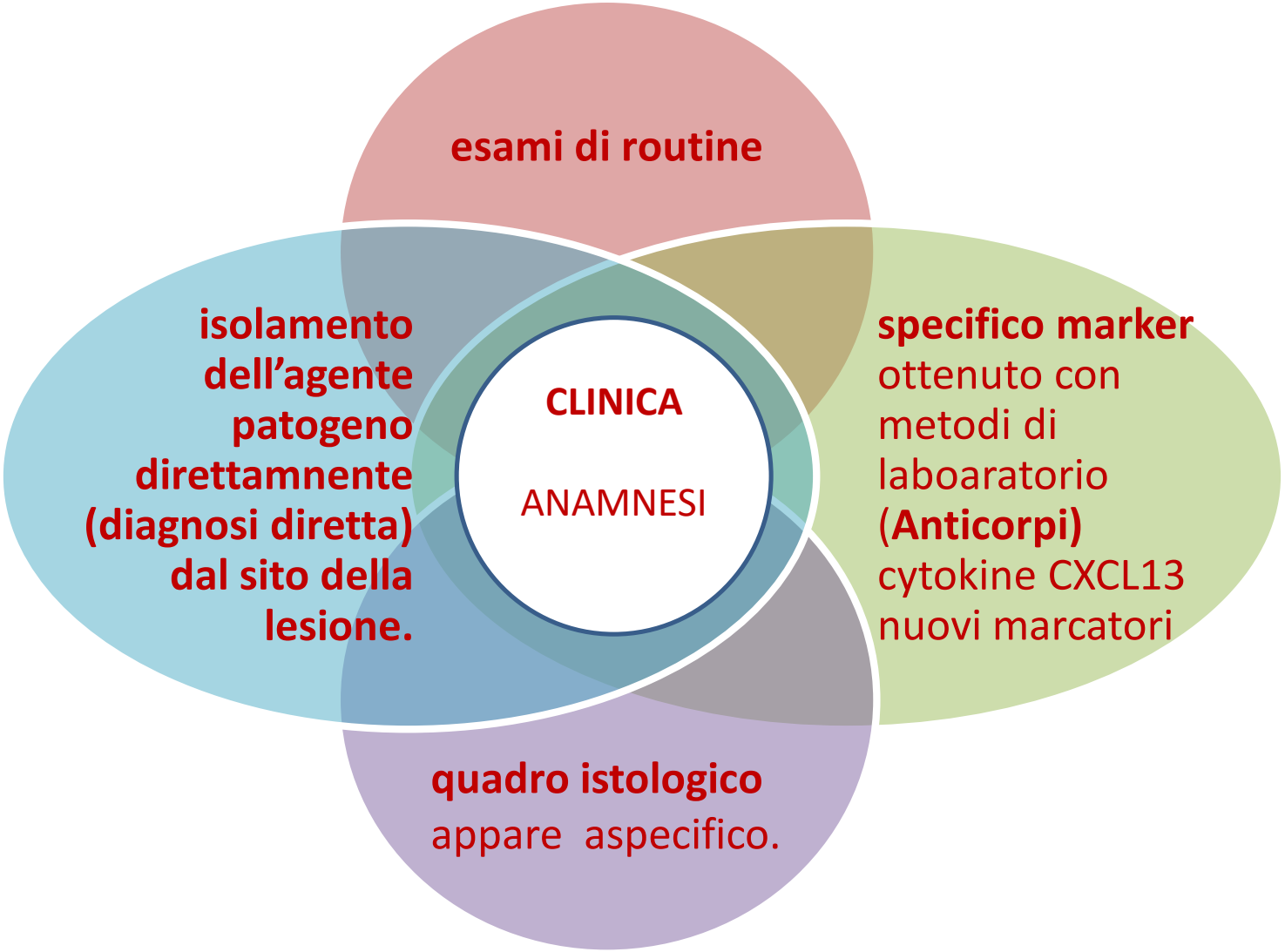
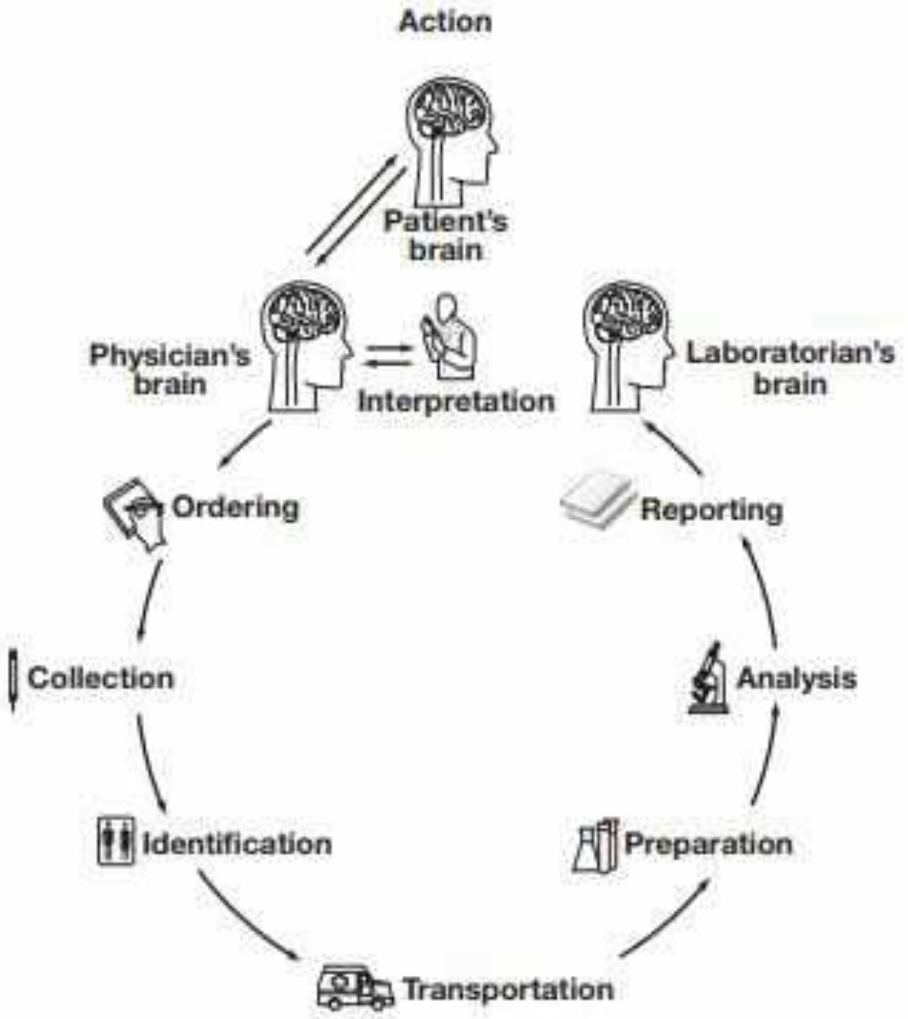
IL LABORATORIO NELLA MALATTIA DI LYME : la diagnosi indiretta

Maurizio Ruscio

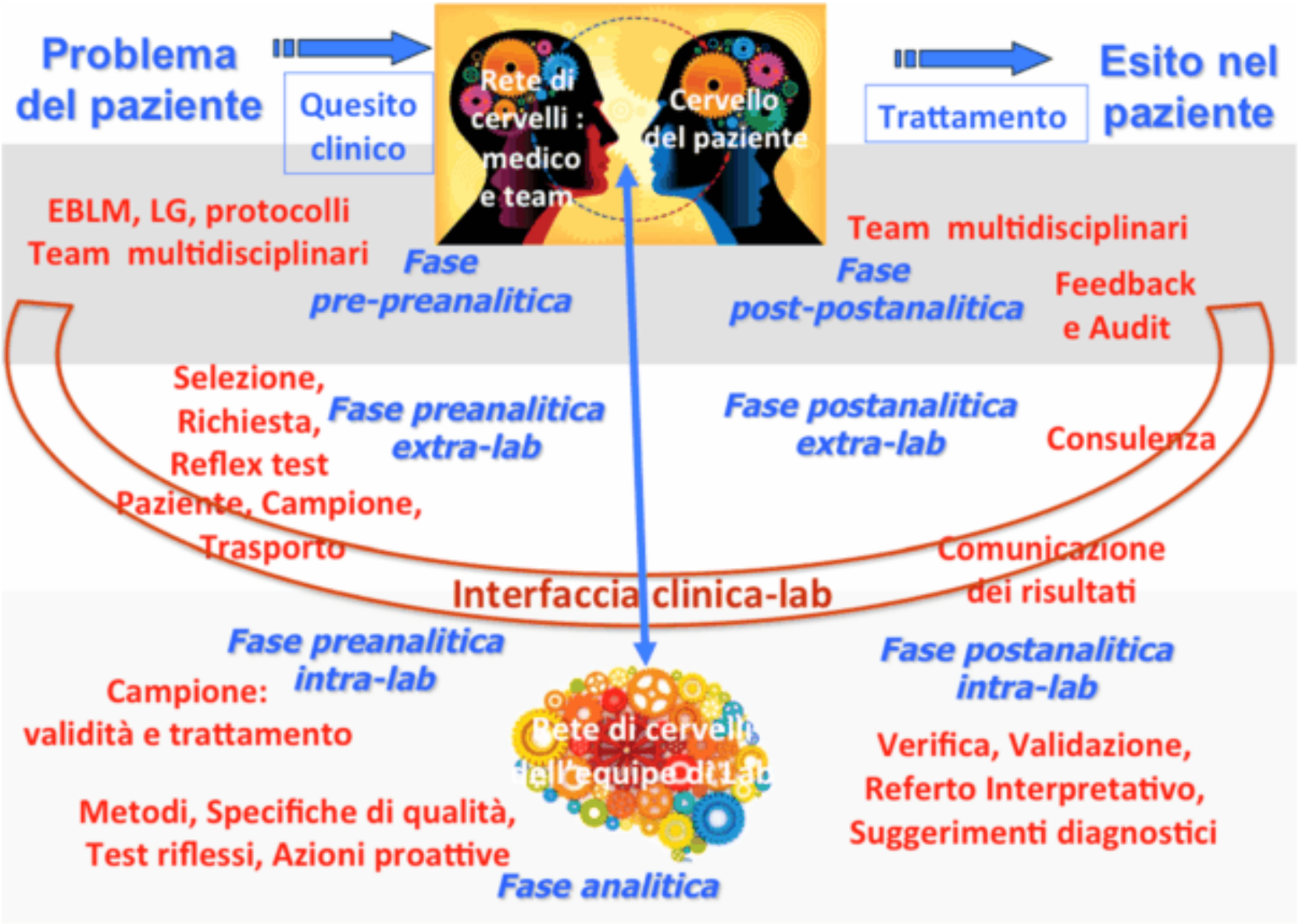
"Azienda Sanitaria Universitaria Integrata di Trieste"

Gli strumenti diagnotici





Lundberg GD. Acting on significant laboratory results. JAMA. 1981;245:1762-1763.



Lundber Brain to brain loop 2019 modificato


Standardizzazione
System status: OK
Stato del sistema: OK
Anlagen-status: OK
系統狀態 行
Sistem durumu: tamam
0101110
0101001

Term	Clinical case definition (indications for testing)	Medical laboratory evidence necessary[b]	Supporting medical laboratory/ clinical evidence
Erythema migrans (early localized infection)	Expanding red or bluish-red patch (>5 cm in diameter)[a], with or without	None in typical erythema	Detection of *B. burgdorferi* s.l. by culture and/or PCR from skin biopsy material
Borrelia (local			ology, culture i-
Lyme ne (early infect			culture cal syn- and/or ri s.l.- ent or
Lyme ca disse			culture dial ncomi- typical
Ocular n (rare) nated			reliosis *burg-* CR from
Lyme ar mani			tion of rarely d/or
Acroder atrop mani			rferi s.l. kin

[a]If <5 cm is requir tick bite

[b]As a ru

[c]In early cases intrathecally produced specific antibodies may still be absent.

