LETTERS TO THE EDITOR

Fludarabine in the treatment of an active phase of a familial haemophagocytic lymphohistiocytosis

EDITOR,—Familial haemophagocytic lymphohistiocytosis (FHL) is a lethal disease with an uncontrolled activation of T lymphocytes and macrophages due to a perforin gene defect.1

The only current curative treatment is bone marrow transplant when in good clinical condition. Nevertheless a series of patients is needed to assess the efficacy of fludarabine for the treatment of active phases of FHL.

We thank Dr JL Stephan for his helpful clinical advice.

Correspondence to: Prof JP Vannier (Jean-Pierre. vannier@chu-rouen.fr)


Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Holiday destination where infected</td>
<td>South of France</td>
<td>Elba</td>
</tr>
<tr>
<td>Interval from exposure to appearance of symptoms (months)</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Interval between appearance of symptoms and diagnosis (weeks)</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Hepatomegaly (%)</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Splenomegaly (cm)</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>HB (mmol/l)</td>
<td>2.9</td>
<td>3.0</td>
</tr>
<tr>
<td>WBC (&lt;10^9/l)</td>
<td>4.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Platelets (&lt;10^7/l)</td>
<td>47</td>
<td>107</td>
</tr>
<tr>
<td>Ferritin (µg/l)</td>
<td>10813</td>
<td>260</td>
</tr>
<tr>
<td>LDH (U/l)</td>
<td>4779</td>
<td>911</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>3.64</td>
<td>6.9</td>
</tr>
<tr>
<td>Serum IgG (g/l)</td>
<td>13.9</td>
<td>15.6</td>
</tr>
</tbody>
</table>

LDH = lactate dehydrogenase

Table 1 Patient characteristics

EDITOR,—We read with interest the report by Grech et al. From their population based study, it seems that the annual incidence of visceral leishmaniasis (VL) declined considerably in Malta as a result of the eradication of stray dogs. VL is still endemic around the Mediterranean Sea and sporadic cases are reported in children living in Northern Europe. It seems likely that with increasing tourism the incidence of VL will also increase in areas where until recently this condition would not even be thought of. During the last 18 months, we have diagnosed three children with VL. As the presentation features can be fairly dramatic and physicians in Northern Europe are not always alert to the possibility of this condition, we would like to call attention again to the possibility of VL in non-endemic countries.

The main clinical features of the patients are shown in table 1. All three children presented with spiking high fevers, anorexia, hepatosplenomegaly, and pancytopenia. The onset of the symptoms was insidious and it took 3–12 weeks to establish the diagnosis. In all three patients this was achieved through bone marrow aspiration and the demonstration of the typical amastigotes in macrophages. The diagnosis was further confirmed through the demonstration of antibodies to the leishmania parasite. All three patients needed erythrocyte transfusions and patient three also needed platelet transfusions. A 5–10 day course of liposomal amphotericin-B was given to all three children. The treatment was well tolerated, and they all became afebrile within a week. Pancytopenia subsided over the ensuing 2–3 weeks and the children gradually returned to normal activity.

Naturally, we cannot draw epidemiological conclusions from such a small number of patients, but it is intriguing to find three unrelated cases within a relatively short time. While the eradication of stray dogs may go a long way to reduce the incidence of VL, vaccination would be more desirable.2 Although resistance and immunity against the leishmania parasites is not well understood, the seemingly increasing incidence of VL in children travelling from Northern Europe might be because they have no transplacental immunity against the parasite and are therefore more prone to develop this condition than local children. There is much in common between the presentation features of the haemophagocytic syndromes and VL. It is noteworthy that all three of our patients showed signs of macrophage activation and haemophagocytosis was observed in their bone marrow smears. With increased awareness of this condition by physicians in non-endemic countries, the time required to reach the correct diagnosis and institute treatment should be reduced.


Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis (years)</td>
<td>1</td>
<td>1.5</td>
</tr>
<tr>
<td>Holiday destination where infected</td>
<td>South of France</td>
<td>Elba</td>
</tr>
<tr>
<td>Interval from exposure to appearance of symptoms (months)</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>Interval between appearance of symptoms and diagnosis (weeks)</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Hepatomegaly (%)</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Splenomegaly (cm)</td>
<td>10</td>
<td>3</td>
</tr>
<tr>
<td>HB (mmol/l)</td>
<td>2.9</td>
<td>3.0</td>
</tr>
<tr>
<td>WBC (&lt;10^9/l)</td>
<td>4.5</td>
<td>1.5</td>
</tr>
<tr>
<td>Platelets (&lt;10^7/l)</td>
<td>47</td>
<td>107</td>
</tr>
<tr>
<td>Ferritin (µg/l)</td>
<td>10813</td>
<td>260</td>
</tr>
<tr>
<td>LDH (U/l)</td>
<td>4779</td>
<td>911</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>3.64</td>
<td>6.9</td>
</tr>
<tr>
<td>Serum IgG (g/l)</td>
<td>13.9</td>
<td>15.6</td>
</tr>
</tbody>
</table>

