

programs might represent a cost-efficient opportunity for monitoring trends of HCV infection in the population.

The study was funded by the Hector Stiftung, Mannheim, Germany, Project M72 and the Cologne/Heidelberg/Lighthouse Partnership through ESTHER, Germany, Deutsche Gesellschaft für Internationale Zusammenarbeit (GIZ), contract no.: 81 166 383.

References

1. Platt L, Easterbrook P, Gower E, McDonald B, Sabin K, McGowan C, et al. Prevalence and burden of HCV co-infection in people living with HIV: a global systematic review and meta-analysis. *Lancet Infect Dis*. 2016;16:797–808. [http://dx.doi.org/10.1016/S1473-3099\(15\)00485-5](http://dx.doi.org/10.1016/S1473-3099(15)00485-5)
2. Joint United Nations Programme on HIV/AIDS. Malawi: HIV and AIDS estimates (2015). [cited 2016 Jul 7]. <http://www.unaids.org/en/regionscountries/countries/malawi>
3. Ahmed SD, Cuevas LE, Brabin BJ, Kazembe P, Broadhead R, Verfoeff FH, et al. Seroprevalence of hepatitis B and C in HIV and HIV in Malawian pregnant women. *J Infect*. 1998;37:248–51. [http://dx.doi.org/10.1016/S0163-4453\(98\)91983-1](http://dx.doi.org/10.1016/S0163-4453(98)91983-1)
4. Maida MJ, Costello Daly C, Hoffman I, Cohen MS, Kumwenda M, Vernazza PL. Prevalence of hepatitis C infection in Malawi and lack of association with sexually transmitted diseases. *Eur J Epidemiol*. 2000;16:1183–4. <http://dx.doi.org/10.1023/A:1010920426795>
5. Candotti D, Mundy C, Kadewele G, Nkhoma W, Bates I, Allain JP. Serological and molecular screening for viruses in blood donors from Ntcheu, Malawi: high prevalence of HIV-1 subtype C and of markers of hepatitis B and C viruses. *J Med Virol*. 2001;65:1–5. <http://dx.doi.org/10.1002/jmv.1093>
6. Chimphambano C, Komolafe IOO, Muula AS. Prevalence of HIV, HepBsAg and Hep C antibodies among inmates in Chichiri prison, Blantyre, Malawi. *Malawi Med J*. 2007;19:107–10.
7. Taha TE, Rusie LK, Labrique A, Nyirenda M, Soko D, Kamanga M, et al. Seroprevalence for hepatitis E and other viral hepatitis among diverse populations, Malawi. *Emerg Infect Dis*. 2015;21:1174–82. <http://dx.doi.org/10.3201/eid2107.141748>
8. Fox JM, Newton R, Bedaj M, Ada Keding, Molyneux E, Carpenter LM, et al. Prevalence of hepatitis C virus in mothers and their children in Malawi. *Trop Med Int Health*. 2015;20:638–42. <http://dx.doi.org/10.1111/tmi.12465>
9. Rao VB, Johari N, du Cros P, Messina J, Ford N, Cooke GS. Hepatitis C seroprevalence and HIV co-infection in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Infect Dis*. 2015;15:819–24. [http://dx.doi.org/10.1016/S1473-3099\(15\)00006-7](http://dx.doi.org/10.1016/S1473-3099(15)00006-7)
10. Graham CS, Baden LR, Yu E, Mrus JM, Carnie J, Heeren T, et al. Influence of human immunodeficiency virus infection on the course of hepatitis C virus infection: a meta-analysis. *Clin Infect Dis*. 2001;33:562–9. <http://dx.doi.org/10.1086/321909>

Address for correspondence: Münevver Demir, Clinic for Gastroenterology and Hepatology, University Hospital of Cologne, Germany, D-50924, Koeln, Germany; email: muenevver.demir@uk-koeln.de

Exposures among MERS Case-Patients, Saudi Arabia, January–February 2016

Raafat F. Alhakeem, Claire M. Midgley, Abdullah M. Assiri, Mohammed Alessa, Hassan Al Hawaj, Abdulaziz Bin Saeed, Malak M. Almasri, Xiaoyan Lu, Glen R. Abedi, Osman Abdalla, Mutaz Mohammed, Homoud S. Algarni, Hail M. Al-Abdely, Ali Abraheem Alsharif, Randa Nooh, Dean D. Erdman, Susan I. Gerber, John T. Watson

