TICKS AND TICK-BORNE DISEASES

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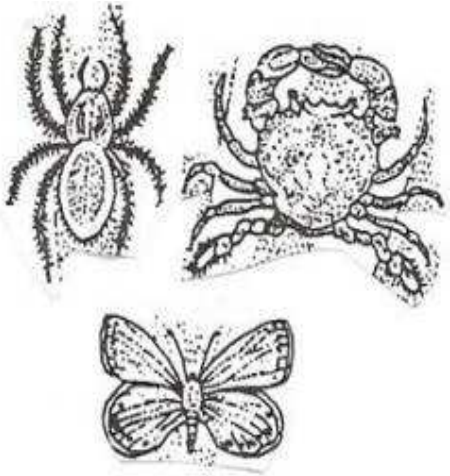
Ticks: taxonomy

Phylum:Arthropoda



Classe:
Arachnida

They don't have: wings and antennae

They have: 4 pairs of articulate legs in the nymphal and adult stages, and chelicera and pedipals

Ordine:Ixodida

Ixodidae: hard ticks

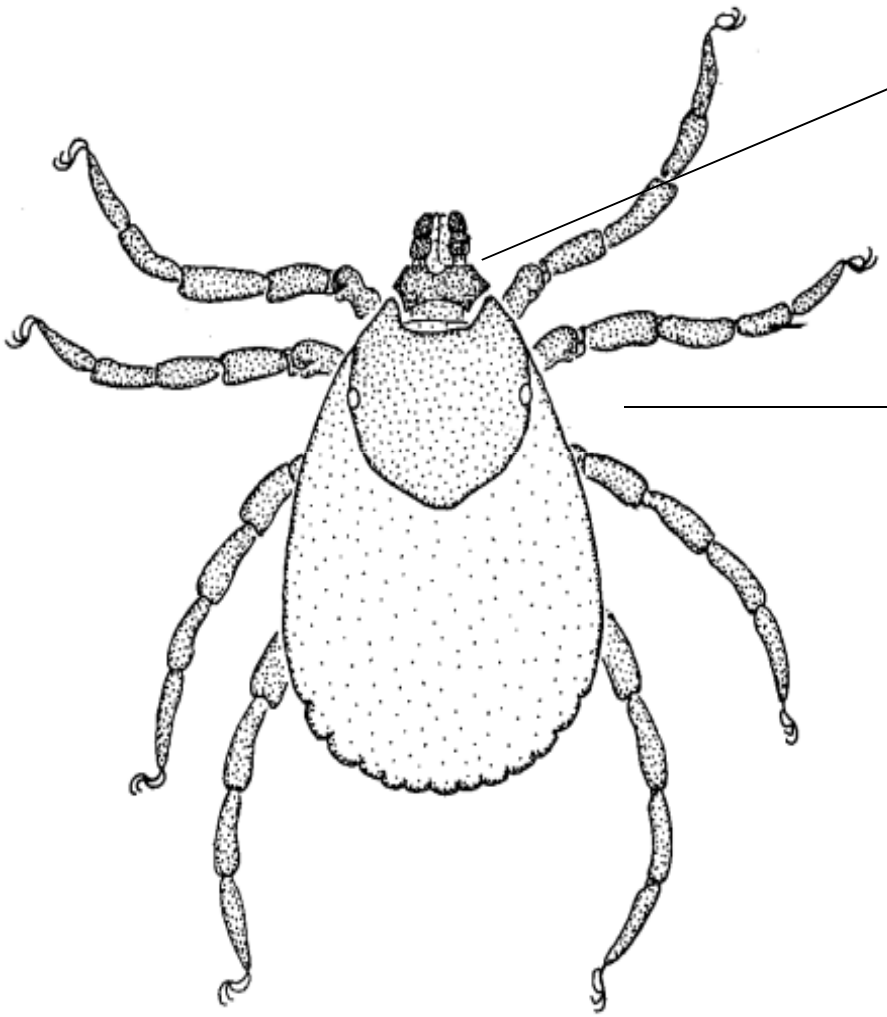
Argasidae: soft ticks

Obligate haematophagus of reptiles, birds and mammals

General Features

Unfed adult ticks are visible to the naked eye (from 2-3 mm to more than 20 mm)

General Features



capitulum or gnatosoma = mouthpart

Idiosoma= body

IXODIDAE and ARGASIDAE

Soft ticks

Capitulum dorsally invisible
scutum absent
males are identical to females
medium/short feeders (from 15 min up to 1 h)

Hard ticks

- Capitulum dorsally visible
  Hard scutum present
  sexual dimorphism
  Long-feeders (from 1 to 10 days)

ARGASIDAE-SOFT TICKS

- Strictly associated with their hosts, birds and chiropters
- Some species are considered urban pest, Argas reflexus- pigeons ticks frequently infest houses and public historical buildings
- Ornithodoros species are vector of Tick-borne Relapsing Fever

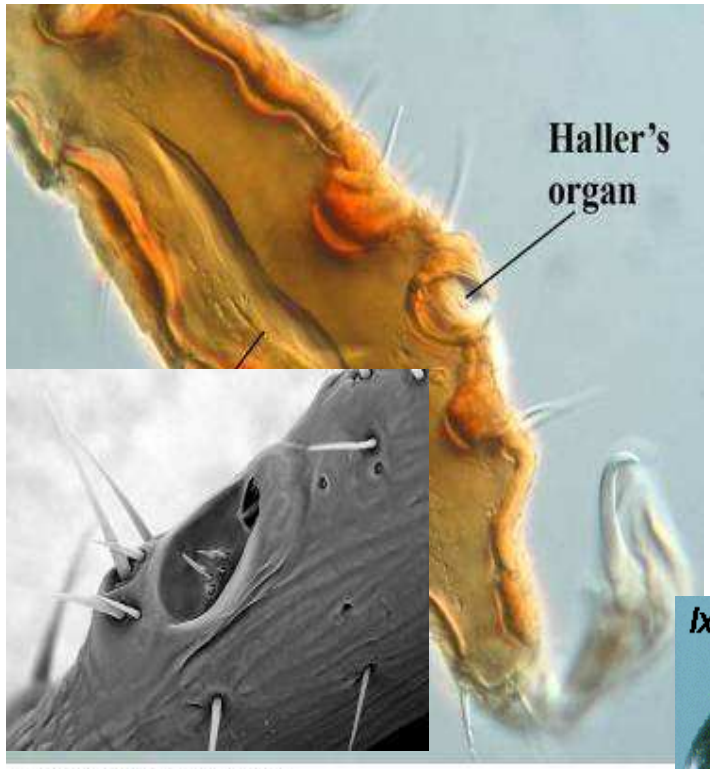
Morphological features

Ticks have very limited mobility: need to optimize the single blood meal

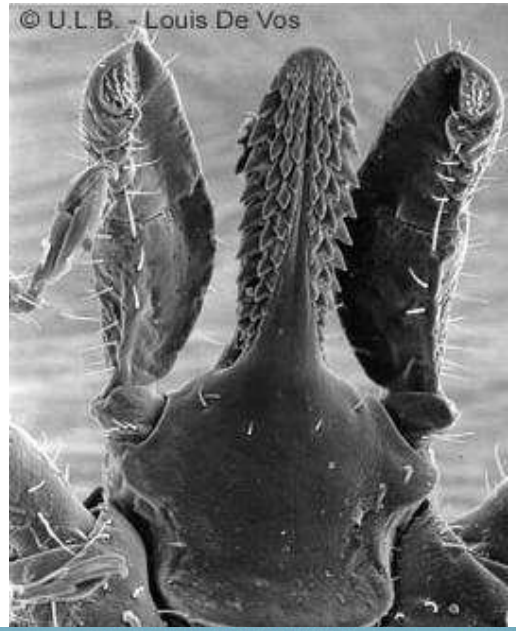
-Chelicera and pedipalps

-Haller's organ on the first pair of tarsus

-Very elastic skin; can weigh up to 100 times their unfed body weight



9, Ixodida Haller's organ on tarsus 1.



Blood meal

They can survive only by feeding on a verterbrate host. Blood is the only food source

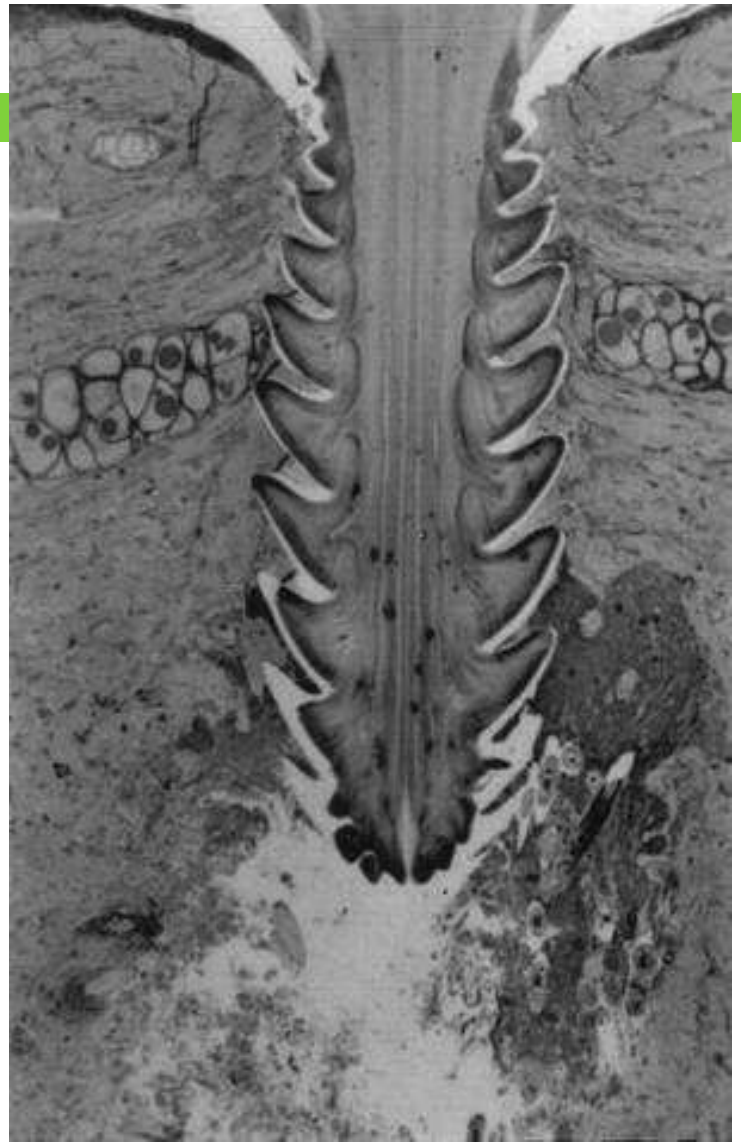
1. the tick select a suitable location on the host
2. cut the skin with the chelicerae
3. then insert the hypostomeinto the wound created by the chelicerae
4. the ticks begin to secret salivafrom its salivary glands
5. the salivary fluids contains proteins that form a cement layer
6. once the tick is firmly attacched , it start sucking blood

Blood meal

No other blood-feeding arthropods have succeeded in assuming large quantities of blood as well as ticks.

Ticks secrete bioactive compounds like anticoaugulants, anti-inflammatory proteins, vasodilatation proteins and immunoglobulin binding proteins, enzyme thst cleave complement.

