



# Borréliose de Lyme

Yves Hansmann

Hôpitaux Universitaires de  
Strasbourg

# Borréliose de Lyme

## Actualités

- Pas de conflit



# PLAN : actualités/recherche

- Prévention
  - Faire plus ou faire moins ?
- Epidémiologie
  - Sommes nous face à une pandémie ?
  - *Borrelia*...et tout le reste
- Manifestations cliniques
  - Formes chroniques ?
- Diagnostic : LA polémique
- Traitement : jusqu'où aller ?



Quoi de neuf...



...pour la prévention ?

Faire plus ou faire moins ?

# Prophylaxie post piqûre de tique



## Topical azithromycin for the prevention of Lyme borreliosis: a randomised, placebo-controlled, phase 3 efficacy trial

*Michael Schwameis, Thomas Kündig, Gustave Huber, Luzi von Bidder, Lorenz Meinel, Roland Weisser, Elisabeth Aberer, Georg Härter, Thomas Weinke, Tomas Jelínek, Gerd Fätkenheuer, Uwe Wollina, Gerd-Dieter Burchard, Roland Aschoff, Ruth Nischik, Gerhard Sattler, Georg Popp, Wolfgang Lotte, Dirk Wiechert, Gerald Eder, Olga Maus, Petra Staubach-Renz, Andrea Gräfe, Veronika Geigenberger, Ingomar Naudts, Michael Sebastian, Norbert Reider, Ridwan Weber, Marc Heckmann, Emil C Reisinger, Georg Klein, Johannes Wantzen, Bernd Jilma*

- Application d'une crème à l'azithromycine 2 x par jour pendant 3 jours dans les 72 heures suivant une piqûre de tique avérée
- Critère d'évaluation : survenue d'un EM ou séroconversion à S8

Lancet, 2017

	ITT population (n=995)		Per-protocol population (n=134)		Reanalysed ITT population (n=174)	
	Azithromycin (n=505)	Placebo (n=490)	Azithromycin (n=62)	Placebo (n=72)	Azithromycin (n=87)	Placebo (n=87)
Seroconversion, erythema migrans, or both at 8 weeks	11	11	3	5	3	9
Erythema migrans	6	8	1	5	2	8
Seroconversion	6	6	2	2	1	3
Seroconversion and erythema migrans	1	3	0	2	0	2
Erythema migrans at day 30	2	8	0	5	0	7
Negative tick bite and seroconversion as the failure event*	1	2	0	0	0	0
Negative tick bite and erythema migrans as the failure event	1†	0	0	0	0	0

ITT=intention-to-treat. \*None of these seroconversion events could be confirmed with reanalysis by the German Reference Centre for Borreliosis. †Erythema migrans was poorly described with no details on size or progression.

**Table 2: Numbers of patients with treatment failure events**

# Recommandations allemandes 2017

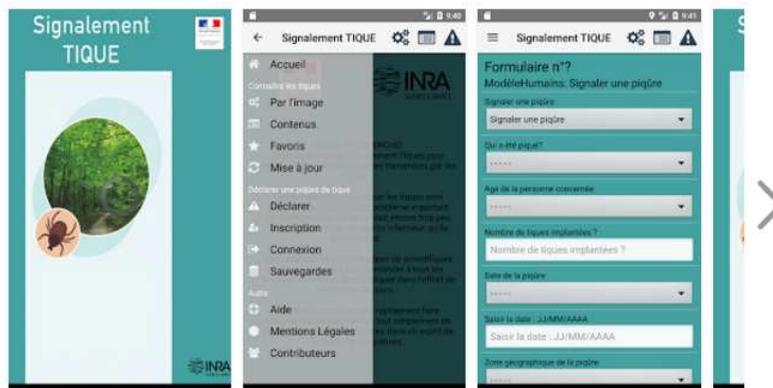
- Pas de prophylaxie en cas de piqûre de tique

...sans autres précisions

- En attendant le PNDS français

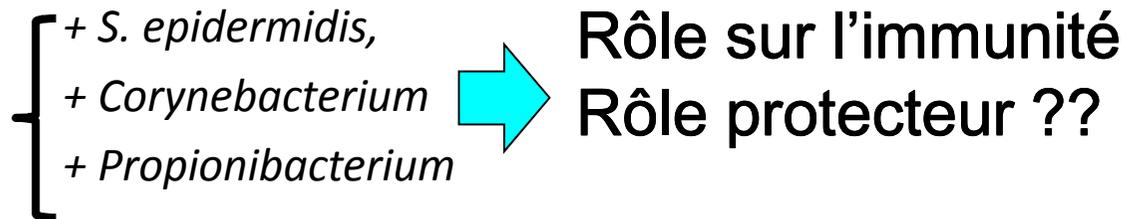
# La prévention

- Médecine participative
  - Applications smartphone



## ...et la recherche ?

- Microbiome cutané et transmission de *Borrelia*
  - Bactéries commensales: rôle dans l'attraction des tiques
    - Peau à tique et identification (Collaboration ONF)
  - Rôle des bactéries commensales de la peau dans la transmission de *Borrelia* ?

  
+ *S. epidermidis*,  
+ *Corynebacterium*  
+ *Propionibacterium* → Rôle sur l'immunité  
Rôle protecteur ??

- mise au point d'un vaccin en cours



Quoi de neuf...



...pour l'épidémiologie ?

Sommes nous face à une pandémie ?

# Etude Alsacétique

- Nombre de cas estimés/ an: 2200
- Ti annuel: 117 cas/10<sup>5</sup> [IC95%: 109-126]
  - 2014: 121 cas/10<sup>5</sup> [IC95%:109-133]
  - 2015: 113 cas/10<sup>5</sup> [IC95%:101-125]
- Ti cantonal annuel
  - Lieux d'exercice des médecins
  - Min: 9 cas/10<sup>5</sup> [IC95%: 1-64]
  - Max: 264 cas/10<sup>5</sup> [IC95%: 125-556]

Tableau 4 : Répartition des cas certains et possibles par tableau clinique.  
Étude ALSA(CE)TIQUE. Janvier 2014 – décembre 2015 (n = 672)

Tableau clinique	Nombre	%
Erythème migrant unique	530	78,9
Formes disséminées	142	21,1
<i>Arthrite de Lyme</i>	68	10,3
<i>Neuroborréliose de Lyme</i>	54	8,0
<i>Erythème migrant multiple</i>	9	1,3
<i>Acrodermatite chronique atrophiante</i>	6	0,7
<i>Lymphocytome borrélien</i>	3	0,4
<i>Atteinte cardiaque</i>	1	0,1
<i>Atteinte oculaire</i>	1	0,1



Quoi de neuf...



