Mycoplasma pneumoniae

EDITOR,—The report from Thomas et al may lead us to alter our current understanding of the association of Mycoplasma pneumoniae and central nervous system dysfunction.1 The suggestion, however, that M pneumoniae should be considered in all cases of encephalopathy, regardless of preceding respiratory infection, could potentially lead to considerable overdiagnosis for the following reasons.

Complement fixation serology, which is raised as a function of both IgG and IgM, may not be seen as a result of a potentially cross-reactive glycolipid antigen. Complement fixation titres may be raised in the diagnostic range in a small subset of normal individuals, and therefore a background of high titres should exist as well in patients with neurological disorders regardless of the diagnosis. Furthermore, specific increases have been previously found in some central nervous system disorders, for example, Kleemola and Kayhty previously demonstrated a fourfold change in complement fixation titres in 40-7% of paired sera from patients with bacterial meningitis and 10-3% of patients with bacteremias.2 Most commercially available assays will also yield positive results in approximately 2-10% of asymptomatic populations, and therefore a similar frequency is at least likely in all patient populations regardless of illness. The frequency of true disease in a patient population will affect the predictive value of a positive test. A positive serological test for M pneumoniae is more likely to be truly positive in patients who have had respiratory manifestations in contrast to those who have not. Therefore, if one were to adopt a diagnostic strategy of encephalopathy should be screened serologically for M pneumoniae despite the low frequency of true positives, there would be a good chance of false positives equalling or exceeding true positive results. The problems here are analogous to those encountered in the use of screening tests for populations with low endemicity. The potential for endemic seropositivity needs to be especially considered when association between a positive test and an uncommon disease is made. It would be preferable then to establish more definitively the diagnostic utility of M pneumoniae infection by adopting independent methods such as direct bacterial isolation, IgM anti-P1 immunoblotting,3 and/or direct polymerase chain reaction assay of respiratory secretions.4

The respiratory manifestations of M pneumoniae infection are variable and may range from a mild sore throat to atypical pneumonia. In the context of an acute encephalopathy, it would be easy to disregard a mild form of respiratory illness when the focus of history taking and physical examination is the neurological illness. The existing body of medical literature still indicates that the majority of M pneumoniae-associated central nervous system diseases are associated with a preceding or coexisting respiratory illness. N CIMOLAI Department of Pathology

Chart to estimate surface area from body weight

<table>
<thead>
<tr>
<th>Weight (BSA) (m²)</th>
<th>Weight (BSA) (m²)</th>
<th>Weight (BSA) (m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.4</td>
<td>0.049</td>
<td>8</td>
</tr>
<tr>
<td>0.5</td>
<td>0.058</td>
<td>9.4</td>
</tr>
<tr>
<td>0.6</td>
<td>0.066</td>
<td>10</td>
</tr>
<tr>
<td>0.7</td>
<td>0.074</td>
<td>11.5</td>
</tr>
<tr>
<td>0.8</td>
<td>0.082</td>
<td>12.9</td>
</tr>
<tr>
<td>0.9</td>
<td>0.096</td>
<td>14</td>
</tr>
<tr>
<td>1.0</td>
<td>0.110</td>
<td>15.5</td>
</tr>
<tr>
<td>1.1</td>
<td>0.126</td>
<td>16.9</td>
</tr>
<tr>
<td>1.2</td>
<td>0.141</td>
<td>18.4</td>
</tr>
<tr>
<td>1.3</td>
<td>0.159</td>
<td>20</td>
</tr>
<tr>
<td>1.4</td>
<td>0.172</td>
<td>21.6</td>
</tr>
<tr>
<td>1.5</td>
<td>0.187</td>
<td>23.1</td>
</tr>
<tr>
<td>1.6</td>
<td>0.203</td>
<td>24.7</td>
</tr>
<tr>
<td>1.7</td>
<td>0.219</td>
<td>26.3</td>
</tr>
<tr>
<td>1.8</td>
<td>0.235</td>
<td>27.9</td>
</tr>
<tr>
<td>1.9</td>
<td>0.251</td>
<td>29.5</td>
</tr>
<tr>
<td>2.0</td>
<td>0.267</td>
<td>31.1</td>
</tr>
</tbody>
</table>

