Hepatitis E virus (HEV) is a major cause of acute hepatitis worldwide (1). Four HEV genotypes belonging to the species Orthohepevirus A are commonly found in humans (HEV-1 through HEV-4). Genotypes 1 and 2 seem to be restricted to humans, whereas genotypes 3 and 4 also occur in domesticated and wild animals. Zoonotic transmission by ingestion of contaminated meat, mainly from pigs, is the most likely zoonotic source of infection (1).

Recently, HEV sequences were reported from 3 dromedary samples in the United Arab Emirates (UAE) in 2013 and were classified as a new orthohepevirus A genotype, HEV-7 (2,3). Afterwards a human patient also from the UAE who had chronic hepatitis after liver transplantation was shown to carry HEV-7 (4,5). Until now, knowledge on HEV-7 and its zoonotic potential relied on these 2 studies, which provide no insight into the prevalence and distribution of HEV-7. To determine the geographic distribution of HEV-7, we conducted a geographically comprehensive study of HEV-7 prevalence in dromedaries by testing 2,438 specimens sampled in 6 countries during the past 3 decades.

The Study

Serum and fecal samples were collected from dromedary camels in the UAE, Somalia, Sudan, Egypt, Kenya, and Pakistan during 1983–2015 (6–7). A total of 2,171 serum samples and 267 fecal samples were tested for HEV RNA by using reverse transcription PCR (RT-PCR) as previously described (8). Seventeen samples were positive for HEV RNA: 12 (0.6%) of 2,171 serum samples and 5 (1.9%) of 267 fecal samples (Table). Positive samples originated from UAE, Somalia, Kenya, and Pakistan and dated to 1983 (Figures 1, 2). Viral loads were measured by using real-time RT-PCR (9) calibrated on the basis of the World Health Organization International Standard for HEV RNA (10). Viral RNA concentrations ranged from 3.2 × 10^4 to 3.6 × 10^7 IU/g in feces and 6.2 × 10^2 to 8.3 × 10^4 IU/mL in serum.

We sequenced a 283-nt fragment of the RNA-dependent RNA polymerase gene of all positive samples for phylogenetic analyses. All camel HEV clustered in a monophyletic clade with the human HEV-7 sequence (Figure 2), supporting the classification of camel-associated HEV to a separate Orthohepevirus A genotype (11).

African viruses from Somalia and Kenya formed a monophyletic clade, whereas viruses from UAE and Pakistan were intermixed (Figure 2). Distances based on nucleotide identities were calculated for all sequences from this study and 1 reference strain from each orthohepevirus A genotype as defined by Smith et al. (11). This subset of references comprised GenBank accession nos. M73218 (HEV-1), M74506 (HEV-2), AF082843 (HEV-3), AJ272108 (HEV-4), AB573435 (HEV-5), AB602441 (HEV-6), and KJ496143 (HEV-7). Nucleotide diversity was remarkable among viral sequences from dromedaries, reaching a maximum distance of 22.7%, compared with a maximum distance of 29.9% among all genotypes. The internal distance among the African viruses was 14.2%, compared with 17.4% distance within viruses from UAE and Pakistan. The African viruses were 16.7%–22.7% distant from UAE and Pakistan viruses, which corresponds to the distance threshold of 22%–25%.

A new hepatitis E virus (HEV-7) was recently found in dromedaries and 1 human from the United Arab Emirates. We screened 2,438 dromedary samples from Pakistan, the United Arab Emirates, and 4 African countries. HEV-7 is long established, diversified and geographically widespread. Dromedaries may constitute a neglected source of zoonotic HEV infections.

DOI: http://dx.doi.org/10.3201/eid2207.160168

Hepatitis E Virus Infection in Dromedaries, North and East Africa, United Arab Emirates, and Pakistan, 1983–2015


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Table. Sample characteristics and detection rates of orthohepevirus Agenotype 7 in 6 countries, 1983–2015

<table>
<thead>
<tr>
<th>Country</th>
<th>Time period</th>
<th>Virus RNA</th>
<th>Antibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudan</td>
<td>1983</td>
<td>0/60</td>
<td>15/35 (42.9)</td>
</tr>
<tr>
<td>Somalia</td>
<td>1983–1984</td>
<td>1/105 (0.9)</td>
<td>14/35 (40.0)</td>
</tr>
<tr>
<td>Egypt</td>
<td>1997</td>
<td>0/50</td>
<td>22/35 (62.9)</td>
</tr>
<tr>
<td>Kenya</td>
<td>1992–2015</td>
<td>2/889 (0.2)</td>
<td>11/35 (31.4)</td>
</tr>
<tr>
<td>United Arab Emirates</td>
<td>2013</td>
<td>1/500 (0.2)</td>
<td>5/267 (1.9)</td>
</tr>
<tr>
<td>Pakistan</td>
<td>2012–2015</td>
<td>8/867 (1.4)</td>
<td>21/35 (60.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>12/2,171 (0.5)</td>
<td>96/210 (45.7)</td>
</tr>
</tbody>
</table>

