Influenza A accounted for 80% (75/94) of cases. Seventy-nine percent (74/94) received antiviral therapy. Underlying conditions included 63% (59/94) immunocompromising condition, 51% (48/94) chronic lung disease, 22% (21/94) renal disease, and 15% (14/94) asthma. Forty-eight percent of patients (45/94) required intensive care. At the time of discharge, 60% (56/94) were diagnosed with pneumonia and 14% (13/94) died.

Conclusion. Over one-third of patients with invasive aspergillosis did not have a documented immunosuppressive condition. ICD codes are likely an imperfect way to identify invasive aspergillosis, and further studies are needed to characterize risk factors and verify diagnoses for aspergillosis among patients with severe influenza.

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355. Invasive Pulmonary Aspergillosis (IPA) Complicating Respiratory Viral Infections in Patients With Hematological Malignancies

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Background. Data regarding respiratory viral infections (RVIs) in patients with leukemia and/or stem cell transplantation (LSCT) and their predisposition to invasive pulmonary aspergillosis (IPA) are limited. To that end, we conducted a case–control study of post-RVI-IPA in LSCT patients.

Methods. We analyzed all consecutive adult patients (2006–2016) with culture-documented IPA (EORTC/MSG criteria). Cases were patients with confirmed (either by nasal wash and/or BAL PCR and/or respiratory viral culture) RVIs [respiratory syncytial virus (RSV), Influenza A/B (INFA/B), or parainfluenza virus (PIV)] followed by IPA up to 5 weeks after. Controls were patients with IPA without evidence of RVIs.

Results. We identified 54 cases (proven 1, probable 53), and 142 patients with IPA (proven 12, probable 130) as controls. The distribution of viruses were 34 PIV (52%), 18 INFA/B (27%), and 14 RSV (21%). The median days of post-RVIs-IPA infection was 8(−6–57) days. Among cases, the most common hematological malignancies were AML (34%) and CLL (26%). Most cases had prior allogeneic SCT (57%). Non-*fumigatus Aspergillus* species were the cause of IPA in 58% of cases. In univariate analysis, patients with post-RVs-IPA infection were more likely to be in complete or partial remission (43.9% vs. 22.3% $P = 0.007$), to have prior allogeneic SCT (57% vs. 31%, $P = 0.0009$) and an absolute lymphocyte count between 500 and 1,000/mm^3 at RVI diagnosis (41% vs. 27%, $P = 0.04$). In addition, coinfections within 2 weeks after viral infection (58% vs. 18%, $P = 0.0001$), especially of the lower respiratory tract (37% vs. 18%, $P = 0.004$) were more common in patients with post-RVIs-IPA. RVIs-IPA patients were less likely to have an absolute neutrophil count <100 mm^3 at IPA diagnosis (17% vs. 37%, $P = 0.005$). Need for ICU post-RVIs-IPA disease (31% vs. 26% $P = 0.5$) and 42 days crude mortality (22% vs. 27%, $P = 0.45$) were no different between cases and controls.

Conclusion. Post-RVIs-IPA occurs more frequently in patients with prior transplantation and is less associated with leukemia relapse and neutropenia. Although co-infections are common, this entity does not appear to be associated with worse outcome compared with IPA without preceding RVI.

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356. Bronchoalveolar Lavage Fluid Cytology by GMS Stain for the Diagnosis of Invasive Pulmonary Aspergillosis in Patients With Hematologic Malignancies: Analysis of 67 Episodes

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Background. The yield of direct fungal visualization by GMS (Gomori–methenamine–silver) stain in bronchoalveolar lavage (BAL) cytology has rarely been studied in the diagnosis of invasive pulmonary aspergillosis (IPA) in patients with hematological malignancies (HM).

Methods. We analysed a series of patients with proven or probable culture-documented IPA (EORTC/MSG criteria) in HM patients (1999–2015). All patients had BAL cultures that were positive for *Aspergillus* spp. and had concurrently obtained BAL cytology GMS available for analysis.

Results. We identified 67 such patients. BAL cytology based on GMS showed hyalohyphomycetes consistent with *Aspergillus* in 28/67 (41.8%) patients, whereas only in 2/67 (3.6%) direct smear Calcofluor White stain was positive. Based on BAL GMS cytology, co-infections were identified in six patients: two *Pneumocystis* and five viral infections with cytopathic changes (one had both). The yield of cytology was not different in patients with IPA caused by non-*fumigatus Aspergillus*, although patients with IPA and >1 *Aspergillus* in BAL culture had more often positive cytology GMS (100% vs. 0%, p 0.027). Cytology was also more often positive when obtained from a lesion-targeted BAL as compared with non-targeted bronchial washings (60.7% vs. 7.1%, p 0.038). Patients with IPA and cavitary lesions (32.1% vs. 5.1%, $P = 0.006$), history of SCT (64.3% vs. 33%, $P = 0.015$) or prior exposure to itraconazole (75% vs. 41%, $P = 0.007$) had positive cytology GMS results more often than did patients without these characteristics. In the multivariate analysis, only cavitary lesions were significantly associated with positive BAL GMS cytology.

