have been in contact with TOSV and show asymptomatic or mild, unidentified symptoms, as it is the case for many other arbovirus infections (10). Such findings raise concerns about the risks of virus transmission to virus-naïve persons by blood transfusions and organ transplants.

Further investigation is needed to better assess how widespread TOSV is in populations. For example, a donor–recipient investigation might confirm virus transmission by blood transfusion, and studies related to the behavior of sandfly vectors, virus biology, and mammalian reservoir hosts could help define populations at higher risk for exposure.

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Quinine-Resistant Malaria in Traveler Returning from French Guiana, 2010

To the Editor:

Resistance of Plasmodium falciparum to antimalarial drugs is one of the most worrying problems in tropical medicine. For P. falciparum malaria acquired in French Guiana, the combination of quinine and doxycycline is one of the first-line recommended treatments (1). Since 1996, only 2 treatment failures with quinine have been reported from that country (2). An elevated 50% inhibitory concentration (IC50), classified as in vitro quinine resistance, was reported for 17% of 32 P. falciparum isolates obtained during 1983–1987 in French Guiana (3). Throughout 1994–2005, isolates were susceptible to quinine, with a mean IC50 <200 nmol/L (4).

We report quinine treatment failure in a 35-year-old man who was infected during a 3-month stay in Saül, a rural area of French Guiana. The patient did not use antivectorial or antimalarial prophylaxis. The patient sought treatment with fever 4 days after returning to France on June 22, 2010 (day 0), and a diagnosis of P. falciparum malaria was made on the basis of results of a rapid diagnostic test performed by a private medical laboratory. The man, who weighed 58 kg, was treated as an outpatient with 500 mg of quinine to be taken orally 3×/d for 7 days; he did not receive doxycycline. He was admitted to the Laveran Military Teaching Hospital in Marseille on July 15 (day 24 and first day of recrudescence) for uncomplicated malaria with a P. falciparum parasitemia level of 4%. He was given artemether, 80 mg/d, by intramuscular injection for 3 days. Blood samples taken on day 27 (third day of recrudescence) and day
52 (4 weeks of recrudescence) were negative for *P. falciparum*.

In vitro testing of drug susceptibility was performed by the standard 42-hour ³H-hypoxanthine uptake inhibition method (5). We assessed susceptibility to 11 antimalarial drugs on the fresh isolate and after culture adaptation (Table). The laboratory-adapted strain 3D7, tested 3× on the same batch of plates, was used as reference. The strain isolated from the blood sample on day 24 (first day of the recrudescence) showed reduced susceptibility to quinine (1,019 nmol/L), chloroquine (427 nmol/L), and monodesethylamodiaquine (157 nmol/L). The isolate was susceptible to all other antimalarial drugs tested. We assessed gene polymorphisms of *pfcr* (*P. falciparum* chloroquine resistance transporter), *pfmdr1* (*P. falciparum* multidrug resistance 1 protein), and *pfnhe-1* (*P. falciparum* Na+/H+ exporter 1); the copy number of *pfmdr1* involved in quinoline resistance; and gene polymorphisms of *dhfr* (dihydrofolate reductase, involved in proguanil or pyrimethamine resistance), *dhps* (dihydropteroate synthetase, involved in sulfadoxine resistance), and *cytB* (cytochrome B, involved in atovaquone resistance) (6).

The *pfnhe* ms4760 microsatellite showed a profile 3, with 1 repeat of DNNND and 2 repeats of DDDNHNDNHN. Studies of the *pfnhe-1* polymorphism of worldwide culture-adapted isolates showed that increased numbers of DNNND were associated with decreased quinine susceptibility (7). Association of 2 repeats of DNNND and a high quinine IC₅₀ value was found in a case of clinical failure of quinine in a traveler returning from Senegal (8).

Reinfection was excluded because the patient had stayed in mainland France since his return. The patient reported that he took the quinine as instructed. We report here a clinical and parasitologic failure of quinine treatment associated with high IC₅₀, but not linked with the ms4760 *pfnhe-1* profile involved with quinine in vitro reduced susceptibility. A hypothesis that may explain our data is that unlike previous studies (7), in which the less susceptible strains originated from Asia, this isolate came from South America. The profile associated with quinine resistance for chloroquine resistance and *pfcr* genotypes could be different in the 3 malaria-endemic continents. There are no data on ms4760 *pfnhe-1* of *P. falciparum* isolates from South America. In another recent study (9), a multivariate analysis performed on 83 clinical isolates from Madagascar and 13 African countries did not confirm this association between quinine susceptibility and *pfnhe-1* microsatellite polymorphisms.

The *pfcrt* gene had a point mutation on codon 76 (76T) and *pfmdr1* on codons 184F, 1034C, 1042D, and 1246Y. These data are in agreement with those from previous studies that showed the mutation 76T in the *pfcrt* gene led to decreased susceptibility to chloroquine, amodiaquine, and quinine. The isolate had only 1 copy of *pfmdr1*. The data on mutations and copy number of *pfmdr1* are consistent with data in Brazil (10). Nevertheless, the lack of gene amplification and specific point mutations in *pfmdr1* were not associated with decreased in vitro susceptibility of quinine. *dhfr* and *dhps* genes had a 5-mutation haplotype, 511 C59 108N 1164-S436 437G 540E 581G A613, which suggested in vitro resistance to proguanil, pyrimethamine, and sulfadoxine. This case confirms the need to always add doxycycline to quinine for treatment of *P. falciparum* malaria acquired in French Guiana as well as other parts of South America.

