Cystic Fibrosis our focus

***Pseudomonas aeruginosa* infection in people with cystic fibrosis. Suggestions for Prevention and Infection Control**

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Fighting for a Life Unlimited

The UK Cystic Fibrosis Trust Infection Control Group

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Pseudomonas aeruginosa infection in people with cystic fibrosis

Suggestions for Prevention and Infection Control Report of the UK Cystic Fibrosis Trust Infection Control Group

Contents

Preface

This document describes precautions that may need to be taken in Specialist CF Centres and CF Clinics where there is a possibility of spread of transmissible strains of *Pseudomonas aeruginosa* between patients. The majority of *P. aeruginosa* is acquired from the environment and not from other patients with CF or from the hospital. However, it is important that all Specialist CF Centres and CF Clinics are vigilant that a problem of cross-infection is not developing amongst their patients.

Whether or not segregation of patients, according to the organisms present in their respiratory secretions, is practised in a clinic, the highest standards of personal hygiene, particularly with regard to respiratory secretions and hand washing, are necessary at all times by patients, relatives and all clinic personnel who have any contact with patients.

Regular expert microbiological surveillance of people with CF is recommended if spread of a transmissible organism amongst patients is to be identified and dealt with at an early stage. For this, expert microbiological laboratory services are required by the clinic. The reference laboratories mentioned in the document are prepared, after discussion, to examine cultures from Specialist CF Centres and CF Clinics who wish to investigate whether they have a cross-infecting strain of *Pseudomonas aeruginosa*.

The present document reviews much of the available information on the prevention and control of *P. aeruginosa* infection in people with cystic fibrosis. Some of the recommendations in this document are based on firm evidence and many on experience. The UK Cystic Fibrosis Trust Infection Control Group has considered the available evidence and considers that there is a risk from cross-infection with some strains of *Pseudomonas aeruginosa*. The recommendations are considered to represent best practice for the prevention and control of *P. aeruginosa* infection with the present state of knowledge; it is hoped that they may serve to provide some guidance for local policies. It is intended that the present recommendations will be revised every two years to take account of new developments.

Finally, the ultimate responsibility for the infection control policy in an individual Specialist CF Centre or CF Clinic lies with the clinic director and staff in consultation with their microbiologist and their hospital infection control committee; together they can decide on the precise precautions that are necessary in their particular clinic.

The UK Cystic Fibrosis Trust Infection Control Group
November 2004

Grading scheme for recommendations used in *Pseudomonas aeruginosa* Infection in People with Cystic Fibrosis

The criteria for the grading of recommendations in this document are based upon a paper by Petrie et al published on behalf of the Scottish Intercollegiate Guidelines Network.

Much of the data in the document are derived from observational studies where randomisation is not appropriate or possible but many are from peer reviewed scientific studies therefore this grading in not always appropriate.

Levels of evidence

Level	Type of evidence (based on AHCPR, 1992)
Ia	Evidence obtained from meta-analysis of randomised controlled trials.
Ib	Evidence obtained from at least one randomised controlled trial.
IIa	Evidence obtained from at least one well designed controlled study without randomisation.
IIb	Evidence for at least one other type of quasi-experimental study.
III	Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies.
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.

Grading of recommendations

Grade	Type of recommendation (based on AHCPR, 1992)
A (levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.
B (levels IIa, IIb, III)	Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of the recommendation.
C (level IV)	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

Petrie GJ, Barnwell E, Grimshaw J, on behalf of the Scottish Intercollegiate Guidelines Network. Clinical guidelines: criteria for appraisal for national use. Edinburgh: Royal College of Physicians, 1995.

Agency for Health Care Policy and Research. Acute pain management, operative or medical procedures and trauma 92-0032. Clinical practice guidelines. Rockville, Maryland, USA: Agency for Healthcare Policy and Research Publications, 1992.

Summary of main recommendations

- All Specialist CF Centres and CF Clinics should have a policy on cross-infection that addresses *Pseudomonas aeruginosa* and considers issues of surveillance, hygiene and segregation.
- All Specialist CF Centres and CF Clinics should provide guidance on the importance of hygiene to people with CF, their carers and all staff involved in their care.
- All Specialist CF Centres and CF Clinics should undertake pro-active surveillance to ensure that evidence of cross-infection is rapidly detected and appropriate measures put in place to limit spread.

1. Introduction

Pseudomonas aeruginosa is the most frequent and important pathogen responsible for chronic infection in people with cystic fibrosis (Cystic Fibrosis Foundation Patient Registry, 1996 [III]; Lyczak, et al 2002 [IV]). There are many different strains of *P. aeruginosa* and these may behave differently. Cross-infection can be defined as acquisition of infection with the same strain directly from another person or, indirectly, from the environment. Cross-infection with *P. aeruginosa* has been reported in some Specialist CF Centres and guidelines are required to reduce the spread of transmissible strains (Govan, 2000 [IV]; Jones & Webb, 2003 [IV]; Saiman, et al 2003 [IV]).

