Use of cyclosporin A as a steroid sparing agent in cystic fibrosis

Editor,—In cystic fibrosis (CF) chronic respiratory infection is countered by an intense inflammatory reaction. Systemic steroids been shown to improve lung function and reduce morbidity in patients with CF and reduce markers of chronic inflammation; however, there are significant side effects associated with their long term use. Low dose cyclosporin A (CyA) has been shown to be effective in the treatment of inflammatory and autoimmune diseases, corticosteroid dependent chronic severe asthma in adults, and refractory childhood asthma.1

We report six paediatric CF patients where CyA had been used as a steroid sparing agent. These patients were on treatment with high dose inhaled or nebulised steroids prior to the commencement of oral steroids, and repeated attempts at reducing the steroid dose were unsuccessful. All patients exhibited steroid related complications including Cushionoid features, growth suppression, impaired glucose tolerance, hypertension, osteoporosis, and bone fractures. The dosage of CyA was adjusted to maintain whole blood trough levels between 100 and 150 ng/ml, using CyA doses ranging from 2 to 37 mg/kg/day.

In the four patients who benefited from CyA therapy the mean steroid dose decreased from 0.86 mg/kg/day in the one month prior to commencement of CyA to 0.30 mg/kg/day six months later and 0.25 mg/kg/day 12 months later. These patients were able to discontinue oral steroids within 18 months of commencement of CyA. Two patients did not show a reduction in mean steroid dosage, one of which underwent a successful heart–lung transplantation.

In the four patients who responded to CyA, lung function was maintained or improved, as were Chripin–Norman chest x ray scores. Height velocity was also improved. Three patients did develop transient renal impairment, of whom only one required discontinuation of CyA. This dose was related and reversible but is infrequent with lower dose regimens used for anti-inflammatory therapy.2 Other side effects due to CyA were minimal, including mild hypertrichosis and gingival hyperplasia. There was no evidence of hypertension, hepatotoxicity, or neurotoxicity. The side effect profile of CyA is no more severe than for other immunosuppressive agents.

It is evident that CyA is a powerful but potentially toxic therapeutic agent and its use should be balanced against the risks of the disease and the long term use of steroids. These results suggest that CyA can be beneficial as a steroid sparing agent in CF patients; these data may be of help to the clinician in comparable clinical circumstances.

Patricia A Maguire
1 MF BOWLER

Subnormal growth in children with Helicobacter pylori infection

Editor,—We read with interest the study by Choe and colleagues1 in which they investigated the effect of Helicobacter pylori infection and iron deficiency anaemia on growth, especially in pubescent children. In this study, height values were found to be below the 25th centile in 18 of 63 (28.6%) H pylori positive children. The prevalence rate of H pylori infection was 15.9% in children without iron deficiency anaemia and 31.3% in those with iron deficiency anaemia (p = 0.022). They also revealed that the mean height of subjects who had both H pylori infection and iron deficiency anaemia decreased significantly. In this study, they concluded that H pylori infection accompanied by iron deficiency anaemia, 

<table>
<thead>
<tr>
<th>Table 1 Replies to questionnaire (% of all units)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Assessed yearly or more</strong></td>
</tr>
<tr>
<td>---</td>
</tr>
<tr>
<td>Aspergillus precipitins</td>
</tr>
<tr>
<td>Aspergillus specific IgE</td>
</tr>
<tr>
<td>CXR infiltrates</td>
</tr>
<tr>
<td>Blood eosinophilia (&gt;500/mm^3)</td>
</tr>
<tr>
<td>Aspergillus fumigatus skin test</td>
</tr>
<tr>
<td>Total serum IgE (&gt;1000 ng/ml)</td>
</tr>
<tr>
<td>Bronchiectasis</td>
</tr>
<tr>
<td>Wheeze/cough</td>
</tr>
</tbody>
</table>

*Six major criteria investigations.

