

Species	Number	Percentage
<i>C. albicans</i>	20	21
<i>C. glabrata</i>	22	23.40
<i>C. parapsilosis</i>	34	36.10
<i>C. tropicalis</i>	8	8.50
<i>C. krusei</i>	2	2.10
<i>C. orthopsilosis</i>	3	3.10
<i>C. nivariensis</i>	1	1.06
<i>C. kefyr</i>	1	1.06
<i>Pichia norvegensis</i>	1	1.06
<i>C. lusitane</i>	1	1.06
<i>Trichosporum</i> spp.	1	1.06
Total	94	100

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#### 2046. FungiScope™: News on the Global Emerging Fungal Infection Registry

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**Background.** Numbers of rare invasive fungal diseases (IFD) are rising worldwide due to increasing patient population at risk. To broaden the knowledge on epidemiology of rare IFD and eventually improving diagnosis and clinical outcome, FungiScope™, a global registry for rare IFD, has been initiated.

**Methods.** FungiScope™ uses web-based data capture (www.clinicalsurveys.net). Eligible are cases with proven or probable infection due to rare, non-endemic fungi. Data collected include demographics, underlying conditions, clinical presentation, diagnostics, antifungal therapy and outcome. Clinical isolates are collected for centralized identification, susceptibility testing and exchange between collaborators.

**Results.** To date, 728 valid cases of rare IFD from 41 countries are included in the registry: IFD due to Mucormycetes ( $n = 358$ ), *Fusarium* spp. ( $n = 87$ ), rare yeasts ( $n = 83$ ), dematiaceae ( $n = 69$ ), and *Scedosporium* spp. ( $n = 55$ ) are the most frequently reported. FungiScope™ is supported by central labs in the Czech Republic, India, Russia, and Spain. Recently, FungiScope™ collaborators jointly published results on (I) invasive mucormycosis in children analyzed together with cases from the registry study Zygomycosis.net, (II) disseminated fusariosis in 10 children, and (III) invasive infections due to *Saprochaete* and *Geotrichum* spp. in 23 patients.

**Conclusion.** The clinical relevance and by this the awareness of emerging IFD is increasing. FungiScope™ is a valuable resource used for collaborative studies on rare IFD. Operating and management of the registry requires considerable effort to ensure high data quality for comprehensive analyses, which provide insights into current clinical management of the diseases and thus, hold the potential to identify strategies for early diagnosis and effective treatment.

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#### 2047. Study of Molecular epidemiology, risk factor analysis and comparison of diagnostic methods for rapid diagnosis of fungal pneumonia in critically ill cirrhotics

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**Background.** Liver cirrhosis causes immune dysregulation and increased susceptibility to fungal infections. We studied risk factors, molecular epidemiology and compared the rapid diagnostic methods and biomarkers for fungal pneumonia in critically ill cirrhotics

**Methods.** Single-center, prospective cohort study of 50 critically ill cirrhotics with fungal pneumonia between January and September 2017. Comparative analysis of culture, real-time PCR and biomarkers; Bronchoalveolar lavage and serum galactomannan, serum procalcitonin were measured by ELISA and chemiluminescence assay on Days 1, 3, 7. Final outcome were mortality within 1 month after diagnosis or discharge. Genotyping of clinical and air sampling *Aspergillus* isolates was done

**Results.** *Aspergillus flavus* was most common species (34/50, 68%). Risk factors were, neutropenia ( $P 0.03$ ), steroids prior to ICU admission ( $P 0.02$ ), prolonged hospitalizations  $>21$  days ( $P 0.05$ ). Culture positivity was 80%. Culture was not inferior to real-time PCR for diagnosis of fungal pneumonia. BAL Galactomannan was early prognostic marker with median rise above  $>1$  index value on Day 1. Median PCT level was higher from Day 1 in the fungal pneumonia nonsurvivor group (3.29 vs. 0.8 ng/mL) with higher 30-day mortality (72%). Higher PCT was associated with bacterial co-infection (48%), antibiotic (74%) and antifungal therapy and renal failure and mortality. Clinical isolates from patients matched those recovered from air in two clusters.

**Conclusion.** Fungal pneumonia complicates cirrhotics with neutropenia, prolonged hospitalization and steroids as risk factors. *Aspergillus* species predominate as in Asian epidemiology. Culture methods are reliable and combination of molecular test with BAL galactomannan is useful for rapid diagnosis. Serum PCT is raised in patients with fungal pneumonia and associated with higher mortality. In our study the baseline PCT at admission to ICU was higher in nonsurvivor group, levels on D3 and D7 were persistently higher. High serum procalcitonin level is an independent prognostic biomarker of mortality risk in fungal pneumonia. Genetic relatedness of clinical and environmental sample necessitates infection control measures to prevent invasive aspergillosis in high-risk patients.