Author affiliations: Ministry of Health, Riyadh, Saudi Arabia (R.F. Alhakeem, A.M. Assiri, M. Alessa, H. Al Hawaj, A. Bin Saeed, M.M. Almasri, O. Abdalla, M. Mohammed, H.S. Algarni, H.M. Al-Abdely, A.A. Alsharif, R. Nooh); US Centers for Disease Control and Prevention, Atlanta, Georgia, USA (C.M. Midgley, X. Lu, G.R. Abedi, D.D. Erdman, S.I. Gerber, J.T. Watson)

DOI: <http://dx.doi.org/10.3201/eid2211.161042>

To the Editor: Risk factors for primary acquisition of Middle East respiratory syndrome (MERS) coronavirus (CoV) include recent direct contact with dromedary camels (1), but secondary transmission, associated with healthcare settings (2–4) or household contact (5), accounts for most reported cases. Because persons with MERS often do not report any of these risk factors, we investigated MERS cases in Saudi Arabia during an apparent period of limited hospital transmission. Through telephone interviews of case-patients and information from routine investigations, we aimed to characterize exposures and to explore additional factors potentially important in disease transmission. We also genetically sequenced MERS-CoV from respiratory specimens to identify circulating strains.

For confirmed MERS cases (6) reported in Saudi Arabia during January–February 2016, we assessed exposures during the 2 weeks before illness onset (exposure period), including direct (1) and indirect camel contact; indirect contact was defined as 1) having visited settings where camels were kept but without having direct contact or 2) exposure to friends or household members who themselves had direct camel exposure (1). We assessed whether case-patients had worked at, visited, or been admitted to a healthcare setting or had contact with a person known to have MERS during the case-patient's exposure period. We also asked about recent travel and if any household members were healthcare personnel. For persons too ill to participate or deceased, we interviewed relatives or close friends.

We classified as secondary any case identified through routine case-contact tracing and testing. We considered persons whose cases were identified through routine testing

of occupational contacts of MERS-CoV-positive camels to have had direct camel contact. For the remaining cases, we used interview responses to characterize exposures.

All MERS cases reported during January–February 2016 were confirmed in Saudi Arabia by testing of respiratory specimens with real-time reverse transcription PCR assays targeting the MERS-CoV upstream envelope protein gene and the open reading frame (ORF) 1a gene (7,8). Available specimens (or RNA extracts) were shipped to the US Centers for Disease Control and Prevention (Atlanta, GA, USA) for full genome sequencing. Methods for sequencing and phylogenetic analysis have been described previously (9).

During January–February 2016, a total of 27 MERS case-patients were reported by public health officials from 6 of the 13 administrative regions of Saudi Arabia (online Technical Appendix 1, <http://wwwnc.cdc.gov/EID/article/22/11/16-1042-Techapp1.xlsx>). Case-patients were evaluated at 20 different hospitals, 3 of which reported >1 case during the investigation period. Among the 27 case-patients, 4 (15%) were identified through routine contact tracing and testing as having secondary cases. Two case-patients (7%) were identified as occupational contacts of MERS-CoV-positive camels. Of the remaining 21 case-patients, 17 (81%) were interviewed during March 13–16, 2016; three were unavailable for interview, and 1 provided incomplete data. Ten (59%) of the 17 interviews were completed by proxy.

Among the 17 case-patients interviewed, 5 (29%) reported direct camel contact (1 of these also reported visiting a healthcare facility), and 4 (24%) reported indirect camel contact (2 of these also reported visiting a healthcare facility) during the exposure period (online Technical Appendix 1). Three case-patients reported having close acquaintances who regularly interacted with camels but reported they had not seen these acquaintances during the exposure period. One case-patient was the spouse of a healthcare worker employed in a facility with a reported MERS patient during the putative exposure period; the spouse was found to be MERS-CoV-negative by real-time reverse transcription PCR of a respiratory specimen. The 4 remaining cases could not be further characterized.

Viruses from 13 of the 27 case-patients were sequenced, and all belonged to the MERS-CoV recombinant subclade NRC-2015 (9), first detected in humans in January 2015; these 13 case-patients were from the Riyadh and Makkah regions (online Technical Appendix 1). Full genome sequences were obtained from the specimens of 11 case-patients (online Technical Appendix 2, <http://wwwnc.cdc.gov/EID/article/22/11/16-1042-Techapp2.pdf>). Continued and predominant circulation of NRC-2015 supports increased epidemiologic fitness compared with other clades, as postulated previously (9).

