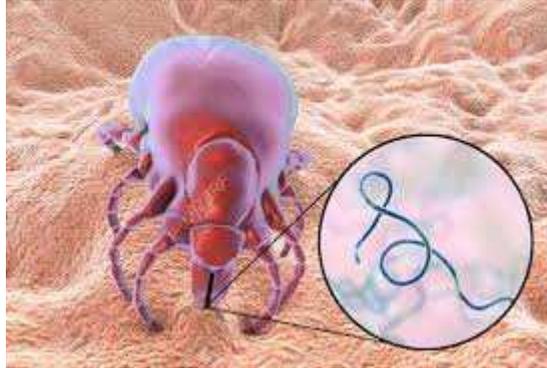
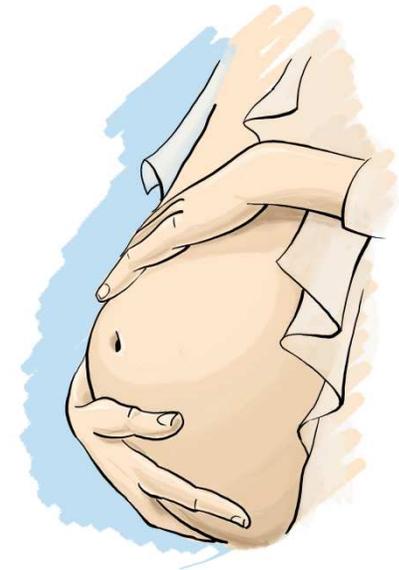


# Maladie de Lyme



Pr Olivier Picone

Hôpital L. Mourier, Colombes, Univ Paris 7  
Unité Inserm IAME UMR1137, Equipe BIPID, Axe 4  
CNGOF, GRIG



Groupe de Recherche sur les  
Infections pendant la Grossesse



ASSISTANCE  
PUBLIQUE  HÔPITAUX  
DE PARIS



Centre Pluridisciplinaire  
de Diagnostic Prénatal  
LEONARD DE VINCI



université  
**PARIS**  
DIDEROT

Aucun conflit d'intérêt en lien  
avec la question traitée

Lyme borreliosis and other tick-borne diseases. Guidelines from the French scientific societies (II). Biological diagnosis, treatment, persistent symptoms after documented or suspected Lyme borreliosis

*Borreliose de Lyme et autres maladies vectorielles à tiques. Recommandations des sociétés savantes françaises. Argumentaire 2: diagnostic biologique, traitement, symptômes persistants au décours d'une borreliose de Lyme documentée ou suspectée*

B. Jaulhac<sup>a</sup>, A. Saunier<sup>b</sup>, E. Caumes<sup>c</sup>, K. Bouiller<sup>d</sup>, J.F. Gehanno<sup>e</sup>, C. Rabaud<sup>f</sup>, S. Perrot<sup>g</sup>, C. Eldin<sup>h</sup>, T. de Broucker<sup>i</sup>, F. Roblot<sup>j</sup>, J. Toubiana<sup>k</sup>, F. Sellal<sup>l</sup>, F. Vuillemet<sup>l</sup>, C. Sordet<sup>m</sup>, B. Fantin<sup>n</sup>, G. Lina<sup>o</sup>, C. Sobas<sup>o</sup>, X. Gocko<sup>p</sup>, J. Fignon<sup>q,r</sup>, C. Chirouze<sup>d</sup>, Y. Hansmann<sup>s</sup>, V. Hentgen<sup>t</sup>, P. Cathebras<sup>u</sup>, M. Dieudonné<sup>v</sup>, O. Picone<sup>ag</sup>, B. Bodaghi<sup>w</sup>, J.P. Gangneux<sup>x</sup>, B. Degeilh<sup>x</sup>, H. Partouche<sup>y</sup>, C. Lenormand<sup>z</sup>, A. Sotto<sup>aa</sup>, A. Raffetin<sup>ab</sup>, J.J. Monsuez<sup>ac</sup>, C. Michel<sup>ad</sup>, N. Boulanger<sup>n</sup>, C. Lemogne<sup>af,\*</sup>, P. Tattevin<sup>af,\*</sup>, endorsed by scientific societies<sup>1</sup>

*E-mail address:* pierre.tattevin@chu-rennes.fr (P. Tattevin).

<sup>1</sup> Société française de dermatologie (SFD), Société française de rhumatologie (SFR), Fédération française de neurologie (FFN), Société française de neurologie (SFN), Collège national des généralistes enseignants (CNGE), Collège de la médecine générale (CMG), Société nationale française de médecine interne (SNFMI), Société française de microbiologie (SFM), Collège national des professionnels en psychiatrie - Collège national pour la qualité des soins en psychiatrie (CNPP-CNQSP), Association française de psychiatrie biologique et de neuropsychopharmacologie (AFPBN), Société de psychologie médicale et de psychiatrie liaison de langue française (SPMPLLF), Société française de médecine du travail (SFMT), Société française de cardiologie (SFC), Société française de pédiatrie (SPD), Groupe de pathologies infectieuses pédiatriques (GPIP), Société française de rhumatologie et médecine interne pédiatrique (SOFREMIP), Société française d'ophtalmologie (SFO), Société française de mycologie médicale (SFMM), Société française de parasitologie (SFP), Collège des universitaires de maladies infectieuses et tropicales (CMIT), Collège national des gynécologues et obstétriciens français (CNGOF), Société française d'étude et de traitement de la douleur (SFETD), Société de pathologie infectieuse de langue française (SPILF).

# Introduction

Borréliose de Lyme : anthroponose la plus fréquente.  
= transmission d'une maladie d'un animal vertébré à l'homme.

Due à des spirochètes du genre *Borrelia*.

Transmis par piqûre de tiques du genre *Ixodes*.

Schramm, Revue francophone des laboratoires 2013

Premières manifestations articulaires de la maladie décrites en 1977.

A Lyme, USA.

Mise en évidence du spirochète en 1982.

