The rise and fall of *Escherichia coli* O15 in a London Teaching Hospital

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Summary. A marked increase in the prevalence of bacteraemia due to *Escherichia coli* of serogroup O15 was noted during November and December 1986 at Charing Cross Hospital. This multiresistant strain had been reported by several hospitals in south London. All isolates of *E. coli* from patients with bacteraemia between October 1986 and the end of September 1988 were assessed for the presence of the O15 antigen and for the unusual pattern of resistance to six antimicrobial agents. As a guide to faecal carriage, isolates from urine were similarly assessed during seven 4-week periods between January 1987 and June 1988. Of the 123 *E. coli* isolates from blood, 25 (20%) were serogroup O15 and 20 of these expressed the same pattern of multiresistance; 17 of these multiresistant isolates occurred in the 4-month period 1 Nov. 1986–28 Feb. 1987. During the remaining 19 months of the study only eight isolates were serogroup O15 of which only three were multiresistant. In the first 4-week period that urine isolates were studied 21 Jan. 1987–17 Feb. 1987, 26 (13.2%) of the 195 isolates were serogroup O15 of which 20 were multiresistant. The proportion of serogroup O15 isolates fell gradually until, in June 1988, the last period studied, only 8 (4.2%) of the 189 isolates were serogroup O15, of which only one was multiresistant. In a preliminary study of plasmids in six serogroup O15 isolates from blood, three multiresistant isolates and one that was sensitive to chloramphenicol appeared to carry a similar plasmid of c. 100 Mda. A strain that expressed the multiresistance pattern except for tetracycline sensitivity carried four plasmids, the largest of which was c. 70 Mda. No plasmids were found in the one fully sensitive strain studied.

Introduction

During November and December 1986 we noticed a marked increase in the number of cases of septicaemia with *Escherichia coli* isolated from blood cultures at Charing Cross Hospital. Following the report of an outbreak in London of infection caused by a strain of *E. coli* serogroup O15 resistant to ampicillin, streptomycin, tetracycline, sulphamethoxazole, trimethoprim and chloramphenicol,1 we examined the antibiotic resistance patterns and O-serogroups of our *E. coli* isolates from blood cultures.

The increase in septicaemia appeared to reflect an increased rate of isolation of multiresistant *E. coli* O15; therefore, we decided to monitor the prevalence of this strain in our blood cultures. Because the numbers of blood cultures are small in relation to the total specimen throughput, and because strains generally cause urinary tract infec-

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Characterisation of bacteria

All isolates were identified by standard biochemical tests\(^3\) or by API 20E (API-bioMerieux, Basingstoke). O-serogrouping was done as described previously\(^4\) with antisera against 14 of the most common O-serogroups (1, 2, 4, 5, 7, 8, 9, 11, 15, 17, 18, 25, 75). Antibiotic sensitivities were determined by the Stokes method on DST agar (Oxoid; CM 261) with Oxoid disks containing (\(\mu g\)) ampicillin 10, chloramphenicol 10, streptomycin 10, sulphamethoxazole 25, tetracycline 10 and trimethoprim 1.25 and with \(E.\ coli\) NCTC 10418 as control; isolates resistant to all six antibiotics will be referred to as 'multiresistant'.

Plasmid carriage

The carriage of plasmids by six \(E.\ coli\) O15 isolates with various antibiotic sensitivities was assessed by agarose gel electrophoresis of lysed cells prepared by a method based on that of Kado and Liu.\(^5\)

Results

Blood-culture isolates

The numbers of non-duplicate blood culture isolates of \(E.\ coli\) for each month from October 1985 to September 1988 are shown in fig. 1; for several years before this period there were no more than seven isolates in any one month. The isolates before October 1986 and two from the beginning of that month were no longer available for serogrouping. However, none of 100 isolates, randomly collected between 1984 and 1986 for another purpose, was of serogroup O15.\(^6\)

The 123 isolates of \(E.\ coli\) from blood cultures collected between October 1986 and September 1988 were examined for O-serogroup and multiresistance. During this period, 25 (20\%) of the isolates were serogroup O15, of which 20 (16-3\% of total) expressed the multiresistance pattern described. However, 17 of the isolates, all multiresistant, were obtained in the 4-month period 1 Nov. 1986–28 Feb. 1987 (fig. 1). During the remaining 19 months of the study, only eight isolates were serogroup O15 and only three were multiresistant. The O-serogroup and sensitivity patterns of all isolates are summarised in table I. Eight isolates that were not serogroup O15 were resistant to all six antibiotics; four were non-typable, three autoagglutinated, and one was serogroup O6.

