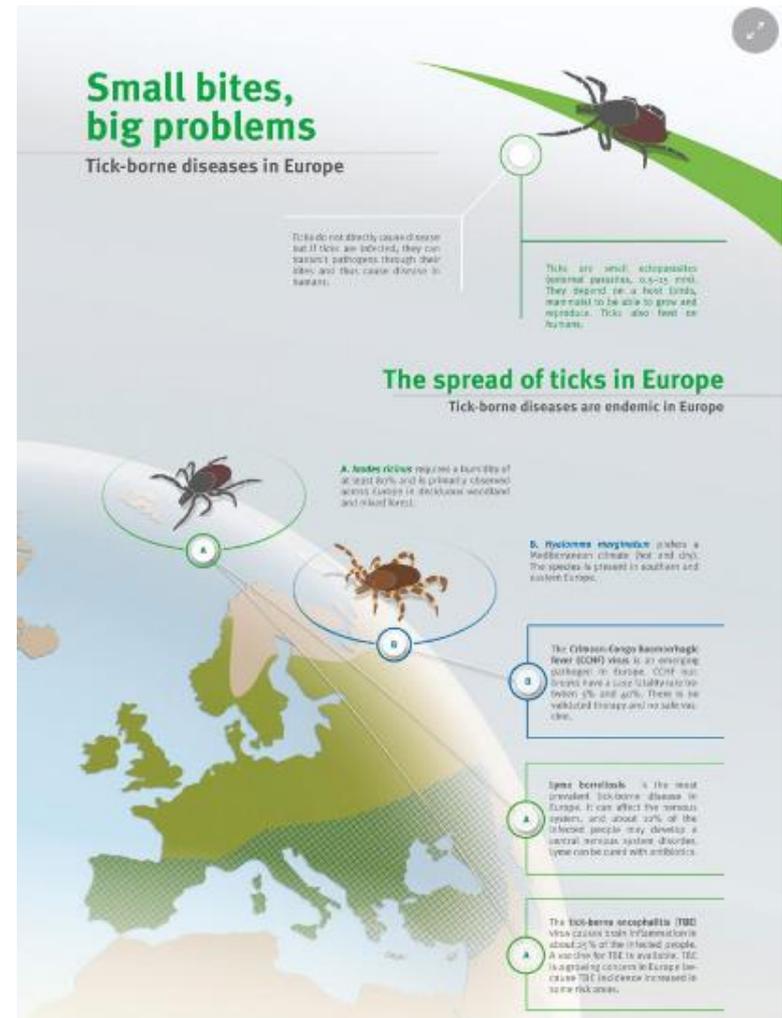




**INSTITUTE  
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# ASCID: Tick Borne Diseases: Clinical Aspects



DR ULA MANIEWSKI



## Pathogens transmitted by ticks

- Lyme (*Borrelia Burgdorferi*/*Afzelii*, *Garinii*)
- *Borrelia*: Tick Borne Relapsing Fever (TBRL)
- *Anaplasma*
- *Ehrlichia*
- *Rickettsia*: RMSF, MSF, Japanese Spotted fever, TIBONEL, ...
- *Bartonella*
- *Babesia*
- Tularemia: *Francisella tularensis*
- Colorado Tick fever
- Hemorrhagic fevers: Crimean-Congo, Omsk,..
- FSME (Frühsommer meningo-encephalitis) = TBE
- Powassan
- ...



A tularemia lesion on the dorsal skin of the right hand

# Case 1

- Consultation emergencies
  - man, 61 y old
  - Long and adventurous holiday to Zimbabwe, South Africa, Zambia
  - Fever, chills since 2 days





## Case 2

- Man
- Spent 1 month in Portugal
- Visited several natural reserves
- Complaints: fever, myalgia, sick since day of return





Inoculation eschar



Copyright @ITG



**inoculation eschars**



# Rickettsioses

## General

- very small Gram-negative bacteria
- zoonotic
- Most transmission via arthropods
- new species are frequently discovered
- treatment with antibiotics (tetracyclines)



Howard Taylor **Ricketts**



# Rickettsia : Transmission

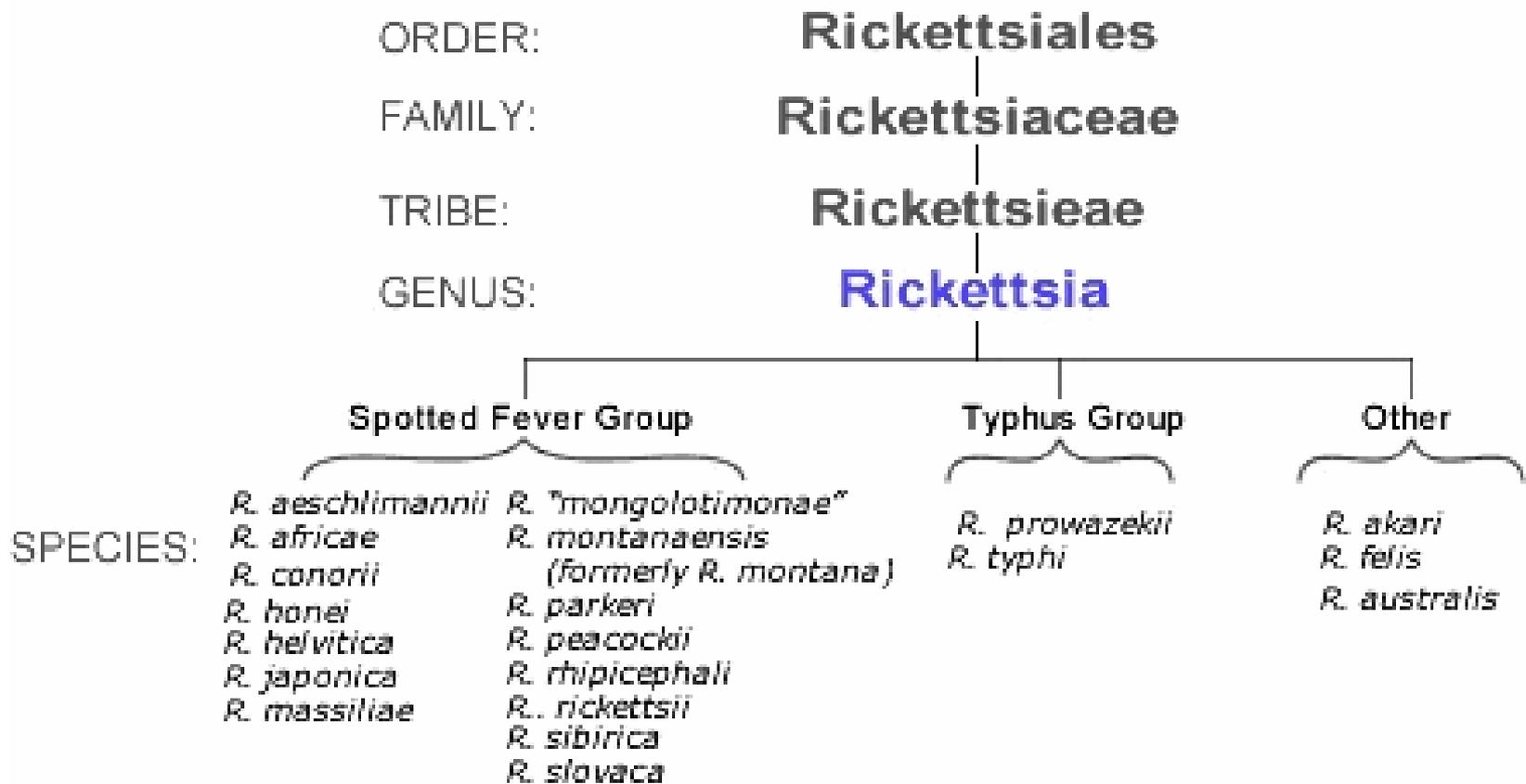
## ■ Via arthropods:

- Body louse: faeces in bite and aerosol
- Fleas : faeces
- Ticks : via bite
- Mites : via bite

**Infectious for months**

## ■ Transovarial transmission in ticks and mites





## Often mild to moderate severity

<i>R. typhi</i> ( <i>mooseri</i> )	: Endemic typhus	flea	World wide
<i>R. felis</i>	: Californian flea typhus	flea	USA, Europe
<i>R. conorii</i>	: Fièvre boutonneuse	tick	Mediterr, Africa (India?)
<i>R. conorii</i> var. <i>pijperi</i>	: Fièvre boutonneuse	tick	Southern Africa
<i>R. africae</i>	: African Spotted Fever (SF)	tick	Africa, Caribbean
<i>R. sharoni</i>	: Israelian SF	tick	Middle East
<i>R. sibirica</i>	: Nord Asiatic SF	tick	Siberia, Mongolia
<i>R. japonicum</i>	: Japanese SF	tick	Japan
<i>R. australis</i>	: Queensland SF	tick	Australia
<i>R. honei</i>	: Flinders Island SF	tick	Australia
<i>R. mongolotimonae</i>	: Atypical fièvre boutonneuse	tick	Asia, Europe
<i>R. helvetica</i>	: Fluellike illness	tick	Europe
<i>R. slovaca</i>	: insufficient data	tick	Europe
<i>R. aeschlimannii</i>	: Fièvre boutonneuse	tick	Marocco
<i>R. akari</i>	: Rickettsial pox	mite	USA, Africa

## Often severe or dramatic course

- <i>R. prowazekii</i>	: Epidemic typhus	lice	World wide
- <i>R. rickettsii</i>	: Rocky Mountain SF	tick	America
- <i>O. tsutsugamushi</i>	: Scrub typhus	mite	SE-Asia, Australasia



# Clinical picture

- Incubation 1-3 weeks (average 12d)
  - 8 d for RMSF
- Fever, myalgia, headache, dry cough,
- Maculopapular - petechial skin rash after 2-4 days (“spotted fever”)
- Eschar
  - fièvre bouttoneuse, Brazilian RMSF, sometimes scrub typhus
  - Not in RMSF, only 50% in scrub typhus
- Locally swollen lymph nodes
- Splenomegaly



