EUROIMMUN
a PerkinElmer company

Medizinische
Labordiagnostika
AG

Professional serological Borrelia diagnostics

using recombinant and native antigens

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com

Lyme borreliosis

Borrelia are the causative agent of Lyme borreliosis, a bacterial disease which is transmitted through bites from ticks of the genus Ixodes. The most important human pathogenic Borrelia genospecies are together termed as "Borrelia burgdorferi sensu lato". These include Borrelia afzelii, Borrelia burgdorferi sensu stricto and Borrelia garinii. Infection with Borrelia can manifest itself dermatologically, neurologically or through internal disorders. The clinical expression of borreliosis is divided into three stages:

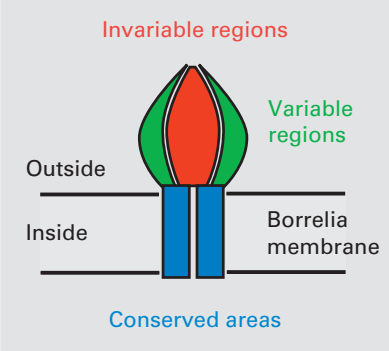
Stage I: In the foreground is a characteristic **erythema migrans**, which occurs a few days to several weeks after the infection and spreads radially with central clearing. This is often accompanied by influenza-like general symptoms, such as fever, shivering, headaches and vomiting. In rare cases, bulging nodular skin infiltrates develop, which consist predominantly of lymphocytes (lymphadenosis cutis benigna). Serologically, antibodies against Borrelia of the immunoglobulin classes IgM and IgG can be detected. A stage I infection can be followed by spontaneous healing or can develop into a general borreliosis (stages II and III).

Stage II: This stage of the disease, characterised by **neurological, cardiac** (e.g. myocarditis) **and rheumatological** (e.g. arthritis) **manifestations**, develops several weeks to months after the tick bite. The attack on the nervous system frequently appears as radiculitis (Bannwarth's syndrome), mono- or plexusneuritis, and motor (mostly facial paralysis) and sensory disorders. Meningitis, myelitis, encephalitis and cerebral vasculitis occur less frequently. IgG antibodies against Borrelia burgdorferi can be detected in more than 90 % of stage II patients.

Stage III: The characteristic manifestation of the late stage of the disease, months to years after the occurence of the Borrelia infection, is a chronic involvement of the joints, skin and CNS. Destructive arthritis develops in many cases, predominantly in the large joints and mostly in the knee joints. A typical acrodermatitis chronica atrophicans is formed in the epidermis of the extremities. IgG antibodies can be detected in 90 %–100 % of stage III patients, while IgM antibodies no longer play a role.

The diagnosis of Lyme disease is based on the patient anamnesis, clinical findings and the detection of antibodies against Borrelia antigens. Serology played a leading role in the discovery of Lyme disease and nowadays helps to achieve a diagnostic breakthrough for many patients. The prevalence of antibodies against Borrelia in Germany is around 20 % in the case of forest workers, and below 5 % for town dwellers. Following a tick bite, a serological baseline status should be determined and a check made for Borrelia antibodies in the ensuing weeks. For the diagnosis of neuroborreliosis, the determination of intrathecal synthesised antibodies is of decisive importance.

