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Anxiety and depression symptoms affect health status in patients with stable COPD
http://ow.ly/r5452

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Molecular epidemiological analysis suggests cross-infection with *Pseudomonas aeruginosa* is rare in non-cystic fibrosis bronchiectasis

To the Editor:

In both cystic fibrosis (CF) and non-CF bronchiectasis (NCFBr) chronic *Pseudomonas aeruginosa* infection is adversely prognostic [1, 2]. In CF, epidemic infections with specific clones of *P. aeruginosa* are associated with further adverse outcomes [3, 4]. This cross-infection risk has led to segregation of patients [5]. There are few data on *P. aeruginosa* cross-infection in NCFBr. As a result, segregation in NCFBr has not been addressed in guidelines [6].

Our aim was to undertake a cross-infection study in NCFBr. This was undertaken in an adult bronchiectasis service in the north-east of England (UK) that is separated from the regional CF unit (sited 2 miles (3 km) away). The service was initiated in 2007 with a weekly specialist clinic without a *Pseudomonas*-specific clinic. When NCFBr patients are hospitalised, there is a preference for cubicle-based (single-patient room) management, but when cubicles are unavailable, patients are managed in six-bed bays. All patients had computed tomographic confirmation and had predominantly idiopathic or post-infectious bronchiectasis with CF excluded following current guidelines [6]. The study had ethical permission and Caldicott approval (Newcastle and North Tyneside National Research Ethics Service Committee).

56 isolates were selected for analysis. Six were chosen from CF patients as laboratory controls. 50 were NCFBr isolates collected between 2008 and 2011 from 40 NCFBr patients. 36 patients (patients 1–36) attending the adult bronchiectasis service were randomly selected. Longitudinal isolates were included from 10 patients with a mean (range) 16 months (2–35 months) between isolates. Additionally, single isolates were chosen from four NCFBr patients (patients 37–40) as potential patient controls who had not attended the specialist clinic and had not been hospitalised. Isolates were cultured from spontaneous sputum and identified as *P. aeruginosa* by routine biochemical methods and matrix-assisted laser desorption/ionisation-time-of-flight (MALDI-TOF) mass spectrometry.

We used two genotyping methods; in each case, testing was blinded. First, we used the ArrayTube (AT genotyping; Alere, Jena, Germany) as per the manufacturer's protocol. This system detects 13 single-nucleotide polymorphisms within conserved *P. aeruginosa* genes and the presence/absence of 38 variable genetic markers in the accessory genome. The data were converted into a four-digit hexadecimal code and then compared to a database [7, 8]. Secondly, we used variable number tandem repeat (VNTR) analysis based on variation in the number of DNA repeats at specified sites across the genome at nine variable loci [9] with comparison to a VNTR database [10].

The vast majority of the 36 NCFBr patients attending the service (patients 1–36) harboured their own strains (fig. 1). Patients 11 and 27 had distinct variants of clone C, which is a lineage that is widely found globally [10]; two patients in the nonhospitalised control group also had further variants of this clone (patients 39 and 40). Among the 34 remaining NCFBr patients attending the service, there were three pairs (patients 2 and 34; 12 and 19; and 16 and 17) whose isolates of *P. aeruginosa* shared very similar profiles by at least one method (fig. 1). For patients 12 and 19, this was confirmed by pulsed-field gel electrophoresis of *Spe*I-digested genomic DNA; this is an unusual profile and that these patients shared the same strain almost certainly does reflect cross-infection. Patients 2 and 34 both had a widely found type belonging to sequence type 27, while patients 16 and 17 had clearly distinct strains by VNTR, suggesting only one probable case of cross-infection.

