Crimean-Congo Hemorrhagic Fever Virus in Cattle and Ticks, Israel

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We conducted a nationwide serologic and molecular survey to elucidate the epidemiologic status of Crimean-Congo hemorrhagic fever virus in Israel. We found serologic and molecular evidence of virus circulation in the country. Future human cases could be prevented by increasing public awareness and implementing public health measures.

Crimean-Congo hemorrhagic fever virus (CCHFV) is an enveloped segmented negative-sense RNA virus belonging to the *Nairoviridae* family of the *Bunyavirales* order (*1*). The virus is the etiologic agent of Crimean-Congo hemorrhagic fever (CCHF), a severe tickborne zoonotic illness with a wide geographic distribution, infecting ≈10,000–15,000 humans annually worldwide (*2*). Ticks, primarily of the genus *Hyalomma*, are considered the vector and the reservoir of CCHFV (*3*). CCHFV can infect various animal hosts, including livestock, that, although remaining asymptomatic, can act as amplifying hosts of the virus (*4*). CCHFV is transmitted to humans primarily through the bite of an infected tick but also by direct contact with blood or body fluids of infected animals or humans or through improperly sterilized medical equipment (*1*).

Neither CCHFV infection in humans nor positive serologic test results in humans or in animals were previously reported in Israel. However, outbreaks of the disease and seropositivity among livestock have been reported in neighboring countries (*5*). Moreover, the main vector of CCHFV, the *Hyalomma marginatum* tick, is endemic in Israel (*6*). Hence, the risk for CCHFV emergence in Israel is considered high, and undetected viral circulation might already exist in specific regions of the country (*6*).

During April 2024–February 2025, we sampled whole blood, serum specimens, and ticks from 19 beef cattle herds from different regions in Israel. We tested serum samples by using an ELISA commercial kit (ID Screen CCHF Double Antigen Multi-species; Innovative Diagnostics, https://www.innovative-diagnostics.com). We classified the ticks morphologically and extracted RNA to identify CCHFV presence (Appendix, https://wwwnc.cdc.gov/EID/article/31/11/25-0622-App.pdf).

Sixteen beef cattle herds had serologic evidence of prior exposure to CCHFV; seropositivity ranged from 3% to 100% (Table). We detected virus exposure eliciting an immune response in locations across Israel (Figure). Those serologic results are comparable with

Table. Seroprevalence of Crimean-Congo hemorrhagic fever virus in cattle, Israel, April 2024–February 2025

Site of sampling (district)	No. sampled animals	No. (%) seropositive	Average age of sampled animals, y
Kidmat Tzvi (Golan Heights)	34	17 (50)	8.3
Merom Golan (Golan Heights)	39	14 (35.9)	9.3
Ramat Magshimim (Golan Heights)	39	6 (15.4)	8.6
Keshet (Golan Heights)*	30	0	<2
Keshet (Golan Heights)	20	20 (100)	8.08
Ortal (Golan Heights)	25	22 (88)	8.8
Gazit (Yizrael Valley)	30	9 (30)	7.7
Zipori (Yizrael Valley)	17	5 (29.4)	7.05
Alonim (Yizrael Valley)	31	1 (3.2)	2†
Na'aura (Gilboa)	21	6 (28.6)	7.5
Nurit (Gilboa)	22	1 (4.7)	5†
Gal'ed (Ramat Menashe)	33	10 (30.3)	5.8
Ein Yaakov (Western Galilee)	24	19 (79.1)	8.5
Shetula (Western Galilee)	24	2 (8.3)	2.5
Lapidot (Western Galilee)	30	2 (6.6)	11.8
Kochav Hayarden (Jordan Valley)*	17	0	<2
Kfar Szold (Hula Valley)	30	1 (3.3)	3†
Sha'alabim (Gezer)	32	27 (84)	5.7
Avi'ezer (Adulam)*	9	0	<2
Binyamina (Haifa)	29	19 (65.5)	6.07
Total no. samples	536	181 (34)	

*Heifers only.
†Estimated average age provided by owner.

rates reported in CCHFV-endemic countries with confirmed human cases, such as Turkey (Türkiye) (*7*) and Pakistan (*8*). Consistent with prior publications linking older age with seropositivity (*9*), the age of the sampled animals from the 2 herds that were seronegative was <2 years. Moreover, although all serum samples from the heifers (<2 years of age) of the Keshet herd (Golan Heights) were seronegative, subsequent

