case. More importantly, decisions were taken on selective aspects of information and members were highly influenced by the language in which the information was presented. This might indicate a need for tribunal members and representatives to receive advice and training, which is the principal objective of Representing the Mentally Ill and Handicapped.

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Early intervention in Down's syndrome

Sir,—May I challenge a report in your “Views” column (21 June, p 1541)? Minerva cited a study by Piper and Pless,1 which claimed to show that early intervention had no significant effect on infants with Down's syndrome and she ended by saying that such negative results, though disheartening, were welcome evidence of a more rigorous approach. Unfortunately, Piper and Pless claimed a major result of their study, by my mother and a colleague,2 which reached the opposite conclusion but appeared too late to be considered by Piper and Pless. As I was involved in the statistical analysis of my mother’s data I would like to comment on the discrepancy between these studies.

Neither study was completely satisfactory. The Griffiths scales were recorded at intervals within the first two years of life, without any between-group differences. However, as pointed out by the second author of the present study, the final test results did not suffer from this and in other respects the groups were well matched. Piper and Pless did not say whether they controlled for any other possible confounders. A second point of concern is that many of the tests were done by the authors, although numerous problems have arisen from this dependence. It was felt that there was no good correlation between Griffiths and Stanford Binet results. However, neither of these criticisms should be deemed excessive, as they were based on the results of the study of Drs. L. and W. Griffiths, which showed that the proportion of children placed by independent assessors in normal schools or for moderately educationally subnormal training was always overwhelmingly greater in the treated group than in the controls. A 2 x 2 table showed that there was about one chance in 3 000 000 that this was a random effect.

While Ludlow and Allen have done one of the largest and most rigorous studies, they are also supported by many earlier authors and there is every justification for the view that early intervention is extremely beneficial to children with Down’s syndrome. As Piper and Pless themselves say, the Griffiths scales measure only some of the possible benefits of such intervention. Others are less tangible but may be even more important, and I hope that your report did nothing to alter that view.

Finally, I trust that you will quote sample size in all future reports on research. That would be welcoming more evidence of rigorous reporting.

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Can insulin-treated diabetics be given beta-adrenergic-blocking drugs?

Sir,—The article by Dr Anthony H Barnett and others (5 April, p 976) makes the broad assumption that any beta-blocking drug can safely be used in patients with hyperglycaemia. The study, however, only related to a relatively rare, albeit important, aspect of hyperglycaemia—namely, hyperglycaemic coma. The major causes for concern in using beta-blocking agents in diabetic coma to hyperglycaemia are: (1) an increased risk of hyperglycaemic coma; (2) masking of the major hyperglycaemic warning signals; (3) a delayed rate of fall of the hyperglycaemia; and (4) an altered haemodynamic reaction to hyperglycaemia.

(1) The article by Dr Barnett and others shows that beta-blocking agents are not a major cause of hyperglycaemic coma, with which we fully agree. However, in our experience a non-selective agent (propranolol) can indeed change the hyperglycaemic response and produce sudden uncontrolled loss of consciousness.3 Neither placebo nor a cardioselective agent (metoprolol) produced this response despite the broader use of propranolol by many patients taking it in diabetes without any medication, Dr Barnett and his colleagues also found that one of their five patients treated with beta-blockade attributed his occurrence of hyperglycaemia to the institution of propranolol therapy. Since this effect of propranolol may be due to its effect on the cardiovascular reflex,3 it is possible that as discussed below, it would be of interest to know if this patient improves by withdrawing the drug.

(2) The finding of similar incidences of hyperglycaemic symptoms in the untreated and beta-blocked groups does not mean that beta-blockade leaves the hyperglycaemic symptoms unchanged. Additionally, it is possible that some true hyperglycaemic attacks are not recorded as such. In our main study patients on a non-selective drug such as propranolol is increased sweating. However, tremor or palpitations might not have been noted by the observer, prouing that Dr Barnett and his colleagues found a higher incidence of palpitations in the beta-blocked group (17% vs 7%) during the alleged hyperglycaemia. This raised possibility that all patients were indeed hyperglycaemic when they reported hyperglycaemia, and whether they had adequate beta-blockade. We have recently finished a prospective, double-blind study where five insulin-dependent diabetics were in a cross-over fashion (metoprolol vs a cardioselective agent (metoprolol) for totals of 71 and 77 weeks, respectively. The patients were not able to record possible hyperglycaemic episodes and symptoms. One of the patients noted that with metoprolol the hyperglycaemic symptoms were less pronounced and not as sudden in onset. The remaining patients noted no clear difference. Thus we feel that a cardioselective agent may be used in insulin-dependent diabetics, but some caution should still be exercised and patients should be informed that the symptoms may be mitigated.

