Lyme Science Links

Research Publications on Lyme Disease/ *Borrelia burgdorferi*

1982

- Lyme disease is characterized by skin, joint, heart, and central or peripheral neurologic disease. We studied a patient with typical Lyme disease, including a demyelinating neuropathy, who had many characteristics of the Guillain-Barré syndrome, although it was accompanied by CSF pleocytosis. Immunologic abnormalities occurring in Lyme disease suggest immune pathogenesis of the peripheral demyelination."
  - **https://n.neurology.org/content/32/11/1302.short**

- "The following results indicated that the 34K-range proteins were exposed on the surface of the spirochetes. (i) Antibody H6831 agglutinated the spirochetes; (ii) immune electron microscopy showed that the H6831 determinant was associated with the outer membrane; (iii) radiolabeled H6831 bound to live organisms; and (iv) proteases effectively removed the 34K-range proteins from intact cells. With their demonstrated variability and exposure on the surface, the 34K-range proteins may contribute to the serotype specificity of Lyme disease spirochetes."
  - **https://iai.asm.org/content/45/1/94.short**

- "Later, during active neuritis, carditis, or arthritis, the trend was toward heightened phytohemagglutinin responsiveness and less suppression than normal. By multiple regression analysis, serum IgM levels correlated directly with disease activity ($p = 0.025$) and inversely with the number of T cells ($p = 0.02$); during acute disease only, elevated IgM levels correlated with increased phytohemagglutlnin responsiveness ($p = 0.004$) and decreased suppressor cell activity ($p = 0.03$). Decreased suppression, observed later in the disease, may permit damage to host tissues because of either autoimmune phenomena or a heightened response to the Lyme spirochete"
  - **https://www.sciencedirect.com/science/article/abs/pii/0002934384903528**

1986

- Lymphocytes, plasma cells, and mononuclear phagocytes are frequently found in human tissues infected by the Lyme disease spirochete, Borrelia burgdorferi. Experience has shown that these cells comprise the tissue bed inflammatory infiltrate in Lyme disease affecting the joint synovia, myocardium, and skin. While many differences otherwise exist, Lyme synovitis has lymphoplasmacellular similarities with rheumatoid synovitis, lymphoplasmacellular epimyocarditis similarities with syphilitic myocarditis, and occasionally synovial endarteritis obliterans. Silver staining can demonstrate the spirochete if a careful search is done.
  - **https://www.sciencedirect.com/science/article/pii/S0176672486801201**

- "Lyme disease has recently begun to emerge as a significant threat to human health, both in Europe and the United States. Late sequellae, resembling those of neurosyphilis and multiple sclerosis, may occur many years after initial infection. Spontaneous abortion accompanies arthritis, carditis and neuritis as burdensome short-term sequellae. Thousands of new infections are recognized each year on each side of the Atlantic, although reporting may be incomplete. The disease was described in Europe nearly a century ago and named erythema chronicum migrans, but its etiology has only recently been defined. The name "Lyme disease" was coined to describe a particularly intense American focus of disease, but the term has gained wide acceptance on both continents. The identity of the American and European etiological agents involved has yet to be determined.

  Due to the dispersed nature of Lyme disease and its recent emergence as an important hazard to health, measures for prophylaxis have only recently been devised. Lyme disease can be treated with antibiotics. But the effectiveness of such therapy depends upon correct and prompt diagnosis; delayed treatment is less effective, presumably because the spirochete becomes sequestered in immune-privileged sites"
    - **https://link.springer.com/article/10.1007/BF01193900?fbclid=IwAR3XarFve5oNcJVU_DKcpiQ9hAtzgojHi8vCXTAwRs6qf807e-TzGCNbgvA**

- Lymphocytes, plasma cells, and mononuclear phagocytes are frequently found in human tissues infected by the Lyme disease spirochete, Borrelia burgdorferi. Experience has shown that these cells comprise the tissue bed inflammatory infiltrate in Lyme disease affecting the joint synovia, myocardium, and skin. While many differences otherwise exist, Lyme synovitis has lymphoplasmacellular similarities with rheumatoid synovitis, lymphoplasmacellular epimyocarditis similarities with syphilitic myocarditis, and occasionally synovial endarteritis obliterans. Silver staining can demonstrate the spirochete if a careful search is done.
    - **https://www.sciencedirect.com/science/article/pii/S0176672486801201**