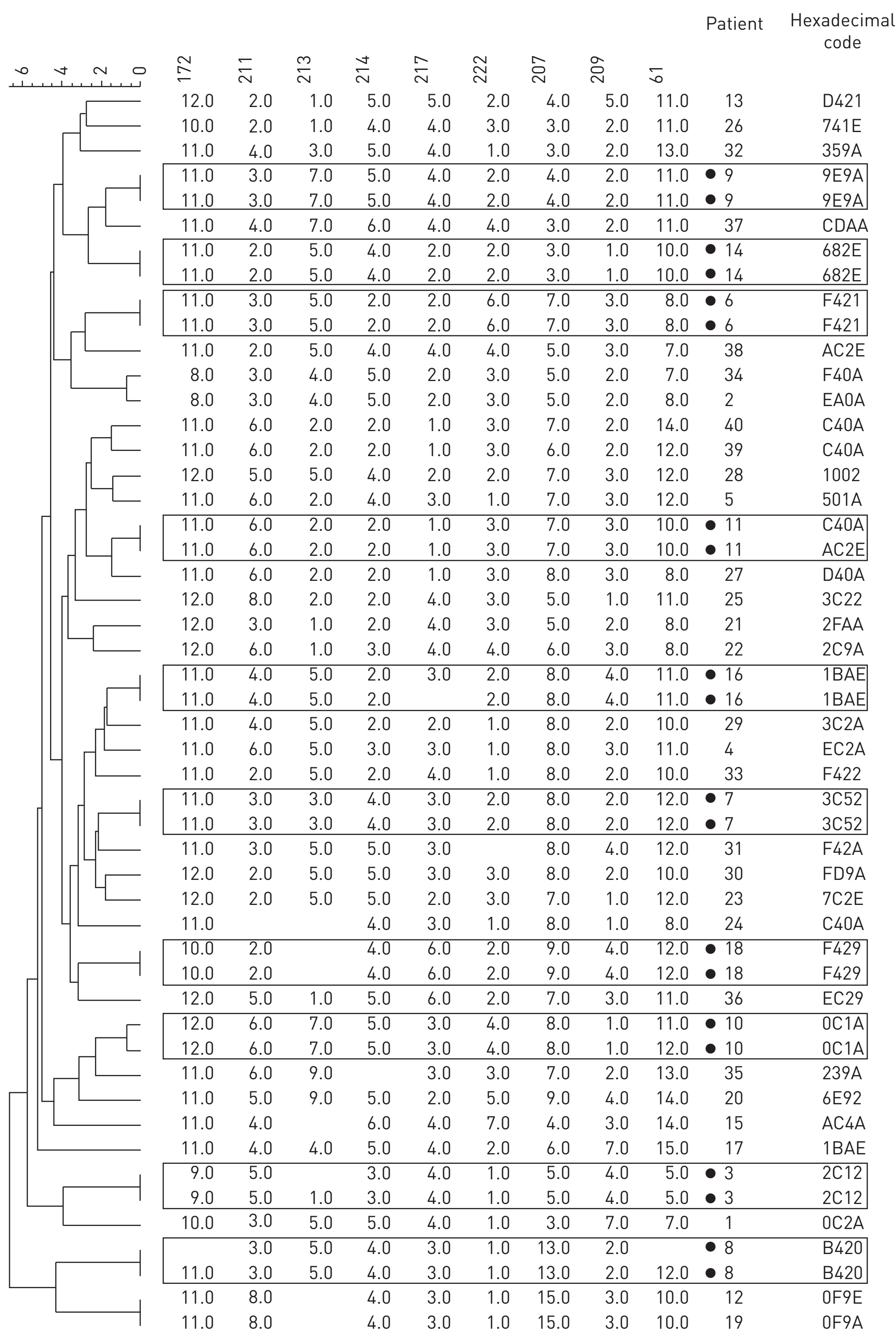
The location of the NCFBr isolates among the wider population structure of *P. aeruginosa*, based on AT genotype, was mapped (not shown) and demonstrated that NCFBr isolates were widely distributed. AT analysis found several pattern matches with the AT database: matches were with AT clones A2, K, E, I, A7, A, L, J, A5 and U. Both methods correctly identified the known control strains from CF patients.

Longitudinally paired isolates from 10 patients were examined (patients 3, 6–11, 14, 16 and 18). For nine patients, the first and second isolates were indistinguishable by both AT and VNTR genotyping, confirming persistence of the initial strain. In one patient (patient 11), VNTR analysis indicated that both isolates were identical, but AT genotyping did not.