Steere, Arthritis Rheum 1977 ; Burgdorfer, Science 1982

# Spirochète : *Borrelia burgdorferi*

Taxonomie :

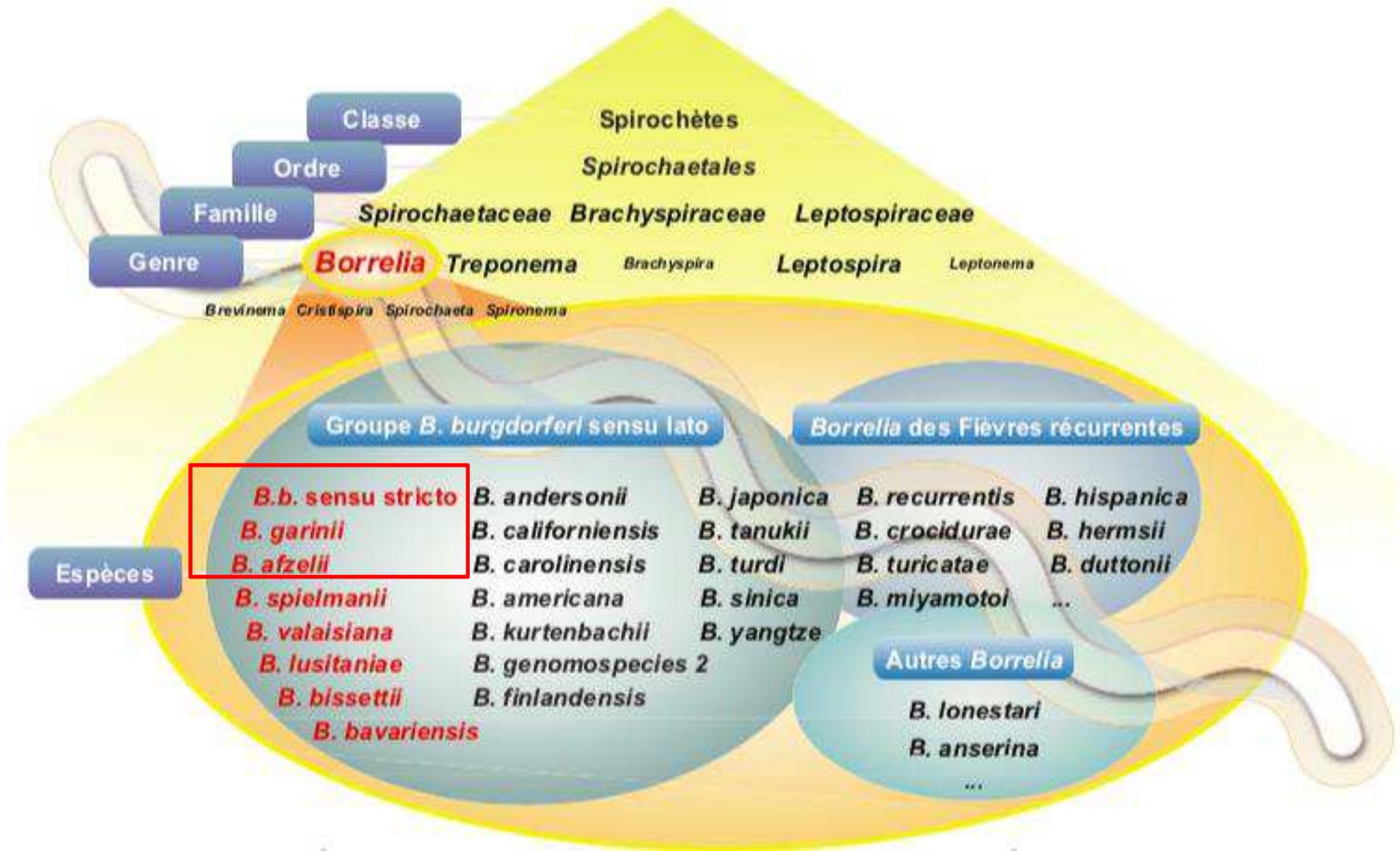
Classe : Spirochètes (bactéries spiralées).

Ordre : Spirochaetales.

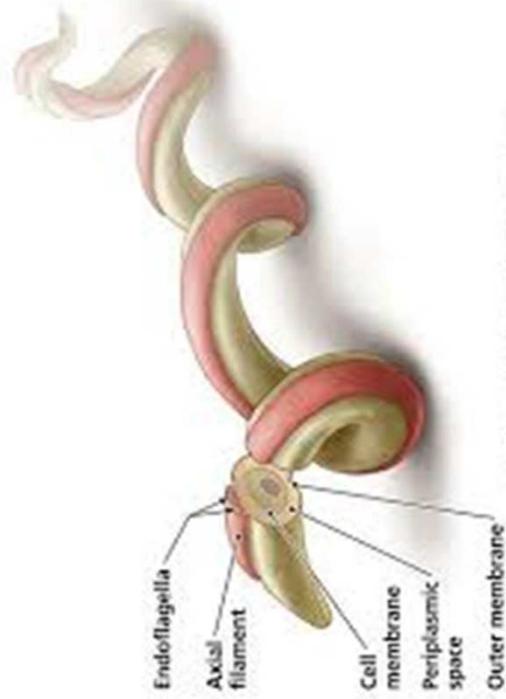
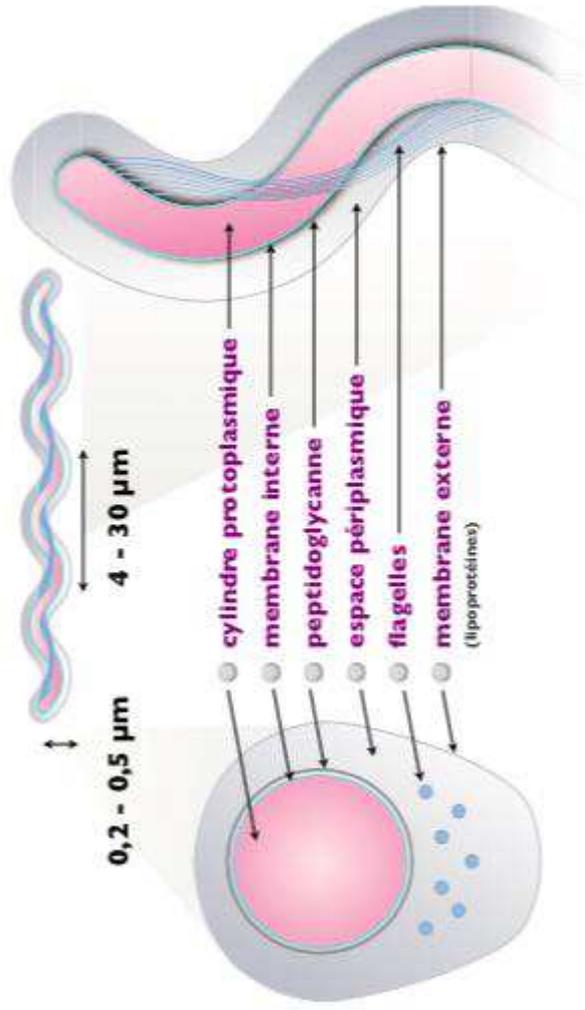
Famille : Spirochaetaceae.

