

## Serologie Lyme – Borreliose

### Immunglobulin G Halbwertszeit, Half-life of immunoglobulin G

Morell A, Terry WD, Waldman TA (1970) Metabolic properties of IgG sub classes in man. J clin. Invest. 49, 673-680.

Riesen W (1980) Struktur und biologische Eigenschaften von Immunglobulinen und  $\gamma$ -Globulin-Präparaten. 1. Struktur und Funktion von Immunglobulinen. Schweiz. med. Wschr. 110, 74-79.

Boger RH, Bode-Boger SM, Frolich JC (1995) Intravenöse Immunglobuline Grundlagen, Auswahlkriterien und Indikationen für ihren prophylaktischen und therapeutischen Einsatz. Medizinische Klinik 90, 520-526 (Nr. 9), Urban & Vogel, München

[http://www.med.uni-magdeburg.de/fme/institute/ikp/publikationen/publikationen1995/med\\_klinik520.pdf](http://www.med.uni-magdeburg.de/fme/institute/ikp/publikationen/publikationen1995/med_klinik520.pdf)

„Die mittlere biologische Halbwertszeit von Immunglobulin G beträgt etwa 21 Tage“.

“The mean biological half-life of immunoglobulin G is 21 days.”

Irani V, Guy AJ, Andrew D et al. (2015) Molecular properties of human IgG subclasses and their implications for designing therapeutic monoclonal antibodies against infectious diseases. *Mol Immunol*. pii: S0161-5890(15)00359-4. doi: 10.1016/j.molimm.2015.03.255.

<http://www.ncbi.nlm.nih.gov/pubmed/25900877>

[Burgdorfer W](#), [Barbour AG](#), [Hayes SF](#), [Benach JL](#), [Grunwaldt E](#), [Davis JP](#). (1982) **Lyme disease-a tick-borne spirochetosis?** *Science*. 216(4552), 1317-9.

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Burgdorfer+w+science+1982>

„Samples of serum from patients with Lyme disease were shown by indirect immunofluorescence to contain antibodies to this agent. It is suggested that the newly discovered spirochete is involved in the etiology of Lyme disease.“

[Steere AC](#), [Grodzicki RL](#), [Kornblatt AN](#), [Craft JE](#), [Barbour AG](#), [Burgdorfer W](#), [Schmid GP](#), [Johnson E](#), [Malawista SE](#) (1983) **The spirochetal etiology of Lyme disease.** *N Engl J Med*.

308(13), 733-40. <https://www.ncbi.nlm.nih.gov/pubmed/6828118>

Ackermann R, Boisten HP, Kabatzki J, Runne U, Krüger K, Herrmann WP (1984) Serumantikörper gegen Ixodes-ricinus-Spirochäte bei Acrodermatitis chronica atrophicans (Herxheimer). Dtsch med Wochenschr 109(1), 6-10 DOI: 10.1055/s-2008-1069128

<https://www.thieme-connect.com/ejournals/abstract/10.1055/s-2008-1069128>

“Using indirect immunofluorescence, IgG antibodies against the recently detected Ixodes-ricinus-spirocheta, which causes erythema chronicum migrans, could be demonstrated in all 21 persons with acrodermatitis chronica atrophicans. Titers were from 1 : 64 to 1 : 1024, specific IgM antibodies were demonstrable in only 5 patients in a titer of 1 : 64. Even after treatment with penicillin high IgG antibody titers of up to 1 : 1024 were found”.

Craft J, Fischer DK, Shimamoto GT, Steere AC. (1986) Antigens of Borrelia burgdorferi Recognized during Lyme Disease appearance of a **new Immunoglobulin M response** and expansion of the immunoglobulin G response late in the illness. J. Clin.Invest.1978: 934-939.

[Dattwyler RJ](#), [Volkman DJ](#), [Luft BJ](#), [Halperin JJ](#), [Thomas J](#), [Golightly MG](#) (1988)

**Seronegative Lyme disease.** Dissociation of specific T- and B-lymphocyte responses to Borrelia burgdorferi. *N Engl J Med*. 319(22), 1441-6. DOI: 10.1056/NEJM198812013192203

<http://www.nejm.org/doi/full/10.1056/NEJM198812013192203>

Hansen K, Asbrink E. (1989) Serodiagnosis of erythema migrans and acrodermatitis chronica atrophicans by the *Borrelia burgdorferi* flagellum enzyme-linked immunosorbent assay. *J Clin Microbiol* 27(3), 545-41.

Luger SW, Krauss PJ. (1990) Serologic tests for Lyme disease: interlaboratory variability. *Arch Intern Med* 150, 761-763.

Schutzer SE, Coyle PK, Belman AL, Golightly MG, Drulle J (1990) Sequestration of antibody to *Borrelia burgdorferi* in **immune complexes** in **seronegative Lyme disease**. *Lancet* 335, 312-315.

DORWARD DW, SCHWAN TG, GARON CF (1991) **Immune Capture and Detection of *Borrelia burgdorferi* Antigens in Urine, Blood, or Tissues from Infected Ticks, Mice, Dogs, and Humans**. *JOURNAL OF CLINICAL MICROBIOLOGY*, 1162-1170. 0095-1137/91/061162-09\$02.00/0  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC269963/pdf/jcm00042-0088.pdf>  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC269963/>

Hansen K, Pii K, Lebech AM (1991) **Improved immunoglobulin M serodiagnosis** in Lyme borreliosis by using a  $\mu$ -captured enzyme-linked immunosorbent assay with biotinylated *Borrelia burgdorferi* flagella. *J Clin Microbiol* 29, 166-173.

[Schierz G, Weber K, Burgdorfer W](http://www.amazon.de/Aspects-Lyme-Borreliosis-G-Schierz/dp/3540556281) (1992) *Aspects of Lyme Borreliosis*. Springer; Auflage: 1  
<http://www.amazon.de/Aspects-Lyme-Borreliosis-G-Schierz/dp/3540556281>

Bakken LK, Case KL, Callister SM, Bourdeau NJ, Schell RF. (1992) Performance of 45 laboratories participating in a proficiency testing program for Lyme disease serology. *JAMA* 268, 891-5.