Primary sclerosing cholangitis in childhood inflammatory bowel disease

EDITOR,—The strong association between primary sclerosing cholangitis (PSC) and inflammatory bowel disease, ulcerative colitis in particular, was realised after the introduction of endoscopic retrograde cholangiopancreatography (ERC).5 Furthermore it is well known that primary sclerosing cholangitis is an important risk factor for neoplastic transformation in adults.6 In Swedish adults with ulcerative colitis, primary sclerosing cholangitis is seen in 2-3-6%.7 The occurrence of primary sclerosing cholangitis in children, however, is less well documented.8 Over the past four years we have treated 31 children with inflammatory bowel disease, 11 of whom were 10 years or younger at diagnosis. There were 14 with ulcerative colitis, eight with indeterminate colitis, and nine with Crohn's disease diagnosed


A further advantage of Boyd's formula is that it allows data expressed per unit BSA and per unit W to be calculated easily one from the other, provided W is known. For this example, approach enabled the comparison of glomerular filtration measurements in newborns from 12 different studies, despite the fact that the data had been expressed variously as per m² or per kg, because body weight values were also available.4 None of the studies gave body length measurements, so data conversion would not have been possible using conventional formulae for estimating BSA.

M G COULTHARD Paediatric Nephrology Unit, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP


Primary sclerosing cholangitis in childhood inflammatory bowel disease

EDITOR,—The strong association between primary sclerosing cholangitis (PSC) and inflammatory bowel disease, ulcerative colitis in particular, was realised after the introduction of endoscopic retrograde cholangiopancreatography (ERC).5 Furthermore it is well known that primary sclerosing cholangitis is an important risk factor for neoplastic transformation in adults.6 In Swedish adults with ulcerative colitis, primary sclerosing cholangitis is seen in 2-3-6%.7 The occurrence of primary sclerosing cholangitis in children, however, is less well documented.8 Over the past four years we have treated 31 children with inflammatory bowel disease, 11 of whom were 10 years or younger at diagnosis. There were 14 with ulcerative colitis, eight with indeterminate colitis, and nine with Crohn's disease diagnosed
according to the criteria set up by Holmqquist et al. Liver function tests showed signs of cholestasis in six patients with ulcerative colitis. Further investigation with ERCAP and liver biopsy verified primary sclerosing cholangitis in three children with ulcerative colitis, two of whom had a newly diagnosed mild pancolitis and one had had an almost symptomless colitis for six years and impaired liver function tests for the last two years. The remaining three children with cholestatic liver function tests have, for various reasons, not yet been investigated with ERCAP.

Thus of 14 children at our department with ulcerative colitis at least three and probably six have primary sclerosing cholangitis. This indicates a high prevalence of primary sclerosing cholangitis in childhood ulcerative colitis and emphasises the need for regular testing of liver function in children with inflammatory bowel disease, even those with a clinically mild disease.

LARS STENHAMMAR
LOTTA HÖGBORG
PER LIEWANDER
Department of Paediatrics,
Norrköping Hospital
S-601 82 Norrköping, Sweden


Guidelines for ethical conduct of medical research in children

EDITOR—In the research report and commentaries on venepuncture several references were made to the BPA Guidelines for the Ethical Conduct of Medical Research Involving Children 1990. The guidelines were quoted as classifying venepuncture as low, not minimal, risk. However, the guidelines actually say: ‘Many children fear needles and for them low rather than minimal risks are often incurred by injections and venepuncture’ (emphasis added). Although risk probability has objective measures, the severity of any harms which are risked is partly a subjective estimation. The guidelines allow for possible differences in risk assessment by the doctor, parents and child, and among various groups of children. Clear explanations, expert phlebotomists, and the offer of EMLA cream can all help each child to decide whether the risks associated with venepuncture are worthwhile undertaking. The research reported in this journal suggests that most healthy children are willing to cooperate in research venepunctures.

