

Prevention of Cross-Infection in Cystic Fibrosis: How relatively simple initiatives have improved the prognosis for people with CF in Denmark

By Claus Moser, MD PhD and Niels Højby, MD

The majority of adult patients with cystic fibrosis (CF) have chronic bacterial lung infection. The most common pathogens in CF around the world are:

- *Pseudomonas aeruginosa* (*P. aeruginosa*), followed by
- *Staphylococcus aureus* (*S. aureus*),
- *Burkholderia cepacia* (*B. cepacia*) complex,
- *Achromobacter xylosoxidans* (*A. xylosoxidans*),
- *Stenotrophomonas maltophilia* (*S. maltophilia*)
- non-tuberculous mycobacteria (NTM).

Prevalence (or the number of people infected) with these bacteria, varies greatly between different CF centers around the world.

Once the chronic infection is established, it can only rarely be eradicated from the lungs of CF patients, due to the ability of the bacteria to form protected microcolonies called bio-films. Some of the bacteria may become very slimy (mucoïd) making them even more difficult to treat. The bio-film mode of growth, and the propensity to become mucoïd, protects the bacteria from the immune system of the CF patient and the antibiotics given to the patient to treat the infection. Furthermore, it is now widely accepted that the ongoing inflammatory response to the chronic lung infections, is responsible for damage of the lung tissue and loss of lung function observed in patients with CF.

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The major contributor to prolonged life expectancy in recent years, and markedly improved prognoses in CF, is improved treatment of chronic lung infections. Other initiatives such as prompt treatment of diabetes, physiotherapy and treatment with DNase (Pulmozyme) also add to the increased quality of life for CF patients. If CF patients could escape the chronic lung infection or at least delay the onset of chronic infection as long as possible, this would dramatically add to their life expectancy. This article describes how relatively simple initiatives implemented in Denmark have improved the prognosis in patients with CF.

Mode of acquisition

To avoid lung infection, the mode of acquisition (how you get infected) has to be taken into consideration. Since this varies with the kind of organism that is present, we will describe the mode of acquisition of the three most common and most feared infections in people with CF.

Acquisition of *Pseudomonas aeruginosa*

In general, *P. aeruginosa* can be acquired from both the environment and from infected patients.

In nature, *P. aeruginosa* is present in fresh water and soil contaminated by humans and animals. Other environmental sources are inadequately chlorinated swimming pools and whirlpools.



More potential sources of *P. aeruginosa* have also been recognized in intensive care units, dentists, sinks, toys and hand-soaps in CF wards. A possible explanation for the relatively high presence of *P. aeruginosa* in the CF wards is that *P. aeruginosa* in sputum can survive for up to 8 days on dry surfaces. Therefore, hospital locations and the immediate surroundings of CF patients must be considered contaminated until they are properly cleaned, if chronically infected patients have been attending.

“...The most important evidence of cross infection is the dramatic reduction in *Pseudomonas aeruginosa* incidence which has resulted from segregation of non-infected from chronically infected patients”

Dr. Niels Høiby

Cross-infection with *P. aeruginosa* from other patients is considered likely due to the fact that siblings often carry the same strain and the transmission of specific strains during social events like summer and winter camps from chronically infected to previously uninfected patients. The epidemic spread of antibiotic resistant strains and the relationship between the increase in the number of chronically infected patients and time spent in the CF center, also points to cross-infection between patients. The most important evidence of cross infection is the dramatic reduction in *P. aeruginosa* incidence, which has resulted from segregation of non-infected from chronically infected patients. Although not the major topic of this article, it should be mentioned that the early aggressive treatment upon isolation of *P. aeruginosa* has significantly reduced numbers of chronically infected CF patients, further resulting in decreased transmission of *P. aeruginosa*.

Acquisition of *Staphylococcus aureus*

In contrast to *P. aeruginosa*, a relatively high frequency, up to 10-30% of healthy carriers of *S. aureus* can be observed, and the most important route of transmission to CF patients is thought to be from healthy carriers or non-CF patients, although transmission of methicillin resistant *S. aureus* between CF patients has been reported. The major mode of transmission is believed to be by hand contact. In the pre-antibiotic era the majority of patients with CF died before 10 years of age, and most patients actually succumbed due to *S. aureus* lung infections. Regular microbiological examinations followed by aggressive antibiotic treatment can possibly reduce the prevalence of CF patients with chronic *S. aureus* lung infection below 10%. Furthermore, the risk of acquiring methicillin resistant *S. aureus* in the CF center is reduced in this way.

