Editorials

Antibodies against *Pseudomonas aeruginosa* in patients with bronchiectasis: helpful or harmful?

N Høiby

The measurement of antibodies against pathogens is mainly done for diagnostic purposes in order to detect the aetiology of infections or to confirm that protection following vaccination is present against a certain disease.

In some diseases such as chronic *Pseudomonas aeruginosa* lung infection in patients with cystic fibrosis antibodies induced by the infection obviously do not offer any protection against the infection. On the contrary, high and rapidly increasing levels of antibodies are correlated with a poor prognosis.¹ The reason for this is that immune elimination is not mediated by the antibody response because the alginate producing bacteria which are so characteristic of this disease grow as biofilms in the bronchioles.² The biofilm mode of growth is an ancient survival strategy developed by bacteria living in the environment to exploit the micro-milieu of nutrients on surfaces and to avoid being killed by amoeba and toxic chemicals.² As a consequence, antigen-antibody reactions take place around the surface of the *P aeruginosa* biofilm in the airways of patients with cystic fibrosis, eventually leading to chronic inflammation dominated by polymorphonuclear leucocytes. The process of frustrated phagocytosis around the biofilm leads to liberation of proteolytic enzymes such as elastase and oxygen radicals which gradually destroy the tissue of the lungs in patients with cystic fibrosis.² The antibody response against *P aeruginosa* in cystic fibrosis is therefore both a marker of chronicity of the infection and a marker of the inflammation and tissue damage. Measurement of antibodies against *P aeruginosa* in patients with cystic fibrosis is therefore done in some centres to distinguish between intermittent *P aeruginosa* colonisation, which does not give rise to a significant antibody response, and chronic *P aeruginosa* infection characterised by a significant antibody response.¹⁻³ The predictive values of both a positive and a negative antibody test to discriminate between intermittent colonisation and chronic infection is about 90%.⁴

This has important therapeutic consequences as it is possible to prevent chronic *P aeruginosa* infection in 80% of patients by early aggressive antibiotic treatment of the intermittent colonisation.⁵ Likewise, with aggressive suppressive antibiotic treatment of chronic *P aeruginosa* infection it is possible to maintain lung function for many years and to improve the prognosis of patients with cystic fibrosis, although the infection is virtually never eradicated.⁶ Generation of the knowledge behind these results has only been possible because patients with cystic fibrosis are followed and treated in large specialised centres. It is therefore possible to obtain blood samples for antibody measurements before and during the onset and course of the intermittent and chronic *P aeruginosa* infection and to correlate the results with the clinical status and laboratory findings of the patients in longitudinal studies.

This is obviously seldom the case with other diseases. One is therefore forced to rely on the results of transversal studies and to search for any pathogenetic, clinical, or immunological findings which may show an analogy with the chronic *P aeruginosa* infection in cystic fibrosis. Such hypothesis generating observations may then initiate clinical trials to investigate whether the principles of treatment of infections in cystic fibrosis may also be of benefit to other groups of patients. More than 30 years ago Burns and May⁷⁻⁹ initiated such a series of studies in patients with cystic fibrosis and in adult patients with other chronic bronchial disorders. Similar studies were started in other countries.¹⁰⁻¹⁵ The results were concordant in cystic fibrosis patients as described above and also showed that a few non-cystic fibrosis patients with *P aeruginosa* lung infection had high levels of anti-*P aeruginosa* antibodies and were harbouring mucoid strains.¹⁶⁻¹⁷ However, none of these authors continued the research in the non-cystic fibrosis patients and it is therefore not known whether the information gathered from the studies in cystic fibrosis can be extrapolated to non-cystic fibrosis patients.

In this issue of *Thorax* Caballero *et al*¹⁸ have used the Western blot technique to detect IgG antibodies to outer membrane antigens of *P aeruginosa* in patients with bronchiectasis who were classified as having no *P aeruginosa*, alternating *P aeruginosa* and other bacteria, or continuously colonised with *P aeruginosa*. They found that the antibody response distinguished between these groups of patients at the level of approximately 75% sensitivity and specificity. Their results are therefore a valuable extension of the previously published results in non-cystic fibrosis patients but await further clinical studies as outlined above.

