

µL). Non-HIV patients were significantly older ( $P < 0.001$ ) and had higher rates of altered mental status (AMS) on presentation (58.3% vs. 25%,  $P = 0.05$ ). There was no significant variation in temperature, blood pressure, white blood cell count, serum sodium, or CSF opening pressure. Non-HIV patients had significantly higher CSF cell count ( $P = 0.02$ ) and protein ( $P < 0.001$ ), and lower glucose ( $P = 0.005$ ) compared with HIV patients. There was no significant variation in length of stay or rates of intensive care unit admission. Overall, 90-day all-cause mortality was 19.4%; mortality rates were significantly higher in non-HIV patients at both 90 days ( $P = 0.017$ ) and one year ( $P = 0.047$ ).

**Conclusion.** Compared with individuals with HIV, non-HIV cryptococcal meningitis patients have a more inflammatory CSF profile at the time of diagnosis, higher rates of AMS on presentation, and higher rates of 90-day and 1-year all-cause mortality. We postulate that reversible immunosuppression among HIV patients may partially explain these findings. Further research is needed to identify hallmarks of cryptococcal meningitis in non-HIV patients to facilitate early intervention.

	HIV (n=24)	Non-HIV (n=12)	p-value	Total Cohort (n=36)
Mean age (±SD, years)	42.2 ± 9.9	62.2 ± 7.4	<0.001*	48.8 ± 13.2
Male sex (%)	21 (87.5)	9 (75)	0.343	30 (83.3)
White (%)	16 (66.7)	7 (58.3)	0.624	23 (63.9)
Median CSF cell count/µL (IQR)	27.5 (12-63)	84 (53-265)	0.02*	53 (14-118)
Mean CSF glucose (±SD, mg/dL)	44 ± 17.2	25.6 ± 16.1	0.005*	37.4 ± 18.8
Median CSF protein (IQR, mg/dL)	57 (47-89)	171 (101-292)	<0.001*	89 (51-171)
Altered mental status (%)	6 (25)	7 (58.3)	0.05*	13 (36.1)
ICU Admission (%)	5 (20.8)	5 (41.7)	0.188	10 (27.8)
90-day mortality (%)	2 (8.3)	5 (41.7)	0.017*	7 (19.4)
1-year mortality (%)	3 (12.5)	5 (41.7)	0.047*	8 (22.2)

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### 1718. The Natural History of Chronic Pulmonary Coccidioidomycosis in the Pre-Antifungal Era

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**Background.** Prior studies to characterize pulmonary coccidioidomycosis (CM) have been limited by small samples. The historical VA-Armed forces CM patient group provides a unique cohort of patients not treated with conventional antifungals to better characterize and describe chronic pulmonary CM with an emphasis on chronic nodules and cavities.

**Methods.** A retrospective study of 374 VA-Armed forces non-disseminated CM patients diagnosed between 1955 and 1958 and followed to 1966. Patients had a pulmonary nodule or a pulmonary cavity secondary to CM. Basic demographic information, complement fixation serology, and details regarding the nodules and cavities were investigated.

**Results.** The studied population had a median age of 34 with 97% men and 84% white. Eighty percent had no underlying pulmonary disease and concurrent tuberculosis was the most common comorbid pulmonary condition (11%). Patients with cavities had a median complement fixation (CF) serology of 1:2 (interquartile range (IQR) negative 1:8). Patients with nodules had a median CF serology of negative (IQR negative 1:2). The median number of pulmonary nodules was 1 with a median size of 1-1.9 cm. Sixty-nine percent of the nodules had a sharp, well-defined border, while 10% had a calcified border. The median number of cavities was 1 with a median size of 3-3.9 cm. Forty-five percent of the cavity walls were thin, 31% were thick, and 19% were variable in size. Twenty-six percent of the cavities developed during acute infection with 46% developing without a prior history of primary infection. Twenty-nine percent of the cavities were stable in size, 20% increased in size, 5% disappeared, 4% ruptured, and 2% decreased in size.

**Conclusion.** This study helps further characterize chronic pulmonary nodules and cavities caused by CM. To the best of our knowledge, this is the largest study of the natural history of chronic CM pulmonary cavities and nodules providing valuable descriptive features.

