case. More importantly, decisions were taken on selective aspects of information and members were highly influenced by the hospital authority's report. The results 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 you overlooked a much larger 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 scale development quotients decline most rapidly over the first two years, at about eight points per year[2] and this decline is not linear, being more rapid at first. Consequently children should be tested at exactly the same ages to be comparable, but that is not practical. The resulting errors in pooling data from children even two months apart are appreciable and make the study of treatment effects particularly difficult in infants. Piper and Pless confined their attention to infants, whereas Ludlow and Allen followed their children through for up to eight years. In neither case were the ages of testing synchronised.

In addition, Piper and Pless studied rather a small sample (21 experimental and 16 control children). From the standard deviations in their table 2 it is possible to calculate the smallest difference between controls and experimentals which would be statistically significant. These turn out to be rather large (5·67 to 10·44 points on the Griffiths scale) and differences as large as this could not have developed within six months unless the treatment had completely arrested or even reversed the usual decline in development quotients. In other words, given their sample size and the observed variation in children, Piper and Pless could not have shown a significant effect of early intervention unless the treatment had been totally effective. Sadly, no one is able to make that claim.

The non-statistical reader may be surprised that Piper and Pless detected no difference at all between groups, but this is a perennial problem in statistics. Even a biased coin may come up the "wrong" way more often than not unless the sample is very large. That is precisely why statistical tests are necessary. Piper and Pless were aware of this and did not claim that early intervention was useless. They were careful to point out that their results disagreed with those of previous studies and discussed possible explanations. Indeed, their careful scientific work deserves better than the scant report you gave.

One of their suggestions was that a longer period of observation might have produced different results. This seems likely since Ludlow and Allen found the largest differences at about 4 years. Piper and Pless also pointed out that the experimental group was assessed over the autumn and winter, while the control children were studied over the spring and summer when more frequent play outdoors with other children may have been as beneficial as the therapy they missed. It is also possible that the control group children in Canada were less deprived or better counselled than the corresponding group in England, with the result that treatment was less necessary in Canada.

Ludlow and Allen studied 192 children, with 77 in the treated group and 82 and 43 in two control groups. They found highly significant differences between the groups although two features of their study might be criticised. The initial assessment of the stimulated children took place two or three weeks after the first counselling session, since an academic study was not then envisaged. By the time of the assessment, therefore, the children had already received some treatment. More importantly, the experimental group children were younger than the control group when first tested, and therefore scored higher. However, the final test results did not suffer from this problem and in other respects the groups were well matched. Piper and Pless do not say whether their control group received any counselling.

A second point of concern is that many of the tests were done by the authors, although numerous independent tests agreed closely and there was good correlation between Griffiths and Stanford Binet results. However, neither of these criticisms can be levelled at the final result of the study, which showed that the proportion of children placed by independent assessors in normal schools or schools for moderately educationally subnormal children was overwhelmingly greater in the treated group than in the controls. A χ^2 test shows that there was about one chance in 3 000 000 that this was a spurious difference.

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 welcome evidence of more rigorous reporting.

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[1] Piper CM, Pless IB, *Pediatrics* 1980;**65**:463-8.
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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 statement that any beta-blocking drug can safely be used in diabetics prone to hypoglycaemia. The study, however, only related to a relatively rare, albeit important, aspect of hypoglycaemia—namely, hypoglycaemic coma. The major causes for concern in using beta-blocking agents in diabetics prone to hypoglycaemia are: (1) an increased risk of hypoglycaemic coma; (2) masking of the major hypoglycaemic warning signals; (3) a delayed rate of recovery from the hypoglycaemia; and (4) an altered haemodynamic reaction to hypoglycaemia.

