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Because the NIS reports hospital discharges rather than unique patients, we were unable to identify patients with multiple hospitalizations or estimate the per-person costs of hepatitis A inpatient care. We were also not able to separately report the costs associated with liver transplantation.

Even though using highly sensitive inclusion criteria might have introduced an element of cost overestimation in some patients incidentally diagnosed with hepatitis A while admitted for other conditions, our results almost certainly underestimate hospitalization costs associated with the ongoing hepatitis A outbreaks because NIS does not include hospital-based physician fees. Moreover, the national \$306.8 million estimate does not account for outpatient visits, emergency department visits that did not result in an admission to the same hospital, lost productivity, out-of-pocket costs to patients or their informal caregivers, or public health costs associated with the hepatitis A outbreaks, further reinforcing the conservative nature of this estimate.

Given the high proportion of hospitalized patients during the ongoing hepatitis A outbreaks, we estimated the average hepatitis A-related hospitalization costs to highlight the preventable economic burden of these outbreaks on healthcare systems and state governments. Hepatitis A is a vaccine-preventable disease. Despite longstanding vaccination recommendations for adults at increased risk for hepatitis A virus infection or adverse consequences of infection, self-reported adult hepatitis A vaccination coverage with ≥ 2 doses was only 10.9% for persons ≥ 19 years of age in 2017 (6). Our findings underscore the importance of improving hepatitis A vaccination coverage among at-risk adults, in accordance with Advisory Committee on Immunization Practices recommendations (7).

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References

- Centers for Disease Control and Prevention. Surveillance for viral hepatitis—United States, 2017 [cited 2020 Feb 13]. <https://www.cdc.gov/hepatitis/statistics/2017surveillance/pdfs/2017HepSurveillanceRpt.pdf>
- Centers for Disease Control and Prevention. Widespread outbreaks of hepatitis A across the United States [cited 2020 Feb 11]. <https://www.cdc.gov/hepatitis/outbreaks/2017March-HepatitisA.htm>
- Agency for Healthcare Research and Quality. Introduction to the HCUP National Inpatient Sample (NIS) 2017 [cited 2020 Feb 13]. <https://www.hcup-us.ahrq.gov/db/nation/nis/NISIntroduction2017.pdf>
- Agency for Healthcare Research and Quality. Cost-to-charge ratio files [cited 2019 Jun 13]. <https://www.hcup-us.ahrq.gov/db/state/costtocharge.jsp>
- Agency for Healthcare Research and Quality. Requirements for publishing results with HCUP data [cited 2019 Apr 24]. <https://www.hcup-us.ahrq.gov/db/publishing.jsp>
- Centers for Disease Control and Prevention. Vaccination coverage among adults in the United States, National Health Interview Survey, 2017: hepatitis A vaccination [cited 2019 Dec 2]. <https://www.cdc.gov/vaccines/imz-managers/coverage/adultvaxview/pubs-resources/NHIS-2017.html#box2>
- Freedman MS, Hunter P, Ault K, Kroger A. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older—United States, 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69:133–5. <https://doi.org/10.15585/mmwr.mm6905a4>

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Crimean-Congo Hemorrhagic Fever Virus Antibodies among Livestock on Corsica, France, 2014–2016

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We conducted a serologic survey for Crimean-Congo hemorrhagic fever virus antibodies in livestock (cattle, sheep, and goats; N = 3,890) on Corsica (island of France) during 2014–2016. Overall, 9.1% of animals were seropositive, suggesting this virus circulates on Corsica. However, virus identification is needed to confirm these results.

Crimean-Congo hemorrhagic fever (CCHF), the most widespread tickborne viral infection in humans, is a zoonotic disease caused by an orthornairovirus of the *Nairoviridae* family. Symptoms in humans vary from a nonspecific mild febrile syndrome to severe hemorrhagic disease that sometimes leads to death (1,2), and a wide range of animals are asymptomatic reservoirs (1). Corsica is an island of France located in the northwestern part of the Mediterranean Sea (Figure, panel A). Entomologic surveys have revealed that one of the main vectors of CCHF virus (CCHFV), the *Hyalomma marginatum* tick, is abundant on this island (1,3,4). Therefore, we performed a serologic cross-sectional survey to assess the prevalence of antibodies against CCHFV in domestic ruminants

on Corsica. This work was approved by the French Ministry of Agriculture (Direction Départementale de la Cohésion Sociale et de la Protection des Populations of Corse-du-Sud and Haute-Corse and General Directorate for Food).

