never carried to the site where they were housed or taken out for grazing. Thus, the only way for the infant patient to be infected would be environmental exposure. Since the infant had not been carried to the animal sites, the pathogen must have been transmitted to the household by the clothes or skin of the father or grandfather, who had been shepherding the infected animals. Subsequently, the baby became infected either by inhaling infected aerosolized particles or by direct transmission of the pathogen through minor skin abrasions (which were specifically looked for on admission but were not seen) or mucosal surfaces.

This case suggests that *B. melitensis* may even affect persons who are not directly exposed to infected animals, through direct contact with contaminated persons or the environment. In this context, brucellosis can be considered as not simply a household disease but as a disease of the house.

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**Hepatitis E Virus Genotype 1, Cuba**

To the Editor: Hepatitis E virus (HEV) causes acute viral hepatitis, which in rare cases leads to fulminant hepatitis with high death rates, especially among women in their third trimester of pregnancy (*I*). Sporadic infections and epidemics have been reported from all parts of the world, especially Asia, Africa, and Latin America. Although indigenous hepatitis E has rarely been observed in industrialized countries, higher than expected anti-HEV prevalence has been detected in these areas (*I*). In the Caribbean region, many countries including Cuba, Haiti, Guatemala, and Honduras have reported hepatitis E (2,3), but the viruses have not been characterized.

The transmission of HEV is primarily fecal–oral, through contaminated drinking water; limited zoonotic transmission has also been reported. Despite only 1 serotype, 4 major genotypes of HEV have been reported (*I*). Genotype 1 is mainly responsible for sporadic infections and large outbreaks in Asia and Africa. Genotype 2 was first found in Mexico and later on the African continent. Genotypes 3 and 4 have been reported from the United States, Europe, China, Japan, and Taiwan; this group also includes the related swine HEV (*I*).

We report the phylogenetic analysis of 11 HEV isolates from 2 outbreaks and sporadic cases in Havana, Cuba. The first outbreak occurred in 1999 in a factory; 20 persons were affected (12 women, 8 men; median age 45 years, range 22–53 years). The second outbreak was in 2005 in a suburb of Havana and involved 26 persons (15 women, 11 men; median age 24 years, range 17–45 years). We also analyzed HEV in 12 sporadic clinical cases obtained from the Cuban national surveillance program for viral hepatitis. Most patients reported asthenia, epigastric pain, nausea, and vomiting. None had any history of international travel, contact with persons traveling from disease-endemic areas, or consumption of exotic foods. Serologic screening showed all patients to be negative for immunoglobulin (Ig) M against hepatitis A and hepatitis C viruses. One patient had positive results for hepatitis B surface antigen but negative results for anti-hepatitis B core antigen IgM and hepatitis B virus DNA. All patients were positive for anti-HEV IgM (Genelab Diagnostics, Singapore) according to the manufacturer’s criteria. A total of 22 serum samples (outbreak 1, n = 9; outbreak 2, n = 7; sporadic cases, n = 6) were tested for HEV RNA; only 2 (both from sporadic cases) were positive. A total of 31 serum samples were also tested for anti-HEV IgG (Genelab Diagnostics), of which 22 were positive...
(outbreak 1, n = 7/10; outbreak 2, n = 10/13; sporadic cases, n = 5/8).

A total of 44 stool samples were collected 2–4 weeks after onset of symptoms and stored at –70°C until use. Fecal samples were screened for HEV open reading frame (ORF) 2 by using reverse transcription (RT)–PCR. For genotyping, nested RT-PCR was then performed for the ORF1 RdRp region on 18 samples that were positive for ORF2. Of the 12 PCR products obtained, 11 fragments were cloned into pGEMT Easy Vector (Promega, Madison, WI, USA). At least 3 positive clones for each sample were sequenced, and the consensus sequence was used for phylogenetic analysis. The GenBank accession numbers of ORF1 for the HEV outbreak cases from Cuba are CUB10-1999 (EU165504), CUB11-1999 (EU165502), CUB13-1999 (EU1655019), CUB19-1999 (EU165500), CUB24-1999 (EU165499), CUB68-2005 (EU165496), and CUB71-2005 (EU165495). For the sporadic cases they are CUB9-2005 (EU165503), CUB1803-2005 (EU165494), CUB2-2005 (EF493155), and CUB27-2005 (EU165498). Additionally, nested RT-PCR was conducted with ORF2-specific primer pairs for 2 HEV isolates, 1 each from outbreak and sporadic cases, and sequences were obtained. The accession numbers for ORF2 are outbreak CUB10D-1999 (EU284749) and sporadic CUB2D-2005 (EU284748).