Genre : *Borrelia*.

Espèce : *burgdorferi* sensu lato



En Europe



Copyright © 2014 Pearson Education, Inc., publishing as Benjamin Cummings

# Un vecteur : la tique Ixodes

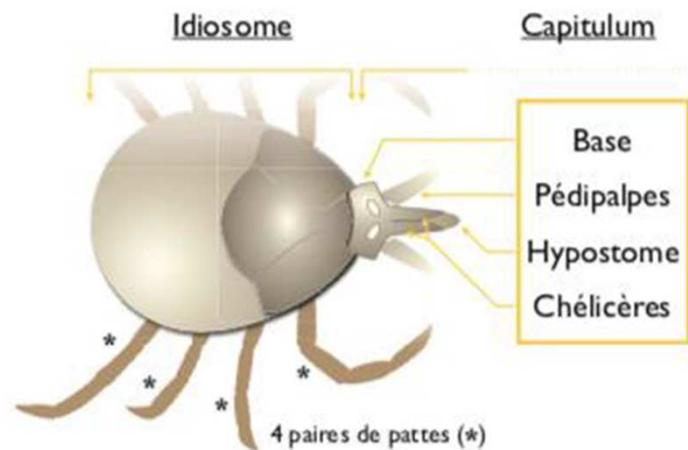
Taxonomie simplifiée :

Arthropode

Arachnide

Acariens

Ixodidae : tiques dures



# Tique

Ectoparasite hématophage strict :

Diapause hivernale

Arthropodes forestiers, en-dessous de 1500m.

Recherche d'un hôte vertébré

Fixation pendant 3 à 10 jours :

la tique se « gorge » de sang.



# Transmission à l'Homme

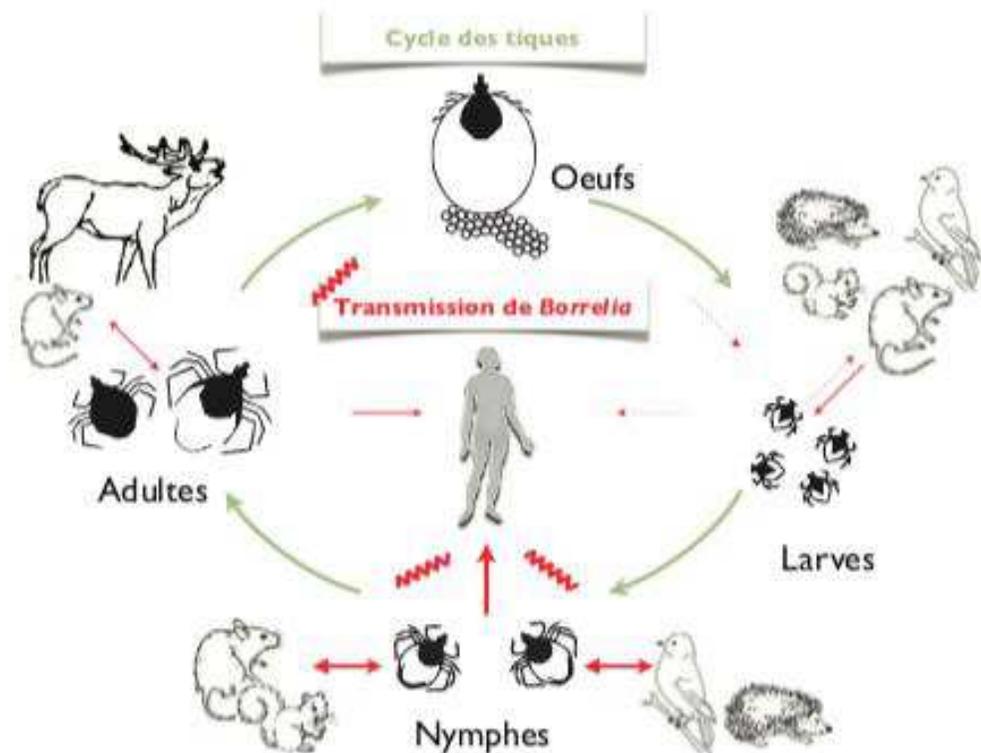
Homme : hôte accidentel et terminal.

« Régurgitation » des spirochètes :

A partir de 48 heures.

Risque augmente avec la durée.

Transmission par la salive.



# 2019

Recommendations/Recommandations

Lyme borreliosis and other tick-borne diseases. Guidelines from the French scientific societies

*Borréliose de Lyme et autres maladies vectorielles à tiques. Recommandations des sociétés savantes françaises*

Med Mal Infect. 2019 Aug;49(5):335-346

Med Mal Infect. 2019 Aug;49(5):318-334

# Epidémiologie

Incidence annuelle en France : réseau Sentinelles de médecins généralistes.

2009 – 2017 : 53 cas / 100 000 habitants

2016 : 84 cas / 100 000 habitants

95% erythème migrant, 5% forme disséminée

25% des adultes ont déjà rapporté une piqûre de tique

Disparité régionale : taux plus élevés en Alsace, Lorraine et Limousin.

