
# Zoonosi da morso di zecca

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# ZOONOSI DA MORSO DI ZECCA

| Batteri | Virus |
| --- | --- |
| - Malattia di Lyme<br>- Anaplasmosi<br>- Erlichiosi<br>- Febbre ricorrente<br>- Rickettsiosi<br>- Febbre delle montagne rocciose<br>- Tularemia<br>- ..... | -Tick-borne encephalitis<br>-Febbre delle zecche del Colorado<br>-Febbre emorragica Crimea-Congo<br>-Powassan<br>-Heartland virus<br>-..... |

**Protozoi**

- Babesiosi

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## Protozoi

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# Malattia di Lyme: eziologia e patogenesi

- ***Borrelia burgdorferi sensu lato complex***: Spirochetaceae family

In Europe, most infections are caused by **B. afzelii, B. garinii, B. burgdorferi sensu stricto**

- B. burgdorferi: particular affinity for the joint

- B. garinii: exclusively found in Europe and has selectivity for causing encephalitis

- B. afzelii: affinity for the skin and is found at the site of the infection

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1. Replication of *B. burgdorferi* at the site of its inoculation after the tick bite (*I. ricinus* ticks may transmit *B. afzelii* within 24 h)

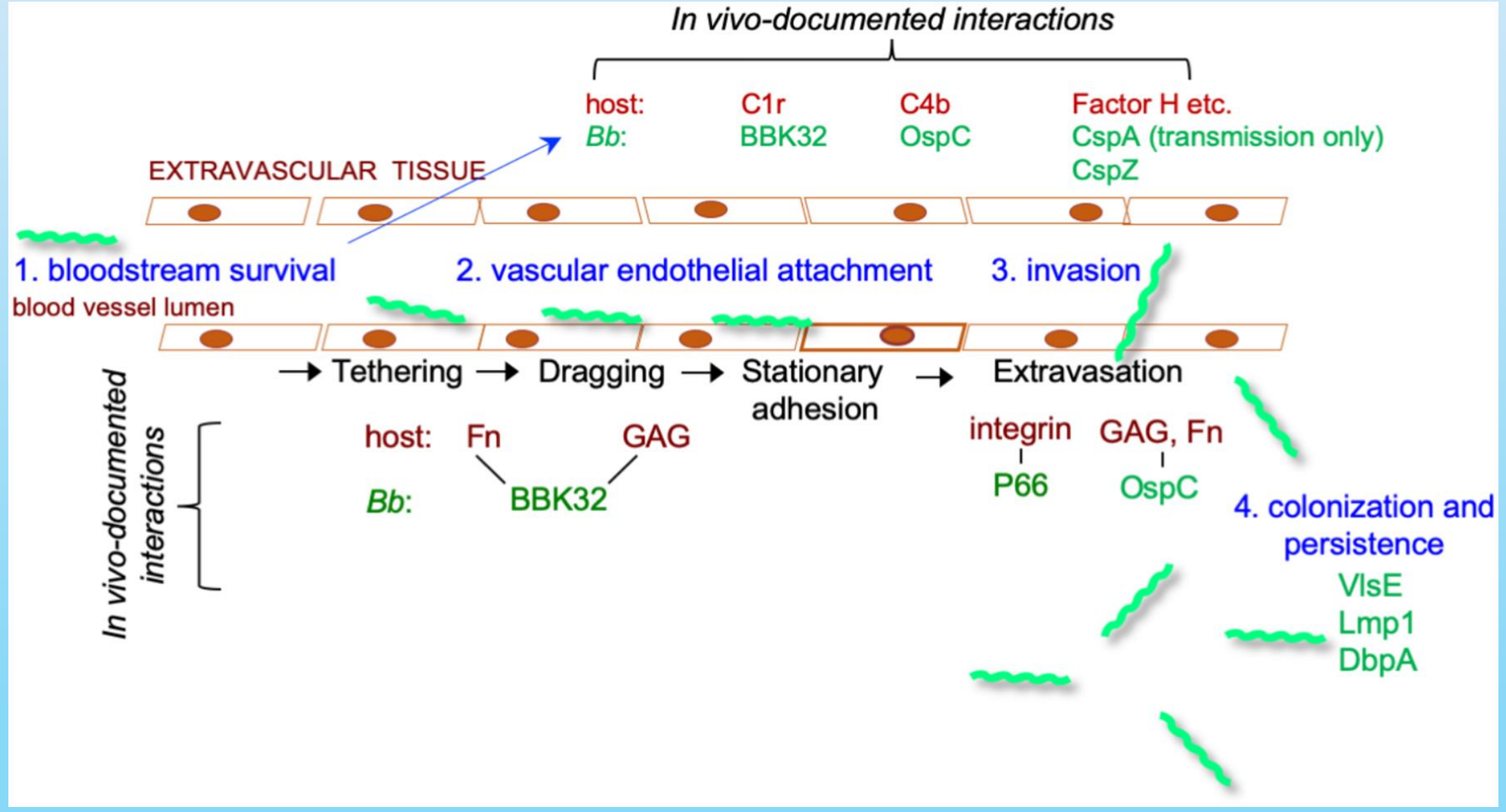
2. Innate/adaptive cellular immune response arises at the site of spirochete entry (from a few days to a month)

3. Spirochete, with the help of several proteins and other substances found in the body, spreads to the central nervous system, eye, muscle, liver, spleen, and heart

# Malattia di Lyme: eziologia

The **OspC** surface protein is required for the survival of Borrelia

The **VlsE** surface protein can also lead to immune evasion by inactivating the host's immune system



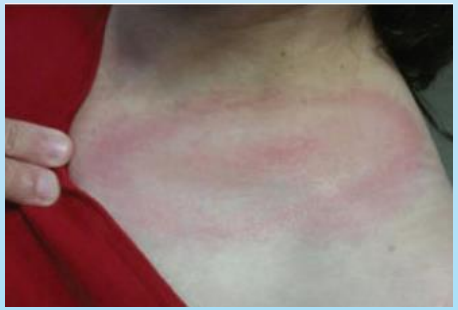
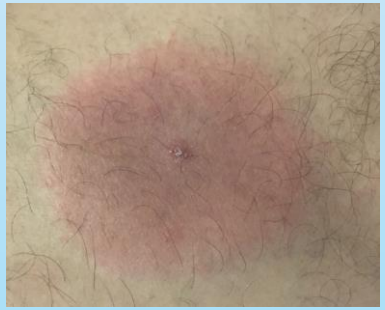
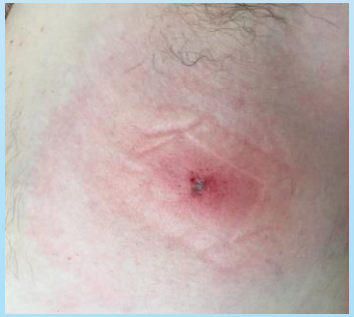
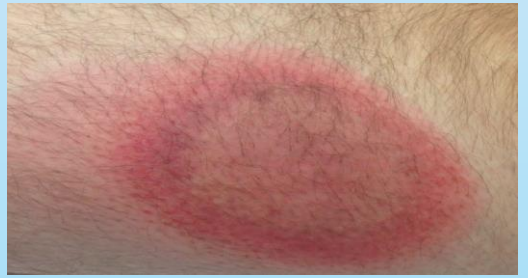
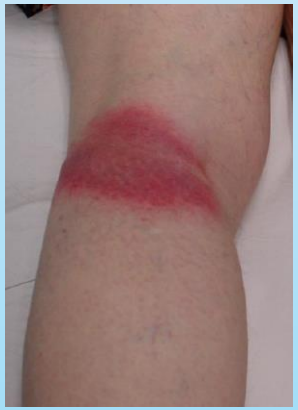

Coburn J, Garcia B, Hu LT, Jewett MW, Kraiczy P, Norris SJ, Skare J. Lyme Disease Pathogenesis. Curr Issues Mol Biol. 2021;42:473-518. doi: 10.21775/cimb.042.473. Epub 2020 Dec 23. PMID: 33353871; PMCID: PMC8046170.†

# Malattia di Lyme: clinica

| Stage | Skin manifestations | Manifestations in other organs |
|---|---|---|
| **Early localised** | Erythema migrans | |
| | Borrelial lymphocytoma | |
| **Early disseminated** | Multiple erythemata migrantia<br>Multiple borrelial lymphocytoma | Flu-like symptoms (muscle and joint pain, fever, swelling of the lymph nodes, reduced performance) |
| | | Neuroborreliosis<br>- Lymphocytic meningitis<br>- Meningo-radiculitis (Bannwarth's syndrome)<br>- Cranial nerve palsy<br>- Myelitis |
| | | Ophthalmoborreliosis |
| | | Myositis |
| | | Acute Carditis |
| | | Acute intermittent Lyme arthritis (monoarthritis) |
| **Late** | Acrodermatitis chronica (atrophicans) | Peripheral neuropathy associated with ACA |
| | - Oedematous stage | |
| | - Atrophic stage | Chronic arthritis |
| | - Fibroid nodules<br>- Pseudo scleroderma | |
| | - With B cell lymphoma | Chronic encephalomyelitis (very rare) |
| | | Cerebral vasculitis (very rare) |

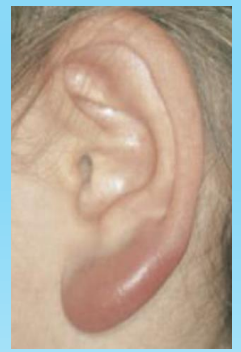
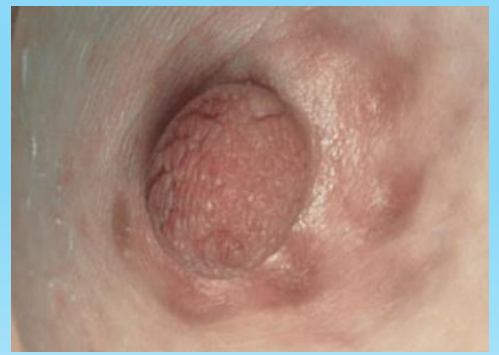
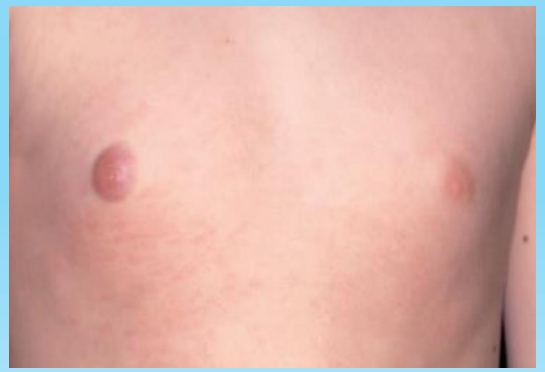
# Malattia di Lyme: clinica, early localised

**<u>Erithema migrans</u>**: expanding, erythematous, often annular skin lesion at the site of inoculation of *Bb (70-80%) 1-2 weeks after tick-bite*

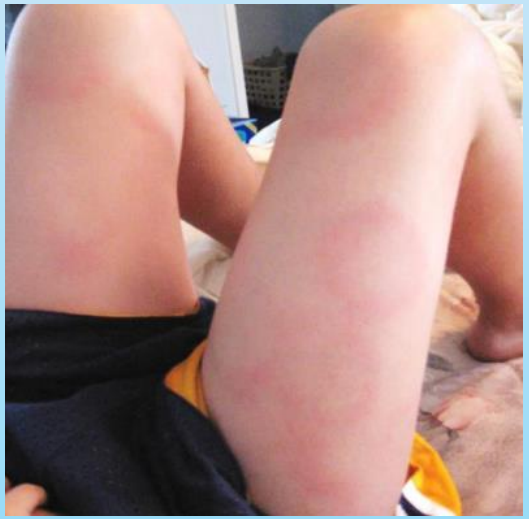
**Lymphocytoma (lymphadenosis benigna cutis)** **usually B. afzelii-B. bissettii**

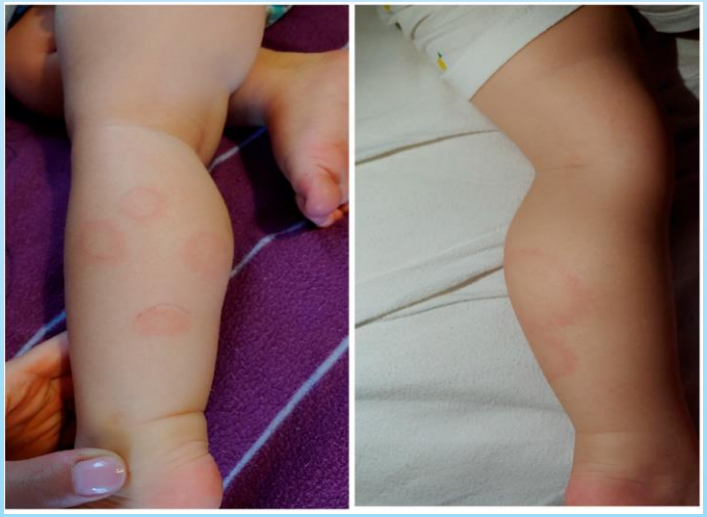
Bluish red nodule usually in the ear, nipple or scrotum (lymphocyte infiltrate), can be painful; it can persist for months. Usually lymph nodes

