PostScript

LETTERS

Adverse effects of methylprednisolone pulse therapy in refractory Kawasaki disease

The efficacy and safety, including arrhythmia and sudden death,^{1,2} of intravenous methylprednisolone pulse (IVMP) therapy in patients with Kawasaki disease (KD) are uncertain.

We conducted a control study in KD patients with persistent or recurrent fever ($\geq 37.5^{\circ}\text{C}$) 48 hours after a single infusion of initial intravenous immunoglobulin (IVIG) 2 g/kg. At enrolment (day 1), the subjects were randomised to receive IVMP (30 mg/kg/day of methylprednisolone for three days), or additional IVIG (2 g/kg). Heparin was also continuously infused (15–20 units/kg/h) in the IVMP group. The study was halted prematurely because of adverse effects of IVMP when 22 patients were recruited; they accounted for 13% of KD patients treated with initial IVIG.

The antipyretic effect of IVMP was superior to that of additional IVIG on day 2 ($p = 0.02$, repeated measures analysis), but not on day 3 and later (fig 1). The fraction of febrile patients was significantly lower in the IVMP

Table 1 Adverse effects

	IVMP (n = 11)	Additional IVIG (n = 11)	p value
Heart rate (/min)	68 (63, 76)	98 (76, 110)	0.01
Sinus bradycardia (%)	82	18	0.01
Body temperature ($^{\circ}\text{C}$)	35.4 (0.4)	36.1 (0.5)	0.002
Hypothermia $<35.0^{\circ}\text{C}$ (%)	9	0	1.00
Systolic blood pressure (mm Hg)	119 (8)	113 (12)	0.24
Hypertension (%)	91	55	0.15
Blood glucose (mmol/l)	7.0 (1.4)	5.4 (0.6)	0.007
Hyperglycaemia ≥ 7.0 mmol/l (%)	55	0	0.01
Shortening of activated partial thromboplastin time (%)	27	18	1.00
Embolism (%)	0	0	
Stool blood (%)	0	0	

We analysed continuous variables with the normal distribution, expressed as mean (SD), by the unpaired *t* test, and those with any non-normal distribution, expressed as median (first quartile, third quartile), by the Wilcoxon rank sum test. For nominal variables, we used the Fisher exact test. All statistical tests were two tailed. Heart rate and body temperature are minimum values and systolic blood pressure is the maximum value within 72 hours after the start of IVMP or additional IVIG. Bradycardia is defined as heart rate <2 percentile of the normal standard (*Pediatr Cardiol* 1979;1:123–52) and hypertension as systolic blood pressure >95 percentile of the normal standard (*Pediatrics* 1996;98:649–58). Blood glucose level is the maximum value obtained on days 2, 4, and 7 after treatment with IVMP or additional IVIG. Shortening of activated partial thromboplastin time is defined as the minimum value on days 2, 4, and 7 $<80\%$ of the value on day 1.

group until day 3 (1/11 v 8/11, $p < 0.001$, Fisher exact test), but not on day 4 and later (6/11 v 6/11). Coronary artery dimensions

and the prevalence of coronary artery lesions (2/11 v 3/11) were similar in the two groups. Regarding adverse effects, sinus bradycardia and hyperglycaemia occurred more often in the IVMP group (table 1). Hypertension occurred in 91% of the IVMP group, but the fraction did not differ significantly, probably due to the small sample size. All of the adverse effects were transient. There were no convulsions, gastrointestinal symptoms, infection, malignant arrhythmia, or sudden death in any subjects.

KD patients refractory to initial IVIG should be treated with additional IVIG,^{3,4} because IVMP induced faster but temporary resolution of fever and more adverse effects. Further investigations with steroid therapy are necessary to determine the indication and the appropriate dose in KD.

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Figure 1 Changes in the maximum body temperature attained each day after treatment with IVMP or additional IVIG. The starting day of IVMP or additional IVIG was defined as day 1. Body temperature dropped more rapidly in the IVMP group than in the additional IVIG group ($p = 0.006$, repeated measures analysis); the antipyretic effect of IVMP was superior to that of additional IVIG on day 2 ($p = 0.02$, repeated measures analysis), but not on day 3 and later. The upper and lower ends of a box show the first and third quartiles, and the line inside the box the median value. The upper fence of a whisker represents the largest value within 1.5 times the interquartile range above the third quartile and the lower fence of a whisker the smallest value within 1.5 times the interquartile below the first quartile. Values beyond the fences are marked with circles.

