***Pseudomonas aeruginosa* and Cystic Fibrosis – A Nasty Bug Gets Nastier**

Shawn D. Aaron

Department of Medicine, University of Ottawa, The Ottawa Hospital, Ottawa, Canada

In this issue of *Respiration* Lechtzin et al. [1] describe outcomes in adult cystic fibrosis (CF) patients at the Johns Hopkins CF clinic who were infected with multiply antibiotic-resistant *Pseudomonas aeruginosa* (MARPA) bacteria. Of 75 adults followed in their clinic, 21 developed antibiotic-resistant *P. aeruginosa* during a 33-month study period and 13 were infected with antibiotic-resistant *P. aeruginosa* throughout the study period. The authors demonstrate using survival analyses that patients who were infected with MARPA had an increased risk of death or lung transplantation compared to those patients who were infected with antibiotic-susceptible *P. aeruginosa*. Multivariable analyses also suggested that these patients had more rapid declines in FEV₁ per year.

P. aeruginosa has long been a scourge of CF patients and CF clinics. Approximately 70% of adults in North American CF clinics are chronically infected with *P. aeruginosa*. Once established, the infection is virtually impossible to eradicate in adults. Studies have shown that *P. aeruginosa* forms biofilms within the CF airway, and that most adults are infected with a single clone of *P. aeruginosa* in their airway secretions even when multiple morphotypes are isolated from sputum [2].

Large database analyses of CF patients from the US and Canada have confirmed that infection with *P. aeruginosa* is an independent risk factor for mortality [3]. Those patients infected with *P. aeruginosa* have a relative

risk of mortality that is 2–3 times higher than similar patients who are not infected with *P. aeruginosa*. Data from the study by Lechtzin et al. suggests that even amongst those patients already infected with *P. aeruginosa*, there exists a subgroup of patients infected with multiply antibiotic-resistant isolates who fare even more poorly.

Why do these patients have unfavourable outcomes? It is possible, but not confirmed in this study, that some of the patients infected with antibiotic-resistant isolates may have been infected with a clonal strain of *P. aeruginosa* bacteria common to the Johns Hopkins clinic. The study by Lechtzin et al. did not utilize molecular typing of isolates and it is therefore impossible to determine if these antibiotic-resistant isolates represent epidemic clones. However, studies from Australia and the UK have shown evidence of clonal epidemic strains of *P. aeruginosa* that have infected a majority of CF patients in certain clinics [4, 5]. One small retrospective study of 12 patients from Liverpool suggested that patients infected with the Liverpool multiresistant epidemic strain had poorer outcomes compared to 12 matched patients infected with unique strains of *P. aeruginosa* [6].

Why else might these patients do more poorly? Bacteria such as *P. aeruginosa* are known to develop antibiotic resistance through development of multidrug efflux systems, altered membrane permeability, and plasmid-mediated resistance. Many of these bacterial resistance

mechanisms are induced by exposure to antibiotics. This study by Lechtzin et al. suggests that patients who developed multiply resistant infections had repeated courses of antibiotics before isolation of MARPA. It is possible that isolation of MARPA simply represents a marker of a sicker CF patient who has frequent exacerbations, requires more courses of antibiotics, and therefore is more likely to have an unfavourable prognosis.

In any case, this study by Lechtzin et al. has yielded interesting information. The study will need to be confirmed using regular surveillance of *P. aeruginosa* isolates from multiple CF clinics with clinical outcomes collected prospectively. In the meantime, the study provides further impetus to stress the potential importance of infection control efforts to prevent patient-to-patient spread of *P. aeruginosa*.

References

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