

### 137 *Exophiala dermatitidis* in cystic fibrosis: prevalence and risk factors

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**Aims:** To prospectively assess the prevalence of *Exophiala dermatitidis* (ED) in respiratory secretions of patients with CF and to identify risk factors for its presence. **Methods:** The results of all cultures performed over a 2 years period in non lung-transplanted patients were considered. To detect fungi, cultures were grown on Sabouraud Gentamicin-Chloramphenicol Agar medium (Becton-Dickinson) and incubated at 35°C for 2 days and then at ambient temperature (15–25°C) for 3 weeks. Group A included all patients with one or more sputum cultures + for ED, Group B ED– patients ≥12 y.

**Results:** The study group included 154 patients (76M, 48% >18 y, median number of cultures/patient/2 years: 12). Out of 2,065 cultures, ED was isolated from 58 specimens (2.8%), in 9 patients (5.8%). All ED+ patients were PI and ≥12 y of age. Comparison of Groups A and B (n=90) revealed that isolation of *Aspergillus fumigatus* at the last culture of the study period was more frequent in patients from Group A (44.4 % vs 10%, p=0.017). A larger proportion of patients homozygous for the F508 del mutation was also observed in this group (88.9% vs 48.9%, p=0.052). There was no significant difference in terms of predominant bacterial pathogen or treatment.

**Conclusion:** ED was isolated in 5.8% of patients without lung transplant (9% >12 y). *Aspergillus fumigatus* colonization and genotype seem to be predisposing factors.

### 138 *Scedosporium* colonisation challenges in cystic fibrosis (CF) lung transplantation (LT) – a report of 7 monocentric series

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*Scedosporium* (S) spp. are associated with poor outcome in immunocompromised patients due to low susceptibility to conventional antifungal (AF) drugs. Azole arsenal recently provided 2 active drugs voriconazole (VRZ), posaconazole (PSZ). We present our experience in managing CFLT with S colonisation over the past 10 years.

All CFLT S+ were recorded with mycology, clinical outcome, immunosuppressants (IS) and AF data; S was assessed by direct examination on respiratory samples, specific cultures, morphologic identification, AF susceptibility (Etest®). Therapeutic drug monitoring (TDM) of both azole and IS were routinely performed using analytical methods.

Out of 122 CFLT (2000–09), we observed n=7 S (7 *S. apiospermum* +1 *S. prolificans*), 5/7 before T, pre-treated with classical susceptibility (VRZ, PSZ) of isolates. Demographics – 19.9±4.4 yrs, 48.4±9.3 kg, 4M/3F – fitted our usual CFLT. LT surgery exposed to bronchial stenosis.

AF was introduced de novo (except 1 at S+) as VRZ (6) or PSZ (1); VRZ stopped (n=3), 1 after 1 yr without relapse, 1 for photosensitisation with S fungal ball, ablation and PSZ, 1 for resistance and PSZ. Mean VRZ and PSZ maintenance doses were respectively 572±207 and 1550±638 mg/d with 1.4±0.7 and 0.8±0.6 mg/L; IS treatment were steroids, tacrolimus and adjuvants. Survival ranged from 12 to 102 mths after T, 2 died (BOS), 5 ongoing.

S colonisation may be controlled in CFLT, using de novo probably lifelong VRZ or PSZ. VRZ de novo is more appropriate if IV, but exposes to photosensitisation (n=3) (skin protection) and neuropathy (n=1). Azole PK variability in CF need higher dosage, long time to steady-state and careful TDM to achieve compliance with safe DDI management.

### 139 *Scedosporium apiospermum* colonization in cystic fibrosis patients: incidence and clinical outcome

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**Introduction:** The *Scedosporium apiospermum* is the second most frequent filamentous fungus that can be found in patients with CF after *Aspergillus fumigatus*. Filamentous fungi may contribute to the local inflammatory response and under special circumstances could be pathogenic and invasive.

**Aim:** The incidence of colonization by *Scedosporium apiospermum* in CF patients and its association with several clinical characteristics.

**Population and Method:** All 416 CF patients of our department (206 boys, 210 girls, mean age: 13.9 years) were surveyed for colonization with *Scedosporium apiospermum* during the last 3 years. Sputum cultures collected during their routine clinical visits or on admission to the hospital were inoculated on yeast extract-peptone-dextrose agar plates. The colonization was associated with several clinical factors: the age of the patients, pancreatic function, chronic colonization with *Pseudomonas aeruginosa*, chronic use of inhaled antibiotics, prolonged use of inhaled and systematic steroids.

**Results:** The incidence of *Scedosporium apiospermum* in our CF population was 2%. The mean age of the patients at the age of first colonization was 17.6 years. There was a strongly positive relation with chronic use of inhaled antibiotics (p<0.001) and systematic steroids (p<0.001). Colonization with *Scedosporium apiospermum* was not associated with any deterioration in patients' clinical condition, apart from one child, who developed signs of infection.

**Conclusion:** The intensification of therapy in CF patients with antibiotics and steroids may facilitate the colonization by *Scedosporium apiospermum*, so monitoring with suitable fungal culture methods is mandatory.

### 140 *Scedosporium apiospermum* seroprevalence study in a large cohort of patients with cystic fibrosis in France

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*Scedosporium apiospermum* (*S.a*) is an emerging filamentous fungus described as one of the major fungal agents responsible for chronic airway colonisation in cystic fibrosis (CF) patients. Although the significance of patients' respiratory tract colonisation by *S.a* is still unclear, this fungus may contribute to the local inflammatory response, and therefore to the progressive deterioration of lung function. We studied *S.a* seroprevalence in a large prospective cohort of CF patients and compared the clinical features of seropositive and seronegative patients. Serum samples from 395 CF patients were analysed retrospectively. Total antibodies against *S.a* were determined by ELISA using cytosolic antigens extracted by mechanical disruption. Patients' demographic and clinical data were obtained by a systematic review of medical records and univariate analysis was performed to compare the clinical characteristics of seropositive and seronegative patients. Antibodies against *S.a* were detected in 98 patients (24.1%), the median age of seropositive patients was 20.5 years [1.7–53 years]. The prevalence of immunisation against *S.a* regularly increased with age and reached 46% in patients older than 35 years. Results of univariate analysis revealed that seropositivity to *S.a* was associated with age, diabetes mellitus, *Aspergillus* spp airway colonisation and poor pulmonary function. In conclusion, our results show that an immune response against *S.a* can be detected in almost one-fourth of cystic fibrosis patients. The clinical relevance of the immunisation against *S.a* is unknown and a prospective study will be planned to evaluate the long-term clinical outcome of seropositive patients.