...pour l'épidémiologie ?

Borrelia...et tout le reste

RESEARCH ARTICLE

# Molecular Detection of Tick-Borne Pathogens in Humans with Tick Bites and Erythema Migrans, in the Netherlands

**Setareh Jahfari \***, Agnetha Hofhuis, Manoj Fonville, Joke van der Giessen, Wilfrid van Pelt, Hein Sprong

Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), Bilthoven, the Netherlands

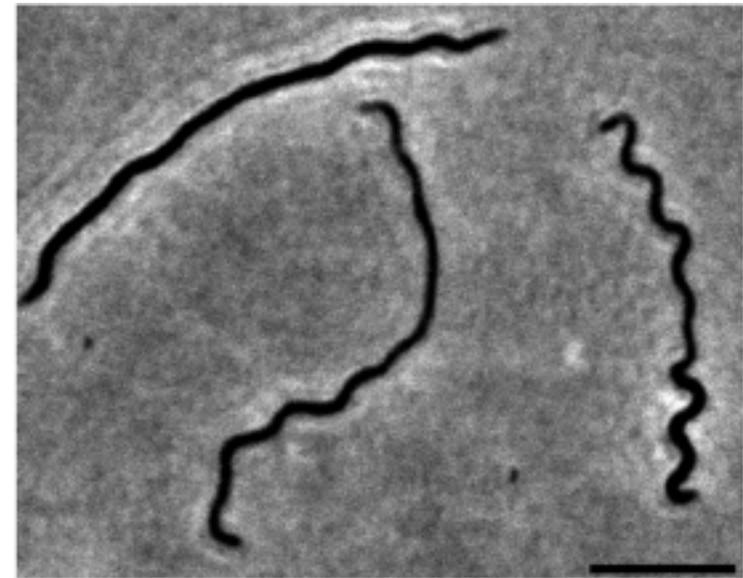
Table 1. Detected DNA sequences in 314 ticks obtained from 293 participants. The results on *B. burgdorferi* s. l. have been published by Hofhuis et al. 2013 [29].

Detected DNA sequences	n / N	% (95%CI)	Estimated human exposure with 1.1 million tick bites
<i>Borrelia burgdorferi</i> sensu lato [29]	92 / 314	29.3% (24.5%-34.5%)	322293
<i>B. afzelii</i> [29]	36 / 314	11.5% (8.3%-15.4%)	126115
<i>B. garinii</i> [29]	11 / 314	3.5% (1.9%-6.0%)	38535
<i>B. burgdorferi</i> sensu stricto [29]	7 / 314	2.2% (1.0%-4.4%)	24522
<i>B. valaisiana</i> [29]	4 / 314	1.3% (0.4%-3.0%)	14013
Untypeable* <i>Borrelia burgdorferi</i> [29]	36 / 314	11.5%	
<i>Borrelia miyamotoi</i>	7 / 302	2.3% (1.0%-4.5%)	25497
<i>Babesia</i> spp	11 / 314	3.5% (1.8%-6.0%)	
<i>B. microti</i>			21019
<i>B. veneta</i>			14013
<i>B. divisa</i>			3503
<i>Ehrlichia</i> spp			
<i>A. phagocytophilum</i>			10510
Untypeable*			
<i>Candidatus</i>			59936
Spotted fever rickettsia's	70 / 314	22.3% (18.0%-27.2%)	
<i>R. helvetica</i>	59 / 314	18.8% (14.8%-23.4%)	206688
<i>R. monacensis</i>	1 / 314	0.3% (0.0%-1.6%)	3503
Untypeable* <i>Rickettsia</i> spp	10 / 314	3.2%	
Co-infections with <i>B. burgdorferi</i> sensu lato**	30		105096
<i>Babesia</i> spp	3 / 314	1.0% (0.2%-2.6%)	
<i>Ehrlichia</i> / <i>Anaplasma</i> spp	10 / 314	3.2% (1.6%-5.6%)	
<i>Candidatus Neoehrlichia mikurensis</i>			
Spotted fever rickettsia's	21 / 314	6.7% (4.3%-9.9%)	
<i>Borrelia miyamotoi</i>	1 / 302	0.3% (0.0%-1.6%)	

Aucune manifestation clinique corrélée à la présence d'un micro-organisme différent de *Borrelia*

# *B. myamotoi*

- Agent de fièvre récurrentes
- Identifié en Amérique du nord, en Europe et en Asie
- En Alsace: 1 à 2 % des tiques infectées
- Qq cas de méningo encéphalites
- Diagnostic repose sur frottis sanguin ou PCR
- Risque de réaction de Jarish Herxheimer
- Traitement par doxy ou beta lactamines



Manifestation	% Patients		
	<i>B. miyamotoi</i> , n=46	<i>B. garinii</i> , n = 21	<i>B. burgdorferi</i> , n = 92
Individual			
EM	9	91	89
Multiple EM	0	14	7
Fever <sup>†</sup>	98	67	32
Fatigue	98	86	74
Headache	89	57	63
Chills	35	10	43
Myalgia	59	52	63
Arthralgia	28	29	62
Nausea	30	10	24
Vomiting	7	5	7
Neck stiffness	2	0	38

Clinical manifestations in patients with *Borrelia* spp. infection, Yekaterinburg City, Russia, 2009, and northeastern United States, 1991–2008. Adapted from Platonov AE, Karan LS, Kolyasnikova NM, Makhneva NA, Toporkova MG, Maleev VV, Fish D, Krause PJ. Humans infected with relapsing fever spirochete *Borrelia miyamotoi*, Russia. *Emerg Infect Dis* 2011;17:1816–23 [10].

# Et la recherche ?

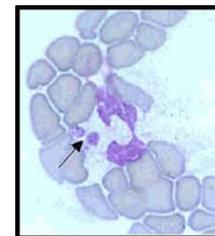
- Evolution de la population des tiques



**Suivi mensuel** des *Ixodes* en zones rurales et périurbaines en Alsace et en Bretagne

- Analyse moléculaire des microorganismes :
  - PCR
  - Génomique : OH ticks
  - Protéomique identifier les tiques et les pathogènes associés :  
CNR

Iconographie : CNR Strasbourg



*Anaplasma* spp.