- To further define cellular immunity in Lyme disease, the responses of lymphocytes from patients with active Lyme disease were assessed to Con a, PHA, PWM, tetanus toxoid, and whole live B. burgdorferi. In addition, the natural killer cell (NK) function of these patients was assayed. As compared to the controls the lymphocyte response to Con A was reduced and the response to PHA was increased. There was a significant profilerative response to B. burgdorferi in all patients with no response in the controls. The responses

to PWM and tetanus toxoid were not different in the two groups. NK cell function in the patients with active disease was reduced as compared to the normal controls and patient's who were not clinically active. We conclude that there is a significant alteration in cellular immunity in active LD consistent with a defect in the induction of suppressor cells leading to a vigorous humoral response."

- **https://www.sciencedirect.com/science/article/abs/pii/S0176672486801183**

1987

- "We compared phenoxymethyl penicillin, erythromycin, and tetracycline, in each instance 250 mg four times a day for 10 days, for the treatment of early Lyme disease (stage 1). None of 39 patients given tetracycline developed major late complications compared with 3 of 40 penicillin-treated patients and 4 of 29 given erythromycin (p = 0.07). However, with all three antibiotic agents, nearly half of patients had minor late symptoms. For neurologic abnormalities (stage 2), 12 patients were treated with high-dose intravenous penicillin, 20 million U a day for 10 days. Pain usually subsided during therapy, but a mean of 7 to 8 weeks was required for complete recovery of motor deficits.

  For the treatment of established arthritis (stage 3), 20 patients were assigned treatment with intramuscular benzathine penicillin (7.2 million U) and 20 patients received saline. Seven of the 20 penicillin-treated patients (35%) were apparently cured, but all 20 patients given placebo continued to have attacks of arthritis ($P < 0.02$). Of 20 arthritis patients treated with intravenous penicillin G, 20 million U a day or 10 days, 11 (55%) were apparently cured. Thus, all 3 stages of Lyme disease can be treated with antibiotic therapy, but some patients with late disease may not respond."

  - https://www.sciencedirect.com/science/article/pii/S0176672487800925

1988

- From 1988 before they falsified the case definition (Dearborn-1994) and fraudulently used the two-tier testing. Allen Steere basically describing Lyme as post-sepsis and like a pseudoleukemia, probably from the reactivated Epstein-Barr:
  - **http://www.actionlyme.org/clinical-pathologic-correlations-of-lyme-disease-by-stage-Steere-Duray.pdf?fbclid=IwAR3MiwKS84ETy6_ig3bGwo6MvdZjf3lJpmq-pcwJcksaN3IGFrASqcNyM34**

- "We describe four patients with marked chronic meningoencephalomyelitis caused by tick-transmitted Borrelia burgdorferi infection. Imaging techniques showed either MS-like lesions or evidence of vascular involvement, as in other spirochetal infections, especially in meningovascular syphilis."

- **https://n.neurology.org/content/38/6/863.short**

- "The illness usually occurs in stages with many different clinical manifestations. The disease starts with a typical cutaneous lesion called erythema cronicum migrans, that usually develops at the site of the tick bite.

  After weeks or months, some patients develop neurological abnormalities, particularly meningitis, cranial nerve paralysis, peripheral radiculoneuritis, or cardiac involvement, such as atrioventricular blockade, myopericarditis and cardiomegaly, or migratory musculoskeletal pain.

  Months or years later, many patients develop arthritis, which usually occurs in intermittent attacks for several years. Lyme disease was only recently recognized in the United States.