ORIGINAL ARTICLE INFECTIOUS DISEASES

Lyme borreliosis: Clinical case definitions for diagnosis and management in Europe

G. Stanek[1], V. Fingerle[2], K.-P. Hunfeld[3], B. Jaulhac[4], R. Kaiser[5], A. Krause[6], W. Kristoferitsch[7], S. O'Connell[8], K. Ornstein[9], F. Strle[10] and J. Gray[11]

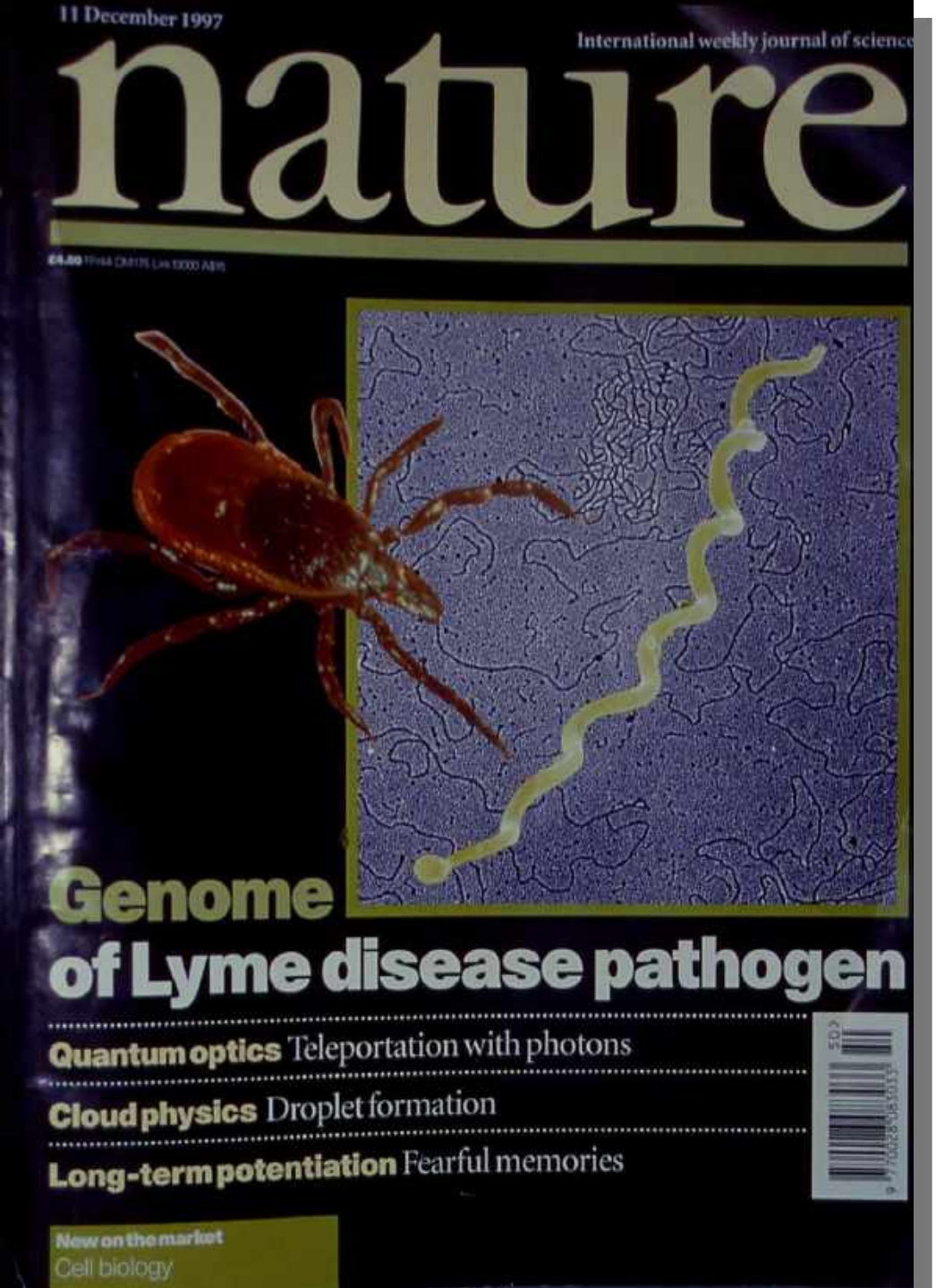
1) Medical University of Vienna, Department of Hygiene and Applied Immunology, Vienna, Austria, 2) National Reference Centre for Borrelia, Bavarian Food and Health Safety Authority, Munich, Germany, 3) Institute for Laboratory Medicine, Northwest Medical Center, Academic Teaching Hospital of The Johann Wolfgang Goethe-University, Frankfurt/Main, Germany, 4) National Reference Centre for Borrelia, Department Laboratory of Bacteriology, Strasbourg University Hospital, Strasbourg, France, 5) Neurology Clinic, Klinikum Pforzheim, Pforzheim, Germany, 6) Rheumatology Clinic, Immanuel-Krankenhaus, Berlin, Germany, 7) Department of Neurology, Sozialmedizinisches Zentrum Ost, Donauspital, Vienna, Austria, 8) Health Protection Agency Lyme Borreliosis Unit, HPA Microbiology Laboratory, Southampton General Hospital, Southampton, UK, 9) Department of Clinical Sciences, Section for Clinical and Experimental Infection Medicine, Lund University, Lund, Sweden, 10) Department of Infectious Diseases, University Medical Center Ljubljana, Ljubljana, Slovenia, and 11) UCD School of Biology and Environmental Science, University College Dublin, Dublin, Ireland

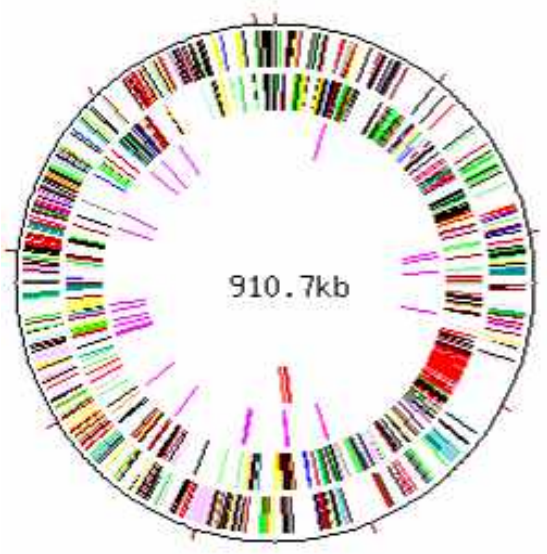
Abstract

Lyme borreliosis, caused by spirochaetes of the *Borrelia burgdorferi* genospecies complex, is the most commonly reported tick-borne infection in Europe and North America. The non-specific nature of many of its clinical manifestations presents a diagnostic challenge and concise case definitions are essential for its satisfactory management. Lyme borreliosis is very similar in Europe and North America but the greater variety of genospecies in Europe leads to some important differences in clinical presentation. These new case definitions

Ricerca ac anti B.Borrelia burgdorferi *sl*

La positivita’ degli anticorpi specifici è necessaria per confermare la diagnosi in tutte le manifestazione della ML della fase acuta disseminata e tardiva

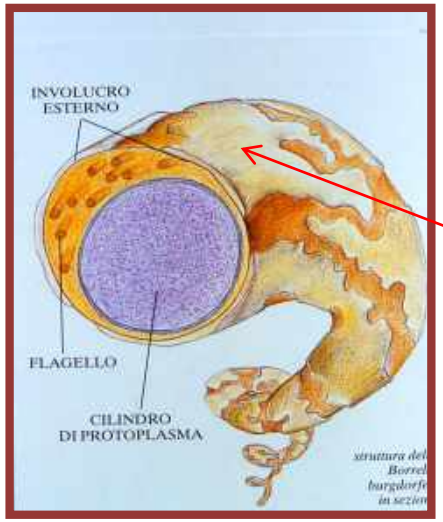




The genome is quite small (approximately 1.5 megabases) and consists of a linear chromosome of 910 kilobases as well as 9 linear and 12 circular plasmids.

Fraser, 1997

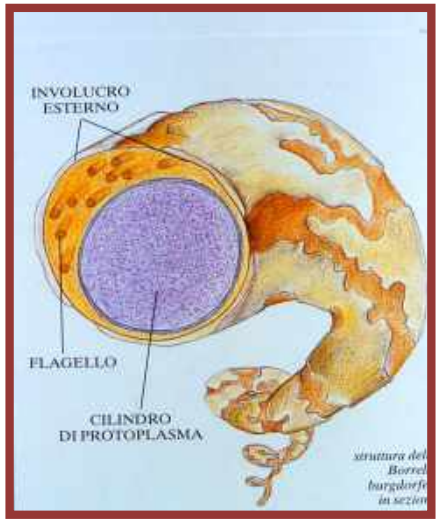
Borrelia burdorferi *sensu lato complex*



The organism has few proteins with biosynthetic activity

The only known virulence factors of B.b. are surface proteins (**OSP A-F**) that allow the spirochete to attach to mammalian cells

Borrelia burdorferi Sensu Lato Complex



Genospecie EU patogene : ***B. afzeli, garinii, bavariensis*** *(formalmente garinii Osp A tipo 4),* ***burgdorferi ss, spielmani.***

Mentre *bisetti, valaisiana, lusitaniae* segnalate patogene in un singolo caso. *(Picken,1966-Maraspin, 2006, Fingerle, 2008-Stanek,2012, Stupica, 2015*)

La Borrelia burgdorferi sl

Borrelia afzelii
Borrelia garinii
Borrelia burgdorferi ss
Borrelia bavariensis
Borrelia spielmanii

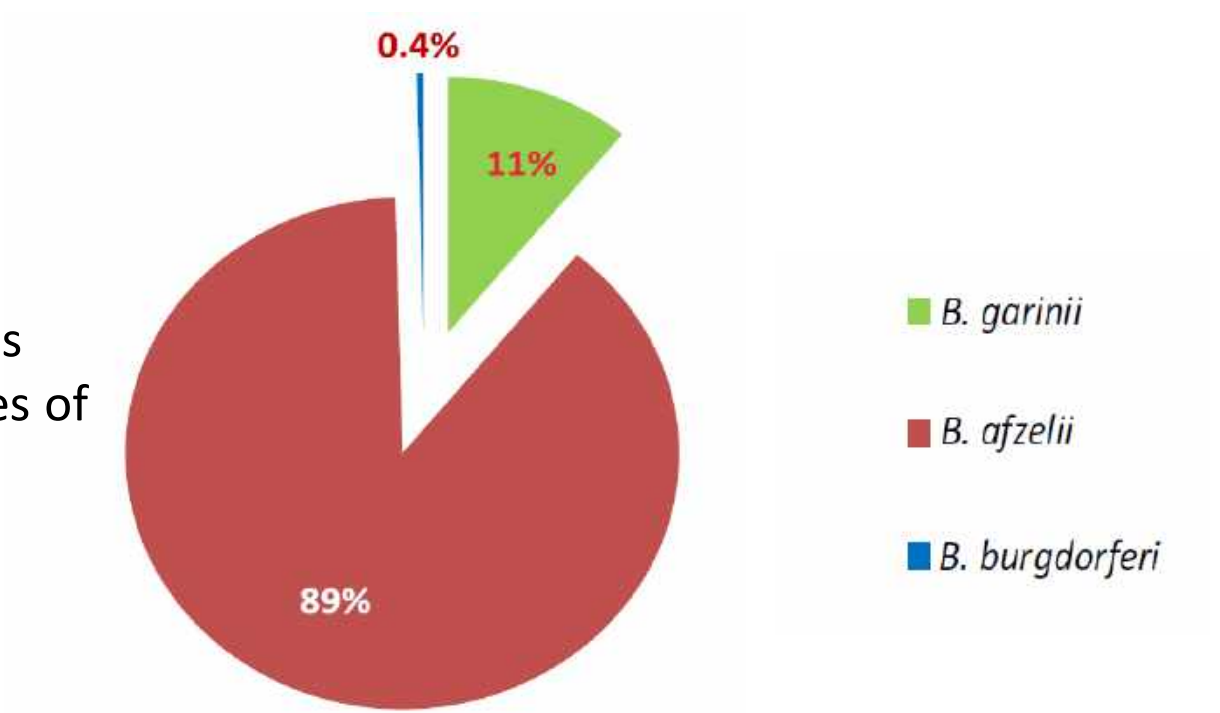
Borrelia burgdorferi ss
Borrelia spielmanii
Borrelia bisetti
americana
Borrelia andersoni

Borrelia japonica,
tanukii, turdae, sinica

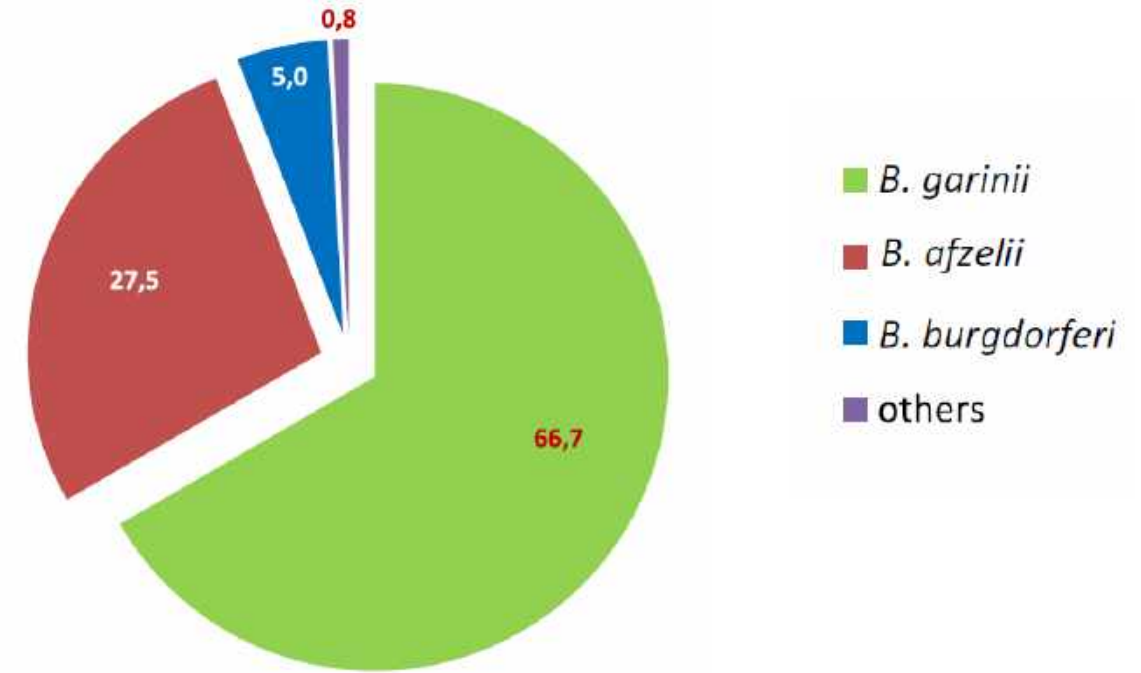
Borrelia miyamotoi
(Pitt, 2016)

Borrelia lonestari

Distribution of genospecies (%) among 488 skin isolates of *B. burgdorferi*s.l. from **erythema migrans** (Ruzic-Sablji´c 2002).