N HØIBY

Department of Clinical Microbiology and Danish Cystic Fibrosis Centre, Rigshospitalet, University of Copenhagen, DK-2100 Copenhagen Ø, Denmark
hoiby@inet.uni2.dk

- 1 Høiby N, Frederiksen B. Microbiology of cystic fibrosis. In: Hodson ME, Geddes D, eds. *Cystic fibrosis*. 2nd ed. London: Arnold, 2000: 83-107.
- 2 Høiby N, Johansen HK, Moser C, *et al*. *Pseudomonas aeruginosa* and the bio-film mode of growth. *Microbes and Infection* 2001;3:1-13.
- 3 Döring G, Conway SP, Heijerman HGM, *et al*. Antibiotic therapy against *Pseudomonas aeruginosa* in cystic fibrosis: a European consensus. *Eur Respir J* 2000;16:749-67.
- 4 Høiby N. *Pseudomonas aeruginosa* infection in cystic fibrosis. Diagnostic and prognostic significance of *Pseudomonas aeruginosa* precipitins determined by means of crossed immunoelectrophoresis. A survey. *Acta Pathol Microbiol Scand Suppl* 1977;262C:3-96.
- 5 Frederiksen B, Koch C, Høiby N. Antibiotic treatment of initial colonization with *Pseudomonas aeruginosa* postpones chronic infection and prevents deterioration of pulmonary function in cystic fibrosis. *Pediatr Pulmonol* 1997;23:330-5.
- 6 Frederiksen B, Lanng S, Koch C, *et al*. Improved survival in the Danish cystic fibrosis centre: results of aggressive treatment. *Pediatr Pulmonol* 1996; 21:153-8.
- 7 Burns MW, May JR. Bacterial precipitins in serum of patients with cystic fibrosis. *Lancet* 1968;i:270-2.

- 8 Burns MW. The pattern of bacterial infection in bronchial diseases in Australia: a serological and bacteriological survey. *Med J Aust* 1972;2:697-701.
- 9 Burns MW. Significance of *Pseudomonas aeruginosa* in sputum. *BMJ* 1973;3:382-.
- 10 Doggett RG, Harrison GM. *Pseudomonas aeruginosa*: immune status in patients with cystic fibrosis. *Infect Immun* 1972;6:628-35.
- 11 Hoiby N, Axelsen NH. Identification and quantitation of precipitins against *Pseudomonas aeruginosa* in patients with cystic fibrosis by means of crossed immunoelectrophoresis with intermediate gel. *Acta Pathol Microbiol Scand Sect B* 1973;81:298-308.
- 12 McCrae WM, Raeburn JA. The patterns of infection in cystic fibrosis. *Scot Med J* 1974;19:187-90.
- 13 Ericsson Hollsing A, Granström M, Vasil ML, et al. Prospective study of serum antibodies to *Pseudomonas aeruginosa* exoproteins in cystic fibrosis. *J Clin Microbiol* 1987;25:1868-74.
- 14 Brett MM, Simmonds EJ, Ghoneim ATM, et al. The value of serum IgG titres against *Pseudomonas aeruginosa* in the management of early pseudomonal infection in cystic fibrosis. *Arch Dis Child* 1992;67:1086-8.
- 15 Pedersen SS. Lung infection with alginate-producing, mucoid *Pseudomonas aeruginosa* in cystic fibrosis. *Acta Pathol Microbiol Immunol Scand* 1992;100(Suppl 28):5-79.
- 16 Hoiby N. Prevalence of mucoid strains of *Pseudomonas aeruginosa* in bacteriological specimens from patients with cystic fibrosis and patients with other diseases. *Acta Pathol Microbiol Scand Sect B* 1975;83:549-52.
- 17 Hoiby N. Antibodies against *Pseudomonas aeruginosa* in sera from normal persons and from patients colonized with mucoid or non-mucoid *Pseudomonas aeruginosa*: results obtained by means of crossed immunoelectrophoresis. *Acta Pathol Microbiol Scand Sect C* 1977;85:142-8.
- 18 Caballero E, Drobnic M-E, Pérez M-T, et al. Anti-*Pseudomonas aeruginosa* antibody detection in patients with bronchiectasis without cystic fibrosis. *Thorax* 2001;56:669-74.

Free access to *Thorax* for low income countries

By the time this article appears in print, individual readers and institutions with internet access in any of the 65 countries defined by the World Bank as "low income economies"¹ will be given free access to articles printed in *Thorax* via the website.²

Readers wishing to take advantage of this should simply log on to the *Thorax* website² and the software will recognise the country of origin of the request and implement free access. A similar facility is being introduced for most of the other BMJ specialist journals.³ We hope that this service will increase the availability and use of *Thorax* and other BMJ journals in developing countries, and also encourage submission of papers for publication from researchers in these countries.

For some time now the BMJ group and the British Thoracic Society have provided a limited number of free

paper subscriptions to *Thorax* for hospital or university libraries in low income countries, and will continue to look sympathetically at individual applications from institutions still experiencing difficulty in accessing the internet. Applicants wishing to take advantage of this should contact Alex Williamson, BMJ Publishing Group, BMA House, Tavistock Square, London WC1H 9JR, UK.

A WILLIAMSON
Publishing Director,
BMJ Specialist Journals

A KNOX
J BRITTON
Executive Editors

1 <http://www.bmjournals.com:80/subscriptions/countries.shtml>

2 <http://thorax.bmjournals.com>

3 <http://www.bmjpg.com/template.cfm?name=specjou>