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Hepatitis E Virus Infection in Solid Organ Transplant Recipients, France.

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were almost identical to those of the Japanese broad tapeworm available in the GenBank database (sequence similarities of 99% [GenBank accession no. KY000483] and 100% [KY000484], respectively), thus providing unequivocal support that this plerocercoid was a larva of the *D. nihonkaiense* tapeworm reported from North America.

This report provides additional evidence that salmon from the Pacific coast of North America may represent a source of human infection. Because Pacific salmon are frequently exported unfrozen, on ice, plerocercoids may survive transport and cause human infections in areas where they are not endemic, such as China, Europe, New Zealand, and middle and eastern United States (1). It is probable that most diphyllbothriosis cases originally attributed to *D. latum* may have been caused by *D. nihonkaiense* tapeworms. For more effective control of this human foodborne parasite, detection of the sources of human infection (i.e., host associations), and critical revision of the current knowledge of the distribution and transmission patterns of individual human-infecting tapeworms are needed.

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References

1. Kuchta R, Scholz T, Brabec J, Narduzzi-Wicht B. *Diphyllbothrium*, *Diplogonoporus* and *Spirometra*. In: Xiao L, Ryan U, Feng F, editors. *Biology of Foodborne Parasites Section III. Important Foodborne Helminths*. Boca Raton (FL): CRC Press; 2015. p. 299–326.
2. Yamane Y, Kamo H, Bylund G, Wikgren B. *Diphyllbothrium nihonkaiense* sp. nov. (Cestoda: Diphyllbothriidae): revised identification of Japanese broad tapeworm. *Shimane Journal of Medical Science*. 1986;10:29–48.
3. Choi S, Cho J, Jung B-K, Kim D-G, Jeon SJ, Jeon H-K, et al. *Diphyllbothrium nihonkaiense*: wide egg size variation in 32 molecularly confirmed adult specimens from Korea. *Parasitol Res*. 2015;114:2129–34. <http://dx.doi.org/10.1007/s00436-015-4401-7>
4. Arizono N, Shedko M, Yamada M, Uchikawa R, Tegoshi T, Takeda K, et al. Mitochondrial DNA divergence in populations of the tapeworm *Diphyllbothrium nihonkaiense* and its phylogenetic relationship with *Diphyllbothrium klebanovskii*. *Parasitol Int*. 2009;58:22–8. <http://dx.doi.org/10.1016/j.parint.2008.09.001>
5. Muratov IV. A new type of diphyllbothriosis foci in the Far East [in Russian]. *Med Parazitol (Mosk)*. 1992;61:25–7.
6. Gorman-Kadoshnikov PB, Chizhova TP, Yakovleva TA. A new type of diphyllbothriid plerocercoid from chum salmon from Kamchatka [in Russian]. *Med Parazitol (Mosk)*. 1970;39:237–9.
7. Dovgalev AS, Valovaya MA, Piskunova YA, Romanenko NA, Khobakova VI, Artamoshin AS. The morphology of human diphyllbothriosis agent in the Far East [in Russian]. *Med Parazitol (Mosk)*. 1991;60:42–6.
8. Bryan HM, Darimont CT, Hill JE, Paquet PC, Thompson RC, Wagner B, et al. Seasonal and biogeographical patterns of gastrointestinal parasites in large carnivores: wolves in a coastal archipelago. *Parasitology*. 2012;139:781–90. <http://dx.doi.org/10.1017/S0031182011002319>
9. Catalano S, Lejeune M, Tizzani P, Verocai GG, Schwantje H, Nelson C, et al. Helminths of grizzly bears (*Ursus arctos*) and American black bears (*Ursus americanus*) in Alberta and British Columbia, Canada. *Can J Zool*. 2015;93:765–72. <http://dx.doi.org/10.1139/cjz-2015-0063>
10. Fang FC, Billman ZP, Wallis CK, Abbott AN, Olson JC, Dhanireddy S, et al. Human *Diphyllbothrium nihonkaiense* infection in Washington State. *J Clin Microbiol*. 2015;53:1355–7. <http://dx.doi.org/10.1128/JCM.00065-15>

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Hepatitis E Virus Infection in Solid Organ Transplant Recipients, France

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The rate of transfusion-transmitted hepatitis E virus (HEV) in transplant recipients is unknown. We identified 60 HEV-positive solid organ transplant patients and retrospectively assessed their blood transfusions for HEV. Seven of 60 patients received transfusions; 3 received HEV-positive blood products. Transfusion is not the major route of infection in this population.