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Blood pressure measurement in a district general paediatric A&E department

Blood pressure is a simple physiological measure routinely estimated in many paediatric clinical environments. The recommended frequency and requirement for this measure in children is debatable, particularly in casualty departments. However the rising burden to healthcare systems from hypertension should perhaps be used to review current practice.¹

One thousand and six consecutive patient records from a district general hospital in west London from May to August 2004 were audited retrospectively. Blood pressure was measured in 9% of those 16 years or younger. By contrast aural temperature and manually estimated pulse rates were recorded in 91% of the group. Age was the largest single determinant for measurement ($p < 0.001$); triage priority, arrival time, and presenting complaint had lower impacts. Only 32% of children with a high priority triage had a measure of blood pressure. Appropriate follow up of abnormal results was patchy; 14% of raised blood pressures documented in casualty received no follow up or repeat measure. Interviews with staff indicated that there was no perceived need to check blood pressure unless specific medical directions were received. Equipment and appropriate age related normal charts were readily available and did not limit the service.

Although no evidence supports population based blood pressure screening in children, studies have suggested advantages to the measurement of blood pressure in the hospital setting.^{2–4} This strategy identifies hypertension early, particularly in teenagers, who are infrequent attendees in general practice.⁵ In urban British populations a hospital casualty is frequently their sole point of contact with health services (local audit results).

Following the audit period in this centre two cases of essential hypertension were subsequently identified in children aged 14 and 16 years. Neither had blood pressure measured on earlier visits to casualty. As documented recently the global burden of hypertension is likely to increase.⁶ While A&E departments are not designed to carry out primary prevention, the valuable opportunity to prevent disease and improve outcomes with a simple measurement should not be overlooked.

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Intima-media thickness in obesity: relation to hypertension and dyslipidaemia

Obesity in childhood contributes to cardiovascular risk factors, such as hypertension and dyslipidaemia.¹ Exposure to these cardiovascular risk factors may induce atherogenic changes in the arteries.¹ Measurement of the intima-media thickness (IMT) of the common carotid artery (CCA) is an acknowledged non-invasive marker for early atherosclerotic changes and is a feasible, reliable, valid, and cost effective method.^{2,3} It has not yet been studied whether hypertension and dyslipidaemia are related to IMT in obese children. Therefore, we measured clinical data (age, gender, degree of overweight as standard deviation score of BMI (SDS-BMI⁴), IMT, serum lipids (triglycerides and HDL, LDL, and total cholesterol), systolic (SP) and diastolic blood pressure (DP) in 46 obese children (median age 9.6 years). The control group was comprised of 16 lean age and gender matched children. IMT was measured at CCA near the bifurcation at the far wall by B-mode ultrasound using a 14 Mhz linear transducer and compared between obese and lean children by Mann-Whitney U test, since IMT was not normally distributed. IMT as dependent variable and age, gender, SDS-BMI, blood pressure, and serum lipids as independent variables were determined in a multiple linear regression analysis. Blood pressure and lipids were compared between obese children with IMT above the upper quartile of IMT and children with IMT below or equal to the upper quartile of IMT by Student's *t* test for unpaired observations. Obese children showed a significant ($p < 0.001$) thicker intima media (median 0.06 cm) compared to the control group (median IMT 0.04 cm). In multiple linear regression analysis, IMT correlated significantly to triglycerides ($p = 0.023$) and systolic and diastolic blood pressure ($p < 0.001$). The children with IMT above the upper quartile (0.06 cm) showed significantly increased triglycerides ($p = 0.038$, median 142 mg/dl versus 103 mg/dl) and blood pressure ($p < 0.001$, median SP 137 mm Hg versus 119 mm Hg, median DP 71 mm Hg versus 60 mm Hg), while they did not differ significantly from the other children in respect of gender, age, SDS-BMI, and HDL, LDL, or total cholesterol.