As part of national surveillance for animal diseases, veterinarians collected cattle, goat, and sheep blood samples during 2014–2016. In total, 3,890 animals (1,731 cattle, 1,035 goats, 1,124 sheep) were sampled from 269 farms, originating from 46% (137/298) of the municipalities with ruminant farming activities (3).

We tested the collected serum samples for the presence of CCHFV IgG using a double-antigen ELISA kit (ID Screen CCHF Double Antigen Multi-species, ID.Vet, <https://www.id-vet.com>) according to the manufacturer's instructions (Appendix Figure, <https://wwwnc.cdc.gov/EID/article/26/5/19-1465-App1.pdf>). For this kit, the 95% CI for sensitivity is 96.8%–99.8%, and 95% CI for specificity is 99.8%–100% (5). To confirm ELISA results, we sent 35 ELISA-positive and 5 ELISA-negative serum samples to a Biosafety Level 4 laboratory (Laboratory Jean Mérieux, Lyon, France) to be analyzed by the World Health Organization and World Organisation for Animal Health national reference center for CCHFV (Institut Pasteur and Institut de Recherche Biomédicale des Armées, Paris, France). We used the pseudo-plaque reduction neutralization test (PPRNT) (6) to measure the neutralizing antibodies against IbAr10200 (same antigen used in ELISA) in triplicate. We included Hazara virus (same serogroup as CCHFV) and Dugbe virus (closely related virus, Nairobi sheep disease serogroup) to detect possible immune cross-reactions. We estimated overall and species-specific IgG prevalence against CCHFV using a β -binomial logistic regression model of data grouped by farm.

The overall estimated seroprevalence was 9.1% (95% CI 6.9%–11.9%); estimated seroprevalence in cattle was 13.3% (95% CI 10.2%–17.3%), goats 3.1% (95% CI 1.4%–7.0%), and sheep 2.5% (95% CI 1.0%–5.9%). CCHFV antibodies were detected across the island; 35.8% (49/137; 95% CI 27.8%–44.4%, estimated by exact binomial test) of the investigated municipalities had ≥ 1 positive ELISA test result. Because serum samples were not available from all municipalities, we used Voronoi polygons to draw regional boundaries and estimate the spatial distribution of seroprevalence across the island. Seroprevalence was high in the northwest corner of Corsica; however, most regions lacked evidence of seropositivity (Figure panel A). In areas corresponding to negative polygons, the probability of nondetection of positive serum samples was estimated assuming 3 levels of estimated serop-

