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


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

EDITORS,—Allergic bronchopulmonary aspergillosis (ABPA) creates a difficult diagnostic and management problem in patients with cystic fibrosis (CF). The six major diagnostic criteria for ABPA were adapted from asthma guidelines. 1 Retrospective studies report significant variability in prevalence and the numbers of criteria for diagnosis. 2 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 based on 42 replies (72%) from 14 adult clinics (33%), 23 paediatric (55%) clinics, and five (12%) mixed adult/paediatric clinics. Units had a median of 100 patients (interquartile range (IQR) 63 to 160).

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, preferred to be present, or were not considered important. It was considered that a median of two factors (IQR 1 to 2.3) must be present, three preferred to be present (IQR 2 to 5), and one factor was not considered important (IQR 1 to 2.3). Forty per cent of centres considered one or more further factors in addition to those provided.

Thirty eight per cent of centres would begin treatment without clinical deterioration (62% treat on deterioration). Initial treat-ment in all centres (100%) was prednisolone: in paediatric patients 1 mg/kg in 21% and 2 mg/kg in 76%; in adults 30 mg/day in 50% (range 20–60 mg/day). In response to failure of steroid treatment 33% would add an antifungal agent, 17% would increase steroid dose (17% no experience against steroid failure, 12% other, 21% no reply). Oral antifungals had been used by 60% of respondents, itraconazole in all cases. Paediatric centres were much more likely to use oral antifungals (88% ± 31%, p = 0.004, Mann–Whitney U test). Nebulised antifungals were used by 21%, amphotericin in all cases.

We also asked how many patients would currently be diagnosed as having ABPA in that unit using: (a) criteria stated as “must be present” earlier in the questionnaire; and (b) if major criteria were strictly adhered to. Clinicians considered that 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 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 15.3% 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,

Table 1 Replies to questionnaire (% of all units)

<table>
<thead>
<tr>
<th>Must be present</th>
<th>Prefer to be present</th>
<th>Not important</th>
</tr>
</thead>
<tbody>
<tr>
<td>Assessed yearly or more</td>
<td>83</td>
<td>42</td>
</tr>
<tr>
<td>Aspergillus precipitins</td>
<td>83</td>
<td>42</td>
</tr>
<tr>
<td>Aspergillus specific IgE</td>
<td>52</td>
<td>45</td>
</tr>
<tr>
<td>cXr infiltrates</td>
<td>93</td>
<td>38</td>
</tr>
<tr>
<td>Blood eosinophilia (&gt;500/mm&lt;sup&gt;3&lt;/sup&gt;)</td>
<td>83</td>
<td>42</td>
</tr>
<tr>
<td>Aspergillus fumigatus skin test</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Total serum IgE (&gt;1000 ng/ml)</td>
<td>79</td>
<td>45</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>16</td>
<td>12</td>
</tr>
<tr>
<td>Wheez/cough</td>
<td>8</td>
<td>11</td>
</tr>
</tbody>
</table>
| *Six major criteria investigations.

rather than *H pylori* infection alone, might delay pubertal 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. In the study, the mean age was 11.5 (2.0) years (range 8–15). We found 11 (36.7%) *H pylori* positive patients. 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 it is not related to iron deficiency anaemia.

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**Growth monitoring**

**EDITOR—**Garner and colleagues recently reviewed the need for growth monitoring. This is a component of primary health care on which so much finance and health workers’ time is being expended. No doubt this review will stimulate more necessary trials.

However, they did not touch on one important aspect of growth monitoring—that is, whether health workers using growth charts comprehend the weight for age curve. Piaget (1896–1980) considered the line graph to be one of the more difficult subjects to teach. Graphic representation of numbers is not taught in primary schools in developing countries and colleagues with knowledge of primary education suggest that primary school teachers in these countries would not be able to teach it. Experience with postgraduate doctors in the 1970s suggested that a proportion could not complete a weight chart and even fewer would have problems in interpreting it. A similar problem has arisen with midwives in the use and interpretation of the partograph to plot the progress of labour. Fortunately, an alternative method of weighing may overcome this difficulty. This method involves weighing in or near the community, presenting to general practice, and reported to national surveillance. BMJ 1999;318:1046–50.

