Clinical assessment of neonatal hyperbilirubinemia

The study by Keren and colleagues is a retrospective study, using infants in whom pre- and post-discharge TSB has been carried out, hence causing an inherent bias towards the same group.

The data for clinical risk have been collected from documents such as admission, intrapartum, and discharge forms. This retrospective collection can result in missing or ambiguous data, as has been accepted by the authors. Ideally, a study should be prospective using both methods on all neonates in a study group and then the sensitivity and specificity (that is, false positives and false negatives) should be compared using actual data on follow up.

The clinical risk factor score includes factors that are interrelated such as vacuum and cephalhaematoma. In cases where the cephalhaematoma is caused by the use of vacuum the neonate gets a double rating. Obviously, authors have not found clinical risk factors more specific than pre-discharge TSB.

Contrary to this study, the AAP guidelines promote and support breast feeding and state that effective breast feeding can reduce substantially the risk for hyperbilirubinemia. It is known that inadequate feeds increase the level of neonatal jaundice; hence the emphasis on “effective” breast feeds. The study subjects date from 1993–97 and the increase the level of neonatal jaundice; hence the same group.

The study by Keren and colleagues found that the cost was $5 743 905 for routine predischarge TSB, $2 495 423 for cephalhaematoma, and $57460 for vacuum extraction. By decreasing the number of patients with “negative” test results, this bias has the effect of over-estimating test sensitivity and underestimating specificity. However, as we point out in our manuscript, we studied infants enrolled in an early discharge follow up programme and minimized the potential for verification bias by restricting our sampling frame to months during which >75% of enrolled infants had post-discharge TSB measurements performed. In fact, for the majority of these months, >90% of enrolled infants had post-discharge TSBs measured.

The second point on which Drs Kanjilal and Prasad are mistaken concerns the inclusion of “interference factors” factors “like vacuum and cephalhaematoma” in our clinical risk factor scoring system. As summarised in table 2, vacuum extraction is included in the scoring system but cephalhaematoma is not. In fact, contrary to our expectation, cephalhaematoma was not associated with development of post-discharge TSB >95th centile. This simply may be a result of poor documentation of cephalhaematoma in the admission and discharge physical examination (misclassification bias), but it raises concerns about the use of subjective factors in clinical risk factor scoring systems. Our results suggest that using more objective findings, such as cephalhaematoma or vacuum extraction during delivery—a common cause of cephalhaematoma—may provide more accurate information about subsequent risk of hyperbilirubinemia.

Finally, our finding that breast feeding increases the risk of hyperbilirubinemia is not new and should not be interpreted as a recommendation against breast feeding. As paediatricians who routinely care for newborn infants, we recognise the benefits of breast feeding and strongly support its use. However, at the same time we are cognizant of the potential risks of dehydration and hyperbilirubinemia posed by inadequate intake in breast fed infants. The results of our study should be interpreted as another reminder that healthcare systems and providers must work to ensure adequate lactation support for breast feeding mothers and early identification and intervention of breast feeding problems that may result in inadequate intake for infants.

As Drs Kanjilal and Prasad suggest, a prospective validation of alternative risk assessment strategies is needed to confirm the results of our study as well as other studies of alternative screening strategies. Additional studies are also needed to evaluate the incremental benefit of using clinical risk factors in addition to the pre-discharge TSB to predict which infants are at risk of developing severe hyperbilirubinemia. And finally, more studies are needed to evaluate the cost effectiveness of alternative strategies for screening and tracking infants for their risk of developing severe hyperbilirubinemia in order to prevent the occurrence of kernicterus, an uncommon but devastating, costly, and entirely preventable condition.

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Biopsychosocial approach to functional abdominal pain

We read with interest the article by Lindley and colleagues outlining their concerns about consumerism in health care focusing on the potential detrimental effects on the child with functional abdominal pain (FAP). All of the children had extensive investigations carried out by the authors according to in-house clinical service guidelines for the management of children with abdominal pain.

