81 Susceptibility of *Exophiala dermatitidis* to antifungal agents

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Objectives: Patients with cystic fibrosis (CF) are at constant risk for pulmonary colonization by opportunistic microorganisms. The black yeast, *Exophiala dermatitidis*, has consistently been isolated from patients with CF. The aim of this study was to determine the minimal inhibitory concentrations (MIC) for itraconazole, voriconazole, posaconazole, flucytosine and amphoterricin against *E. dermatitidis*.
Methods: Since *E. dermatitidis* grows initially in the yeast form and acquires mould form with age, two methods i.e. the Clinical and laboratory Standards Institute (CLSI) for moulds and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for yeasts have been used. The results obtained from the two analytical systems were compared.
Results: The overall agreement between CLSI and EUCAST was good (>90%), with the exception for posaconazole and flucytosine.
Conclusion: The antifungal susceptibility testing of 53 clinical isolates, using CLSI and EUCAST shows that *p*osaconazole was the most active drug against *E. dermatitidis in vitro* followed by voriconazole and itraconazole in both systems.

82 Effect of ivacaftor on CF clinical isolates of *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Streptococcus* sp. in comparison to antimicrobial peptides

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Objectives: It has been suggested that, as there is a quinolone ring in the structure of ivacaftor, it may have some antimicrobial activity against CF pathogens. Therefore, the aims of this study were to (1) determine whether ivacaftor demonstrates any antimicrobial activity against CF clinical isolates, and (2) compare the activity of ivacaftor to a standard panel of antibiotics used in CF therapy and human antimicrobial peptides (AMPs) which are naturally produced as part of the innate immune response.
Methods: The minimum inhibitory concentration (MIC) ivacaftor, Colistin, and a range of AMPs against clinical isolates from CF patients (*P. aeruginosa, Streptococcus* sp. and *S. aureus*) were determined using radial diffusion assays. Antibiotic susceptibility was determined by Etest®.
Results: See the table. At the concentrations tested ivacaftor had no direct antimicrobial activity against any of the clinical isolates tested. Human β-defensin 3 was the most effective AMP against the Gram positive isolates tested.

Table: MICs of ivacaftor, AMPs and antibiotics

	MIC (μg/ml)		
	P. aeruginosa	*Streptococcus* sp.	*S. aureus*
Ivacaftor	>50	>50	>50
Lysozyme	19.5–57.2	–	>250
β-defensin 3	–	1.38–21.78	5.65–47.5
Colistin	1.5–7.7	1–1.3	>10
Tobramycin	0.38–8	0.094–>256	0.094–34
Meropenem	0.016–12	0.016–0.75	0.125–>32
Ciprofloxacin	0.064–4	0.38–1.5	0.19–>32

Conclusion: Ivacaftor does not have any direct antimicrobial activity against the clinical isolates tested. The MIC values for the AMPs tested varied between and within the different genera tested, suggesting that isolates possess a range of virulence factors which affect AMP activity.
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83 Bronchopulmonary infection/colonization in cystic fibrosis: results from a Spanish multicenter study

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Objectives: To identify and characterize the lung microbiota of Spanish cystic fibrosis (CF) patients from a national multicenter study (March-November, 2013) focusing in the major pathogens, including *Pseudomonas aeruginosa* and *Staphylococcus aureus*.
Methods: 13 adult and 11 paediatric CF-Units from 17 Hospitals covering different areas in Spain participated in the study. Each one collected respiratory samples and clinical data of 15 non-selected consecutive patients. Samples were immediately stored (−80ºC) and sent to our hospital for quantitative culture, identification (MALDI-TOF MS) and antibiotic susceptibility (MicroScan).
Results: 340 patients were included, 177 adults (52.1%) and 163 children (47.9%), median age of 24.5 and 10 years, respectively. 33.9% of patients were homozygous for F508del and 46.4% were heterozygous. Pulmonary function had a mean (SD) FVE_1 of 59.1% (34.0) and 69.5% (30.2) for adults and children, respectively. *P. aeruginosa* was isolated in 49 (27.7%) adult and 25 (15.3%) paediatric patients. Other CF pathogens isolated are in the table below. Co-colonization was a frequent event.
Conclusion: *S. aureus* was the most frequent CF pathogen, followed by *P. aeruginosa* and other non-fermenting Gram-negative rods (NFGNR). *P. aeruginosa* colonization was lower than expected, especially in the adult subset. This could reflect an improvement in the clinical and therapeutic approach to CF and a positive impact of the neonatal screening.

	Frequency of colonization (%)		
	Total	Adults	Children
S. aureus	59.7	57.6	62.0
P. aeruginosa	21.8	27.7	15.3
NFGNR	25.6	25.9	25.2

84 Respiratory microbiota in children with cystic fibrosis and healthy controls

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Background: The CF respiratory microbiome contains diverse bacterial species that are not routinely cultured. Few studies have examined airways microbiota in young children with CF from whom sputum samples are difficult to obtain. Studies such as these are important to understand the changes in airway microbiota over time and how this affects long term respiratory health in CF.
Aims: To characterise the airways microbiota of young children with CF and compare microbial diversity with older CF and healthy children.
Methods: Sputum and BAL samples were collected from children with CF respiratory exacerbations and healthy controls. Bacterial density was quantified by a real-time PCR assay targeting the 16S rRNA gene and identified by 454-pyrosequencing of a fragment of the same gene, with these data assessed for richness, diversity and equability.
Results: Microbiome sequencing revealed that diversity and richness were highest in control patients. In CF patients there was a correlation between patient age and declining diversity although these trends were not statistically significant. Diversity was lowest in samples containing known pathogens from genera such as *Staphylococcus, Achromobacter, Pseudomonas* and *Stenotrophomonas*. We found no significant differences in microbiota richness or diversity between BAL and sputum samples from young children.
Conclusions: These data highlight the complicated bacterial population structures within the airways of young children and changes occurring over time in CF patients. A more complete understanding of the dynamics of these populations will be beneficial in improving the management of respiratory infection in CF.