Ma B, Christen B, Leung D, Vigo-Pelfrey C. (1992) Serodiagnosis of Lyme borreliosis by Western immunoblot: reactivity of various significant antibodies against *Borrelia burgdorferi*. *J Clin Microbiol* 30, 370-6.

Feder HM Jr, Gerber MA, Luger SW, Ryan RW. (1992) **Persistence of serum antibodies** to *Borrelia burgdorferi* in patients treated for Lyme disease. *Clin Infect Dis* 15, 788-93.

Banyas GT. (1992) Difficulties with Lyme serology. *J Am Optom Assoc* 63(2), 135-139.

Dressler F, Whalen JA, Reinhardt BN, Steere AC (1993) Western blotting in the serodiagnosis of Lyme disease. *J Infect Dis* 167, 392-400. [Abstract/FREE Full Text](#)

[Aguero-Rosenfeld ME](#), [Nowakowski J](#), [McKenna DF](#), [Carbonaro CA](#), [Wormser GP](#). (1993) Serodiagnosis in early Lyme disease. *J Clin Microbiol*. 31(12), 3090-5  
<http://www.ncbi.nlm.nih.gov/pubmed/8308100>

**“Seroconversion was observed in 74 and 64% of evaluable patients by ELISA and IB, respectively, despite the use of antibiotic therapy”.**

Wilske B, Fingerle V, Herzer P, Hofmann A, Lehnert G, Peters H, Pfister HW, Preac-Mursic V, Soutschek E, Weber K. (1993) Recombinant immunoblot in the serodiagnosis of Lyme borreliosis. Comparison with indirect immunofluorescence and enzyme-linked immunosorbent assay. *Med Microbiol Immun* 182(5), 255-70.

Schubert HD, Greenebaum E (1994) Cytologically proven **seronegative Lyme** choroiditis and vitriitis. *Retina* 14, 39-42.

(1995) Centers for Disease Control and Prevention. Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR Morb Mortal Wkly Rep 44, 590–1.

Engstrom SM, Shoop E, Johnson RC. (1995) Immunoblot interpretation criteria for serodiagnosis of early Lyme disease. J Clin Microbiol 33, 419–27. **[Spezifität 96%, Sensitivität 55%]**

Oksi J, Uksila J, Marjamäki M et al. (1995) Antibodies against Whole Sonicated *Borrelia burgdorferi* Spirochetes, 41-Kilodalton Flagellin, and P39 Protein in Patients with PCR- or Culture-Proven Late Lyme Borreliosis. J Clin Microbiol. 33(9), 2260-2264.

Lawrence C, Lipton R, Lowy R, Coyle PK (1995) **Seronegative chronic relapsing neuroborreliosis.** Eur Neurol 35(2), 113-117.

Coyle PK, SE Schutzer et al. (1995) Detection of *Borrelia burgdorferi* specific antigen in **antibody-negative cerebrospinal fluid** in neurologic Lyme disease. Neurology 45, 2010-2015.

[M E Aguero-Rosenfeld](#), [J Nowakowski](#), [S Bittker](#), [D Cooper](#), [R B Nadelman](#), and [G P Wormser](#) (1996) Evolution of the serologic response to *Borrelia burgdorferi* in treated patients with culture-confirmed erythema migrans. J Clin Microbiol. 34(1), 1–9. PMID: PMC228718 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC228718/>  
“We investigated the appearance and evolution of immunoglobulin M (IgM) and IgG antibodies to *Borrelia burgdorferi* in 46 patients with culture-proven erythema migrans (EM). All patients received antimicrobial treatment and were prospectively evaluated for up to 1 year. A total of 257 serially collected serum samples were tested by commercial IgG-IgM enzyme-linked immunosorbent assay and separate IgM and IgG immunoblots (IBs). At the baseline, 33% of the patients had a positive ELISA result and 43% of the patients had a positive IgM IB result by using the criteria of the Centers for Disease Control and Prevention-Association of State and Territorial Public Health Laboratory Directors for the interpretation of IB results. Positive serology at the baseline and the rate of seroconversion correlated directly with disease duration and/or evidence of dissemination prior to treatment.”

Mouritsen CL, Wittwer CT, Litwin CM, Yang L, Weis JJ, Martins TB, Jaskowski TD, Hill HR (1996) Polymerase chain reaction detection of Lyme disease: correlation with clinical manifestations and serologic responses. Am J Clin Pathol 105, 647-654.  
<http://www.ncbi.nlm.nih.gov/pubmed/8623775>

“In 29 serologic positive samples (14 IgG and IgM positive, 9 IgM alone and 6 IgG alone), *B burgdorferi* DNA was not detected. In contrast, nine serum samples and one synovial fluid from patients with definite clinical features of Lyme disease were found to be negative by EIA and Western blot analysis for IgG and IgM antibody, but contained *B burgdorferi* DNA, as detected by PCR. Polymerase chain reaction analysis of serum and synovial fluid may be of significant diagnostic value in Lyme disease, especially in the absence of a serologic response in early, partially treated and seronegative chronic disease.”

Aguero-Rosenfeld ME, Nowakowski J, McKenna DF et al. (1996) Evolution of the serologic response to *Borrelia burgdorferi* in treated patients with culture-confirmed erythema migrans. J Clin Microbiol 34, 1-9.

Johnson BJ, Robbins KE, Bailey RE, et al. (1996) Serodiagnosis of Lyme disease: **accuracy of a two-step approach using a flagella-based ELISA and immunoblotting.** J Infect Dis 174, 346–53.

Wormser GP, Horowitz HW, Dumler SJ, Schwartz I, Aguero-Rosenfeld M (1996) **False-positive Lyme disease serology in human granulocytic ehrlichiosis.** Lancet 347,981-2.  
[CrossRefMedlineWeb of Science](#)

Luft BT, Dattwyler RJ, Johnson RC, Luger SW, Bosler EM, Rahn DW, Masters EJ, Grunwaldt E, Gadgil SD (1996) Azithromycin compared with amoxicillin in the treatment of erythema

migrans. A double-blinded, randomized controlled trial. *Ann Int Med* 124, 785-791.  
<http://www.ncbi.nlm.nih.gov/pubmed/8610947>

**57% of patients who had relapsed were seronegative at the time of relapse.**

Hilton E, Devoti J, Sood S. (1996) Recommendation to include OspA and OspB in the new immunoblotting criteria for serodiagnosis of Lyme disease. *J Clin Microbiol* 34, 1353–4.