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#### 2048. Comparison Between Endpoint and Real-Time (RT) Polymerase Chain Reaction (PCR) for the Diagnosis of Pneumocystis Pneumonia (PCP)

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**Background.** The definitive diagnosis of PCP requires direct visualization of the organism by silver or direct fluorescent antibody stain, but in recent years PCR has become a widely used diagnostic tool. Varying results have been noted with different PCR assays; one concern has been that RT-PCR will be more sensitive and not differentiate colonization from infection. For this study, we compared the performance of RT-PCR with that of endpoint PCR for detection of PCP.

**Methods.** All adult patients who had a bronchoalveolar lavage (BAL) or sputum sample positive for *Pneumocystis* by PCR at the U. Michigan Hospitals from February 2014–February 2018 were studied. Before February 2017 samples were tested with endpoint PCR followed by agarose gel electrophoresis and after February 2017 with RT-PCR. For each patient, a strict case definition based on host factors, clinical presentation, radiological and pathologic findings, was used to classify PCP as proven, probable, possible, and unlikely. Based on this classification, endpoint PCR and RT-PCR results were designated as true positive or false-positive presumably colonized (FP).

**Results.** The number of specimens tested each year was similar, ranging from 751 to 791. One hundred and fifty-three patients tested positive: 77/2318 (3%) by endpoint PCR and 76/783 (10%) by RT-PCR. One hundred and twenty-six patients had risk factors for PCP: hi-dose steroids (39), hematologic malignancy (38), chemotherapy within 3 months (24), HIV (14), solid-organ transplant (12), stem cell transplant (9), and 27 patients had no PCP risk factors. By our definitions, patients were classified as proven (2), probable (70), possible (46) and unlikely (35). RT-PCR gave a higher FP rate (27/76, 35%) than endpoint PCR (8/77, 10%,  $P < 0.0001$ ), especially in those with chronic lung disease,  $P = .001$  and those with no known PCP risk factors,  $P < 0.0001$ . More patients with no risk factors tested positive with RT-PCR (20) than with endpoint PCR (7),  $P = .006$ . FP rates RT-PCR were similar in sputum (34%) and BAL (36%).

**Conclusion.** RT-PCR gave significantly more FP results, likely due to increased detection of *Pneumocystis* colonization. Pretest probability should be considered when ordering a highly sensitive test such as RT-PCR and positive results must be interpreted in the context of the clinical presentation, radiological findings and risk factors.

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**2049. *Pneumocystis jirovecii* Detection by Nested PCR in HIV-Infected Peruvian Patients**

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**Background.** *Pneumocystis jirovecii* (PJ) is considered a common cause of pneumonia in HIV-AIDS patients. PJ detection now is facilitated by molecular techniques using non-invasive samples; however, there are few PJ colonization studies in HIV population using these techniques. The study aim was to evaluate the frequency and factors related to PJ colonization among HIV-patients with CD4 account <500 cells/mm<sup>3</sup>.

**Methods.** We performed a cross-sectional study evaluating HIV patients older than 18 years old with or without respiratory symptoms with CD4 account <500 cells/mm<sup>3</sup> who attended Hospital Cayetano Heredia in Lima, Peru during May 2017–March 2018. After patients signed an inform consent, clinical information was obtained from the medical chart and a non-induced sputum sample was collected. If patient did not have cough, an oral wash sample using saline was obtained. PJ detection was based on the amplification of the mitochondrial large subunit ribosomal RNA (mtLSU rRNA) in two stages. First, single round PCR was done using external primers (pAZ102E and pAZ102H); then, PCR products were amplified (nested PCR) using internal primers (pAZ102X and pAZ102Y). If the single round PCR was positive in a patient with respiratory symptoms, it was considered a PJ infection. If only the nested PCR was positive, this was considered as PJ colonization.

**Results.** A total of 177 patients were included, 75 (42.4%) with respiratory symptoms. Three cases were considered PJ infections. A total of 15 cases (8.6%) were colonized by PJ, 7/72 (9.7%) cases with respiratory symptoms and 8/102 (7.8%) among asymptomatic patients. A higher proportion of colonization was seen in patients in whom an oral wash was obtained (14/156, 9.0%) compared with those in whom a non-induced sputum was analyzed (1/18, 5.5%). The frequency of PJ colonization based on CD4 account was 6.5 and 10.3% among patients with ≤200 and >200 cells/mm<sup>3</sup>, respectively.

**Conclusion.** PJ colonization was seen in 8.6% of HIV patients. The proportion of PJ detection was higher when oral wash was analyzed compared with non-induced sputum. Patients with lower CD4 account did not show a higher proportion of colonization.

