Crimean-Congo hemorrhagic fever virus (CCHF) in Iberia

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No conflict of interest

About the virus

Overview of the virus

Iberian case series (2013-2025)

Restrospective study of all cases identified nationwide

Tick-borne diseases

Why is this happening?

Future directions

Resources for optimal management of these disease

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CCHFV

History

- 1944


- 1956

- 1969

- 1976: Confirmation of differents strains
- 1980: Cases in Europe, Asia and Africa
- 1990: Cases in Balcanes, Turkey and Middle East
- 2000: Expantion to Africa, Asia, China
- 2010: Outbreaks in Iran and Pakistan
- 2020

What is Crimean-Congo haemorrhagic fever?

VIRUS

Order *Bunyaviridae* → family *Nairoviridae*
Negative single-strand RNA viruses [1]

VECTOR

Genus *Hyalomma*
Hyalomma marginatum marginatum

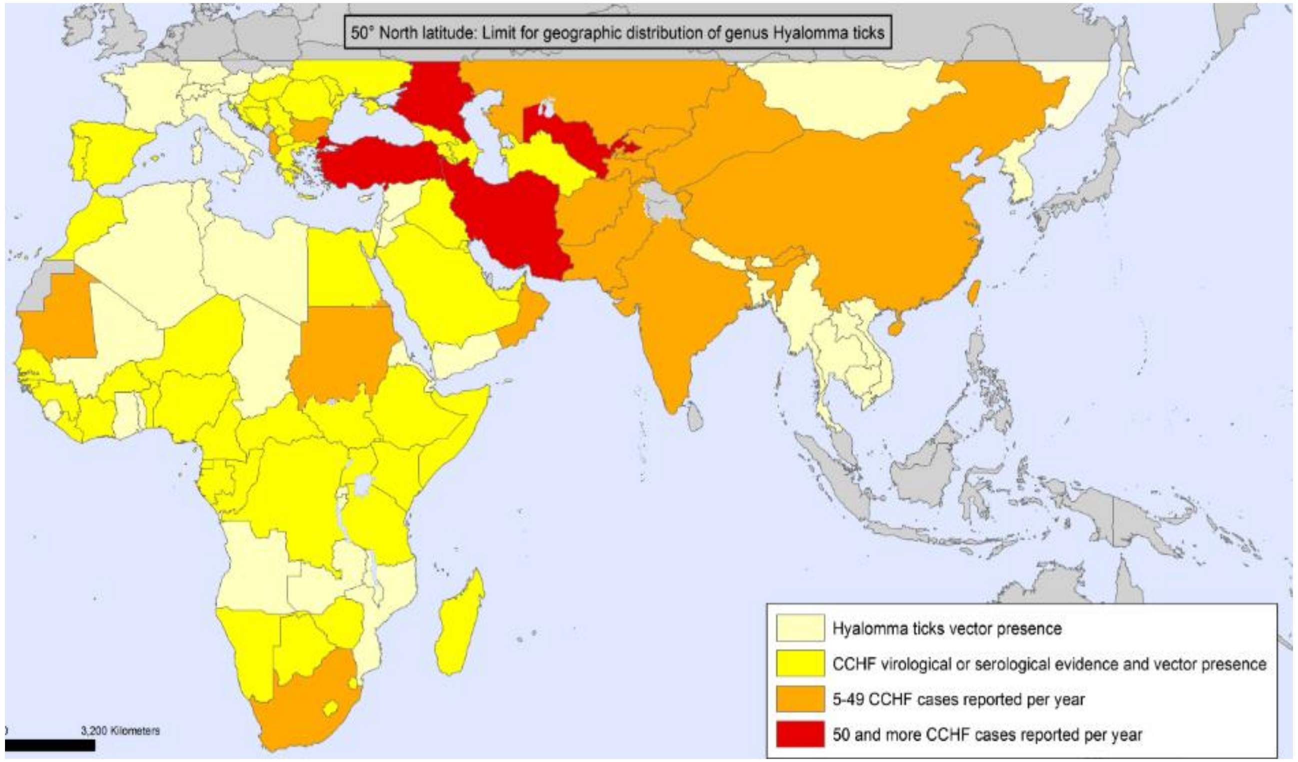
GEOGRAPHICAL DISTRIBUTION

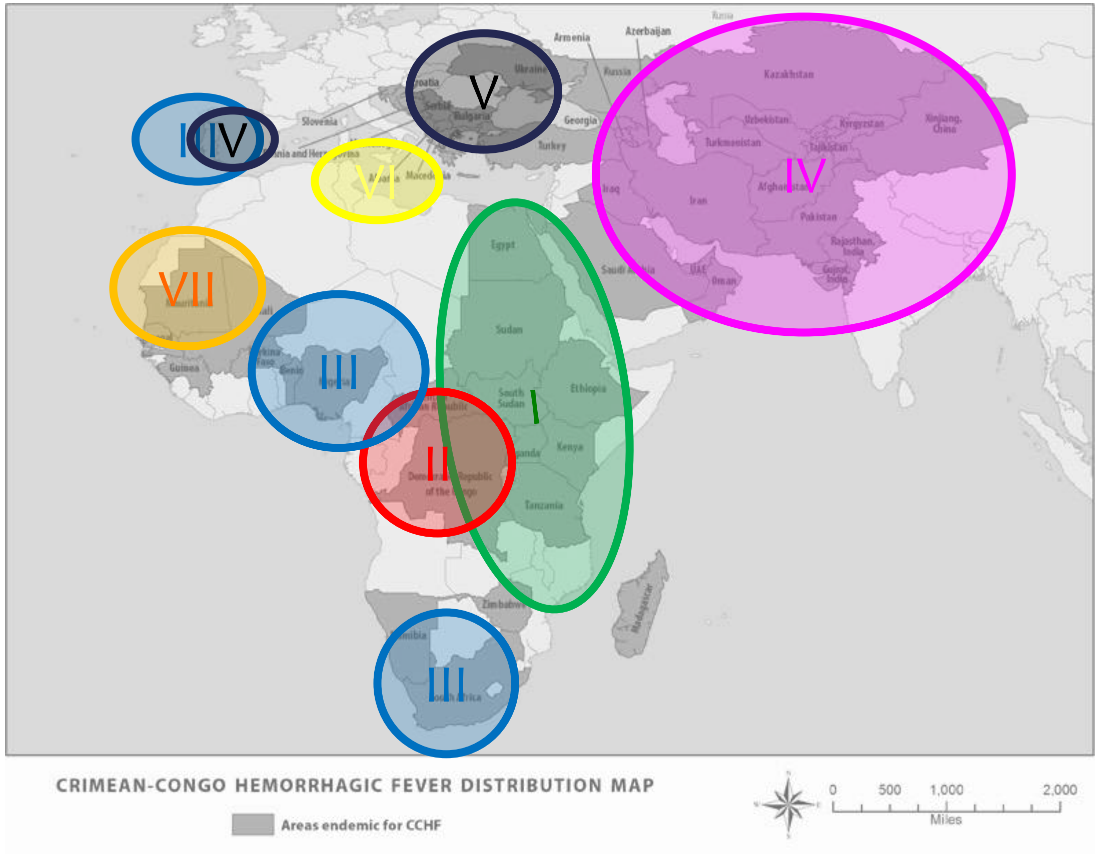
Africa: Central and South African countries
Asia: Turkey, Iran, Pakistan, India, China…
Europe: Ukraine, Romania, Balkan countries, **Portugal**, **Spain** [2]

1.Ergönül; Lancet Infect Dis 2006; 6: 203–14 2. World Health Organization (WHO); https://www.who.int/health-topics/crimean-congo-haemorrhagic-fever#tab=tab_1