# Malattia di Lyme: clinica, early disseminated

**Multiple erythemata migrantia**





may be accompanied by general flu-like symptoms, headache, joint pain, and neurological symptoms

# Malattia di Lyme: clinica, early disseminated

Lymphocitic meningitis/encephalitis

radiculoneuritis

- facial (VIIth) nerve the most common
- nerves to the extraocular muscles (IIIth IVth VIth)
- trigeminal (Vth) nerve
- acousticovestibular (VIIIth) nerve

mononeuropathy multiplex

Encephalopathy

- deficits in concentration
- memory loss
- changes in personality
- irritability and depression

Raised intracranial pressure (children)

- Radicular pain (night)
- Peripheral paresis
- Headache
- Anxious-depression syndrome
- Insomnia

# Malattia di Lyme: clinica, early disseminated

**Lyme carditis**

*Manifestation of early disseminated infection (weeks/months-average 21 days after initial infection)*

***conduction system disturbances (heart block), myocarditis, endocarditis, pericarditis, valvular disease***

**Lyme arthritis**

*- Swelling of 1-5 large joints with less pain than expected based on the degree of swelling*

*- Intermittent = spontaneous resolution of inflammation after a few weeks or months*

*- Small joint involvement of the hands and feet is very unusual*

*. «Migrans arthritis of large joints»*

**Ophtalmoborreliosis**

*conjunctivitis*
*papillitis*

*anterior-posterior uveitis*
*episcleritis*

*keratitis*
*neuritis*
*panophthalmitis*

# Malattia di Lyme: clinica, late disease

Months or years after the initial infection

- Acrodermatitis chronica atrophicans (mostly B. afzelii)
- Arthritis: mostly knee
- Neurological involvement: septic meningitis, Bell palsy, dysesthesias, radicular pain, encephalomyelitis (ataxia, seizures, hemiparesis, autonomic dysfunction, hearing loss)
- Neurocognitive involvement (cerebral vasculitis) and psychiatric symptoms
- Cardiac involvement: arrhythmias, transient heart block

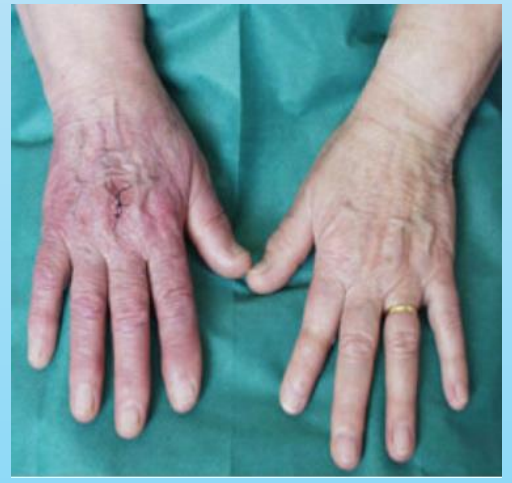
*Many patients may not have a history of erythema migrans*

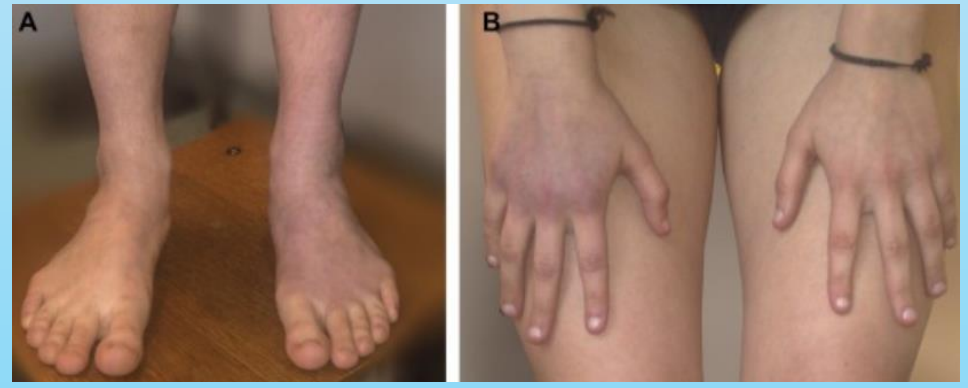
*Symptoms mimic fibromyalgia….*

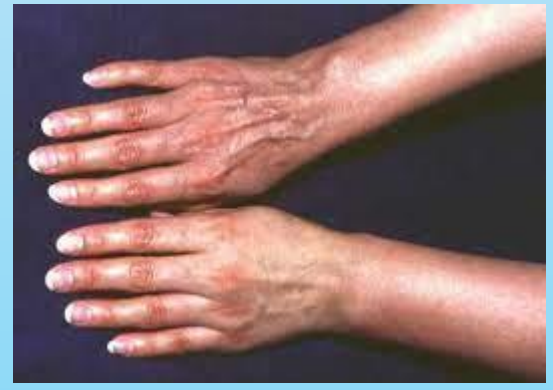
# Malattia di Lyme: clinica, late disease

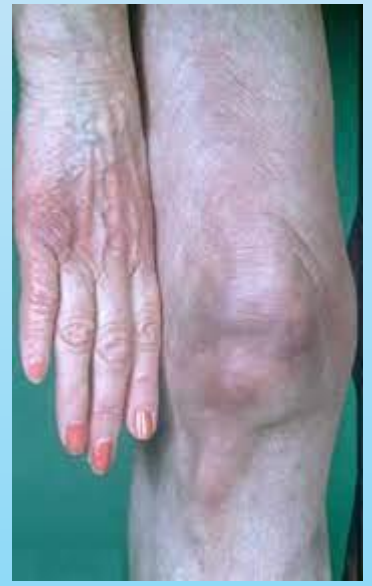
**Acrodermatitis Chronica Atrophicans**

*Older women, tends to occur on the dorsum of the hands and feet, rarely prior symptoms (20% EM)*
*If untreated, it progresses from an early inflammatory stage to a chronic, atrophic phase, which can be complicated by neuropathy, arthralgias, and cutaneous malignancy*





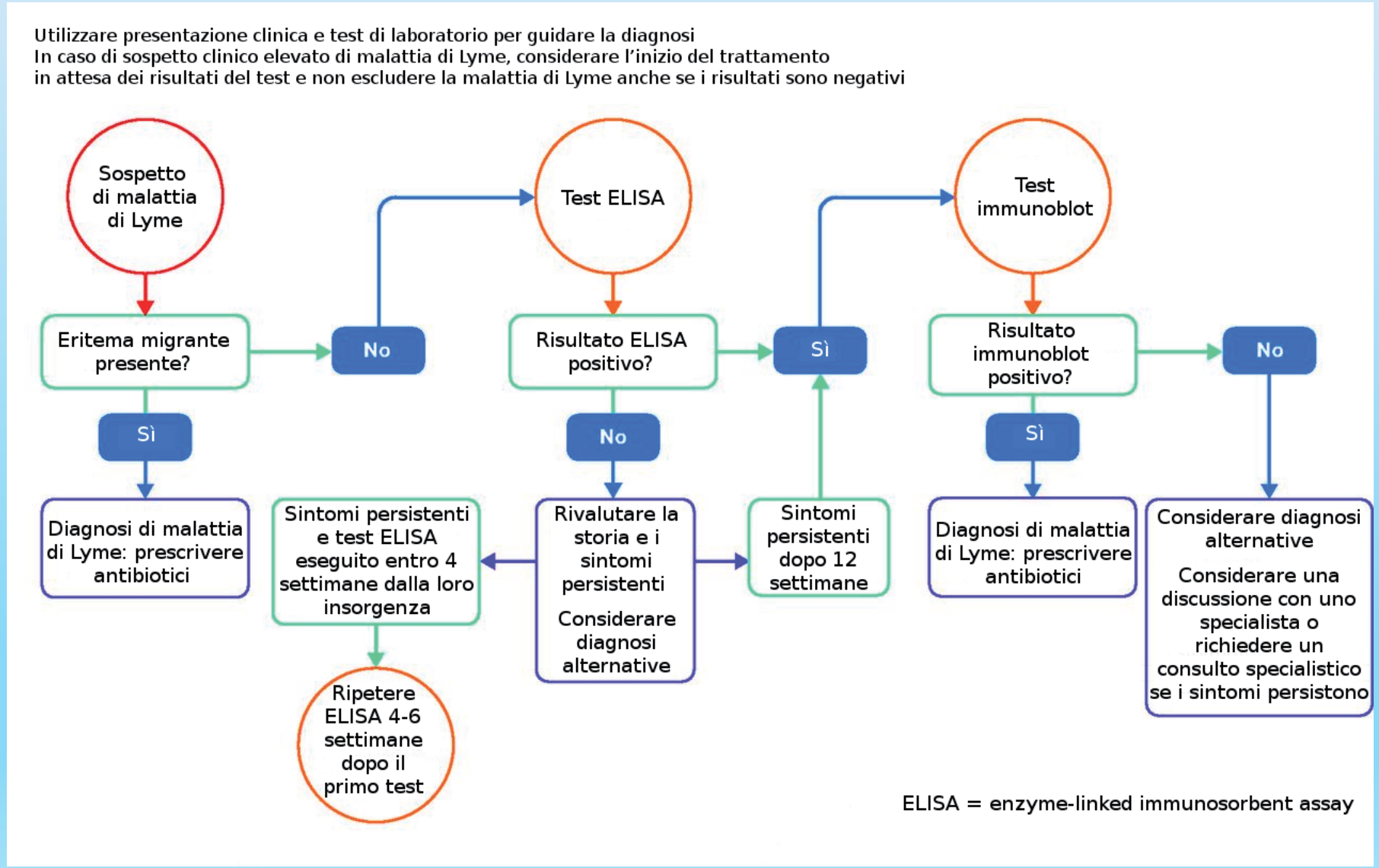





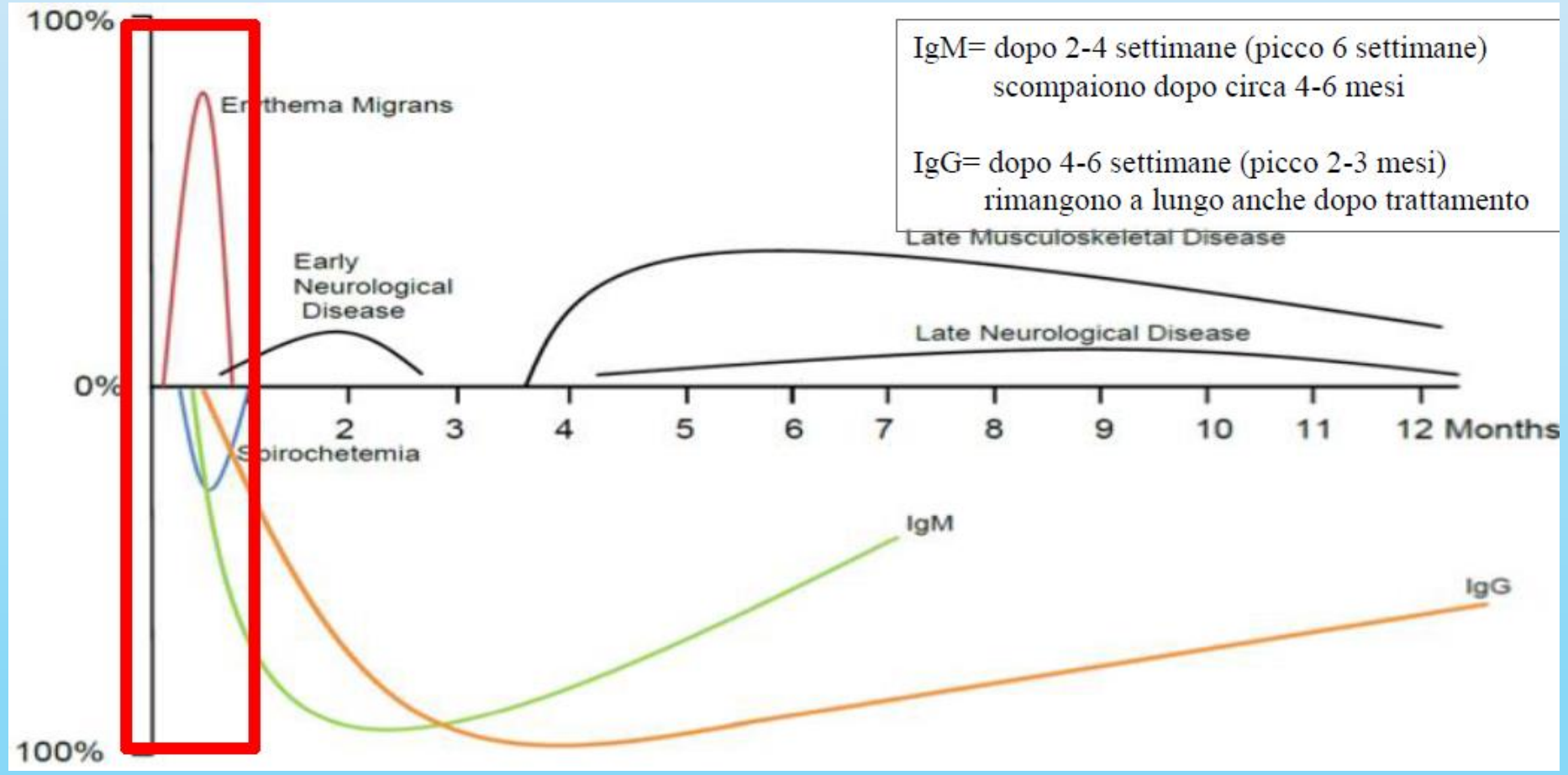
**Chronic encephalomyelitis**

If the infection remains untreated in months-years after initial infection:
*Neurological symptoms of encephalomyelitis, migraines, dizziness, sleep disturbances, concentration issues, brain fog, memory loss*

# Malattia di Lyme: diagnosi, linee guida italiane



# Malattia di Lyme: diagnosi




IgM= dopo 2-4 settimane (picco 6 settimane)
scompaiono dopo circa 4-6 mesi

IgG= dopo 4-6 settimane (picco 2-3 mesi)
rimangono a lungo anche dopo trattamento

Ma…positività IgM può persistere per diversi anni: ATTENZIONE ALLE FALSE DIAGNOSI!!!

