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# Infection control and the significance of sputum and other respiratory secretions from adult patients with cystic fibrosis

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## Abstract

**Background:** There is limited data available on the environmental and public health impact of the microbiological hazards associated with sputa from patients with cystic fibrosis [CF]. *Pseudomonas aeruginosa*, *Burkholderia cenocepacia* (formerly *Burkholderia cepacia* genomovar III), *Staphylococcus aureus* and *Stenotrophomonas maltophilia* are bacterial pathogens which are commonly found in the sputum of CF patients. A study was performed to ascertain the amount of sputum produced relating to microbial loading, as well as the diversity of bacteria present in a population of adult patients, with particular attention to pathogenic organisms.

**Methods:** Sputum from adult [>18 years old] CF patients [n = 20], chosen randomly from a population of 138 CF patients, was collected over a 24 h period on admission to the in-patient CF unit and enumerated quantitatively, as well as the sputa from 138 adult CF patients was examined qualitatively for the presence of infecting microflora. In addition, all different phenotypes from the sputum of each patient were identified phenotypically employing a combination of conventional identification methods [e.g. oxidase], as well as the API Identification schemes [API 20 NE, API 20 E].

**Results:** This study demonstrated that patients with cystic fibrosis generate large numbers of bacteria in their sputum, approximating to $10^9$ organisms per patient per day. Although these organisms are introduced to the environment from the respiratory tract mainly via sputum, relatively few represent true bacterial pathogens and therefore are not clinically important to the general public who are immunocompetent. The greatest risk of such environmental microbial loading is to other patients with CF and therefore CF patients should be made aware of the hazards of acquiring such organisms from the environment, as well as socializing with other CF patients with certain transmissible types, such as *Pseudomonas aeruginosa* and *Burkholderia cenocepacia*.

**Conclusions:** Environmental health professionals should therefore be aware that CF patients are a greater risk to their peer grouping rather than to the general public or health care workers and that good personal hygiene practices with CF patients should be encouraged to minimize environmental contamination and potential acquistion.

## Introduction

Cystic fibrosis [CF] is the most commonly inherited disease in persons originating from a white and European background, currently affecting approximately 30,000 adults and children in the US [1]. The defective gene carrying the mutation is carried in one in every 31 Americans [one in 28 Caucasians], equating to more than 10 million people being a symptomless carrier of the defective gene [1]. It is an autosomal recessive condition whereby two alleles carrying a polymorphism in the cystic fibrosis transmembrane conductance regulator [CFTR] gene phenotypically manifest the disease state through a variety of multiorgan problems, associated with a pharmacological disfunction to regulate anion [chloride] secretion across cell membranes. The most common complication of CF is the recurrence of chronic chest infections usually caused by bacterial pathogens [2]. CF patients continue to suffer from recurrent and chronic respiratory tract infections and most of their morbidity and mortality is due to such infections throughout their life [3]. These infections are usually dominated by Gram-negative organisms, especially by the pseudomonads, including *Pseudomonas aeruginosa*, *Burkholderia cepacia* and *Stenotrophomonas maltophilia*. However, with modern antibiotic management with improved antimicrobial agents, such as the carbapenems, CF patients have an improved survival, resulting in more adults in employment.

One important manifestation of the CF patient's disease morbidity is the constant presence of a cough, which generally increases in frequency during an infective pulmonary exacerbation [4]. Patients with CF also need to perform daily physiotherapy which involves a variety of techniques designed to enhance the expectoration of sputum from the lungs. Quantitative microbiology of sputum has been included as an important endpoint in several studies [5-8] and these have demonstrated that bacterial loading of CF sputum is in the order $10^7$-$10^9$ colony forming units [cfu] per gram sputum [9] and that the proportion of individual pathogens may vary, depending on the microbial ecology present. To date, the majority of CF clinics routinely monitor the microbiological status of patients through qualitative [presence/absence] examination of sputum specimens from the patient, employing a combination of selective and non-selective culture media to detect which bacteria are present, so that the most appropriate antibiotics are administered to help control the pulmonary infection and also to avoid transmissible respiratory pathogens spreading from person-to-person.

There is limited data available on the environmental and public health impact of the microbiological hazards associated with CF sputum and respiratory secretions outside of CF, particularly on: – [i]. various patient groupings [healthy immunocompotent individuals, immunocompromised patients, other CF patients], [ii]. environmental loading and contamination, [iii]. veterinary medicine and [iv]. food. Therefore, the main aim of this study was to determine the mass of sputum produced on a daily basis by adult CF patients and the range and public health significance of the resident microflora/microbiota of sputum in order to evaluate the infection control and environmental burden due to such secretions.

## Materials & Methods

### *Determination of mass of daily sputum production in CF patients*

Sputum from adult [>18 years old] CF patients [n = 20], chosen randomly from a population of 138 CF patients, was collected over a 24 h period on admission to the inpatient CF unit. All sputum produced by each individual patient was collected in disposable collection containers and was pooled and weighed on digital scales [Sartorius, Germany], to the nearest gram, to determine total daily mass of sputum produced per patient.