VlsE: The main antigen for Borrelia serology

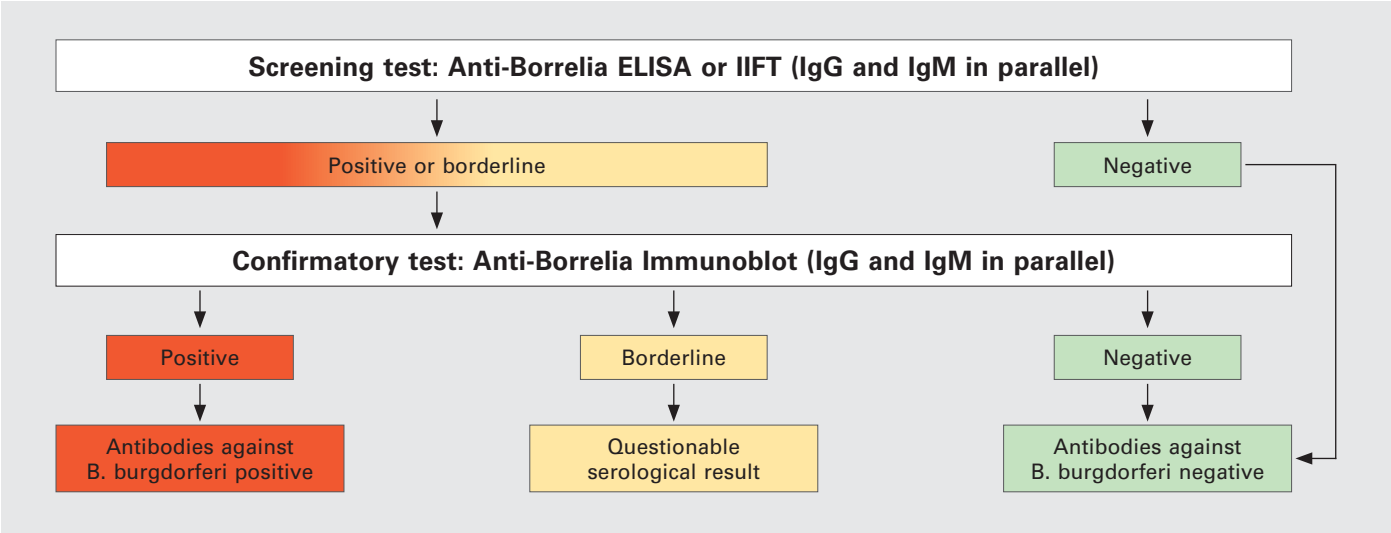


VlsE on the Borrelia surface

VlsE (variable major protein-like sequence, expressed) is a **surface protein of Borrelia burgdorferi** which plays a key role in the survival strategy of Borrelia. After penetration into the host organism, Borrelia bacteria constantly change their surface-expressed VlsE and, in this way, try to escape recognition and elimination by the immune system. Borrelia do not express VlsE when cultivated, but only in vivo under immunological stress. Therefore the antigen can only be produced using recombinant techniques.

The VlsE protein is divided into several sections: conserved regions, which serve as transmembrane domains and anchor VlsE in the bacterial membrane, as well as variable and invariable regions. The variable regions of VlsE facing outwards are constantly changed by recombination, whereby the attacking immune system consistently encounters new, altered antigen epitopes. The invariable regions are masked by the variable regions and, in living Borrelia bacteria, are protected from direct attack by the immune system. When deceased Borrelia bacteria are processed by antigen-presenting cells, the complete VlsE protein is presented to the immune system and the host also forms **antibodies against the invariable and conserved regions of VlsE**. These antibodies are **highly suitable for diagnosis of borreliosis because of the high level of conservation of their target antigens:** Using monospecific test systems (IIFT, ELISA, EUROLINE-WB, EUROLINE) Lyme borreliosis can be diagnosed in 85 % of cases, regardless of the species, through the detection of antibodies against VlsE alone.

Serological two-tier strategy in infections with Borrelia burgdorferi



EUROIMMUN is one of the leading manufacturers of reagents for the diagnosis of Borrelia burgdorferi infections. EUROIMMUN provides screening and confirmatory tests for the determination of antibodies against Borrelia burgdorferi which allow a qualified **two-tier diagnostic procedure** as **recommended by the German Society for Hygiene and Microbiology, the Robert Koch Institute and the Centers for Disease Control and Prevention (USA)**.

In the first step a preferably **sensitive screening test (ELISA or IIFT)** which also detects antibodies against the Borrelia major antigen VlsE is performed. During the early stage of borreliosis, the test result may still be negative. A second analysis should therefore be carried out after one to two weeks if borreliosis is indicated. In suspected cases of neuroborreliosis Borrelia-specific antibodies are investigated simultaneously in CSF and serum.

If the screening test result is positive or borderline, it should be followed up by a **confirmatory test**. The **immunoblot** is the **method of choice** because it allows a reliable differentiation between antibodies against the individual specific and unspecific antigens. By printing an additional antigen band with VlsE onto the strip, the sensitivity of the IgG test can be increased, e.g. from 40% to 62% in erythema migrans. The reaction pattern of the different antigen bands is decisive for the diagnosis of borreliosis and the evaluation of the infection stage. Positive reactions of specific antigen bands in combination with significant clinical symptoms are considered to be an indication of an acute or past infection. If the immunoblot shows a negative result for IgG and IgM (after a positive screening test), an infection can generally be excluded. If the clinical suspicion of borreliosis persists, components of alternative Borrelia strains are used as test substrates in individual cases. Borderline immunoblot results combined with clinical symptoms should be followed up by further tests to monitor the disease course. For computer-aided evaluation of the incubated immunoblot strips and for archiving of the results EUROIMMUN offers the computer programms EUROLineScan and EUROLabOffice. Possible result interpretations of anti-Borrelia immunoblots are outlined in the following table.