Distribution of genospecies (%) of *B. burgdorferi* s.l. among 120 CSF isolates from **Lyme neuroborreliosis** (Strle, 2006).



Morso di zecca e trasmissione della Bb

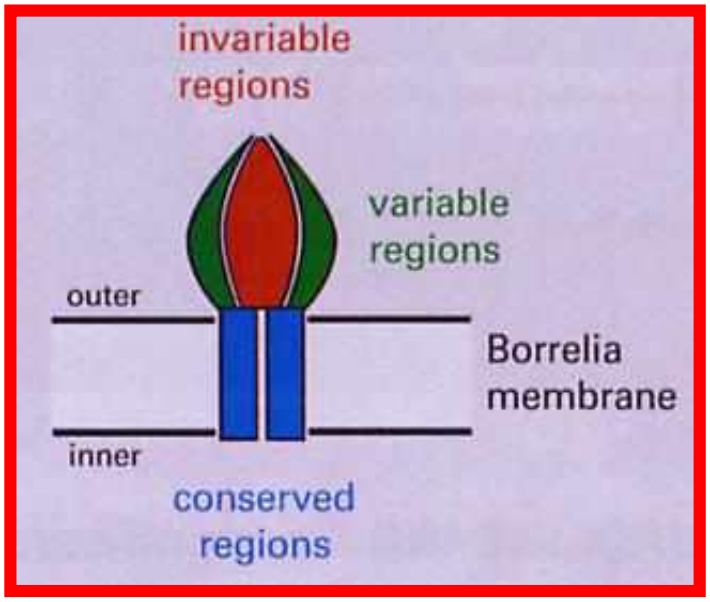
Morso di zecca e trasmissione della Bb

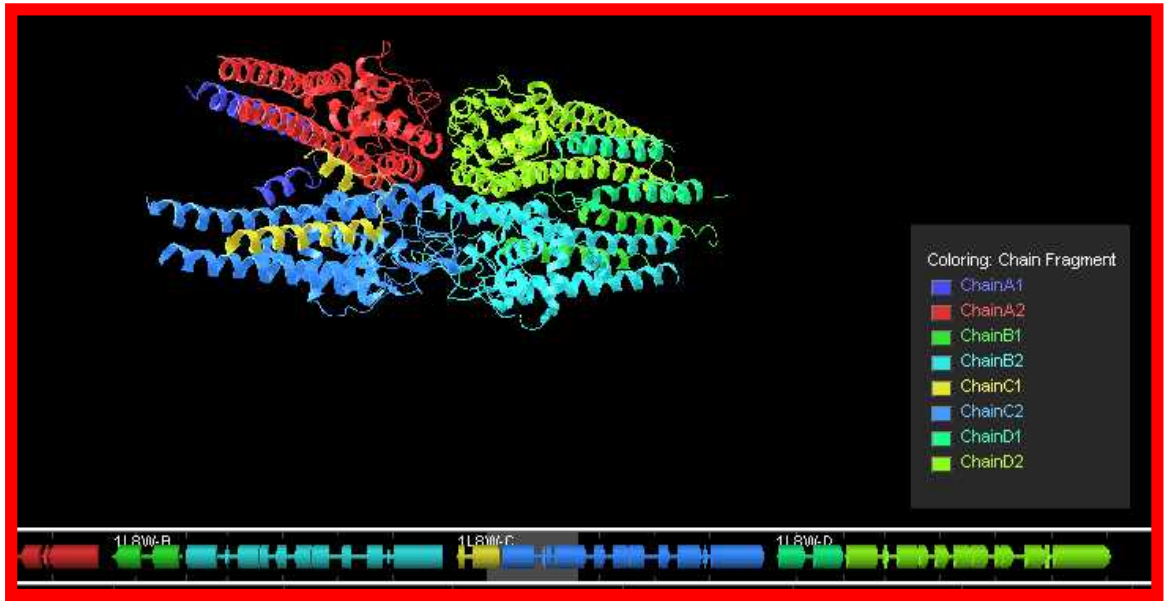
Il pasto di sangue è lo stimolo per la Bb a regolare la produzione di **OspC, DbpA, DbpB** e **p66** e a ridurre la produzione di **OspA e B**.

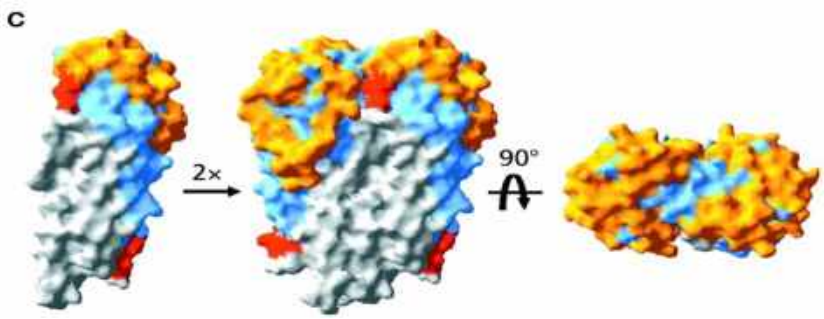
Il **co-feeding** accresce le varianti di **Osp C** *(Rosa, 2005, Pérez, 2011)*

L’evoluzione dei test sierologici per LD

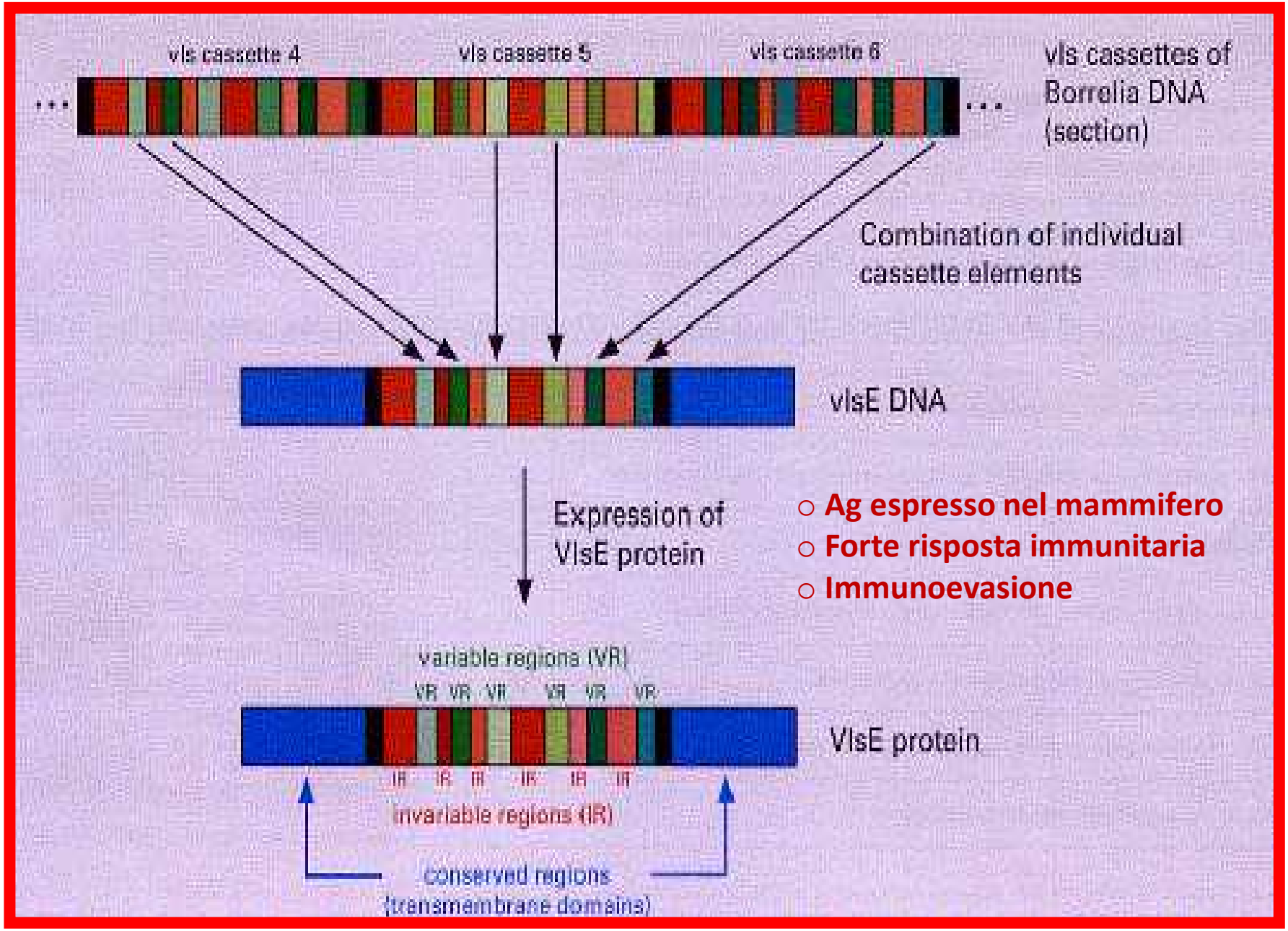
VLsE (Variable major protein – Vmp 35 kDa)







Il complesso VlsE è formato da 3 domini definiti: 2 regioni costanti ai terminali COOH e NH2; 1 regione VARIABILE interna



- **Ag espresso nel mammifero**
- **Forte risposta immunitaria**
- **Immunoevasione**

L’evoluzione dei test sierologici per LD

VLsE (Variable major protein – Vmp 35 kDa)

C6 (VLsE – IR6 epitopo immunodominante) ricombinante 26 aminoacidi ELISA

OspC (Outer surface protein C 23 kDa)
pepC10 (kinetic ELISA)
(rVLsE/pepC10) e OspC1

I test sierologici per LD e la loro evoluzione

Indirect Immunofluorescenza, Hemoagglutination assays, Complement fixation.

enzyme-linked immunosorbent assay (**ELISA**)

enzyme-immunoassay (**EIA**)

enzyme-linked fluorescence assay (**ELFA**)

chemiluminescence immunoassay (**CLIA)**

luminex, fluoro-immunoassay (**FIA**)