In 11 of the 20 patients (12 female, 8 male) with the multi resistant O15 strain in their blood, the septicaemia followed a clinical diagnosis of urinary tract infection. In the other nine patients, clinical diagnoses were: acute orchitis, chronic lymphocytic leukaemia, non-Hodgkins lymphoma, carcinoma

![Fig. 1. Monthly incidence of \(E.\ coli\) bacteraemia at Charing Cross Hospital from October 1985 to September 1988: serogroup O15 multiresistant (■), O15 not multiresistant (□), other O-serogroups (□□), serogroup not known (□).](image-url)

of the cervix and meningitis following a surgical operation in a boy with medulloblastoma. Four patients had pyrexia of unknown origin. Twelve of the patients were aged over 60 years and six were over 80 years old.

Urine isolates

Isolates were collected during five consecutive 4-week periods from 21 Jan. 1987 to 9 June 1987 and two further 4-week periods from 31 Dec. 1987 to 27 Jan. 1988 and from 6 June 1988 to 4 July 1988. The prevalence of serogroup O15 isolates for each 4-week period is shown in fig. 2.

During the first 4-week period, 26 (13.3%) of the 195 isolates were serogroup O15, of which 20 expressed multiple resistance; this was considerably more than the three serogroup-O15 isolates among 400 urinary isolates collected up to August 1986. The prevalence of serogroup O15 fell from January to May 1987, but then rose again in late May to June. By January 1988 the prevalence of serogroup O15 had fallen to 7%, of which only 2% were multiresistant. In June 1988 the percentage of serogroup O15 had fallen again to 4.2% with only 0.5% resistant to all six antibiotics. Thus, the prevalence of the multiresistant strain of serogroup O15 in the urine followed a similar pattern to that in the blood cultures, but over a longer period.

The O-serogroup and sensitivity patterns of all 1286 urinary isolates are shown in table II. Of these isolates, 115 (8.9%) were serogroup O15 and 74 (5.7% of total) were multiresistant. Among the 13 other O-serogroups examined, only O6 occurred more frequently (12.9% of the total isolates). Multiresistance was found more widely among the various serogroups from urine but less frequently than in the blood.

Although we were unable to conduct an epidemiological survey, we noted that about half the multiresistant serogroup O15 strains were from patients in the community where they are likely to have been acquired. An analysis of the patients' home addresses reflected the catchment area of the hospital rather than any geographical clustering and patients living north and south of the River Thames were affected.

Plasmid carriage

The result of agarose gel electrophoresis of plasmids released from six serogroup O15 strains and two control strains is shown in fig. 3. Tracks 1 and 10 are from a control strain of E. coli known not to contain any plasmids and tracks 2 and 9 are
Fig. 3. Agarose gel electrophoresis of plasmids released from *E. coli* strains. Tracks 1 and 10: control strain of *E. coli* with no plasmids; 2 and 9: plasmids of mol. wt. standard strain, *E. coli* NCTC 50192; 3 and 6: serogroup O15 isolates with the multiresistance pattern except for sensitivity to tetracycline and chloramphenicol respectively; 4, 5 and 8: multiresistant serogroup O15 isolates; 7: fully sensitive serogroup O15 isolate.