(3) Most studies,2,3 but not all,7 show that a non-selective agent will delay the recovery from hyperglycaemia, probably by reducing hepatic glucose production. Although a selective agent might influence this variable there is less pronounced than that of a non-selective drug.4,5 Insulin-dependent diabetics have an already lowered rate of glucose production and recovery from hyperglycaemia.4,5 Any additional attenuation is obviously unwanted.

The normal haemodynamic pattern in hyperglycaemia (tachycardia, reduced diastolic pressure, and raised systolic pressure) is changed by a non-selective agent to bradycardia, which may be pronounced and lead to heart rates below 30 beats/min, and elevated diastolic blood pressure.1,6 Ventricular arrhythmias have also been reported.8 We have previously reported5 that the blood pressure in a diabetic patient during hyperglycaemia and propranolol treatment was changed from 120/70 to 180/120. We propose that the increased incidence of cardiovascular disease in diabetics is certainly a potentially hazardous change. In addition, the bradycardia produced by metoprolol may also be hazardous,9 possibly one reason for the hyperglycaemic coma we noted with propranolol. A cardioselective agent influences the haemodynamic pattern less than a non-selective agent 1 and does not lead to bradycardia during hyperglycaemia.

Thus a non-selective agent influences the hyperglycaemic symptoms, attenuates the blood glucose recovery rate, and leads to a more alarming haemodynamic reaction during hyperglycaemia. A cardioselective agent influences these aspects less and should there-
was noticed that she had unexpected severe ketoacidosis. The diagnosis of diabetes mellitus was made in January 1979 by Dr J M Steel (10 May p 1167) and Dr Joan R Gomez (5 July, p 61) I submit the case of a 20-year-old girl.

Insulin-dependent diabetes mellitus was diagnosed in 1973 at 131 years. She menstruated regularly for 14 years, when her weight was 444 kg. In 1976 frequent ketonuria was noted and she admitted to reducing her insulin to control her weight. In February 1978 she was started on phenytoin 100 mg for symptomatic nocturnal epilepsy. In January 1979 her weight had fallen to 385 kg (expected weight 52 kg). She admitted that this was due to dieting and was underweight but not confined to bed. Initially frequent hypoglycaemic attacks occurred and it was noticed that she disappeared into the toilets immediately after meals and would refuse to eat her urine for sugar. She was discharged with no recorded weight gain. A further four episodes of ketoacidosis occurred in 1979, each seeming to follow a record of weight gain in the clinic. She complains of frequent hypoglycaemia, which she confirms with Dextrostix. Reductions in insulin dosage have therefore been confined despite clinic Dextrostix readings in excess of 22 mmol/l (400 mg/100 ml). HbA1 ranges from 10-1% to 15%. Her urine contains little sugar and she is suspected of diluting the samples. She remains unwell and was managed with a low caloric diet and has gained 40 kg and amnorrheic (see figure), single, and lives with her parents, but does have a boyfriend.

Reluctance to diagnose anorexia nervosa in this notably difficult young female diabetic may contribute to the infrequent reports.

I thank Dr R de Mowbray for permission to report this case.

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Site of action of intrathecal morphine

Sr,—May I somewhat tardily comment on your correspondents' responses (27 September, p 870) to my letter (6 September, p 680)? Dr P J W Knell's suggestion that the intrathecal catheter, which we injected intrathecally did not reach the target sites in the spinal cord is reasonable, although I would have anticipated that the lower sacral segments would have been blocked; yet this was not the case. Anticipating Dr Knell's idea, in our own investigation (report awaiting publication) we injected morphine (2 mg in 10 ml) extradurally via a cannula inserted through the T10/11 interspace, yet still failed totally to relieve the pain of labour.

Dr Jacobson's letter reiterates one of the more pressing arguments favouring the spinal cord as the site of action of intrathecal morphine, namely, that opiate receptors have been identified in the spinal cord. This has never seemed to me to be a very convincing argument, as it assumes that narcotics, when attached to these receptors, necessarily effect a classical analgesia. The case becomes even more tenuous in the light of recent publications. It has been demonstrated that there are receptors to opiates and opioid substances (including naloxone) in the placenta and in the hypophysial-hypothalamic region, and indeed that the placenta synthesises endorphins. It is beginning to look as though there are cell membranes which contain specific receptors for narcotics scattered throughout the body. Possibly it will emerge that endorphins are analogous to substances like the prostaglandins, having a multitude of functions depending on the exact configuration of the molecule and on the identity of the receptors. If such considerations rang true, the analogues of endorphins—will act in accordance with the local situation, and in the case of the spinal cord they might well not be acting as depressants of pain impulses. The onus remains with others to confirm that intrathecal (or extradural) morphine exerts analgesic activity at spinal cord level rather than in brain.

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2 Sinamot RV, Scharow SH, Brain Res 1979;174:178-84.