

**Alert Coordination Center and
Health Emergencies**

Detection of cases of hemorrhagic fever of Crimea-Congo in El Bierzo (León)

August 5, 2022

Summary of the situation and conclusions

In July 2022, two cases of Crimean-Congo hemorrhagic fever (CCHF) have been confirmed in two men residing in the Bierzo region. The first case, a 49-year-old hunter, with a history of tick bite, began symptoms on July 12 and is in stable condition. The second case, 51 years old, was diagnosed retrospectively on July 20, after having died on June 19 of an unknown cause with suspected poisoning by sulfur compounds.

The CCHF virus (CCHFV) is mainly transmitted by ticks of the *Hyalomma* genus and person-to-person transmission can also occur through contact with the blood or secretions of a sick person. FHCC manifests clinically with fever, headache, muscle pain and in a few cases it evolves into severe forms with hemorrhagic manifestations. There is no specific treatment.

Between 2013 and 2022, a total of 12 cases with 4 deaths have been confirmed in Spain: 1 in 2013 in Ávila, 2 in 2016, one of them in Ávila and a secondary case to this in a health worker, 2 in 2018 in Badajoz and Salamanca, 3 in 2020 in Salamanca, 2 in 2021 in Salamanca and León (el Bierzo) and 2 in 2022 in León (el Bierzo).

The circulation of the virus in our country has been known since 2010. Studies have been carried out on ticks and wild and domestic animals to find out the extent of the circulation, having been detected in large areas of Castilla y León, Castilla-La Mancha, Extremadura, and Andalucía. . They have also recently been detected in animal serology studies carried out in Galicia and Catalonia. The province of León and in particular the Bierzo region was considered low risk, given the low presence of *Hyalomma* and the low prevalence of antibodies against the virus in wild and domestic animals in the serological studies carried out, in which was around 1-2%.

The risk of more sporadic cases of CCHF occurring in areas where ticks of the *Hyalomma* genus are present, especially in the population that resides or frequents these areas and carries out activities with greater exposure to their bites, is considered moderate. The impact of the disease is considered low given that, although a low percentage of infections may be a serious illness, the number of people affected would not be high and adequate means of isolation and control of cases are available.

It is recommended to intensify public health measures in areas with the presence of the virus, especially in the area where cases have been recently detected, emphasizing recommendations to the population for the prevention and management of tick bites, active and passive surveillance of cases, and entomological study and virus circulation in animals and humans.

Rationale for risk assessment

In the month of July 2022, two confirmed cases of Crimean-Congo hemorrhagic fever (CCHF) have been reported in two men residing in the Comarca del Bierzo, province of León. CCHF is considered an emerging disease in Eastern European countries. In Spain until 2021 only 10 cases had been detected.

The detection of these two new cases grouped over time and in a specific geographic area considered low risk, where another case had also been detected in 2021, justifies this rapid risk assessment.

In 2019, an analysis of the situation and a broader assessment of the risk of this virus in Spain was carried out, which can be consulted at the following link: <https://www.msbs.gob.es/profesionales/saludPublica/ccayes/analisisituacion/infoSitua.htm>

CCAES team and experts consulted

CCAES team that has participated in this risk assessment, in alphabetical order:

Esteban Aznar Cano, Lucía García San Miguel Rodríguez-Alarcón, Gabriela Saravia Campelli, María José Sierra Moros (CIBERINFEC), Fernando Simón Soria (CIBERESP).

Arbovirus Laboratory. National Center for Microbiology. Carlos III Health Institute.

Anabel Negredo Antón, M^a Paz Sánchez-Seco (CIBERINFEC) and Ana Vázquez González (CIBERESP).

National Epidemiology Center. Carlos III Health Institute.

Beatriz Fernández Martínez (Public Health Surveillance of Communicable Diseases. CIBERESP)

General Directorate of Public Health. Ministry of Health. Castilla and Leon meeting

Rufino Alamo Sanz, Maria del Carmen Pacheco Martinez

General Directorate of Public Health of Galicia

Elvira Iñiguez Pichel and Beatriz Alonso Rodríguez

Ministry of Agriculture, Fisheries and Food

Luis José Romero González; German Caceres Garrido, Elena Garcia Villaceros

National Laboratory of Reference of Infectious Diseases Transmitted by Vectors/National Institute of Health Doutor Ricardo Jorge. Portugal.

