadine overdose

Drs ANTHONY J DAVIES, V HARINDRA, A MCEWAN, and R R GHOSE (Singleton Hospital, Swansea SA2 8QA) write:

Terfenadine (Triludan) is a specific, selective, histamine H_1 receptor antagonist with few side effects. Four adults have developed prolonged QT intervals with doses of 120-240 mg/day, and ventricular arrhythmias occurred 15 hours after overdose with 3·36 g in conjunction with 7 g cephalexin and 1·2 g ibuprofen. Complications were not observed in 12 other overdoses, six exceeding 1·0 g (H C Masheter, Merrrell Dow, personal communication). We report a quinidine-like effect on the myocardium with convulsions in a patient with terfenadine toxicity.

A healthy 21 year old woman developed two generalised convulsions lasting two minutes 12 and nine hours before admission. There was no incontinence or tongue biting and no residual signs in the central nervous system but an irregular pulse. The patient had been given terfenadine for pruritus seven days earlier. Two tablets daily were prescribed (120 mg) but she took four tablets daily (240 mg), except for the day when the convulsions occurred, when she took none. Although 56 tablets had been prescribed only three remained in the packet; the patient claimed she had thrown the rest away.

On admission there were no abnormal physical signs and blood pressure was normal. An electrocardiogram showed prolonged QT_c intervals, however, with widened notched and inverted T waves and a single premature beat. These changes remained on the second day but reverted to normal. Serial QT_c intervals were: 0·57 s on day 1, 0·47 s on day 2, 0·47 s on day 3, 0·43 s on day 4, and 0·40 s on day 5 (normal 0·35-0·42 s). On admission the plasma concentration of terfenadine, measured by radioimmunoassay, was: metabolite 1, 504 μg/l; unmetabolised terfenadine 43 μg/l. Nine hours later metabolite 1 had fallen to 389 μg/l and unmetabolised terfenadine to 26·5 μg/l. Liver function values were normal.

The high levels of metabolite 1 and unmetabolised terfenadine on admission, with lowered levels nine hours later, pointed to overdose, although delayed metabolic clearance could not be excluded. These raised concentrations coincided with prolonged QT_c intervals and widened notched T waves, consistent with a quinidine-like effect. Terfenadine is completely absorbed from the gut, thereafter undergoing extensive first pass metabolism in the liver. Less than 1% of the oral dose reaches the systemic circulation. The half life is about 17 hours.[1] Terfenadine is widely distributed throughout the body, but the blood-brain barrier is not breached in animals. Although extrasystoles were noted by the general practitioner, only one was observed in hospital, but convulsing may have resulted from such arrhythmias arising from a cardiotoxic effect. Since 1981, 773 reactions to terfenadine have been reported to the Committee on Safety of Medicines including one case of arrhythmia, one of extrasystole, and one of cardiac arrest. Central nervous system effects included one report of convulsions and two cases of aggravated epilepsy. Cardiotoxic effects may be more common than realised because electrocardiograms are not routinely obtained.

We thank Merrell Dow Research Institute for arranging for measurement of plasma concentration of terfenadine.

1 Okerholm RA, Weiner DL, Hook RH, *et al*. Bio-availability of terfenadine in man. *Biopharm Drug Dispos* 1981;2:185-90.

Pseudopolymyalgia rheumatica during treatment with enalapril

Professor X LELOËT, Dr N MOORE, and Professor P DESHAYES (Department of Rheumatology and Centre Régional de Pharmacovigilance, Hôpital de Boisguillaume, BP 100, 76233 Boisguillaume Cedex, France) write:

A 76 year old woman was treated for hypertension from July 1985 with enalapril 20 mg/day. She took no other drugs. Three weeks after starting enalapril she started complaining of muscular aches in the right arm. These progressively extended to the other arm, shoulders, and then to the pelvic girdle and legs. These aches occurred day and night, causing insomnia, and were accompanied by severe asthenia and morning stiffness lasting three to four hours. Weakness was pronounced and made dressing and getting up from a low stool impossible. She had no dyspnoea, swallowing problem, fever, wasting, or other signs, in particular no headache or eye or skin manifestations.