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rather than *H pylori* infection alone, might delay puberal growth. We investigated the frequency of diminished growth in 30 *H pylori* positive children (21 girls and 9 boys) diagnosed by serology and histology. The mean age was 11.5 (2.0) years (range 8–15). We found 11 (36.7%) *H pylori* positive patients with height values below the 25th centile. Anaemia was determined in none of the patients. Mean haemoglobin concentration was 130 (9) g/l. *H pylori* infection is a chronic persistent infection, leading to diminished growth. Chronic gastric inflammation, dyspepsia, decreased nutritional intake, and malnutrition, leading to diminished growth. We did not detect anaemia in *H pylori* positive patients with diminished growth. We suggest that the development of short stature in *H pylori* positive patients may be due solely to *H pylori* infection itself, and is not related to iron deficiency anaemia.

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Growth monitoring

EDITOR,—Garner and colleagues recently presented a much needed review of growth monitoring.1 It is, whether health workers using growth charts comprehend the weight for age graph. Experience with post-school teachers in these countries would not be able to teach it. Therefore, if the suggested policy was introduced, a toiletting record constitutes a starting point, a toiletting record constitutes a systematic review of trials. *Arch Dis Child* 2000;82:197–201.


Dr Salmon comments:

Children who attend out of home care are at increased risk for infectious diseases of which gastro-intestinal tract infections are among the most common.1 Numbered among these are VTEC *E coli* O157 infections which, as this outbreak showed, can cause severe disease. The challenge is to identify disease in a timely manner.

In this outbreak, given that the first two cases attended the nursery for two days after the onset of their disease on 21 August and the first case from the nursery was not reported until 1 September by which time 13 further symptomatic cases had occurred, our claim that 10–12 cases could have been prevented by taking further action, at this point, is straightforward. The toiletting record might have constituted a prompt to such action. We list a range of possible responses, particularly when the bowel motion is loose or offensive (inquiring about symptoms at home, suggesting a visit to the family doctor, arranging a faecal sample, and informing and seeking the advice of public health agencies). We were aware of the issue of specificity and did not suggest that all these activities should necessarily be carried out on every occasion that more than one child with more than one bowel motion was recorded. Most agree that faecal sampling needs, generally, to be encouraged. However, to combine the activities into a workable algorithm was beyond the scope of the report. Constructing an algorithm is worth attempting, however, as, starting a point, a toiletting record constitutes a straightforward record used in a number of care settings.

R L SALMON
Consultant Epidemiologist


Detecting outbreaks of *E coli* O157 infection in nurseries


1 Holmes SJ, Marrow AL, Pickering LK. Childhood infectious intestinal disease in England: rates in children treated at our hospital for meningococcal disease due to serogroup W135, type 2A, subtype P1.2, P1.5, within a one month period from April 2000. We would like to report four children treated at our hospital for meningococcal infection due to serogroup W135, type 2A, subtype P1.2, P1.5, within a one month period from April 2000. We had been vaccinated recently with meningococcal serogroup C conjugate vaccine, and had all been

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Table 1  Clinical presentation, severity and outcome

<table>
<thead>
<tr>
<th>Case</th>
<th>Contact with travellers</th>
<th>Presentation</th>
<th>Resuscitation fluid*</th>
<th>Mechanical ventilation (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Grandmother</td>
<td>Petechiae, septicemia</td>
<td>80 ml/kg fluid</td>
<td>2</td>
<td>Discharged</td>
</tr>
<tr>
<td>2</td>
<td>Father</td>
<td>Purpura fulminans, septicemia</td>
<td>350 ml/kg fluid adrenaline 2.2 µg/kg/min</td>
<td>11</td>
<td>Peripheral gangrene</td>
</tr>
<tr>
<td>3</td>
<td>6 family members</td>
<td>Meningitis, seizures, no rash</td>
<td>No fluid</td>
<td>0</td>
<td>Neurological sequelae</td>
</tr>
<tr>
<td>4</td>
<td>2 Aunts</td>
<td>Purpura, septicemia</td>
<td>90 ml/kg fluid dopamine 10 µg/kg/min</td>
<td>2</td>
<td>Discharged</td>
</tr>
</tbody>
</table>

*Total resuscitation fluid required in first 24 hours

in contact with travellers returning from Mecca. The clinical features of these cases are outlined in table 1.