Our key finding was the absence of dominant clones of *P. aeruginosa* with little evidence of cross-infection and many strains that were "unique". While there is distinct clustering of AT clone types in ocular keratitis, the isolates from NCFBr were widely distributed in the *Pseudomonas* population structure. Collectively, this suggests that sporadic infection is the most common mode of infection in NCFBr. Clone C was found in only 6% of the NCFBr patients and is known to be widely distributed within the environment [8]. Cross-infection with clone C seems unlikely, as the VNTR profiles varied at two or three loci, suggesting that they were independently acquired. Other isolates matched those previously isolated from various clinical and environmental sources [8]. These data may suggest a risk of environmental acquisition in NCFBr [5, 8].

The absence of a dominant *P. aeruginosa* clone in NCFBr may reflect many factors, including the lower incidence of *P. aeruginosa* infection in NCFBr (<50%) as compared to CF (⩽80%). The probable lower rate of hospitalisation in NCFBr compared to CF may also limit cross-infection exposures. The standard infection prevention and control measures used in our NCFBr centre are less stringent than those implemented in designated CF centres. The absence of significant cross-infection herein is therefore unlikely to be due to a higher standard of infection control practices.

Notably, our study is solely focused on *P. aeruginosa* cross-infection and we cannot exclude cross-infection in the NCFBr population with *Staphylococcus aureus*, *Haemophilus influenzae* or nontuberculous



172	211	213	214	217	222	207	209	61	Patient	Hexadecimal code
12.0	2.0	1.0	5.0	5.0	2.0	4.0	5.0	11.0	13	D421
10.0	2.0	1.0	4.0	4.0	3.0	3.0	2.0	11.0	26	741E
11.0	4.0	3.0	5.0	4.0	1.0	3.0	2.0	13.0	32	359A
11.0	3.0	7.0	5.0	4.0	2.0	4.0	2.0	11.0	● 9	9E9A
11.0	3.0	7.0	5.0	4.0	2.0	4.0	2.0	11.0	● 9	9E9A
11.0	4.0	7.0	6.0	4.0	4.0	3.0	2.0	11.0	37	CDAA
11.0	2.0	5.0	4.0	2.0	2.0	3.0	1.0	10.0	● 14	682E
11.0	2.0	5.0	4.0	2.0	2.0	3.0	1.0	10.0	● 14	682E
11.0	3.0	5.0	2.0	2.0	6.0	7.0	3.0	8.0	● 6	F421
11.0	3.0	5.0	2.0	2.0	6.0	7.0	3.0	8.0	● 6	F421
11.0	2.0	5.0	4.0	4.0	4.0	5.0	3.0	7.0	38	AC2E
8.0	3.0	4.0	5.0	2.0	3.0	5.0	2.0	7.0	34	F40A
8.0	3.0	4.0	5.0	2.0	3.0	5.0	2.0	8.0	2	EA0A
11.0	6.0	2.0	2.0	1.0	3.0	7.0	2.0	14.0	40	C40A
11.0	6.0	2.0	2.0	1.0	3.0	6.0	2.0	12.0	39	C40A
12.0	5.0	5.0	4.0	2.0	2.0	7.0	3.0	12.0	28	1002
11.0	6.0	2.0	4.0	3.0	1.0	7.0	3.0	12.0	5	501A
11.0	6.0	2.0	2.0	1.0	3.0	7.0	3.0	10.0	● 11	C40A
11.0	6.0	2.0	2.0	1.0	3.0	7.0	3.0	10.0	● 11	AC2E
11.0	6.0	2.0	2.0	1.0	3.0	8.0	3.0	8.0	27	D40A
12.0	8.0	2.0	2.0	4.0	3.0	5.0	1.0	11.0	25	3C22
12.0	3.0	1.0	2.0	4.0	3.0	5.0	2.0	8.0	21	2FAA
12.0	6.0	1.0	3.0	4.0	4.0	6.0	3.0	8.0	22	2C9A
11.0	4.0	5.0	2.0	3.0	2.0	8.0	4.0	11.0	● 16	1BAE
11.0	4.0	5.0	2.0		2.0	8.0	4.0	11.0	● 16	1BAE
11.0	4.0	5.0	2.0	2.0	1.0	8.0	2.0	10.0	29	3C2A
11.0	6.0	5.0	3.0	3.0	1.0	8.0	3.0	11.0	4	EC2A
11.0	2.0	5.0	2.0	4.0	1.0	8.0	2.0	10.0	33	F422
11.0	3.0	3.0	4.0	3.0	2.0	8.0	2.0	12.0	● 7	3C52
11.0	3.0	3.0	4.0	3.0	2.0	8.0	2.0	12.0	● 7	3C52
11.0	3.0	5.0	5.0	3.0		8.0	4.0	12.0	31	F42A
12.0	2.0	5.0	5.0	3.0	3.0	8.0	2.0	10.0	30	FD9A
12.0	2.0	5.0	5.0	2.0	3.0	7.0	1.0	12.0	23	7C2E
11.0			4.0	3.0	1.0	8.0	1.0	8.0	24	C40A
10.0	2.0		4.0	6.0	2.0	9.0	4.0	12.0	● 18	F429
10.0	2.0		4.0	6.0	2.0	9.0	4.0	12.0	● 18	F429
12.0	5.0	1.0	5.0	6.0	2.0	7.0	3.0	11.0	36	EC29
12.0	6.0	7.0	5.0	3.0	4.0	8.0	1.0	11.0	● 10	0C1A
12.0	6.0	7.0	5.0	3.0	4.0	8.0	1.0	12.0	● 10	0C1A
11.0	6.0	9.0		3.0	3.0	7.0	2.0	13.0	35	239A
11.0	5.0	9.0	5.0	2.0	5.0	9.0	4.0	14.0	20	6E92
11.0	4.0		6.0	4.0	7.0	4.0	3.0	14.0	15	AC4A
11.0	4.0	4.0	5.0	4.0	2.0	6.0	7.0	15.0	17	1BAE
9.0	5.0		3.0	4.0	1.0	5.0	4.0	5.0	● 3	2C12
9.0	5.0	1.0	3.0	4.0	1.0	5.0	4.0	5.0	● 3	2C12
10.0	3.0	5.0	5.0	4.0	1.0	3.0	7.0	7.0	1	0C2A
	3.0	5.0	4.0	3.0	1.0	13.0	2.0		● 8	B420
11.0	3.0	5.0	4.0	3.0	1.0	13.0	2.0	12.0	● 8	B420
11.0	8.0		4.0	3.0	1.0	15.0	3.0	10.0	12	0F9E
11.0	8.0		4.0	3.0	1.0	15.0	3.0	10.0	19	0F9A

