Migrants have recently been presented as a major risk group for imported malaria in European countries. We would like to emphasize that some European tropical medicine centers can serve as surveillance sites for malaria (as well as other infectious diseases) for the countries from which a dominant migrant community originates. In addition, different approaches regarding pre-travel medical advice in specific migrant populations can be studied. Thus, we have in Europe the opportunity to participate in the fight against malaria in certain tropical countries. This is the case with our unit in Marseilles, where there is a significant community of migrants from the Comoros Islands.

Background

The Comoros archipelago (43°11' to 45°19' E, 11°20' to 13°00' S) includes four islands located in the Mozambic Canal of the Indian Ocean, 300 km north of Madagascar. Three islands, including Grande Comore (Ngazidja), Mohéli (Mwali), and Anjouan (Ndziouani), form the Federal Islamic Republic (FIR) of the Comoros, independent since 1975. On the other hand, Mayotte Island remains a French territory (Department de Mayotte). The total area (four islands) covers less than 2,300 km² and has a population of some 726,000 inhabitants. Although much effort has been put into malaria control during recent years, malaria still constitutes a major public health problem in the FIR of Comoros, where it represents 15% to 30% of the hospitalization cases and 15% to 20% of the registered deaths in the pediatric services. Plasmodium falciparum remains predominant, as it is responsible for 95% of the malaria cases.

There have been two waves of immigration from Comoros to France, the first before 1970 (students, sailors, cooks), and the second in the 1970s, particularly after 1975, following the independence of the three islands. In Marseilles, the population originating from Comoros has been estimated at 50,000 to 70,000 inhabitants. The precise number is difficult to assess. Within this community, people of French nationality (including people from Mayotte, people who chose to become French nationals after the independence of the three islands, and French-born offspring of migrants) are not registered as “Comorians” anymore. The second part of this community includes visiting foreigners, whose actual number as well as duration of stay are difficult to evaluate. Regarding the size of the Comorian population in Marseilles, our city can be considered the second “Comorian capital”.

Furthermore, it has been estimated that 4,000 to 5,000 people originating from Comoros and living in France travel back to Comoros every year, primarily to visit their families. Such a population of first- or second-generation migrants is particularly susceptible to malaria, as stated by Schlagenhauf and Loutan.

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Malaria Imported From Comoros to Marseilles

Our unit in Marseilles, which is located near Comorian neighborhoods, is the reference center for tropical diseases. During the past 4 years, the proportion of people originating from Comoros among patients hospitalized for imported malaria in our unit was as follows: 74/132 (56.1%) in 1999, 51/89 (57.3%) in 2000, 49/76 (64.5%) in 2001, and 60/90 (66.7%) in 2002.5,6 (Patella F, unpublished data). The decrease in the total number of people hospitalized for imported malaria after 1999 is explained by the fact that our unit moved from one hospital to another site, although this was located near the previous one. However, the recruitment of people from Comoros remains unique. We constitute the main source of this community in the French databank surveillance of imported diseases,6 and Comoros dramatically appeared in the databank of the European network on Surveillance of Imported Infectious Diseases (TropNetEurope) after we joined the network several years ago.7

Among the 221 patients hospitalized in our unit for acute imported malaria in 1999–2000, several characteristics at baseline were recorded (age, sex, weight, country visited, symptoms and clinical signs). We compared two groups of patients with *falciparum* malaria, Comorians (50% of the patients, all having acquired malaria in Comoros) and non-Comorian patients (including French travelers and people originating from the African mainland, all having acquired malaria in tropical settings other than Comoros). We found no significant differences regarding sex ratio and mean age. However, the following differences emerged: (1) the Comorian group complied with malaria chemoprophylaxis less frequently than non-Comorians (16/47 = 34% vs. 17/25 = 68%; p = .006); (2) the Comorians consulted family doctors less frequently than non-Comorians before presenting to emergency units with malaria (43/90 = 48% vs. 41/64 = 64%; p = .046); (3) the Comorians more frequently reported headache and vomiting than non-Comorians (67/90 = 74% vs. 35/64 = 55%, and 36/90 = 40% vs. 14/64 = 22%, respectively; p = .018); and (4) Comorians developed severe malaria less frequently than non-Comorians (1/112 = 0.9% vs. 11/85 = 13%; p < .0005).

