ERJ open research
THE BEST IN OPEN ACCESS BASIC, TRANSLATIONAL & CLINICAL RESPIRATORY RESEARCH

Early View

Research letter

Family case studies: absence of *Pseudomonas aeruginosa* transmission in bronchiectasis

Ruth Sobala, Kristian Brooks, John Davison, Joanna Lumb, Anthony De Soyza

Please cite this article as: Sobala R, Brooks K, Davison J, *et al*. Family case studies: absence of *Pseudomonas aeruginosa* transmission in bronchiectasis. *ERJ Open Res* 2022; in press (https://doi.org/10.1183/23120541.00280-2022).

Family Case Studies: Absence of *Pseudomonas aeruginosa* transmission in Bronchiectasis

Ruth Sobala[1], Kristian Brooks[1], John Davison[1], Joanna Lumb[1], Anthony De Soyza[1, 2]

Affiliation Addresses:

1. Freeman Hospital, High Heaton, Newcastle Upon Tyne NE7 7DN
2. Population Health Science Institutes, Newcastle University, Newcastle Upon Tyne NE2 4HH

Correspondence Address:
Ruth Sobala

Regional Bronchiectasis Service
Freeman Hospital
High Heaton
Newcastle Upon Tyne
NE7 7DN
Ruth.sobala1@nhs.net

Bronchiectasis, sometimes referred to as non-CF (cystic fibrosis) bronchiectasis (NCFB), is a chronic lung disease in which one or more bronchi become permanently dilated, resulting in mucus retention and airway inflammation.[1] It is characterised by repeat infective exacerbations, and bacterial colonisation. In bronchiectasis, *Pseudomonas aeruginosa (Pa)* is a significant pathogen, associated with increased mortality and acute hospital admission.[2] *Pa* is an aerobic Gram-negative bacillus and a common nosocomial pathogen.[3]

Cross-infection with *Pa* in cystic fibrosis is well recognised, and has been described between CF patients, and from CF to non-CF individuals. [4][5].This transmission occurs both in the community and nosocomial. Consequently, guidelines for CF advise strict segregation.[6][7] However, the prevalence of cross-infection in NCFB is indeterminate.

To date, two single centre studies identified *Pa* cross-infection in NCFB, through genotyping strains of *Pa*.[8][9]. De Soyza et al. demonstrated one case of cross-infection in 36 non-segregated NCFB.[9] This finding was confirmed by a multi-centre analysis of 91 NCFB patients in which whole genome sequencing showed certain isolates had genetic similarity, implying cross-infection or common source acquisition.[10] Furthermore Mitchelmore et al. analysed *Pa* in a non-segregated NCFB population (n=46) and detected 3 cases of cross-infection in patients who shared a waiting room and lung function room.[11]

The British Thoracic Society guidelines state that for NCFB there is no evidence of *Pa* transmissibility and that segregation is not routinely required [1] while the EMBARC Patient Advisory Group and the European Reference Network (ERN-Lung) Bronchiectasis Network recommend that currently there is insufficient evidence to advise segregation.[12]

We present two family case studies, all of whom have NCFB, in which household *Pa* transmission does not occur, despite a significant contact history amongst the paired subjects. This supports the hypothesis that *Pa* is less communicable in the NCFB population, compared to CF.[10][13]

Case 1: Patient A is a 79 year old man with an established diagnosis of severe idiopathic bronchiectasis. His Bronchiectasis Severity Index (BSI) was 17 indicating a 16.7-52.6% risk of hospitalisation at one year[14]] and his Bronchiectasis Aetiology Comorbidity Index (BACI) is 2, indicating 5 year mortality 11.7%.[15] He has multimorbidity which include Parkinson's disease, percutaneous endoscopic gastrostomy (PEG) (weight 56.15 kg) and significant high volume daily sputum production (estimated ≥60mls/ day).

Patient A is colonised with *Pa*. Over a 13 year period (2009 – 2022) he produced fifty purulent sputum samples for culture, with *Pa* first isolated in 2009. *Pa* has been isolated a further twenty-eight times, with *in vitro* ciprofloxacin resistance developing in 2011. Additional bacteria isolated from sputum samples include: *Haemophilus influenzae:* 23 isolates with two isolates demonstrating co-trimoxazole resistance*, Escherichia coli:* 6 isolates, *Coliforms*: 4 isolates, *Moraxella catarrhalis:* 2 isolates, *Streptococcus pneumonia:* 1 isolate*,* and *Achromobacter xylosoxidans*: 1 isolate.

His bronchiectasis is managed with inhaled beclomethasone/formoterol, carbocisteine and prophylactic co-trimoxazole, reflecting an intolerance of azithromycin.

