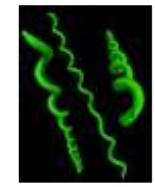
Serological diagnosis of Lyme disease

Borrelia

- Gram-negative bacteria of the family Spirochaetaceae
- At least 36 genospecies are known, the group of pathogenic strains is referred to as Borrelia burgdorferi sensu lato
- Pathogenic species for humans:

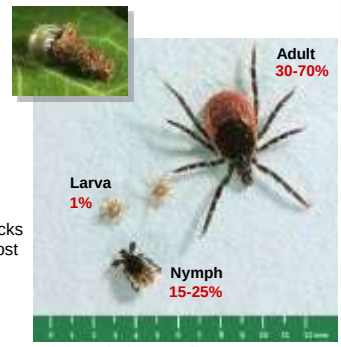
Europe:	*Borrelia burgdorferi* sensu stricto *Borrelia garinii* *Borrelia afzelii* (*Borrelia spielmanii*)
USA:	*Borrelia burgdorferi* sensu stricto



- Causative agent of Lyme disease (Borreliosis)

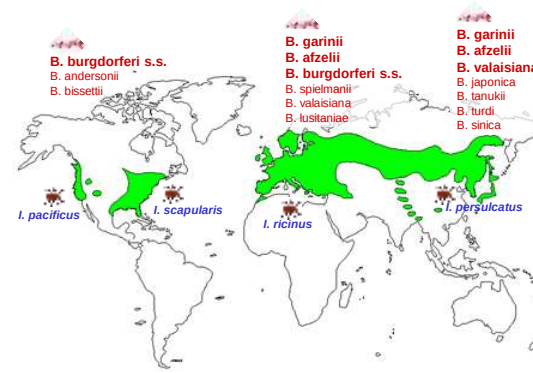
Ticks (genus Ixodes): Vectors of Lyme disease

- 3 developmental stages: larva, nymph, adult
- Blood feeding is necessary before every moult
- Transmission of Borrelia by ticks of all development stages, most frequently by nymphs
- Whole life cycle: ≈ 3 years



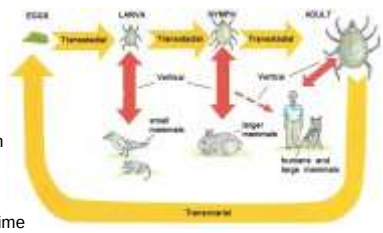
% infected with Borrelia

Global distribution of ticks transmitting Borrelia



How do ticks become infected with Borrelia?

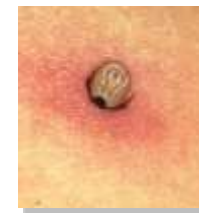
- Blood feeding on an already infected host
- Co-feeding in close vicinity to an infected tick
- Transovarial transmission to unfertilised eggs (→ infected larvae)
- Infection is kept for a lifetime



Transmission risk after tick bite (Germany)

- 743 ticks collected from humans (Maiwald et al., 1998)

57%	Nymphs
41%	Adult female Ticks
2%	Larvae



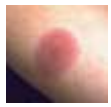
- 11% of the ticks were infected with Borrelia
- 27% of bites from infected ticks resulted in a human infection
- In total, ≈ 4% of all tick bites lead to an infection

Infection prophylaxis (no vaccine available!):

1. Avoid tick exposure
2. After tick bite: avoid squeezing, remove tick quickly

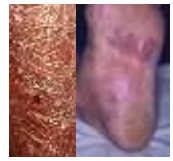
Clinical symptoms and stages

Early local *Days to weeks* → **Disseminated** *Weeks to months* → **Chronic** *Months to years*



Erythema migrans (EM)

Facial paresis



Acrodermatitis chronica atrophicans (ACA)

Lymphocytoma

Lyme arthritis

Problem: sometimes no EM, unspecific symptoms

Distribution of pathogenic Borrelia species

EUROPE	Ticks (n=90)	CSF (n=43)	Skin (n=68)	Synovial fluid (n=32)
B. burgdorferi s.s.	20%	19%	6%	33%
B. afzelii	9%	12%	84%	29%
B. garinii	71%	69%	10%	38%

Wilske et al. Diagnosis of Lyme borreliosis in Europe. Vector-Borne and Zoonotic Diseases.3(2003):215-227.