# Malattia di Lyme: diagnosi, neuroborreliosi

## DIAGNOSTIC TESTING STRATEGY FOR LYME NEUROBORRELIOSIS

1. <u>serum antibody testing:</u> most sensitive test *(strong recommendation, moderate quality evidence)*

2. If CSF testing is performed:

- obtaining simultaneous samples of CSF and serum for

**Formula for the Borrelia-specific antibody index (AI)**

$$\frac{\dfrac{\text{Borrelia-specific Ig in CSF}}{\text{Borrelia-specific Ig in serum}}}{\dfrac{\text{total Ig in CSF}}{\text{total Ig in serum}}} = \text{AI}$$

**<u>determination of the CSF:serum antibody index</u>** (sensitivity 56-79%)

- recommend <u>against CSF without measurement of the CSF:serum antibody index</u>
- recommend against routine PCR or culture of CSF or serum *(strong recommendation, moderate quality evidence)*

Detection of *B. burgdorferi* in CSF by PCR: sensitivity 5-17%

Detection of *B. burgdorferi* in blood by PCR: sensitivity 1-28%

# Malattia di Lyme: diagnosi

| Early antigens | Early/Late antigens | Late antigens |
|---|---|---|
| OspC (p21-p25, Major outer surface lipoprotein C) | VlsE (vmp-like sequence E) | OspA (p31) |
| BbK32 (Fibronectin-binding protein) | Dbpa (p17-p18, Decorin-binding protein A) | p30 |
| Flagellin (p41) | OppA-2 (p58, Oligopeptide-binding protein) | p66 |
| | BmpA (p39) | p83/100 |
| | p14 | p93 |
| | p28 | |
| | p43 | |
| | p45 | |

Variations in the *Borrelia* immunodominant antigen expression during human infection

(Talagrand-Reboul, E.; Raffetin, A.; Zachary, P.; Jaulhac, B.; Eldin, C. Immunoserological Diagnosis of Human Borrelioses: Current Knowledge and Perspectives. *Front. Cell. Infect. Microbiol.* **2020**, *10*, 241. https://doi.org/10.3389/fcimb.2020.00241.)

# Malattia di Lyme: terapia (IDSA guidelines)

**Erythema migrans**

Doxycycline 10 days

Or

Amoxicillin 14 days

Or

Cefuroxime axetil 14 days

Second-line agent:

Azithromycin 7 days

**Lyme carditis**

Ceftriaxone ev

Or

Doxycycline

Or

Amoxicillin

Or

Cefuroxime axetil

(Or

Azithromycin)

*For 14-21 days*

**Lymphocytoma**

Doxycycline

Or

Amoxicillin

Or

Cefuroxime axetil

(Or

Azithromycin)

*For 14 days*

**Acrodermatitis chronica atrophicans**

Doxycycline

Or

Amoxicillin

Or

Cefuroxime axetil

(Or

Azithromycin)

*For 21-28 days*

Benefit from the anti-inflammatory effects of aspirin or corticosteroid therapy? ←

Weak recommendation, low quality evidence

# Malattia di Lyme: terapia (IDSA guidelines)

**Acute neurological manifestations**

Ceftriaxone IV

Or

Cefotaxime IV

Or

Penicillin G IV

Or

Doxycicline

} For 14-21 days

**Corticosteroid in facial nerve palsy?**

Corticosteroid not recommended in addition to antibiotics

>16 years with acute facial nerve palsy but without other objective clinical or serologic evidence of Lyme disease, corticosteroid treatment should be administered within 72 hours in accordance with current facial nerve palsy guideline recommendations

# Malattia di Lyme: terapia (IDSA guidelines)

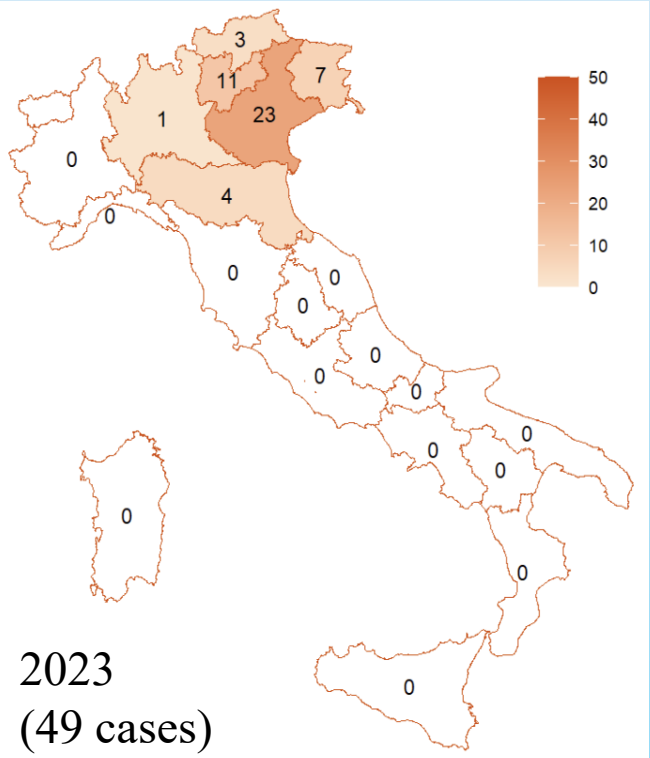
## Lyme Arthritis

| | | |
|---|---|---|
| Doxycycline<br>Or<br>Amoxicillin<br>Or<br>Cefuroxime axetil<br>Or<br>Azithromycin<br>*For 28 days* | **No or minimal response** (moderate to severe joint swelling with minimal reduction of the joint effusion) **to an initial course of oral antibiotic**:<br><br>Ceftriaxon IV 2-4-weeks<br>*For 28 days* | **Partial response** (mild residual joint swelling) **after a first course of oral antibiotic**<br><br>no recommendation for a second course of antibiotic versus observation |

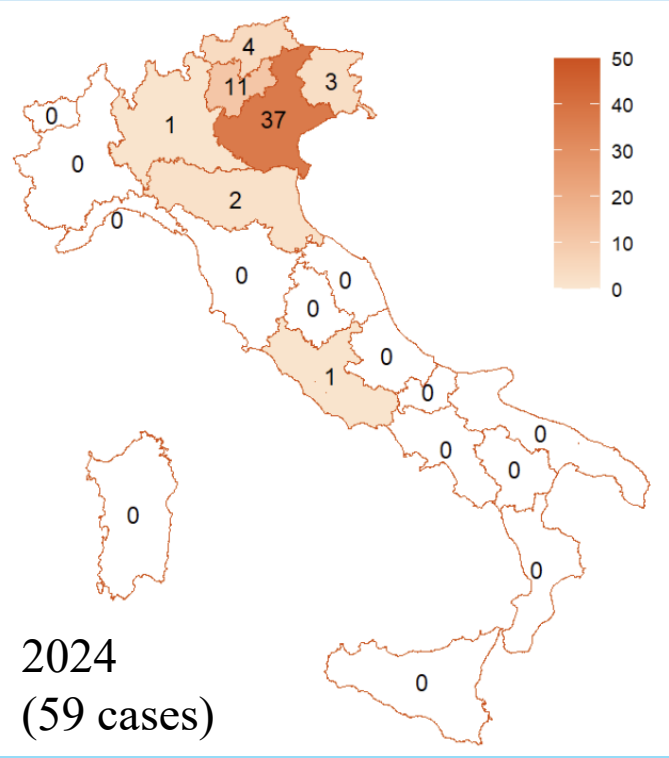
Patients failed 1 course of oral and 1 course of IV antibiotics (post Lyme arthritis): refer to a rheumatologist (for DMARDs, biologic agents, intra-articular steroids, arthroscopic synovectomy).

***Antibiotic therapy for longer than 8 weeks is not expected to provide additional benefit to patients with persistent arthritis if that treatment has included 1 course of IV therapy***

# TICK BORNE-ENCEPHALITIS (TBE)



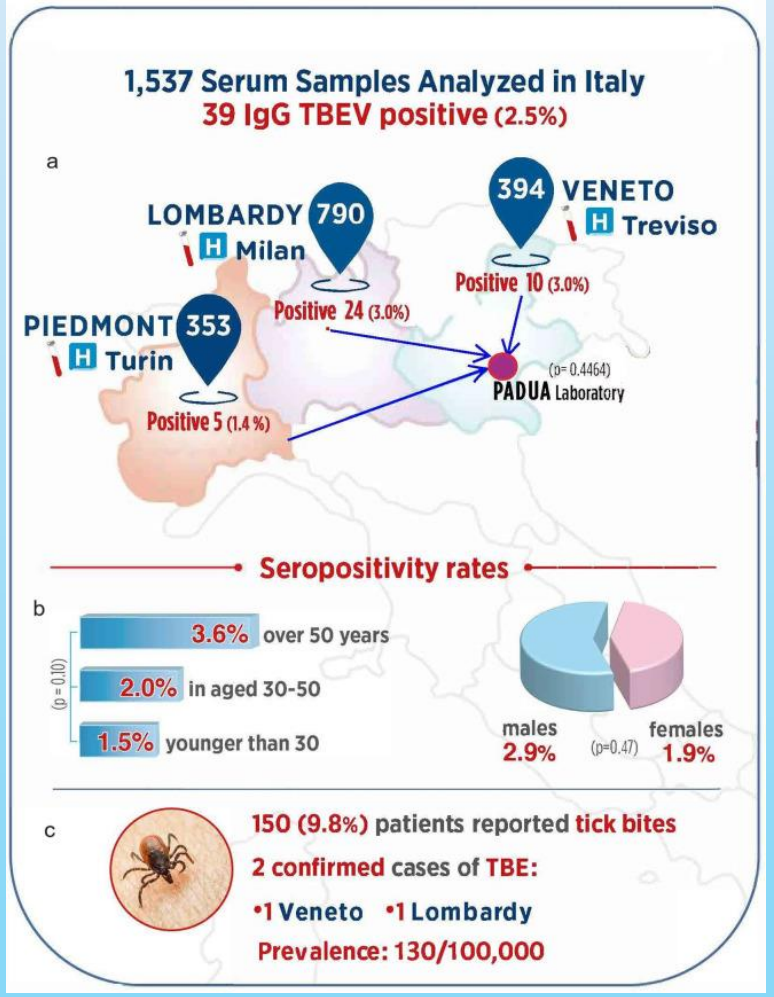

2023
(49 cases)




2024
(59 cases)

N° casi per regione anno

https://www.epicentro.iss.it/arbovirosi




**First Human Case of Tick-Borne Encephalitis in Non-Endemic Region in Italy: A Case Report**

*Barp N et al. Pathogens. 2022*
(Modena)

Tick-Borne Encephalitis, Lombardy, Italy

*Gaffuri A et al. Emerg Infect Dis. 2024*
(Bergamo)

*Castagna A et al. Tick-borne encephalitis seroprevalence in northern Italy: a cross-sectional study on a randomly selected population. IJID Reg. 2024 Jul 14;12:100404*

# TICK BORNE-ENCEPHALITIS

- **Flavivirus**

- Europeo o Estremo Occidente (European o Western Tick-Borne Encephalitis Virus, TBEV-Eu)

  Europa centrale, orientale e settentrionale;  Russia occidentale

- Estremo Oriente o Virus dell'Encefalite Russa Estiva/Primaverile (Far Eastern Tick-Borne Encephalitis Virus o Russian Spring Summer Encephalitis Virus, TBEV-FE o RSSEV)

  Russia, Cina, Giappone, alcuni casi in Europa orientale

- Siberiano (TBEV-Sib)

  Urali, Siberia, Russia, Europa nord-orientale

- "178-79 group" "Baikalian subtype 1" (TBEV-Bkl-1)  Irkutsk, Russia
- "886-84 group" o  "Baikalian subtype 2" (TBEV-Bkl-2)  Siberia dell'est (lago Baikal), nord della Mongolia
- Himalayan TBEV (TBEV-Him)  China nell'altopiano del Qinghai-Tibeti (roditore Marmota himalayana)
- TBEV-2871 o "Obskaya subtype "  (TBEV-Ob)