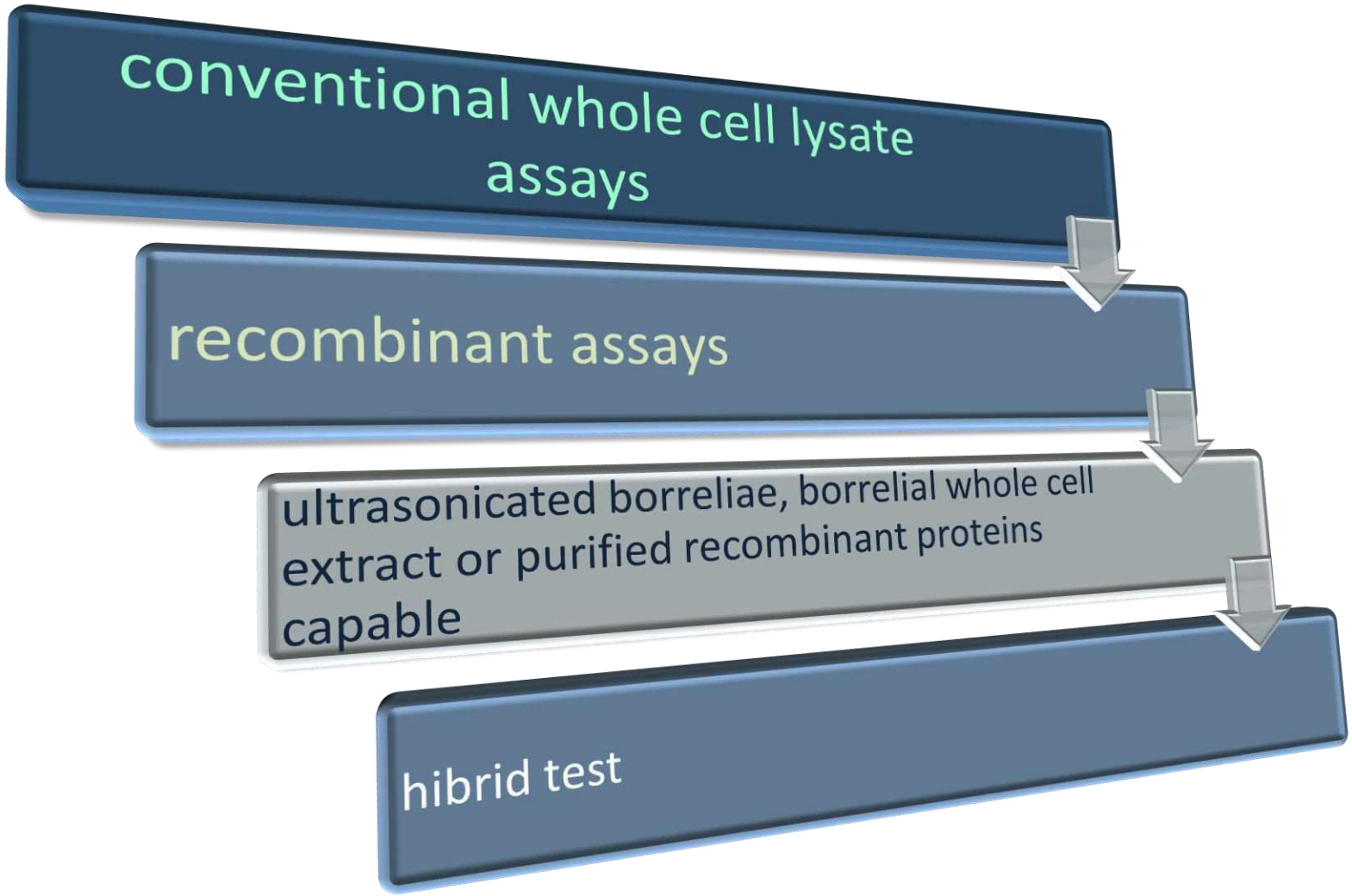
immuno-fluorimetric assay (**IFMA**)

immuno-enzimometricassay (**IEMAI**)

immuno-chemiluminometric assay (**CMA**)

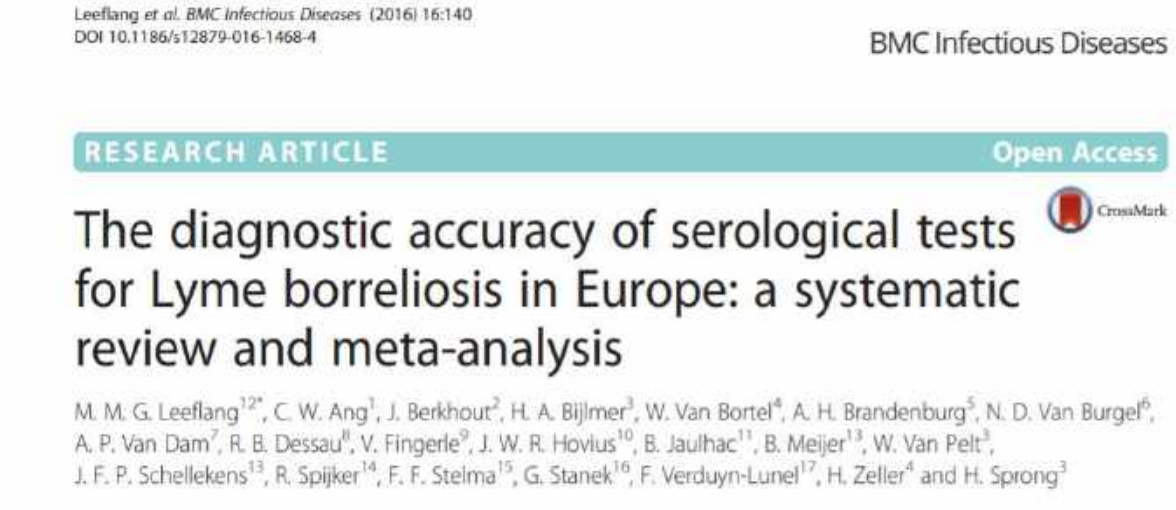
elettrochemiluminescence immunoassay (**ECLIA)**

Preparazione degli Ag



L’evoluzione dei test sierologici per LD

Specificità 80- 90 %



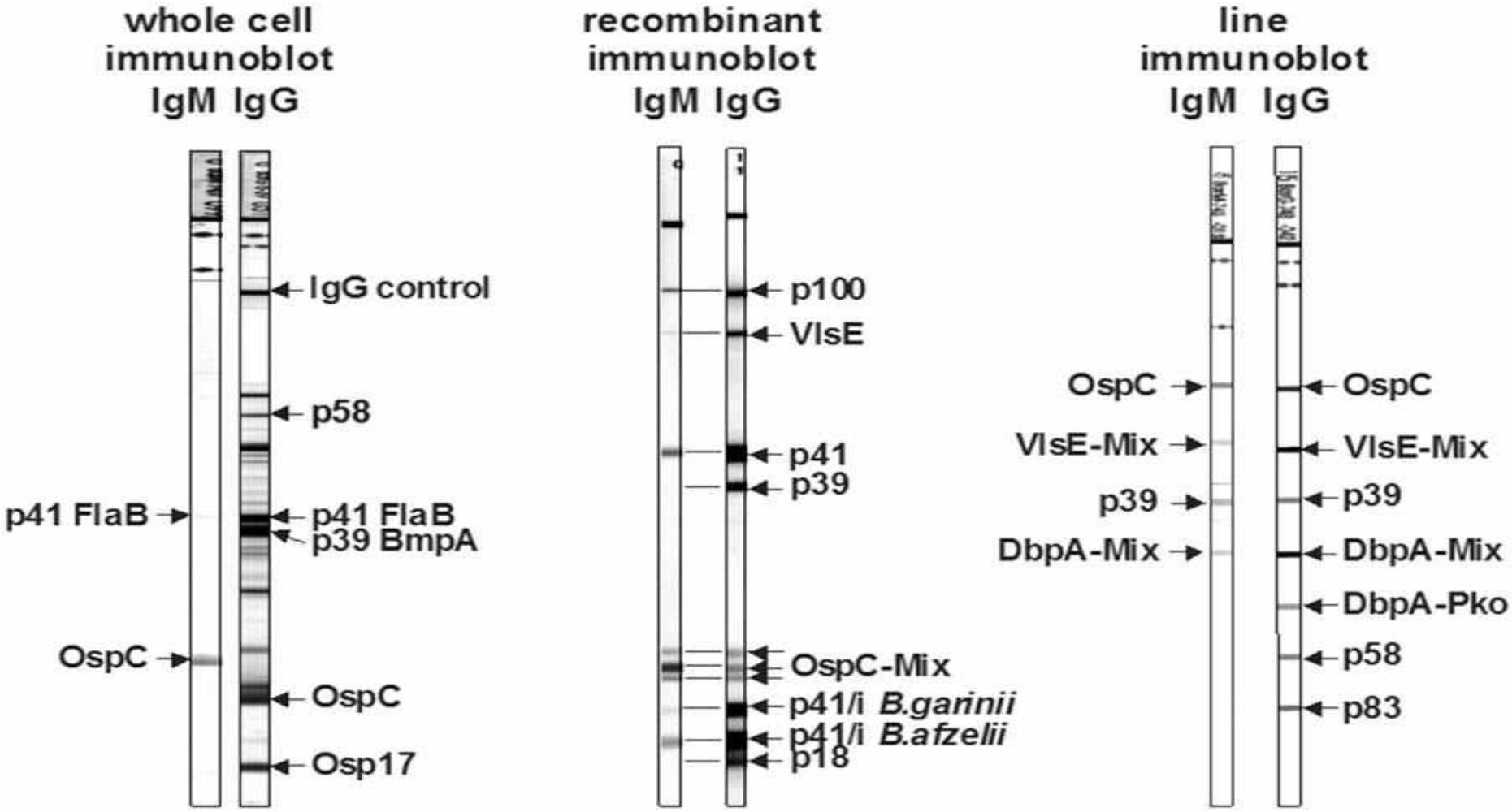
Leeflang et al. BMC Infectious Diseases (2016) 16:140
DOI 10.1186/s12879-016-1468-4

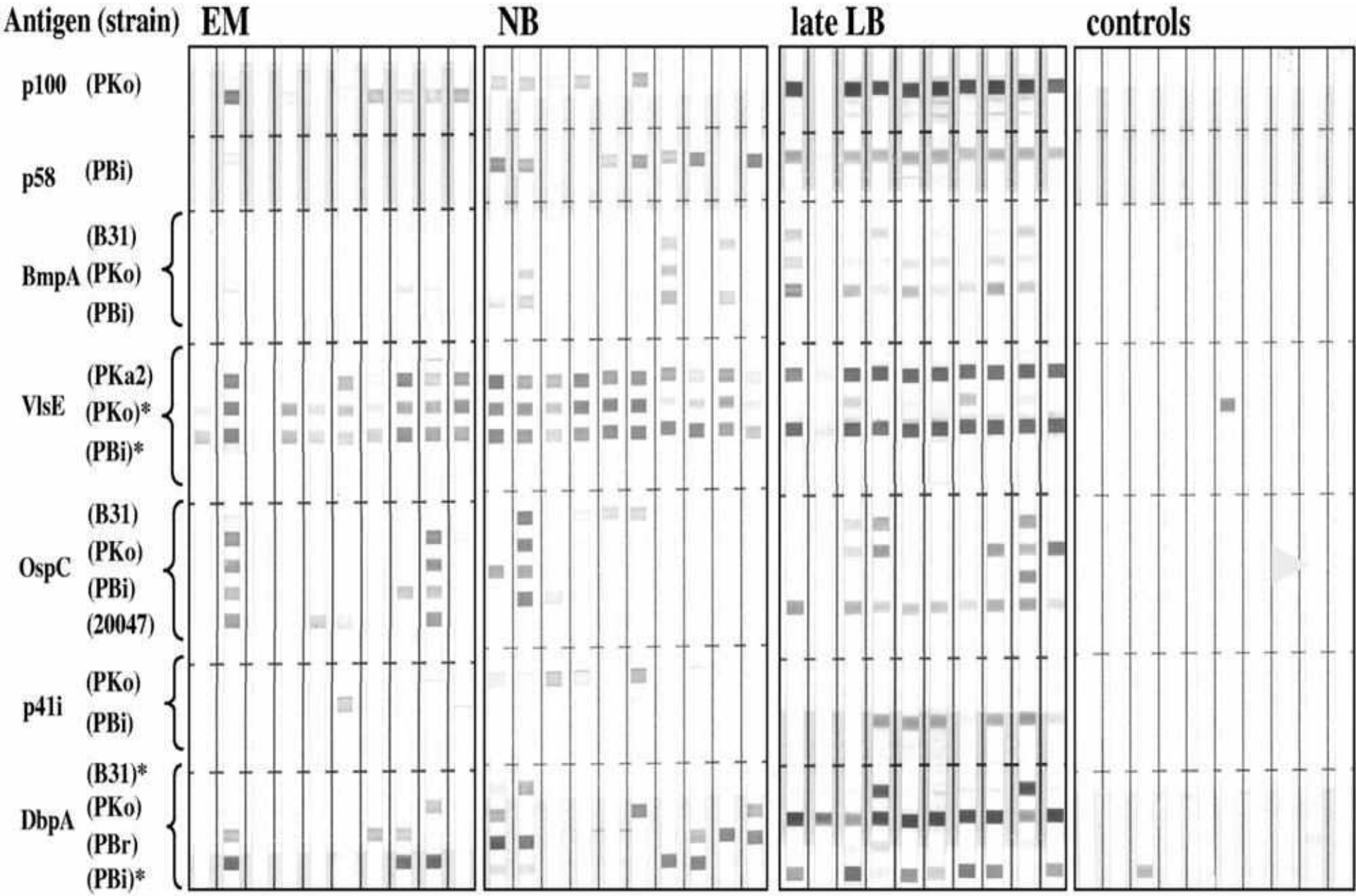
BMC Infectious Diseases

RESEARCH ARTICLE Open Access

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

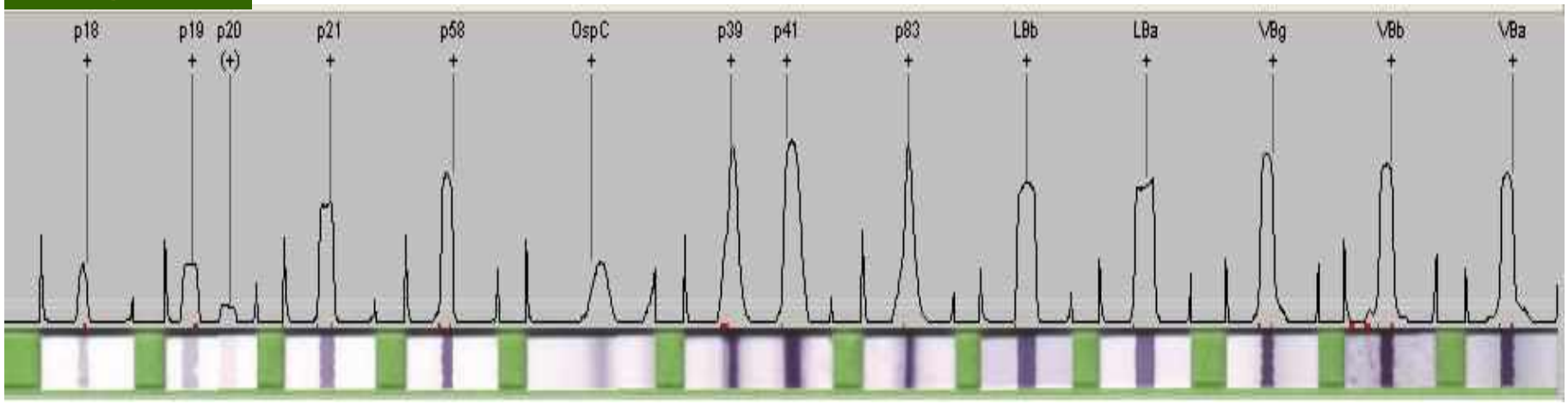
M. M. G. Leeflang[12*], C. W. Ang[1], J. Berkhout[2], H. A. Bijlmer[3], W. Van Bortel[4], A. H. Brandenburg[5], N. D. Van Burgel[6], A. P. Van Dam[7], R. B. Dessau[8], V. Fingerle[9], J. W. R. Hovius[10], B. Jaulhac[11], B. Meijer[13], W. Van Pelt[3], J. F. P. Schellekens[13], R. Spijker[14], F. F. Stelma[15],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