CCHFV

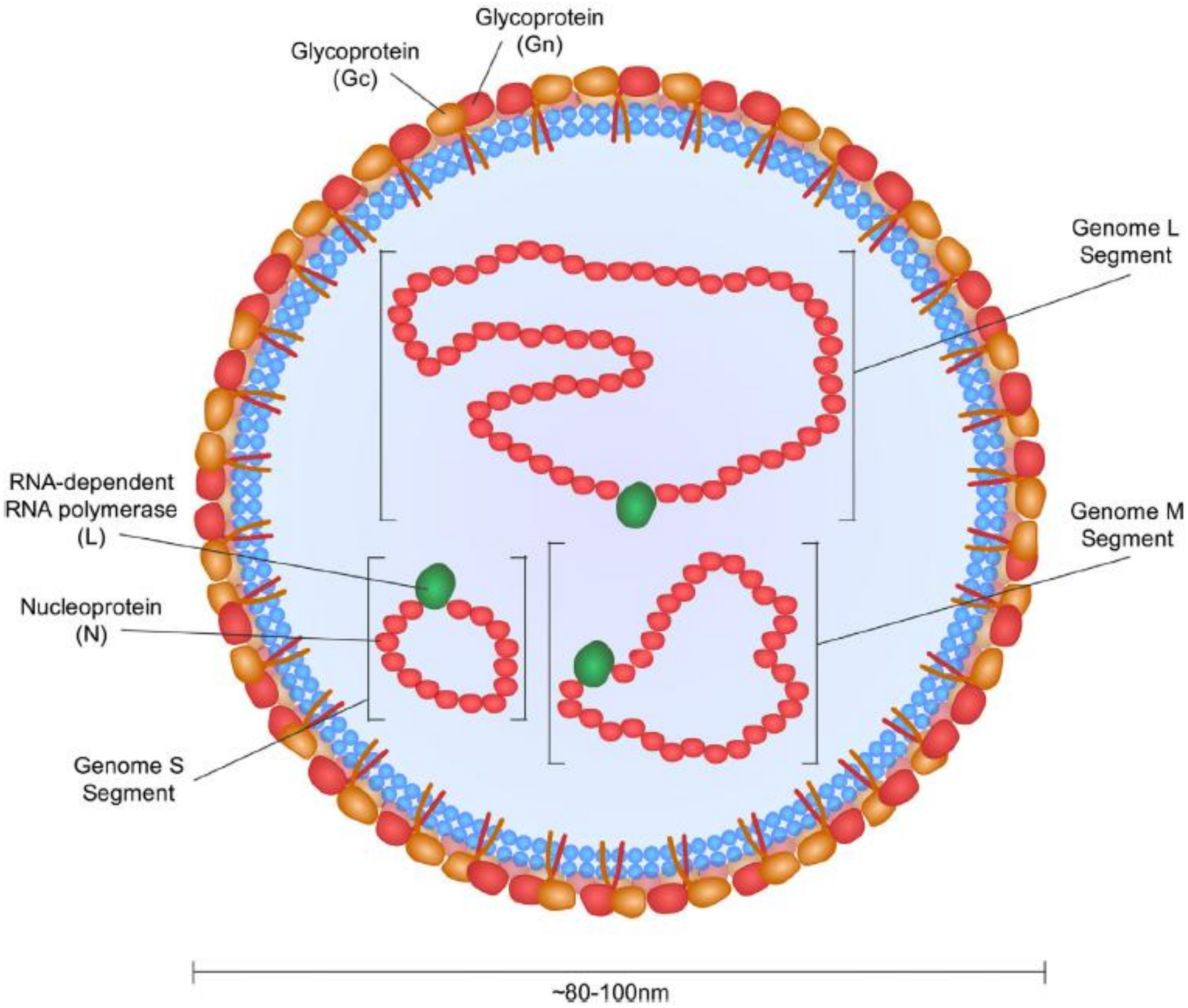
World distribution



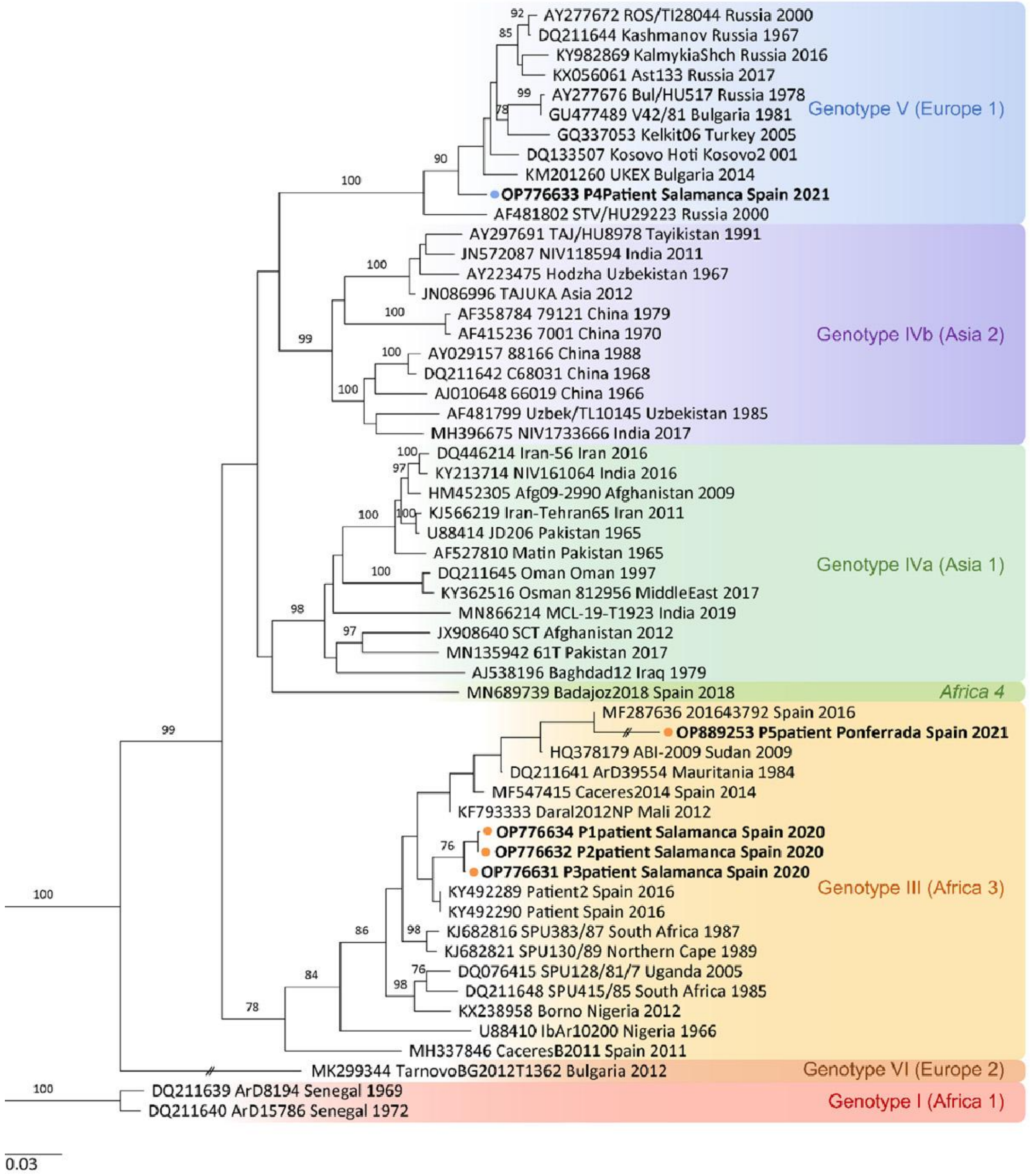


CCHFV

Virus

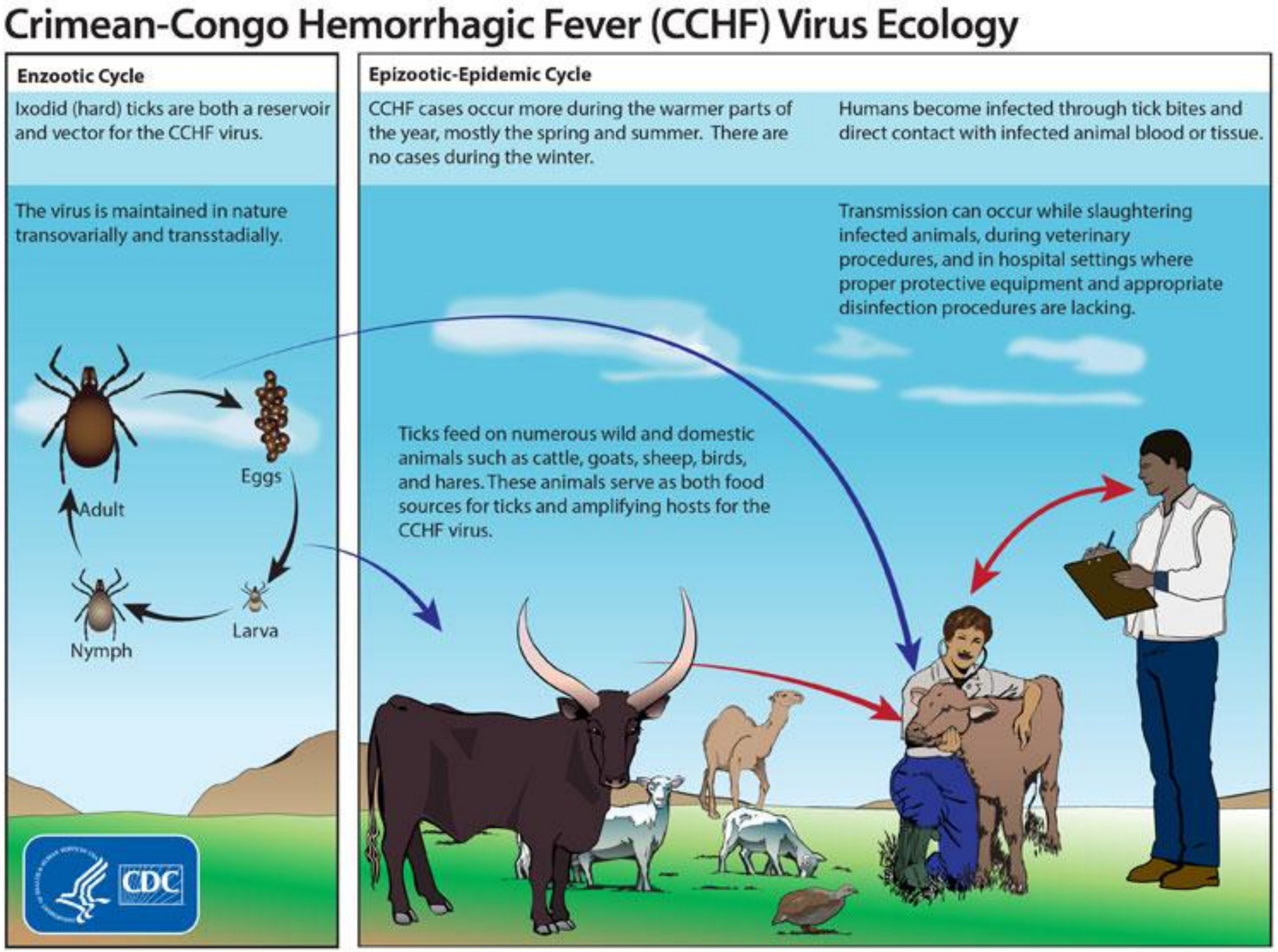


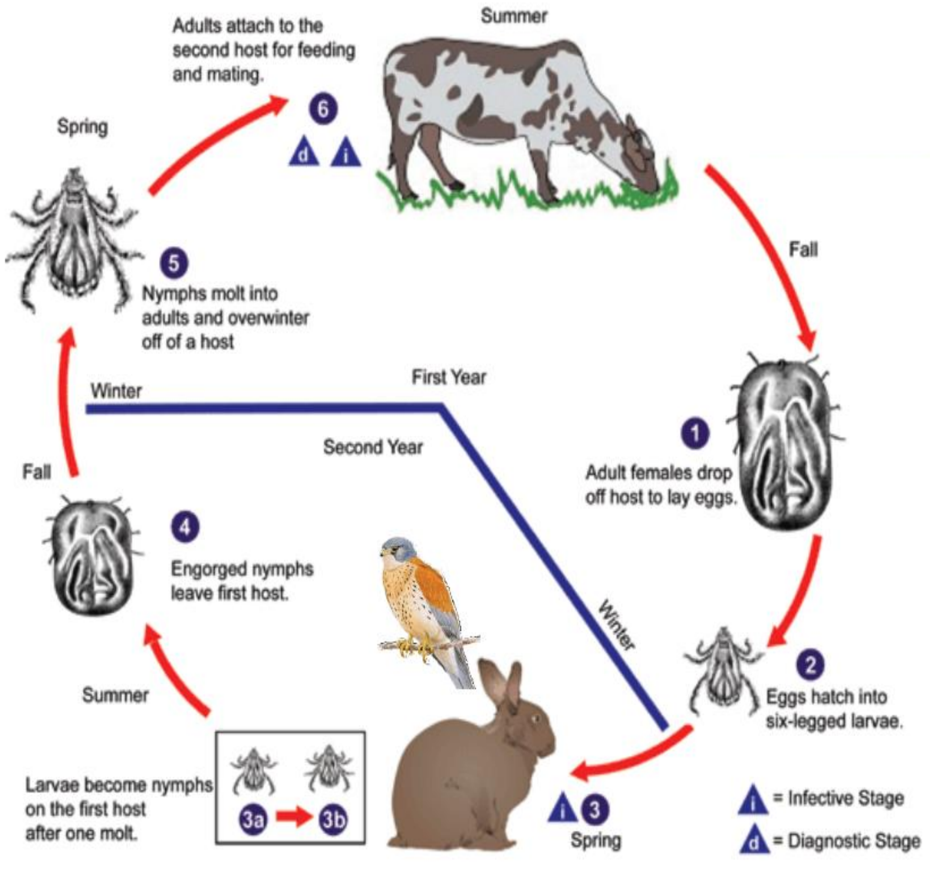
Glycoprotein (Gn)
Glycoprotein (Gc)
Genome L Segment
RNA-dependent RNA polymerase (L)
Genome M Segment
Nucleoprotein (N)
Genome S Segment
~80-100nm



AY277672 ROS/TI28044 Russia 2000
DQ211644 Kashmanov Russia 1967
KY982869 KalmykiaShch Russia 2016
KX056061 Ast133 Russia 2017
AY277676 Bul/HU517 Russia 1978
GU477489 V42/81 Bulgaria 1981
GQ337053 Kelkit06 Turkey 2005
DQ133507 Kosovo Hoti Kosovo2 001
KM201260 UKEX Bulgaria 2014
OP776633 P4Patient Salamanca Spain 2021
AF481802 STV/HU29223 Russia 2000
Genotype V (Europe 1)
AY297691 TAJ/HU8978 Tayikistan 1991
JN572087 NIV118594 India 2011
AY223475 Hodzha Uzbekistan 1967
JN086996 TAJUKA Asia 2012
AF358784 79121 China 1979
AF415236 7001 China 1970
AY029157 88166 China 1988
DQ211642 C68031 China 1968
AJ010648 66019 China 1966
AF481799 Uzbek/TL10145 Uzbekistan 1985
MH396675 NIV1733666 India 2017
Genotype IVb (Asia 2)
DQ446214 Iran-56 Iran 2016
KY213714 NIV161064 India 2016
HM452305 Afg09-2990 Afghanistan 2009
KJ566219 Iran-Tehran65 Iran 2011
U88414 JD206 Pakistan 1965
AF527810 Matin Pakistan 1965
DQ211645 Oman Oman 1997
KY362516 Osman 812956 MiddleEast 2017
MN866214 MCL-19-T1923 India 2019
JX908640 SCT Afghanistan 2012
MN135942 61T Pakistan 2017
AJ538196 Baghdad12 Iraq 1979
Genotype IVa (Asia 1)
MN689739 Badajoz2018 Spain 2018
Africa 4
MF287636 201643792 Spain 2016
OP889253 P5patient Ponferrada Spain 2021
HQ378179 ABI-2009 Sudan 2009
DQ211641 ArD39554 Mauritania 1984
MF547415 Caceres2014 Spain 2014
KF793333 Daral2012NP Mali 2012
OP776634 P1patient Salamanca Spain 2020
OP776632 P2patient Salamanca Spain 2020
OP776631 P3patient Salamanca Spain 2020
KY492289 Patient2 Spain 2016
KY492290 Patient Spain 2016
KJ682816 SPU383/87 South Africa 1987
KJ682821 SPU130/89 Northern Cape 1989
DQ076415 SPU128/81/7 Uganda 2005
DQ211648 SPU415/85 South Africa 1985
KX238958 Borno Nigeria 2012
U88410 IbAr10200 Nigeria 1966
MH337846 CaceresB2011 Spain 2011
Genotype III (Africa 3)
MK299344 TarnovoBG2012T1362 Bulgaria 2012
Genotype VI (Europe 2)
DQ211639 ArD8194 Senegal 1969
DQ211640 ArD15786 Senegal 1972
Genotype I (Africa 1)
0.03

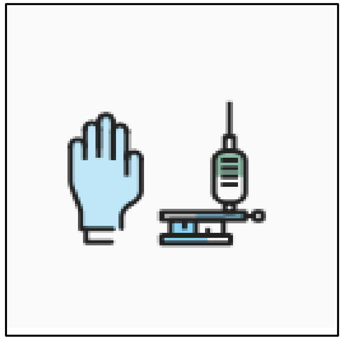
Biological cycle of Crimean Congo Hemorrhagic Virus



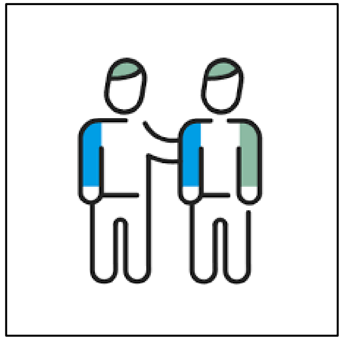


Transmission

Nosocomial transmission

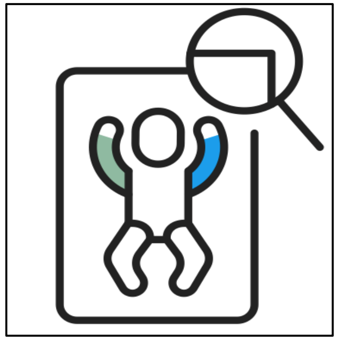


Health professional transmission

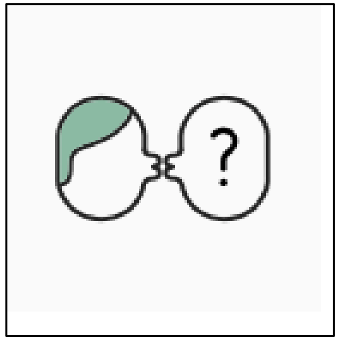


Community spread

Vertical transmission



Transmission through breastfeeding?



Sexual transmission?

Transmission by hemodonation?

Laboratory regulations

8

- Germany → 2
- Switzerland → 1
- France → 1
- Italy → 1
- United Kingdom → 1
- Sweden → 1
- Hungary → 1
- Spain → 2* →
  - Centro de Investigación Sanidad Animal (CISA), Valdeolmos
  - Centro Nacional de Microbiología (CNM), Majadahonda

LA GACETA

El laboratorio de alta contención de la Universidad ya estudia distintos virus

La sala, con un nivel de protección 3, ha sido utilizada por investigadores de enfermedades tropicales para estudiar garrapatas que transmiten la fiebre hemorrágica Crimea-Congo

R.D.L / 08 FEB 2020 / 22:26 H.

Expertos en seguridad biológica dentro del laboratorio de alta contención de la Universidad de Salamanca. | CUESTA

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The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Autochthonous Crimean–Congo Hemorrhagic Fever in Spain

A. Negredo, F. de la Calle-Prieto, E. Palencia-Herrejón, M. Mora-Rillo, J. Astray-Mochales, M. P. Sánchez-Seco, E. Bermejo Lopez, J. Menárguez, A. Fernández-Cruz, B. Sánchez-Artola, E. Keough-Delgado, E. Ramírez de Arellano, F. Lasala, J. Milla, J.L. Fraile, M. Ordobás Gavín, A. Martinez de la Gándara, L. López Perez, D. Diaz-Diaz, M.A. López-García, P. Delgado-Jimenez, A. Martín-Quirós, E. Trigo, J.C. Figueira, J. Manzanares, E. Rodriguez-Baena, L. Garcia-Comas, O. Rodríguez-Fraga, N. García-Arenzana, M.V. Fernández-Díaz, V.M. Cornejo, P. Emmerich, J. Schmidt-Chanasit, and J.R. Arribas, for the Crimean Congo Hemorrhagic Fever@Madrid Working Group*

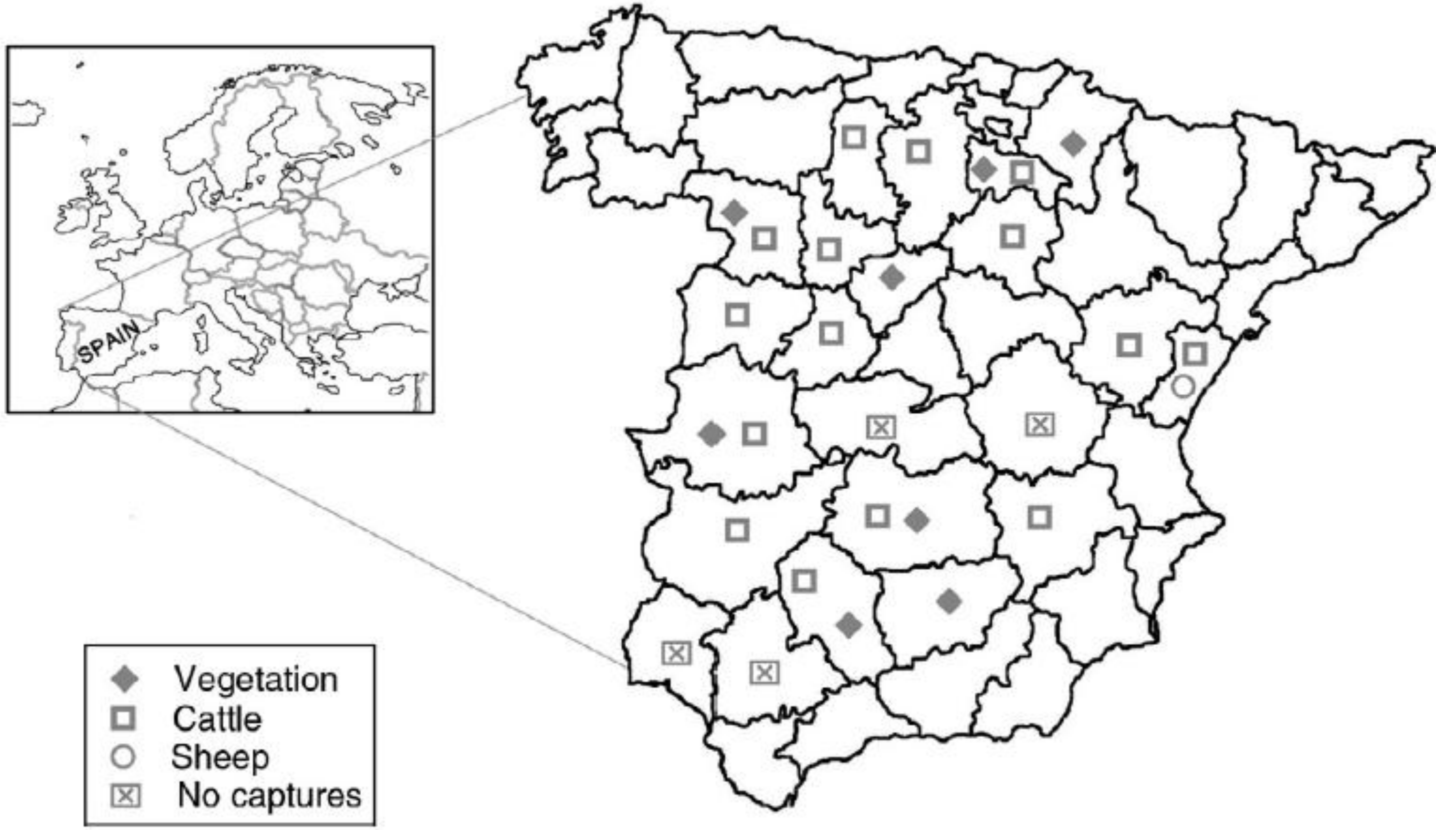
Enfermedades Infecciosas y Microbiología Clínica
www.elsevier.es/eimc

Original article

Molecular (ticks) and serological (humans) study of Crimean-Congo hemorrhagic fever virus in the Iberian Peninsula, 2013–2015

Ana M. Palomar[a], Aránzazu Portillo[a], Sonia Santibáñez[a], Lara García-Álvarez[a], Agustín Muñoz-Sanz[b], Francisco J. Márquez[c], Lourdes Romero[a], José M. Eiros[d], José A. Oteo[a,*]

[a] Centro de Rickettsiosis y Enfermedades Transmitidas por Artrópodos Vectores, Departamento de Enfermedades Infecciosas, Hospital San Pedro-CIBIR
[b] Servicio de Patología Infecciosa, Hospital Universitario de Badajoz, Badajoz, Spain
[c] Departamento de Biología Animal, Biología Vegetal y Ecología, Universidad de Jaén, Facultad de Ciencias Experimentales, Jaén, Spain
[d] Facultad de Medicina, Universidad de Valladolid, Microbiología, Valladolid, Spain



RESEARCH

Epidemiologic Survey of Crimean-Congo Hemorrhagic Fever Virus in Suids, Spain

Mario Frías, Kerstin Fischer, Sabrina Castro-Scholten, Caroline Bost, David Cano-Terriza, Maria Ángeles Risalde, Pelayo Acevedo, Saúl Jiménez-Ruiz, Balal Sadeghi, Martin H. Groschup, Javier Caballero-Gómez, Ignacio García-Bocanegra

Table 1. Distribution and seroprevalence of Crimean-Congo hemorrhagic fever in wild boars and extensively raised Iberian pigs, Spain*

	Wild boars			Iberian pigs		
Variable	No. positive/no. analyzed	Seroprevalence, % (95% CI)	p value	No. positive/no. analyzed	Seroprevalence, % (95% CI)	p value
Season						
2015–16	10/20	50.0 (28.8–71.1)	0.8885	NA	NA	
2016–17	16/45	35.5 (22.6–50.2)		NA	NA	
2017–18	27/66	40.9 (29.5–53.0)		1/126	0.8 (0–2.3)	0.0123
2018–19	26/63	41.2 (29.6–53.6)		6/77	7.8 (1.8–13.8)	
2019–20	20/52	38.4 (26.0–52.1)		0/48	0 (0–0)	
2020–21	7/21	33.3 (15.9–55.1)		NA	NA	
Province						
Badajoz	7/32	21.9 (7.6–36.2)	0.0119	0/79	0 (0–0.3)	<0.001
Cáceres	20/45	44.4 (30.5–59.1)		6/46	13.0 (3.3–22.8)	
Córdoba	51/100	51.0 (41.2–60.8)		1/126	0.8 (0–2.3)	
Jaén	13/44	29.5 (17.5–44.1)		NA	NA	
Sevilla	15/46	32.6 (19.1–46.2)		NA	NA	
Age						
Yearling	9/45	20.0 (0–26.1)	<0.001	NA	NA	NA
Subadult	23/70	32.9 (21–38.6)		NA	NA	
Adult	72/147	49.0 (41.0–57.0)		NA	NA	
Sex						
M	41/124	33.1 (25.2–41.7)	0.0435	NA	NA	NA
F	64/139	46.0 (37.8–54.3)		NA	NA	

*NA, not applicable.