**Disclosures.** All authors: No reported disclosures.

### 1719. Incidence and Characterization of Invasive Fungal Infections (IFIs) in Patients with Chronic Lymphocytic Leukemia (CLL) Treated with Ibrutinib (IBR)

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**Background.** IBR is a Bruton's tyrosine kinase inhibitor, and plays a key role in the treatment of CLL. In randomized clinical trials, <1% of IBR-treated CLL patients developed IFIs. However, several IFIs were reported with real-life use of IBR.

**Methods.** This is a retrospective observational study of all CLL patients (> 18 years) treated with IBR (2/2014-8/2018) at MD Anderson Cancer Center. We excluded patients with active IFI (proven and probable, EORTC/MSG criteria) at the start of IBR and patients with <6 months of follow-up.

**Results.** Of the 821 CLL IBR-treated patients, 24 developed probable or proven IFI (2.9%). Of these infections, 21 occurred within 30 days (d) of last IBR dose, while 3 IFIs occurred at 94, 135 and 221 d post IBR, respectively. The majority of patients with IFI were male (83%) with a median age of 66 years at IFI diagnosis. The median prior lines of therapy for CLL was 1 (range 0-7), with 29% receiving IBR as frontline treatment. Five patients had evidence of Richter's transformation at the time of IFI diagnosis, while two patients had prior stem cell transplant. The average time from start of IBR to diagnosis of IFI was 338 d, with only 7 cases of IFI within the first 3 months of IBR. The majority of IFIs were proven/probable aspergillosis (63%), including 9 cases of *Aspergillus fumigatus*. The remaining infections consisted of *Cryptococcus neoformans* (21%), *Fusarium spp.* (8%), with one case each of candidiasis, histoplasmosis, mucormycosis, and *Pneumocystis jirovecii* pneumonia. Three patients had evidence of poly-fungal IFI. The sites of infection were pulmonary (88%), blood (13%), CNS (13%), and sinus (8%). Five patients were diagnosed with disseminated IFI, including *Cryptococcus spp.* (2 cases), *Rhizopus spp.*, *Aspergillus spp.*, and *Candida spp.* The 42-day mortality rate post IFI diagnosis was 25%.

**Conclusion.** We report the largest single-center cohort of CLL patients on IBR to date. The IFI incidence of 2.9% (24/821) is consistent with most previous reports estimating a 0.5-4% incidence. In contrast to published reports, close to 1/3 of our patients with IFI received IBR as frontline therapy and most IFIs (71%) were diagnosed > 3 months after starting IBR. We are currently conducting a case-control comparison with IBR-treated CLL patients with no infection to uncover risk factors associated with IFIs in these patients.

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### 1720. Isolation and Characterization of *Candida auris* From an Active Surveillance System in Texas

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**Background.** *Candida auris* is an emerging new multi-drug-resistant fungal pathogen spreading globally. *C. auris* is associated with outbreaks due to the bloodstream, ear, and wound infections with a high mortality rate (30 to 60%). As part of our multi-pathogen surveillance system, we began screening for *C. auris* to understand the ecology, sources, and epidemiology of this important pathogen from leftover stool samples collected from hospitalized patients.

**Methods.** Four hundred and seventeen stool samples were collected, enriched in brain heart infusion broth for 2-3 days at 37°C, and sub-cultured onto selective *Candida* agar plates. Agar plates were incubated at 37°C for another 2-3 days and suspected *Candida* colonies were stocked for DNA extraction, PCR identification, and whole-genome sequencing. PCR amplicons were sequenced to confirm the identification *C. auris*. Enrichment samples were also screened by PCR to directly detect *C. auris*. Minimum inhibitory concentration (MIC) of various anti-fungal drugs was determined by the micro-dilution method using a commercial MIC plate (Sensititre "YeastOne").

**Results.** Three *C. auris* samples were identified by PCR (0.7%; 3/417) of which one was able to be cultured. The isolated strain was resistant to fluconazole, itraconazole, voriconazole, posaconazole, and caspofungin. WGS data analysis demonstrates our isolate has high similarity with the Pakistani strains.

**Conclusion.** We have detected *C. auris* from stool samples of hospitalized patients in Texas for the first time. WGS data indicate our isolate has high similarity with South Asian patient strains. Long-term surveillance of *C. auris* is essential to understand the infection or colonization sources and epidemiology of this newly emerging fungal pathogen.