*Deviatkin et al. Viruses.2020*

# TICK BORNE-ENCEPHALITIS

***Incubation period*** → Alimentary transmission → < 4 days

Tick bite → 2-28 days (usually 7-8 days)

***If the virus takes over the immune system...***

***First viremia*** = Infection of peripheral tissues and organs (liver, spleen, bone marrow, lymphnodes)

Then…

***Second viremia*** may occur = CNS involvement

***Abortive TBEV infection*** = no CNS involvement

*Ruzek D et al. Antiviral Res. 2019*

# TICK BORNE-ENCEPHALITIS

**BIFASICO** = prima fase viremica con sintomi aspecifici + intervallo asintomatico + seconda fase neurologica

**MONOFASICO** = quadro clinico con o senza sintomi neurologici, senza identificazione di intervallo asintomatico

**TBE ABORTIVA** = decorso monofasico senza sintomi neurologici

# INFEZIONE DA TBEV: *clinical features, biphasic course, phase I*

*Flu-like syndrome* ⟶ *Stop = abortive form*

⟶ *Progression = after an asymptomatic interval (1-21 days)*

⟲ *CNS involvement*

| | |
|---|---|
| Fever | 88.7% (212/239) |
| Asthenia | 58.6% (140/239) |
| Headache | 36.4% (87/239) |
| Arthromyalgia | 36.4% (87/239) |
| Nausea/vomiting | 17.2% (41/239) |
| Diarrhea | 14.2% (34/239) |
| Abdominal pain | 7.1% (17/239) |
| Sorethroat | 4.2% (10/239) |
| Cough | 2.9% (7/239) |
| Syncope | 2.5% (6/239) |
| Weight loss | 2.1% (5/239) |

| | |
|---|---|
| Limphadenopathy | 2.1% (5/239) |
| Skin rush | 1.3% (2/239) |
| Constipation | 1.3% (2/239) |
| Conjunctival hyperaemia | 0.4% (1/239) |
| Othalgia | 0.4% (1/239) |

*Unpublished data from a retrospective Italian study: clinical features of the first phase of TBEVi*

# INFEZIONE DA TBEV: *clinical features, biphasic course, phase II*

CNS involvement (meninges, encephalic regions, spinal cord, nerve roots)

Meningitis (50%)

Meningoencephalitis (40%)

Meningoencephalomyelite (5-10%)

Meningoencephaloradicolite (rare)

Myeloradicolite (rare)

*Ruzek D et al. Antiviral Res. 2019*

# INFEZIONE DA TBEV: *clinical features, biphasic course, phase II*

| | |
|---|---|
| Fever | 99.2% (237/239) |
| Asthenia | 90.8% (217/239) |
| Headache | 83.7% (200/239) |
| Nausea/vomiting | 53.1% (127/239) |
| Arthromyalgia | 48.1% (115/239) |
| Ataxia | 37.2% (89/239) |
| Tremors | 23.8% (57/239) |
| Constipation | 21.3% (51/239) |
| Ideomotor slowing | 18% (43/239) |
| Disorientation | 14.2% (34/239) |
| Meningism | 13% (31/239) |
| Dizziness | 12.6% (30/239) |
| Diarrhea | 9.2% (22/239) |

| | |
|---|---|
| Photophobia | 8.8% (21/239) |
| Abdominal pain | 8.8% (21/239) |
| Paresthesia | 8.8% (21/239) |
| Soporous state | 7.9% (19/239) |
| Upper limb palsy | 6.7% (16/239) |
| Cranial nerve palsy | 5.4% (13/239) |
| Diplopia | 5.4% (13/239) |
| Amnesia | 4.2% (10/239) |
| Lower limb palsy | 3.8% (9/239) |
| Weight loss | 3.8% (9/239) |
| Dysarthria | 3.8% (9/239) |
| Syncope | 3.3% (8/239) |
| Limphadenopathy | 3.3% (8/239) |

**Other symptoms**:

- tinnitus, aphasia, epilepsy, 2.9% (7/239) each;
- urinary retention, insomnia, hypovisus, anxious-depressive state 2.5% (6/239) each;
- sorethroat 2.1% (5/239;
- hypotension, respiratory failure, hypertension, othalgia, conjunctival hiperaemia 1.7% (4/239) each;
- dysphagia 1.3% (3/239);
- hallucinations, bradycardia, emineglect, hearing loss, fasciculation, urinary incontinence, skin rash 0.8% (2/239) each;
- nystagmus, SIADH, hiccups, cough, dysgeusia 0.4% (1/239) each

*Unpublished data from a retrospective Italian study: clinical features of the second phase of the biphasic course of TBEVi*

# INFEZIONE DA TBEV: *clinical features, sequelae*

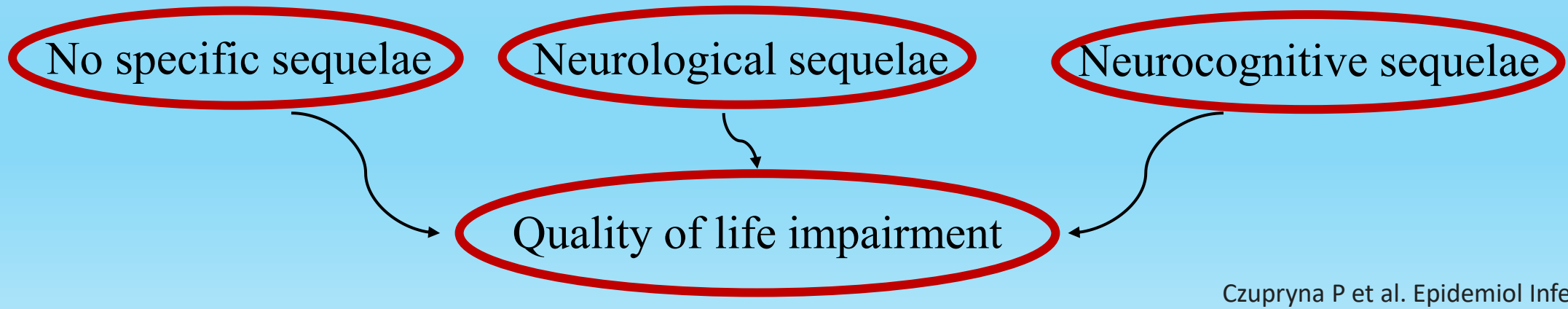
Mortality < 2% ⟶ < 0.5% if < 70 years

⟶ 2% if 71-79 years

⟶ 3.1% if > 80 years

**Sequelae: incidence 20-60%**

signs, symptoms, neurological/neurocognitive changes persisting from the acute phase or appearing in the following period, even months and years later




Czupryna P et al. Epidemiol Infect. 2018

# INFEZIONE DA TBEV: *clinical features, sequelae*

## (sequelae at 30 days)

| | |
|---|---|
| Asthenia | 46.6% (211/455) |
| Ataxia | 10.8% (49/455) |
| Arthromyalgia | 9.9% (45/455) |
| Tremors | 8.8% (40/455) |
| Deficit of attention | 8.8% (40/455) |
| Headache | 5.9% (27/455) |
| Upper limb palsy | 5.3% (24/455) |
| Lower limb palsy | 4.9% (22/455) |
| Amnesia | 3.5% (16/455) |
| Anxious-depressive state | 3.1% (14/455) |
| Paresthesia | 2.6% (12/455) |
| Ideomotor slowing | 2% (9/455) |
| Insomnia | 1.5% (7/455) |

| | |
|---|---|
| Nausea | 1.5% (7/455) |
| Dizziness | 1.3% (6/455) |
| Fever | 1.3% (5/455) |
| Urinary retention | 1.1% (5/455) |
| Dysarthria | 1.1% (5/455) |
| Behaviour alteration | 1.1% (5/455) |
| Tinnitus | 0.9% (4/455) |
| Soporous state | 0.9% (4/455) |
| Respiratory failure | 0.9% (4/455) |
| Disorientation | 0.7% (3/455) |
| Hypoacusia | 0.7% (3/455) |
| Coma | 0.4% (2/455) |

***272/455 (59.8%) presented sequelae at 30 days***

**<u>Other symptoms</u>**:
Hiccup, clonia, photophobia, ageusia
0.2% (1/455) each

*Unpublished data from a retrospective Italian study: sequelae at 30 days*

# INFEZIONE DA TBEV: *clinical features, sequelae*

## (sequelae at 6 months)

| | |
|---|---|
| Asthenia | 16.2% (39/244) |
| Arthromyalgia | 7.5% (18/244) |
| Amnesia | 6.2% (15/244) |
| Upper limb palsy | 5.4% (13/244) |
| Ataxia | 5.0% (12/244) |
| Lower limb palsy | 4.1% (10/244) |
| Tremors | 2.9% (7/244) |
| Anxious-depressive state | 2.9% (7/244) |
| Headache | 2.5% (6/244) |
| Dizziness | 0.8% (2/244) |
| Disorientation | 0.8% (2/244) |
| Behaviour alteration | 0.8% (2/244) |
| Respiratory failure | 0.8% (2/244) |

***84/244 (34.4%) presented sequelae at 6 months***

| | |
|---|---|
| Dysphagia | 0.8% (2/244) |
| Ideomotor slowing | 0.4% (1/244) |
| Tinnitus | 0.4% (1/244) |
| Soporous state | 0.4% (1/244) |
| Dysarthria | 0.4% (1/244) |
| Dysgeusia | 0.4% (1/244) |

*Unpublished data from a retrospective Italian study: sequelae at 6 months*

# INFEZIONE DA TBEV : *diagnosis*

***Criteri presentati dall'Eurosourveillance nel 2012, stessi criteri utilizzati dal Ministero della Salute in Italia***

| | |
|---|---|
| **CRITERI CLINICI** | **qualsiasi persona che presenti sintomi clinici di infiammazione del SNC (es. meningite, meningoencefalite, encefalomielite, encefaloradicolite).** |
| **CRITERI DI LABORATORIO** | Caso probabile:<br>• Identificazione degli anticorpi IgM o di IgM e IgG specifici in un unico campione di siero.<br><br>Caso confermato: almeno uno dei seguenti 5 criteri:<br>• Identificazione di RNA virale su CSF e/o siero;<br>• Presenza di IgM e IgG specifici nel siero;<br>• Presenza di IgM o IgM e IgG nel CSF;<br>• Siero-conversione o aumento significativo degli anticorpi specifici per TBE in coppie di campioni di siero;<br>• Isolamento del TBEV da un campione clinico. |
| **CRITERI EPIDEMIOLOGICI** | • Possibile esposizione a morso di zecca in un'area endemica o risiedere in un'area endemica;<br>• Persona esposta alla stessa fonte alimentare (derivati del latte non pastorizzato) di un caso confermato di TBE durante un focolaio epidemico |

- **Caso probabile** = criteri clinici e di laboratorio per caso probabile o criteri clinici + epidemiologici
- **Caso confermato** = criteri clinici + almeno uno dei criteri di laboratorio per caso confermato

***Identificano solamente TBE e non l'infezione da TBEV, che si può presentare anche con assenza di sintomi neurologici***

# INFEZIONE DA TBEV : *diagnosis*

***Criteri presentati dall'Eurosourveillance nel 2012, stessi criteri utilizzati dal Ministero della Salute in Italia***

| | |
|---|---|
| **CRITERI CLINICI** | **qualsiasi persona che presenti sintomi clinici di infiammazione del SNC (es.** |
| **CRITERI DI LABORAT** | …ero. |
| | …pie di |
| **CRITERI EPIDEMIOLOGICI** | …nica;<br>• Persona esposta alla stessa fonte alimentare (derivati del latte non pastorizzato) di un caso confermato di TBE durante un focolaio epidemico |