  However this borreliosis has now been recognized in every continent except South America. In this paper we review the clinical and laboratorial features of Lyme borreliosis and discuss the possibility of its presence in Brazil or other parts of South America, where it has recently been recognized that ixodid ticks are common."
  - **http://europepmc.org/abstract/med/2690198**

- **OspA patent**
  - Borrelia burgdorferi antigen OspA, gene encoding it and uses thereof
    - **https://patents.google.com/patent/EP1092774A2/tr**

- "It is clear that B. burgdorferi can be transmitted in the blood of infected pregnant women across the placenta into the fetus. This has now been documented with resultant congenital infections and fetal demise. Spirochetes can be recovered or seen in the infant's tissues including the brain, spleen and kidney. The chorionic villi of the placenta show an increase in Hofbauer cells as in luetic placentitis. Inflammatory changes of fetal or neonatal changes are not as pronounced as in the adult, but cardiac abnormalities, including intracardiac septa1 defects, have been seen. It is not known why inflammatory cells are so sparse from maternal transmission, but it is possible that an immature immune system plays a role."
  - https://docs.wixstatic.com/ugd/47b066_3b7e265fc3c74de898683ed57cedad6a.pdf
  - https://t.co/2nTyFQFstD

1989

- "Only patients with an MS-like illness had abnormal EPs, elevated IgG index, and oligoclonal bands in the cerebrospinal fluid. Twelve of 18 patients with encephalopathy,

meningitis, or focal CNS disease had evidence of intrathecal synthesis of anti-B burgdorferi antibody, compared with no patients with either MS-like or psychiatric

illnesses, and only 2/24 patients with neuropathy. MRIs were abnormal in 7/17 patients with encephalopathy, 5/6 patients with an MS-like illness, and no others. We conclude that (1) intrathecal concentration of specific antibody is a useful marker of CNS B burgdorferi infection; (2) Lyme disease causes an encephalopathy, probably due to infection of the CNS; (3) MS patients with serum immunoreactivity against B burgdorferi lack evidence of CNS infection with this organism."

- **https://n.neurology.org/content/39/6/753.short**

1990

- "In a manner that is 'like what occurs in syphilis, we found Lyme infection can have long periods of latency and then cause slowly progressive disease leading to chronic problems including memory loss, fatigue, sleep disorders, numbness and spinal pain, Steere said."

  The 14 men and 13 women in the new study, who ranged in age from 25 to 72, developed neurological abnormalities an average of 26 months after the initial infection. However the range of time spanned from one month to 14 years, Steere said.

  He said 24 of them developed a mild form of encephalopathy, a brain disease characterized by memory loss. 'They forgot names, missed appointments, or misplaced objects. To compensate, they often made daily lists,' the researchers said. Ten patients also had symptoms of depression and five had 'subtle symptoms of a language disturbance, with difficulty finding words"

  Of those who showed no improvement, Steere said it is possible they suffered irreversible brain damage or that their symptoms were not caused by live bacteria susceptible to antibiotics. He said it may also be that they needed longer drug therapy or treatment with different types of drugs."
  - **https://www.upi.com/Archives/1990/11/21/Lyme-disease-can-remain-dormant-for-years/8201659163600/?fbclid=IwAR16GStFi_w4rGAJmaobcfGBSZaoqzS2RFmjFI8hrS4l7b72bNN9124zdh0**

- **New York Times 1990:Lyme Disease Shows Latent Effects**
  - "Some victims of Lyme Disease may suffer memory loss, mood changes, tingling sensations, shooting pains and other signs of nerve damage that strike years after the initial tick bite and may not disappear with antibiotic therapy"

"This is similar to syphilis," said Dr. Allen Steere. "Although the neurological symptoms and consequences are different, in both diseases there are long periods of latent infection followed by a variety of neurological disorders" – Allen Steere
  - **https://t.co/mfJe95s0tK**

- "Western blot analysis of immune serum from each of the persistently infected mice demonstrated that spirochetes used to infect the mice reacted differently when compared with the spirochetes subsequently reisolated from the mice, demonstrating for the first time that changes in antigenic reactivity had occurred in the spirochete populations during persistent infection"
  - **https://www.nrcresearchpress.com/doi/abs/10.1139/m91-074**