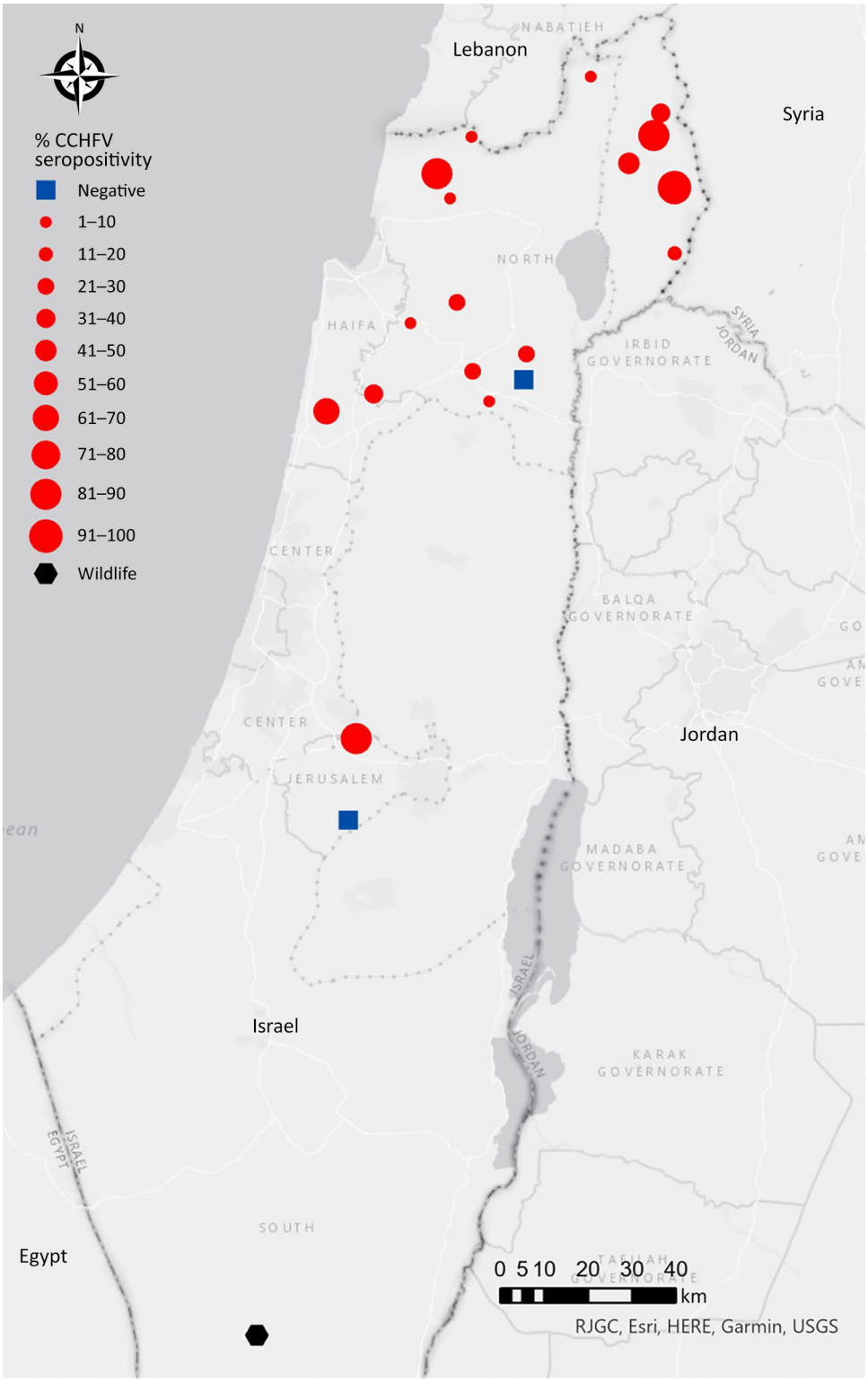

Figure. Distribution of samples seropositive for CCHFV in study of serologic and molecular evidence of CCHFV in cattle and ticks, Israel, April 2024–February 2025. Red dots represent seropositive beef cattle herds. Size of dots correlates with percentage of CCHFV seropositivity. Blue rectangles represent CCHFV seronegative herds. Black hexamer represents 2 of 200 CCHFV seropositive wild animals that were tested. Map created by using ArcGIS software (Esri, https://www.esri.com). CCHFV, Crimean-Congo hemorrhagic fever virus.

sampling of older cows (3–15 years of age) in the herd revealed 100% positive serologic test results (Table). We also tested serum samples that were randomly collected from 200 wild animals dispersed through the country (including boars, foxes, jackals, ibexes, dogs, deer, oryxes, gazelles, and porcupines) during 2023–2024. We found that only 2 samples, from ibexes (*Capra nubiana*) residing in the Negev Desert (southern Israel), were seropositive for CCHFV antibodies (Figure).

