

Epidemiology of *Pseudomonas cepacia* in cystic fibrosis

STATEMENT FROM THE MEDICAL/SCIENTIFIC ADVISORY COMMITTEE
CANADIAN CYSTIC FIBROSIS FOUNDATION

PSEUDOMONAS CEPACIA HAS BECOME AN IMPORTANT PATHOGEN in patients with cystic fibrosis (CF) during the past decade with colonization rates in some North American CF clinics of 20 to 30%. Furthermore, it is the opinion of some clinicians that colonization/infection with *P cepacia* is associated with a very poor prognosis, with some patients dying from necrotizing pneumonia (a syndrome quite dissimilar to that seen with *Pseudomonas aeruginosa*) (1).

Issues related to the epidemiology of *P cepacia* colonization and infection in patients with CF have engendered substantial confusion and debate over the past few years. The debate has focused on issues of nosocomial spread and the attributable risks associated with contact between colonized and noncolonized CF patients in both social and medical environments. This controversy has been fuelled by widely divergent opinions and recommendations regarding the best and safest infection control policies for limiting the rate of acquisition of *P cepacia* by CF patients. The debate has become highly polarized with some clinicians recommending that patients who are colonized with *P cepacia* should be prohibited from having any contact (in either social or medical settings) with uncolonized patients. This strong interdiction (which is far more extreme than that recommended by the Medical/Scientific Advisory Committee of the Canadian Cystic Fibrosis Foundation)

has created substantial discord and anxiety among patients with CF, their families and their caregivers. Although much remains to be learned about the biology, pathogenetic mechanisms and epidemiology of *P cepacia*, the current 'state-of-the-art' does not support such extreme recommendations.

As a result of this controversy, the Canadian Cystic Fibrosis Foundation convened a one-day workshop in Toronto in July 1991 to reach a consensus on infection control recommendations for prevention of spread of *P cepacia* among CF patients. The participants at the workshop concluded the following:

- Ribotyping is the best method currently available for typing *P cepacia* for epidemiological purposes;
- Although acquisition of *P cepacia* by CF patients is associated with widely variable clinical outcome, on balance the prognosis is worse for patients colonized than for those who are culture-negative;
- Close and sustained contact among patients with CF appears to facilitate acquisition of *P cepacia*. The mechanism by which this occurs has not been determined nor have the optimum precautions required to prevent new acquisition;
- Until more is known about the mode(s) of *P cepacia* acquisition, patients with CF who are

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colonized should not sleep in the same hospital room with those who are culture-negative;

- The incidence of *P cepacia* colonization has decreased substantially in at least two large North American CF centres during the past decade. The role of infection control practices in effecting these changes remains to be determined. Nonetheless, cohorting appears to have decreased the rate of new acquisition.

The Medical/Scientific Advisory Committee of the Canadian Cystic Fibrosis Foundation has recently reviewed new information since the 1991 workshop and has drawn the following conclusions:

CURRENT STATE OF KNOWLEDGE (1993)

- Patients with CF who are colonized with *P cepacia* have a worse prognosis than those who are uncolonized (2,3).
- Acquisition of *P cepacia* is rarely associated with necrotizing pneumonia and a precipitous clinical deterioration, as was observed in the syndrome described about 10 years ago (1).
- In CF centres where colonized patients have been cohorting and restricted from having contact with uncolonized patients, the rate of new acquisition has decreased substantially.
- Although there is strong circumstantial evidence that *P cepacia* may be spread from one patient with CF to another (4), direct proof is lacking. The data accumulated to date also support the possibility of acquisition of *P cepacia* from the environment.

RECOMMENDATIONS FOR INFECTION CONTROL

Based upon the available evidence that acquisition of *P cepacia* is associated with an adverse prognosis and that spread from patient to patient may occur, measures to prevent such spread should be instituted as follows:

- Patients with CF who are colonized with *P cepacia* should avoid prolonged close contact with patients who are uncolonized;
- Patients who are colonized with *P cepacia* should not share a hospital room with patients who are uncolonized;
- Further measures to prevent contact between colonized and uncolonized CF patients should be determined by individual clinic directors as determined by the local experience with *P cepacia* and the feasibility of cohorting patients.

