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Imported Hepatitis E Virus, Central African Republic, 2011

To the Editor: Hepatitis E virus (HEV) is endemic to India (*1,2*) and Central African Republic (*3,4*), although different strains circulate in the countries. In May 2011, a case of jaundice and fever in an expatriate Indian worker (a 33-year-old man) was reported to Institut Pasteur de Bangui, Bangui, Central African Republic. HEV RNA and IgM were detected in serum samples from the patient, and liver enzyme levels were raised (alanine aminotransferase 840 U/L, reference value 11–66 U/L). Symptoms lasted for ≈10 days and resolved without specific treatment. The patient was working and living at a construction site in Central African Republic with 51 other men (22–62 years of age) from India.

We investigated this case to determine whether it was linked to an outbreak and whether disease-control measures were needed. The protocol for surveillance and investigation was approved by the national ethical and scientific committee in Central African Republic.

Background information and blood and stool samples were obtained from the patient's coworkers. The Bioelisa HEV IgM 3.0 kit (Biokit, Barcelona, Spain), which has sensitivity >98%, was used to test serum samples for HEV IgM; real-time reverse transcription PCR (rRT-PCR) was used to test serum and stool samples for viral RNA (*5*). Test results provided evidence of early HEV infection. Liver enzymes (aspartate aminotransferase and alanine aminotransferase) were measured in serum by using an ABX Pentra 400 benchtop analyzer (Horiba Medical, Montpellier, France).

For genetic analysis of HEV strains from viremic study participants, we performed nested RT-PCR on serum and stool samples to amplify a 348-bp portion of the open reading frame 2 region (*6*). We directly sequenced the purified amplicons and compared the resulting sequences with HEV sequences in GenBank (*7*) and those from autochthonous HEV cases from 2008–2011. ClustalW2 (www.ebi.ac.uk/Tools/msa/clustalw2/) was used to align sequences. MEGA5 (*8*) was used to construct a phylogenetic tree (300-nt sequences) by the neighbor-joining method. The genotypes and subtypes were identified as described (*7*).

The 52 men arrived in Central African Republic in several groups during July 2010–June 2011. During May–July 2011, a total of 40 (77%) men had a febrile illness; 9 illnesses were accompanied by digestive signs or symptoms, such as nausea and vomiting (Technical Appendix Table, wwwnc.cdc.gov/EID/article/12-0670-Techapp1.pdf). Only the patient whose case was reported was jaundice. Early HEV infection was biologically confirmed for 11 (21%) men, including the -patient whose case was reported; 8 of the 11 men had IgM only, 1 was HEV positive according to rRT-PCR and IgM negative, and 2 were HEV positive according to rRT-PCR and IgM positive. The 2 other men with viremia were asymptomatic, but liver enzyme levels were elevated in 1 of them.

Illnesses in infected and noninfected men did not differ, and, except for the notified case, we cannot say with certainty that the illnesses were caused by HEV. We found IgG against HEV in 14 (34%) uninfected men, which is close to the prevalence for the general population in India (*2*).

HEV subtype 1a isolates from the notified case-patient (serum-derived isolate) and a co-worker (stool-derived isolate) were sequenced (GenBank accession nos. JN863908 and JQ074213, respectively) and found to be 100% similar and to share 97%– 99% similarity with other HEV strains in India and Nepal (Technical Appendix Figure). The sequences obtained from persons with autochthonous HEV (GenBank accession nos. JN863909, JN863910, and JQ740782) clustered with HEV subtype 1e and type 2 strains and were closely related to strains from Africa and Mexico (93% and 82% similarity, respectively). Similarity between strains was not as high for the strain from the notified case-patient and those from persons with autochthonous infection (87% similarity with the subtype 1e strain and 77% similarity with the type 2 strain).

IgM titers typically rise after the incubation period, which is >3 weeks for HEV (*9*). Thus, for the purpose of this study, we assumed that men who

were positive for IgM against HEV or who had positive rRT-PCR results <3 weeks after their arrival in Central African Republic were probably infected while in India (Table, study participants 2–4 and 9). The notified case-patient and study participants 1, 5, 7, 8, and 10 had positive IgM or rRT-PCR results 4–20 weeks after arrival (Table) and, thus, could have become infected in India or Central African Republic. Study participant 6 was IgM positive >7 months after arriving in Central African Republic; thus, he was infected locally. Housing conditions for the workers were conducive to waterborne transmission of HEV, so it is likely that study participant 6 was infected with the imported strain. However, this participant was not viremic, and we cannot eliminate the possibility of autochthonous infection.

During the past few decades, concern that communicable diseases are emerging or re-emerging because of population mobility has focused mainly on mobility within industrialized countries. However, because of humanitarian and economic reasons, migration within low-income regions is also increasing. Resource-limited countries have weak infrastructures; thus, the consequences of imported outbreaks may be more serious in such countries. Our findings further demonstrate the need to improve cooperation among countries in terms of health policy, surveillance, and control, particularly in resource-limited countries. Such countries should immediately implement the International Health Regulations (2005) (10).