HOSPITAL UNIVERSITARIO DE SALAMANCA
URGENCIAS

Research

Crimean-Congo haemorrhagic fever (CCHF) virus-specific antibody detection in blood donors, Castile-León, Spain, summer 2017 and 2018

Lía Monsalve Arteaga[1] , Juan Luis Muñoz Bellido[2,3,4] , María Carmen Vieira Lista[1] , María Belén Vicente Santiago[1] , Pedro Fernández Soto[1] , Isabel Bas[5] , Nuria Leralta[5] , Fernando de Ory Manchón[6] , Ana Isabel Negredo[5] , María Paz Sánchez Seco[5] , Montserrat Alonso Sardón[1] , Sonia Pérez González[7] , Ana Jiménez del Bianco[7] , Lydia Blanco Peris[7] , Rufino Alamo-Sanz[8] , Roger Hewson[9] , Moncef Belhassen-García[1] , Antonio Muro[1]

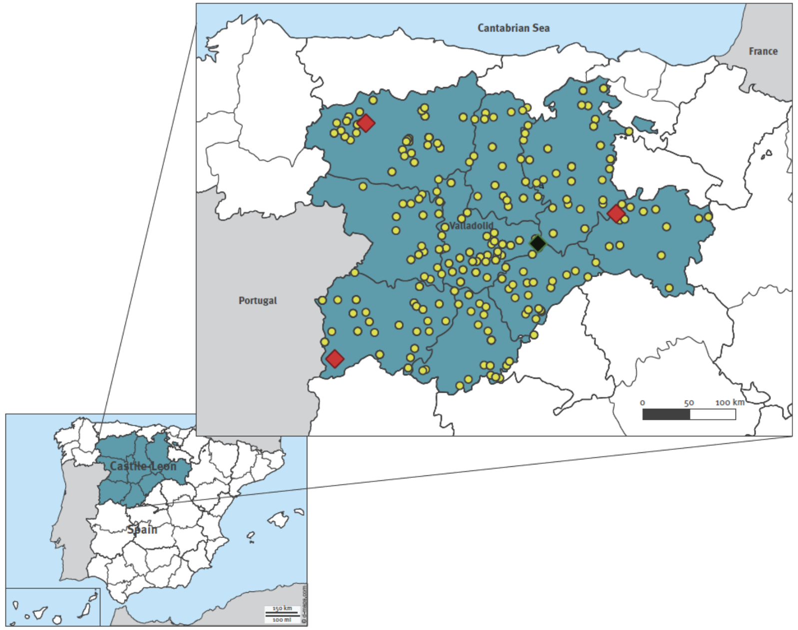
1. Infectious and Tropical Diseases Group (e-INTRO). IBSAL-CIETUS (Biomedical Research Institute of Salamanca-Research Center for Tropical Diseases at the University of Salamanca), Faculty of Pharmacy, University of Salamanca, Salamanca, Spain
2. Instituto de Investigación Biomédica de Salamanca (IBSAL), Universidad de Salamanca, CSIC, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain
3. Servicio de Microbiología y Parasitología, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain
4. Departamento de Ciencias Biomédicas y del Diagnóstico, Universidad de Salamanca, Salamanca, Spain
5. Arbovirus and Imported Viral Diseases Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Red de Investigación Colaborativa en Enfermedades Tropicales, Madrid, Spain
6. Centro Nacional de Microbiología, Ciber en Salud Pública (CIBERESP), Instituto de Salud Carlos III, Majadahonda, Madrid, Spain
7. Center for Hemodonation and Hemotherapy of Castilla y León (CHEMCYL), Valladolid, Spain
8. Consejería de Sanidad Junta Castilla y León, Valladolid, Spain
9. Public Health England, Porton Down, Wiltshire, Salisbury, United Kingdom

Correspondence: Moncef Belhassen-García (belhassen@usal.es)

Prevalence study in healthy donors: 2017-2018, 516 donors (0,58-1,16%)

Characteristics	n	%
Age (years), mean ± SD	46.3 ± 11.2	
Male sex	353	68.4
Professional activities at risk	109	21.1
Agriculture/shepherding activities	81	15.7
Slaughtering	6	1.2
Hunting	2	0.4
Veterinarians	1	0.2
Healthcare workers (nurses and laboratory technicians)	10	1.9
Rural population	448	86.8
Contact with animals	354	68.6
Animal husbandry practices	108	20.9
History of a tick bite	79	15.3

SD: standard deviation.



CCHFV: Crimean-Congo haemorrhagic fever virus.

Yellow circles: blood donors' places of residence; red diamonds: individuals with confirmed serology for IgG antibodies against CCHFV; black diamond: individual with a result concluded as indeterminate.

	ELISA IgG		IFA IgG		ELISA IgM		IFA IgM		Final result
	Vector Best[a]	In house[b]	GPC	NP	Vector Best[a]	In house[b]	GPC	NP	
1	10.01 (+)	3.4 (+)	–	–	0.50 (–)	0.3 (–)	–	–	+
2	10.01 (+)	0.1 (–)	–	–	0.01 (–)	Not done	Not done	Not done	–
3	10.01 (+)	6.4 (+)	Indeterminate	Indeterminate	0.01 (–)	Not done	Not done	Not done	+
4	2.59 (+)	0.2 (–)	–	–	0 (–)	Not done	Not done	Not done	–
5	0.90 (+)	0.5 (–)	+	Indeterminate	0.01 (–)	Not done	Not done	Not done	+
6	0.01 (–)	0.3 (–)	Indeterminate	+	0 (–)	Not done	Not done	Not done	Indeterminate

+: positive; –: negative; GPC: glycoprotein precursor construct; ELISA: enzyme-linked immunosorbent assay; IFA: immunofluorescence assay; NP: nucleoprotein.

ELISA results are expressed as a ratio sample absorbance/cut-off. IFA is expressed as a qualitative result obtained at 1:10 dilution.

[a] This assay was performed in triplicate.

[b] In-house ELISA performed at the National Centre of Microbiology.

RESEARCH ARTICLE

New circulation of genotype V of Crimean-Congo haemorrhagic fever virus in humans from Spain

Lia Monsalve Arteaga[1], Juan Luis Muñoz Bellido[2], Ana Isabel Negredo[3], Jorge García Criado[4], Maria Carmen Vieira Lista[1], Jesús Ángel Sánchez Serrano[4], María Belén Vicente Santiago[1], Amparo López Bernús[1,5], Fernando de Ory Manchón[6], María Paz Sánchez Seco[3], Nuria Leralta[6], Montserrat Alonso Sardón[1], Antonio Muro[1]*, Moncef Belhassen-García[1,5]*

1 Infectious and Tropical Diseases Group (e-INTRO), IBSAL-CIETUS (Biomedical Research Institute of Salamanca-Research Center for Tropical Diseases at the University of Salamanca), Faculty of Pharmacy, University of Salamanca, Salamanca, Spain, **2** Servicio de Microbiología y Parasitología, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain, **3** Arbovirus and Imported Viral Diseases Unit, Centro Nacional de Microbiología, Instituto de Salud Carlos III, Red de Investigación Colaborativa en Enfermedades Tropicales, Madrid, Spain, **4** Emergency Department, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain, **5** Internal Medicine and Infectious Disease Department, Complejo Asistencial Universitario de Salamanca, Salamanca, Spain, **6** Centro Nacional de Microbiología, Instituto de Salud Carlos III, Majadahonda, Madrid, España; Ciber en Salud Pública (CIBERESP), Instituto de Salud Carlos III, Spain

* ama@usal.es (AM); belhassen@usal.es (MB-G)

ED, 2017-2018, 133 Febrile syndromes (4 CCHF, 1 acute infection y 3 past infections)

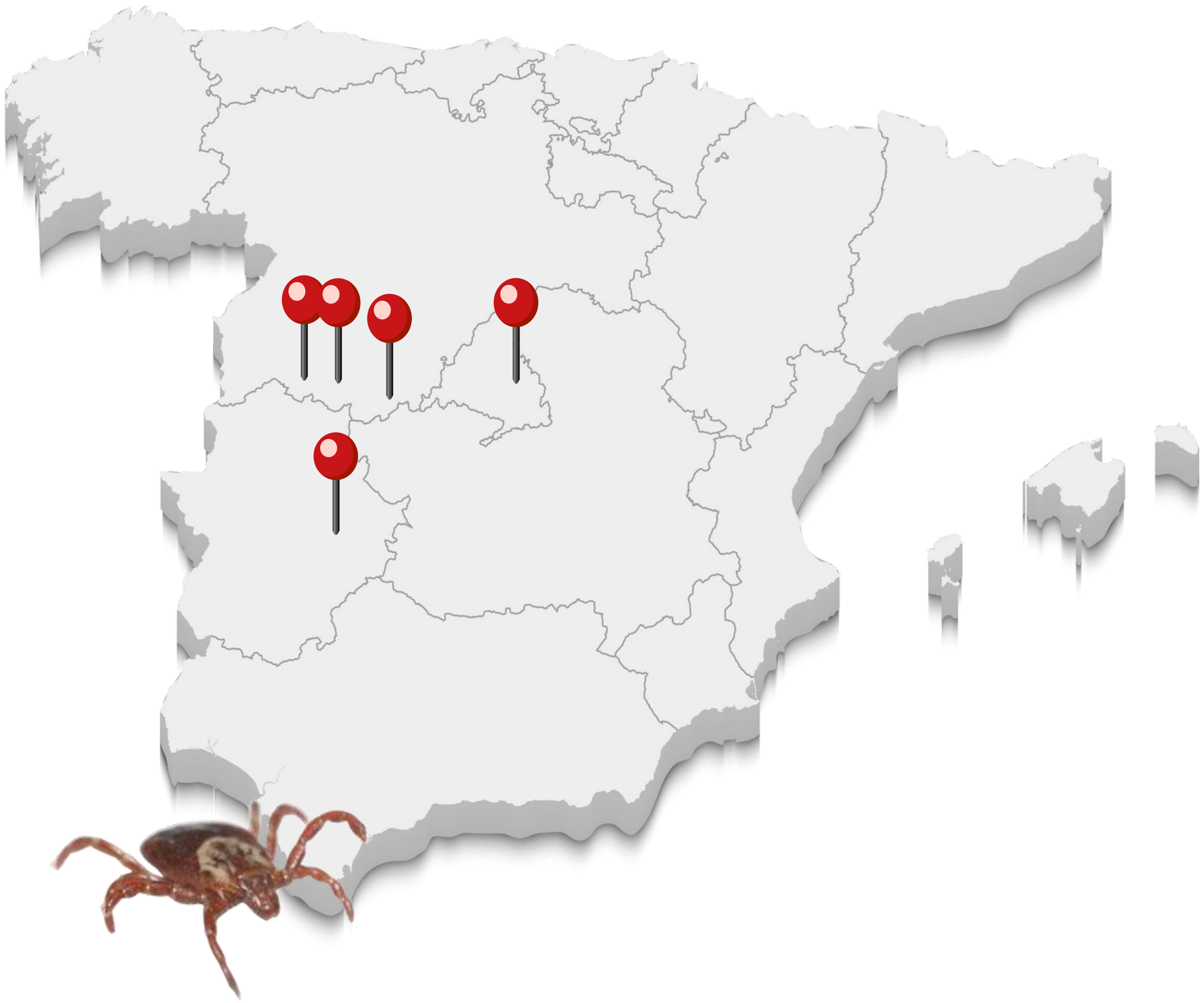
Table 1. Main epidemiological and clinical characteristics of patients.

Characteristics	N = 133, n (%)
Age mean ± SD, years	67.6 (18.8)
Median age, years	73 (IQR, 54.5–82)
Male gender	81 (60.9)
Urban population	101 (68.7)
Emergency department initial diagnosis	
Respiratory syndrome	37 (27.8)
Genito-urinary syndrome	**32 (24.0)**
Febrile syndrome without focus	30 (22.5)
Fever after tick exposure	8 (6.0)
Neurological syndrome	6 (4.5)
Gastrointestinal syndrome	6 (4.5)
Biliary and hepatic infection	**4 (3.0)**
Cutaneous affectation	4 (3.0)
Mononucleosis syndrome	2 (1.5)
ENT infection	2 (1.5)
Fever associated to haemodialysis process	2 (1.5)

ENT: Ear, nose, and throat disorder

	Acute infection by CCHFV, N = 1	Previous infection by CCHFV, N = 3
Age mean ± SD, years	53	68 ± 28.2
Sex	Male	2 males / 1 female
Urban population	Yes	2/3
Comorbidity	Non	2/3 arterial hypertension 1/3 chronic renal failure, hypothyroidism, depressive syndrome, dyslipidemia and stroke 1/3 essential thrombocytosis
First clinical diagnosis	Acute viral hepatitis	2/3 genitourinary tract infection 1/3 acute pancreatitis
Range fever duration, days	5–10	3–7
Chills	Yes	2/3
Abdominal pain	Non	1/3
Cutaneous signs (suggesting tick bite)	Leg sore	0
Muscles soreness	Leg myalgias	1/3
Any bleeding symptomatology	Non	Non
Risk factors	Cattle husbandry	Non
Laboratory data		
Hemogram, ±SD		
Haemoglobin, g/dL	14.1	9.6 ± 2.4
White blood cells, x $10^3/mm^3$	3.1	7.0 ± 1.9
Polymorphonuclear leukocytes x $10^3/mm^3$	8.1	5.4 ± 1.5
Lymphocytes x $10^3/mm^3$	3.6	1.1 ± 5.6
Platelets, x $10^3/mm^3$	41	207.6 ± 158.5
Liver function tests, ±SD		
C-Reactive Protein (CRP), mg/L	15.16	20.2 ± 15.5
Activated Partial Thromboplastin Time, sec	43.8	34.2 ± 5.1
Aspartate Aminotransferase (AST), U/L	347	151.3 ± 110.2
Alanine Aminotransferase (ALT), U/L	161	74.7 ± 50.1

CCHF situation in the Iberian peninsula



2018-2019

1 case in Ávila (retrospective) and 1 Madrid

1 case in Badajoz/Ávila: retrospective

1+1 cases in Salamanca: retrospective

Retrospective Identification of Early Autochthonous Case of Crimean-Congo Hemorrhagic Fever, Spain, 2013

Ana Negredo,[1] María Sánchez-Ledesma,[1] Francisco Llorente, Mayte Pérez-Olmeda, Moncef Belhassen-García, David González-Calle, María Paz Sánchez-Seco,[2] Miguel Ángel Jiménez-Clavero[2]

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DOI: https://doi.org/10.3201/eid2706.204643

Before this report, 7 autochthonous human cases of Crimean-Congo hemorrhagic fever had been reported in Spain, all occurring since 2016. We describe the retrospective identification of an eighth case dating back to 2013. This study highlights that the earliest cases of an emerging disease are often difficult to recognize.

Crimean-Congo hemorrhagic fever (CCHF) is a widely distributed tickborne disease in humans, emerging in different parts of the world (*1*). In Western Europe, the first and currently only country affected by this disease is Spain, where the etiologic agent, Crimean-Congo hemorrhagic fever virus (CCHFV) (family *Nairoviridae*, genus *Orthonairovirus*), was first identified in ticks in 2010 (*2*). Of note, the first autochthonous cases of CCHF were reported in 2016. In this hitherto first incidence, the index case-patient presumably acquired the infection from a tick bite, whereas a nurse (secondary case-patient) became infected while caring for the index patient (*3*). Since then, 5 more CCHF cases have been reported (Table): 2 in 2018 (1 of them retrospectively diagnosed in 2019) and 3 more in 2020 (*4*,*5*). All these cases (except the nosocomial case in 2016) arose in summer in rural areas of west-central Spain; 5 occurred in the southernmost part of the autonomous community of Castile and León. Field studies have confirmed that these areas are at risk for CCHF occurrence because of the abundance of *Hyalomma lusitanicum* tick vectors; CCHFV has been verified in specimens collected there, and high seroprevalences have been observed in wild and domestic animals (*4*).

[1]These first authors contributed equally to this article.

[2]These senior authors contributed equally to this article.

Table. Human cases of Crimean-Congo hemorrhagic fever reported to date, in chronological order, Spain

Year	No. cases	Autonomous community/province	Reference
2013	1	Castile and León/Ávila	This study
2016	2	Castile and León/Ávila (index case); community of Madrid/Madrid (secondary case)	(*3*)
2018	2	Extremadura/Badajoz; Castile and León/Salamanca	(*4*)
2020	3	Castile and León/Salamanca	(*5*)

In August 2020, we were contacted by a person who recovered from a severe disease in May 2013, described as "caused by a tick bite," that occurred in the high-risk region referenced previously, and the etiology remained unknown. The patient's occupation did not expose her to animals, and she stated that she had not noticed any tick bites since then. The case was suggestive enough to warrant review of the patient's medical history: 3 days after being bitten by a tick during a walk through the mountains (40°18′26.8″N, 5°40′40.7″W), the patient (then a 32-year-old previously healthy woman) sought medical care after experiencing fever and chills. The patient's general condition worsened the next day (arthromyalgia, nausea, vomiting, and diarrhea), and she was admitted to a local hospital. Physical examination revealed erythema (Figure, panels A, B) and a necrotic lesion on the patient's back in the area of the tick bite (Figure, panel C). Platelet count dropped from 136,000/µL to 17,000/µL in 3 days, accompanied by remarkable leukopenia and neutropenia. Her general condition deteriorated rapidly and she experienced anasarca, gum bleeding, petechiae, and melena; she was transferred to a tertiary hospital.

Laboratory findings included pancytopenia, hypoalbuminemia, and hyperbilirubinemia with elevated transaminases (aspartate aminotransferase [AST] ≤4,000 U/L [reference range 0–33U/L] and alanine aminotransferase [ALT] ≤1,000 U/L [reference range 0–32 U/L]). Intracytoplasmic inclusions (morulae) were described in buffy coat examination.

Despite treatment, septic shock occurred, and supportive treatment was started in the intensive care unit. After 10 days of hospitalization, the patient recovered and was discharged.

Final laboratory diagnostic tests ruled out infection by most common tickborne illnesses (i.e., *Rickettsia* spp., *Borrelia burgdorferi*, *Anaplasma* spp., and *Ehrlichia* spp.) and other suspected etiologies (i.e., cytomegalovirus, *Coxiella* spp., hepatitis C virus, hepatitis B virus, HIV). Stool and blood cultures were negative.

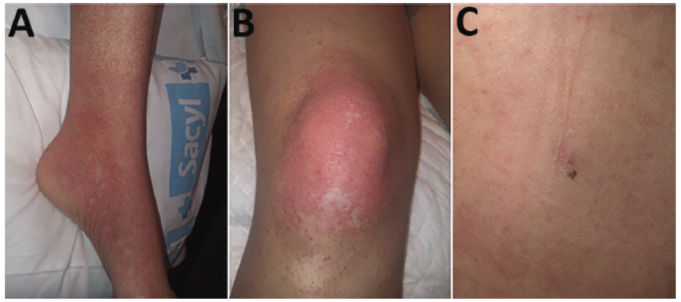

Figure. Retrospectively identified early autochthonous case of Crimean-Congo hemorrhagic fever in a woman in Spain, 2013. A, B) Erythema in the patient's ankle (A) and knee (B) 3 days after a tick bite during a leisure walk. C) Necrotic lesion on patient's back at site of tick bite.

At the time of discharge CCHF was not suspected, probably because this disease had never occurred in Spain or other nearby countries, and buffy coat examination suggested ehrlichiosis. Evidence indicates CCHFV was present in 2010 in ticks ≈150 km from the location where the patient was bitten (*2*), but this finding was not deemed medically relevant at that time. However, examined retrospectively, and with the perspective of 7 CCHF cases in 4 years in Spain, 5 of them in the same area, the case strongly suggested CCHFV infection. In agreement with the patient, a new serum sample was collected and tested by the ID Screen CCHF Double Antigen Multi-species ELISA (ID-Vet, https://www.id-vet.com). The serum sample tested positive for antibodies to CCHFV, further confirmed by Crimean-Congo fever virus Mosaic 2 indirect immunofluorescence test for CCHFV-GPC and CCHFV-N, yielding positive results to both GPC and N antigens (EUROIMMUN, https://www.euroimmun.com). Meanwhile, we located and analyzed whole blood and serum samples that were collected 10 days after symptom onset and subsequently stored. CCHFV genome was detected in blood by nested PCR (*3*) and real-time reverse transcription PCR (*6*), whereas CCHFV-N–specific IgG and IgM were found in serum by indirect immunofluorescence test as described previously. Thus, the most likely cause of the disease suffered by the patient in 2013 was CCHF.

