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Review

Arthropods as vectors of transmissible diseases in Spain[☆]Aránzazu Portillo, Ignacio Ruiz-Arrondo, José A. Oteo^{*}

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ABSTRACT

Different aspects related to globalization together with the great capacity of the arthropod vectors to adapt to a changing world favour the emergence and reemergence of numerous infectious diseases transmitted by them. Diptera (mosquitoes and sandflies), ticks, fleas and lice, among others, cause a wide spectrum of diseases with relevance in public health. Herein, arthropod-borne disease are reviewed, with special emphasis on the existing risk to contract them in Spain according to different parameters, such as the presence of arthropod and the circulation or the possible circulation of the causative agents.

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Artrópodos vectores en España y sus enfermedades transmisibles

RESUMEN

Diferentes aspectos relacionados con la globalización junto a la gran capacidad de los artrópodos vectores para adaptarse a un mundo cambiante propician la emergencia y reemergencia de numerosos procesos infecciosos transmitidos por los mismos. Dípteros (culícidos y flebótomos), garrapatas, pulgas y piojos, entre otros, provocan un variado espectro de enfermedades con gran importancia en Salud Pública. En esta revisión se repasan las diferentes afecciones transmitidas por artrópodos vectores, haciendo un especial hincapié en el riesgo existente para contraerlas en España en función de diferentes parámetros, como la presencia del artrópodo y la circulación o posible circulación de los agentes causales.

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Palabras clave:

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Arthropods are the most abundant invertebrates of the animal kingdom. Their classification is very complex and among them are very diverse orders (spiders, scorpions, ants, crabs, butterflies, lice, centipedes, mosquitoes, ticks, etc.). Without entering into their different actions and functions in nature, some of them have great importance in Public Health and Animal Health due to the diseases they are capable of transmitting and/or for their capacity to act as reservoirs of infectious processes.¹

We can define an arthropod vector (AV) as an invertebrate that has a segmented body covered by a cuticle (exoskeleton), with articulated appendages, with the ability to transmit

infectious agents. Most AVs belong to *Insecta* and *Arachnida* classes (Table 1).

To review the broad subject of arthropod vector-borne diseases (AVBD) in Spain is a complex task. Just listing the arthropods that transmit diseases in our environment, such as dipterans (culicids and phlebotominae sand flies), fleas, lice, bed bugs and ticks, among others, and the diseases they transmit, or that they can transmit at any given time, would be a reason for one or several treatises. In any case, before discussing the subject, it should be remembered that the infections that they transmit are usually included in the so-called zoonoses. In this regard, the World Organization for Animal Health estimates that at least 60% of infections that affect humans have a zoonotic origin² and, according to the Pandemic Emerging Threats Program of the American Agency for International Development, almost 75% of current threats also have this origin.³ One of the many known routes for the acquisition of zoonoses, apart from direct contact with animals or their products, faecal-oral or respiratory routes, bites or scratches, the consumption of undercooked

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Table 1
Main arthropod vectors with health significance.

Class	Order	Genus	Common name
Insecta	Siphonaptera	<i>Ctenocephalides, Pulex</i>	Fleas
		<i>Pediculus</i>	Lice
	Phthiraptera	<i>Pthirus</i>	Crab louse
		<i>Rhodnius, Triatoma</i>	Triatoma infestans
	Hemiptera	<i>Cimex^a</i>	Bed bugs
		Diptera	<i>Anopheles, Culex, Aedes, etc.</i>
	<i>Simulium</i>		Black flies
	<i>Glossina</i>		Tse-tse flies
	<i>Tabanus</i>		Horseflies
	<i>Phlebotomus, Lutzomya</i>		Phlebotominae
<i>Culicoides, Leptoconos, etc.</i>	Sand fly		
<i>Ixodes, Dermacentor, Rhipicephalus, Hyalomma, Amblyomma, Argas, Ornithodoros, etc.</i>	Ticks		
<i>Neotrombicula, Demodex</i>	Trombiculids, scabies mites, red bugs and other mites		
Arachnida	Ixodida	<i>Sarcoptes</i>	
		<i>Dermanyssus</i>	
	Trombidiforms		
	Sarcoptiforms		
	Mesostigmata		

^a Vector capacity not demonstrated.

products or the intake of milk, is AV transmission.⁴ It is difficult to limit this issue to our country, since the setting is global and very dynamic, and diseases do not understand political borders. Only a few months ago new threats appeared, such as the re-emergence of yellow fever in Brazil or the epidemic of plague in Madagascar.⁵ However, in this review we will put the focus on AVBD with greater risk to humans in our environment, without losing the “one health” perspective.