Fournier, Bull Epidemiol Hebd. 2018

Med Mal Infect. 2019 Aug;49(5):335-346

Med Mal Infect. 2019 Aug;49(5):318-334

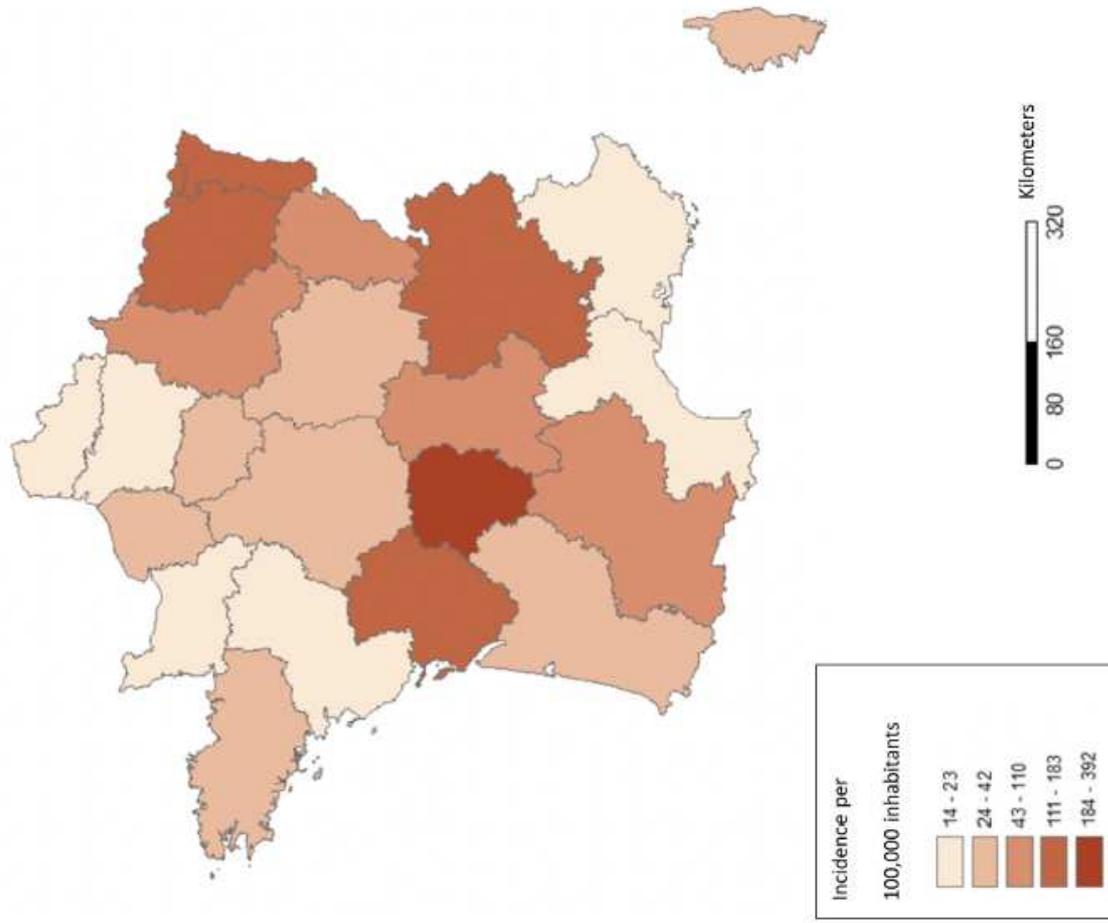


Fig. 3. Estimated incidence of Lyme borreliosis by region, 2013–2017, metropolitan France.  
*Estimation de l'incidence de la Borréliose de Lyme par région, 2013–2017, France métropolitaine.*  
Santé publique France, based on data from the Sentinel network, 2019.

# Prévention primaire

Port de vêtements longs et clairs, port de casquette (enfants+++)

Avis d'Expert

Répulsifs: Peu efficace, à mettre sur peau non couvertes, à éviter chez bb et femmes enceintes

Grade B

Huiles essentielles, bracelets, vêtements imprégnés: non recommandés

Avis d'Expert



# CAT si tique retrouvée (Avis d'Expert)

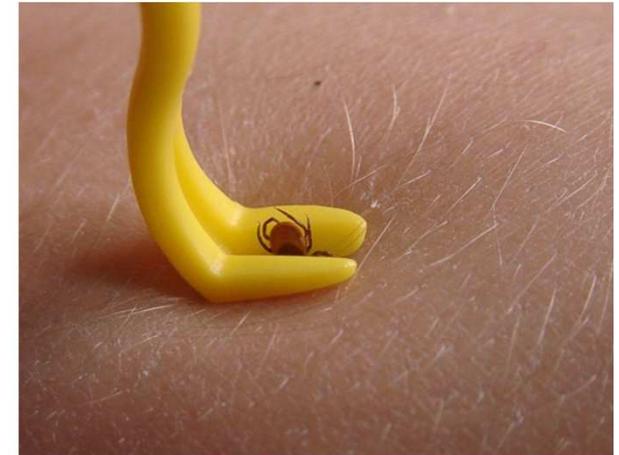
Extraction mécanique

Pincette, Tire-tiques, Pas d'éther

Désinfection cutanée et des mains

Photo de la tique

Surveillance de la piqûre pendant 4 semaines



Reaction to the tick's saliva



Necrosis

Fig. 2. Examples of cutaneous inflammatory reaction after a tick bite. Reaction to the tick's saliva. Necrosis.