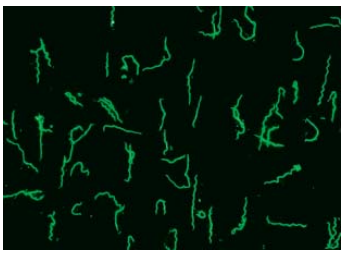
Serological result		Interpretation
IgG	IgM	
Borderline or negative	**Borderline or negative**	No reliable detection of specific Borrelia antibodies. In the case of continued clinical suspicion, retest after one or two weeks, if required (possibility of retarded antibody formation).
Borderline or negative	**Positive**	Detection of specific Borrelia antibodies indicates an early infection stage. Presence of chronic borreliosis unlikely. Possibility of a residual result with persisting IgM antibodies after successful therapy.
Positive (1-2 specific bands)	**Borderline or negative**	Detection of specific Borrelia antibodies indicates an early infection stage. Further tests for monitoring the disease course recommended to exclude past infections. The clinical symptoms should be taken into account!
Positive (1-2 specific bands)	**Positive**	Detection of specific Borrelia antibodies indicates an early infection stage. Also possibility of late manifestations, although untypical. Past infections with persisting IgM only occur in exceptional cases, particularly after therapy. Serological monitoring of the disease course, if required.
Positive (>2 specific bands)	**Borderline or negative**	Detection of specific Borrelia antibodies indicates chronic borreliosis (late clinical manifestation). An early infection stage is unlikely. A definitive differentiation between a florid infection and a residual result is not possible. Serological monitoring of the disease course, if required.
Positive (>2 specific bands)	**Positive**	Detection of specific Borrelia antibodies indicates chronic borreliosis (late clinical manifestation). An early infection stage in secondary infections cannot be excluded. Residual antibodies after a recently cured borreliosis are possible (persisting IgM).

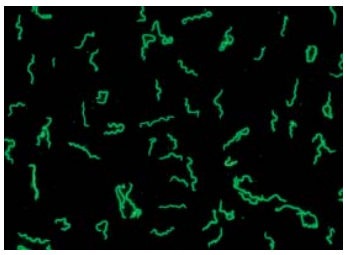
Note: Antibodies against several different variants of an antigen (e.g. VlsE, lipids) are considered as one band.

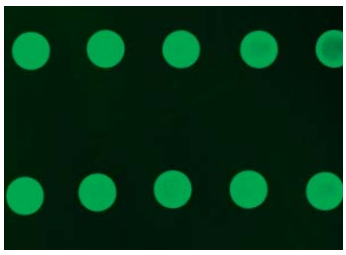
EUROIMMUN
a PerkinElmer company

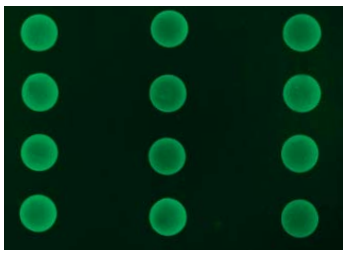
Medizinische
Labordiagnostika
AG

Screening test I: Anti-Borrelia IIFT plus VlsE and OspC (EUROPLUS)


Borrelia afzelii


Borrelia burgdorferi


OspC antigens


VlsE antigens

By combining bacteria smears (B. afzelii and B. burgdorferi) with recombinant VlsE and purified OspC, the serological hit rate is increased compared to conventional immunofluorescence tests. In cell smears the VlsE antigen is missing because Borrelia can only express VlsE in vivo and not in cell cultures. With its broad antigen spectrum the EUROPLUS: Anti-Borrelia IIFT plus VlsE and OspC is able to provide a very high sensitivity. It is therefore ideally suited for screening.

Clinical data: In a study 577 Polish forest workers and 100 healthy blood donors were tested for antibodies against Borrelia antigens. For the substrate combination of Borrelia afzelii and Borrelia burgdorferi a sensitivity of 94% (IgG), and 77% (IgM) was found (reference: 137 (IgG) and 34 (IgM) sera were positive in ELISA and westernblot). Using BIOCHIPs coated with VlsE or OspC these values can be increased to 98% and 91%. The single antigens showed a specificity of 100% (VlsE) and 98% (OspC) (reference: 234 (IgG) and 181 (IgM) sera were negative in ELISA and westernblot).