**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-Jader and colleagues recommend that more than one child with more than one bowel motion in a nursery should trigger action including “inquiring and seeking the advice of public health agencies”.

Using data on healthy children reported in the paper we have calculated the additional work that would be generated for the Public Health Department in the district where 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 at least one of the half day sessions attended during the surveillance period. Well children attended 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 day nurseries and playgroups in North Wales, with an average of 23 children per nursery. 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 almost unworkable, and the claim that it could have prevented 10–12 of the 31 cases in the outbreak needs to be reviewed.

**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 following meningococcal infection due to serogroup W135, type 2A, subtype P1.2, P1.5, within a one month period from April 2000. They had been vaccinated recently with meningococcal serogroup C conjugated vaccine, and had all been...
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>Case number</th>
<th>Sex</th>
<th>Contact with travellers</th>
<th>Presentation Resuscitation fluid* (72 hours)</th>
<th>Mechanical ventilation (days)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10m/F</td>
<td>Grandmother</td>
<td>Petechiae, septicaemia</td>
<td>2</td>
<td>Discharged</td>
</tr>
<tr>
<td>2</td>
<td>27m/M</td>
<td>Father</td>
<td>Purpura fulminans, septicaemia</td>
<td>11</td>
<td>Peripheral gangrene, Neurological sequelae</td>
</tr>
<tr>
<td>3</td>
<td>4m/F</td>
<td>6 family members</td>
<td>Purpura, septicaemia</td>
<td>90 ml/kg fluid</td>
<td>Discharged</td>
</tr>
<tr>
<td>4</td>
<td>19m/F</td>
<td>2 Aunts</td>
<td>Purpura, septicaemia</td>
<td>10 µg/kg/min fluid</td>
<td>Discharged</td>
</tr>
</tbody>
</table>

*Total resuscitation fluid required in first 24 hours

in most neonatal screening tests for galactosaemia. 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 neurological problems in healthy children. Galactose is a functionally important component of milk in all mammalian species, it is unclear whether a lactose free diet plays a role in the clinical neurological abnormalities of children with galactosaemia. However, lactose is essential for patients with UDP-galactose-4 epimerase deficiency. 

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;84:615–16.

Prevention and treatment of cow’s milk allergy

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 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 phenobarbitone, phenytoin, and clonazepam. At 48 hours, an EEG showed a burst

*aemia* overlooks 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. 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.7 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.
Are sleep studies worth doing?

Editor,—If sleep studies are worth doing, they are worth doing well. The study of sleep is sometimes all too readily treated as a cure for the physician who has difficulty in sleep. We began a study of sleep in children with epilepsy unrecognised and difficult epilepsy unrecognised and inadequately treated. The use of sleep studies in children with epilepsy is common and can leave a treatable cause of difficult epilepsy unrecognised and inadequately treated.

M HUTTON
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Visilab has not been satisfactorily validated for use in children and even suggest that some things might be better with a different testing modality for pediatric obstructive sleep apnea syndrome. 6th World Congress on Sleep Apnea, Sydney, Australia, March 2000.


Are sleep studies worth doing?

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 referred 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 1979–1992). Only one of these children was recorded as having received a trial of pyridoxine, which included 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 the present.

S CUNNINGHAM M HARRIS Department of Paediatric Respiratory and Sleep Medicine, Mater Children's Hospital, Brisbane, Australia email: steve.cunningham@talk21.com

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 total milk consumed, as well as the percentage of energy from fat and, particularly, saturated fats.1 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 be our attitude towards young people as a group. It is 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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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.2 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 (inertial deposition, etc) following actuation into 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.

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The various theories of feeding difficulties from physiological (oral motor, regulatory, neurological), psychological (behavioural, cognitive behavioural, and psychoanalytical) and cultural perspectives are covered. These are discussed to multi-disciplinary 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 information on 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.


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 are much more impressive shelf-fillers than 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.

JACKIE BLISSETT
School of Psychology, University of Birmingham

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.

www.archdischild.com
Subnormal growth in children with *Helicobacter pylori* infection

HÜLYA DEMIR, INCI NUR SALTIK, NURTEN KOÇAK, AYSEL YÜCE, HASAN ÖZEN and FIGEN GÜRAKAN

*Arch Dis Child* 2001 84: 89
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