### *Qualitative isolation of culturable microflora in sputum*

Sputum was collected immediately after a standardized session of physiotherapy and was stored at ambient temperature and was processed within 4 h from collection. Fresh sputum [1 ml min ] was mixed with an equal mass [1:1] of Sputasol [Oxoid SR089A, Oxoid Ltd., Poole, England] and was incubated in a water bath at 37°C for 15 min, before further processing. Processed sputa from 138 adult CF patients attending the regional CF centre was obtained and 20 μl were inoculated individually and incubated, onto several selective media, including: – Columbia Blood Agar [Oxoid CM0331] supplemented with 5% [v/v] defribinated horse blood, Chocalate Agar [incubated microaerophilically in 5% [v/v] $CO_2$], MacConkey Agar [Oxoid CM0007], *Pseudomonas* Isolation Agar [PIA] [Oxoid CM0559 + SR0102] and *Burkholderia cepacia* Selective Agar [BCSA] [MAST, MAST DM253E + SV22, MAST Diagnostics Ltd., Merseyside, UK]. All media were incubated aerobically at 37°C for 48 h, unless otherwise stated. The PIA and BCSA plates were incubated at room temperature for a further three days following initial 48 hrs incubation. In addition, all different phenotypes from the sputum of each patient were identified phenotypically employing a combination of conventional identification methods [e.g. oxidase], as well as the API Identification schemes [API 20 NE, API 20 E] [Biomérieux, Les Halles, France].

## Results and Discussion

Of the 20 adult patients examined randomly on admission, a mean value of 26.8 ± 17.8 g sputum was expectorated per patient per day, with a range of 7 – 69 g. Qualitative examination of a larger population of adult patients [n = 138] demonstrated 25 infection/co-coloniz-

**Table 1: Microbiological co-colonizing/infection patterns isolated from the sputum of 138 adult patients with cystic fibrosis**

| Microflora/Microbiota present | Number of patients | Percentage of adult CF population |
|---|---|---|
| *Pseudomonas aeruginosa* | 50 | 36.2 |
| *Burkholderia cenocepacia* | 17 | 12.3 |
| *Staphylococcus aureus* | 14 | 10.1 |
| *Pseudomonas aeruginosa &Staphylococcus aureus* | 7 | 5.1 |
| *Stenotrophomonas maltophilia* | 5 | 3.6 |
| *Pseudomonas aeruginosa &Burkholderia cenocepacia* | 4 | 2.9 |
| *Burkholderia multivorans* | 3 | 2.2 |
| *Candida* sp. | 3 | 2.2 |
| *Burkholderia cenocepacia &Staphylococcus aureus* | 2 | 1.5 |
| *Candida sp. &Burkholderia cenocepacia* | 2 | 1.5 |
| *Aspergillus* sp. *&Pseudomonas aeruginosa* | 2 | 1.5 |
| *Pseudomonas fluorescens* | 1 | 0.7 |
| *Aspergillus* sp. | 1 | 0.7 |
| Commensals | 1 | 0.7 |
| *E. coli* | 1 | 0.7 |
| *Haemophilus influenzae* | 1 | 0.7 |
| *Haemophilus parainfluenzae* | 1 | 0.7 |
| *Moraxella catarrhalis* | 1 | 0.7 |
| *Morganella morganii* | 1 | 0.7 |
| *Neiserria* sp. | 1 | 0.7 |
| *Aspergillus* sp. *&Staphylococcus aureus* | 1 | 0.7 |
| *Candida* sp. *&Pseudomonas aeruginosa* | 1 | 0.7 |
| *Haemophilus influenzae &Burkholderia cenocepacia* | 1 | 0.7 |
| *Staphylococcus aureus &Burkholderia cenocepacia &Pseudomonas aeruginosa* | 1 | 0.7 |
| *Candida* sp. *&Burkholderia cenocepacia &Pseudomonas aeruginosa* | 1 | 0.7 |
| No significant growth | 16 | 11.3 |

ing patterns in 122 adult patients [Table 1], with 16 [11.3%] patients exhibiting no significant microbiological findings. *Pseudomonas aeruginosa* and *Burkholderia cepacia* complex [BCC] organisms were the most commonly isolated CF pathogens, occurring in 47.1% and 22.5% patients, respectively. Yeasts and filamentous fungi were isolated from 11/138 [8.0%] patients. No pneumococci [*Streptococcus pneumoniae*], *Mycobacterium tuberculosis*, *Pneumocystis jiroveci* or *Legionella pneumophila* were isolated from any of the patients. Additionally, *Staphylococcus aureus* was isolated from the sputum of 25/138 patients [18.1%]. Previously we have shown in our CF centre that quantitative microbiology on patients' sputum had a mean cell density of 8.25 ± 0.85 log cfu $g^{-1}$ sputum and a range of 5.91 – 9.74 log cfu $g^{-1}$ sputum [Moore *et al.*, unpublished data]. Therefore, theoretically, by considering the mean values obtained, each CF patient may potentially transfer 4.77 billion [$4.77 \times 10^9$; $\log_{10}$ 9.68 colony forming units [cfu]] organisms per day to the environment, particularly at the onset of an infective pulmonary exacerbation.

