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Lyme Disease

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ABSTRACT:

Lyme disease is an animal-borne multisystem disease caused by the spirochete of Borrelia bergdorferi (Bb) and usually affects the skin, nervous system, musculoskeletal system, and heart. A history of exposure to tick bites, the typical signs and symptoms of Lyme disease, and a positive test for anti-Bb antibodies are the basis for diagnosis. A two-step diagnosis is required.

The first step is based on the highly sensitive His ELISA test and positive results are confirmed by the more specific Western blot His assay. Most cases are cured with antibiotic therapy, but some patients develop chronic symptoms that do not respond to antibiotics. The purpose of this review is to summarize current knowledge about Lyme disease symptoms, clinical diagnosis and treatment of Lyme borreliosis

Keywords: Lyme disease, causes of Lyme Disease, symptoms risk, diagnosis, treatment , prevention ,test etc

Introduction:

Lyme disease is the most common tick-borne disease in the United States and Europe. Lyme disease is caused by a deer tick-borne Borrelia burgdorferi infection. Ticks infect humans by biting them. This is a bacterial infection caused by his six species in the family Borreliaceae Spirochetidae. The taxonomy of these spirochetes is under revision and the genus name can be presented as Borrelia or Borreliella. According to the Centers for Disease Control and Prevention (CDC), the number of vector-borne illnesses reported to the National Reportable Disease Surveillance System (NNDSS) totaled 642,602 between 2004 and 2016.For most people, antibiotic treatment is highly effective in relieving symptoms, preventing disease complications, and curing infections. Some symptoms improved rapidly with this treatment whereas others symptoms gradually improve over week to month.

Lyme disease is an infectious cause of recurrent bouts of arthritis often part of a multi-system disease that involves cardiac, skin and neurologic manifestations. It typically begins with an erythematous rash but can also include a number of other dermatologic abnormalities. Approximately 20% of patients experience only dermatologic features and do not progress further. However, 40–60% of patients eventually develop an inflammatory arthropathy.

What is Lyme disease?

Lyme disease is a bacterial infection that is transmitted through the bite of an infected tick. Lyme disease in its early stages usually causes symptoms such as rash, fever, headache, and fatigue. However, if not treated early, the infection can spread to the joints, heart, and nervous system. Prompt treatment can help you recover quickly.





What Causes Lyme Disease?

Lyme disease is caused by bacteria. In the United States, this is a bacterium usually called Borrelia burgdorferi. Humans are infected by being bitten by an infected tick. The tick that spreads it is the black-legged tick (or deer tick). They are usually located at:

- northeast
- Mid-Atlantic
- midwest upper
- Pacific coast, especially Northern California

These mites can attach to any part of the body. However, they are more common in hard-to-see areas such as the groin, armpits, and scalp.Usually, a tick needs to stick to the body for 36 to 48 hours, or more to spread bacterium .

Who is at Risk for Lyme Disease?



Anyone can be bitten by a tick. But people who spend a lot of time outdoors in wooded grasslands are at higher risk. This includes campers, hikers, and people working in gardens and parks.

Most tick bites occur during the summer months when ticks are most active and people spend more time outdoors. However, bites may occur during the warm months of early fall and late winter when temperatures are unusually high. Also, if the winter is mild, ticks may emerge earlier than usua.

What are the symptoms of Lyme Disease?

- A red rash called erythema migrans (EM). Most people with Lyme disease develop this rash. It will grow over a few days and may feel warm. There is usually no pain or itching. As it gets better, the part can get thinner. This can cause the rash to look like a "bull's eye".
- Heat
- Cold
- headaches
- Malaise
- Muscle and joint pain
- Swollen lymph nodes

If the infection is not treated, it can spread to the joints, heart, and nervous system. Symptoms include:

- Severe headache and neck stiffness
- Additional EM spikes elsewhere on your body
- Facial nerve palsy weakens the muscles of the face. It can cause sagging on one or both sides of the face. Arthritis with severe joint pain and swelling, especially in the knees and other large joints
- Pain going in and out of tendons, muscles, joints and bones
- Palpitations are the feeling that your heart is jumping, thumping, pounding, or beating too hard or too fast.
- Arrhythmia (Lyme carditis)
- Episodes of dizziness or shortness of breath
- Inflammation of the brain and spinal cord
- Neuralgia
- Tingling, numbness, or tingling in hands or feet

How is Lyme disease diagnosed?