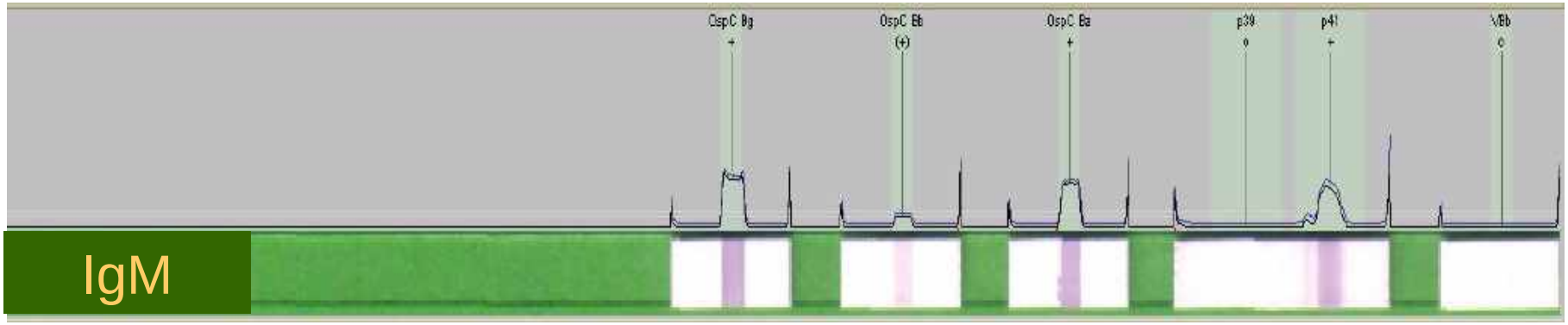

whole cell
immunoblot
IgM IgG
IgG control
p58
p41 FlaB
p41 FlaB
p39 BmpA
OspC
OspC
Osp17
recombinant
immunoblot
IgM IgG
p100
VlsE
p41
p39
OspC-Mix
p41/i B.garinii
p41/i B.afzelii
p18
line
immunoblot
IgM IgG
OspC
VlsE-Mix
p39
DbpA-Mix
OspC
VlsE-Mix
p39
DbpA-Mix
DbpA-Pko
p58
p83


Antigen (strain)
EM
NB
late LB
controls
p100 (PKo)
p58 (PBi)
BmpA (B31)
(PKo)
(PBi)
VlsE (PKa2)
(PKo)*
(PBi)*
OspC (B31)
(PKo)
(PBi)
(20047)
p41i (PKo)
(PBi)
DbpA (B31)*
(PKo)
(PBr)
(PBi)*

I test di conferma in Immunoblot (secondo livello)

IgG





IgM

I test di conferma in Immunoblot (US)

IgG: positive if >=5 bands of the following are present: p18,p23,p28,p30,p39,p41,p45,p58,p66, p93

IgM: positive if >=2 bands of the following is/are present: p23 OspC, p39 BmpA, p41

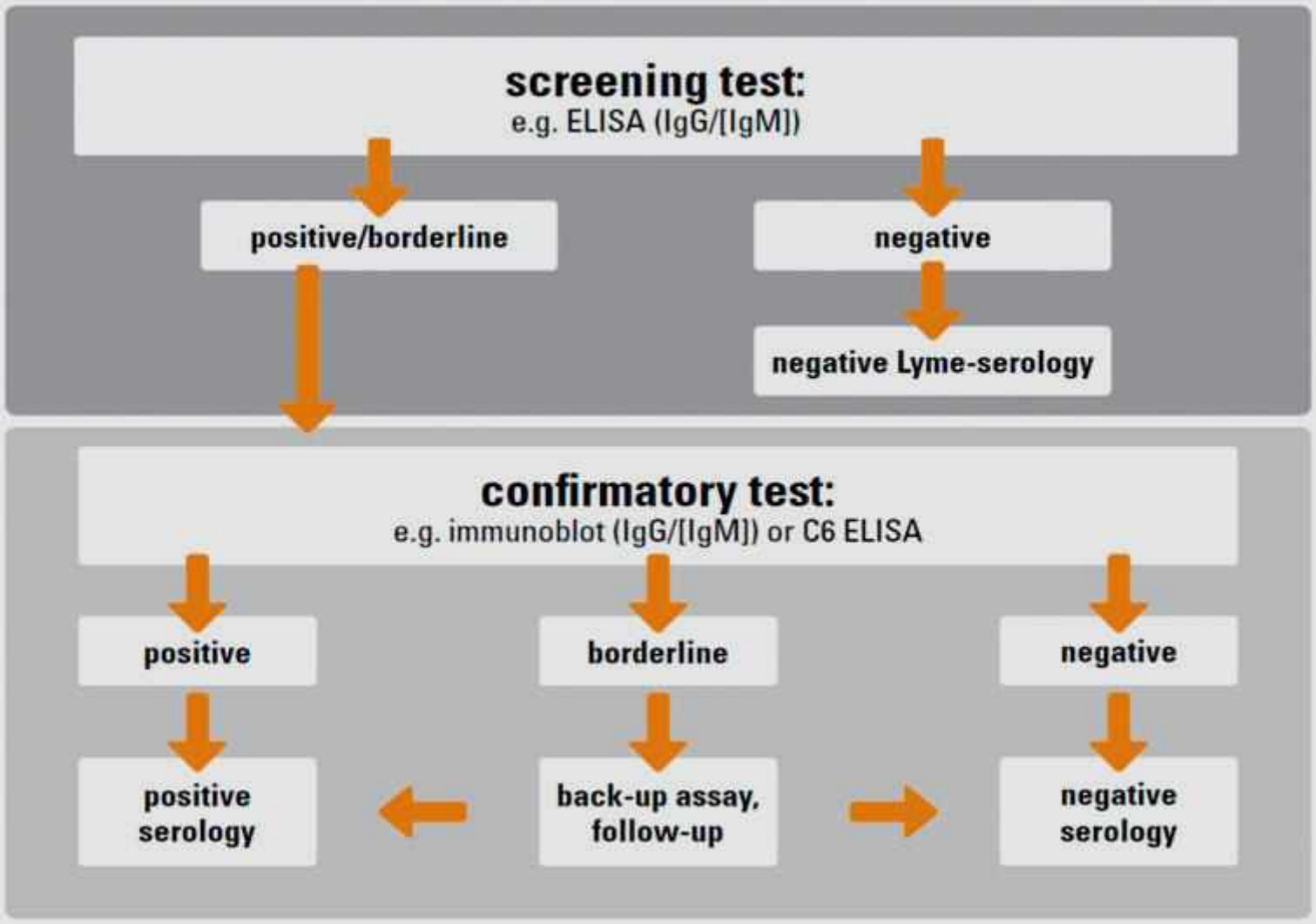
Dresler et al, Engstrom et al

I test di conferma in Immunoblot (EU)

L' **EUCALB** (*European Union Concerted Action on Lyme Borreliosis*) ha effettuato uno studio multicentrico a fine di individuare dei criteri iterpretativi standard per l'immunoblot in EU.

Sebbene sia stato identificato un set di **8 bande significative**, dai laboratori partecipanti, **non è stato possibile individuare uno schema unico per tutta l'EU** (Robertson 2000).

Two-tiered laboratory testing strategy



	Sensitivity (%)		Specificity (%)		
Assay[a]	Early (stage 1)	Late (stages 2, 3)	Healthy donors[b]	Patients with non-LD infections or conditions	Reference
WCS ELISA	74.9	97.7, 98.4	96.4	89.3	*Wormser, 2012*
WCS ELISA + WB	35.2	77.3, 95.9	99.5	99.2	
C6 ELISA	66.5	88.6, 98.4	98.8	99.5	
C6 ELISA + WB	34.5	75, 95.1	99.5	99.5	
VlsE CIA[c]	69.8	100	99.5	93.7	*Ledue, 2008*
pepC10 kELISA	47.3	46.1, 10.3	100	98.0	
VlsE/pepC10 kELISA	67.2	88.5, 94.1	99.2	96.7	*Bacon, 2003*

[a] WCS, whole-cell sonicate; VlsE, variable major protein (Vmp)-like sequence, expressed; WB, Western blot; ELISA, enzyme linked immunosorbent assay; CIA, chemiluminescent immunoassay; kELISA, kinetic ELISA.

[b] Data from healthy donors from regions in which Lyme disease is endemic and from those in which it is not endemic were combined.

Thell 2016 mod

L'evoluzione dei test sierologici per LD

Diagnostic Microbiology and Infectious Disease 75 (2013) 9–15

Contents lists available at SciVerse ScienceDirect

Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Single-tier testing with the C6 peptide ELISA kit compared with two-tier testing for Lyme disease☆,☆☆,★

Gary P. Wormser [a,*], Martin Schriefer [b], Maria E. Aguero-Rosenfeld [c], Andrew Levin [d], Allen C. Steere [e], Robert B. Nadelman [a], John Nowakowski [a], Adriana Marques [f], Barbara J.B. Johnson [b], J. Stephen Dumler [g]

[a] Division of Infectious Diseases, New York Medical College, Valhalla, NY 10595, USA
[b] National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, CO 80521, USA
[c] Department of Pathology, New York University Langone Medical Center, New York, NY 10016, USA

combination with supplemental Western blot testing

	Sensitivity (%)		Specificity (%)		
Assay[a]	Early (stage 1)	Late (stages 2, 3)	Healthy donors[b]	Patients with non-LD infections or conditions	Reference
WCS ELISA	74.9	97.7, 98.4	96.4	89.3	14
WCS ELISA + WB	35.2	77.3, 95.9	99.5	99.2	

Wormser, 2012

Un approccio alternativo

Two-Tiered Antibody Testing for Lyme Disease With Use of 2 Enzyme Immunoassays, a Whole-Cell Sonicate Enzyme Immunoassay Followed by a VlsE C6 Peptide Enzyme Immunoassay

John A. Branda,[1] Katy Linskey,[1] Yeowon A. Kim,[1] Allen C. Steere,[2] and Mary Jane Ferraro[1,2]

[1]Department of Pathology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; and [2]Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

Background. Lyme disease (LD) antibody testing currently involves a 2-tiered algorithm with a whole-cell sonicate (WCS) enzyme immunoassay (EIA), followed by IgM/IgG Western immunoblots. A single EIA using the C6 peptide of the *Borrelia burgdorferi* variable-major protein-like sequence expressed lipoprotein provides similar or better sensitivity but less specificity, compared with standard 2-tiered testing. Here, we investigated an alternative 2-tiered strategy, in which the first step remained a WCS EIA, but immunoblotting was replaced by a C6 EIA.

Methods. We determined the sensitivity of the 3 testing strategies with use of 91 serum samples from research study patients with LD and 78 serum samples from patients with LD whose samples were submitted to our hospital's clinical laboratory. Specificity was measured using 54 patients with other illnesses and 1246 healthy subjects from areas where the infection is endemic and nonendemic.

Results. The 2-EIA algorithm in early LD had similar sensitivity as C6 testing alone, and both strategies had better sensitivity than did standard 2-tiered testing (61% and 64%, respectively, vs 48%; $P = .03$ and $P = .008$). For late disease, all 3 strategies had 100% sensitivity. The specificity of the 2-EIA algorithm was equal to that of standard 2-tiered testing, and both 2-tiered strategies were more specific than C6 testing alone (for both, 99.5% vs 98.4%; $P = .01$). The positive predictive value of the 2-EIA algorithm was 70%, compared with 66% for standard 2-tiered testing and 43% for the C6 EIA alone.

