966. Infectious Diseases among US Resident Student Travelers after Return to the United States: A GeoSentinel Analysis, 2007–2017

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Session: 124. Adventures with Globally Acquired Infections

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Background. The number of US students studying abroad has more than tripled over the past 20 years. As study abroad programs diversify their destinations, more students are traveling to developing regions, increasing their risk of infectious diseases. Few data exist describing infections acquired by US students while traveling internationally. We describe the spectrum of disease among students who have returned from international travel and suggest how to reduce illness among these travelers.

Methods. GeoSentinel is a global network of travel and tropical medicine providers that monitors travel-related morbidity. Records of US resident student travelers, 17–24 years old, who returned to the United States and were given a confirmed travel-related diagnosis at one of 15 US GeoSentinel sites during 2007–2017. Those without ascertainable exposure regions were excluded. Records were analyzed to describe demographic and travel characteristics and diagnoses.

Results. There were 432 students included. The median age was 21 years; 69% were female. Over 70% had a pretravel consultation with a healthcare provider. The most common exposure region was sub-Saharan Africa (112 travelers; 26%); the most common exposure countries were India (44 students; 11%), Ecuador (28; 7%), Ghana (25; 6%), and China (24; 6%). Students presented to a GeoSentinel site a median of 8 days (range: 0–181) after travel; 98% were outpatients. The most common diagnosis categories were gastrointestinal (45%) and dermatologic (17%). Of 581 confirmed diagnoses, diarrheal illnesses were most common (165; 28%). Thirty-one (7%) students had a vector-borne disease; 14 (41%) of these were diagnosed with malaria (13 had a pretravel consultation) and 11 (32%) with dengue. Two students were diagnosed with acute HIV. Three had a vaccine-preventable disease (two typhoid; one hepatitis A).

Conclusion. Students experienced travel-related infections despite a large proportion receiving pretravel consultations. Students (especially those traveling to a less developed region) should receive specific pretravel instructions (including suggestions for behavioral modification, vaccination, and medication prophylaxis when applicable) to prevent gastrointestinal, vector-borne, sexually transmitted, and vaccine-preventable diseases.

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967. Inhibition of Host Neuraminidase Increases Susceptibility to Invasive Pulmonary Aspergillosis

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Session: 125. Fungal Infections

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Background. Influenza-associated aspergillosis (IAA) is an emerging fungal infection with high mortality and morbidity and the pathogenesis of this disease is not well understood. Interestingly, the number of IAA case reports has increased since the widespread use of neuraminidase inhibitors, such as oseltamivir in 2009. We set out to determine whether oseltamivir could contribute to the pathogenesis of IAA by modulating host responses.

Methods. First, peripheral blood mononuclear cells (PBMCs) and neutrophils from healthy donors were stimulated with neuraminidase (NA)-treated *A. fumigatus* or were pre-exposed to NA prior to stimulation with *Aspergillus* conidia. In addition, PBMCs and neutrophils were pretreated with oseltamivir carboxylate prior to stimulation. Cytokines were measured from supernatants after 24 hours of incubation at 37˚C. C57BL/6 and BALB/c mice were treated with oseltamivir prior to intranasal challenge with *A. fumigatus*. Immunosuppression was induced by corticosteroid or cyclophosphamide.

Results. We demonstrate that *Aspergillus* treated with NA induced an enhanced immune response. Moreover, PBMCs and neutrophils treated with NA produced increased cytokine responses. Blocking NA in vitro with oseltamivir reduced *Aspergillus*-induced cytokine responses. Next we investigated the effects of blocking neuraminidase activity with oseltamivir in vivo. Immunocompetent mice and mice treated with corticosteroids showed increased mortality, lung fungal burden, and decreased cytokine production when treated with oseltamivir. These effects were not observed in cyclophosphamide-treated mice, suggesting that the effects of NA activity in anti-*Aspergillus* host defense acts mainly via myeloid cells.

Conclusion. Our results provide evidence that host neuraminidase activity is important for protective anti-*Aspergillus* immune responses. Treatment with oseltamivir, thus blocking host NA activity, in a setting of corticosteroid use might therefore increase susceptibility to *Aspergillus* infection. These results warrant further study on the role of neuraminidase and the effects of oseltamivir on susceptibility to invasive pulmonary aspergillosis during active influenza infection.

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968. Managing Invasive Aspergillosis in the Era of Diagnostic PCR and Increasing Triazole Resistance: A Modeling Study of Different Strategies

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Session: 125. Fungal Infections

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Background. Triazole resistance in *Aspergillus* spp. is emerging and complicates prophylaxis and treatment of invasive Aspergillosis (IA) worldwide. New polymerase chain reaction (PCR) tests on broncho-alveolar lavage (BAL) fluid allow for detection of triazole resistance on a genetic level, which opened up new possibilities for targeted therapy. In the absence of clinical trials, a modeling study delivers estimates of the added value of resistance detection with PCR and which empiric therapy would be optimal when local resistance rates are known.

Methods. We performed a decision-analytic modeling study based on epidemiological data of IA, extended with estimated dynamics of resistance rates and treatment effectiveness. We compared 6 clinical strategies that differ in the use of PCR diagnostics (A: not used, B: used) and in empiric therapeutic choice in case of unknown triazole susceptibility: Voriconazole (1, VOR), Liposomal Amphotericin B (2, LAmB), or both (3). Outcome measures were proportion of correct treatment, survival, and serious adverse events.

Results. Implementing Aspergillus PCR tests was projected to result in residual treatment susceptibility mismatches of <5% for a triazole resistance rate up to 20% (using VOR). Empiric LAmB outperformed VOR at resistance rates higher than 5–20%, depending on PCR use and estimated survival benefits of VOR over LAmB (Figure 1). Combination therapy of VOR and LAmB performed best at all resistance rates but the advantage over the other strategies should be weighed against the expected increased number of drug-related serious adverse events (Figure 2). The advantage of combination therapy over LAmB monotherapy became smaller at higher triazole-resistance rates.

Conclusion. Introduction of current Aspergillus PCR tests on BAL-fluid is an effective way to increase the proportion of patients that receive targeted therapy for IA. The results indicate that close monitoring of background resistance rates and of adverse drug events are important to attain the potential benefits of LAmB. The choice of strategy ultimately depends on the probability of triazole resistance, the availability of PCR, and individual patient characteristics.