



# ALS and Lyme Disease

## Questions from Patient and Families – Responses from Medical Experts

### **Introduction:**

When anyone receives a diagnosis of ALS, it is normal and understandable to ask why you've developed this disease, and to look for the reasons. Although there has been an avalanche of new research knowledge in the past 10 years about how ALS progresses and what contributes to developing the disease, we don't yet have a complete understanding of the cause or causes of ALS.

Additionally, because the treatments available today don't offer a cure, or significant slowing of ALS, the possibility that you have a more treatable or reversible disease, and not ALS, offers great hope. Indeed, there are many other conditions that need to be ruled out before concluding that a person has ALS. This is one reason that it is important to seek an initial evaluation or second opinion from a neurologist knowledgeable and experienced in motor neuron diseases.

The purpose of this paper is to provide general information to help people with ALS and their loved ones learn more about the current scientific and medical information concerning ALS and Lyme disease. By being well informed, you and your physician can make decisions knowing as much as possible. The absence of a cure for ALS today naturally leads patients to seek treatments outside of the mainstream ALS medical community. The ALS Association seeks to help people with ALS become informed about the disease and possible treatments.

In most cases, there is agreement among the medical experts as to the answers to the questions posed in this paper. For some questions, there is more than one response included which may reflect variations in the physicians' approaches to care and treatment, and their interpretations of the available medical evidence. This variation in physician perspective is not unusual nor is it limited to the topic of ALS and Lyme disease. New scientific research information to clarify questions surrounding ALS and Lyme disease are needed.

This information paper is meant to provide general information and is not intended to be used for individual medical advice. As always, The ALS Association urges people with ALS to discuss this information and their treatment decisions with their ALS physician to determine the most appropriate and individualized plan of care.

Note: For more information on Lyme disease and the geographic distribution of risk, visit the Centers for Disease Control and Prevention web site: <http://www.cdc.gov/ncidod/dvbid/lyme/index.htm>

**Q: What is Lyme disease and where are the geographic areas in the United States where people are at risk to become infected with the Lyme bacterium?**

A: Lyme disease is an infection caused by a bacterium, *Borrelia burgdorferi*. In some people (how frequent is this?), Lyme disease may result in a more chronic neurologic disease (neuroborreliosis) because of its ability to produce chronic meningitis (inflammation of the lining surfaces of the brain and spinal cord). The potential neurologic consequences of an overt infection of the nervous system by the Lyme bacterium include headache, weakness, sensory problems such as numbness, tingling, pain in the arms or legs; cognitive disturbances and/or difficulty controlling bladder and/or bowel functions.

*Leo McCluskey, MD; University of Pennsylvania\**

A. There are large regional differences in the frequency of positive Lyme antibodies in the blood. The likelihood of detecting the Lyme antibody in a person with a previous, adequately treated Lyme infection unrelated to ALS is relatively low on the West Coast, in contrast to this being a more common occurrence on the East Coast and in the Midwest. Thus, this testing approach may make more sense in areas where the prevalence of exposure to Lyme disease is quite low, in contrast to areas of the country where the prevalence of exposure to Lyme disease is much higher.

*Richard Olney, MD; University of California, San Francisco*

**Q: Does Lyme disease cause ALS?**

A: It is extremely unlikely that an infection such as Lyme disease would cause classical ALS. It would be unusual for the bacterium that is responsible for Lyme disease to lead to both upper and lower motor neuron signs and symptoms as well as the progressive motor weakness and paralysis that characterize ALS. Adding the further evidence of sparing sensation and bladder and bowel control, make it very improbable to look to Lyme disease as a cause of ALS.

*Leo McCluskey, MD; University of Pennsylvania\**

**Q: Can Lyme disease mimic the symptoms of ALS including absence of sensory symptoms such as pain?**

A. There have been a few isolated cases reported in the medical literature of people with Lyme disease who do not have many of the usual symptoms of Lyme disease, and who do have some of the symptoms and signs of ALS. In these extremely rare cases, the patients did improve with antibiotics.

*John Halperin, MD; North Shore University Hospital, NY*

**Q: Should people who are diagnosed with ALS routinely get a test for Lyme disease?**

A: People with a diagnosis of classical ALS should not undergo Lyme disease testing as a matter of course. The probability that the disease is Lyme, and not ALS, is very low. At this time, there

are not convincing data that Lyme disease is a cause of classical ALS. However, for someone with a reasonable history of exposure to the Lyme disease organism, sensory symptoms, and/or symptoms in one area of the body, Lyme disease testing could be considered.