Ledue TB, Collins MF, Craig WY. (1996) New laboratory guidelines for serologic diagnosis of Lyme disease: evaluation of the two-test protocol. *J Clin Microbiol* 34, 2343–50. [**Spezifität 100%, Sensitivität 44%**]

Tilton RC, Sand MN, Manak M. (1997) The Western immunoblot for Lyme disease: determination of sensitivity, specificity, and interpretive criteria with use of commercially available performance panels. *Clin Infect Dis* 25(Suppl 1), S31-4. [**Spezifität 100%, Sensitivität 45%**]

Bakken LL, Callister SM, Wand P et al. (1997) Interlaboratory comparison of test results for detection of Lyme disease by 516 participants in the Wisconsin State Laboratory of Hygiene/College of American Pathologists Proficiency Testing Program. *J Clin Microbiol* 35(3), 537-43.

Tugwell P, Dennis DT, Weinstein A, et al. (1997) Laboratory evaluation in the diagnosis of Lyme disease. *Ann Intern Med* 127, 1109-23. [Abstract/FREE Full Text](#)

Hilton E, Tramontano A, DeVoti J, and Sood SK. (1997) Temporal study of **immunoglobulin M seroreactivity** to *Borrelia burgdorferi* in patients treated for Lyme borreliosis. *J Clin Microbiol* 35(3), 774-776.

Coyle PK. (1997) Advances and pitfalls in the diagnosis of Lyme disease. *FEMS Immun Med Microbiol* 19, 103-109.

Akin E, McHugh GI, Flavell RA, Fikrig E, Steere AC (1999) The immunoglobulin (IgG) antibody response to OspA and OspB correlates with severe and prolonged Lyme arthritis and the IgG response to P35 with mild and brief arthritis. *Infect Immun* 67, 173-181.

Trevejo RT, Krause PJ, Sikand VK, et al (1999) Evaluation of two-test serodiagnostic method for early Lyme disease in clinical practice. *J Infect Dis* 179, 931-8. [Abstract/FREE Full Text](#) [**Spezifität 100%, Sensitivität 29%**]

Brown SL, Hanson SL, Langone JJ. (1999) Role of serology in the diagnosis of Lyme disease. *JAMA* 282, 62–6.

Logigian EL, Kaplan RF, Steere AC. (1999) Successful treatment of Lyme encephalopathy with intravenous ceftriaxone. *J Infect Dis* 180 377–83.  
**17% of the patients with documented Lyme encephalopathy were seronegative.**

Liang FT, Steere AC, Marques AR, Johnson BJ, Miller JN, Philipp MT (1999) Sensitive and specific serodiagnosis of Lyme disease by enzymelinked immunosorbent assay with a peptide based on an immunodominant conserved region of *Borrelia burgdorferi* VlsE. *J Clin Microbiol* 37, 3990-6. [Abstract/FREE Full Text](#)

Lawrenz MB, Hardham JM, Owens RT et al. (1999) Human antibody responses to **VlsE** antigenic variation protein of *Borrelia burgdorferi*. *J Clin Mikrobiol.* 37, 3997-4004

Kaiser R. (2000) **False negative serology in patients with neuroborreliosis** and the value of employing of different borrelial strains in serological assays. J Med Microbiol 49(10), 911-915.

Wilmers A (2000) Die **Antikörperdynamik** bei der Lyme Borreliose. Inauguraldissertation Med. Fak. Köln.  
[http://books.google.de/books/about/Die\\_Antik%C3%B6rperdynamik\\_bei\\_der\\_Lyme\\_Borr.html?id=d6RfywAACAAJ&redir\\_esc=y](http://books.google.de/books/about/Die_Antik%C3%B6rperdynamik_bei_der_Lyme_Borr.html?id=d6RfywAACAAJ&redir_esc=y)

Kalish RA, McHugh G, Granquist J, Shea B, Ruthazer R, Steere AC (2001) **Persistence of IgM or IgG** antibody responses to Borrelia burgdorferi 10 to 20 years after active Lyme disease. Clin Infect Dis 33, 780-5. [Abstract/FREE Full Text](#) <http://cid.oxfordjournals.org/content/33/6/780.full>

Dumler JS (2001) Molecular diagnosis of Lyme disease: review and metaanalysis. Mol Diagn 6, 1–11

Nowakowski J, Schwartz I, Liveris D et al. (2001) Laboratory Diagnostic Techniques for Patients with Early Lyme Disease Associated with Erythema Migrans: A Comparison of Different Techniques. Clinical Infectious Diseases 33, 2023–7 \_ 2001 by the Infectious Diseases Society of America. **[Spezifität 99%, Sensitivität 68%]**

Van Dam AP (2001) Recent advances in the diagnosis of Lyme disease. Expert Rev Mol Diagn 1, 413–27

Breier F, Khanakah G, Stanek G, Aberer E, Schmidt B, Tappeiner G. (2001) Isolation and polymerase chain reaction typing of Borrelia afzelii from a skin lesion in a **seronegative patient** with generalized ulcerating bullosus lichen sklerosus et atrophicus. Br J Dermatol 144, 387-392

Grignolo MC, L Buffrini, P Monteforte, G Rovetta. (2001) Reliability of a polymerase chain reaction (PCR) technique in the diagnosis of Lyme borreliosis. Minerva Med. 92(1), 29-33  
<http://www.ncbi.nlm.nih.gov/pubmed/11317136>

**True positives at clinical examination but negatives at serologic tests. “The obtained results suggested a good reliability of positive results obtained with the PCR technique used in this study and allowed the false negatives of serologic tests to be detected ....”**

Dejmková H, D Hulinska, D. Tegzová, K Pavelka, J Gatterová, and P Vavřík. (2002) **Seronegative Lyme arthritis** caused by Borrelia garinii. Clin Rheumatol 21, 330-334.

