**Burkholderia cepacia complex**


**Introduction**

The bacteriae previously known as ‘*Burkholderia cepacia*’ have been reclassified as nine closely related species, sometimes referred to as ‘genomovars’ (Table 1), (Coenye et al, 2001; Mahenthiralingam et al, 2002). Collectively these are commonly referred to as ‘*Burkholderia cepacia complex*’ (Bcc). The various genomovars have different pathogenic potential (Keig et al, 1999; Bevivino et al, 2002; Chu et al, 2002; Cystic Fibrosis Trust Infection Control Group, 2004).

<table>
<thead>
<tr>
<th>Genomovar</th>
<th>Species</th>
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<tbody>
<tr>
<td>I</td>
<td><em>Burkholderia cepacia</em></td>
</tr>
<tr>
<td>II</td>
<td><em>Burkholderia multivorans</em></td>
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<tr>
<td>III</td>
<td><em>Burkholderia cenocepacia</em></td>
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<tr>
<td>IV</td>
<td><em>Burkholderia stabilis</em></td>
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<td>V</td>
<td><em>Burkholderia vietnamiensis</em></td>
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<tr>
<td>VI</td>
<td><em>Burkholderia dolosa</em></td>
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<tr>
<td>VII</td>
<td><em>Burkholderia ambifaria</em></td>
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<tr>
<td>VIII</td>
<td><em>Burkholderia anthina</em></td>
</tr>
<tr>
<td>IX</td>
<td><em>Burkholderia pyrrocinia</em></td>
</tr>
</tbody>
</table>

Table 1. Taxonomy of the *Burkholderia cepacia complex* – genomovar status and species name

The prevalence of chronic respiratory infection with multiresistant Bcc increased in the 1980s and 1990s mainly due to hospital and social patient-to-patient transmission (Chen et al, 2001; Walsh et al, 2002). Further spread of Bcc infection has been very successfully interrupted by separating these patients from others attending the clinic. Some members of the complex are more closely associated with acute clinical deterioration (‘cepacia syndrome’) and patient-to-patient spread, in particular *Burkholderia cenocepacia* (Mahenthiralingam et al, 2001; Jones et al, 2004; Manno et al, 2004). Other species such as *Burkholderia multivorans* have also been associated with ‘cepacia syndrome’ (Blackburn et al, 2004) and some, such as *Burkholderia dolosa* appear as invasive in vitro as *B. cenocepacia* (Caraher et al, 2007). Chronic infection with *B. dolosa* has been associated with an accelerated decline in lung function (Kalish et al, 2006). Studies suggest that the epidemiology of Bcc has changed in recent years in CF Units. Successful segregation policies have resulted in a decline in the prevalence of *B. cenocepacia* and in many European CF Centres, including Leeds, the most common Bcc species is now *B. multivorans* (Brisse et al, 2004; De Boeck et al, 2004). Even in countries where *B. cenocepacia* remains the predominant species, such as the USA, most recent acquisitions have been with *B. multivorans* (Reik et al, 2005). Genotyping evidence also suggests that most isolates of *B. multivorans* appear largely unrelated between different patients, suggesting acquisition from the environment (Turton et al, 2003) rather than from other patients with CF. Isolates of Bcc can be found in environmental niches such as soil (LiPuma et al, 2002), although exactly how patients with CF acquire Bcc species such as *B. multivorans* remains uncertain.

Although the clinician is faced with an increasingly complex nomenclature for Bcc, it is important to remember that the genomovar classification alone cannot predict clinical outcome in any individual patient. Some patients infected with the same genomovar of Bcc may remain clinically stable, whereas others may experience a decline in lung function. It is also imperative that all patients with Bcc are strictly segregated from each other at all times, as some less virulent species may be replaced by highly virulent and transmissible species, such as *B. cenocepacia* (Mahenthiralingam et al, 2001).
As with *P. aeruginosa*, some isolates of Bcc, particularly *B. multivorans*, can be successfully eradicated with early aggressive antibiotic therapy before chronic infection becomes established (Etherington *et al.*, 2003). We therefore treat all patients with new growths of Bcc with a regimen of three intravenous antibiotics (e.g. tobramycin plus meropenem plus ceftazidime) for two weeks followed by three consecutive months of nebulised TOBI®. There is also anecdotal evidence that eradication can be enhanced by giving aerosolised amiloride and tobramycin in combination (Middleton *et al.*, 2005), a new strategy that we will pursue on a case-by-case basis.

Although in the laboratory the organism is often resistant to most intravenous antibiotics, most patients will respond to standard therapy (Peckham *et al.*, 1994). A proportion of patients may have a more rapid decline in lung function. The reasons for this are unclear. There does not appear to be a greater inflammatory response to *B. cepacia complex* than to *P. aeruginosa* (Hendry *et al.*, 1999). The optimum antibiotic treatment for ‘cepacia syndrome’ remains unclear and mortality unfortunately remains very high. However, survival has been described in a few patients following aggressive antibiotic therapy and in one case was associated with the use of steroids (Kazachkov *et al.*, 2001; Weidmann *et al.*, 2008).

*Burkholderia cepacia complex and lung Transplant*

Pre-operative infection with Bcc, particularly *B. cenocepacia*, is associated with a worse outcome. One and five year survival has been documented as 60% and 36% compared to 86% and 64% in non-Bcc infected patients (Egan *et al.*, 2002). This high risk seems to relate to *B. cenocepacia* (genomovar III), infection exclusively (De Soyza *et al.*, 2004; Meachery *et al.*, 2008). The greatest danger to Bcc infected patients seems to be in the perioperative period. Beyond six months from the transplant the actuarial survival curves of Bcc infected patients and other patients with CF run parallel. Patients with Bcc infection have a poorer outcome (Meachery *et al.*, 2008) and *B. cenocepacia* is now a contra-indication to lung transplantation as it is associated with such poor prognosis and post transplant sepsis.

**Key points**

- Bcc includes nine genomovars (different bacterial types) each with varying degrees of virulence
- Bcc genomovar classification alone cannot predict clinical outcome
- It is essential that patients with Bcc infection are isolated from other patients and from each other
- Early eradication may be possible

**References**


Turton JF, Kaufmann ME, Mustafa N, et al. Molecular comparison of isolates of Burkholderia


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