*Eric Logigian, MD, University of Rochester Medical Center, NY*

- A. Although the probability of Lyme disease is extremely low in a person who presents with typical features of classical ALS, I routinely obtain the Lyme antibody test on all my patients. There have been at least two patients in the world, who presented with a classical ALS presentation, were found to have Lyme disease, and in whom the symptoms and signs reversed with antibiotic treatment (Halperin JJ et al. Archives of Neurology 1990; 47:586-594; Hemmer B et al. Journal of Neurology, Neurosurgery and Psychiatry 1997; 63:257-258). Although the pretest probability is much higher for the results to be a false positive than identifying the third patient with this presentation, most of my patients read about Lyme disease and seek out a physician who will test them for Lyme disease. I would rather know the Lyme antibody status and discuss this with my patients before they may seek out a physician who specializes in Lyme disease, but is unfamiliar with ALS. This is the reason I routinely obtain Lyme antibody tests on all my patients, not because there is a high probability of a positive Lyme antibody test result that could be associated with ALS.

*Richard Olney, MD; University of California, San Francisco*

- A: Screening for Lyme disease is not advised in patients who have classical ALS, unless there is a definite history of exposure to ticks or the clinical examination warrants this testing.

*Rup Tandan, MD; University of Vermont*

- A. It is a medically appropriate approach to order a Lyme disease test for a patient with early ALS-like symptoms in one area of the body, known exposure to Lyme disease or who has other symptoms suggestive of Lyme disease. Communication between the physician and the patient can include a discussion of the low likelihood of the patient having Lyme disease and that if the test is positive, it's probably a false positive. However, discussing the importance of the test result with patients and supporting them in understanding the meaning and implications of positive and negative results is an important way physicians can help their patients.

*John Halperin, MD; North Shore University Hospital, NY*

Note: The medical experts agree that if the patient has a known exposure to appropriate ticks and has medical and/or neurologic symptoms, the opinion of a physician should be sought. It may be appropriate or reasonable to test for the Lyme antibody and conduct further tests. If you decide to seek Lyme disease testing, consult your ALS physician to discuss the testing and the possible meaning of both a negative and a positive result.

**Q: Are ALS and Lyme disease the same illness?**

- A: No. There is no evidence in the medical literature to support that these two conditions are the same, or that there is a causative effect. Some patients with Lyme disease develop a type of muscle weakness as also seen in ALS, but this pattern of weakness is non-specific and does not mean that Lyme disease is ALS or ALS is Lyme disease.

*Eric Logigian, MD, University of Rochester Medical Center, NY*

**Q: Should a person diagnosed with ALS take antibiotics, just in case?**

A: If the signs and symptoms confirm that the patient has classical ALS and there is no history of possible tick exposure, testing for the bacterium antibody is not indicated. Without clinical or laboratory evidence of the Lyme bacterium exposure, antibiotics are not indicated. If blood tests suggest Lyme bacterium exposure, a spinal fluid examination may be warranted to assess for involvement of the brain or spinal cord.

*Stephen Scelsa, MD, Beth Israel Medical Center, NY*

Note: Several neurologists whom The ALS Association consulted in the development of this informational material report that, in their clinical practice settings, they have not seen any patient with ALS convincingly respond to a course of antibiotics with objective improvements in neurologic testing.

**Q: How valid and reliable are the tests for Lyme disease? How useful are these tests?**

A: The currently available tests for Lyme disease can be problematic. Some of the tests being used today, such as the urine antigen test and even PCR tests done in some laboratories, are invalid or unreliable. The most commonly performed antibody tests for Lyme disease indicate past exposure to the bacterium, and not active disease. The bottom line is that Lyme disease is a clinical diagnosis and that the various tests, when performed in a reliable laboratory, can be used to help confirm the diagnosis. A positive "Lyme disease" test carries little diagnostic weight in and of itself and only has diagnostic value when used in conjunction with the patient's specific clinical features.

*Eric Logigian, MD, University of Rochester Medical Center, NY*

A: The serological testing is performed by many laboratories and good correlation does not exist between the results from one laboratory to the next in the same patient. In some patients with possible Lyme disease, repeat serological testing does not show a rise in the antibody titer against the Lyme agent, or Western blot testing does not confirm the diagnosis. False positive testing clearly exists and can be attributed to laboratory error, laboratory technique, or the quality of reagents used. Positive results of the Lyme antibody test (ELISA) can indicate active disease, but it may also reflect a previous case of Lyme disease that was adequately treated, yet serological testing did not revert to normal.

*Peter Donofrio, MD; Wake Forest University Baptist Medical Center, NC*

**Q: What are the tests that should be done if Lyme disease is suspected?**

A: When it is indicated to conduct a screening Lyme antibody test, and this ELISA test and the confirmatory Western immunoblot test are positive, a spinal tap should be performed to determine if there is evidence of meningitis (inflammation of the lining of the brain and spinal cord). At the same time as the spinal tap, simultaneous blood and spinal fluid Lyme antibody tests are done. The diagnosis of neurologic Lyme disease - the only manifestation that is capable of producing an ALS mimic syndrome - is made when there is evidence of meningitis

(increased number of white blood cells) and there is evidence of Lyme antibody production as demonstrated by a comparison of the blood Lyme titer/albumin ratio to that of the spinal fluid.

