9. Nordmann P, Poirel L. Emerging carbapenemases in gram-negative aerobes. *Clin Microbiol Infect* 2002; 8: 321–331.
10. Bennet JW, Herrera ML, Lewis JS, Wickes BW, Jorgensen JH. KPC-2 producing *Enterobacter cloace* and *Pseudomonas putida* co-infection in a liver transplant recipient. *Antimicrob Agents Chemother* 2009; 53: 292–294.
11. Anderson KF, Lonsway DR, Rascheed JK *et al.* Evaluation of methods to identify the *Klebsiella pneumoniae* carbapenemase in Enterobacteriaceae. *J Clin Microbiol* 2007; 45: 2723–2725.
12. Naas T, Cuzon G, Villegas MV, Lartigue MF, Quinn JP, Nordmann P. Genetic structures at the origin of acquisition off the beta-lactamase blaKPC gene. *Antimicrob Agents Chemother* 2008; 52: 1257–1263.
13. Pournaras S, Protonotariou E, Voulgari E *et al.* Clonal spread of KPC-2 carbapenemase-producing *Klebsiella pneumoniae* strains in Greece. *J Antimicrob Chemother* 2009; 64: 348–352.
14. Woodford N, Tierno PM, Young K Jr *et al.* Outbreak of *Klebsiella pneumoniae* producing a new carbapenem-hydrolyzing class A β-lactamase, KPC-3, in New York Medical Center. *Antimicrob Agents Chemother* 2004; 48: 4793–4799.
15. Maltezou HC, Giakkoupi P, Maragos A *et al.* Outbreak of infections due to KPC-2-producing *Klebsiella pneumoniae* in a hospital in Crete (Greece). *J Infect* 2009; 58: 213–219.
16. Clinical Laboratory Standards Institute. *Performance standards for antimicrobial susceptibility testing 19th informational supplement*. Document M100-S19. Wayne, PA: CLSI, 2009.
17. Otto TD, Vasconcellos EA, Gomes LHF *et al.* ChromaPipe: a pipeline for analysis, quality control and management for a DNA sequencing facility. *Genet Mol Res* 2008; 7: 861–871.
18. Marschall J, Tibbetts RJ, Dunne WM Jr, Frye JG, Fraser VJ, Warren DK. Presence of the KPC carbapenemase gene in Enterobacteriaceae causing bacteremia and its correlation with in vitro carbapenem susceptibility. *J Clin Microbiol* 2009; 47: 239–241.
19. Tenover FC, Kalsi RK, Williams PP *et al.* Carbapenem resistance in *Klebsiella pneumoniae* not detected by automated susceptibility testing. *Emerg Infect Dis* 2006; 12: 1209–1213.
20. Sader HS, Jones RN, Gales AC, Silva JB, Pignatari AC, SENTRY Particicpants Group (Latin America). SENTRY antimicrobial surveillance program report: Latin American and Brazilian results for 10997 through 2001. *Braz J Infect Dis* 2004; 8: 25–79.
21. Mermel LA, Allon M, Bouza E *et al.* Clinical practice guidelines for the diagnosis and management of intravascular catheter-related infection: 2009 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2009; 49: 1–45.

Clinical impact of a highly prevalent *Pseudomonas aeruginosa* clone in Dutch cystic fibrosis patients

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Abstract

Studies suggest that infection with highly prevalent *Pseudomonas aeruginosa* clones in cystic fibrosis (CF) is associated with an unfavourable clinical outcome. We studied the clinical characteristics of patients infected with a recently described, highly prevalent *P. aeruginosa* clone (ST406) in two CF centres in The Netherlands. Multilocus sequence typing data were available for 219 patients, of whom 40 (18.3%) were infected with ST406 and 179 with other sequence types. ST406 infection was independently associated with age, having a sibling with ST406 infection and use of inhaled antibiotics, but not with unfavourable clinical outcome, suggesting that high transmissibility is not necessarily associated with high virulence.

Keywords: Clone, cross-infection, cystic fibrosis, MLST, *Pseudomonas aeruginosa*

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Of patients with cystic fibrosis (CF), 60–80% become chronically infected with *Pseudomonas aeruginosa* [1], which is associated with increased morbidity and mortality [2]. The original perception that each patient acquires his or her own *P. aeruginosa* strain from the environment and that transmission only occurs in siblings with CF [3] is disputed by later reports of the occurrence of highly prevalent clones of *P. aeruginosa* in CF centres in Australia and Europe. Many of these clones are highly resistant to antibiotics and appear to be associated with unfavourable clinical outcome [4–8]. To prevent the further spread of transmissible *P. aeruginosa* clones, infection control policies and measures have been put into practice in several countries [9,10]. Recently, a cross-sectional study using multilocus sequence typing (MLST) revealed a highly prevalent clone in the patient population of two large CF centres in The Netherlands (together,

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these centres manage about 45% of the total Dutch CF population), designated ST406 [11]. Genetically, this clone was not closely related to any of the earlier described 'epidemic' *P. aeruginosa* clones, and it has no specific antibiotic resistance profile. We aimed to study whether infection with ST406 is associated with unfavourable clinical outcome in the CF patient population of the CF centres of Utrecht and The Hague, The Netherlands.