Anti-Borrelia antigens	Sensitivity (precharact. panel)		Prevalence blood donors	
	IgG n=137	IgM n=34	IgG n=87	IgM n=92
Borrelia afzelii	94%	77%	28%	3%
Borrelia burgdorferi	93%	71%	28%	3%
VlsE	89%	–	5%	–
OspC	–	85%	–	4%
B. afzelii + B. burgd.	94%	77%	28%	3%
B. afzelii + B. burgd. + VlsE	98%	–	29%	–
B. afzelii + B. garinii + OspC	–	91%	–	7%

Reference range: In healthy blood donors (origin of samples: Germany) the following antibody prevalences were obtained (titers: IgG >1:100, IgM >1:10).

Anti-Borrelia antigens	Prevalence IgG		Prevalence IgM	
VlsE	5.0%	(n=201)	–	–
OspC	–	–	1.5%	(n=68)
Borrelia afzelii	17.0%	(n=150)	3.0%	(n=159)
Borrelia burgdorferi	18.0%	(n=150)	4.0%	(n=159)

Technical data

Sample dilution
IgG
Qualitative determination: 1:100; **quantitative determination:** 1:100, 1:1000, etc.
There is no upper limit to the measurement range.
IgM
Qualitative determination: 1:10; **quantitative determination:** 1:10, 1:100, etc.
There is no upper limit to the measurement range.

Test procedure 30 min / 30 min (room temperature). Fully automatable.

Reagents Ready for use, with the exception of the PBS Tween buffer (for dilution and washing steps).

EUROIMMUN IIFT test systems for Borrelia diagnostics

Order number	IIFT test system	Antigens
FI 2131-1 G	EUROPLUS: Anti-Borrelia afzelii IIFT plus VlsE (IgG)	Smears of Borrelia afzelii and EUROPLUS BIOCHIPs with the antigen VlsE
FI 2131-2 M	EUROPLUS: Anti-Borrelia afzelii IIFT plus OspC (IgM)	Smears of Borrelia afzelii and EUROPLUS BIOCHIPs with the antigen OspC
FI 2132 G/M	Anti-Borrelia burgdorferi IIFT (IgG/IgM)	Smears of Borrelia burgdorferi (CH)
FI 2133 G/M	Anti-Borrelia burgdorferi IIFT (IgG/IgM)	Smears of Borrelia burgdorferi (USA)
FI 2134 G/M	Anti-Borrelia garinii IIFT (IgG/IgM)	Smears of Borrelia garinii
FI 2136-1 G/M	EUROPLUS: Anti-Borrelia afzelii and burgdorferi IIFT plus VlsE und OspC (IgG/IgM)	Smears of Borrelia afzelii, B. burgdorferi (USA) and EUROPLUS BIOCHIPs with the antigens VlsE and OspC
FI 2138-2 G/M	Anti-Borrelia-afzelii, burgdorferi and garinii IIFT (IgG/IgM)	Smears of Borrelia afzelii, B. burgdorferi (CH), B. burgdorferi (USA) and B. garinii

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com

EUROIMMUN
a PerkinElmer company

Medizinische
Labordiagnostika
AG

Screening test II: Anti-Borrelia plus VlsE ELISA (IgG) and Anti-Borrelia ELISA (IgM)

Reference range: Levels of anti-Borrelia burgdorferi antibodies were measured in a cohort of 500 healthy blood donors (University Hospital of Luebeck, Germany) using the EUROIMMUN ELISA. With a cut-off value of 20 RU/ml, 5 % (IgG) and 2 % (IgM) of blood donors were anti-Borrelia positive, in agreement with the known infection level in adults.

Reproducibility: Coefficients of variation (CVs) were determined using data from three sera with values at different points on the standard calibration curve. The intra-assay CVs (each 20 determinations) ranged from 3.5 % to 3.6 % (IgG) and 2.9 % to 4.3 % (IgM). The intra-assay CVs (4 determinations on 6 different days) ranged from 3.6 % to 3.8 % (IgG) and 4.7 % to 6.9 % (IgM).

Clinical data: 364 sera from patients with clinically characterised borreliosis in different disease stages and 573 control sera (53 patients with other infectious diseases, 20 patients with rheumatic diseases, 500 healthy blood donors) were screened using the EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG) and the EUROIMMUN Anti-Borrelia ELISA (IgM). In the parallel investigation of IgG and IgM antibodies the test systems achieved a sensitivity of 91 % to 100 %, depending on the patient cohort.