While this is surprising in itself, it is even of more concern when it is noted that most children already had extensive investigations in other centres. Clinical service guidelines should take into account the fact that children referred with abdominal pain to a tertiary referral practice have a high probability of having a functional disorder. Rather than embark on an extensive, expensive, and traumatic list of procedures, protocols should encompass a biopsychosocial approach to the management of abdominal pain. We are potentially doing a great disservice to children if we first resort to invasive investigations while failing to make a positive diagnosis of FAP.

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Reference

Is timing of haemorrhage by spectrophotometry similar for haemorrhages in the subdural and subarachnoid space?

We investigated whether quantifying the spectral peaks for oxyhaemoglobin, methaemoglobin, and bilirubin (and their ratios) and comparing them to established standards for timing subarachnoid haemorrhage, might permit timing of the subdural haemorrhage.

If red cells enter the subarachnoid space, they are visible for a few days to several weeks. Lysis of red cells results in oxyhaemoglobin release predominantly between 2 and 12 hours but continues up to 48 hours. A microsomal enzyme haeme oxygenase, released from macrophages (and the arachnoid membrane) converts oxyhaemoglobin to bilirubin. Bilirubin usually appears after 3–4 days but may exceptionally occur as early as 9–10 hours. The “bilirubin transformation capacity” is a rate limiting reaction, and when the concentration of oxyhaemoglobin rises rapidly, additional amounts are oxidised non-enzymatically to methaemoglobin.

Spectrophotometry performed on centrifuged, undiluted samples of subdural aspirates from 14 infants (mean age 4.6 months) admitted with subdural haematoema/effusion of suspected non-accidental origin, were reviewed retrospectively and peaks of oxyhaemoglobin (absorption peak at 413–415 nm), bilirubin (peak at 450–460 nm), and methaemoglobin (absorption peak at 405 nm) identified.

The haemoglobin (Hb) and bilirubin (Bil) spectral amplitudes were converted to micro-moles per litre using a nomogram and the Haemoglobin Index (HBI = Hb (μmol/l)/Bil (μmol/l)) and Haemoglobin Coefficient (HC = arc sine (?HBI/Hb + Bil + 1)) calculated on the 30 spectrophotograms. Absorbance indices (HBI and HC) of oxyhaemoglobin and bilirubin in subdural specimens did not correspond with those reported for subarachnoid haemorrhage and were unrelated to the time from admission. Pigment concentrations were higher than those reported from patients with subarachnoid haemorrhage, confirming similar observations reported by Tichy and Lindquist who suggested that this was due to “packing” of the erythrocytes and their subsequent lysis. Unlike a subarachnoid haemorrhage which disperses within the cerebrospinal fluid space and will dilute and disappear fast, the subdural haemorrhage is in a more encapsulated space without a natural cistern.

We concluded that while spectrophotometry of the subarachnoid space can identify fresh blood, oxyhaemoglobin, bilirubin, or methaemoglobin in the aspirate, and the presence of bilirubin indicates that bleeding has occurred between 24 hours and 3 days prior to admission, it is not possible to time the original haemorrhage by using the spectral peaks data from existing models of subarachnoid haemorrhage.

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Melatonin and epilepsy

There have been conflicting reports of the effects on seizure control of prescribing melatonin for people with epilepsy. We undertook a retrospective before-and-after observational study of 13 young people prescribed melatonin for sleep disturbances at the David Lewis Centre, a residential school for children and young adults with severe epilepsy and learning difficulties situated in Cheshire, UK, with particular focus on any changes in seizure frequency. At the David Lewis Centre each patient has a comprehensive record of their daily seizure profiles (seizure numbers and seizure types over 24 hours) carefully documented by care workers. Daily seizure rates were tabulated for each young person at 3 months, 1 month, 1 week, and 24 hours before and after the start of melatonin administration. Data were analysed using the Wilcoxon signed ranks test.