- "The encephalitis involves white matter more often than gray; severity varies widely. Of six patients with this antibiotic-responsive encephalitis, five were positive for HLA DQw3(DQw7). We conclude that (1) measurement of intrathecal antibody production is a reliable indicator of CNS infection, (2) North American neuroborreliosis includes the same spectrum of neurologic dysfunction as described in Europe, and (3) HLA typing may be useful in furthering our understanding of severe CNS involvement"
  - **https://n.neurology.org/content/41/10/1571.short**

- "We developed an in vitro assay showing that Borrelia burgdorferi organisms were killed by serum from patients with Lyme disease. Twenty of 20 Lyme disease serum samples caused B. burgdorferi killing in a range of 36 to 99% compared with the mean number of viable spirochetes when sera from 10 healthy individuals were used. The percentage of killing of B. burgdorferi increased with convalescent serum from patients with early Lyme disease. The borreliacidal activity was detectable in some sera diluted 640-fold and was abrogated after treatment with anti-human immunoglobulin G. In contrast, pooled or individual normal human serum did not cause a decrease in the number of viable B. burgdorferi. Borreliacidal activity was also not detected in sera from patients with relapsing fever, rocky mountain spotted fever, syphilis, mononucleosis, rheumatoid factor, or DNA antibodies. Our results show that borreliacidal activity can be used as a specific serodiagnostic test for detecting Lyme Disease"
  - **https://jcm.asm.org/content/29/9/1773.short**

1992

- **Lyme Test (Band 41) Patented by Yale**
  - **https://patents.google.com/patent/US5618533A/en**

- "At the time of our evaluation, late in the course of their illness, 11 patients had positive immunoglobulin (lg) G antibody responses to Borrelia burgdorferi by enzyme-linked immunosorbent assay (ELISA), one had a positive Western blot, and the three

seronegative patients had positive cellular immune responses to borrelial antigens. Four patients had abnormal cerebrospinal fluid analyses that showed an elevated protein level, a slight pleocytosis, or intrathecal antibody production to the spirochete.

The signs of Lyme disease resolved with antibiotic therapy, usually intravenous

ceftriaxone, 2 g/d for 2 to 4 weeks, except in one patient with persistent knee swelling. However, 14 of the 15 patients continued to have symptoms of fibromyalgia. Currently, only one patient is completely asymptomatic. ▪Conclusions: Lyme disease may trigger fibromyalgia, but antibiotics do not seem to be effective in the treatment of the fibromyalgia."

- **https://annals.org/aim/article-abstract/705732/lyme-disease-associated-fibromyalgia**

1993

- "Correlative evidence and adsorption experiments indicated that antibodies to cardiolipin had separate specificities from those directed against the gangliosides. IgM antibodies to Gal(β1–3) GalNac gangliosides appeared to have similar specificities since these were positively correlated and inhibitable by cross adsorption assays. Given the clinical associations of patients with neuroborreliosis and syphilis with IgM reactivity to gangliosides sharing the Gal(β1–3) GalNac terminus, we suggest that these antibodies could represent a response to injury in neurological disease or a cross reactive event caused by spirochetes."
  - **http://www.jns-journal.com/article/0022-510X(93)90175-X/references**

1994

- "Lyme arthritis can usually be treated successfully with oral antibiotics, but patients may still develop neuroborreliosis. Patients with certain genetic and immune markers may have persistent arthritis despite treatment with oral or intravenous antibiotics."
  - **https://www.ncbi.nlm.nih.gov/m/pubmed/8003060/?i=21&from=OspA%20and%20persistent%20disease**

1997

- "Only patients with primary CBCL were selected. In all cases, monoclonality of the infiltrate was confirmed by immunohistological pattern of immunoglobulin light chains or molecular analysis of JH gene rearrangement, or both. Specific DNA sequences of Borrelia burgdorferi were identified in cutaneous lesions from 9 patients (follicle center lymphoma: 3/20; immunocytoma: 3/4; marginal zone B-cell lymphoma: 2/20; diffuse large B-cell lymphoma: 1/6). Specificity was confirmed by Southern blot hybridisation in all positive cases. We could show that Borrelia burgdorferi DNA is present in skin lesions from a small proportion of patients (18%) with various types of CBCL.