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Event information

On July 18, the Autonomous Community of Castilla y León informed the Center for the Coordination of Health Alerts and Emergencies and the National Center for Epidemiology of a suspicion of Crimean Congo hemorrhagic fever (FHCC). It was a 49-year-old male, hunter, resident in Ponferrada (Comarca del Bierzo, León) with a history of tick bites who on July 12 began with gastrointestinal symptoms (abdominal pain, diarrhea and vomiting) along with headache and fever. . On July 16, he was hospitalized with elevated transaminases and thrombocytopenia. On July 19, the National Center for Microbiology (CNM) confirmed positivity against the CCHF virus (CCHF) using real-time PCR. The case was transferred on July 20 to the high-level isolation unit in Donostia, where it is evolving favorably.

On July 20, the National Institute of Toxicology and Forensic Sciences sent the CNM blood samples from a 51-year-old man, an environmental agent, who had died on June 19, 2022 at the Hospital del Bierzo, León, with a probable diagnosis of intoxication. due to cuprocalcium sulfate 20%, hemorrhagic shock and coagulopathy.

Real-time PCR was positive against CCHFV in blood. The case did not refer to a history of tick bite, but he had been sulphating his garden and symptoms began 24 hours later (06.15.2022). He was initially diagnosed with respiratory infection with headache; subsequently he developed abdominal discomfort, diarrhea and on June 16 he was admitted with severe coagulopathy, experiencing progressive deterioration until his death 3 days later. As a consequence of this case, four close contacts were identified who performed the autopsy and another four who handled the samples in the laboratory. Currently, follow-up has ended with no secondary cases detected.

Likewise, in the Bierzo hospital, 50 professionals have been identified who were in contact with the patients (Emergency Services, Internal Medicine and ICU). Health professionals used standard personal protective equipment (PPE) and no secondary cases have been detected.

It is not the first time that a case of FHCC has been detected in El Bierzo. On June 10, 2021, another case of FHCC was confirmed, a woman resident in El Bierzo who had also been in some places in Ourense, around the Ribera Sacra, Galicia. This was the first case in this area, considered until then a low-risk area (see entomological and serological studies carried out).

In Castilla y León, the prevention public health activities of the FHCC have focused in recent years on educating citizens about tick bites and also health professionals on how to remove them and avoid antibiotic chemoprophylaxis. Since the identification of the cases in the Comarca del Bierzo, these communication and health education tasks have intensified. In a complementary way, new entomological and serological studies are being designed in risk groups (health professionals, risk groups due to their work activity (environmental agents, agriculture and livestock veterinarians, hunters) as well as the possibility of population study in the region and seroprevalence in animals to determine the extent of CCHFV circulation in the affected area.

Information about the disease

CCHF is one of the most widespread tick-borne diseases in the world, affecting populations in various parts of Africa, Asia, Eastern Europe and the Middle East. The disease-producing agent is CCHFV, transmitted by the bite of hard ticks (*Ixodidae*), mainly of the genus *Hyalomma* (1). Humans can be infected either through the bite of the tick, which also acts as a reservoir, or through direct contact with secretions or fluids of an infected animal host during the acute phase. Person-to-person transmission may occur through direct contact with blood, secretions, other body fluids, or aerosols from infected individuals or with contaminated inanimate objects, which occurs with

It is more frequent in health personnel, although some studies indicate that this transmission with adequate protection measures is infrequent (2).

After an incubation period of 5-6 days, the majority of symptomatic cases present mild symptoms of 4-5 days. days of evolution characterized by fever, headache, myalgia and dizziness. In a few cases, the disease progresses to a severe clinical picture with hemorrhagic manifestations on the skin and mucous membranes, such as petechiae or bleeding, which can progress to death (3). The fatality rate ranges from 3% to 40%, depending on the studies (4). Serological studies carried out in endemic countries indicate that infection in humans can be asymptomatic, although it is difficult to establish the percentage (5,6).

It is unknown whether the infection produces immunity against the virus, although no cases of CCHFV reinfection have been identified (7). Diagnosis is made by virus isolation, genome detection by PCR (specific, sensitive and rapid method) or serology (IgM and IgG antibodies are detected by ELISA and immunofluorescence assays from about 7 days after the onset of the disease) (8). There is no vaccine for this disease and no specific treatment, although ribavirin has been used with apparent benefit.