This study demonstrates that the occurrence of CCHF cases in Spain started ≥3 years before the previously reported first known case (Table). This case is the second to be identified retrospectively (*4*), so it would be possible that additional CCHF cases dating even earlier might be diagnosed in the future, since antibodies seem to be long-lasting (>7 years). CCHF should be included in the differential diagnosis after tick bites in areas in which it is endemic. Furthermore, awareness of CCHF is key to prevent nosocomial infections among exposed healthcare workers.

Acknowledgments

We are indebted to the patient without whose initiative and kind collaboration this work would not have been possible. We thank Giovanni Fedele and Raquel Escudero for their valuable help providing stored samples from the patient.

This study has been supported in part from ISCIII, Project RD16CIII/0003/0003, "Red de Enfermedades Tropicales," Subprogram RETICS Plan Estatal de I+D+I 2013-2016, and cofunded by FEDER "Una manera de hacer Europa."

About the Author

Dr. Negredo is a senior researcher at the Arbovirus and Imported Viral Diseases Laboratory, National Center of Microbiology, Madrid, Spain. Her primary research interests are viral hemorrhagic fevers and detection of emerging viruses that circulate in Spain.

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3. Negredo 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

Crimean-Congo Hemorrhagic Fever, Spain, 2013–2021

Helena Miriam Lorenzo Juanes,[1] Cristina Carbonell,[1] Begoña Febrer Sendra, Amparo López-Bernus, Alberto Bahamonde, Alberto Orfao, Carmen Vieira Lista, María Sánchez Ledesma, Ana Isabel Negredo, Beatriz Rodríguez-Alonso, Beatriz Rey Bua, María Paz Sánchez-Seco, Juan Luis Muñoz Bellido, Antonio Muro, Moncef Belhassen-García

Table 1. Main epidemiologic data of patients with Crimean-Congo hemorrhagic fever, Spain, 2013–2021*

	Patient no. and source									
Characteristic	1 (*10*)	2 (*10*)	3 (*12*)	4 (*13*)	5	6	7	8 (*11*)	9	10
Age, y	62	50	74	53	70	54	69	32	59	30
Sex	M	F	M	M	M	M	M	F	M	F
Rural location	No	No	No	Yes	Yes	Yes	Yes	No	Yes	No
Date	2016 Aug	2016 Aug	2018 Jul	2018 Aug	2020 Jun	2020 Jul	2020 Aug	2013 May	2021 Apr	2021 Jun
Risk factors†	Leisure	Nurse	Hunting	Ag	Ag	Ag	Leisure	Leisure	Ag	Leisure
Comorbidities	HTN, OSA	None	None	Hepatic steatosis, active drinker	Tongue cancer	TB, brucellosis, active drinker	HTN	None	Diabetes mellitus, dyslipemia	Diabetes mellitus
Bakir scale at admission	7	0	7	6	6	4	8	5	2	5
Outcome	Died	Good	Died	Good	Good	Good	Died	Good	Good	Good

*Source is indicated if other than this study. Ag, agriculture; HTN, hypertension; OSA, obstructive sleep apnea.
†Risk factors include high-risk occupations; agriculture includes shepherding activities.

Seroprevalence in the Salamanca province (Bejar), 2023, 658 pacients (0,6%)

Enfermedades Infecciosas y Microbiología Clínica 43 (2025) 23–27

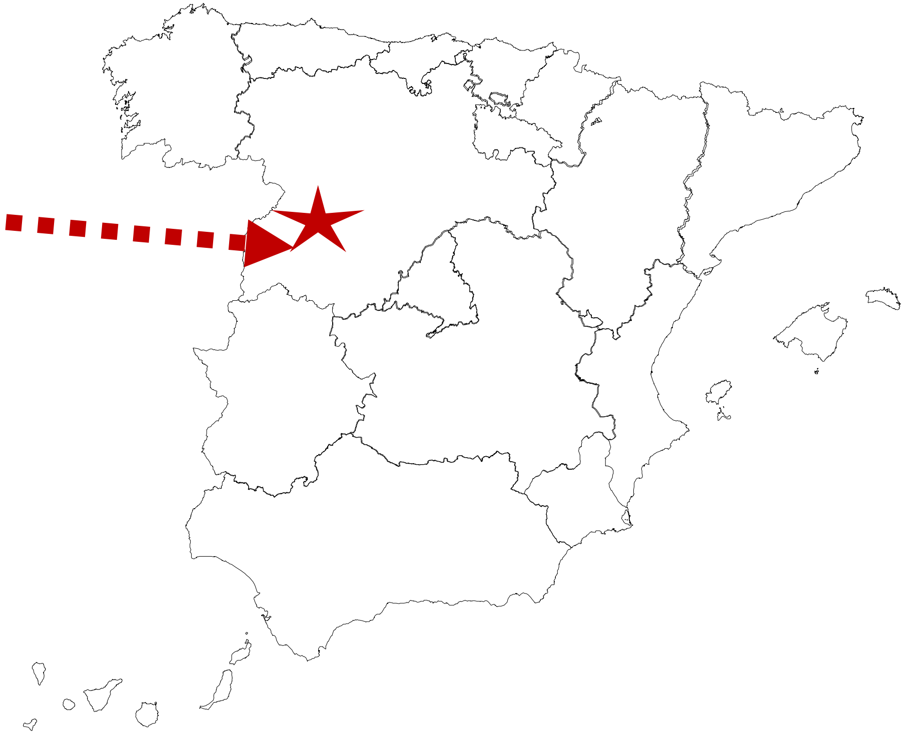
Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc

Original article

Screening for Crimean-Congo Haemorrhagic Fever Virus antibodies in humans living in an endemic area of Spain

Helena Miriam Lorenzo Juanes[a], Montserrat Alonso-Sardón[b], Belen Vicente[c], Beatriz Rodríguez Alonso[d], Amparo López-Bernus[d], Josue Pendones Ulerio[e], Rufino Alamo Sanz[f], Antonio Muro[g], Juan Luis Muñoz Bellido[f], Moncef Belhassen-García[h,*]



Variable categories	N = 658
Gender	
Male	370 (56.2%)
Female	288 (43.8%)
Age	
Mean (±SD)	58.6 (±14.3)
Median (IQR)	60 (68–50)
Range	(6, 92)
Contact with CCHF patients	
No	633 (96.2%)
Yes	5 (0.8%)
No data	20 (3.0%)
Contact with animals	
No	326 (49.5%)
Yes	321 (48.8%)
No data	11 (1.7%)
Symptoms	
No	631 (95.9%)
Yes	11 (1.7%)
No data	16 (2.4%)
Previous history of tick bite	
Yes	7 (1.1%)
Anti-CCHFV IgG	
Negative	654 (99.4%)
Positive	2 (0.3%)
Low positive	2 (0.3%)

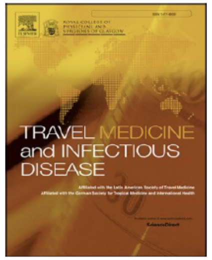
Impact of African migrant populations

Travel Medicine and Infectious Disease 64 (2025) 102814

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid



Crimean-Congo haemorrhagic fever virus screening among African individuals in Spain: Lessons to learn

Helena Miriam Lorenzo Juanes [a,1], Amparo López-Bernus [b,1], Belen Vicente [c], Montserrat Alonso-Sardón [d], Beatriz Rodríguez Alonso [e], Josue Pendones Ulerio [f], Pedro Fernandez Soto [g], Juan Luis Muñoz Bellido [f], Antonio Muro [g], Moncef Belhassen-García [h,*]

[a] *Servicio de Microbiología y Parasitología, Hospital Universitario de Salamanca (HUS), Instituto de Investigación Biomédica de Salamanca (IBSAL), Centro de Investigación en Enfermedades Tropicales (CIETUS), Universidad de Salamanca, Salamanca, Spain*

[b] *PhD Servicio de Medicina Interna, Unidad de Infecciosas. HUS. IBSAL. CIETUS. Universidad de Salamanca, Salamanca, Spain*

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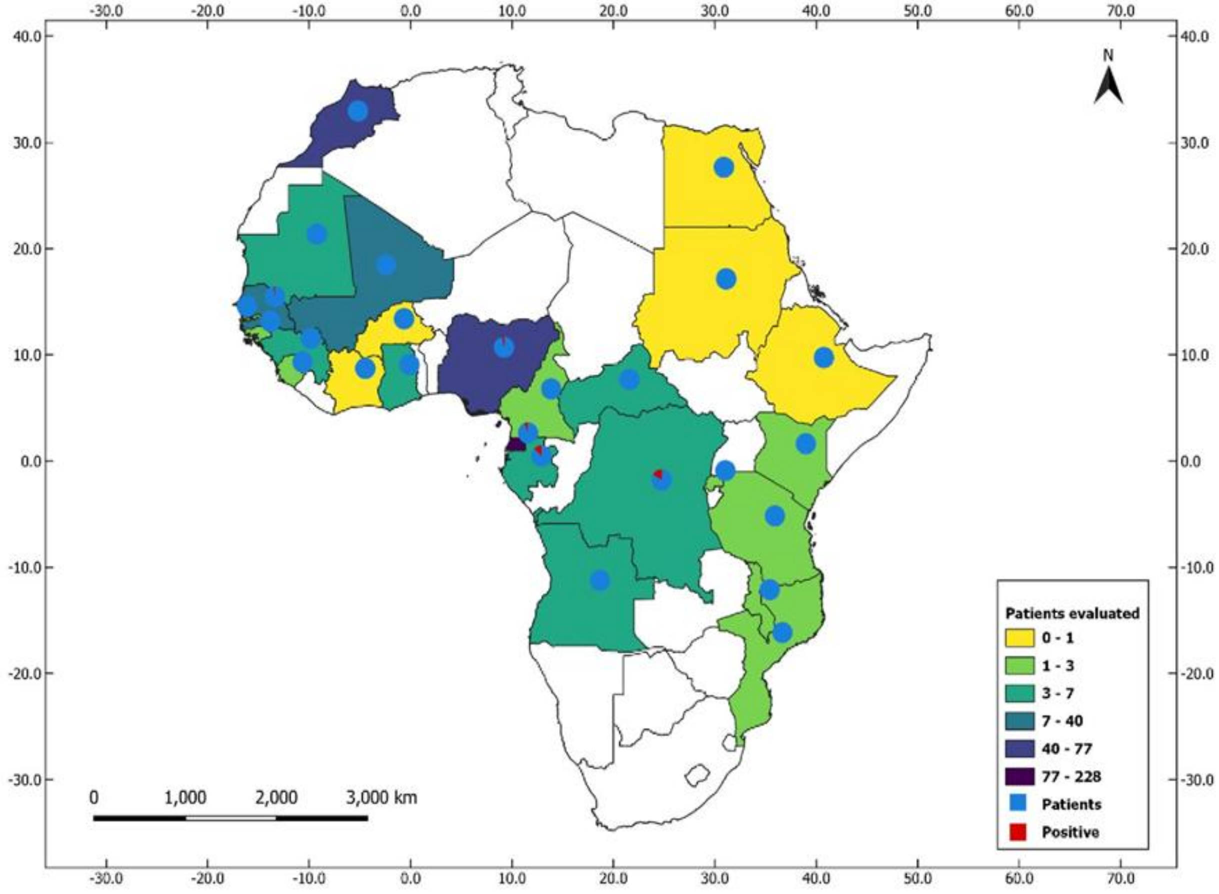
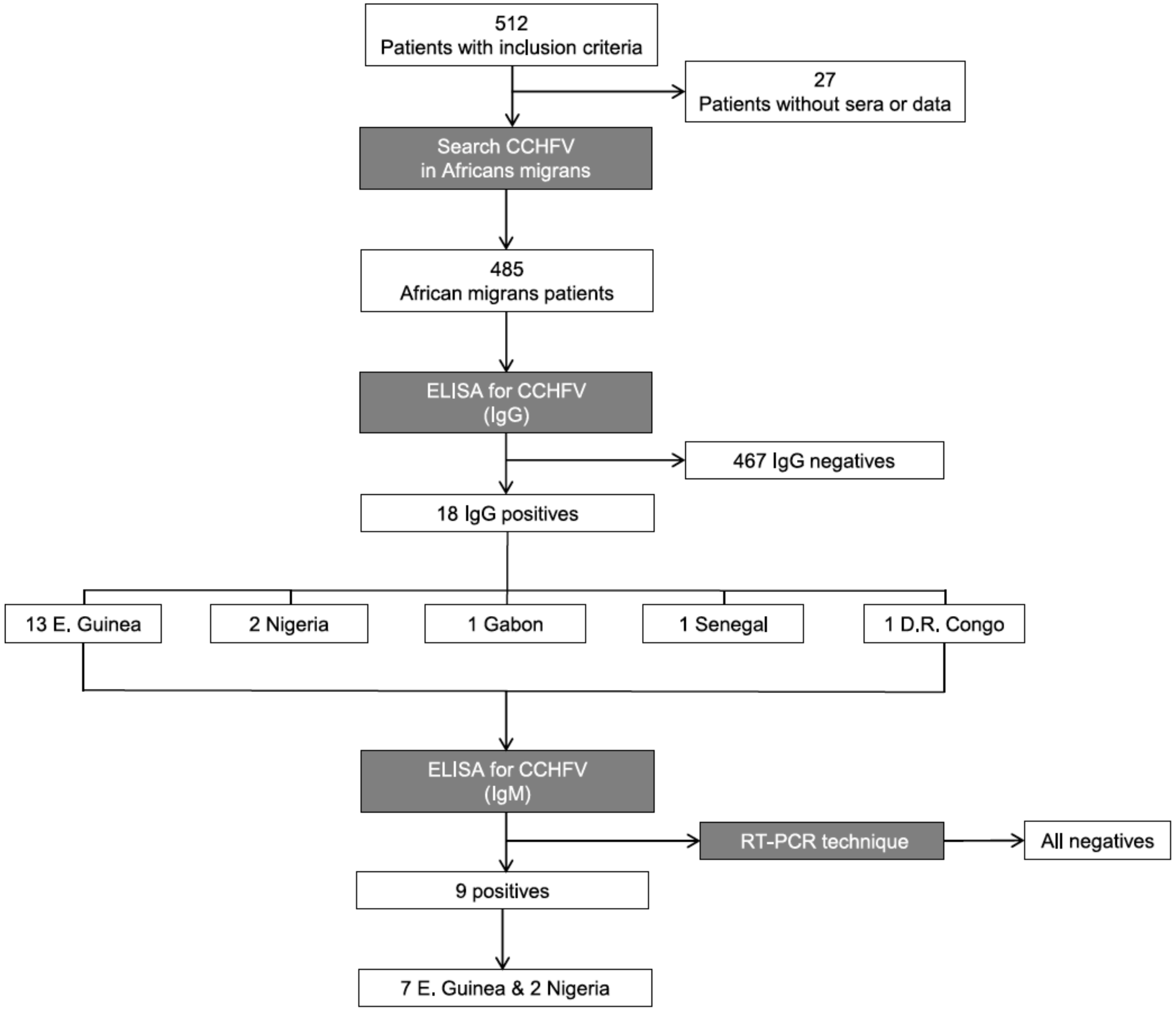
Impact of African migrant populations





Impact of endemic zones travelers

Travel Medicine and Infectious Disease 64 (2025) 102806

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: www.elsevier.com/locate/tmaid

Changes in the epidemiology of Crimean-Congo hemorrhagic fever: Impact of travel and a One Health approach in the European region

Francesca F. Norman [a,b,*], Octavio A. Arce [c], Marta Díaz-Menéndez [d], Moncef Belhassen-García [e], Marta González-Sanz [a,b]

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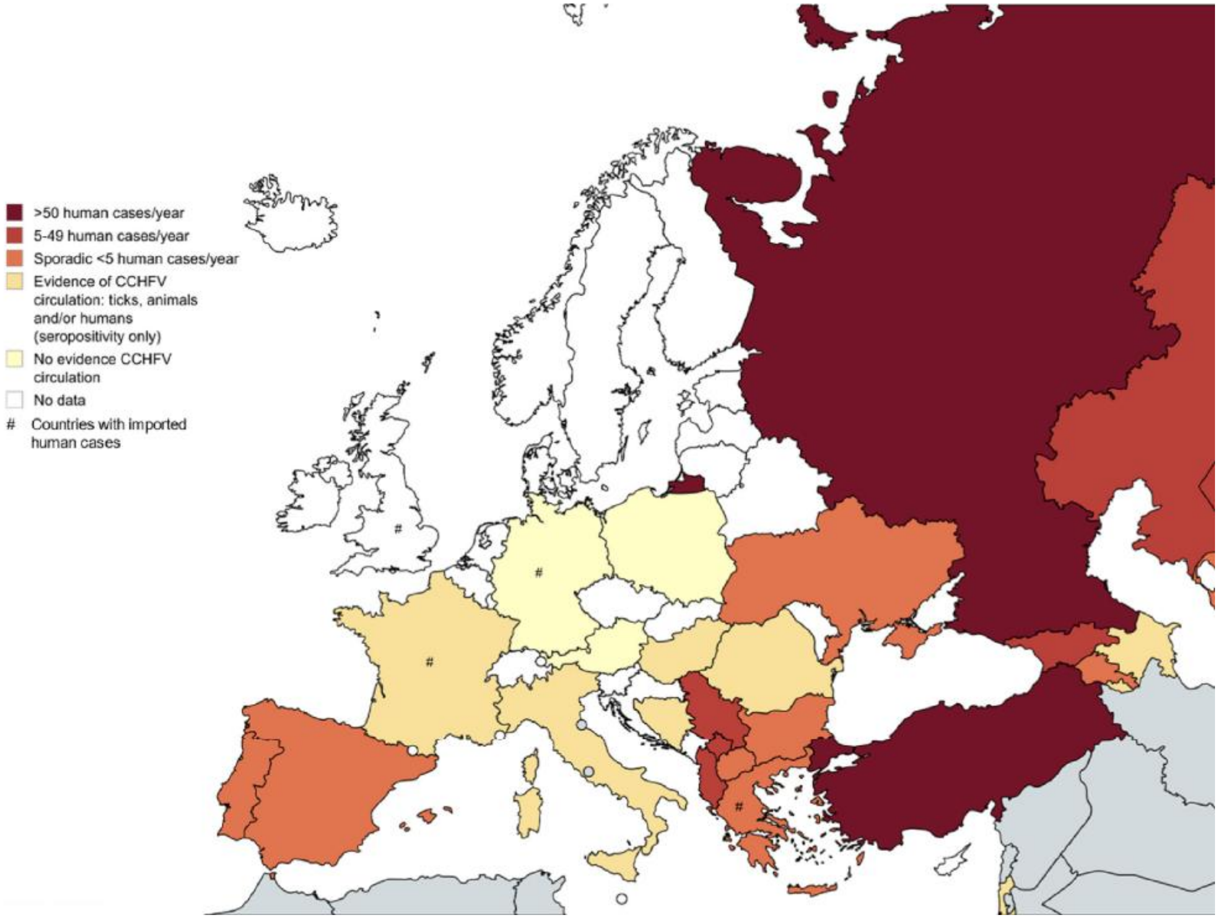
[e] *Infectious Diseases Section, Internal Medicine Department, CAUSA, IBSAL, CIETUS, University of Salamanca, Salamanca, Spain*