Hepatitis E virus (HEV; family *Hepeviridae*, genus *Orthohepevirus*) is a single-stranded, positive-sense RNA virus of ≈ 7.2 kb. At least 4 genotypes are responsible for hepatitis E in humans (HEV-1–4). HEV-1 and HEV-2 infect only humans, while HEV-3 and HEV-4 have animal reservoirs (1). In developed countries, the main source of HEV transmission is the consumption of raw or undercooked, infected meat or direct contact with infected animals. Cases of bloodborne transmission have also been reported (1–3).

Transfusion-transmitted infections in solid organ transplant (SOT) patients remains a major concern; the frequency at which these infections occur is unknown (4). SOT patients receiving transfusions are at risk of contracting HEV because systematic screening for the virus is rare. For SOT patients exposed to HEV, infection can become chronic, with rapidly progressing liver disease (1). Because of the high incidence of HEV infection in the Midi-Pyrénées area (1), SOT patients are regularly screened for HEV RNA, and diagnosis of HEV infection is made at the time of alanine aminotransferase elevation.

We investigated retrospectively the extent to which transfusion-transmitted HEV infections occurred in a cohort of 60 SOT patients infected with HEV from January 1, 2009, through June 30, 2014. We found that 7 (11.7%) of these SOT patients were potentially infected through transfused blood products because they were given transfusions in the 6 months preceding the diagnosis (online Technical Appendix Table 1, <https://wwwnc.cdc.gov/EID/article/23/2/16-1094-Techapp1.pdf>); the remaining 53 HEV-positive patients were infected by other modes. The median HEV RNA concentration in recipient blood was 5.4 log copies/mL (range 3.6–6.8 log copies/mL) or 5.2 log IU/mL (range 3.4–6.6 log IU/mL). The median interval between transfusion and diagnosis was 4 months (range 0.2–5.0 months). HEV infections developed in 4 patients (R1, R3, R4, and R5) 6 months after transplantation. Transmission of HEV by the graft was excluded in these patients by examining the samples from the organ donors at the time of donation. None of them tested positive for HEV RNA.

We collected the 231 blood samples corresponding to the 7 patients' donors (stored by the French Blood Agency) and tested them individually for HEV RNA and HEV IgM/IgG (online Technical Appendix). Of these samples, 7 (3.0%) tested positive for HEV RNA (online Technical Appendix Table 2). This analysis revealed that 3 patients (recipients R1, R2, and R3) received ≥ 1 blood components derived from the 7 HEV RNA-positive donations; 4 patients were not given viremic donations.

The median HEV RNA dose given to the recipients was 5.1 log copies (range 3.8–8.4 log copies) or 4.9 log IU (range 3.6–8.2 log IU). Recipient R1 received blood components from 1 viremic donor (D1), while R2 and R3 received blood

components from 3 HEV RNA-positive donors (D2.1–D2.3 and D3.1–D3.3, respectively). Phylogenetic analyses of the 348-nt partial sequences of the open reading frame (ORF) 2 region (online Technical Appendix) showed that R1/D1 and R3/D3.1 sequences clustered together (Figure); nucleotides were $>99.0\%$ identical in both cases, confirming transfusion-transmitted HEV infection. Phylogenetic analysis of R2/D2.3 showed they clustered together but had a lower sequence identity (84.2%), suggesting transmission could have been mediated by another mechanism.