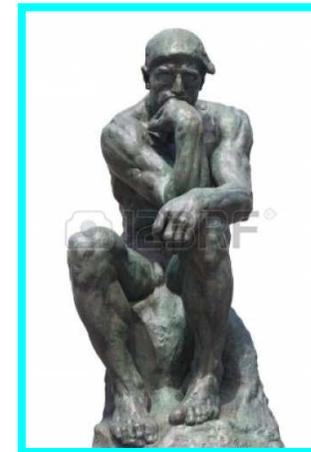
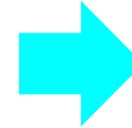
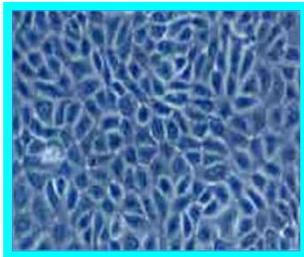
Quoi de neuf ?



...pour la physio-pathologie

# Recherche: Approche translationnelle

Analyse du rôle de la peau dans la transmission et dans la persistance bactérienne



**Modèles *In vitro* :**  
Cellules résidentes de la peau  
Fibroblastes et kératinocytes  
humaines primaires

**Modèle *In vivo***  
Souris C3H/HeN

**Patients:**  
Validation

**Techniques de protéomique à l'interface chimie-biologie**

Source : Nathalie Boulanger, CNR, Strasbourg



Quoi de neuf...



...pour les manifestations ?

...et les formes chroniques ?

RESEARCH ARTICLE

Open Access



# Common and uncommon neurological manifestations of neuroborreliosis leading to hospitalization

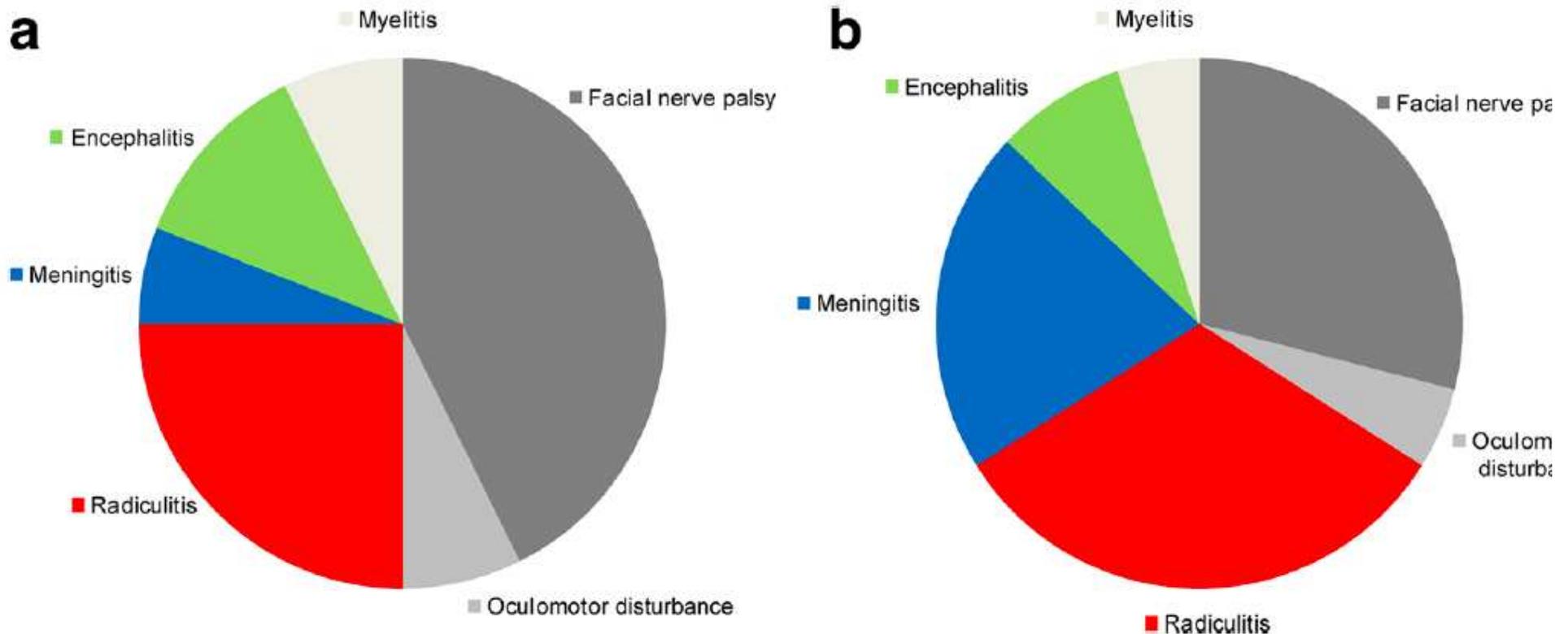
Philipp Schwenkenbecher<sup>1†</sup>, Refik Pul<sup>1†</sup>, Ulrich Wurster<sup>1</sup>, Josef Conzen<sup>2</sup>, Kaweh Pars<sup>1</sup>, Hans Hartmann<sup>3</sup>, Kurt-Wolfram Sühs<sup>1</sup>, Ludwig Sedlacek<sup>4</sup>, Martin Stangel<sup>1</sup>, Corinna Trebst<sup>1†</sup> and Thomas Skripuletz<sup>1\*†</sup>

- Service de neurologie
- Hôpital de Hanovre en Allemagne
- 68 patients entre 1999 et 2014

# Description des manifestations neurologiques

Mode d'entrée vers le diagnostic

Nombre total de manifestations



# Durée des symptômes au moment du diagnostic

**Table 1** Patient's characteristics. Age and duration of symptoms to diagnosis are presented by median with lowest and highest values