(1) The article by Dr Barnett and others shows that beta-blocking agents are not a major cause of hypoglycaemic coma, with which we fully agree. However, in our experience a non-selective agent (propranolol) can indeed change the hypoglycaemic response and produce sudden unconsciousness.[1] Neither placebo nor a cardioselective agent (metoprolol) produced this response despite similar or lower blood glucose levels.[1] We have in our subsequent studies seen another patient treated with propranolol react in an identical fashion. Although this reaction may indeed occur in diabetics without any medication, Dr Barnett and his colleagues also found that one of their five patients treated with beta-blockade attributed the occurrence of hypoglycaemic coma to the institution of propranolol therapy. Since this effect of propranolol may be due to its effect on the haemodynamic reaction during hypoglycaemia, as discussed below, it would be of interest to know if this patient improves by withdrawing therapy or by switching to a cardioselective drug.

(2) The finding of similar incidences of hypoglycaemic symptoms in the untreated and beta-blockade groups does not mean that beta-blockade leaves the hypoglycaemic symptoms unchanged. Additionally, it is possible that some true hypoglycaemic attacks are not recorded as such. In our experience the main hypoglycaemic symptom on a non-selective drug such as propranolol is increased sweating. However, tremor or palpitations were not experienced by our patients. It is surprising that Dr Barnett and his colleagues found a higher incidence of palpitations in the beta-blockade group (26% *v* 17%) during the alleged hypoglycaemia. This raises the questions whether all patients were indeed hypoglycaemic when they reported hypoglycaemia, 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 and random fashion treated with placebo or a cardioselective agent (metoprolol) for totals of 71 and 77 weeks, respectively. The patients were asked to record possible hypoglycaemic episodes and symptoms. One of our patients noted that with metoprolol the hypoglycaemic 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,[1–5] but not all,[6 7] show that a non-selective agent will delay the recovery from hypoglycaemia, probably by reducing hepatic glucose production. Although a selective agent may also influence the rate of recovery this effect is less pronounced than that of a non-selective drug.[3–5] Insulin-dependent diabetics have an already reduced rate of spontaneous blood glucose recovery from hypoglycaemia.[1 6] Any additional attenuation is obviously unwanted.

(4) The normal haemodynamic pattern during hypoglycaemia (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 8] Ventricular arrhythmias have also been reported.[8] We have previously reported[1] that the blood pressure in a diabetic patient during hypoglycaemia and propranolol treatment was changed from 110/70 to 200/120 mmHg. When we consider the increased incidence of cardiovascular disease in diabetics this is certainly a potentially hazardous change. In addition, the bradycardia produced by hypoglycaemia and a non-selective agent is probably one reason for the hypoglycaemic coma we noted with propranolol. A cardioselective agent influences the normal haemodynamic pattern less than a non-selective agent[1] and does not lead to bradycardia during hypoglycaemia.

Thus a non-selective agent influences the hypoglycaemic symptoms, attenuates the blood glucose recovery rate, and leads to a more alarming haemodynamic reaction during hypoglycaemia. A cardioselective agent influences these aspects less and should there-

fore be used when a beta-blocking agent is required in diabetics prone to hypoglycaemia. However, with these drugs also patients should be informed that institution of treatment may modify the normal hypoglycaemic symptoms. Additionally, until further experience has been gained we think that special care should be exercised with any of these drugs in diabetics with clear autonomic neuropathy, where both symptoms and recovery may be further compromised.

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Anorexia nervosa in diabetes mellitus

SIR,—Further to the reports of anorexia nervosa in diabetics by Drs C G Fairburn and 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-dependant diabetes was diagnosed in 1973 at 13½ years. She menstruated regularly from 14 years, when her weight was 44½ 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 38·5 kg (expected weight 52 kg). She admitted that this was due to dieting and adamantly refused admission as her skeletal appearance was "about right." She had last menstruated in May 1978, when her weight was 51 kg. In April 1979 she was admitted in severe ketoacidosis. The diagnosis of anorexia nervosa was guarded because of the diabetes and "epilepsy." She was managed with a high-dose insulin regimen but not confined to bed. Initially frequent hypoglycaemic attacks occurred and it was noticed that she disappeared into the toilets immediately after meals "to test 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 condoned despite clinic Dextrostix readings in excess of 22 mmol/l (400 mg/100 ml). HbA_1 ranges from 10·1% to 15%. Her urine contains little sugar and she is suspected of diluting the samples. She remains underweight at 46 kg and amenorrhoeic (see figure), is single, and lives with her parents, but does have a boyfriend.