Our results may have therapeutic implications. In analogy to Helicobacter pylori-associated MALT-lymphomas, which in some cases can be cured by eradication of Helicobacter pylori infection, a proportion of CBCL may be cured with antibiotic therapy against Borrelia burgdorferi. Although yet speculative, adequate antibiotic treatment for

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patients with primary CBCL should be considered before more aggressive therapeutic options are applied, particularly in countries where infection by Borrelia burgdorferi is

endemic. PCR analysis of Borrelia burgdorferi DNA is a fast test that should be performed in all patients with CBCL to identify those who more likely could benefit from an early antibiotic treatment."

  - **https://www.ncbi.nlm.nih.gov/pubmed/9331890**

2000

- "Dr. Allen C. Steere, who directed SmithKline Beecham's trials of the vaccine, told the committee that it was hypothetically possible that the vaccine could set off an autoimmune reaction in which the body's immune system attacks its own tissue, and that this could cause treatment-resistant arthritis."
  - **https://www.nytimes.com/2000/11/21/science/concerns-grow-over-reactions-to-lyme-shots.html?fbclid=IwAR1JAsRG9Sxo24E1fdtwb6SgUxCXMBFzow5YcDVi328A3WtyeisQokKHjzk**

2002

- "We demonstrated that this hyporesponsiveness to OspA vaccination was associated with decreased cell surface expression of TLR1. Moreover, TLR1- and TLR2-deficient mice did not develop significant levels of OspA antibodies following vaccination with OspA, providing a correlation with human hyporesponsiveness to OspA. These data suggest that defects in the TLR1/2 signaling pathway are associated with an impaired ability to generate antibodies following immunization with OspA lipoprotein."
  - **https://www.ncbi.nlm.nih.gov/m/pubmed/12804162/?i=14&from=lyme%20and%20TLR1**

2003

- "Next, we investigated whether these Borrelia-specific stimuli render monocytes tolerant, i.e. hyporesponsive, towards another Toll-like receptor 2 (TLR2) agonist, such as lipoteichoic acid from gram-positive bacteria, or towards the TLR4 agonist lipopolysaccharide. Cross-tolerance towards all tested stimuli was induced.

  Furthermore, using primary bone marrow cells from TLR2-deficient mice and from mice with a nonfunctional TLR4 (strain C3H/HeJ), we demonstrated that the TLR2 was required for tolerance induction by Borrelia, and using neutralizing antibodies, we

identified interleukin-10 as the key mediator involved. Although peripheral blood mononuclear cells tolerized by Borrelia exhibited reduced TLR2 and TLR4 mRNA levels, the expression of the respective proteins on monocytes was not decreased, ruling out the possibility that tolerance to Borrelia is attributed to a reduced TLR2 expression.

In summary, we characterized tolerance induced by B. burgdorferi, describing a model of

desensitization which might mirror the immunosuppression recently attributed to the persistence of Borrelia in immunocompetent hosts."

- **https://www.ncbi.nlm.nih.gov/m/pubmed/12819085/**

2004

- "Despite specific antibodies, the pathogen burden was 250-fold higher in MyD88−/− mice than in WT mice 45 days after infection; by 90 days of infection, the pathogen burden had diminished substantially in MyD88−/− mice, but it was still elevated compared to that in WT mice.
The elevated pathogen burden may be explained in part by the finding that MyD88−/− peritoneal macrophages could ingest spirochetes but degraded them more slowly than WT macrophages. Our results show that MyD88-dependent signaling pathways are not required for B. burgdorferi-induced inflammation but are necessary for the efficient control of the pathogen burden by phagocytes."
  - **http://iai.asm.org/content/72/6/3195.short**

2005

- "In this study, we investigated the presence of cross-reactive human neural epitopes that share amino acid sequences with Borrelia burgdorferi OspA protein. Sequence similarity analysis was carried out by searching known cDNA sequences from brain tissue. The cDNA database search yielded three sequences that were identical to sequences in OspA. Corresponding peptides were synthesized and antibodies were generated against them in rabbits. Antibodies against two of the homologous OspA peptides were found to react with neurons in human brain, spinal cord and dorsal root ganglia by immunohistochemistry."
  - **https://www.ncbi.nlm.nih.gov/m/pubmed/15652419/?i=12&from=OspA%20and%20persistent%20disease**