Video



Ecology

aproximately 890 known tick species can be divided in two major groups, based on their ecology:

-nidicolous ticks or endophilic

-nonnidicolous ticks or exophilic

Host seeking

<u>Ambushing</u>:

ticks climb onto weeds, grasses, bushes or leaf vegetation to wait for passing host

the height to which the ticks climb depends upon many factors:

- Larvae : closest to the ground (small mammals, ground feeding birds)

- Nymphs: up to 30-40 cm

- Adults: up to 150 cm (large mammals such as deer, carnivores or humans)

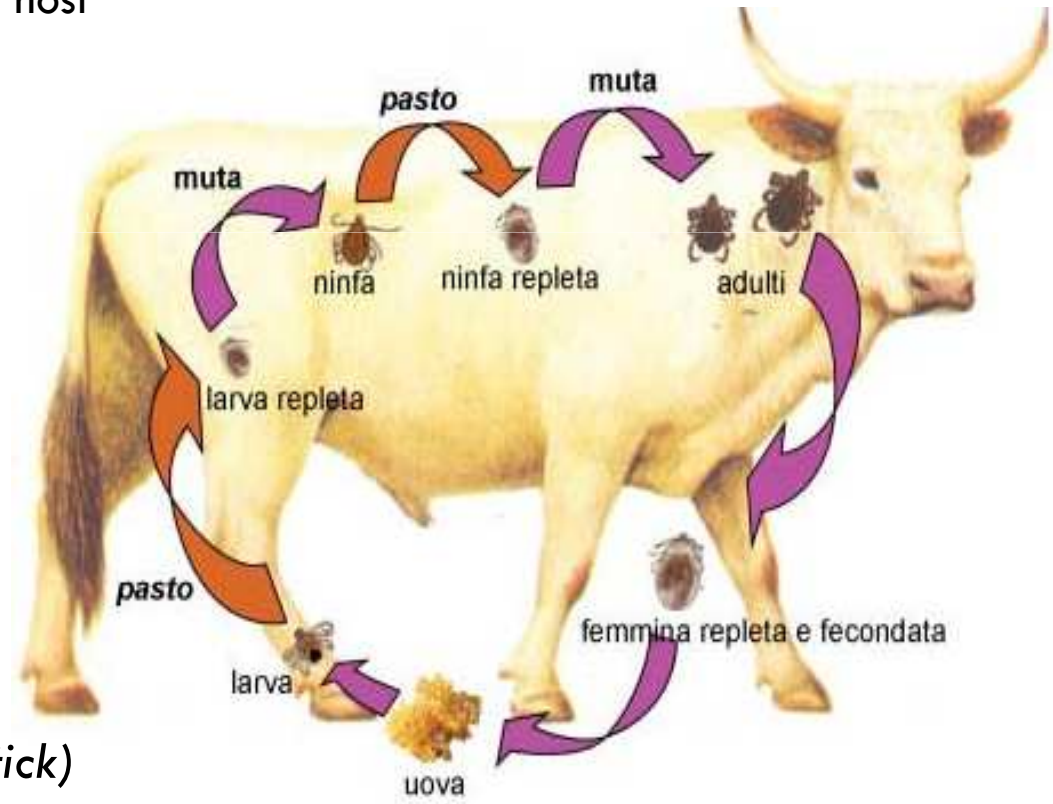
Ticks wait under leaves until increasing desiccation initiates a descent to the cooler and humid ground layer, then climb again

Host seeking

- Hunting: method used by several species that parasitize large mammals in arid zone, such as *H.dromedarii* or *Amblyomma* species.
- They remain buried in soil protected from desiccation and when excited by host (odor, CO2, vibration, sound) the tick emerged and run rapidly to attack the host

Ecological features: one-host tick

Ticks that spend the entire cycle on the host

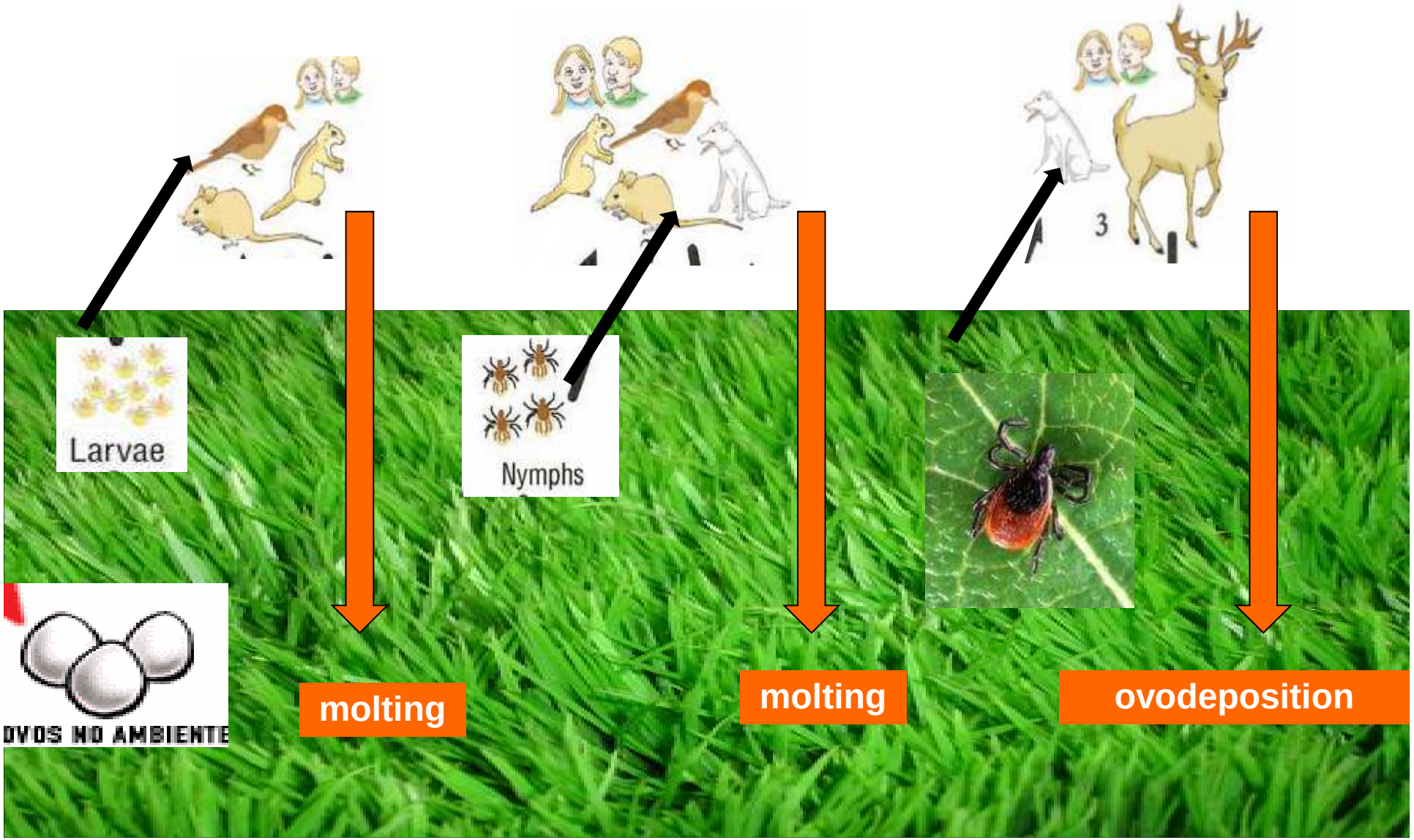


Rhipicephalus annulatus (bovine tick)

Rhipicephalus bursa (horse tick)

Ecological features : three-host ticks (*Ixodes ricinus*)

each life stage engorged and drop off its host to develop (molt) in environment



European tick species

Transmitting zoonoses

If you know the vector, you know the risk

What we know in Montenegro

Vet Parasitol. 1996 May;63(1-2):25-40.
Ticks of domestic animals in the Macedonia region of Greece.
Papadopoulos B[1], Morel PC, Aeschlimann A.

Glas Srp Akad Nauka Med. 1993;(43):87-91.
[Distribution of Ixodes ricinus ticks in Yugoslavia].
[Article in Serbian]
Petrović Z, Milutinović M.

Ixodes ricinus: deer tick or sheep tick

Vector of:

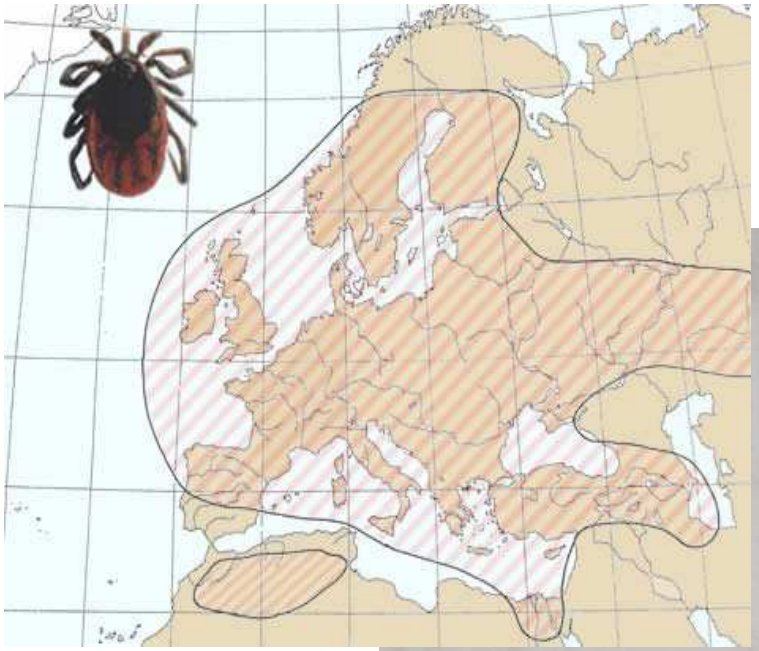
TBE

LYME DISEASE

HGE

RICKETTSIOSIS

BABESIOSIS



Dermacentor marginatus

VECTOR OF.

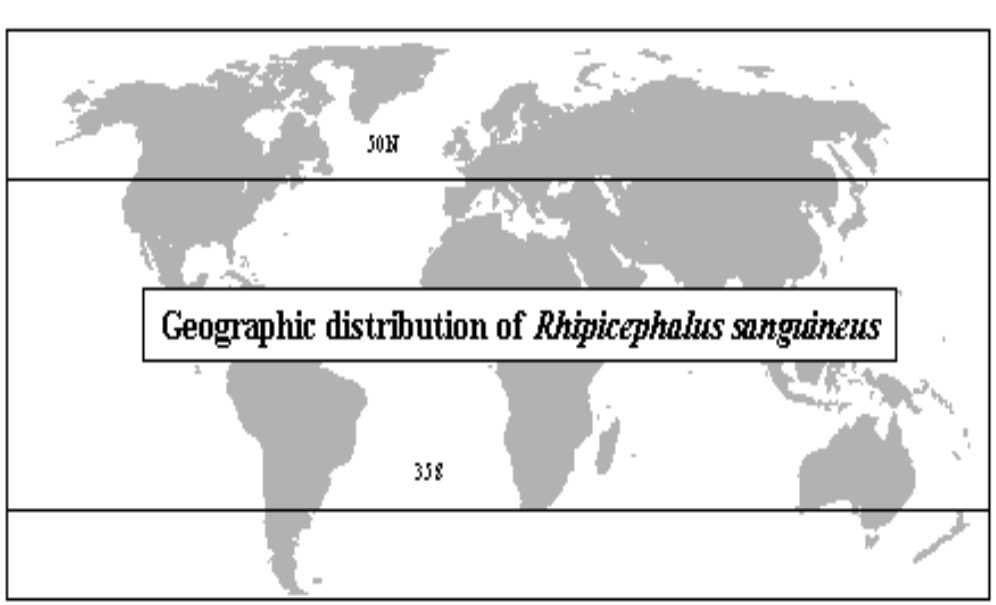
SENLAT (R. slovaca and raoultii)

Tularemia

Rhipicephalus sanguineus: brown dog tick

VECTOR OF:

Mediterranean Spotted fever and other rickettsiosis



Hyalomma marginatum

VECTOR OF:

CCHF

R. AESCHLIMANNII

Sampling ticks

<u>Questing ticks</u>:

Dragging/ Flagging

CO^2 trap

<u>Engorged tick:</u>

Remove from hosts

Preventing tick-bites

In areas where ticks are present it is important to know how to prevent and check for tick bites.

Main risk groups in endemic areas:

- People with recreational or occupational outdoor activities (e.g. hunting, fishing, hiking, camping, collecting mushrooms and berries, forestry and farming) are potentially at risk of infection by contact with infected ticks.

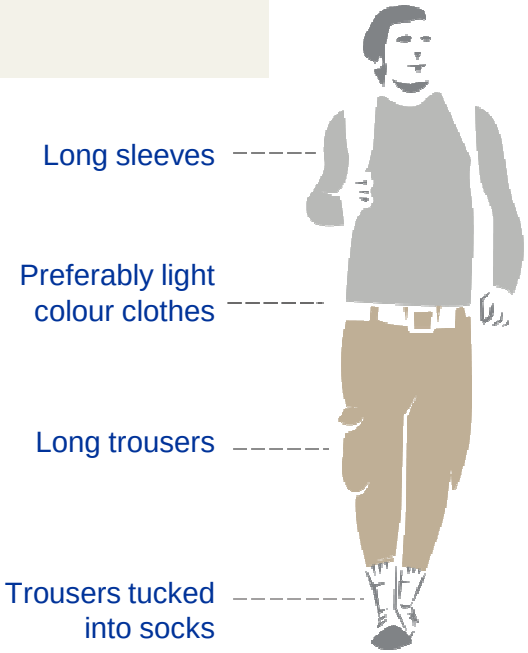
Preventing tick-bites

Key recommendations:

Avoid tick bites and remove the tick rapidly but safely!

Protection against ticks:

- Wear long-sleeved shirts and long trousers tucked into socks.
- Wear preferably clothes with light colours to make it easier to spot ticks.
- Use tick repellent on clothes and skin.
- Avoid areas with ticks: high grasses, ferns etc.