Information about the circulation of the virus in Spain and in the Bierzo region.

In the Iberian Peninsula, *Hyalomma marginatum* and *Hyalomma lusitanicum* are the most abundant species of this genus of ticks (9). VFHCC was identified for the first time in Spain in 2010, in ticks captured on deer from a hunting estate in Cáceres, on the banks of the Tagus River on the Portuguese border (10). A subsequent study carried out in various areas of the country, in different species of ticks (2,053) obtained from cattle and vegetation and sera from people exposed to ticks in Cáceres (114) and La Rioja (114), did not show the presence of the virus in any sample (11). In another study carried out between 2011 and 2015, 1,579 ticks were captured on wild and domestic ungulates in Cáceres, Toledo, Segovia and Huesca.

CCHFV RNA was detected in *H. lusitanicum* and *H. marginatum* in 3.25% of the ticks captured in Cáceres and was not detected in the rest of the provinces studied (12).

Given the detection of the first two human cases of CCHF in 2016, a three-phase study was launched to assess the situation and risk of CCHFV infection in Spain. The first phase was carried out between September 2016 and February 2017 with the aim of detecting the virus in ticks of the *Hyalomma* genus, both in wildlife and in domestic livestock animals. For this purpose, tick captures were carried out in the area where the virus had previously been identified in this vector and the area where the infection was transmitted in the first human case. CCHFV-positive ticks were identified in seven of the eleven regions studied (belonging to Extremadura, Castilla-La Mancha, Castilla y León and Madrid). All positive ticks were captured on wild animals. The second phase of the study was carried out with ticks collected in the vegetation and ticks infected with the virus were identified in several regions of Andalusia in the provinces of Cádiz and Córdoba (Figure 1). Subsequently, in this second phase and during 2018, a serological study was carried out on domestic and wild animals from the five autonomous communities in which ticks had been studied (Andalusia, Castilla-La Mancha, Castilla y León, Extremadura and Madrid).). Three zones were defined based on the results obtained in the studies on ticks: zone 1, counties with identification of infected *Hyalomma* ticks; zone 2, counties with the presence of *Hyalomma* ticks but which were negative; and zone 3, counties with a very low risk of the presence of ticks of the *Hyalomma* genus. The prevalence of infection in wild/domestic animals detected was 69.5%/15.8% in zone 1, 25.7%/3.7% in zone 2 and 2.7%/6.7% in zone 2. zone 3. The results of this study in the province of León resulted in a positivity of 1% in domestic animals (2 positives out of 199 samples) and 2.2% in wild animals (1 positive out of 45 samples). On the other hand, the autonomous community of Galicia, in June 2021, carried out a serological study in the wild horses of the Sierra da Groba,

Pontevedra. A total of 182 horse samples were analyzed, confirming a seroprevalence of 1.1% (95% CI, 0-3%) of antibodies against CCHFV.

Since 1995 in the autonomous community of Castilla y León, entomological surveillance of ticks has been carried out, mainly from those fixed on people who are sent by health centers for analysis. In 2021, 388 ticks from the province of León were studied, 159 from the Bierzo health area. In that area, the ticks studied included specimens belonging to 8 species, the most frequent being *Ixodes ricinus* (41.51%) and *Dermacentor marginatus* (18.87%). *Hyalomma* sp. accounted for 12.58% (*H. marginatum* 7.55% and *H. lusitanicum* 5.03%), exceeding the percentage found in the health area of León, which accumulated 7.11% of the total (with 4.89% and 2.22%, respectively). Likewise, differences are observed between the months of *Hyalomma* activity in both health areas. In the León health area, *Hyalomma marginatum* was only collected from May to August, while in the Bierzo health area *Hyalomma marginatum* was detected associated with stings from January to September and *Hyalomma lusitanicum* from June to August. Since 2020 all ticks of the genus *Hyalomma* are sent to the National Center for Microbiology to investigate VFHCC. To date, the virus has not been detected in any of the ticks removed from people. The virus has only been detected in this autonomous community in *Hyalomma* in the only positive specimen of the first phase of the national study, located on a fallow deer in an intensive preserve, and punctually in other bovine ticks in the provinces of Salamanca and Ávila in the year 2021. However, between 2014 and 2019 a clear increase in *H.lusitanicum* ticks that have bitten people has been detected (13).

