practitioners can immunise most patients in return for what.

ANDREW DICKER

Ivinghoe LU7 9EB

The truth about juniors' hours

SIR,—In highlighting the results of the recent work study performed in the Royal Infirmary of Edinburgh[1] Dr Stella Lowry failed to mention some of the features which are seen locally to be of greatest value.

The study examined the work of the preregistration house officers (not junior doctors more generally) in our medical wards and was requested by the house officers themselves, who felt that their current workload potentially compromised good patient care. Present arrangements mean that the house officers work in a superficially legitimate 1 in 3 rota, which was introduced two years ago by implementing a cross cover system, with one house officer sometimes being responsible at night for over 100 acute medical beds. The concern was conveyed to the hospital's unit general manager, who commissioned Lothian Health Board's management efficiency unit to undertake a study examining not only the house officers' hours of work but also the nature and pattern of the work, so that information about both workload and hours of work would be available as a basis for considering changes.

The first lesson learnt from the study is that with careful planning involving all interested parties, and with good briefing of the individuals concerned, modern work study methods can be applied to the diverse work of junior doctors. Thus we now have information compiled on a minute to minute basis about the daytime work of 12 house officers and their work during nights and weekends on call. Because the study design and some of the results may be of interest in other hospitals we intend to produce a detailed report for publication.

The need to reduce the out of hours duties of many junior doctors is widely appreciated, but it is not easily achieved. In this instance we are convinced that the wholehearted commitment of junior doctors, consultants, and managers to the work study was an important factor in its success. The skill of the work study team in obtaining, analysing, and presenting the information about workload then enabled all concerned to see what measures were needed and where they would be most effective in resolving the difficulties. Doctors and managers in the hospital are in complete agreement on the actions now to be taken, which will include the appointment of additional house officers to some of the wards.

ROBERT C HEADING
PETER J LESLIE
ANDREW DOIG
CHARLES J MCKENNA

Royal Infirmary,
Edinburgh EH3 9YW

1 Lowry S. The truth about juniors' hours. *Br Med J* 1989;**298**: 1338. (20 May).

Drug Points

Death after flumazenil

Dr WILLIAM BURR, Mr PAUL SANDHAM (Pinderfields General Hospital, Wakefield WF1 4DG), and Dr ALAN JUDD (Leeds Poisons Information Centre, Leeds LS1 3EX) write: We report a case in which the use of flumazenil was implicated in a death after ingestion of a tricyclic antidepressant and benzodiazepines.

A 31 year old woman was admitted via the casualty department a few hours after taking an unknown quantity of dothiepin, chlordiazepoxide, and temazepam together with alcohol. She was drowsy but rousable and was treated by gastric lavage. After about an hour she became deeply unconscious with no response to painful stimuli. Breathing was spontaneous but laboured; she was not cyanosed. Pulse was regular (120 beats/min) and blood pressure 130/70 mm Hg. Pupils were dilated but responded normally to light, and she had decreased tone in all four limbs. She was placed on a cardiac monitor. Screening for salicylate and paracetamol produced negative results.

About 12 hours after ingestion she was still deeply unconscious and her pupils were responding sluggishly to light. Her heart rate had fallen to 70 beats/min, though still in sinus rhythm, and blood pressure was 110/80 mm Hg. Respiration was laboured at 15 per minute. Flumazenil 250 μg intravenously was given. She regained consciousness briefly, had a grand mal seizure, and went into status epilepticus. Intravenous benzodiazepines had no effect. A chlormethiazole infusion was started at 60 drops/min (about 24 mg/min). The seizures were brought under control and she was in sinus rhythm at 60 beats/min with a respiratory rate of 12 per minute and fixed pupils. Ninety minutes after the administration of flumazenil she developed bradycardia then went into asystole. She died 25 minutes later despite continued resuscitation attempts.

