work for reasons similar to those described above. Once more, after pressure from the patients, we reached agreement with the health authority and the community health councils to have two short visiting spells each day—one in the afternoon and one in the early evening. The precise times and duration depend on the ward concerned.

We agree that the patient's needs are paramount but not the exclusive consideration. One patient's wishes should not be inflicted on other sick patients in neighbouring beds. The caring professions have a duty to tend their patients, but if this is constantly hindered by the excessive and prolonged presence of visitors we have a duty to consider where the priority lies.

BRIAN ALDERMAN

Arrowe Park Hospital,
Upton,
Wirral,
Merseyside L49 5PE

Case-control study of cutaneous malignant melanoma

SIR,—The abstract of the paper by Drs Dallas R English and Bruce K Armstrong on identifying people at high risk of cutaneous malignant melanoma (7 May, p 1285) is misleading in stating that "... time spent outdoors in summer from the age of 10 to 24 ... provided good discrimination between patients [with malignant melanoma] and controls. ...". In fact table I, which shows odds ratios for variables independently predicting risk of cutaneous malignant melanoma, and a small section in the results state that increasing exposure to sunlight between the ages of 10 and 24 was associated with a decreasing incidence of cutaneous malignant melanoma. It would therefore seem that increasing exposure to sunlight between the ages of 10 and 24 years has a protective effect on the development of cutaneous malignant melanoma.

This is an interesting finding, particularly in view of the large amounts of money currently spent by the Australian government on the "Slip, Slop, Slap" campaign aimed at children and discouraging prolonged exposure to sunlight. I was disappointed that Drs English and Armstrong chose not to discuss the implication of this important finding in their paper.

N S BROUGHTON

Department of Orthopaedics,
Luton and Dunstable Hospital,
Luton,
Bedfordshire LU4 0DZ

AUTHORS' REPLY.—The model we developed did provide good discrimination between patients with melanoma and controls. Mr Broughton seems to have inferred that an apparent protective effect of time spent outdoors cannot help distinguish patients from controls. In fact, whether the effect of an "exposure" is to increase or decrease the risk of developing the disease makes no difference to its contribution to the model's ability to discriminate. Time spent outdoors was not the only variable that decreased the risk of melanoma—arrival in Australia after the age of 10 had the same effect. For such factors people in high risk categories are those with the least amount of exposure.

With respect to Mr Broughton's comment about the implications of decreasing the risk of melanoma by increasing the time spent outdoors, we reiterate that the purpose of our paper was to determine whether it was possible to identify a group of people at high risk of melanoma, not to identify risk factors for melanoma. Our finding of a protective effect of increasing time spent outdoors was not new and has been discussed in more detail.¹

Although it seems that a reduction in exposure to the sun by Australians may increase the incidence of melanoma, our study also showed that arrival in Australia after the age of 10 was a strong independent predictor of a reduced risk of melanoma. The prevalence of naevi, which was the strongest risk factor for melanoma, was also reduced in these migrants. As most migrants to Australia come from countries that have less sun it is reasonable to assume that their lower risk is a result of less exposure to the sun early in childhood. Thus the "Slip, Slop, Slap" campaign directed at children should, if successful, reduce the incidence of melanoma.

In addition, the "Slip, Slop, Slap" campaign is directed primarily at the prevention of non-melanocytic skin cancer, which is the commonest cancer in Australia. Because of its high incidence non-melanocytic skin cancer is an important contributor to the use of medical and hospital resources. The indirect evidence from its distribution by age, sex, and site on the body and, to a lesser extent, its association with outdoor occupations would suggest that the incidence of non-melanocytic skin cancer increases with increasing total accumulated exposure to the sun and would be reduced by reducing exposure to the sun.

DALLAS ENGLISH
BRUCE ARMSTRONG

National Health and Medical Research Council,
Unit in Epidemiology and Preventive Medicine,
University Department of Medicine,
Queen Elizabeth II Medical Centre,
Nedlands 6009,
Western Australia

I Holman CDJ, Armstrong BK, Heenan PJ. Relationship of cutaneous malignant melanoma to individual sunlight exposure habits. *JNCI* 1986;76:403-14.

Diet and inequalities in health

SIR,—Dr J E Cade and others (14 May, p 1359) shows that, contrary to established wisdom, the fat content of diet in middle age is not related to the death rate from ischaemic heart disease. In fact, if the data from the three towns studied were taken in isolation they would suggest that a high fat diet conferred some protection.

