Disasters like the 2010 earthquake in Haiti placed evacuees at high risk for infection, mostly by mosquito bites during November–February. On January 12, 2010, a 7.0 magnitude earthquake struck Haiti and left many homeless.

On January 2010, a 7.0 magnitude earthquake struck Haiti and left many homeless. The main malaria vector in Haiti, Anopheles albimanus, which is mostly active during November–February, can transmit malaria among travelers returning from Haiti to Canada and France by using genotypic and phenotypic methods.

The main study developed by Myriam Gharbi, Dylan R. Pillai, Rachel Lau, Véronique Hubert, Krishna Khairnar, Alexandre Existe, Eric Kendjo, Sabina Dahlström, Philippe J. Guérin, Jacques Le Bras, and members of the French National Reference Center for Imported Malaria Study, investigated chloroquine sensitivity to Plasmodium falciparum in travelers returning to France and Canada from Haiti during a 23-year period. Two of 19 isolates obtained after the 2010 earthquake showed mixed pfcr76K+T genotype and high 50% inhibitory concentration. Physicians treating malaria acquired in Haiti should be aware of possible chloroquine resistance.

We investigated chloroquine sensitivity to Plasmodium falciparum in travelers returning to France and Canada from Haiti during a 23-year period. Two of 19 isolates obtained after the 2010 earthquake showed mixed pfcr76K+T genotype and high 50% inhibitory concentration. Physicians treating malaria acquired in Haiti should be aware of possible chloroquine resistance.

In Haiti (2011 population ≈9.7 million), malaria is endemic. Approximately 30,000 malaria infections are confirmed annually, among ≈200,000 estimated malaria cases, mainly Plasmodium falciparum infections (1). On January 12, 2010, a 7.0 magnitude earthquake struck Haiti near Port-au-Prince, leaving much of the population homeless.

The main malaria vector in Haiti, Anopheles albimanus mosquitoes, which mostly bite outdoors during November–January, placed evacuees at high risk for infection (2,3).

Author affiliations: Université Paris-Descartes, Paris, France (M. Gharbi, J. Le Bras); École des Hautes Études en Santé Publique, Rennes, France (M. Gharbi, P.J. Guérin); Worldwide Antimalarial Resistance Network, Paris (M. Gharbi, S. Dahlström, J. Le Bras); Public Health Ontario, Toronto, Ontario, Canada (D.R. Pillai, R. Lau, K. Khairnar); University of Calgary, Calgary, Alberta, Canada (D.R. Pillai); Hospital Bichat-Claude Bernard, Paris (V. Hubert, J. Le Bras); Laboratoire National de Santé Publique, Port-au-Prince, Haiti (A. Existe); Centre National de Référence Paludisme, Paris (V. Hubert, E. Kendjo, J. La Bras); Hospital Pitité-Salpêtrière, Paris (E. Kendjo); Université Pierre et Marie-Curie-Paris VI, Paris (E. Kendjo); Worldwide Antimalarial Resistance Network, Oxford, UK (P.J. Guérin); Centre for Tropical Medicine, Oxford (P.J. Guérin); University of Oxford, Oxford, UK (P.J. Guérin); and Institut National de la Santé et de la Recherche Médicale, Paris (P.J. Guérin).

DOI: http://dx.doi.org/10.3201/eid1808.111779
Chloroquine-Resistant Malaria

The number of confirmed malaria cases imported from Haiti doubled during 2009–2010 (Figure 1). Approximately half of the travelers were in Haiti 2–4 weeks before the earthquake and >1 month after the earthquake. The main purpose of travel, visiting friends and relatives, decreased from 59% before to 44% after the earthquake. More than 75% of travelers did not take prophylactic medication. The proportion of severe malaria increased from 3% to 11% after January 2010 (Table 1).

Before the earthquake, all 29 isolates had the wild-type Pfcrt K76 allele according to analysis by PCR–restriction fragment-length polymorphism. The mean 50% inhibitory concentration (IC_{50}) of chloroquine for the 24 isolates tested ex vivo by the 3H-hypoxanthine uptake inhibition method was 27 nM (95% CI 23–31). These results are consistent with those of an unpublished study conducted in Haiti during 2007 to monitor chloroquine resistance (Jean-François Vely, unpub. data). In that study, Haiti’s National Malaria Program, in collaboration with the National Malaria Reference Centre in France, found the chloroquine-sensitive genotype in 146 P. falciparum–positive samples in 6 departments (Artibonite, Centre, Grand’Anse, Nord, Nord-Ouest, Ouest) (Figure 2) (12). After the earthquake, 2 (11%) of 19 isolates analyzed by pyrosequencing and PCR–restriction fragment-length polymorphism showed a mixed Pfcrt76K+T genotype. The ratios of K to T genotypes before and after in vitro adaptation were 0.75:0.25 and 0.23:0.77, respectively, for patient 1, and 0.58:0.42 and 0.25:0.75, respectively, for patient 2. The Pfcrt72–76 haplotype was CVMNK before adaptation and CVIET after adaptation for both patients by sequencing. Resistance was confirmed by in vitro methods after culture adaptation. Both isolates had high chloroquine IC_{50} (506 nM and 708 nM, respectively) and high chloroquine IC_{50} isolate:Pf3D7 (chloroquine susceptible clone) ratio (20 and 27, respectively) (Table 2).

Patient 1, a 58-year-old woman, was in Haiti during October 2009–January 2010; she returned after the earthquake to Canada, where she sought care for malaise, fever, diarrhea, and vomiting. She reported no previous malaria and no other travel during the previous 2 years. For patient 2, a 16-year-old girl, malaria was diagnosed in Canada on February 25, 2010, after 3 days of fever. She had traveled to Haiti in the past 2 months before malaria was diagnosed and did not report any other recent travel.

