In Response:

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In Response: Alanio et al. comment that the prevalence of azole-resistant Aspergillus disease may differ, depending on location of the hospital where patients are admitted and the patients’ underlying disease (1). Determining local or regional epidemiology, especially in areas where azole-resistant isolates are found in the environment, is indeed important. These isolates commonly harbor the TR14/L98H or TR34/Y121F/T289A resistance mechanism. Patients may inhale azole-resistant spores in the air and subsequently develop azole-resistant disease, even when they have never been treated with azoles (2). Although risk for inhalation of azole-resistant Aspergillus spores arguably might be similar for all patients, surveillance of Aspergillus isolates in the Netherlands indicates that resistance rates vary among hospitals. When all A. fumigatus isolates cultured from patients were investigated for azole resistance, resistance rates in the Netherlands ranged from 4.3% to 19.2% in 2013 and 3.8% to 13.3% in 2014 (3). The highest and lowest resistance rates were found in hospitals only 39 km from each other, supporting the observation made by Alanio et al. about variations in prevalence of azole-resistant Aspergillus disease (1).

More detailed surveillance is required to determine if local treatment guidelines should be reassessed. Two recent studies in the Netherlands investigated the risk of azole-resistant invasive aspergillosis in high-risk populations. One study conducted in a 33-bed tertiary-care university hospital intensive-care unit (ICU) showed that 26% of culture-positive patients with presumed invasive aspergillosis harbored azole-resistant isolates, a proportion 14% higher than that found in other departments in the hospital (p = 0.06) (4). The second study, which investigated azole resistance in the primary routine culture (including respiratory cultures) of 105 ICU and hematology patients, showed that the resistance rate (24.6%) for hematology patients was higher than the rate (4.5%) for ICU patients (5). Other countries have also reported higher prevalence of resistance in high-risk populations than in other populations.

One problem with assessing prevalence of azole resistance is that the recovery of A. fumigatus in culture may vary considerably among different patient groups. A recent audit in our hematology department over the past 5 years indicated that A. fumigatus was cultured in only 35% of patients who underwent bronchoalveolar lavage as part of a diagnostic work-up for pulmonary infection (P.E. Verweij, unpub. data). This outcome indicates that in culture-negative patients, presence of azole resistance will be missed.

In agreement with Alanio et al. (1), recent studies show a need to determine frequency of azole resistance at the hospital level and within different patient groups or departments. Although surveillance of unselected clinical cultures provides resistance rates at a national level and offers information about the epidemiology of resistance mechanisms, regular audits in specific patient populations are warranted to determine the frequency of azole resistance among different risk groups. These audits will enable clinicians to determine whether reassessment of azole monotherapy as a primary treatment option is necessary. Given the low and variable rates of positive cultures, culture-negative patients should also be included in azole-resistance surveillance programs.

References
Schistosomiasis Screening of Travelers to Corsica, France

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To the Editor: As members of the French Ministry of Health Working Group on autochthonous urinary schistosomiasis, we read with interest the 2 recently published articles regarding schistosomiasis screening of travelers to Corsica, France (1,2). Surprisingly, the authors of both articles lacked evidence to support the diagnosis of schistosomiasis in most of what they referred to as confirmed cases. The diagnostic standard for confirmation of urinary schistosomiasis is identification of eggs by microscopic examination of urine samples (3–5). If this criterion were applied in both reports, only 1 patient of the 7 allegedly confirmed cases would actually be confirmed.

The low sensitivity of microscopy is well known. Therefore, different serologic tests have been developed, including Western blot (WB). In the study based on travelers from Italy (1), the SCHISTO II WB IgG test (LDBIO Diagnostics, Lyon, France) was used. This test, available since 2015, is based on both Schistosoma haematobium and S. mansoni antigens and has not been evaluated by anyone other than the manufacturer. Moreover, the authors did not report any details regarding the molecular weight and number of specific bands observed on the strip.

In the study by authors from the GeoSentinel Surveillance Network (2), both cases that could have been infected after 2013, since exposure occurred only in 2014, and 4 cases which reported bathing in rivers in Corsica other than the Cau River had just 1 weakly positive serologic screening test. Hence, irrespective of the criteria for a confirmed case of schistosomiasis described above, it appears difficult to conclude that confirmation could rely on only 1 positive serologic test, even a WB.

Altogether, these 2 studies identified only 1 patient with parasitological evidence of infection that was attributable to the already known 2013 focus in Cau River. Therefore, these articles do not provide evidence of transmission of schistosomiasis in Corsica after 2013 or outside the Cau River.

References