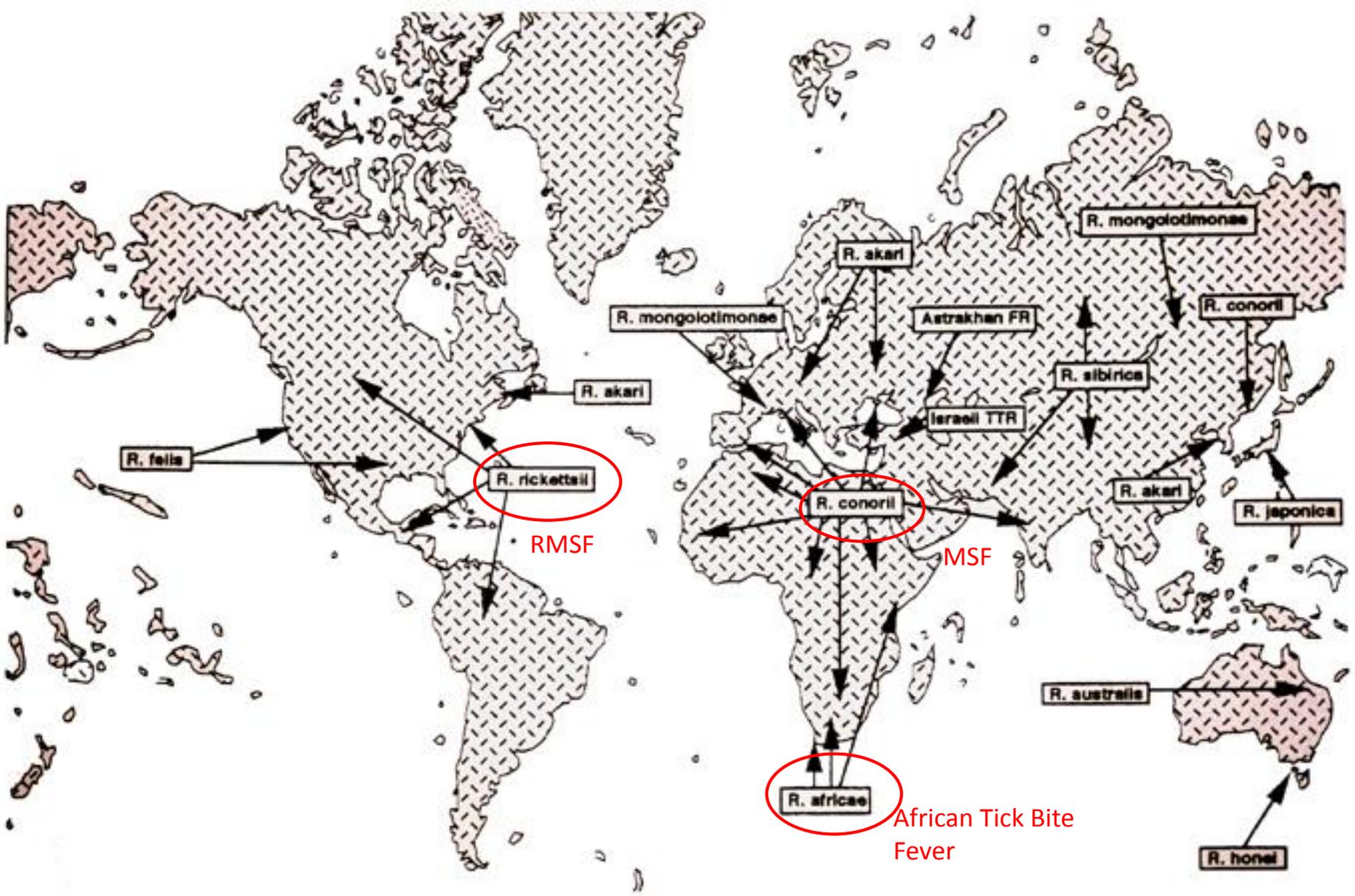
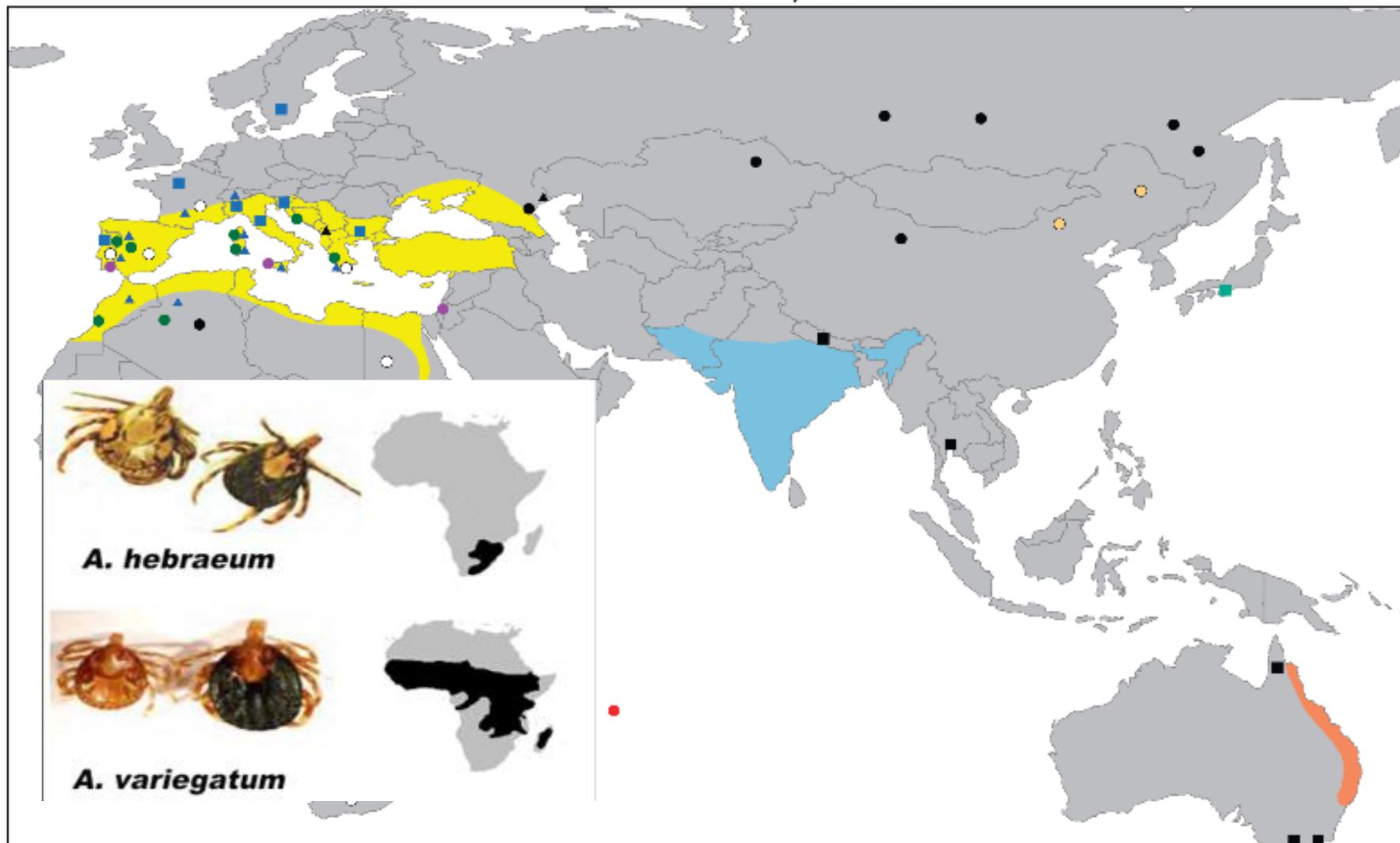


FIG. 7. Geographical distribution of pathogenic rickettsiae.

# Tick-borne Rickettsioses, Old World



## Distribution of Tick-borne *Rickettsiae*

- |                                      |                                 |                       |
|--------------------------------------|---------------------------------|-----------------------|
| ● <i>R. africae</i>                  | ○ <i>R. heilongjiangensis</i>   | ■ <i>R. helvetica</i> |
| ● <i>R. sibirica sibirica</i>        | ● <i>R. conorii conorii</i>     | ■ <i>R. honei</i>     |
| ○ <i>R. sibirica mongolittimonae</i> | ● <i>R. conorii israelensis</i> | ■ <i>R. japonica</i>  |
| ● <i>R. aeschlimannii</i>            | ▲ <i>R. conorii caspia</i>      | ▲ <i>R. massiliae</i> |

## Endemic areas for

- |                             |
|-----------------------------|
| ■ <i>R. australis</i>       |
| ■ <i>R. conorii conorii</i> |
| ■ <i>R. conorii indica</i>  |
| ■ No data                   |