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### 1721. A Transcriptional Signature of Acute *Aspergillus* Infection Offers High Diagnostic Accuracy Despite the Presence of Immunosuppression

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**Background.** Invasive aspergillosis (IA) is a major cause of critical illness in immunocompromised (IC) patients. However, current fungal testing methods have significant limitations and there is a clear need for new diagnostic options. Disease-specific gene expression patterns in circulating host cells show promise as novel diagnostics; however, it is unknown whether such a "signature" exists for IA. Additionally,

there is a need for better understanding of the effect of iatrogenic immunosuppression (present in most cases of IA) on such host response-driven biomarkers.

**Methods.** Male BALB/c mice were separated into an *Aspergillus fumigatus* inhalational exposure group and a placebo group. These two groups were each subdivided into three additional sets based on immunocompromised status (no immunosuppression, cyclophosphamide, and corticosteroids) for a total of six experimental groups. Mice were sacrificed 4 days post-infection. Whole blood was assayed for transcriptomic responses via microarray. Bayesian techniques were utilized to develop classifiers of IA and leave one out cross-validation was used to estimate predictive probabilities.

**Results.** *Aspergillus* infection triggers a powerful response in non-IC hosts, with 2996 genes differentially expressed between IA and controls. We generated a 146-gene expression classifier able to discriminate between non-IC mice with IA and uninfected non-IC mice with 100% accuracy. However, the presence of immunosuppressive drugs exhibited a strong confounding effect on the transcriptomic classifier that was derived in the absence of immunosuppression. After controlling for the genomic effects of immunosuppressive drugs, we were able to generate a 187-gene classifier with a sensitivity of 100% and specificity of 97% across all IC states.

**Conclusion.** The host transcriptomic response to IA is robust and highly conserved. Pharmacologic perturbation of the host immune response unsurprisingly has powerful effects on gene expression-based classifier performance and must be taken into account when developing novel diagnostics. When appropriately designed, host-derived peripheral blood transcriptomic responses to IA demonstrate the ability to accurately diagnose *Aspergillus* infection, even in the presence of immunosuppression.

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### 1722. Histoplasmosis Acquired in Alberta, Canada, 2011–2018

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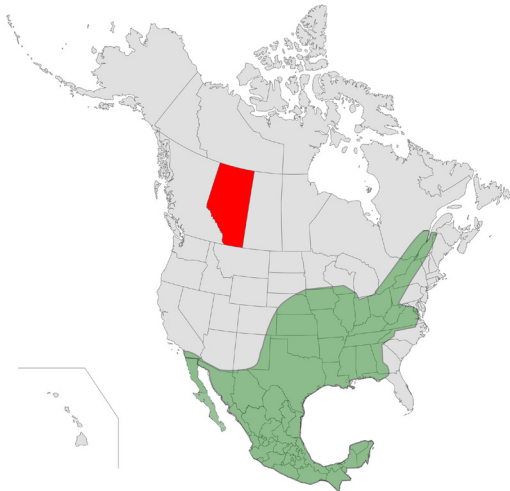
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**Background.** Histoplasmosis is a serious fungal infection caused by the geographically restricted, dimorphic fungus *Histoplasma capsulatum*. In Canada, the geographic range of *H. capsulatum* is classically thought to be restricted to southern parts of Ontario and Quebec. Over the past decade, histoplasmosis has occasionally been diagnosed in patients in Alberta without travel to areas of known geographic risk (Figure 1). We studied the epidemiology and geographic distribution of histoplasmosis in Alberta to assess evidence for locally-acquired infections.

**Methods.** We retrospectively reviewed all laboratory-confirmed (culture, antigen and/or immunodiffusion positive) cases of histoplasmosis diagnosed from January 1, 2011 to June 30, 2018. Data collected by public health and clinical charts were reviewed for clinical presentation, exposure and travel histories, and geographic distribution of cases. Cases of histoplasmosis in patients who had not left Alberta or associated with a local point source were classified as definite local acquisition; cases in patients with remote travel but with local exposures and appropriate timing of disease onset were deemed “probable” cases of local infection. University of Alberta’s Research Ethics Board approved this study.