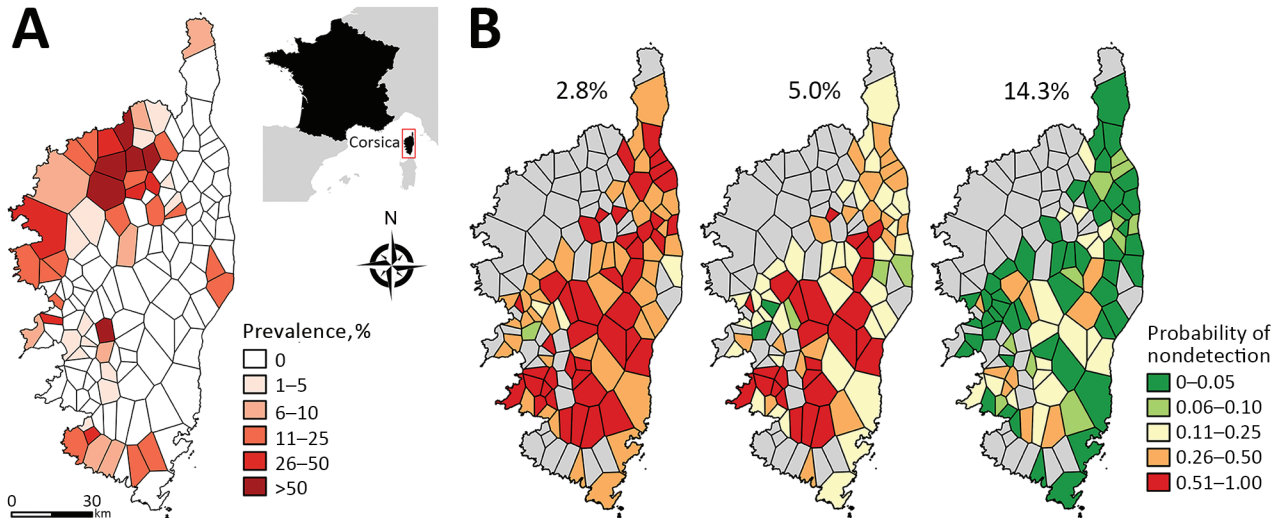


Figure. Prevalence and probability of nondetection of antibody against Crimean-Congo hemorrhagic fever virus (CCHFV) in ruminants, Corsica, France, 2014–2016. A) Spatial variability of CCHFV antibody prevalence. Inset indicates location of the island of Corsica in relation to France. B) Probability of nondetection of CCHFV antibody in areas where estimated prevalence was null. Three different probabilities were estimated in accordance with different assumptions of the estimated true seroprevalence, corresponding with the 10% quantile (2.8% seroprevalence), 25% quantile (5.0% seroprevalence), and 50% quantile (14.3% seroprevalence). In this analysis, a Voronoi diagram was used to divide the island into regions; the centroids of Voronoi polygons corresponded to municipalities where blood samples were collected.

revalence corresponding with the 10% quantile (2.8% seroprevalence), 25% quantile (5.0% seroprevalence), and 50% quantile (14.3% seroprevalence) (Figure, panel B) and by accounting for sample size. These data show that if seroprevalence in these regions is $\leq 5\%$, the probability of nondetection is high (Figure, panel B), and if the seroprevalence in these regions is $\geq 14.3\%$, the probability of nondetection is low. Therefore, the chance that we missed hotspots of transmission is highly unlikely.

Of 35 ELISA-positive serum samples tested, none showed neutralizing antibodies against Hazara and Dugbe viruses, and no ELISA-negative serum sample showed neutralizing antibodies against CCHFV, Hazara virus, or Dugbe virus (at lowest dilution 1:20; Appendix Table). Of 35 ELISA-positive serum samples, 23 had neutralizing antibodies against CCHFV at the 1:40 dilution, and 10 remained positive at the 1:80 dilution (including 2 positive at the 1:320 and 1:640 dilutions).

Our serologic survey results suggest CCHFV circulates in livestock on Corsica. Relative discrepancies between ELISA (35 positives) and PPRNT (23 positives) findings might result from their different target epitopes; the ELISA measures total immunoglobulin (neutralizing and nonneutralizing antibodies) and PPRNT just a subset (functional neutralizing antibodies) (7). Seroprevalence estimates were higher in cattle than smaller ruminants, probably reflecting

that cattle in Corsica are more infested by *Hy. marginatum* ticks (3).

As of February 2020, CCHFV has not been detected in ticks on Corsica (8), and no clinical human case has been reported. The presence of a genetically close and less virulent strain in ticks on Corsica might help explain the lack of these findings. CCHFV was detected in ticks in Spain, where the first human cases were reported in 2016 (9), and in a tick collected on a migratory bird in Italy (10). Entomologic and epidemiologic investigations to identify the incriminated strain and characterize its spatial distribution are ongoing. This work will be essential to assess the risk for human CCHFV exposure and raise public health awareness on Corsica and in neighboring areas.