Eleven children (ages 6–18 years, mean age 14.1) and two adults were included. All had severe learning disabilities and behavioural problems, 12 had autistic spectrum disorders, and 11 suffered from severe epilepsy. All of the young people had severe sleep disturbances. The dose of melatonin ranged from 2–6 mg nocte with a mean dose of 4.8 mg (SD 1.54) (0.1 mg/kg/d, SD 0.05). Eleven of the 13 young people slept better with melatonin. Two discontinued melatonin due to lack of efficacy. For the remainder the mean length of time on melatonin was 2.6 years. One person showed worsening behaviour following melatonin initiation, but no other side effects were observed. Of those with epilepsy three had an increase in seizure severity, seven had a decreased seizure rate, and one patient had no observable difference. The Wilcoxon signed ranks test was applied to the data using a significance level of 0.05. The p value was insignificant (<0.05) for all four time parameters, indicating that in this study melatonin had no effect on seizure frequency. Our experience has been that melatonin can be helpful for sleep disturbance in young people with significant neurological impairment without a demonstrable influence on seizure control.

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Nutritional rickets is increasingly diagnosed in children of ethnic origin

We noted with interest the article published by Ladhani and colleagues highlighting the increase in vitamin D deficiency. We agree that this remains a problem, especially in “at risk” ethnic minority groups. In Oldham, which has a population of 49 992 children, 20.8% are Asian (Census 2001). Between December 2002 and March 2004, we identified nine cases of hypocalcaemia/riboflavin deficiency secondary to vitamin D deficiency. We excluded those with vitamin D deficiency secondary to other conditions or non-nutritional aetiologies. All of the nine children had biochemical changes of raised alkaline phosphatase and levels of 25-OHD below 10 ng/ml; three had radiological evidence of rickets. Eight were of Asian origin and five were male.

Presentation of these children was divided into those with hypocalcaemic symptoms and those with clinical rickets. Six of them presented with hypocalcaemic symptoms and their ages ranged from 6 days to 13 years of age. These included two neonates who presented with focal seizures; two toddlers under 2 years who presented with generalised seizures; and two 13 year olds who presented with cramps/carpopedal spasms. Three of the nine presented with signs of rickets and were aged 15–19 months.

The two neonates involved were born at term with their birth weights on the 25th centile. Calcium levels were 1.39 and 1.54 mmol/l respectively. Both were on formula feeds, and tests on maternal blood revealed levels of parathyroid hormone and calcium suggestive of vitamin D deficiency. Four toddlers were still breast fed, all of whom were confirmed from dietary history to have had limited solid intake. Of the two teenagers, one had a diet low in calcium and the other had background problems of abdominal pain. All the children were treated with vitamin D, and three children also received oral calcium supplements. All responded to treatment with normalisation of biochemical bone profiles and vitamin D/parathyroid hormone levels.

There is no information on the prevalence of rickets in the UK; however, there are reports to say that this is growing. Our

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experience and reports across the UK show that the ethnic minority population still remains at risk of vitamin D deficiency. Efforts to promote vitamin D supplementation as recommended by the Department of Health need to be implemented and targeted at the risk group.

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References

A vaccine scare in 19th century Northampton

The controversy regarding immunisation is longstanding. Records from 1806 concerning a vaccine scare in Northampton give a flavour of how this issue has been a contemporary chord. The revelation of Edward Jenner’s 1798 seminal work meant smallpox mortality fell from 31% in unvaccinated children compared to 1.2% in vaccinated.

A register was however established with the hope: “By these means the practice of vaccination and its merits as a complete security against the smallpox will be gradually brought to the test of unprejudiced experience.”

One could regard this as common sense, which today would be described as “clinical governance”.

Doctors beleaguered in the present time through similar “misrepresentations” regarding immunisations should take heart that this is not a new problem, but perhaps managers could learn from the more robust attitude taken by our medical forebears when dealing with the media in these matters.

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More evidence is needed in the antibiotic treatment of Pseudomonas aeruginosa colonisation

In presenting various therapeutic approaches for the management of cystic fibrosis (CF), Smyth primarily cites evidence obtained from The Cochrane Library as either systematic reviews of randomised controlled trials (RCTs) or RCTs. The antibiotic treatment of Pseudomonas aeruginosa (PA) when first isolated, is still an open question. When discussing this topic, he considers only the RCT by Valerius and colleagues.