She was examined in December 1985; her muscles seemed normal and were not painful on palpation, but active mobilisation of the arms and legs caused intense pain in the scapular and pelvic girdles. There was no muscular deficit or ptosis. The neurological examination was normal. The rest of the physical examination was totally unremarkable, and blood pressure was 140/85 mm Hg. Laboratory test results were also all normal, with a normal blood count and no sign of inflammation (erythrocyte sedimentation rate 17 mm in the first hour, fibrinogen 3·1 g/l); creatinine, creatine phosphokinase, and aldolase values were normal; no antinuclear antibodies were found; and latex and Waaler-Rose tests gave negative results. Protein electrophoresis and triiodothyronine and thyroxine concentrations were normal, as were a chest radiograph and electromyograms of all four limbs.

Treatment with indomethacin 75 mg/day by mouth was started on 28 December and partially relieved the daytime muscle pain but not the asthenia or night pain. Having eliminated most known causes of such inflammatory like muscle pain, we suspected enalapril. It was withdrawn on 7 January 1986 and the muscle pain had disappeared completely by 10 January, when indomethacin was also stopped. In January 1988 she was completely symptom free and her hypertension was being treated successfully with reserpine and diuretics.

The typical diagnoses for the symptoms at that age are polymyalgia rheumatica and rheumatoid arthritis affecting the hips and shoulders. Both were excluded, as were other diagnoses such as hypothyroidism and polymyositis. There was no evidence for any other of the usual causes, either viral, bacterial, sarcoid, or metabolic. The paucity of biological signs led us to suspect a drug, a suspicion that seems confirmed by the evolution. Despite the absence of rechallenge enalapril seems the likely cause. There was a clear temporal relation with both the onset and the resolution of the symptoms; no other drug was taken; and no other cause was found. The fact that two years later there was no recurrence of symptoms may provide further support, since this would be unusual with any other cause.

Though no case of severe myalgia induced by enalapril has been reported to our knowledge, data from the French adverse drug reaction monitoring system and from the manufacturer indicate that a few other cases of muscular symptoms (myalgia and weakness) exist. The mechanism responsible for these manifestations is unclear. In the event of such incapacitating muscle pain during treatment with enalapril, and once the more common causes have been eliminated, it would seem advisable to test the effects of stopping enalapril before resorting to more invasive or costly tests.

Hair loss in a child associated with naproxen

Dr DENNIS A C BARTER (Paediatric Department, Queen Elizabeth Hospital, King's Lynn PE30 4ET) writes:

I report an unfortunate side effect of naproxen (Syntex) when used for the treatment of monarticular arthritis in a 2 year old. She presented at the age of 22 months with a three week history of swelling and limp in the right leg. There was no history of trauma. On examination she appeared well nourished, was afebrile, and cried on taking weight on the right leg. The right knee was swollen and hot and 1·5 cm greater in circumference than the left. Radiographs of both knees showed no abnormality apart from soft tissue swelling on the right. Although there was no evidence of fracture, the clinical diagnosis was at first thought to be toddler fracture and she was treated with paracetamol. At review, however, monarticular juvenile arthritis was clinically diagnosed. The erythrocyte sedimentation rate at that time was 46 mm in the first hour. She was stiff in the mornings and limped during the day. Naproxen was started in a dose of 10 mg/kg (70 mg twice daily). She was given night splints. At review a month later she had made a dramatic improvement, although she still had a morning limp. The swelling was considerably reduced and the redness and temperature change less noticeable. The dose of naproxen was increased to 100 mg twice daily (13·6 mg/kg). A further month later the mother stated that her hair was falling out and showed a photograph of her hair taken in the previous six months, which showed a full head of very curly hair. The knee had improved dramatically: she had no limp or morning stiffness.

Our pharmacy found reports of 58 cases of hair loss in adults associated with naproxen and the Committee of Safety of Medicines had reports of 13. None had occurred in children. Dr Barbara Ansell said that she had never seen hair loss at the Medical Research Council's Clinical Research Centre associated with naproxen, though it had not been used in a child as young as this. Naproxen was stopped, and the child's hair regrew dramatically, although without its curls. Fortunately, the monarticular arthritis remained quiescent with no symptoms and no loss of function, although there was still marginal swelling of the right knee.

Naproxen should be used with caution in young children with juvenile chronic arthritis.