A novel nucleotide substitution was identified in the MERS-CoV sequence from 1 case-patient (online

Technical Appendix 1) at position 337 located in the stop codon of ORF8b (TAA [Stop] >CAA [Gln] = Stop113Q), predicted to yield a 143aa protein versus the 112aa wild-type. ORF8b is an internal ORF overlapped by the nucleocapsid protein gene (10); the corresponding substitution in the nucleocapsid protein gene predicts a conserved amino acid change (V178A). The virologic and clinical significance of these findings is unknown.

Since the emergence of MERS-CoV in 2012, virus acquisition has been associated with direct exposure to camels (1) and with person-to-person transmission in households and healthcare settings (2–5); other sources of infection are less clear. Among the patients in our study whose cases were successfully characterized (23/27), 4 had contact with other known case-patients, and 7 reported direct camel contact. Among the remaining 12 case-patients without these risk factors, 7 were identified as having at least some exposure to persons with direct camel contact. Our findings suggest that community and household exposure to persons with direct camel contact might play a role in MERS-CoV acquisition. Further investigation is needed to determine any specific roles of these interactions in MERS-CoV transmission.

Acknowledgments

Thanks to Senthilkumar K. Sakhivel and Shifaq Kamili for specimen shipment and processing.

This work was funded by the Saudi Arabia Ministry of Health and the US CDC as part of an emergency response. The authors declare no competing interests.

References

- Alraddadi BM, Watson JT, Almarashi A, Abedi GR, Turkistani A, Sadran M, et al. Risk factors for primary Middle East respiratory syndrome coronavirus illness in humans, Saudi Arabia, 2014. *Emerg Infect Dis*. 2016;22:49–55. <http://dx.doi.org/10.3201/eid2201.151340>
- Assiri A, Abedi GR, Bin Saeed AA, Abdalla MA, al-Masry M, Choudhry AJ, et al. Multifacility outbreak of Middle East respiratory syndrome in Taif, Saudi Arabia. *Emerg Infect Dis*. 2016;22:32–40. <http://dx.doi.org/10.3201/eid2201.151370>
- Balkhy HH, Alenazi TH, Alshamrani MM, Baffoe-Bonnie H, Al-Abdely HM, El-Saed A, et al. Notes from the field: nosocomial outbreak of Middle East respiratory syndrome in a large tertiary care hospital—Riyadh, Saudi Arabia, 2015. *MMWR Morb Mortal Wkly Rep*. 2016;65:163–4. <http://dx.doi.org/10.15585/mmwr.mm6506a5>
- Oboho IK, Tomczyk SM, Al-Asmari AM, Banjar AA, Al-Mugti H, Aloraini MS, et al. 2014 MERS-CoV outbreak in Jeddah—a link to health care facilities. *N Engl J Med*. 2015;372:846–54. <http://dx.doi.org/10.1056/NEJMoa1408636>
- Drosten C, Meyer B, Müller MA, Corman VM, Al-Masri M, Hossain R, et al. Transmission of MERS-coronavirus in household contacts. *N Engl J Med*. 2014;371:828–35. <http://dx.doi.org/10.1056/NEJMoa1405858>
- Command and Control Center Saudi Arabia Ministry of Health. Infection prevention and control guidelines for Middle East

- respiratory syndrome coronavirus (MERS-CoV) infection. Third edition [cited 2016 Aug 26]. <http://www.moh.gov.sa/en/CCC/Regulations/2015%20update.pdf>
7. Corman VM, Müller MA, Costabel U, Timm J, Binger T, Meyer B, et al. Assays for laboratory confirmation of novel human coronavirus (hCoV-EMC) infections. *Euro Surveill*. 2012;17:20334.
 8. World Health Organization. Laboratory testing for Middle East respiratory syndrome coronavirus—interim guidance [cited 2016 Aug 26]. http://www.who.int/csr/disease/coronavirus_infections/mers-laboratory-testing
 9. Assiri AM, Midgley CM, Abedi GR, Bin Saeed A, Almasri MM, Lu X, et al. Epidemiology of a novel recombinant MERS-CoV in humans in Saudi Arabia. *J Infect Dis*. 2016;214:712–21. <http://dx.doi.org/10.1093/infdis/jiw236>
 10. van Boheemen S, de Graaf M, Lauber C, Bestebroer TM, Raj VS, Zaki AM, et al. Genomic characterization of a newly discovered coronavirus associated with acute respiratory distress syndrome in humans. *MBio*. 2012;3:e00473–12. <http://dx.doi.org/10.1128/mBio.00473-12>