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<table>
<thead>
<tr>
<th>Antimalarial drug</th>
<th>Fresh isolate IC₅₀, nmol/L</th>
<th>Cultured isolate IC₅₀, nmol/L, mean ± SD†</th>
<th>3D7 clone IC₅₀, nmol/L, mean ± SD</th>
<th>I₅₀, isolate:3D7</th>
<th>Resistance cutoff value, nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quinine</td>
<td>1,019</td>
<td>1,087 ± 145</td>
<td>171 ± 26</td>
<td>6.0:6.4</td>
<td>&gt;800</td>
</tr>
<tr>
<td>Chloroquine</td>
<td>427</td>
<td>492 ± 39</td>
<td>13.9 ± 2.2</td>
<td>30.7:35.4</td>
<td>&gt;100</td>
</tr>
<tr>
<td>Monodesethylamodiaquine</td>
<td>157</td>
<td>157 ± 27</td>
<td>16.3 ± 3.5</td>
<td>9.6:9.6</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Mefloquine</td>
<td>16.4</td>
<td>14.9 ± 2.2</td>
<td>53.4 ± 5.2</td>
<td>0.31:0.28</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Lumefantrine</td>
<td>8.9</td>
<td>9.0 ± 3.0</td>
<td>46.0 ± 6.0</td>
<td>0.19:0.20</td>
<td>&gt;150</td>
</tr>
<tr>
<td>Pyronaridine</td>
<td>45.2</td>
<td>37.8 ± 8.4</td>
<td>18.3 ± 1.6</td>
<td>2.5:2.1</td>
<td>ND</td>
</tr>
<tr>
<td>Piperaquine</td>
<td>80.4</td>
<td>99.5 ± 11.7</td>
<td>56.3 ± 5.4</td>
<td>1.4:1.8</td>
<td>ND</td>
</tr>
<tr>
<td>Dihydoartemisinin</td>
<td>2.18</td>
<td>2.46 ± 0.28</td>
<td>2.58 ± 0.13</td>
<td>0.84:0.95</td>
<td>&gt;10.5</td>
</tr>
<tr>
<td>Artesunate</td>
<td>1.86</td>
<td>1.68 ± 0.28</td>
<td>2.27 ± 1.15</td>
<td>0.82:0.74</td>
<td>&gt;10.5</td>
</tr>
<tr>
<td>Atovaquone</td>
<td>6.5</td>
<td>5.2 ± 0.8</td>
<td>4.2 ± 0.7</td>
<td>1.5:1.2</td>
<td>&gt;490</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>11,600</td>
<td>12,600 ± 1,700</td>
<td>12,600 ± 1,000</td>
<td>0.92:1.0</td>
<td>&gt;35,000</td>
</tr>
</tbody>
</table>

*Isolate was obtained from a man who returned to France from French Guiana in June 2010. IC₅₀, 50% inhibitory concentration; ND, not determined. †Mean IC₅₀ and standard deviation of 3 different tests on the isolate after culture adaptation.
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Kyasanur Forest Disease Virus Alkhurma Subtype in Ticks, Najran Province, Saudi Arabia

To the Editor: The lineage of Kyasanur Forest disease virus (KFDV) found in the Kingdom of Saudi Arabia is commonly referred to as Alkhurma hemorrhagic fever virus (AHFV). This virus was first isolated from a specimen collected in 1994 from a butcher living in Makkah Province, who was hospitalized for a hemorrhagic fever from which he died (1). The virus was assigned to the genus Flavivirus on the basis of reactivity with genus-specific monoclonal antibodies and sequencing of a fragment of the nonstructural 5 (NS5) gene, which showed >89% identity with KFDV. Ten other cases were confirmed among patients who had leukopenia, thrombocytopenia, and elevated liver enzymes. Observations of patients in the original study or in a subsequent analysis (2) suggested that Alkhurma hemorrhagic fever (AHF) disease was associated with contact with blood from infected animals, bites from infected ticks, or the drinking of raw milk. However, the exact mode of transmission to humans has still not been fully elucidated. More recently, AHFV RNA was detected in a single pool of sand tamps (Ornithodoros savignyi, soft ticks), collected in western Saudi Arabia (3), which suggests a link with these ticks.

To analyze the virus association with arthropods further, we collected and identified ticks and mosquitoes in Najran Province, southern Saudi Arabia, during May and June 2009 from different sites close to where human AHF cases had been recently confirmed (4,5). Camel ticks (Hyalomma dromedarii) (130 adults) were collected while they fed on camels, and O. savignyi sand tamps (243 adults) were collected from the ground in camel resting places (except 1 collected while feeding on a camel). Mosquitoes were collected by using light traps (203 Culex decens females) or as larvae that were then raised in the laboratory (9 Culiseta sp. females). Ticks and mosquitoes were stored at room temperature and killed by overnight freezing the day before shipping to the Centers for Disease Control and Prevention (Atlanta, GA, USA). All arthropods were processed in the BioSafety Level 4 laboratory by injecting Vero E6 cells and by intracerebrally inoculating suckling mice with ground pools of either 5 ticks or 10 mosquitoes. All the tick material was used for the tested pools. Isolates of AHFV were obtained from 1 of 13 pools of H. dromedarii ticks and 1 of 6 pools of O. savignyi sand tamps, both from Al Mishaalyya...