Tylewska-Wierzbanowska S, Chmielewski T. (2002) Limitation of serological testing for Lyme borreliosis: evaluation of ELISA and western blot in comparison with PCR and culture methods. Wien Klin Wochenschr 114(13-14), 601-5. <http://www.ncbi.nlm.nih.gov/pubmed/12422608>

**“No correlation was found between levels of specific B. burgdorferi antibodies detected with a recombinant antigen ELISA and the number of protein fractions developed with these antibodies by immunoblot. Moreover, Lyme borreliosis patients who have live spirochetes in body fluids have low or negative levels of borrelial antibodies in their sera. This indicates that an efficient diagnosis of Lyme borreliosis has to be based on a combination of various techniques such as serology, PCR and culture, not solely on serology.”**

Magnarelli LA, Lawrenz M, Norris S, Fikrig S (2002) Comparative reactivity of human sera to recombinant VlsE and other Borrelia burgdorferi antigens in class-specific enzyme-linked immunosorbent assays for Lyme borreliosis. J. Medical Microbiol. 51, 649-655.

Hunfeld KP, Stanek G, Straube E, Hagedorn HJ, Schörner C, Mühlischlegel F, Brade V. (2002) Quality of Lyme disease serology. Lessons from the German Proficiency Testing Program 1999-2001. A preliminary report. Wien Klin Wochenschr.114(13-14), 591-600.  
<http://www.ncbi.nlm.nih.gov/pubmed/12422607>

**“In view of our results further standardisation of Lyme disease serology is not just desirable but is urgently needed. Moreover, stronger criteria for the validation of available test kits must be applied.”**



Bacon RM, Biggerstaff BJ, Schriefer ME, et al (2003) Serodiagnosis of Lyme disease by kinetic enzyme-linked immunosorbent assay using recombinant **VlsE** or peptide antigens of *Borrelia burgdorferi* compared with 2-tiered testing using whole-cell lysates. *J Infect Dis* 187, 1187-99. [Abstract/FREE Full Text](#) [**Spezifität 99%, Sensitivität 67%**]

(2003) Seronegativity in Lyme borreliosis and Other Spirochetal Infections.

<http://www.lymeinfo.net/medical/LDSeronegativity.pdf>

**"If false results are to be feared, it is the false negative result which holds the greatest peril for the patient."**

Panelius J, Lahdenne P, Saxen H et al. (2003) Diagnosis of Lyme Neuroborreliosis with Antibodies to Recombinant Proteins DbpA, BBK32, and OspC, and VlsE IR6 Peptide. *Journal of Neurology*, 250, 1318-1327. <http://dx.doi.org/10.1007/s00415-003-0205-2>

Ekerfelt C, Ernerudh J, Forsberg P, et al. (2004) Lyme borreliosis in Sweden—diagnostic performance of five commercial *Borrelia* serology kits using sera from well-defined patient groups. *APMIS* 112, 74–8.

Mogilyansky E, Loa CC, Adelson ME, Mordechai E, Tilton RC (2004) Comparison of Western immunoblotting and the C6 Lyme antibody test for laboratory detection of Lyme disease. *Clin Diagn Lab Immunol* 11, 924-9. [CrossRefMedline](#)

Marangoni A, Sparacino M, Cavrini F et al. (2005) Comparative evaluation of three different ELISA methods for the diagnosis of early culture-confirmed Lyme disease in Italy. *J Med Microbiol* 54, 361-367

DePietropaolo DL, Powers JH, Gill Jm Foy AJ (2005) Diagnosis of Lyme disease. *Am Fam Physician* 72(2), 297-304 <http://www.ncbi.nlm.nih.gov/pubmed/16050454>

[Aguero-Rosenfeld](#) ME, [Wang](#) G, [Schwartz](#) I, [Wormser](#) GP (2005) Diagnosis of Lyme Borreliosis. *Clin Microbiol Rev.* 18(3), 484–509. doi: [10.1128/CMR.18.3.484-509.2005](https://doi.org/10.1128/CMR.18.3.484-509.2005) PMID: PMC1195970 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1195970/>

Coulter P, Lema C, Flayhart D et al. (2005) Two-Year Evaluation of *Borrelia burgdorferi* Culture and Supplemental Tests for Definitive Diagnosis of Lyme Disease. *J Clin Microbiol.* 43(10), 5080–5084. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1248466/> [**Sensitivität 25%**]

(2005) Centers for Disease Control and Prevention. Notice to readers: caution regarding testing for Lyme disease. *MMWR Morb Mortal Wkly Rep* 54, 125–6.

Smismans A, Goossens VJ, Nulens E et al. (2006) Comparison of five different immunoassays for the detection of *Borrelia burgdorferi* IgM and IgG antibodies. *Clin Microbiol Infect.* 12, 648-655 <http://www.ncbi.nlm.nih.gov/pubmed/16774561>

Sillanpää H, Lahdenne P, Sarvas H, Arnez M, Steere A, Peltomaa M, Seppälä I. (2007) Immune responses to borrelial VlsE IR6 peptide variants. *Int J Med Microbiol* 297, 45-52.

Gomes-Solecki MJ, Meirelles L, Glass J, Dattwyler RJ. (2007) Epitope length, genospecies dependency, and serum panel effect in the IR6 enzyme-linked immunosorbent assay for detection of antibodies to *Borrelia burgdorferi*. *Clin Vaccine Immunol* 14, 875-9.

Stricker RB, Johnson L. (2007) Lyme wars: let's tackle the testing. *BMJ.* 335(7628),1008.

Holl-Weiden A, Suerbaum S, Girschick HJ. (2007) **Seronegative Lyme arthritis.** *Rheumatology International* 11, 1091-1093.