CCHF situation in the Iberian peninsula

Tropical Animal Health and Production (2022) 54: 237
https://doi.org/10.1007/s11250-022-03238-z

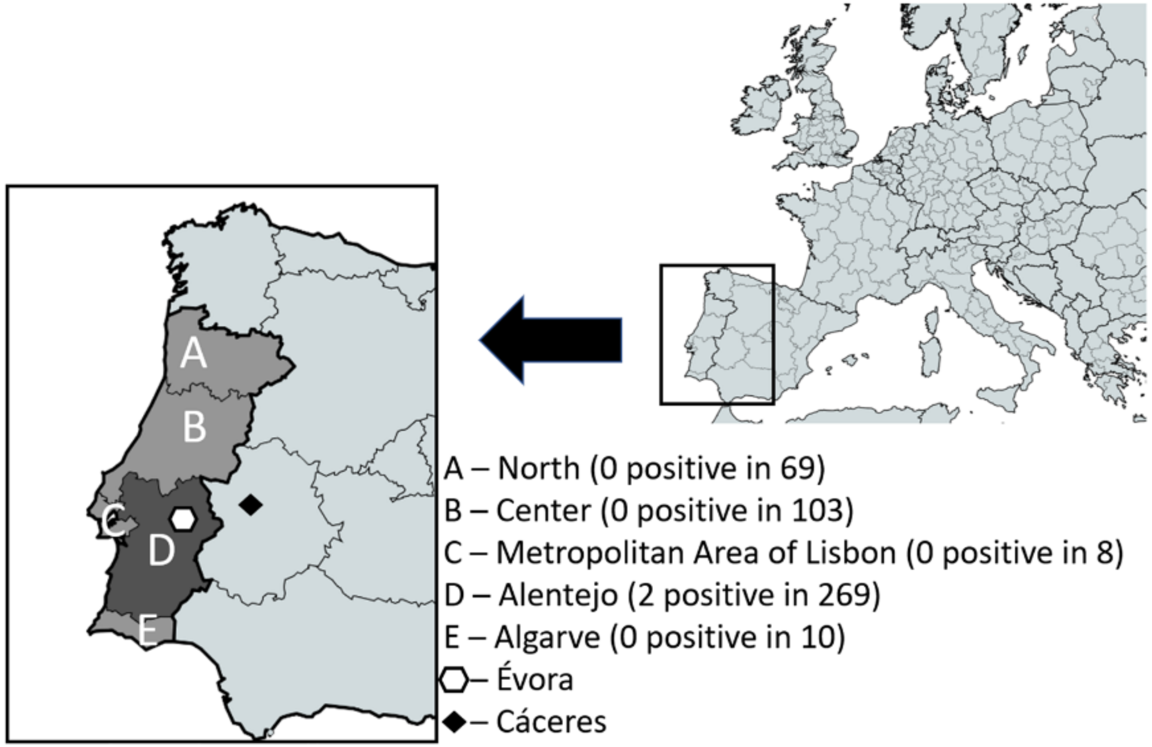
SHORT COMMUNICATIONS

Check for updates

Crimean-Congo hemorrhagic fever virus circulating among sheep of Portugal: a nationwide serosurvey assessment

João R. Mesquita[1,2] · Rita Cruz[3,4] · Fernando Esteves[3,4] · Carla Sa
Ana Cristina Mega[3] · Carmen Nóbrega[3,5] · Helena Vala[3,5] · Chris
Maria São José Nascimento[10] · Patrícia Ferreira Barradas[2,11,12]

Fig. 1 Map of the five NUTS II of continental Portugal. Alentejo region (dark grey) was the region where anti-CCHFV IgG seropositive sheep; Cáceres (where infected ticks were identified by Estrada-Peña et al. 2012) are depicted



n=459 samples
20 farms
0,4% seroprevalence
[CI 0,04-1,56%]

OPEN

Evidence of Crimean–Congo hemorrhagic fever virus in livestock and wildlife in Northeastern Portugal

Fábio Abade dos Santos[1,2,3], Margarida D. Duarte[1,2,4]✉, António Caçote[5], António Lourenço[6], Diogo Maroco[1,7], Ana Rita Varela[1,8], Luís Bonifácio[1,9], Miguel Pimpão[1], Margarida Henriques[1], Ana Duarte[1,2,4] & Sílvia C. Barros[1,10]

CCHF situation in the Iberian peninsula

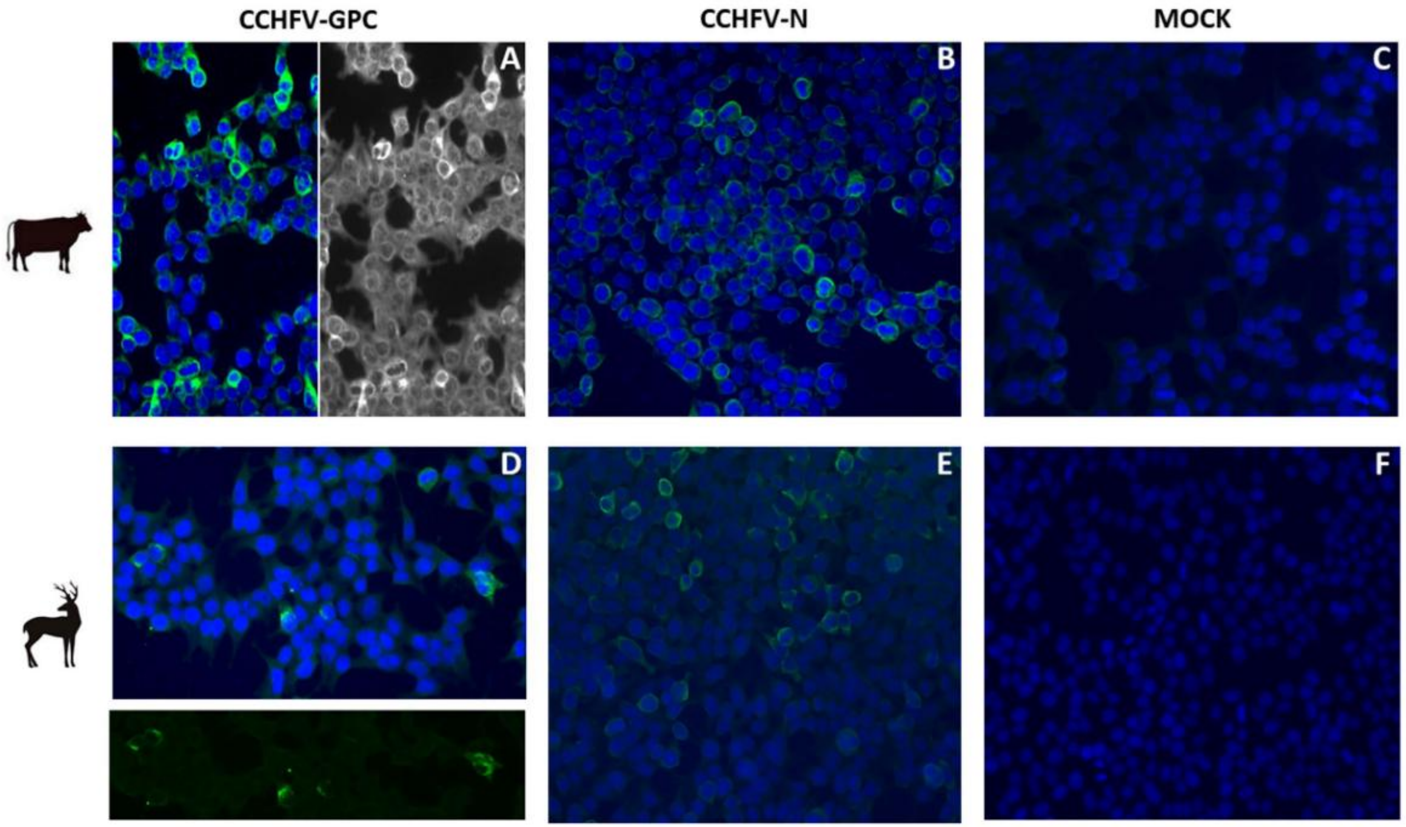
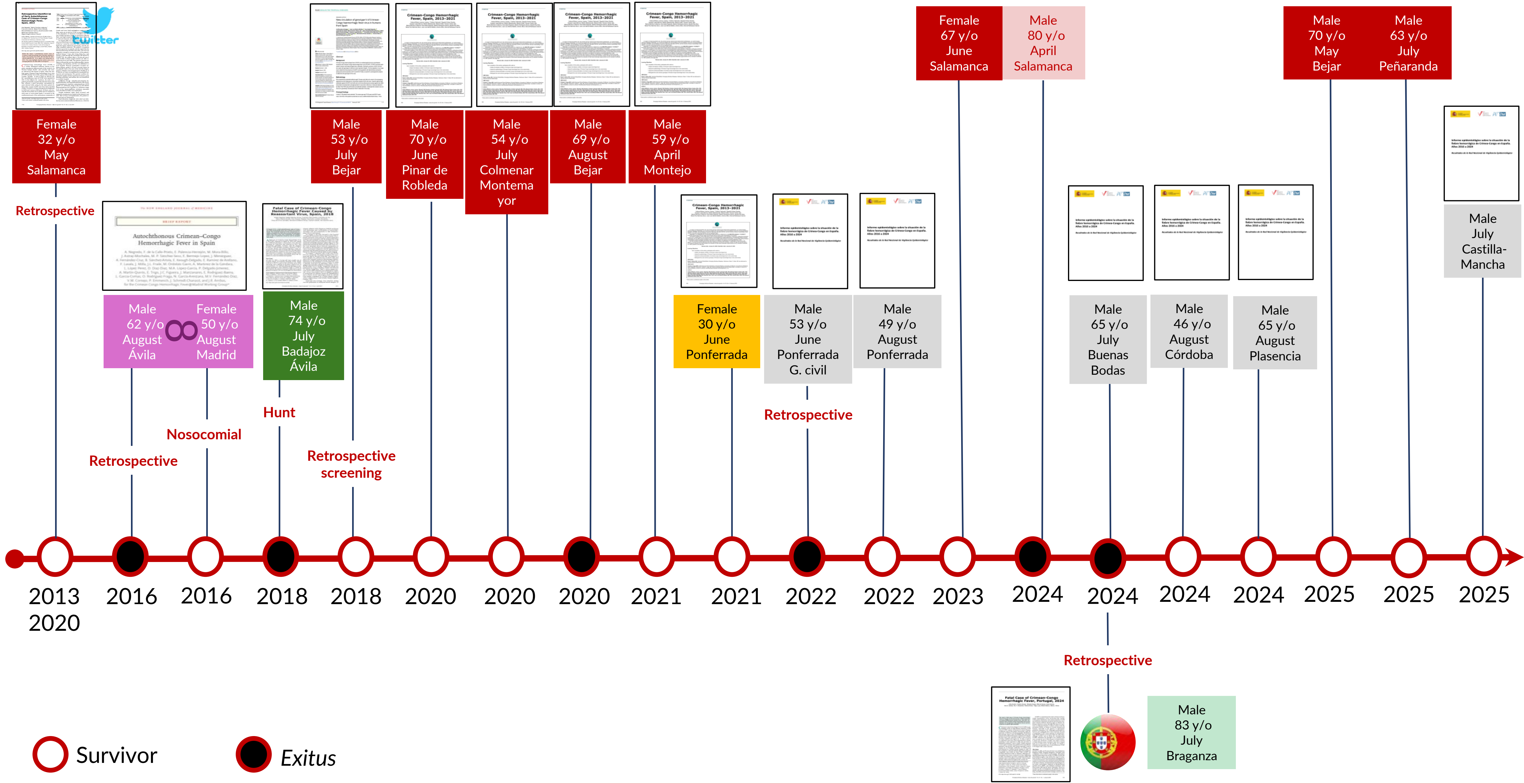


Fig. 2. Immunofluorescence of ruminant sera for positive detection of CCHFV-antibodies. Antigens (GPC and N) or MOCK cells are indicated at the top of the figures. Green represents antibodies recognizing the viral antigens. Blue stains nuclei DNA. A, B, C- ELISA positive bovine sample (serum 2, Supplementary Table 1); D, E, F– ELISA positive deer sample (serum 102, Supplementary Table 1). 100x total magnification.

N=94 cattle 3,33%
N=30 sheep 38,29%
N=10 red deer 60%

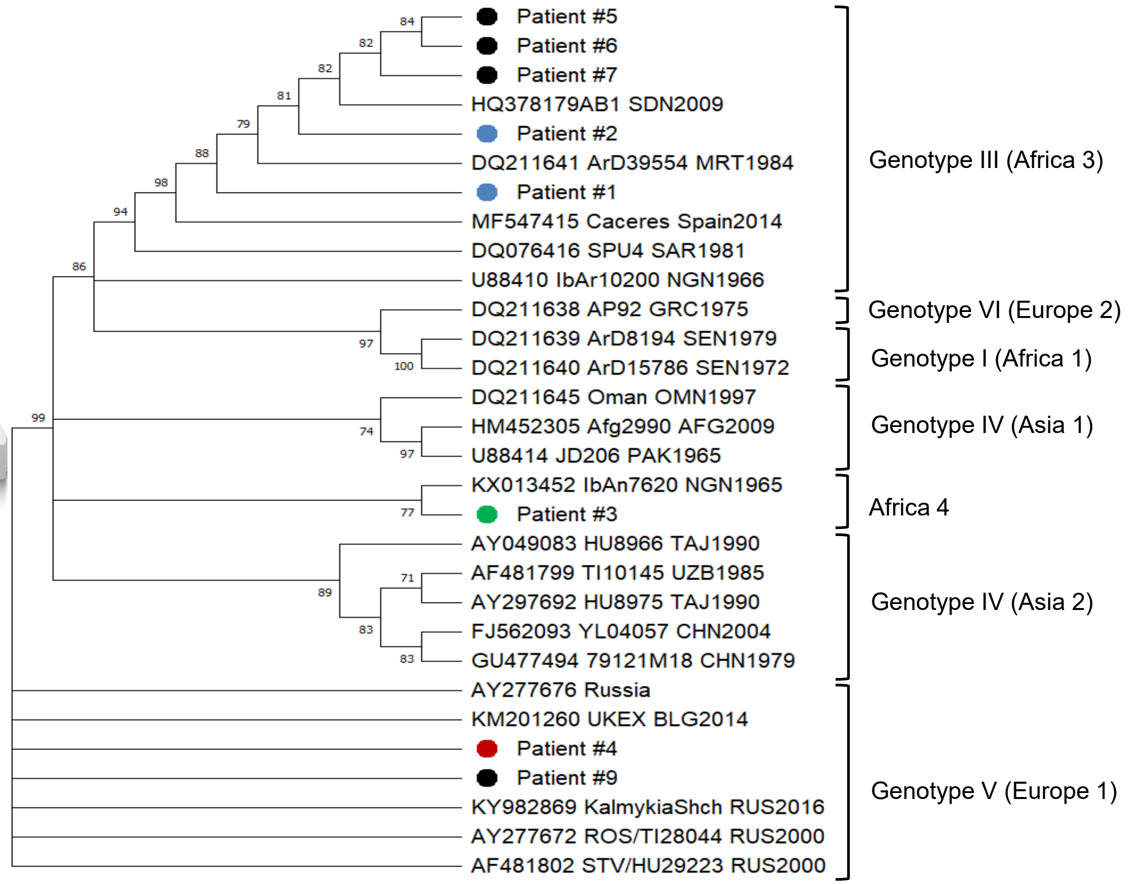
PCR testing was negative for all samples

Historic evolution of the Spanish cohort of patients with CCHF (2013-2025)



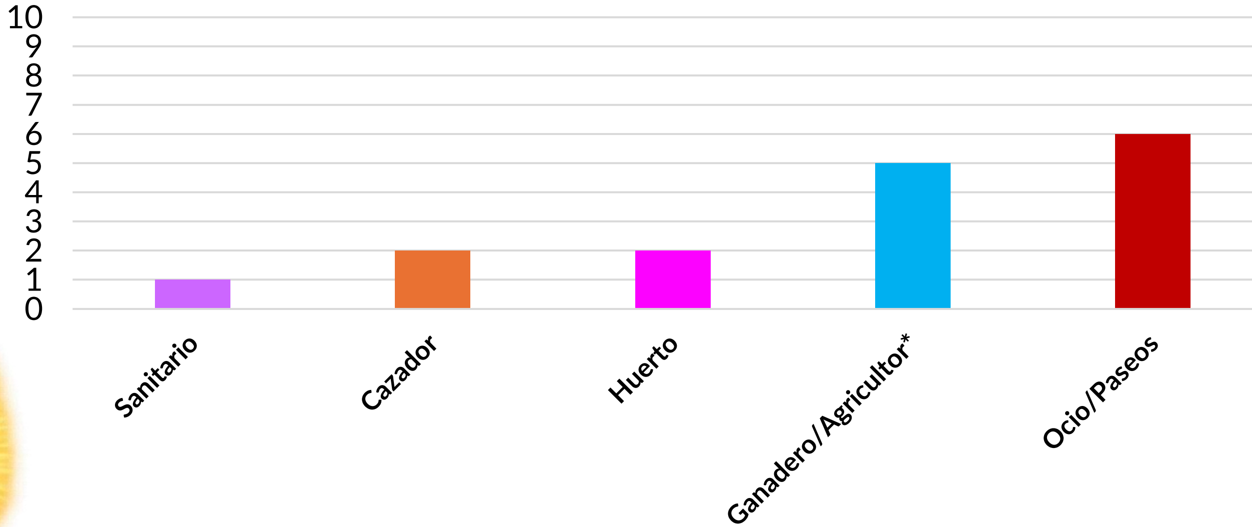
CCHF situation in the Iberian peninsula, 2025

