Identification of airborne dissemination of epidemic multiresistant strains of *Pseudomonas aeruginosa* at a CF centre during a cross infection outbreak


Background: Chronic *Pseudomonas aeruginosa* infection is a major cause of morbidity and mortality for individuals with cystic fibrosis (CF). *P aeruginosa* cross infection outbreaks have recently been reported at CF holiday camps and specialist centres. The mechanism of cross infection is unknown. A study was performed to look for the presence of epidemic strains of *P aeruginosa* in the environment of a CF centre during a cross infection outbreak and to examine their potential modes of spread between patients.

Methods: Microbiological sampling of the environment of the CF facility was performed, including room air sampling. Individual *P aeruginosa* strains were identified by bacterial fingerprinting. The typing patterns were compared with those of epidemic strains responsible for cross infection among the patients.

Results: Epidemic *P aeruginosa* strains were isolated from room air when patients performed spirometric tests, nebulisation, and airway clearance, but were not present in other areas of the inanimate environment of the CF centre.

Conclusions: Aerosol dissemination may be the most important factor in patient-to-patient spread of epidemic strains of *P aeruginosa* during recent cross infection outbreaks at adult CF centres.

*Pseudomonas aeruginosa* is an aerobic Gram negative bacterium that is widely distributed in nature. It may be recovered from water, soil, plants and the general environment, including domestic and hospital locations. It is an opportunistic pathogen for humans and causes chronic pulmonary infection in individuals with cystic fibrosis (CF). Once chronic infection is established, it is virtually impossible to eradicate, even with intensive antibiotic therapy. Chronic *P aeruginosa* infection is associated with an increase in morbidity and mortality for individuals with CF.

Most patients with CF have developed chronic infection with *P aeruginosa* by adulthood. While CF siblings often share the same strain of *P aeruginosa*, the majority of unrelated patients typically harbour unique isolates. *P aeruginosa* cross infection outbreaks have recently been documented in CF holiday camps and CF centres, including the Manchester Adult CF Centre. We identified two epidemic strains of *P aeruginosa* associated with a cross infection outbreak at our CF centre—a novel strain and another also known to have been responsible for epidemic spread at another UK CF centre.

The source and mechanism of acquisition of sporadic *P aeruginosa* infection in individuals with CF is poorly understood. Most patients who successfully eradicate early *P aeruginosa* infection subsequently become re-infected with different strains. Similarly, the mechanism of *P aeruginosa* cross infection during epidemic spread is unknown. We carried out a study to look for the presence of epidemic strains of *P aeruginosa* within the environment of our CF centre during a cross infection outbreak and to explore the potential mechanism of spread of *P aeruginosa* between CF patients.

**METHODS**

The Manchester Adult CF Centre is housed in a modern purpose built facility. All patients have single bedrooms. All treatment, including nebulisation and airway clearance, is performed in the patient’s own room with the door closed. All nebulisers are single patient use only. At the time of a *P aeruginosa* cross infection epidemic the following sampling was performed.

**Inanimate surfaces**

Environmental samples were taken from locations in the CF centre inpatient ward and outpatient facility, including patient rooms and communal areas. Particular attention was paid to moist areas such as washbasins, taps, showers, baths, and soap dispensers, where *P aeruginosa* is known to proliferate. Door handles and objects in communal areas such as the television remote control unit were also sampled. Samples were taken using sterile moistened PROBACT swabs (Technical Service Consultants Ltd, Heywood, UK) which were smeared directly onto selective *Pseudomonas* isolation agar (CM559/SR102, Oxoid Ltd, Basingstoke, UK). The same swabs were transferred to sterile selective broth (CM559/SR102, Oxoid Ltd) and subcultured to the selective agar as described.

**Spirometers**

Patients perform spirometric tests at each outpatient visit and at least twice weekly during inpatient stays using a dry bellows spirometer (Vitalograph, UK). The exterior and interior surfaces of the spirometer tubing, spirometer head, and exterior surface of the spirometer were sampled between patients using the same technique as described above. Disposable mouthpieces with one way valves are used for spirometry. These were not sampled as they are known to become heavily contaminated during spirometric testing (J R W Govan, unpublished data) and therefore are single use and changed by the staff between each patient.

**Hand samples**

Two methods were used to sample the hands of staff. Method 1: Moistened PROBACT swabs were smeared across the palm
and fingers. Swabs were taken from each hand and the presence of \textit{P} \textit{aeruginosa} investigated as previously described. Method 2: Hands were also placed into sterile gloves containing 30–40 ml of maximum recovery diluent (Public Health Laboratories, UK) and all parts of the hands, fingers, and nail areas were massaged for 1 minute. Separate samples were taken from both hands. The solution was then streaked onto the selective agar as described above.