Wilske B, Fingerle V, Schult-Spechtel U (2007) Microbiological and serological diagnosis of Lyme borreliosis. FEMS Immunol Med Microbiol 49, 13-21  
<http://www.ncbi.nlm.nih.gov/pubmed/17266710>

Canadian Public Health Laboratory Network. (2007) The laboratory diagnosis of Lyme borreliosis: Guidelines from the Canadian Public Health Laboratory Network. Can J Infect Dis Med Microbiol 18(2), 145-148 <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2533539/>

Gasiorowski J, Witecka-Knysz E, Knysz B, et al. (2007) Diagnostics of Lyme disease. Med Pr 58(5), 439-47. [Abstract](#)

Skarpaas T, Liostad U, Sobyte M, Mygland A (2007) Sensitivity and Specificity of a Commercial **C6 Peptide Enzyme Immuno Assay** in Diagnosis of Acute Lyme Neuroborreliosis. European Journal of Clinical Microbiology Infectious Diseases, 26, 675-677. <http://dx.doi.org/10.1007/s10096-007-0336-y>

Tjernberg I, Schon T, Ernerudh J, Wistedt AC, Forsberg P, Eliasson I (2008) **C6-Peptide Serology** as Di-agnostic Tool in Neuroborreliosis. APMIS, 116, 393-399.  
<http://dx.doi.org/10.1111/j.1600-0463.2008.00842.x>

Marangoni A, Moroni A, Accardo S, et al. (2008) Borrelia burgdorferi VlsE antigen for the serological diagnosis of Lyme borreliosis. Eur J Clin Microbiol Infect Dis 27(5), 349-54.  
[Abstract](#)

Weinstein A. (2008) Laboratory Testing for Lyme Disease: Time for a Change? Clin Infect Dis. 47 (2), 196-197. <http://cid.oxfordjournals.org/content/47/2/196.full>

Stricker RB, Johnson L (2008) Serologic tests for lyme disease: more smoke and mirrors. Clin Infect Dis 47(8), 1111-2; author reply 1112-3. [Full Citation](#)

Lencáková D, Fingerle V, Stefancíková A, et al. (2008) Evaluation of recombinant line immunoblot for detection of Lyme disease in Slovakia: comparison with two other immunoassays. Vector Borne Zoonotic Dis 8(3), 381-90. [Abstract](#)

Steere AC, McHugh G, Damle N, Sikand VK (2008) Prospective study of serologic tests for Lyme disease. Clin Infect Dis 47,188-95. [Abstract/FREE Full Text](#) [**Spezifität 99%, Sensitivität 18%**]

Binnicker MJ, Jespersen DJ, Harring JA, Rollins LO, Bryant SC, Beito EM. (2008) Evaluation of two commercial systems for the automated processing, reading and interpretation of Lyme Western blots. J Clin Microbiol 46, 2216–21. [**Spezifität 100%, Sensitivität 49%**]

Petersen E, Tolstrup M, Capuano F, Ellermann-Eriksen S. (2008) Population based study of diagnostic assays for Borrelia infection: comparison of purified flagella antigen assay (IDEIA, Dako Cytomation) and recombinant antigen assay (Liaison, DiaSorin). BMC Clin Pathol 8, 4.

Vermeersch P, Ressler S, Nackers E, Lagrou K (2009) The **C6 Lyme Antibody Test** Has Low Sensitivity for Antibody Detection in Cerebrospinal Fluid. Diagnostic Microbiology and Infectious Disease, 64, 347-349. <http://dx.doi.org/10.1016/j.diagmicrobio.2009.03.013>

Stricker RB (2009) IDSA hearing presentation: Problems with diagnosis and treatment of Lyme disease. [http://www.ilads.org/lyme\\_disease/media/lyme\\_video\\_stricker.html](http://www.ilads.org/lyme_disease/media/lyme_video_stricker.html)

Maloney EL (2009) The need for clinical judgment in the diagnosis and treatment of Lyme disease. *Journal of American Physicians and Surgeons*. 14, 82-89.

**“Available laboratory tests for Lyme disease have poor sensitivity. “**

Melby KK, Skar AG (2009) Borrelia--serologic tests for benefit and problems. *Tidsskr Nor Laegeforen* 129(20), 2135. [Full Citation](#)

Kristiansen BE, Grude N, Tveten Y, et al. (2009) Laboratory diagnosis of Lyme borreliosis. *Tidsskr Nor Laegeforen* 129(20), 2132-4. [Full Citation](#)

Stricker RB (2009) Challenge to Recommendation Requiring Diagnostic Test Confirmation of Lyme Disease. *IDSA Guidelines* (p. 1090): “Diagnostic testing performed in laboratories with excellent qualitycontrol procedures is required for confirmation of extracutaneous Lyme disease....” [http://www.ilads.org/lyme\\_disease/written\\_testimony/3%20Stricker-Diagnostic%20Test%20Confirmation.pdf?storyid=/templatedata/parents/story/data/1182531760403.xml](http://www.ilads.org/lyme_disease/written_testimony/3%20Stricker-Diagnostic%20Test%20Confirmation.pdf?storyid=/templatedata/parents/story/data/1182531760403.xml)

Ang CW, Notermans DW, Hommes AM. et al. (2010) Large differences between test strategies for the detection of anti-Borrelia antibodies are revealed by comparing eight ELISAs and five immunoblots. *Eur J Clin Microbiol Infect Dis* DOI 10.1007/s10096-011-1157-6 <http://www.springerlink.com/content/w64170894v08654g/>  
<http://www.springerlink.com/content/w64170894v08654g/fulltext.pdf>

Branda JA, Aguero-Rosenfeld ME, Ferraro MJ et al. (2010) 2-Tiered Antibody Testing for Early and Late Lyme Disease Using Only an Immunoglobulin G Blot with the Addition of a VisE Band as the Second-Tier Test *Clinical Infectious Diseases* 50(1), 20-26 [Abstract](#) [Full Text \(HTML\)](#) [Full Text \(PDF\)](#)

Schwarzbach A (2010) Vergleich Borrelia-ELISA unterschiedlicher Testhersteller mit Immunoblot: Hochspezifische, aber niedrig-sensitive Testverfahren. [**Sensitivität 92%, ELISA Spezifität 32 - 43 %, Immunoblot 60%**] <http://www.borreliose-nachrichten.de/wp-content/uploads/2011/12/Schwarzbach-2010-Vergleich-Elisa-Blot.pdf>

Gajović O, Todorović Z, Nesić L, et al. (2010) Lyme borreliosis--diagnostic difficulties in interpreting serological results. *Med Pregl* 63(11-12), 839-43. [Abstract](#)