Conclusions. The 2-EIA strategy matched the individual strengths of the C6 EIA and Western blotting, without the drawbacks. The 2 EIAs provided sensitivity comparable to that of the C6 EIA but maintained the specificity of standard 2-tiered testing.

MAJOR ARTICLE

Performance of United States Serologic Assays in the Diagnosis of Lyme Borreliosis Acquired in Europe

John A. Branda,[1] Franc Strle,[4] Klemen Strle,[3] Nikhil Sikand,[3] Mary Jane Ferraro,[1,2] and Allen C. Steere[2,3]

[1]Department of Pathology, [2]Department of Medicine, and [3]Center for Immunology and Inflammatory Diseases, Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital and Harvard Medical School, Boston and [4]Department of Infectious Diseases, University Medical Centre Ljubljana, Slovenia

(See the Editorial Commentary by Schoen on pages 341–3.)

Background. Physicians in the United States sometimes need to evaluate a patient for suspected Lyme borreliosis (LB) who may have acquired the infection in Europe. Using serum samples from European LB patients, we compared the performance of European and US serodiagnostic tests, including newer-generation assays containing Vmp-like sequence, expressed or its C6 peptide.

Methods. The sensitivity of each assay was determined using 64 serum samples from LB patients with early or late disease manifestations who acquired the infection in Europe. Specificity was measured using 100 sera from healthy subjects from a nonendemic area.

Results. For the detection of European-acquired infection, conventional 2-tiered testing (enzyme-linked immunosorbent assay [ELISA] followed by immunoblotting) using US assays had an overall sensitivity and specificity of 52% and 100%, compared with 81% ($P = .0007$) and 99% ($P = 1.00$) using analogous European tests. The sensitivity of a US C6 ELISA used as a stand-alone test (88% overall) was statistically comparable to that of conventional 2-tiered testing using European tests ($P = .47$) and was 100% specific. Similarly, an alternative 2-tiered algorithm using a standard US ELISA followed by a C6 ELISA was comparably sensitive (84% overall) compared with conventional 2-tiered testing using European assays ($P = .82$), and specificity remained 100%.

Conclusions. European assays outperformed analogous US assays in a conventional 2-tiered testing algorithm. However, a C6 ELISA used as a stand-alone test or in the second tier of a 2-tiered algorithm performed comparably to conventional 2-tiered testing using European assays, and can be used for evaluation of any patient, regardless of travel history.

'One size fits all' approach

ORIGINAL ARTICLE INFECTIOUS DISEASES

Lyme borreliosis: Clinical case definitions for diagnosis and management in Europe

G. Stanek[1], V. Fingerle[2], K.-P. Hunfeld[3], B. Jaulhac[4], R. Kaiser[5], A. Krause[6], W. Kristoferitsch[7], S. O'Connell[8], K. Ornstein[9], F. Strle[10] and J. Gray[11]

Critical Reviews in Clinical Laboratory Sciences

ISSN: 1040-8363 (Print) 1549-781X (Online) Journal homepage: http://www.tandfonline.com/loi/ilab20

Laboratory diagnosis of Lyme borreliosis: Current state of the art and future perspectives

Benedikt Lohr, Volker Fingerle, Douglas E. Norris & Klaus-Peter Hunfeld

Clin Chem Lab Med 1999; 37(7):771 © 1999 by Walter de Gruyter · Berlin · New York

Book Review

Clinical Laboratory Diagnostics

Use and Assessment of Clinical Laboratory Results
By Thomas Lothar, editor

TH-Books Verlagsgesellschaft, Frankfurt/M., 1998
pp. 1527; Price: DM 248,–. ISBN 3-9805215-4-0

laboratory methods]. The last chapter presents concise information on the production of clinical laboratory results.

This book reviews about all the tests which can be used for quantitative or qualitative measurements in

Un approccio alternativo

TABLE 2 Comparison of the traditional TTTA to a 2-EIA TTTA and the C6 ELISA alone in sera from patients with well-characterized Lyme disease[a]

	Sensitivity (%)			Specificity (%)	
Testing algorithm	Stage 1 (n = 114)	Stage 2 (n = 26)	Stage 3 (n = 29)	Healthy donors[b] (n = 1,246)	Patients with a non-LD infection or condition (n = 54)
Traditional[c]	42.1	73.1	100	99.4	100
C6 ELISA alone	56.1	100	100	98.4	98.1
2-ELISA[d]	52.6	100	100	99.4	100

[a] Adapted from reference 17.
[b] Data from healthy donors from regions in which Lyme disease is endemic and from those in which it is not endemic were combined.
[c] Traditional TTTA, WCS ELISA followed by Western blot analysis.
[d] 2-ELISA, WCS ELISA followed by C6-ELISA.

US 3.4 milioni test/anno

37.000 Falsi Positivi

35.000 Casi di LD/anno

Thell 2016 mod

Interpretazione dei risultati dei tests sierologici

Bayes' Theorem

predictive values of the test

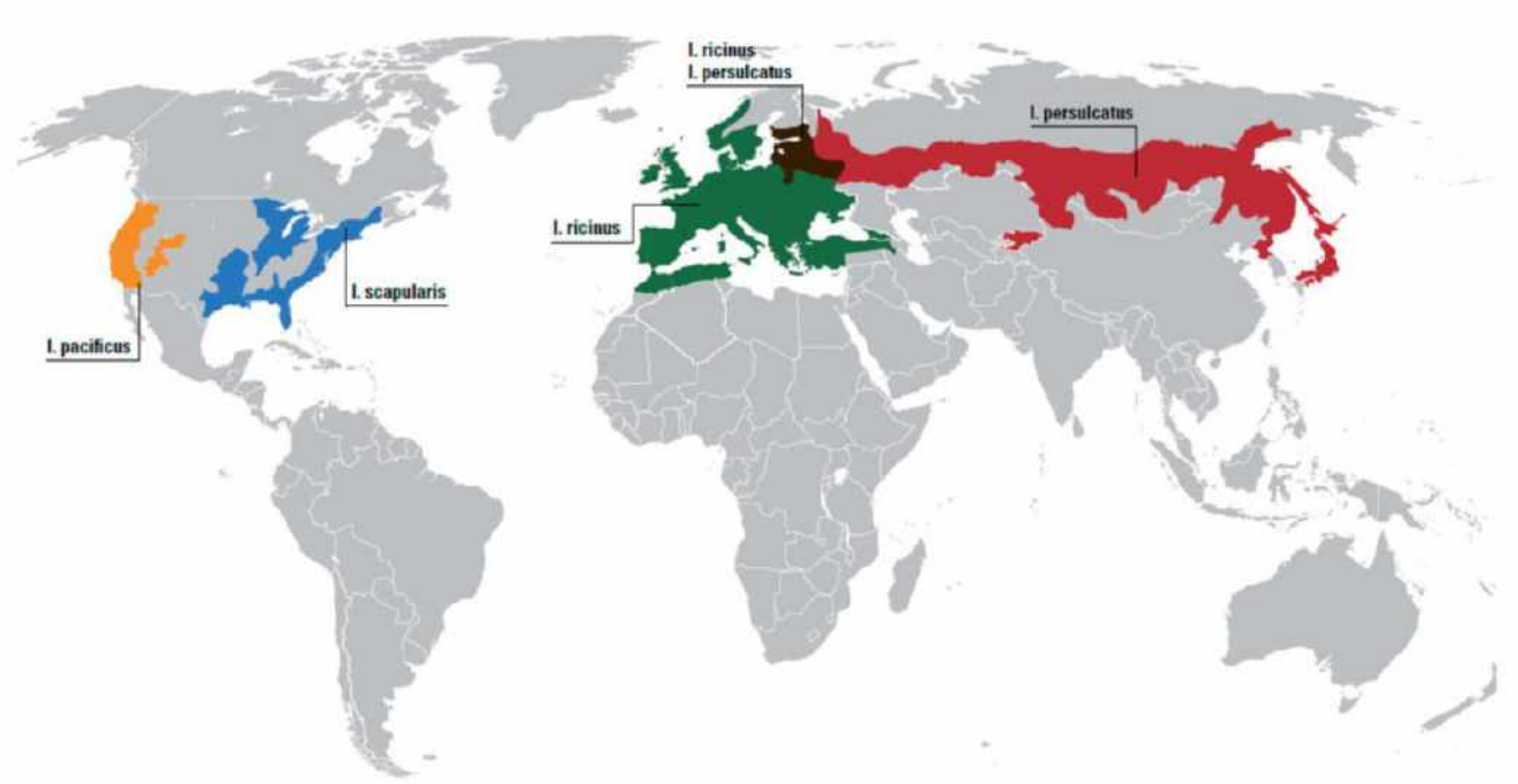
accuracy (sensitivity and specicficity)

---

pretest likelihood (prior probability)

Valutazione del Contesto

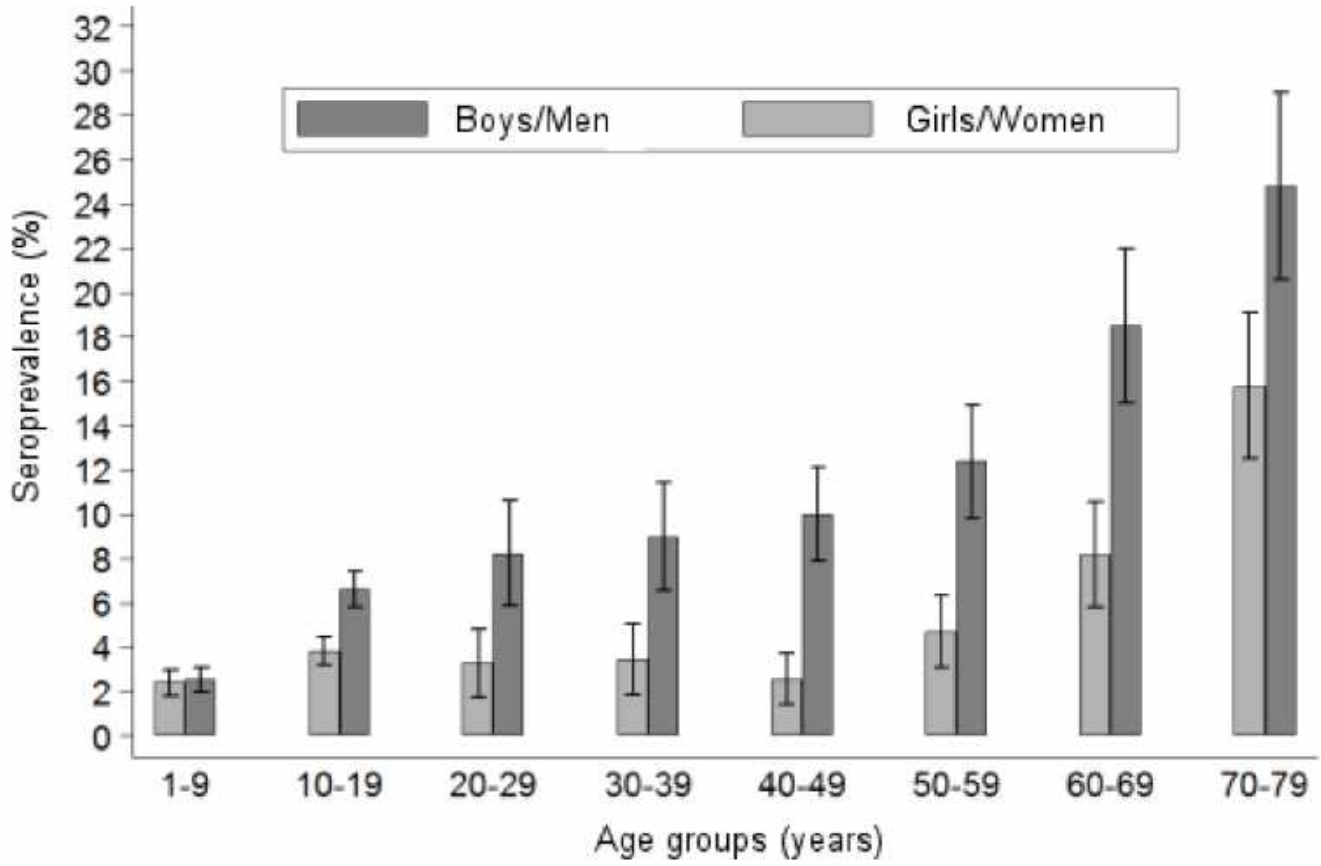
Diffusione del vettore



Stanel, 2016 Modificato

Diffusione della malattia di Italia

Fonte personale



Wilking H, et al.
Antibodies against Borrelia burgdorferi sensu lato among Adults, Germany, 2008-2011. Emerging Infect Dis. 2015