Reluctance to diagnose anorexia nervosa in the notoriously 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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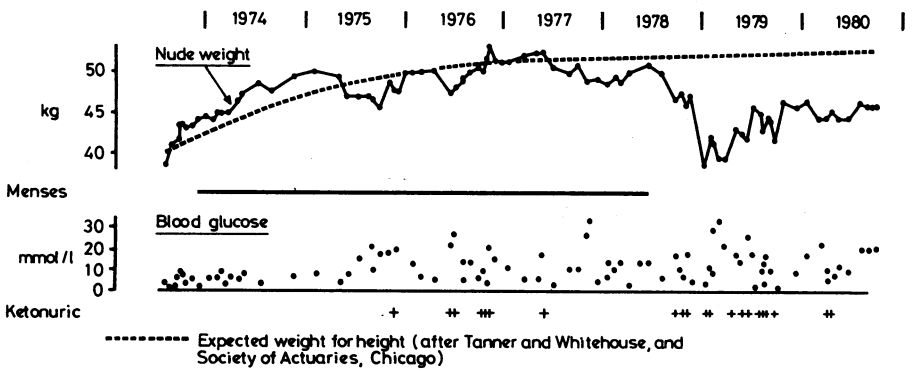

Patient's clinic record.

Conversion: SI to traditional units—Glucose: 1 mmol/l = 18 mg/100 ml.

Site of action of intrathecal morphine

SIR,—May I somewhat tardily comment on your correspondents' responses (27 September, p 870) to my previous letter (6 September, p 680)? Dr P J W Knell's suggestion that the hyperbaric solution of morphine 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 "opiate" activity. The suggestion becomes even more tenuous in the light of recent publications. It has been demonstrated[1] that there are receptors to opiates and opioid substances (including naloxone) in the placenta and in the hypophyseal-hypothalamic region,[2] and indeed that the placenta synthesises endorphins.[3] 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 analagous to substances like the prostaglandins, having a multitude of functions depending on the exact configuration of the molecule and on the identity of the target cell. If such is the case, opiates—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 depresssants 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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Community medicine—a second chance?

SIR,—Your leading article (27 September, p 826) raises a number of important points and I hope that, together with the recent report of the joint working party, it may stimulate some necessary change.

I believe that there are two key issues in community medicine today: firstly, the question of administrative and technical support and, secondly, the danger of professional isolation of those working in community medicine. Given adequate recourse to a good information unit and to the general administrative system much can be achieved, but these things are not adequate on their own. Community medicine specialists need to have secretarial, administrative, and research services accountable and responsible to them and not to anybody else. The total resources do not need to be great but they do need to exist. Without them the practice of the specialty will become ineffective and this will inevitably result in low morale and an inadequate advertisement of the subject to clinical colleagues and to other professionals in the Health Service. Would-be entrants to the specialty could scarcely be blamed if they did not wish to continue their studies in a specialty which achieved little and offered less. Professional isolation can be overcome provided the danger is recognised. Community medicine specialists need the stimulus and even the irritation of professional conversation with colleagues in the same specialty. The formation of departments of community medicine, providing they are adequately serviced and supported, and provided they can be motivated not to self-destruct, will do much to improve the situation.

Outside the specialty, two bodies could help to improve the situation. Regional health authorities should provide the stimulus and opportunity for regional meetings of community medicine specialists, to be held on a routine basis, and indicate that it is expected that such meetings are supported. The British Medical Association should publicise those health authorities that decline to provide adequate support for community medicine, and if this has no effect use the mechanism of the "important notice" procedure in the advertisement section of the journal.

Consideration could also be given to more firmly establishing district community physicians as the physicians with overall