The children represent four out of 38 cases (with five fatalities) of serogroup W135 Neisseria meningitidis infection in England and Wales within the six week period from March to May 2000 (PHLS Meningococcal Reference Unit, personal communication), with hundreds of cases of the identical subtype being reported throughout Europe. ¹ Saudi Arabia has reported over 225 cases, with almost 25% mortality to the end of April 2000. It is thought that this large outbreak of an unusual strain originated in Saudi Arabia, with the pilgrimage of a record 1.3 million people to the Hajj between 15–18 March 2000.²

A similar outbreak occurred in 1987, due to serogroup A, subgroup III. This also followed the yearly pilgrimage to Mecca, and spread throughout Europe, USA, and Africa over the next two years.³ Requirements for pilgrims entering Saudi Arabia now include documented vaccination with meningococcal A and C polysaccharide preparation. This public health measure has been effective in irradiating serogroup A disease in these travellers.⁴ A quadrivalent vaccine is available for serogroup W135 as well as serogroups A, C, and Y. This vaccine, however, is not licenced in the UK, and is only available on a named patient basis. This raises public health issues, including whether people returning from Mecca to the UK should be screened or given prophylaxis.

Even with the anticipated beneficial effects of the meningococcal C vaccination programme in England and Wales, it is important to remember that other serogroups of meningococci will continue to cause significant disease in the UK.

Until 1950, England was predominantly affected by epidemics of serogroup A meningococcal disease. The switch to serogroup B and C disease occurred after the second world war, and serogroup A disease is now rarely seen in the UK. Neisseria meningitidis has the potential to alter its capsular polysaccharide antigen through recombinational exchanges at the capsular locus. In his commentary in the Lancet in 1999, Martin Maiden expressed concern that new hypervirulent strains of serogroups including B, W135, and Y may emerge as serogroup C disease is eliminated.⁵ This recent outbreak of serogroup W135 infection does not seem to represent such selection pressure. However, it highlights the need for continued clinical, laboratory, and epidemiological vigilance for meningococcal infection, particularly now that there may be a theoretical risk of other serogroups becoming more prevalent as meningococcal serogroup C disease is controlled.

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References


Prevention and treatment of cow's milk allergy

Editor,—Divergences in existing guidelines on the prevention and treatment of cow's milk allergy (CMA) in infants⁶ seemed settled when a joint statement by the committees of ESPACI/ESPAGAN appeared in *Arch Dis Child* 1999;81:80–4. However, we take exception to some of the assumptions, which have been left open to challenge from both nutritional and allergological points of view. Our concern is that lactose free diets from birth may cause false negative results in most neonatal screening tests for galactosaemia.⁷

The assertion that “...formulas based on intact soy protein isolates are not recommended for the initial treatment of food allergy in infants, although a proportion of infants with cow's milk protein allergy tolerate soy formula⁸” is based on the ESPGAN Committee on nutrition (and on the AAP recommendations).⁹ While the former concerns itself with clinical gastrointestinal manifestations, the latter recommendations state in conclusion (point 8): “Most infants with documented IgE-mediated allergy to cow milk protein will do well on isolated soy protein-based formula⁹.” Initial treatment for allergic disease is avoidance of the incurred allergen. Soy formula has been recommended in treatment of CMA on grounds of efficacy, adequate nutrient intake, and cost.⁴ In the absence of prospective studies comparing the allergenicity of cow's milk hydrolisates against soy formulas in children with CMA, the rationale to alter this indication appears to be lacking.

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Pyridoxine dependent and pyridoxine responsive seizures

Editor,—Seizures in infancy and early childhood responsive to pyridoxine are well recognised but rare. Baxter has recently observed that almost a third of neonatal cases of pyridoxine dependency present with apparent birth asphyxia and/or suspected hypoxic ischaemic encephalopathy, and recommended that, because of the high proportion of atypical cases, all children with early onset (younger than 3 years old) intractable seizures or status should receive a trial of pyridoxine whatever the suspected cause.¹ Following this recommendation can be of remarkable benefit.