Laboratory diagnosis of Lyme disease

Direct detection methods: Microscopy, Culture, PCR

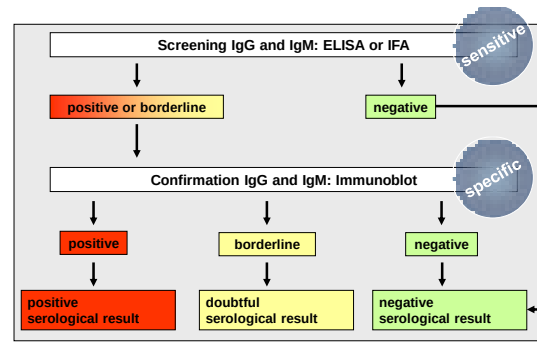
- low sensitivity (10-70%), time consuming, not standardised

Serological techniques: ELISA, Immunoblot, IFA

Stage	Symptoms	Sensitivity*	Comments
Local	Erythema migrans	20-50%	Predominantly IgM → *Sensitivity can be significantly increased by detection of anti-VlsE antibodies (IgG)*
Disseminated	Neuro-borreliosis	70-90 %	IgM and IgG → with longer lasting disease predominance of IgG
Chronic	Lyme arthritis	90-100%	Normally only IgG

**taken from MIQ 12-2000*

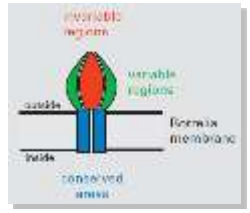
Serological two-step strategy (CDC, RKI, …)



VlsE: the main antigen for Borrelia serology

VlsE **V**ariable major protein (VMP)-**l**ike **s**equence, **E**xpressed

- 35 kDa surface lipoprotein of Borrelia only expressed *in vivo* !
- Constant VlsE recombination protects the bacteria from elimination by the immune system
- Lyme disease patients show an early and strong IgG antibody response to VlsE



Prevalences of IgG antibodies against VlsE

Cohort	Anti-VlsE ELISA IgG positive (%)
Culture-positive EM (n = 41)	63
Early disseminated (n = 12)	92
Acute neuroborreliosis (n = 17)	100
Lyme arthritis (n = 23)	87
Controls (n = 110)	2

Lawrenz et al., 1999 (group of Prof. Norris, University of Houston, Texas, USA)

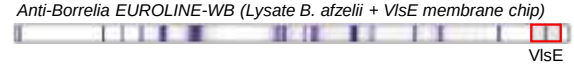
Diagnostic value of VlsE: ELISA

Erythema migrans n = 50		EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG)		
		positive	negative	
full-extract ELISA without VlsE	positive	22	0	44%
	negative	13	15	
		70%		

⇒ **VlsE increases sensitivity in early stage by 26% !**

Diagnostic value of VlsE: Immunoblot

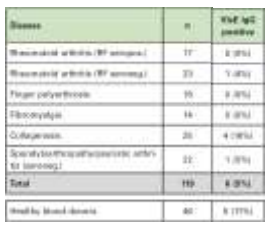
Anti-Borrelia EUROLINE-WB (Lysate B. afzelii + VlsE membrane chip)



	B. afzelii IgG	B. afzelii plus VlsE IgG	B. afzelii IgM	B. afzelii plus VlsE IgM	Effect of VlsE on blot sensitivity IgG + IgM
EM (n=47)	40%	62%	68%	70%	80 → 89%
NB (n=27)	78%	93%	48%	48%	85 → 96%
Arthritis (n=33)	94%	94%	15%	15%	94 → 94%
ACA (n=8)	100%	100%	13%	13%	100 → 100%

The addition of VlsE leads to a significant increase of sensitivity!

Specificity of VlsE



Specificity of anti-VlsE antibodies investigated in patients with rheumatic diseases *(Käßer et al., 2006)*

Test system: Blot

Study group	Sera tested	Anti-VlsE reactive sera (IgG)
Syphilis (secondary or latent)	24	0 (0 %)
Louse-borne relapsing fever	11	1 (9 %)
Oral infections	6	0 (0 %)
Rheumatoid arthritis	7	0 (0 %)
Healthy subjects	28	0 (0 %)

Magnarelli et al., 2002 Test system: ELISA

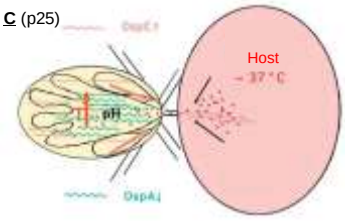
European Patent Application: EP 2 199 303 A1