Clinical features	Patients (number)	Age (years)	Males (number)	Tick bite and/or erythema migrans (number)	Duration of symptoms (days)
All patients	68	45 (5–93)	44/68	23/68	16 (1–733)
Cranial nerve palsy	34	40 (6–77)	23/34	10/34	7 (1–121)
Facial nerve palsy	29	34 (6–77)	16/29	9/29	7 (1–121)
Isolated facial nerve palsy	11	26 (6–73)	7/11	4/11	4 (1–15)
+ Radiculitis	8	57 (18–77)	6/8	2/8	18 (2–49)
+ Meningitis	6	67 (30–93)	4/6	2/6	7 (3–21)
+ Radiculitis + meningitis	4	(34, 43, 44, 57)	3/4	1/4	(2, 21, 28, 121)
Oculomotor nerve palsy	5	53 (38–76)	2/5	1/5	53 (38–76)
Isolated oculomotor nerve palsy	2	(76, 42)	1/2	0/2	(2, 7)
+ Meningitis/Radiculitis	3	(26, 38, 53)	1/3	1/3	(11, 25, 26)
Radiculitis	17	67 (5–93)	10/17	9/17	20 (3–379)
Isolated radiculitis	14	67 (5–93)	8/14	8/14	18 (3–379)
+ Meningitis	3	(13, 65, 75)	2/3	0/3	(3, 22, 30)
Encephalitis	8	70 (8–79)	7/8	2/8	183 (1–732)
Chronic course	5	74 (67–79)	4/5	0/5	186 (81–732)
Acute/Subacute onset	3	(8, 11, 45)	3/3	2/3	(1, 1, 38)
Myelitis	5	37 (7–64)	4/5	0/5	126 (23–733)
Meningitis	4	(22, 34, 45, 64)	0/4	2/4	(1, 4, 7, 120)

# Suicide and Lyme and associated diseases

This article was published in the following Dove Press journal:  
Neuropsychiatric Disease and Treatment  
16 June 2017

- All of these patients met the clinical criteria for the diagnosis of LAD.
- Many patients fulfilled CDC Surveillance Case Definition, while in other patients, Surveillance Case Definition was not used as the sole criteria for establishing the clinical diagnosis
- Many had a history of erythema migrans rashes
- most had laboratory confirmation
- some had findings demonstrated by single photon emission tomography
- most tested positive for a number of coinfections which included *Babesia*, *Bartonella*, *Anaplasma*, *Ehrlichia chaffeensis*, *Rickettsia rickettsii*, Epstein–Barr virus, cytomegalovirus, human herpesvirus-2, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and hepatitis C virus

# « The death formula »

...ou comment trouver une définition de « sophisme »

Lyme and associated diseases infection→  
Persistent proinflammatory cytokines→  
Dysregulation of tryptophan metabolism→  
Quinolinic acid→NMDA receptor agonism→  
Glutamate dysregulation→  
Neural circuit dysfunction→  
Psychiatric dysfunction→  
Suicidal, sometimes also homicidal

**Figure 2** The death formula.

**Abbreviation:** NMDA, N-methyl-D-aspartate.

## ...et la recherche

- Centres spécialisés
  - évaluation clinique des patients
- Piq tiq : cohorte socio-microbio-clinique
  - Hypothèse : tiques poly infectées
    - Qu'est ce qui est transmis ?
    - Qu'est ce que risque l'homme ?
  - Méthodologie
    - Cohorte de sujets piqués par les tiques



Quoi de neuf...



...pour le diagnostic ?

# LA polémique

Diagnostic Microbiology and Infectious Disease xxx (2017) xxx-xxx



Studies that  
borrelia – a

Gary P. Worms

<sup>a</sup> Division of Infectious Dis

<sup>b</sup> Departments of Pediatric

<sup>c</sup> Department of Infectious

Philipps, 1998 : patients traités au préalable  
par antibiothérapie, sérologie négative

Sapi (2013) : 94 % des patients testés  
sont positifs

Essai non reproductible :  
contamination de laboratoire  
probable

Rudenko, 2016 : probable  
contamination de laboratoire



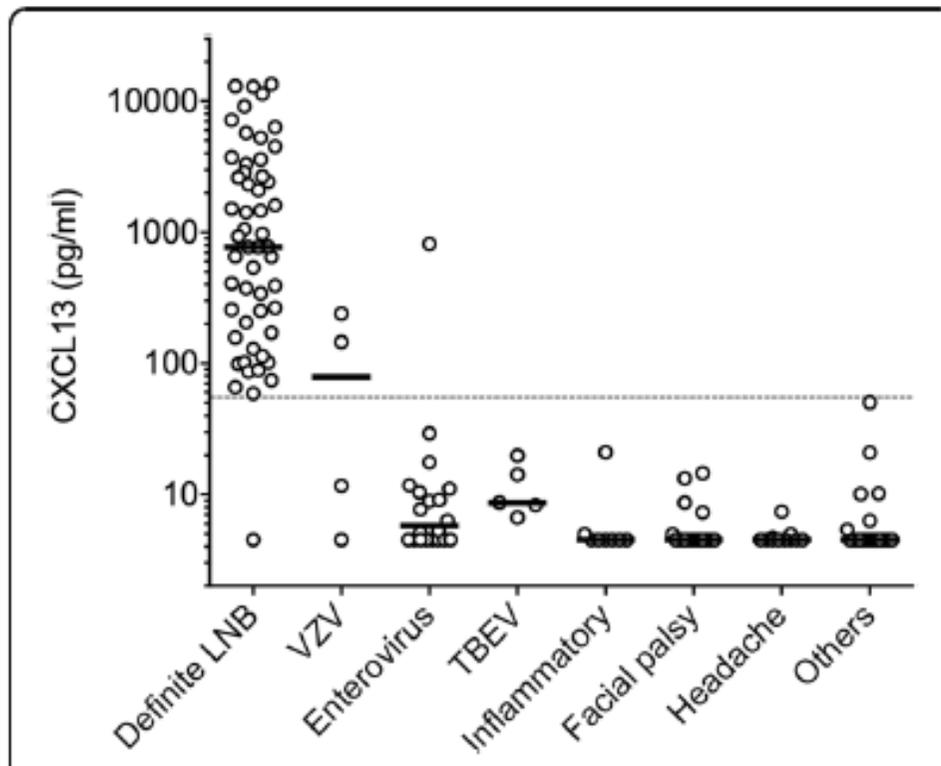
RESEARCH

Open Access



# Cerebrospinal fluid CXCL13 as a diagnostic marker of neuroborreliosis in children: a retrospective case-control study

M. M. Remy<sup>1†</sup>, N. Schöbi<sup>2†</sup>, L. Kottanattu<sup>2</sup>, S. Pfister<sup>1</sup>, A. Duppenhaler<sup>2</sup> and F. Suter-Riniker<sup>1</sup>



## Groupe Lyme

- majorité de paralysie faciale
- Présence d'une réaction cellulaire
- Durée des symptômes : maximum 109 jours spécifiques