FIGURE 1 Variable number tandem repeat dendrogram showing the diversity of types among the 50 non-cystic fibrosis bronchiectasis isolates analysed. The similarity coefficient was calculated using Euclidian distance, and strains were clustered using the unweighted pair group method with arithmatic mean using BioNumerics software (Applied Maths, Sint-Martens-Latem, Belgium). Pairs of longitudinal isolates are marked in boxes and with a dot. The hexadecimal code derived by ArrayTube analysis (Alere, Jena, Germany) is included for reference, as are the patient numbers (see text).

mycobacteria. Furthermore, limitations of our study include the single-centre design. Our observations may have been different if our NCFBr centre facilities were shared with our regional CF clinic. We therefore advocate further multicentre studies to delineate the cross-infection risks.

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Cross-infection with *Pseudomonas aeruginosa* is rare in non-cystic fibrosis bronchiectasis
http://ow.ly/sjvKz

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Rapidly progressing tuberculosis outbreak in a very low risk group

To the Editor:

We report an unusual tuberculosis (TB) outbreak, centred on a professional basketball team in Montevideo, Uruguay, a country with a low TB incidence (21 cases per 100 000). Uruguay has a relatively high income (2010 gross domestic product USD14 338 *per capita*), a low HIV prevalence (305 cases per 100 000) and a very low rate of multidrug-resistant TB (0.24%) [1]. In August 2008, a young male member of the basketball team was diagnosed with TB, with positive microscopic examination and Ziehl-Nielsen staining of a sputum sample (graded 1). Chest radiography indicated a bilateral pulmonary form with cavities. TB was bacteriologically confirmed 20 days later, with a *Mycobacterium tuberculosis* isolate pan-susceptible to antituberculous drugs. The patient was compliant with first-line treatment (2HRZ/4H_2R_2: 2 months daily