PANCREATIC ENZYME SUPPLEMENTATION IN CYSTIC FIBROSIS

Sir,—Pharmacological advances in pancreatic enzyme supplementation have produced a dramatic improvement in nutritional status of cystic fibrosis patients, contributing to ever improving life expectancy.1 Compliance is sometimes problematic due to the large number of capsules required per meal. For these reasons and the introduction of higher strength enteric coated microsphere preparations (for example Creon 25000, Duphar) is particularly welcome. One group which has not been previously considered where improved acceptability is concerned is the younger child. In our clinic 76% of children under 5 years and 29% of children aged 5–10 years are unable to swallow conventional treatment schedules. Pancreatic preparations. To overcome this problem capsules are opened and the free granules taken with food.

We have performed an open, prospectively randomised, crossover study to compare the probability of a group of cystic fibrosis patients for two different presentations of enteric coated microspheres of pancreatin (Creon): the conventional gelatin capsule and a foil sachet. Patients who had been taking Creon capsules for a minimum of four weeks were invited to participate. Each child was randomised to receive either capsules or sachets for the initial six week block after which they crossed over to the second preparation. On entry to the study and at the six and 12 week intervals parents completed a questionnaire detailing their response to each preparation and in the final assessment stated their preference.

Seventeen patients were recruited, 11 girls and six boys (mean age 4·1 years, range 4 months–12 years). Their average daily intake of Creon was 30 capsules (range 10–45). In the final assessment 10 patients preferred the foil wrapped preparation, five preferred the capsules, and two expressed no preference. Comments made about the preparations highlighted flaws that the practitioner may overlook. Most found conventional capsules too large to swallow and found the quantities of medication required excessive. Problems were also encountered with the disposal of empty capsule shells and the tendency of capsules to disintegrate when wet. The consensus (10 of 17 patients) was that sachets were more easily manipulated and easier to dispose of.

Cystic fibrosis management demands of the child and his family a lifetime of rigorous treatments schedules. Pancreatic supplements are a constant companion and compliance and ease of administration must be priorities if treatment is to succeed. While the ultimate objective must be for children to learn to swallow capsules whole, for the substantial group who through age or idiosyncrasy cannot achieve this, a non-capsule preparation offers several advantages in administration.

CATHRINE M HILL
CHRISTOPHER J ROLLES
PATRICIA KEAN
RAJ CHAND
Paediatric Medicine Unit, Southampton General Hospital, Southampton, UK

Cystic Fibrosis and Control Costs Controls

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>Cystic fibrosis patients</th>
<th>Controls</th>
<th>p Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>0·28</td>
<td>1440 (2140–8)</td>
<td>2556 (991·2)</td>
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<tr>
<td>[n=56]</td>
<td>[n=56]</td>
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<tr>
<td>0·3–3·9</td>
<td>6359 (3336–3)</td>
<td>3688 (156–0)</td>
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<td>[n=7]</td>
<td>[n=5]</td>
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<tr>
<td>4·7–7·9</td>
<td>4675 (1997·4)</td>
<td>2194 (954–0)</td>
<td>0·0095</td>
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<td>[n=8]</td>
<td>[n=9]</td>
<td></td>
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<tr>
<td>8·1–11·9</td>
<td>4114 (1993·7)</td>
<td>2498 (903·8)</td>
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<tr>
<td>12·8–15·9</td>
<td>4007 (1732·5)</td>
<td>2498 (1029·4)</td>
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<td>[n=33]</td>
<td>[n=10]</td>
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†P Value by Kruskal-Wallis test.
Positive hepatitis serologies with treatment for Kawasaki syndrome

Sir,—Intravenous immune globulin (IVIG) is currently the treatment of choice for Kawasaki syndrome in that it shortens the duration of symptoms and lowers the incidence of coronary artery aneurysms associated with this disorder. We describe a 3 year old boy who also had hepatomegaly and raised hepatic transaminases associated with Kawasaki syndrome and transiently developed false positive serologies to hepatitis B and hepatitis C after treatment with IVIG.

Case report
Seven days before hospitalisation, this 3 year old boy developed fever, abdominal pain, and vomiting. During the next five days he developed a generalised maculopapular skin eruption sparing the palms and soles, diffuse tender cervical adenopathy, oedema of the hands and feet, non-purulent conjunctivitis, right upper quadrant abdominal tenderness with mild hepatomegaly, and a systolic ejection murmur. Serum alanine aminotransferase was 133 IU/l (normal 6–65), serum aspartate aminotransferase was 191 IU/l (normal 7–40), and serum lactate dehydrogenase was 775 IU/l (normal 232–619). Prothrombin time, alkaline phosphatase, and bilirubin values were normal, as was an abdominal sonogram. Past and family history were negative; he had received no transfusions nor been exposed to infectious hepatitis. A diagnosis of Kawasaki syndrome was made and IVIG administered.