Table II. O-serogroup and multiresistance of isolates from urine

<table>
<thead>
<tr>
<th>O-serogroup</th>
<th>Number (%) of isolates</th>
<th>Number (%) of total multiresistant</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>46 (3.6)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>2</td>
<td>76 (5.9)</td>
<td>4 (0.3)</td>
</tr>
<tr>
<td>4</td>
<td>67 (5.2)</td>
<td>3 (0.2)</td>
</tr>
<tr>
<td>5</td>
<td>1 (0.1)</td>
<td>...</td>
</tr>
<tr>
<td>6</td>
<td>166 (12.9)</td>
<td>...</td>
</tr>
<tr>
<td>7</td>
<td>23 (1.8)</td>
<td>...</td>
</tr>
<tr>
<td>8</td>
<td>27 (2.1)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>9</td>
<td>7 (0.5)</td>
<td>...</td>
</tr>
<tr>
<td>11</td>
<td>9 (0.7)</td>
<td>...</td>
</tr>
<tr>
<td>15</td>
<td>115 (8.9)</td>
<td>74 (5.7)</td>
</tr>
<tr>
<td>17</td>
<td>12 (0.9)</td>
<td>...</td>
</tr>
<tr>
<td>18</td>
<td>53 (4.1)</td>
<td>...</td>
</tr>
<tr>
<td>25</td>
<td>44 (3.5)</td>
<td>2 (0.2)</td>
</tr>
<tr>
<td>75</td>
<td>73 (5.7)</td>
<td>1 (0.1)</td>
</tr>
<tr>
<td>NT</td>
<td>364 (28.3)</td>
<td>29 (2.3)</td>
</tr>
<tr>
<td>AA</td>
<td>203 (15.8)</td>
<td>17 (1.3)</td>
</tr>
<tr>
<td>Total</td>
<td>1286 (100)</td>
<td>133 (10.3)</td>
</tr>
</tbody>
</table>

See footnotes to table I.

Discussion

Several hospitals in south London have reported an outbreak of septicaemia mainly affecting the elderly, frequently associated with infections of the urinary tract, and caused by a virulent strain of *E. coli* serogroup O15 with a characteristic resistance pattern.9 Such strains were not found in the Bristol area.9 We also observed such an epidemic in our district, which straddles the Thames, from November 1986 to February 1987. Some of the infections occurred in patients resident north of the Thames. It was important to establish the occurrence of the strain in the normal population. Clearly, the prevalence in the faecal flora of hospital in-patients or in faecal samples routinely submitted for examination by general practitioners cannot be regarded as normal. As urinary tract infections are generally caused by the predominant serogroup in the patient's faecal flora in proportion to the occurrence of the serogroup in the normal population,2 we considered that the prevalence of the strain in urinary isolates was a better indication of normal faecal carriage. We found the epidemic strain initially to be present more frequently than would have been expected from its prevalence before August 19866 but to have reverted now to former levels.

In our previous studies of *E. coli* strains from urine, blood or faeces4, 6, 10–12 none of the most common O-serogroups (6, 18 and 75) accounted for more than 12.2% of total isolates, whereas serogroup O15 accounted for almost 60% of the isolates from blood between November 1986 and January 1987 (fig. 1) and for over 13% of isolates from urine between 21 Jan. 1987 and 17 Feb. 1987. Because this study was done as a result of an observed increase in blood-culture isolates, statistical comparisons are clearly invalid but the results of the prospective study of urinary isolates can be compared statistically with previous findings. The increased prevalence of all serogroup O15 strains—
115 (8.9%) of the 1286 urine isolates—compared to that found previously—3 (<1%) of 400—was highly significant ($\chi^2$ with Yates's correction = 30.214, $p < 0.001$). It is interesting that the prevalence of serogroup O15 strains without the multiresistance pattern—41 (3.2%)—was also significantly increased ($\chi^2 = 6.209, p < 0.025$).

The origin of this epidemic strain remains obscure but the unusual antimicrobial resistance pattern suggests that it may have arisen in veterinary practice. The distribution so far reported indicates that spread via food from farm animals is unlikely. With the Thames apparently providing some barrier to dissemination, this may have occurred through transient contamination of the drinking-water supply or, perhaps, via relatively free roaming domestic pets, such as cats and dogs, with little cross-river contact.

A likely explanation for the rapid increase in the prevalence of serogroup O15 isolates could be the acquisition of one or more plasmids specifying virulence factors. Resistance to antibiotics alone is unlikely to account for the increased virulence of this strain but two of the three multiresistant serogroup O15 strains examined appeared to contain only one plasmid (fig. 3; tracks 3 and 4) of c. 100 Mda, whereas the third had a plasmid of similar size and at least one smaller plasmid (track 8). If the common 100-Mda, plasmid determined the multiresistance and any other virulence factors responsible for the increased prevalence of this strain, then a change in sensitivity to one agent can be seen with little or no change in the plasmid (track 6) or with a major change (track 3). This observation and the fact, noted above, that the prevalence of serogroup O15 of all antibiotic sensitivity patterns has increased significantly, raises the possibility that chromosomal changes may also have played a part in the success of this strain. So far, we have studied too few strains from which to draw firm conclusions and we are currently assessing plasmid carriage in all the serogroup O15 strains as well as those isolates from other serogroups with the same multiresistance pattern.

REFERENCES