

## POSTER ABSTRACT

**142. Emergence and Spread of *Candida auris* in New York State**

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**Background.** *Candida auris*, an emerging yeast, has been detected in New York State (NYS). *C. auris* is often resistant to antifungal medications and has caused healthcare-associated outbreaks. We describe the emergence and spread of *C. auris* in NYS in multiple healthcare facilities.

**Methods.** *C. auris* cases were identified through active or passive surveillance. Isolates were identified using matrix-assisted laser desorption/ionization-time of flight mass spectrometry, and antifungal susceptibility testing was performed. Cases of *C. auris* were classified as clinical or screening depending on the reason for culture (diagnostic or surveillance). Invasive cases of *Candida haemulonii* were classified as probable if the yeast identification method used could not reliably identify *C. auris* and the isolate was not available. Surveillance methods included culturing contacts, conducting point prevalence surveys, and collecting environmental cultures. Facility site visits were conducted to review infection control practices when transmission was suspected.

**Results.** As of May 15, 2017, 53 clinical, 17 screening, and four probable cases had been reported. Twenty-three of the 53 clinical cases died. Clinical cases were identified in 18 hospitals, one long-term acute care hospital (LTACH), and one private medical office, but the cases passed through 24 hospitals, 24 long-term care facilities, and one LTACH in the 90 days before diagnosis through May 15, 2017. Although the facilities were located eight counties, 42 of 53 (79%) of the cases were residents in three downstate metropolitan counties. Site visits identified areas for improvement in infection control, including adherence to recommended hand hygiene practices, standard and contact precautions, and environmental cleaning practices. Isolates from 52 of 53 clinical cases were resistant to fluconazole. Amphotericin B susceptibility varied. Initial isolates from all clinical cases were susceptible to echinocandins; one case developed echinocandin resistance during treatment.

**Conclusion.** *C. auris* has emerged as a novel pathogen in NYS and has been detected in multiple healthcare facilities. The spread to many facilities likely reflects the challenges of detection and demonstrates the need for strict infection control practices.

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**143. Mitigating *Candida auris* at a Busy Community Hospital: A Quasi-Experimental Near Real-Time Approach**

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**Background.** *Candida auris*, an emerging multidrug-resistant pathogen associated with increased mortality, can disseminate on hospital surfaces and resist disinfection. Transmission dynamics remain poorly understood at community hospitals. Immediately following identification of a *C. auris* infection in an unsuspected patient admitted to a semi-private room 6 days previously, we sought to limit and determine the extent of *C. auris* contamination at Rochester General (RG), a 528-bed hospital in New York, using available resources.

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**Methods.** The index and roommate were placed on enhanced contact precautions and moved to private rooms. Their former room was terminally cleaned with peracetic acid/hydrogen peroxide (PAHP) and UV light. Ten high-touch environmental surfaces in the new rooms of the index and roommate, the nursing stations, and throughout the ward were sampled immediately before and after, and between daily cleaning. The nares, axillae, and groin of the index, the roommate, and all concurrent ward patients were also sampled. All patients on the involved ward were sequentially moved from their initial rooms into vacated rooms that were terminally cleaned with PAHP and UV light. Prior to the index event, RG laboratory began sending all possible *C. auris* isolates to the state public health laboratory for confirmation, and using PAHP for all cleaning. RG also leverages preexisting agreements with other referral laboratories to support outbreak investigations. Hand-hygiene compliance averaged 80–90% on the ward. Hospital leaders, laboratory, nursing, environmental services, and local public health personnel regularly participate in infection prevention efforts.

**Results.** *C. auris* was isolated from 3 of 132 surface samples on the eighth, ninth, and 15th day of ward occupancy, and 0 of 48 patient samples from 18 co-located patients. The index remained colonized until death on hospital Day 21. No surfaces were *C. auris*-positive 1 month later.

**Conclusion.** Compared with prior reports, dissemination at RG was limited. This, the first such quantitative assessment, illustrates how community hospitals can enhance surveillance and patient safety when formal agreements, vigilance, and multi-disciplinary and interagency teamwork exist before outbreaks occur.

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**144. Public Health Response to US Cases of *Candida auris*, a Globally Emerging, Multidrug-Resistant Yeast, 2013–2017**

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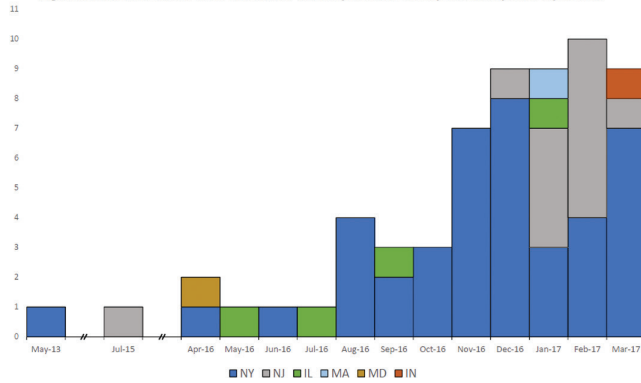
**Background.** *Candida auris* is an often multidrug-resistant yeast that causes invasive infections and, unlike most *Candida* species, spreads in healthcare facilities. CDC released a clinical alert in June 2016 requesting reporting of *C. auris* cases. We investigated cases to contain transmission and inform prevention measures for this novel organism.