To make a diagnosis, doctors consider:

• Your Symptoms

How likely is it that you have been exposed to an infected black foot tick?

Other diseases can cause similar symptoms

• Results of all laboratory tests

Most Lyme disease tests look for antibodies that your body produces in response to infection. It can take several weeks for these antibodies to develop. Getting tested right away may not always mean you have Lyme disease. So you may need to do another test later.

What is the treatment for Lyme disease?

Lyme disease is treated with antibiotics. The sooner treatment is started, the better. This will give you the best chance of a quick and complete recovery.

Some patients continue to have pain, fatigue, or difficulty thinking for more than 6 months after treatment. This is called post-treatment Lyme disease syndrome (PTLDS). Researchers don't know why some people have PTLDS. There is no proven cure for PTLDS. Long-term antibiotics have not been proven effective. However, there are ways to alleviate the symptoms of PTLDS. If you've been treated for Lyme disease but still feel unwell, contact your doctor to learn how to manage your symptoms. Most people get better over time. But it may take months before you feel better.

| Clinical picture | Suggested regimens | Dosage | Administration | Duration of the treatment [days] |
|---|-----------------------|--|----------------|--|
| EM BLC | Doxycycline | 100 mg bid | po | 14-21 |
| | Amoxicillin | 508 mg tid (children: 50 mg/kg/day) | po | 14-21 |
| | Cefuroxime | 500 mg bid (children: 30 mg/kg/day) | po | 14-21 |
| Lyme disease with joint involvement | Amoxicillin | 500-1000 mg tid (children: 50 mg/kg/day) | ро | 14-28 |
| | Doxycycline | 100 mg bid or 200 mg q24h | ро | 14-28 |
| | Cefuroxime | 500 mg bid (children: 15 mg/kg/day) | po | 14-28 |
| Lyme disease with nervous system, heart or recurrent joint involvement | Ceftriaxone | 2000 mg q24h (children: 50-75 mg/kg/day) | îv | 14-28 |
| | Cefotaxime | 2000 mg tid (children: 150-200 mg/kg/day: divided in 3-4 doses) | iv | 14-28 |
| | Penicillin G | 3-4 mu q4h (children: 0.2-0.4 mu/kg/day divided in 4- 6 doses) | iv | 14-28 |
| ACA | Amoxicillin | 500-1000 mg tid | po | 14-28 |
| | Doxycycline | 100 mg bid or 200 mg q24h | po | 14-28 |
| | Ceftriaxone | 2000 mg q24h | iv | 14-28 |
| | Cefotaxime | 2000 mg tid | iv | 14-28 |
| | Penicillin G | 3-4 mu q4h | ÎV | 14-28 |

Table I. Dosage and duration of Lyme disease treatment

EM – erythema migrans, BLC – borrelial lymphocytoma catls, ACA – atrophic chronic acrodermatitis, bid – twice a day, tid – 3 times a day, po – per os (by mouth), iv – intravenously; q4h – in each 4 h, q24h – in each 24 h

Can I Lyme disease be prevented?

To prevent Lyme disease, you need to reduce your risk of tick bites.

- Avoid places where ticks live. B. Grassy, bushy or wooded areas. When hiking, walk in the middle of the trail avoiding bushes and grass.
- Use insect repellent with DEET
- Treat clothing and gear with a repellent containing 0.5% permethrin
- Wear light-colored protective clothing so attached ticks can be easily spotted
- Wear long-sleeved shirts and long pants. Also, tuck your top into your pants and your pant legs into your socks. Check yourself, your kids and pets each day for ticks. Carefully remove any ticks you find.
- Wash and dry your clothes in a hot shower after going outdoors

What is the Lyme disease test?

Lyme disease is an infection caused by bacteria infected by tick bites. The Lyme disease test looks for signs of infection in a blood or cerebrospinal fluid (CSF) sample. CSF is a clear fluid that flows in and around the brain and spinal cord. This test checks samples for antibodies that your immune system makes to fight the bacteria that cause Lyme disease. If you get bitten by an infected tick, you can get Lyme disease. Ticks can bite anywhere on the body, but usually in invisible places such as the groin, scalp, behind the knees, and under the armpits.