Stricker RB, Johnson L (2010) Lyme disease diagnosis and treatment: lessons from the AIDS epidemic. *Minerva Med* 101(6), 419-25. [Abstract](#)

Jiang Y, Hou XX, Geng Z, et al. (2010) Interpretation criteria for standardized Western blot for the predominant species of *Borrelia burgdorferi* sensu lato in China. *Biomed Environ Sci* 23(5), 341-9. [Abstract](#) | [Full Citation](#)

Dessau RB, Bangsberg JM, Ejlertsen T, et al. (2010) Utilization of serology for the diagnosis of suspected Lyme borreliosis in Denmark: survey of patients seen in general practice. *BMC Infect Dis* 317. [Abstract](#)

Evans R, Mavin S, McDonagh S, et al. (2010) More specific bands in the IgG western blot in sera from Scottish patients with suspected Lyme borreliosis. *J Clin Pathol* 63(8), 719-21. [Abstract](#)

Shah JS, Du Cruz I, Narciso W, Lo W, Harris NS. (2010) Improved clinical sensitivity for detection of antibodies to *Borrelia burgdorferi* by Western blots prepared from a mixture of two strains of *B. burgdorferi*, 297 and B31, and interpreted by in-house criteria. *European Infect. Dis.* 4, 56-60  
<http://www.touchinfectiousdisease.com/articles/improved-clinical-sensitivity-detection-antibodies-borrelia-burgdorferi-western-blots-prepa>



Dessau RB, Ejlersen T, Hilden J (2010) Simultaneous use of serum IgG and IgM for risk scoring of suspected early Lyme borreliosis: graphical and bivariate analyses. *APMIS* 118(4), 313-23. [Abstract](#)

Branda JA, Aguero-Rosenfeld ME, Ferraro MJ, et al. (2010) 2-tiered antibody testing for early and late Lyme disease using only an immunoglobulin G blot with the addition of a VlsE band as the second-tier test. *Clin Infect Dis* 50(1), 20-6. [Abstract](#)

Durovska J, Bazovska S, Ondrisova M, et al. (2010) Our experience with examination of antibodies against antigens of *Borrelia burgdorferi* in patients with suspected Lyme disease. *Bratisl Lek Listy* 111(3), 153-5.

Burbelo PD, Issa AT, Ching KH, et al. (2010) Rapid, simple, quantitative, and highly sensitive antibody detection for Lyme disease. *Clin Vaccine Immunol* 17(6), 904-9. [Abstract](#)

Mavin S, McDonagh S, Evans R, et al. (2011) Interpretation criteria in Western blot diagnosis of Lyme borreliosis. *Br J Biomed Sci* 68(1), 5-10. [Abstract](#)

Ang CW, Notermans DW, Hommes M, et al. (2011) Large differences between test strategies for the detection of anti-*Borrelia* antibodies are revealed by comparing eight ELISAs and five immunoblots. *Eur J Clin Microbiol Infect Dis* 30(8), 1027-32. [Abstract](#)

Wojciechowska-Koszko I, Mączyńska I, Szych Z, et al. (2011) Serodiagnosis of borreliosis: indirect immunofluorescence assay, enzyme-linked immunosorbent assay and immunoblotting. *Arch Immunol Ther Exp (Warsz)* 59(1), 69-77. [Abstract](#)

Branda JA, Linskey K, Kim YA, et al. (2011) 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. *Clin Infect Dis* 53(6), 541-7. [Abstract](#)

Racine R., McLaughlin M. Jonesa DD. et al. (2011) **IgM Production by Bone Marrow Plasmablasts Contributes to Long-Term Protection against Intracellular Bacterial Infection.** *J Immunol* 186, 1011-1021 Prepublished online 8 <http://www.jimmunol.org/content/186/2/1011>

Ang CW, Notermans DW, Hommes M, Simoons-Smit, Herremans T. (2011) Large differences between test strategies for the detection of anti-*Borrelia* antibodies are revealed by comparing eight ELISAs and five immunoblots. *Eur J Clin Microbiol Infect Dis* 30, 1027-1032. [CrossRef](#) | [PubMed](#)

CDC (2011) Lyme Disease (*Borrelia burgdorferi*), Case Definition [http://www.cdc.gov/osels/ph\\_surveillance/nndss/casedef/lyme\\_disease\\_current.htm](http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/lyme_disease_current.htm)  
"This webpage does not contain the latest information on NNDSS, and does not meet current CDC accessibility and branding standards. After December 21, 2012 this website will no longer be available".

CDC NNDSS Diseases & Conditions (2011) Lyme disease (*Borrelia burgdorferi*) Case Definition. Lyme disease Summary. <https://wwwn.cdc.gov/nndss/conditions/lyme-disease/case-definition/2011/>  
"This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis."

**Seriburi V**, Ndukwe N, Chang Z, Cox ME, Wormser GP (2011/2012) High frequency of **false positive IgM** immunoblots for *Borrelia burgdorferi* in Clinical Practice. *Clin Microbiol Infect*, European Society of Clinical Microbiology and Infectious Diseases. 18, 1236-1240  
10.1111/j.1469-0691.2011.03749.x

Stricker RB. (2012) Lyme Disease: The hidden Epidemic. House Committee on Foreign Affairs, Subcommittee on Africa, Global Health, and Human Rights.  
<http://foreignaffairs.house.gov/hearings/view/?1455>

Dehnert M, Fingerle V, Klier C, Talaska T et al. (2012) **Seropositivity** of Lyme Borreliosis and Associated Risk Factors: A Population-Based Study in Children and Adolescents in Germany (KiGGS). PLOS ONE | www.plosone.org, 7(8) e41321

Berghoff W. (2012) Serologie Lyme-Borreliose Stadium III.  
<http://www.praxis-berghoff.de/dokumente/SerologieLymeBorrelioseStadiumIII.pdf>

Barclay SS, Melia MT, Auwaerter PG (2012) Misdiagnosis of late Lyme arthritis by inappropriate use of synovial fluid Borrelia burgdorferi immunoblot testing. Lyme Synovial Immunoblot. *Clin Vaccine Immunol*. 2012 Sep 12. <http://www.ncbi.nlm.nih.gov/pubmed/22971779>