**Methods.** Clinical cases were defined as *C. auris* from any clinical specimen from a patient in the United States. Response to cases included implementation of infection control measures, enhanced cleaning and disinfection, and testing of close contacts for *C. auris* colonisation (isolation from a person's axilla or groin was defined as a screening case). Microbiology records were reviewed at reporting facilities for missed cases. All isolates were forwarded to CDC for confirmation, antifungal susceptibility testing, and whole-genome sequencing (WGS).

**Results.** As of April 13, 2017, 61 clinical cases of *C. auris* were reported from six states: New York (39), New Jersey (15), Illinois (4), Indiana (1), Maryland (1), and Massachusetts (1). All but two occurred since 2016 (Figure). An additional 32 screening cases were identified among contacts. Median age of clinical case-patients was 70 years (range 21–96); 56% were male. Nearly, all had underlying medical conditions and extensive exposure to healthcare facilities before infection. Most clinical isolates were from blood (38, 62%), followed by urine (8, 13%) and respiratory tract (5, 8%). Among the first 35 isolates, 30 (86%) were resistant to fluconazole, 15 (43%) to amphotericin B, and one (3%) to caspofungin. No isolate was resistant to all three. WGS revealed isolates from each state were highly related and different from other states, suggestive of transmission. Microbiology record reviews did not identify additional cases before 2016.

**Conclusion.** *C. auris* is an emerging pathogen, with similarities to multidrug-resistant bacteria, that has been transmitted in US healthcare settings. CDC and public health partners are committed to prompt and aggressive action through investigation of cases and heightened infection control practices to halt its spread.

Figure: Number of clinical cases of *Candida auris* reported to CDC by state, May 2013-April 2017



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#### 145. Assessment of *Candida auris* Response to Antifungal Drugs Using Time-Kill Assays and an Animal Model

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**Background.** *Candida auris* is an emerging nosocomial pathogen that is resistant to Fluconazole and variably susceptible to other systemic drug classes. Treatment with echinocandins has been recommended based on MICs in the susceptible range, but supporting in vivo data is lacking.

**Methods.** We tested the MIC of *C. auris* strains ( $n = 12$ ) to fluconazole, voriconazole, posaconazole, anidulafungin, amphotericin B and flucytosine. Representative *C. auris* strains from Israel and South Africa, and a reference *C. albicans* strain were analysed using time-kill curve assays. Fungicidal activity was defined as reduction of  $\geq 3$  log from baseline CFU/ml. Response to caspofungin treatment was assessed in BALB/c mice immunosuppressed with cyclophosphamide and inoculated with  $7 \times 10^7$  *C. auris* cells by tail vein injection. Mice were treated from day +1 to day +7 with caspofungin (IP) at doses of 1 or 5 mg/kg and compared with sham-treated controls. Survival was assessed daily. Kaplan-Meier survival analyses were performed and treatment arms were compared using the log-rank test.

**Results.** Drug susceptibility results (MIC<sub>50</sub> and MIC<sub>90</sub>) were: fluconazole, 64 and 128 mg/l; voriconazole, 0.5 and 24 mg/l; posaconazole, 0.5 and 27 mg/l; anidulafungin, 0.03 and 0.06 mg/l; amphotericin B, 2 and 8 mg/l; flucytosine, 0.3 and 1 mg/l. Time-kill curve analyses showed log reduction from baseline CFU concentration of -3.0 to -2.8 for fluconazole (MIC  $\times 1$ ), 5.6-6.1 for amphotericin B (MIC  $\times 4$ ) and -0.4 to -0.9 for caspofungin (MIC  $\times 16$ ), consistent with fungicidal activity of amphotericin B and weak fungistatic activity of caspofungin. In the mouse model, survival rate was similar with sham treatment (33%) and treatment with caspofungin 1 mg/kg/day (44%) and 5 mg/kg/day (22%),  $P = 0.7$ .

**Conclusion.** Despite generally low MIC, caspofungin has only mild fungistatic activity on *C. auris* and no effect on survival in a mouse infection model. Amphotericin B has fungicidal activity against *C. auris*.

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#### 146. Pharmacodynamic Optimization for the Treatment of Invasive *Candida auris* Infection

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**Background.** *Candida auris* is an emerging, nosocomial multidrug-resistant threat with high treatment failure rate and mortality. The optimal antifungal agent to use and susceptibility breakpoints are based on limited clinical data.