Disparition sans traitement en 24 à 48h

Risque de Borreliose <5%

Pas de sérodiagnostic, Pas d'analyse de la tique

Grade A

Pas d'antibiothérapie

Grade B

# Quand évoquer une borreliose de Lyme?

## Signes cutanés++++

Erythème migrans isolé ou multiple	Grade B
Pas d'ex compl (faux neg++)	Grade B
Lymphocytomes	Grade B
Biopsie cutanée	Avis d'Expert
Acrodermite chronique atrophique	Grade B
Biopsie cutanée	Avis d'Expert



## Signes neurologiques

90% sont des formes précoces disséminées	Grade B
Sérologies / PL (index iGG CSF/S)	Grade B

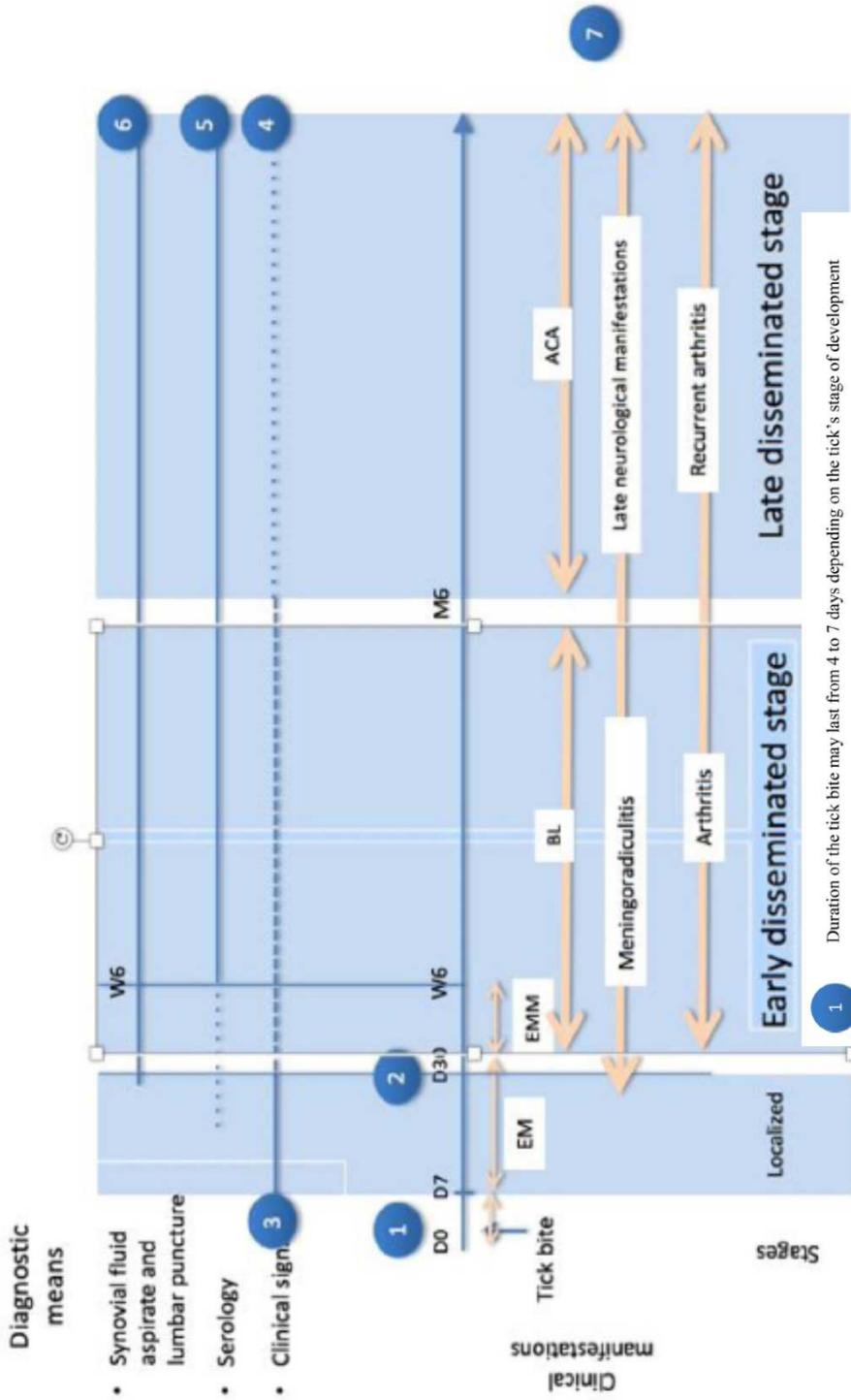
## Signes rhumatologiques

Arthralgies (genou): apparition jusqu'à 2 ans, 10% chronique  
Myalgies



## Signes cardiologiques

BAV (0,3-4%), tachycardies, fibrillations	Grade B
Myocardites, Pericardites	



1 Duration of the tick bite may last from 4 to 7 days depending on the tick's stage of development

2 Erythema migrans may still be observed at meningoradiculitis onset

3 Diagnosis at the early stage only relies on clinical signs

4 Clinical signs are less specific at disseminated stages, especially at late disseminated stages.

5 Serology may be negative at the early stages, but its sensitivity is satisfactory from the sixth week on. For late stages, serology has excellent negative predictive value.

6 *Borrelia* identification in synovial fluid or CSF and meningitis associated with intrathecal synthesis of specific antibodies ascertain Lyme borreliosis diagnosis.

7 50% to 70% of disseminated presentations are not preceded by erythema migrans and patients do not necessarily recall or notice the tick bite.

Management of patients presenting with symptoms within four weeks of a tick bite sustained in France.  
*Stratégie de prise en charge en cas de symptômes débutant dans les 4 semaines suivant une piqûre de tique en France.*

Clinical presentation	Pathologies to consider	Exposure/clinical features	Biological parameters	Diagnostic strategy	Treatment to consider
Fever + signs of meningitis OR encephalitis	TBE	Eastern France, French region of Savoie (people traveling to endemic areas)	Lymphocytic meningitis	IgM and IgG serology in serum and CSF	Symptomatic
Fever + lymphadenopathy + black spot	Tularemia			PCR/culture of pus from a lymph node; black spot swab; serology	ciprofloxacin or doxycycline
	Senlat/Tibola	Localization on the scalp		PCR on black spot swab, lymph node aspiration PCR, serology	doxycycline
Fever + splenomegaly	Lymphangitis-associated Rickettsia Babesiosis	Lymphangitis signs ± maculopapular rash			doxycycline
Fever + maculopapular rash	Rickettsioses	Mediterranean region, localization on the palms of the hands and on the soles of the feet	Cytopenia	Blood smear, PCR	Combination of an antibiotic and an antiparasitic treatment <sup>a</sup> doxycycline
	Anaplasmosis		Cytopenia + lymphocyte activation + cytolytic hepatitis	Lymph node aspiration PCR, serology	doxycycline
Skin ulcer with or without fever	Mediterranean spotted fever	Mediterranean region	Cytopenia	Blood PCR, serology	doxycycline
	Tularemia			PCR on black spot swab, lymph node aspiration PCR, serology	doxycycline
	TIBOLA, SENLAT	Scalp		PCR/culture of pus from a lymph node; black spot swab; serology	ciprofloxacin OR doxycycline
				PCR on black spot swab, lymph node aspiration PCR, serology	doxycycline

# Tests biologiques

Performance of diagnostic tests (sensitivity/specificity) in European Lyme borreliosis.