AVBD are subject to complex interactions (demographic, social and cultural changes, climate change, wars and famine or evolution of microorganisms) among which, undoubtedly, global transport systems and the consequent invasion of exotic species⁶ stand out. Generally speaking, travel, migration and globalization contribute to the emergence of infectious diseases. Its importance has been debated for many years and, possibly, dates back to ancient times.⁷ Humans carry their usual microbiota, pathogens, ectoparasites and other possible vectors, the immunological history of past infections and vaccines, the genetic load (greater or lesser susceptibility), cultural preferences, behaviours, habits and customs, as well as luggage (pets, goods and others).⁷ In the case of AVBD, the equation for the appearance of a certain disease would be the following: the presence of competent vector arthropods plus susceptible population, together with the presence of reservoirs and/or intermediate hosts (sick people), could give result an epidemic. The introduction of the tiger mosquito (*Aedes albopictus*) and the threat of its expansion could be a good example.

Diptera (mosquitoes and phlebotominae sand flies) overview in Spain and its impact on Public Health

It is thought that *A. albopictus* was introduced in Europe in 1979 through Albania, by the trade of used tyres, although the first publication on its introduction in the European continent dates back to 1990 in Italy.⁸ Since then, *A. albopictus* has expanded throughout the Mediterranean area. In Spain, this aggressive mosquito is well established in Catalonia, Levante, in the coastal area of Murcia and Andalusia. It has also been detected in Guipúzcoa,⁹ and little by little it is introduced in other non-coastal areas such as Aragon, extending through travel routes (for example, motorways).¹⁰ The last detection was carried out in the Community of Madrid¹¹ (Fig. 1). A few months ago, the first specimens of this species were also identified in the North of Portugal. This mosquito has been incriminated as a vector of numerous arboviruses in different parts

of the world, including Europe. *A. albopictus*, is the chikungunya virus vector. In this regard, most of the cases in Europe are imported, although in the last two decades there have been different epidemic outbreaks in Italy¹² and, recently, in France.¹³ In Spain, only imported cases have been reported.¹⁴ This mosquito (next to *Aedes aegypti* which, as will be detailed later, has been detected in a timely manner in Europe) can act as a vector of the dengue virus and with less effectiveness of the Zika virus.¹⁵ In France, *A. albopictus* was responsible for the first autochthonous cases of dengue¹⁶ and of those reported in the same country during the following years, one of them with a history of travel to Madeira, where a large outbreak had been reported (more than a thousand cases) between 2012 and 2013.¹⁷ In 2011, the occurrence of autochthonous cases of dengue in Croatia were also attributed to *A. albopictus*, establishing the transmission by this mosquito in Europe.¹⁸ In Spain we are only suffering from their annoying bites, for now.¹⁹

Table 2 shows arbovirus infection and Table 3 shows other infections transmitted by dipterans worldwide, with the risk of transmission in Spain. We have evaluated the risk of emergence and/or re-emergence of these diseases in Spain according to the existing studies for each pathogen, the experience according to other diseases, previous immunity and other criteria, some of them subjective, that do not appear in the text.

A. aegypti is the main Zika vector and also a transmitter of yellow fever, dengue and chikungunya. In principle, this species is not a problem because it is not settled in Europe, although it has been detected in some areas, such as in an airport in the Netherlands and, more recently, in Fuerteventura²⁰ (Canary Islands) (Fig. 1).

In view of the Zika epidemic in the Americas, the Ministry of Health, Social Services and Equality, in collaboration with the Carlos III Health Institute and the Autonomous Regions, has established a Zika virus disease surveillance in Spain. To date (last update in July 2017), 325 confirmed cases have been reported, all imported, except 4 congenital cases whose mothers were infected in the risk zone and 2 autochthonous cases of sexual transmission.²¹

It should be noted that it is not necessary to resort to invasive or exotic species to refer to AVBD. Thus, *Anopheles atroparvus* is present in Spain, a good malaria vector. The official map of the distribution of this mosquito is not updated; however, although the risk of a malarial outbreak is low in our country,²² recent events have involved this species in the two cases of autochthonous malaria registered in the north of the peninsula.²³ Spain was an endemic country of malaria until 1964, when WHO declared it a

Table 2
Arboviruses transmitted by culicoides with impact on Public Health.