Flumazenil is a competitive benzodiazepine antagonist. It has not been licensed specifically for managing benzodiazepine overdose but it is understandable that it has been used for this indication. Concern has been expressed that its use may produce problems related to precipitation of benzodiazepine withdrawal effects in dependent individuals or related to removal of a protective action of benzodiazepines in multiple drug overdose.[1,2]

Until now the fears relating to multiple drug overdose seem only to have been theoretical. The sequence of events in this case, however, strongly suggests that flumazenil precipitated status epilepticus and fatal cardiovascular toxicity after combined ingestion of a tricyclic antidepressant and benzodiazepines in a patient who was taking one or both of these types of drugs regularly. Flumazenil should be used with extreme caution and should be used only exceptionally when treating ingestion of several drugs including benzodiazepines.

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Autoimmune haemolytic anaemia associated with interferon alfa-2a in patient with mycosis fungoides

Drs L R BRAATHEN (Department of Dermatology) and P STAVEM (Section of Haematology, Medical Department A, Rikshospitalet, Oslo, Norway) write: A 58 year old man with multiple cutaneous lesions of mycosis fungoides and bilateral exophthalmos was admitted to hospital on 22 April 1985. Diagnosed in 1979, he had been treated with psoralens and ultraviolet A and several courses of a combination regimen of bleomycin, cyclophosphamide, etretinate, and prednisolone. In 1981 a right orbital biopsy showed sialoadenitis with lymphoid hyperplasia and computed tomography of the orbit showed bilateral supralateral soft tissue masses, largest on the right. Lymphadenopathy was detected retroperitoneally using computed tomography. Baseline investigations showed haemoglobin 103 g/l, erythrocyte sedimentation rate >100 mm in the first hour, white cell count $15{\cdot}6\times10^9$/l, red cell count $3{\cdot}4\times10^{12}$/l, thrombocytes 95×10^9/l. Immunoelectrophoresis showed an increased IgG fraction but no well defined monoclonal component. A direct Coombs test was negative.

Having become refractory to treatment and with rapidly deteriorating vision, he was given 50 mg etretinate orally and subcutaneous injections of 3× 10 units of interferon alfa-2a (Roferon-A, Roche) daily from 25 April. His anaemia deteriorated. Several transfusions with saline-adenine-glucose blood were given without apparent effect, and on 29 May a direct Coombs test was positive and a strongly reacting autoantibody to his own and donor red cells was detected. Etretinate and interferon alfa-2a were stopped. His haemoglobin was then 59 g/l. He was given prednisone and chlorambucil. By 2 July his haemoglobin had risen to 91 g/l and by 6 August to 144 g/l. A Coombs test was not performed.

Interferon alfa-2a and etretinate were restarted on 13 August because of progressive retrobulbar tumour growth but discontinued 10 days later owing to lack of response. On 28 August prednisone and chlorambucil were stopped. A Coombs test was again negative on 21 October.

During the autumn of 1986 his mycosis fungoides progressed, and on 20 October 1986 interferon was restarted with daily subcutaneous injections of 3×10 units and within a week increased to 18×10 units. He also received 2·5 mg prednisone orally but no etretinate. On 5 January 1987 interferon was discontinued owing to recurrence of a weakly positive direct Coombs test. His haemoglobin fell by 79 g/l and prednisone was increased to 10 mg three times daily. The Coombs test became negative within three weeks, and on 17 February his haemoglobin was 115 g/l. The time from restarting interferon to recurrence of the anaemia was longer than in 1985, possibly because of the concomitant prednisone. He also received much higher doses of interferon.

Etretinate[1] and systemic[2] and intralesional[3] recombinant leucocyte A interferon are effective treatments for cutaneous T cell lymphomas. Interferon is probably the more immunologically active of the two drugs, and a wide variety of immunomodulatory actions have been shown.[4] Recent reports of the development of primary hypothyroidism,[5] autoimmune thyroid disease,[6] parotitis and epididymitis,[7] immune thrombocytopenia,[8] and immune haemolytic anaemia[9] after treatment with interferon suggest that interferon may be associated with the development of autoimmune disease. Autoimmune haemolytic anaemia has also been documented with mycosis fungoides.[10] The transient autoimmune haemolytic anaemia observed twice in this patient was probably induced or exposed by treatment with interferon alfa-2a.

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