The incidence of ischaemic heart disease in the towns studied rises the further north the town is located, and this supports the suggestion that environmental cold stress may play an important part in explaining the geographical differences in the distribution of ischaemic heart disease, since the degree of cold stress is dependent on absolute temperature, air movement, and dampness.¹

Although the social class distribution was similar in the three towns, the socioeconomic indices were worse in the two northern towns. Social class is usually closely related to socioeconomic indices, and the lower the social class the more likely it is that people are living in cold, damp housing. Low income, more common in the lower social classes, means that house repairs may have to be neglected, clothing may be of inferior quality and quantity, and energy intake may be marginal. Lower social class is also associated with smaller houses, poor insulation, and a higher number of people in each room. These factors increase the risk of damp.^{1,2}

The lower the social class, or the worse the socioeconomic indices, the greater the potential for exposure to cold stress, a relation which matches the known gradation of incidence of ischaemic heart disease through the social classes.^{3,4} One of the physiological responses to exposure to cold stress is a rise in the circulating concentrations of catecholamines,¹ and it has been suggested that these play a part in the aetiology of ischaemic heart disease.⁵ It seems probable that cold stress acts

through catecholamines, and a paper is being prepared which reviews the evidence for the role of cold stress in the aetiology of ischaemic heart disease.

E I LLOYD

Department of Anaesthetics,
Princess Margaret Rose Hospital,
Edinburgh EH10 7ED

- 1 Lloyd EL. *Hypothermia and cold stress*. London: Croom Helm, 1986:77-157.
- 2 Stephens DH. Sleeping snugly in cold damp bedrooms. *J R Soc Health* 1982;6:272-5.
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- 4 Whitehead M. *The health divide: inequalities in health in the 1980s*. London: Health Education Council, 1987.
- 5 Carruthers ME. Aggression and atheroma. *Lancet* 1969;ii:1170-1.

Restraining infants in cars

SIR,—Dr M A Mason (14 May, p 1345) highlights the important problem of mortality and morbidity from road traffic accidents among infant car occupants. Unpublished Scottish Office statistics between 1981 and 1985 show that 288 (just over 7%) of the 3931 children injured while travelling by car were infants. Of these 75% were unrestrained.

We carried out a pilot study in Fife to see if the success of infant car seat loan schemes overseas could be repeated in Britain.¹ Our project was a success with 79% of the babies travelling regularly by car in the intervention population being carried in a rear facing infant car seat compared with only 8% of the control population. In the intervention group 93% of parents said that if they had another baby they would buy or hire an infant car seat. Interestingly, 82% of the mothers given a seat indicated that if one had not been provided they would have carried their baby in their arms or in a carrycot.

We urge health authorities and local government in other areas to give serious consideration to starting infant car seat loan schemes.

ERIC BAIJAL

Fife Health Board,
Glenrothes,
Fife KY7 5PB

1 Baijal E, Carter H, Jones IG, Walkingshaw IW. The role of infant car seats in road safety. *Journal of the Institute of Health Education* (in press).

Clinical carpal scaphoid injuries

SIR,—I thank Mr M Reichl and Dr M A Khan (23 April, p 1198) and Dr J J Langham-Brown (30 April, p 1259) for their comments on my and my colleagues' paper (19 March, p 825).

Traditional management by plaster cast for the clinical scaphoid injury is still practised in many hospitals throughout Britain. Awareness of the potential sequelae of scaphoid fractures has promoted this conservative approach.

Our study showed a low incidence of delayed radiological visualisation of scaphoid fractures (2%). We therefore concluded that the clinical scaphoid syndrome is a soft tissue injury and hence appropriate splintage should be sufficient; it is not the cause of the dangerous sequelae initially thought. As the *BMJ* has a wide distribution among junior and senior doctors we hoped that our article would give guidance to change from a policy of plaster cast management.

We also have reported the use of radionuclide bone imaging¹ and like Mr Reichl and Drs Khan and Langham-Brown would recommend it for diagnosis and management decisions. But not every hospital has an isotope department or immediate access to one. We would suggest that two

to three days is not the optimal time for scanning as bone healing is only just beginning and soft tissue hyperaemia may interfere with the image. A more reliable delay after trauma is seven to 10 days.² Isotope scans are indeed less expensive and more sensitive than conventional radiographs.

Our aim is to give medical staff, especially junior doctors, confidence to treat this condition by adequate soft tissue splintage when they do not have access to isotope departments.

M R A YOUNG

Ulster Hospital,
Dundonald,
Belfast BT16 0RH

- 1 Young MRA, Lowry JH, Laird JD, Ferguson WR. ^{99m}Tc-MDP bone scanning of injuries of the carpal scaphoid. *Injury* 1988;19:14-7.
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Drug points

Addendum to guidelines for reporting adverse drug reactions

Drs LOUISE GLASSNER COHEN and JOHN P ROVERS (Department of Pharmacy Services, Brigham and Women's Hospital, Boston, Massachusetts) write: Accurate reporting of adverse drug reactions requires that they be adequately identified and reported in complete detail. Several algorithms have been published as aids to this.^{1,2} Venulet *et al* evaluated 5737 such reports and determined that only 19% included complete information.³ Minimal guidelines for reports have been published,⁴ but we would include one additional requirement. Both the outpatient and inpatient records should be checked when preparing reports of adverse drug reactions.