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References

1. Bente DA, Forrester NL, Watts DM, McAuley AJ, Whitehouse CA, Bray M. Crimean-Congo hemorrhagic fever: history, epidemiology, pathogenesis, clinical syndrome and genetic diversity. *Antiviral Res.* 2013;100:159–89. <http://dx.doi.org/10.1016/j.antiviral.2013.07.006>
2. Dreshaj S, Ahmeti S, Ramadani N, Dreshaj G, Humolli I, Dedushaj I. Current situation of Crimean-Congo hemorrhagic fever in Southeastern Europe and neighboring countries: a public health risk for the European Union? *Travel Med Infect Dis.* 2016;14:81–91. <http://dx.doi.org/10.1016/j.tmaid.2016.03.012>
3. Grech-Angelini S, Stachurski F, Lancelot R, Boissier J, Allienne JF, Marco S, et al. Ticks (Acari: *Ixodidae*) infesting cattle and some other domestic and wild hosts on the French. *Parasit Vectors.* 2016;9:582. <http://dx.doi.org/10.1186/s13071-016-1876-8>
4. Gargili A, Estrada-Peña A, Spengler JR, Lukashev A, Nuttall PA, Bente DA. The role of ticks in the maintenance and transmission of Crimean-Congo hemorrhagic fever virus: a review of published field and laboratory studies. *Antiviral Res.* 2017;144:93–119. <http://dx.doi.org/10.1016/j.antiviral.2017.05.010>
5. Sas MA, Comtet L, Donnet F, Mertens M, Vatansever Z, Tordo N, et al. A novel double-antigen sandwich ELISA for the species-independent detection of Crimean-Congo hemorrhagic fever virus-specific antibodies. *Antiviral Res.* 2018;151:24–6. <http://dx.doi.org/10.1016/j.antiviral.2018.01.006>
6. Canakoglu N, Berber E, Ertek M, Yoruk MD, Tonbak S, Bolat Y, et al. Pseudo-plaque reduction neutralization test (PPRNT) for the measurement of neutralizing antibodies to Crimean-Congo hemorrhagic fever virus. *Virology.* 2013;10:6. <http://dx.doi.org/10.1186/1743-422X-10-6>
7. Ravault S, Friel D, Di Paolo E, Caplanusi A, Gillard P, Povey M, et al. Assessment of mumps virus-specific antibodies: comparison of plaque reduction neutralization test and enzyme-linked immunosorbent assay estimates. *J Infect Dis.* 2019;220:1462–8. <http://dx.doi.org/10.1093/infdis/jiz345>
8. Grech-Angelini S, Stachurski F, Vayssier-Taussat M, Devillers E, Casabianca F, Lancelot R, et al. Tick-borne pathogens in ticks (Acari: *Ixodidae*) collected from various domestic and wild hosts in Corsica (France), a Mediterranean island environment. *Transbound Emerg Dis.* 2019;tbed.13393. <http://dx.doi.org/10.1111/tbed.13393>
9. Negro A, de la Calle-Prieto F, Palencia-Herrejón E, Mora-Rillo M, Astray-Mochales J, Sánchez-Seco MP, et al.; Crimean Congo Hemorrhagic Fever@Madrid Working Group. Autochthonous Crimean-Congo hemorrhagic fever in Spain. *N Engl J Med.* 2017;377:154–61. <http://dx.doi.org/10.1056/NEJMoa1615162>
10. Mancuso E, Toma L, Polci A, d'Alessio SG, Di Luca M, Orsini M, et al. Crimean-Congo hemorrhagic fever virus genome in tick from migratory bird, Italy. *Emerg Infect Dis.* 2019;25:1418–20. <http://dx.doi.org/10.3201/eid2507.181345>

Rise in Murine Typhus in Galveston County, Texas, USA, 2018

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Murine typhus, an undifferentiated febrile illness caused by *Rickettsia typhi*, is increasing in prevalence and distribution throughout Texas. In 2018, a total of 40 cases of murine typhus were reported in Galveston County. This increase, unprecedented since the 1940s, highlights the importance of awareness by physicians and public health officials.

Murine typhus is an undifferentiated febrile illness endemic worldwide in tropical and subtropical seaboard regions, where rats and rat fleas (*Xenopsylla cheopis*) are involved in the maintenance and transmission of the etiologic agent, *Rickettsia typhi* (1). Once prevalent in the United States, the disease was nearly eradicated following vector control practices of the 1940s using DDT (2). In 2012, murine typhus was identified in 2 patients from Galveston, Texas. The identification of cases in a city where murine typhus was perceived to have been eliminated prompted the investigation and identification of 12 patients from Galveston County in 2013 (3). Since then, murine typhus has been reported to the Galveston County Health District (GCHD) yearly (1 case in 2014, 8 in 2015, 2 in 2016, and 17 in 2017). Murine typhus has also increased in prevalence and distribution throughout Texas (4). To call attention to this increasingly prevalent disease, we