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 have been shown to improve lung function 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. 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 Cushingsoid 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 Chripisin–Norman chest x ray scores. Height velocity was also improved. Three patients did not develop transient renal impairment, of whom only one required discontinuation of CyA. This was dose related and reversible but is infrequent with lower dose regimens used for anti-inflammatory therapy. 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.

We are grateful to Dr CE Daman-Willems, Dr R Dinwiddie, Prof JF Price, Dr HA Wyatt, and Dr GJ Connett for allowing us to use their patients in this report.

G K BHAL
S A MAGUIRE
I M BOWLER


Survey of criteria used to diagnose allergic bronchopulmonary aspergillosis in cystic fibrosis

Editor,—Allergic bronchopulmonary aspergillosis (ABPA) creates a difficult diagnostic and management problem in patients with cystic fibrosis (CF). The six major diagnostic criteria for ABPA in CF were adapted from asthma guidelines. Retrospective studies report significant variability in prevalence and the numbers of criteria used for diagnosis. This is important as CF databases (UK CF database, European CF Register, and the North American CF database) report ABPA frequency either without ascertaining the criteria used, or using limited diagnostic criteria. We have assessed consensus current practice of criteria used by UK clinicians to support a diagnosis of ABPA and how cases were treated.

This retrospective, descriptive postal questionnaire survey was addressed to senior consultants in the 58 CF specialist clinics identified by the UK CF Trust. A total of 45 replies were received (78%); three were illegible/incomplete. Results are presented.

Of six ABPA major criteria investigations (table 1), centres routinely tested (at least yearly) a median of four (mode five). Clinicians were also asked how many of eight factors (table 1) associated with ABPA diagnosis must be present, if major criteria were strictly adhered to. Clinicians considered they had a median of 5% of patients with ABPA (IQR 1 to 8), using their own criteria, falling to a median of 0% (IQR 0 to 3) when all major criteria were strictly adhered to.

This questionnaire shows considerable variability in the criteria used to diagnose ABPA in CF. Prospective reporting of cases with defined criteria will be the only way to reliably identify the true prevalence of ABPA. Database surveys may overestimate the true prevalence.

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Subnormal growth in children with Helicobacter pylori infection

Editor,—We read with interest the study by Choe and colleagues 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 15.5% 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. They concluded that H pylori infection accompanied by iron deficiency anaemia,
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 (5) g/l. H pylori infection is a chronic persistent infection, leading to diminished growth. Chronic gastric inflammation, dyspepsia, decreased nutritional intake, and malnutrition could all be factors leading to 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 They concluded that primary education suggest that primary schools in developing countries and colleagues with knowledge of cult subjects of primary education suggest that primary


Detecting outbreaks of E coli O157 infection in nurseries

Editor,—In their report of a serious outbreak of E coli O157 in a nursery in North Wales, Al-Jadder and colleagues recommend that more than one child with more than one bowel motion in a nursery should trigger action including “informing and seeking the advice of public health agencies.”1 Using data on healthy children in nurseries in the paper we have calculated the additional work that would be generated for the Public Health Department in the district in which the outbreak occurred if this policy was implemented.

Of 19 well children on the ground floor of the nursery, six had more than one bowel motion on or about one of the half day sessions attended during the surveillance period.2 Well children attending nursery for six days during the period, giving an approximate total number of sessions attended of 228 (19×6/2). The probability of a well child having more than one bowel motion during any half day session was therefore about 0.026 (6/228). There are 385 nursery and playgroups in North Wales, with an average of 23 children per nursery.3 In an average nursery the probability that two or more well children would have more than one bowel motion in a session on any one day is 0.12, equivalent to a false alarm every eight days.

Therefore, if the suggested policy was implemented, and incidents were reported to the Public Health Department, this would result in approximately 46 inappropriate calls per day (0.12×385)—that is, 230 per week. Even if the normal background rate was ten times lower than that seen among well children during this outbreak, this would still result in just over three calls a week to the department reporting false alarms. The proposed “early warning system” is therefore straightforward. The toiletting procedure that would prevent more than one child with more than one bowel motion was recorded. Most agree that faecal sampling needs, generally, to be encouraged.4 However, to combine the activities into a workable algorithm was beyond the scope of the report. Constructing an algorithm is worth attempting, however, since, as a starting point, a toiletting record constitutes a straightforward record used in a number of care settings.