# ESGBOR

Clinical suspicion of	Detection of antibodies to <i>B. burgdorferi</i>	<sup>c</sup> Expected sensitivity	<sup>d</sup> Incidence per 100,000 population
Tick bite	Not relevant	Not relevant	High
Erythema migrans	Not recommended	50%(40-61)	10-100
Lyme neuroborreliosis Clinical duration < 6 weeks	Specific CSF/serum antibody index	77%(67-85)	
Lyme neuroborreliosis Clinical duration >6 weeks	Specific CSF/serum antibody index	>99%	<10
Long-lasting Lyme neuroborreliosis > 6 months	Specific CSF/serum antibody index	>99%	<1
Lyme carditis	Serum IgG and/or IgM	>80%	<1
Borrelial lymphocytoma	Serum IgG and/or IgM	>80%	<1
Lyme arthritis	Serum IgG	96%(93-100)	<1
Acrodermatitis chronica atrophicans <sup>a</sup>	Serum IgG	98%(84-100)	1
Ocular manifestations <sup>b</sup>	Serum IgG	?	Rare

<sup>a</sup>Including ACA-associated peripheral neuropathy, <sup>b</sup>Specialist care only, also consider other diagnoses.

<sup>c</sup>Sensitivities from the systematic review of European studies are indicated with 95% confidence intervals for erythema migrans and Lyme neuroborreliosis and with median and range for Lyme arthritis and acrodermatitis chronica atrophicans [65]. <sup>d</sup>Incidences are approximate magnitude and vary in different parts of Europe.

# Quelle valeur diagnostique de la sérologie ?

Leeflang et al. *BMC Infectious Diseases* (2016) 16:140  
DOI 10.1186/s12879-016-1468-4

BMC Infectious Diseases

RESEARCH ARTICLE

Open Access

## The diagnostic accuracy of serological tests for Lyme borreliosis in Europe: a systematic review and meta-analysis



M. M. G. Leeflang<sup>12\*</sup>, C. W. Ang<sup>1</sup>, J. Berkhout<sup>2</sup>, H. A. Bijlmer<sup>3</sup>, W. Van Bortel<sup>4</sup>, A. H. Brandenburg<sup>5</sup>, N. D. Van Burgel<sup>6</sup>, A. P. Van Dam<sup>7</sup>, R. B. Dessau<sup>8</sup>, V. Fingerle<sup>9</sup>, J. W. R. Hovius<sup>10</sup>, B. Jaulhac<sup>11</sup>, B. Meijer<sup>13</sup>, W. Van Pelt<sup>3</sup>, J. F. P. Schellekens<sup>13</sup>, R. Spijker<sup>14</sup>, F. F. Stelma<sup>15</sup>, G. Stanek<sup>16</sup>, F. Verduyn-Lunel<sup>17</sup>, H. Zeller<sup>4</sup> and H. Sprong<sup>3</sup>

IgT

Estimate (95 % CI)

0.606 (0.503 to 0.700)

**Table 4** Summary estimates of sensitivity

		IgG (IgT)	IgT
		Estimate (95 % CI)	Estimate (95 % CI)
Erythema migrans	S	0.293 (0.293 to 0.431)	0.606 (0.503 to 0.700)
	S	0.939 (0.939 to 0.975)	0.919 (0.885 to 0.944)
Neuroborreliosis	S	0.515 (0.515 to 0.659)	0.865 (0.812 to 0.906)
	S	0.935 (0.935 to 0.971)	0.913 (0.869 to 0.942)
Lyme arthritis	S	0.857 (0.857 to 0.977)	0.945 (0.842 to 0.982)
	S	0.942 (0.942 to 0.983)	0.921 (0.837 to 0.964)
Acrodermatitis Chronica Atrophicans	S	0.821 (0.821 to 0.999)	0.978 (0.874 to 0.996)
	S	0.952 (0.952 to 0.976)	0.932 (0.883 to 0.962)
Unspecified Lyme borreliosis*	S	0.448 (0.448 to 0.661)	0.792 (0.960 to 0.867)
	S	0.877 (0.877 to 0.998)	0.947 (0.725 to 0.992)
IgT refers to assays measuring IgM and IgG simultaneously; estimates for studies including cross-reacting controls are not possible for healthy controls; these are the		0.978 (0.874 to 0.996)	

0.932 (0.883 to 0.962)

0.792 (0.960 to 0.867)

0.947 (0.725 to 0.992)

# Valeur des IgM ELISA



Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: [www.elsevier.com/locate/diagmicrobio](http://www.elsevier.com/locate/diagmicrobio)



Evaluation of commercial screening tests and blot assays for the diagnosis of Lyme borreliosis<sup>☆</sup>

Laurent Busson <sup>a,\*</sup>, Marijke Reynders <sup>b</sup>, Sigi Van den Wijngaert <sup>a</sup>, Hafid Dahma <sup>a</sup>, Marc Decolvenaer <sup>a</sup>, Liesbet Vasseur <sup>a</sup>, Olivier Vandenberg <sup>a,c</sup>

**Table 3**

Percentage of false-positive and equivocal results.

	Screening tests			
	DiaSorin liaison		Euroimmun anti-Borrelia	
	IgG	IgM	IgG	IgM
Equivocal	3/180	15/181	11/196	11/196
Equivocal (%)	1.66	8.28	5.61	5.61
False positive	13/180	50/181	4/196	14/196
False positive (%)	7.22	27.62	2.04	7.14

**Table 2**

Overall sensitivity, specificity, positive, and negative predictive value, and sp

	Screening tests			
	Diasorin liaison		Euroimmun anti-Borrelia	
	IgG	IgM	IgG	IgM
Overall sensitivity (%)	100	92.31	100	100
Overall specificity (%)	91.39	67.11	97.44	91.62
Specificity in control group (%)	95.83	85.11	100	97.96
Positive Predictive Value (%)	60.61	19.35	84	53.33
Negative Predictive Value (%)	100	98.03	100	100