1.1 Chronic infection with *Pseudomonas aeruginosa* should be avoided

Chronic infection with *P. aeruginosa* is defined in this document as the regular culture of the organism from the sputum or respiratory secretions, on 2 or more occasions extending over 6 months or a shorter period if accompanied by a sustained rise of anti-Pseudomonal antibodies (Hoiby, 1974 [III]; Brett et al, 1992 [III]). Recently a more precise definition into 4 groups "chronic", "intermittent", "free" and "never" has been suggested (Lee et al, 2003 [III]). It is now well established that the clinical state can worsen when chronic *P. aeruginosa* infection becomes established.

- The 64% of patients chronically infected with *P. aeruginosa* by the age of 7 years in Toronto had a mean FEV1 that was 10% lower than those who were uninfected (Kerem et al, 1990 [III]).
- The outcome for 81 patients followed for 8 years was as follows: 21/50 (42%) of those with mucoid *P. aeruginosa*, 2/19 (11%) of those with non-mucoid *P. aeruginosa* and only 1/12 (8%) of those with no P. aeruginosa had died (Henry et al, 1992 [III]).
- Culture of *P. aeruginosa* from patients in the first 2 years was associated with increased morbidity, and the finding of *P. aeruginosa* with Staphylococcus aureus with significantly increased mortality, during the first 10 years after diagnosis (Hudson et al, 1993 [III]).
- Despite optimal respiratory management, the pulmonary function of patients who were chronically infected with *P. aeruginosa* deteriorated more rapidly than that of uninfected patients (Pamukcu et al, 1995 [III]).
- In the Danish CF Centre, the age at death correlated with the age of onset of chronic *P. aeruginosa* infection. Six of 135 (4.4%) uninfected patients died and 60 of the 228 (26.3%) of those with chronic *P. aeruginosa* infection died (Frederiksen et al, 1996 [III]).
- The median survival of patients with CF reported to the US CF Foundation database that were chronically infected with P. aeruginosa was 28 years and with Burkholderia cepacia only 16 years but for patients with neither infection it was 39 years (Cystic Fibrosis Foundation Patient Registry, 1996 [III]).
- The pulmonary function of patients who were prevented from developing chronic P. aeruginosa infection by appropriate antibiotic treatment did not deteriorate over 2 years in contrast to those who became chronically infected (Frederiksen et al, 1997 [IIa]).
- Screened infants in Wisconsin who acquired chronic *P. aeruginosa* infection had a more rapid decline in chest X-ray scores than those who were uninfected (Kosorok et al, 2001 [IIb]).

1.2 Variable prevalence of chronic *Pseudomonas aeruginosa* infection

The prevalence of chronic *P. aeruginosa* infection differs considerably between Specialist CF Centres, possibly reflecting varying opportunities for new infections and different treatment policies of early infections (Taylor et al, 1993 [III]; Bauernfeind et al, 1996 [IV]). Other factors may include clinic and ward practices relating to infection control, general hygienic measures such as cleaning, hand washing, care of respiratory equipment, number of patients attending the clinic and segregation of patients according to their microbiological status. Out-of-clinic social mixing and participation in holidays for people with CF are other relevant factors (Ojeniyi et al, 2000 [III]).

An important factor in determining the prevalence of chronic infection is the clinic policy for eradication therapy following first isolation of *P. aeruginosa* (Lee et al, 2004a [III]). Early treatment is only 80% successful (Littlewood et al, 1985 [III]; Valerius et al, 1991 [Ib]; Vasquez et al, 1993 [IIb]; Frederiksen et al, 1997 [IIb]; Wiesemann et al, 1998 [Ib]; Lee et al, 2004b [III]), therefore avoidance of early *P. aeruginosa* infection would be preferable, and economically advantageous (Robson et al, 1992 [III]; Littlewood & Cross, 2000 [III]). Various studies have used different treatment regimens and the optimal method to be used remains unclear. Recent evidence indicates that 28 days of preservative free tobramycin solution for inhalation (TOBI), 300 mg twice daily, provides a safe and effective alternative to eradicate or reduce lower airway density of P. aeruginosa in young children with cystic fibrosis (Gibson et al, 2003 [Ib]).

This report will consider how to reduce the risk of acquisition and cross-infection, from the environment and patients, both outside and within the hospital.

Recommendations

- When *P. aeruginosa* first grows from respiratory culture, eradication should be attempted. Nebulised colistin and oral ciprofloxacin is recommended as first choice

(Valerius et al, 1991 [Ib]) [A].

- If eradication fails, a course of intravenous anti-Pseudomonal antibiotics and nebulised colistin should be given (Antibiotic Treatment for Cystic Fibrosis. UK Cystic Fibrosis Trust. 2002. Section 4.4 [IV]) [C].
- For practical purposes, at least 3 consecutive negative respiratory cultures spread over a 6-month period would indicate that the organism had been eradicated [C].
- The same recommendations apply should reinfection occur [A].

2. Sources of *Pseudomonas aeruginosa*

Pseudomonas aeruginosa is found in many natural environments and also in hospitals.

