Acta Tropica 121 (2012) 315–323

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Prospects for malaria elimination in non-Amazonian regions of Latin America

Sócrates Herrera[a,b,*], Martha Lucia Quiñones[c], Juan Pablo Quintero[a], Vladimir Corredor[c], Douglas O. Fuller[d], Julio Cesar Mateus[e], Jose E. Calzada[f], Juan B. Gutierrez[g], Alejandro Llanos[h], Edison Soto[i], Clara Menendez[j], Yimin Wu[k], Pedro Alonso[j], Gabriel Carrasquilla[l], Mary Galinski[m], John C. Beier[d], Myriam Arévalo-Herrera[a,b]

[a] *Centro de Investigación Científica Caucaseco, Colombia*
[b] *School of Health, Valle State University, Colombia*
[c] *National University, Colombia*
[d] *University of Miami, USA*
[e] *Fundación para la Educación Superior, Colombia*
[f] *Gorgas Memorial Institute of Health, Panama*
[g] *Ohio State University, USA*
[h] *Cayetano Heredia University, Peru*
[i] *The Global Fund to Fight AIDS, Tuberculosis and Malaria,Colombia*
[j] *Barcelona Centre for Internacional Health Research (Hospital Clinic, Universitat de Barcelona), Spain*
[k] *Laboratory of Malaria Immunology and Vaccinology, NIAD/NIH, USA*
[l] *Santa Fe de Bogotá Foundation, Colombia*
[m] *Emory University Atlanta, USA*

ARTICLE INFO

Article history:
Received 22 February 2011
Received in revised form 31 May 2011
Accepted 23 June 2011
Available online 14 July 2011

Keywords:
Malaria
Plasmodium falciparum
Plasmodium vivax
Anopheles mosquitoes
Vector control
Epidemiology
Malaria elimination
Malaria pathogenesis
Non-Amazon regions
Latin America

ABSTRACT

Latin America contributes 1–1.2 million clinical malaria cases to the global malaria burden of about 300 million per year. In 21 malaria endemic countries, the population at risk in this region represents less than 10% of the total population exposed worldwide. Factors such as rapid deforestation, inadequate agricultural practices, climate change, political instability, and both increasing parasite drug resistance and vector resistance to insecticides contribute to malaria transmission. Recently, several malaria endemic countries have experienced a significant reduction in numbers of malaria cases. This is most likely due to actions taken by National Malaria Control Programs (NMCP) with the support from international funding agencies. We describe here the research strategies and activities to be undertaken by the Centro Latino Americano de Investigación en Malaria (CLAIM), a new research center established for the non-Amazonian region of Latin America by the National Institute of Allergy and Infectious Diseases (NIAID). Throughout a network of countries in the region, initially including Colombia, Guatemala, Panama, and Peru, CLAIM will address major gaps in our understanding of changing malaria epidemiology, vector biology and control, and clinical malaria mainly due to *Plasmodium vivax*. In close partnership with NMCPs, CLAIM seeks to conduct research on how and why malaria is decreasing in many countries of the region as a basis for developing and implementing new strategies that will accelerate malaria elimination.

1. Malaria control in non-Amazonian regions of Latin America

Approximately 170 million people, corresponding to almost 60% of the total population of Latin America (LA) and the Caribbean, live in malaria endemic areas where 1–1.2 million clinical malaria cases occur every year (Guerra et al., 2010; WHO, 2009). Sixty percent of these cases are reported from Brazil whereas the remaining 40% of the cases occur in another 20 countries mainly located in the Andean region (PAHO and WHO, 2008; WHO, 2008). *Plasmodium vivax* is the predominant species (~74%) followed by *Plasmodium falciparum* (~26%) and *Plasmodium malariae* (<0.1%) (Guerra et al., 2010; WHO, 2009).

During the Global Malaria Eradication Program (GMEP) from 1955 to 1969, several countries in LA made significant progress toward malaria elimination (Gabaldon, 1983; Gabaldon et al., 1961). Importantly, even highly endemic countries such as Venezuela, Colombia, Peru, and Panama significantly reduced malaria transmission. However, parasite resistance to several

* Corresponding author at: Centro de Investigación Científica Caucaseco, Cali 760042, Colombia. Tel.: +57 2 521 6228; fax: +57 2 557 0449.
E-mail address: sherrera@inmuno.org (S. Herrera).

0001-706X/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.actatropica.2011.06.018

anti-malarial drugs (Corredor et al., 2010; Feachem et al., 2009; WHO, 2005), mosquito resistance to DDT and other insecticides, economical constraints, and unclear malaria control policies significantly limited the progress of this early program (Roberts and Andre, 1994; WHO, 1998).

Since 1969 when the GMEP ended, most countries of the region experienced overall increases in malaria incidence. However, since 2000, substantial decreases in malaria incidence have been observed due to regional policies and efforts to improve malaria surveillance, early case detection, prompt diagnosis and treatment, integrated vector management, and health systems strengthening (WHO, 2009). The initiation of other programs like the "Malaria Control Program in Andean-country Border Regions" (PAMAFRO) sponsored by the Andean Health Organization (ORAS), The Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), and The Amazon Network for the Surveillance of Antimalarial Drug Resistance (RAVREDA) sponsored by the Pan American Health Organization/World Health Organization (PAHO/WHO) have significantly influenced the Annual Parasite Index (API) in this region. Moreover, some of the countries from the Mesoamerican region like El Salvador, Costa Rica, Mexico and Nicaragua have decreased malaria incidence by over 90% through intensive control activities (SM2015, 2010). To date, three countries, Argentina, El Salvador and Mexico, have scaled-up their malaria control strategies and are working toward malaria elimination (WHO, 2006). Significantly, these success stories in malaria control strongly encourage the initiation of strategically focused efforts toward malaria elimination throughout the LA region.