In our critical review of published clinical studies evaluating the early antibiotic treatment in asymptomatic PA colonised CF patients, we identified three relevant RCTs (two versus placebo). Our study also included eight cohort studies, two of which were with historical controls. Overall, 309 patients (range 7–91) were recruited. There was a high variability between the individual studies for age, outcome measures, duration of follow up, and treatment (three studies: two RCTs; 1 cohort used only aerosol tobramycin, 1 colistin, 4 aerosol colistin plus ciprofloxacin, 1 intravenous treatment, and 2 miscellaneous therapy).

An overall critical evaluation indicated that early antibiotic treatment can reduce the rate of positive cultures and of anti-PA antibody titres. Long term benefit is expected but not yet proven. Moreover, we recently conducted an observational study which found that nearly all CF centres in Italy treat asymptomatic PA colonised patients in order to prevent or postpone chronic pulmonary infection (unpublished data). However, the adopted prescribing practice varies largely even within the same centre, highlighting the existing lack of formal consensus on this subject.

Several therapeutic options (aerosol therapy alone or oral therapy associated with aerosol inhalation) are available for the early treatment of PA colonisation, but no direct comparison has so far been made. Prospective multicentre randomised studies with relevant outcomes measures are needed to investigate which of the different proposed antibiotic schemes has the best benefit/risk ratio and the best patient compliance.

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Community needlestick injuries may still be dangerous

We read with interest the report by Makwana and Riordan on community needlestick injuries in children.1 We do not believe, however, that the authors have presented sufficient data to support their conclusion that routine follow up after community needlestick injury is unnecessary.

In their study only 25 children had complete serological follow up. Their literature review cites three additional papers in which children were followed up after needlestick injury. Adding all of these children gives a total of 138 children who had...
serological testing following needlestick injury. This is an insufficient number to allow one to conclude with confidence that the risk of transmission is low.

Indeed, all these needles contained HIV positive blood, applying the rule of threes to the pooled data, we can say with 95% confidence that the risk of HIV transmission following needlestick injury in children is less than 2%. The transmission rate in healthcare workers following HIV positive needlestick injury is around 0.35%. Their study, therefore, does not provide sufficient evidence to state that these children are at a lower risk of acquiring HIV following needlestick injury than healthcare workers in similar circumstances. Until such evidence becomes available, there seems to be no good reason to treat these children differently to healthcare workers following needlestick injury.

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Authors’ reply
We were interested to read this letter. The authors feel that children with community needlestick injuries should be treated the same as healthcare workers. This seems to miss the point of our paper. Hospital needlestick injuries are very different to out-of-hospital needlestick injuries: the blood is generally dry, so therefore less likely to be infectious; the injuries are often superficial—again less likely to be infectious; and, although the HIV status of the needlestick user is often unknown, the incidence outside of London is very low.

The risk of HIV transmission is estimated to be less than 0.01%.

We therefore read with interest the data presented by Booy et al of responses to primary series immunisation in Asian infants born in the UK to a population of parents of whom “most” were born abroad.

While Booy et al comment on their study as descriptive, we feel, to offer follow up to those patients who have high risk injuries or in whom parents have a high level of anxiety.

Interpreting immunogenicity data in UK studies
It has become increasingly clear that interaction between seroconversion rate in discarded syringes of intravenous drug users.

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Car seat safety for premature and LBW infants
Recent advances in neonatal intensive care have resulted in improved survival rates of premature and low birth weight infants. These infants are frequently transported in the mother’s own vehicle when discharged from hospital. Commercially available infant car seats are primarily designed for a typical
We carried out an anonymous questionnaire survey to examine prescribing practices of members of the British Association for Community Child Health (BACCH) and the British Academy of Childhood Disability (BACD) (see ADC website: http://www.archdischild.com supplemental).

From a newsletter circulation reaching an estimated 926 paediatricians, responses to the questionnaire were received from 148 (about 15%) (table 1).