2.1 General environmental sources

Pseudomonas aeruginosa is found in many natural and domestic environments including plants, soils and surface water, especially warm moist environments containing organic material or contaminated by human or animal waste. Although *P. aeruginosa* thrives in moist environments, it is not considered to be a marine organism because the high salt concentrations inhibit its growth. Hydrotherapy pools and Jacuzzis have been reported as a risk for people with CF because the combination of water, warmth, aeration and human contamination impair adequate disinfection whilst providing ideal growth conditions for *P. aeruginosa* (Govan & Nelson, 1993 [III]; Govan, 2000 [IV]). Swimming pools are generally safe provided chlorination is maintained at recommended levels. Showers have not been reported as a source of *P. aeruginosa* cross-infection.

2.2 Equipment

Although not proved with *P. aeruginosa* specifically, contaminated equipment may be a source of infection e.g. respiratory function equipment. However, respiratory function equipment has not proved to be a major source of infection provided there are appropriate standards of hygiene.

The home nebulisers of 34 people with CF with chronic P. aeruginosa infection did not harbour the organism although other pathogens were identified. Drying was an important part of the cleaning procedure (Hutchinson et al, 1996 [III]).

Dental equipment may be a source of *P. aeruginosa* but is a relatively low risk and patients should not be deterred from visiting the dental surgeon. Three of 103 (2.9%) water samples from 25 dental sessions in an oral health care service were positive for *P. aeruginosa*. Eighteen of 327 samples (5.5%) from 9/82 (11%) sessions from various dental clinics were positive for P. aeruginosa; one was the same strain as isolated from a patient with cystic fibrosis (Jensen et al, 1997 [III]).

2.3 Other factors

The increase in first isolations (66%) and onset of chronic *P. aeruginosa* infection (68%) between October and March has been attributed to the increased likelihood of viral infections (Johansen & Hoiby, 1992 [III]).

There is some historical evidence that prophylactic anti-staphylococcal therapy with a broad spectrum antibiotic (cephalexin) increased the incidence of new *P. aeruginosa* infections (Stutman et al, 2002 [Ib] but a recent systematic review shows the evidence is inconclusive (Smyth & Walters, 2003 [1a]).

2.4 Hospital

Pseudomonas aeruginosa is frequently found in some hospital environments, particularly intensive care units. In one study, washbasins and sinks were found to be contaminated and identical strains were identified on the hands of staff. The contamination level of *P. aeruginosa* in aerosols from the sinks was greater in the mornings, presumably because of the opportunity for overnight bacterial growth (Doring et al, 1991 [III]; Doring, 1993 [III]).

In a 4-week study 88% of all hospital ward washbasin drains contained *P. aeruginosa*, which correlated with the strains isolated from patients; 4 of 16 patients grew the organism from hand cultures. The organisms were detected for up to 180 minutes from hands experimentally contaminated with sputum. Genomic fingerprinting of the bacteria did not distinguish between contamination of the environment from secretions or cross-infection i.e. patient-to-patient transmission (Doring et al, 1996 [III]).

Rates of faecal carriage of *P. aeruginosa* differ widely; carriage rates are generally low (less than 10%) in healthy individuals but may rise to 40% in hospitalised patients (Agnarsson et al, 1989 [III]). Several studies suggest that faecal contamination of patients with CF with *P. aeruginosa* follows primary infection of the airways rather than secondary spread from the gut (Agnarsson et al, 1989 [III]; Taylor et al, 1992 [III]; Speert et al, 1993 [III]).

In a recent study from the Danish CF Centre, where precautions are taken to avoid cross-infection, including segregation of patients according to their microbiological status and good hygienic practice, there was no evidence that the hospital environment was an important source of infection (Zambruska-Sadkowska et al, 1995 [III]). Following their policy of segregation and early treatment, the mean age of acquisition of

chronic *P. aeruginosa* infection in the Danish CF Centre has risen from 6 to 15 years over the past decade (Hoiby & Pedersen, 1989 [III]; Hoiby, 1998 [III]; Hoiby & Frederiksen, 2000 [III]). The effect of segregating patients with chronic *P. aeruginosa* infection in reducing the incidence of infection amongst Danish patients is based on historical controls i.e. the falling annual incidence of new infections following the introduction of segregation (1970-75 8.4%, 1976-80 17% and after segregation in 1981 6.5% falling to the present 3% of new infections per year) (Hoiby & Frederiksen, 2000 [III]). A similar reduction in prevalence of chronic *P. aeruginosa* infection has been reported from another regional paediatric centre and attributed to early diagnosis following neonatal screening, early identification and eradication treatment and patient segregation according to microbiological status (Lee, et al 2004a [III]). As a number of measures were introduced, it is not clear which was the most important.

3. Cross-infection with *Pseudomonas aeruginosa*

3.1 Cross-infection between siblings who have cystic fibrosis

There is evidence that siblings with CF commonly carry the same strain of *Pseudomonas aeruginosa* suggesting that, in closely related individuals sharing the same household for prolonged periods, cross-infection is common or there is a common environmental source.

