Increased treatment requirements of patients with cystic fibrosis who harbour a highly transmissible strain of *Pseudomonas aeruginosa*

A M Jones, M E Dodd, C J Doherty, J R W Govan, A K Webb

**Background**: A group of patients who harbour the same highly transmissible strain of *Pseudomonas aeruginosa* were identified at a cystic fibrosis (CF) centre. Isolates of this strain display a number of unusual phenotypic features including resistance to most typical antipseudomonal antibiotics. A study was undertaken to see if there was a difference in treatment requirements between CF patients with chronic infection with their own unique *P aeruginosa* strains (group 1) and those who harbour a highly transmissible strain (group 2).

**Methods**: Data on treatment requirements for the year 2000 were collected from the case records of CF patients with chronic *P aeruginosa* infection who had received inpatient treatment. Patients co-infected with *Burkholderia cepacia* or other highly transmissible strains of *P aeruginosa* were excluded.

**Results**: There were 2/56 and 3/22 deaths in groups 1 and 2, respectively; these patients were excluded from the analysis. No difference was found between the two groups for mean age, % predicted forced expiratory volume in 1 second (FEV1), % predicted forced vital capacity (FVC), and body mass index. Patients in group 2 had a greater median (range) number of intravenous antibiotic days (60 (17–216) v 33 (4–237) days; p=0.01), inpatient days (39 (7–183) v 16 (1–172) days; p<0.01), and inpatient episodes (3 (1–9) v 2 (1–6); p<0.01), and more respiratory exacerbations (mean (SD) 8.2 (3.4) v 6.1 (3.2); p<0.01).

**Conclusions**: Patients who harbour the highly transmissible *P aeruginosa* strain have a greater treatment burden than patients with CF who harbour their own unique strains. These findings support the need for microbiological surveillance for highly transmissible *P aeruginosa* and the implementation of infection control measures to prevent cross infection.
RESULTS
There were 56 patients (33 male) and 22 patients (10 male) in groups 1 and 2, respectively; two patients died in group 1 and three in group 2. A multiresistant P. aeruginosa isolate was identified in sputum samples on at least one occasion during the year 2000 for 28 (50%) of the 56 patients in group 1 and 20 (91%) of the 22 patients in group 2. There was no difference between the two groups in mean age, % predicted FEV1, % predicted FVC, and body mass index. There were, however, significant differences between the two groups in median number of days receiving intravenous antibiotics (p=0.01), outpatient episodes (p=0.005), inpatient days (p=0.003), and mean number of respiratory exacerbations (p=0.01; table 1).

DISCUSSION
This study has examined the differences in treatment requirements between patients with CF who have chronic P. aeruginosa infection with their own unique strains and those who harbour a highly transmissible strain. Patients who harbour the highly transmissible P. aeruginosa strain had more respiratory exacerbations and a greater requirement for intravenous antibiotics and inpatient treatment.

The emergence and spread of highly transmissible strains of P. aeruginosa is, at present, a topic of great concern and controversy among CF physicians. Isolates of highly transmissible strains may display unusual phenotypic features, including antibiotic resistance. Most (20/22) of the isolates from patients in group 2 were found to be multiresistant; however, P. aeruginosa strains from 50% (28/56) of the patients in group 1 were also found to exhibit antibiotic resistant phenotypes. Although the increased morbidity seen in patients in group 2 may be a reflection of the difficulty in treating a multiresistant strain, it is also possible that highly transmissible strains possess other properties that allow adaptation to and spread among CF patients, and which makes them more difficult to treat. We have previously described two “Pseudomonas naïve” patients who acquired initial infection with the highly transmissible P. aeruginosa strain. In both cases the recommended eradication regimes failed and the patients developed chronic infection. There are also reports of superinfection by a highly transmissible strain at another UK CF centre.

The two groups in the current study were well matched in terms of spirometric parameters and body mass index. However, it is still not clear whether infection by the highly transmissible strain is the cause of the increased treatment requirements or a marker for CF patients who require a high intensity of treatment. The contact density of cases may be important in determining the risk of cross infection, therefore highly transmissible strains may be more likely to spread among inpatients, selecting CF patients who already have increased treatment requirements. We therefore limited the patients in the study to those who have received inpatient treatment with intravenous antibiotics during the year 2000.

The CF Trust advocates surveillance for highly transmissible strains of P. aeruginosa. This study shows that there may be resource implications associated with spread of infection by multiresistant highly transmissible P. aeruginosa strains and an increased morbidity for the CF patient. These findings support the need for microbiological surveillance for P. aeruginosa cross infection and the implementation of cross infection control measures to limit spread of highly transmissible strains.

Table 1 Demographic data and treatment requirements of adult CF patients with chronic infection by unique (group 1) and highly transmissible strains (group 2) of P. aeruginosa

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group 1 (n=56)</th>
<th>Group 2 (n=22)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.6 (7.2)</td>
<td>26.6 (7.4)</td>
<td>NS</td>
</tr>
<tr>
<td>FEV1 (% pred)</td>
<td>55.1 (19.3)</td>
<td>54.9 (18.0)</td>
<td>NS</td>
</tr>
<tr>
<td>FVC (% pred)</td>
<td>75.4 (19.2)</td>
<td>75.3 (20.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index</td>
<td>21.2 (2.8)</td>
<td>20.6 (3.4)</td>
<td>NS</td>
</tr>
<tr>
<td>Outpatient episodes*</td>
<td>10 (2–26)</td>
<td>9.5 (3–32)</td>
<td>NS</td>
</tr>
<tr>
<td>Inpatient episodes*</td>
<td>2 (1–6)</td>
<td>3 (1–9)</td>
<td>0.005</td>
</tr>
<tr>
<td>IV antibiotic days*</td>
<td>16 (1–172)</td>
<td>39 (7–183)</td>
<td>0.003</td>
</tr>
<tr>
<td>Respiratory exacerbations*</td>
<td>33 (4–237)</td>
<td>60 (17–216)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

FEV1 = forced expiratory volume in 1 second; FVC = forced vital capacity.
Results expressed as mean (SD) or *median (range).

REFERENCES

Authors’ affiliations
A M Jones, M E Dodd, A K Webb, Bradbury Cystic Fibrosis Unit, South Manchester NHS Trust, Wythenshawe Hospital, Manchester M23 9LT, UK
C J Doherty, J R W Govan, Department of Medical Microbiology, University of Edinburgh, Edinburgh EH8 9AG, UK
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