Selmi M, Bertolotti L, Tomassone L, Mannelli A. *Rickettsia slovaca* in *Dermacentor marginatus* and Tick-borne Lymphadenopathy, Tuscany, Italy. *Emerg Infect Dis.* 2008;14(5):817-820. <https://dx.doi.org/10.3201/eid1405.070976>

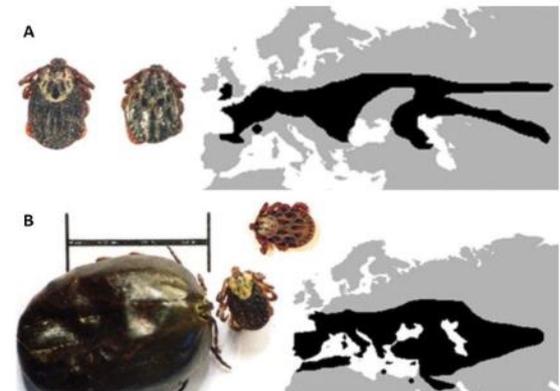
# Tick borne lymphadenopathy (TIBONEL)

- Spain, France, Hungary,
- More often in autumn-winter-spring
- Often bite on the scalp
- Eschar
- Fever- lymphopathy- astheny- myalgia-rash

Ticks Tick Borne Dis. 2014 Oct;5(6):656-9. doi: 10.1016/j.ttbdis.2014.04.016. Epub 2014 Jul 8.

## Tick-borne lymphadenopathy, an emerging disease.

Silva-Pinto A<sup>1</sup>, Santos Mde L<sup>2</sup>, Sarmento A<sup>2</sup>.



[Download full-size image](#)

Fig. 1. (A) *Dermacentor reticulatus* (left hand side: female; center: male; right hand side: distribution). (B) *Dermacentor marginatus* (left hand side: engorged female; center left: unfed female; center right: male; right hand side: distribution; scale bar: 1 cm). *Dermacentor marginatus* is commonly found in Mediterranean areas of Europe and North Africa and *D. reticulatus* in colder areas of western Europe and in the former Soviet Union. From Parola et al. (2009), also at <http://wwwnc.cdc.gov/eid/article/15/7/08-1440.htm>.

# Diagnosis+ treatment rickettsioses

- Think of it!
- Look for rash/ eschar
- Labo: not specific: inflamm-sometimes liverdysfunction-thrombopenia
- PCR on eschar
- Serology
- R/ doxy 100 mg 2/d, 2w



# Be Aware of Tick-Borne Relapsing Fever

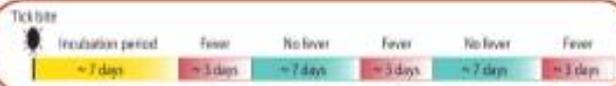


Before feeding After feeding  
TBRF is spread through the bite of soft ticks, which feed very quickly and painlessly. Above, a soft tick before and after feeding (not to scale).

For more information about TBRF, visit [www.cdc.gov/relapsing-fever/](http://www.cdc.gov/relapsing-fever/)

## What is tick-borne Relapsing Fever (TBRF)?

Tick-borne relapsing fever (TBRF) is a rare infection linked to sleeping in rustic cabins, particularly cabins in mountainous areas of the western United States. The main symptoms of TBRF are high fever (e.g., 103° F), headache, muscle and joint aches. Symptoms can reoccur, producing a telltale pattern of fever lasting roughly 3 days, followed by 7 days without fever, followed by another 3 days of fever. Without antibiotic treatment, this process can repeat several times.



## How do you get TBRF?

The bacteria that cause TBRF are transmitted by certain types of ticks, called "soft" ticks (see photo) that live in the nests of squirrels, chipmunks, and other small animals. People become exposed when they sleep in cabins and other rustic buildings in which rodents have built nests. These nests are usually located inside the walls or in the attic or crawl space. Soft ticks emerge at night and feed briefly, like bed bugs. Because the bites are quick and painless, most people do not know that they have been bitten.

## What should I do if I think I may have TBRF?

Call or visit your healthcare provider. Explain your symptoms and your concerns.

## How is TBRF diagnosed and treated?

TBRF is usually diagnosed by examining a sample of blood under a microscope. Other blood tests are available but require that the patient has been sick for several weeks. TBRF is treated with antibiotics. Your healthcare provider will need to monitor you during the first dose of antibiotics in case of a bad reaction. Although deaths are very rare, TBRF can be a particularly serious disease for pregnant women and the elderly.

## What can I do to prevent TBRF?

- Avoid sleeping in rodent-infested buildings whenever possible. Although rodent nests may not be visible, other evidence of rodent activity (e.g., droppings) are a sign that a building may be infested.
- Prevent tick bites. Use insect repellent containing DEET (on skin or clothing) or permethrin (applied to clothing or equipment).
- If you are renting a cabin and notice a rodent infestation, contact the owner to alert them.
- If you own a cabin, consult a licensed pest control professional who can safely:
  - » Identify and remove any rodent nests from walls, attics, crawl spaces, and floors. (Other diseases can be transmitted by rodent droppings—leave this job to a professional!)
  - » Treat "cracks and crevices" in the walls with pesticide.
  - » Establish a pest control plan to keep rodents out.

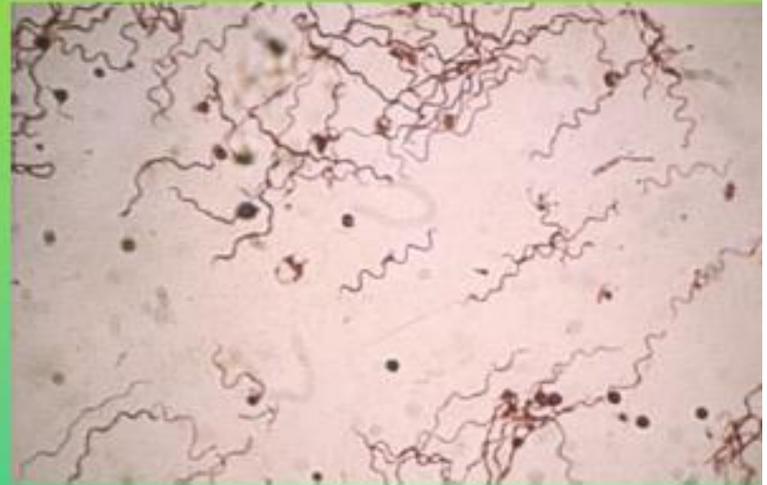
National Center for Emerging and Zoonotic Infectious Diseases  
Division of Vector Borne Diseases



11/20/2016

# Recurrent fever – Borreliosis

- Very thin spiral-shaped bacteria
- Two clinical forms:
  - ✓ Epidemic (body lice)
    - ✓ **Humans** are reservoir
  - ✓ Endemic (soft ticks)
    - ✓ **Rodents** are reservoir



*O. hermsi* tick, before and after feeding.  
Photo taken by Gary Hettrick RML,  
NIAID.