Although CF is the most commonly inherited disease, relatively little is known about the manifestations and morbidity of this disease outside of the CF community, which has led to confusion regarding the transmissibility of CF respiratory bacterial pathogens to the general public, through coughing and expectorating sputum. Our study demonstrated the infrequent isolation of bacterial pathogens, which are commonly associated with respiratory tract infections with the immunocompetent population. However, the study demonstrated the presence of *Moraxella catarrhalis* and *Haemophilus influenzae* in a small proportion of patients examined, namely in one and two patients, respectively. These pathogens are more commonly seen in non-CF patients with chest infections. Consequently, even though the microbial burden generated by CF patients is large, the types of colonizing organisms of the CF lungs do not generally represent a significant cross-infection risk with members of the general public or to veterinary medicine, which can be minimized through good personal hygiene of the CF patient. The greatest health risk of such secretions is to other CF patients particularly in relation to the transmission of *Pseudomonas aeruginosa* and *Burkholderia* cepacia either directly from patient-to-patient or indirectly via environmental contamination. Hence, any exposure of CF patients to the respiratory secretions of other CF patients should be avoided, including sharing of communal toothbrushes, cutlery at mealtimes and all respiratory equipment [e.g.

nebulizers, oxygen equipment, etc.]. Environmental health professionals should be aware of the recently published guidelines entitled "*Infection control recommendations for patients with cystic fibrosis: Microbiology, important pathogens, and infection control practices to prevent patient-to-patient transmission*" [10], which describe how to minimize the transmission of infections amongst CF patient, particularly where the environment acts as reservoir of such CF pathogens.

Although there is no evidence in the literature to suggest that CF patients, who are chronically infected with *Staphylococcus aureus*, are at greater risk of acquiring more frequent episodes of gastroenteritis due to enterotoxigenic staphylococcal food-poisoning, there is a theoretical increased risk of its occurrence due to the high cell density of coagulase-positive staphylococci in respiratory secretions. Of particular concern is the situation where CF patients with chronic *Staphylococcus aureus* pulmonary infection, work or are involved in commercial food production or catering activities, particularly involving "ready-to-eat" [RTE] foodstuffs. Most concern in the food industry relates to the carriage of gastrointestinal bacterial pathogens including *Salmonella* and *Campylobacter* in the gut of production personnel. However, CF patients present an unusual scenario in that their respiratory tract is loaded with organisms, which is not the case in non-CF patients. Therefore, careful consideration should be given in terms of applying HACCP principles to this particular group of patients. Although various HACCP type II controls measures can be adopted to minimize the potential of transfer of organism to RTE foodstuffs, including the wearing of face masks, increased hand washing, such controls are not absolute. Therefore, it may be prudent for CF patients who are known to be positive for *Staphylococcus aureus* to avoid the handling of RTE foodstuffs in commercial operations and to pay particular attention to food hygiene in the domestic setting. In any case, it is particularly important to assess infected patients and the circumstances of each case, including type of employment, provision of sanitation facilities at work and standards of personal hygiene. For example, an infected food handler with CF whose work involves touching unwrapped foods to be consumed raw or without further cooking represents a greater risk than an infected CF patient working in the dispatch area of a food manufacturer.

In conclusion, patients with cystic fibrosis generate large numbers of bacteria in their sputum, approximating to $10^{12}$ organisms per patient per year. Although these organisms are introduced to the environment from the respiratory tract mainly via sputum, relatively few represent true bacterial pathogens and therefore are not clinically important to the general public who are immunocompetent. The greatest risk of such environmental microbial loading is to other patients with CF and therefore CF patients should be made aware of the hazards of acquiring such organisms from the environment, as well as socializing with other CF patients with certain transmissible types, such as *Pseudomonas aeruginosa* and *Burkholderia cenocepacia*. Infection control healthcare professionals should therefore be aware that CF patients are a greater risk to their peer grouping rather than to the general public, through the production of large quantities of sputum and that good personal hygiene practices should be encouraged to minimize environmental contamination. Further guidance on infection control practices is available [11-13].

## Authors' contributions

JEM conceived the study, designed and executed the quantitative aspects of experimentation, analyzed the data and prepared the manuscript. AS executed and analyzed the qualitative aspects of the experimentation and critically reviewed the final manuscript. JLH interacted with the CF patients, was involved in study design and critically reviewed the final manuscript. JSGD provided expert microbiological analysis and interpretation of data. JSE provided clinical expertise in interpretation of data and critically reviewed the final manuscript. All authors read and approved the final manuscript.

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