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Acquisition of *Burkholderia cepacia* complex

The *B. cepacia* complex consists of different so-called genomovars of which some occasionally can lead to chronic lung infections in CF patients. The most common is *B. cenocepacia* and *B. multivorans* but in addition *B. cepacia*, *B. vietnamensis* and *B. gladioli* have also been recognized as CF pathogens. *B. cepacia* complex is responsible for different clinical patterns of lung infections, the most serious being the *B. cepacia* syndrome. The *B. cepacia* complex is a common part of the microflora in soil and can act as a plant pathogen. In addition, the *B. cepacia* complex has been isolated from food stores, salad bars, and greenhouses, and it may be more common in rural than in urban environments. Even though the overall prevalence of *B. cepacia* complex in CF centers is relatively low, some centers have higher prevalence (e.g. over 31% of CF patients in Toronto have been reported to be diagnosed with *B. cepacia* complex)².

An important reason seems to be cross-infection, and there are several reports of spread among CF patients, including by social contact outside the CF centers. A famous outbreak was reported from UK in 1990-92, where the index patients acquired the *B. cepacia* complex strain in Canada during a summer camp, and subsequently spread it while attending weekly fitness classes.

Intensive investigations have identified routes of transmission by direct contact between infected and non-infected patients, as well as through contaminated equipment, and an important observation is that CF centers which do not segregate these patients have had ongoing transmission of *B. cepacia* complex.

Control of cross-infection by intervention

Intervention by cohorting of CF patients and improved hygiene precautions were implemented in Denmark in 1981, in order to avoid transmission of pathogens from infected to non-infected CF patients by physical contact or coughing at close range². Cohorting means dividing CF patients into separate subgroups according to their infection status, and also segregating the patients geographically (different wards or rooms) and/or segregating the patients by time (different days).

The “being infective” status is based on bacteriological findings, and on whether the patient is intermittently infected (pathogen is eradicated at later controls,- and the patient does not develop an immune response) or chronically infected (the pathogen is currently being isolated over a 6 month period and/or the patient does develop an immune response).

Seeing the patients frequently allows rapid detection of infection, giving the opportunity for early aggressive treatment and thereby reducing the risk for transmission of the pathogen. Cohort segregation (patients with the same bacterial species) inhibits transmission of the bacteria by physical contact or coughing to unaffected persons. Indeed, the mean time from first isolation of *P. aeruginosa* to onset of chronic *P. aeruginosa* lung infection increased from 1 to 3 years after implementation of cohorting of CF patients in Denmark.

The CF patients in the Copenhagen CF center in Denmark are segregated based on identification of the following bacteria from the lower airways of the patients:

- 1) no *P. aeruginosa*,

- 2) intermittent *P. aeruginosa* infection,
- 3) chronic infection with antibiotic sensitive strain of *P. aeruginosa*,
- 4) chronic infection with multiply resistant strains of *P. aeruginosa*, and
- 5) intermittent or chronic infection with organisms belonging to the *B. cepacia* complex (each patients with *B. cepacia* complex forms a unique cohort).

Five wards are ideal but not possible in most hospitals. Patients in cohort 2 can be hospitalized with patients from cohort 1, however in different rooms, since intermittent colonized patients have low number of bacteria and often do not produce sputum. Cohort 1) and 2) can also be seen in out-patient clinic on the same days, since cohort 2) is either free of *P. aeruginosa* in the last sputum sample taken 4 weeks earlier or on anti- *P. aeruginosa* treatment. Cohorts 3) and 4) are seen on separate days and all clinic rooms are cleaned using hypochlorite disinfectants every morning. Patients with *B. cepacia* complex are seen in separate rooms, which are cleaned after every patient.

Furthermore, the staff must disinfect hands with chlorhexidine-ethanol and change gowns between patients belonging to different cohorts, and between each patient with *B. cepacia* complex. Following lung function, elbow-piece, mouthpiece and nose clip are changed after each patient and sterilized in ethanol.

For the first four cohorts separate camps and social events are advised, where each patient with *B. cepacia* complex is considered unique, and they are therefore advised against contact with any other CF patient. If a chronically infected patient (cohort 3) or 4)) get rid of the bacteria as judged by negative culture results and antibody response normalizes they can attend camps if they remain culture negative for 6 months.

In addition to general universal precautions for preventing cross-infection, cohorting has proven efficient in preventing cross-infection with *P. aeruginosa* and *B. cepacia* complex. Seeing patients on different days and disinfecting the clinic thoroughly between cohorts enables cohorting in the out-patient clinic, and cohort patients who are admitted to hospital can be seen in separate wards.

Claus Moser, MD, Ph.D specializes in Clinical Microbiology. He has worked with Professor Høiby for more than ten years. His research interests include chronic infections - especially chronic Pseudomonas aeruginosa lung infections in patients with CF, urinary tract infection in patients with spinal cord injuries, and the significance of immune responses during chronic infections.

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Editor's Note

Dr. Moser and Dr. Høiby treat patients within an extremely high standard of care in Denmark. We appreciate the fact that they have provided some detailed information on microbiology, mode of Infection, and Infection Control Measures. It is important to understand that well-defined Infection Control Measures exist, for example as defined by CDC – U.S. American Centers for Disease Control and Prevention. This article is a product of long and careful consideration by international CF experts, and we appreciate the effort Dr. Moser and Dr. Høiby put forth to produce this article.

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