Family/virus	Geographical distribution	Presence in Spain	Risk of emergence or re-emergence in Spain					
			Disease cases	Presence of the vector	Virus pathogenicity	Risk	Risk according to authors	
<i>Bunyaviridae</i>								
Batai	Africa Asia Europe	–	1	1	1		Moderate	Low
La Crosse encephalitis	North America	–	0	0	0		Low	Low
Rift Valley fever	Africa Middle East	–	0	1	0		Moderate	Moderate
Inkoo	North Europe	–	1	1	0		High	Low
Tahyna	Africa Asia Europe	Only serological evidence	1	1	0		High	Low
<i>Flaviviridae</i>								
Dengue	Africa America Asia Oceania	Present in the past	1	1	0		High	High
Murray Valley encephalitis	Oceania	–	0	0	0		Low	Low
Saint Louis encephalitis	America	–	0	1	0		Moderate	Low
Japanese encephalitis	Asia	–	0	1	0		Moderate	Low
Yellow fever	Africa South America	–	1	1	0		High	Low
West Nile Virus	Africa Asia Europe North America Middle East Oceania	Sporadic communication	1	1	0		High	High
Usutu	Africa Europe	Sporadic communication	1	1	1		Moderate	Low
Zika	Africa America Asia Oceania	–	1	1	0		High	Moderate
<i>Togaviridae</i>								
Chikungunya	Africa America Asia Oceania	–	1	1	0		High	High
Eastern equine encephalitis	America	–	0	1	0		Moderate	Low
Western equine encephalitis	America	–	0	0	0		Low	Low
Equine encephalitis of Venezuela	America	–	0	1	0		Moderate	Low
Mayaro	South America	–	0	1	0		Moderate	Low
O'nyong-nyong	Africa	–	0	0	0		Low	Low
Ross River	Oceania	–	0	0	0		Low	Low
Sindbis	Africa Asia Europe Oceania	Only serological evidence	1	1	0		High	Low

The risk of emergence/re-emergence is calculated based on three factors: (a) presence of cases of the disease in humans in the last 5 years in Europe, Mediterranean, Central and South American countries with a significant relationship with Spain; (b) presence of the vector in Spain; (c) pathogenicity of the virus for humans. Each factor is scored with one point (presence in the first two factors and low pathogenicity in the third factor) or with zero points (absence in the first two factors and high pathogenicity in the third factor). The first two factors are added and the third is subtracted. The total score can range between 0 and 2, with 0 being: low risk; 1: moderate risk; 2: high risk.

Table 3
Main human diseases transmitted by diptera.

Disease	Causal agent	Diptera		Geographical distribution	Endemic presence in Spain	Risk of emergence or re-emergence in Spain			
		Family	Genus/species			Disease cases	Presence of the vector	Risk	Risk according to authors
Oropuche fever	Oropuche virus	Ceratopogonidae	<i>Culicoides paraensis</i>	Caribbean, South America	No	0	0	Low	Low
Mansonellosis	<i>Mansonella ozzardi</i>	Ceratopogonidae	<i>Culicoides Leptoconos equaerti</i>	Caribbean, South America	No	0	0	Low	Low
	<i>M. ozzardi</i>	Simuliidae	<i>Simulium</i>	South America, Panama	No	0	0	Low	Low
	<i>Mansonella perstans</i>	Ceratopogonidae	<i>Culicoides</i>	Africa, Caribbean, South America	No	0	0	Low	Low
Malaria	<i>Mansonella streptocera</i>	Ceratopogonidae	<i>Culicoides</i>	Africa	No	0	0	Low	Low
	<i>Plasmodium</i> spp.	Culicidae	<i>Anopheles</i>	Africa, Asia, Central and South America, Pacific	No	1	1	High	Moderate
Filariasis	<i>Wuchereria bancrofti</i> , <i>Brugia malayi</i> , <i>Brugia timori</i>	Culicidae	<i>Aedes/Ochlerotatus</i> , <i>Anopheles</i> , <i>Culex</i> , <i>Mansonia</i>	Africa, Asia, Caribbean, Western Pacific, South America	No	0	0	Low	Low
Trypanosomiasis	<i>Trypanosoma gambiense</i> , <i>T. rhodesiense</i>	Glossinidae	Tse fly (<i>Glossina</i>)	Africa	No	0	0	Low	Low
Leishmaniasis	<i>Leishmania</i> spp.	Physicodidae	<i>Phlebotomus/Lutzomya</i>	Africa, Asia, Europe, Central and South America	Yes	1	1	High	High
Bartonellosis	<i>Bartonella bacilliformis</i>	Physicodidae	<i>Lutzomya</i>	Central and South America	No	0	0	Low	Low
Fever by phlebotominae sand flies	Virus Toscana, Naples, Sicily, Granada, etc.	Physicodidae	<i>Phlebotomus/Lutzomya</i>	Central and South America, China, Mediterranean, North Africa	Yes ^a	1	1	High	High
Vesicular stomatitis	Vesicular stomatitis virus	Physicodidae	<i>Lutzomya</i>	America	No	0	0	Low	Low
Onchocerciasis	<i>Onchocerca volvulus</i>	Simuliidae	<i>Simulium</i>	Africa, Central and South America	No	0	0	Low	Low
Loiasis	<i>Loa</i>	Tabanidae	<i>Chrysops</i>	Tropical Africa	No	0	0	Low	Low
Tularemia	<i>Francisella tularensis</i>	Tabanidae	<i>Chrysops</i>	North America, Russia, Japan	No	0	0	Low	Low

^a There are 7 serotypes included in the phlebotomy fever group that have been isolated in Europe; Toscana and Granada viruses have been detected in Spain.