Most Lyme disease is caused by bites by tiny baby ticks no bigger than the head of a pin. Generally, an infected tick must adhere to the body for 36 to 48 hours before he can transmit the Lyme disease bacteria. Without treatment, Lyme disease can cause serious health problems that affect the joints, heart, and nervous system. Cures. If discovered later, treatment may last up to 8 weeks.

Other name:

Lyme antibody detection, Borrelia burgdorferi antibody test, Borrelia DNA detection, IgM/IgG by Western blot, Lyme disease test (CSF), Borrelia antibody, IgM/IgG

Why do I need a Lyme disease test?

If you have symptoms of an infection and have been or may have been exposed to ticks that carry the bacteria that cause Lyme disease, testing may be necessary. The first symptoms of Lyme disease usually appear 3 to 30 days after the tick bite.

What happens during a Lyme disease test?

A test for Lyme disease is usually done using a blood sample. In some cases, a CSF test can be performed.

For Lyme disease blood tests:

A medical professional uses a small needle to take a blood sample from a vein in your arm. After the needle prick, a small amount of blood is drawn into a test tube or vial. There may be a slight tingling sensation when inserting and removing the needle. Usually this takes him no more than five minutes.

For CSF examination:

- A CSF test may be needed if Lyme disease may affect the nervous system, such as: B. Stiffness in the neck and numbness in the limbs. A health care provider may order a CSF test if blood test results indicate that Lyme disease is likely, or if the results are uncertain.
- To take a sample of cerebrospinal fluid, your provider will perform a procedure called a spinal tap, also known as a spinal tap. During the procedure:

Lie down or sit on the examination table.

Your provider will clean your back and inject an anesthetic into your skin so you won't feel any pain during the procedure. Your doctor may apply an anesthetic cream to your back before this injection.

If the back area is completely paralyzed, the doctor will insert a thin, hollow needle between her two vertebrae in the lower spine. Vertebrae are the small spines that make up your spine. Your doctor will take a small amount of CSF and test it. This takes about 5 minutes.

You must remain still while drinking liquids.

Your doctor may ask you to lie on your back for 1-2 hours after surgery.

Need to prepare for the test?

No special preparation is required for the Lyme disease blood test.

If you have a spinal tap, you may be asked to empty your bladder (pee) and intestines (poop) before the test.

Are there any risks with the Lyme test?

The risks of blood tests and spinal taps are minimal. A blood test may show mild pain or bruising where the needle was inserted, but most symptoms resolve quickly.

A cerebrospinal fluid test may feel a slight pressure or tightness when the needle is inserted. After the test, the back where the needle was inserted may be sore or tender.

You may also experience bleeding and headaches at the site. A headache can last for hours or a week or longer, but your doctor may suggest treatments to reduce the pain.

What do the results mean?

Lyme disease is difficult to diagnose. Symptoms are common to many diseases, and test results alone cannot diagnose the disease. To make a diagnosis, health care providers consider test results along with medical history, exposures, and symptoms. Also, other tests may be required. A negative blood test result means that no antibodies to Lyme disease were detected in the blood. If he had symptoms for more than 30 days before the test, he may not have Lyme disease.

- However, if you have symptoms within 30 days of the blood draw, you may need to get another Lyme disease test, which takes several weeks for your body to make enough antibodies to show up for the test. If you test too early, you can still be infected even if the test result is negative. This is called a "false negative".
- A positive blood test result means that antibodies to Lyme disease have been found in the blood. In this case, the Centers for Disease Control and Prevention (CDC) recommends a second blood test for her using the same blood sample. If the second test is positive and you have symptoms of an infection, you may have Lyme disease.
- However, a positive test result does not necessarily mean that Lyme disease is the cause of your symptoms. It's possible that your body has
 antibodies from previous cases of Lyme disease that you've successfully fought months or years ago. There is also the possibility of "false
 positives". This means that you don't have antibodies that fight Lyme disease bacteria, even if the test shows it. B. Certain autoimmune
 diseases. And these diseases, not Lyme disease, may be causing your symptoms.

The CSF test (CSF) results can help show whether Lyme disease has spread to the nervous system.

A negative CSF test result means that Lyme disease antibodies were not detected in the CSF. However, Lyme disease of the nervous system is not ruled out. Further testing may be required.

A positive CSF test result means that antibodies to Lyme disease were detected in the cerebrospinal fluid. If there are more antibodies in the cerebrospinal fluid than in the blood, Lyme disease may have spread to the nervous system.