*Performances des tests diagnostiques (sensibilité/spécificité) dans la borréliose de Lyme européenne.*

Clinical suspicion	ELISA	Sensitivity ELISA	Specificity ELISA	PCR	Other useful examinations
Tick bite	Not useful	/	/	/	No
Erythema migrans	Not recommended	IgG: 36% (29–43) IgM: 42% (36–49)	IgG: 96% (94–97) IgM: 95% (92–97)	PCR on skin biopsy: Sensitivity 69% (35–81)	PCR on skin biopsy
Early Lyme neuroborreliosis < 6 weeks	IgG + IgM	67–85%	92–97%	PCR in CSF: variable sensitivity	Intrathecal synthesis (antibody index) CSF cytology (lymphocytosis)
Semi-early neuroborreliosis, 6 weeks–6 months	IgG + IgM	90–99%	92–97%	PCR in CSF: not useful	Intrathecal synthesis CSF cytology (lymphocytosis)
Borrelial lymphocytoma	IgG + IgM	≥ 80%	92–97%	PCR on skin biopsy	Histology
Late Lyme neuroborreliosis > 6 months	IgG	99%	92–97%	PCR in CSF: not useful	/
Lyme arthritis	IgG	IgG: 94% (86–98) IgM: 39% (28–52)	IgG: 97% (94–98) IgM: 95% (88–98)	PCR in synovial fluid: sensitivity 36–85%	PCR in synovial fluid and/or synovial biopsy
Ocular symptoms	IgG + IgM	Variable depending on the manifestations	92–97%	PCR in aqueous humor, CSF (variable sensitivity)	Intrathecal synthesis CSF cytology (lymphocytosis)
Cardiac symptoms	IgG + IgM	> 80%	92–97%	/	No
Acrodermatitis chronica atrophicans	IgG	IgG: 99% (82–99) IgM: 18% (9–34)	IgG: 97% (95–98) IgM: 97% (93–98)	PCR on skin biopsy: sensitivity 16–92%	Histology

CSF: cerebrospinal fluid.

- The sole persistence of IgM beyond six weeks should be considered a false positive result, because of the high risk of non-specific cross-reactions.
- Performing a serological test at four weeks in patients presenting with reinfection may help detect increased IgG levels.
- A positive serology does not distinguish an active infection from a serological scar.
- High levels of antibodies can be observed in treated patients several years after recovery. The treatment should in that case not be resumed.

# Traitements atteintes cutanées

## Grade B

**Table 3**

Treatment of erythema migrans (single or multiple) and of borrelial lymphocytoma.

Traitement de l'érythème migrant, unique ou multiple, et du lymphocytome borrélien.

Antibiotics	Dosing regimen duration	Duration
Adults and children from 8 years of age		
1st line	Doxycycline 100 mg twice daily Children: 4 mg/kg/day as two intakes (maximum 100 mg/intake, and 200 mg/day)	14 days for erythema migrans, 21 days for borrelial lymphocytoma
2nd line	amoxicillin 1 g thrice daily Children: 50 mg/kg/day as three intakes, every 8 hours if possible* (maximum 1 g per intake)	
Children <8 years of age		
1st line	amoxicillin 50 mg/kg/day as three intakes, every 8 hours if possible <sup>a</sup>	14 days for erythema migrans, 21 days for borrelial lymphocytoma
2nd line	azithromycin 20 mg/kg/day without exceeding 500 mg/day	5 days for erythema migrans, 10 days for borrelial lymphocytoma

<sup>a</sup> If the 8-hour interval between each intake is not possible, 25 mg/kg every 12 hours.

# Traitements neuroborreliose

## Grade AE

340

*B. Jaulhac et al. / Médecine et maladies infectieuses 49 (2019) 335–346*

**Table 4**

Treatment of Lyme neuroborreliosis.

*Traitement des neuroborrélioses.*

Antibiotics	Adults	Children	Duration
Early Lyme neuroborreliosis (symptom onset <6 months)			
Doxycycline	100 mg twice daily	From 8 years of age: 4 mg/kg/day (maximum 200 mg/day) as two intakes	14 days
IV ceftriaxone	2 g once daily	80 mg/kg once daily (maximum 2 g)	14 days
Late Lyme neuroborreliosis (symptom onset >6 months)			
Doxycycline <sup>a</sup>	100 mg twice daily 200 mg twice daily in case of central nervous system impairment**	From 8 years of age: 4 mg/kg/day (maximum 200 mg/day) as two intakes 8 mg/kg/day (maximum 400 mg/day) as two intakes in case of central nervous system impairment <sup>b</sup>	21 days
IV ceftriaxone	2 g once daily	80 mg/kg once daily (maximum 2 g)	21 days

<sup>a</sup> Some studies showed the good tolerability of doxycycline as a short treatment ( $\leq 14$  days) in children below 8 years of age. Treatment with doxycycline could be discussed on a case-by-case basis in children, especially when beta-lactams are contraindicated or when the IV line is difficult to insert or manage, after having informed the parents that such treatment does not have a marketing authorization in France for use in children aged below 8 years.

<sup>b</sup> Central nervous system impairment = encephalitis, myelitis, vasculitis.

# Traitements arthralgies

## Grade AE

*B. Jaulhac et al. / Médecine et maladies infectieuses 49 (2019) 335–346*

341

**Table 5**

Treatment of joint manifestations of Lyme borreliosis.