R L SALMON
Consultant Epidemiologist


Meningococcal disease due to W135: fresh public health concerns

Editor,—The paediatric intensive care unit at St Mary’s Hospital in London admits more than 100 cases of meningococcal disease each year from over 50 different hospitals in the south east of England. Since 1992, the unit has treated over 650 patients with the disease, but had not treated a single case of serogroup W135 meningococcal infection until April 2000. We would like to report four children treated at our unit for meningococcal disease due to serogroup W135, type 2A, subtype P1.2, P1.5, within a one month period from April 2000. They had been vacccinated recently with meningococcal serogroup C conjugate vaccine, and had all been


Dr Salmon comments:

Children who attend out of home care at is increased risk for infectious diseases of which gastrointestinal tract infection is among the most common.1 Numbered among these are VTE+ E coli O157 infections which, as this outbreak showed, can cause severe disease. The challenge is to identify disease in the early stage.

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 the trigger for 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 normally be entered on 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, since, as a starting point, a toiletting record constitutes a straightforward record used in a number of care settings.

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

Table 1 Clinical presentation, severity and outcome

<table>
<thead>
<tr>
<th>Age (months)/Contact with</th>
<th>Presentation Resuscitation fluid*</th>
<th>Mechanical ventilation (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case sex</td>
<td></td>
<td>Maximum isotopes</td>
<td>Dopamine 10 µg/kg/min</td>
</tr>
<tr>
<td>1 10m/F Grandmother</td>
<td>Petechiae, septicaemia</td>
<td>80 ml/kg fluid</td>
<td>2 Discharged</td>
</tr>
<tr>
<td>2 27m/M Father</td>
<td>Purpuric fulminans, septicaemia</td>
<td>350 ml/kg fluid adrenaline 2.2 µcg/kg/min</td>
<td>11 Peripheral gangrene</td>
</tr>
<tr>
<td>3 4m/F 6 family members</td>
<td>No fluid</td>
<td>0 Discharged</td>
<td></td>
</tr>
<tr>
<td>4 19m/F 2 Aunts</td>
<td>Purpuric, septicaemia</td>
<td>90 ml/kg fluid</td>
<td>2 Discharged</td>
</tr>
</tbody>
</table>

*Total resuscitation fluid required in first 24 hours

in most neonatal screening tests for galactosaemia, the use of screening tests “overdiagno-
oses or status should receive a trial of pyridoxine. Fo-

Pyridoxine dependent and pyridoxine responsive seizures

EDITOR,—Seizures in infancy and early childhood responsive to pyridoxine are well recog-
nised but rare. Baxter has recently observed that almost a third of neonatal cases of pyridoxine dependency present with apparent birth asphyxia and/or suspected ischaemic encephalopathy, and recom-
mended 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 presented at delivery in a state of unexpected collapse requiring intubation and resuscitation. He developed tonic seizures within hours of birth and was treated with phenobarbital, phenytoin, and clonazepam. At 48 hours, an EEG showed a burst

Despite the fact that these tests do not establish blood galactose levels but the presence/deficiency of the enzymes responsible for galactosaemia, 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 formula” is based on the ESPGAN Committee on nutrition and on the AAP recommendations.2 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 formula”. Initial treatment for allergic disease is avoidance of the incriminated allergen. Soy formula has been recommended in treatment of CMA on grounds of efficacy, adequate nutrient intake, and cost.3 In the absence of prospective studies comparing the allergenicity of cow’s milk hydrolysates against soy formulas in children with CMA, the rationale to alter this indication appears to be lacking.

embrace. disordered breathing is another area of they are worth doing well. The study of sleep recorded as having received a trial of their early epilepsy management has been undertaken at many di...ies, which started before they were 3 years old, were identified (dates of birth 1979–1992). Only one of these children was recorded as having received a trial of pyridoxine early in the evolution of their epilepsy. The true prevalence of pyridoxine responsive epilepsy is difficult to assess if the recommendations of Baxter are seldom applied. Giving pyridoxine can be diagnostic and therapeutic—not giving a trial of pyridoxine is common and can lead to 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 disordered breathing is another area of paediatrics that the UK has stumbled to embrace.1 Sleep medicine has exponentially increased in adults in recent years, yet in paediatrics many questions remain unanswered. Although van Someren and colleagues made a valiant attempt to answer an important question,2 they did so by assessing clinical scores in relation to a standard which was far from gold and, as such, accuracy could not be determined, only inferred. Clinical scores or simple oximetry are limited in their ability to identify obstructive sleep apnoea (OSA), as they are able to identify significant OSA but not mild to moderate cases.3 Data is now accumulating that even mild OSA may be associated with significant neurocognitive morbidity in children.4 Full polysomnography is the current gold standard. The Vslab has not been satisfactorily validated against full polysomnography, and the results presented in van Someren and colleague’s paper showed a discrepancy in two of 10 simultaneous recordings (a 20% error rate) with important differences in mean oxygen saturation between the two systems (93% v 95%). It is true that full polysomnography may not be offered in all children for the diagnosis of OSA, but this process should be one of working down from a gold standard rather than edging up towards it. The arguments used by van Someren and colleagues against the use of full polysomnography are weak. Children in dedicated sleep areas tolerate full polysomnography well: in the 54 full polysomnographic OSA studies performed in this unit in the past six months, sleep efficiency was a mean of 90% (SD 8%), which includes children with frequent wakening as a result of their OSA!