2006

- Toll-like receptors (TLRs) trigger innate immune responses via the recognition of conserved pathogen-associated molecular patterns. Lipoproteins from Borrelia burgdorferi, the agent of Lyme disease, activate inflammatory cells through TLR2 and TLR1. We show that stimulation of human monocytes with B. burgdorferi lysate, lipidated outer surface protein A, and triacylated lipopeptide Pam3CysSerLys4 results in

the up-regulation of both TLR2 and TLR1 but the down-regulation of TLR5, the receptor for bacterial flagellin, and that this effect is mediated via TLR2. TLR4 stimulation had no effect on TLR2, TLR1, and TLR5 expression. Human monocytes stimulated with TLR5 ligands (including p37 or flaA, the minor protein from B. burgdorferi flagella) up-regulated TLR5. In addition, TLR2 stimulation rendered cells hyporesponsive to a TLR5 agonist. These results indicate that diverse stimuli can cause differential TLR expression, and we hypothesize that these changes may be useful for either the pathogen and/or the host.

- **https://www.ncbi.nlm.nih.gov/pubmed/16479520**

- Toll-like receptors (TLRs) trigger innate immune responses via the recognition of conserved pathogen-associated molecular patterns. Lipoproteins from Borrelia burgdorferi, the agent of Lyme disease, activate inflammatory cells through TLR2 and TLR1. We show that stimulation of human monocytes with B. burgdorferi lysate, lipidated outer surface protein A, and triacylated lipopeptide Pam3CysSerLys4 results in the up-regulation of both TLR2 and TLR1 but the down-regulation of TLR5, the receptor for bacterial flagellin, and that this effect is mediated via TLR2. TLR4 stimulation had no effect on TLR2, TLR1, and TLR5 expression. Human monocytes stimulated with TLR5 ligands (including p37 or flaA, the minor protein from B. burgdorferi flagella) up-regulated TLR5. In addition, TLR2 stimulation rendered cells hyporesponsive to a TLR5 agonist. These results indicate that diverse stimuli can cause differential TLR expression, and we hypothesize that these changes may be useful for either the pathogen and/or the host.
  - **https://www.ncbi.nlm.nih.gov/pubmed/16479520**

2007

- "An association between Borrelia burgdorferi with primary cutaneous B-cell lymphoma (PCBCL) has long been suspected but just recently, thanks to a polymerase chain reaction technique, it had been possible to demonstrate B. burgdorferi-specific DNA in skin lesions of patients with different PCBCL subtypes. Locating cases of PCBCL that are related to B. burgdorferi infection could be really important for therapeutic implications; in fact, there are several reports of PCBCL responding to antibiotic therapy against B. burgdorferi. We report a case of B. burgdorferi-associated primary cutaneous marginal-zone B-cell lymphoma that, after specific antimicrobial therapy, did not show any clinical regression. We can conclude that additional studies are necessary in order to establish the use of antimicrobial therapy in B. burgdorferi-associated PCBCL."
  - **https://www.ncbi.nlm.nih.gov/pubmed/17823520**

2009

- "Three different polymerase chain reaction (PCR) protocols targeting the hbb, flagellin, and Osp-A genes were used. Direct sequencing of both sense and antisense strands of purified PCR products confirmed the specificity of the amplified fragments. Sequence specificity was assessed using the Basic Local Alignment Search Tool, and MultAlin
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  software was used to investigate the heterogeneity of target gene sequences across the different samples.

