to a population vulnerable to VPDs in the United States.

Finally, in Mr. Trump's vision of "America first," economic aspects tend to be prioritized, and global challenges such as climate change tend to be neglected. However, Mr. Trump's doubts about climate change [8] must be discussed from a scholarly point of view because if countermeasures to control climate change are not taken, mosquito-borne diseases may be left untreated. As a fact, we should take note that since 2015, 220 cases of locally acquired mosquito-borne Zika infection have been reported in some parts of Florida and Texas [9]. We believe that any policies and orders should be announced after the due deliberation of several aspects including the scientific facts.

Our challenge is to control possible outbreaks of infectious diseases, and Mr. Trump's challenge is to protect his country and the children of the United States from the view of a "globalized world." We believe that not only the guarantee of vaccine service to all children irrespective of their nationality, ethnicity, or race but also addressing climate change honestly will create a stronger wall than any that might be built at a border.

Notes

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Artemether-Lumefantrine Treatment Failure in Nonimmune European Travelers With *Plasmodium falciparum* Malaria: Do We Need to Reconsider Dosing in Patients From Nonendemic Regions?

We read with interest the recent article by Sóden and colleagues [1], which describes 310 imported *Plasmodium falciparum* malaria cases in Sweden treated with oral regimens: 95 of 310 with artemether-lumefantrine (AL), 162 of 310 with mefloquine, 36 of 310 with atovaquone-proguanil, and 17 of 310 with other regimens. Among patients treated with AL, a high rate of late treatment failures was observed: 5.3% (5/95) of patients showed recrudescence of *P. falciparum* 20–28 days after completion of treatment, whereas no late treatment failures were seen in patients treated with other oral regimens. While genotyping did not reveal any evidence of underlying drug resistance, pharmacokinetic data suggest that the observed treatment failures may be attributable to subtherapeutic lumefantrine plasma concentrations [1].

As the area under the curve of plasma lumefantrine concentration vs time is the main determinant for eradication of residual parasites not cleared by artemether, and thus the determinant of clinical efficacy [2–4], this explanation appears plausible.

Sóden and colleagues also provide a review of published reports on AL treatment, which includes the only prospective study on the efficacy of AL including nonimmune European travelers published in 2008 [5]. In this study, 165 nonimmune patients from Europe and nonmalarious regions of Colombia with uncomplicated falciparum malaria were treated with the standard 6-dose AL regimen. We would like to highlight that, although the cited overall failure rate of AL treatment in this study was 3.6% (6/165), the failure rate in the subgroup analysis of European travelers (not shown) was 5.3% (3/57), and thus identical to the rate now reported by Sóden and colleagues in Swedish patients.

Considering that (*i*) the currently used 6-dose regimen of AL was a consequence of the unacceptably high recrudescence rates following the initially recommended 4-dose regimen of AL [6, 7], that (*ii*) nonimmune patients lacking acquired partial immunity have a higher risk of treatment failure compared with patients from endemic regions [3], that (*iii*) at the time of AL registration, almost no data from nonimmune patients were available, that (*iv*) the observed treatment failures with AL are very likely attributable to low lumefantrine plasma levels, and that (*v*) the now reconfirmed failure rate of 5.3% in nonimmune patients challenges the current treatment strategy, reconsideration of the dosing strategy of AL in this patient population is warranted.

To achieve sufficiently high lumefantrine plasma levels over time, either the extension of the current 3-day AL regimen to a 5-day "augmented regimen" [3] or the spreading

of the 6-dose regimen from currently 3 days (0, 8, 24, 36, 48, 60 hours) to 5 days (0, 8, 24, 48, 72, 96 hours) may be discussed [8]. The question of whether a higher cumulative dose of lumefantrine in an augmented regimen may increase the rate of gastrointestinal side effects (primarily vomiting [3]) will be answered once the results of the "AL3vs5" study, comparing the 3-day AL regimen with a 5-day regimen, are published [9].

Note

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