1. Lyme titer is usually normalized to IgG, not albumin.
2. This assumes sensitivity of intrathecal antibody production testing is 100%, which is not believed to be established.

*Leo McCluskey, MD; University of Pennsylvania\**

**Q: If my ALS physician finds that I do have active neurologic Lyme disease – along with ALS, or instead of ALS - what is the standard treatment?**

A: The treatment for active neurologic Lyme disease is two weeks to up to one month of intravenous antibiotics.

*Leo McCluskey, MD; University of Pennsylvania\**

**Q: Why are ALS researchers interested in two antibiotics as possible treatments for ALS if there is only rare association between Lyme disease and ALS, as when one person has both diseases?**

A: Both minocycline and ceftriaxone are of potential interest in the treatment of ALS. In independent laboratory studies using in-vitro culture systems, these two antibiotics have shown preservation of motor neurons and/or protection of the nerves from other kinds of neurological injury and prolongation of life in the transgenic SOD1 ALS mouse model. Researchers have determined that it is likely not the antibiotic actions of these compounds that are being observed in the encouraging experiments, but rather other drug actions unrelated to the antibiotic effects.

*Rup Tandan, MD; University of Vermont*

**Q: Are there other diseases besides Lyme disease that may need to be considered when confirming a diagnosis of ALS?**

A: Yes. The present consensus of the World Federation of Neurology criteria for the diagnosis of ALS includes a list of symptoms and signs that, if present, should cast doubt upon the diagnosis of ALS. This list includes significant pain, numbness, bowel or bladder control difficulties, involuntary movements and difficulty with eye movements. Additionally, the list also includes blood and spinal fluid studies and neuroimaging studies, such as CT scans or MRIs, that, if abnormal, are inconsistent with the diagnosis of ALS and that may indicate another disorder that may be mimicking ALS.

*Leo McCluskey, MD; University of Pennsylvania\**

Note: For more medical information, visit the web site of the World Federation of Neurology/ALS at <http://www.wfnals.org/guidelines/1998elescorial/elescorial1998.htm>, or refer to Mitsumoto, H, Chad, D.A., Pioro, E. P. *Amyotrophic Lateral Sclerosis*, Contemporary Neurology Series, 1998, F.A. Davis Company, and Belsh, J. M., Shiffman, P. L. *Amyotrophic Lateral Sclerosis: Diagnosis and Management for the Clinician*. 1996, Futura Publishing Company.

**Q: Why is there so much information on the Internet about ALS and Lyme disease?**

A: With such a serious disease as ALS for which there is no current diagnostic test, and given the media attention Lyme disease has received over the past few years, it is understandable that there would be interest in, and many questions about, ALS and Lyme disease. Other contributing factors that make this topic one of such interest to the general public and the ALS community are:

- ALS is often a diagnosis of exclusion. It is important to consider up to 40 or more other diseases and conditions before making the diagnosis of ALS. There are treatments for most of the alternative diagnoses.
- Some people with ALS do not have easy access to neurologists experienced in making the diagnosis of ALS.
- Tests and laboratories that are used to reach a diagnosis of Lyme disease may not produce reliable results. This promotes over-diagnosis of Lyme disease by clinicians who are not skilled and experienced in making the ALS diagnosis.

*Leo McCluskey, MD; University of Pennsylvania\**

**Q: Is it common for a person to have both ALS and Lyme disease?**

A: No. While it is certainly possible for a person to have both ALS and active Lyme disease, there is no evidence that this is common.

*John Halperin, MD; North Shore University Hospital, NY*

**Q: What should I do if I am in the process of being diagnosed and have been told that I may have ALS, or I have already been diagnosed with ALS?**

A: Seek a physician who has experience, training and expertise in diagnosing ALS and providing ongoing clinical care. He or she will be the best equipped to make a correct diagnosis, ruling out other diseases and conditions. If you have had a definite history of known tick exposure, be sure to tell your physician. Screening for Lyme disease is not routine unless the clinical signs and symptoms warrant the tests and/or the patient has known tick exposure. In most cases, ALS can be distinguished from Lyme disease by the physical examination by a physician experienced with diagnosing ALS. As with any serious disease, it is important to get a second opinion.

*Stephen Scelsa, MD, Beth Israel Medical Center, NY*

\* Excerpts with permission from *Ask the Neurologist* Column, Winter 2004, Newsletter of The ALS Association's Greater Philadelphia Chapter.