Hospital admission and benzodiazepine use

EDITOR,—Suren-drakumar and colleagues are right to express concern that admission to hospital might result in patients starting to use benzodiazepines.¹ I attempted to answer the same question by looking at the admissions to a district general hospital in north London.

I sought the case notes of medical and surgical (general surgery, urology, and orthopaedics) patients admitted in one week in June 1986. I recorded data on the length of stay and on drugs taken on admission, prescribed during the admission, and prescribed on discharge, making particular note of the benzodiazepines.

There were 157 admissions during the week of the study, and case notes could be found for 127 patients (81%). Four patients were treated as day cases, 79 were inpatients for up to seven days, 24 for 8-14 days, 10 for 15-21 days, and 10 for longer than three weeks. On admission three patients were taking benzodiazepines for epilepsy and one for anxiety; only four patients were taking them apparently as hypnotics. Records were incomplete for one patient.

Of the patients who were not taking benzodiazepines before admission, 80 were not prescribed them during the admission or on discharge; 34 were prescribed them during the admission but not on discharge; and four started taking them while in hospital and were prescribed them on discharge.

My impression from these data is that although a moderate proportion of patients who have fairly brief inpatient medical or surgical admissions are prescribed benzodiazepines while in hospital, few continue them after discharge. If there is a problem that admission is followed by long term use of benzodiazepines it may be that doctors are prescribing these drugs de novo to patients who stay in hospital longer than a month and these are the patients to whom attention should be directed.

ROBERT M COHEN

Gordon Hospital,
London SW1V 2RH

1 Suren-drakumar D, Dunn M, Roberts CJC. Hospital admission and the start of benzodiazepine use. *BMJ* 1992;304:881. (4 April.)

Bovine spongiform encephalopathy and risk to health

EDITOR,—Paul J Harrison and Gareth W Roberts' editorial on spongiform encephalopathies seems simultaneously to be offering unjustified reassurance and highlighting worrying uncertainties about the risk to human health of bovine spongiform encephalopathy.¹

On the reassurance side of the equation the authors say that the characteristics of Creutzfeldt-Jakob disease do not point to an infective origin. Yet it is fairly well established that in a few cases the disease has been transmitted between humans both by corneal transplantation and by the therapeutic administration of growth hormone derived from the pituitary.^{2,3}

Furthermore, the editorial does not refer to an important epidemiological study of sporadic cases of Creutzfeldt-Jakob disease in the United Kingdom, which looked at cases occurring just before the epidemic of bovine spongiform encephalopathy in cattle was recognised.⁴ This case-control study showed modest but significant associations between several biologically plausible risk factors and Creutzfeldt-Jakob disease. These factors included contact with cats (odds ratio 2.0) and ferrets (odds ratio 2.1) and the consumption of offal (odds ratio not given). The authors of

this study acknowledged that multiple tests of significance were performed in identifying these associations. Though the weight of evidence offered is relatively small, it nevertheless offers some support to the notion that sporadic cases of Creutzfeldt-Jakob disease may be due to transmission through contact with animals or through the food chain.

In the light of such evidence, Harrison and Robert's obvious awareness of the glaring gaps in our knowledge deserves much greater emphasis. In particular, they refer briefly to the opportunity for a natural experiment offered by the entry into the human food chain of material infected with bovine spongiform encephalopathy. What they fail to mention is that relevant data must be collected systematically. A case register of human spongiform encephalopathy should be compiled and dietary and other data collected in the context of case-control or cohort studies, or both, to permit formal examination of the hypothesised association with bovine spongiform encephalopathy. Until that is done nationally—and we know of no organisation undertaking or funding such work—the results of this crucial natural experiment may never be known.

E COYLE

South Glamorgan Health Authority,
Cardiff CF1 3NW

IAN HARVEY

Centre for Applied Public Health Medicine,
Cardiff CF1 3NW

- 1 Harrison PJ, Roberts GW. How now mad cow? *BMJ* 1992;304: 929-30. (11 April.)
- 2 Koch TK, Berg BO, De Armond SJ, Gravina RF. Creutzfeldt-Jakob disease in a young adult with idiopathic hypopituitarism: possible relation to the administration of cadaveric human growth hormone. *N Engl J Med* 1985;313:731-3.
- 3 Gibbs CJ, Joy A, Heffner R, Franko M, Miyazaki M, Asher DM, et al. Clinical and pathological features and laboratory confirmation of Creutzfeldt-Jakob disease in a recipient of pituitary-derived human growth hormone. *N Engl J Med* 1985;313:734-8.
- 4 Harries-Jones R, Knight R, Will RG, Cousens S, Smith PG, Matthews WB. Creutzfeldt-Jakob disease in England and Wales, 1980-84: a case-control study of potential risk factors. *J Neurol Neurosurg Psychiatry* 1988;51:1113-9.