The child's symptoms resolved within 48 hours but serum transaminases remained raised. On the third hospital day, alanine aminotransferase was 164 IU/l and aspartate aminotransferase was 191 IU/l. Alkaline phosphatase and bilirubin values remained normal. Serum was obtained for measurement of transaminases and antibodies to hepatitis A, B, and C virus; these were negative. Serum was unavailable for hepatitis B surface antigen but hepatitis C virus antibodies were detected (HCV Ab ELISA, Ortho Diagnostics), as were antibodies to core and surface antigens of hepatitis B virus. Clinically the child did well and was discharged from the hospital at the conclusion of IVIG treatment. In the year since hospital discharge he has remained asymptomatic and his serum transaminases have remained normal. Three months after discharge, antibodies to hepatitis C virus but not core or surface antigens of hepatitis B virus were detectable. However, at six, nine, and 12 months after discharge, all antibody studies were negative.

The history and serological findings in this case suggest that hepatitis B and C viruses were passively transferred by infusion of IVIG. The disappearance of detectable antibody to both viruses six months after the infusion is consistent with the 30 day half life of IVIG.2 Passive transfer of antibody to hepatitis B virus has been described after infusions of IVIG.2 Similarly, passive transfer of antibody to human immunodeficiency virus has been described after infusions of hepatitis B immune globulin and raises the possibility of transfer of hepatitis C virus.5

The increases in serum transaminases in this case may have been due to Kawasaki disease. Increases in serum transaminases and bilirubin values occur frequently in Kawasaki disease and may correspond microscopically to cholangitis, periadnitis, vasculitis, and portal perivasculitis.6

IVIG has become an important therapeutic agent with ever increasing uses. This patient demonstrates that infusion of IVIG may induce false positive serological and immunohematological tests, and therefore the results of such studies must be interpreted with caution.

STEPHEN M BOROWITZ
Department of Pediatrics,
University of Virginia Health Sciences Center,
Box 131, Charlottesville,
Virginia 22908, USA


Recent parotitis

SIR,—Cohen et al report 11 children with recurrent parotitis.1 They state that immunological factors may be involved in the pathogenesis of this condition, although in general the immunological abnormalities described have been fairly subtle.2,3 We report a recent case which supports the theory that auto-immune mechanisms are important.

A 2 year old boy recently saw his 11 year old girl who presented with a 12 month history of four episodes of right sided parotid swelling, without redness or tenderness, but associated with low grade fever. There was a history of recurrent upper respiratory tract infections and unexplained fever from infancy until 7 years of age. She also gave a history of dry, sore eyes since infancy, recently diagnosed by an ophthalmologist as being allergic conjunctivitis. She had a chronic non-productive cough for four years and had had recurrent ear infections from 5 years of age, for which adenotonsillectomy was performed and ventilating tubes inserted, and had a chronic non-productive sialiaisis since age 7 years.

Sialogram showed right sided sialaiosis with a normal left parotid duct. Chest radiography was normal. Full blood count was normal, with no eosinophilia. Serum immunoglobulin concentrations that were performed on two occasions showed serum IgG 3-2 and 2-4 g/l (normal 6-5–15-0), serum IgA 0-07 and 0-09 g/l (normal 0-5–5-0), and serum IgM 0-13 and 0-25 g/l (normal 0-3–2-5). HIV antibodies were not detected. There was a family history of normal but B cells were raised (CD19 27%, normal 1–15%). A diagnosis of common variable immunodeficiency (late onset hypo-gammaglobulinaemia) was made, and the patient was started on intravenous immunoglobulin replacement treatment.

It is well recognised that autoimmune phenomena may occur in common variable immunodeficiency, including recurrent parotitis. Conley et al described parotitis in two of eight children with common variable immunodeficiency, although it did not state whether or not it was recurrent.1 One of the two patients described by Friis et al had IgA deficiency, gluten enteropathy and high titres of antinuclear antibodies, all features of evolving common variable immunodeficiency.4 As long ago as 1960, Mosbeck and Kristensen felt that autoimmunity might play some role in the pathogenesis of recurrent parotitis.5 We believe the case we report here supports that theory. Our case shows the importance of measuring serum immunoglobulin concentrations on children with recurrent parotitis.
The value of proximal small intestinal biopsy in the differential diagnosis of chronic diarrhoea.
J A Walker-Smith, A D Phillips and A G Thomas

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