*Traitement des manifestations articulaires de la borréliose de Lyme.*

Antibiotics	Adults	Children	Duration
Oral doxycycline <sup>a</sup> as first-line treatment	100 mg twice daily	From 8 years of age: 4 mg/kg/day (maximum 200 mg/day) as two intakes	28 days <sup>a</sup>
IV ceftriaxone, 2nd line, in case of failure or contraindication to doxycycline	2 g once daily, IV	80 mg/kg once daily (maximum 2 g)	
Oral amoxicillin as third-line treatment	1 g thrice daily	80 mg/kg/day as three intakes (maximum 3 g)	

<sup>a</sup> When the first-line antibiotic therapy has failed, the parenteral route should be favored for the second-line antibiotic therapy

# Traitements ophtalmo

## Grade AE

**Table 6**

Treatment of ophthalmologic manifestations of Lyme borreliosis.

*Traitement des manifestations ophtalmologiques de la borréliose de Lyme.*

Antibiotics	Adults Dose/day	Children Dose/kg/day	Duration
Surface lesions, except for keratitis: conjunctivitis, episcleritis			
Oral doxycycline	100 mg twice daily	From 8 years of age: 4 mg/kg/day (maximum 200 mg/day) as two intakes	14 days
IV ceftriaxone	2 g once daily	80 mg/kg once daily (maximum 2 g/day)	14 days
Keratitis, scleritis, uveitis, retinitis, optical neuropathy, oculomotor nerve palsy, orbitopathy			
IV ceftriaxone	2 g once daily 80–100 mg/kg/day in case of central nervous system impairment	80 mg/kg once daily	21 days
Oral doxycycline (2nd line)	100 mg twice daily 200 mg twice daily in case of central nervous system impairment	From 8 years of age: 4 mg/kg/day (maximum 200 mg/day) as two intakes	21 days

# Femme enceinte

RESEARCH ARTICLE

A systematic review on the impact of gestational Lyme disease in humans on the fetus and newborn

Lisa A. Waddell<sup>1\*</sup>, Judy Greig<sup>1</sup>, L. Robbin Lindsay<sup>2</sup>, Allison F. Hinckley<sup>3</sup>, Nicholas H. Ogden<sup>4</sup>

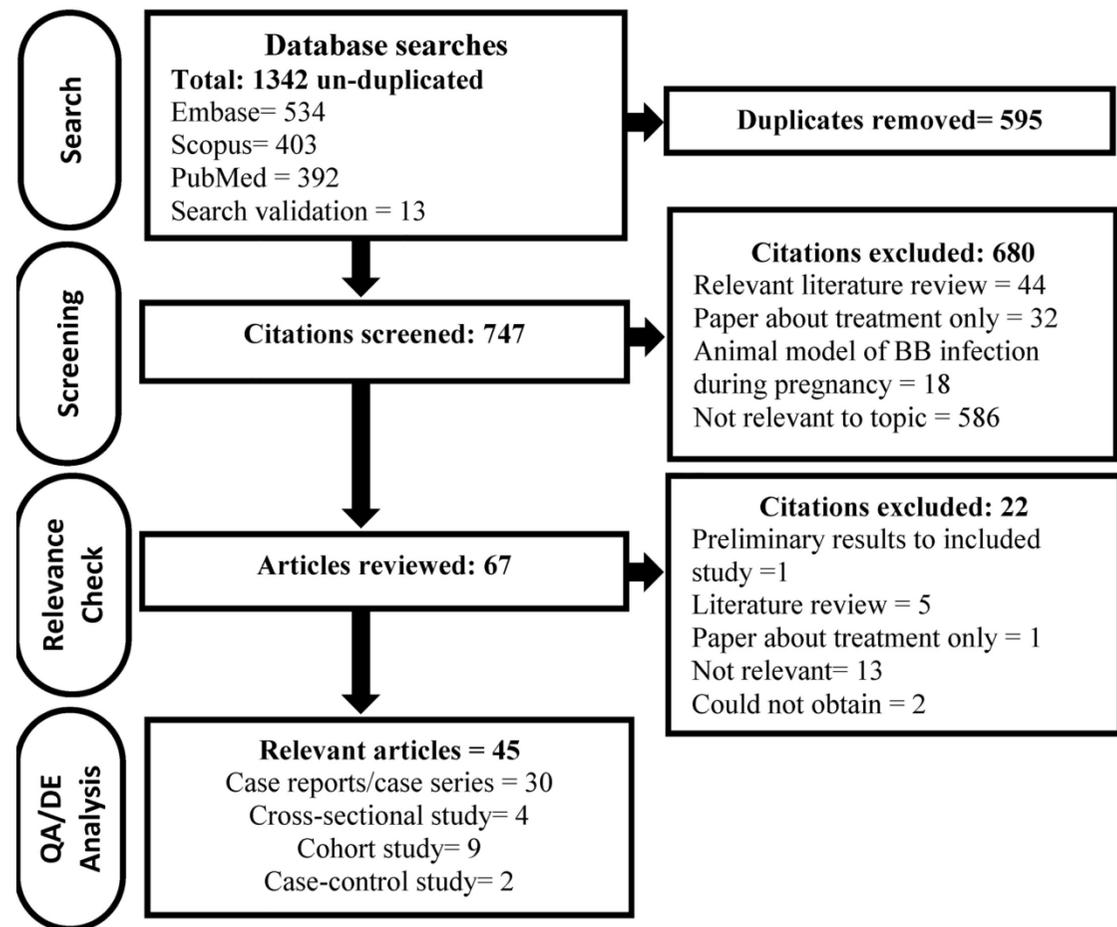
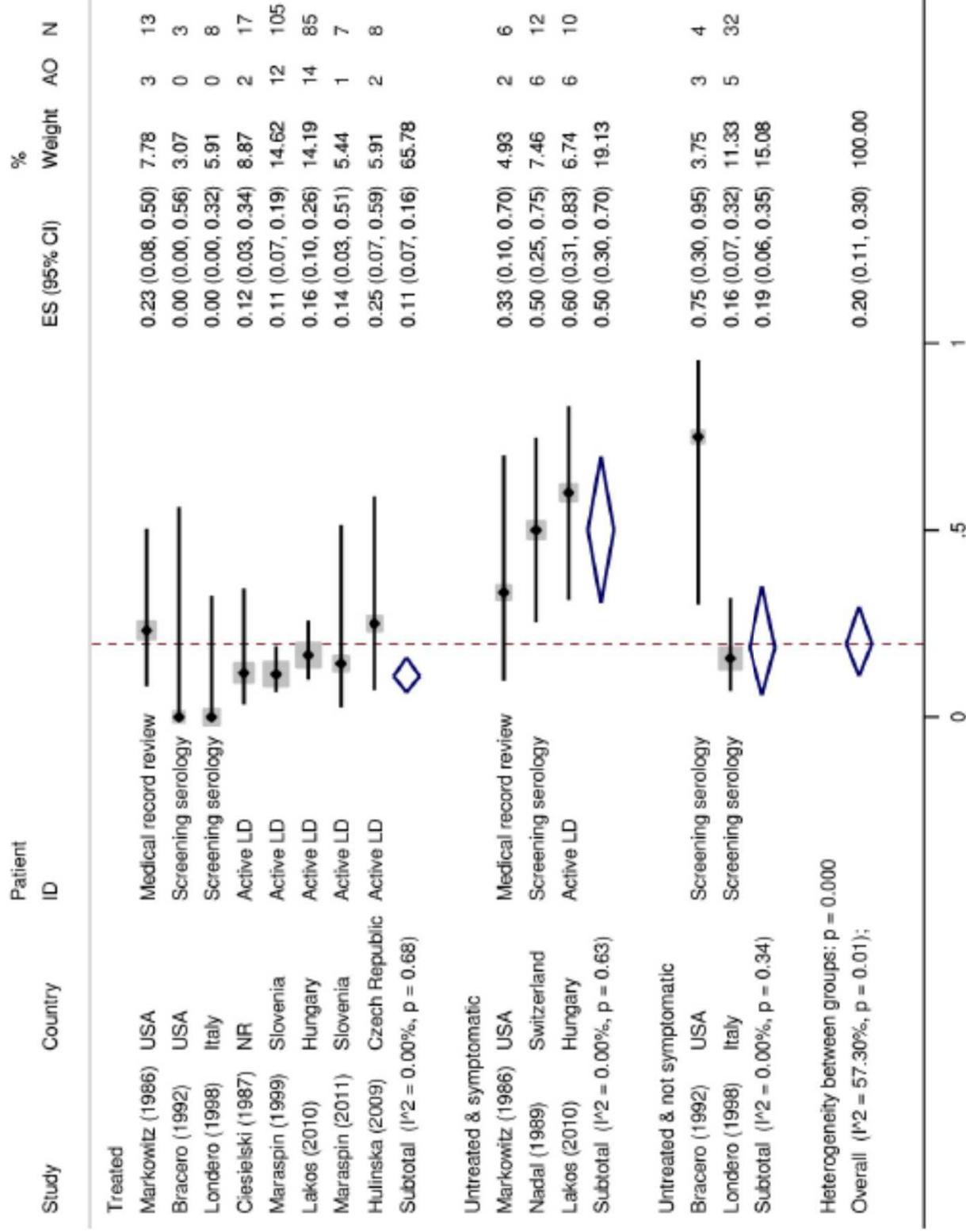