In 2017, the REGAVIVEC (Galician Vector Surveillance Network) was created through the signing of a collaboration agreement between the Ministry of Health (General Directorate of Public Health), the Ministry of Rural Environment (Animal Health) and the University of Santiago de Compostela. In 2019, surveillance of ticks in human bites was incorporated into these activities through the collaboration of health centers throughout the autonomous community of Galicia. The year 2020 was the first time that the tick *H. marginatum*, in the province of Ourense in the Trives area. In 2021, it was detected in the southern area of Ourense, which borders Zamora and Portugal, and in the south of the province of Lugo, in Quiroga. These ticks come from human bites. In addition, *Hyalomma* ticks were detected on horses from the Sierra de Groba in the regions of Pontevedra, Baixo Miño and Val Miño. All ticks collected have been PCR VFHCC negative.

In Portugal, the presence of *H. lusitanicum* has been detected mainly in the south of the country and *H. marginatum* throughout the territory. Since 1985, when 2 cases confirmed by CCHF neutralizing serology were detected in the Alentejo region, no human cases have been detected again. The REVIVE network (Rede Vigilância de Vetores) was implemented in 2008. Since 2016, all ticks captured on game animals have been negative.

In 2019, around 50 *H. lusitanicum* and *H. marginatum* were captured on deer and wild boar 2 km from the border with the province of Cáceres that were negative for VFHCC. All samples of suspected cases detected in hospitals have been negative.

In Catalonia, data from serological studies carried out between 2014 and 2020 in wild animals have been published, with positive results in Hispanic goats and wild boars in the Ebro delta area (14).

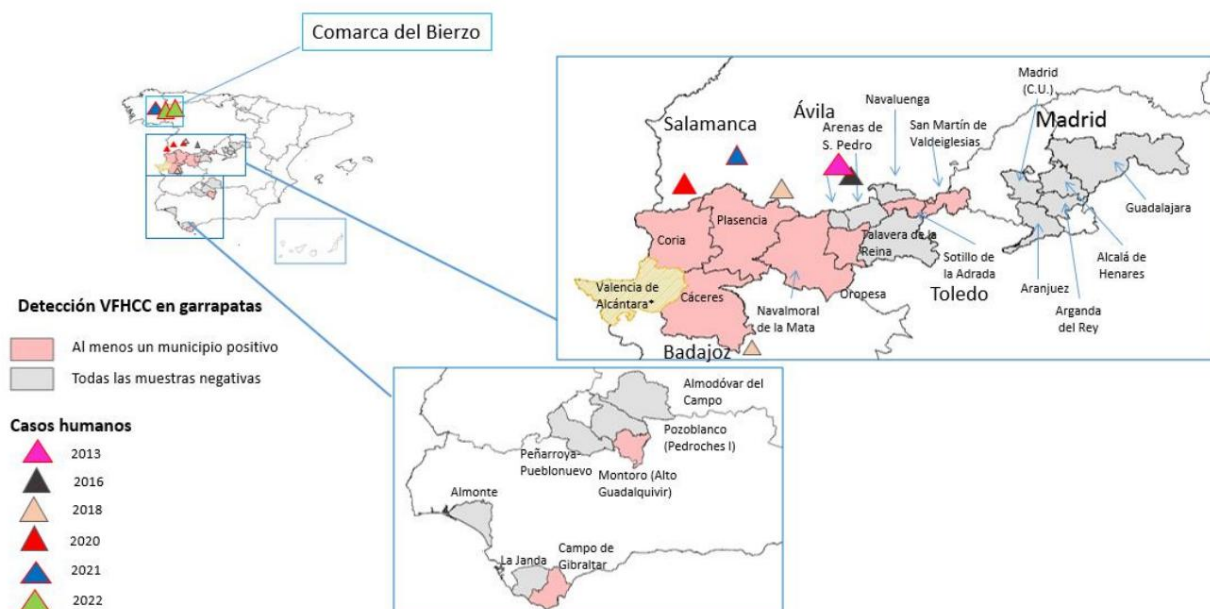
In Spain, from 2013 to 2022, 12 human cases of CCHF have been confirmed with 4 deaths.