In November 2016, Patient A was noted to have a weak cough and a reduced mean peak cough flow of 145 L/min (<270 L/min indicates ineffective airway clearance). Lung function testing demonstrated forced expiratory volume (FEV1) 1.4 (49%) and FVC 3.1 (80%). This was initially managed with a lung volume recruitment bag (2017) and flutter valve, but as his symptoms

progressed he was prescribed a cough assist device in 2020. Due to the patient's frailty, his wife assists him with this device.

Patient B, the wife of patient A, is a 74 year old female who also has a diagnosis of idiopathic bronchiectasis, diagnosed in 2013 on CT scan. Her lung function is FEV1 2.33 (102%), FVC 2.77 (102%), and weight 73 kg. She has produced 27 sputum samples from 2012-2022 and is colonised with *Haemophilus influenzae:* 19 isolates which twice demonstrated co-trimoxazole resistance. She has isolated additional bacteria from her sputum: *Moraxella catarrhalis:* 4 isolates and *Streptococcus pneumonia:* 1 isolate. She is the main carer for her husband assisting him with his PEG feeding, and his cough assist device. Additionally, in 2020 she shared her husbands disused flutter valve.

We conclude that despite cohabiting and close daily contact (including handling a cough assist device with purulent sputum within) that patient A has not coinfected patient B with *Pa.* This is despite a 12 year period of *Pa* isolates, daily close proximity and 2 years of handling a cough assist device.

Case 2: Patient C is a 60-year-old male diagnosed with idiopathic bronchiectasis in 2009. He is a heavy smoker of cigarettes and has regularly smoked cannabis, and HRCT (high resolution computed tomography) scan shows upper-lobe predominant emphysema in addition to bronchiectasis. He has well maintained lung function: FEV1 3.05 (87% predicted) and FVC 4.80 (103% predicted). His BSI is 5, indicating moderate bronchiectasis and he is managed with inhaled beclomethasone/formoterol and carbocisteine.[14] His main symptom is persistent cough with high sputum volumes, however he infrequently exacerbates (approximately one per year).

Between 2018-2022, Patient C produced 5 purulent sputum samples. He has been colonised with *Pa* since 2020. Culture has also grown *Streptococcus pneumoniae* once.

Patient D is an 84-year-old female, and the mother of patient C. She has a long-standing history of bronchiectasis with a background of recurrent pneumonia, sinusitis and otitis media. She has a BSI of 11 and a comorbid diagnosis of asthma. Spirometry shows FEV1 1.25 (77% predicted), FVC 1.68 (83% predicted). In contrast to her son, she has never smoked and has regular exacerbations requiring 3-4 antibiotic courses per year. She has high sputum volumes and is managed with nebulised hypertonic saline, high-dose inhaled budesonide/formoterol, montelukast and carbocisteine.

From 2014-2019, Patient D produced 13 sputum samples which predominantly show *Staphylococcus aureus* colonisation. She has also grown non-tuberculous mycobacteria (*M.chimaera* and *M.avium*) twice, but never *Pa*.

Since undergoing a total hip replacement in February 2019, Patient D has required increasing care from Patient C. This has included daily visits and manual labour to assist in household refurbishment. Despite this daily contact, and both patients having significant cough, Patient D has not become colonised or infected with *Pa*.

We have demonstrated two separate cases where *Pa* transmission has not occurred, despite significant household contact. Understanding the transmissibility of *Pa* in NCFB is important. These patients do not segregate in waiting rooms, inpatient wards or during therapy i.e. pulmonary rehabilitation, and meta-analysis demonstrates *Pa* in NCFB is common (21.4%).[2]

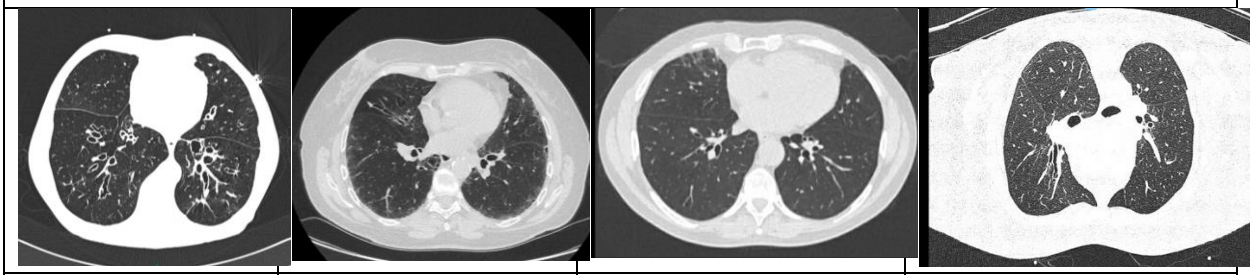
UK studies have demonstrated that there is not a prevalent infectious *Pa* strain in NCFB [10] and Cramer et al. showed low risk of *Pa* transmission in an outpatient clinic: no evidence of patient to patient transmission in 49 patients.[13] It has been proposed that due to decreased time spent in

inpatient settings, NCFB patients have reduced time to cross-infect in hospital.[9] Additionally, NCFB attend outpatients at a reduced frequency compared with CF patients.