Table 3. An overview of the features of 59 case reports diagnosed with gestational Lyme disease.

Case characteristic	Positive / total cases	Not reported/ not done
<b>Pregnant Women</b>		
Pregnant women with clinical manifestations of LD	41/54	5
Pregnant women with laboratory test results	23/33	26
Pregnant women with test results from currently recommended laboratory tests <sup>1</sup>	4/4	N/A
Pregnant women where clinical symptoms were not reported (n = 2) or not specific (n = 8), but laboratory test results were reported <sup>2</sup>	7/10	N/A
<b>Other samples tested</b>		
Spirochetes detected in placenta	5/11	N/A
Cord blood serology	1/5	N/A
<b>Fetus, Newborn or Child</b>		
Any test result for a fetus, newborn or child	18/31	28
Spirochete identified in tissue collected at autopsy	15/18	2
Spirochetes identified following autopsy conducted on fetus from pregnant women not diagnosed with gestational LD.	5/5	N/A
Spirochete identified in tissue sample from a live child	1/1	N/A
Serology results in the newborn or child	2/13	34
<b>Frequency of Negative Birth Outcomes</b>		
1 <sup>st</sup> trimester miscarriage	3/59	N/A
2 <sup>nd</sup> trimester miscarriage	7/59	N/A
3 <sup>rd</sup> trimester fetal death/ stillbirth	2/59	N/A
Death shortly after birth	8/59	N/A
Abnormalities/ health issues <sup>3</sup>	16/59	N/A
Long term conditions	6/16	N/A
Healthy Infants	23 (1 set of twins)/59	N/A



**Fig 3. Random effects meta-analysis of nine studies that reported the proportion of women with gestational Lyme disease that experienced an adverse birth outcome.** Studies were sub-grouped by treatment status: treated active LD, untreated LD that had a clinical history of LD symptoms, and seropositive with no history of LD. LD status was determined by retrospective medical record review, clinical diagnosis with and without serology or culture, or positive IgG and/or IgM serology. (NR = not reported, AO = Adverse outcome).

# Femmes enceintes

La transmission materno fœtale est possible

MacDonald AB, Gestational Lyme borreliosis. Implications for the fetus. Rheum Dis Clin North Am 1989;15:657-77.

Le lien entre l'infection maternelle et la morbi mortalité est faible

Il semblerait qu'il y ai moins de conséquences quand les patientes sont traitées

Waddell LA, Greig J, Lindsay LR, Hinckley AF, Ogden NH. A systematic review on the impact of gestational Lyme disease in humans on the fetus and newborn. PLoS One 2018;13:e0207067.

Le borelia à été décelée dans le lait sans conséquences

Schmidt BL, Aberer E, Stockenhuber C, Klade H, Breier F, Luger A. Detection of Borrelia burgdorferi DNA by polymerase chain reaction in the urine and breast milk of patients with Lyme borreliosis. Diagn Microbiol Infect Dis 1995;21:121-8.

# Femme enceinte - traitement

Le traitement doit être le même que la population générale

Grade A

En première intention Amoxicilline ou ceftriaxone selon le stade

Grade B

Doxycycline peut être utilisée au premier trimestre pas après  
(coloration des dents) (Lecrat.org)

Grade B