Panel	n	EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG) Anti-Borrelia ELISA (IgM)		
		IgG [%]	IgM [%]	IgG/IgM [%]
Erythema migrans	205	76	68	**91**
Neuroborreliosis	80	90	49	**96**
Borrelia arthritis	49	84	43	**94**
Acrodermatitis chron. atrop.	14	93	21	**93**
Facial paralysis	16	100	50	**100**

Prevalence: The prevalence of anti-Borrelia antibodies in the control panels (other infectious diseases: anti-CMV positive n = 18, anti-EBV positive n = 28, anti-Toxoplasma positive n = 7; rheumatic diseases: APF positive n = 10, RF (IgM) positive n = 10) corresponds to the data found in literature (Robert Koch Institute, Epidemiological Bulletin 14/98).

Panel	n	EUROIMMUN Anti-Borrelia plus VlsE ELISA (IgG) Anti-Borrelia ELISA (IgM)	
		IgG [%]	IgM [%]
Other infectious diseases	53	13	11
Rheumatic diseases	20	15	0
Blood donors	500	5	2
Total	**573**	**6**	**2**

Agreement with quality assessment results: 156 (IgG) and 172 (IgM) clinically characterised patient samples (quality assessment: EQUALIS, Sweden; INSTAND and IQS Germany, LABQUALITY, Finland) were investigated using the EUROIMMUN Anti-Borrelia ELISA (IgG and IgM). The results of both ELISAs were 99 % in agreement with the target values given by the providers of the quality assessment schemes (borderline sera excluded).

n = 181		Target (IgG) EQUALIS, INSTAND, IQS, LABQUALITY		
		pos.	borderl.	neg.
EUROIMMUN Anti-Borrelia-plus-VlsE ELISA (IgG)	pos.	101	1	1
	borderl.	1	2	1
	neg.	0	0	74

n = 195		Target (IgM) EQUALIS, INSTAND, IQS, LABQUALITY		
		pos.	borderl.	neg.
EUROIMMUN Anti-Borrelia ELISA (IgM)	pos.	45	1	1
	borderl.	1	1	3
	neg.	0	2	141

Technical data

Sample dilution	Serum or plasma; 1 : 101 in sample buffer.
Calibration	Quantitative, in relative units per milliliter (RU/ml). **Calibration serum 1:** 200 RU/ml, **Calibration serum 2:** 20 RU/ml, **Calibration serum 3:** 2 RU/ml.
Interpretation (IgG, IgM)	**< 16 RU/ml:** negative, **≥ 16 to < 22 RU/ml:** borderline, **≥ 22 RU/ml:** positive. Optional semiquantitative evaluation.
Test procedure	30 min / 30 min / 15 min (room temperature). Fully automatable.

EUROIMMUN ELISA test systems for Borrelia diagnostics

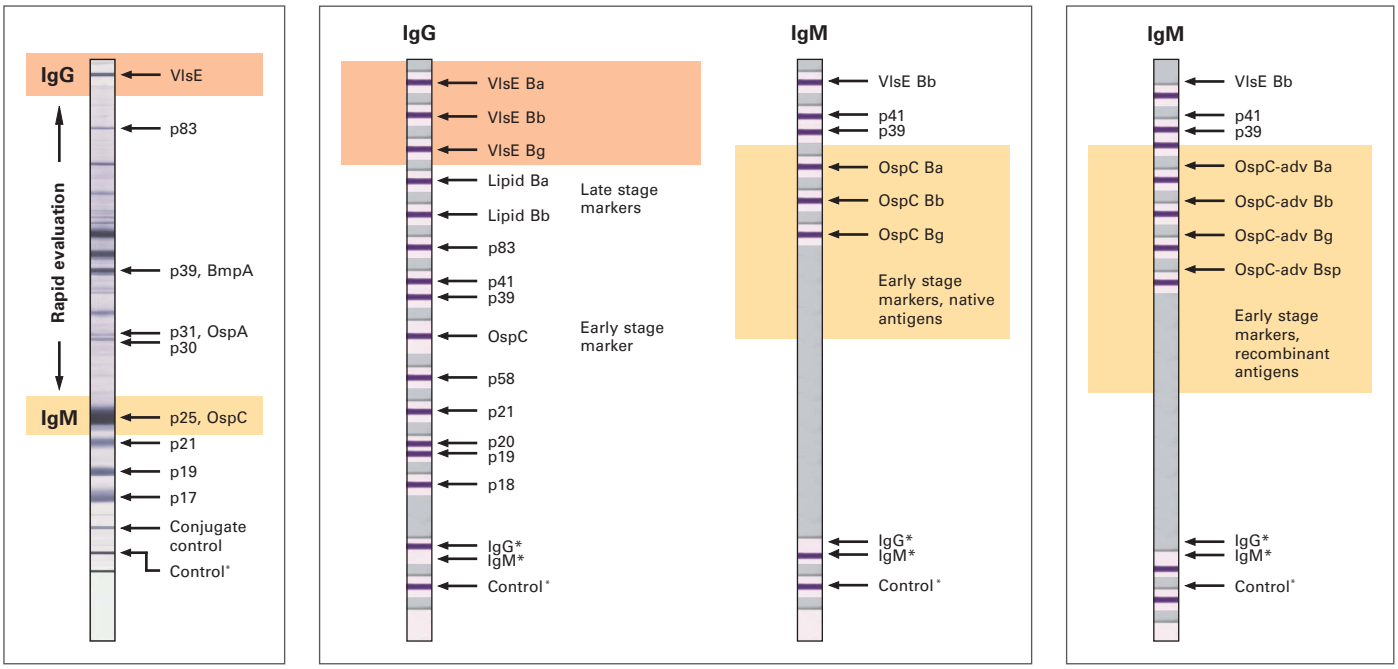
Order number	ELISA test system	Antigens
EI 2132-9601 M	Anti-Borrelia ELISA (IgM)	Whole antigen, SDS extract of Borrelia burgdorferi sensu stricto, B. garinii and B. afzelii
EI 2132-9601-2 G	Anti-Borrelia plus VlsE ELISA (IgG)	Whole antigen, SDS extract of Borrelia burgdorferi sensu stricto, B. garinii and B. afzelii plus recombinant VlsE of B. burgdorferi sensu stricto
EI 2132-9601-10 G	Lyme Trace ELISA (IgG)	Recombinant VlsE of Borrelia burgdorferi sensu stricto and B. afzelli

