**LETTERS TO THE EDITOR**

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

**Editor,—**Familial haemophagocytic lymphohistiocytosis (FHL) is a lethal disease with an unpredictable clinical course. The haemophagocytic syndromes and visceral leishmaniasis are closely related and have many points in common.2–3 We report the case of a 16 month old boy, BL, who presented with fever, pallor, hepatosplenomegaly, and pancytopenia, initially diagnosed as having acute myeloid leukaemia, but subsequently proven to have familial haemophagocytic lymphohistiocytosis. 

**Table 1 Patient characteristics**

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<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>7</td>
<td>12</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>1</td>
<td>1</td>
</tr>
<tr>
<td>Interval between appearance of symptoms and diagnosis (weeks)</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
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<td>6</td>
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</tr>
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LDH = lactate dehydrogenase

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**Visceral leishmaniasis: also beware of these deceptive microbes in non-endemic countries!**

**Editor,—**We read with interest the report by Grech et al.1 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, anaemia, 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.
I have explored the validity of this assay for use in supernatants of faecal homogenates in children with cystic fibrosis and found it wanting. Recovery of a 500 pg/ml spike of IL-8 progressively increased from 41% in samples which were a 12-fold dilution of faeces to 180% in samples which were a 120,000-fold dilution of faeces, when used according to manufacturer’s instructions. Pre-diluting the samples 50/50 in newborn calf serum, and using cell culture supernatants for further dilutions gave this assay (R&D catalogue no DB8000) mean (SD) spike recovery of 92.1 (12.5%) and coefficients of variation of 3.46% (intra-assay) and 6.85% (interassay).

Without knowledge of the IL-8-ELISA validation data of Smyth et al, I assume that this assay returns similarly spuriously high IL-8 concentrations in polyethylene glycol based whole gut lavage fluid to my 120,000-fold dilution faecal supernatant. The absence of a significant difference between CF patients and controls in their α1 antitrypsin outputs suggests that intestinal inflammation was not present in the CF patients. Overestimation of the WGLF IL-8 concentration would explain the apparently implausibly large volumes of swallowed sputum that the authors estimate would be required to account for their findings. In this study which could not turn off the mucociliary escalator, but did dramatically increase the rate of intestinal transit and exclude exogenous pancreatic enzymes, swallowed sputum is the most likely explanation for the results.

Letters to the editor

Intestinal inflammation in cystic fibrosis

EDITOR,—Following their studies of whole gut lavage fluid, Smyth et al have suggested that a non-idiopathic intestinal inflammation occurs constitutively in patients with cystic fibrosis (CF), as a consequence of a proinflammatory effect of the patient’s CFTF mutations. They reported marginally elevated excretion of IgG, IgM, interleukin 1 (IL-1), neutrophil elastase, and eosinophil cationic protein, and much more significant increase in excretion of IL-8 and albumin, but no increase in excretion of α1 antitrypsin or IgA. In this study where lavage fluid was administered continuously, and intestinal effluent was collected in discrete samples, pooling of the effluent before analysis would have allowed small differences in calculated inflammatory marker outputs to be interpreted as representative of gastrointestinal output. Of all the inflammatory markers presented, only IL-8 shows a range of cytokine outputs in CF patients with or without fibro-mucosal abnormalities which did not extend into the range seen in controls, in these non-parametric datasets. The author’s evidence for intestinal inflammation therefore relies heavily on the validity of their IL-8 Quantikine assay (R&D Minneapolis) protocol.

Dr Grech comments:

The development of visceral leishmaniasis after travel to endemic countries is not a new facet of this problem. At the time of writing, a Medline search using the key words visceral leishmaniasis and Malta yields 16 papers. Of these, almost a third (n=5) deal with patients who colonised Malta and contracted the disease.1,2

2 Herwaldt B. Leishmaniasis.

V GRECH
Paediatric Department, St Luke’s Hospital, Guardamangia, Malta

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. While it is understandable that one is not able 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 cerebrovascular compromise and raised intracranial pressure, both of which are recognised contraindications to lumbar puncture.

There are clear and recognised performances of 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 a clear diagnosis has been obtained.

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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 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. In the CB post code population, the RSV related admission rate (95% CI) from our under 6 month old population was in the range 19–41 per 1000 (denominator estimated from the number of live births with a CB post code; personal communication with A Sneddon, Office for National Statistics, London). In the pre-ex pertrem infants who were under 6 months the proportion admitted during the two winters (1998–99 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 more than double hospital authority costs for RSV, with little impact on our so-called “low risk” more major caseload.

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PHILIP DEBENHAM
ROBERT TASKER
Department of Paediatrics, University of Cambridge Clinical School, Addenbrooke’s Hospital, Hills Road, Cambridge CB2 2QG, UK

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 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.

2 Fearon C, Mohammed MH, Strickland GT. The role of parental antischistosomal therapy in the spread of hepatitis C virus in Egypt. Lance

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>1998–99</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.)
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