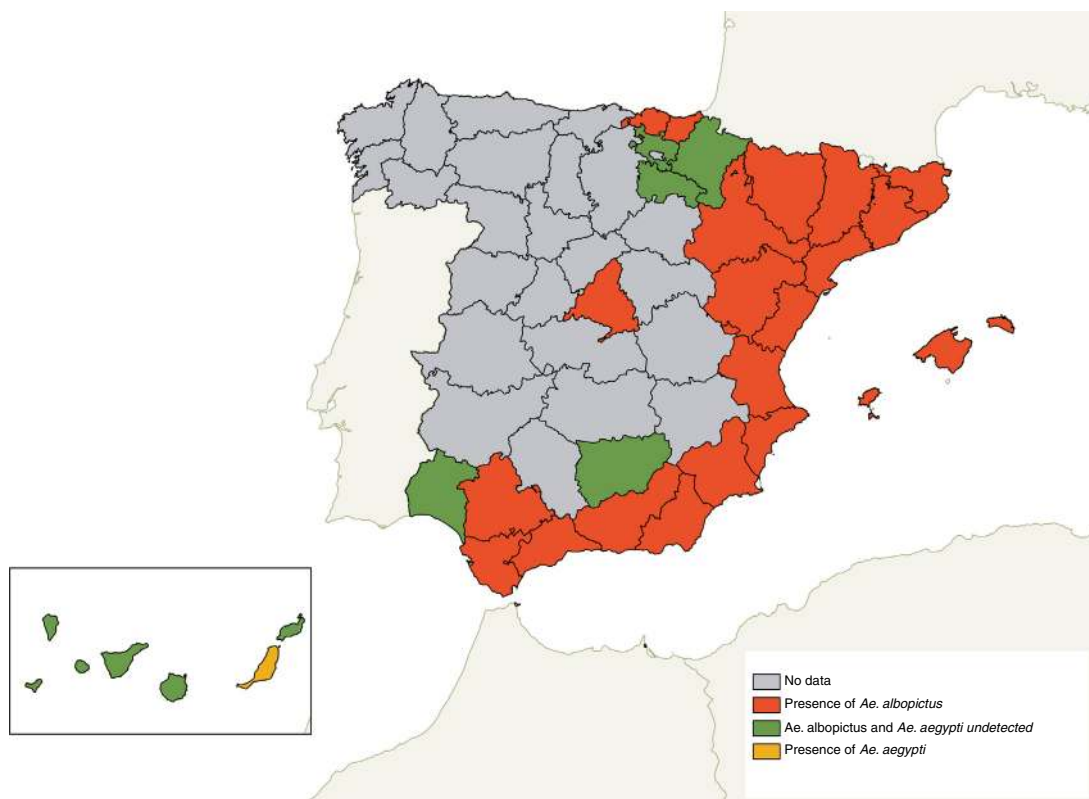


Fig. 1. Updated distribution map of *Aedes albopictus* in Spain. Ae: *Aedes*.

free zone. In Europe, after the eradication of malaria, most cases are imported, although sporadic cases have recently been reported in many Mediterranean countries such as France, Italy, Greece.²⁴ The emergence of autochthonous cases in Greece between 2009 and 2017 has raised doubts about the real situation in Europe as a malaria-free zone.²⁵

Other diptera present in Spain which we cannot ignore are phlebotominae sand flies. The species *Phlebotomus perniciosus* and *Phlebotomus ariasi*, are the competent vectors of the leishmaniasis agent (*Leishmania infantum*). There are also other potential vectors of *L. infantum* in Spain, as they are *Phlebotomus papatasi* and *Phlebotomus sergenti*. Leishmaniasis is endemic throughout the Mediterranean basin in Europe and its geographic scope is spreading. Usually, the epidemiology of leishmaniasis was linked to the rural habitat with the presence of dogs. The great epidemic outbreak of Fuenlabrada with a high number of cases in an urban area, in which leishmaniasis was not common, showed the dangers of changing the urban model in Spain. Many houses were built in rural agricultural areas with gardens and peri-urban green spaces where wildlife was present. In these places the concentration of phlebotominae sand flies was high, and, in their environment, there were not only dogs but also other *L. infantum* reservoirs, such as hares and rabbits. This fact together with mild temperatures in recent years, decreasing the mortality of the vector, seems to be what caused the great outbreak.^{26–28} Undoubtedly, the presence of phlebotominae sand flies throughout the Iberian Peninsula is a great threat, since not only do they transmit leishmania, but they are also Toscana virus vectors, which is causing numerous cases of meningoencephalitis in some areas of Spain²⁹ and other

phleboviruses such as the Granada virus (without proven pathogenic power), the Naples virus or the Sicily virus.³⁰