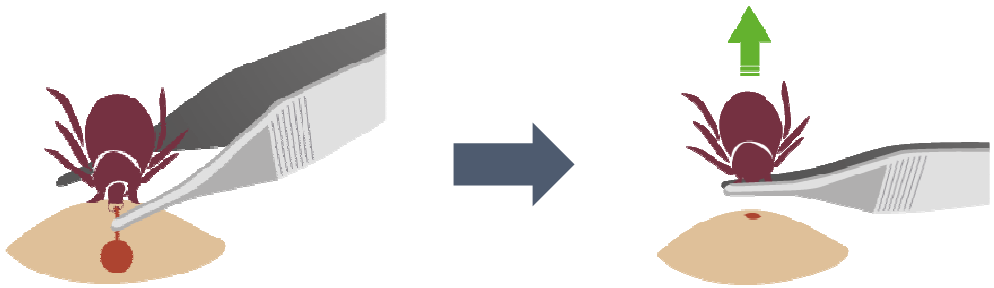


Preventing diseases

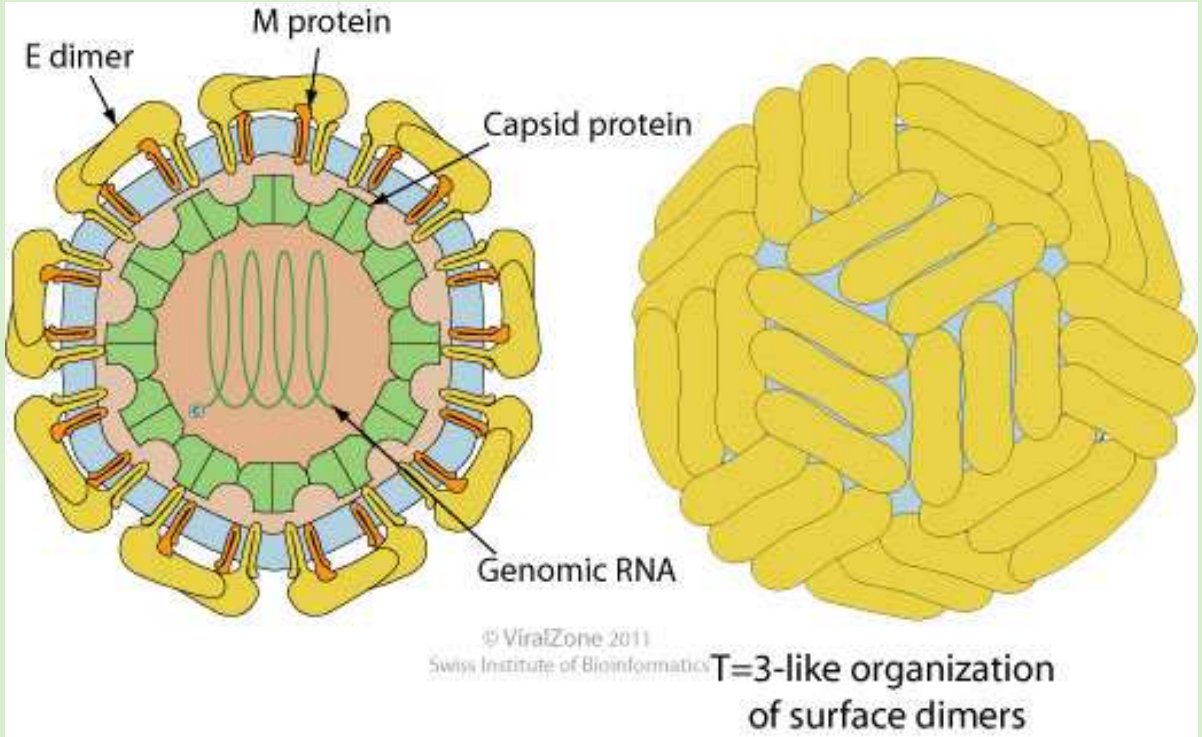
Detection and Removal

- Body inspection after outdoor activities.
  - Areas of particular attention: armpits, groin, legs, navel, neck and head.
  - On children: head at the hairline.
- Using tweezers or ticks-removal tools to remove the tick(s). video
- Cleaning the wound afterwards and applying antiseptic.
- Still using tweezers, wrap the tick in some toilet paper and flush it in the toilet.

Note: Vaccine is available for TBE

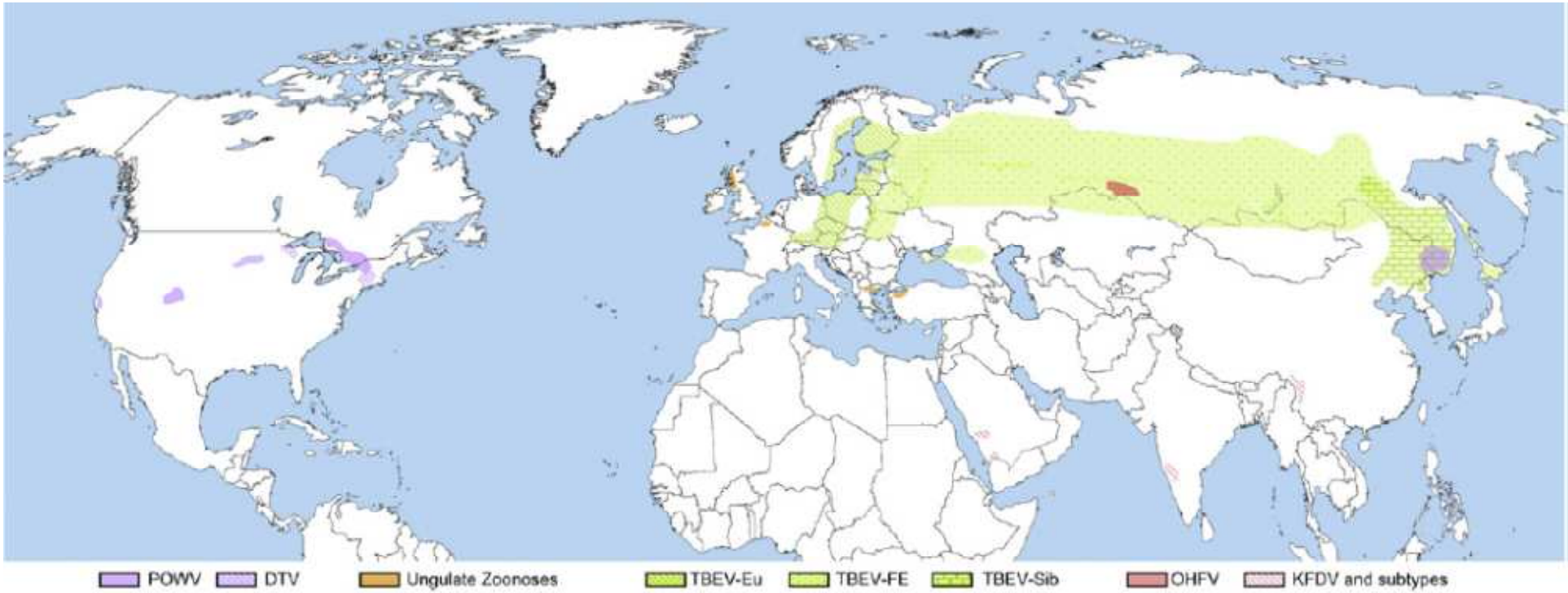


Viruses



Flaviviridae

Tick-transmitted Flavivirus



Congruencies between phylogeny and biogeographic properties, (principal tick vector, principal vertebrate host, global distribution)

Tick-borne flavivirus

- Except for tick-borne encephalitis virus, which is distributed over large parts of Europe and Asia, all other tick-borne flaviviruses have rather limited geographical distributions, probably due to their necessary ecological prerequisites.
- Because of changing ecological conditions new, so far unidentified tick-borne flaviviruses may emerge or virus strains of well-known tick-borne flaviviruses could emerge with altered pathogenetic characteristics.

Flavivirus of tick-borne encephalitis (TBEV)

There are three recognized TBEV subtypes:

1. Western or European subtype (TBEV-W), also called Central European (CEEV)
2. (Ural-)Siberian subtype (TBEV-Sib) sometimes called "persulcatus" subtype, causing Russian spring–summer encephalitis (RSSEV)
3. Far Eastern subtype (TBEV-FE)

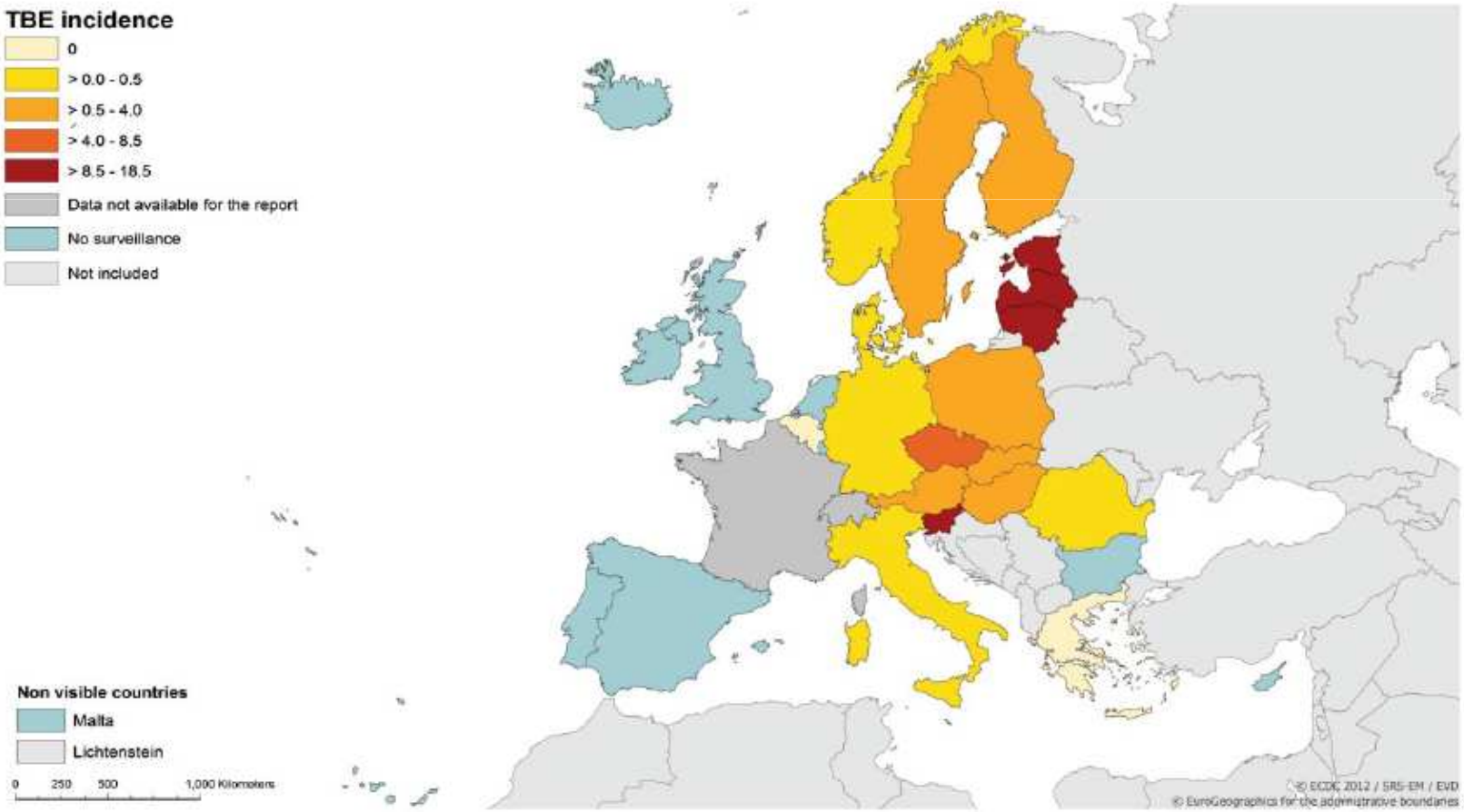
Principal arthropod vectors are ticks of the *Ixodes persulcatus* complex; the infection rate may attain 0.5 % to 3 % in natural foci