\textbf{Air samples}

Air samples (900 l over 5 minutes) were obtained from a surface air system sampler (Cherwell Laboratories, Bichester, UK) using \textit{P} \textit{seudomonas} isolation agar plates. The air sampler was positioned approximately 500–1000 cm from the patient. Sampling was performed immediately after spirometry, nebulisation, and airway clearance. Samples were also taken in the clinical and communal areas occupied by CF patients.

\textbf{Patients}

We continued to survey the \textit{P} \textit{aeruginosa} strain types harboured by the patients and including cases of new acquisition of \textit{P} \textit{aeruginosa}.

\textbf{Bacterial isolates}

All plates were incubated for a minimum of 72 hours at 37°C. All Gram negative species were further identified using the API 20 NE system (BioMerieux, Basingstoke, UK). Different colonial morphotypes on the same plate were investigated individually. Each isolate was typed using the pyocin typing method for \textit{P} \textit{aeruginosa}\textsuperscript{t} and by genomic fingerprinting by pulsed field gel electrophoresis (PFGE; CHEF-DRII System, BioRad, Hemel Hempstead, UK) following total bacterial DNA digestion with endonuclease \textit{XbaI}.\textsuperscript{t} Typing patterns were compared with \textit{P} \textit{aeruginosa} isolates cultured from the sputum of CF patients attending the Manchester Adult CF Centre.

\textbf{RESULTS}

\textbf{Inanimate surfaces}

306 specimens were taken from the inanimate environment of the CF ward and outpatient department, excluding spirometers and room air samples. The following organisms were isolated from the ward environment: \textit{P} \textit{aeruginosa} (n=5), other \textit{P} \textit{seudomonas} species (n=23), \textit{Alcaligenes xylosoxidans} (n=11), \textit{Enterobacter cloacae} (n=3), \textit{Morganella morgani} (n=1), and \textit{Citrobacter freundii} (n=1). These organisms were all isolated from damp areas such as washbasins, showers, and baths. None of the environmental \textit{P} \textit{aeruginosa} isolates had the same typing profile as the strains of \textit{P} \textit{aeruginosa} responsible for the cross infection outbreak.

\textbf{Spirometer samples}

Forty seven samples were taken from the spirometers. \textit{P} \textit{aeruginosa} was grown from a sample taken from the exterior surface of the spirometer tubing; this isolate had a different bacterial fingerprint from those of the epidemic \textit{P} \textit{aeruginosa}. None of the remaining spirometer samples (n=46) yielded growth of \textit{P} \textit{seudomonas} species.

\textbf{Hand samples}

One hundred and two samples were taken from the hands of staff, 48 using method 1 and 54 using method 2. \textit{P} \textit{seudomonas putida} was grown from the left and right hands of the same member of staff. All other staff hand samples were negative for growth of \textit{P} \textit{seudomonas} species.

\textbf{Room air samples}

Fifty eight air sampling plates were taken from the CF outpatient (n=22) and inpatient (n=36) facilities. \textit{P} \textit{aeruginosa} was isolated from seven of the 58 plates (12.1%), 4/26 immediately after spirometry, 1/9 after air clearance techniques, 1/14 after nebulisation, and 1/9 in a communal waiting room. Typing confirmed the isolates on three plates (one after airway clearance with 1 colony forming unit (CFU) \textit{P} \textit{aeruginosa}/m\textsuperscript{3} air, one after spirometric testing with 1 CFU/m\textsuperscript{3}, one after nebulisation with 2 CFU/m\textsuperscript{3}) as epidemic strains of \textit{P} \textit{aeruginosa} (fig 1).

\textbf{Patients}

At the same time as the environmental sampling was being carried out, a previously "\textit{P} \textit{seudomonas} naive" CF patient resident on the ward developed infection with a multiresistant strain of \textit{P} \textit{aeruginosa}. This patient had been resident on the ward for 4 weeks before \textit{P} \textit{aeruginosa} was isolated. All previous sputum cultures had been negative for \textit{P} \textit{aeruginosa}. Typing confirmed the isolate to be an epidemic strain (\textit{P} \textit{aeruginosa} strain MA). Six other patients who were also resident on the CF ward at the same time are now known to harbour this particular strain of \textit{P} \textit{aeruginosa}.