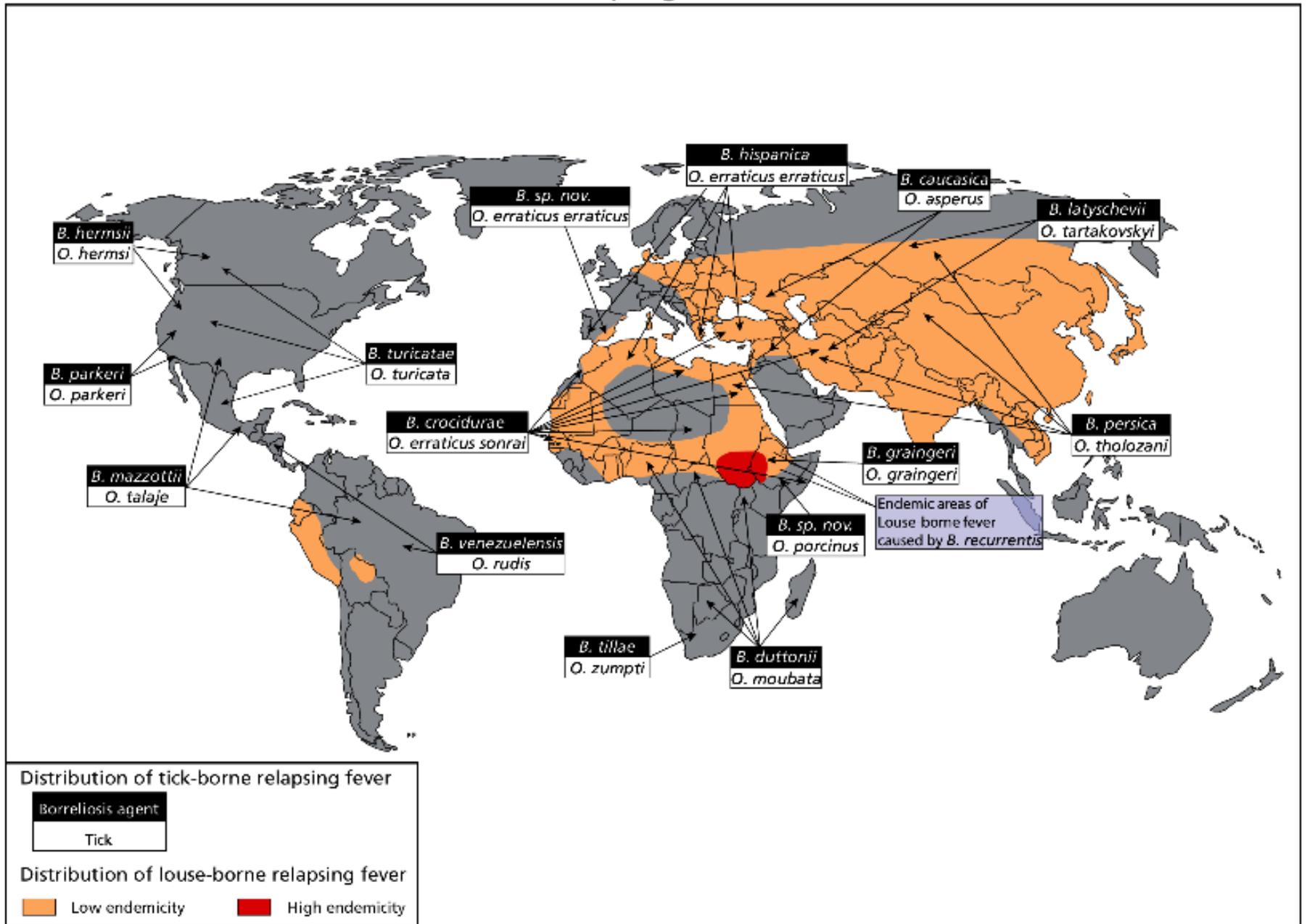


# Treatment recurrent fever

- Doxycycline (penicilline is less efficacious)
- Jarish-Herxheimer reaction may be cause of complications!
- Steroids not very useful
- IV-fluid
- Symptomatic (e.g. O<sub>2</sub> and inotropics)



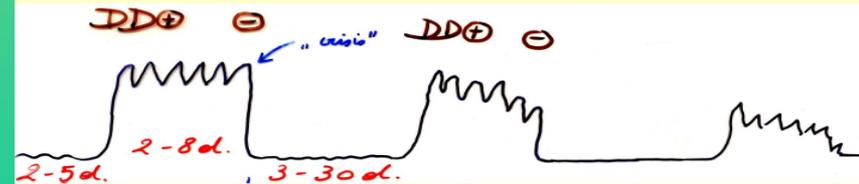
# Relapsing Fever



# Relapsing fever: Clinical presentation

- Sporadic
- Incubation 1 week
- Sudden onset fever
  - ✓ Recurrent fever
- Malaise, headache
- Myalgia, arthralgia
- Red eyes
- Discrete rash
- Symptoms worse at the end of febrile episode

episode



les *Borrelia* subissent des variations antigéniques qui leur permettent d'échapper aux réactions immunitaires établies contre la structure antigénique antérieure

# Recurrent fever: Complications

- Myocarditis, dyspnea, dry cough
- Abdominal pain, diarrhea, subicterus
- Hepatosplenomegaly, swollen LN
- Aseptic meningitis
  - ✓ residual facial paralysis
  - ✓ Deafness
  - ✓ N. III-IV-VI lesions (strabism)
- Bleeding tendency, DIC
- Abortion and preterm labor (50%)
- Mortality
  - ✓ epidemic form: 30-80%
  - ✓ Endemic form: 2-5%
  - ✓ Neonatal: 50%



