MALARIA EPIDEMIOLOGY AND CONTROL IN RURAL AMAZONIA

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Figure 1. Study children in the Remansinho settlement, Amazonas State, Brazil. Photography by Alessandra Fratus

Malaria remains a major public health concern in Brazil. With 243,000 slide-confirmed infections, this country contributed 52% of the malaria burden in the Americas in 2012. Most transmission in Brazil occurs in open mining enclaves, logging camps and farming settlements across the Amazon Basin. Since the early 1970s, colonization projects have attracted migrant farmers from the malaria-free South and Southeast regions to frontier settlements in densely forested areas of Amazonia. Land clearing for agriculture and logging resulted in an increased abundance of the local malaria vector, the mosquito *Anopheles darlingi*. Not surprisingly, recent frontier settlements constitute malaria hotspots until these communities become more stable, with improved health infrastructure and reduced mobility of settlers. Although the two main human malaria parasites *Plasmodium falciparum* and *P. vivax* are widespread across Amazonia, the latter species accounts for 85% of the malaria cases in the region. The presence of dormant liver stages (hypnozoites) and the early circulation of infectious stages (gametocytes) in peripheral blood render *P. vivax* less responsive than *P. falciparum* to available control strategies based on early diagnosis and treatment of infections. With the long-term goal of providing scientific evidence that can be translated into effective public health interventions for malaria control, over the past 10 years we have carried out population-based prospective cohort studies in frontier settlements in rural Amazonia. We focused on the relative contribution of low-density and asymptomatic infections, which are missed by routine control measures, to ongoing *P. vivax* transmission. Furthermore, we used molecular genotyping to examine how community-level genetic diversity of malaria parasites varies across time and space and to track the spread of new parasite strains associated with outbreaks. The combined analyses of malaria morbidity data and individual and household-level risk factors provided the bases for new strategies for eliminating residual malaria in areas where most infections are asymptomatic and parasite densities are often below the detection.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

Clinical and laboratory surveillance of malaria in the agricultural settlement of Granada, Acre State, revealed year-round transmission of both *P. falciparum* and *P. vivax*, mostly associated with logging and farming. Individuals with the Fya+b- phenotype in the Duffy blood group, a major red cell receptor for *P. vivax*, have a 30-80% reduced risk of clinical vivax in this prospective cohort. Molecular methods were 5.4-fold more sensitive than conventional microscopy for diagnosing infections, especially in asymptomatic parasite carriers. High rates of *P. vivax* recurs after malaria treatment, a finding with major implications for control. Nearly all recurrences involved parasite genotypes not found in the primary infection, revealing a high turnover rate of parasite strains. Since 2010, focusing on malaria transmission during the early stages of frontier settlements, population-based cohort study in Remansinho area, documented a major decline in the prevalence of *P. vivax* infection (from 23.8% to 3.0%) over three years, with vanishing P. falciparum transmission but a *P. vivax* outbreak in October 2012. Molecular genotyping of *P. vivax* isolates revealed a moderate to high genetic diversity, with a large proportion (78.5%) of infections comprising more than one strain. The lowest parasite diversity and the smallest proportion of mixed-strain infections were observed at the time of the outbreak. Risk of both infection and *P. vivax*-related disease in Remansinho decreased with increasing cumulative exposure to malaria, consistent with anti-parasite and anti-disease immunity being acquired. Up to 73.1% of the *P. vivax* infections were missed by microscopy as malaria transmission declined and most (56.6%) of these infections caused no clinical signs or symptoms. Few (17.0%) asymptomatic *P. vivax* infections that were left untreated eventually progressed to clinical disease, becoming detectable by routine malaria surveillance, over 6 weeks of follow-up. Moreover, nearly all *P. vivax* infections that were undetected by microscopy had gametocytes, the parasite's blood stages responsible for malaria transmission to mosquito vectors, detected by molecular methods. These findings indicate that apparently healthy carriers of low-density infections, who are often missed by conventional diagnosis, contribute significantly to ongoing *P. vivax* transmission and further complicate residual malaria elimination in rural Amazonia.

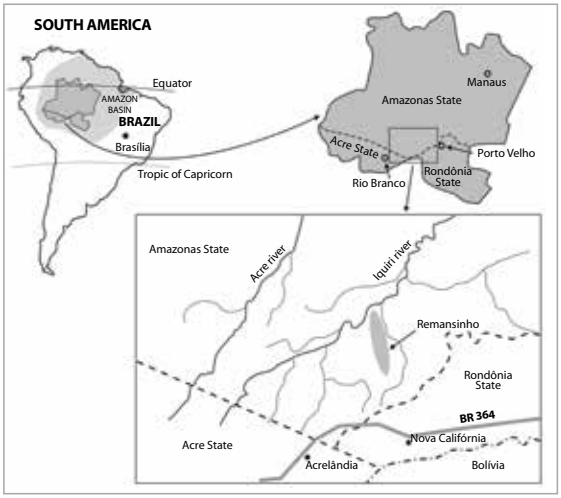

Figure 2. Location of the field site, Remansinho, southern Amazonas State

MAIN PUBLICATIONS

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