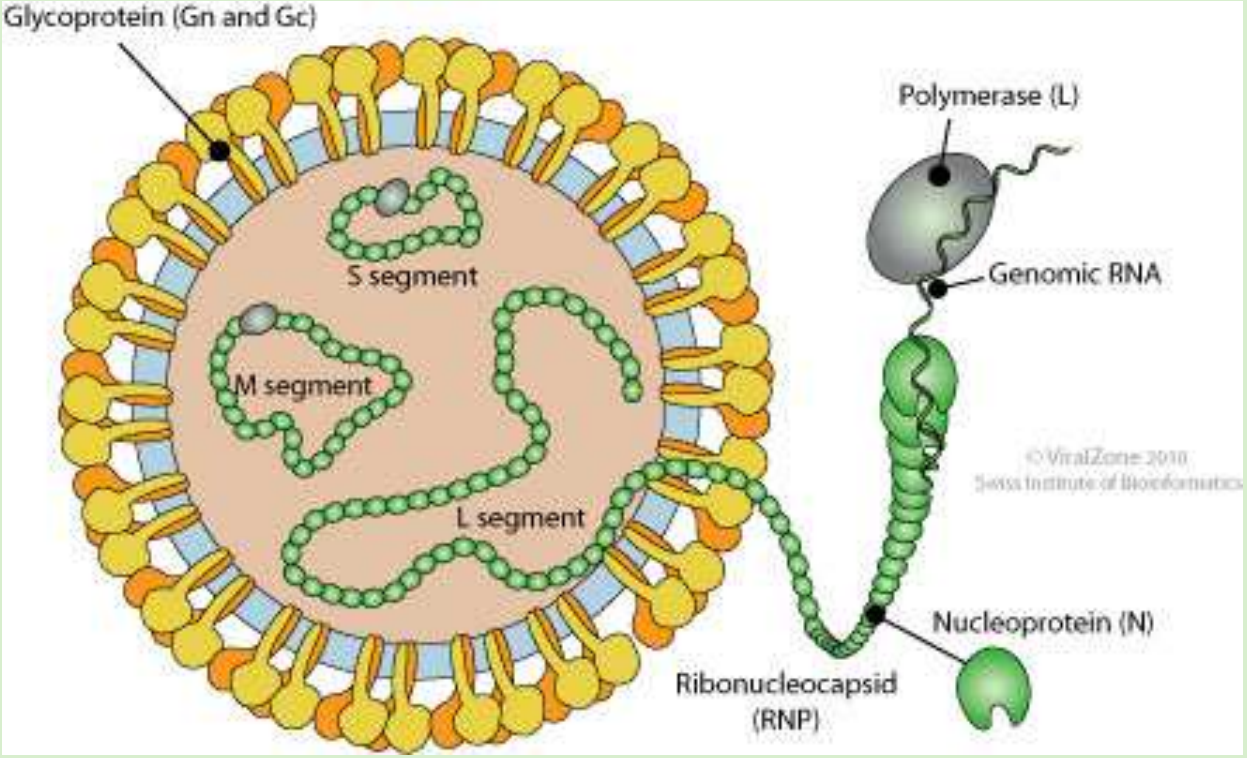
Competent vertebrate hosts are small forest mammals, especially rodents and insectivores (*Apodemus flavicollis, Apodemus sylvaticus, Myodes glareolus, Myodes rufocanus, Microtus agrestis, Sciurus vulgaris, Talpa europaea, Sorex araneus, Erinaceus concolor*)

TBE in Europe

Figure 5. TBE average annual incidence rate per 100 000 inhabitants in the EU/EFTA. (A) At country level, (B) at lower administrative level NUTS 2 (Italy) or NUTS 3.

A

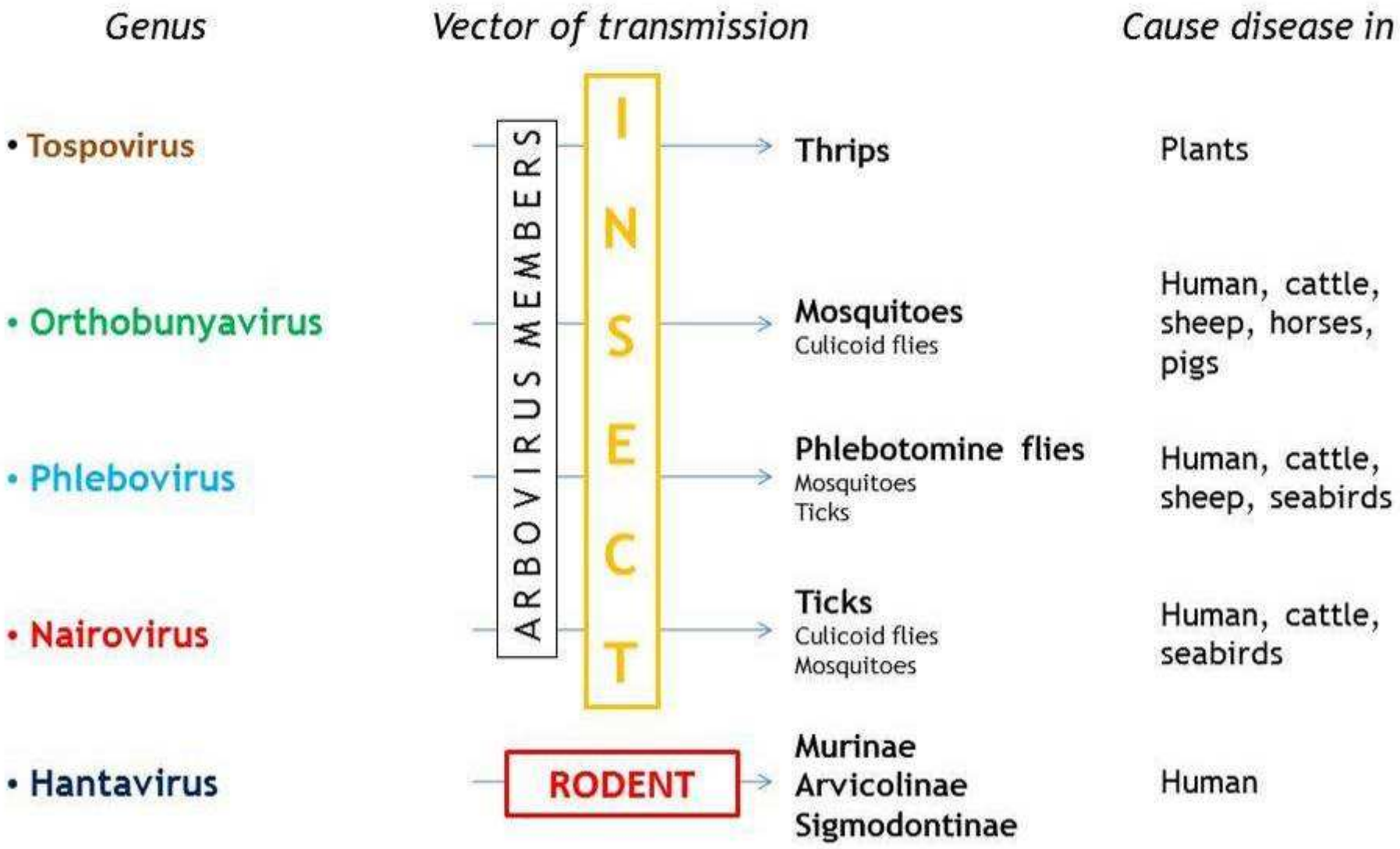




Bunyaviridae

5 genera

Except for the hantaviruses, bunyaviruses in the other four genera are transmitted by arthropods

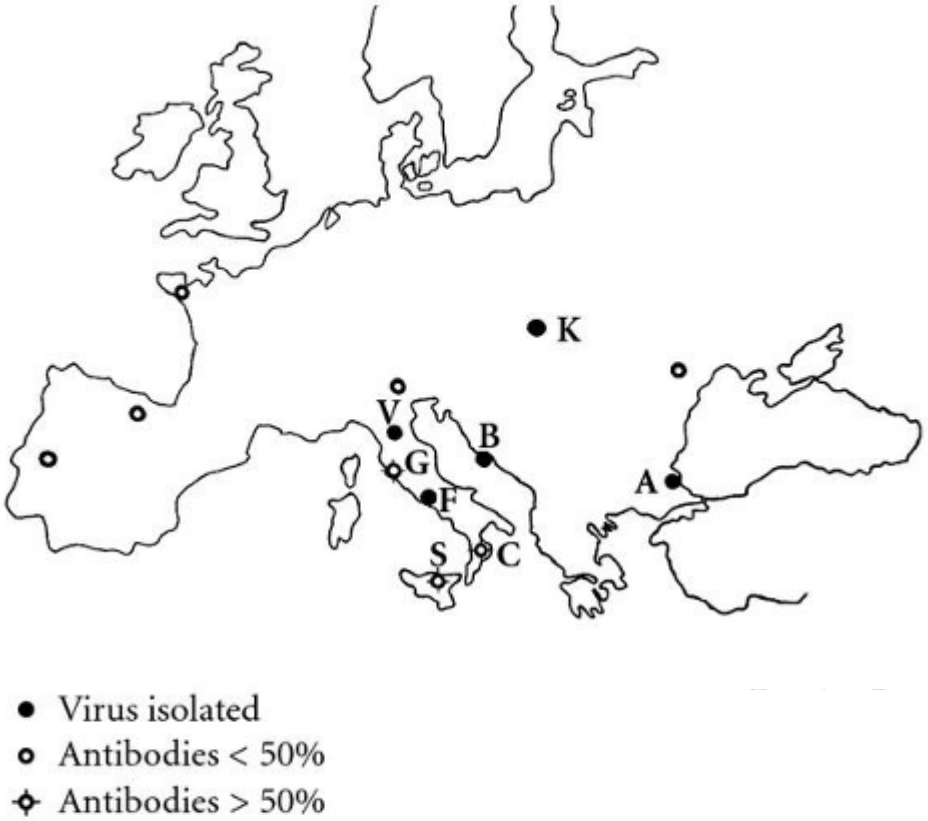


Bunyaviridae

	Name	Vector	GEOGRAPHIC DISTRIBUTION
Ortobunyaviru s	California Encephalitis virus	mosquitoes	East USA
Phlebovirus	Sandfly transmitted Phlebovirus	sandflies	Mediterranean basin
	Tick transmitted Phlebovirus (UUkuniemi/SFTS/HRTLV)	ticks	North Europe; China; USA
	Rift Valley Fever	mosquitoes	Africa, Madagascar, Saudi Arabia
Nairovirus	CCHF	ticks	Africa, Asia, middle East Europe
	Nairobi sheep disease/ Ganjam virus	ticks	Africa and India

Bhanja virus

- The virus is transmitted by metastriate ixodid ticks: in addition to *H. intermedia*, it was also isolated from *Haemaphysalis punctata, H. sulcata, Dermacentor marginatus, Hyalomma marginatum, H. detritum, H. dromedarii, H. truncatum, H. asiaticum, Rhipicephalus bursa, R. appendiculatus, Boophilus decoloratus, B. annulatus, B. geigyi, and Amblyomma variegatum.*
- 10 cases of BHAV febrile illness have been described in humans, with symptoms including photophobia, vomiting, meningoencephalitis, and pareses



Phlebovirus- Recently discovered

Heartland virus

- The Heartland virus (HRTV) is a novel, tick-borne Phlebovirus discovered in northwestern Missouri
- first appeared in humans in June 2009 when two farmers, living 60 miles (97 km) apart, presented with the following symptoms: fever, fatigue, diarrhea, thrombocytopenia, and leukopenia.[
- The reservoir host has yet to be identified.
- *Amblyomma americanum*

closely related virus (>90% identity)