# Actualités diagnostiques

INFECTIOUS DISEASES, 2016  
<http://dx.doi.org/10.3109/23744235.2016.1144931>

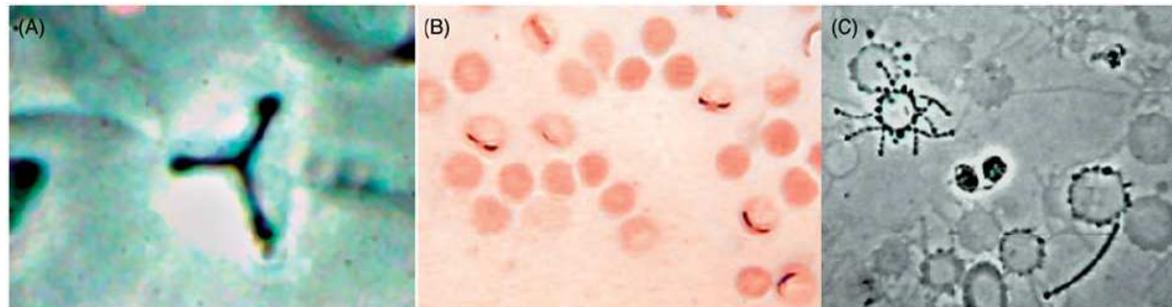


ORIGINAL ARTICLE

## Validate or falsify: Lessons learned from a microscopy method claimed to be useful for detecting *Borrelia* and *Babesia* organisms in human blood

Audun Aase<sup>a</sup>, Ondrej Hajdusek<sup>b</sup>, Øivind Øines<sup>c</sup>, Hanne Quarsten<sup>d</sup>, Peter Wilhelmsson<sup>e</sup>, Tove K. Herstad<sup>a</sup>, Vivian Kjelland<sup>f,g</sup>, Radek Sima<sup>b</sup>, Marie Jalovecka<sup>b</sup>, Per-Eric Lindgren<sup>e,h</sup> and Ingeborg S. Aaberge<sup>a</sup>

Groupe témoin : 88 % de positifs  
Groupe infectés : 66 % de positifs



# ...et la recherche ?

- Recherches génomiques systématiques chez patients piqués par des tiques : piq tiq
- Protéomique ciblée : Diabolyc
  - Diagnostic précoce : idex, PHRC interrégional
  - Diagnostic tardif
    - Recherche de marqueurs protéiques d'infection active
- Vésicules lipidiques

**Bioaster**

Agence Nationale de la Recherche  
**ANR**

Projet générique 2016-2019



Quoi de neuf...



...pour le traitement ?

Jusqu'où aller ?

## Identification of novel activity against *Borrelia burgdorferi* persists using an FDA approved drug library

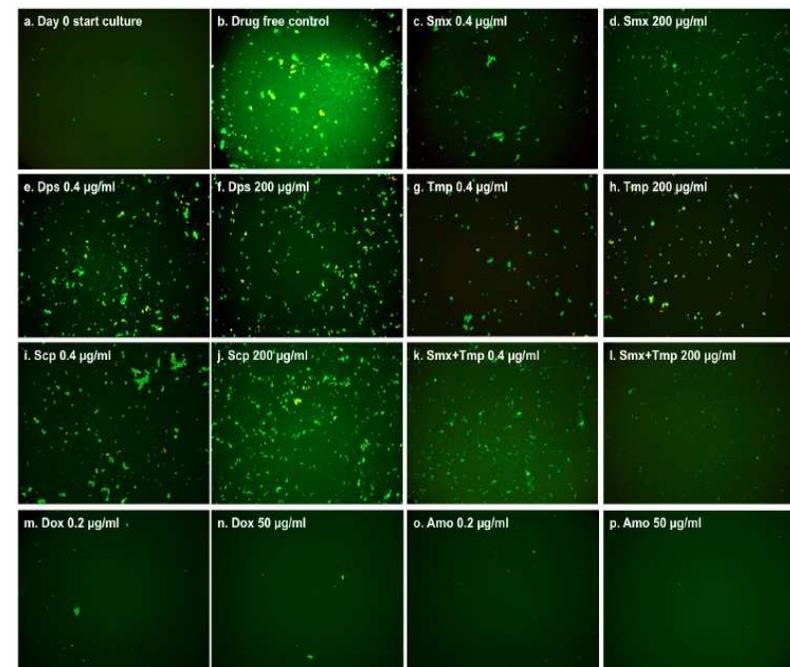
Jie Feng<sup>1</sup>, Ting Wang<sup>1</sup>, Wanliang Shi<sup>1</sup>, Shuo Zhang<sup>1</sup>, David Sullivan<sup>1</sup>, Paul G Auwaerter<sup>2</sup> and Ying Zhang<sup>1</sup>

- *Borrelia* en phase de croissance stationnaire vs formes métaboliquement actives

**Table 2** Comparison of the MIC values and anti-persister activity of selected antibiotics against *B. burgdorferi*

Antibiotics	MIC ( $\mu\text{g/mL}$ )	$C_{\text{max}}$ ( $\mu\text{g/mL}$ ) <sup>a</sup>	Activity against persisters
Doxycycline	$\leq 0.25$	3.6–4.6	–
Amoxicillin	$\leq 0.25$	1.5–13.8	–
Metronidazole	25	12.5–19.4	–
Daptomycin	12.5–25	57.8–93.9	++++
Clofazimine	6.25	0.47–0.7	+++
Carbomycin	$\leq 0.25$	0.625	+++
Cefoperazone	$\leq 0.25$	111–375	+++
Cefotiam	$\leq 0.25$	30–170	++
Vancomycin	0.2–0.4	19–23	+
Tazobactam	12.5	14.8–33.8	–
Sulfamethoxazole	$\leq 0.25$	46.3	–

<sup>a</sup>  $C_{\text{max}}$  values are derived from the literature.



*The* **NEW ENGLAND**  
**JOURNAL** *of* **MEDICINE**

ESTABLISHED IN 1812

MARCH 31, 2016

VOL. 374 NO. 13

Randomized Trial of Longer-Term Therapy for Symptoms  
Attributed to Lyme Disease

Anneleen Berende, M.D., Hadewych J.M. ter Hofstede, M.D., Ph.D., Fidel J. Vos, M.D., Ph.D.,  
Henriët van Middendorp, Ph.D., Michiel L. Vogelaar, M.Sc., Mirjam Tromp, Ph.D., Frank H. van den Hoogen, M.D., Ph.D.,

- Etude randomisée, double aveugle contre placebo
- Patients avec manifestations chroniques, en échec d'un traitement par ceftriaxone
- Traitement par doxycycline vs clarithromycine + hydroxy chloroquine vs placebo pendant 12 semaines

0.69

0.94

0.85

0.44

0.84

0.42

0.41

1.00

0.11

0.32

0.85

Placebo  
Group  
(N=98)

P Value†

Doxycycline Group  
vs. Placebo GroupClarithromycin-  
Hydroxychloroquine Group  
vs. Placebo Group