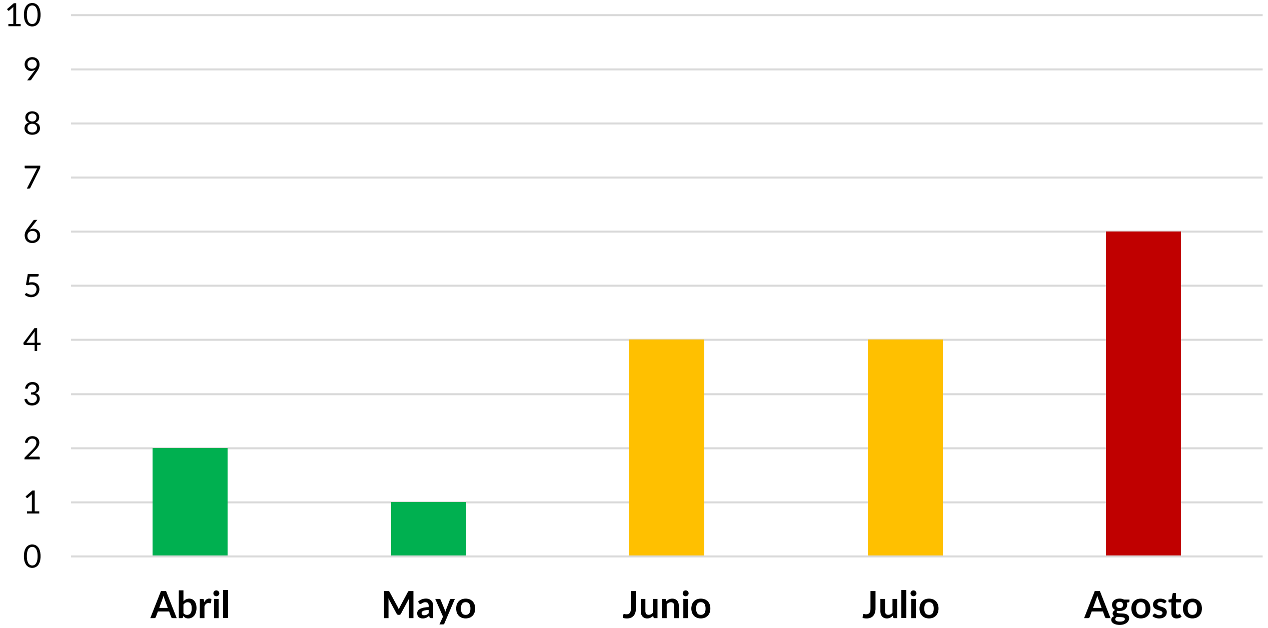
20+1 Human cases | **14 Castilla y Leon** | **10 Salamanca**



Patients background and activities

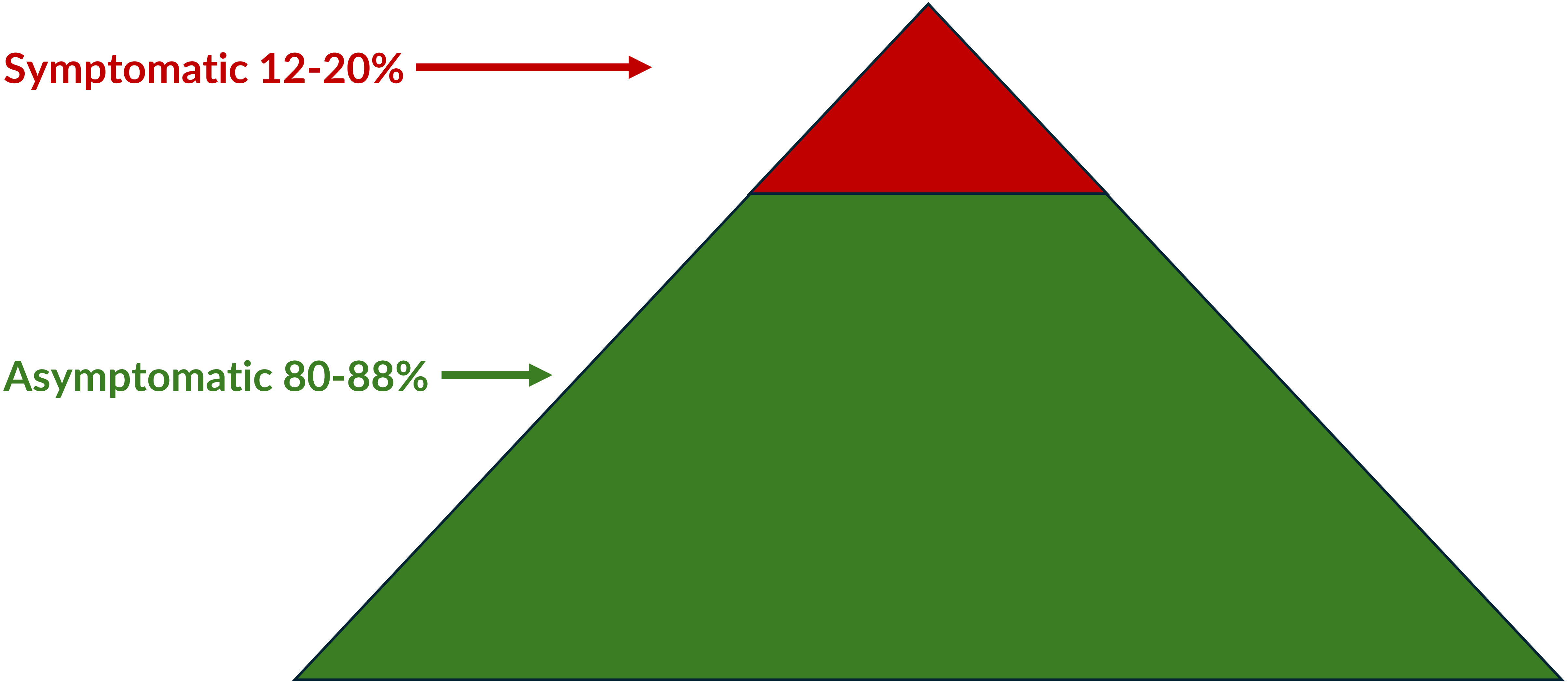
Variables	N=18 patients, N%
Gender (male)	14/18
Age (years), mean ± SD	57.5 ± 13.3
Range (years)	(30-80)
Rural habitat	53%
Urban habitat	47%
Wilderness exposure	94%
Bite history	88%
Exposure to symptoms (days)	3.6 ± 1.65
Tick-bite to hospital admission (days)	8.8 ± 3.8





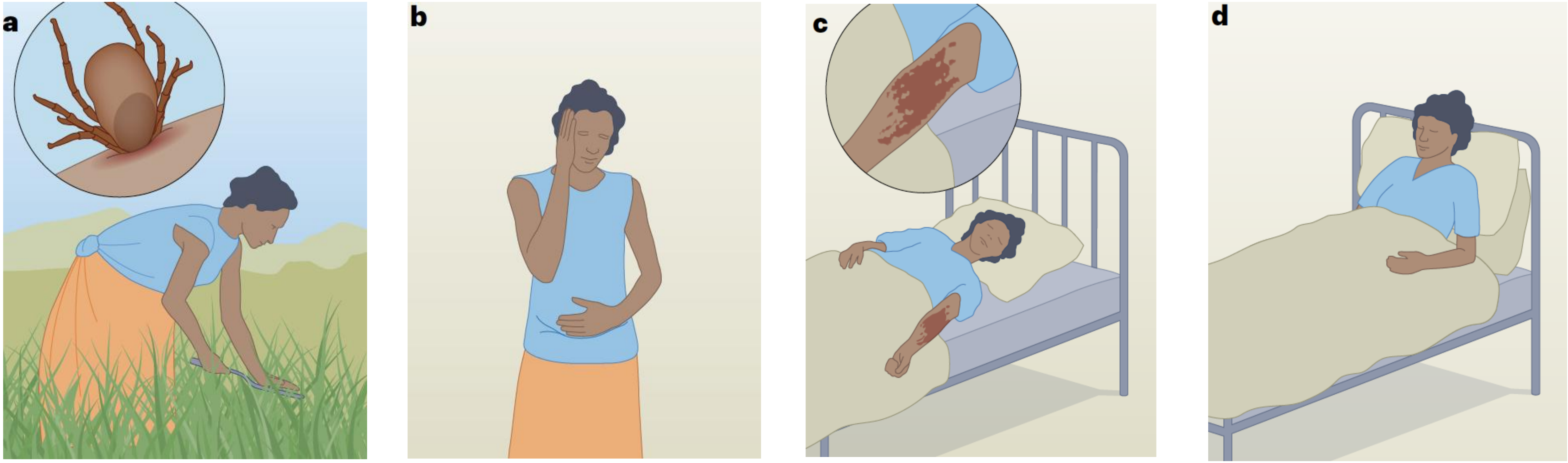
*2 ganaderos/agricultores realizaban actividades de caza

Manifestaciones Clínicas



Bodur H. *Emerg Infect Dis* 2012. Ergonul O. *Lancet* 2006

Clinical manifestations



Incubation (1-9 days)

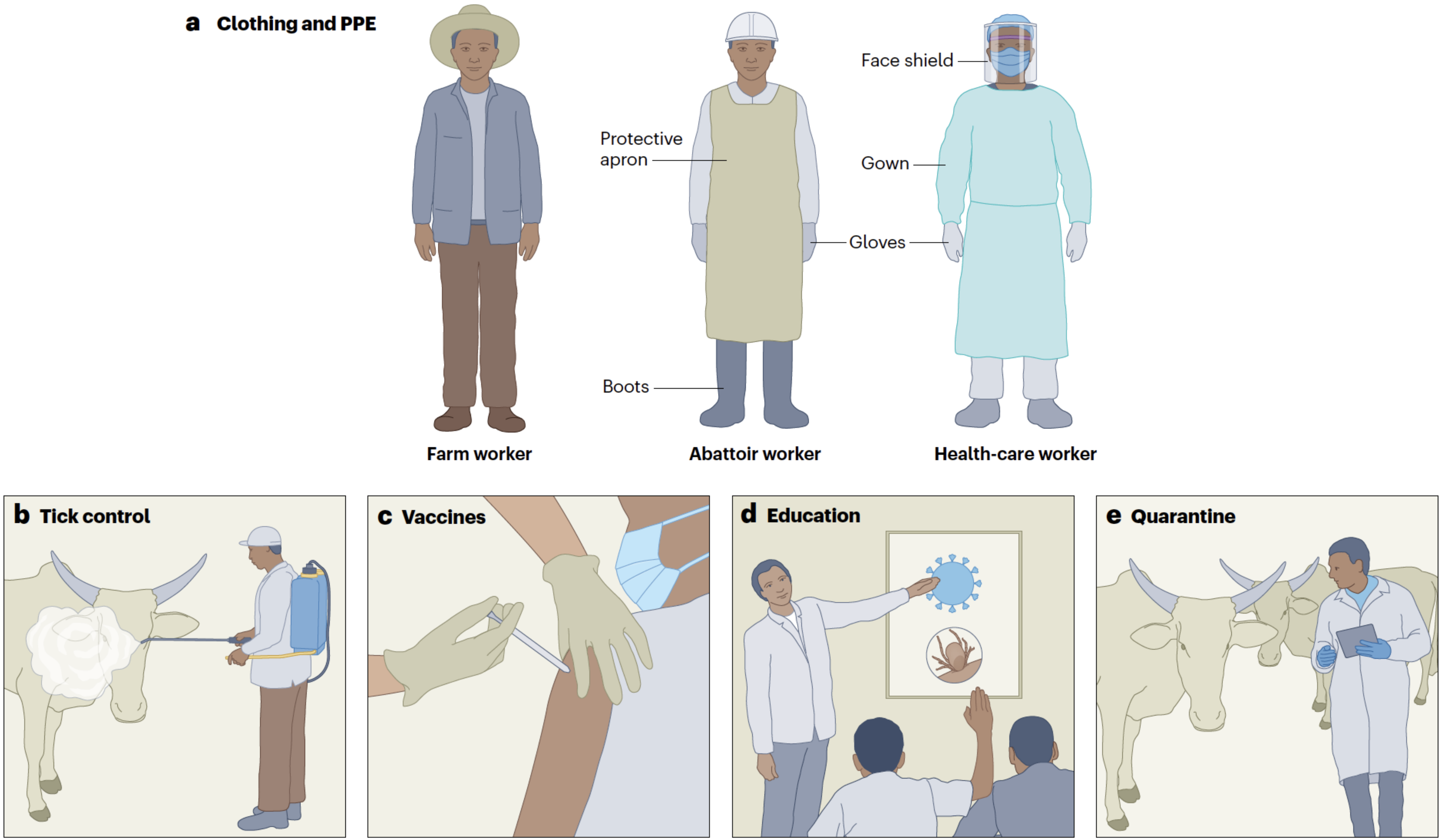
Pre-hemorrhagic phase (1-7 days)

Flu-like symptoms

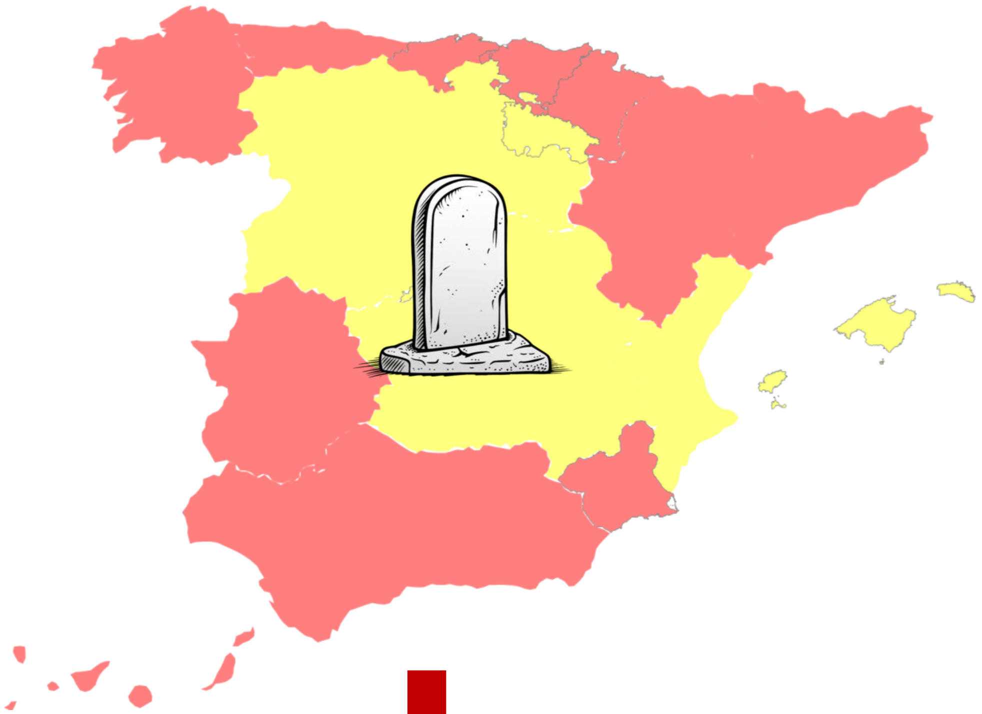
Hemorrhagic phase (2-3 days)

Convalescence (weeks)

Manejo del Virus Hemorrágico de Crimea Congo



Mortality



6/20=30%

7/21=33%

S. No	Country	Cases Reported	Mortality Rate	Key Information
1.	Pakistan	In June 2023, investigated 81 suspected cases.	Approx 30%	CCHF poses a significant public health concern in Pakistan because the disease is present in livestock and tick vectors and has been reported in human cases.
2.	China	As of 2021, reported 4,47,848 cases.	80%	Between 1951 and 2021, researchers reported 447,848 cases of bunyaviruses viruses, with CCHFV causing a significant disease burden alongside three other viruses.
3.	Kazakhstan	Approximately 16 cases occur per year.	14.8%	The study finds that the CCHF virus is present in 2.4% of sheep and 3.8% of the cattle population in the Zhambyl region.
4.	India	In 2019, reported 34 cases.	50%	The first case in Gujarat state is linked to Pakistan, while multiple outbreaks occur in Uttar Pradesh, Rajasthan, and Gujarat.
5.	Afghanistan	On September 20, 2023, there were 352 cases reported.	9.7%	Afghanistan's CCHF instances provide an unparalleled difficulty, particularly for women, children, and other marginalized populations.
6.	Iran	The Iran Ministry of Health announced in July 2019 that there had been 1501 cases of CCHF, including 195 fatalities.	13%	The worldwide distribution and re-emergence of CCHF underscore the necessity for conducting additional research on prevention and treatment agents, understanding pathophysiology, elucidating transmission routes, and evaluating the efficacy of drugs like favipiravir through double-blind, randomized clinical trials.
7.	Oman	Between 2011 and 2017, individuals reported 80 cases.	23.8%	From 2011 to 2017, the Eid-Al-Ahda festival, typically occurring during the summer months, contributed to around 23.8% of cases, highlighting increased transmission risk during this period.
8.	Iraq	In August 2023, authorities confirmed 511 cases.	12.7%	Increased temperatures influence vector behavior, and uncontrolled animal movement with neighboring countries contributes to variations in CFR among provinces during religious ceremonies, highlighting the necessity for a unified public health intervention strategy.
9.	Turkey	From 2014 to 2017, medical professionals identified 76 suspected cases, confirming CCHF in 46.1% of them.	9.6%	Turkey is considered a hub for CCHF, with increasing cases and a high fatality rate initially. The disease is highly prevalent in eastern regions.