However, a minority of children deeply fears needles. In a recent multicentre study we interviewed 120 young people aged 8 to 15 years having orthopaedic surgery. They have chronic conditions and on average had had four previous operations. They were asked what they (a) most and (b) least looked forward to about being in hospital. In answer to question (b) 59 gave two or more examples which mainly included ‘needles’ and ‘having stitches taken out’, 14 said ‘nothing particular’, and 13 said ‘the operation’. They were all having major surgery, nearly half were waiting for spinal surgery; 15 year olds were as likely as 8 year olds to object to needles.

In all but the most life threatening circumstances it amounts to an abuse of a child’s rights as members of society to demand a refusal to consent to treatment if the child seems to have made a fully informed and considered decision.1 How much more does this standard apply to children taking part in research which is not of direct benefit to them?

PRISCILLA ALDERSON
Social Science Research Unit, Institute of Education, University of London, Woburn Square, London WC1H ONS


Use of enteric coated prednisolone in Crohn’s disease

EDITOR—A new patient, aged 13 years, presented to our paediatric inflammatory bowel clinic with abdominal pain, weight loss, and bloody diarrhoea. Full investigation including barium meal and follow through, colonoscopy and biopsy demonstrated active Crohn’s disease of the terminal ileum and colon. He was treated with prednisolone initially at 40 mg/day with good relief of his symptoms.

As an outpatient he was prescribed enteric coated prednisolone by his general practitioner instead of the non-enteric type prescribed in our clinic. On the same dose as before his symptoms (abdominal pain and diarrhoea) recurred. Non-enteric coated prednisolone was represcribed and he improved.

This is not an isolated occurrence in our unit. We frequently hear from parents that their children have deteriorated with a switch from non-enteric coated to enteric coated prednisolone.

The pharmacokinetics of enteric coated and non-enteric coated prednisolone have been studied in normal subjects. The bioavailability is similar but peak plasma concentrations of the enteric coated are delayed after approximately two hours using non-enteric coated formulations and at around four hours using enteric coated ones.1 2 The absorption of drugs in Crohn’s disease is known to be erratic associated with the last meal, anticipation, rapid transit time, and diarrhoea3 and enteric coated prednisolone is likely to be less well absorbed. There are other reports in the literature of adults with Crohn’s disease who have had to restart enteric coated prednisolone and responded to the non-enteric coated formulation.4 A recent review suggested that the advantages of enteric coated prednisolone in the prevention of duodenal ulceration are only theoretical.5

We advocate the use of non-enteric coated prednisolone in the treatment of Crohn’s disease and suggest that in any condition where there is a rapid transit time or diarrhoea enteric coated prednisolone should be used with caution.

LEWANDER
S-601 82 Norrköping, Sweden


Symptoms of diabetes insipidus

EDITOR—It is well recognised that in children presenting with symptoms of diabetes insipidus the investigations should include a brain scan to exclude a hypothalamic tumour. It has been our policy to perform a second brain scan six months later if the first is negative to ensure that such tumour has not been missed. We have recently seen a child where this strategy failed.

The child, a girl aged 9 years, presented with a short history of enuresis and was found to have diabetes insipidus. She was also of short stature and investigations confirmed that she had not only diabetes insipidus but also growth hormone deficiency. There was a hypothalamic thalamic syndrome stimulating hormone response to thyroid releasing hormone but she was euthyroid and cortisol concentrations were normal. Two brain scans, child in contrast and performed six months later, were normal. She was started on desmopressin and growth hormone with excellent response. Four years later she presented with vague symptoms of tearfulness, lethargy, and tiredness after a series of winter respiratory illnesses. Examination at that time was normal, her growth was excellent and it was thought that her symptoms were related to a variety of illnesses during the winter months in association with family upheaval. She was referred to a child psychiatrist. Within a few weeks, however, she had deteriorated and was found to have a decrease in her visual fields. She had no hard neurological signs. Magnetic resonance imaging (MRI) confirmed the presence of a hypothalamic tumour which proved to be a dysgerminoma.

This tumour must have been present when the child was first seen and it is possible that MRI then rather than computed tomography may have confirmed its presence. There must be a number of children with congenital diabetes insipidus who have had computed tomography only and we would recommend that they have MRI as soon as possible. We