In these centres, segregation policies have been adopted since 2005. Sputum samples and throat swabs were collected regularly and were cultured according to the standard diagnostic laboratory protocols of each CF centre. Phenotypically different isolates were collected by randomly taking one *P. aeruginosa* colony of each different colony morphology (based on rough, smooth and mucoid characteristics and colony size) per sample. MLST was performed on all phenotypically different isolates of the first *P. aeruginosa*-positive culture from each patient in 2007 (Utrecht) and the first half of 2008 (The Hague), as described in a previous study [11]. Patients were designated as chronically infected if *P. aeruginosa* was present in more than 50% of all cultures performed in 2006 and 2007. Patients infected with more than one sequence type including ST406, were regarded as being infected with ST406. Demographic data, CF genotype and clinical parameters were collected from the centres' databases. All patients gave written informed consent for storage and evaluation of their clinical data in the CF database for scientific purposes. Statistical analyses were performed using SPSS for Windows version 15.0.1 (SPSS, Chicago, IL, USA).

In total, 561 patients were under treatment at the CF centres of Utrecht and The Hague, excluding patients with a history of lung transplantation. Cultures were collected from 515 patients (92%), and ten patients were excluded because of chronic *Burkholderia cepacia* infection. There were 265 patients (52%) chronically infected with *P. aeruginosa*, and MLST data were available for 219 of these. Forty (18%) patients were infected with ST406, and 179 patients were infected with other sequence types (not ST406). Table 1 shows that chronic *P. aeruginosa* infection is associated with increased age, increased use of inhaled antibiotics and decreased lung function. Factors associated with infection with the highly prevalent clone ST406 are shown in Table 2. There was no significant association between sequence type and percentage of predicted forced expiratory volume in 1 s , body mass index and the number of hospitalization days. In the multiple logistic regression model, the presence of a sibling with ST406, age and the use of inhaled antibiotics were independently associated with ST406 infection. This strong association with having a sibling with the same *P. aeruginosa* sequence type was not a unique feature of ST406: the proportion of concordant siblings was not significantly different between those infected with ST406 (75%) and those infected with sporadic sequence types (58%) (p 0.67).

The observations of an association between chronic *P. aeruginosa* infection and increased age, decreased lung function and increased use of inhaled antibiotics are in accordance with the literature [12,13]. However, the findings regarding the Dutch clone ST406 are different from those described in other countries, as many of the published clones are associated with decreased lung function [4,6,7], decreased nutritional status [6] and/or increased treatment requirements [4,5,7,14,15]. An important difference between the clones

TABLE 1. Association between clinical and demographic variables and chronic *Pseudomonas aeruginosa* infection (results of logistic regression analysis) in 505 cystic fibrosis patients

	Simple logistic regression				Multiple logistic regression	
	OR (95% CI)	*Pseudomonas*-positive (*n* = 265)	*Pseudomonas*-negative (*n* = 240)	p	OR (95% CI)	p
Male gender	0.85 (0.60–1.21)	133 (50.2%)	130 (54.2%)	0.37		
Age (years)						
1–12 (reference category)		42 (15.8%)	118 (49.2%)	<0.001		<0.001
13–24	5.20 (3.21–8.44)	100 (37.7%)	54 (22.5%)	<0.001	3.69 (1.98–6.88)	<0.001
≥25	5.08 (3.21–8.05)	123 (46.4%)	68 (28.3%)	<0.001	2.31 (1.17–4.57)	0.02
Homozygosity for dF508	1.39 (0.96–2.01)	154 (63.4%)	127 (55.5%)	0.08	1.62 (0.99–2.64)	0.05
Pancreatic insufficiency	1.02 (0.65–1.60)	217 (81.9%)	196 (81.7%)	0.95		
ABPA	2.32 (1.30–4.16)	42 (15.8%)	18 (7.5%)	<0.01	1.49 (0.74–3.00)	0.27
Diabetes	2.26 (1.38–3.70)	59 (22.3%)	27 (11.3%)	<0.01	0.90 (0.47–1.70)	0.74
rhDNase	2.67 (1.84–3.88)	132 (49.8%)	65 (27.1%)	<0.001	1.15 (0.69–1.91)	0.59
Inhaled antibiotics	10.66 (6.90–16.47)	173 (65.3%)	36 (15.0%)	<0.001	7.38 (4.46–12.19)	<0.001
Hospitalization days	1.02[a] (1.01–1.04)	7.59 (SD 16.7)	3.50 (SD 13.2)	<0.01	1.00[a] (0.99–1.02)	0.82
BMI z-score	0.92[a] (0.78–1.09)	−0.40 (SD 1.1)	−0.31 (SD 1.0)	0.35		
FEV_1 (% of predicted value)	0.97[a] (0.96–0.98)	63.78 (SD 24.0)	82.39 (SD 24.2)	<0.001	0.98[a] (0.97–0.99)	0.003

ABPA, allergic bronchopulmonary aspergillosis; BMI, body mass index; FEV_1, forced expiratory volume in 1 s; rhDNase, recombinant human DNase; SD, standard deviation.
[a]Change per unit of variable.

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