OspC advanced

A new designer antigen

OspC – Target of early IgM antibodies

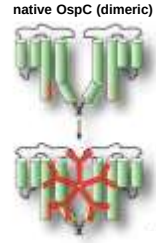
OspC **O**uter **s**urface **p**rotein **C** (p25)



- Most important target of IgM mediated immune response
- Upregulated during blood feeding
- Enables Bacteria to migrate into salivary glands

Starting point

native OspC (dimeric)



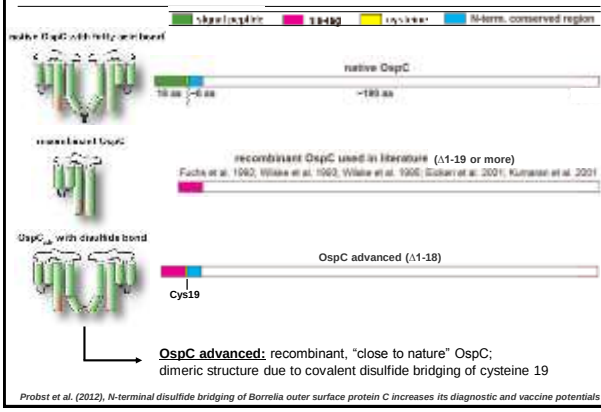
- Optimal antigen with high sensitivity and specificity
- Bivalent IgM binding with high affinity
  → low antigen input needed
- Very difficult to produce

recombinant OspC (monomeric)

- Easier production
- Monovalent IgM binding with low affinity
  → high antigen input needed
  → higher number of unspecific reactions

Objective: development of recombinant OspC with properties of native OspC

Results



OspC advanced: recombinant, "close to nature" OspC;
dimeric structure due to covalent disulfide bridging of cysteine 19

Probst et al. (2012), N-terminal disulfide bridging of Borrelia outer surface protein C increases its diagnostic and vaccine potentials

OspC advanced: Comparison with native OspC

Cohort	n	Prevalence of anti-OspC (IgM)					
		B. afzelii		B. burgdorferi		B. garinii	
		adv	native	adv	native	adv	native
Active borreliosis	150	85%	81%	88%	84%	66%	84%
Past infection (persisting IgM)	10	13%	13%	13%	13%	13%	19%
Acute EBV	10	0%	0%	0%	0%	0%	0%
Pregnant women	50	2%	2%	2%	2%	2%	2%
Blood donors	50	4%	4%	6%	4%	4%	2%

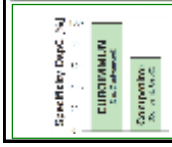
Scientific presentation at the 21st European Congress of Clinical Microbiology and Infectious Diseases (ECCMID), Milan, Italy, May 2011

Same sensitivity and specificity as native OspC!

OspC advanced: Specificity

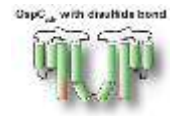
Poster presentation at the 12th ICLB congress, Ljubljana, Slovenia, September 2010

	n	Anti-OspC-IgM positive sera			
		Native OspC	OspC-adv	OspC-adv monomeric mutant	Mikrogen recomLine IgM
Patients with erythema migrans (+)	20	14	13	14	16
Sensitivity (%)	20	70	65	70	80
Healthy blood donors (+)	25	0	0	4	0
Specificity (%)	25	100	100	84	68
Diagnostic accuracy (%)	45	87	84	76	76



32% higher specificity than recombinant OspC of competitor

OspC advanced: "Close to nature" rec. OspC



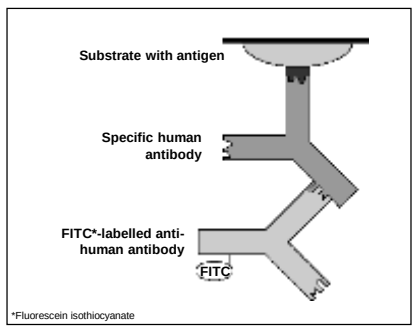
OspC advanced

- Combines advantages of native and recombinant OspC
- Same diagnostic characteristics as native OspC
- Easier to produce than native OspC
  → less costly, consistent quality
- 32% more specific than monomeric rec. OspC

N-terminal disulphide-bridging of Borrelia outer surface protein C increases its diagnostic and vaccine potentials

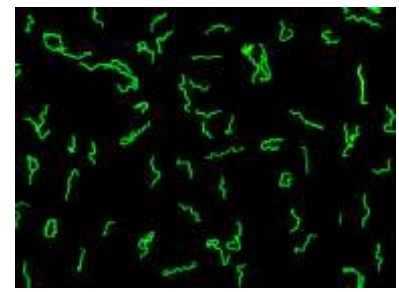
Christian Probst, Anthonina Ott, Thomas Scheper, Wolfgang Meyer, Winfried Stöcker, Lars Komorowski*