Another study conducted from January 2004 through June 2009 in France found that the risk factors associated with HEV transmission in SOT patients were eating pork meat, game, and mussels (5). Thus, the risk for transfusion-transmitted HEV infection is lower than the risk for acquiring an HEV infection from other sources in the environment in this population. Our study supports these results; we identified viremic donors as the source of infection in 2 (or possibly 3) of 60 HEV-positive SOT patients using phylogenetic analyses.

In France, HEV-positive samples were found in 1/2,218 blood donations, with HEV RNA concentrations of <60 to 29,796 IU/mL (6). In the Netherlands, 1/2,671 donations was viremic, with HEV RNA concentrations from <25 to 470,000 IU/mL (7). Published data indicate that the minimum infectious dose in donations is 7,056 IU (3.85 log IU) (8). A recent study found that donations associated with HEV-transmission had higher HEV RNA concentrations than did those that were not associated with HEV transmission (9). In our study, the 3 blood donations implicated in HEV transmission had HEV RNA doses >5.7 log copies (i.e., 5.5 log IU). Another parameter that must be considered is the presence of HEV antibodies in the donor or in the recipient, although the concentration needed to protect against an HEV infection is still unclear.

We conclude that, although transfusion-transmitted HEV infection can occur in SOT patients, blood transfusion is not the main source of transmission in these patients in France. Optimal policies for screening blood donations for HEV must be defined according to epidemiologic data.

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The authors have no conflicts of interest to declare.

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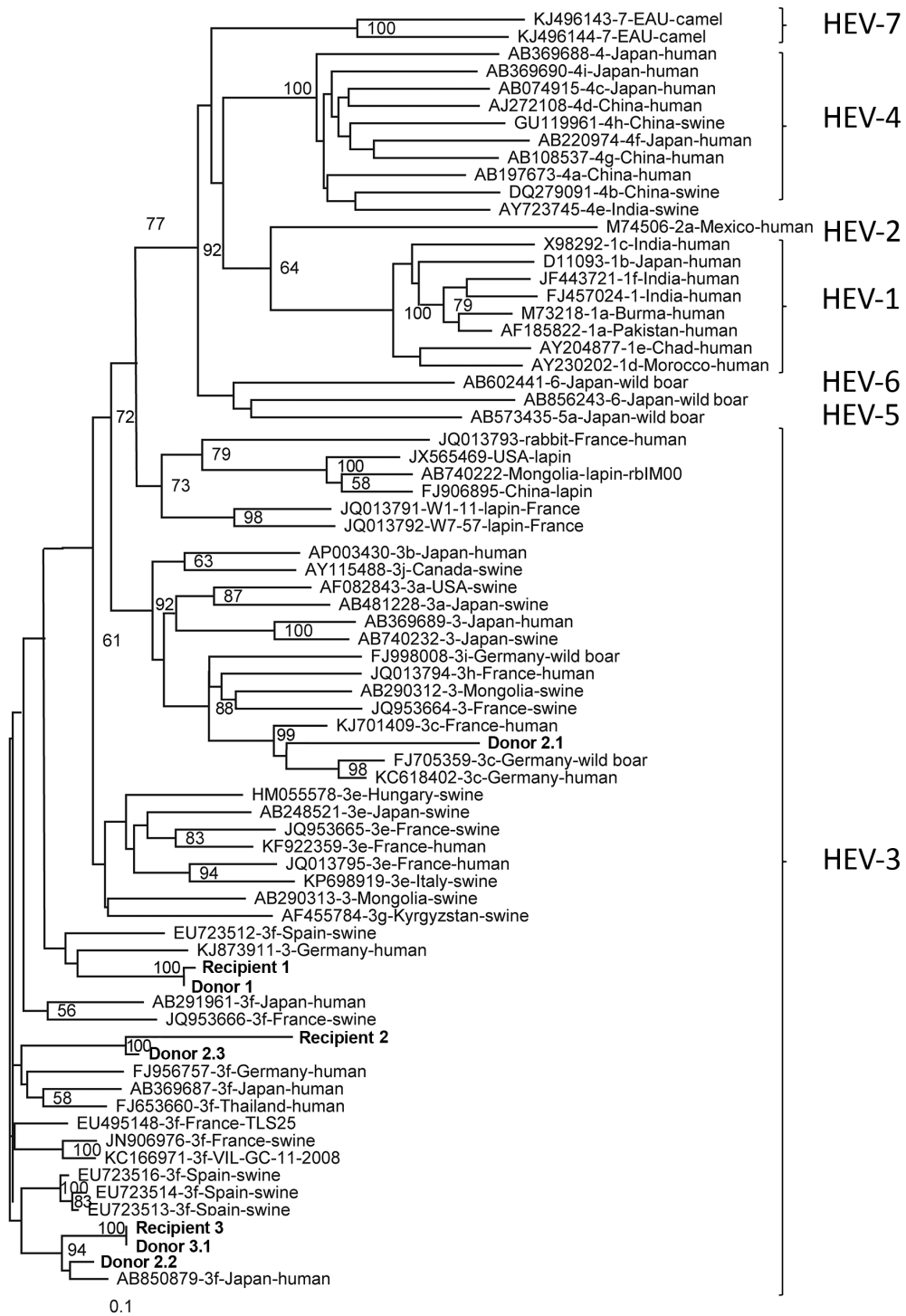