- The early studies (Kelly, et al 1982 [III]; Speert & Campbell, 1987 [III]), mentioned in Section 3.2, suggested that cross-infection with *P. aeruginosa* did occur between siblings with cystic fibrosis.
- In a 3-year surveillance study involving 835 isolates from 72 unrelated patients with CF and 22 siblings, genomic fingerprinting, serotyping, bacteriophage and pyocin typing showed that all unrelated patients were harbouring different strains. However, siblings with CF were harbouring identical or closely related strains. Transmission within the family was thought to be the most likely cause (Grothues et al, 1988 [III]; Kubesch et al, 1988 [III]).
- In a study of 6 pairs of sibling with CF, 2 pairs of the 6 developed chronic infection with the same strain; in all families transient cross-infection was observed. The authors concluded that cross-infection or acquisition of the same environmental strain exists within the family situation but does not always result in chronic infection (Renders et al, 1997 [III]).

3.2 Evidence for and against infection and/or acquisition at Specialist CF Centres and CF Clinics

Not all studies have revealed evidence of *P. aeruginosa* cross-infection in Specialist CF Centres and CF Clinics.

- Early evidence for cross-infection in Specialist CF Centres and CF Clinics was scanty except for its occurrence in sibling pairs with cystic fibrosis (Kelly et al, 1982 [III]; Speert & Campbell, 1987 [III]; Govan & Nelson, 1993 [III]; Bingen et al, 1993 [IV]).
- A recent study using a reliable genomic typing technique, randomly amplified polymorphic DNA (RAPD), did not reveal evidence of significant cross-infection in the Vancouver CF Clinic (Campbell et al, 1998 [III]). More recently these authors concluded that there is an extremely low risk in the Vancouver CF

Clinic for patients with CF to acquire *P. aeruginosa* from other patients. It appears that prolonged close contact, such as occurs between siblings, is necessary for patient-to-patient spread (Speert et al, 2002 [III]).

- A recent prospective study using pulsed-field gel electrophoresis (PFGE), presently recognised as a gold standard for bacterial fingerprinting, has not shown cross-infection within the Edinburgh paediatric Specialist CF Centre (Govan, unpublished data).

However, there are well-documented reports of outbreaks involving epidemic antibiotic resistant *P. aeruginosa* and data suggesting that *P. aeruginosa* infection may be acquired from the hospital environment when the patient density increases in the clinic.

- In early 1983, in the Danish CF Centre, there was an outbreak of infection with *P. aeruginosa* resistant to aminoglycosides, carbenicillin, ureidopenicillins, ceftazidime, cefsoludin and imipenem. The phenotypic bacterial fingerprinting systems available at the time did not provide unequivocal evidence that a single strain was responsible. However, segregating the affected patients stopped the epidemic and it was felt that clustering of increasingly large numbers of the patients in the CF Centre had been a factor in the outbreak. Close monitoring and immediate isolation of patients with resistant strains was recommended (Pedersen et al, 1986a [III]; Pedersen et al, 1986b [III]).
- *Pseudomonas aeruginosa* infection was more common in the 192 patients treated in the Danish CF Centre than in the 19 treated at other hospitals (Pedersen et al, 1986b [III]). The risk of *P. aeruginosa* infection increased between 1970-1987 when the number of patients increased from 54 to 226 and the prevalence of chronic infection increased from 35% to 59%. (Pedersen et al, 1986b [III]).
- In the Liverpool paediatric CF Clinic, 92 (76.7%) of 120 patients with CF had chronic *P. aeruginosa* infection and 65 of the 92 harboured ceftazidime resistant isolates. The isolates from 55 of these patients were shown to be the same strain by reliable genomic finger printing techniques, pulsed-field gel electrophoresis (PFGE) and flagellin gene polymorphisms. The authors recommended there should be careful regular surveillance and that patient segregation should be instituted to prevent cross-infection (Cheng et al, 1996 [III]).
- Screened infants with CF in Wisconsin were seen at two CF Centres. There was earlier acquisition of *P. aeruginosa* in the clinic where newly diagnosed infants mixed with older patients who were already infected with *P. aeruginosa*. There was a higher prevalence of chronic *P. aeruginosa* infection in patients at the non-segregating centre - in patients 0-3 years (30% vs. 21%) and 3-9 years (80% vs. 63%) and overall (75% vs. 65%). The median "Pseudomonal-free period" was only 52 weeks in the centre where the patients mixed, but was 289 weeks in the centre where segregation was practised (Farrell et al, 1997 [III]; Kosorok et al, 1998 [III]).
- In Australia, 5 children with CF who died before 5 years of age at the Royal Children's Hospital Melbourne during 1991-1995 were all infected by a single clonal strain of mucoid P. aeruginosa. Sputum was examined from the 166 children attending that clinic who produced sputum (51% of the whole clinic). Mucoid P. aeruginosa was grown from the sputum of 115 children of whom 59 shared the same strain, which was not reliably predicted by the antibiotic patterns. This study provides direct molecular evidence of a long-term outbreak by a virulent, resistant mucoid P. aeruginosa strain in a large paediatric CF Clinic. Following this study, segregation was introduced in the clinic (Armstrong et al, 2002 [III]). Widespread use of microbiological surveillance was recommended following subsequent studies which suggested that *P. aeruginosa* cross-infection may be more common than previously believed (Armstrong, et al 2003 [III]).
- Infection by a multi-drug resistant strain of *P. aeruginosa* has been reported from the Manchester Adult CF Centre. Twenty-two (14%) of 154 patients with chronic *P. aeruginosa* infection shared the same clonal strain. Two patients, previously free of *P. aeruginosa* infection, became infected with a transmissible multi-resistant strain: both became chronically infected despite prompt antibiotic therapy (Jones et al, 2001 [III]). A subsequent study found no evidence of an environment reservoir for the transmissible strain at the centre, but did demonstrate significant aerosol dissemination, suggesting this may be an important route for patient-to-patient spread (Jones et al, 2003a [III]).
- Four of 6 children with CF who acquired colistin resistant *P. aeruginosa* between 1995 and 2000 in the paediatric Specialist CF Centre in Leeds harboured the same strain as judged by PFGE genotyping; 2 were sisters. Two of the children were on the same ward together at the time of their first isolation and have both since had overlapping admissions with one of the sisters (Denton et al 2002 [III]).
- In the Liverpool adult Specialist CF Centre, a longitudinal study of *P. aeruginosa* isolates from all patients with CF using PFGE, demonstrated super-infection by a transmissible *P. aeruginosa* strain in 4 patients previously chronically infected with unique strains of the organism. All 4 episodes followed inpatient stays where these patients were not segregated from those who were subsequently shown to be chronically infected with the same transmissible strain. Other patients, who had only attended the outpatient department, did not become infected with the transmissible strain. Extensive investigation of the inpatient facilities did not detect an environmental reservoir for the transmissible strain. The authors concluded that the transmissible strain had been acquired by cross-infection from the previously infected patients and advocated a policy of segregation by genotype of *P. aeruginosa* (McCallum et al, 2001 [III]).