# Crimean Congo Hemorrhagic Fever

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## Iran reports 120 CCHF cases in six months, Tehran spared so far

by NEWS DESK

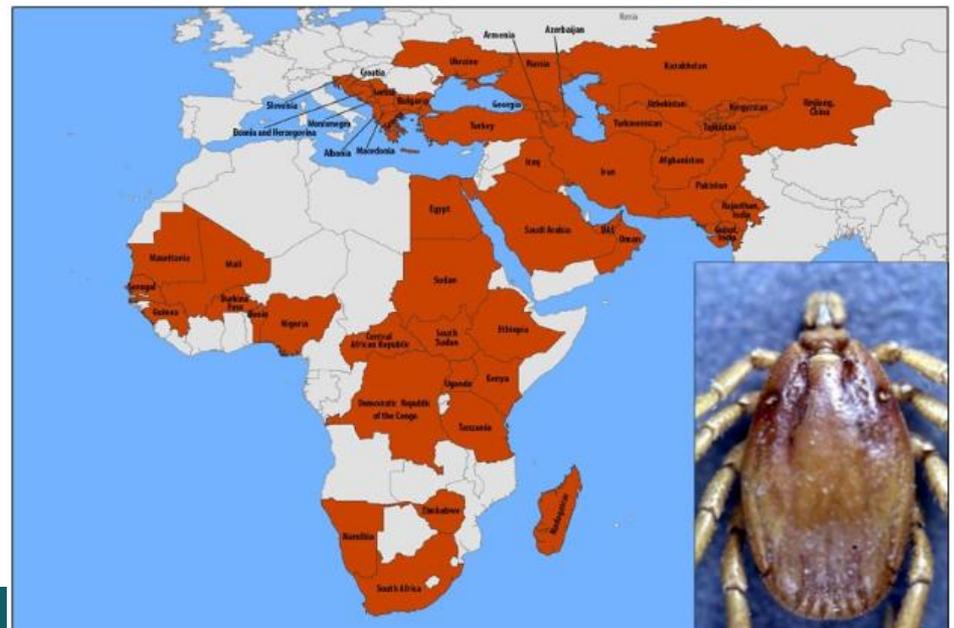
September 29, 2017 [Headlines, Middle East](#) [No Comments](#)

2372 views

Turkey: +/- 10 000 cases-CFRR almost 5%

## One Dead, One In Isolation After Two Cases Of Crimean-Congo Hemorrhagic Fever Confirmed In Madrid

*Sep 01 2016—NEWS—200 people who came into contact with the infected patients are being checked, and some confined to their homes.*

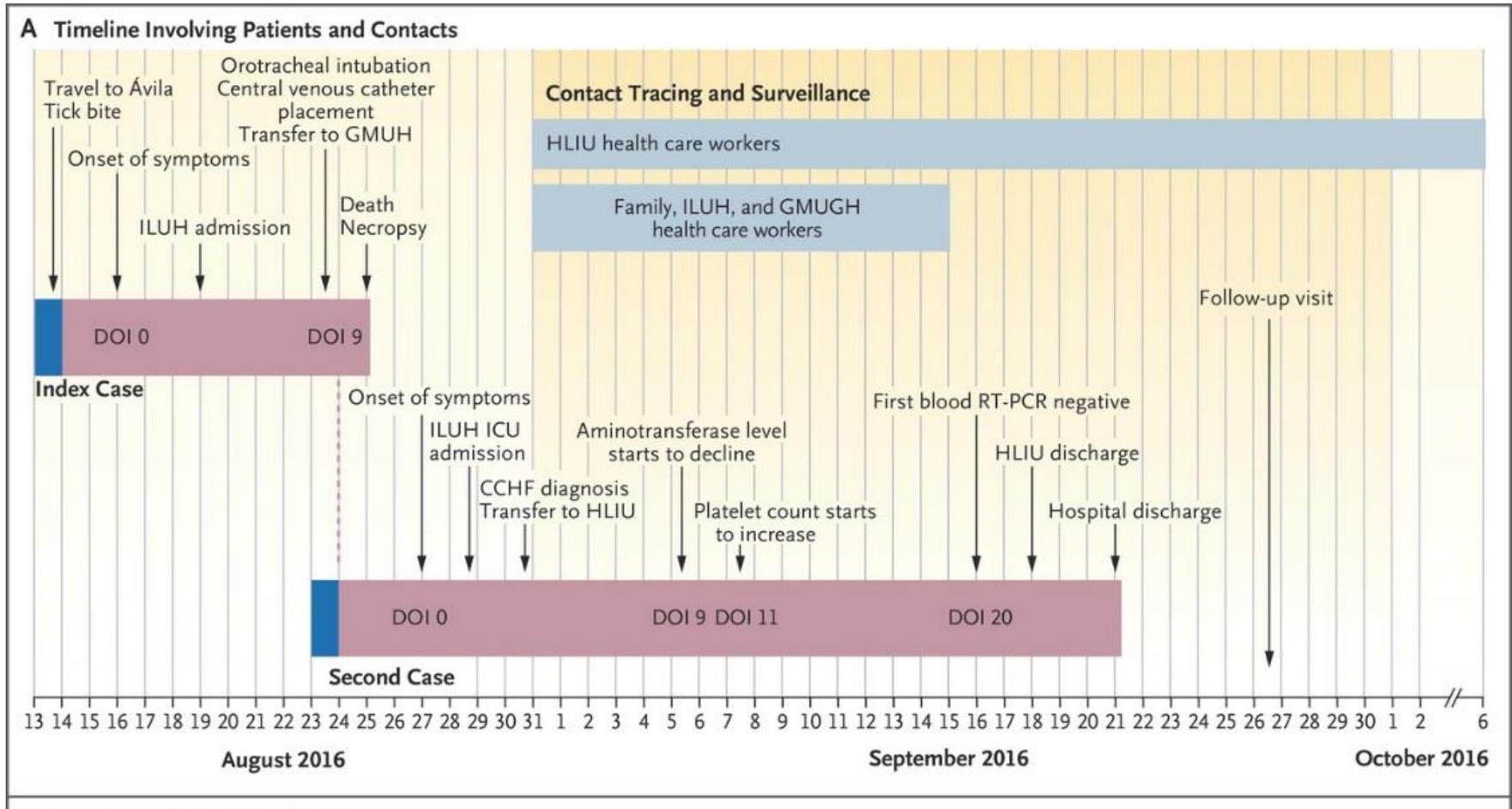


# Crimean-Congo HF

- CCHF virus : family Bunyaviridae, genus Nairovirus
- 1944-45 (Crimean HF), 1956 (Congo HF), 1967 : identical => CCHF
- Zoonosis in wide range of wild / domestic vertebrates, incl small mammals, cattle, sheep, goats, ostriches
- Enzootic in sub-Saharan Africa, Middle East, rare elsewhere (Albania, Kosovo)
- Occasional epidemics
- Transmission via
  - Ticks, esp. *Hyalomma* sp. - transovarial and venereal in
  - Larvae bite viremic small mammals
  - Direct contact with blood / tissue of livestock
  - Nosocomial : aerosol