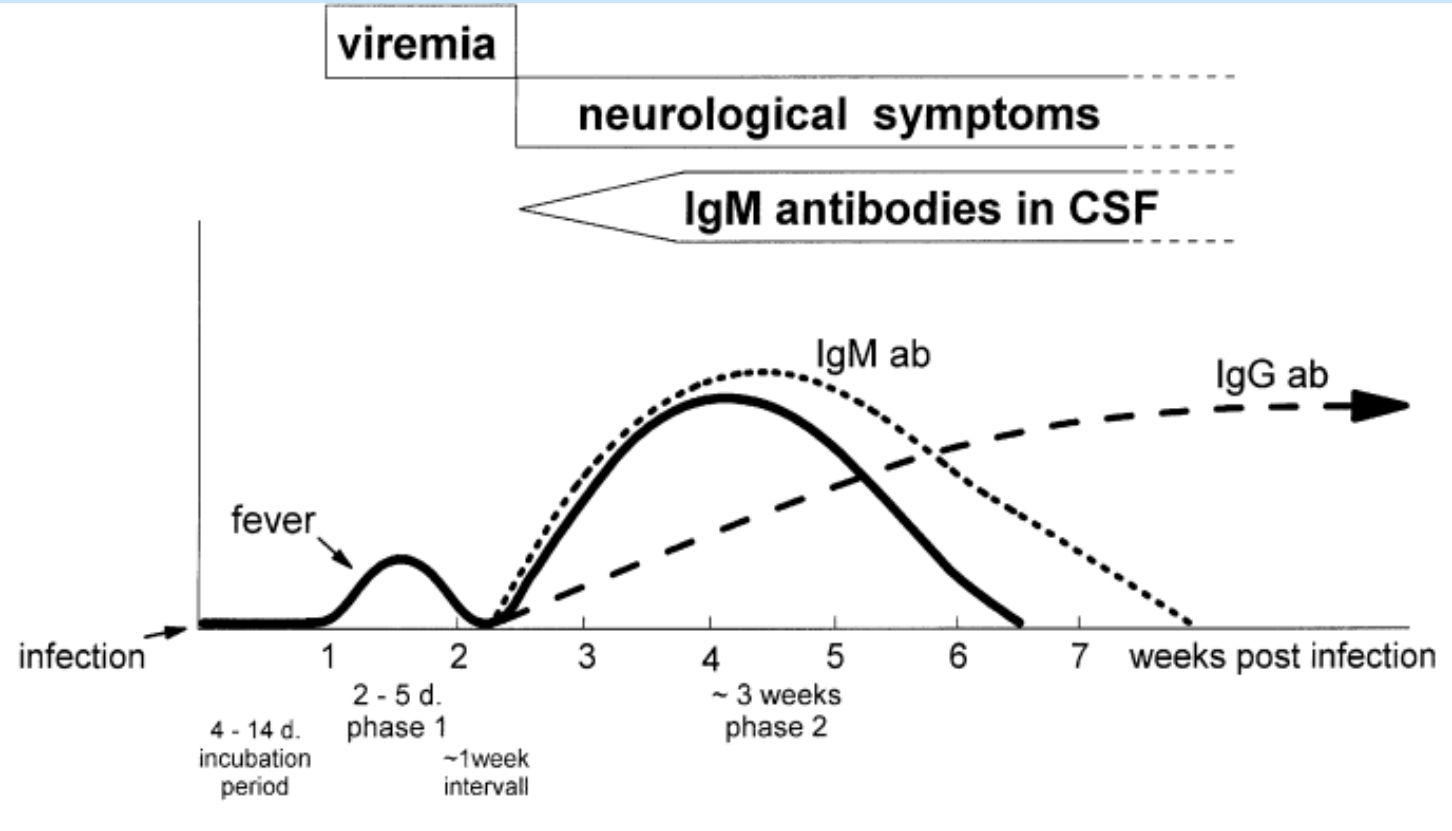
**96 pazienti (16,5% di tutte le TBEVi) hanno presentato la forma abortiva**

*Unpublished data from a retrospective Italian study*

- **Caso probabile** = criteri clinici e di laboratorio per caso probabile o criteri clinici + epidemiologici
- **Caso confermato** = criteri clinici + almeno uno dei criteri di laboratorio per caso confermato

***Identificano solamente TBE e non l'infezione da TBEV, che si può presentare anche con assenza di sintomi neurologici***

# INFEZIONE DA TBEV : *diagnosis*




## IgM

- peak within 14 days after the onset of neurological symptoms
- persist for 6-7 weeks, rarely months and years

## IgG

- with CNS involvement
- Peak in the 6° week following the onset of neurological symptoms

*Persistence of IgG results in permanent protection from further TBEV infection*

Holzmann H et al. *Vaccine.* 2003

# INFEZIONE DA TBEV : *therapy and vaccine*

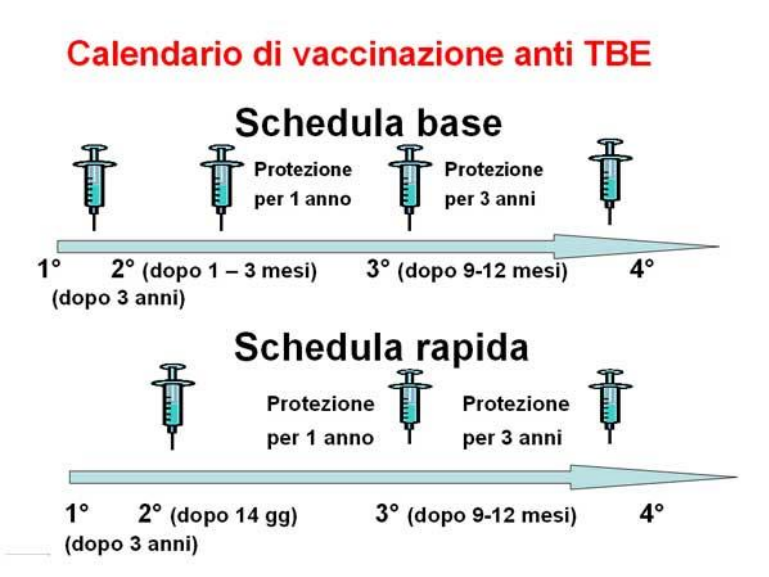
**Symptomatic therapy**

*Paracetamol, NSAD, intensive care…*

**Schedule vaccinali**

- Standard: tempo 0, tempo 1-3 mesi, tempo 5-12 mesi / 9-12 mesi (in base al vaccino, disponibili 2 formulazioni)

- Booster: I booster a 3aa, poi → ogni 5aa se <60aa per FSME-IMMUN;
  → ogni 3aa se >60aa per FSME-IMMUN;




***Effetti avversi (16-25%)***

dolore nel sito di iniezione — febbre — cefalea — artromialgie — astenia

*Efficacia 95-99% dei casi se eseguita intera schedula vaccinale*

*La scheda rapida utilizzata nel periodo estivo per ridurre intervallo tra prima e seconda somministrazione, garantendo protezione più precoce, ma minore risposta immunitaria e declino più rapido delle IgG protettive*

# ZOONOSI DA MORSO DI ZECCA

## Batteri

- **Malattia di Lyme**
- Anaplasmosi
- Erlichiosi
- Febbre ricorrente
- Rickettsiosi
- Febbre delle montagne rocciose
- Tularemia
- .....

## Virus

- **Tick-borne encephalitis**
- Febbre delle zecche del Colorado
- Febbre emorragica Crimea-Congo
- Powassan
- Heartland virus
- .....

## Protozoi

- Babesiosi

# **ANAPLASMOSI:** *Anaplasma phagocytophilum*

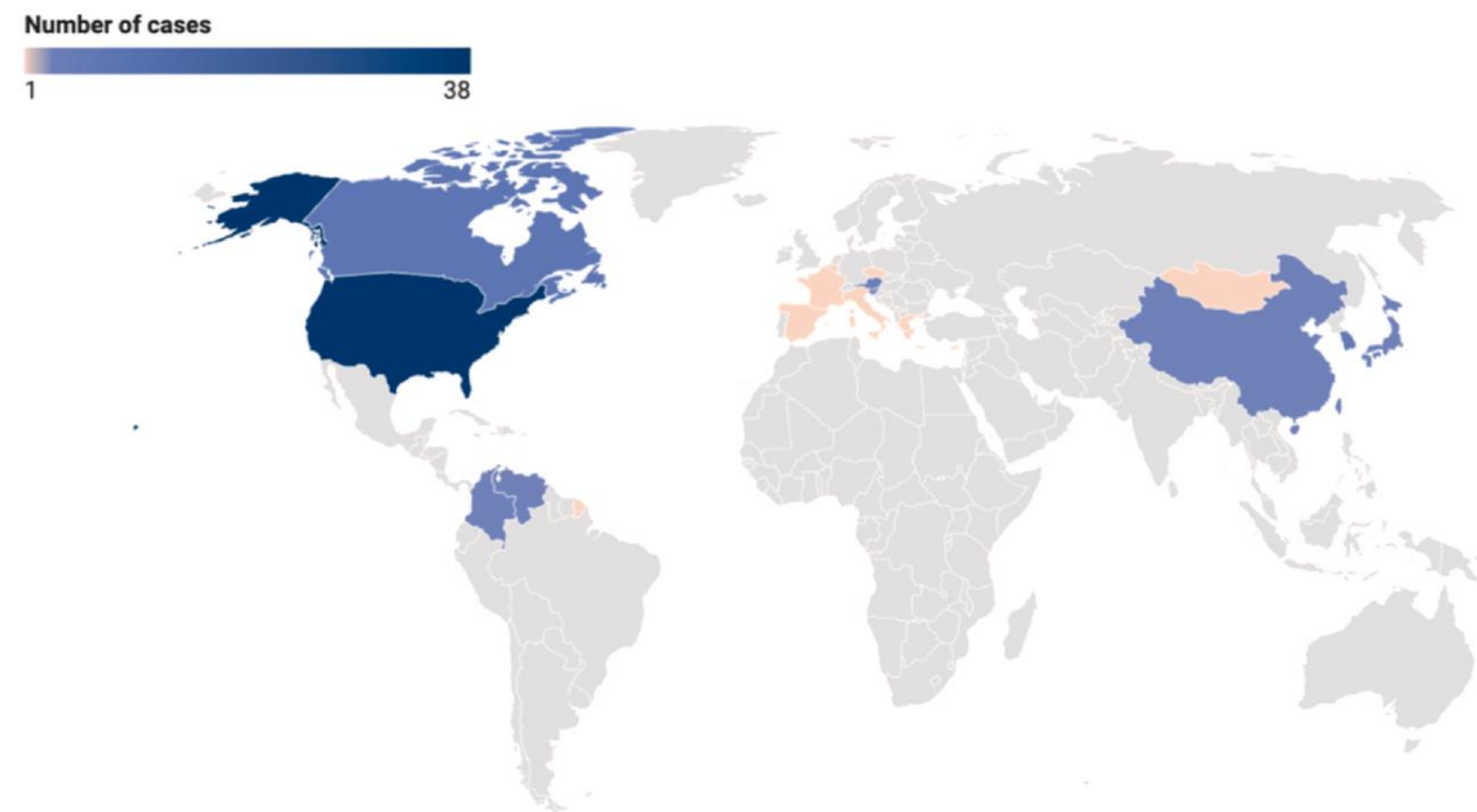
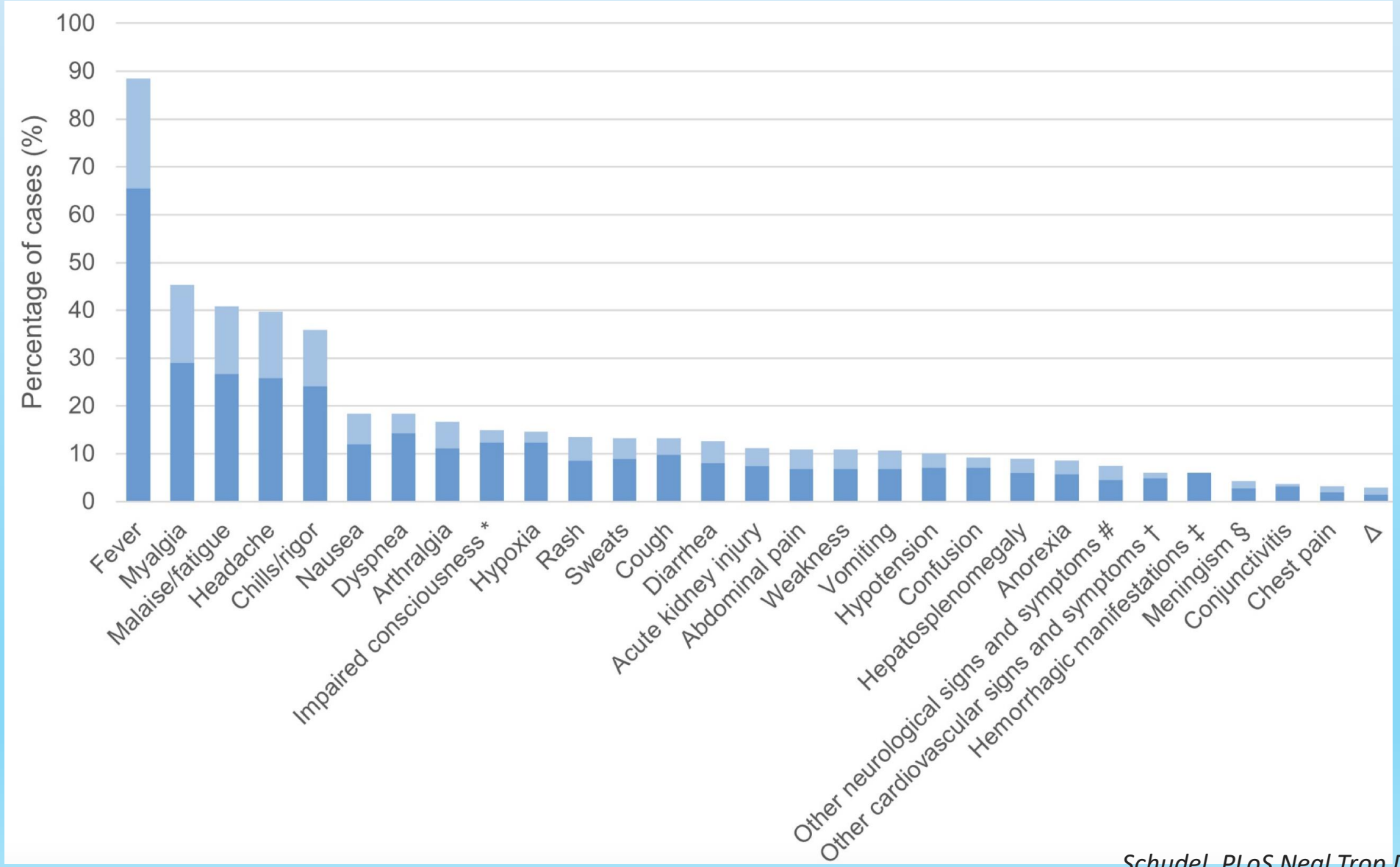