Difference in score (95% CI)‡

4.8  
to 36.00.1  
to 41.76.0  
to 37.51.0  
to 42.33.9  
to 35.89.4  
to 40.97.5  
to 38.95.1  
to 46.42.6  
to 44.87.5  
to 39.51.9  
to 43.48.4  
to 92.48.3  
to 40.2**P = 0,69**

2.8)

0.9  
(-1.6 to 3.3)

0.94

0.85

0.44

0.84

0.42

0.41

1.00

0.11

0.32

0.85

0.84

0.73

0.3

1.1

-1.3  
(-8.3 to 5.6)0.3  
(-3.1 to 3.7)**Table 2. Treatment Effect at the End of the Treatment Period in the Modified Inter**

Outcome	Doxycycline Group (N=86)	Clarithromycin-Hydroxychloroquine Group (N=86)	Placebo Group (N=98)	P Value†	Doxycycline Group vs. Placebo Group	Clarithromycin-Hydroxychloroquine Group vs. Placebo Group
Primary outcome: SF-36 physical-component summary§	35.0 (33.5 to 36.5)	33.0 (34.2 to 36.0)	4.8 to 36.0	0.69	2.8)	0.9 (-1.6 to 3.3)
Secondary outcomes						
RAND SF-36§						
Mental-component summary	40.2 (38.6 to 41.9)	40.1 (38.9 to 41.7)	0.1 to 41.7)	0.94	0.1 (-2.7 to 2.9)	0.4 (-2.3 to 3.1)
Global-health composite	36.1 (34.5 to 37.8)	36.0 (35.1 to 36.9)	6.0 to 37.5)	0.85	0.1 (-2.6 to 2.9)	0.6 (-2.1 to 3.2)
Physical-functioning scale	41.9 (40.5 to 43.3)	41.0 (40.8 to 41.2)	1.0 to 42.3)	0.44	0.9 (-1.4 to 3.2)	1.1 (-1.1 to 3.4)
Role-physical scale	33.6 (31.6 to 35.6)	33.0 (32.5 to 33.5)	3.9 to 35.8)	0.84	-0.3 (-3.7 to 3.1)	0.5 (-2.8 to 3.8)
Bodily pain scale	39.1 (37.5 to 40.7)	39.5 (39.0 to 40.0)	9.4 to 40.9)	0.42	-0.3 (-2.9 to 2.4)	1.1 (-1.5 to 3.6)
General-health scale	37.1 (35.6 to 38.6)	37.0 (37.0 to 37.0)	7.5 to 38.9)	0.41	-0.4 (-2.9 to 2.0)	0.9 (-1.5 to 3.3)
Mental-health scale	45.1 (43.8 to 46.4)	45.0 (43.9 to 46.1)	5.1 to 46.4)	1.00	0.0 (-2.3 to 2.2)	0.0 (-2.1 to 2.2)
Role-emotional scale	44.7 (42.4 to 47.0)	44.0 (39.2 to 48.8)	2.6 to 44.8)	0.11	2.1 (-1.7 to 6.0)	-1.2 (-5.0 to 2.6)
Social-functioning scale	36.3 (34.2 to 38.4)	36.6 (36.6 to 36.6)	7.5 to 39.5)	0.32	-1.2 (-4.7 to 2.3)	1.0 (-2.4 to 4.4)
Vitality scale	42.5 (40.9 to 44.0)	42.0 (41.0 to 43.0)	1.9 to 43.4)	0.85	0.5 (-2.0 to 3.1)	0.5 (-2.0 to 3.0)
Checklist Individual Strength¶						
Total score	88.7 (84.4 to 92.9)	88.0 (83.0 to 93.0)	8.4 to 92.4)	0.84	0.3 (-6.9 to 7.4)	-1.3 (-8.3 to 5.6)
Fatigue-severity scale	39.4 (37.3 to 41.5)	39.0 (36.6 to 41.4)	8.3 to 40.2)	0.73	1.1 (-2.4 to 4.6)	0.3 (-3.1 to 3.7)

# Que disent les dernières recommandations ?

## Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift

An open access, online journal • [www.smw.ch](http://www.smw.ch)

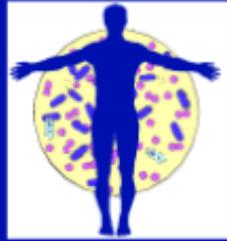
**Review article: Biomedical intelligence** | Published 5 December 2016, doi:10.4414/smw.2016.14353

Cite this as: Swiss Med Wkly. 2016;146:w14353

### Update of the Swiss guidelines on post-treatment Lyme disease syndrome

*Johannes Nemeth<sup>a</sup>, Enos Bernasconi<sup>b</sup>, Ulrich Heininger<sup>c</sup>, Mohamed Abbas<sup>d</sup>, David Nadal<sup>e</sup>, Carol Strahm<sup>f</sup>, Stefan Erb<sup>g</sup>, Stefan Zimmerli<sup>h</sup>, Hansjakob Furrer<sup>h</sup>, Julie Delaloye<sup>i</sup>, Thierry Kuntzer<sup>j</sup>, Ekkehardt Altpeter<sup>k</sup>, Mathias Sturzenegger<sup>l</sup>, Rainer Weber<sup>a</sup>, for the Swiss Society for Infectious Diseases and the Swiss Society for Neurology*

« Finally, there is no evidence for specific treatment for PTLDS. »



## 5.1 Erythème migrant

Molécules	Posologie adulte	Posologie pédiatrique	Durée du traitement
<b>1er choix:</b> Doxycycline <sup>1</sup>	100 mg 2x/j	4 mg/kg/j en 2 prises (max. 100 mg/prise)	10 jours <sup>2</sup>
<b>2è choix:</b> Amoxicilline	500 mg 3x/j	50 mg/kg/j en 3 prises (max. 500 mg/prise)	14 jours <sup>3</sup>
<b>3è choix:</b> Cefuroxime-axetil	500 mg 2x/j	30 mg/kg/j en 2 prises (max. 500 mg/prise)	14 jours <sup>3</sup>
<b>4è choix:</b> Macrolides <sup>4</sup>	Azithromycine <sup>5</sup> 1g le premier jour puis 500 mg/j pendant 4 jours ou 500 mg/j pendant 7 jours	20 mg/kg en une prise le premier jour puis 10 mg/kg/j en une prise pendant 4 jours	5 ou 7 jours
	Clarithromycine 500 mg 2x/j	15 mg/kg/j en 2 prises	14 jours <sup>3</sup>

<sup>1</sup>Contre-indiqué chez la femme enceinte et l'enfant de < 8 ans.