If Lyme disease is possible, your doctor will prescribe antibiotics. Most people treated with antibiotics in the early stages of their illness make a full recovery.

Can I get Lyme disease again?

If you are treated for early Lyme disease, you may become infected again if you are bitten by another infected tick. However, Lyme antibodies (proteins that the immune system makes to fight bacteria) can remain in the blood for years after treatment. As a result, it can be difficult for doctors to determine whether a positive blood test means reinfection. Therefore, if a new rash typical of Lyme disease develops after possible exposure to deer ticks, reinfection is usually diagnosed. If you have been treated for late-stage Lyme disease, you are less likely to get it again because people with late-stage Lyme disease have a stronger and more longer lasting antibody response.

Conclusion:

Lyme disease is the tick-borne disease in the United States and Europe. Lyme disease is caused by a deer tick-borne Borrelia burgdorferi infection. Ticks infect humans by biting them. For most people, antibiotic treatment is highly effective in relieving symptoms, preventing disease complications, and curing infections. Some symptoms

References:

1. Cechová L, Durnová E, Sikutová S, Halouzka J, Nemec M. Characterization of spirochetal isolates from arthropods collected in South Moravia, Czech Republic, using fatty acid methyl esters analysis. J Chromatogr B Analyt Technol Biomed Life Sci. 2004;808:249–54. [PubMed] [Google Scholar]

2. Flisiak R, Prokopowicz D. Antibodies against Borrelia garinii in diagnosis of Lyme borreliosis [Polish] Przegl Lek. 2000;57:147–9. [PubMed] [Google Scholar]

3. Halouzka J, Wilske B, Stünzner D, Sanogo YO, Hubálek Z. Isolation of Borrelia afzelii from overwintering Culex pipiens biotype molestus mosquitoes. Infection. 1999;27:275–7. [PubMed] [Google Scholar]

4. Stańczak J, Racewicz M, Kubica-Biernat B, et al. Prevalence of Borrelia burgdorferi sensu lato in Ixodes ricinus ticks (Acari, Ixodidae) in different Polish woodlands. Ann Agric Environ Med. 1999;6:127–32. [PubMed] [Google Scholar]

5. de Carvalho IL, Fonseca JE, Marques JG, et al. Vasculitis-like syndrome associated with Borrelia lusitaniae infection. Clin Rheumatol. 2008;27:1587–91. [PubMed] [Google Scholar]

6. Derdáková M, Lencáková D. Association of genetic variability within the Borrelia burgdorferi sensu lato with the ecology, epidemiology of Lyme borreliosis in Europe. Ann Agric Environ Med. 2005;12:165–72. [PubMed] [Google Scholar]

7. Murray TS, Shapiro ED. Lyme disease. Clin Lab Med. 2010;30:311-28. [PMC free article] [PubMed] [Google Scholar]

8. Asbrink E, Hovmark A. Classification, geographic variations, and epidemiology of Lyme borreliosis. Clin Dermatol. 1993;11:353–7. [PubMed] [Google Scholar]

9. Hubálek Z, Halouzka J. Distribution of Borrelia burgdorferi sensu lato genomic groups in Europe, a review. Eur J Epidemiol. 1997;13:951–7. [PubMed] [Google Scholar]

10. Nau R, Christen HJ, Eiffert H. Lyme disease – current state of knowledge. Dtsch Arztebl Int. 2009;106:72–81. [PMC free article] [PubMed] [Google Scholar]

11. Stanek G, Wormser GP, Gray J, Strle F. Lyme borreliosis. Lancet. 2012;379:461-73. [PubMed] [Google Scholar]

12. Marques A. Chronic Lyme disease: a review. Infect Dis Clin North Am. 2008;22:341-60. [PMC free article] [PubMed] [Google Scholar]

13. Müllegger RR, Glatz M. Skin manifestations of lyme borreliosis: diagnosis and management. Am J Clin Dermatol. 2008;9:355–68. [PubMed] [Google Scholar]

14. Bitar I, Lally EV. Musculoskeletal manifestations of Lyme disease. Med Health R I. 2008;91:213-5. [PubMed] [Google Scholar]

15. Grygorczuk S, Pancewicz S, Zajkowska J, Kondrusik M, Moniuszko A. Articular symptoms in Lyme borreliosis. Pol Merk Lek. 2008;24:542–4. [PubMed] [Google Scholar]

