more than one Candida spp. isolated were excluded. Patient data were collected using electronic medical records and microbiology laboratory reports.

**Results.** Out of 835 VAT patients screened, there were 57 candidemia episodes across 38 patients resulting in an incidence of 6.2%. *C. glabrata* was the most common species (13/38, 34.2%), followed by *C. albicans* (10/38, 26.3%), *C. parapsilosis* (6/38, 15.8%), and *C. tropicalis* (5/38, 13.2%), and C. krusei (3/38 (7.9%). Ten patients had an echinocandin nonsusceptible first isolate (26.3%). In patients with recurrent candidemia, echinocandin nonsusceptibility rose as high as 55.6%. Candida species was the only independent risk factor for antifungal nonsusceptibility (OR, 1.9; 95% CI, 1.0–3.4). Micafungin was the most common initial antifungal (69/86, 80% of patients required salvage therapy with amphotericin and/or combination therapy (18.4%). Nineteen patients died prior to discharge (50.0%) and 29 patients died within 1 year (76.3%). Independent risk factors for in hospital mortality included APACHE II score (OR, 1.4; 95% CI, 1.1–1.8) and persistent candidemia (OR, 12.9; 95% CI, 1.3–129.6). Only three patients survived to heart transplant (7.9%).

**Conclusion.** Resistance and mortality rates in this patient population are extremely high. Micafungin was the most common antifungal used but antifungal choice did not appear to impact 1-year mortality. While this is the largest cohort of patients with VAT-associated candidemia to date, larger, prospective studies are needed to guide management of these infections.

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**378. Candida auris Fungemia: Risk Factors and Outcome**

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**Background.** *Candida auris* emerged as a human pathogen in 2009 and has subsequently been identified around the world as a cause of invasive candidiasis. Published clinical information on this organism consists primarily of case reports and small case series; thus, data from a single institution will allow us to examine risk factors for acquiring *C. auris* candidemia in comparison to other Candida species.

**Methods.** Aga Khan University Hospital Nairobi is a 280-bed referral center with 50 critical care beds. Candida species account for 34% of hospital-acquired bloodstream infections (Maina et al., 2016). Blood cultures were monitored continuously using the Bactec and the Vitrek™ was used for identification and susceptibility. The Vitrek™ identified *C. auris* as *Candida haemulonii*, but species determinations were done for 21 of the isolates and all were identified as *C. auris* using published methods (Pfaffer et al., 2012).

**Results.** From September 2010 to December 2016, 201 patients had 228 episodes of candidemia. Further analyses were performed only for first episodes. *C. auris* accounted for 38% of candidemia cases and 25% for *C. albicans*. A case–control analysis was done to compare patients with *C. auris* vs. *Candida albicans* fungemia. *C. auris* patients were more likely to be from critical care beds (78% vs. 52%, *P = 0.003) and had been hospitalized longer (mean 33 days vs. 13 days; *P < 0.001) prior to the positive blood culture. There was a trend toward more pre-existing renal failure (39% vs. 24%; *P = 0.09) in *C. auris* patients and during the two weeks prior to candidemia, they were more likely to have central lines (84% vs. 54%, *P < 0.001). *C. auris* patients received a mean 3.35 antifungal classes vs. 2.6 for *C. albicans* (p = 0.01). 75% of *C. auris* patients received carbapenems vs. 54% for *C. albicans* (*P = 0.02*). Eighteen percent of *C. auris* patients had 214 days of candidemia, despite frequent lack of followup blood cultures. Prolonged candidemia was not associated with development of in vitro resistance. The crude mortality was 29%, compared with 36% for *C. albicans* and 39% for other Candida spp. (NS).

**Conclusion.** These findings suggest an opportunistic pathogen that may be less virulent, but difficult to eradicate and that control efforts should focus on antimicrobial usage.

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**379. Pediatric Bloodstream Infections by Candida auris in Colombia: Clinical Characteristics and Outcomes of 34 Cases**

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**Background.** *Candida auris* is an emerging multi-drug-resistant human pathogen. Experimental data on the pathogenicity of *C. auris* are scarce, especially regarding its virulence compared with *C. albicans*. Additionally, studies of drug efficacy against *C. auris* rely on conventional animal models that are laborious and low throughput; alternative, less cumbersome models are desirable. To that end, we developed a *C. auris* infection model.