Figure. Phylogenetic tree of hepatitis E virus (HEV) isolates from 3 HEV-positive blood donors and 3 solid organ transplant recipients (shown in bold), France, compared with reference isolates. The tree was constructed by using partial open reading frame 2 sequences (348 nt). HEV genotypes are indicated at right. A confirmed case of transfusion-transmitted HEV infection requires evidence of infection in the recipient and donor and that the nucleotide sequences of these isolates be identical. The isolates from France were deposited in GenBank under accession nos. KX452928–KX452935; accession numbers, sources, and location of isolation for other isolates are indicated. Scale bar indicates nucleotide substitutions per site.

References

1. Kamar N, Dalton HR, Abravanel F, Izopet J. Hepatitis E virus infection. *Clin Microbiol Rev*. 2014;27:116–38. <http://dx.doi.org/10.1128/CMR.00057-13>
2. Boxall E, Herborn A, Kochethu G, Pratt G, Adams D, Ijaz S, et al. Transfusion-transmitted hepatitis E in a ‘nonhyperendemic’ country. *Transfus Med*. 2006;16:79–83. <http://dx.doi.org/10.1111/j.1365-3148.2006.00652.x>
3. Mahajan R, Collier MG, Kamili S, Drobeniuc J, Cuevas-Mota J, Garfein RS, et al. Hepatitis E virus among persons who inject drugs, San Diego, California, USA, 2009–2010. *Emerg Infect Dis*. 2013;19:1664–6. <http://dx.doi.org/10.3201/eid1910.130630>
4. Mezocho AK, Henry R, Blumberg EA, Kotton CN. Transfusion-transmitted infections in solid organ transplantation. *Am J Transplant*. 2015;15:547–54. <http://dx.doi.org/10.1111/ajt.13006>
5. Legrand-Abravanel F, Kamar N, Sandres-Saune K, Garrouste C, Dubois M, Mansuy JM, et al. Characteristics of autochthonous hepatitis E virus infection in solid-organ transplant recipients in France. *J Infect Dis*. 2010;202:835–44. <http://dx.doi.org/10.1086/655899>
6. Gallian P, Lhomme S, Piquet Y, Sauné K, Abravanel F, Assal A, et al. Hepatitis E virus infections in blood donors, France *Emerg Infect Dis*. 2014;20:1914–7. <http://dx.doi.org/10.3201/eid2011.140516>
7. Slot E, Hogema BM, Riezebos-Brilman A, Kok TM, Molier M, Zaaijer HL. Silent hepatitis E virus infection in Dutch blood donors, 2011 to 2012. *Euro Surveill*. 2013;18:20550. <http://dx.doi.org/10.2807/1560-7917.ES2013.18.31.20550>
8. Huzly D, Umhau M, Bettinger D, Cathomen T, Emmerich F, Hasselblatt P, et al. Transfusion-transmitted hepatitis E in Germany, 2013. *Euro Surveill*. 2014;19:20812. <http://dx.doi.org/10.2807/1560-7917.ES2014.19.21.20812>
9. Hewitt PE, Ijaz S, Brailsford SR, Brett R, Dicks S, Haywood B, et al. Hepatitis E virus in blood components: a prevalence and transmission study in southeast England. *Lancet*. 2014;384:1766–73. [http://dx.doi.org/10.1016/S0140-6736\(14\)61034-5](http://dx.doi.org/10.1016/S0140-6736(14)61034-5)