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com

EUROIMMUN
a PerkinElmer company

Medizinische
Labordiagnostika
AG

Confirmatory tests: Anti-Borrelia Immunoblots (EUROLINE-WB and EUROLINE-RN-AT and EUROLINE-RN-AT-adv)



Anti-Borrelia-EUROLINE-WB

Anti-Borrelia-EUROLINE-RN-AT

Anti-Borrelia-EUROLINE-RN-AT-adv

Bb Borrelia burgdorferi, Ba Borrelia afzelii, Bg Borrelia garinii, Bsp Borrelia spielmanii, * Control bands for all incubation steps

I. EUROLINE-WB: A combination of line blot and westernblot

The **Anti-Borrelia EUROLINE-WB** combines the advantages of both methods: **EUROLINE and Westernblot.** A whole-antigen extract from Borrelia afzelii together with a membrane chip containing recombinant VlsE as an early-stage disease marker (regardless of the species) enable the identification of atypical reactions and ensure a high sensitivity. Presence of a positive VlsE (IgG) or p25/OspC antigen band (IgM) allows at-a-glance evaluation.

Clinical data: A panel of 115 clinically defined patient samples was investigated using the EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG, IgM). The following prevalences were detected (only positive results were taken into account):

Panel	n	EUROIMMUN Anti-Borrelia EUROLINE-WB (IgG, IgM)		
		IgG [%]	IgM [%]	IgG/IgM [%]
Erythema migrans	47	51	57	83
Neuroborreliosis	27	78	33	81
Borrelia arthritis	33	94	6	94
Acrodermatitis chronica atrophicans	8	100	13	100

Technical data

Sample dilution Serum or plasma; 1:51 in universal buffer.

Test procedure 30 min / 30 min / 10 min (room temperature).

Automation Compatible with all commercial blot processing systems, e.g. the EUROBlotOne or EUROBlotMaster from EUROIMMUN. Computer-aided evaluation and archiving of results using the program EUROLineScan.

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com

EUROIMMUN
a PerkinElmer company

Medizinische
Labordiagnostika
AG

II. EUROLINE-RN-AT: Unique combination of Borrelia-specific antigens

The Anti-Borrelia EUROLINE-RN-AT provides a comprehensive range of diagnostically relevant Borrelia antigens in a user-friendly line blot format. In addition to the most important serological early phase markers OspC and VlsE from different genospecies, it includes highly specific p39 (Bmp) and the late phase marker p83. The test also contains native immunogenic lipids which were extracted in native form from Borrelia and printed as lines onto membranes.

Furthermore, immunoreactive antigens with a high specificity for the detection of anti-Borrelia antibodies were produced by means of bioinformatic analysis of the Borrelia genome and molecular designing.