\textbf{DISCUSSION}

Extensive microbiological screening of the inpatient and outpatient environment has identified a number of \textit{P} \textit{seudomonas} and other Gram negative species; however, we failed to find an environmental reservoir or environmental contamination for the epidemic strains of \textit{P} \textit{aeruginosa}. Epidemic \textit{P} \textit{aeruginosa} could, however, be isolated from room air in the presence of CF patients known to harbour these strains.

At the same time as the environmental sampling was performed, an inpatient acquired infection with an epidemic strain of \textit{P} \textit{aeruginosa}. Six other patients resident on the CF ward at the same time are now known to harbour this strain. Patient-to-patient spread is suggested by our failure to culture the epidemic \textit{P} \textit{aeruginosa} from the inpatient and outpatient environment at this time. The isolation of epidemic \textit{P} \textit{aeruginosa} from room air in the presence of CF patients raises the possibility that there may be airborne spread of epidemic \textit{P} \textit{aeruginosa} strains between patients with CF.

The Manchester Adult CF Centre is housed in a modern purpose built facility with single bedrooms for all patients and close attention is paid to infection control techniques. Although we were unable to isolate the epidemic \textit{P} \textit{aeruginosa} strains from the environment of the CF facility, we did isolate a number of Gram negative organisms. This level of contamination with \textit{P} \textit{aeruginosa} at our CF Centre is less than might be
expected from previous studies of *P. aeruginosa* contamination in hospital environments, but is similar to more recent studies. These differences may reflect changes in cleaning methods and use of modern cleaning agents. In addition to hospitals, such organisms can be found in domestic areas including patients’ homes. A previous study has shown that some CF patients harboured *P. aeruginosa* strains that were also present in the hospital environment. However, it is difficult to know whether this merely represents secondary contamination of the environment by patients with chronic *P. aeruginosa* infection. This study and most previous studies have shown that CF patients harbour different strains of *P. aeruginosa* from those found in the environment of specialist centres. Importantly, it should be emphasised that regular attendance at CF specialist centres is associated with better health for individuals with CF, even at the time of cross infection outbreaks.

If nebuliser equipment is inadequately cleaned, it can become contaminated with *Pseudomonas* and other Gram negative species. Nebulisation equipment should be single patient use and be cleaned and dried thoroughly after each use. On our unit there is no patient sharing of nebuliser equipment, so nebulisers are unlikely to be a source of cross infection. However, sampling of the room air detected *P. aeruginosa* immediately after patients had used their nebuliser. Based on these new data, we recommend that CF patients should not use nebulisers in the same room as other patients with CF. Similarly, when individuals with CF perform airway clearance, other patients should not be present in the same room as epidemic strains of *P. aeruginosa* can be isolated in room air at this time. There is concern that spirometers are a potential source for cross infection, although this is partly dependent on the type of spirometer used. We use dry bellows spirometers with disposable single use mouthpieces fitted with one way valves. We isolated *P. aeruginosa* on one occasion from the exterior surface of the proximal tubing. This was a different strain from that associated with the cross infection outbreak at our centre. An epidemic *P. aeruginosa* strain was isolated from room air after a patient had performed spirometric tests. Although the risk of cross infection from spirometry equipment is minimal provided it is properly cleaned and maintained, spirometry associated airborne spread may present a risk of cross infection to other CF patients if they are present in the same room.

*P. aeruginosa* was not recovered from the hands of staff in the present or previous studies at other CF centres. Neither contamination of the environment nor a breakdown in simple infection control practices has played a role in the *P. aeruginosa* cross infection outbreak at this CF centre. The isolation of epidemic strains of *P. aeruginosa* from room air suggests that aerosol dissemination may be the most important factor in patient-to-patient spread during the recent cross infection outbreaks. Air sampling was done at a distance of 500–1000 cm, which suggests that close contact may be important for cross infection. The duration of airborne contamination following spirometric testing, nebulisation, and airway clearance was not determined in this study but warrants further investigation. The required level of exposure necessary for acquisition is unknown and cannot be identified by ethical experimentation.

In conclusion, in our clinic the reservoir for epidemic multi-resistant strains of *P. aeruginosa* is not the inanimate environment of a CF facility but the patients. It seems likely that cross infection by epidemic strains of *P. aeruginosa* between individuals with CF is by airborne dissemination. To control the spread of *P. aeruginosa* in CF centres we recommend that patients should have single rooms to enable spirometric tests, airway clearance techniques, and nebulisation to be performed without risk to other patients, and cohort segregation of patients who harbour epidemic strains of *P. aeruginosa* should be introduced.

**REFERENCES**

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