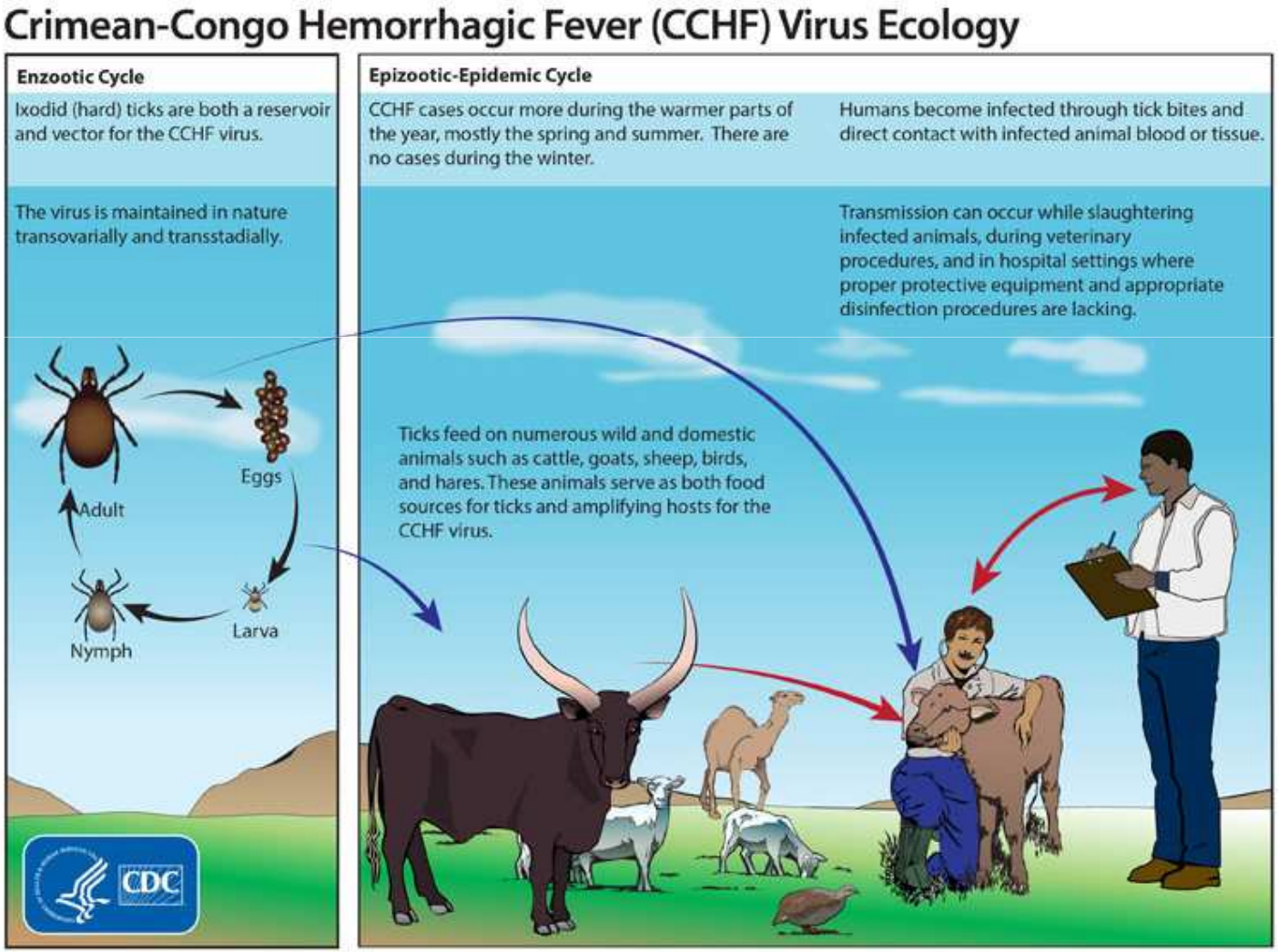
Severe fever with thrombocytopenia syndrome

- SFTS is an emerging infectious disease recently described (1° isolation in 2010) in northeast and central China. SFTS has a fatality rate of 12% and as high as 30% in some areas
- life cycle of the SFTSV is not yet known, but seems most likely to involve arthropod vectors and mammaliam hosts, including cats, mice, hedgehogs, weasels, possums and yaks.
- *Haemaphysalis longicornis*

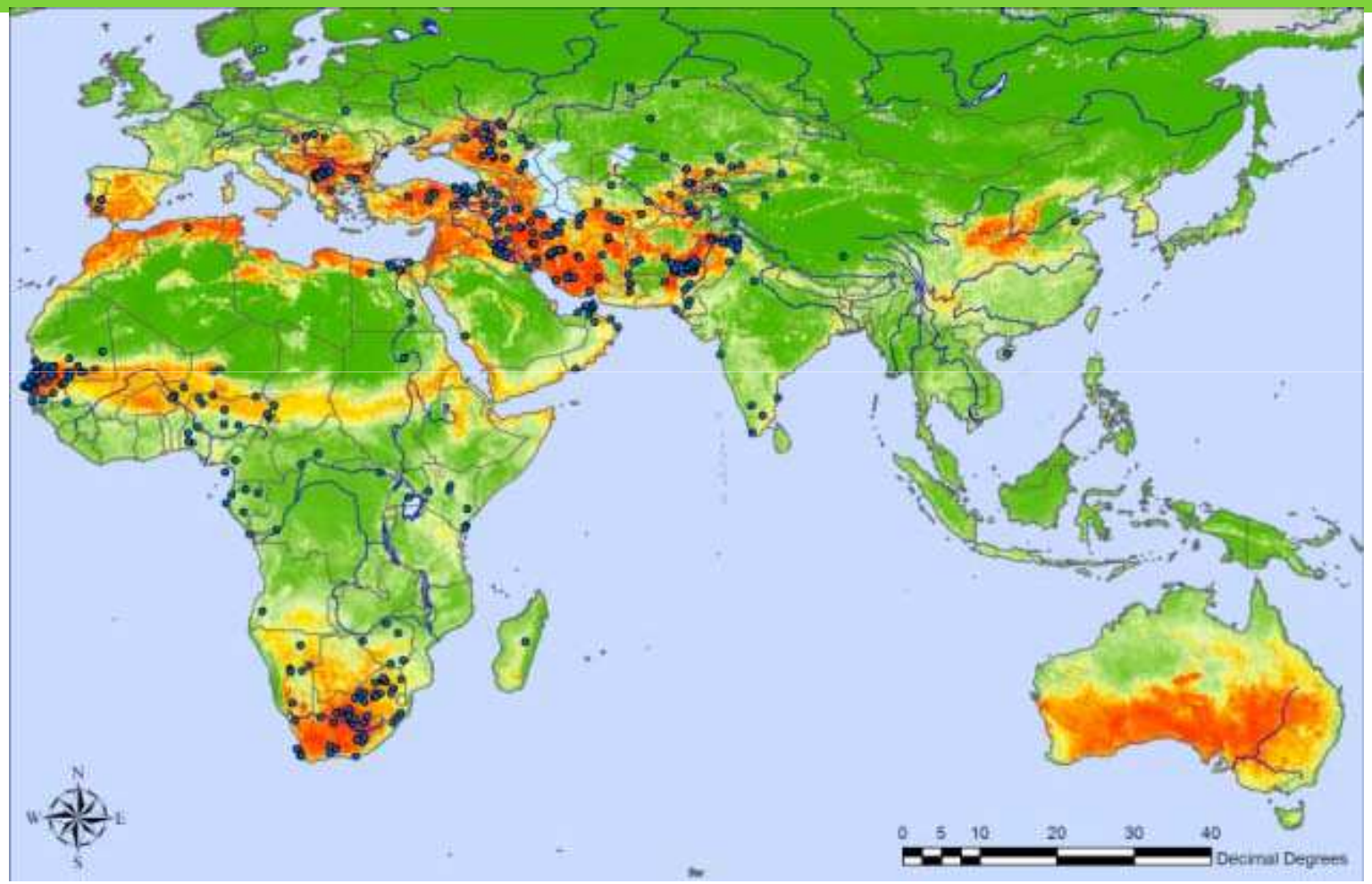
Bunyaviridae-Nairovirus

- A primary characteristic of the viruses of the genus Nairovirus , distinguishing them from most of the other members of the family Bunyaviridae , is that they are all transmitted by ticks
- 7 serogroup
- the most important is CCHFv serogroup

Crimean-Congo haemorrhagic fever is endemic in the Balkan region and a few cases are reported on a regular basis from Bulgaria (four cases in 2011, six cases in 2010, eight cases in 2009, and 14 cases in 2008). In the wider European region, Turkey remains the most affected country.

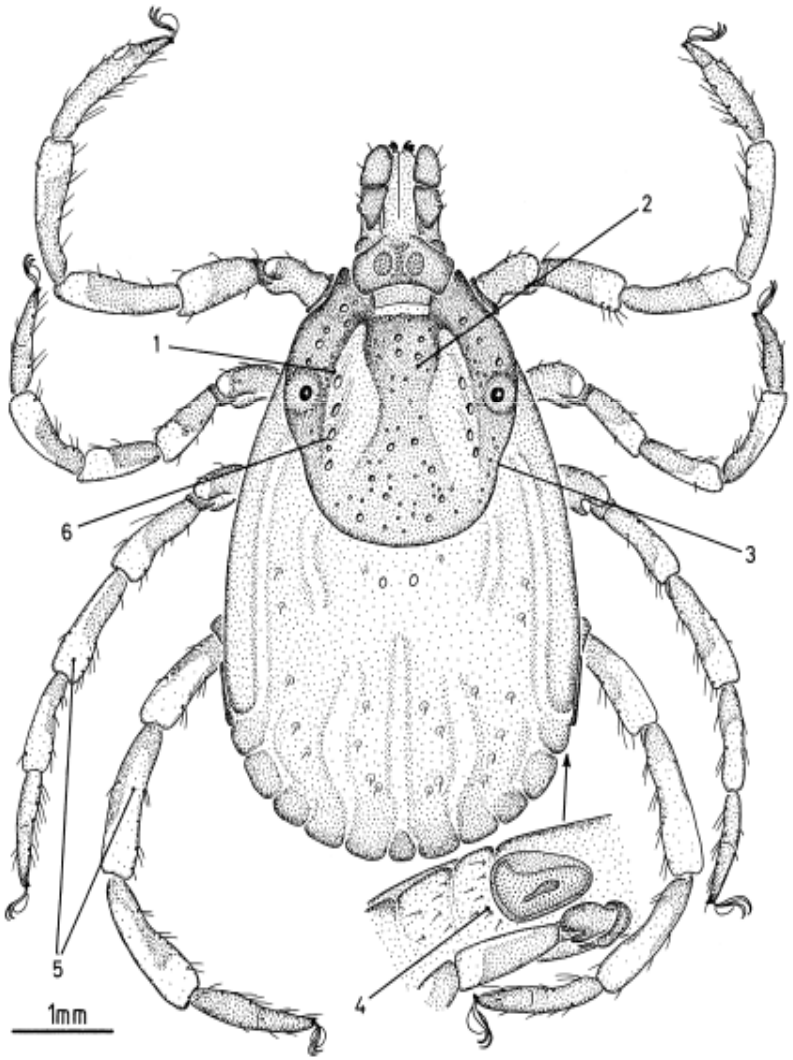


CCHF: the occurrence of the disease is linked to the geographical distribution of its hard tick vectors, mostly from the *Hyalomma* genus



Randolph S, In: Ergonul & Whitehouse (eds), CCHF, Springer, 2007

Vector



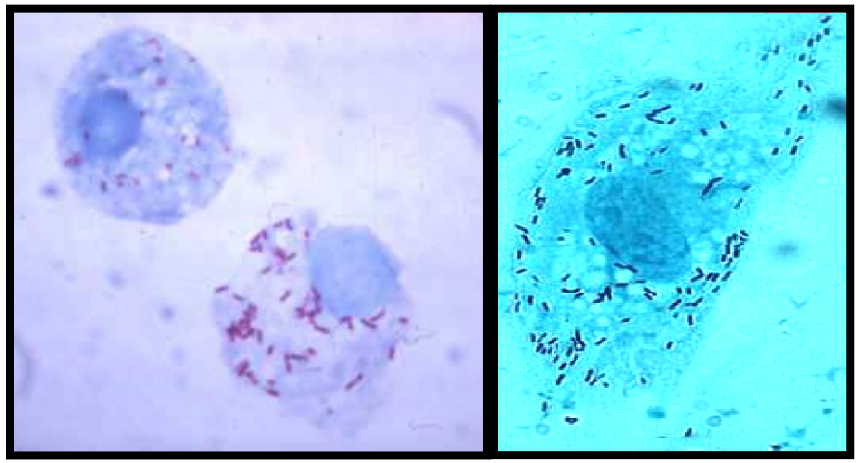
Genus *Hyalomma* is the virus reservoir

- Two-host exophlic tick: immature stage feed on small mammals and ground-feeding birds and adult stages feed on big mammals such as ruminants, wild boars, hares and humans
- the tick could transmit the virus to a vertebrate host after a long overwintering time (about 4 months at 10°)