Influence of early life on later health

EDITOR,—David Barker and colleagues' "programming hypothesis" is not entirely new.^{1,2} It is nearly 20 years since Baird showed that a woman's risk of giving birth to a low birthweight baby was related to the socioeconomic circumstances in which she herself had spent her early childhood.³ This long term effect accounts for slightly under half of the total social class gradient in the rate of low birth weight, or slightly more than half if selective mating is taken into account.⁴ Seemingly a beneficial socioeconomic environment in early life can compensate for hardship later on and vice versa. Whereas effects on low birth weight of social class at birth and in adult life can be shown, this is not true of social class at age 16.

Lumey has shown that the Dutch "hunger winter" of 1944-5 also had late effects. Women who as fetuses had been exposed to famine in the first or second, but not the third, trimester had babies with lower mean birth weights than did those who had not been exposed to famine; this was due partly to slower fetal growth and partly to shorter gestation.⁵ The immediate effect of the famine on the exposed pregnancies was in sharp contrast: birth weight was reduced only after exposure in the third trimester.

Biomedical events in early life are also relevant to future childbearing. Women who were born before term seem to have relatively heavy babies.⁶ Conversely, adults who were low birth weight infants tend to have babies of relatively low mean birth weight; this is true of women to a greater extent than men, suggesting that it may not

entirely be due to genetic control of fetal growth rate.

What biological mechanisms underlie these findings is unclear as we have only a few pieces of the jigsaw at present. What does seem clear is that observed health status is a product of the interaction of early and later events operating on a genetic background. This seems to hold true for the reproductive and cardiovascular systems and for certain other processes such as blood clotting⁷ and glucose tolerance.⁸ It may plausibly, therefore, be a general principle. To avoid misleading "either/or" paradigms perhaps this hypothesis should be referred to as the two stage model of environmental influence.

MICHAEL JOFFE

Academic Department of Public Health,
St Mary's Hospital Medical School,
London W2 1PG

- 1 Robinson RJ. Is the child father to the man? *BMJ* 1992;304: 789-90. (28 March.)
- 2 Fall CHD, Barker DJP, Osmond C, Winter PD, Clark PMS, Hales CN. Relation of infant feeding to adult serum cholesterol concentration and death from ischaemic heart disease. *BMJ* 1992;304:801-5. (28 March.)
- 3 Baird D. The epidemiology of low birth weight: changes in incidence in Aberdeen, 1948-72. *J Biosoc Sci* 1974;6:323-41.
- 4 Joffe M. Social inequalities in low birth weight: timing of effects and selective mobility. *Soc Sci Med* 1989;28:613-9.
- 5 Lumey LH. Decreased birthweights in infants after maternal in utero exposure to the Dutch famine of 1944-45. *Paediatr Perinat Epidemiol* 1992;6:240-53.
- 6 Alberman E, Emanuel I, Filaki H, Evans JW. The contrasting effects of parental birthweight and gestational age on the birthweight of offspring. *Paediatr Perinat Epidemiol* 1992;6: 134-44.
- 7 Barker DJP, Meade TW, Fall CHD, Lee A, Osmond C, Phipps K, et al. Relation of fetal and infant growth to plasma fibrinogen and factor VII concentrations in early life. *BMJ* 1992;304:148-52. (18 January.)
- 8 Hales CN, Barker DJP, Clark PMS, Cox LJ, Fall C, Winter PD. Fetal and infant growth and impaired glucose tolerance at age 64. *BMJ* 1991;303:1019-22.

Hospital mortality of patients injured by antipersonnel mines

EDITOR,—Last year Korver and I reported the experience of the International Committee of the Red Cross with regard to injuries caused by antipersonnel mines; we found a hospital mortality of 0.8%.¹ Since then we have created and analysed a simple data collection system giving information about all patients admitted to four hospitals (including the two hospitals that we studied in our report). In the past 18 months data on 12 958 patients have been collected; 2706 were injured by antipersonnel mines, and their hospital mortality was 2.5% (69 patients).

Readers should know that there was probably an error in our original study. It has since become apparent that some of the records of the dead patients may not have been returned to store. Loss of these records is unlikely seriously to have altered the results except in relation to mortality.

ROBIN M COUPLAND

Medical Division,
International Committee of the Red Cross,
CH-1202 Geneva,
Switzerland

1 Coupland RM, Korver A. Injuries from antipersonnel mines: the experience of the International Committee of the Red Cross. *BMJ* 1991;303:1509-12.

Urine albumin, total protein, and glomerular proteinuria

EDITOR,—P H Winocour reviews the association of microalbuminuria with impending nephropathy and with risk markers for coronary heart disease.¹ He states that many of the associations are more pronounced in the presence of overt proteinuria.

Urine total protein consists of a complex mixture