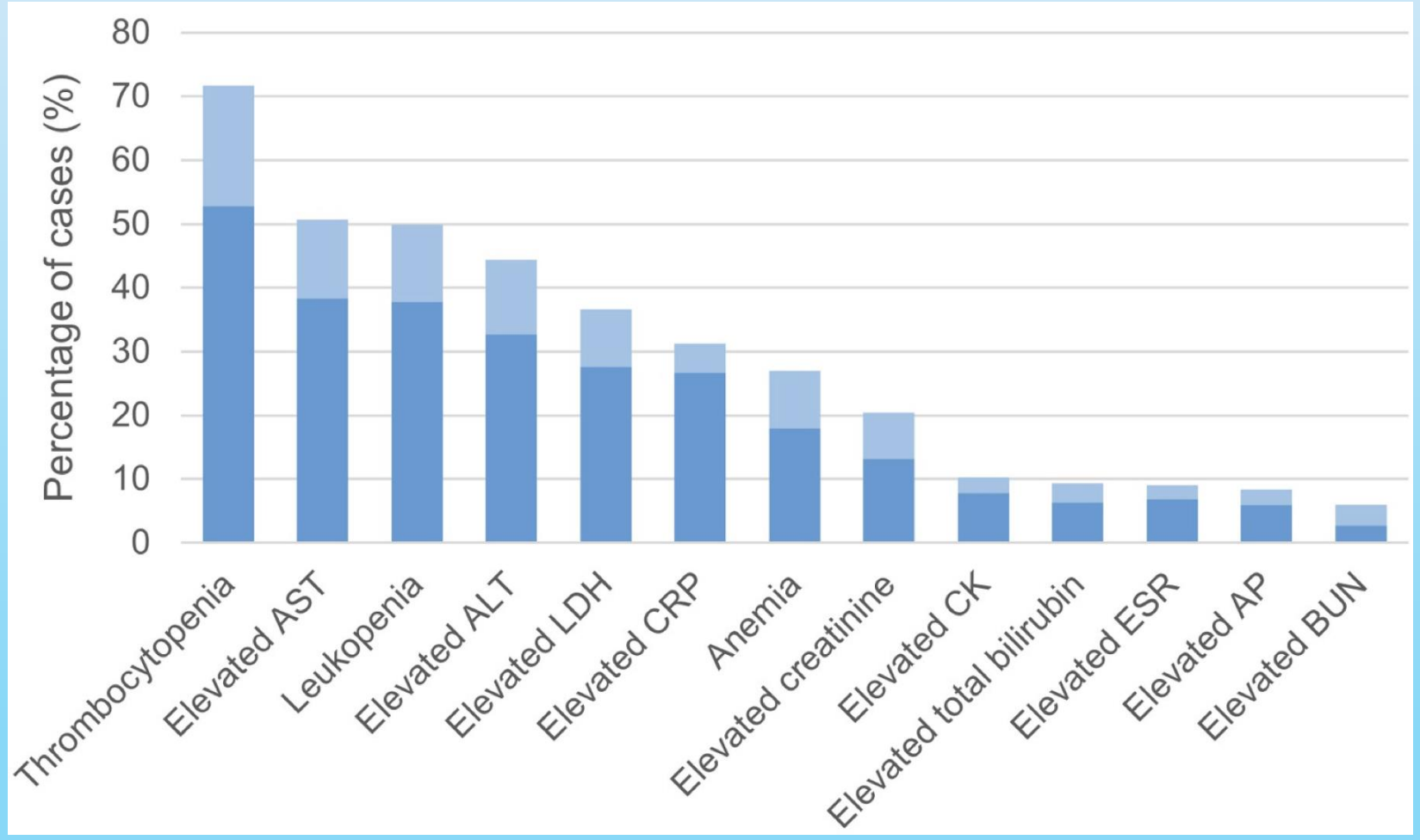

**Fig. 3.** Heatmap of anaplasmosis cases in humans by reporting country.

# **ANAPLASMOSI:** *Anaplasma phagocytophilum*




*Schudel, PLoS Negl Trop Dis. 2024*

# **ANAPLASMOSI:** *Anaplasma phagocytophilum*




*Schudel, PLoS Negl Trop Dis. 2024*

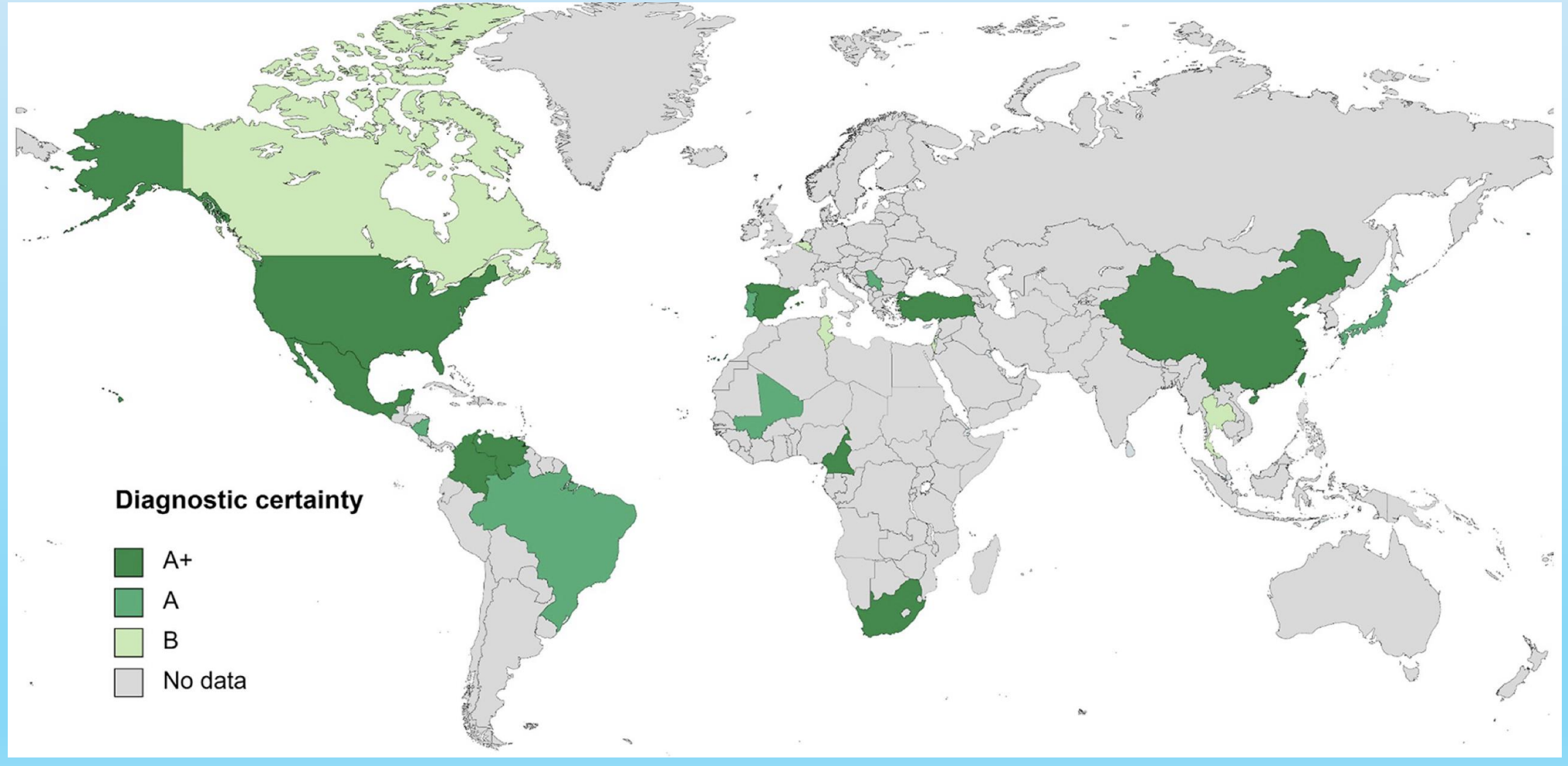
# ANAPLASMOSI: *Anaplasma phagocytophilum*

| Diagnostic method | Description | Grade of diagnostic certainty | Case classification (provided illness clinically compatible with anaplasmosis) | Comment |
|---|---|---|---|---|
| **PCR** | Detection of *Anaplasma* spp. DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay | A+ | Direct evidence, confirmed diagnosis | High level of evidence, especially in the first week of illness and before start of antibiotics, mostly done from whole blood specimens, also possible in solid tissue and bone marrow specimens |
| **Culture** | Isolation of *Anaplasma* spp. from a clinical specimen in cell culture | A+ | Direct evidence, confirmed diagnosis | High level of evidence, especially in the first week of illness and before start of antibiotics, difficult to carry out, time demanding |
| **Immunostaining of biopsy/autopsy tissue** | Demonstration of anaplasmal antigen in a biopsy/autopsy sample by immunohistochemical methods | A+ | Direct evidence, confirmed diagnosis | High level of evidence, difficult to carry out, time demanding |
| **Serology—IgG IFA, paired samples** | Serological evidence of a fourfold rise in IgG-specific antibody titer to *A. phagocytophilum* antigens by indirect immunofluorescence assay (IFA) in paired serum samples (i.e. an acute phase sample [first week of infection] and a convalescent phase sample [2–4 weeks later]) | A | Indirect evidence, confirmed diagnosis | High level of evidence, serological gold standard, cross-reaction with other rickettsial diseases possible |