Anti-Borrelia IFA



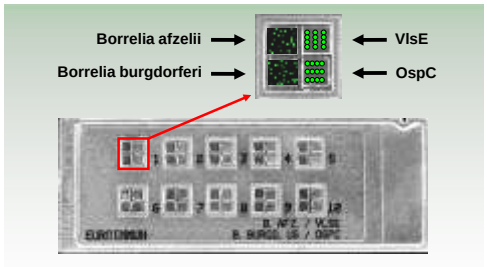
Principle of the IFA test

Anti-Borrelia IFA



Antibodies to Borrelia spirochetes in the IFA test

EUROPLUS (IgG, IgM): Anti-Borrelia IFA



Ig class specific EUROPLUS tests:

- Borrelia afzelii plus VlsE antigen (IgG)
- Borrelia afzelii plus OspC antigen (IgM)

Anti-Borrelia plus VlsE (IgG)
Anti-Borrelia (IgM)

Clinical studies with anti-Borrelia ELISAs

Cohort	n	Anti-Borrelia plus VlsE IgG	Anti-Borrelia IgM	Anti-Borrelia IgG / IgM
Erythema migrans	205	76%	68%	91%
Neuroborreliosis	80	90%	49%	96%
Facial paresis	16	100%	50%	100%
Arthritis	49	84%	43%	94%
ACA	14	93%	21%	93%
Healthy blood donors	500	5%	2%	

Summarized results of various studies

EUROIMMUN Anti-Borrelia ELISA (IgG, IgM) agree 99% with the results from EQUALIS, INSTAND, IQS and Labquality quality assurance schemes

n = 137		Designated result from EQUALIS, INSTAND, IQS, Labquality (IgG)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG)	positive	75	1	1
	borderline	0	2	1
	negative	0	0	51

n = 151		Designated result from EQUALIS, INSTAND, IQS, Labquality (IgM)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia ELISA (IgM)	positive	24	1	1
	borderline	0	1	3
	negative	0	1	110

Anti-Borrelia ELISAs in external QAS

EQUALIS: 10/2004-09/2010 | INSTAND: 10/2006-11/2010 | Labquality 02/2008-01/2011

	EQUALIS				INSTAND				Labquality			
	IgG		IgM		IgG		IgM		IgG		IgM	
	n	%	n	%	n	%	n	%	n	%	n	%
EUROIMMUN	73	97	73	93	347	95	415	91	161	98	158	97
Serion	191	96	189	88	707	94	893	97	106	93	152	88
DiaSorin LIAISON (CLIA)	125	94	125	93	36	100	41	92	184	94	178	94
Mikrogen	24	73	30	90	309	98	359	92	-	-	16	100
DAKO / Oxoid	872	70	871	88	-	-	12	100	-	-	80	87
Virion\Serion	-	-	-	-	255	94	388	92	-	-	-	-
Virotech	-	-	-	-	333	85	341	93	40	93	35	86
Abbott	-	-	-	-	8	63	-	-	-	-	-	-
Biomedica	-	-	-	-	-	-	-	-	45	87	43	97
IBL	-	-	-	-	-	-	-	-	21	62	21	90

n = number of participants % = percentage of correct results

NEW

Anti-Borrelia Select (IgG)
Anti-Borrelia Select (IgM)

Tested Borrelia antigens

IgG

Antigens:
VlsE
p17/p18
DbpA
OspC
BmpA (p39)
p100/p83

Species:
Borrelia burgdorferi
Borrelia garinii
Borrelia afzelii
Borrelia spielmanii

IgM

Antigens:
OspC – native purified
OspC – recombinant monomer
OspC – recombinant dimer (*advanced*)
VlsE
BmpA (p39)
DbpA

Species:
Borrelia burgdorferi
Borrelia garinii
Borrelia afzelii
Borrelia spielmanii

Anti-Borrelia Select ELISA (IgG, IgM):
Mixture of recombinant antigens from various pathogenic Borrelia species
- IgG test with VlsE
- IgM test with dimeric *OspC advanced* (optimised for use in ELISA)

Anti-Borrelia Select ELISA: Specificity

	Positive and grey zone results of ELISA			
	IgG		IgM	
	Lysate Ba, Bb, Bg plus VlsE	Anti-Borrelia Select	Lysate Ba, Bb, Bg	Anti-Borrelia Select
Anti-Treponema positive (n=92)	65 (71 %)	3 (3 %)	26 (28 %)	6 (7 %)
Autoantibody positive (n=28)	6 (22 %)	5 (19 %)	7 (26 %)	1 (4 %)
Sera from daily laboratory routine (IgG: n=187 / IgM: n=185)	33 (18 %)	11 (6 %)	10 (5 %)	6 (3 %)

According to the literature, the prevalence of anti-Borrelia antibodies in healthy blood donors is 5 – 10% (IgG) and about 2% (IgM), respectively.