  Borrelia DNA was not detected in 19 controls, 23 cases of follicular lymphoma, 31 cases of extranodal marginal zone lymphoma, or 30 cases of mycosis fungoides. A single case of 14 diffuse large B-cell lymphoma cases was positive for B. burgdorferi. This study

  does not support a pathogenic role of B. burgdorferi in primary cutaneous B- and T-cell lymphomas from areas non endemic for this microorganism and the consequent rationale for the adoption of antibiotic therapy in these patients."
    - **https://www.ncbi.nlm.nih.gov/pubmed/22071292**

- "This review is focused on the role of infectious agents in the development of some lymphoma entities. Associations involving bacterial infections mostly regard marginal zone B-cell lymphomas of mucosa-associated lymphoid tissue (MALT)-type. Some paradigmatic examples of these associations include the Helicobacter pylori-related gastric MALT lymphoma and the more recently reported links between Chlamydophila psittaci and ocular adnexal MALT lymphomas and Borrelia burgdorferi and cutaneous MALT lymphomas.

  The well-documented association between Epstein-Barr virus infection and related lymphoproliferative disorders are analysed as an example of lymphotropic virus with tumourigenic activity. Molecular, biological and clinical features as well as therapeutic implications of these associations are analysed and future perspectives in this field are discussed."
    - **"https://www.ncbi.nlm.nih.gov/pubmed/19298458**

2010

- "A relationship between Borrelia burgdorferi and the development of cutaneous B-cell lymphoma (CBCL) has been long discussed. B. burgdorferi DNA has been detected in patients with CBCL and a response of CBCL to antibiotics has been observed.
  In our patient with a Borrelia infection, a marginal zone lymphoma (SALT) regressed after ceftriaxone therapy. This further case of a combined appearance of CBCL and B.
-

burgdorferi underlines a possible relationship as an example of an infectious trigger in tumorigenesis."

- **https://www.ncbi.nlm.nih.gov/pubmed/19399378**

2011

- "We report on a 69-year-old female patient with specific cutaneous manifestations of B-cell chronic lymphocytic leukemia that arose at the site of erythema chronicum migrans due to Borrelia burgdorferi infection. Histological examination revealed the presence of dense infiltrates of small hyperchromatic lymphocytes admixed with clusters of plasma

  cells. Immunohistology showed a CD5+/CD20+ phenotype of the lymphocytes and monoclonal expression of kappa immunoglobulin light chain by the plasma cells. Presence of Borrelia DNA was confirmed by polymerase chain reaction studies. The unusual histopathological and phenotypic findings described in this case of cutaneous manifestations of B-cell chronic lymphocytic leukemia associated with Borrelia burgdorferi infection may lead to the misdiagnosis of cutaneous marginal zone B-cell lymphoma."
  - **https://www.ncbi.nlm.nih.gov/pubmed/21946761**

2013

- "A 66-year-old woman presented with severe shooting pains throughout her back and legs, followed by progressive deafness, weight loss and headache. She had a history of marginal zone B-cell lymphoma stage IV-B, for which she was successfully treated with immunochemotherapy and rituximab maintenance therapy. A relapse was suspected, but chemotherapy was not administered, since, despite elaborate investigations, malignancy could not be proven. Because of a history of tick bites she was tested for antibodies against Borrelia burgdorferi in serum and cerebrospinal fluid (CSF), which were negative. However, a B burgdorferi PCR on CSF came back positive. The patient was treated for seronegative Lyme neuroborreliosis with ceftriaxone intravenously and dramatically improved. This case presentation demonstrates that, in immunocompromised patients, it is important not to solely rely on antibody testing and to use additional diagnostic tests to avoid missing or delaying the diagnosis."
  - **https://www.ncbi.nlm.nih.gov/pubmed/23417373**

2015

- **This is one of the best papers (by Nicole Baumgarth & others), demonstrating how immune system collapses with Lyme. B-cell germinal centers collapse in #Lyme (tick bite post sepsis or LYMErix) victims resulting in the inability to fight off viral or opportunistic infections, similar to AIDS (acquired immune deficiency syndrome):**

  "Lyme Disease caused by infection with Borrelia burgdorferi is an emerging infectious disease and already by far the most common vector-borne disease in the U.S. Similar to

many other infections, infection with B. burgdorferi results in strong antibody response induction, which can be used clinically as a diagnostic measure of prior exposure. However, clinical studies have shown a sometimes-precipitous decline of such antibodies shortly following antibiotic treatment, revealing a potential deficit in the host's ability to induce and/or maintain long-term protective antibodies.