About the virus

Overview of the virus

Iberian case series (2013-2025)

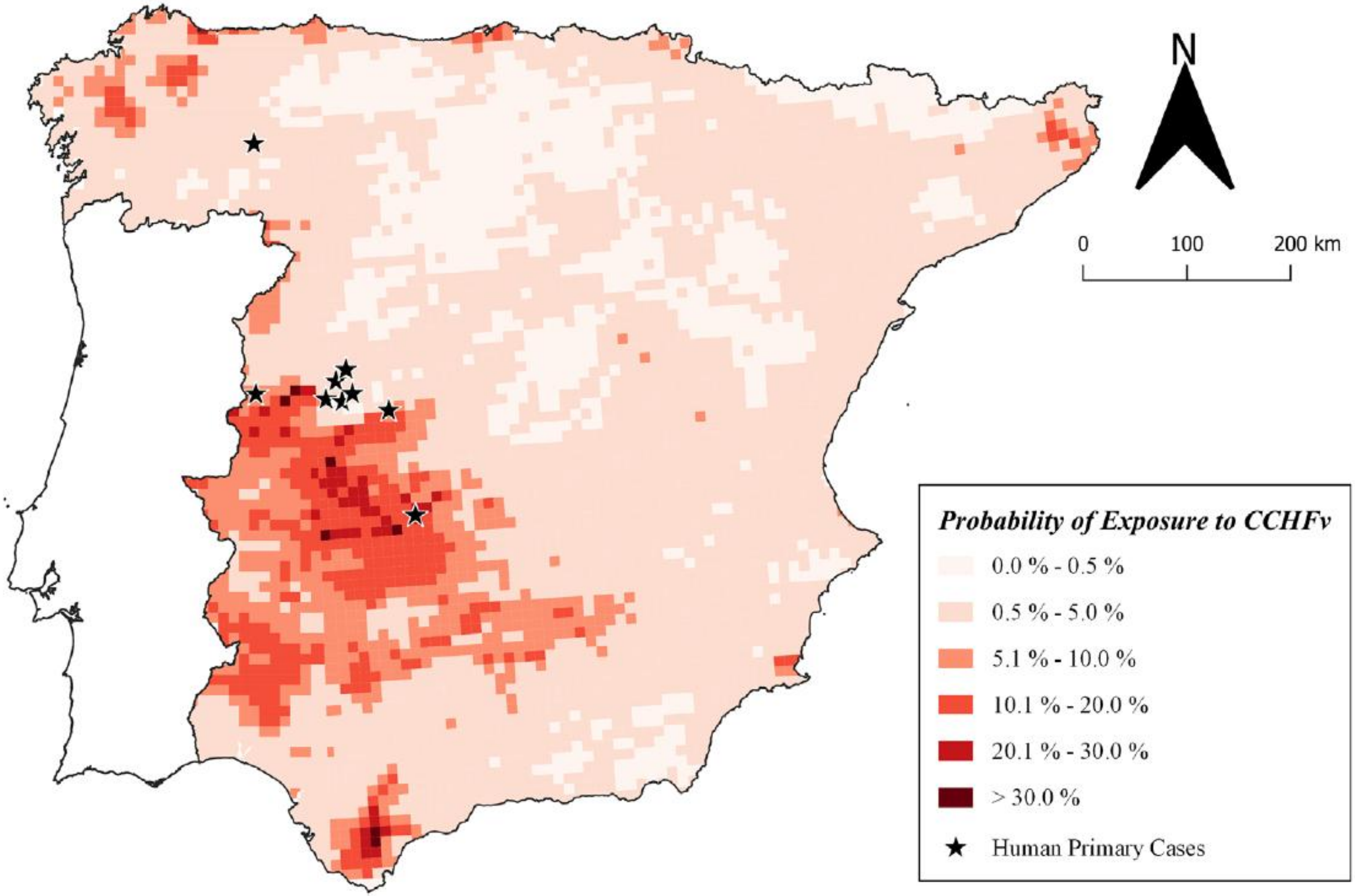
Restrospective study of all cases identified nationwide

Tick-borne diseases

Why is this happening?

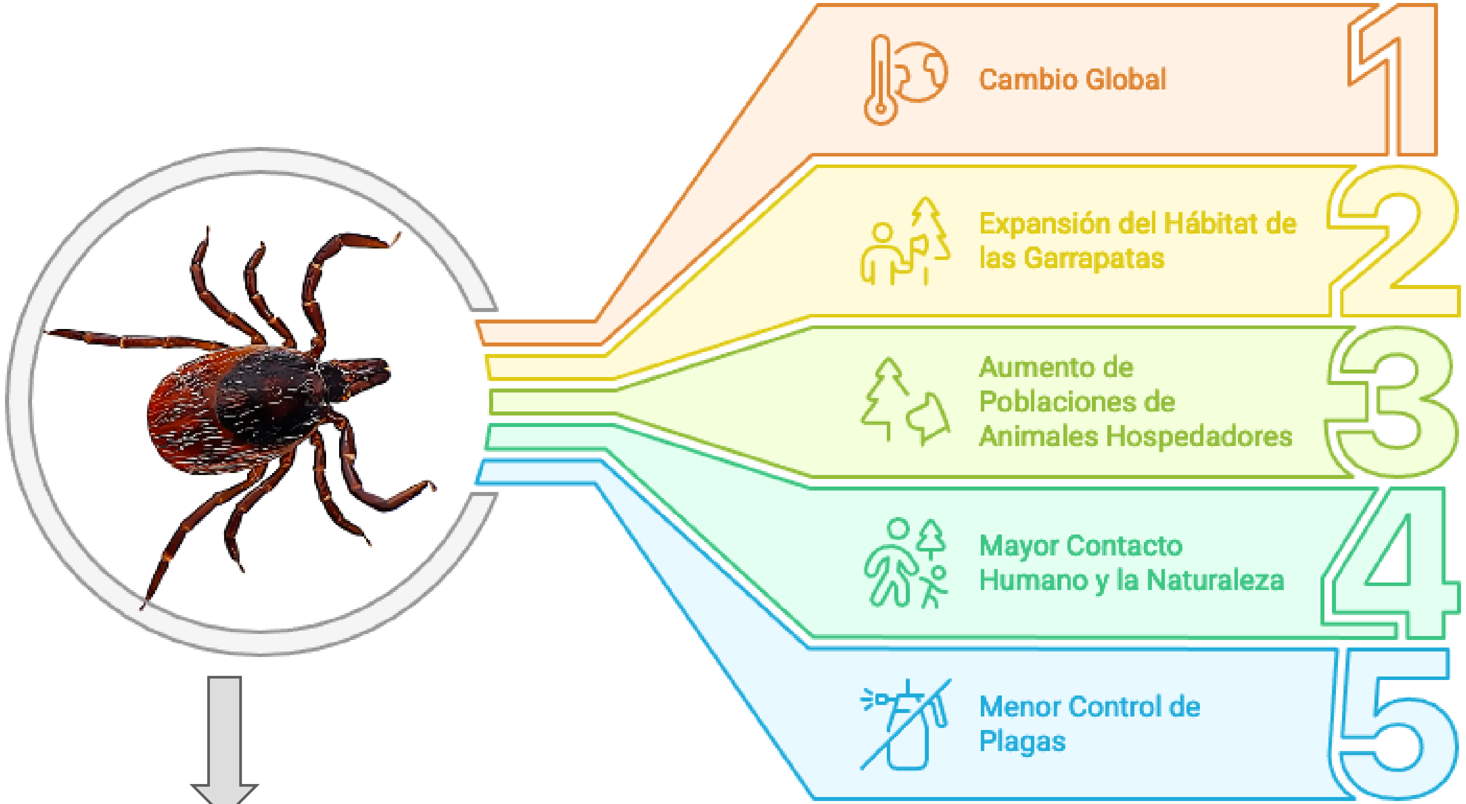
Future directions

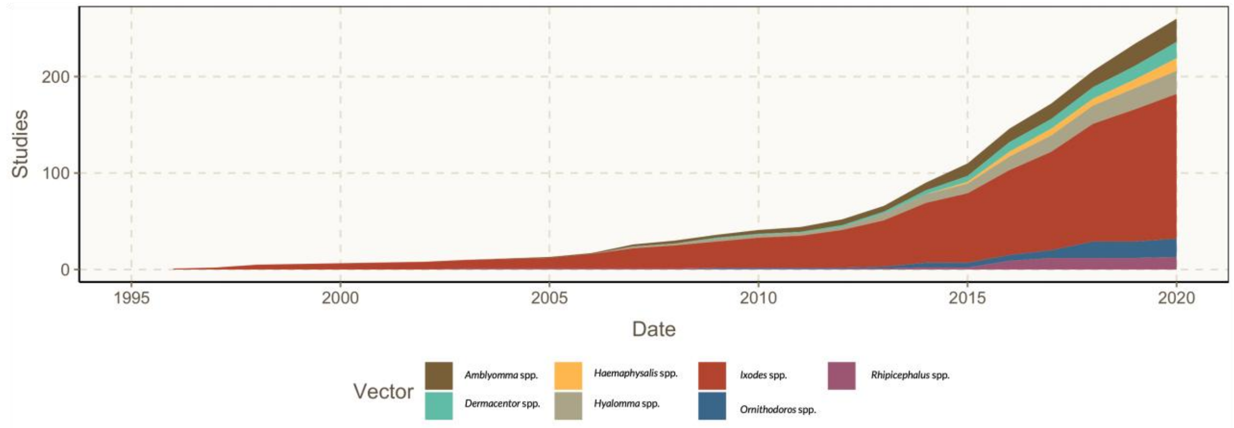
Resources for optimal management of these disease


N
0
100
200 km
Probability of Exposure to CCHFv
0.0 % - 0.5 %
0.5 % - 5.0 %
5.1 % - 10.0 %
10.1 % - 20.0 %
20.1 % - 30.0 %
> 30.0 %
Human Primary Cases

Factors associated with the rise in tick populations

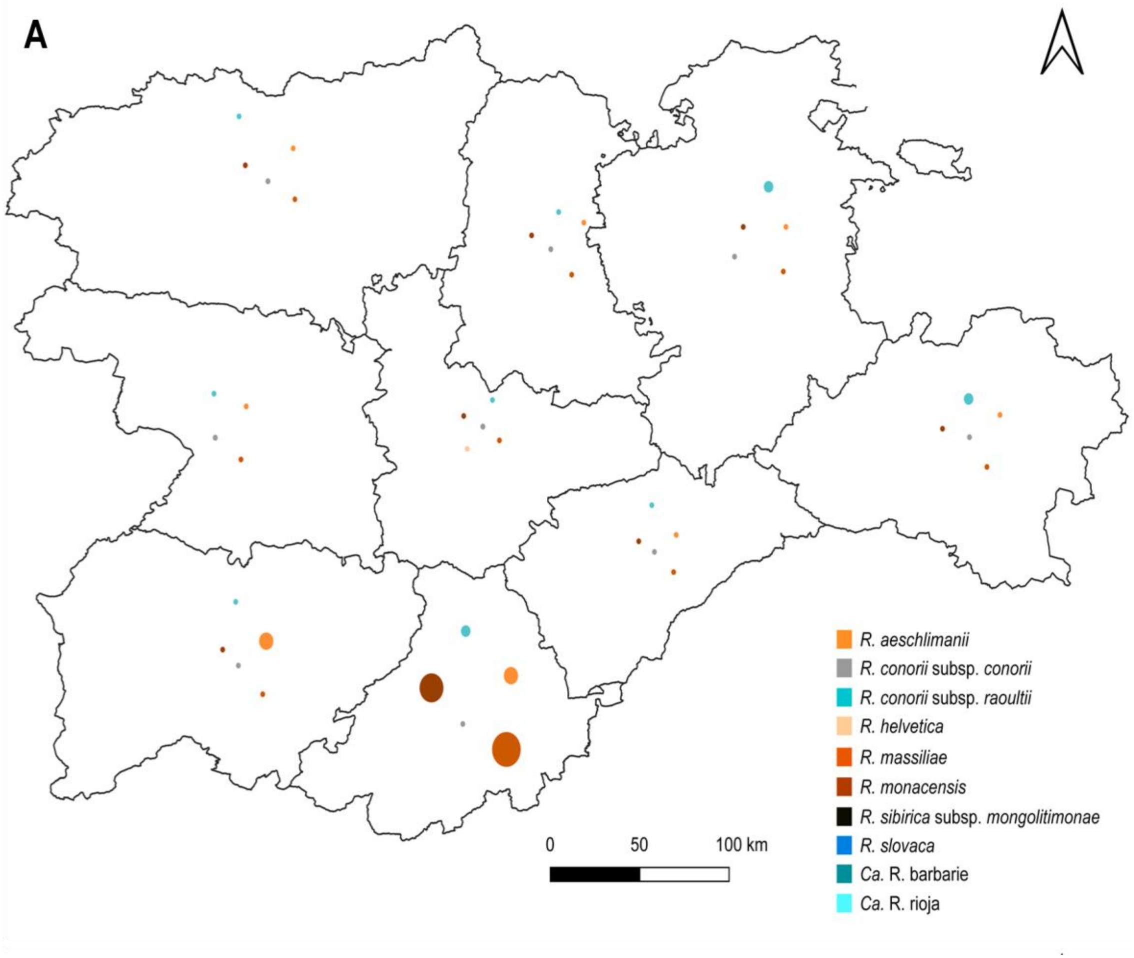
- Arthropods, Hematophagous, Present all over the world
- They parasitize humans and different species of mammals, birds and reptiles.
- Efficient vectors of a wide group of pathogens: bacteria, protozoa, viruses and helminths
- Many of them have a great impact on public health.



