

PostScript

LETTERS TO THE EDITOR

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Burkholderia infection and survival in CF

We read with interest the paper by Jones *et al*¹ indicating the experience of the Manchester Adult CF Unit in the survival of patients with cystic fibrosis (CF) in the first 5 years following chronic infection with the *B cepacia* complex (Bcc).

The authors appear to have shown that 31 patients with *B cenocepacia* had a worse prognosis than *Pseudomonas aeruginosa* infected patients. Despite the title of the paper, they had insufficient patients chronically infected with *B multivorans* to draw any similar conclusions. Although these are not new findings, we congratulate them on their attempt to throw light on a difficult topic within the microbiology of CF. However, there are several anomalies in the study that cause concern. Firstly, they state that the 5 year survival in the *B cenocepacia* group was 66.6%, yet the figure (which incidentally contains data for 7 years) clearly shows the rate to be around 30%. Also, table 2 states that 19 (of 31) of these patients (61%) died within the study period, a value that fits with neither of the two previous statements. Secondly, although there were significantly more deaths in the *B cenocepacia* group, these patients apparently did not have increased treatment requirements or diminution in spirometric parameters compared with the matched group. This implies deterioration in respiratory function that was rapid enough to not affect the statistical calculation, but that falls short of the "cepacia" syndrome, which seems unlikely. We wonder whether a different statistical method may have produced more meaningful results. Finally, the authors state in the discussion that the only other studies of outcome of Bcc infection are in CF patients following transplantation. We are surprised that they appear to be unaware of the well conducted study by Ledson *et al* from our unit, published in this journal in 2002,² which showed the outcome for 37 CF patients chronically infected with *B cenocepacia*, none of whom were listed for transplantation. This study used a more robust method of statistical analysis to show that *B cenocepacia* infected patients had an accelerated loss of

lung function with a fourfold increased risk of mortality and a trend towards worsening nutrition—results in keeping with those produced by the US CF Foundation.³

However, we do agree with the authors that further work needs to be done to assess the effect of infection by other genomovars (including *B multivorans*) on morbidity and mortality in patients with CF.

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References

- 1 Jones AM, Dodd ME, Govan JRW, *et al*. Burkholderia cenocepacia and Burkholderia multivorans: influence on survival in cystic fibrosis. *Thorax* 2004;59:948–51.
- 2 Ledson MJ, Gallagher MJ, Jackson M, *et al*. Outcome of Burkholderia cepacia colonisation in an adult cystic fibrosis centre. *Thorax* 2002;57:142–5.
- 3 Fitzsimmons S. The Cystic Fibrosis Foundation Patient Registry report 1996. *Pediatr Pulmonol* 1996;21:267–75.

Authors' reply

We thank Drs Ledson and Walshaw for their interest in our recent paper,¹ although we are not in agreement with some of their comments. They feel that there are anomalies for fig 1; they need to inspect it again more carefully. The survival for 1 year (12 months) and 5 years (60 months) is given in the table as 80% and 66%, as is represented in the figure. The timescale on the x axis in fig 1 is given in months. The data in the figure are not limited to 5 years as it contains survival data for patients throughout the entire study period. For some patients, data were available and are presented for over a decade rather than the 7 years suggested by Ledson and Walshaw.

As is clearly stated in the paper, the data for spirometry, body mass index and treatment requirements were, however, limited to 5 years from onset of infection. We collected annual spirometry figures from time of acquisition of infection. We did not demonstrate a significant difference in the decline in FEV₁ or FVC between the two groups of patients infected with *Burkholderia cenocepacia* and *Pseudomonas aeruginosa*, respectively, but we are unable to exclude the possibility that there may have been a large fall in spirometric parameters in the last few months before death in patients infected with *B cenocepacia*. If the rate of decline in spirometric data is linear, the use of linear regression—as suggested by Drs Ledson and Walshaw—would not significantly alter the findings. We note that they reported a linear rate of decline in their previous study.² We also observe that the study by Ledson *et al* did not match the patients for spirometry at baseline. The effect of the *B cepacia* complex (Bcc) on lung function and spirometry is complex and, as mentioned in our discussion, other studies have also shown a decreased survival among patients with Bcc without any demonstrable difference in lung function decline.^{3,4}

Drs Ledson and Walshaw have looked at survival at their own centre.² Although a relatively recent paper, they used the redundant term of *B cepacia* in their title rather than the *Burkholderia cepacia* complex which is the current nomenclature. It is accepted that infection with the ET12 *B cenocepacia* strain confers a clinical disadvantage, and many authors have reported their own experiences of a poor clinical outcome following infection over the past two decades. Our study was the first to compare survival between *P aeruginosa* infected patients and those with different Bcc genomovars (other than the papers discussed in our article that look at this after transplantation). It presents data to show that adults with cystic fibrosis (CF) infected with some Bcc genomovars have the same outcome as those infected with *P aeruginosa*. Our study has been supported by another recently published paper from the Belfast CF Centre.⁵

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References

- 1 Jones AM, Dodd ME, Govan JRW, *et al*. Burkholderia cenocepacia and Burkholderia multivorans: influence on survival in cystic fibrosis. *Thorax* 2004;59:948–51.
- 2 Ledson MJ, Gallagher MJ, Jackson M, *et al*. Outcome of Burkholderia cepacia colonisation in an adult cystic fibrosis centre. *Thorax* 2002;57:142–5.
- 3 Frangolias DD, Mahenthalingam E, Rae S, *et al*. Burkholderia cepacia in cystic fibrosis. Variable disease course. *Am J Respir Crit Care Med* 1999;160:1572–7.
- 4 Isles A, MacLusky I, Corey M, *et al*. Pseudomonas cepacia infection in cystic fibrosis: an emerging problem. *J Pediatr* 1984;104:206–10.
- 5 Courtney JM, Dunbar KEA, McDowell A, *et al*. Clinical outcome of Burkholderia cepacia complex infection in cystic fibrosis adults. *J Cystic Fibrosis* 2004;3:93–8.

CORRECTION

CARD 15 GENE MUTATIONS IN SARCOIDOSIS

The order of the authors of this letter which appeared on pages 354–355 of the April issue of *Thorax* was published incorrectly. The correct order is: L-P Ho, F Merlin, K Gaber, R J O Davies, A J McMichael, and J-P Hugot. The publishers apologise for the error.