Guidelines should be based on systematic reviews of the evidence

EDITOR.—After surveying 39 intensive care units D R Jeevaratnam and D K Menon conclude that many use treatments that are “at odds with an emerging consensus about the management of patients with severe head injury.”¹ Use of steroids despite “increasing evidence of their lack of efficacy” is given as an example of this. The authors call for clinical guidelines.

Although guidelines may reduce variations in practice, we believe that a more important obstacle to the effective management of head injury is the lack of reference to large scale randomised evidence on the effectiveness of treatment.² This evidence could be obtained by conducting systematic reviews of all relevant previous trials and, when necessary, by conducting large scale randomised trials. Like Jeevaratnam and Menon, we will use steroids as our example.

Worldwide, head injury is a major cause of premature death. For a problem as important as this even a moderate reduction in mortality from an intervention as simple and inexpensive as steroids could save thousands of lives.² In support of their statement that steroids are ineffective Jeevaratnam and Menon cite three randomised trials.³⁻⁵ Table 1 shows the effect of steroids on six month mortality in these trials. The pooled result has a wide confidence interval, and it is impossible to exclude a moderate intervention effect. Much larger trials would be required to detect a moderate effect of steroids on mortality.

Table 1—Result of pooling data from trials showing effect of steroids on six month mortality

Trial	Steroid	Placebo	Odds ratio (95% confidence interval)
Gianotta <i>et al</i>	34/72	7/16	0.86 (0.30 to 2.45)
Cooper <i>et al</i>	26/49	13/27	1.14 (0.38 to 3.37)
Saul <i>et al</i>	8/50	9/50	1.21 (0.47 to 3.08)
Trials pooled	68/171	29/93	1.07 (0.59 to 1.92)

Another reason why the possibility that steroids may prove useful should not be dismissed is that Jeevaratnam and Menon cite only a fraction of the evidence available. We are conducting a systematic review of steroids in head injury and have so far identified 15 randomised trials. Inclusion of all the randomised evidence in a systematic review minimises random error and avoids systematic error, which can arise when a biased selection of trials is reviewed. Guidelines are needed for the management of severe head injury, but these should be based on a systematic review of all the relevant randomised trials⁶ and not on an emerging consensus ignoring the evidence. If systematic reviews fail to provide clear answers then the answers should be sought in large randomised trials.

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1 Jeevaratnam DR, Menon DK. Survey of intensive care of severely head injured patients in the United Kingdom. *BMJ* 1996;312:944-7. (13 April.)

2 Peto R, Collins R, Gray R. Large-scale randomized evidence: large simple trials and overviews of trials. *J Clin Epidemiol* 1995;48:23-40.

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Author's reply

EDITOR.—The primary purpose of our audit was to document clinical practice in this aspect of intensive care, and we believe that our results provide strong evidence for the variability in practice among centres. These findings are echoed in the data provided by M D D Bell.

We were careful to discuss the deficiencies of a telephone based audit and are interested in the data provided by J D Palmer and colleagues. Since our paper was accepted for publication, however, we have undertaken (at the suggestion of one of the reviewers of the paper) a documentary survey that covered the issues addressed in our original telephone survey. The survey was sent to senior medical staff in the neurosurgical units that were targeted in the telephone survey, and, as might be expected, resulted in a lower response rate.¹ Except for data on the use of corticosteroids, the findings from the two surveys were similar, in support of the general accuracy of data in our paper.

We agree with Graham Teasdale and colleagues that the report by the task force of the American Association of Neurological Surgeons and Joint Section in Neurotrauma and Critical Care is an important advance in the management of patients with acute head injuries,² and we believe that its findings support the case for guidelines based on the available evidence. While we were unaware of the activities of the working party of the Society of British Neurological Surgeons, its agreement that there is a need for synthesis of such activities and the production of national guidelines is welcome, and we strongly support the case for national research.

The report by the task force provides a clear level I recommendation against the use of corticosteroids in acute head injury, one of the few areas in which it thought that the evidence was sufficient for it to make such a firm recommendation. We look forward with interest to the results of the meta-analysis being undertaken by Ian Roberts and colleagues. Clearly, practice may change on the basis of new evidence or a new analysis of available evidence, and we agree that there is a case to be made for both reducing variations in practice and analysing the efficacy of treatments. The purpose of our paper, however, was to highlight the first of these two issues.

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1 Matta BF, Menon DK. Audit of intensive care of acute head injury in the United Kingdom. *Crit Care Med* (in press).

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Assay used in serum screening for Down's syndrome may depend on ethnic make up of population

EDITOR.—The purpose of our report on serum screening for Down's syndrome was to “highlight the need for outcome data on [such screening] to

be collected by ethnic group.”¹ We argued that only when this is done can problems specific to different ethnic groups (such as important differences in the incidence of Down's syndrome pregnancies and in the medians of biochemical markers, etc) be identified and addressed. We are pleased to have achieved this objective, as three laboratories with data on large numbers of ethnic minorities have now reported their results,²⁻⁴ which are interesting.

Clare Ford and colleagues use intact human chorionic gonadotrophin (as we did), and their results are similar to ours,² with a higher false positive rate in Indian Asians, indicating that the median value of intact human chorionic gonadotrophin is higher in that group. P J Holloway and S Bulusu³ and Kevin Spencer's laboratories⁴ use free β human chorionic gonadotrophin, and their results suggest that when this assay is used the false positive rate is lower in South Asian and Indian Asians and higher in Afro-Caribbeans. These reports therefore support our recommendation that “medians for the biochemical markers and risk estimates should be derived from within the population.” It also seems that certain assays may be better in certain populations.

There is much dispute among laboratories over the best assay or combination of assays for screening maternal serum, and Connor, in an editorial on biochemical screening for Down's syndrome, made a plea that commercial considerations should not interfere with the publication of data.⁵ We hope that, despite the pressure of the internal market and competition among laboratories for providing screening services, the laboratories will continue to publish data that will help determine which assay is best for each population.

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Why interferon beta 1b was licensed is a mystery

EDITOR.—Patients with multiple sclerosis are interested in whether they can still go to work, get out of bed to go to the lavatory, or stand on one leg to put the other one through their pants—that is to say, they are interested in disability. Interferon beta 1b has been shown to reduce the rate of relapse in relapsing multiple sclerosis by one third¹ and to diminish the accretion of disease as shown by magnetic resonance imaging.² Unfortunately, neither of these two variables has any convincing or direct relation to disability. I have patients who have several relapses a year, or who seem on magnetic resonance imaging to have no brains left, who lead full and active lives; I have patients who are seriously disabled after one or two relapses; I have patients with severe disability whose scans apparently show trivial disease.