LDH = lactate dehydrogenase

www.archdischild.com
Intestinal inflammation in cystic fibrosis

Editor,—We thank Dr Briars for his recent comments and are aware of his opinions regarding the potential source of the intestinal cytokines that we discussed in paper, including reference to his previous paper.1

We do not agree that our data is dependant upon IL-8 alone. We have shown statistically significant differences for a whole range of proteins and types of assays that we have performed, we have not carried out the extensive experiments for IL-8, as reported by Dr Briars. We do know that the polyethylene glycol, a key constituent of the lavage fluid, does not affect the IL-8 assay. There are two reasons why variable recovery is unlikely to be a major factor in our results. Firstly, by collecting whole gut lavage, any intestinal secretions present, including bile, intestinal enzymes and mucus, which are found in the controls, this still shows statistically significant differences for the lavage fluid proteins.

In summary, we believe that the IL-8 is a highly sensitive marker of intestinal inflammation in children with cystic fibrosis. The source of the IL-8 is the mucosa and not the stool. If a stool sample is taken, the IL-8 concentrations in polyethylene glycol should be measured.


3 We also showed eosinophilic cationic protein to be raised in children with cystic fibrosis. With α1 antitrypsin, this is relatively stable in faeces at room temperature (approximately 21% loss over 24 hours). This loss would be considerably lower during whole gut lavage. Thus, degradation would be unlikely to explain this difference.


Letters to the editor

Intestinal inflammation in cystic fibrosis

Editor,—We thank Dr Briars for his recent comments and are aware of his opinions regarding the potential source of the intestinal cytokines that we discussed in paper, including reference to his previous paper.1

We do not agree that our data is dependant upon IL-8 alone. We have shown statistically significant differences for a whole range of proteins and types of assays that we have performed, we have not carried out the extensive experiments for IL-8, as reported by Dr Briars. We do know that the polyethylene glycol, a key constituent of the lavage fluid, does not affect the IL-8 assay. There are two reasons why variable recovery is unlikely to be a major factor in our results. Firstly, by collecting whole gut lavage, any intestinal secretions present, including bile, intestinal enzymes and mucus, which are found in the controls, this still shows statistically significant differences for the lavage fluid proteins.

In summary, we believe that the IL-8 is a highly sensitive marker of intestinal inflammation in children with cystic fibrosis. The source of the IL-8 is the mucosa and not the stool. If a stool sample is taken, the IL-8 concentrations in polyethylene glycol should be measured.


3 We also showed eosinophilic cationic protein to be raised in children with cystic fibrosis. With α1 antitrypsin, this is relatively stable in faeces at room temperature (approximately 21% loss over 24 hours). This loss would be considerably lower during whole gut lavage. Thus, degradation would be unlikely to explain this difference.

Lucrative puncure should not be performed in meningococcal disease

Editor,—I was dismayed to see your publication of the letter by Dr Sam regarding the role of lumbar puncture in meningococcal disease.1 While fully understanding the need to get as much information as possible, the benefits of isolating the causative organism need to be weighed against the risk of causing benefit of isolating the causative organism. It is generally accepted that throat swabs should not be taken from children with epiglottitis until the child's airway has been protected, because of the risk of clinical deterioration. It is time that textbooks of emergency paediatrics stated clearly that lumbar punctures on children with a haemorrhagic rash, and clinical signs of meningococcal meningitis should not be carried out until the clinical condition has been stabilised, and only if the procedure will add further valuable information that cannot be obtained elsewhere.

SIMON NADEL
Consultant in Paediatric Intensive Care, St Mary's Hospital, London, UK
s.nadel@ic.ac.uk

Lumbar puncture should not be performed in meningococcal disease

Editor,—I was dismayed to see your publication of the letter by Dr Sam regarding the role of lumbar puncture in meningococcal disease.1 While fully understanding the need to get as much information as possible, the benefits of isolating the causative organism need to be weighed against the risk of causing clinical deterioration in a patient who may have carcinogenic compromise and increased intracranial pressure, both of which are recognised contraindications to lumbar puncture.2 There are clear and recognised risks of performing the procedure in such patients. The potential benefits of lumbar puncture include making a diagnosis of meningitis and isolation of the organism for epidemiological and sensitivity testing. In the UK the typical haemorrhagic rash of meningococcal infection is pathognomonic of the disease and should be treated as such prospectively, until further confirmatory evidence is available. With polymerase chain reaction (PCR) of meningococcal DNA in blood allowing up to 100% sensitivity for diagnosis in the first 24 hours of illness,3 there is little to be gained from looking for bacteria or cells in the cerebrospinal fluid (CSF).

The antibiotic regimen is no different for either meningococcal meningitis or septicaemia, with seven days of a third generation cephalosporin being the treatment of choice because of improved CSF penetration.4 There are no reports of meningococcal resistance to this treatment in the UK, so performance of a lumbar puncture for bacterial sensitivity testing appears to be unnecessary.