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Emergence of *bla*_{NDM-7}–Producing *Enterobacteriaceae* in Gabon, 2016

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Reports of carbapenemase-producing *Enterobacteriaceae* in Africa remain rare and assess mostly *bla*_{OXA-48}–producing isolates from Mediterranean countries and South Africa. We identified *bla*_{NDM-7}–producing *Enterobacteriaceae* in Gabon in 2016. The isolates contained *bla*_{NDM-7} *IncX3* plasmids that were unusual and similar to the one described in a colistin-resistant *Klebsiella pneumoniae* SZ04 isolate from China.

Carbapenems are used as last-line antimicrobial drugs for treating infections caused by multidrug-resistant gram-negative bacilli. Their effectiveness is challenged by the emergence of carbapenemase-producing *Enterobacteriaceae* (CPE). A new type of β -lactamase, *bla*_{NDM?} was reported from a patient in Sweden in 2007 (1). Since then, *bla*_{NDM} CPE have been identified worldwide and described as endemic to the Indian subcontinent and the Balkans (2). In countries to which they are nonendemic, CPE are reported mainly from patients with a history of hospitalization in a CPE-endemic area and, more rarely, in patients without history of travel (3). Reports on CPE in Africa are scarce, likely because monitoring of antimicrobial resistance remains uncommon. *bla*_{OXA-48} and *bla*_{NDM-1} CPE have been reported from the Maghreb area, Nigeria, Kenya, and South Africa, and single cases of *bla*_{NDM-4} and *bla*_{NDM-5} *Escherichia coli* have been reported in Cameroon, Algeria, and Uganda (2,4,5).

In January 2016, we conducted a point-prevalence study in all patients at the military general hospital of Libreville, Gabon. We collected demographic and clinical data and screened patients by rectal swabbing with Amies medium transport swabs (Copan Italia SPA, Brescia, Italy). The swabs were placed in 0.5 mL sterile water; 0.1 mL of the resulting suspension was streaked onto a selective agar plate provided for the identification of bacteria resistant to third-generation cephalosporins (CHRO-Magar, Paris, France). The plates were incubated for 48 h at 35°C. We used matrix-assisted laser desorption/ionization time-of-flight mass spectrometry technology (Bruker, Bremen, Germany) to confirm each isolate thought to be *Enterobacteriaceae*.

We performed antimicrobial drug susceptibility testing by the agar disk diffusion method (<http://www.eucast.org/>). Isolates resistant to second- and third-generation cephalosporins were investigated for MIC of ertapenem using Etest (bioMérieux, Marcy-L’Étoile, France) and for carbapenemase production by the CarbaNP test (bioMérieux). For molecular characterization, we performed Sanger sequencing of PCR amplicons of the gene. Purified genomic DNA of the *bla*_{NDM}–producing isolates was subjected to whole-genome sequencing on a HiSeq system (Illumina, San Diego, CA, USA). Reads were filtered for quality with fastq-mcf (Ea-utils: <http://code.google.com/p/ea-utils/>).