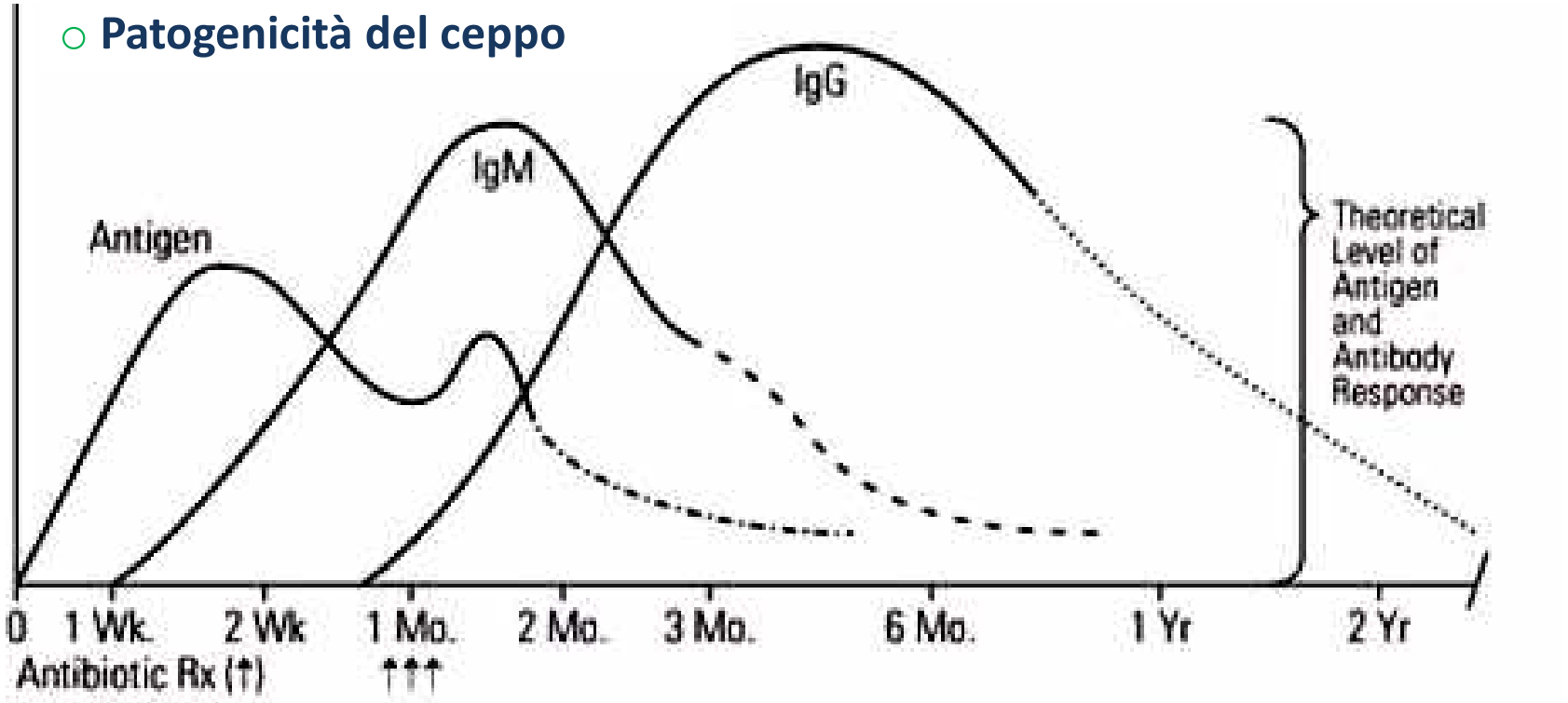
Infezione asintomatica

In US la Bb determina una **infezione asintomatica** nel **10%** dei casi (Steere, 2003)

Svezia il **50%** delle persone sieropositivi resta asintomatica (Wilhelmsson, 2016)

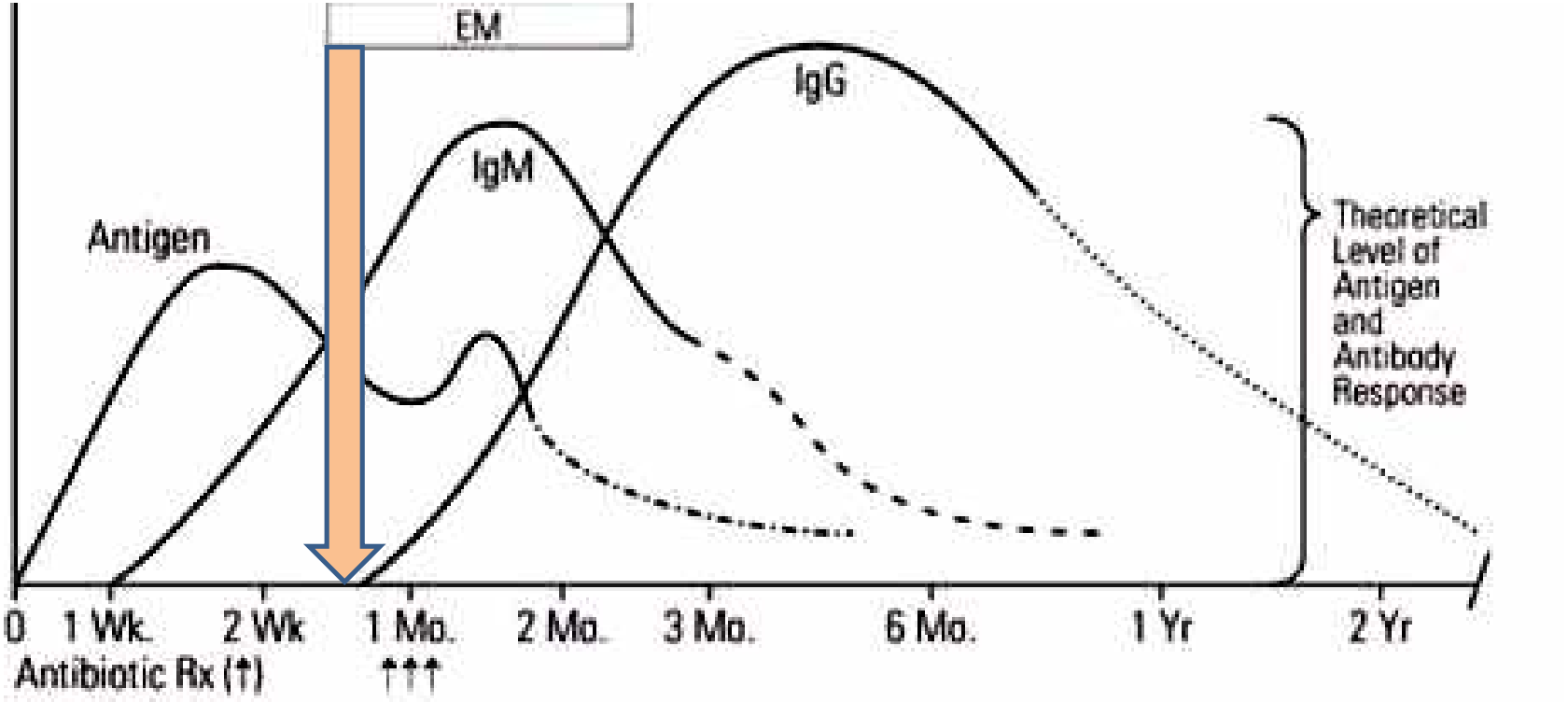
Cinetica Anticorpale

- **Fattori proinfiammatori**
- **Dose di inoculo**
- **Patogenicità del ceppo**



Cinetica Anticorpale

Fase precoce
localizzata
IgM+ nel 20-50%



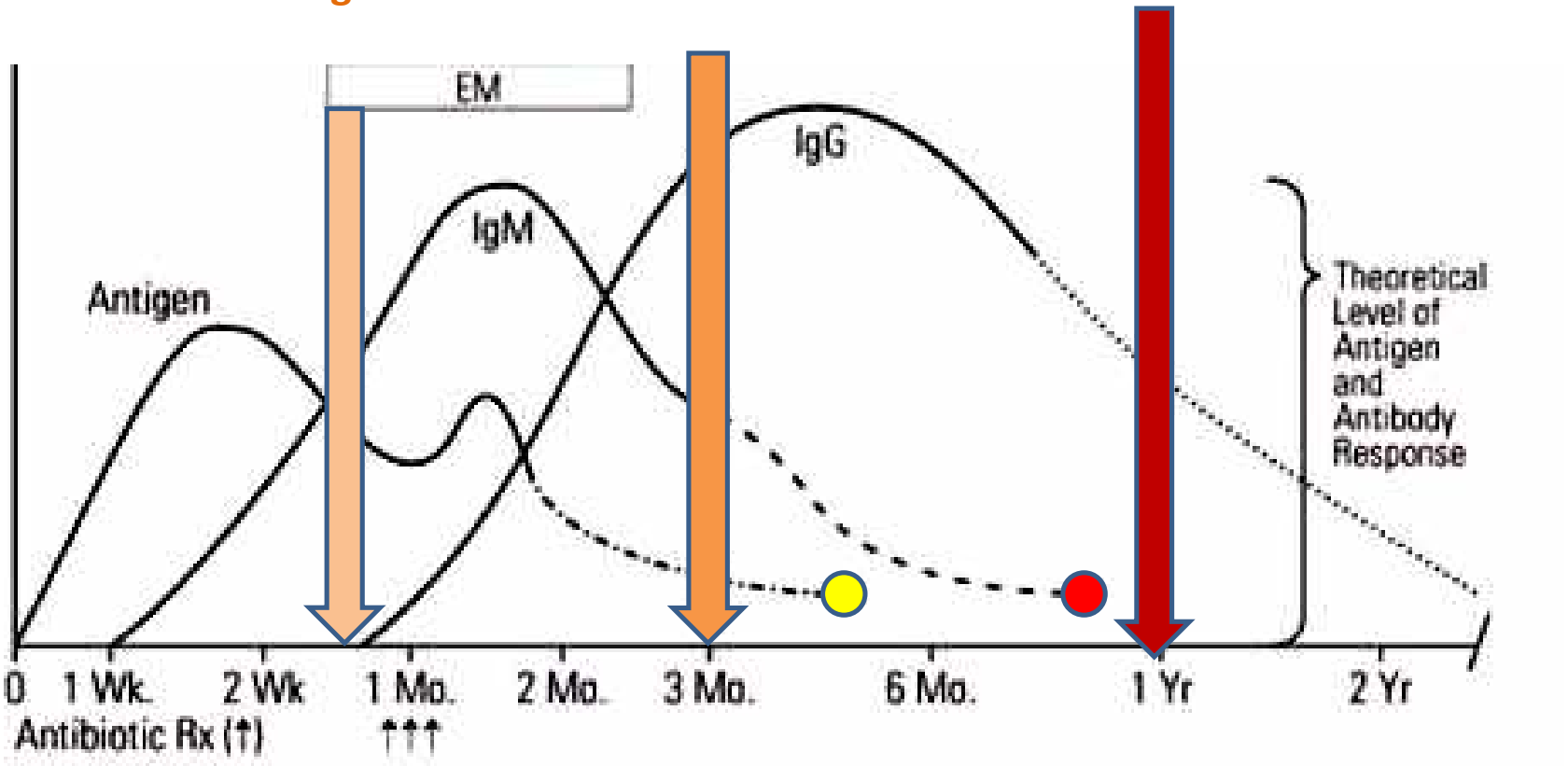
La diagnosi di *erythema migrans tipico* non richiede l'esecuzione gli esami sierologici

Cinetica Anticorpale

Fase precoce localizzata IgM+ nel 20-50%

Fase precoce generalizzata IgG-IgM 70-90%

Fase tardiva IgG 100%



Per sintomi riferibile alla LD iniziati da oltre 6 mesi, la presenza di IgG specifiche è (di regola) mandatoria

La positività protratta di IgM specifiche non ha rilevanza diagnostica

Test di screening NEGATIVO

Va interpretata in relazione alla clinica

Test di screening POSITIVO

Va interpretata in relazione alla clinica

Test di conferma Negativo

Test di screenig positivo e test di conferma negativo

Test di conferma POSITIVO

Classe

Tipo di bande

Numero

Intensità delle bande

La positività dei test sierologici non discrimina tra infezione latente, attiva o uno stato post-infettivo

Neuroborreliosi

- Il **CSF** presenta una **pleiocitosi linfocitaria** da alcune centinaia a molte migliaia di cell/l; la protidorrachia è normale o leggermente aumentata; la glicorrachia è normale o solo poco diminuita.
- In corso della **paralisi del nervo facciale** il CSF presenta spesso pleiocitosi linfocitaria anche in assenza di segni e sintomi di meningite (Lotric-Furla, 1999).
- Dopo l'esordio dei sintomi neurologici, per breve tempo, può non essere **rilevabile la sintesi intratecale** e può **essere assente la pleocitosi** del CSF specialmente nei bambini con la paralisi isolata del VII°nc (Millner *et al.* 1989).
- La produzione di ac intratecale continua anche dopo la guarigione.

CSF parameter	Early LNB	Comparison of CSF findings in early and late LNB [173]	
		Early LNB, $N = 37$	Late LNB, $N = 10$
Cell count (/μL)	170.5 (57.0; 369)[a]	218 (6–757)[b]	95 (23–312)[b]
Total protein (g/L)	1.232 (697; 1926)[a]	n.n.	n.n.
Albumin quotient ($\times 10^{-3}$)	17.2 (9.7; 28.4)[a]	19.6 (8–58.4)[b]	45 (8–140)[b]
IgG-synthesis-rated	n.n.	20 % (17)[c]	50 % (20)[c]
Pathologic at:	19.5 %	81 %	100 %
IgM-synthesis-rate[d]	n.n.	54 % (32)[c]	9 % (13)[c]
Pathologic at:	70.2 %	84 %	40 %
IgA-synthesis-rate[d]	n.n.	7 % (17)[c]	39 % (28)[c]
Pathologic at:	9 %	19 %	80 %
Lactate	2.0 (1.6; 2.6)[a]	n.n.	n.n.