This is further supported by reports of frequent repeat infections with B. burgdorferi in endemic areas. The mechanisms underlying such a lack of long-term humoral immunity, however, remain unknown. We show here that B. burgdorferi infected mice show a similar rapid disappearance of Borrelia-specific antibodies after infection and subsequent

antibiotic treatment. This failure was associated with development of only short-lived germinal centers, micro-anatomical locations from which long-lived immunity originates. These showed structural abnormalities and failed to induce memory B cells and long-lived plasma cells for months after the infection, rendering the mice susceptible to reinfection with the same strain of B. burgdorferi.

The inability to induce long-lived immune responses was not due to the particular nature of the immunogenic antigens of B. burgdorferi, as antibodies to both T-dependent and T-

independent Borrelia antigens lacked longevity and B cell memory induction. Furthermore, influenza immunization administered at the time of Borrelia infection also failed to induce robust antibody responses, dramatically reducing the protective antiviral capacity of the humoral response. Collectively, these studies show that B. burgdorferi-infection results in targeted and temporary immunosuppression of the host and bring new insight into the mechanisms underlying the failure to develop long-term immunity to this emerging disease threat."

- **https://journals.plos.org/plospathogens/article?id=10.1371%2Fjournal.ppat.1004976&fbclid=IwAR3lUfW3vDiZFtVHgj4q5epD4jeVJ1SIJXP7VMndS2sj36wuIC-75cl1pdY**

2016

- "Patients with chronic HCV infection have 5 times higher risk to develop MZL, in particular, an association with splenic and nodal MZL has been shown in several studies. Moreover, there is evidence of lymphoma regression after antiviral therapy with interferon+ribavirin, thus raising hope that newly available drugs, extremely efficient against HCV replication, could improve outcome also in HCV-driven lymphomas. Another case-study are represented by those rare cases of MZL localized to orbital fat and eye conjunctivas that have been associated with Chlamydophila psittaci infection carried by birds. Efficacy of antibacterial therapy against C. psittaci are conflicting and generally poorer than gastric MALT. Finally, some case reports will cover the relationship between primary cutaneous B-cell Lymphomas and Borrelia Burgdorferi."
  - **https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4696464/**

2017

- "OspA from B. burgdorferi is able to cross the BBB by binding to CD40 of brain-microvascular endothelial cells [4]. OspA in the brain activates TLR2 on microglia and astrocytes, which initiates immune activity and causes damage to brain tissue

  OspA expressed from Escherichia coli (prepared by the Biomaterials and Advanced Drug Delivery Laboratory at Stanford University) showed that ospA significantly decreased the number of presynaptic sites (i.e., synapsin) ($p = 0.04$), whereas it did not affect the

  number of postsynaptic sites (i.e., PSD-95) ($p > 0.05$) (Figure 2). This result suggests that ospA directly disrupts neuronal function by damaging presynapses exclusively"
  - **https://www.intechopen.com/books/advances-in-lipoprotein-research/lipoproteins-and-diseases-of-the-brain**

2018

- **Public comments on the record of the TBDWG (Tick-borne Disease Working Group).**
  - **https://www.youtube.com/watch?v=1tUii_UUyq0&fbclid=IwAR3QFrpwrS1Yj057BhxwjnB1Rst9sQhohejfDq7qEayhZmYiapXzs1u7zmA**

- "We provide the first report of a Bbsl-positive Amblyomma longirostre larva parasitizing a bird; this bird parasitism suggests that a Willow Flycatcher is a competent reservoir of Bbsl. Our findings show that Bbsl is present in all provinces, and that multiple tick species are implicated in the enzootic maintenance cycle of this pathogen. Ultimately, Bbsl poses a serious public health contagion Canada-wid"
  - **https://www.mdpi.com/2227-9032/6/4/131?fbclid=IwAR2wW1yccyupEebQKUI6an5w-m7LIYNWz4O7jQ_QVk2F1BeywPno5BciCss**