As we pointed out, the proposed mechanism for the interaction between eproxindine and flupenthixol is speculative. However, Simister and Jorgensen's suggestion that this fatality could have been due to an idiosyncratic reaction to eproxindine is also speculative. Their comment that the volunteer who died had higher blood levels of eproxindine than the other volunteer who had received the same dose sequence is misleading, since in the man who died the only sample analysed for eproxindine was taken at necropsy, over 24 h after death. Blood levels of this drug in the two volunteers cannot therefore be compared.

Simister and Jorgensen also suggest that high blood levels of unbound active flupenthixol, which could be due to displacement from protein binding sites, "would only be possible for drugs with a small apparent volume of distribution" whereas "flupenthixol has a very large volume of distribution". It is, however, possible that greatly increased amounts of free flupenthixol could have reached the heart before redistribution of the drug had occurred. In discussing drug-displacement interactions Lindup and Orme[2] point out that after displacement "the potentiation of pharmacological activity is transient and fades as a new steady state is established, during co-administration of the drugs". The time required to reach a new steady state would clearly be of critical importance in the present case. The suggestion that a level of free flupenthixol of 0·5 ng/ml is equivalent to a total plasma level of 50 ng/ml would only be true if the extent of protein binding of flupenthixol were exactly 99%. Since the binding of this drug is so high that it cannot be accurately determined, the equivalent total plasma concentration could be much higher; for example, if binding were 99·9% a free-drug level of 0·5 ng/ml would represent a total plasma concentration of 500 ng/ml, much higher than therapeutic plasma levels.

Dr Pereira Gray and Dr Jones and Dr Good (Feb 9, p 343) raised the question of the medical history of drug-study volunteers. The difficulty in obtaining a comprehensive medical history for volunteers participating in phase I studies is a matter of serious concern to all clinical pharmacologists. We have often discussed the possibility that consulting the volunteer's general practitioner would add to the dimensions of safety in phase I studies. However, in our experience healthy adults in the 18–25 age group are often living apart from their family and may not have been seen by their family doctor for several years. Furthermore, seeking a certificate of suitability for all volunteers from their GPs would be impracticable and would place the GPs in a vulnerable position medicolegally, which few would be prepared to accept. In our opinion, therefore, the burden of responsibility for making a full disclosure of his medical history must ultimately rest on the volunteer.

Dr Watkins (this issue) asks why debrillation was attempted when the patient was asystolic and why cardiac pacing was not done. Direct current countershock was applied to this volunteer in the remote hope of inducing a reversible arrhythmia. In the situation of established asystole without P waves the attendant consultant physician decided to continue resuscitative procedures and not to undertake temporary cardiac pacing.

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1 Turbott J, Smeeton WMI. Sudden death and flupenthixol decanoate. *Aust NZ J Psychiatry* 1984; **18:** 91–94.
2 Lindup WE, Orme MCLE'E. Plasma protein binding of drugs. *Br Med J* 1981; **282:** 212–14.

SODIUM BALANCE IN LOW BIRTHWEIGHT BABIES AFTER ORAL REHYDRATION

SIR,—Dr Sachdev (Dec 22/29, p 1474) asks why we saw scant evidence of hypernatraemia in our low birth weight (LBW) neonates with diarrhoea on oral rehydration (Oct 6, p 818) when he and his colleagues saw so much in theirs. We now have experience with 63 LBW neonates, of whom 3 died; 53 received oral rehydration therapy (ORT) only. Only 2 had mild, asymptomatic hypernatraemia. We did not see oedema in any child. We have reviewed the paper by Sachdev and co-workers[1] as well as our own data and find substantial differences, perhaps instructive. We believe that our patients were protected against sodium overload for several reasons. In our patients diarrhoea developed while they were in our unit and since we knew their pre-illness weight we could replace their deficits and losses to within a few grams. Sachdev's patients were admitted with diarrhoea, and with severe acidosis in nearly two-thirds. Over 75% of our patients received soy-based formula 6 h after ORT began (98% after 12 h), with 80% getting it half-strength and thus an ample quantity of free water. 92% of our children had diarrhoea for less than 1 day (an effect, we believe, of early feeding), while the average course of diarrhoea in Sachdev's patients was about twice as long. It may yet be correct that with serious and prolonged diarrhoea in LBW neonates a lower concentration of sodium in the rehydrating and maintenance fluid produces less imbalance. We stated in our first letter that, "Even LBW neonates may be safely given deficit therapy using ORT with the WHO formulation although they are . . . likely to need . . . far more meticulous attention".

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1. Bhargave SK, Sachdev HPS, Das Gupta B, Daral TS, Singh HP, Man Mohan Oral rehydration of neonates and young infants with dehydrating diarrhoea: Comparison of low and standard sodium content in oral rehydration solutions. *J Pediatr Gastroenterol Nutr* 1984, **3:** 500–05.

LEU M1 MONOCLONAL ANTIBODY STAINING OF REED-STERNBERG CELLS

SIR,—We would like to comment on Professor Wright's statement (Feb 9, p 340) about the specificity of the Leu M1 monoclonal antibody for Reed-Sternberg (RS) cells in Hodgkin's disease (HD). Although we found that RS cells and their variants and Hodgkin's (H) cells stained with Leu M1 in forty cases of lymphocyte predominance, nodular sclerosis, and mixed cellularity HD which had been fixed in B5 or formalin and embedded in paraffin, RS-like cells also stained with Leu M1 in five of six cases of immunologically proven T-cell lymphoma. Therefore, it appears that the Leu M1 monoclonal antibody stains RS-like cells in both T and B-cell (see Dr Linch and colleagues' reply to Wright's letter) lymphomas and is less specific than originally thought.

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MIGRAINE AND LEFT-HANDEDNESS

SIR,—In a television programme (*Horizon*, BBC 2, Feb 4) the late Dr Norman Geshwind, professor of neurology at Harvard University, expressed the opinion that there might be a link between migraine and left-handedness. I therefore questioned fifty consecutive patients with migraine and another fifty with neurological conditions but without migraine headaches, with the following results:

	Migraineurs	*Neurological patients without migraine*
Right handed and right footed	30	31
Right handed and uncertain about foot	15	14
Left handed and left footed	3	1
Left handed and uncertain about foot	2	4

These observations indicate that there is no link between handedness and migraine. When, as a registrar, I used to put ideas such as this to my late chief, Lord Brain, he would reply, with flattening brevity, "Ingenious but incorrect".

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