Conclusions

The number of P. falciparum–infected travelers returning from Haiti has increased since January 2010, ...
probably because of the higher number of aid workers and visitors and increased *P. falciparum* malaria transmission. Data suggest that the earthquake and ensuing hurricane and floods created the necessary conditions—inadequate shelters, population movement, and still water—to increase the incidence of malaria and possibly spread the recently identified chloroquine-resistant strains of *P. falciparum* (10). In France and Canada, laboratory surveillance for malaria found that 2 travelers from Haiti carried chloroquine-resistant strains. In vitro culture might have selected resistant strains not observed initially by ex vivo methods. After carefully interviewing these patients about their travels, we found no evidence to cause doubt that they had acquired malaria in Haiti. Alternatively, the resistant strains could have come to Haiti after the earthquake through human activity, as occurred in the cholera outbreak (13).

The origin of the chloroquine-resistant strains identified in Haiti is uncertain. The *Pfcrt* CVIET haplotype is common in Southeast Asia and sub-Saharan Africa and was found in the 2006–2007 study in Haiti (10).

Regardless of origin, containing the spread of chloroquine-resistant parasites is crucial. Malaria elimination is a goal in Haiti, and it has been strengthened after recent events, but the effects of malaria and many other factors affect the achievability of this goal (14). Control measures, possibly mirroring those used to contain artemisinin resistance in Southeast Asia, should be concentrated in Haiti to prevent resistance spreading to the rest of Hispaniola (15). However, lack of consensus on the use of molecular and in vitro data for policy change will hamper decision making. Neither the chloroquine-resistant *Pfcr76T* genotype nor the elevated chloroquine IC$_{50}$ perfectly predicts treatment failure because of confounding factors like acquired immunity.

Our study has several limitations. Returning travelers are not a representative sample of the Haitian population, and the sample of isolates was limited. The origin of the resistant strains is not defined. Also, the precise location of infection is not reported. Nevertheless, travelers are useful sentinels of emerging resistance in areas where little information is available, providing surveillance data in real time with standardized methods. This nonimmune population also facilitates detection of resistant isolates.

Our data highlight the need to implement a therapeutic efficacy surveillance study for assessing in vivo chloroquine sensitivity, which is essential for providing information for rational control strategies and guiding prophylaxis recommendations in Haiti. In addition, physicians treating malaria acquired in Haiti should be aware of the possibility of chloroquine-resistant infections. Patients with persistent fever despite treatment and infected travelers reporting adherence to chloroquine prophylaxis should be treated with alternate antimalarial drug therapy.

Members of the French National Reference Center for Imported Malaria Study who contributed to this article: Amhed Aboubacar, Patrice Agnamey, Adela Angoulvant, Didier Basset, Ghania Belkadi, Anne-Pauline Bellanger, Dieudonné Bemba, Françoise Benoît-Vical, Antoine Berry, Olivier Bouchaud, Patrice Bourée, Bernadette Buret, Enrique Casalino, Frédérique Conquere de Monbrison, Martin Danis, Pascal Delaunay, Anne Delaval, Michel Develoux, Jean Dunand, Remy Durand, Odile Eloy, Madeleine Fontrouge, Françoise Gayandrieu, Nadine Godineau, Céline Gourmel, Samia Hamane, Sandrine Houze, Houria Ichou, Anne-Sophie Le Guern, Anne Marfaing Koka, Denis Mechali, Bruno Megarbane, Olivier Patey, Isabelle Poilane, Denis Pons, Bruno Pradines, Christophe Rapp, Marie-Catherine Receveur, Claudine Sarfati, Jean-Yves Siriez, Marc Thellier, and Michel Thibault.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Before earthquake, n = 49</th>
<th>After earthquake, n = 30</th>
</tr>
</thead>
<tbody>
<tr>
<td>In vitro analysis</td>
<td>n = 24</td>
<td>n = 10</td>
</tr>
<tr>
<td>IC$_{50}$ for chloroquine, nmol/L (mean 95% CI)</td>
<td>27 (23–31)</td>
<td>35 (12–105)*</td>
</tr>
<tr>
<td>No. isolates resistant†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>No</td>
<td>24</td>
<td>8</td>
</tr>
<tr>
<td>Molecular marker analysis, no. (%) isolates</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PICRT K76</td>
<td>29</td>
<td>17 (89.5)</td>
</tr>
<tr>
<td>PICRT K76+76T</td>
<td>0</td>
<td>2 (10.5)</td>
</tr>
</tbody>
</table>

*The 2 resistant isolates are included with an IC$_{50}$ of 506 nmol/L and 708 nmol/L. IC$_{50}$, 50% inhibitory concentration.
†A threshold of IC$_{50}$ = 100 nmol/L is applied to determine resistant isolates (consensus between the laboratories in France and Canada) and in vitro susceptibility (IC$_{50}$) for the isolates from patients returning from Haiti.
Acknowledgments

We thank Valerie Tate for critical reading of the manuscript and Vely Jean-François (deceased) for his contribution to the study.

This study was supported in part by a grant for doctoral studies to M.G. from the Doctoral Network of the École des Hautes Études en Santé Publique, Rennes, France.

Dr Gharbi holds a doctoral degree in pharmacy and is pursuing a PhD degree in epidemiology at the Université Pierre et Marie-Curie, Paris. Her primary research interest is the epidemiology of antimalarial drug resistance.

References


Address for correspondence: Myriam Gharbi, UMR216, Faculté de Pharmacie Paris Descartes, 4 Ave l’Observatoire, 75270 Paris, Cedex 06, France; email: m.gharbi@yahoo.fr