<sup>2</sup>Dans les études, il n'y a pas de différence entre 10 et 14 jours de traitement par doxycycline.<sup>78</sup>

<sup>3</sup>Certains experts préconisent jusqu'à 21 jours en cas d'EM multiples, mais il n'y a pas d'études établissant la supériorité par rapport à 14 jours.

<sup>4</sup>Amoxicilline, amoxicilline-clavulanate, cefuroxime-axetil, ceftriaxone, cefixime, cefepime, cefazolin, cefotaxime, cefotaxime sodium, cefotaxime sodium et cefotaxime sodium et cefepime.

<sup>5</sup>Azithromycine, clarithromycine, clarithromycine et clarithromycine.

## Atteinte articulaire

<b>Molécules</b>	<b>Posologie adulte</b>	<b>Posologie pédiatrique</b>	<b>Durée du traitement</b>
<b>Doxycycline<sup>1</sup></b>	100 mg 2x/j	4 mg/kg/j en 2 prises (max. 100 mg/prise)	28 jours
<b>Amoxicilline</b>	500 mg 3x/j	50 mg/kg/j en 3 prises (max. 500 mg/prise)	28 jours
<b>Ceftriaxone</b>	2g 1x/j	100 mg/kg/j en 1prise (max.2g)	14 à 28 jours

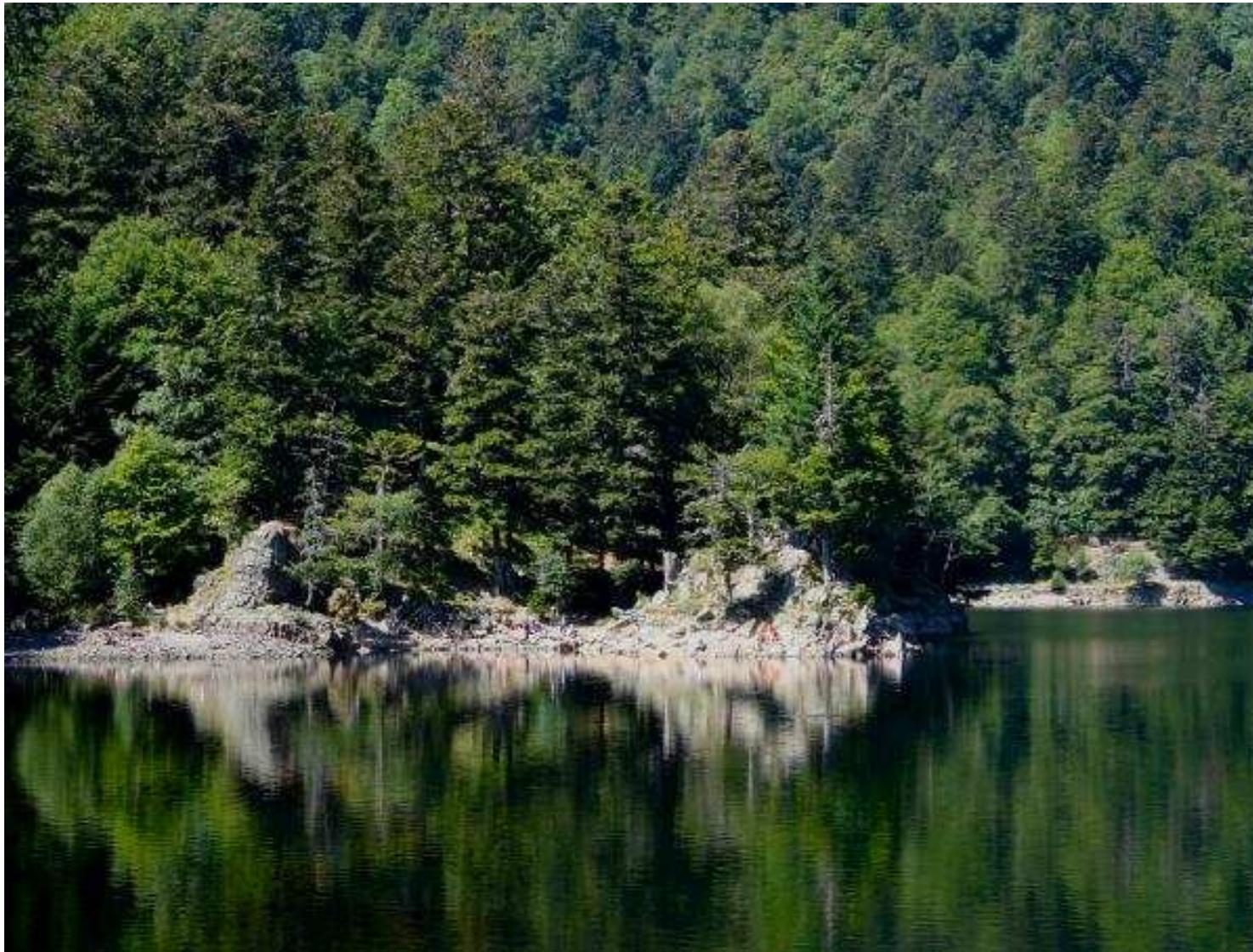
## Neuroborréliose aiguë

<b>Molécules</b>	<b>Posologie adulte</b>	<b>Posologie pédiatrique</b>	<b>Durée du traitement</b>
<b>Doxycycline<sup>1</sup></b>	100 mg 2x/j	4-8 mg/kg/j en 2 prises (max 100 mg/prise)	14 jours
<b>Ceftriaxone</b>	2g 1x/j	100 mg/kg/j en 1 prise (max.2 g)	14 jours

## ...et la recherche ?

- Ce qu'il manque
  - Les pathologies chroniques
    - quelles relations avec la borréliose de Lyme ?
  - Les traitements prolongés
    - Quelle efficacité : absence d'évaluation

# Rendez vous dans nos belles forêts vosgiennes



**Table 3** Accuracy of CSF CXCL13 test to diagnose definite LNB in children using a 55 pg/ml cut-off

Sensitivity %	96.7 (90.7–99.3)
Specificity %	98.1 (89.9–100.0)
Positive LR	29.8 (9.8–90.6)
Negative LR	0.02 (0.0–0.14)
Diagnostic odds ratio	1525.3 (154.6–15047.4)

Definite LNB cases ( $n = 53$ ) were compared to control non-LNB cases ( $n = 96$ )  
LR likelihood ratio. 95% confidence interval is indicated in parentheses