Address for correspondence: Claire M. Midgley, Centers for Disease Control and Prevention, 1600 Clifton Road NE, Atlanta, Georgia, 30329-4027, USA; email: ydk5@cdc.gov

***Leishmania major* Cutaneous Leishmaniasis in 3 Travelers Returning from Israel to the Netherlands**

Justin S. Kuilder, Pieter J. Wismans, Ewout M. Baerveldt, Jaap J. van Hellemond, Mariana de Mendonça Melo, Perry J.J. van Genderen

Author affiliations: Harbour Hospital, Rotterdam, the Netherlands (J.S. Kuilder, P.J. Wismans, E.M. Baerveldt, J.J. van Hellemond, M. de Mendonça Melo, P.J.J. van Genderen); Erasmus University Medical Center, Rotterdam, the Netherlands (E.M. Baerveldt, J.J. van Hellemond)

DOI: <http://dx.doi.org/10.3201/eid2211.161154>

To the Editor: Cutaneous leishmaniasis (CL) is a protozoan disease transmitted by sand flies that usually runs a relatively mild course. Classic CL starts as a red papule at the place of the insect bite; it gradually enlarges into a painless nodule or plaque-like lesion, which eventually becomes encrusted. When the crust falls off, a typical ulcer with raised and indurated border becomes apparent. CL can cause considerable illness and may leave disfiguring and disabling scars after healing. The interplay between *Leishmania* species and host immune response is complex, and, as a result, disease manifestations may vary substantially

among species as well as among infected persons (1,2). An estimated 0.7–1.2 million new CL cases occur annually in tropical and subtropical regions of the world. CL is currently endemic in >98 countries worldwide; Afghanistan, Algeria, Colombia, Brazil, Iran, Syria, Ethiopia, North Sudan, Costa Rica, and Peru together account for up to 75% of global estimated CL incidence (3).

We report 3 travel companions from the Netherlands who all acquired CL after they participated in a short-term study course in Israel during September–October 2015. The travelers visited several places in the Negev Desert in southern Israel. All cases were confirmed by PCR with additional sequence analysis of the mini-exon locus and the 3' untranslated region of the HSP70 locus, demonstrating *L. major* as the causative species (4).

The first case-patient was a 55-year-old man who observed red papules on his head and shoulder 1 month after he returned to the Netherlands. Gradually, these papules increased in size, and number and showed a tendency to ulcerate. On examination at the Institute for Tropical Diseases in Rotterdam, 12 painless, hyperkeratotic, plaquelike, sharply demarcated lesions were identified, some partially ulcerated, located on the head, shoulders, arms, legs, and across the chest. Histopathologic examination on skin biopsy specimens acquired from 1 lesion revealed *Leishmania* amastigotes, consistent with a diagnosis of CL. The patient was treated with miltefosine (50 mg orally 3×/d for 28 d). Clinical recovery followed gradually.

