

Burkholderia cepacia: another twist and a further threat

A K Webb, J R Govan

Patients with cystic fibrosis present a continuum of complex medical problems to their carers. It is for this reason that cystic fibrosis care is best delivered by a multidisciplinary team from recognised paediatric and adult cystic fibrosis centres. The consequences of this practice are that, over time, patients are better nourished with a slow decline in respiratory function.¹ The ultimate benefit of better care is increased survival.² Despite this greater knowledge and better management, cystic fibrosis as a disease repeatedly produces unpleasant novel management problems; the recent descriptions of a six fold increase in the incidence of digestive tract cancer and the remarkably high prevalence of osteoporosis are typical examples of the cystic fibrosis Pandora's box.^{3,4}

The current stigma of acquiring *Burkholderia cepacia* are both medical and social. The medical consequences of acquiring *B cepacia* may be accelerated lung disease, more intense treatment requirements, and doubt about suitability for transplantation due to a greater mortality following surgery with some strains.⁵ The social consequences are segregation from other patients with cystic fibrosis in hospital, in social settings, and a ban from attending cystic fibrosis conferences or holiday schemes. It is not surprising that patients with cystic fibrosis infected by *B cepacia* have felt isolated by their peers and have done their best to organise their own social groups.

The current strict infection control measures which are currently recommended to reduce *B cepacia* acquisition are restrictive enough but in this issue of *Thorax* Ledson *et al* describe further cross infection problems associated with this multi-resistant respiratory pathogen.^{6,7} The implications of the Liverpool findings require a considerable reappraisal of the current management of cross infection with *B cepacia*.

The first report describes a previously healthy mother who acquired *B cepacia* from her children with cystic fibrosis, as a result of which she has developed severe bronchiectasis with the potential to progress. This worrying observation is unique and somewhat undermines the absolute reassurance given to parents and non-cystic fibrosis siblings that cross infection of *B cepacia* from cystic fibrosis infected patients never occurs. In future it may be informative to test partners and close relatives of *B cepacia* positive patients in sufficiently large numbers to assess whether an immunological response takes place to this respiratory pathogen in normal individuals. However, this case report is very unusual and *B cepacia* has been present in the cystic fibrosis population for over a decade with no previous reports of infection with *B cepacia* occurring in the close companions of cystic fibrosis patients.

The second report by Ledson *et al* which describes cross infection of a second *B cepacia* (epidemic) strain between cystic fibrosis patients already infected by one *B cepacia* strain is of greater concern. It has considerable implications for cystic fibrosis patients infected with *B cepacia* and the centres which care for them.

For some years it has become increasingly evident that the transmissibility of *B cepacia* is strain dependent. Different groups in the UK and North America have found by different typing systems that the epidemic strain described in this paper has a strong transatlantic lineage^{8–11}; a clonal relationship between the UK patients (Edinburgh, Man-

chester and Liverpool) and the Canadian patients for this strain was first described in 1993.⁹ It should be appreciated that the cable pilus (so described for its length and intertwining properties) is not exclusive to this strain of *B cepacia*, neither does possession of the cable pilus gene alone explain transmission.^{8,11} Interestingly, this strain—known as the Edinburgh/Toronto lineage or ET 12 clone^{10,12}—is unusual in containing both the cable pilus gene and a conserved 1.4 kbp DNA fragment found in other epidemic strains and designated the “*B cepacia* epidemic strain marker” (BCESM).¹¹

The historical background to the *B cepacia* ET 12 strain and the issue of nomenclature for different strains of *B cepacia* have recently been extensively reviewed.¹² Isolates identified as *B cepacia* by present laboratory methods belong to a *B cepacia* complex of at least five distinct species; in the absence of easily identifiable markers and obeying taxonomic rules these are called genomovars. Isolates identified with the cepacia syndrome and epidemics tend to cluster in genomovar III; however, it is important to appreciate that transmissibility and virulence are independent factors. The *B cepacia* strain responsible for the first described UK case of the cepacia syndrome in a nine year old girl did not carry the cable pilus gene and did not transfer to her cystic fibrosis sibling.¹³

Although the clinical course of *B cepacia* is determined by the host-pathogen response and cannot be predicted, epidemic forms of *B cepacia* belonging to genomovar III may be more pathogenic due to a greater antibiotic resistance and its association with the lethal cepacia syndrome which three of the five Liverpool patients developed. Recognition of the spread of *B cepacia* led to the segregation of *B cepacia* infected (BC+) patients from non-infected patients (BC-) in cystic fibrosis centres. *B cepacia* positive patients are now segregated as inpatients, outpatients and socially. They have encouraged each other and expressed unhappiness at their isolation from the larger cystic fibrosis community. The disquieting report by Ledson *et al* suggests that this protective collectiveness may now be disrupted. They have shown that the epidemic ET 12 strain can be readily transmitted to patients with other strains of *B cepacia* with resulting lethal consequences for some patients. Their paper also raises the question of whether the presence of one *B cepacia* strain primes a patient for a potentially nastier clinical outcome if a second *B cepacia* strain can achieve colonisation. Is virulence enhanced by multiple strains of the same pathogen?