- A recent survey of over 1225 CF isolates of *P. aeruginosa* from 31 Specialist CF Centres and Clinics in England and Wales revealed that at least 72% of patients haboured strains with unique genotypes. Small clusters of related strains were evident in some centres presumably indicating limited transmission of local strains. The most prevalent strain was indistinguishable from that previously described as the 'Liverpool' genotype and accounted for 11% of the patient isolates from 15 centres. The second most common genotype (termed Midlands 1) was recovered from 86 patients in 9 centres and the third genotype, which matched closely the PGFE profile of Clone C, a genotype originally described in Germany, was found in 15 patients in 8 centres: a fourth genotype identical to the published Manchester strain was found in 3 centres. The two most common genotypes accounted for more than 20% of the isolates examined and transmissible genotypes were found in all but 3 centres studied. These data strongly suggest that cross-infection has occurred not only between patients in individual Specialist CF Centres but also between patients attending different centres (Scott & Pitt, 2004 [III]).
- In paediatric and adult CF Clinics in Brisbane the presence of the same transmissible strain of P. aeruginosa was demonstrated in 59% of patients (O'Carroll et al, 2004 [III]).

3.3 Acquisition of *Pseudomonas aeruginosa* at CF holidays and camps

Cross-infection with *P. aeruginosa* has been reported to occur at camps and during holidays for people with CF but with low frequency.

- Earlier studies showed that patients who were Pseudomonas-negative remained negative after the CF camp and those who were Pseudomonas-positive kept the same strain when checked immediately after the camp. The authors suggested there was a low risk of person-to-person transmission (Speert et al, 1982 [III]). However, the cultures may have been taken too soon to identify the true incidence of cross-infection.
- A later study showed that, over a 4-year period, 12 of 40 patients who were newly colonised with *P. aeruginosa* had apparently acquired it at CF recreation camps, clinics or rehabilitation centres. After hygienic precautions were introduced only one episode of transmission was detected in 2 years (Tummler et al, 1991 [IIb]).
- Ninety-one patients with CF who attended a CF camp had respiratory cultures performed on arrival then at 2 weeks, 2 months later and regularly thereafter. The incidence of sputum conversion to Pseudomonas-positive was 7% in previously Pseudomonas-negative children with cystic fibrosis. The eventual incidence of new chronic *P. aeruginosa* infection was approaching 2%. The authors concluded that the eventual risk was comparable to that occurring in the community and "trivial compared with the obvious joy and social benefit derived from a holiday camp" (Hoogkamp-Korstanje et al, 1995 [III]).
- Eighteen German patients were studied before and one week after attending a CF holiday camp and also 12 Israeli patients who joined them after a week. The study supported the occurrence of cross-infection between the patients with cystic fibrosis (Hunfeld et al, 2000 [III]).
- Another publication reviews data from a one-week winter camp in Spain using reliable genomic typing methods. Twenty-seven patients attended the camp and 22 were studied. Seventeen of the 22 were chronically infected with *P. aeruginosa* before the camp but after the camp all 22 harboured *Pseudomonas aeruginosa*. The 5 that were initially Pseudomonas-negative acquired identical strains to those isolated from the other patients with chronic infection. The authors recommended holiday camps should be organised based on infection status to avoid P. aeruginosa cross-infection (Ojeniyi et al, 2000 [III]).