16. Halperin JJ, Shapiro ED, Logigian E, et al. Practice parameter: treatment of nervous system Lyme disease (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2007;69:91–102. [PubMed] [Google Scholar]

17. Halperin JJ. Nervous system lyme disease: diagnosis and treatment. Rev Neurol Dis. 2009;6:4-12. [PubMed] [Google Scholar]

18. Hildenbrand P, Craven DE, Jones R, Nemeskal P. Lyme neuroborreliosis: manifestations of a rapidly emerging zoonosis. AJNR Am J Neuroradiol. 2009;30:1079–87. [PMC free article] [PubMed] [Google Scholar]

19. Wormser GP, Dattwyler RJ, Shapiro ED, et al. The clinical assessment, treatment, and prevention of lyme disease, human granulocytic anaplasmosis, and babesiosis: clinical practice guidelines by the Infectious Diseases Society of America. Clin Inf Dis. 2006;43:1089–134. [PubMed] [Google Scholar]

20. Wormser GP, Nadelman RB, Dattwyler RJ, et al. Practice guidelines for the treatment of Lyme disease. The Infectious Diseases Society of America. Clin Infect Dis ; 31 Suppl. 2000;1:1–14. [PubMed] [Google Scholar]

21. Bacon RM, Kugeler KJ, Mead PS. Centers of Disease Control and Prevention (CDC) Surveillance for Lyme disease – United States, 1992-2006. MMWR Surveill Summ. 2008;57:1–9. [PubMed] [Google Scholar]

22. Bartuněk P, Gorican K, Veiser T, Táborský M, Hulinská D. Significance of Borrelia infection in development of dilated cardiomyopathy (a pilot study) Prague Med Rep. 2007;108:339–47. [PubMed] [Google Scholar]

23. Flisiak R, Pancewicz S. Diagnostics and treatment of Lyme borreliosis. Recommendations of Polish Society of Epidemiology and Infectious Diseases [Polish] Przegl Epidemiol. 2008;62:193–9. [PubMed] [Google Scholar]

24. Aberer E. Lyme borreliosis - an update [German] J Dtsch Dermatol Ges. 2007;5:406-14. [PubMed] [Google Scholar]

25. Kaplan RF, Trevino RP, Johnson GM, et al. Cognitive function in post-treatment Lyme disease: do additional antibiotics help? Neurology. 2003;60:1916–22. [PubMed] [Google Scholar]

26. Klempner MS, Hu LT, Evans J, et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. N Engl J Med. 2001;345:85–92. [PubMed] [Google Scholar]

27. Gasiorowski J, Witecka-Knysz E, Knysz B, Gerber H, Gladysz A. Diagnosis of Lyme disease [Polish] Med Pr. 2007;58:439–47. [PubMed] [Google Scholar]

28. Hermanowska-Szpakowicz T, Świerzbińska R, Zajkowska J, Iżycka-Herman A. Actual diagnostic possibilities of Lyme borreliosis [Polish] Pol Merk Lek. 2000;7:69–71. [PubMed] [Google Scholar]

29. Hunfeld KP, Fingerle V, Stanek G, et al. European multicenter study for evaluation of a new enzyme immunoassay for detection of IgG antibodies against Borrelia burgdorferi sensu lato. 10th Int. conference on Lyme borreliosis and other tick-borne diseases; 2005. Sep 11-15, [Google Scholar]

30. "Lyme Disease: MedlinePlus" https://medlineplus.gov/lymedisease.html

31. Kugeler K, Schwartz A, Delorey M, Mead P, Hinckley A. Estimating the frequency of Lyme disease diagnoses, United States, 2010–2018. Emerg Infect Dis J. (2021) 27:616–9. 10.3201/eid2702.202731 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

32.https://www.researchgate.net/publication/234134823_Lyme_disease_Review

33. Nelson CA, Saha S, Kugeler KJ, Delorey MJ, Shankar MB, Hinckley AF, et al.. Incidence of clinician-diagnosed Lyme disease, United States, 2005-2010. Emerg Infect Dis. (2015) 21:1625–31. 10.3201/eid2109.150417 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

34. Steere AC, Strle F, Wormser GP, Hu LT, Branda JA, Hovius JWR, et al.. Lyme borreliosis. Nat Rev Dis Primers. (2016) 2:16090. 10.1038/nrdp.2016.90 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

