Low incidence of rifampicin-resistant tubercle bacilli

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ABSTRACT  In a six-year survey 10 (0.15%) of 6849 patients with European names and 31 (1.0%) of 3079 patients with non-European names yielded cultures of Mycobacterium tuberculosis that were resistant to rifampicin. Only two of each group had organisms resistant to rifampicin alone. Resistance to one or more other antituberculous drugs was found in eight of the European and 29 of the non-European group. Two patients in each group were known to have received treatment for the first time in the United Kingdom; 17 of the non-Europeans were known to have been treated abroad; precise information was not available for the other 12. The overall six-year incidence of patients with rifampicin-resistant Mycobacterium tuberculosis was only 0.41%. The very low incidence among Europeans is probably the result of stricter regimens than are possible in some other areas.

All cultures of Mycobacterium tuberculosis received and identified in this laboratory since the beginning of 1975 have been tested for sensitivity to rifampicin as well as other antituberculous drugs. Experience suggested that resistance to rifampicin was uncommon and confined to certain groups of patients. We thought therefore that a retrospective analysis of the results obtained over a period of six years might be informative.

Methods

From 1 January 1975 to 31 December 1980 cultures were received from 9928 patients who were new to the laboratory register. Of these patients 6849 (69%) had European names; the remaining 3079 (31%) had Asian, Middle Eastern, or African names and included recent immigrants and visitors. When resistance was found, information about treatment was sought and, when available, was kindly provided by the physicians and microbiologists concerned.

Cultures were tested by the modal resistance method1 2 using Lowenstein Jensen medium. In this method the minimal inhibitory concentration of the drug for each strain is compared with that of the modal average of a group of recently isolated and known sensitive strains to give the resistance ratio. If this ratio is 1 or 2 the test strain is reported as sensitive. If it is 4 or more the strain is reported as resistant.

Tests were repeated on all cultures found to be resistant when first examined. More than one culture was examined from most patients over the six years.

Results

Ten out of 6849 (0.15%) patients with European names and 31 out of 3079 (1.0%) with non-European names had rifampicin-resistant strains of M tuberculosis, the overall resistance rate in the 9928 patients being 0.41%. Eight patients in the European group and 29 in the non-European group were resistant to at least one other drug (table 1). Only two of the non-European patients with rifampicin-resistant strains were known to have been treated in the United Kingdom, but all 10 of the European group were (table 2).

Table 1  Resistance of Mycobacterium tuberculosis to rifampicin and other drugs, 1975–80

<table>
<thead>
<tr>
<th>Drugs to which resistance shown</th>
<th>Patients with resistance shown</th>
<th>European names</th>
<th>Non-European names</th>
<th>All patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rifampicin alone</td>
<td>2</td>
<td>2</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Rifampicin and other drug</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>Rifampicin and two or more other drugs</td>
<td>3</td>
<td>21</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>31</td>
<td>41</td>
<td></td>
</tr>
</tbody>
</table>

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Table 2. Number of patients with rifampicin-resistant Mycobacterium tuberculosis treated in the United Kingdom and elsewhere

<table>
<thead>
<tr>
<th>Where treated</th>
<th>Patients with rifampicin-resistant bacilli</th>
<th>European names</th>
<th>non-European names</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>10</td>
<td>2*</td>
<td>8</td>
</tr>
<tr>
<td>Other countries</td>
<td>0</td>
<td>17</td>
<td>9</td>
</tr>
<tr>
<td>Not known</td>
<td>0</td>
<td>12</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>10</td>
<td>31</td>
<td>17</td>
</tr>
</tbody>
</table>

*Both had been treated with rifampicin and other antituberculous drugs before arriving in Britain, but resistance to rifampicin developed during treatment here.

Discussion

These results confirm the low incidence of rifampicin-resistant strains of M. tuberculosis. The overall figure of 0.41% over the six years compares well with the 0.3% obtained by Kapanoff et al from 3146 patients in the United States who showed primary resistance. The information we received did not enable us to determine which of our patients had primary resistance (no previous treatment) and which had initial resistance (when first tested). Only four, two Europeans and two non-Europeans, had bacilli that became resistant between 1975 and 1980; no pretreatment results were available for the other patients. In Poland Janowiec et al* found no primary resistance to rifampicin among 509 patients tested from 1974 to 1977. Macdonald* found no cases of primary resistance in cultures from 84 patients with tuberculosis who lived in Wales, but reported 66 cases of acquired resistance.

The difference between the numbers of rifampicin-resistant cultures from patients with European names and from patients with non-European names is striking. Kapanoff et al also found more resistance among non-Europeans (though our results cannot properly be compared with theirs); their highest resistance rate, 20.7%, was among Asians and the lowest, 5.8%, among white patients.

Only two patients in the European group acquired resistance during the period of the survey. Both had been treated with isoniazid and ethambutol, and both yielded isoniazid-resistant as well as rifampicin-resistant organisms. Both patients were described by their physicians as "non-compliant." The two patients with non-European names who acquired their resistance in Britain arrived with histories of treatment with several drugs, including rifampicin. One had tubercle bacilli that were resistant to streptomycin and isoniazid; the other had organisms resistant to streptomycin, isoniazid, p-aminosalicylic acid, and ethambutol. Both were treated in Britain with several drugs, including rifampicin, and resistance emerged within a year.

Resistance to rifampicin was accompanied by resistance to one or more other drugs in all but two cultures from both the European and the non-European group. Siddiqi et al.,* writing from Pakistan, examined cultures from 1063 patients and found that all of the 21 that were resistant to rifampicin were also resistant to isoniazid, and 17 of them were resistant to other antituberculous agents as well. A further 34 strains, obtained from the United States, were resistant to both rifampicin and isoniazid. Thus resistance to rifampicin alone appears to be uncommon. Nineteen of the 31 patients with non-European names and rifampicin-resistant organisms (Table 2) had a history of treatment with rifampicin and other antituberculous drugs before they arrived in the United Kingdom. Precise information about the other 12 was lacking, but as they were visitors or recent immigrants we may assume that they had been treated outside Europe.

These results confirm opinions expressed by physicians that successful treatment with rifampicin, as with other drugs, is associated with strict regimens and the prevention of self-medication. This is possible in developed countries, but often very difficult to achieve in the third world.

We thank the physicians and microbiologists who supplied information about treatment of patients, and Lepetit Pharmaceuticals for the rifampicin used in the tests.

References