Conclusion. GMS stain in cytology of BAL in patients with HM and culture-documented IPA had a sensitivity of 41.8% and was more often positive in patients with cavitary lesions. Although there were no differences in the proportion of GMS-positive cytology rates among differing *Aspergillus* spp. causing IPA, mixed *Aspergillus* spp. IPA was associated with an increase in positive cytology. BAL cytology was diagnostic for co-infections in more than 10% of patients. BAL cytology should be part of the diagnostic wok up in HM patients with suspected IPA.

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357. Aspergillus Isolates Remain Largely Susceptible to Azoles and Other Antifungals at a Large Transplant Program Using Azole Prophylaxis

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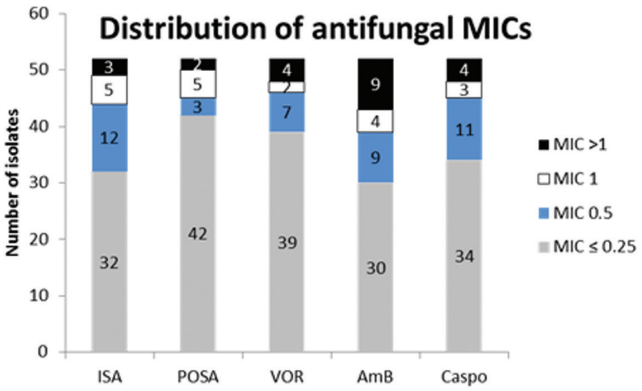
Background. The emergence of azole resistance globally among *Aspergillus* species has major clinical and agricultural implications. At our center, isavuconazole (ISA), posaconazole (POS), and voriconazole (VOR) have been used as antifungal prophylaxis in solid-organ transplant recipients. We determined susceptibility to azoles and other antifungals among *Aspergillus* isolates from our center.

Methods. Fifty-two patient isolates of *Aspergillus* species were collected from the UPMC Microbiology Laboratory between December 2016 and April 2018. Minimum inhibitory concentrations (MICs) of ISA, POS, VOR, amphotericin B (AmB), and caspofungin (CAS) were measured using EUCAST Antimicrobial Susceptibility Testing methods. *Candida parapsilosis* ATCC 22019 and *Candida krusei* ATCC 6258 were used as quality control.

Results. Seventy-one percent (37/52) of isolates were from solid-organ transplant recipients (34 lungs, two liver, and one heart). *Aspergillus* spp. were *A. fumigatus* (29), *A. terreus* (*At*, 6), *A. niger*, *A. flavus* and *Aspergillus calidoustus* (five of each species), and *A. lentulus* and *A. thermomutatus* (one of each species). Thirteen breakthrough (BT) isolates were recovered from patients on azoles: *A. calidoustus* (5), *A. niger* (4), *A. flavus* (2), *A. fumigatus* (1) and *At* (1). *A. calidoustus, A. flavus*, and *A. niger* were more likely than other species to be recovered from azole BT (75% (12/16) vs. 5% (2/36), $P = 0.06$). For all isolates, ISA, VOR, and POSA MIC_{50} were 0.25 μg/mL, 0.04 μg/mL, and 0.25 μg/mL, respectively. One *A. calidoustus* and one *At* were resistant to all antifungals (azoles, AmB, and caspofungin MICs were >16 μg/mL); both were associated with azole BT. ISA, POS, and VOR MIC_{50} vs. azole BT isolates (0.5, 0.125, and 0.5 μg/mL, respectively) were higher than those vs. non-BT isolates (0.25, 0.03, and 0.25 μg/mL, respectively; $P < 0.01$ for all).

Conclusion. Despite widespread use of azole prophylaxis in transplant recipients at our center, we did not observe high rates of resistance to azoles or other antifungals among *Aspergillus* isolates, although azole MICs were higher against BT isolates. Azole BT isolates were more likely to be non-*A. fumigatus* species. Clinicians should understand that antifungal resistance rates can vary by center and geographical location, and use their local epidemiology to guide decisions about the utility of specific agents in their populations.



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