35. Adrion ER, Aucott J, Lemke KW, Weiner JP. Health care costs, utilization and patterns of care following Lyme disease. PLoS ONE. (2015) 10:e0116767. 10.1371/journal.pone.0116767 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

36. TBDWG . Tick-Borne Disease Working Group: Report to Congress 2018. HHS; (2018). Available online at: https://www.hhs.gov/sites/default/files/tbdwg-report-to-congress-2018.pdf (accessed July 22, 2021). [Google Scholar]

37. Moon KA, Pollak J, Poulsen MN, Hirsch AG, DeWalle J, Heaney CD, et al.. Peridomestic and community-wide landscape risk factors for Lyme disease across a range of community contexts in Pennsylvania. Environ Res. (2019) 178:108649. 10.1016/j.envres.2019.108649 [PubMed] [CrossRef] [Google Scholar]

38. Nigrovic LE, Bennett JE, Balamuth F, Levas MN, Chenard RL, Maulden AB, et al.. Accuracy of clinician suspicion of Lyme disease in the emergency department. Pediatrics. (2017) 140:e20171975. 10.1542/peds.2017-1975 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

39. Burlina PM, Joshi NJ, Mathew PA, Paul W, Rebman AW, Aucott JN. AI-based detection of erythema migrans and disambiguation against other skin lesions. Comput Biol Med. (2020) 125:103977. 10.1016/j.compbiomed.2020.103977 [PubMed] [CrossRef] [Google Scholar]

40. Mead PS. Epidemiology of Lyme disease. Infect Dis Clin North Am. (2015) 29:187–210. 10.1016/j.idc.2015.02.010 [PubMed] [CrossRef] [Google Scholar]

41. Hirsch AG, Poulsen MN, Nordberg C, Moon KA, Rebman AW, Aucott JN, et al.. Risk factors and outcomes of treatment delays in Lyme disease: a population-based retrospective cohort study. Front Med. (2020) 7:560018. 10.3389/fmed.2020.560018 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

42. Hirsch AG, Herman RJ, Rebman A, Moon KA, Aucott J, Heaney C, et al.. Obstacles to diagnosis and treatment of Lyme disease in the USA: a qualitative study. BMJ Open. (2018) 8:e021367. 10.1136/bmjopen-2017-021367 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

43. Rebman AW, Bechtold KT, Yang T, Mihm EA, Soloski MJ, Novak CB, et al.. The clinical, symptom, and quality-of-life characterization of a welldefined group of patients with posttreatment Lyme disease syndrome. Front Med. (2017) 4:224. 10.3389/fmed.2017.00224 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

44. Johnson L, Aylward A, Stricker RB. Healthcare access and burden of care for patients with Lyme disease: a large United States survey. Health Policy. (2011) 102:64–71. 10.1016/j.healthpol.2011.05.007 [PubMed] [CrossRef] [Google Scholar]

45. Tibbles CD, Edlow JA. Does this patient have erythema migrans? JAMA. (2007) 297:2617–27. 10.1001/jama.297.23.2617 [PubMed] [CrossRef] [Google Scholar]

46. Diuk-Wasser MA, Hoen AG, Cislo P, Brinkerhoff R, Hamer SA, Rowland M, et al.. Human risk of infection with Borrelia burgdorferi, the Lyme disease agent, in eastern United States. Am J Trop Med Hyg. (2012) 86:320–7. 10.4269/ajtmh.2012.11-0395 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

47. Nieto NC, Porter WT, Wachara JC, Lowrey TJ, Martin L, Motyka PJ, et al.. Using citizen science to describe the prevalence and distribution of tick bite and exposure to tick-borne diseases in the United States. PLoS ONE. (2018) 13:e0199644. 10.1371/journal.pone.0199644 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

48. California Department of Public Health Vector-Borne Disease Section . Epidemiology and Prevention of Tick-Borne Diseases in California. Available online at: https://westnile.ca.gov/pdfs/EpidemiologyandPreventionofTBDinCA.pdf (accessed July 7, 2021).