Bacteria

Rickettsia: Formal Description

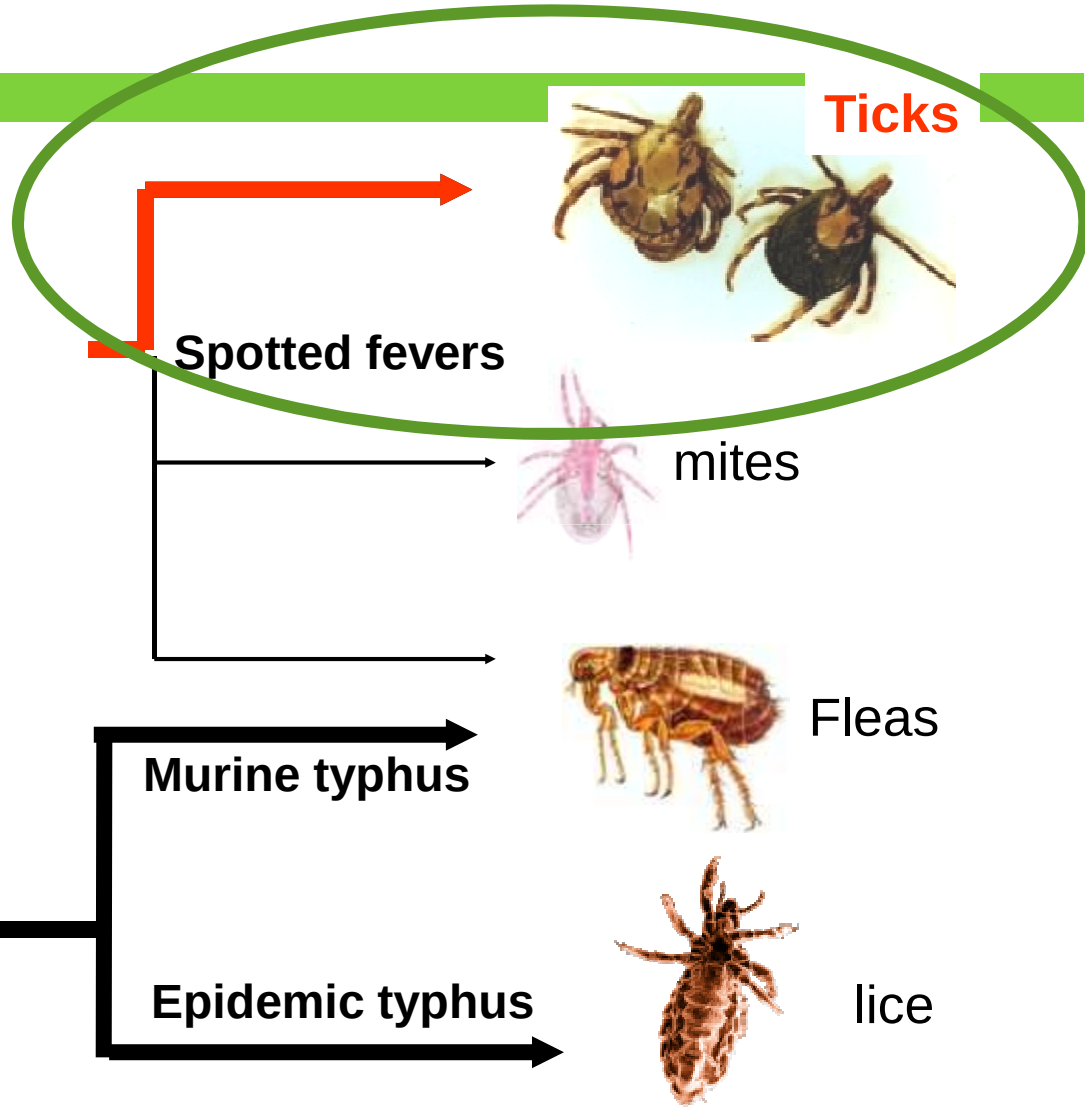
- **Obligate** intracellular rod-shaped bacteria
- Cell culture , Slow growing
- Surrounded by typical Gram –negative membrane
  a. Not stained well by the Gram method
  b. Retain basic fuschin when stained by Gimenez



- Infect endothelial cells *in vivo*
- Infect arthropod cells
- Very promiscuous in cell culture

The genus *Rickettsia*

Spotted fever group



Typhus group

Parola 2014

Rickettsioses around the word

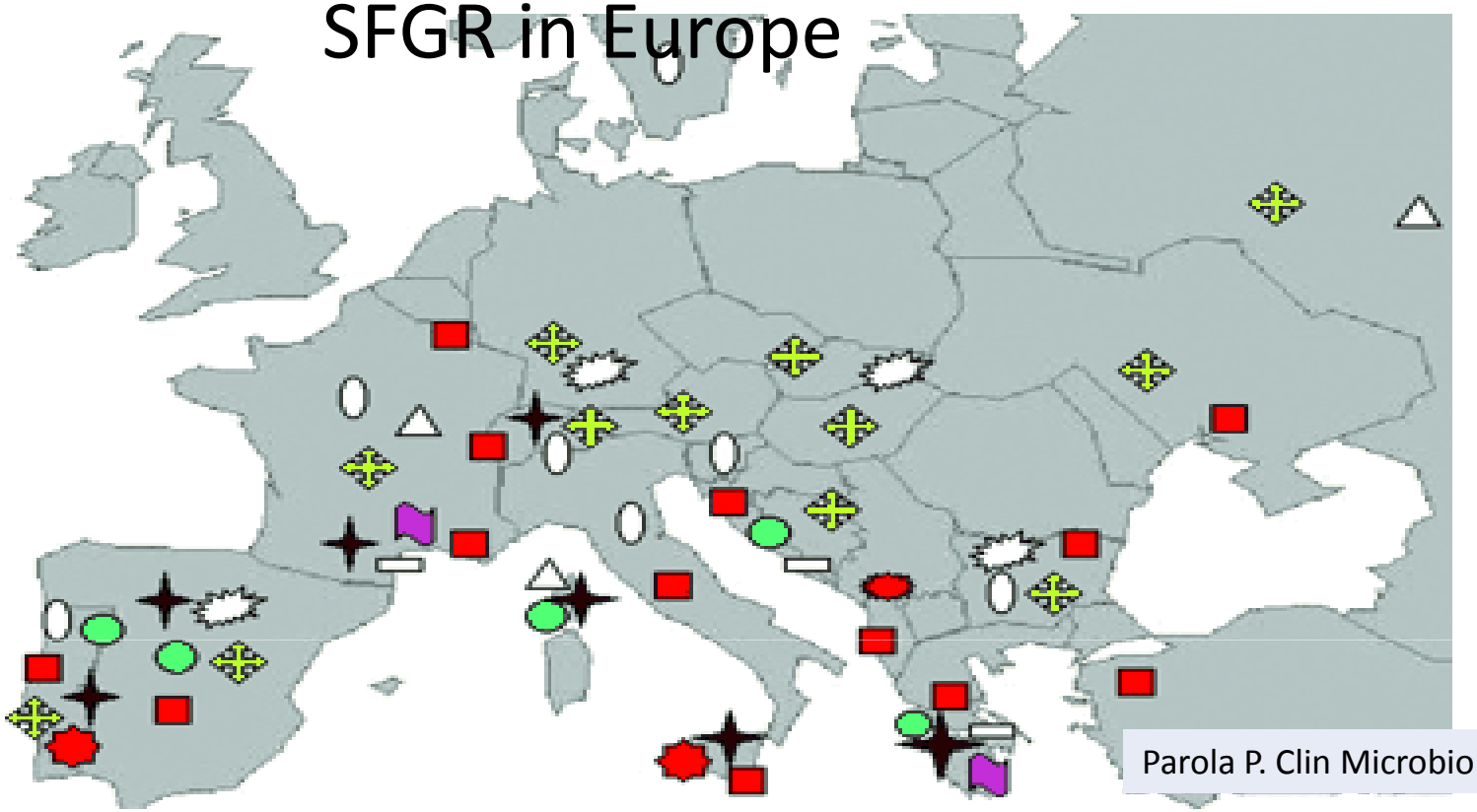
CMR
Journals.ASM.org

Update on Tick-Borne Rickettsioses around the World: a Geographic Approach

Philippe Parola,[a] Christopher D. Paddock,[b] Cristina Socolovschi,[a] Marcelo B. Labruna,[c] Oleg Mediannikov,[a] Tahar Kernif,[d] Mohammad Yazid Abdad,[e] John Stenos,[e] Idir Bitam,[f] Pierre-Edouard Fournier,[a] Didier Raoult[a]

Clinical Microbiology Reviews , October 2013

SFGR in Europe



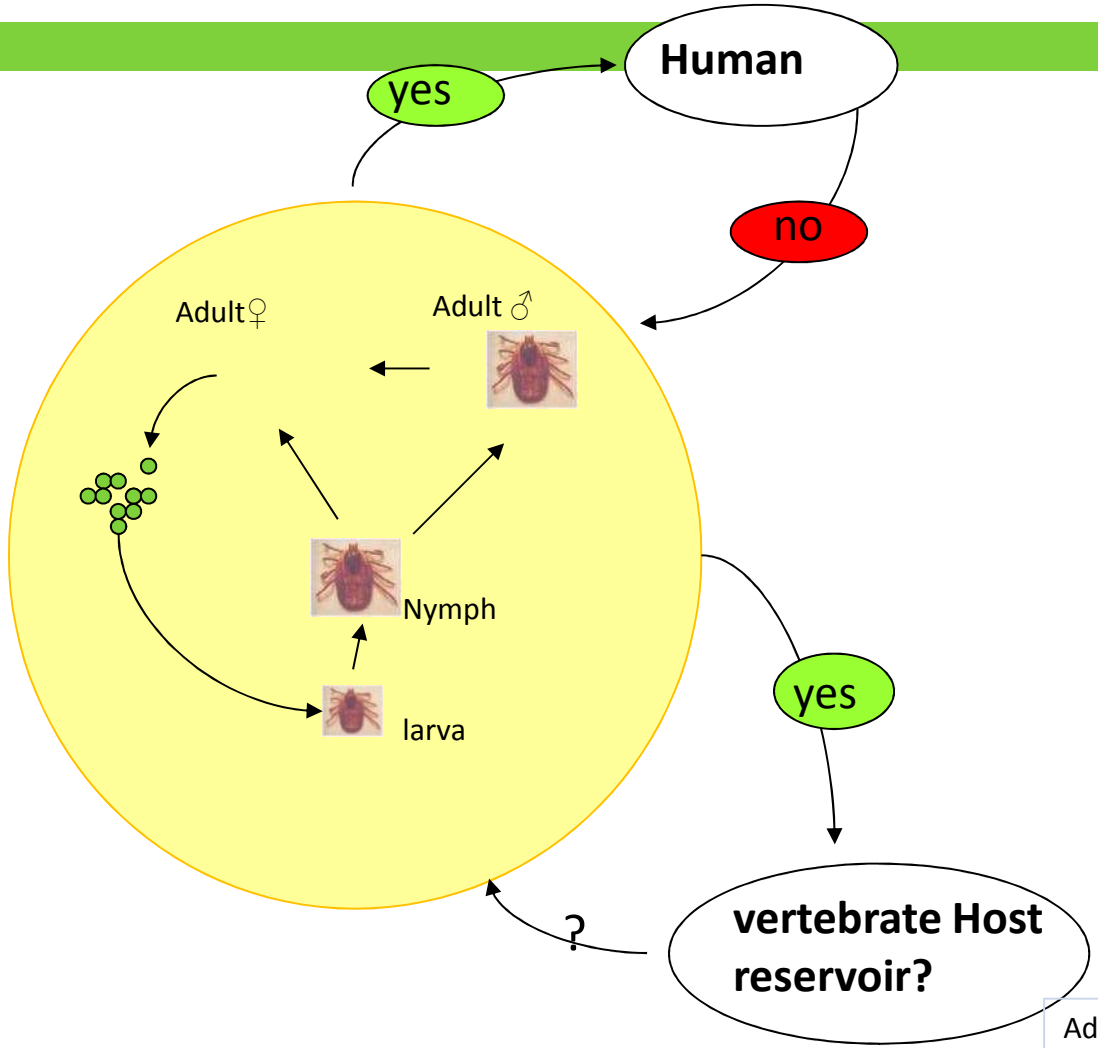
Parola P. Clin Microbiol Reviews, 2005

- *R. conorii conorii*
- *R. conorii israelensis*
- *R. conorii caspia*
- *R. sibirica mongolitimonae*
- *R. aeschlimannii*
- *R. slovaca*
- *R. helvetica*
- *R. massiliae*
- « *R. monacencis* » and related rickettsias
- *R. rhipicephali*
- *Rickettsia sp.* RpA4

Ecology- human infection

TICK :

Vector and Reservoir !



