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impetus to definitely conclude that an increase and subsequent decrease of GM after administration of caspofungin represents treatment failure. In our patient, this was not the case. An increase and decrease in GM during therapy does not necessarily presage the outcome in one way or another. Our point was that one should exercise caution in interpreting the GM serum ratio in patients who receive caspofungin—or any other antifungal, for that matter.

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Illness in Travelers Visiting Friends and Relatives: What Can Be Concluded?

To the Editor—We were interested to read the GeoSentinel report by Leder et al. [1] that focused on an important group of international travelers who, to date, have not been clearly defined in terms of demographic characteristics and travel-related morbidity. We suggest that there are significant issues related to the design, analysis, interpretation, and conclusions of the study that require comment. Although Leder and colleagues acknowledge several limitations in their report, practitioners who are not familiar with the nature of the GeoSentinel program and/or who do not work with migrant travelers may not fully appreciate the significance of these limitations.

First, although the classification of travelers into 3 groups looks appealing, the classifications have been applied retroactively to the data, and the consequences of this are significant. The retrospective cohort nature of the study design limits the interpretation of outcomes to a cohort association and diminishes the generalizability of the conclusions to wider practice outside of the participating GeoSentinel centers.

Second, there is no design evidence that the recategorization of travelers into "immigrant visiting friends and relatives," "traveler visiting friends and relatives," and "tourist," as defined within the report, is either robust or reliably discriminating for travel-related risk or for health outcomes.

Third, the data recruitment allows for the introduction of both patient referral and selection bias. This may create epidemiological associations that may not be representative of travelers outside of the study group. GeoSentinel sites are often academic or tertiary care centers, and are predominantly based in America; thus, they may be biased towards recruiting tourists rather than travelers visiting friends and relatives. Patterns of access to medical service by migrants may differ from those of the host population [2]. Allowable health insurance coverage and issues of willingness to pay for services in the visited nation [3] may influence pretravel and posttravel service use by travelers visiting friends and relatives. Insurance coverage may be linked to the study's observations of early clinical presentation by tourist travelers, compared with the travelers visiting friends and relatives (who have limited insurance) .

Other design considerations include the acquisition of diseases, such as malaria, which are primarily related to the destination rather than the reason for travel. Analysis of travel to regions of West Africa and East and southern Africa would have been more reflective of actual risk than reasons for travel. There is evidence that travelers visiting friends and relatives are overrepresented as travelers [4] to both Asia and sub-Saharan Africa, and the relative high proportion of disease prevalence in the group may be a reflection of greater exposure to and not increased likelihood of disease. The differing pattern of morbidity among the groups of travelers and immigrants visiting friends and relatives may relate to their economic status, access to and use of services, and medical care–seeking behavior, rather than to travel-associated risk.

All of these factors combined are design issues that we believe makes studies like the Leder et al. [1] study difficult to extend

beyond the participating GeoSentinel clinics. Nonetheless, the report by Leder and colleagues and similar studies highlight the importance of defining and determining population-based risk factors in cohorts of travelers. Existing limitations of current data at this time do not allow the associations of outcomes that are demonstrated in the report to be extended to all travelers and immigrants visiting friends and relatives or migrant travelers.

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Reply to Behrens et al.

To the Editor—We appreciate the opportunity to discuss several points addressed by Behrens et al. [1], some of which were already addressed in our original article [2]. GeoSentinel is a network of 33 globally dispersed clinics, mostly at academic or tertiary care centers. We have acknowledged the possibility of referral or selection biases that may limit generalizability of our findings beyond specialized travel and/or tropical medicine clinics.

GeoSentinel data are not predominantly from the US population. Of the 60,000 patients in the entire database, 42% were seen at clinic sites in Asia, 26% in Europe, 20% in the United States, 9% in Canada, and 3% in Australia and New Zealand. For our study [2], 44% of the immigrants visiting friends and relatives were seen at clinic sites in Europe, 30% in Canada, 21% in the United States, and 5% in Australia and New Zealand.

GeoSentinel clinics serve diverse patient populations; some clinics see greater proportions of immigrants, and others see more travelers. At the average US GeoSentinel site, 25% of the patients are immigrants visiting friends and relatives. Eleven percent of patients at European sites and 23% of patients at Canadian sites are immigrants visiting friends and relatives.

The categorization of travelers as "visiting friends and relatives" in itself implies a number of differences, including previous exposure, genetic predisposition, types of exposure during travel, and medical care–seeking patterns. We agree with Behrens et al. [1] that, in most countries, access to and use of medical services may differ between groups of travelers visiting friends and relatives and other travelers. The different patterns of morbidity among the groups of travelers visiting friends and relatives may relate not only to their travel-associated risk, but also to behavioral, cultural, and economic factors.

As noted by Behrens et al. [1], certain diagnoses primarily relate to the region visited, and travelers visiting friends and relatives are overrepresented as travelers to some regions. To correct for this, we presented results by region (tables 2–4), with logistic regressions to adjust for destination and other possible confounders (figure 1) [2]. Insufficient data precluded separation of West from East and southern Africa. As stated in the article, our results do not indicate the rate of incidence of disease or absolute risk of disease, but rather reflect relative morbidity.

Because travelers visiting friends and relatives generally do not seek medical care prior to travel [3], prospective studies do not exist. In our study [2], patient data were collected in a standardized way, with predesignated data fields; thus, the retroactive classification into 3 groups is irrelevant. As stated, some misclassification of immigrants visiting friends and relatives and travelers visiting friends and relatives may have occurred. However, by categorizing travelers and immigrants visiting friends and relatives into subgroups, we have shown significant differences between groups in the relative morbidity for a number of travel related diseases. As with any original approach to an issue, we have not claimed that the groups are robust; our results require validation to determine whether they can be replicated.

A recent exhaustive literature review concluded that "there are no published recommendations and little data on providing care to this population of travelers" [4, p. 2857]. Other recent authoritative reviews have found few primary studies of this population [5, 6]. Our results represent, to our knowledge, the first data focused solely on populations of travelers and immigrants visiting friends and relatives from a global surveillance network and clearly highlight significant issues of morbidity among this population, compared with tourist travelers. Our findings suggest important considerations for additional understanding of migrant populations.

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