Busson L, Reynders M, Van den Wijngaert S, et al. (2012) Evaluation of commercial screening tests and blot assays for the diagnosis of Lyme borreliosis. *Diagn Microbiol Infect Dis* 73(3), 246-51. [Abstract](#)

Gerritzen A, Brandt S (2012) Serodiagnosis of Lyme borreliosis with bead based immunoassays using multiplex technology. *Methods* 56(4), 477-83. [Abstract](#)

Reiber H (2013) **Instand Ringversuch für Neuroborreliose: „Liquordiagnostik und Qualitätskontrolle, CSF und Complexity Studies“**, Sao Paulo, Brasil; Instand e.V. 22. 11. <http://www.borreliose-gesellschaft.de/de/TagungenFortbildung/2013Hamburg/Programm/Reiber>  
**“Die Methodenbezogene Auswertung ergibt mittlere AI Werte, die um einen Faktor 8 variieren können”**

Lerner MB, Dailey J, Goldsmith BR et al. (2013) Detecting lyme disease using antibody-functionalized single-walled carbon nanotube transistors. *Biosensors and Bioelectronics*.  
<http://dx.doi.org/10.1016/j.bios.2013.01.035>

Donta ST (2013) Reinfection versus Relapse of Lyme Disease. *N Engl J Med* 361, 11  
<http://www.nejm.org/doi/full/10.1056/NEJMc1215615>

SERONEGATIVE LYME DISEASE (causes, Ursachen)  
<http://www.mentalhealthandillness.com/seronegativelymedisease.html>

[Elsner](#) RA, [Hastey](#) CJ, [Baumgarth](#) N (2014) **CD4<sup>+</sup> T cells promote antibody production but not sustained affinity maturation during Borrelia burgdorferi infection.** doi: 10.1128/IAI. <http://iai.asm.org/content/early/2014/10/08/IAI.02471-14.abstract>  
**« Previous studies showed that immune response to Borrelia burgdorferi (Bb) appear to lack robust T-dependent B cell responses, as neither long-lived plasma cells nor memory B cells form for months after infection and non-switched IgM antibodies are continuously produced during this chronic disease ».**

Fallon BA, Pavlicova M, Coffino SW, Brenner C (2014) **A comparison of Lyme disease serologic test results from four laboratories in patients with persistent symptoms after antibiotic treatment.** *Clinical Infectious Diseases*, online before print. pii: ciu703.  
<http://doi.org/10.1093/cid/ciu703>  
<http://bobcowart.blogspot.de/2014/09/a-comparison-of-lyme-disease-serologic.html>  
**« While there was surprisingly little difference among the labs in percentage of positive results on most assays using CDC criteria, interlaboratory variability was considerable and remains a problem in LD testing. »**

Dattwyler RJ, Arnaboldi PM (2014) **Comparison of Lyme Disease Serologic Assays and Lyme Specialty Laboratories.** EDITORIAL COMMENTARY. *CID* 2014, 59, 1711-1713  
<http://www.ncbi.nlm.nih.gov/pubmed/25182243>  
<http://cid.oxfordjournals.org/content/early/2014/09/02/cid.ciu705.extract>

„We should all remember that poor specificity was a major issue that led to the adoption of the 2-tier paradigm in the first place.“

Norris SJ (2014) **The vls antigenic variation systems of Lyme disease Borrelia: eluding host immunity through both random, segmental gene conversion and framework heterogeneity.** Microbiol Spectr. 2(6): . doi:10.1128/microbiolspec.MDNA3-0038-2014.  
<http://www.asmscience.org/content/journal/cm/10.1128/microbiolspec.MDNA3-0038-2014>

[Moore A](#), [Nelson C](#), [Molins C](#), [Mead P](#), [Schriefer M](#). (2016) **Current Guidelines, Common Clinical Pitfalls, and Future Directions for Laboratory Diagnosis of Lyme Disease, United States.** *Emerg Infect Dis.* 22(7). doi: 10.3201/eid2207.151694.

<http://www.ncbi.nlm.nih.gov/pubmed/27314832>

[Raphael Stricker](#) 2016 Jun 18 05:43 a.m. Circular Reasoning in CDC Lyme Disease Test Review Raphael B. Stricker, MD; Lorraine Johnson, JD, MBA Previous studies have shown that commercial two-tier serolo ... more

<https://www.researchgate.net/publication/304210330> <http://www.ncbi.nlm.nih.gov/pubmed/27314832>

Cook MJ, Puri BK (2016) **Commercial test kits for detection of Lyme borreliosis: a meta-analysis of test accuracy.** *International Journal of General Medicine, Volume 9*

<https://www.dovepress.com/commercial-test-kits-for-detection-of-lyme-borreliosis-a-meta-analysis-peer-reviewed-fulltext-article-IJGM>

<https://www.ncbi.nlm.nih.gov/pubmed/27920571>

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5125990/>

Leeflang M, Ang C, Berkhout J, Bijlmer H, Van Bortel W, Brandenburg H, et al. (2016) **The diagnostic accuracy of serological tests for Lyme borreliosis : a systematic review and meta-analysis** . BMC Infect Dis. BMC Infectious Diseases; 16, 1–17.

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4807538>

Zeller H, Van Bortel W. (2016) **A systematic literature review on the diagnosis accuracy of serological tests for Lyme borreliosis** [Internet]. (Based on Leeflang et al).

<http://ecdc.europa.eu/en/publications/Publications/lyme-borreliosis-diagnostic-accuracy-serological-tests-systematic-review.pdf>

Cook MJ, Puri BK. (2017) **Application of Bayesian decision-making to laboratory testing for Lyme disease and comparison with testing for HIV Application of Bayes to Lyme disease testing.** Int J Gen Med. 2017;10: 113–123.

<https://www.ncbi.nlm.nih.gov/pubmed/28435311>

## Persistierende IgM-Titer

Craft J, Fischer DK, Shimamoto GT, Steere AC. (1986) Antigenen von *Borrelia burgdorferi* während der Lyme-Disease-Erkrankung: Erkennung einer neuen **Immunoglobulin M**-Antwort und Expansion der Immunoglobulin G-Antwort **spät in der Erkrankung**. J. Clin. Invest. 1978, 934-39

[Morakote N](#), [Sukhavat K](#), [Khamboonruang C](#) et al. (1992) **Persistence of IgG, IgM, and IgE antibodies in human trichinosis.** *Trop Med Parasitol.* 1992 Sep;43(3):167-9.