Another species of mosquito to which special attention is to be paid is *Culex pipiens*. This species, which is distributed and well represented throughout the Iberian Peninsula, is capable of transmitting the West Nile virus (WNV). West Nile fever is becoming a serious problem in some areas of Europe, as in Greece, where there has been an outbreak with numerous neuroinvasive forms,³¹ and in 2017 cases have been reported in France, Italy, Romania, Hungary, Croatia, Serbia and Austria.³² In Spain, according to the data from the situation report and WNV risk assessment, published in 2013, there are several species of mosquitoes capable of virus transmission. For example, *Culex modestus*, *Culex perexiguus* and *Culex theileri* show a high vector competence, while *C. pipiens* and *A. albopictus* have a moderate vector competence.³³ The first human case of neuroinvasive disease due to WNV in our country was identified, retrospectively, in a patient diagnosed with meningitis in September 2004 who, in the days before the onset of symptoms, visited a village in Badajoz, Extremadura (Spain).³⁴ In 2010, the Ministry of the Environment reported the detection of WNV in 36 equine farms in the provinces of Cádiz, Sevilla and Málaga.³⁵ Through this active surveillance, 15 suspected cases were investigated and two human cases of WNV meningoencephalitis were confirmed.³⁵ Between 2011 and 2016, virus activity was detected in equines, suggesting that the virus is endemic in our country.³⁶ In addition, there was previous evidence about its circulation in birds that were considered for the development of a predictive virus circulation model in our country.³⁷

Influence of climate change

Another factor that clearly influences infections transmitted by arthropod vectors is climate change. In 2017 the International Conference on Climate Change and Health was held in Atlanta, which revolved around the idea that: “Health is the human face of climate change”. Following this meeting, a special article was published in the *New England Journal of Medicine* which stated that the distribution of infectious diseases such as Lyme borreliosis, rickettsiosis or West Nile fever are expanding at the same rate as their AVs.³⁸ We know that climate variations and extreme weather events have a profound impact on AVBD.³⁹

Mosquitoes and ticks are devoid of temperature regulation mechanisms and, for this reason, fluctuations in temperature greatly affect their reproduction and survival.⁴⁰ In our country, it is more than possible that the great increase in the number of ticks in recent years is due to the fact that winters, in general, are much milder than years ago. Just to mention an example, *Ixodes ricinus*, the tick that most frequently bites people in the north of Spain, is very sensitive to climate warming. This, among other factors, is increasing its survival.⁴¹ This species of tick transmits very prevalent diseases in Europe, such as Lyme disease or tick-borne encephalitis, or others such as *Rickettsia monacensis* infection, human anaplasmosis, and babesiosis.^{42,43} In Spain, human cases of all of them have been described, except for tick-borne encephalitis. Although there is a high suspicion of the circulation of the virus in Spain, the molecular screening of hundreds of ticks has been carried out in our laboratory, with negative results.⁴³ In addition, other pathogens have been detected in *I. ricinus* specimens collected in Spain, such as *Rickettsia helvetica*, *Candidatus Neorhlichia mikurensis* or *Borrelia miyamotoi*, which leads us to be alert to the possible occurrence of human cases.^{44–46} As a consequence of climate change, the hypothesis about the probable changes in the distribution of another species of tick, *Hyalomma marginatum*, which is the Crimean-Congo hemorrhagic fever (CCHF) vector in Europe, has also been established. Under warmer climate conditions, according to prediction models, it is expected that the distribution of this tick species will extend to new areas which were previously free of the vector. In relation to this issue, the epidemiology of Mediterranean spotted fever seems clearly associated with climate change, especially with low rainfall values⁴⁷ and it has been shown that warming causes greater aggressiveness in its AVs. Table 4 shows the tick-borne diseases throughout the world, with the prediction of risk for Spain (subjective assessments).

Surveillance and diagnosis of infections transmitted by arthropod vectors

To be able to show a perspective on the AVBD, it is essential to monitor and identify microorganisms in vertebrates and arthropods, designing strategies before their transmission to humans. Early detection and implementation of control strategies allow minimizing the impact on the population. Between 1990 and 2010, 91% of emerging infections spread from a wild-type focal point.² Occasionally, the infection is spread directly from reservoirs such as bats, rats or chimpanzees to domestic animals, which amplify the infection, or to people; other times, infection dissemination (*spill-over*) occurs through AV such as ticks, fleas or mosquitoes. In any case, it is essential to carry out a surveillance and to know the microorganisms carried by AV. A recent example in Spain is the detection of CCHFV in ticks of the species *Hyalomma lusitanicum* collected in deer a few years ago⁴⁸ in the province of Caceres and the explanation of one of the possible ways of the arrival of the virus to our country.⁴⁹ Both findings contributed to the early