Of these 98% were currently prescribing, or had prescribed melatonin in the last year; data on a total of 1918 children were obtained.

The dose prescribed (0.5–24 mg) varied widely (table 2).

Autism (68%) and attention deficit hyperactivity disorder (44%) were the most frequent clinical diagnoses in the children prescribed melatonin. On a crude four point scale of perceived effectiveness (never, rarely, usually, always), over 95% of respondents found melatonin "usually" or "always" effective. Adverse events were reported by 18% (n = 27) of respondents including: new onset seizure activity (n = 2), increased seizure frequency (n = 3), hyperactivity (n = 5), agitation/behavioural changes (n = 6), worsening sleep pattern (n = 6), nightmares (n = 2), and constipation (n = 2).

As this survey was opportunistic, and unfunded, we did not have the opportunity...
to further interrogate the non-responders and determine to what extent they systematically differed from the responders. Information on frequency of prescribing is also missing on a national level, as exact numbers of melatonin prescriptions are not recorded, but since November 2002, 239 UK hospitals/trust pharmacies have requested melatonin (personal communication, Peter Stephens, IMSHealth, 2004).

Reports of adverse events from our study mirror those in the literature. Although 27 respondents in this limited survey reported adverse events, only 13 reports, involving 25 adverse events, were notified to the UK Medicines and Healthcare products Regulatory Agency (MHRA) (Committee for Safety of Medicines, Drug Analysis Print: Melatonin; personal communication, 2004) and two notified to the UK Food Standards Agency in the same period (personal communication, Cath Mulholland, 2004). Whether these “adverse events” represent a significant rise above events that would be seen by chance in this population will need further studies over a longer period.

It remains crucial to establish just how effective melatonin is for children with developmental disorders, through large scale, multicentre randomised controlled trials. This survey suggests that problems agreeing appropriate and safe dose ranges, the heterogeneity of underlying developmental problems, and a potentially wide range of underlying sleep disorders are just a few of the hurdles that will need to be overcome.

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The questionnaire can be viewed on the ADC website (http://www.archdischild.com/supplemental)

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unique to this book and provide a good revision of the basics for the generalist.

The next section forms the core of the book. It is divided into organ systems, but the approach is problem based. The book does not provide exhaustive information, but acts as a guide.

For example, in the section ‘approach to child with headache’ the authors do not provide an exhaustive list of causes of headache and their treatment. They give only pointers. There are boxes highlighted with a red flag, which make sure that a generalist does not miss the salient points in history and examination.

Other than the core medical problems, the book also contains sections on adolescence care, mental health care, and social aspects of childcare. These sections are quite exhaustive. These chapters have been handled with a very practical approach.

Other important features of the book are that it is very colourful. All the sections are colour coded for easy access. The book is well illustrated. In particular, the chapter on skin conditions contain many photographs, which are very informative.

The book also comes with a CD-Rom. The CD is not the textbook in a digital format. The CD contains videos of clinical conditions, medical procedures, colour atlases of dermatological conditions, etc; all the tables and pictures on the CD are provided in a PowerPoint format that can be downloaded for educational use.

All in all, a very useful book to have as a part of the generalist’s library.

M S H Madhava

Abnormalities in puberty: scientific and clinical advances

Edited by H A Dellemarre-van de Waal. Karger, 2005; €117.00 (hardback), pp 182. ISBN 3 8055 7867 9

This book is described in the foreword as being of interest to paediatric and adult endocrinologists as well as workers involved with puberty. It is one of a series of books on endocrine development and has a strongly European dominated authorship.

The book is set out in 11 chapters which read like scientific papers, have useful explanatory abstracts, and are extensively refereenced. A broad range of topics pertaining to puberty are covered, including the potential effects of fetal nutritional status on the timing of puberty, and adolescent topics such as polycystic ovarian syndrome and fertility preservation in cancer sufferers. The chapters are stand-alone articles and the reader is likely to pick and choose specific areas of interest rather than reading from cover to cover.