A patient with sepsis secondary to AIDS had had previous adverse drug reactions. After receiving treatment with a new antimicrobial agent he noticed a rash and was readmitted to hospital with a condition resembling toxic epidermal necrolysis, to which he eventually succumbed. His illness was consistent with other reports of drug induced toxic epidermal necrolysis. Literature searches and information from the manufacturer showed no reports of reactions of this type with this drug. The inpatient chart was used to prepare a report for publication. As a final check the outpatient chart was obtained, and, unlike the inpatient chart, this record indicated that he had previously undergone a skin biopsy, whose result had been suggestive of erythema multiforme. We re-evaluated the cause and effect relation of this adverse drug reaction and did not submit it for publication.

Like most adverse drug reaction reports ours concerned a patient in hospital.⁵ Presumably many such reports relied solely on the inpatient record. In large teaching hospitals the patient may not be known to the team, and the history obtained from an abbreviated summary may be incomplete. Therefore reports prepared from only inpatient documents may lack relevant information.

New drugs are often held responsible for otherwise unexplained clinical situations. Using only inpatient documents the published algorithms classify our case as a possible adverse drug reaction.^{1,2} Consequently, even objectively identified reports which include the requisite information⁴ may be incorrect. We concur with previously proposed requirements and additionally recommend that the patient's outpatient record should be consulted before the clinician concludes that an adverse drug reaction has occurred.

- 1 Kramer MS, Leventhal JM, Hutchinson TA, Feinstein AR. An algorithm for the operational assessment of adverse drug reactions. 1. Background, description and instructions for use. *JAMA* 1979;242:623-32.
- 2 Karch FE, Lasagna L. Toward the operational identification of adverse drug reactions. *Clin Pharmacol Ther* 1977;21:247-54.
- 3 Venulet J, Blattner R, Von Bulow J, Berneker GC. How good are articles on adverse drug reactions? *Br Med J* 1982;284:252-4.
- 4 Venulet J. Informativity of adverse drug reactions data in medical publications. *Drug Information Journal* 1985;19:357-65.
- 5 Karch FE, Lasagna L. Adverse drug reactions. A critical review. *JAMA* 1975;234:1236-41.

Neutropenia following intravenous immunoglobulin

Drs P A VEYS, M G MACEY, C M OWENS, and A C NEWLAND (Department of Haematology, The London Hospital, London E1 1BB) write: Drs R V Majer and P J Green reported the occurrence of temporary neutropenia in two patients receiving high dose intravenous immunoglobulin (30 April, p 1262) and concluded that this was a side effect that had not been reported previously. This is, however, a frequently observed although not widely reported effect.

We studied the neutrophil counts in 48 patients with idiopathic thrombocytopenic purpura who received intravenous immunoglobulin. There was a significant decrease ($p < 0.001$) from the count before treatment (mean $6.0 \times 10^9/l$) to that on days three and four (mean $3.0 \times 10^9/l$). There was a correlation

Platelet count (□), neutrophil count (●), and FcR III expression (○) after intravenous immunoglobulin given on days 0 and 1 to a patient with longstanding idiopathic thrombocytopenic purpura.

between the decrease in neutrophil count and the increase in platelet count ($p < 0.01$). The neutropenic period was brief, and counts returned to normal by day seven.

We studied six patients in detail. Five developed a significant but brief reduction in absolute neutrophil count during the infusion of immunoglobulin. Using flow cytometric studies of patient and donor leucocytes we confirmed specific binding of intravenous immunoglobulin to the neutrophil surface *in vivo* and *in vitro*.¹ Ultracentrifugation of the immunoglobulin to remove IgG aggregates before testing reduced the amount of IgG binding *in vitro*. The expression of neutrophil FcR III, a receptor which has a low affinity for monomeric IgG,² varied in a reciprocal fashion to the amount of bound IgG, suggesting that the small amount of IgG aggregates remaining in the intravenous immunoglobulin is responsible for the specific binding of IgG to the FcR III.

Clarkson *et al* reported a temporary platelet increment accompanied by a profound neutropenia in a patient with refractory idiopathic thrombocytopenic purpura after a monoclonal antibody to the FcR III was given.³ This also suggests that the neutropenia might be mediated through this receptor.