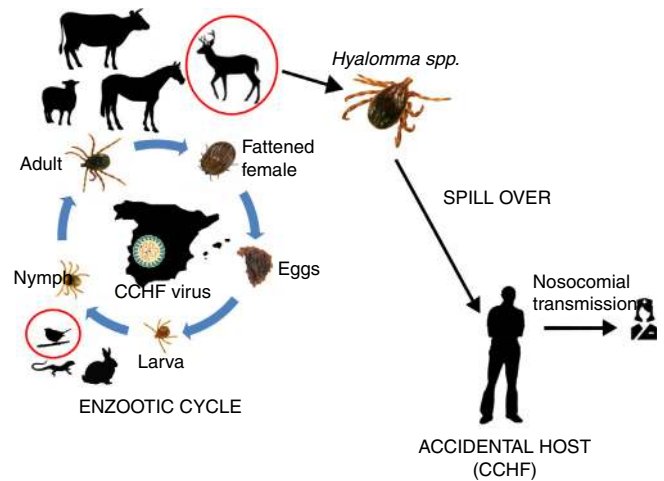


Fig. 2. Transmission cycle of Crimean-Congo haemorrhagic fever in Spain, 2016 (*spill-over*). CCHF: Crimean-Congo haemorrhagic fever.

detection of the disease that appeared in 2016 as, to some extent, it was predictable. On September 1, 2016, the Ministry of Health issued a press release reporting the death of a man by CCHF and the contagion of the nurse who had taken care of him in the ICU of the Vallecas Hospital where he had been treated. The first two autochthonous cases of CCHF in Spain were confirmed⁵⁰ (Fig. 2). In the last CCHFV situation report and transmission risk assessment in Spain,⁵¹ the virus has been found in a low percentage of ticks of the species *H. lusitanicum*. This tick does not bite people very often and does not seem to be a good virus vector, although it shares an ecological niche with another very active species (*H. marginatum*) which bites humans more often. Given this situation, two scenarios could be developed: that of Turkey, where in 2002 the first case was reported and there are currently around 1,000 cases/year, or the scenario in Greece, where the first case was reported in 1975; the second, in 2008 and to date, no new cases have been reported.⁵²

The diagnosis of tick-borne diseases is not always easy. We must bear in mind that a tick bite history is usually absent in at least half of the cases and that incubation periods can be very long. Depending on the size of the tick, they can be very difficult to see (they can simulate a small mole), and their bite is painless. Unless there is awareness or a high index of suspicion when faced with certain signs and/or clinical symptoms, who is going to think of a tick-borne disease? It is clear, “*what is not sought, is not found*”.⁵² In 2018, WHO revised the list of emerging pathogens that could cause serious epidemics in the future and those that need to be investigated, including CCHFV, Ebola/Marburg virus, Zika virus, Middle East respiratory syndrome coronavirus (MERS-CoV), severe acute respiratory syndrome coronavirus (SARS-CoV), Lassa virus, Nipah virus and Rift Valley fever virus. In addition, this year the list is completed with disease X, referring to an international epidemic that could be caused by a pathogen whose pathogenic potential and route of transmission is unknown at the moment. This list takes into account the transmissibility between humans, the severity of cases and the percentage of mortality, the difficulty of control and diagnosis and the context of public health and global expansion. In addition, there are other diseases that need more attention as soon as possible: hemorrhagic fevers by other arenaviruses, chikungunya virus, diseases by other highly pathogenic coronaviruses or by emerging enteroviruses and febrile syndrome with severe thrombocytopenia.⁵³ Many of these diseases are AV-borne.

Table 4
Main tick-borne diseases with impact on Public Health.