**Results.** We identified 45 laboratory-confirmed cases of histoplasmosis, including 17 cases that were locally acquired. Among these, there were 12 cases of definite local acquisition, including 8 patients from 3 point-source outbreaks—all involving exposure to bats and/or their droppings in chimneys or attics of private dwellings or churches—and 4 sporadic cases in patients who had never traveled. Of the other 5 cases probably acquired in Alberta, patients had previously traveled ( $n = 4$ ) or travel history was incomplete ( $n = 1$ ) but local exposures preceding infection were considered compelling. The mean incidence rate of locally acquired infection was 0.062/100,000 population with incidence increasing since 2014. Table 1 shows features of locally acquired cases.

**Conclusion.** This study, for the first time, establishes Alberta as a region of geographic risk for histoplasmosis. The diagnosis should be considered in patients with compatible symptoms and exposure history, even in the absence of travel.



**Table 1.** Characteristics of patients with locally acquired histoplasmosis in Alberta

Characteristic, No. of Patients	No (%)
<b>Age, Median (Range) in years</b>	49 (17-64)
<b>Sex, 17</b>	
M	15 (88)
F	2 (12)
<b>Diagnostics, 17</b>	
Culture confirmed	6 (35)
Not culture confirmed	11 (65)
Antibody only	5
Antigen only	4
Antibody and antigen	2
<b>Epidemiology, 17</b>	
Point-source outbreak	8 (47)
Sporadic	9 (53)
<b>Exposure History, 12</b>	
Bats/bat guano	9 (75)
Workplace (excavation, moldy/humid soil)	2 (17)
Proximity to Construction Site	1 (8)
<b>Disease Localization, 15</b>	
Disseminated	7 (47)
Soft Tissue	1 (7)
Pneumonia	10 (67)
<b>Immunocompromised, 7</b>	
Yes	4 (57)
No	3 (43)
<b>Hospitalized, 15</b>	
Yes	7 (47)
No	8 (53)
<b>Seasonality, 16</b>	
Summer	10 (63)
Spring/Fall	6 (37)
<b>Outcome, 17</b>	
Death	2 (12)
Survival	15 (88)

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### 1723. Human Serum Albumin Regulates the Growth of *Candida auris* in vitro

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**Background.** *Candida auris* is commonly detected in human ear secretions. However, *C. auris* occasionally causes bloodstream infections even in immunocompetent patients resulting in poor prognosis. It was speculated that *C. auris* growth within the blood might be regulated by proteins in the bloodstream. Thus, in this study, the potential role of blood proteins in the regulation of *C. auris* growth was investigated.

**Methods.** Five *Candida* species (*C. albicans*, *C. auris*, *C. glabrata*, *C. parapsilosis*, and *C. tropicalis*) were incubated overnight. Colony suspensions for each species were prepared and adjusted to OD 1.0 at absorbance 0.1. Then, human serum albumin (HSA) and bovine serum albumin (BSA) were diluted (2.5 g/dL–0.002 g/dL) and mixed with the suspensions. Mixed samples were adjusted to 100 µL and incubated on MHA plates at 35°C for 2 days. Then, 50 µL of the combined sample was extracted and streaked onto Yeast extract–Peptone–Dextrose (YPD) agar. The remaining 50 µL sample was analyzed using an XTT assay. Further testing was then conducted on the effects of a specific blood protein albumin on *Candida*. Thereby, *C. albicans* and *C. auris* were cultured following the procedure above and stained with Annexin V and PI.

**Results.** The growth of *C. auris* mixed with a high albumin concentration (2.5–0.15 g/dL) was regulated compared with that of other *Candida* species ( $P < 0.01$ ) (Figures 1 and 2); however, the growth of *C. auris* mixed with a lower albumin concentration was similar to that of other species. The wash-out study showed that *C. auris* growth and survival in the high albumin concentration was not different than that of other species.

**Conclusion.** HSA and BSA regulated *C. auris* growth which led to increased necrosis of *C. auris*. Conversely, growth of the other *Candida* species was not regulated. Therefore, albumin might be involved in the growth and necrosis of *C. auris*. As the highest concentration at which albumin regulated *C. auris* growth was similar to that found in human serum, it is possible that serum albumin might help prevent *C. auris* from entering the bloodstream via the ear or skin.