In one patient with longstanding idiopathic thrombocytopenic purpura who had a temporary platelet response to intravenous immunoglobulin there was a reduction in the absolute neutrophil count from 5.1 to $2.2 \times 10^9/l$ after the first two infusions. The count remained low for about 10 days (figure). The neutrophil FcR III expression was reduced in the same manner, returning to normal only with the cessation of the platelet response.

We suggest that the reduction in neutrophil count after intravenous immunoglobulin is not just a side effect. Indeed, a reduction in neutrophil phagocytic

capability and mononuclear phagocyte blockade by neutrophils coated with IgG might contribute to the platelet increment in some patients with idiopathic thrombocytopenic purpura. None of our 54 patients suffered any infective complications during the neutropenic episodes, and we think that, while fairly common, the neutropenia after intravenous immunoglobulin is of little clinical concern.

- 1 Minchinton RM, McGrath K. Binding and antibody blocking effects of intravenous IgG preparation on peripheral blood cells. *Clin Lab Haematol* 1987;9:49-58.
- 2 Anderson CL, Looney RJ. Human leucocyte IgG Fc receptors. *Immunology Today* 1986;7:264-6.
- 3 Clarkson SB, Bussell JB, Kimberly RP, *et al*. Treatment of refractory immune thrombocytopenic purpura with an anti-Fc gamma-receptor antibody. *N Engl J Med* 1986;314:1236-9.

Henoch-Schönlein purpura after influenza vaccination

Drs UDAY PATEL, JOHN R BRADLEY, and DAVID V HAMILTON (Department of Renal Medicine, West Norwich Hospital, Norwich NR2 3TU) write: Vaccination against influenza is recommended for patients at increased risk of lower respiratory tract infections. The safety of the vaccine is well established, the usual side effects being a mild serum sickness with fever, malaise, and myalgia.¹

A 77 year old man developed malaise, diarrhoea, and arthralgia 10 days after receiving 0.5 ml of inactivated influenza vaccine surface antigen (Influvac). On admission his blood pressure was 95/60 mm Hg, and ankle and sacral oedema were present. His abdomen was distended, and bowel sounds were reduced. A purpuric rash was present over his buttocks and legs, and the knee and ankle joints were tender.

The haemoglobin concentration was 147 g/l, the white cell count $13.6 \times 10^9/l$ (92% neutrophils), the platelet count $407 \times 10^9/l$, and the erythrocyte sedimentation rate 30 mm in the first hour. Plasma urea and creatinine concentrations were raised at 21.1 mmol/l and 204 $\mu\text{mol/l}$ respectively, and the albumin concentration was reduced at 30 g/l. A midstream urine specimen contained 50×10^6 red cells/l and showed pronounced proteinuria.

After admission the patient developed haematemesis and melaena. Renal function deteriorated further, and percutaneous renal biopsy was performed. All of the glomeruli were abnormal with an increase in mesangial cells and matrix and patchy deposition of IgA, IgM, and C2 in relation to glomerular capillaries. The tubules and interstitial tissue were unremarkable. Oral prednisolone 60 mg daily was started. Renal function improved and the rash, arthralgia, and gastrointestinal disturbance resolved. Four weeks later the plasma creatinine concentration was 137 $\mu\text{mol/l}$, and there was no blood or protein on analysis of urine.

Immunological investigations were performed on serum collected 10 days after admission. No antibodies to influenza A or B, cytomegalovirus, *Mycoplasma pneumoniae*, chlamydia, or Q fever were detectable by complement fixation tests, but antibodies to Influvac (IgG 1/12800, IgA 1/400) were detected by enzyme linked immunosorbent assay (ELISA). No antibodies to ovalbumin were detected.

Henoch-Schönlein purpura is commonly preceded by symptoms of an upper respiratory tract infection, and relapses may be related to further infections. Pre-existing Henoch-Schönlein purpura may be exacerbated by influenza vaccination² but we are unaware of any report of Henoch-Schönlein purpura caused by the vaccination. Hypersensitivity reactions to influenza vaccine are thought to relate to allergy to vaccine components such as egg protein. It is possible, however, that immune complexes may form as a result of interaction between influenza vaccine antigens and native antibodies, initiating a vasculitic syndrome.³

- 1 Centers for Disease Control. Influenza vaccine 1980-1981. Recommendations of the public health service immunization practices advisory committee. *Ann Intern Med* 1980;93:466-8.
- 2 Damjanov J, Amato J. Progression of renal disease in Henoch-Schönlein purpura after influenza vaccination. *JAMA* 1979;242:2555-6.
- 3 Blumberg S, Bienfang D, Kantrowitz FG. A possible association between influenza vaccination and small-vessel vasculitis. *Arch Intern Med* 1980;140:847-8.