Since IMT is increased in obese children, vascular changes in obesity seem to occur already in childhood. Childhood obesity may

be a risk factor for developing atherosclerosis, since higher IMT of the CCA is reported to be predictive and is related to the severity and extent of coronary artery disease and strokes.^{5,6} Our findings suggest that hypertension and hypertriglyceridaemia, which are part of the metabolic syndrome, have the highest atherogenic potential in childhood obesity.

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How to improve patients' understanding in biomedical research?

We read with interest the recent paper from Barnett and colleagues,¹ reporting the impact of different styles of informed consent forms proposed to children; it is one of the few papers on this important topic. Indeed, the content of informed consent documents (ICD) is a crucial element in the process of providing information to participants in biomedical research. Clear comprehension of this information—that is, the ability to understand its meaning and its consequences, is of great importance. However, investigators sometimes have the feeling that volunteers do not fully understand the major concepts of the study in which they are enrolled, and this issue is specifically relevant to children. This feeling has been confirmed by several studies in adults. A study conducted in two public hospitals² showed that 40.7% and 74.5% of patients respectively did not understand the content of the ICD for clinical studies in which they were enrolled. In a third study, 156 veterans were

interviewed to determine their degree of understanding of a clinical protocol for which they had signed a consent form.³ Less than 10 weeks after signing, only 10% could totally describe the objective of the study. More recently, Joffe *et al* validated a questionnaire to determine the quality of informed consent in phases 1, 2, and 3 of cancer clinical trials.⁴ The main result was that many patients did not recognise non-standard treatment (74%), the potential for incremental risk (63%), or the uncertainty of benefit to themselves (29%).

We carried out an initial study, QuIP-1⁵ in which we compared the lexico-syntactic readability of informed consent documents, from the Rhône-Alpes region (France) with reference texts corresponding to five school levels, using the Flesch and Cordial readability scores. We showed that lexico-syntactic readability of French informed consent documents was worse than the readability score of the most difficult reference texts (university level). In a subsequent study, QuIP-3, we further showed that review by French Ethic committees did not improve the lexico-syntactic readability of an ICD,⁶ while increasing its length.

In the present study, Barnett *et al* suggest that a story format was clearly superior in maximising children's understanding. Such data are important in our practice of biomedical research, as they should trigger investigators to promote such types of leaflets. However, several questions remain unanswered. Firstly, the questionnaire used probably only reflects part of the whole comprehension. The development of a questionnaire is usually a long term process that involves item generation, review, and selection. Its validation needs a survey carried out on a small group of subjects, and implies an analysis of the content and construct validity. Although a lighter process may be used for the present study, it would be interesting to know how these items were selected and whether a survey was performed prior to the general study. Secondly, this directive questionnaire prompts answers, whereas free recall would provide data on the amount and the type of information spontaneously understood, which could differ from that prompted.⁷ However, free recall itself is debated as most studies use the percentage of discrete bits of information memorised, which is a poor indicator of comprehension. A more accurate analysis needs the use of specific language analyser software that requires specific knowledge to be used. Thirdly, another potential pitfall is the place where the study took place. It is tempting to conclude that children's answers would be the same at hospital or at the doctor's office, but this is probably wrong, as in different locations, their attention would differ. It would add much to our knowledge to determine whether such a story format increases children's comprehension in a real situation.

In conclusion, the work of Barnett *et al* further suggests that we may, and should, improve adults' and children's comprehension in biomedical research. As patients become more and more associated in the process of clinical research, this is an important area of improvement for the future.

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True status of supplement not made clear to reader

As current or previous members of the ADC editorial board, we wish to register our disquiet about your recent supplement on ADHD.

Firstly, we are concerned at the principle of publishing something of this kind at all. One of ADC's great strengths has been the fact that it has not, until now, rented out editorial space to those prepared to pay. Such commercially funded supplements, even if peer reviewed, will always tend to emphasise aspects that favour the funding company. This supplement illustrates this, with two of the seven articles mentioning the same Eli Lilly drug in their titles, with no other drugs mentioned at all. We feel that this sort of covert advertising is not in keeping with ADC's reputation for academic rigour.