**Methods.** Nine clinical *C. auris* strains were used. MICs were determined by CLSI standards. Drug treatment studies consisted of: fluconazole (FLC) dose range 0.78-200 mg/kg/12 h, micafungin (MFG) dose range 0.3125-80 mg/kg/24 h, or amphotericin B deoxycholate (AMB) dose range 0.078-20 mg/kg/24 hours. Plasma PK was previously determined in the murine model for all three drugs. A 96 h neutropenic murine model of invasive candidiasis (IC) was used for all studies. The Emax Hill equation was used to model the dose-response data to PK/PD index AUC/MIC (FLC and

MFG) and Cmax/MIC (AMB). The static and 1 log kill doses (when achieved) and the associated PK/PD targets (AUC/MIC or Cmax/MIC) were determined and compared with previous murine IC studies with *C. albicans*, *C. glabrata*, and *C. parapsilosis*.

**Results.** MIC range: FLC 2-256 mg/l, MFG 0.125-4 mg/l, and AMB 0.38-6 mg/l. Dose-dependent activity was observed with all three drugs. Net stasis was achieved against seven strains for FLC, eight strains for MFG, and eight strains for AMB. However, MFG performed significantly better than comparators for cidal endpoints. A 1 log kill endpoint was achieved in eight strains for MFG, whereas this endpoint was only achieved in one strain for FLC and three strains for AMB. PK/PD analyses demonstrated a strong relationship between AUC/MIC and treatment outcome for FLC ( $R^2$  0.61) and MFG ( $R^2$  0.77); and Cmax/MIC and treatment outcome for AMB ( $R^2$  0.64). The median static dose and 1 log kill dose (MFG only) and associated AUC/MIC or Cmax/MIC values are shown (Table).

Drug	Stasis		1 log kill	
	Dose (mg/kg/24 hours)	AUC/MIC or [Cmax/MIC]	Dose (mg/kg/24 hours)	AUC/MIC
FLC	107	26.3		
MFG	1.25	53.7	3.36	130
AMB	3.86	[0.87]		

**Conclusion.** MFG was the most potent drug over the dose range achieving up to 2 log kill against eight of nine strains. PK/PD targets for *C. auris* against FLC and AMB were similar to other *Candida* species; however, MFG targets were  $\geq 20$ -fold lower than *C. albicans*, *C. glabrata*, and *C. parapsilosis*. Using the median stasis targets and human PK for each drug, resistance thresholds could be 16 mg/l for FLC, 2-4 mg/l for MFG, and 1-2 mg/l for AMB.

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#### 147. Risk Predictive Model for 90-Day Mortality in *Candida* Bloodstream Infections

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**Background.** *Candida* bloodstream infections (CBSI) continue to be associated with high mortality, despite changes in antifungal treatment and diagnostics.

**Methods.** All patients age 18 or greater with a first episode of CBSI by blood culture from 1/2002 to 1/2015, admitted to Barnes-Jewish Hospital, a tertiary referral hospital in St. Louis, MO, were included. We collected data on demographics, comorbidities, laboratory values, vital signs, indwelling devices, and medical treatments of interest from the electronic medical record. We analyzed the potential predictor variables using univariate logistic regression. Variables associated with mortality were considered for model inclusion. The final model was built using multivariable binary logistic regression. A predictive equation was created, and a receiver-operator curve (ROC) was calculated to determine the appropriate cut-off points and c-statistic.

**Results.** Of the 1873 episodes of CBSI identified, 789 (42%) resulted in death in 90 days. The variables included in this model were age (40-49: OR 0.463, 95% CI 0.291-0.736; 50-69: 0.542, 0.342-0.860;  $\geq 70$ : 0.560, 0.400-0.785); history of CAD (1.616, 1.171-2.230), chronic liver disease (2.247, 1.327-3.806); maximum heart rate (1.496, 1.126-1.989) and temperature (0.537, 0.408-0.708); AST (1.817, 1.343-2.459) and platelet count (1.563, 1.178-2.073); the presence of ventilator (1.847, 1.321-2.582), urinary catheter (1.365, 1.008-1.847), two or more central lines (1.658, 1.020-2.694); removal of lines after positive culture (0.259, 0.181-0.370); ophthalmology consult during admission (0.441, 0.329-0.592); thoracentesis/chest tube (3.827, 1.550-9.448); diagnosis of secondary malignancy (2.131, 1.488-3.053); whether antimetabolites (2.119, 1.353-3.318), dapsone (4.507, 1.450-14.012), linezolid (1.605, 1.059-2.435), quinolones (1.384, 0.998-1.920) were ordered 90 days before positive culture. An ROC curve was calculated with an internal c-statistic of 0.806.

**Conclusion.** We created a risk predictive model for 90-day mortality in patients with CBSI, with 81% probability of predicting mortality. This model can lead to development of point-of-care applications to aid decision-making regarding escalation/de-escalation of care.

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#### 148. Time Trends in the Burden of Hospitalizations with Invasive Aspergillosis in the United States, 2004-2013

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