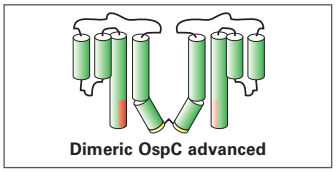
Anti-Borrelia antigens	EUROLINE-RN-AT, IgG (n=617*)	
	Sensitivity [%]	Specificity [%]
VlsE B. afzelii	65.5	98.6
VlsE B. burgdorferi	88.5	98.6
VlsE B. garinii	67.6	95.3
Lipid B. afzelii	25.1	100.0
Lipid B. burgdorferi	25.1	99.6
p83	53.7	95.3
p39	61.3	98.6
OspC	48.7	95.7
p58	20.7	97.5
p21	8.9	99.3
p20	7.1	100.0
p19	9.1	99.3
p18	22.4	99.3

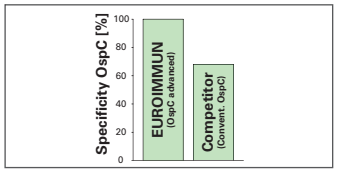
Anti-Borrelia antigens	EUROLINE-RN-AT, IgM (n=644*)	
	Sensitivity [%]	Specificity [%]
VlsE B. burgdorferi	4.9	99.4
p39	15.9	99.0
OspC native B. afzelii	88.2	99.0
OspC native B. burgdorferi	77.1	99.2
OspC native B. garinii	84.1	96.8

*Analysed sera (IgG/IgM): 274/236 patients with active borreliosis, 198/204 patients with suspected borreliosis, 28/45 patients with other infections, 117/159 healthy blood donors.

III. EUROLINE-RN-AT-adv: 30% more specific due to OspC advanced

Antibodies against OspC are the most important serological marker for the detection of Borrelia infections (sensitivity: up to 90%). Numerous research results have shown that native OspC purified from Borrelia (dimeric form) is the ideal antigen substrate. However, the standardised production of native OspC dimers is complicated, which means that the use of recombinant, monomeric OspC is often preferred. Since Borrelia infections cannot be detected using only moderate amounts of monomeric OspC, high concentrations must be employed. In this way, an acceptable detection rate is achieved, but this comes at the price of a higher number of unspecific reactions. Scientists from EUROIMMUN AG have successfully produced recombinant covalently bonded dimeric OspC (European Patent No. EP 2 199 303 B1) by genetic engineering. This **OspC advanced is 30% more specific than conventional recombinant OspC** (Probst et al., ICLB, 2010, see figure), with the same sensitivity as native OspC (Ott et al., ECCMID/ICC, 2011). The OspC advanced is used in the **EUROIMMUN Anti-Borrelia EUROLINE-RN-AT-adv (IgM)**. This line blot allows reliable detection of antibodies against all relevant human pathogenic Borrelia genospecies, since OspC advanced from B. spielmanii is also included.


Dimeric OspC advanced



Panel	n	Prevalence of anti-OspC (IgM) [%]					
		B. afzelii		B. burgdorferi		B. garinii	
		adv	native	adv	native	adv	native
Active borreliosis	150	65	61	69	54	66	64
Past infection (persisting IgM)	16	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

Technical data

Sample dilution **Serum or plasma**; 1:51 in universal buffer.
CSF/serum pair, in universal buffer: CSF 1:4, Serum dilution calculated with $LSQ_{ges.}$ or $LSQ_{lim.}$.

Test procedure **Serum or plasma** 30 min/30 min/10 min; **CSF/serum pair** 180 min/60 min/20 min; room temperature.

Automation Compatible with all commercial blot processing systems, e.g. the EUROBlotOne or EUROBlotMaster from EUROIMMUN. Computer-aided evaluation and archiving of results using the program EUROLineScan.

EUROIMMUN immunoblots for Borrelia diagnostics

Order number	Immunoblot	Antigens
DN 2131 G	Anti-Borrelia EUROLINE-RN-AT (IgG)*	p18, p19, p20, p21, p58, OspC, p39, p41, p83, LBb, LBa, VlsE Bg, VlsE Bb, VlsE Ba
DN 2131 M	Anti-Borrelia EUROLINE-RN-AT (IgM)*	OspC Bg, OspC Bb, OspC Ba, p39, p41, VlsE Bb
DN 2131-2 M	Anti-Borrelia EUROLINE-RN-AT-adv (IgM)*	OspC-adv Bsp, OspC-adv Bg, OspC-adv Bb, OspC-adv Ba, p39, p41, VlsE Bb
DY 2131-1 G/M	Anti-Borrelia EUROLINE-WB (IgG/IgM)	Whole antigen, SDS extract of Borrelia afzelii plus recombinant VlsE
DY 2131 G/M	Anti-Borrelia afzelii Westernblot (IgG/IgM)	Whole antigen, SDS extract of Borrelia afzelii
DY 2132 G/M	Anti-Borrelia burgdorferi Westernblot (IgG/IgM)	Whole antigen, SDS extract of Borrelia burgdorferi sensu stricto
DY 2134 G/M	Anti-Borrelia garinii Westernblot (IgG/IgM)	Whole antigen, SDS extract of Borrelia garinii