**Discussion**

We derive two conclusions from Marseille’s “Comorian” experience. The first one concerns advice for travelers and malaria chemoprophylaxis in this specific population. Currently, mefloquine is primarily recommended in France for travelers to Comoros. Alternatives include doxycycline and atovaquone–proguanil. Among our patients hospitalized for fever after returning from Comoros, 85% do not take any chemoprophylaxis against malaria and 11% take inadequate regimens (Patella F, personal communication). Reasons include lack of information, as well as the belief in continued immunity against malaria because of birth in Comoros, and the relatively high cost of the drugs recommended for chemoprophylaxis, particularly mefloquine and atovaquone–proguanil. An improved approach to educate the Comorian population regarding malaria risks and prophylaxis needs to be explored. It should involve people with good relationships with the Comorian residents in Marseilles, and include people within the Comorian community such as those at schools, health centers, and other community-based programs.

The second point concerns *falciparum* drug resistance, one of the major problems in the control of malaria. Although some in vivo tests can be conducted in Comoros, in vitro testing of *Plasmodium* susceptibility is difficult there, due to the lack of laboratory facilities, expertise and funding. The closest reference center is located at the Institut Pasteur in Madagascar, where strains from Comoros are sometimes studied.9 Thus, obtaining *Plasmodium* strains from Comoros to be tested in Marseilles, where all these facilities are available, represents a unique opportunity to establish surveillance of *falciparum* drug resistance.

Between 1996 and 2002, 41 *Plasmodium falciparum* strains obtained from patients returning from Comoros were cultured and tested at the National Reference Laboratory for Malaria Chemosusceptibility in Marseilles. Of the 22 strains obtained in 2000–2002, 59% were shown to be resistant in vitro to chloroquine (IC$_{50}$ > 100 nM), 50% were resistant to pyrimethamine (IC$_{50}$ > 2,000 nM), 44% were resistant to cycloguani (IC$_{50}$ > 500 nM), 19% were resistant to atovaquone (IC$_{50}$ > 6 nM) and 7% were resistant to mefloquine (IC$_{50}$ > 30 nM) (Pradines B, personal communication). All these strains were, however, susceptible to quinine and halofantrine. Moreover, 117 strains were tested by molecular methods for the presence of mutations that have been associated in recent years with resistance to antimalarial drugs. Details of these results will be reported elsewhere. For example, 44% of the strains tested by molecular methods were shown to have the Ser108Asn mutation in the dihydrofolate reductase gene, the basic mutation associated with antifolate resistance.

Such information is valuable in establishing policies for chemoprophylaxis for travelers. It is also important in establishing therapeutic recommendations. Indeed, travelers returning to France with *falciparum* malaria are usually treated with quinine (7-day regimen) or mefloquine,10 and more recently with a 3-day quinine–clindamycin15 or atovaquone–proguanil regimen.11 The high rate of mutation in the dihydrofolate reductase gene (associated with resistance to antifolates such as proguanil), and the appearance of resistance to atovaquone, raise doubts...
regarding the efficiency of atovaquone–proguanil in the treatment of \textit{falciparum} malaria acquired in the Comoros. As a consequence, the use of atovaquone–proguanil is currently under surveillance in our unit. Additionally, the FIR currently still uses chloroquine as the first-line regimen to treat acute uncomplicated \textit{falciparum} malaria for the native population, whereas sulfadoxine–pyrimethamine is the second-line drug. As demonstrated in Marseilles, both chloroquine and pyrimethamine in vitro resistance levels are high in \textit{P. falciparum} parasites acquired in Comoros, and malaria treatment failure is of concern. The results of in vitro studies are essential for the planning of appropriate antimalarial policy, including the choice of first- and second-line treatment, in endemic areas. Thus these studies have important public health implications. Finally, we are attempting to improve our ability to culture the malaria strains obtained from our patients. This is sometimes difficult because of prior self-treatment, low parasitemia ($<0.01\%$) or delay in inoculation. Finally, all mutations recently associated with antimalarial drug resistance are now being tested in our laboratory.

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\textbf{References}


Marseilles: a surveillance site for malaria from the Comoros islands

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