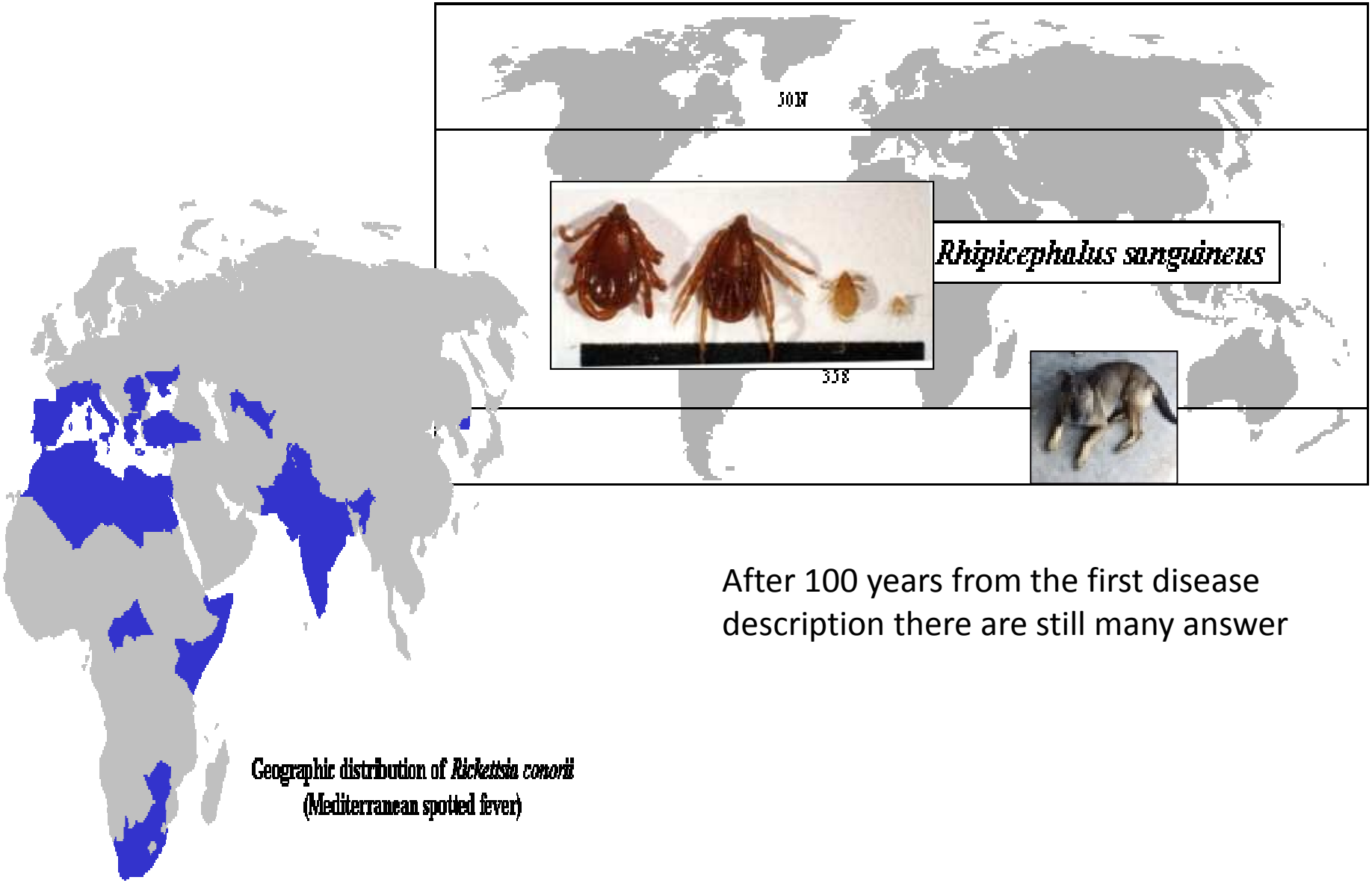
Adapted from
Beati L, in Zoonoses Ed 1998

Spotted Fever Group Rickettsioses

- Typically
  Abrupt onset : fever + rash + Headache
  +/- Eschar
- +/- report of arthropod-bite

- However, symptoms and epidemiology vary according to causative species and host

Mediterranean Spotted Fever (*R. conorii*)



After 100 years from the first disease description there are still many answer

Mediterranean Spotted Fever

- Incubation 4-7 days
- Abrupt Fever + Headache
- Day 3-5 : generalized maculo-papular rash

- Typical triad : fever + rash + eschar

Mediterranean Spotted Fever (*R. conorii*) rash

TIBOLA – DEBONEL
SENLAT (Scalp Eschar and Neck LymphAdenopaThy)

- ***Rickettsia slovaca***
- **vector = *Dermacentor marginatus* and *D. reticulatus***
  (tropism for hairy zones)
- **1997: First description** **(Lakos. Lancet. 1997)**

THE LANCET Vol 350 • July 12, 1997

A new tick-transmitted disease due to *Rickettsia slovaca*

D Raoult, Ph Berbis, V Roux, W Xu, M Maurin

- **Incubation 7 days , Cold season**
- **Females and children**

TIBOLA – DEBONEL

SENLAT (**S**calp **E**schar and **N**eck **L**ymph**A**denopa**T**hy)

SENLAT
Scalp Eschar and Neck Lymphadenopathy after Tick bite

-Rickettsia slovaca,
-R.raoultii
but Not only

Scalp Eschar and Neck Lymphadenopathy Caused by *Bartonella henselae* after Tick Bite

Emmanouil Angelakis,[1] Céline Pulcini,[2] Julie Waton,[3] Patrick Imbert,[4] Cristina Socolovschi,[1] Sophie Edouard,[1] Pierre Dellamonica,[2] and Didier Raoult[1]

BRIEF REPORT • CID 2010:50 (15 February) • 549

Aneruptive Fever Associated with Antibodies to *Rickettsia helvetica* in Europe and Thailand†

Pierre-Edouard Fournier,[1] Caroline Allombert,[1] Yupin Supputamongkol,[2] Giuseppe Caruso,[3] Philippe Brouqui,[1] and Didier Raoult[1]*

TABLE 1. Epidemiological and clinical findings for 13 patients with *R. helvetica* infection

Patient	Age[b]	Sex	Geographic area	Month of onset	Fever[a]	Headache[a]	Myalgia[a]	Arthralgia[a]	Conjunctivitis[a]	Report of tick bite (location)[a]	Inoculation eschar (location)[a]	Cutaneous rash[a]	Treatment[a]	Recovery[a]
1	70	M	Northern Italy	May	+	+	−	+	−	+ (right thigh)	+ (right thigh)	−	No treatment	−
2	58	M	Northern Italy	May	+	+	+	+	−	+ (left buttock)	−	−	No treatment	−
3	50	F	Northern Italy	May	+	+	+	+	−	+	−	−	No treatment	−
4	37	M	Northeastern France	August	+	+	+	+	−	−	−	−	No treatment	−
5	63	F	Northeastern France	June	+	+	−	+	−	+ (leg)	−	−	No treatment	−
6	27	M	Northeastern Thailand	January	+	+	+	−	−	−	−	−	Doxycycline	−
7	43	M	Northeastern Thailand	December	+	+	+	−	+	−	−	−	Cefotaxime	−
8	57	M	Northeastern Thailand	October	+	+	+	−	+	−	−	−	Doxycycline	−
Total (%)		6M, 2F			8 (100)	8 (100)	6 (75)	5 (62)	2 (25)	4 (50)	1 (12.5)	0		8 (100)

Rickettsia massiliae Human Isolation

To the Editor: The number of new rickettsial species that cause diseases in humans is rapidly increasing (*1*). Moreover, many of the species first described in ticks have been recently shown to be pathogenic. Of the 10 species or subspecies found to be pathogens after 1984, a total of 7 were first isolated from ticks (*2*). We report the first isolation of *Rickettsia massiliae* from a patient. The bacterium was isolated in Sicily in 1985 and identified in 2005.

Other pathogenic Rickettsiae found in Europe

Rickettsia monacensis and Human Disease, Spain

Isabel Jado,* José A. Oteo,† Mikel Aldamiz,‡ Horacio Gil,* Raquel Escudero,* Valvanera Ibarra,† Joseba Portu,‡ Aranzazu Portillo,† María J. Lezaun,‡ Cristina García-Amil,* Isabel Rodríguez-Moreno,* and Pedro Anda*

We identified *Rickettsia monacensis* as a cause of acute tickborne rickettsiosis in 2 humans. Its pathogenic role was assessed by culture and detection of the organism in patients' blood samples. This finding increases the number of recognized human rickettsial pathogens and expands the known geographic distribution of Mediterranean spotted fever–like cases.

Flea spotted Fever

- ***Rickettsia felis***
- **1918: First detection in cat fleas** Sikora. Arch Inst Cardiol Mex. 1918
- **Vector: C. felis ++ *(c*at flea)**

Prevalence in fleas: 1- 20% in wild fleas

***Rickettsia felis*: from a rare disease in the USA to a common cause of fever in sub-Saharan Africa**

P. Parola
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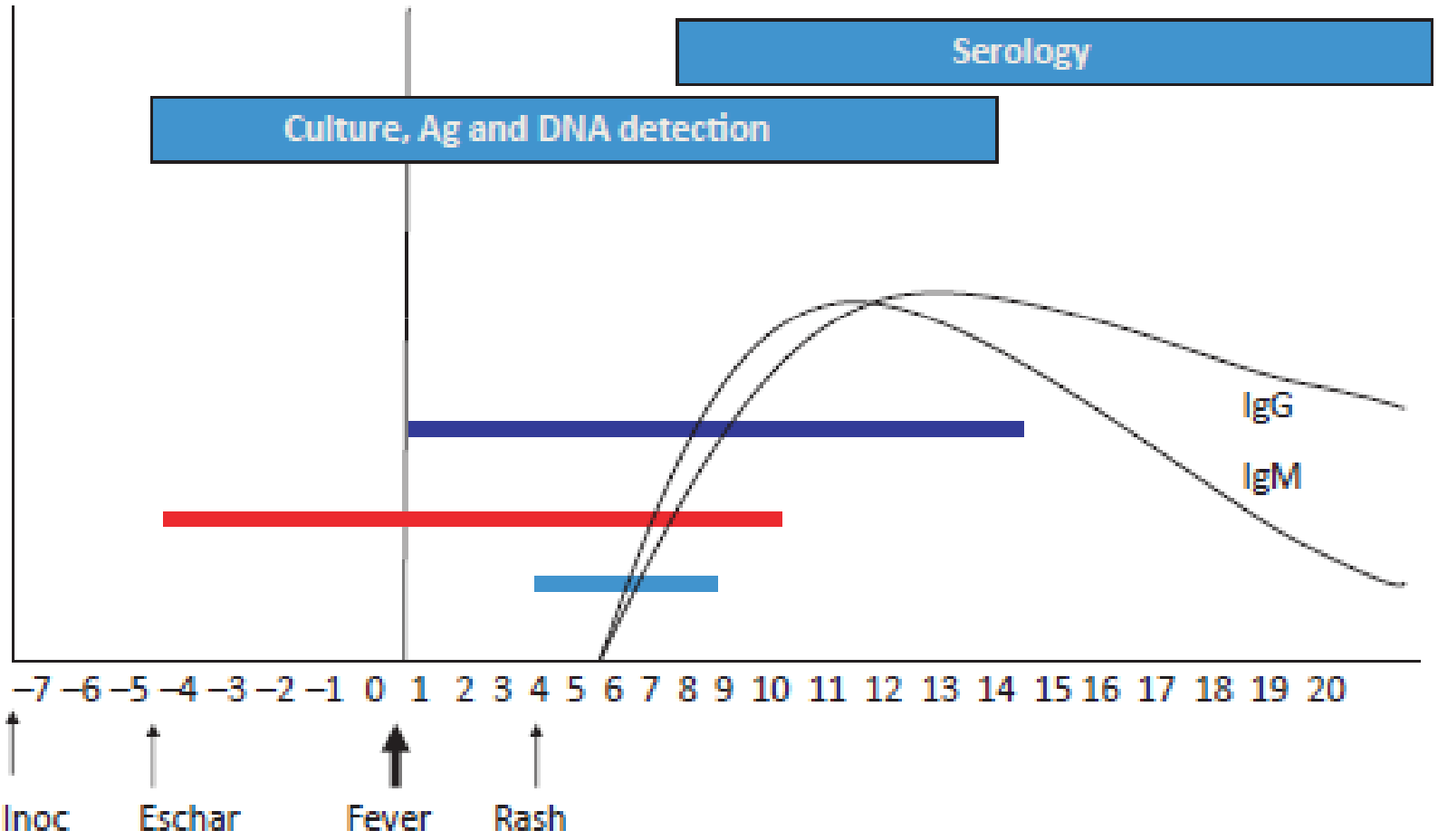
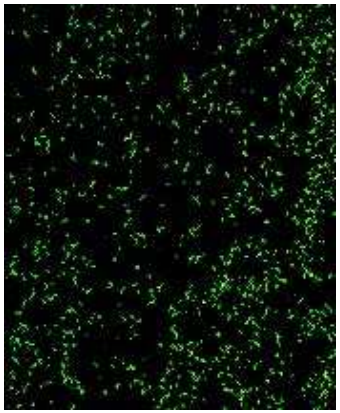
Parola P, Clin Microbiol Infect 2011

Time course of markers of rickettsial infection



Indirect diagnosis- SEROLOGY

Indirect immunofluorescence



Reference method

Cell-cultivated antigens, formalin-inactivated

Variable seroconversion (10 - 25 jours)