* Also suited for analysis of CSF/serum pairs.

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com

EUROIMMUN
a PerkinElmer company

Medizinische
Labordiagnostika
AG

CSF diagnostics

Borrelia-specific intrathecal antibodies

I. EUROIMMUN CSF ELISA

- Standardised dilution and incubation schemes enable an efficient, standardised automation
- 4-point standard curve for highest accuracy; extended measurement range owing to optionally usable, additional calibrators (included in the test kit)
- Very good reproducibility of results over the total measurement range
- High clinical sensitivity and specificity (sensitivity >95 % in clinically confirmed cases of neuroborreliosis; specificity >95 % in patients with other neurological diseases)
- Excellent correlation with results from quality assessment schemes (INSTAND e.V.)
- Automated calculation of results (evaluation software: EUROLabCSF)
- CSF/serum control pairs available

II. Anti-Borrelia EUROLINE-RN-AT (IgG or IgM) Anti-Borrelia EUROLINE-RN-AT-adv (IgM)

- High specificity (100 %) and sensitivity (>97 %), determined using clinically characterised CSF/serum pairs
- Wide antigen spectrum
- One fixed dilution factor for CSF (1:4) — no complicated calculations are necessary
- Short incubation periods (test result after approx. 300 min)
- Small sample volumes for CSF (250 µl)
- Automatic processing with the EUROBlotMaster or EUROBlotOne (adapted incubations for CSF/serum pairs)
- Computer-supported evaluation using EUROLineScan (available from EUROIMMUN)

Activity and therapy marker

Detection of the CXCL13 antigen: EUROIMMUN CXCL13-ELISA

- First test to be CE-labelled
- Early-stage marker for acute neuroborreliosis: high concentrations of CXCL13 can frequently be measured already at the start of the illness, often even before antibodies against Borrelia are detectable
- Marker for monitoring the disease course: with successful antibiotic treatment, the CXCL13 concentration in the CSF sinks rapidly
- Differentiation between acute and past neuroborreliosis: A pathological ASI/LSQrel, together with
  - a low CXCL13 level in CSF: indicates that an acute neuroborreliosis is unlikely
  - a high CXCL13 level in CSF: indicates that an acute neuroborreliosis is very likely
- 6 calibrators and 2 controls included in the test

EUROIMMUN test systems for CSF diagnostics in neuroborreliosis

Order number	Test system	Antigens
EI 2132-L G	Anti-Borrelia plus VlsE ELISA (IgG) Antibody detection in CSF	Whole antigen, SDS extract of Borrelia burgdorferi sensu stricto, B. garinii and B. afzelii plus recombinant VlsE of B. burgdorferi sensu stricto
EI 2132-L M	Anti-Borrelia ELISA (IgM) Antibody detection in CSF	Whole antigen, SDS extract of Borrelia burgdorferi sensu stricto, B. garinii and B. afzelii
DN 2131 G	Anti-Borrelia EUROLINE-RN-AT (IgG)	p18, p19, p20, p21, p58, OspC, p39, p41, p83, LBb, LBa, VlsE Bg, VlsE Bb, VlsE Ba
DN 2131 M	Anti-Borrelia EUROLINE-RN-AT (IgM)	OspC Bg native, OspC Bb native, OspC Ba native, p39, p41 and VlsE Bb
DN 2131-2 M	Anti-Borrelia EUROLINE-RN-AT-adv (IgM)	OspC-adv Bsp, OspC-adv Bg, OspC-adv Bb, OspC-adv Ba, p39, p41 and VlsE Bb
EQ 6811-L	CXCL13 ELISA	Monoclonal anti-CXCL13 antibody

EUROIMMUN AG · Seekamp 31 · 23560 Lübeck (Germany) · Tel +49 451/5855-0 · Fax 5855-591 · info@euroimmun.de · www.euroimmun.com
HI_2132_I_UK_C10, 11/2018