We report a case of a caucasian boy, born at term, who presents at delivery in a state of unexpected collapse requiring intubation and resuscitation. He developed tonic seizures within hours of birth and was treated with phenobarbitone, phenytoin, and clonazepam. At 48 hours, an EEG showed a burst

"www.archdischild.com"
suppression pattern. There was biochemical evidence of multi-organ damage. He was extubated on day 5 and discharged on day 16 on phenobarbitone. He continued to have frequent myoclonic seizures. At 6 months, phenobarbitone was replaced by sodium valproate with some initial benefit. By 7 months, he was having focal motor seizures affecting his right arm up to 40 times a day and additional atypical absences and tonic seizures. He also showed signs of an emerging spastic quadraparesis. EEG showed right sided spike and wave discharge with a frontal emphasis. At 8 months a trial of oral pyridoxine (30 mg/kg/day) was given. No seizures have been observed since pyridoxine was started. He is now 16 months old. He is maintained on pyridoxine 15 mg/kg/day; valproate has been discontinued. The EEG no longer shows spike and wave activity. The signs of spastic quadraparesis remain.

We have reviewed the notes of children attending The David Lewis Centre, a residential school for children with severe epilepsy. Children at The David Lewis Centre are recruited from all over the UK and their early epilepsy management has been undertaken at many different centres. 31 children with intractable cryptogenic epilepsies, which started before they were 3 years old, were identified (dates of birth 1979–1998). Only one of these children was recorded as having received a trial of pyridoxine early in the evolution of their epilepsies. The true prevalence of pyridoxine responsive epilepsy is difficult to assess if the recommendations of Baxter are seldom followed. Giving pyridoxine can be diagnostic and therapeutic—not giving a trial of pyridoxine is common and can leave a treatable cause of difficult epilepsy unrecognised and inadequately treated.

Are sleep studies worth doing?

Editor,—If sleep studies are worth doing, they are worth doing well. The study of sleep may be an emerging paediatric subspeciality that the UK has stumbled to enter and pyridoxine responsive seizures in the UK.

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Data presented do not justifi

Editor,—In a recent article, Cavaddini and colleagues told us that during the past thirty years the youth of today are decadent and unhealthy. The old fashioned disciplinarian mother is probably desirable. However, the current practice of using empty drink bottles is common in some countries (either by necessity or choice), but we are highly concerned about the support to the hypothesis, given by implication in this paper, that coffee cup or drink bottle spacers are as effective as properly designed add on devices.

Spacers and holding chambers: Not the last word, we hope

Editor,—Zai and colleagues compared homemade spacers with two commercially available valved holding chambers (VHCs) for the treatment of children with acute asthma.1 As the manufacturer of one of the VHCs that was evaluated, acknowledge that the practice of using empty drink bottles is common in some countries (either by necessity or choice), but we are highly concerned about the support to the hypothesis, given by implication in this paper, that coffee cup or drink bottle spacers are as effective as properly designed add on devices.

In this paper, the production technique did not simulate the release of medication from a pressurised metered dose inhaler (pMDI). Instead, the technique created a radio labelled aerosol by pneumatic nebulisation into a bag (which would have acted as a particle pre-selector). This set up would not have reproduced accurately the ballistic component (polydispersed particles) that is inevitably released at actuation of a pMDI. It has already been shown that these particles are more effectively separated by a VHC than a spacer (with no valve). Had a pMDI containing the radio-labelled aerosol been used (as is the normal practice in gamma scintigraphic studies evaluating pMDI systems), we believe that the dynamic aerosol behaviour (in particular the impact of the ballistic component, turbulent deposition, etc.) following actuation into the chamber would have been quite different to that observed by having patients drawing in the already formed aerosol from a nebuliser bag. Simply put, the protocol more closely simulated a continuous jet nebuliser releasing a liquid phase aerosol into a bag that was then connected to a chamber/spacer device and may therefore have introduced bias to what occurs inside a VHC used with a pMDI.

A well designed holding chamber (with a valve) will retain a significant portion of the coarse component of the emitted dose (parti-
in feeding problems, which may highlight the refreshing focus on the role of organic factors. Several chapters of this book are dedicated to the understanding of feeding difficulties. In health, it is important for all health professionals involved in the assessment or treatment of feeding difficulties, to the development and maintenance of feeding problems in children, and is also essential to facilitate culturally sensitive intervention strategies. The perspectives of Indian culture are discussed and whilst one text alone cannot cover the breadth of multicultural issues that are relevant to the UK population, there is useful and informative sections which are specifically related to cultural practices and those which are related to social disadvantage and poverty in general. Whilst some chapters focus on clinical practice and opinion that may not appeal to an academic audience, practical advice, such as special issues in tube feeding, neurological impairment, and chronic illness, combined with generally sound theoretical discussion, makes this text a useful resource for health professionals involved in the assessment or treatment of feeding difficulties.