Doxycycline for 7-14 days

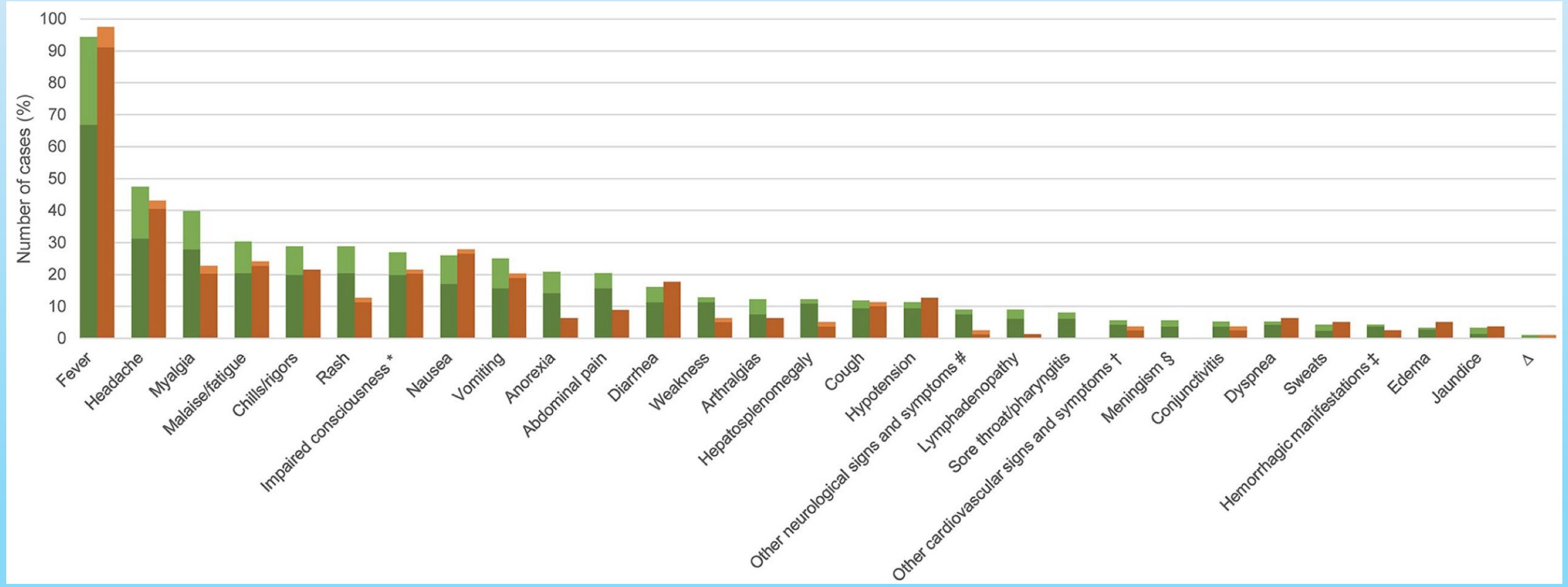
*Schudel, PLoS Negl Trop Dis. 2024*

# **ERLICHIOSI:** *Erlichia chaffeensis – ewingii - canis*



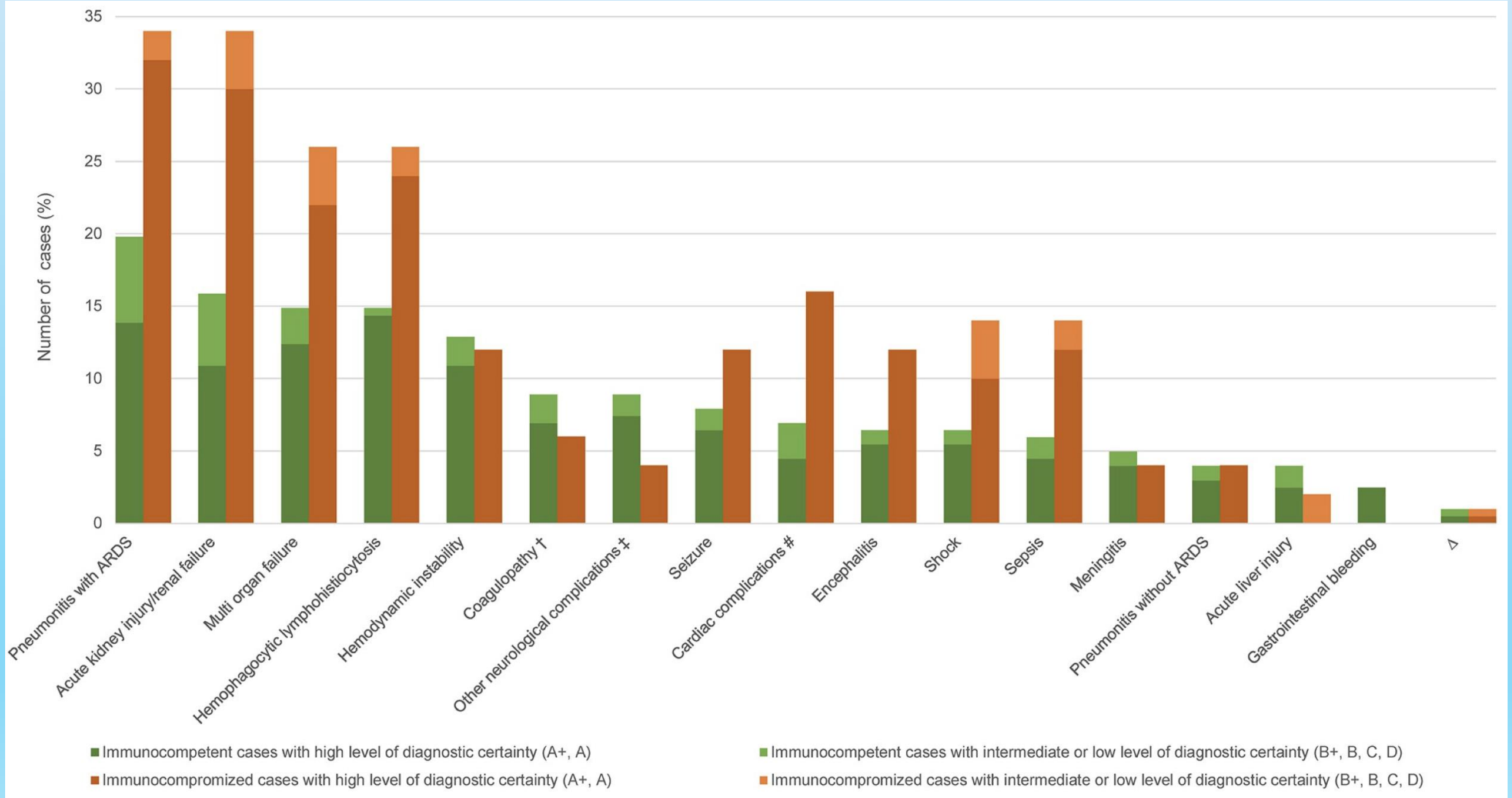

Gygax L, PLoS Negl Trop Dis. 2024

# **ERLICHIOSI:** *Erlichia chaffeensis – ewingii - canis*



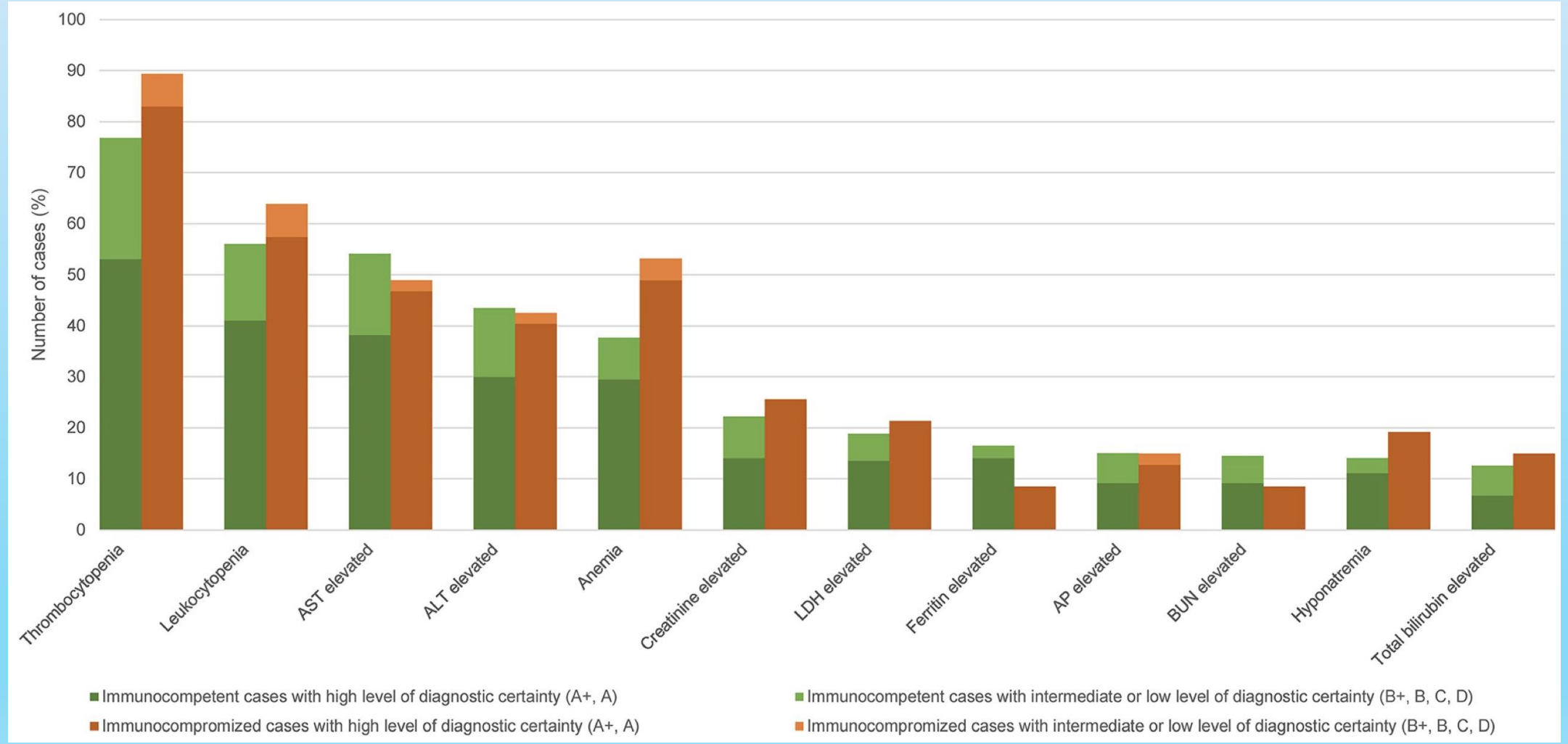

Gygax L, PLoS Negl Trop Dis. 2024

# **ERLICHIOSI:** *Erlichia chaffeensis – ewingii - canis*




Gygax L, PLoS Negl Trop Dis. 2024

# **ERLICHIOSI:** *Erlichia chaffeensis – ewingii - canis*




Gygax L, PLoS Negl Trop Dis. 2024

# ERLICHIOSI: *Erlichia chaffeensis – ewingii - canis*

| Diagnostic method | Description | Grade of diagnostic certainty | Case classification (provided illness clinically compatible with ehrlichiosis) | Comment |
|---|---|---|---|---|
| PCR | Detection of *Ehrlichia* spp. DNA in a clinical specimen via amplification of a specific target by polymerase chain reaction (PCR) assay | A+ | Direct evidence, confirmed diagnosis | High level of evidence, especially in the first week of illness and before start of antibiotics, mostly done from whole blood specimens, also possible in solid tissue and bone marrow specimens |
| Culture | Isolation of *Ehrlichia* spp. from a clinical specimen in cell culture | A+ | Direct evidence, confirmed diagnosis | High level of evidence, especially in the first week of illness and before start of antibiotics, difficult to carry out, time demanding |
| Immunostaining of biopsy/autopsy tissue | Demonstration of ehrlichial antigen in a biopsy/ autopsy sample by immunohistochemical methods | A+ | Direct evidence, confirmed diagnosis | High level of evidence, difficult to carry out, time demanding |
| Serology—IgG IFA, paired samples | Serological evidence of a fourfold rise in IgG-specific antibody titer to *E. chaffeensis/E. canis* antigens by indirect immunofluorescence assay (IFA) in paired serum samples (i.e. an acute phase sample [first week of infection] and a convalescent phase sample [2–4 weeks later]) | A | Indirect evidence, confirmed diagnosis | High level of evidence, serological gold standard, cross-reaction with other rickettsial diseases possible |

Doxycycline for 7-14 days

Gygax L, PLoS Negl Trop Dis. 2024

# FEBBRE RICORRENTE: *Borrelia*

**Table 2.** Clinical and laboratory findings for persons who have confirmed and possible hard tick relapsing fever caused by *Borrelia miyamotoi* among reported cases with available laboratory findings identified by public health surveillance, United States, 2013–2019*

| Characteristic | Confirmed, n = 165 | Possible, n = 133 | p value |
|---|---|---|---|
| Hospitalized | 20 (12) | 19 (14) | 0.61 |
| Median duration of illness, d† (IQR) | 3 (2–7) | 9 (3–29) | 0.03 |
| Required symptoms | | | |
| Fever | 157 (95) | 108 (81) | <0.0001 |
| Chills | 115 (70) | 87 (65) | 0.27 |
| Supporting signs and symptoms | | | |
| Headache | 118 (72) | 96 (72) | 0.85 |
| Myalgia | 104 (63) | 94 (71) | 0.20 |
| Arthralgia | 79 (48) | 84 (63) | 0.02 |
| Malaise/fatigue | 125 (76) | 99 (74) | 0.55 |
| Rash | 21 (13) | 28 (21) | 0.06 |
| Abdominal pain | 16 (10) | 27 (20) | 0.01 |
| Nausea | 55 (33) | 36 (27) | 0.26 |
| Vomiting | 23 (14) | 15 (11) | 0.44 |
| Diarrhea | 8 (5) | 17 (13) | 0.01 |
| Dizziness | 26 (16) | 33 (25) | 0.06 |
| Confusion | 7 (4) | 24 (18) | <0.0001 |
| Photophobia | 8 (5) | 11 (8) | 0.29 |
| Leukopenia‡ | 31 (46) | 8 (22) | 0.02 |
| Thrombocytopenia§ | 40 (58) | 9 (25) | 0.001 |
| Increased levels of aminotransferases¶ | 27 (45) | 13 (36) | 0.41 |
| Other symptoms | | | |
| Recurring fevers | 37 (22) | 47 (35) | 0.01 |
| Shortness of breath | 5 (3) | 14 (11) | 0.01 |
| Cough | 15 (9) | 10 (8) | 0.53 |
| Anorexia | 32 (19) | 26 (20) | 0.99 |
| Jaundice | 2 (1) | 4 (3) | 0.21 |
| Lymphadenopathy | 0 (0) | 0 (0) | NA |
| Cognitive impairment/mood disturbance | 7 (4) | 21 (16) | 0.0004 |
| Meningitis/encephalitis | 0 (0) | 5 (4) | 0.01 |
| Neutropenia | 6 (4) | 2 (2) | 0.11 |
| Abnormal chest radiograph | 11 (7) | 2 (2) | 0.04 |

*Values are no. (%) unless indicated otherwise. IQR, interquartile range; NA, not available.

Thrombocytopenia
+
Leukopenia
+
high transaminase levels

McCormick DW Emerg Infect Dis. 2023

# FEBBRE RICORRENTE: *Borrelia*

**Table 3.** Diagnostic results for confirmed and possible cases of hard tick relapsing fever caused by *Borrelia miyamotoi* reported by public health surveillance, United States, 2013–2019*

| Characteristic | Confirmed, n = 166† | Possible, n = 134 |
|---|---|---|
| PCR results | | |
| Detected | 162/164 (99) | 0/5 (0) |
| Not detected | 0/164 (0) | 5/5 (100) |
| Serologic analysis results | | |
| Single IgM alone | | |
| Positive | 2/2 (100) | 36/127 (28) |
| Negative | 0/2 (0) | 89/127 (70) |
| Indeterminate | 0/2 (0) | 2/127 (2) |
| Single IgG alone | | |
| Positive | 0/2 (0) | 111/127 (87) |
| Negative | 2/2 (100) | 16/127 (13) |
| Indeterminate | 0/2 (0) | 0/127 (0) |
| Single combined IgM/IgG | | |
| Positive | 1/2 (50) | 6/7 (86) |
| Negative | 0/2 (0) | 1/7 (14) |
| Indeterminate | 1/2 (50) | 0/7 (0) |
| Paired serologic samples | | |
| ≥4-fold change in titer | 1/1 (100) | 0/18 (0) |
| <4-fold change in titer | 0/1 (0) | 18/18 (100) |

*Values are no. positive/no. tested (%).
†Missing diagnostic information for 2 cases.