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Table. Chronology of events and clinical test results for 11 immigrants from India participating in a study of imported hepatitis E virus, Central African Republic, 2011*

Participant, region of origin	Arrived in Central African Republic	Symptomatic period, 2011	Biological specimen collected	Test result				
				IgM	rRT-PCR blood	rRT-PCR stool	AST, U/L†	ALT, U/L‡
1, Orissa	2011 Apr 29	NS	Mid Jun	+	+	+	852	791
2, Orissa	2011 Jun 4	NS	Mid Jun	–	+	–	22	14
3, Orissa	2011 Jun 4	Late Jun	Mid Jun	+	–	–	26	12
4, Orissa	2011 Jun 4	NS	Mid Jun	+	–	–	25	23
5, West Bengal	2011 Apr 5	Late Jun	Mid Jun	+	–	–	31	23
6, West Bengal	2010 Oct 10	Early Jul	Mid Jun	+	–	–	9	7
7, Orissa	2011 Apr 29	Late May	Mid Jun	+	–	–	23	18
8, Karnatanka	2011 Feb 23	Early May	Mid Jun	+	–	–	16	7
9, Orissa	2011 Jun 4	Early Jul	Mid Jun	+	–	–	19	12
10, West Bengal	2011 Apr 5	Early Jul	Mid Jun	+	–	–	24	23
NC, Orissa	2011 Apr 29	Early Jun	Early Jun	+	+	NA	2,100	840

*rRT-PCR, real-time reverse transcription PCR ; AST, aspartate aminotransferase; ALT, alanine aminotransferase; NS, not symptomatic; NC, participant whose case was notified ; NA, not available.
†Reference value 5–34 U/L.
‡Reference value 11–66 U/L.

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Clustered Cases of Rickettsia sibirica mongolitimonae Infection, France

To the Editor: *Rickettsia sibirica mongolitimonae,* a member of the tick-borne spotted fever group (SFG) of rickettsia, was first isolated from *Hyalomma asiaticum* ticks in China (*1*). The first human case was described in France in 1996, and 7 new cases were described in 2005 (*1*). This rickettsiosis was named lymphangitis-associated rickettsiosis because lymphangitis was observed in 50% of the patients (*1*). Only 17 cases have been reported, for which 7 patients had lymphangitis, and 13 had inoculation eschars, including 2 patients with 2 eschars (*1,2*). We report a cluster of cases of *R. sibirica mongolitimonae* infection.

Patient 1, a 73-year-old man in France, had fever, rash, lymphadenopathies, and an axillary inoculation eschar in February 2011. A diagnosis of lymphangitis-associated rickettsiosis was suspected because of the season (most cases occur in spring in France) and clinical manifestations.

The patient was confined to bed for several weeks after surgical placement of a knee prosthesis when his disease occurred; the domestic cat was suspected to have introduced ticks into the home.

In April, his wife (67 years of age) (patient 2) became febrile, had popliteal lymphadenopathies associated with lymphangitis, and had an eschar on the leg from which a swab specimen was obtained. Patient 3 was their neighbor; he had the same symptoms in March 2011 but samples were not collected from him.

None of patients reported tick bites, but they were in regular contact with animals, including a cat, a dog, horses, and birds. Both patients who lived with the cat reported that it would return home with ticks. Infections in these patients were successfully treated with doxycycline.

An immunofluorescence assay for antibodies against SFG antigens showed IgG/IgM titers of 128/0 for patient 1 and 64/16 for patient 2 (*3*). DNA was extracted from the skin swab specimen of patient 2 by using the QIAamp Mini Kit (QIAGEN, Hilden, Germany). A fragment of the citrate synthase gene of *Rickettsia* spp. was amplified by PCR and sequenced. The sequence show 99.7% homology with that of the same gene sequence of *R. sibirica mongolitimonae* in GenBank (accession no. DQ423370) (*4*).

Ticks were collected from the property of the 2 patients: from the garden by flagging vegetation (*3*), from animals, and near the cat litter (Table). SFG rickettsiae were detected by specific quantitative PCR. Species identification was confirmed by specific quantitative PCR for *R. massiliae* and sequencing of outer membrane protein A gene for others species (*5*). A negative control (sterile water) and positive control (DNA from *R. montanensis* or *R. massiliae*) were included in each PCR.

Ticks were morphologically identified as adult *Rhipicephalus sanguineus*. Molecular identification of these ticks harboring rickettsiae was performed by amplification of the 12S rRNA gene. DNA from *R. massiliae* was found in 3 ticks collected from the dog and near the cat litter morphologically identified as *Rh. sanguineus*. This DNA showed 98% homology with the sequence in GenBank (accession no. AY559843). *R. sibirica mongolitimonae* with 99.8% homology for the outer membrane protein gene sequence in GenBank (accession no. DQ097082) was isolated from 1 tick collected from the cat. This tick was identified as *Rh. pusillus* and showed 99.7% homology with the sequence in GenBank (accession no. FJ536547). *R. massiliae* was cultured from an *Rh. sanguineus* tick, and *R. sibirica mongolitimonae* was cultured from an *Rh. pusillus* tick.

A cluster of 1 documented case and 2 probable cases of lymphangitis-associated rickettsiosis in southern France was linked to a cat and *Rh. pusillus* ticks. Infection with *R. massiliae* for the 2 probable case-patients was unlikely because clinical findings

Table. Ticks collected from property of 2 patients infected with *Rickettsia sibirica mongolitimonae*, France, 2011*

Location of tick collection	No. ticks collected	Tick species identification†	No. ticks (*Rickettsia* species)	
			Harboring rickettsial DNA	From which rickettsiae were cultured
Garden	2	ND	0	0
Dog	21	*Rhipicephalus sanguineus*	2 (*R. massiliae*)	0
Cat litter	7	ND	1 (*R. massiliae*)	1 (*R. massiliae*)
Cat	9	*Rh. pusillus*	1 (*R. sibirica mongolitimonae*)	1 (*R. sibirica mongolitimonae*)
Scrub land	5	ND	0	0

*ND, not done.
†Based on 12S rRNA gene. All adult ticks were morphologically identified as *Rh. sanguineus*.