

paper. A total of 3068 female doctors, a highly motivated group, were asked for details of their entire reproductive history. The outcome studied was fetal death—stillbirth, ectopic pregnancy, or detected spontaneous abortion. For present purposes the main limitation is the fact that reproductive histories are incomplete for some members of the later-born cohorts in the study.

The two most pertinent features of the results of Professor Bakketeig and Mr Hoffman may be observed in those of Roman also. Analysis of all pregnancies irrespective of final gravidity indicated a U-shaped dependence of failure rate on birth order, overall rates of fetal loss being 13.6%, 12.5%, 13.9%, and 18.3% in the first four pregnancies. Within groups defined according to gravidity reached by the time of the study the failure rate fell with increasing pregnancy order.

In order to compare loss rates in pregnancies 1 and 2 it is most appropriate to take into account all women of final gravidity 2 or more. In analysing Roman's data thus, we deduct the women of gravidity 1 from the "all pregnancies" figures, obtaining loss rates of 13.8% and 12.5% in pregnancies 1 and 2. Similarly, losses in pregnancies 2 and 3 may be compared among all women of ultimate gravidity 3 or higher—17.7% and 13.9%. The corresponding figures for pregnancies 3 and 4, among all women with four or more pregnancies, are 22.0% and 18.3%. Thus the biological processes involved are best represented by decreases in loss rate by factors of .904, .783, and .834 from each pregnancy to the next, or a decrease from 26.8% to 18.3%, a factor of .683, from first to fourth.

Nevertheless, it will be noted that each successive group defined according to ultimate gravidity has higher losses at a given birth order than the previous group. When we observe outcome in women pregnant for the fourth time, we observe the balance of a biological process that has apparently improved with each successive pregnancy against the possible implications of self-selection for such a gravidity.

R G NEWCOMBE

Department of Medical Statistics,
Welsh National School of Medicine,
Cardiff CF4 4XN

¹ Roman, E, et al, *Early Human Development*, 1978, 2, 131.

Non-compliance: does it matter?

SIR,—In questioning the value of programmes to improve compliance, your leading article (10 November, p 1168) deals exclusively with drug treatment. There are nevertheless other aspects of management which require the active co-operation of patients, one of which is that patients should attend for treatment in the first place.

A significant number of patients who are referred to psychiatric outpatient clinics fail to keep their first appointment. During a recent 12-month period, for instance, 26% of new outpatient appointments at this department were not kept, a figure of similar magnitude has been reported at other centres.^{1,2} Although many of these patients may have managed without specialist help—indeed it has been argued that a waiting list is a useful screening device for this very reason³—this degree of non-compliance with referral procedures represents, at the very least, an appreciable waste of administrative, clinical,

and teaching time. It is, however, probably that a significant proportion of patients who fail to co-operate in this way will remain unwell.⁴ Moreover, when outpatient time has been reserved for patients who do not use it, other patients—who may well have benefited from an earlier appointment—are subjected to unnecessary delay. Finally, a non-compliance rate of 26% raises important questions about the whole process of psychiatric referral such as the selection of patients for referral and the suitability of existing administrative procedures.

T PASTOR

Department of Psychiatry,
St Mary's Hospital
(Harrow Road),
London W9 3RL

¹ Skuse, D H, *British Medical Journal*, 1975, 3, 469.

² Whyte, R, *British Journal of Psychiatry*, 1975, 127, 160.

³ Robin, A, *British Journal of Psychiatry*, 1976, 128, 138.

⁴ Bridges, P, and Woollacott, S, *Comprehensive Psychiatry*, 1972, 13, 63.

Adverse reactions to drugs in general practice

SIR,—I welcome Dr C R Martys's study of adverse reactions to drugs in general practice (10 November, p 1194). It is good that the extent of such adverse reactions is being demonstrated and studied. Dr Martys found that 41% of the 817 patients given single-drug treatment were thought to have "certainly" or "probably" had a reaction to the drug prescribed. But unfortunately the frequency of adverse reactions to prescribed drugs is likely to be greater than this.