=> obtain a convalescent-phase serum

Sensitive but cross-reactions among *Rickettsia* species

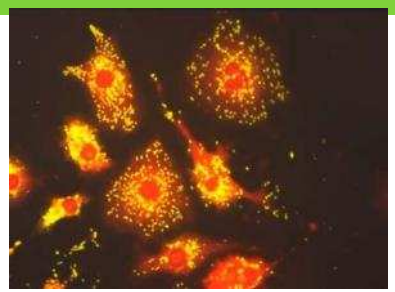
IgG >=1:128 ; IgM >=1:32

Fournier . Clin.Diagn.Lab.Immunol. 2002

Direct diagnosis

Best specimen = inoculation eschar biopsy

Culture



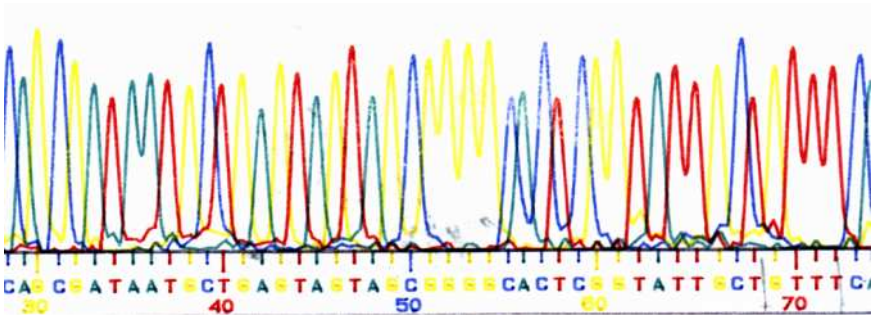
Reserved to specialized laboratories
- Vero, HEL, XTC cells
- In shell vials

≥ 2 weeks

Gimenez stain or IFA

Molecular detection

Polymerase Chain Reaction



Standard or **real-time PCR, and qPCR**

Specimens:

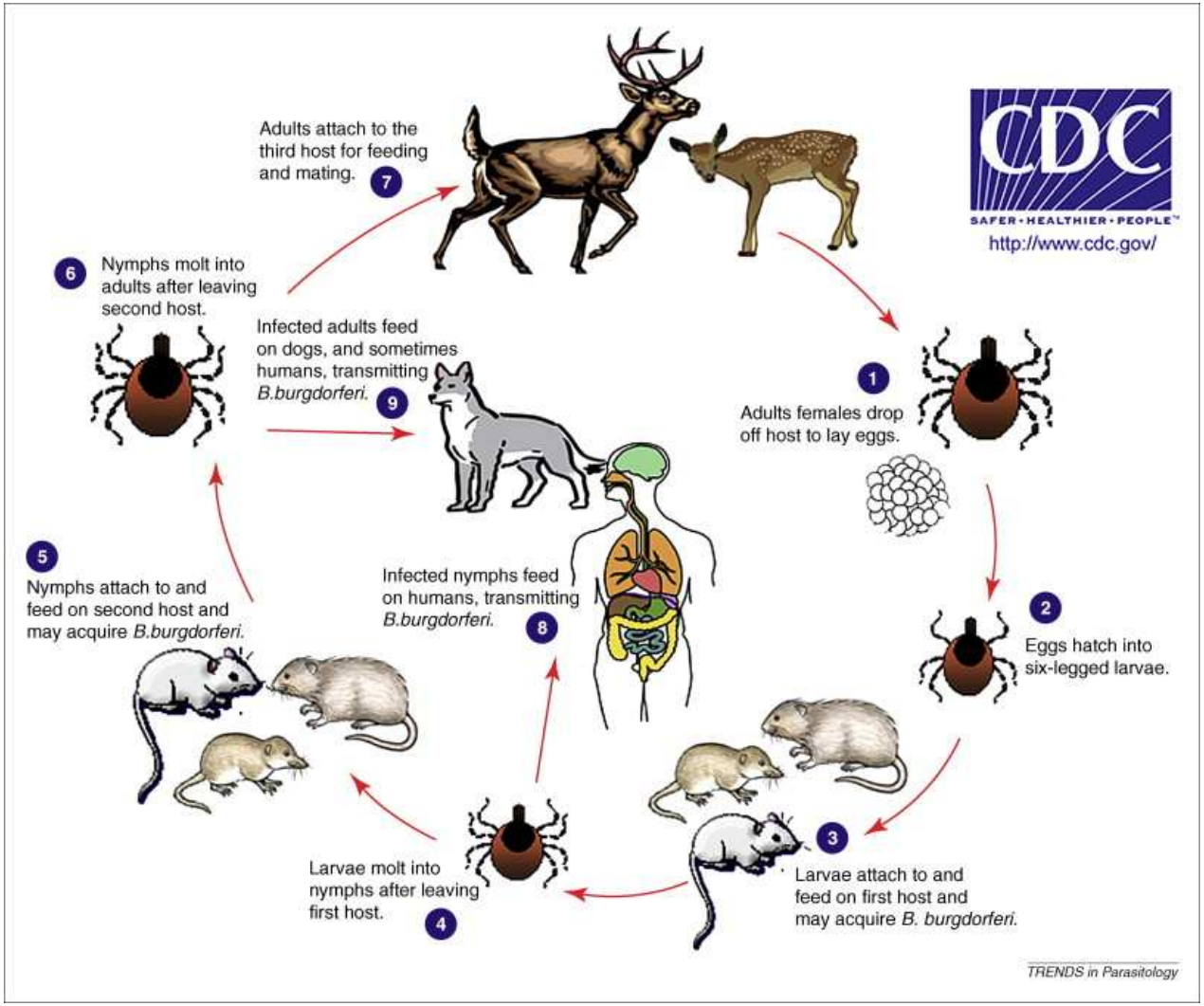
arthropods,
eschar biopsies/swab
EDTA blood,
culture supernatant

Lyme disease

The causative agents of Lyme borreliosis are tick-transmitted spirochaetes belonging to the Borrelia burgdorferi species complex (B. burgdorferi sensu lato (s.l.)) in which there are known to be at least 19 genospecies with a worldwide distribution

- in Europe, four additional pathogens, Borrelia garinii, Borrelia afzelii, Borrelia spielmanii and Borrelia bavariensis, also occur.
- Three further European genospecies, Borrelia valaisiana, Borrelia lusitaniae and the recently described Borrelia finlandensis are involved in human cases

Lyme disease ecology



Lyme borreliosis - Symptoms

- Clinical presentation: *Borrelia burgdorferi* infection can be asymptomatic.

Early manifestations

- Erythema migrans, the early skin rash of localised infections, occurs in about 80-90% of cases.
- It is an erythematous rash that gradually expands from the site of a tick bite.
- Some patients may also have systemic 'flu-like' illness but without significant respiratory symptoms.
- *Borrelial lymphocytoma* is an uncommon skin manifestation of early infection.

Lyme borreliosis - Symptoms

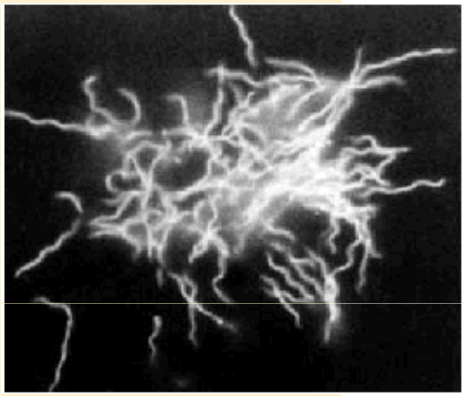
Late manifestations:

- Neuroborreliosis is the main complication (occurs in approximately 10% of cases). (usually occurs withing aprox. 6-12 weeks of infection).

  Meningoencephalitis is a less common feature.
- Presentations of late (previously untreated) Lyme borreliosis can affect the skin, nervous and musculoskeletal systems.

Lyme borreliosis - Diagnosis

- No laboratory tests are required in the diagnosis of erythema migrans, which depends on a clinical evaluation and assessment of tick exposure risk.
- Laboratory tests are necessary to confirm a diagnosis of later stage infection.
- Antibodies to *B. burgdorferi* are usually detectable within 4-8 weeks of infection.
- Patients with late-stage infection are rarely seronegative and usually have very strongly positive antibody tests.
- False-positive tests can lead to misdiagnosis and inappropriate treatment.



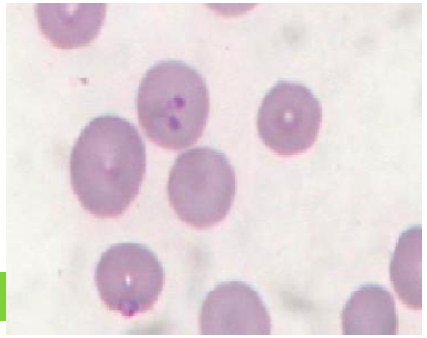
Lyme borreliosis - Treatment

- All patients with symptomatic *B. burgdorferi* infection should be treated with appropriate antibiotics.
- Early treatment can prevent the risk of developing late stage complications.
- Even patients with late stage Lyme can benefit from antibiotics, although clinical recovery may be incomplete.

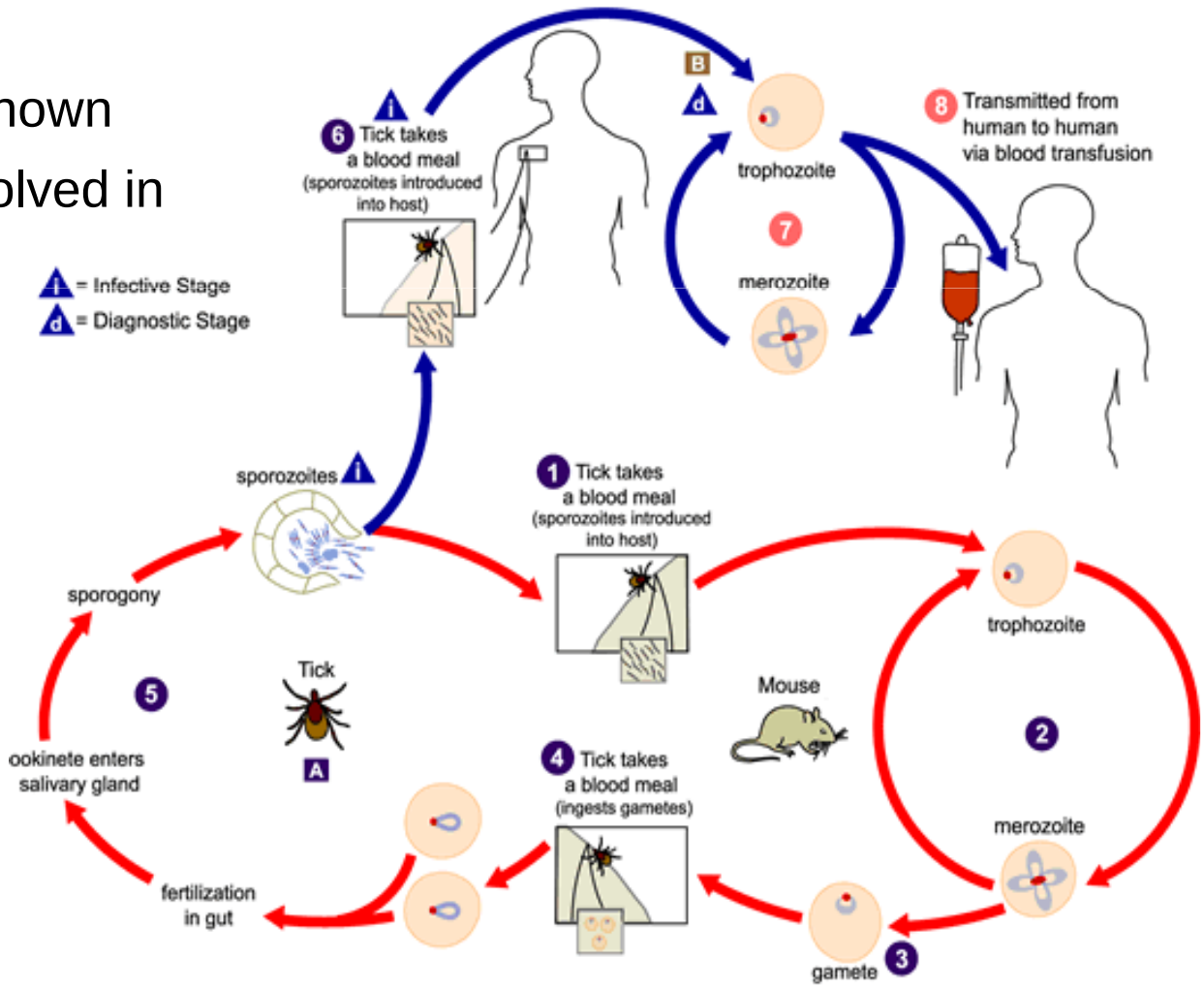
Note: No licensed vaccine against Lyme borreliosis is currently available for prevention

Parasites

Babesiosis



- First recognised parasite transmitted by ticks
- More than 100 species known
- Only few species are involved in human diseases
- *B. microti*
- *B. divergens*



Zoonotic babesia

Babesia divergens

- Europe
- Vector: Ixodes ricinus
- Reservoir/main host: ruminants

Babesia microti

- In US, first human cases described in SWz in 2007
- Ixodes ricinus and triamnguliceps

“BETTER THAN KNOWING EVERYTHING, IS KNOWING WHO CALL WHEN YOU NEED IT”

Cit. Mauro Ferri