This case report series has some intrinsic limitations. The absence of cross-infection described can be accounted for by a number of different reasons (i.e. both host and pathogen factors). Possible explanations for the results found are that: *Pa* is poorly transmits in the NCFB cohort, or that the strains of *Pa* seen in this series were not readily transmissible, or that the hosts were not sufficiently susceptible. The latter is particularly important as most bronchiectasis patients are not colonised with *Pa* (despite *Pa* being widespread in the environment). It is therefore important to note our findings can not be generalised to the whole NCFB community.

In conclusion, large scale longitudinal studies are required to determine the incidence of cross-infection in NCFB.[12] Previous work has demonstrated cross-infection is rare, and in some instances the primary source from CF.[4] We have provided evidence showing lack of transmission of *Pa* in NCFB, in patients with a significant exposure history. To our knowledge, these are the first cases demonstrating this, supporting evidence that in NCFB, *Pa* is poorly transmissible by direct contact. This is of interest to the bronchiectasis community, with implications for inpatient and outpatient management strategies.

Figure 1: CT image slices demonstrating bronchiectasis



Patient A	Patient B	Patient C	Patient D

References:

1. Hill AT, Sullivan AL, Chalmers JD et al. British Thoracic Society Guideline for bronchiectasis in adults. Thorax. 2019 Jan;74(Suppl 1):1-69. doi: 10.1136/thoraxjnl-2018-212463.
2. Finch S, McDonnell MJ, Abo-Leyah H, et al. A Comprehensive Analysis of the Impact of Pseudomonas aeruginosa Colonization on Prognosis in Adult Bronchiectasis. Ann Am Thorac Soc. 2015;12(11): 1602-11.
3. UK Standards for Microbiology Investigations Identification of Pseudomonas species and other Non-Glucose Fermenters. SMI ID 17: identification of Pseudomonas species and other non glucose fermenters - GOV.UK (www.gov.uk). Date last updated April 2015. Date last accessed May 2022.
4. Robinson P, Carzino R, Armstrong D, et al. Pseudomonas cross-infection from cystic fibrosis patients to non-cystic fibrosis patients: implications for inpatient care of respiratory patients. J Clin Microbiol. 2003; 41(12): 5741.
5. LiPuma JJ, Dasen SE, Nielson DW, et al. Person-to-person transmission of Pseudomonas cepacia between patients with cystic fibrosis. *Lancet.* 1990; 336(8723):1094–1096.

6. Saiman L, Siegel JD, LiPuma JJ, et al. Cystic Fibrous Foundation; Society for Healthcare Epidemiology of America. Infection prevention and control guideline for cystic fibrosis: 2013 update. Infect Control Hosp Epidemiol. 2014; 35 Suppl 1:S1-S67.
7. Smyth AR, Bell SC, Bojcin S, et al. European Cystic Fibrosis Society European cystic fibrosis society standards of care: best practice guidelines. *J Cyst Fibros.*2014;13(Suppl 1):S23–S42.
8. Mitchelmore PJ, Randall J, Bull MJ, et al. Molecular epidemiology of *Pseudomonas aeruginosa* in an unsegregated bronchiectasis cohort sharing hospital facilities with a cystic fibrosis cohort. Thorax 2018; 73: 677–679.
9. De Soyza A, Perry A, Hall AJ et al. Molecular epidemiological analysis suggests cross-infection with *Pseudomonas aeruginosa* is rare in non-cystic fibrosis bronchiectasis. European Respiratory Journal. 2014, 43 (3) 900-903.
10. Hilliam Y, Moore MP, Lamont IL, et al. Pseudomonas aeruginosa adaptation and diversification in the non-cystic fibrosis bronchiectasis lung. European Respiratory Journal 2017, 49(4), 1602108.
11. Mitchelmore P, Wilson C, Hettle D. Risk of Bacterial Transmission in Bronchiectasis Outpatient Clinics. *Curr Pulmonol Rep*. 2018;7(3):72-78.
12. Chalmers JD, Ringshausen FC, Harris B, et al. Cross-infection risk in patients with bronchiectasis: a position statement from the European Bronchiectasis Network (EMBARC), EMBARC/ELF patient advisory group and European Reference Network (ERN-Lung) Bronchiectasis Network. Eur Respir J 2018; 51: 1701937.
13. Cramer N, Sedlacek L, Tümmler B, et al. Low transmission risk of *Pseudomonas aeruginosa* in a bronchiectasis clinic based on the knowledge of bacterial population biology. Eur Respir J. 2019 Mar 28;53(3):1802191.
14. Chalmers JD, Goeminne P, Aliberti S, et al. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med. 2014 Mar 1;189(5):576-85.
15. McDonnell MJ, Aliberti S, Goeminne PC, et al. Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicentre cohort study. *Lancet Respir Med*. 2016;4(12):969-979