Secondly, we are concerned that a casual reader might not have realised that this publication was commercially motivated. The sponsorship was not mentioned on the cover and then was mentioned only elliptically by referring to an "educational grant" from Eli Lilly. Most importantly, there was no explicit acknowledgment that the drug featured prominently in the supplement was produced by the sponsors of the supplement; we had to go on the web to establish the connection. We have additional concerns that none of the authors of the articles declared either the presence or absence of a conflict of interest, in contrast to articles appearing in the main journal, when it seems likely that at least some of them have received grant funding or sponsorship from Eli Lilly; indeed one is a Lilly employee.

We hope very much that this supplement is not part of a new trend to prioritise advertising income over ethics and represents instead merely a slip-up in ADC's usual editorial rigour. Either way, we suggest that ADC publish a clarification about the status of the supplement to alert the unwary reader.

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BOOK REVIEWS

Recent advances in paediatrics, 22nd edition

Edited by Timothy J David. London: The Royal Society of Medicine Press Limited, 2004, £35.00, pp 242. ISBN 1 85315 597 7

Like many paediatricians, I first became familiar with the Recent Advances series when I was a trainee and have been reading it faithfully ever since. I was therefore delighted to be invited to review the latest edition. There is something of interest in this book to any practising paediatrician, from a generalist in a rural hospital in India to a specialist in a tertiary paediatric hospital in the western world. Having said that, this book is probably most relevant to a paediatrician, like me, working in a bog standard general hospital, who looks after children from birth to adulthood in hospital and community settings. One can see that the topics are chosen with care, to be relevant to as wide an audience as possible. The editor acknowledges the fact that there is a bias towards more community paediatric topics in this particular edition, because this area is generally not very well covered in textbooks and journals dealing with general paediatrics. I welcome this trend, as most paediatric trainees have less than adequate exposure to care of children in the community, and any attempt to address this gap in knowledge is very welcome.

The book opens with chapters on abusive head trauma and sudden unexpected death in infancy. This will grab the attention of any paediatrician straight away, as child protection has been a high profile and controversial area recently. Any authoritative and evidence based review of this difficult and controversial area of paediatric practice will help day to day clinical practice.

Chapters on neonatal thrombocytopenia, neonatal abstinence syndrome, and jaundice in preterm infants provide an up to date review of these common neonatal clinical problems. The chapter on congenital brachial palsy provides very detailed information about this rare but potentially disabling condition and is clearly written by experts in the field who have done original work.

As a general paediatrician with an interest in paediatric rheumatology, I found the chapter on DXA scanning particularly interesting. It highlights the importance of knowing the limitations as well as the advantages of any new investigation. There is a similar review of the use of MRI scanning of the preterm brain to help with predicting developmental prognosis of premature babies who have gone through neonatal intensive care.

There is also an interesting chapter on trachoma, which is the second most important cause of blindness worldwide. This is a reminder that, in low income countries, there

are a lot of children who are still suffering from disability secondary to eminently preventable communicable diseases.

At the end of the book there is an excellent literature review. It provides the most succinct review of interesting articles published during the year in question.

In the era of continuing professional development, personal learning plans, appraisals, learning objectives, and revalidation, it has become vital to show that every doctor is keeping up to date with the developments in their chosen field of medical practice. A lot of paediatricians depend on the recent advances series to achieve this.

It is a well produced book with high quality printing in a very readable layout. It is difficult to suggest how this book can be improved, but more illustrations and introduction of colour could be one way of making this already good book into an excellent one.

Even though reviews from experts come low down in the hierarchy of evidence based medicine, this book always provides well referenced and up to date practical information, which will save a lot of hours for a busy clinician. I would recommend this book to any paediatrician who wants to keep themselves up to date. It is excellent value for money and should be an essential addition to every departmental and hospital library.

V Reddy

Adolescents and sex: the handbook for professionals working with young people

Edited by Sarah Bekaert. Oxford: Radcliffe Publishing Limited, 2005, £21.95, pp 200. ISBN 1 85775 880 3

This book has been written primarily for health professionals as a guide to setting up young people's clinics, but it actually provides more than that. Anyone who comes into contact with young people within their work will find this easy to read book full of

helpful practical suggestions about how to make any service "young person friendly". Each chapter is well referenced and there is an extensive web based list of resources making this book an excellent teaching aid.

