mycoses
Diagnosis, Therapy and Prophylaxis of Fungal Diseases

Abstracts

Proffered Oral

PO1

Histoplasmosis in Israeli Travelers

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Histoplasmosis is one of the more common endemic human mycoses. The majority of infections are acquired in the Americas. We report 23 cases of histoplasmosis in Israeli travelers. All traveled to endemic areas; 22 to Latin America, one to North America. Fourteen cases had visited bat habitats, including 9 who visited a specific cave infested by bats in Lanquin, Guatemala. Fourteen of the 23 patients were symptomatic; all presented within 3 months of their return from Latin America. The majority had respiratory symptoms; however 28% presented with prolonged febrile illness only.

Asymptomatic patients were diagnosed during the evaluation of incidental radiological findings or because a travel partner had been suspected of *Histoplasma* infection. These patients were diagnosed 16-120 months after their return from the endemic region.

Serological testing was positive in 75% of symptomatic cases but only 22% of asymptomatic cases.

Histoplasmosis should be considered in travelers returning from Central or South America with respiratory or febrile illness within weeks of return, particularly if exposed to bat habitats. Serological and urinary antigen testing are useful for diagnosis of "early" presenters but wane over time, and thus are of limited utility in late presenters. Evaluation of travel partners may be a useful adjunct in the returning traveler suspected of having current or healed histoplasmosis. The histoplasmin skin test, if available, may be of use when attempting to diagnose histoplasmosis in non-endemic areas.

PO2

Occupational Exposure to *Aspergillus* spp. in Poultry and Swine Feed Production

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Workers from feed production often develop allergic respiratory symptoms and fungi, are likely to be a significant contributing factor to these symptoms. This study intended to characterize fungal contamination in two feed production units, one for poultry and other for swine consumption. We aimed at identifying which unit presented the highest risk of occupational exposure to *Aspergillus* spp. Twelve air and twelve surfaces' samples were collected from the two studied units through impaction and swabbing methods, respectively. After laboratory processing and incubation of the collected samples, quantitative and qualitative results were obtained, with the identification of the isolated fungal species. For molecular analysis, 300L of air were also collected from each same sampling site using the impinger method. Real Time PCR (RT-PCR) was done to perform the molecular detection of the *Aspergillus* sections *Fumigati* and *Flavi* (only the toxigenic strains). In the poultry feed production isolates belonging to the *Aspergillus fumigatus* species-complex (section *Fumigati*) were the most abundant in air (46.6%). In the swine feed production no isolate from *Aspergillus* genus was collected. Regarding the results obtained through molecular methods, *A. fumigatus* complex was detected in one sampling site in poultry feed production and in two sampling sites in swine feed production where this species-complex was not isolated by conventional methods. Altogether, the results we obtained with cultural methods showed that feed production on poultry was the setting where the highest number of isolates belonging to *Aspergillus* spp was found. Importantly, the molecular tools applied during this study enabled to target selected fungal indicators, allowing a more precise characterization of the *Aspergillus* spp. occupational burden in these settings.

PO3

The Fungi: Silent Neighbors or Hidden Threat?

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Introduction The pathogenesis of fungal rhinosinusitis/FRS was widely investigated but the relationship of the fungal presence in environment and development of FRS is not yet revealed. We evaluated the relationship of the presence of fungi on sinonasal mucosa with fungal presence in home air of patients with their clinical characteristics.

Material and methods The prospective study with 136 patients with chronic rhinosinustis/CRS was conducted in the National Reference Medical Mycology Laboratory, Faculty of Medicine, University of Belgrade. Study design included: 1) anamnesis data; 2) measurements of molds specific IgE/sIgE and total IgE Ab, absolute eosinophile/Eo count and skin prick test; 3) rhinologic and CT observation; 4) mycological finding of sinonasal nasal aspirate and 5) air sampling from the patient's bedroom.

Results (i) 30.4% patients with positive molds sIgE Ab had severe forms of CRS with more often presence of NP (p=0.025); (ii) 46.4% of patients with positive sIgE Ab had positive fungal finding on nasal mucosa; (iii) in Serbia the prevalence is 1.3% for allergic FRS/AFRS and 2.8% for FRS; (iv) patients with AFRS had more frequent asthma (p=0.024) and CRS lasting more than 10 years (p=0.000); (v) 225 fungus was found in air samples, the most common were *A. niger* (57%) and *Penicillium* sp.(26%).

Conclusion Huge amount of fungal spore in the air of patient's living area should be threat for development of FRS in predisposing patients. Next studies should clarify the mechanism by which airborne fungi turn from 'normal flora' into triggers of immunological reactions, resulting in FRS.