Doxycycline for 7-14 days

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# RICKETTSIOSI

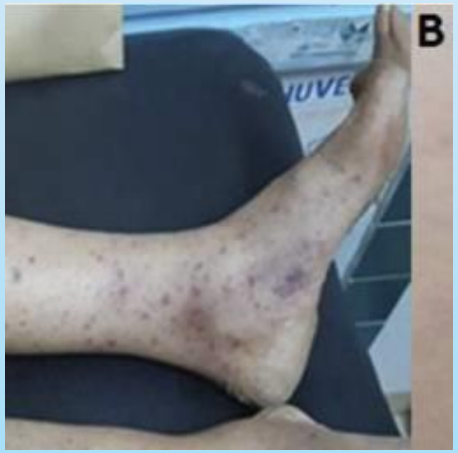
| I Belli Group -BG | II Canadensis Group-CG | III Typhus Group-TG | IV Spotted Fever Group II (Earlier TGR) | V Spotted Fever Group I (Sample *Rickettsia* Species) |
|---|---|---|---|---|
| *R. bellii* | *R. canadensis* | *R. prowzekii* | *R. akari* | *R. monacensis* |
| | | *R. thypi* | *R. australis* | *R. raoultii* |
| | | | *R. hoogstraalii* | *R. aeschlimannii* |
| | | | *R. asemboensis* | *R. rhipicephali* |
| | | | *R. felis* | *R. massiliae* |
| | | *R. helvetica* | | *R. rickettsii* |
| | | | | *R. slovaca* |
| | | | | *R. conorii* |
| | | | | *R. sibirica* |
| | | | | *R. parkeri* |
| | | | | *R. africae* |

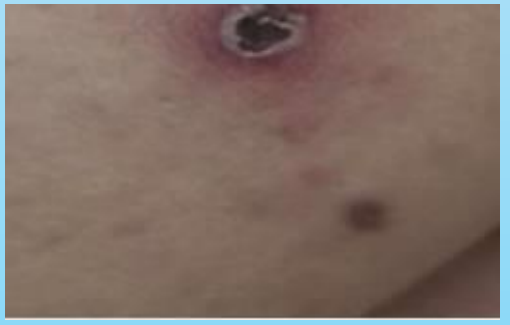
***Febbre bottonosa del Mediterraneo***

McCormick DW Emerg Infect Dis. 2023

# RICKETTSIOSI

| Clinical features | All patients (*n* = 173) | Confirmed/Definite cases (*n* = 47) | Suspected/Probable cases (*n* = 126) |
|---|---|---|---|
| Fever (*n*, %) | 173/173 (100) | 47/47 (100) | 126/126 (100) |
| Skin rash (*n*, %) | 173/173 (100) | 47/47 (100) | 126/126 (100) |
| Inoculation eschar (*n*, %) | 121 (69.9) | 29/47 (61.7) | 92/126 (73) |
| Headache (*n*, %) | 121/173 (64.5) | 35/47 (74.5) | 86/126 (68.2) |
| Myalgia (*n*, %) | 105/173 (60.7) | 31/47 (66) | 74/126 (58.7) |
| Arthralgia (*n*, %) | 99/173 (57.2) | 30/47 (63.8) | 69/126 (54.8) |
| Asthenia (*n*, %) | 73/173 (42.2) | 18/47 (38.3) | 55/126 (43.6) |
| Chills (*n*, %) | 49/173 (28.3) | 14/47 (29.8) | 35/126 (27.8) |
| Sweating (*n*, %) | 27/173 (15.6) | 8/47 (17) | 19/126 (15.1) |
| Cough and dyspnoea (*n*, %) | 10/173 (5.8) | 0/47 (0) | 10/126 (8) |
| Vomiting (*n*, %) | 27/173 (15.6) | 4/47 (8.5) | 23/126 (18.25) |
| Neurological symptoms (*n* = 12); (*n*, %) | Meningeal syndrome | 9/12 (75) | 4/47 (8.5) | 5/126 (4) |
| | Slow walking | 1/12 (8.3) | 1/47 (2.1) | 0/126 (0) |
| | Shaky gait | 1/12 (8.3) | 0/47 (0) | 1/126 (0.8) |
| | Cutaneous hyperesthesia | 1/12 (8.3) | 0/47 (0) | 1/126 (0.8) |
| Complications (*n*, %) | Total | 4/173 (2.3) | 2/47 (4.2) |
| Neurologic complications (*n*, %) | Cerebral vasculitis | 1/4 (25) | 0/47 (0) |
| | Encephalitis | 1/4 (25) | 0/47 (0) |
| | Meningitis | 0/4 (0) | 0/47 (0) |
| | Cerebellitis | 0/4 (0) | 0/47 (0) |
| | Cerebral thrombophlebitis | 0/4 (0) | 0/47 (0) |
| | Ischemic or haemorrhagic stroke | 0/4 (0) | 0/47 (0) |
| Ophthalmic complications (*n*, %) | Chorioretinitis | 1/4 (25) | 1/47 (2.1%) |
| | Anterior uveitis | 1/4 (25) | 1/47 (2.1%) |



Lamloumi M, Epidemiol Infect. 2024

# RICKETTSIOSI

| Biological abnormalities | | All patients ($n$ = 173) |
|---|---|---|
| White-cell count/mm$^3$ (4,000–10,000/mm$^3$) | Mean rate | 8310±6730 /mm$^3$ |
| | Leucocytosis (>10.000/mm$^3$) (n, %) | 63 (36.4) |
| | Leukopenia (<4000/mm$^3$) (n, %) | 10 (5.8) |
| Platelets count/mm$^3$ (150,000–450,000/mm$^3$) | Mean rate | 169 331±125 036 /mm$^3$ |
| | Thrombocytopenia (<150.000/mm$^3$) (n, %) | 83 (48) |
| Aspartate aminotransferase, U/L (10–40 U/L) | Mean rate | 114±70 U/L |
| | Increased level (>40U/L) (n, %) | 88 (50.9) |
| Alanine aminotransferase (10–40 U/L) | Mean rate | 65±43 U/L |
| | Increased level (>40U/L) (n, %) | 70 (40.5) |
| C-Reactive Protein (<5 mg/L) | Mean rate | 160±65 mg/L |
| | Increased level (> 6mg/L) (n, %) | 159 (91.9) |
| Lactate dehydrogenase (190–445 U/L) | Mean rate | 550±123 U/L |
| | Increased level (>445U/L) (n, %) | 114 (65.9) |
| Creatine kinase, U/L (15–200 U/L) | Mean rate | 380±200 U/L |
| | Increased level (>200U/L) (n, %) | 110 (63.6) |
| Natremia (135–142mmol/L) | Mean rate | 136±1.4 mmol/L |
| | Hyponatremia (<135mmol/L) | 88 (50.9) |
| Kalemia (3.5–5 mmol/L) | Mean rate | 3,8±0.3 mmol/L |
| | Hypokalaemia (<3.5mmol/L) | 23 (13.3) |

*Serology and PCR*

*Doxycycline for 7 days*

Lamloumi M, Epidemiol Infect. 2024

# BABESIOSI

**Three Cases of Human Babesiosis, Italy, 2017–2020**

Chiara Sepulcri,[1] Rachele Pincino,[1] Federico Baldi,[1] Giovanni Cenderello, Stefania Zanet, Daniela Boccolini, Anna Rosa Sannella, Mariangela L'Episcopia, Carlo Severini, Matteo Bassetti, Chiara Dentone, Ezio Ferroglio

- 1. F, 20yrs

*arthromyalgia, asthenia, fever, weight loss*

PCR for Babesia

atovaquone+azhithrmoycin for 10 days

- 2. M, 10yrs

*headache, arthromyalgia, fever, hypereosinophilia*

PCR for Babesia

atovaquone + azithrmoycin for 7 days

- 3. M, 20yrs

*fever, cough, night sweats, anemia*

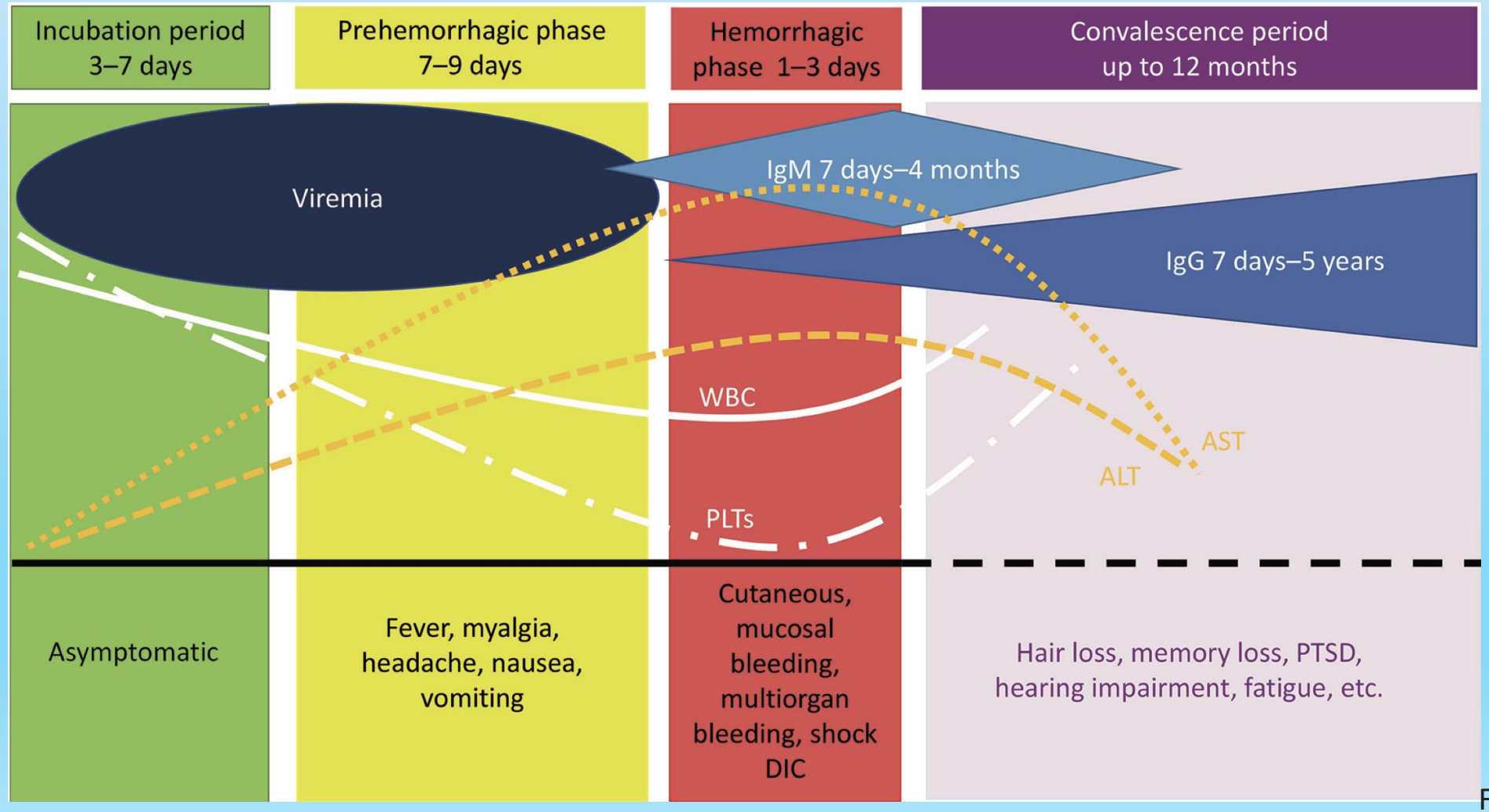
PCR for Babesia

quinine + clindamycin

Sepulcri C. Emerg Infect Dis. 2025

# FEBBRE EMORRAGICA CRIMEA-CONGO

- **Transmission** → *tick bites + touch with infected animals + contact with bodily fluids*




*Serology*

*Ribavirin: 30mg/kg LD, then 15mg/Kg q6h x 4days, then 7.5mg/kg q8h for 6 days*

*Fatality rate 60%*

Frank MG. Emerg Infect Dis. 2024

# Ultime considerazioni…

- Le zoonosi da morso di zecca devono sempre essere considerate in caso di febbre estiva e possibile esposizione a morso di zecca

- Solo il 50% dei pazienti con zoonosi da morso di zecca riportano il precedente morso di zecca

- L'arma fondamentale è la PREVENZIONE (osservazione del proprio corpo dopo frequentazione di luoghi a rischio, doccia, vaccini…)

- La diagnosi precoce avviene solo se queste patologie vengono considerate in diagnosi differenziale






*Grazie per l'attenzione*