The chapters themselves vary from discussion of theoretical ideas about mechanisms of pubertal abnormalities to evidence based summaries of management of conditions, and presentation of trial data. The subject matter is generally well explained, even for the non-endocrinologist, but is quite scientific and specialised and the main appeal will be for those working within the field. Although background information is given as a reminder of pathophysiology, with enough space to set the scene for the new information presented, this is not an easy read and demands full concentration. Perhaps a summary of the points raised would have helped those with shorter attention spans and a desire for easily processed information. However, some relief from the text is provided in the way of data tables and graphs, and there are informative illustrative diagrams of receptors and hormone pathways, as well as clinical radiological images, such as MRI scan pictures of hypothalamic hamartomas.

Overall this book provides new insights into a variety of current topics in pubertal development and will no doubt assist in stimulating further developments in the field. There are interesting nuggets of information such as developments in the understanding of the genetics of hypogonadotropic hypogonadism and some practical information on the diagnosis and management of precocious puberty; however, those revising for examinations or looking to broaden their knowledge of pubertal problems may wish to consult a more standard textbook first.

A Kelly

Paediatric pulmonary function testing


Paediatricians often encounter patients with respiratory problems so most will have reasonable knowledge about the common and chronic respiratory diseases; virtually every paediatric department will have its collection of peak flow devices, spiroimeters, and other instruments for measuring and recording pulmonary function. Research departments and tertiary respiratory centres will have specialised lung function laboratories where more sophisticated tests may provide pages of numerical data to help the clinician best treat the child. But what is the place of pulmonary function testing in the broader clinical context and what does it all mean? This book has been written to provide a comprehensive survey of pulmonary function testing and to review the latest developments in the field.

The pleasingly slim tome is one of a series of books entitled “progress in respiratory research” and is a multi-author book written by experts in the individual areas that form many of the chapters. Despite the brevity, the style is consistent and the content up to date.

As one might expect with a comprehensive review, the book divides logically into lung function testing in infants and toddlers unable to cooperate with most procedures and is followed by analysis of the traditional adult founded techniques as applied to children. Technical and procedural considerations are
Looking after children in primary care: a companion to the Children’s National Service Framework


The recently published leading article on the National Service Framework (NSF) in Archives of Disease in Childhood by our ex-president of this college has also been discussed. All chapters are kicked off with a pithy abstract that lets the reader know what they are in for, which was useful, although the substance of some of the technical sections proved hard going.

While there is no doubting the quality of the book I do wonder whether it will satisfy the potentially diverse needs of the pulmonologists, technicians, and general paediatricians the book claims it is written for. I suspect general paediatricians may find the last half of the book much more useful than the first, while technicians and researchers may find the converse. I would therefore recommend the book to research departments and specialist units more than to the general readership. For those considering buying the book, the price tag of £80.00 is likely to induce some sharp inspiratory manoeuvres in the purchaser.

A Brooke

Looking after Children in Primary Care

Organisation of health care with good examples and principles; setting out an audit checklist for GPs for creating a child and young person friendly environment; providing a box of core curricula for training people who work with parents; and displaying universally available preliminary support to be available to all parents. But the highlight of the book was chapter 18 (listening to young people’s perspectives in relation to adolescent health). It covers smoking, obesity, drinking alcohol, illicit drug use, and sexual health. I liked the poem “Don’t go losing your virginity!”. Overall this book is easy to read and doesn’t falter in its purpose. It is well written by highly experienced authors. The tables and boxes highlight the key features in each chapter. The references are broad and up to date. The immunisation schedule keeps on changing, therefore the readers should update themselves. It is a pity that there is no chapter on resource implications. This book should be beneficial not only to primary healthcare professionals but also to those in secondary and tertiary care. I would recommend that women’s and children’s departments, managers involved with care of children, parents, and carers, and each library should have a copy.

G Sinha

Reference


Book review in Fetal and Neonatal edition

The following book review is published in this month’s Fetal and Neonatal edition:


Pre-published book reviews

Book reviews that have been accepted for publication but have not yet been published in the print journal can be viewed online at http://adc.bmj.com/misc/bookreviews.shtml

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