Letters to the Editor

Histological criteria for childhood coeliac disease

I am writing to confirm the findings by Dr MN Marsh on high mitotic indices in small intestinal mucosal biopsy of patients with gluten-sensitive enteropathy.

I would like to emphasise that in our series a high mitotic index has been one of the most useful pointers in differentiating coeliac disease from other causes of “flat mucosa,” including that of cow’s milk intolerance. The three important morphological criteria used by us in childhood coeliac disease are as follows: (a) a flat mucosa with elongated crypts (the latter is absent in most cases of cow’s milk intolerance), giving the mucosa an appearance of a normal or occasionally increased thickness (>550 μm); (b) infiltration of the surface enterocytes by an increased number of lymphocytes (emperipolesis) and a mitotic index of the lymphocytes of greater than 0.3%; (c) abnormal fat absorption pattern, characterised by accumulation of fat blobs in the supranuclear spaces of the surface enterocytes, which is easily detected by any special fat stain.

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Reference


The in vitro responses of Bacteroides fragilis to Moxalactam, Cefotaxime, Cefmetazole, Josamycin and erythromycin

Although the sensitivity of Bacteroides fragilis to Moxalactam, Cefotaxime, Cefmetazole, Josamycin and erythromycin has been described little has been reported about the bactericidal effect of these antibiotics against this organism. Such an effect may be of considerable importance when the treatment of highly susceptible patients—such as the immunosuppressed—is being considered. Furthermore, little is known about the in vitro and in vivo acquisition of resistance of B fragilis to these drugs. The results of our observations may, therefore, be of interest.

We have studied the susceptibility of two clinically isolated strains of B fragilis ss fragilis (strains A and B) and one of B fragilis ss vulgatus (strain C) to Moxalactam, Cefotaxime, Cefmetazole, Josamycin and erythromycin. Tubes of brucella-enriched broth medium containing serial dilutions of the various antimicrobial drugs were inoculated with approximately 10³ CFU/ml of the strains under test. Anaerobic incubation at 35°C was carried out for 24 h. Subcultures were made using a standard loop, to blood agar. The minimum inhibitory concentration (MIC) was defined as the minimum antibiotic concentration preventing bacterial growth detectable by the naked eye after 24 h incubation. The minimum bactericidal concentration (MBC) was arbitrarily defined as the minimum concentration of the drug producing a 99.9% reduction of the inoculum.

The MIC and MBC values for Moxalactam, Cefotaxime, Cefmetazole, Josamycin and erythromycin against the three strains of Bacteroides tested are shown in the Table. Cefotaxime showed poor activity against the three strains when compared with the other four drugs. Moxalactam, Cefotaxime and Cefmetazole were bactericidal at concentrations equal to or only slightly higher than their inhibitory values. Although sterilisation of the cultures was not achieved—even with concentrations 30-500 times higher than the particular MIC—the average reduction was from 10⁷ CFU/ml to 10³ CFU/ml. The effect of Josamycin and erythromycin was entirely bacteriostatic failing to reduce the initial inoculum at concentrations 30-100 times higher than their MICs.

Resistance to the antibiotics studied was not induced in the Bacteroides strains following a single exposure at concentrations below, equal to, or above the MICs. Resistance following a single exposure, although uncommon, has been shown to occur with clindamycin and in Bacteroides isolated from faeces of patients receiving this drug.

In summary, considerable bactericidal activity against B fragilis has been demonstrated by Moxalactam, Cefotaxime and Cefmetazole although each drug produced “persisters”; these are defined as (bacterial) cells which survive exposure to ostensibly lethal concentrations of bactericidal antibiotics but whose progeny remain fully sensitive to the drug. B fragilis organisms demonstrating such phenotype resistance may play an important part in

### Table: Minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of five antimicrobials against Bacteroides fragilis (mg/l)

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Moxalactam</th>
<th>Cefotaxime</th>
<th>Cefmetazole</th>
<th>Josamycin</th>
<th>Erythromycin</th>
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<tbody>
<tr>
<td>MIC</td>
<td>MBC</td>
<td>MIC</td>
<td>MBC</td>
<td>MIC</td>
<td>MBC</td>
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<td>64</td>
<td>256</td>
<td>4</td>
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<tr>
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<td>2</td>
<td>32</td>
<td>256</td>
<td>4</td>
</tr>
<tr>
<td>B fragilis C</td>
<td>2</td>
<td>4</td>
<td>32</td>
<td>512</td>
<td>4</td>
</tr>
</tbody>
</table>

Technical method

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