In recent years, centres in both North America and Australia have dedicated significant funding to paediatric sleep laboratories and the appropriate training of both nursing and medical staff through specific specialist training criteria; the UK sadly lacks such support. With the exception of one paediatric unit (concentrating on sleep in rare disorders) sleep related research in the UK is linked to adult centres. UK paediatrics needs a sleep medicine wake up call, so that standards can be set from now on.

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Data presented do not justify pessimistic conclusions

Editor,—In a recent article, Cavadini and colleagues told us that during the past thirty years the youth in the US have shown a decrease in the consumption, as well as the percentage of energy from fat and, particularly, saturated fats.4 What are the conclusions of the article? That “these trends... may compromise the health of future US populations.”

In the discussion section the authors expressed concern about low iron and fibre intakes, despite the fact that both have risen steadily in the past 30 years. Concern is also expressed about falling calcium intake, due to a decrease in consumption of dairy products. US milk intake has always been exceptionally high and, being rich in saturated fat, a reduction is probably desirable. However, the current lower intake still supplies levels of calcium much higher than those for children in other developed countries.

There seems little doubt that US children are growing fatter, but I am at a loss to see in what way their dietary intake explains this. Presumably the reduction in energy intake is offset by an even greater reduction in activity, but the effect is that, in composition terms, the diet of today’s adolescents, though supplying more energy than required for current levels of activity, seems healthier than it has ever been.

The old fashioned disciplinary mother used to shout to her children in the next room “whatever you’re doing: stop it!” This seems to have had an effect towards young people as a group. Is it sad to see a scientific article falling back onto the accepted paradigm that the youth of today are decadent and unhealthy. Could the authors not have had the imagination to explore the meaning of these results and even suggest that some things might be improving instead of getting worse?

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Letters, Book reviews, Corrections


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. We, 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 hypoth- esis, 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 the nebuliser bag. Simply put, the protocol more closely simulated a continuous jet nebuliser releasing a liquid phase aerosol into a bag that was then closely connected to a chamber/spacer device and may therefore have led to a greater evanescence 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 (par-
cycles greater than about five microns aerodynamic diameter) from the pMDI. A spacer (homemade or otherwise) will not perform this function effectively. Rather, it will momentarily contain the aerosol and then deliver particles of all sizes to the well coordinated patient who is able to time inhalation with actuation of the pMDI. In the case of corticosteroids, the emitted coarser particles can promote local topical infections—such as oral candidiasis, as well as increases in overall systemic absorption.

The inhalation valve, which distinguishes a VHC from a spacer, needs to be a carefully designed component whose function is to retain the aerosol once created, following actuation of the pMDI, then release it during the inspiratory cycle. Many children, particularly those with an acute exacerbation of asthmatic symptoms, have poor coordination, and are therefore likely to mistime inhalation with pMDI actuation. These patients, who are at greatest risk, are thus likely to derive least benefit from the use of homemade spacers.

Although we have other observations of a technical nature, the information given here should be sufficient to provide the message that this study should not be taken as the final word but rather as a finding concerning the debate about the efficacy of inhalation manufactured add on delivery devices for use in pMDI based treatment.

That said, if a VHC is unavailable for whatever reason, an empty drinking bottle may be better than nothing at all.

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BOOK REVIEWS


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 theories of feeding difficulties from physiological (oral motor, regulatory, neurological), psychological (behavioural, cognitive, cultural, and psychoanalytical) and cultural perspectives are covered. These are distilled into 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 impact 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 reference to issues 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.

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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 paediatrics 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, 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 far more than 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

CORRECTION

In a recent letter by Russell and Gillett (Arch Dis Child 2000;85:456), 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.

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