# Clinical Events and Locations: CCHF in Spain



## Crimean-Congo HF

- Incubation period  $\pm 3$  d after tick bite,  $\pm 6$ d after blood / tissue contact (max 13d)
- Sudden onset fever, flu-like illness, GBP, confusion, lethargy,
- Severe hepatitis, bleeding, hepatorenal and pulmonary failure, no meningitis
- Case fatality rate 30%, death in 2<sup>th</sup> week of illness



## CCHF: Diagnosis

Diagnosis via virus isolation, PCR, ELISA

Isolation pt, barrier nursing (nosocomial:  
airborne possible)

Treatment : ribavirin + supportive

?? value convalescent plasma

No safe vaccine available

Gloves + protective clothing when  
handling animal tissues in endemic  
areas



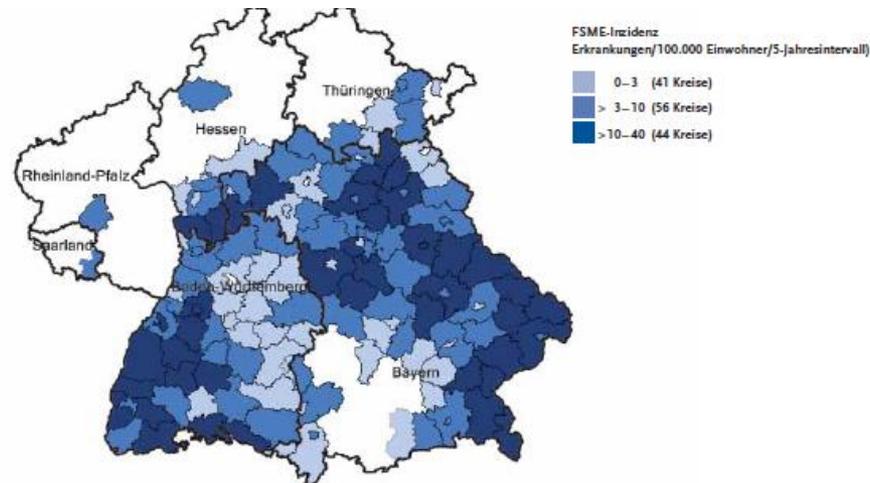
# Ticke Borne Encephalitis (TBE-FSME)



## RAPID COMMUNICATIONS

First human case of tick-borne encephalitis virus infection acquired in the Netherlands, July 2016

JA de Graaf<sup>1</sup>, JHJ Reimerink<sup>2</sup>, GP Voorn<sup>3,4</sup>, EA bij de Vaate<sup>5</sup>, A de Vries<sup>2</sup>, B Rockx<sup>2</sup>, A Schuitemaker<sup>1</sup>, V Hira<sup>4</sup>



# Tick Borne Encephalitis (TBE-FSME)

- Flavivirus
- 3 subtypes:
  - European subtype, transmitted by *Ixodes ricinus* ticks, endemic in rural and forested areas of central, eastern and northern Europe;
  - Far eastern subtype, transmitted mainly by *I. persulcatus*, endemic in far-eastern Russia and in forested regions of China and Japan; and
  - Siberian subtype, transmitted by *I. persulcatus*, endemic in Urals region, Siberia and far-eastern Russia, and also in some areas in north-eastern Europe

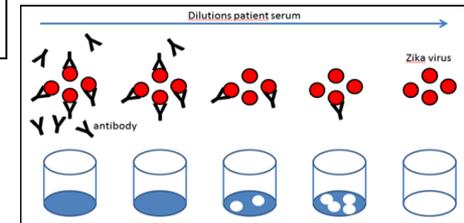
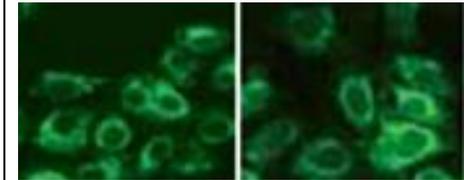
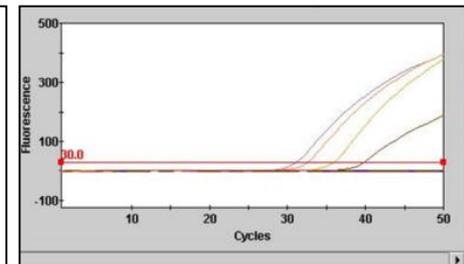
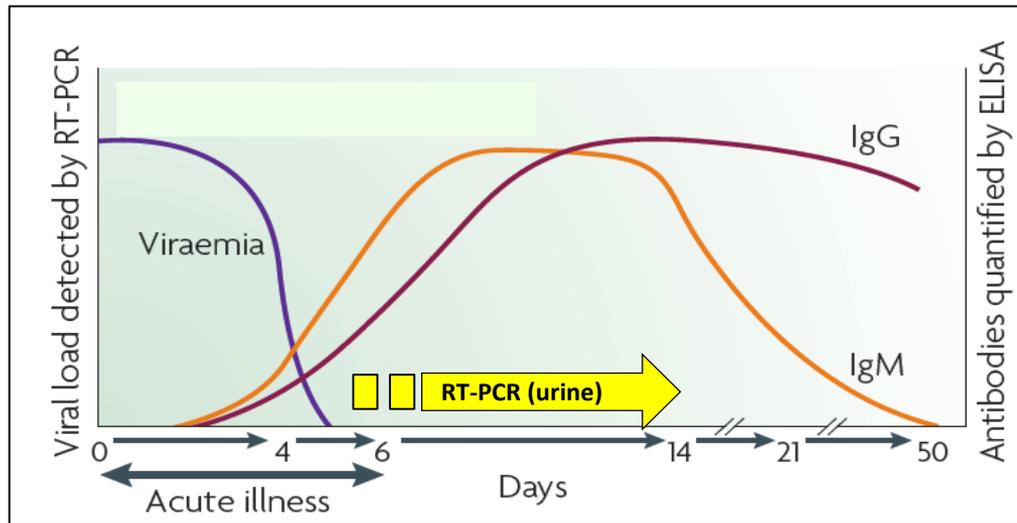