Phylogenetic analysis of ORF1 nucleotide sequences showed that HEV isolates from Cuba clustered in genotype 1 with high bootstrap values (Figure, panel A). The same genotype was detected in an outbreak of hepatitis E in UN peacekeepers deployed from Bangladesh to Haiti (3). Although the outbreak was adequately contained, anti-HEV immunoglobulin was subsequently detected in 3% of civilians in Haiti (3). Nucleotide identity between isolates from Cuba and other HEV strains from genotype 1 ranged from 91.7% to 99%. The strains from Cuba were closely related to the isolates from India and shared 97.8%–99% homology with Yam-67. Absolute ORF1 nucleotide differences (p-distances; MEGA2 software, www.megasoftware.net) of isolates from Cuba ranged from 0% to 1.6%, demonstrating a high degree of relatedness. The ORF2 analysis supported our ORF1 findings because the CUB2D-2005 and CUB10D-1999 sequences also clustered with genotype 1 (Figure, panel B). Both strains from Cuba shared 96.1% nucleotide homology with a prototype strain from Burma (Bur82) and were related to the strains from India (Hyderabad and Yam-67), sharing 97.4%–99% homology. Absolute ORF2 nucleotide differences ranged from 0.8% to 1.9%. This value for ORF1 ranged from 0.05% to 0.08% for the same isolates from Cuba (CUB2-2005 and CUB10-1999).

HEV shows a global presence. The genotype distribution, although dominant in a given geographic area, is not limited to that area. For example, genotype 2, first identified on the American continent in Mexico (8), was later found in Namibia and Nigeria on the African continent (9,10). We report indigenous HEV genotype 1 strains in the Americas.

![Figure](image_url)
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Ciprofloxacin Resistance in Neisseria meningitidis, France

To the Editor: Infections with Neisseria meningitidis may occur as outbreaks or epidemics. Consequently, chemoprophylaxis for contacts is generally recommended. Ciprofloxacin is frequently used in adults in a convenient 1-dose regimen (1). Resistance to this antimicrobial drug in N. meningitidis is rare (MIC > 0.06 mg/L) and has been reported only in sporadic cases in Greece, France, Australia, Spain, Argentina and Hong Kong Special Administrative Region, People’s Republic of China (2–5). However, recent reports have described ciprofloxacin-resistant (Cip-R) serogroup A meningococci from 2 outbreaks in Delhi, India, (6) and a cluster of 3 serogroup B meningococci in the United States (7). This information is of concern because of the high epidemic potential of serogroup A isolates, lack of vaccine against serogroup B meningococci, and possible horizontal Cip-R gene transfer to other meningococcal isolates.

Experimental work was conducted in the Neisseria Unit of the Institut Pasteur in Paris. We screened all clinical N. meningitidis isolates received at the French National Reference Center for Meningococci in Paris since 1999 for ciprofloxacin resistance. Of these isolates, 4,900 were from France and 246 were from African countries (Burkina Faso, Cameroon, Central African Republic, Côte d’Ivoire, Madagascar, Niger, Rwanda, Senegal, and Tunisia). Only 3 isolates tested were resistant to ciprofloxacin (MICs = 0.19 mg/L), and all were isolated from cases of invasive disease in France.

Two serogroup A, serotype 4, serosubtype P1.9, Cip-R isolates belonged to different sequence types (STs), ST-7 (Cip-R1) and ST-4789 (Cip-R2), although they belonged to the same clonal complex (ST-5/subgroup III). Cip-R1, which showed decreased susceptibility to penicillin, was isolated in 2004 from the blood of a 7-year-old girl. This isolate was most likely imported from Africa. Cip-R2 was isolated from the cerebrospinal fluid of a 77-year-old man who had arrived in France from India in 2006. The ST of this isolate (ST-4789) is the same as the ST of isolates from an outbreak in Bangladesh and similar to isolates from an outbreak in India (6; http://neisseria.org/nm/typing/mlstdb). Cip-R3 (serogroup W-135, nontypeable, subtype P1.5), which was isolated from blood and cerebrospinal fluid of a 77-year-old woman who had arrived from France in 2006, belonged to a new ST (ST-6361). Current ciprofloxacin resistance has not been documented among invasive W-135 meningococcal isolates since 2 W-135 resistant meningococci were isolated from sputum samples of elderly patients in Spain (3).