49. Centers for Disease Control and Prevention (CDC). Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR Morb Mortal Wkly Rep. (1995) 44: 590–1. [PubMed] [Google Scholar]

50. Mead P, Petersen J, Hinckley A. Updated CDC recommendation for serologic diagnosis of Lyme disease. MMWR Morb Mortal Wkly Rep. (2019) 68:703. 10.15585/mmwr.mm6832a4 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

51. Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of lyme borreliosis. Clin Microbiol Rev. (2005) 18:484–509. 10.1128/CMR.18.3.484-509.2005 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

52. Theel ES. The past, present, and (possible) future of serologic testing for Lyme disease. J Clin Microbiol. (2016) 54:1191–6. 10.1128/JCM.03394-15 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

53. Horn EJ, Dempsey G, Schotthoefer AM, Prisco UL, McArdle M, Gervasi SS, et al.. The Lyme disease biobank - characterization of 550 patient and control samples from the east coast and upper midwest of the United States. J Clin Microbiol. (2020) 58:26. 10.1128/JCM.00032-20 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

54. Mosel MR, Rebman AW, Carolan HE, Montenegro T, Lovari R, Schutzer SE, et al.. Molecular microbiological and immune characterization of a cohort of patients diagnosed with early Lyme disease. J Clin Microbiol. (2020) 59:e00615–20. 10.1128/JCM.00615-20 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

55. Branda JA, Linskey K, Kim YA, Steere AC, Ferraro MJ. Two-tiered antibody testing for Lyme disease with use of 2 enzyme immunoassays, a wholecell sonicate enzyme immunoassay followed by a VIsE C6 peptide enzyme immunoassay. Clin Infect Dis. (2011) 53:541–7. 10.1093/cid/cir464 [PubMed] [CrossRef] [Google Scholar]

56. Branda JA, Steere AC. Laboratory diagnosis of Lyme borreliosis. Clin Microbiol Rev. (2021) 34:e00018–19. 10.1128/CMR.00018-19 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

57. Wormser GP, Nowakowski J, Nadelman RB, Visintainer P, Levin A, Aguero-Rosenfeld ME. Impact of clinical variables on Borrelia burgdorferispecific antibody seropositivity in acute-phase sera from patients in North America with culture-confirmed early Lyme disease. Clin Vaccine Immunol. (2008) 15:1519–22. 10.1128/CVI.00109-08 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

58. Steere AC, McHugh G, Damle N, Sikand VK. Prospective study of serologic tests for lyme disease. Clin Infect Dis. (2008) 47:188–95. 10.1086/589242 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

59. Rebman AW, Crowder LA, Kirkpatrick A, Aucott JN. Characteristics of seroconversion and implications for diagnosis of post-treatment Lyme disease syndrome: acute and convalescent serology among a prospective cohort of early Lyme disease patients. Clin Rheumatol. (2015) 34:585–9. 10.1007/s10067-014-2706-z [PubMed] [CrossRef] [Google Scholar]

60. Rebman AW, Aucott JN. Post-treatment lyme disease as a model for persistent symptoms in Lyme disease. Front Med. (2020) 7:57. 10.3389/fmed.2020.00057 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

61. Strobino B, Steinhagen K, Meyer W, Scheper T, Saschenbrecker S, Schlumberger W, et al.. A community study of Borrelia burgdorferi antibodies among individuals with prior Lyme disease in endemic areas. Healthcare. (2018) 6:69. 10.3390/healthcare6020069 [PMC free article] [PubMed] [CrossRef] [Google Scholar]

62. Aguero-Rosenfeld ME. Lyme disease: laboratory issues. Infect Dis Clin North Am. (2008) 22:301–13, vii. 10.1016/j.idc.2007.12.005 [PubMed] [CrossRef] [Google Scholar]

63. Seriburi V, Ndukwe N, Chang Z, Cox ME, Wormser GP. High frequency of false positive IgM immunoblots for Borrelia burgdorferi in clinical practice. Clin Microbiol Infect. (2012) 18:1236–40. 10.1111/j.1469-0691.2011.03749.x [PubMed] [CrossRef] [Google Scholar]

64. Eldin C, Raffetin A, Bouiller K, Hansmann Y, Roblot F, Raoult D, et al.. Review of European and American guidelines for the diagnosis of Lyme borreliosis. Med Mal Infect. (2019) 49:121–32. 10.1016/j.medmal.2018.11.011 [PubMed] [CrossRef] [Google Scholar]

65. Sanchez JL. Clinical manifestations and treatment of Lyme disease. Clin Lab Med. (2015) 35:765–78. 10.1016/j.cll.2015.08.004 [PubMed] [CrossRef] [Google Scholar