3.4 Transfer of *Pseudomonas aeruginosa* to non-CF individuals

People with chronic *P. aeruginosa* infection are not usually regarded as presenting an infection risk to non-CF individuals. However, serious respiratory infection with a multiresistant strain of *P. aeruginosa* has been reported recently in both parents of a woman with CF who was chronically infected with an identical strain of multiresistant *Pseudomonas aeruginosa* (McCallum et al, 2002 [III]).

A 14-year old boy with bronchiectasis developed multiresistant *P. aeruginosa* infection following several inpatient periods where accommodation was shared with patients with CF known to be infected with the genetically identical strain of *Pseudomonas aeruginosa* (Robinson et al, 2003 [IV]).

Patients, who do not have CF but who are immunologically compromised may be at increased risk.

3.5 Clinical consequences of transmissible *Pseudomonas aeruginosa* infection

Although there is substantial evidence that some transmissible *P. aeruginosa* strains have adverse clinical consequences, it is not clear this applies to all such strains.

- Patients with CF who were infected with a transmissible strain were shown to have an increased number of exacerbations, days of intravenous antibiotics and hospital days than those with sporadic *P. aeruginosa* (Jones et al, 2002 [III]); although a cross-sectional study showed no difference in levels of inflammatory markers between 20 patients with cystic

fibrosis (Jones et al, 2003b [III]).

- A single clonal strain of *P. aeruginosa* found in the Melbourne clinic caused 5 deaths in children before the age of 5 years (Armstrong et al, 2002 [III]).
- A retrospective study showed that patients infected with an epidemic strain had a greater loss of lung function and deterioration in body mass index than patients with sporadic *Pseudomonas aeruginosa* (Al-Aloul et al, 2004 [III]).
- A cross-sectional survey of 336 separate *P. aeruginosa* isolates in the Liverpool Adult Specialist CF Centre showed those with the Liverpool epidemic strain were significantly more antibiotic resistant than the remaining sporadic varieties. However, some epidemic isolates were fully sensitive, indicating that multiresistance alone cannot be used to indicate the presence of transmissible strains (McManus et al, 2004 [III]).

4. Summary of present evidence

- *Pseudomonas aeruginosa* infection is common in people with cystic fibrosis (Section 1.0, 1.2).
- Chronic infection with *P. aeruginosa* can be associated with decline in pulmonary function and a worse prognosis (Section 1.1).
- Initial and re-infections with *P. aeruginosa* can often be eradicated if treated early and chronic infection delayed and possibly avoided (Section 1.2).
- It is likely that most *P. aeruginosa* infection is acquired outside hospital (Section 3.1, 3.3) but it can be acquired in hospital (Section 3.2).
- *Pseudomonas aeruginosa* can be acquired from other people with cystic fibrosis (Section 3.1).
- Transmissible strains of *P. aeruginosa* are widespread in the Specialist CF Centres in the UK. There is evidence that some transmissible strains are associated with a worse clinical outcome (Section 3.5).
- Transmissible strains are capable of super infecting patients who already have infection with other Pseudomonas strains.
- Evidence suggests that 2 or 3 different genotypes of *P. aeruginosa* have spread beyond and between CF Centres in the UK (Section 3.2).
- *Pseudomonas aeruginosa* can be acquired by cross-infection during holidays and camps for people with cystic fibrosis (Section 3.3).
- In some clinics, effective hygienic measures and patient segregation according to microbiological status, appears to have reduced the incidence of acquisition and cross-infection of *P. aeruginosa* (Section 2.4). It is still not clear which of the measures is most important, or whether all are necessary.

5. Prevention of *Pseudomonas aeruginosa* infection

5.1 Regular microbiological surveillance

Although *Pseudomonas aeruginosa* is widespread in the natural environment, respiratory secretions are an important potential route for transmission of *P. aeruginosa* and every effort should be made to reduce the risk of transfer of these secretions from one patient to another either via infected sputum or aerosol spread (Saiman et al, 2003 [IV]).

Surveillance is important within Specialist CF Centres and CF Clinics, so that the clinical staff and microbiologists are aware of the prevalent strains; also to recognise and identify *P. aeruginosa* following the phenotypic changes that are associated with chronic infection (Miller & Gilligan, 2003 [IV]). Thus, laboratories responsible for processing respiratory cultures from patients with CF are advised to follow the methods which utilise selective media, outlined in Antibiotic Treatment for Cystic Fibrosis, Section 8. Microbiological Appendices. (UK Cystic Fibrosis Trust, 2002 [IV]).

It is important that the strains of *P. aeruginosa* that are, or appear to be, more transmissible than usual are identified at an early stage to reduce the possibilities of spreading to other patients with cystic fibrosis. Such strains may or may not have multiple antibiotic resistance; therefore relying solely on antibiotic resistance patterns may fail to identify transmissible strains. It is for this reason that genomic fingerprinting (PFGE is considered to be the present gold standard) of isolates is the preferable method of surveillance.