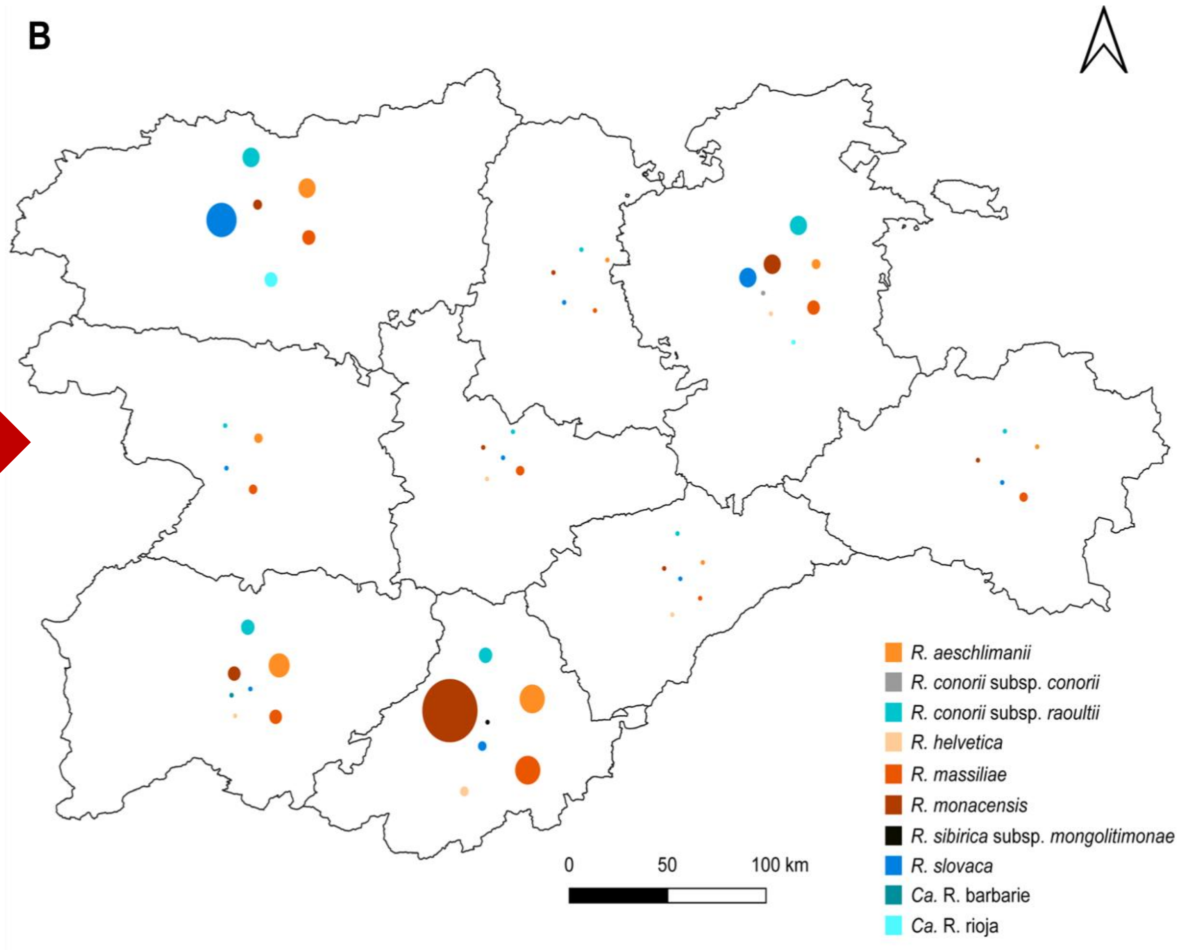


Main *Rickettsias* spp. Found in ticks in Castilla y León

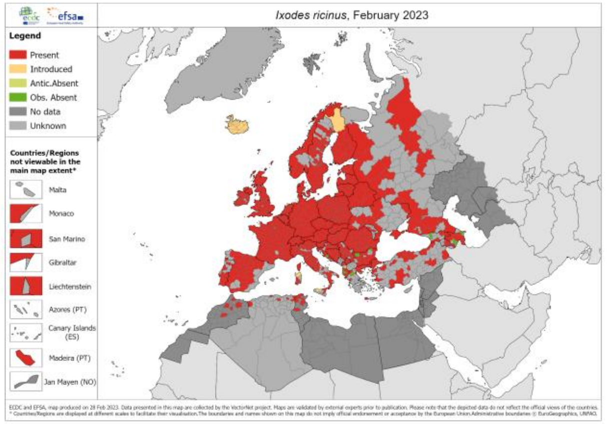
1998-2002

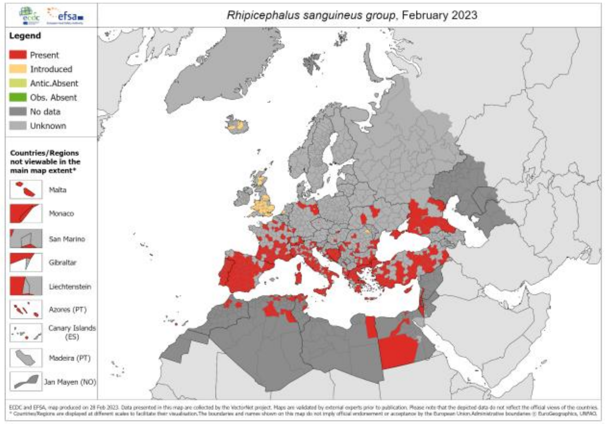


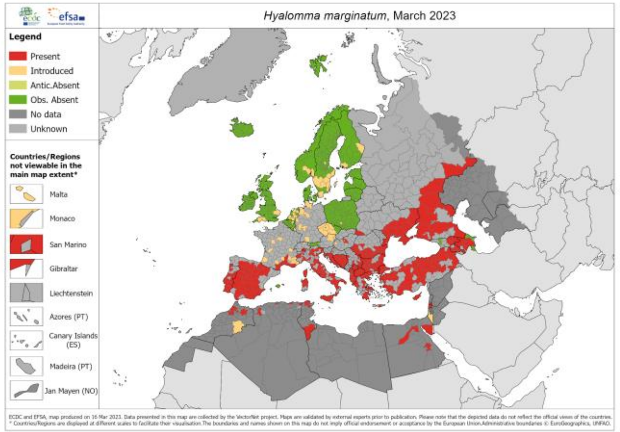
2018-2022

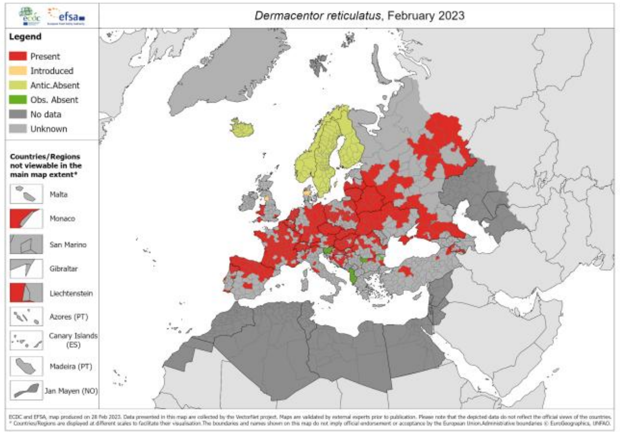


Main species in Europe and Castilla y León

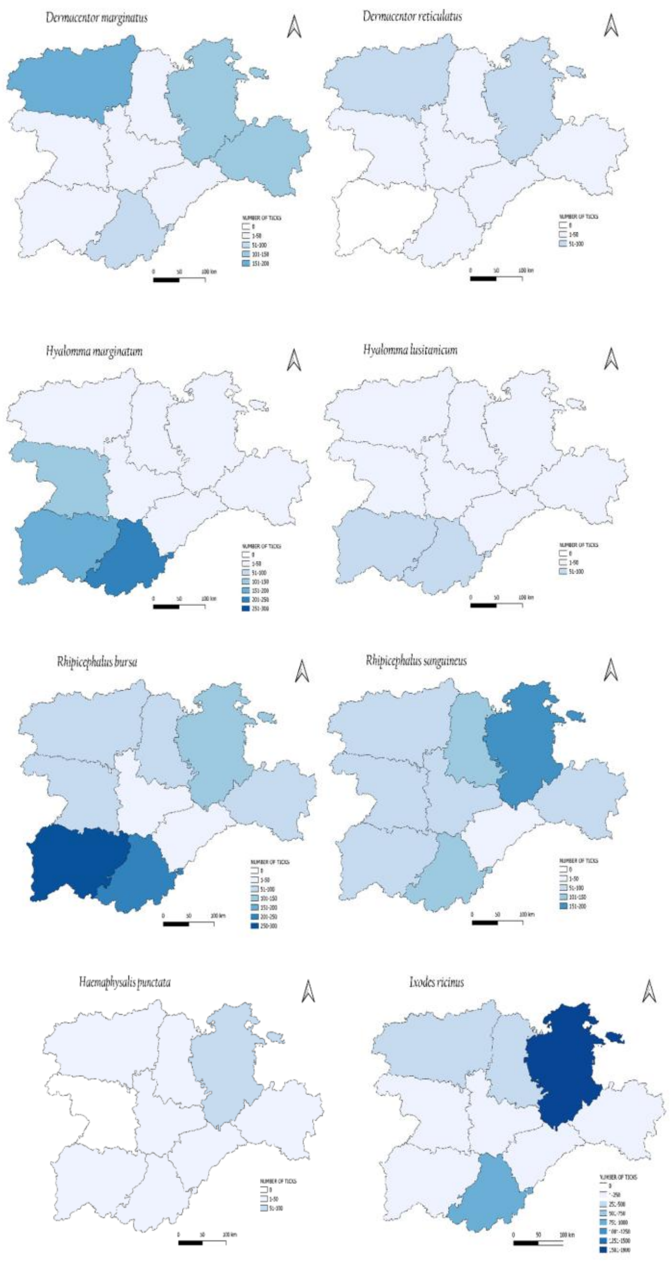








2014-2019



Main species in Castilla y León

***Ixodes* spp. 50%**

Lyme Disease
Anaplasmosis
Babesiosis
Mediterranean Spotted Fever

***Hyalomma* spp. 16%**

Crimean-Congo haemorrhagic fever

***Rhipicephalus* spp. 22%**

Mediterranean Spotted Fever

***Dermacentor* spp. 12%**

Debonel/Tibola*
Tularemia

*Dermacentor-Borne Necrosis Erythema Lymphadenopathy/ Tick-Borne Lymphadenopathy

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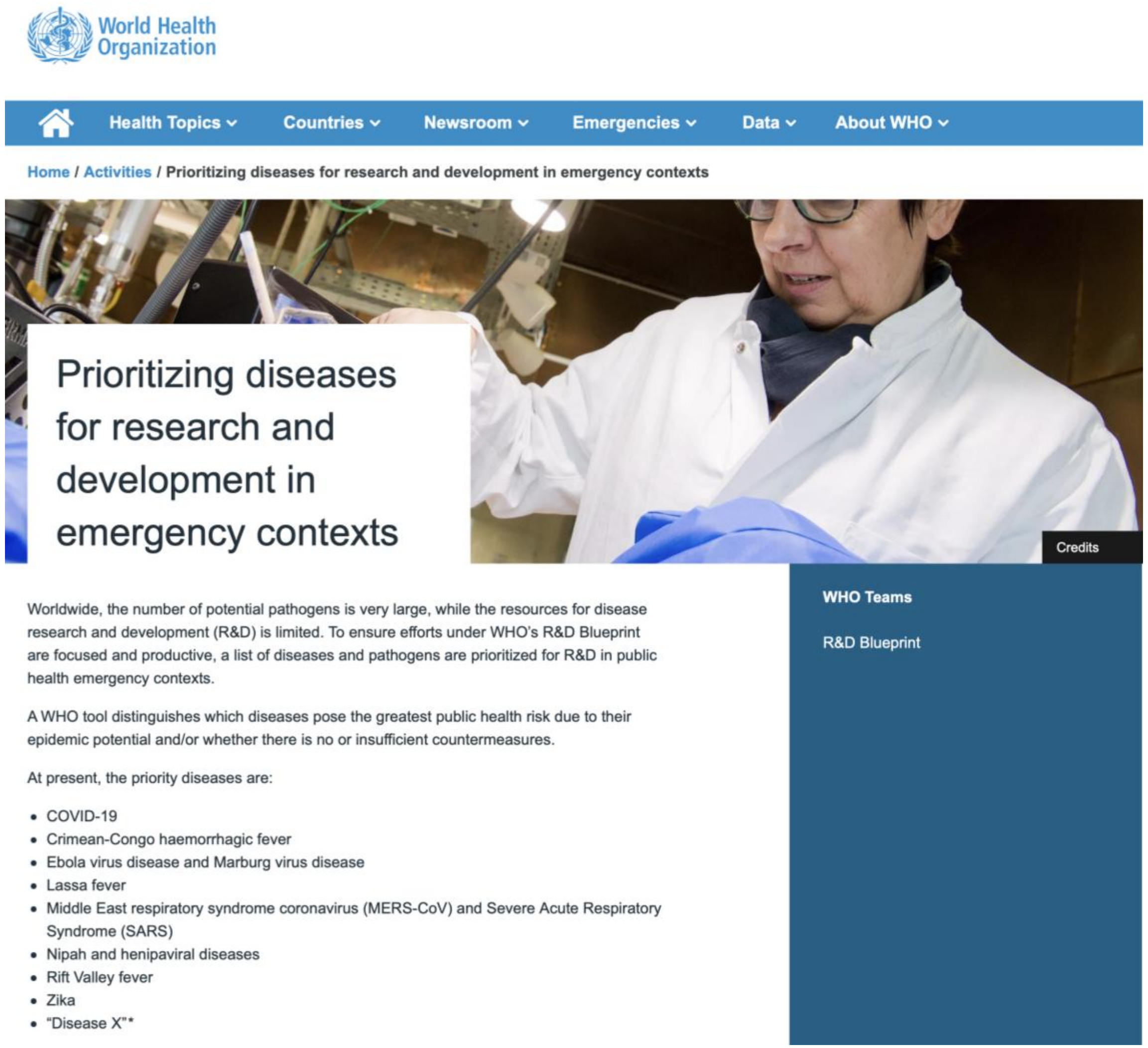
CCHFV

Importance


World Health Organization

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Prioritizing diseases for research and development in emergency contexts

Credits

Worldwide, the number of potential pathogens is very large, while the resources for disease research and development (R&D) is limited. To ensure efforts under WHO's R&D Blueprint are focused and productive, a list of diseases and pathogens are prioritized for R&D in public health emergency contexts.

A WHO tool distinguishes which diseases pose the greatest public health risk due to their epidemic potential and/or whether there is no or insufficient countermeasures.

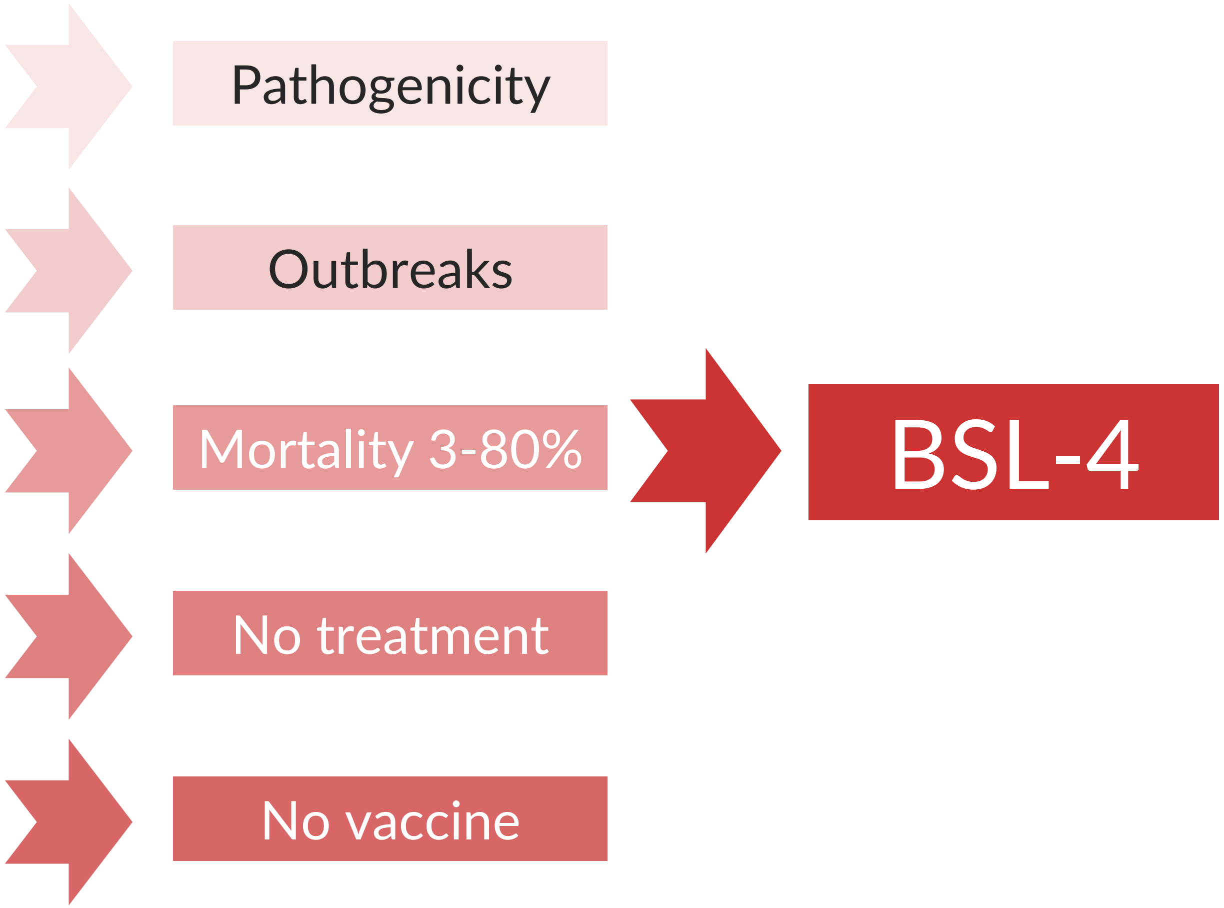
At present, the priority diseases are:

- COVID-19
- Crimean-Congo haemorrhagic fever
- Ebola virus disease and Marburg virus disease
- Lassa fever
- Middle East respiratory syndrome coronavirus (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS)
- Nipah and henipaviral diseases
- Rift Valley fever
- Zika
- "Disease X"*

WHO Teams

R&D Blueprint

Source: World Health Organization



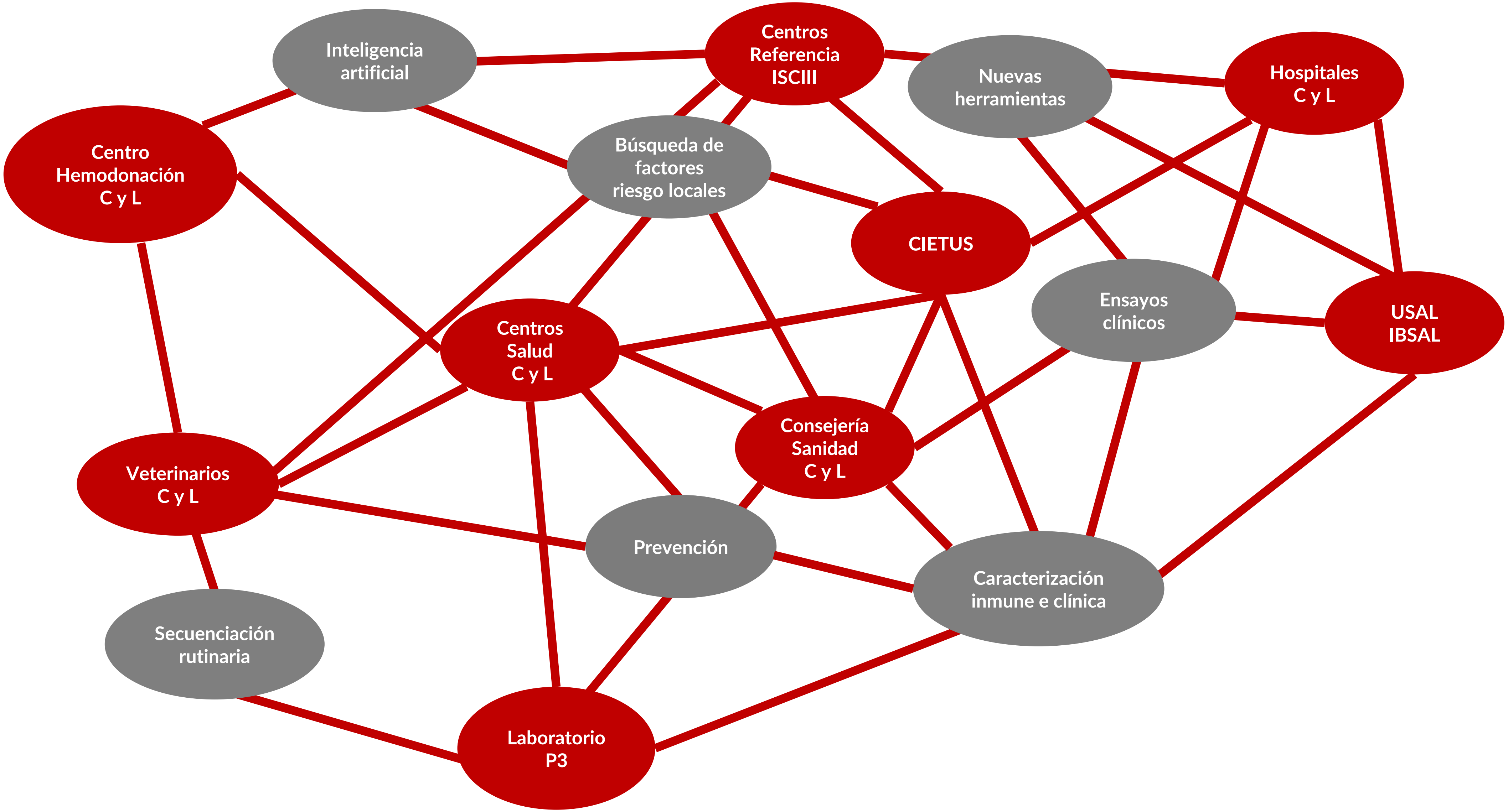
Enhanced, more dynamic implementation of protocols

National Public Health Surveillance Network (RENAVE)

Strengthening and accreditation of reference hospitals in endemic regions

Optimization of programs for the control of vector-borne diseases

Tick-borne disease care network (RAETRAG)



Crimean-Congo Haemorrhagic Fever clinical care training package

Introduction to Crimean-Congo Haemorrhagic Fever

Module 01. Introduction to Crimean-Congo Haemorrhagic Fever link

Health Operations

Module 02. CCHF outbreak preparedness and control Link
Module 03. Laboratory diagnostics for CCHF Link
Module 04. Sample collection and management for CCHF Link
Module 05. Infection prevention and control measures for CCHF Link
Module 06. Mental health and psychosocial support in CCHF care Link
Module 07. Assessment of CCHF ward in existing facilities

Innovation for CCHF: Therapeutics and vaccines

Module 08. CCHF therapeutics and vaccines under development Link

Material available here
Password : CCHF_clinical_management_v1

World Health Organization

Pierre Formenty
Viral Haemorrhagic Fevers (VHF)|
WHO Health Emergencies Programme (WHE) |
World Health Organization (WHO) |

Optimized supportive care for CCHF

Module 09. Screening, triage and initial management Link
Module 10. Overall CCHF patient management and supportive care Link
Module 11. Co-infections management Link
Module 12. Other supportive therapies Link
Module 13. Considerations for CCHF survivor programme

Optimized supportive care for CCHF: Complications

Module 14. Management of sepsis and septic shock Link
Module 15. Management of severe dehydration Link
Module 16. Acute renal failure and acute liver failure
Module 17. Management of acid-base and electrolyte disorders Link
Module 18. Neurological complications Link
Module 19. Respiratory complications Link
Module 20. Management of severe bleeding and anaemia

Optimized supportive care for CCHF: Care for special populations

Module 21. Women's health, pregnancy and puerperium Link
Module 22. Infant and children Link

Guía de manejo clínico de las enfermedades transmitidas por vectores

PLAN NACIONAL DE PREVENCIÓN, VIGILANCIA Y CONTROL DE LAS ENFERMEDADES TRANSMITIDAS POR VECTORES

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