How about sensitivity?

Sera from external quality assessment INSTAND / 2004-2011

n=27	Anti-Borrelia Select (IgG)	Anti-Borrelia Select (IgM)
Sensitivity	100 %	100 %
Specificity	100 %	100 %

Sera from patients with erythema migrans (n=33)

Number of positive results		
Lysate Ba, Bb, Bg plus VlsE (IgG)	27 (82 %)	30 (91 %)
Lysate Ba, Bb, Bg (IgM)	25 (76 %)	
Anti-Borrelia Select (IgG)	21 (64 %)	30 (91 %)
Anti-Borrelia Select (IgM)	22 (67 %)	

EUROIMMUN Anti-Borrelia ELISAs

Anti-Borrelia Screening ELISA (IgG + IgM)

Anti-Borrelia plus VlsE (IgG)
Anti-Borrelia (IgM)

- Lysate based (B. afzelii, B. burgdorferi, B. garinii)
- IgG test with rec. **VlsE**
- IgM test with high concentration of **native OspC**
- Full antigen spectrum
- Highest sensitivity

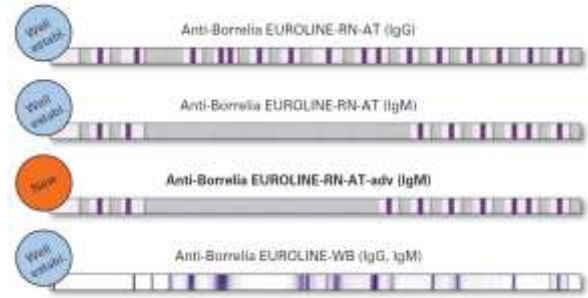
NEW

Anti-Borrelia Select (IgG)
Anti-Borrelia Select (IgM)

- Based on selection of highly specific recombinant Borrelia antigens
- IgG test with **VlsE**
- IgM test with rec. **OspC advanced** (optimized for use in ELISA)
- Fewer cross reactivities (other infectious diseases, autoimmune diseases)

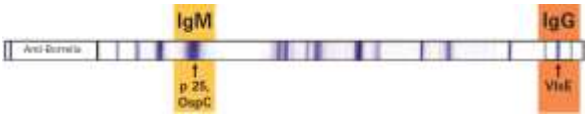
Confirmatory tests

EUROIMMUN immunoblots for confirmation



Anti-Borrelia EUROLINE-WB (IgG, IgM)

Lysate of B. afzelii plus membrane chip with VlsE



- Combines advantages of native and recombinant antigens
- VlsE as a sensitive, cross-species marker (IgG): already in the early phase of an infection
- Contains native OspC as main target of IgM antibodies
- Rapid at-a-glance evaluation:
  Anti-Borrelia IgM: p25/OspC, Anti-Borrelia IgG: VlsE
- Computer based evaluation and data management using the EUROLineScan software

Specificity of Anti-Borrelia EUROLINE-WB

Disease	n	Anti-Borrelia positive			VlsE IgG positive
		IgG	IgM	IgG/IgM	
Rheumatoid arthritis (RF seropos.)	17	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Rheumatoid arthritis (RF seroneg.)	22	1 (4%)	0 (0%)	1 (4%)	1 (4%)
Finger polyarthrosis	18	1 (6%)	0 (0%)	1 (6%)	0 (0%)
Fibromyalgia	14	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Collagenosis	25	4 (16%)	0 (0%)	4 (16%)	4 (16%)
Spondylarthropathy/psoriatic arthritis (seroneg.)	22	1 (5%)	0 (0%)	1 (5%)	1 (5%)
Total	**118**	**7 (6%)**	**0 (0%)**	**7 (6%)**	**6 (5%)**
Healthy blood donors	46	6 (13%)	0 (0%)	6 (13%)	5 (11%)