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**2050. Plasma Next-Generation Sequencing for Pathogen Detection in Pediatric Patients at Risk for Invasive Fungal Infection**

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**Background.** Invasive fungal infection (IFI) is a major cause of mortality and morbidity among immunocompromised patients. Microbiologic culture of biopsy samples remains the diagnostic gold standard. Noninvasive biomarker testing can provide clinically useful information, but does not give species-level identification. Next-generation sequencing (NGS) of cell-free plasma is a noninvasive approach for species-level identification of pathogens, and may guide specific treatment. We sought to describe the diagnostic utility of plasma NGS in high-risk immunocompromised pediatric patients, correlating results with standard microbiology studies.

**Methods.** Plasma from at-risk immunocompromised patients with suspected IFI was tested using cell-free plasma NGS (Karius, Redwood City, CA). Human reads were removed, and remaining sequences aligned to a curated database including >1,000 pathogens. Organisms present above a predefined significance threshold were reported.

**Results.** Forty evaluable patients were enrolled, the majority of whom had underlying oncologic diagnoses. Risk for IFI included prolonged febrile neutropenia (FN) in 22 patients, recrudescence FN in 7, concern for IFI on imaging in 8, and concern for IFI based solely on other clinical findings in 3. Six patients met established criteria for proven IFI, 1 for probable IFI, and 13 for possible IFI. NGS plasma testing identified a pathogen which was cultured from infected tissue or blood in 4 of 6 proven cases; one patient with localized cutaneous *Rhizopus* had negative NGS results. A patient with probable IFI (positive β-D-glucan) had *P. jirovecii* identified by NGS. Among 33 patients without proven or probable IFI, NGS testing identified a fungus in one (*C. glabrata*), no organism in 11, and potential alternative sources of fever in 16.

**Conclusion.** Plasma NGS testing can detect IFI from blood. The test identified fungi from proven IFI, and detected other pathogens in both probable and possible IFI cases. Many patients at risk received prolonged courses of antifungals despite negative testing, suggesting a possible future role for NGS testing in ruling out IFI. Future studies should more definitively evaluate the positive and negative predictive value for NGS testing in patients at risk of IFI.

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**2051. Detection of *Candida auris* Among Previously Unidentified Yeasts Isolated from Ear Discharge Specimens in Japan**

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**Background.** *Candida auris* has not been detected since first report in Japan, despite worldwide reports. We recently reported a second isolate of *C. auris* (TWCC 58191) from ear discharge in Japan. We re-analyzed unidentified yeast strains.

**Methods.** Over 2,000 clinical yeast samples were available. Among these, 16 yeast strains isolated from the ear discharge were not identified using conventional method. *C. auris* was identified by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry and internal transcribed spacer and D1/D2 region sequencing. To determine the minimum inhibitory concentration (MIC), the Clinical and Laboratory Standards Institute broth microdilution method was used. Whole genome sequencing, assembly and error correction was performed (Japanese strains). Average nucleotide identity (ANI) among two Japanese strains and four other strains (India, Pakistan, South Africa) was determined. Our 6 strains and previously reported strains (*n* = 126) were mapped to JCM15448 and single nucleotide variants (SNVs) were detected. An SNV-based phylogenetic tree was constructed.

**Results.** Five were identified as *C. auris*. Our strains exhibited relatively low MICs (Table 1). Japanese strains had susceptibility to nearly all agents. Because all strains were obtained from chronic otitis media, the susceptibility may be explained by a lack of exposure to antifungal agents. JCM15448 was assembled based on 11 contigs. All ANIs were over 99%; therefore, all of these strains are *C. auris*. A total of 168,810 SNVs were detected in 133 strains. The SNV-based phylogenetic tree is shown Figure 1. Since independent clusters were observed from strains from each area, it is possible that *C. auris* emerged independently in different regions worldwide. The SNV-based phylogenetic tree was more effective for the identification of Japanese strains (Figure 2).

**Conclusion.** Despite a general lack of reports, *C. auris* exists in Japan. Clinicians must consider the potential for *C. auris* detection from otorrhea samples.

**A phylogenetic analysis separates native strains from each area.** During an outbreak, an SNV-based phylogenetic tree is suitable for analysis owing to its good identification ability.

**Table 1.** Characteristics of our *C. auris* Strains

Strain No	Date	MIC							
	Specimen isolated	(mg/L)	MCFG	CPFG	AMB	5-FC	FLCZ	ITCZ	VRCZ
13846	Otorrhea	2003	0.03	0.25	0.25	≤0.125	4	0.03	≤0.015
13847	Otorrhea	2003	0.03	0.25	0.25	≤0.125	1	≤0.015	≤0.015
13878	Otorrhea	1997	0.06	0.5	0.25	0.5	16	0.125	0.125
50952	Otorrhea	2008	0.03	0.25	≤0.03	≤0.125	2	0.03	0.03
58191	Otorrhea	2017	0.06	0.5	0.25	0.25	4	0.06	0.03
58362	Otorrhea	2008	0.125	>16	0.25	0.5	>64	0.25	2
	break point		4	2	2	128	32		2

**Figure 1.** Phylogenetic tree based on SNVs