2. Key gaps for effective malaria control/elimination in LA

Although malaria elimination in LA countries appears more feasible than in most other regions of the world (Feachem et al., 2009), moving from control to elimination in low-endemic malaria areas of the region still represents a great challenge. Despite increased funding for malaria control in the region, coverage with preventive measures and access to effective treatments still remain below expected levels in some countries. Major gaps include the availability of suitable diagnostic tests with high sensitivity and specificity for mass use, an adequate understanding of the taxonomy, ecology, and behavior of vector species relative to available tools for vector control, increasing limitations in the availability of effective antimalarials, mapping of the extent and spread of drug resistant parasites, and a limited understanding of *P. vivax* biology and epidemiology (WHO, 2008).

2.1. Vectors of malaria parasite transmission

Nine out of 90 anophelines species described in the region have been incriminated as vectors of primary and secondary importance with regard to malaria parasite transmission (Rubio-Palis and Zimmerman, 1997; Sinka et al., 2010) but there is insufficient information on vector species distribution as well as uncertainties regarding the impact of anthropogenic environmental changes on the dynamics of transmission. The great diversity of *Anopheles* species in LA together with the limited understanding of their taxonomy urgently requires integrated approaches to determine which *Anopheles* species and species complexes are serving as malaria vectors in the region. Moreover, besides limitations in effective tools for vector control, NMCPs are likely to be using under-developed Integrated Vector Management (IVM) strategies (WHO, 2011b). There is only a limited understanding of vector biology, particularly mosquito ecology and behavior, geographic distributions and seasonality of vectors and the dynamics of local malaria parasite transmission, all of which limit the ability of health authorities to select and utilize adequate vector control measures. Appropriate IVM strategies for vector control in the diverse environments of LA must consider local malaria epidemiology and how malaria vector species respond to available tools for vector control.

2.2. Malaria diagnosis and parasite genetic diversity

With malaria, clinical diagnosis is not specific and leads to a high proportion of misdiagnoses, inappropriate use of medicines and exposure to potential drug toxicity, and wastage of economical resources. Although microscopic diagnosis using Giemsa stained thick smears has been the reference method for field malaria diagnosis for ~100 years, it has numerous limitations. These include the lack of personnel with appropriate or adequate training in slide preparation techniques, an overwhelming workload, poor microscope maintenance and the substandard quality of essential laboratory supplies (Wongsrichanalai et al., 2007). Rapid Diagnostic Tests (RDT) have become popular because they are simple to perform, easy to interpret, have high specificity and sensitivity, and do not require electricity or much capital investment. However, although RDTs are sufficiently effective to detect malaria parasites in symptomatic patients seeking medical attention, standardized protocols for Quality Assurance (QA), especially to confirm potentially large numbers of negative results are not yet available. Their usefulness for active case detection programs still needs validation. As an alternative, DNA-PCR techniques are highly sensitive and specific but require further development to be adapted for broad-based field work (Moonen et al., 2010). One of the most serious limitations for malaria control is the difficulty in detecting and treating low-density infections particularly in asymptomatic patients (Coleman et al., 2002a,b). As well, there is a need to define how to approach diagnosis and treatment in those countries moving toward malaria elimination, e.g. El Salvador or Costa Rica where the incidence has decreased by more than 90% (SM2015, 2010).

Another critical issue regarding malaria parasites is the pattern of genetic diversity in parasite populations with low recombination rates and relatively high population differentiation as it occurs in LA. This issue is particularly relevant in the context of parasite drug resistance and the importance of polymorphisms for vaccine development.

Low levels of transmission characterize malaria in LA, and as a consequence, multiplicities of infection are also low, as consequence a low rates of decay of genetic linkage as relatively high indexes of differentiation between parasite populations (Anderson et al., 2000).

These factors constitute a useful epidemiological tool to follow patterns of migration and the dissemination of genotypes of epidemiological relevance (e.g. drug resistance genotypes) in countries where the complex geography creates natural barriers (and a variety of optimal niches for a number of different vector species) that impede the spread of mosquito vectors and contribute to the isolation and genetic differentiation of *Plasmodium* populations (Machado et al., 2004).

An understanding of the population genetics and the nature of *Plasmodium* genetic diversity in LA conditions is key to explain how selective forces, such as immune responses, vaccine trials, and drug administration policies, act upon parasite populations.

2.3. Limitations of the antimalarial drug arsenal

In order to face Malaria Multidrug Resistance (MDR), in 1998 WHO recommended the use of artemisinin based combination therapies (ACTs) (Bosman and Mendis, 2007; WHO, 1998), and since then, countries have been using these antimalarials with the rather common belief that artemisins are not vulnerable to resistance. In 2009, *P. falciparum* strains resistant to artemisinin were