JACKIE BLISSETT
School of Psychology, University of Birmingham


Given the wide prevalence of feeding problems in children and their potential impact on health, it is important for all health professionals working with children to gain an understanding of feeding difficulties. In several chapters of this book there is a refreshing focus on the role of organic factors in feeding problems, which may highlight the wide range of subtle organic features that can contribute to and exacerbate feeding difficulties in children. The impact of other factors on feeding is also covered—for example, the effect of temperament, appetite, growth, developmental stage, prior experience with foods, and cognitive development, all of which are critical in understanding each child's feeding difficulty and creating appropriate intervention strategies.

The various etiologies of feeding difficulties from physiological (oral motor, regulatory, neurological), psychological (behavioural, cognitive behavioural, and psychoanalytical) and cultural perspectives are covered. These are discussed in reference to multidisciplinary teamwork and the development of both hospital and community feeding services. The chapter covering the psychoanalytical perspective sits somewhat oddly within the context of the book. Less helpful advice and practical intervention techniques stem from this chapter than the others, but perhaps those with an interest in psychoanalysis will find it an appealing diversion.

It is vital that health professionals in this field develop an understanding of the impact of cultural factors, from the effect of cultural feeding practices on feeding difficulties, to the perception and importance of food and feeding within cultures. This is critical in understanding the factors that contribute to the development and maintenance of feeding problems in children, and is also essential to facilitate culturally sensitive intervention strategies. The perspectives of Indian culture are discussed and whilst one text alone cannot cover the breadth of multicultural issues that are relevant to the UK population, there is useful and informative sections which are specifically related to cultural practices and those which are related to social disadvantage and poverty in general.


Share prices of dot.com companies have plummeted because, we are told, there are too many players in the market place for them all to be viable. The dot.com bubble has burst. This may also be true of paediatric textbooks. Such thoughts might trouble the authors and publisher of the fourth edition of the ABC of One to Seven, were it not for the pictures it contains. Is there really demand for another general paperback text covering well trodden ground, with predictable text and liberal use of blue boxes to convey the impression that there is a lot more colour than is really the case? Perhaps not, but for those pictures. This book isn’t cheap, but maybe that’s because of the pictures. In short, this book is worth the investment for the pictures alone.

Medical students like to console themselves with thick books because many of us still hold fast to the well known belief that you can learn a lot about a subject by buying a “good book”, even without opening it. Perhaps the same is true of GPs; fat books with hardback covers are much more impressive shelf-fillers than paperbacks with pictures.

But what about when the time comes to learn paediatrics? We need something on which to hang the facts of any textbook, and we all know the daunting effect of long paragraphs of plain text on page after page. This is where pictures and diagrams come into their own, and the ABC of One to Seven has them in spades. They are almost always helpful and relevant—if not adding to the explanation, then proving the useful peg on which to hang a particular fact. Captions though, are few and far between. The reader can sometimes be left confused as to the purpose of a particular illustration. Several of the pictures appear two or three times and others are decidedly outdated. Ambulances and toys seem to be used as space fillers, but others, particularly the dermatological pictures, are excellent.

This is no reference bible, and the text is simple and narrative. Facts are not flung at the reader, and the practical is emphasised over the theoretical. This is a book to demystify infancy and early childhood—the fear of the unknown can quickly be replaced with enthusiasm for such a fun subject area. The Colour Atlas of Kids: this bubble definitely remains intact.

NICK JENKINS

In a recent letter by Russell and Gillett (Arch Dis Child 2000;85:436), the sentence: "The in house assays used for AGA and EmA were performed on 10–20 ml of serum or plasma; thus capillary samples were more than adequate." should have read: “The in house assays used for AGA and EmA were performed on 10–20 microlitres of serum or plasma; thus capillary samples were more than adequate”. We apologise for this error.

Letters, Book reviews, Corrections

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www.archdischild.com
Data presented do not justify pessimistic conclusions

C M WRIGHT

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