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Eosinophilia in Refugees

To the Editor—Refugees are a particularly marginalized and disenfranchised population. Although the rates of infectious disease among this population are excessive, little attention is given to performing research, and little priority is given to publishing results of studies conducted among this population. This disparity has lead to poor information on which to make evidence-based decisions. We would like to applaud Seybolt et al. [1] for their recent article that addressed a frequent scenario and helped to steer the conversation of providing care to this vulnerable population. We would like to add to their conclusions and advocate a more comprehensive approach to the treatment of parasitic diseases in refugees.

In May 1999, the Centers for Disease Control and Prevention recommended that all refugees departing from sub-Saharan Africa receive a single empirical dose of albendazole. In addition, the 15,000 Hmong who recently relocated to the United States from Thailand during 2004–2005 received this treatment. Since that time, the leading pathogen found in stool samples before 1999, Ascaris lumbricoides, has become distinctly uncommon. The second and third most common pathogens, Trichuris trichura and hookworm, have also become less common [2,3]. Although this may seem like a triumph, these parasites account for a minority of illnesses due to helminths. Even without treatment, these parasites have a finite lifespan, and without proper soil conditions, they quickly diminish in number and are eventually lost. In contrast, potential pathogens that are not readily identified on stool examination and that have extended lifespans or autoinfective cycles (e.g., Strongyloides stercoralis, filariae, or trematodes) may have devastating effects even >50 years after migration [4–6]. It is not surprising, with the prevalence of schistosomiasis exceeding 80% in some populations of Africa, that the Centers for Disease Control and Prevention recently described rates of schistosomiasis exceeding 40% in Sudanese refugees, most of whom had resided for prolonged periods in the United States [7–10]. In fact, the same study showed that, when combined with the prevalence of strongyloidiasis, 315 (68%) of 462 Sudanese had evidence of infection with either parasite (203 [44%] had positive test results for schistosomiasis, and 214 [46%] had positive test results for strongyloidiasis) [10]. Although Seybolt et al. [1] focused on refugees with eosinophilia, it should be noted that many refugees with chronic parasitic infections will not have an absolute eosinophilia (eosinophil count >450 cells/μL) with infection (potentially accounting for the predominance of children in their study) [11]. Also, it has been clearly shown that a normal eosinophil count at presentation in a patient with disseminated Strongyloides infection predicts a mortality rate approaching 100% [5]. It also appears that disseminated Strongyloides infection is much more common than has previously been recognized in areas with high refugee populations and where Strongyloides species are not endemic [5,6]. Lastly, because eosinophilia may last for several months after treatment, many refugees may have residual eosinophilia after migration caused by parasitic infections treated before departure with albendazole, making eosinophilia in newly arriving refugees, even when present, very insensitive for predicting the presence of Strongyloides infection.

As Seybolt et al. [1] point out, the only dependable testing for the most pathogenic of these organisms is serological testing. However, commercially available serological tests are relatively expensive, are not well standardized, and are of questionable reliability. Also of concern in this mobile population is the time required for testing. The Centers for Disease Control and Prevention offer serological examination; however, with >50,000 refugees arriving each year from areas of endemicity, routine screening would exceed their capacity. In addition, many refugees do not receive postarrival domestic medical screening in the United States.

Therefore, given the prevalence of infection, the loss to follow-up, the poor screening options, and the duration, complications, and potential life-threatening nature of infection, it would be practical to consider overseas, comprehensive, empirical treatment for S. stercoralis infection and schistosomiasis among populations with known high prevalence rates. After migration, those with persistent eosinophilia should then have a very targeted evaluation recommended to identify other potential causes of eosinophilia (i.e., filariasis). Applying knowledge of the diseases endemic to a refugee’s country of origin should guide the tailoring of recommendations for both predeparture treatment and domestic medical screening.

Acknowledgments


William Stauffer and Patricia Walker
Division of Infectious Diseases and International Medicine, University of Minnesota, Minneapolis, and Regions Hospital/HealthPartners, Center for International Health, St. Paul, Minnesota

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Tenofivir-Associated Kidney Diseases and Interactions between Tenofovir and Other Antiretrovirals

To the Editor—Zimmermann et al. [1] recently described 5 patients with tenofovir-associated acute renal failure and reviewed data on 22 additional patients described in the literature. We have reviewed the charts of all patients who have been treated with tenofovir at our outpatient HIV clinic (G. B. Rossi Hospital, Verona, Italy).

A total of 94 patients (mean age, 37.1 years; range, 27–60 years), 64 of whom were men, were receiving tenofovir for a mean duration of 16 months (range, 4–48 months). Coadministered drugs were lamivudine (62 patients), lopinavir-ritonavir (25), efavirenz (25), didanosine (17), stavudine (9), nevirapine (9), zidovudine (8), atazanavir-ritonavir (6), abacavir (6), nelfinavir (5), tipranavir-ritonavir (3), and amprenavir-ritonavir (2). Thirty-six patients were receiving ritonavir-boosted treatment regimens. Thus far, none of these 94 patients have had tenofovir-related renal failure or kidney disease, including the 3 patients with type 2 diabetes and the 1 patient with type 1 diabetes whose serum creatinine levels were higher than normal (with concomitant proteinuria in 3 patients), before starting to receive this drug.

Our data indicate that, over a reasonable length of time, tenofovir did not cause acute renal failure in any of our patients. This finding is in keeping with the low incidence of tenofovir-related renal abnormalities observed in clinical trials [2–3], retrospective studies [4–6], and in the expanded-access program [7]. Drug discontinuation associated with renal events occurred in <1% of patients during long-term follow-up and among patients enrolled in studies 902 and 907 [2], and it occurred in no patients in study 903 through week 144 of the study [3]. Indeed, the incidence of renal toxicity associated with tenofovir was similar to that associated with stavudine in study 903 and with other antiretroviral agents in retrospective studies [3–6].

Furthermore, the majority of cases of acute renal failure and Fanconi syndrome, which led Gilead to revise, in June 2004, the package insert for tenofovir and to include renal impairment, had identifiable risk factors [8]. Thus, we think that the recommendation by Zimmermann et al. [1] to monitor renal function closely during the first 2 months of therapy should be followed only for patients with identifiable risk factors for kidney disease.

Finally, some of the mechanisms hypothesized by Zimmermann et al. [1] have been ruled out. Indeed, the possibility of ritonavir-related increases in the tenofovir concentration in proximal tubules secondary to decreased urinary secretion has been ruled out by pharmacokinetic data of interaction between tenofovir and lopinavir-ritonavir and atazanavir-ritonavir [9]. Similarly, phosphorylated metabolites of tenofovir appear to inhibit phosphorylation of didanosine by nucleoside phosphorylase by increasing exposure to didanosine [10], rather than through a mechanism of competition between tenofovir and didanosine at proximal renal tubules.

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Massimiliano Lanzafame, Emanuela Lattuada, Francesca Rapagna, Martina Gottardi, and Sandro Vento
Infectious Diseases Unit, G. B. Rossi Hospital, Verona, Italy

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