The maxim that cross infection of different strains of *B cepacia* between BC+ patients is uncommon can no longer be accepted in the light of this report and personal observations of similar instances also involving cross infection of ET 12 from other cystic fibrosis centres (A Greening and A K Webb). In our clinic some BC+ patients who are aware of an epidemic strain have asked to be seen separately from other BC+ patients.

Clearly there is a need for cystic fibrosis centres to review their current policy of the collective segregation of BC+ patients. Patients with cystic fibrosis infected with *B cepacia* may have to be segregated according to the particular defined strain of the organism, placing an even greater strain on limited clinic space, small numbers of cystic fibrosis personnel, and causing more hurt to this vulnerable

group of patients. Cross infection policies also apply as much to equipment as to personnel. Should there be separate lung function equipment for different *B cepacia* strains? Compressors may have to be carefully allocated to BC+ patients according to genomic typing. Optimum laboratory facilities for identification of *B cepacia*, for genomovar analysis, genomic finger printing, and identification of epidemic markers also need to be addressed as the organism can be difficult to culture and identify at a time when the taxonomy of members the *B cepacia* complex are under major review.^{12 14}

Previous carefully thought out guidelines need re-evaluation and revision to incorporate all the clinical and microbiological knowledge which has accrued over the last 3–4 years.

Correspondence to: Dr A K Webb.

Manchester Adult Cystic Fibrosis Unit,
Wythenshawe Hospital,
Southmoor Road,
South Manchester M23 9LT, UK

Department of Medical Microbiology,
University of Edinburgh,
Medical School,
Edinburgh EH8 9AG, UK

A K WEBB

J R GOVAN

- 1 Moorcroft J, Dodd M, Webb AK. Long-term change in exercise capacity, body mass and pulmonary function in adults with cystic fibrosis. *Chest* 1997;111:338–43.
- 2 Dodge JA, Morison S, Lewis PA. Incidence, population, and survival of cystic fibrosis in the UK, 1968–95. *Arch Dis Child* 1997;77:493–6.
- 3 Schoni MH, Maisonneuve P, Schoni-Affolter, et al. Cancer risk in patients with cystic fibrosis: the European data. *J R Soc Med* 1996;89(Suppl 27):38–43.
- 4 Bachrach LK, Loutit CW, Moss RB. Osteopenia in patients with cystic fibrosis. *Am J Med* 1994;96:27–34.
- 5 Webb AK, Egan J. Should patients infected with *Burkholderia cepacia* undergo lung transplantation. *Thorax* 1997;52:671–3.
- 6 Ledson MJ, Gallagher MJ, Walshaw MJ. Chronic *B cepacia* bronchiectasis in a non-cystic fibrosis individual. *Thorax* 1998;53:430–2.
- 7 Ledson MJ, Gallagher MJ, Corkhill JE, et al. Cross infection between cystic fibrosis patients colonised with *Burkholderia cepacia*. *Thorax* 1998;53:432–6.
- 8 Sun L, Jiang RZ, Steinbach S, et al. The emergence of a highly transmissible lineage of cbl+ *Burkholderia cepacia* causing cystic fibrosis centre epidemics in North America and Britain. *Nature Medicine* 1995;1:661–6.
- 9 Govan JW, Brown PH, Maddison J, et al. Evidence for spread of *P cepacia* by social contact in cystic fibrosis patients. *Lancet* 1993;342:15–8.
- 10 Johnson WM, Tyler SD, Rozee KR. Linkage analysis of geographical and clinical clusters in *Pseudomonas cepacia* infections by multilocus enzyme electrophoresis and ribotyping. *J Clin Microbiol* 1994;32:924–30.
- 11 Mahenthiralingam E, Simpson DA, Speert DP. Identification and characterization of a novel marker associated with epidemic *Burkholderia cepacia* strains recovered from patients with cystic fibrosis. *J Clin Microbiol* 1997;35:808–16.
- 12 Govan JRW, Hughes JE, Vandamme P. *Burkholderia cepacia*: medical, taxonomic and ecological issues. *J Med Microbiol* 1996;45:395–407.
- 13 Glass S, Govan JRW. *Pseudomonas cepacia*: fatal pulmonary infection in a patient with cystic fibrosis. *J Infect* 1986;13:157–8.
- 14 Vandamme P, Holmes B, Vancanneyt M, et al. Occurrence of multiple genomovars of *Burkholderia cepacia* in cystic fibrosis patients and proposal of *Burkholderia multivorans* sp nov. *Int J Syst Bacteriol* 1997;47:1188–200.