5.2 National Reference Laboratories at Colindale and Edinburgh

In addition to local facilities, in England and Wales, reference facilities are available through the Laboratory of Hospital Infection, Public Health Laboratory Service, 61 Colindale Avenue, London NW9 5HT under the direction of Dr Tyrone Pitt. Tel 0208 327 7224; Fax 020 8200 7449; Email tyrone.pitt@hpa.org.uk. Complementary facilities are also available at the Cystic Fibrosis Microbiology Laboratory and Strain Repository, Medical Microbiology Division, University of Edinburgh Medical School, Teviot Place, Edinburgh EH8 9AG under the direction of Professor John Govan. Tel 0131 650 3164; Fax 0131 650 6653; Email john.r.w.govan@ed.ac.uk.

The support provided by these laboratories includes the following -

- Confirmatory identification of atypical isolates of *P. aeruginosa* by specific phenotypic tests (where possible) and by PCR-based systems (McIntosh et al, 1992 [III]; da Silva Filho et al, 1999 [III]; Spilker et al, 2004 [III]).
- Strain repositories for storage and comparison of *P. aeruginosa* isolates recovered from Specialist CF Centres in the UK and abroad.
- Genomic fingerprinting to identify clusters of similar strains within patient populations. In such situations, consultation is provided to link local and national developments and exchange strains between Colindale and Edinburgh.
- The Colindale laboratory provides determination of serum antibodies to *Pseudomonas aeruginosa*.

Recommendations for surveillance

- Sputum or cough swabs are cultured regularly at clinic attendances and whenever the patient is unwell using appropriate selective media (e.g. Difco Pseudomonas Isolation Agar). Antibiotic sensitivities should be reported [C].
- Specialist CF Centres and CF Clinics are encouraged to send any organisms that are difficult to identify to one of the reference laboratories [C].
- Genomic fingerprinting is the most reliable way of identifying transmissible strains, and use of this in surveillance is encouraged [B].
- Clinicians and microbiologists should be aware of the identity of strains prevalent in their clinic so they can identify cross-infection at an early stage and can take appropriate action to limit cross-infection. Surveillance should include genotyping of all first-time isolates of *Pseudomonas aeruginosa* [B].

6. Recommendations to limit spread

Available evidence suggests that the risk of cross-infection with *Pseudomonas aeruginosa* does exist. Currently medical opinion is divided as to whether patients with chronic *P. aeruginosa* infection should be segregated from those without this organism, and also whether patients with particular types of *P. aeruginosa* infection, such as transmissible strains, especially if multiresistant, should be segregated from others.

Regular attendance and follow-up at a Specialist CF Centre has been shown to be beneficial to both children and adults (Mahadeva et al, 1998 [III]). Therefore avoiding clinic attendance because of fear of infection is likely to be harmful and seriously interfere with medical care and far outweighs any potential risk of acquiring new infection. Patients and carers should be encouraged to discuss their concerns about infection control measures with the clinic staff.

6.1 Segregation of patients according to their microbiological status

- Every Specialist CF Centre and CF Clinic, large or small, should have a microbiological surveillance and infection control policy for the clinic that considers cross-infection risk. The methods used and extent to which clinics segregate patients should be determined by local policy based on knowledge of the current type and prevalence of organisms infecting the patients. Genomic fingerprinting of *P. aeruginosa* strains is recommended [C].
- Good hygiene should be practised in all outpatient clinics and inpatient facilities to minimise the risk of transmission of *P. aeruginosa* between patients [B].
- Segregation of patients with Burkholderia cepacia complex according to genomovar and from others with CF is mandatory and discussed in detail elsewhere (Burkholderia cepacia complex. Cystic fibrosis Trust, 2004 [IV]). However, Specialist CF Centres and CF Clinics should consider implementing a policy of segregation according to lower respiratory tract bacteriology for all their patients with cystic fibrosis. The risk of cross-infection with P. aeruginosa is small, but it is quite definitely present; although it does not appear to be a problem in some clinics, in others, it can be a significant problem [B]. Segregation of patients is most important where the presence of transmissible strains of P. aeruginosa has been identified [B].
- It is advisable for clinics to monitor the rate of new acquisition of *P. aeruginosa* and prevalence of multiresistant strains. A rise in either may suggest the presence of a transmissible strain although transmissible strains are not necessarily multiresistant [B].
- If a general policy of segregation were implemented, it would be logical for this to cover both inpatient admissions and outpatient clinics. Where appropriate there would be separate clinics for patients chronically infected with *P. aeruginosa* and those who are not. In circumstances where separate clinics were not appropriate infrequent P. aeruginosa growers and those without *P. aeruginosa* infection may instead be seen at the beginning of the clinic or at a different time from those who are chronically infected [C].
- Patients known to have transmissible strains should be seen in separate clinics. They should be separated from both Pseudomonas-positive and Pseudomonas-negative patients [C].
- Depending on the segregation policy adopted, where appropriate the clinics for Pseudomonas-negative, Pseudomonas-positive and for those with transmissible *P. aeruginosa* strains should be ideally held on different days to avoid patients meeting and mixing in other departments e.g. laboratory, pharmacy, X-ray, etc. Alternatively a patient's own local pharmacy may supply the drugs, or the clinic can check that there are no other patients with CF expected in the various departments [C].