PO4

Production of Echinocandins by Fusarium MS-R1

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Fungal infections, especially candidiasis, are on the rise in human populations, leading to a continuous search for novel potential chemicals in order to expand the range of drugs. Filamentous fungi are important sources of bioactive secondary metabolites, many of which are used in medicine. This includes production of anti-fungal metabolites that are used to treat human and animal fungal infections.

Among the antifungal drugs used in medicine, the echinocandins are considered to be relatively safer than those derived from azole or polyene compounds. *Fusarium* strain MS-R1, that produces an anticandidal compound was isolated in our laboratory and identified by molecular means as a member of the *Fusarium brachygibbosum* complex. The active metabolite was extracted, purified and identified as a novel echinocandin. It's activity against range of candida species was determined, showing activity mainly against *Candida albicans* and *C. tropicalis*. Further studies on the production of the antifungal metabolite by the fungal mycelium were conducted in both solid and liquid media, with optimization of cultural conditions such as inoculum age and size and medium manipulations.

PO5

Analysis of Mechanisms of Bacterial (*Serratia marcescens*) Attachment, Migration and Killing of Fungal Hyphae

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Interactions between bacteria and fungi are well documented in the literature. To the best of our knowledge no such interactions have been described regarding the gram negative bacterium *Serratia marcescens*. An incidental finding in our laboratory found a remarkable capacity of *S. marcescens* to migrate along the mycelium of *Zygomycete* molds. In this work, we conducted a series of experiments to better define the nature of this phenomenon. We found that migration of *S. marcescens* along fungal mycelium was restricted to *Zygomycete* molds, and several *Basidiomycete spp.* No migration was seen on any mold of the phylum *Ascomycota*. *S. marcescens* migration did not necessitate fungal viability or surrounding growth medium, as bacteria migrated along aerial hyphae as well. *S. marcescens* did not exhibit growth tropism towards *Zygomycete* mycelium. Bacterial migration along hyphae proceeded only when the hyphae grew into the bacterial colony. *S. marcescens* cells initially swarmed along the hyphae, formed attached microcolonies that grew and coalesced to generate a biofilm covering the mycelium. Flagellum-defective strains of *S. marcescens* were able to migrate along Zygomycete hyphae, although significantly slower than the wild-type strain. Bacterial attachment to the mycelium does not necessitate type 1 fimbrial adhesion since mutants defective in this adhesin migrated equally well or faster than the wild type strain. Killing does not depend on the secretion of *S. marcescens* chitinases as mutants in which all three chitinase genes were deleted retained wild-type killing abilities. Better understanding of the mechanisms by which *S. marcescens* binds, spreads and kills fungal hyphae could serve as an excellent model system for such interactions in general; fungal killing could be employed in agricultural fungal biocontrol.

PO6

Isavuconazole susceptibility of 489 clinical *Aspergillus fumigatus* isolates

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Introduction Isavuconazole (ISA) is a new triazole recently approved for the treatment of invasive aspergillosis. EUCAST has set the clinical breakpoint of ISA for *Aspergillus fumigatus* at >1 mg/L (resistant). In this study, we determined the susceptibility of ISA for 489 *A. fumigatus* isolates and compared the susceptibility to other mold-active azoles.

Methods Isolates were prospectively collected between June 2014 and December 2015. Minimal inhibitory concentrations (MICs) were determined by broth microdilution EUCAST method. Isolates were grouped as azole "wildtype" and "non-wildtype" by the use of epidemiological cutoffs for voriconazole, posaconazole and itraconazole (1 mg/L, 0.25 mg/L and 1 mg/L, respectively). The susceptibility of ISA was compared to voriconazole, posaconazole and itraconazole for all isolates as a group and for the defined subgroups by the Spearman's rank correlation coefficient.

Results 279 isolates exhibited a "wildtype" azole phenotype, and 210 were "non-wildtype". 25/279 "wildtype" isolates had a ISA MIC of >1 mg/L and were thus classified as resistant. 197/210 of "non-wildtype" isolates were classified as resistant. The correlation coefficients for "non-wildtype" isolates were very strong, moderate and weak ($p<0.001$) for ISA compared with voriconazole, posaconazole and itraconazole, respectively. For wildtype isolates the coefficients were all moderate ($p<0.001$).

Conclusion Most "azole non-wildtype" isolates were also resistant for ISA; susceptibility of ISA of non-wildtype isolates had strongest correlation with voriconazole. Additionally, 25/279 "azole wildtype" isolates were classified as ISA-resistant. Thus, isolates with "wildtype" azole susceptibilities, cannot be automatically assumed susceptible for ISA. Consequently, susceptibility testing of ISA is advised before starting ISA treatment.

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CONTENTS

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