Prospective therapy while awaiting results of culture or PCR from blood seems to be a small price to pay in this life threatening illness. An analogy could be drawn from the management of epiglottitis. It is generally accepted that throat swabs should not be taken from children with epiglottitis until the child’s airway has been protected, because of the risk of clinical deterioration. It is time that textbooks of emergency paediatrics stated clearly that lumbar punctures on children with a haemorrhagic rash, and clinical signs of meningococcal meningitis should not be carried out until the clinical condition has been stabilised, and only if the procedure will add further valuable information that cannot be obtained elsewhere.

SIMON NADEL
Consultant in Paediatric Intensive Care, St Mary’s Hospital, London, UK
s.nadel@ic.ac.uk

Prophylaxis for respiratory syncytial virus infection: missing the target

Editor,—Two recent reports about hospitalisation for respiratory syncytial virus (RSV) infection in high risk infants1 2 have suggested that the introduction of prophylaxis may, potentially, be beneficial in certain subgroups. We would like to emphasise that the “bigger picture” also warrants further consideration.

During the winters of 1998–99 and 1999–2000, we recorded our admissions who were RSV positive and had a Cambridge “CB” post code. “At risk” infants—that is, pretermers under 6 months of age, or those with bronchopulmonary dysplasia (BPD) under two years, were identified from the records of the maternity and neonatal units serving our postal region. The total cost for admission was calculated using length of stay on the ward at £255 (appendix $380) and in the intensive care unit (bed day cost of £1136 (appendix $1700)). The potential cost of prophylaxis in the community was also estimated (see table). In the CB post code population, the RSV related admission rate (95% CI) from our under 6 month old population was in the range of 19–41 per 1000 (denominator estimated from the number of live births with a CB post code; personal communication with A Sneeped, Office for National Statistics, London). In the ex-preterm infants who were under 6 months the proportion admitted during the two winters (1998–1999 and 1999–2000) was 5/51 (9.8%, 95% CI 3.3 to 21.4%) and 4/62 (6.5%, 1.8 to 15.7%) respectively. Supposedly “low risk” infants accounted for 92% (66/72) and 90% (54/60) of our RSV related admissions for each winter. There were no deaths in any of the admissions including the two with BPD.

In the first winter, 10 intensive care bed days were needed, none in the “high risk” population. In the second winter, such infants used 12 out of 54 intensive care bed days. Finally, inpatient costs for RSV in “high risk” infants was about 10% and 15% of total RSV related hospital costs for the two winters respectively (see table). Taken together, even if there were potential savings following the introduction of prophylaxis to specific subgroups, a target population—arguably equally in need of protection—is being overlooked. In fact, in our area, the potential effect of introducing prophylaxis would be no more than double hospital authority costs for RSV, with little impact on our so called “low risk” more major caseload.


Hajj and risk of blood borne infections

Editor,—Annually, some two and a half million pilgrims congregate in the city of Mecca in Saudi Arabia to perform the Hajj (pilgrimage), a religious duty for all adult Muslims who are physically and financially able. Because of the very large numbers of peoples from disparate regions, and the hostile climate of the Arabian Desert, the chances of disease are high. Heat exhaustion, sunstroke, and infectious diseases such as pneumonia and meningitis have traditionally caused the greatest disease burden.1

One of the rites of the Hajj is for males to shave their heads, although trimming the hair is also acceptable. Most will choose the former, often in makeshift centres run by opportunistic barbers. A razor blade is commonly used, and may be used on several scalps before ultimately being discarded. The risks of blood borne infections such as HIV and hepatitis B and C are obvious, especially considering that many pilgrims come from regions of the world where such infections are endemic.2 Pilgrims should be aware of the potential dangers and be educated to insist on the use of a new blade. We would also strongly recommend that they be vaccinated against hepatitis B.

AR GATRAD
A SHEIKH
Manor Hospital, Mian Road, Walsall WS2 9PS, UK
A R GATRAD
A SHEIKH
Manor Hospital, Mian Road, Walsall WS2 9PS, UK

Table 1 Potential cost of prophylaxis in the community

<table>
<thead>
<tr>
<th>Year</th>
<th>“Low risk” infants</th>
<th>“High risk” infants</th>
<th>Prophylaxis costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>1998–1999</td>
<td>93940</td>
<td>10455</td>
<td>131440</td>
</tr>
<tr>
<td>1999–2000</td>
<td>97692</td>
<td>15162</td>
<td>16120</td>
</tr>
</tbody>
</table>

£1 equals approximately $1.5 (November 2000).

Intestinal inflammation in cystic fibrosis

N M CROFT, R L SMYTH, U O'HEA and T G MARSHALL

Arch Dis Child 2001 84: 373
doi: 10.1136/adc.84.4.373e

Updated information and services can be found at:
http://adc.bmj.com/content/84/4/373.6

These include:

References
This article cites 6 articles, 1 of which you can access for free at:
http://adc.bmj.com/content/84/4/373.6#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/