Pathogen Family Infection or disease	Geographical distribution	Presence in Spain	Risk of emergence or re-emergence in Spain			
			Disease cases	Presence of the vector	Risk	Risk according to authors
Bacteria						
<i>Rickettsiaceae</i>						
DEBONEL/TIBOLA	Europe	Endemic	1	1	High	High
African tick-bite fever	Sub-Saharan Africa, Caribbean, Oceania, Turkey	–	1	0	Moderate	Low
Mediterranean spotted fever	Mediterranean	Endemic	1	1	High	High
Australian tick-bite fever	Australia	–	0	0	Low	Low
Japanese spotted fever	Japan, Thailand	–	0	0	Low	Low
Flinders Island spotted fever	Australia, Thailand, Nepal	–	0	0	Low	Low
Rocky Mountain spotted fever	America	–	1	1	High	Low
Pacific Coast tick fever	USA	–	0	0	Low	Low
<i>Rickettsia sibirica mongolitimonae</i> infection (LAR)	Africa, Southern Europe	Endemic	1	1	High	High
Far-Eastern tick-borne rickettsiosis	China, Japan, Russia	–	0	0	Low	Low
Queensland Tick Typhus	Australia	–	0	0	Low	Low
Siberian tick typhus	Siberia, Mongolia	–	0	1	Moderate	Moderate
<i>Rickettsia helvetica</i> infection	Central Asia, Europe	Endemic	1	1	High	Moderate
<i>Rickettsia aeschlimannii</i> infection	Africa, Mediterranean	Endemic	1	1	High	Moderate
<i>Rickettsia parkeri</i> infection	America	–	1	0	Moderate	Low
<i>Rickettsia massiliae</i> infection	America, Mediterranean	Endemic	1	1	High	Moderate
' <i>Candidatus Rickettsia kellyi</i> ' infection	India	–	0	0	Low	Low
' <i>Candidatus Rickettsia tarasevichiae</i> ' infection	China	–	0	0	Low	Low
<i>Anaplasmataceae</i>						
Human Anaplasmosis	Europe	Endemic	1	1	High	Low
<i>Anaplasma capra</i> infection	China	–	0	0	Low	Low
<i>Ehrlichia ewingii</i> infection	America	–	0	0	Low	Low
<i>Ehrlichia chaffeensis</i> infection	America	–	0	0	Low	Low
<i>Ehrlichia canis</i> infection	America	–	0	1	Moderate	Low
<i>Ehrlichia muris</i> infection	Asia, USA	–	0	1	Moderate	Low
' <i>Candidatus Neoehrlichia mikurensis</i> ' infection	Asia, Europe	Endemic	1	1	High	High
<i>Borreliaceae</i>						
Lyme borreliosis	America, Asia, Europe	Endemic	1	1	High	High
<i>Borrelia miyamotoi</i> infection	America, Asia, Europe	Endemic	1	1	High	High
<i>Borrelia mayonii</i> infection	North America	–	0	0	Low	Low
Tick-borne relapsing fever	Africa, Asia, America, Mediterranean	Endemic ^a	1	1	High	High
<i>Francisellaceae</i>						
Tularemia	America, Asia, Europe	Endemic	1	1	High	High
Virus						
<i>Bunyaviridae</i>						
Avalon virus infection	Canada, Russia	–	0	0	Low	Low
Bhanja virus infection	Africa, Asia, Europe	Endemic	1	1	High	Low
Crimean–Congo haemorrhagic fever	Europe, Africa, Asia	Sporadic communication	1	1	High	High
Heartland virus infection	USA	–	0	0	Low	Low
Issyk-kul virus infection	Kyrgyzstan, Tajikistan, Kazakhstan	–	0	1	Moderate	Low
Severe fever with thrombocytopenia syndrome or Huaiyangshan	China	–	0	0	Low	Low
<i>Flaviviridae</i>						
Alkhumra virus infection	Saudi Arabia	–	0	0	Low	Low
European subtype tick-borne encephalitis	Europe, South Korea	–	1	1	High	Moderate
Far Eastern and Siberian subtype tick-borne encephalitis	Asia	–	0	0	Low	Low
Kyasanur Forest disease	India	–	0	0	Low	Low
Omsk hemorrhagic fever	Siberia	–	0	1	Moderate	Low
Louping ill virus infection	Europe	Endemic	1	1	High	Low
Powassan virus infection	North America	–	0	1	Moderate	Low
Tyuleni virus infection	Europe, USA, Russia	–	1	0	Moderate	Low
<i>Orthomyxoviridae</i>						
Bourbon virus infection	USA	–	0	0	Low	Low
Dhori virus infection	Mediterranean	–	1	1	High	Low
Thogoto virus infection	Africa, Asia, Europe	–	1	1	High	Low

Table 4 (Continued)

Pathogen Family Infection or disease	Geographical distribution	Presence in Spain		Risk of emergence or re-emergence in Spain			
				Disease cases	Presence of the vector	Risk	Risk according to authors
Reoviridae							
Eyach virus infection	Europe	–	1	1	High	Low	
Colorado tick fever	North America	–	0	0	Low	Low	
Kemerovo virus infection	Egypt, Slovakia, Russia	–	1	1	High	Low	
Tribec virus infection	Europe	–	1	1	High	Low	
Protozoa							
Babesiidae							
Human babesiosis	America, Europe	Endemic	1	1	High	High	

DEBONEL/TIBOLA: *Dermacentor*-borne necrosis, erythema and lymphadenopathy/tick-borne lymphadenopathy; LAR: rickettsiosis associated with lymphangitis.

^a In Spain, *Borrelia hispanica* relapsing fever.

The risk of emergence/re-emergence is calculated based on two factors: (a) presence of cases of the disease in humans in the last 5 years in Europe, Mediterranean countries and Central and South American countries with a significant relationship with Spain; (b) presence of the vector in Spain.