<http://www.ncbi.nlm.nih.gov/pubmed/1470835>

„It was suggested from the data that **IgM-ELISA is a helpful indicator of infection within three years**“.

Hilton E, Tramontano A, DeVoti J, Sood SK. (1997) Temporal study of **immunoglobulin M seroreactivity** to *Borrelia burgdorferi* in patients treated for Lyme borreliosis. J Clin Microbiol 35(3), 774-776.

Kalish RA, McHugh G, Granquist J, Shea B, Ruthazer R, Steere AC (2001) **Persistence of IgM or IgG antibody responses to Borrelia burgdorferi 10 to 20 years after active Lyme disease.** Clin Infect Dis 33, 780-5. [Abstract/FREE Full Text](#)  
<http://cid.oxfordjournals.org/content/33/6/780.full>

**Ulvestad E**, Kristoffersen EK (2002) **False Positive Serological Test in Suspected Borreliosis.** Tidsskrift For Den Norske Laegeforening, 122, 88-90.

Mygland A, Skarpaas T, Ljostad U (2006) Chronic Polyneuropathy and Lyme Disease. European Journal of Neurology, 13, 1213-1215. <http://dx.doi.org/10.1111/j.1468-1331.2006.01395.x>

Racine R., McLaughlin M. Jonesa DD. et al. (2011) **IgM Production by Bone Marrow Plasmablasts Contributes to Long-Term Protection against Intracellular Bacterial Infection.** J Immunol 186, 1011-1021 Prepublished online 8  
<http://www.jimmunol.org/content/186/2/1011>

«Our studies identify a cell population that is responsible for the IgM production in the bone marrow, and they highlight a novel role for IgM in the maintenance of long-term immunity during intracellular bacterial infection».

**Seriburi V**, Ndukwe N, Chang Z, Cox ME, Wormser GP (2012) High frequency of **false positive IgM immunoblots** for Borrelia burgdorferi in clinical practice. Clin. Microbiol. Infect 18, 1236-1240.

[Jones DD](#), [Delulio GA](#), [Winslow GM](#) (2012) **Antigen-driven Induction of Polyreactive IgM during Intracellular Bacterial Infection.** J Immunol. 2012 Aug 1; 189(3): 1440–1447. Published online 2012 Jun 22. doi: [10.4049/jimmunol.1200878](https://doi.org/10.4049/jimmunol.1200878)  
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3401281/>

[Beltrán E](#), [Obermeier B](#), [Moser M](#) et al. (2014) **Intrathecal somatic hypermutation of IgM in multiple sclerosis and neuroinflammation.** Brain. 137(Pt 10):2703-14. doi: 10.1093/brain/awu205. Epub 2014 Jul 23. <http://www.ncbi.nlm.nih.gov/pubmed/25060097>  
« Our data suggest that the intrathecal milieu sustains a germinal centre-like reaction with clonal expansion and extensive accumulation of somatic hypermutation in IgM-producing B cells. »

[Elsner RA](#), [Hastey CJ](#), [Baumgarth N](#) (2014) **CD4<sup>+</sup> T cells promote antibody production but not sustained affinity maturation during Borrelia burgdorferi infection.** doi: 10.1128/IAI. <http://iai.asm.org/content/early/2014/10/08/IAI.02471-14.abstract>  
« Previous studies showed that immune response to Borrelia burgdorferi (Bb) appear to lack robust T-dependent B cell responses, as neither long-lived plasma cells nor memory B cells form for months after infection and non-switched IgM antibodies are continuously produced during this chronic disease ».

[Chernova I](#), [Jones DD](#), [Wilmore JR](#) et al. (2014) **Lasting antibody responses are mediated by a combination of newly formed and established bone marrow plasma cells drawn from clonally distinct precursors.** J Immunol. 193(10), 4971-9. doi: 10.4049/jimmunol.1401264. Epub 2014 Oct 17. <http://www.ncbi.nlm.nih.gov/pubmed/25326027>

[Jones DD](#), [Racine R](#), [Wittmer ST](#) et al. (2015) **The Omentum Is a Site of Protective IgM Production during Intracellular Bacterial Infection.** Infect Immun. 83(5), 2139-47. doi: 10.1128/IAI.00295-15. Epub 2015 Mar 16. <http://www.ncbi.nlm.nih.gov/pubmed/25776744>

[D'Arco Ch](#), [Dattwyler RJ](#), [Arnaboldi PM](#) (2017) **Borrelia burgdorferi-specific IgA in Lyme Disease.** EBiomedicine. DOI: <http://dx.doi.org/10.1016/j.ebiom.2017.04.025>  
[http://www.ebiomedicine.com/article/S2352-3964\(17\)30180-9/abstract](http://www.ebiomedicine.com/article/S2352-3964(17)30180-9/abstract)  
« These results suggest that there may be an association between elevated levels of antigen-specific IgA and particular disease manifestations in some patients with early Lyme disease. »

➔ **IgM persistence**

[https://www.google.de/search?q=IgM+persistence&hl=de&btnG=Google+Search&gws\\_rd=ssl](https://www.google.de/search?q=IgM+persistence&hl=de&btnG=Google+Search&gws_rd=ssl)

➔ **Kommentar zu Lyme Serologie** <http://www.erlebnishaft.de/kommentserollyme.pdf>

➔ **Epidemiologie, Klinik, Gender bias, Fachkontroverse, Cartoons, Epidemiology, clinic, gender bias, controversy, Cartoons**  
[http://www.xerlebnishaft.de/epid\\_klin\\_gend.pdf](http://www.xerlebnishaft.de/epid_klin_gend.pdf)

[Bernt-Dieter Huismans](#) letzte Revision April 2017 [www.Huismans.click](http://www.Huismans.click)



Back to top: <http://www.xerlebnishaft.de/serollyme.pdf>