Letters to the editor

‘Input and outcome, numerators and denominators’

SIR–The ideas on outcome and input by Martin Bax1 are thought-provoking and timely. Although many of us would aspire to the ‘gold standard’ of a randomized clinical trial as the best assessment of intervention efficacy for childhood neurodevelopmental disabilities, there are other studies which can be very useful. In particular, the value of a prospective cohort study has been seriously neglected. As Bax correctly points out, the inclusion and exclusion criteria for such a study will determine to a significant degree the outcome i.e. if the ‘input’ is highly selected then the ‘outcome’ may be an accurate reflection of that particular study, but may not be applicable to the whole population or to other populations. To put it another way, the best way to end up with a good result is to start with a good result! The stated indications for interventions as diverse as intramuscular Botulinum toxin A, selective dorsal rhizotomy and orthopaedic surgery are remarkably similar. Children with spasticity alone will typically have a history of diplegia of prematurity, are cognitively unimpaired, have good family support and access to physiotherapy; these are the children who will do best after interventions. However, these factors are not so much predictors of a good result from these interventions but predictors of a favourable natural history. Therefore, I agree entirely with the comments that the input to cohort studies, and in particular inclusion and exclusion criteria, need to be identified and explicitly stated in order to provide a framework for interpreting results.

A cerebral palsy register, to provide the denominator for the study numerator, is perhaps the best solution.

I would disagree with Dr Bax’s comments, however, that the populations of children with neurodevelopmental disabilities are very different around the world. Whilst agreeing that movement disorders such as ataxia are extremely difficult to define and describe, spastic motor disorders are remarkably consistent and very similar in many parts of the world. The rationale of clinical gait analysis is that spastic gait, although very abnormal is remarkably consistent from day to day and probably from one population to another. It is on this basis that classifications have been developed of spastic motor disorders, the best known of which is the classification of spastic hemiplegia by Winters and coworkers2. Despite this classification being based on 46 children drawn from a single population in Newington, USA, we have found that it provides a coherent basis for understanding and classifying spastic hemiplegia in Melbourne, Australia. The situation is very similar with many other gait patterns and musculoskeletal deformities in children who have spastic cerebral palsy. The clinical problems and the patterns are very similar in different populations from around the world. It should therefore be theoretically and practically possible to measure the ‘input’ to a multicentre study by objective means.*

Dr Bax has drawn attention to an enormously important issue which deserves continuing debate and consideration by all who are involved in clinical trial design and interpretation in the area of neurodevelopmental disabilities.

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Reference

* Editor’s note: I had in mind not populations in USA and Australia, which I agree probably are alike, but the children with cerebral palsy in developing countries about whom we know little; their cerebral palsy may have different characteristics to those in the developed world.

Martin Bax

‘Melatonin as a sedation substitute for diagnostic procedures’

SIR–Melatonin induces sleep by inhibiting the wakefulness generating system3 and also has mild sedative properties.4 It has been found effective in treating chronic sleep disorders in both adult and pediatric populations5, and has more recently been tried as an alternative to sedation for diagnostic procedures for adults6.5 However, there are no studies to date which examine the feasibility of using melatonin as a sedation substitute for Auditory Brainstem Response Threshold (ABR) testing, either in adult or pediatric populations.

As we work in programs serving children with sensory losses (Visually Impaired Program and Hearing Loss Resource Team), the ABR test is routinely utilized as part of multidisciplinary team assessments. The sedation most frequently used for ABR testing has been chloral hydrate. Although effective for most children, there have been difficulties with the administration of the medication, failure to induce sleep, and paradoxical reactions. Therefore, this pilot study examined the potential of melatonin as an alternative to chloral hydrate in ABR testing for children with sensory losses.

A convenience sample of six children (two males, four females) was obtained, and data were collected for a prospective case-series. Children with known hypothalamic dysfunction and/or chronic pain were not included in this study. The ages of the children ranged from 3 to 20 months. The boys’ mean age was 14.5 months, and the girls’ mean age was 8.6 months. Four children were referred for testing because of suspected hearing loss, but only one of these children was found to have an actual hearing loss. The other two children had significant vision loss at the legal blindness level or worse. Four children had disabilities in addition to their sensory losses, including epilepsy, dystonia, developmental delay, and arachnoid cyst. A melatonin dosage of 3 mg was given to children whose bodyweight was at or below the 50th centile for a 2-year-old. Children with bodyweight exceeding the 50th centile for a 2-year-old were given 6 mg. The fast-release form of melatonin was used, and was obtained from Twin Lab,
New York. Two children had previously received sedation for different procedures, but with medication other than chloral hydrate. The remaining four children had never previously received sedation of any type.

Success of melatonin treatment for ABR testing was defined using several criteria including: ease of medication administration, time to sleep onset, number and reasons for waking after medication administration, ability to complete full ABR testing, physiological state after test completion, and effects on test results morphology.

In general, the melatonin was easy to administer regardless of the child’s age. Five of the children fell asleep within 30 minutes of ingesting melatonin. Only one child did not fall asleep during the entire testing time. None of the children maintained sleep to the conclusion of testing. There were no consistent reasons found for awakening. For three of these children, other tests provided enough information so as to avoid repeating ABR testing using chloral hydrate. The remaining three children had repeat ABR testing completed at a later date. Follow-up telephone contact indicated that there were no adverse side-effects for any of the children having received melatonin. Upon review of the audiological data, the morphology of the ABR results was not affected by melatonin.

Although melatonin has been successfully tried as a sedation substitute for EEG testing, the ABR test procedure differs from the EEG procedure as sounds are presented via earphones. Melatonin does not mask environmental disruptions of normal sleep. Therefore, sleep is more likely to be disrupted by ABR testing. Further, the sedative properties of melatonin may be too mild to function adequately as a sedation substitute for this diagnostic procedure.

While melatonin continues to show promise in a variety of settings and with many types of populations, we have concluded that it may not be a viable alternative to chloral hydrate for ABR testing because of the difficulty with sleep maintenance.

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References
can be made early and appropriate management instituted.
In our group of 22 children, 12 of the mothers had
pregestational insulin-dependent diabetes mellitus. Of
these children the diagnosis was made in seven in the first
year of life and in five children after that time. We therefore
feel it is important to exclude sacral agenesis in any child
born with urinary or bowel symptoms, lower limb
orthopadic problems, or a neurological deficit to a mother
with pregestational insulin-dependent diabetes mellitus.

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Mac Keith Meetings

Management and Treatment of Autism (Open meeting)
Royal Society of Medicine, London, UK. October 5, 2000
Organized by Dr Gregory O'Brien and Dr Claire Burns.
Speakers (in order of appearance) will include: Professor
Mary Coleman, Dr Peter Sullivan, Dr Tom Berney, Dr
O'Brien, Dr Burns, Dr Jane Shields, and Dr Rita Jordan.
There will be a panel discussion led by Mary Coleman at
the end of the afternoon.

What Obstetricians Can Do to Prevent Disability (Open
meeting)
Royal Society of Medicine, London, UK. October 23, 2000
Organized by Martin Bax. Speakers will include Professor
Lord Winston, Chair of The Little Foundation.

For further information, and to book places at open
meetings, contact Vesna Milenkovic, CME Department, The
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