The initial chapter provides a summary of some of the issues surrounding adolescence and the physiological and psychological changes which occur during this time. This leads on to a chapter on how to engage young people, and covers some very useful tips on the initial groundwork required and the consultation needed before setting up a service for young people. The importance of confidentiality is highlighted and continues as a main

theme as one would expect throughout the book. The legal issues involved in working with this age group has a dedicated chapter and covers the aspect of consent within the current legal and child protection framework, and is particularly helpful.

Teenage pregnancy is discussed in the context of the government's teenage pregnancy strategy, and the long term social implications of teenage pregnancy are described. The key role of the health professional in providing sexual health information, education, and easy access to services is highlighted, with some examples of good current practice from different areas of the country. The style of writing in the chapter on young people and contraception appears out of keeping with the rest of the book as it is written in a very basic way, assuming little underlying knowledge. This information could however be used directly with the young people as a teaching resource, and it helpfully looks at some of the common myths surrounding contraception.

There has been a huge increase in the rates of sexually transmitted infections, particularly among young people, and within the book there is a chapter looking at the reasons behind this as well as some ways in which this can be addressed when planning sexual health services. There follows a description of the different sexually transmitted diseases, including symptoms and treatment; it is written in a way that again could be used directly with young people.

A particularly helpful chapter is the one covering marginalised groups, and there is an excellent section on working with lesbian, gay, bisexual, and transgender young people. Towards the end of the book there is a definitive guide to setting up a young persons' clinic, giving a step by step approach to establishing a service. Finally, there is chapter on planning sexual health outreach work and an example of a lesson plan which would be particularly helpful for anyone involved in delivering "sex and relationships education".

The sexual health of young people is unlikely to improve until we can feel confident in talking openly with adolescents about their sexual health and contraception needs and have easily accessible services. This book provides an excellent practical guide to this end.

C Grayson

Pediatric nephrology, 4th edition

Edited by R N Srivastava, A Bagga. New Delhi: Jaypee Brothers Medical Publishers, 2005, pp 466. ISBN 81 8061 457 3

Clinical management of children with acute and chronic renal disorders can be complicated, even for the experienced clinician. The practice of paediatric nephrology can commence from fetal presentation to the management and transition of adolescents and

young adults. More patients with complex multi-systemic diseases have shared care management between general paediatric departments, paediatric nephrology, and other subspecialty disciplines. There is a paucity of evidence based practice in paediatric nephrology, with recommendations based on extrapolation of adult data in patients with very different primary diseases. However, to relieve the anxiety of many clinicians, the fourth edition of *Pediatric nephrology* has arrived!

This concise text provides essential information on common nephro-urological disorders, which is both practical and comprehensive. For those who have not had access to the first three editions, this textbook has now been fully revised and updated for the 21st century. The emphasis remains on the diagnostic approach (with clinical, laboratory, and radiological evaluation) and management of children with renal disease. However, there is ample factual information for the clinician on basic anatomy, physiology, embryology, and aetiopathogenesis. The authors understand that busy clinical practice often means that chapters, books, and papers are rarely fully read, so each chapter includes the essential "Key Points" boxes.

The chapters cover the bread-and-butter approach to the clinical diagnoses of acute glomerulonephritis, vasculitis, nephropathies, haematuria/proteinuria, nephrotic syndrome, urinary tract infections, rickets, and hypertension. There is extensive coverage of acute, chronic, and end stage renal failure management with renal replacement therapy, including dialysis and transplantation.

The editorial board has increased the number of authors, with excellent contributions on disorders of micturition (including voiding disorders, nocturnal enuresis, and neurogenic bladders) and imaging of the urinary tract (including a chapter devoted to nuclear medicine scans).

The layout of the book is pleasing to the eye, with excellent anatomical artwork, radiological images, tables, and colour clinical, urinary microscopy, and histopathological photograph plates. Each chapter has a small, but excellent list of suggested references for further reading. There are excellent appendices providing further information, such as drug dosages and adjustments to dose and/or intervals in renal failure.

The textbook highlights specific implications for those practising in India, which I found fascinating comparing my own clinical practice in the UK. This textbook should be readily accessed from the shelves in the offices and libraries of general practitioners, paediatricians, nephrologists, urologists, intensivists, trainees, clinical nurse specialists, and any clinicians who manage children with nephro-urological disorders.

S D Marks

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.bmjournals.com/misc/bookreviews.shtml>