The first case was retrospectively confirmed by positive PCR in a woman who developed symptoms in 2013 in Ávila (14). The first 2 cases detected in the symptomatic phase date back to September 2016: a patient exposed to ticks, possibly in the province of Ávila, who died that year, and a secondary case in health personnel who had close contact with the former during hospital admission.

in Madrid. In August 2018, the third case was reported, a 74-year-old man who had participated in hunting activities in the province of Badajoz, who died during his hospital admission, and in 2019 it was reported, retrospectively in the context of a study of investigation of the University of Salamanca, another case who had been admitted in 2018 to the Salamanca hospital for a non-specific viral infection that was

recovered without problems. In 2020, 3 more cases were detected in the Sierra de Béjar, south of the province of Salamanca, one of them deceased. In 2021 another case was detected in the Sierra de Béjar and the first case in Bierzo. Finally, in 2022 the two cases mentioned previously in the description of the event have been confirmed (Figure 1).

Figure 1. Results of the Crimean-Congo fever virus (FCCV) detection study in ticks collected in animals and in vegetation by livestock regions in 2016-2018, and approximate location of the places where transmission of the virus to human cases detected from 2013 to 2022 could have occurred.



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*municipality where the first studies of positive *Hyalomma* ticks were carried out in 2010

Risk assessment for Spain

CCHFV is present in Spain and its presence has been known since 2010. The circulation of the virus is considered to be uneven depending on the geographical areas. With the data available up to 2021, the Bierzo region, as well as the provinces of León, Orense and Pontevedra, were considered low risk, given the scarcity of *Hyalomma* ticks found through studies and entomological surveillance and prevalence studies carried out on animals, with a percentage of seropositivity between 1 and 2%. The detection of the first human case in 2021 and the two cases in 2022, all residing in the same region, highlight the need for further studies to estimate the current level of virus circulation in this area.

Once the virus is present in ticks in an area, whether it amplifies and ends up being transmitted to people depends on local factors that change from year to year: humidity, temperature, vegetation, abundance of small mammals to larval stages and presence of large ungulates for adult ticks. In this cycle, people would be accidentally bitten by the tick, which can also act as a reservoir. Tick activity is highest in hot and dry seasons

mainly between May and August, without excluding the first months of the year in regions with more benign weather. In the northernmost territories of the country it would be in summer and in the south from spring until the beginning of autumn.

The risk of transmission of CCHFV in the Comarca del Bierzo, as in the rest of the areas where virus circulation has been evidenced in ticks, animals or human cases have been detected, is moderate, especially in the population with greater exposure to tick bites - people in contact with animals or who carry out outdoor activities in the countryside -. For the rest of Spain, it is considered low. The risk is conditioned to the activity of the vectors, whose activity is maximum in the summer season.

In general, the impact of the disease is considered low since, although it can be a serious disease in some cases, the number of people affected would probably not be high, and adequate means of isolation and control of cases are available.

recommendations

- Address the surveillance and control of the Crimean-Congo hemorrhagic fever virus in a comprehensive and multidisciplinary manner within the framework of One Health, especially in the territories where the virus has been identified, including entomological surveillance of tick species. potentially vectors/reservoir and reinforcing coordination at the local, regional and national levels between the human, animal and environmental health sectors.
- Strengthen campaigns for the prevention and management of tick bites in areas where cases have occurred, as well as in known areas with high circulation of the virus, and disseminate information on measures to prevent transmission of the disease to groups risk, health workers and general population. People who work in contact with animals (domestic or wild) should observe the usual individual protection measures to minimize contact with the animal's blood and tissues, as well as to avoid possible tick bites.
- Inform health professionals about this disease in the areas where the cases have occurred, as well as in known areas with high circulation of the virus, so that an early diagnosis and timely management can be carried out if the appearance of the disease occurs. more cases of this infection. In these areas, carry out surveillance of the disease in humans at least during the period of maximum activity of the vector.
- Carry out entomological and seroprevalence studies in animals and humans in the areas where produced the cases.
- Investigate the CCHFV strains detected in Spain to learn about their characteristics and behaviour.

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