IS *PSEUDOMONAS CEPACIA* ACQUIRED PREDOMINANTLY FROM OTHER CF PATIENTS OR FROM THE ENVIRONMENT?

An answer to this question must be found urgently in order to rationalize infection control policies and to minimize the social turmoil which has arisen from this

controversy. In order to resolve the question of whether or not *P cepacia* can spread from one patient with CF to another, the following research goals must be achieved:

- Establish sensitive methods for better identifying *P cepacia* in clinical specimens using molecular diagnostic probes;
- Develop standardized and specific methods for identifying *P cepacia*;
- Establish a standard reference collection of *P cepacia* isolates for collaborative/comparative investigations. This collection should be composed of epidemiologically-characterized 'wild' isolates as well as established 'laboratory' strains;
- Identify the most effective procedure for typing *P cepacia* for epidemiological purposes. Compare newer methods including ribotyping and multilocus enzyme electrophoresis with older methods based on phenotypic differences;
- Determine whether *P cepacia* is merely a marker of disease severity in CF or is responsible per se for deterioration in clinical status;
- Determine why there are such dramatic regional differences in rates of colonization and disease with *P cepacia* in CF patients;
- Determine how *P cepacia* is acquired by patients with CF. Establish if it is spread directly from person to person, if there is an intermediate fomite or if the strains are acquired directly from the environment;
- Determine the optimum infection control practices for prevention of *P cepacia* acquisition;
- Establish an animal model of *P cepacia* infection to better assess differences in virulence among strains.

CREATION OF A REPOSITORY OF *PSEUDOMONAS CEPACIA* STRAINS

To achieve the research goals outlined above and to determine how best to control colonization and infection with *P cepacia*, the Canadian Cystic Fibrosis Foundation supports the establishment of a concerted Canadian effort to answer fundamental questions about the epidemiology of this organism. As a first step in the process, *P cepacia* strains from as many patients and geographical regions as possible should be accumulated in a central repository. Creation of this repository will facilitate standardization of methodologies and will permit rational design of epidemiological studies.

DIRECTIONS FOR SENDING *PSEUDOMONAS CEPACIA* STRAINS

If you or your colleagues are interested in participating in studies designed to answer questions about the epidemiology and pathogenesis of *P cepacia*, kindly send the following to Dr David Speert, Department of Pediatrics, University of British Columbia:

- At least one strain of *P cepacia* from each patient in your clinic who is colonized;
- Sequential isolates of *P cepacia* from individual CF patients if your microbiology laboratory saves such strains;
- Other clinical or environmental isolates of *P cepacia* from your hospital, if available.

For each strain of *P cepacia* you send, please supply the following:

- Name of clinic from which specimen was obtained;
- Patient identification code or environmental source;
- Date of acquisition of specimen;
- Patient's place of residence (if known).

The strains should be prepared, packaged and sent as follows:

- Inoculate each strain of *P cepacia* onto Amies Charcoal Agar Transport swabs (Star Plex Scientific, Mississauga, Ontario);
- Place transport swabs in sealed plastic bag(s) and enclose in a shipping box with plenty of padding;
- Be sure to fill out a Toxic Substance Control Act (TSCA) form and submit it with the package for shipment;

- Send immediately by courier to: Dr David Speert, Room 304, Research Centre, 950 West 28th Avenue, Vancouver, British Columbia V5Z 4H4. Telephone (604) 875-2438, Fax (604) 875-2496.

Please direct enquiries regarding preparation of strains for shipment and other details related to shipment to:

Ms Maureen Campbell
Telephone (604) 875-2469
Fax (604) 875-2496.

REFERENCES

1. Isles A, Maclusky I, Corey M, et al. *Pseudomonas cepacia* infection in cystic fibrosis: An emerging problem. *J Pediatr* 1984;104:206-10.
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3. Tablan OC, Martone WJ, Doershuk CF, et al. Colonization of the respiratory tract with *Pseudomonas cepacia* in cystic fibrosis: Risk factors and outcomes. *Chest* 1987;91:517-32.
4. LiPuma JJ, Dasen SE, Nielson DW, et al. Person-to-person transmission of *Pseudomonas cepacia* between patients with cystic fibrosis. *Lancet* 1990;ii:1094-6.