Dr Martys states that his study was restricted to patients given a single drug because "Most patients in general practice present with relatively straightforward clinical problems, for which treatment with a single drug is entirely appropriate." He gives no figures from his own practice of the proportion of patients receiving more than one drug. In a national study of people on the electoral register in 1969 it was found that the average number of prescribed medicines taken in two weeks by those taking any prescribed medicine was 2.0.¹ And in both this study and another similar one in 1977² half of those taking any prescribed medicine in a two-week period had taken another prescribed medicine.³ Since many adverse reactions are likely to result from interactions between drugs, Dr Martys's estimate of 41% must be regarded as a serious underestimate of the frequency with which such reactions occur.

ANN CARTWRIGHT

Institute for Social Studies
in Medical Care,
London NW3 2SB

¹ Dunnell, K, and Cartwright, A, *Medicine Takers, Prescribers and Hoarders*. London, Routledge and Kegan Paul, 1972.

² Cartwright, A, and Anderson, R, *Journal of the Royal College of General Practitioners*, 1979, Occasional Paper 8.

³ Anderson, R. (In draft.)

Poisoning with chlormethiazole

SIR,—The letter by Dr G T McInnes and others (10 November, p 1218) reports two cases of cardiac arrest during the intravenous infusion of chlormethiazole. That the arrhythmias which occurred were the direct result of the drug must be seriously questioned.

In case 1 ventricular tachycardia developed

after approximately 10 g of chlormethiazole had been given over 16 hours. The tachycardia presumably changed to ventricular fibrillation or asystole if cardiac arrest occurred. How was the patient resuscitated and what was the time course? As the patient survived, one must presume that normal cardiac function resumed quickly despite the fact that the chlormethiazole plasma concentration would take several hours to decrease substantially.

In case 2 the arrest occurred after only 0.66 g of chlormethiazole given over one hour, a dose which in my experience would be expected to cause only a minor degree of sedation. This patient, with severe facial injuries, must have had at least a potential threat to his airway and one wonders if the restlessness for which chlormethiazole was given was not in fact due to hypoxia. The fact that no preceding arrhythmia is reported, no details are given of the cardiac arrest, and resuscitation was unsuccessful brings into doubt the degree of patient monitoring. The bland statement that there was no evidence of respiratory depression prior to arrest is not exactly conclusive.

Dr McInnes and his colleagues are correct in assuming a longer-than-usual half life for chlormethiazole in patients who receive large doses intravenously or who have liver dysfunction. It is difficult to see the relevance of this in regard to cardiac arrest, as neither of their patients would have achieved high plasma concentrations and in case 2 the concentration must have been very low.

Having used chlormethiazole for many years in anaesthesia and in seriously ill patients undergoing intensive care, employing doses much in excess of those reported in these two cases, one is distressed to read that it can cause "potentially lethal cardiac dysrhythmias." Such a charge is surely a complete condemnation of the drug, which if substantiated should lead to its total withdrawal as a sedative. That such an outcome might result from the very inadequate clinical details given by Dr McInnes and his colleagues would be most unfortunate.

D B SCOTT

Department of Anaesthetics,
Royal Infirmary,
Edinburgh EH3 9YW

A reminder to remind the patient

SIR,—I hope you may allow me to respond to the somewhat misguided and subjective view of our poster and pamphlet *Alcohol and Drugs Do Not Mix—A Reminder to the Physician to Remind the Patient* (3 November, p 1138).

This is misguided because the reviewer has obviously not consulted the covering letter, which details the aims and objects of the pamphlet, nor has he given the name of the writer of the pamphlet, which would indicate the authenticity of the data contained in it. The writer is Professor P F D'Arcy, DSc, BPharm, professor of pharmacy at the Queen's University, Belfast, a noted authority on dangerous and adverse drug reactions and a member of the Medicines Commission.

That the pamphlet was intended to remind the physician to remind the patient is clearly stated on the pamphlet. Thus it did not arrogantly assume total ignorance on the part of the medical profession of one of its major concerns, the prescribing of curative drugs. It is quite clearly established that doctors do have many things on their minds and may forget to give these instructions. It is also well