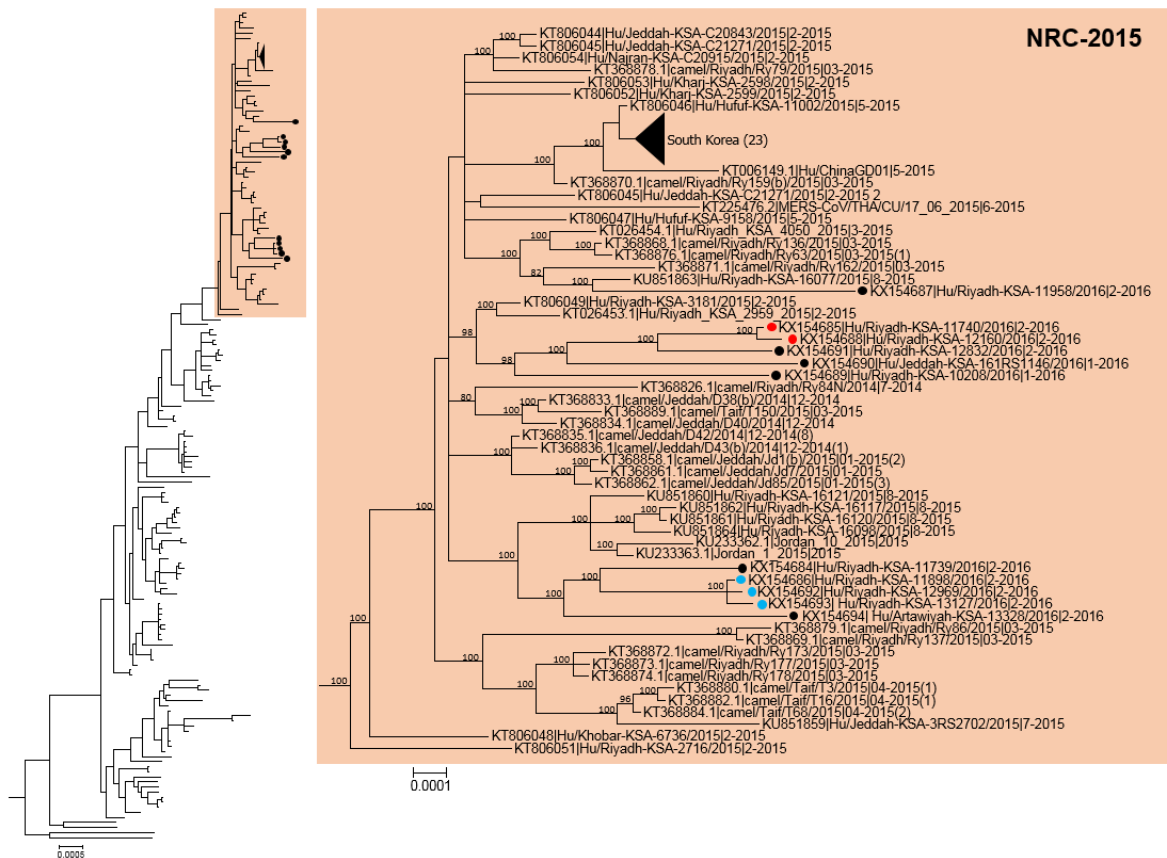
The second case-patient, a 52-year-old woman, noticed some red papules on both legs that gradually increased in size and ulcerated in the 2 months after return to the Netherlands. She was initially treated by a general practitioner for a presumed bacterial skin infection but did not show a clinical response to antibiotic treatment. On examination, also at the Institute for Tropical Diseases, 6 painless ulcers were seen on her legs. CL was suspected after taking into account the clinical manifestations and the recent diagnosis of CL in her travel companion. She was successfully treated with miltefosine after the diagnosis was confirmed.

A third case-patient, a 52-year-old woman, was diagnosed with CL after she sought treatment for a single small, sharply demarcated, painless pretibial plaquelike skin lesion on her arm that had been present for 2 months after her return to the Netherlands. Repeated PCRs of skin biopsy specimens confirmed the diagnosis of *L. major* CL. She preferred a “wait and see” policy over treatment.

The 3 patients with CL, a cluster of travel companions, were conceivably infected in the Negev Desert. Only 1 previous report has documented a traveler returning from Israel who was diagnosed with CL at the Institute for Tropical Diseases during 2007–2016 (Table). Most cases originated from the New World, in particular from South America, followed by Central America (Table). Few of these cases

Exposures among MERS Case-Patients, Saudi Arabia, January–February 2016

Technical Appendix 2



Technical Appendix 2 Figure. Phylogeny of Middle East respiratory syndrome coronavirus (MERS-CoV) genome sequences, Saudi Arabia, January–February 2016. The phylogenetic tree was constructed from MERS-CoV genome sequences obtained from the 11 case-patients reported during January–February 2016, and all near-complete genome sequences available in public domain ($n = 213$) using the program MrBayes version 3.2.6 under a general time-reversible (GTR) model of nucleotide substitution with 4 categories of γ -distributed rate heterogeneity and a proportion of invariant sites (GTR+4 + I). MERS-CoV sequences belonging to the recently described novel recombinant subclade (NRC-2015) are shown in expanded view. The 11 sequences identified in this study are marked with circles. Red circles denote sequences from the hospitalized case-patient and attending healthcare worker; blue circles denote

sequences from the 3 house-hold contacts. Clade-credibility values $\geq 70\%$ are indicated above the respective nodes. Numbers in brackets following some strain identifiers are the number of additional identical sequences with the same geographic location and sample collection year/month. The scale bar shows the genetic distance as nucleotide substitutions per site.