**Methods.** We injected 2-week-old *D.erial* and/or *D. melanogaster* females with a needle dipped in *Candida* solutions (10⁶ yeast cells/mL) in the dorsal side of the thorax. Flies were infected with different 10 *C. auris* strains (source: CDC/FDA) and a *C. albicans* strain. For drug protection studies, *C. auris* isolate AR-BANK#0386 (MFC: fluconazole (FLC) > 64, posaconazole (POSA) 0.125–0.375, isavuconazole (ISA) 0.25–1, voriconazole (VRC) 0.5–2 µg/mL) was used. We assessed survival differences associated with different inocula (10⁵-10⁶ yeast cells/mL and yeast strains. Moreover, protection conferred by addition of FLC, VRC, ISA, POSA, or FLC combined with 5-FC (fluocytosine) and/or nikkomycin Z (NikZ) to fly food was studied. Three independent runs were performed for each experiment.

**Results.** A) All *C. auris* strains and *C. albicans* exhibited comparable in vitro growth rates. B) All strains of *C. auris* exhibited similar virulent than *C. albicans* (P < 0.0001), with all flies dying by day 7 post-infection. C) FLC, VRC, ISA, FLC+5-FC, FLC+NikZ, or FLC+NikZ+5-FC-fed flies infected with *C. auris* #0386 had comparably poor survival outcomes compared with untreated *C. auris* #0386-infected flies. Interestingly, survival rates were improved in POSA-fed infected flies compared with untreated controls.
FLC-treated or untreated infected flies (P < 0.0001). As POSA is a cell-associated drug, we are conducting C. auris phagocytosis assays with Drosophila hemocytes that are co-incubated or not with POSA.

**Conclusion.** Drosophila is a promising, fast, and inexpensive in-vivo model to study pathogenesis and drug activity in C. auris candidiasis.

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381. Morphologic Changes Associated With Echinocandin Tolerance Enhance Immunoevasion of Candida glabrata

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**Background.** Activation of the cell wall integrity pathway and enhanced cell wall chitin synthesis are compensatory mechanisms associated with the incomplete killing of Candida glabrata by echinocandins. Echinocandin-induced morphologic changes in C. glabrata have also been described, yet their correlation with cell wall composition and macrophage responses to echinocandin treated C. glabrata are not well characterized. To identify whether the cell wall compositions is needed to understand how C. glabrata is capable of resisting both echinocandin killing and host immune responses.

**Methods.** Three echinocandin-resistant bloodstream isolates of C. glabrata were grown in liquid RPMI with or without inhibitory concentrations of micafungin (MFG) (0.004 μg/mL) and posaconazole (CAS; 0.008 μg/mL). Cells were stained with fluorescent markers specific for cell wall chitin, mannan, and viability, then imaged utilizing high-content single-cell techniques. Phenotypic characteristics of C. glabrata cells that survive echinocandin exposure were determined by comparing the morphol ogy and antibiotic-optional cell components among the viable and nonviable cell sub-populations. To identify cellular characteristics associated with reduced macrophage phagocytosis, CAS or MFG treated cells were co-incubated RAW 264.7 macrophage and imaged as above. Phenotypic characteristics of the nonphagocytosed yeast cells before and after co-incubation with macrophage were compared.

**Results.** Compared with untreated controls, growth in MFG and CAS significantly increased the proportion of cells with multi-buds (50% ± 10% and 40% ± 18% vs. 12% ± 6%; P < 0.001) and induced cellular enlargement (biovolume; 35 ± 9 μm3 and 80 ± 38 μm3 vs. 26 ± 5 μm3; P < 0.001). Cell enlargement, reduced cell wall mannan, and increased chitin were highly correlated with survival to MFG and CAS exposure (P < 0.001). Comparison of the drug-exposed yeast cell population before and after co-incubation with macrophage found an increased proportion of viable cells and cells with a large diameter (27 μm) remained un-phagocytosed, indicating strong phagocytic avoidance.

**Conclusion.** C. glabrata cells that survive echinocandins have distinct cell wall changes and are large in size. These cells tend to evade phagocytosis by macrophages, suggesting a potential mechanism by which C. glabrata may persist despite echinocandin treatment.

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382. Virulence in Candida glabrata Is Not Attenuated by FKS Mutations but Associated With the Frequency of Cells With Distinct Morphology

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**Session:** Session 56: Fungal Disease: Management and Outcomes

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**Background.** Echinocandins are the first-line treatment for C. glabrata; however, echinocandin resistance is increasingly reported. Acquired FKS-mediated echinocandin resistance has been associated with the chitin expression and attenuated fitness and virulence in C. albicans; however, conflicting data are reported in C. glabrata. Here, the influence of FKS mutations on fitness, virulence, morphology, and cell wall chitin was assessed among clinical strains of C. glabrata.