6.2 In the outpatient clinic (*also applies to inpatient care)

Good hygienic measures are of great importance in any Specialist CF Centre or CF Clinic. These should form part of the local infection control policy for the clinic, but the following are suggestions for best practice:

General hygienic recommendations to limit cross-infection (applicable whether or not a policy of segregating patients is in force).

- *Hand washing, disinfection with alcohol rubs or the use of disposable gloves before and after contact with each patient and at the beginning and end of clinics is recommended to minimise cross-infection [C].
- *Patients are encouraged to cover their mouth and nose when coughing or sneezing [B].
- *Patients should wash or disinfect their hands before use of a spirometer or other handheld apparatus [C].
- *Respiratory function tests should be performed in a well-ventilated room away from other patients [B].

- Local infection control policies should be established to prevent contamination and cross–infection from clinic equipment. This will depend on the nature of the equipment [C].
- *Collection of sputum specimens and cough swabs should be done in a well-ventilated room away from other patients [B].
- *Sputum pots should not be left uncovered and soiled tissues must be disposed of immediately after use in the clinical waste bin. Sputum should not be expectorated down toilets, sinks, and washbasins or in showers [C].
- Airway clearance techniques should be carried out in a separate room away from the waiting area [B].
- The physiotherapists should take appropriate hygienic precautions to prevent contamination of their hands and clothing with respiratory secretions by the use of disposable aprons [B].
- *Cleaning of surfaces and apparatus between patients should be specified by local infection control policies for the clinic. All equipment should be cleaned and dried after use and maintained according to local infection control policies [C].
- Apparatus, stethoscopes, sphygmomanometers, auroscopes etc. should be cleaned between patients [B].
- Consideration should be given to the potential for possible cross-infection afforded by toys, books, computers, game consoles and other communal facilities. Preferably, children should be encouraged to bring their own toys and books [C].

6.3 In the ward

For inpatients it is essential that all staff follow general hygienic precautions. Hygienic measures that apply to inpatients with CF and the staff taking care of them should form part of the local infection control policy for the CF unit, but the following are suggestions for good practice:

General hygienic recommendations to limit cross-infection

- All members of medical, paramedical, nursing and other staff who have physical contact with patients should practice hand washing or appropriate disinfection of hands between dealing with different patients. This includes anyone who comes into contact with the patient [C].
- Patients should have well-ventilated single rooms of adequate size and there should be en suite facilities in all rooms [C].
- Respiratory function tests, exercise tests, nebulisation and airway clearance treatment sessions should be carried out separately either in the physiotherapy department, a treatment room or in the patient's own room with the door closed [C].
- All patients who require them should have their own air compressor and nebuliser system, oxygen therapy delivery devices and airway clearance devices. In general, equipment should not be shared between patients [C].
- All equipment should be cleaned and dried after use and maintained according to the local infection control policies for the CF unit [C].
- Sinks, taps and showers should be cleaned according to local infection control policies for the CF unit [C].
- Apparatus, stethoscopes, sphygmomanometers, auroscopes etc. should be cleaned regularly [C].
- Consideration should be given to minimising the opportunity for cross-infection afforded by the use of communal toys, pens, computers, board games by regular cleaning. Eating and drinking utensils and sweets should certainly not be shared between patients. Ideally, food should be taken in the patients' rooms rather than at a communal table [C].
- Where a policy of segregation is in force in a particular Specialist CF Centre or CF Clinic rooms should be cleaned between patients according to local infection control policies for the unit [C].
- Transmissible Pseudomonas-positive patients, other Pseudomonas-positive patients and Pseudomonas-negative patients should not mix with one another. It is recommended that separate bathroom and toilet facilities are available on the ward if en suite facilities are not provided [C].
- Hospital schooling arrangements should be arranged to avoid mixing Pseudomonas-positive and Pseudomonas-negative patients [C].

6.4 Away from the hospital

Casual meetings between people with CF, including brief encounters indoors and outdoors, carry a risk of infection and this risk is increased the longer and closer the contact.

Recommendations

- Patients should discuss cross-infection issues with their physician and CF team and be aware of their own microbiological status [C].
- All communal CF camps and holidays should be avoided [B].
- Spa and other forms of aerated baths should be avoided [B].
- Schooling: although there is no evidence that *P. aeruginosa* infection can be transmitted between children in the school environment, it is preferable for children with CF attending the same school to be in different classes [C].
- Higher education: students should be aware of their microbiological status and may wish to discuss this with their CF physician, the Student Health Service (who then has legal responsibility) and their personal tutor [C].

- Workplace: people with CF should be aware of their microbiological status and may wish to discuss this with their CF physician and Occupational Health Services who can then take appropriate action to minimise the risk of cross-infection [C].
- Siblings with CF should have separate bedrooms and should carry out their airway clearance and other treatments separately [C].

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At the Trust we are:

- Investing in cutting-edge research
- Driving up standards of clinical care
- Providing support and advice to people with CF and their families
- Campaigning hard for the issues that really matter

Fighting for a Life Unlimited