We tested for CCHFV RNA in 227 ticks retrieved from 8 cattle herds and 51 ticks retrieved from wildlife by using quantitative reverse transcription PCR targeting 2 regions of the small segment (*10*). Because we tested each tick individually, we determined a sample to be positive only when both regions were amplified. In addition, the positive samples were validated at an independent facility (The Central Virology Laboratory, Ministry of Health and Sheba Medical Center, Ramat-Gan, Israel). Of the 227 ticks from cattle, 23 (10%) samples collected from northern Israel (Golan Heights and Western Galilee) were positive for CCHFV (Appendix Table 1). Likewise, among 51 ticks collected from wild animals (all sampled from northern Israel), 7 (13%) were positive for CCHFV (Appendix Table 2). All ticks positive for CCHFV belonged to 2 genera, *Hyalomma* and *Rhipicephalus* (Appendix Tables 1, 2). Sanger sequencing of the 181-bp (1,068–1,248 nucleotides at the small segment) amplicons of 10 samples, which we successfully amplified by using endpoint reverse transcription PCR (*10*), followed by phylogenetic analysis, indicated that the sequences clustered to the Asia-1 genotype (Appendix Figure).

We tested serum samples from 13 persons who had close contact with either CCHFV-positive ticks or seropositive cattle for the presence of CCHF IgG by using ELISA (Euroimmun, https://www.euroimmun.com). All persons tested were seronegative. The study was conducted with the approval of the Shiba Medical Center institutional review board (approval no. 1601–24-SMC).

We present evidence of CCHFV circulation in Israel, expanding the known geographic distribution of CCHFV in the Middle East. We have found serologic evidence of prior exposure to CCHFV in livestock and in wild animals; we also detected CCHFV in the ticks infesting them. Furthermore, the seroprevalence in the cows was found to be comparable to seroprevalence in CCHFV-endemic countries with proven human cases. In addition, the seropositivity prevalence in the cattle and the observation that cows <2 years of age were not seropositive suggest that the virus has been circulating for several years. Still, the route of introduction remains unclear. Our results highlight the importance of raising public and clinical awareness of CCHF, especially among high-risk populations, despite the current absence of human cases.

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About the Author

Dr. Rudoler is head of the virology laboratory at the Kimron Veterinary Institute, Israel. His major interests include veterinary public health, zoonotic diseases, and conducting and implementing One Health research projects.

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Extensively Drug-Resistant Tuberculosis with Conflicting Resistance Testing Results, Lesotho

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A patient with extensively drug-resistant tuberculosis in Lesotho recovered successfully after failed treatment with bedaquiline, delamanid, linezolid, and clofazimine. Whole-genome sequencing and broth microdilution testing results were not in agreement, illustrating the urgent need for studies that correlate phenotypic and genotypic resistance testing with clinical response.

New drugs and regimens for treating tuberculosis (TB) have transformed the way in which healthcare providers manage multidrug-resistant (MDR) TB. Bedaquiline, delamanid, and pretomanid are among the newest drugs developed specifically for treating TB. Other drugs, like linezolid and clofazimine, have demonstrated activity against *Mycobacterium tuberculosis* and have therefore gained status as potential treatments for the disease. Healthcare professionals have reported excellent treatment outcomes in patients receiving those drugs, even in low-resource settings that have the highest burden of MDR TB (*1*,*2*). Resistance to those drugs, however, has been increasing faster than access to accurate laboratory resistance testing. Bedaquiline resistance is increasingly common and problematic, given the drug's prominence in most treatment regimens for MDR TB. (*3*).

In 2016, physicians referred a man in his late 30s to the Botsabelo MDR TB referral hospital in Maseru, Lesotho, for suspicion of drug-resistant TB. The man's only previous exacerbation of TB was 2 years earlier, when he received a standard treatment regimen of 4 first-line drugs. At that time, chest radiographs showed bilateral upper lobe infiltrates, more extensive on the right side; PCR testing with Xpert MTB/RIF assay (Cepheid, https://www.cepheid.com) showed resistance to rifampin. He had HIV infection (CD4 115 cells/μL, viral load 20,000 copies/mL), which appeared to be poorly managed because of inconsistent adherence to abacavir, lamivudine, and efavirenz, especially during episodes of binge drinking.

When the patient sought care in 2016, we performed qualitative in vitro testing with GenoType MTBDR*sl* (Hain Lifescience, https://www.hain-lifescience.de), which showed no evidence of mutations conferring resistance to fluoroquinolones or injectables, so we started a standard treatment regimen for MDR TB: pyrazinamide, kanamycin, levofloxacin, prothionamide, cycloserine, and para-aminosalicylic acid (Figure, panel A). Clinical and bacteriologic response was poor. Repeat testing with GenoType MTBDR*sl* showed resistance to fluoroquinolones but not to injectables; we adjusted the drug regimen at month 10 to include bedaquiline and linezolid. At month 14, we added delamanid and clofazimine. Nevertheless, sputum cultures were persistently TB positive. At month 19, BACTEC MGIT (BD, https://www.bd.com) analysis of a sputum isolate sent to the South Africa National Institute for Communicable Diseases (NICD; Johannesburg, South Africa) revealed susceptibility to all second-line TB drugs except moxifloxacin (0.5 μg/mL).