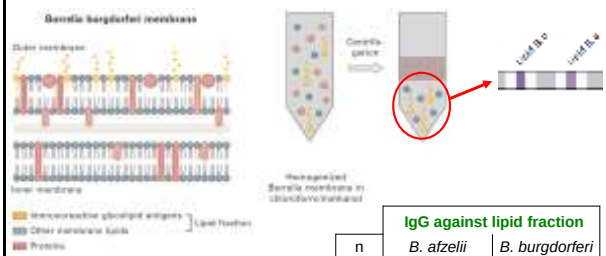
The EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG, IgM) agree 100% with the results from the INSTAND quality assurance scheme

Sera investigated	16 serologically precharacterized sera (IgG) 16 serologically precharacterized sera (IgM)
Origin of sera	INSTAND e. V., Duesseldorf, Germany

n = 16		Designated result from INSTAND (IgG)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG)	positive	7	0	0
	borderline	0	1	1
	negative	0	0	7

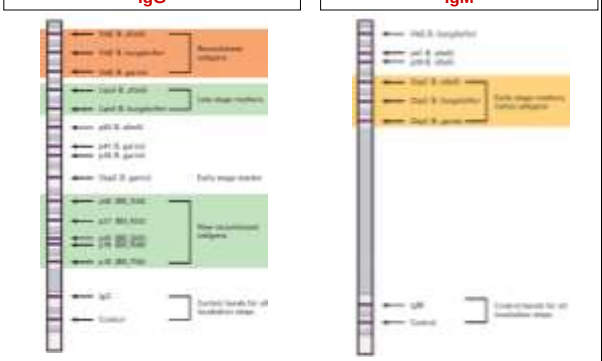
n = 16		Designated result from INSTAND (IgM)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia EUROLINE-WB (IgM)	positive	2	0	0
	borderline	1	2	0
	negative	0	0	11

Lipid antigens



	n	IgG against lipid fraction	
		B. afzelii	*B. burgdorferi*
Erythema migrans	62	4.8 %	8.1 %
Lyme arthritis	17	29.4 %	70.6 %
Specificity		100%	100%

Anti-Borrelia EUROLINE-RN-AT



Performance of EUROLINE-RN-AT

IgG		
Antigen	**Prevalence***	**Specificity***
VlsE Ba	**66%**	**99%**
VlsE Bb	**89%**	**99%**
VlsE Bg	**68%**	**95%**
Lipid Ba	**25%**	**100%**
Lipid Bb	**25%**	**100%**
p83	**54%**	**95%**
p39	**61%**	**99%**
OspC	**49%**	**96%**
p58 (BB_A34)	**21%**	**98%**
p21 (BB_K53)	**9%**	**99%**
p20 (BB_Q03)	**7%**	**100%**
p19 (BB_N38)	**9%**	**99%**
p18 (BB_P38)	**22%**	**99%**

Evaluation of 617 sera from

- suspected LD
- clinically characterised LD
- control groups (blood donors, pregnant women, other infections)

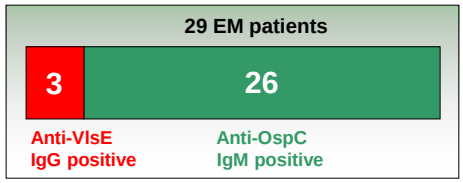
IgM		
Antigen	**Prevalence***	**Specificity***
VlsE Bb	**5%**	**99%**
p39 Ba	**16%**	**99%**
OspC Ba	**88%**	**99%**
OspC Bb	**77%**	**99%**
OspC Bg	**84%**	**97%**

*referring to anti-Borrelia EUROLINE-WB

EL-RN-AT: 100% hit rate for EM patients

Scientific presentation at the 12th ICLB, Slovenia, September 2010

Study group: 29 patients with Lyme disease and Erythema migrans
Test system: Anti-Borrelia EUROLINE-RN-AT (IgG, IgM)



- Serological hit rate: 100%
- Parallel testing of IgG and IgM recommended!