**Methods.** Three sets of isogenic paired strains consisting of an index-West and persistent-FKS mutant (S663P), two un-paired FKS mutant strains (S663F and S629P), and a West reference strain (CBS138) were included. Growth kinetics were measured over 24 hours in 96-well microplate containing liquid RPMI. After overnight growth in RPMI and staining with a chitin-specific fluorescent marker, morphology and cell wall chitin were assessed at the single-cell level utilizing high-content imaging technique. Virulence was evaluated in Galleria mellonella larvae by injecting 107 cells/larvae. Mortality was assessed daily for 5 days.

**Results.** Significant differences in growth kinetics, frequency of morphologic phenotypes within the cell populations (nonbudding, single-bud, multi-bud), and virulence were observed between strains obtained from different patients (P < 0.05 for each). However, no difference was observed between paired index-West and persistent-FKS S663P mutants. Compared with index-WT and the CBS138 reference strain, FKS mutant isolates (S663F, S629P, and S663F) had significantly elevated cell wall chitin content (P < 0.05). Neither chitin content, the presence of an FKS mutation, nor intrator growth characteristics were found to be associated with virulence. Virulence was strongly correlated with the frequency of multi-bud cells within the population however, with 5-day post-injection survival rates of 4% vs. 28% for high frequency (<12% multi-bud) cells and low frequency strains, respectively (P < 0.001).

**Conclusion.** Acquired FKS-mediated echinocandin resistance induced significant alterations in cell wall chitin content but was not observed to attenuate fitness or virulence. Virulence was highly associated with the frequency of cells with distinct morphology.

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383. An Increased Rate of Candida parapsilosis Infective Endocarditis Is Associated With Injection Drug Use

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**Session:** Session 56: Fungal Disease: Management and Outcomes

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**Background.** Candida parapsilosis fungemia typically occurs in patients with intravenous catheters or prosthetic devices. In 2017, we noted an increase in C. parapsilosis infective endocarditis (IE).

**Methods.** We retrospectively reviewed C. parapsilosis fungemia and IE from January 2015 to February 2018. Species were identified using MALDI-TOF, and confirmed by ITS sequencing.

**Results.** Between 2010 and 2017, there was no increase in cases of C. parapsilosis fungemia (mean: 13/year), but there was a significant increase in C. parapsilosis IE (P = 0.048) (Figure 1). From January 2015 to February 2018, 22% (12/54) of C. parapsilosis IE was complicated by IE. Demographics of C. parapsilosis fungemia included: community-acquired infection (87%), presence of vascular catheters (80%), opiate noninjection drug use (non-IDU, 44%), IDU (20%), and presence of cardiac devices (18%). Ninety-one percent (49/54) of C. parapsilosis fungemia was caused by C. parapsilosis sensu strictu (Cps); C. orthopsilosis and C. metapsilosis accounted for 4% (2/54) each (1 isolate could not be subtyped). Cps, C. orthopsilosis, and C. metapsilosis accounted for 83% (10/12), 8% (1/12), and 8% (1/12) of IE, respectively. Ninety-two (11/12) C. parapsilosis IE was left-sided, and 33% (4/12) involved multiple valves. Risk factors for C. parapsilosis IE were post or active IDU (P < 0.001), community-acquired fungemia (P = 0.02), prosthetic heart valve (P = 0.01) or implanted cardiac device (P = 0.03). Receipt of an antibiotic within 30 days was a risk for C. parapsilosis fungemia without IE (P = 0.001). Median age for IE vs. fungemia was 38 ± 57 years (P = 0.09). By multivariable logistic regression, IDU (P < 0.0001), prosthetic valve (P = 0.006) or implanted cardiac device (P = 0.04) were independent risks for C. parapsilosis IE. 70% (71/102), 20% (2/10), and 10% (1/10) of patients with IDU and C. parapsilosis IE primarily used heroin, buprenorphine/naltrexone, and cocaine, respectively. 50% (6/12) of patients with C. parapsilosis IE underwent surgery; most common initial AF regimen were caspofungin and amphotericin B. Nonsurgical patients were suppressed with long-term azole; one relapsed requiring surgery. Thirty-day and in-hospital mortality for patients with fungemia vs. IE were 32% vs. 17% and 26% vs. 17%, respectively.

**Conclusion.** C. parapsilosis IE has emerged at our center. Unique aspects of C. parapsilosis pathogenesis that may account for emergence are a propensity to colonize skin, adhere to prosthetic material and form biofilm. C. parapsilosis IE may be an under-appreciated consequence of IDU and opioid abuse.

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**Figure 1. Cases of C. parapsilosis infective endocarditis**

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