**Evaluation and management of fungal risk in Cystic Fibrosis: first results of a national French study**

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Whilst influence induced by bacterial colonization in cystic fibrosis (CF) is established, prevalence of Aspergillus fumigatus, or other species and factors associated with fungal presence is poorly documented.

Our prospective study aimed to determine which fungal species are present in sputum from CF patients, and which factors are associated with this presence.

The fungal risk was determined according: (i) clinical data, (ii) treatment used (including antibiotics, corticosteroids and antifungal treatments), (iii) fungal presence in sputum using semi-selective growing media according to a unique and standardised protocol of Mycology, and (iv) blood analysis to document patient ABPA status.

300 CF patients have been included and will be followed-up during the next 2 years. The majority were adults with a median age of 28.1 years. The average age in our Paediatric population was 12.8 years old. Aspergillus fumigatus was found in about 30% of patients, with a decreased in vitro sensitivity to azoles in 10 to 15% cases. Correlation between fungal, clinical, environmental, therapeutic or microbiological data is evaluated.

Since fungal presence in CF appears frequent, influence of fungal presence on CF course will be characterized. The 2 years follow-up will allow us to expect a better understanding of filamentous fungus role in CF course, and to establish if patients could benefit from antifungal treatments or preventive measures.

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**Itraconazole (ITZ) resistant Aspergillus fumigatus (Af) in CF patients**

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**Background:** The incidence of ITZ resistance in Af is increasing in the Netherlands. In a small CF center (n ≈ 70) we identified 4 patients with ITZ resistant Af.

**Aim:** To identify possible factors associated with the occurrence of ITZ resistant Af.

**Methods:** We describe baseline characteristics, clinical conditions and medication use of 4 CF patients with ITZ resistant Af.

**Results:** Case 1 is a male (unknown CFTR) born in 1960 who died in 2006. He was known with liver disease and Pseudomonas (Ps.) colonization. In 2002, allergic bronchopulmonary aspergillosis (ABPA) was assessed. ITZ and prednison (PRED) resulted in a remission despite ITZ resistant Af. AFBA relapsed in the following years. In 2006, still using ITZ and PRED, an ITZ sensitive Af was found. Case 2 is a female (df508/dF508) with CF Related Diabettes (CFRD), liver cirrhosis, renal disease and Ps. colonization. First ITZ resistant Af was found in 2004. A probable ABPA led to a successful trial of ITZ and PRED. Only ITZ sensitive Af was found thereafter. She died in 2007 (age 34). Case 3 is a female born in 1974 (df508/dF508), known with CFRD and colonized with Ps. and episodes of ITZ resistant or sensitive Af. Case 4 is a woman born in 1991 (df508/dF508), diagnosed with ABPA and Ps. colonization. Both ITZ resistant and sensitive Af were found during ITZ and PRED use. She had a successful lung transplant in 2006. ITZ resistant Af was more frequent during hospitalization although sampling frequency was irregular.

**Conclusion:** ITZ resistant Af may be found in CF patients. No specific clinical factors associated with their occurrence were found.

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**Fungal allergy in adult cystic fibrosis**

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**Introduction:** Since 1995, the reported incidence and diversity of fungi as lung pathogens in Cystic Fibrosis (CF) has increased. There is emerging evidence that fungi may cause infection but hypersensitivity remains the most common manifestation. This study set out to establish the frequency of fungal atopy in an adult CF cohort.

**Methods:** 46 patients at the Manchester Adult CF Unit underwent immediate hypersensitivity skin prick testing (SPT) to 5 fungal allergens and 5 common allergens. Wheals ≥ 3 mm after 15 minutes were considered positive. Blood was taken for total IgE and fungal specific IgEs by UniCap immunosay (class ≥ 1) is consistent with atopy and ≥ 2 with allergic bronchopulmonary mycosis (ABPM).

**Results:** 76% of patients demonstrated a ≥ class 1 specific IgE response to 1 or more fungal allergens. Aspergillus fumigatus 67%, Alternaria alternata 30%, Cladosporium herbarum, 15%, Candida albicans 15%, Penicillium notatum 48%. SPT had similar results: A. fumigatus 74%, A. alternata 19%, C. herbarum 14%, Calbicins 28%, P. notatum 37%. 19 (46%) patients demonstrated a ≥ Class 2 response to 1 or more fungal allergens. Fungal atopy was more common in patients with atopy to common allergens. 32 (70%) patients demonstrated positive SPT to 1 or more common allergens. Of those with no positive SPT to common allergens, 27% had fungal atopy whereas of those with positive SPT 68% demonstrated fungal atopy. Total IgE was also associated with fungal atopy. Patients with an IgE < 500 demonstrated on average 4 out of 5 positive reactions. Patients with an IgE < 500 demonstrated on average 4 out of 5 positive reactions.

**Conclusion:** Fungal atopy is common in adult CF. There is a high percentage at risk of ABPM. More research into the clinical relevance of this is required.

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**Comparative study of predominant fecal microbiota of cystic fibrosis patients and healthy siblings**

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**Aim:** Because of its controlling and modulating features, the intestinal microbiota plays a key role in the development and homeostasis of the host immune system. External factors, such as multiple high-dose antibiotic treatment courses in cystic fibrosis (CF) patients, may trigger dysbiosis in the gut and therefore contribute to several disorders. This study aims to compare the diversity of predominant members of the fecal microbiota in a group of CF patients with these of healthy siblings.

**Methods:** One general medium for colon bacteria and six selective media were used for cultivation and enumeration of a selection of predominant groups (Enterobacteriaceae, lactic acid bacteria, clostridia, bifidobacteria, Veillonella spp. and Bacteroides & Prevotella spp., resp.). In addition, population profiling of the microbial community was performed with denaturing gradient gel electrophoresis (DGGE) using V3–16S rRNA gene primers.

**Results and Discussion:** For most of the culture media included, plate counts were generally higher for samples of healthy siblings (n=15) compared to CF samples (n=19). Preliminary analysis of DGGE fingerprints revealed highly complex microbial communities in both groups. In some cases, DGGE profiles of the CF patient and his sibling differed in complexity, whereas in other pairs the corresponding profiles were relatively similar. For some patients, DGGE profile complexity from two sampling points remained virtually unchanged, whereas for other patients DGGE profiles indicated temporal instability between subsequent time points. These observations will be confirmed as more samples will be included and culturing and DGGE data will be analyzed in more depth.