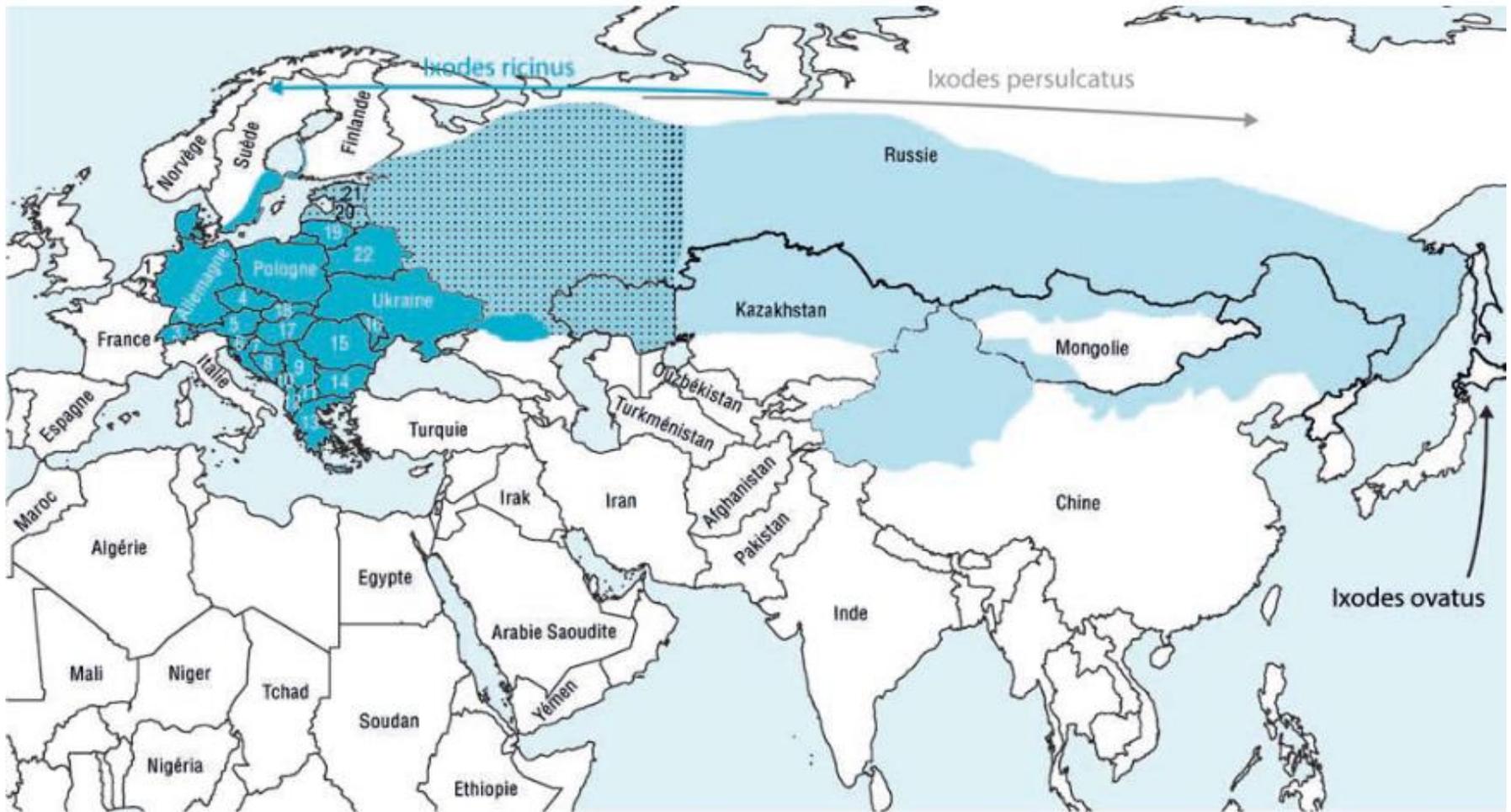
# Clinical features

- Biphasic:
  - First: aspec symptoms (flu like)
  - Asymptomatic interval (1 to4 w)
  - Second phase: neurological symptoms (meningitis, radiculitis, encephalitis, myelitis...)
  
- Sequellae+ severity depend on
  - Age
  - Subtype:
    - European: 30% have second phase, 10 sequellae
    - Far East: often 1phase, 30 mortality rate



# Laboratory diagnosis of TBE

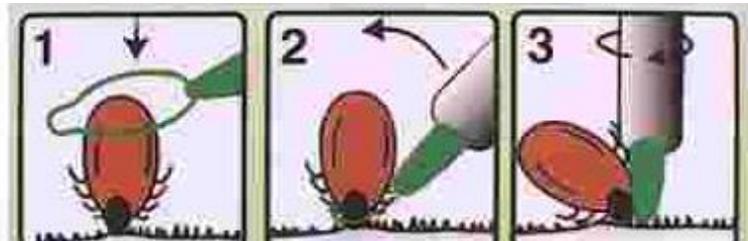




1 : Pays-Bas	4 : République Tchèque	7 : Croatie	10 : Monténégro	13 : Grèce	16 : Moldavie	19 : Lituanie	21 : Estonie
2 : Belgique	5 : Autriche	8 : Bosnie	11 : Macédoine	14 : Bulgarie	17 : Hongrie	20 : Lettonie	22 : Biélorussie
3 : Suisse	6 : Slovénie	9 : Serbie	12 : Albanie	15 : Roumanie	18 : Slovaquie		

# Hoe zich beschermen tegen tick borne diseases?

- Geïmpregneerde kleding
- Insectenrepellent op niet bedekte delen van de huid
- Kousen over broekspijpen trekken
- Huid regelmatig op teken controleren
- FSME: Vaccin beschikbaar



# TBE vaccin

- FSME junior<sup>®</sup> (0.25ml) van 1-16j prijs ~29,60€
- FSME Adult<sup>®</sup> (0.5ml) prijs ~34,50€
  
- Schema:  $M_0 - M_{1-3} - M_{9-12}$
- Versneld schema:  $D_0 - D_{14} - M_{9-12}$
- Booster na 3 jaar en erna om de 5 jaar (bij >60j om de 3j)



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