Correlation ELISA ↔ EUROLINE-RN-AT

Sera: 58 clinically and/or serologically precharacterized sera
(INSTAND, Labquality, IQS)

ELISA	n	EUROLINE-RN-AT	n
positive/borderline	33	positive	30
		negative/borderline	3
negative	25	positive	0
		negative/borderline	25

ELISA	n	EUROLINE-RN-AT	n
positive/borderline	73	positive	7
		negative/borderline	6
negative	46	positive	0
		negative/borderline	46

ELISA	n	EUROLINE-RN-AT	n
positive/borderline	33	positive	31
		negative/borderline	2
negative	25	positive	0
		negative/borderline	25

- 100% agreement according to serological two-step strategy
- No isolated positive blot results

The EUROIMMUN Anti-Borrelia EUROLINE-RN-AT (IgG, IgM) correlate 95–97% with the results from INSTAND and Labquality quality assurance schemes

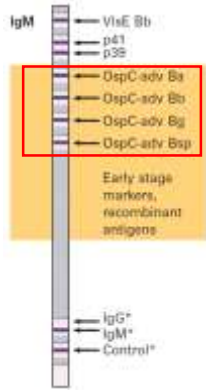
n = 40		Designated result from INSTAND, Labquality (IgG)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia EUROLINE-RN-AT (IgG)	positive	26	0	1
	borderline	0	0	1
	negative	1	0	13

n = 33		Designated result from INSTAND, Labquality (IgM)		
		positive	borderline	negative
EUROIMMUN Anti-Borrelia EUROLINE-RN-AT (IgM)	positive	6	0	1
	borderline	0	0	0
	negative	0	0	26

Advantages Anti-Borrelia EUROLINE-RN-AT

- Antigens at **defined positions** (easy visual evaluation)
- **High specificity** (most important criterion regarding serological two-step strategy)
- At the same time **high sensitivity** (100% hit rate for EM patients; Scheper et al., presentation at the ICLB 2010)
- EUROIMMUN innovations: **lipid antigens** and unique **rec. designer antigens**
- Contains **OspC and VlsE** of all relevant pathogenic genospecies (B. burgdorferi, B. afzelii, B. garinii)
- Excellent performance in **external QAS**
- **Short incubation** time: 30/30/10
- IgG test also suitable for analysis of **CSF/serum pairs**
- Convenient and reliable **automated processing** (EUROBlotMaster), documentation (EUROBlotScanner, EUROBlotCamera), and evaluation (EUROLineScan software)

NEW Anti-Borrelia EUROLINE-RN-AT-adv (IgM)



Product release: June 15th, 2012

Cat. number: DN 2131-2 M
Formats: 32 strips, 240 strips

Includes *OspC advanced* from:
B. afzelii
B. burgdorferi
B. garinii
B. spielmanii

Incubation
EUROBlotMaster: EURO_02
Incubation scheme: 30/30/10
Serum dilution: 1:51
Conjugate dilution: 1:10

EUROLineScan: Evaluation possible with version 3.3.10 or later

Product overview: Anti-Borrelia blots

Test	Anti-Borrelia EUROLINE-RN-AT (IgM)	Anti-Borrelia EUROLINE-RN-AT (IgG)	Anti-Borrelia EUROLINE-RN-AT-adv (IgM)	Anti-Borrelia EUROLINE-WB (IgG / IgM)	Anti-Borrelia Western blots (IgG / IgM)
Antigen / substrate	OspC (Bg, Bb, Ba), p39, p41, VlsE (Bb)	p18, p19, p20, p21, p58, OspC, p39, p41, p83, Lipid (Bb, Ba), VlsE (Bg, Bb, Ba)	OspC-adv (Bsp, Bg, Bb, Ba), p39, p41, VlsE (Bb)	SDS extract B. afzelii plus rec. VlsE	SDS extracts of • B. afzelii • B. burgdorferi • B. garinii
Cat. No.	DN 2131 M	DN 2131 G	DN 2131-2 M	DY 2131-1 G/M	DY 2131 G/M DY 2132 G/M DY 2134 G/M

CSF diagnostics

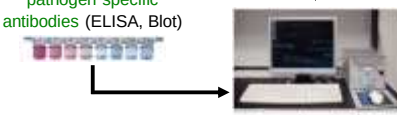
Diagnosis of Neuroborreliosis: Principle

Patient with neurological symptoms

Blood and CSF withdrawn at the same time (within ~ 1h)

Determination of total Ig and albumin concentration (nephelometry)

Determination of pathogen specific antibodies (ELISA, Blot)



Software-based calculation of CSQ_{xx}

Anti-Borrelia CSF ELISA

Anti-Borrelia plus VlsE ELISA (IgG)	EI 2132-9601-L G
Anti-Borrelia ELISA (IgM)	EI 2132-9601-L M

Calibration: 4 point / optional 5 (IgM) or 6 point (IgG)

Sample dilutions: Serum 1:404 / CSF 1:2

Incubation: 60/60/15 (room temperature)