**Conclusions**

We investigated HEV-7 infection in dromedaries. The broad spatial extent, the high diversity of HEV-7 in dromedaries, and the detection of HEV-RNA in a sample collected in 1983 suggest a long evolutionary history of HEV-7 in dromedaries.

Our study has some limitations. First, although most tested dromedaries seemed healthy, no detailed health data were available for all animals. Second, the detection of HEV-RNA does not necessarily indicate active infection, as some samples may have been contaminated during handling. However, the high seroprevalence observed in this study suggests that HEV-7 is widely distributed in dromedaries across the regions studied.
HEV Infection in Dromedaries

information from the RNA-positive animals was available. Second, we studied limited genome fragments that prevented formal classification into genome subtypes (14). Third, although we used 2 different antibody detection methods, the antibody prevalence in camels should be confirmed by larger studies including virus neutralization studies to determine potential genotype variability.

Investigations of camelids other than dromedaries could help to further elucidate the geographic and evolutionary origin of HEV-7. Furthermore, other wild or domestic ungulates with close contact to dromedaries could be investigated to assess the host range of HEV-7. Human infection with HEV is common in all studied areas (1). On the basis of clinical observations and HEV antibody detection tools, several HEV outbreaks mainly linked to water contamination or poor hygienic circumstances have been described for Pakistan, Sudan, Somalia, and Egypt. For Kenya and UAE, data about HEV prevalence is scarce (1). In large parts of the Middle East, human infections are unlikely to be caused by contact with swine or consumption of pork for cultural reasons. Even in Saudi Arabia, where pork is absent in diet, blood donors have antibodies at proportions of up to 18.7% (1). Thus, most HEV infections in the Middle East are assumed to be caused by nonzoonotic genotypes 1 and 2. However, our study and previous studies (12) showed that HEV-7 and other human genotypes form 1 serotype, suggesting a lack of discrimination in seroprevalence studies.

The human HEV seroprevalence in the Middle East region might in fact be caused by HEV-7 infection. Furthermore, human HEV-7 infections might contribute to the HEV prevalence in all studied areas, where camel products are frequent parts of human diet (15). A foodborne transmission scenario is further suggested by the fact that 1 of 12 positive serum in the study was actually sampled in a slaughterhouse, documenting that meat from infected animals can enter the food chain (6). Detections of HEV-7 RNA in feces in this and a previous study (2) point at feces or feces-contaminated camel products, such as milk, as putative additional sources of human infection. Considering the importance of dromedaries as livestock animals (15), risk groups, such as slaughterhouse workers, should be screened for HEV-7 infection.
Acknowledgments
We thank Monika Eschbach-Bludau, Sebastian Brünink, and Tobias Bleicker for providing excellent technical assistance.

This study was supported by the European Commission (project COMPARE), the German Research Foundation (project DR772/12-1). A.L. and V.C.M were supported by the Centrum of International Migration and Development (Contract No. 81195004). The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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References
15. Kadim IT, Mahgoub O, Faye B, Farouk MM, editors. Camel meat and meat products Wallingford (UK): CAB International; 2013. Address for correspondence: Christian Drosten, Institute of Virology, University of Bonn Medical Centre, Sigmund Freud Str 25, 53105 Bonn, Germany; email: drosten@virology-bonn.de
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Technical Appendix

Technical Appendix Figure. Individual optical density (OD) ratios obtained from ELISA testing of serum and fecal specimens from dromedary camels for hepatitis E virus. The OD ratio was calculated by dividing the OD, measured at 450/605 nm, of each sample by the OD of a reference serum (marked with an asterisk), which was obtained from a dromedary 7 months after reverse transcription PCR–confirmed HEV infection and which was tested in parallel in all experiments. Fifty-six samples were also tested in the recomLine Immunoblot (MIKROGEN, Neuried, Germany) for confirmation. These samples were marked red (if Immunoblot testing was positive) or marked cyan (if Immunoblot testing was negative) Dashed line indicates the ELISA cutoff >0.46.