Djukic M, 2012

$$\mathrm{LSI} = \frac{\begin{array}{c}\text{IgG or albumin concentration (serum)} \times \\ \text{specific antibody concentration [ELISA (U/mL)] in CSF}\end{array}}{\begin{array}{c}\text{IgG or albumin concentration (CSF)} \times \\ \text{specific antibody concentration [ELISA (U/mL)] in serum}\end{array}}$$

Djukic M, 2012

Neuroborreliosi

Le diverse genospecie sono spesso correlate a manifestazioni cliniche diverse.

Borrelia garinii causa quello che in EU viene diagnosticata come una tipica LNB precoce (i.e. dolore, meningoradiculoneuritis o sindrome di Bannwarth),

B. afzelii è molto meno specifico e di diagnosi più difficile poichè raramente è presente dolore radicolare e sintomi meningei. E' in grado di atrraversa la barriea emato-encefalica ma ha una limitata capacità di produrre infiammazione nel CSF. Il ruolo di questa genospecie va ancora completamente chiarito.

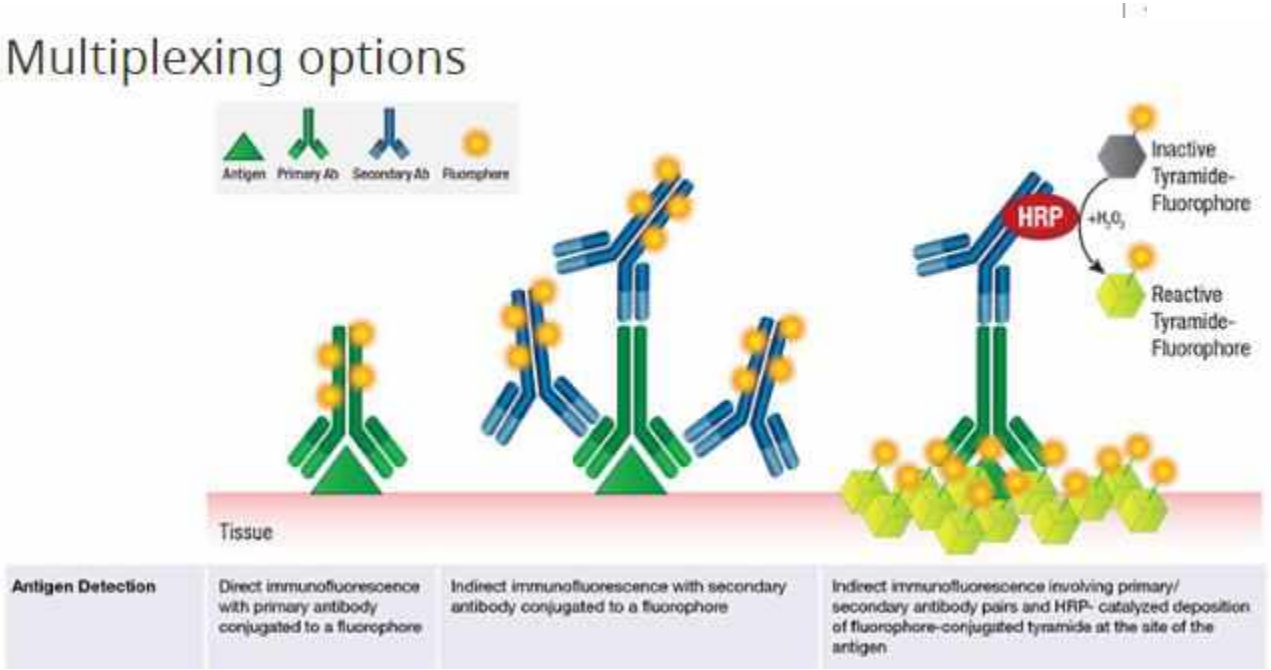
Nuovi approcci

Multiplex assays (10 Ag- Luminex tecnology)

Immuno-PCR (iPCR)
magnetic bead-C6-ac paziente-reporter ac-oligonucleotide tag

Metabolomics LC-MS (modello statistico)
metabolic profile 44 molecole lipofile e lipidi (<1500 kD)*(Sensibilità 88% vs 48% di TTTA) (Molins, 2015)*

Multiple Fluorescence Immunoassay MFI



Chemochina (citochina) **CXCL13**

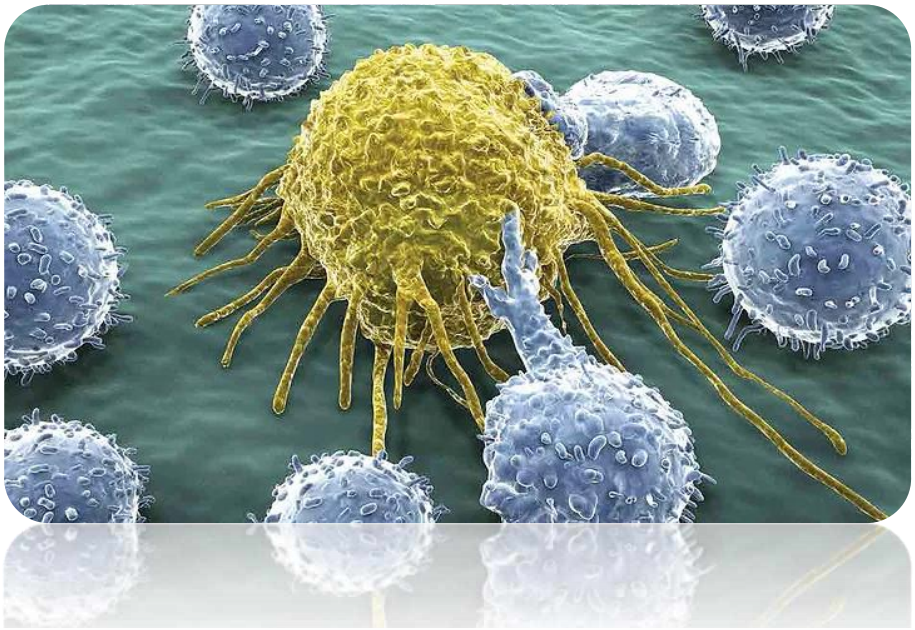
Effetto chemiotattico per i B-lynfociti

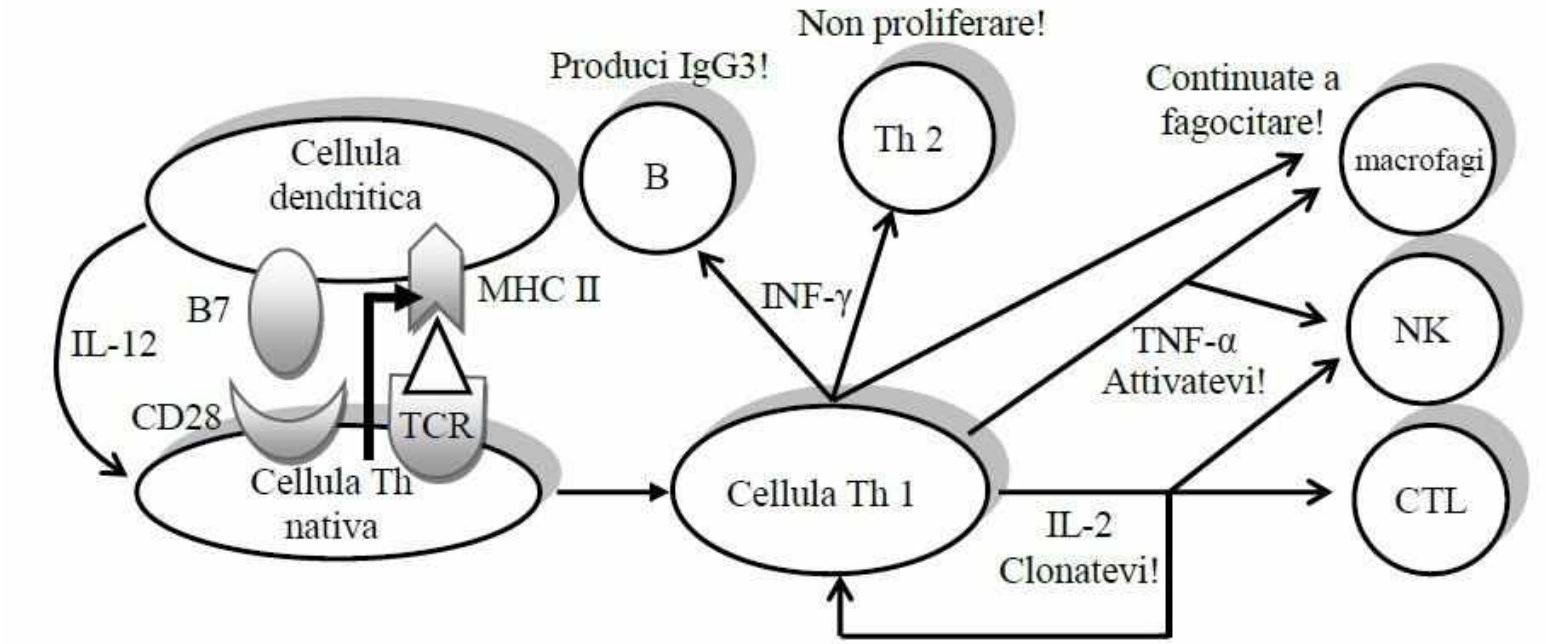
Marcatore precoce

Sensibilità 94–100% e specificità 63–96%

Richiede standardizzazione

Djukic M, 2012




Non proliferare!
Produci IgG3!
Continuate a fagocitare!
Cellula dendritica
B
Th 2
macrofagi
B7
MHC II
IL-12
INF-γ
TNF-α
Attivatevi!
NK
CD28
TCR
Cellula Th nativa
Cellula Th 1
CTL
IL-2
Clonatevi!

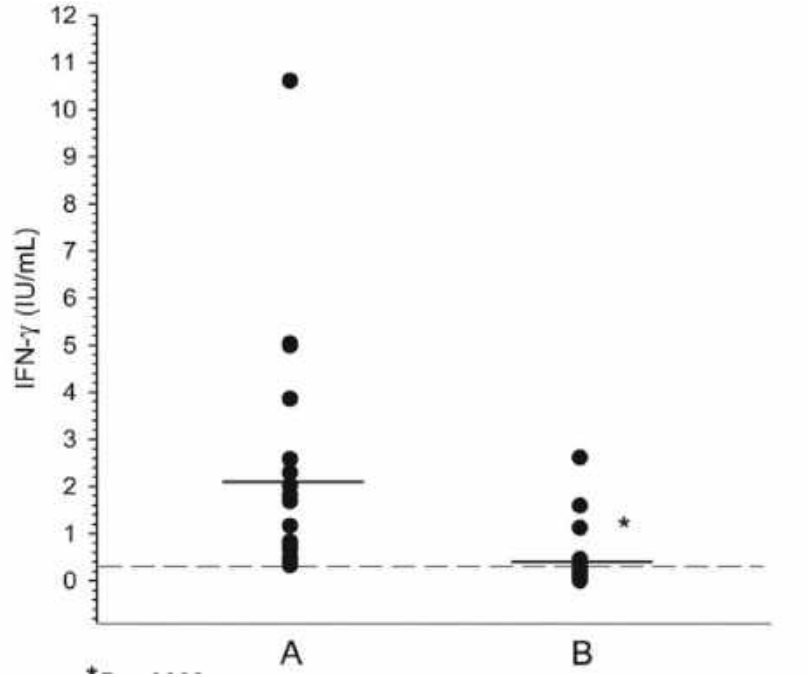
Clinical Infectious Diseases

MAJOR ARTICLE

Detection of IFN-γ Secretion by T Cells Collected Before and After Successful Treatment of Early Lyme Disease

Steven M. Callister,[1] Dean A. Jobe,[1] Aleksandra Stuparic-Stancic,[2] Misato Miyamasu,[3] Jeff Boyle,[3] Raymond J. Dattwyler,[4,5] and Paul M. Arnaboldi[4,5]

[1]Microbiology Research and Molecular Diagnostics Laboratory, and [2]Department of Urgent Care, Gundersen Health System, La Crosse, Wisconsin; [3]Qiagen, Inc, Germantown, Maryland; [4]Biopeptides Corporation, East Setauket, and [5]Department of Microbiology and Immunology, New York Medical College, Valhalla, New York



take-home message

Segni e sintomi specifici indirizzano la diagnosi: non c’è diagnosi di LD

senza clinica.

take-home message

Scorretta interpretazione dei sintomi può portare talora a non corretta interpretazione dei test di Laboratorio.

Talora pazienti con segni clinici tipici non vengono diagnosticati e non trattati

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