Result interpretation:

CSQrel. < 0.6	implausible result
CSQrel. < 1.3	normal range
CSQrel. 1.3 - 1.5	borderline range
CSQrel. > 1.5	indication of pathogen-specific antibody production in CNS

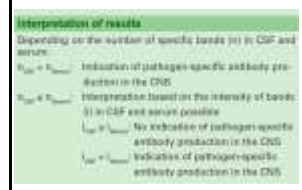
- Excellent correlation of the calculated CSQrel. with clinically proved neuroborreliosis (sensitivity > 95 %)
- Over 95 % of patients with other neurological diseases have non-pathological Borrelia specific CSQrel. (specificity > 95 %)
- Best pass rates in the neuroborreliosis QAS by INSTAND*

**other manufacturers: Virion/Serion, Virotech, Mikrogen, Dade Behring, DiaSorin*

CSF diagnostics with Anti-Borrelia EL-RN-AT (IgG)

CSF

Serum



Advantages:

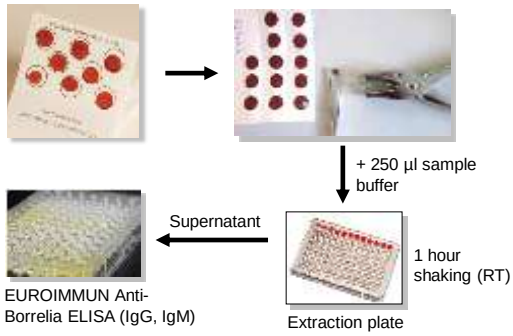
- High specificity (100%) and sensitivity (97%)
- Broad range of antigens
- Standardised dilution for CSF (1:4)
- Low sample volumes for CSF (250 µl)
- Short incubation times (≈ 300 min)
- Automated incubation (EBM) and evaluation (ELS)

Summary

- Lyme disease is a **clinical diagnosis**, based on symptoms!
- Serological **two-step strategy** is recommended: Sensitive screening + specific confirmation
- **VlsE** (IgG antibodies) and **OspC** (IgM antibodies) are the most important antigens
- ELISA and Blot can be used with CSF samples to detect **intrathecally produced** antibodies
- **New EUROIMMUN tests**:
  Anti-Borrelia Select ELISA (IgG, IgM)
  Anti-Borrelia EUROLINE-RN-AT-adv (IgM)

Under Development

Antibody extraction from dried blood spots



Comparison blood spots ↔ serum

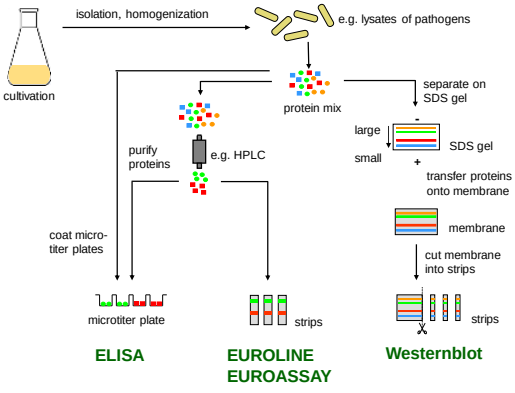
Cohort:
572 forest workers of various districts in Poland

	Dried blood spots vs. serum*	
	IgG ELISA	IgM ELISA
Sensitivity (%)	99.5	100
Specificity (%)	100	99.7
Positive predictive value (%)	100	99.1
Negative predictive value (%)	99.7	100

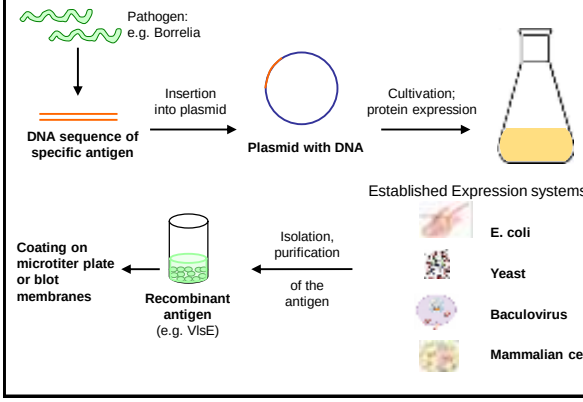
* excluding borderline results

Herbst et al., 12th International Conference on Lyme Borreliosis, Ljubljana, Slovenia (2010)

Antigen Source: Native Proteins



Antigen Source: Recombinant Proteins



Thank you!