Each factor is scored with one point (presence in the two factors) or zero points (absence in the two factors) and both are added. The total score can range between 0 and 2, with 0 being: low risk, 1: moderate risk and 2: high risk.

Other arthropod vectors (lice, fleas and ticks)

Another AV that is said to have killed more people than all wars together is the body louse (*Human pediculus*), transmitting exanthematic or epidemic typhus (*Rickettsia prowazekii*), endemic recurrent fever (*Borrelia recurrentis*) and the trench fever (*Bartonella quintana*). Body lice have been a serious public health problem until recently. They live in the seams of clothes and multiply in cold weather, lack of hygiene and war conditions. A person can be infested with thousands of lice, and each specimen is capable of biting an average of five times a day. It is said that body lice were one of the main problems during the Russian Revolution, where three million people affected by exanthematic typhus died. Thus, Vladimir Ilyich Lenin (1870–1924) stated: *Either Socialism defeats the louse, or the louse will defeat Socialism*.⁵⁴ Here in Spain, it was also a problem during the post-war period and was used as propaganda by Franco's regime. We can ask ourselves: Is there a risk of an epidemic or an epidemic outbreak of exanthematic typhus? It could happen, as it occurred in Burundi in 1996, when a large epidemic affected more than one hundred thousand patients.⁵⁴ All the alarms went off when a Red Cross nurse was diagnosed after returning from work in the affected country. Body lice are not seen on the body surface but live in the seams of clothing, in $20 \pm 2^\circ\text{C}$ temperatures. Parasitism by body lice should be suspected in persons with signs of scratching and lack of hygiene, more frequently in cold times of the year. At present, body lice have reappeared in refugee camps in Europe, as in the Second World War. In November 2015, the European Center for Disease Prevention and Control reported the emergence of 27 cases of recurrent fever due to body lice at different points along the route followed by refugees arriving in Italy from the Syrian war.⁵⁵ In Western Europe, although we have not experienced any epidemic since the post-war period, and the fact that the condition had been eradicated, occasionally, there are *R. prowazekii* and *B. quintana* infection reports in homeless people parasitized by lice⁵⁶ and cases of Brill–Zinsser disease have been described in people who have suffered from exanthematic typhus which could lead to an epidemic outbreak in certain conditions.⁵⁷

Fleas are other bloodsucking insects of worldwide distribution with an impact in Public Health. *Rickettsia* can be transmitted to humans by at least two species: the rat flea (*Xenopsilla cheopis*),

which is the endemic or murine typhus vector (caused by *Rickettsia typhi*), and the cat flea (*Ctenocephalides felis*), which is the key vector of *Rickettsia felis* and, occasionally, of *R. typhi*. As far as we know, rickettsias are not transmitted by the human flea (*Pulex irritans*). In Europe, murine typhus is a common AVBD in Mediterranean countries such as Greece, Cyprus, Croatia and Spain, including the Canary Islands.⁵⁸ It develops as a non-specific febrile disease, with or without rash, which is often underdiagnosed. In clinical practice, murine typhus should be included in the differential diagnosis of any patient with fever of intermediate duration, that is, in a patient with fever (more than 38°C) of more than 7 and less than 28 days of progression, without focality to guide the diagnosis, which remains without a diagnosis after an initial evaluation that includes a complete clinical history, physical examination, complete blood count, chest X-ray and biochemical blood and urine tests.⁵⁹ *R. felis* infection is another rickettsiosis with characteristics similar to murine typhus, of which cases have also been published in Spain⁶⁰ and that should be considered in patients with fever and/or rash, with a history of contact with cats or flea bites. Despite the fact that there have been no reports of autochthonous *Yersinia pestis* infection transmitted by the rat flea (*X. cheopis*) in Spain, there is an alert for travellers at the time of writing this manuscript due to an epidemic outbreak in Madagascar that has affected several thousand people.⁵

Finally, we should remember the phrase written by Hans Zinsser in 1934 in his book entitled: *Rats, lice and history*: “Nothing in the world of living creatures remains constant. Infectious diseases are constantly changing, new ones are in the process of development and the oldest ones are changing or disappearing”.

Currently, ticks are considered the most dangerous AVs in the world, because of their ease in moving from animals to people, because of their ubiquitous nature (they are present on all continents, including Antarctica) and because of their capacity to agglutinate inside them a host of pathogenic microorganisms potentially transmissible through their hematophagous habits. The human tampering of ecosystems (deforestation, erosion of geographical limits to facilitate travel, etc.) or climate change are some of the factors that are favouring a greater contact between wild animals (with their ticks and the diseases they transmit) and people, facilitating the expansion of ticks to new previously unoccupied areas. Diptera, ticks or other AV may play the leading role in the

next pandemic. Therefore, anticipating the next Public Health crisis is in our hands.

Conflict of interests

The authors declare no conflict of interest.

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