Epidemiology and Clinical Features of Lyme Disease

Moderator: Loretta Jackson Brown

Presenter: Alison Hinckley, PhD

Date/Time: March 6, 2012 2:00 pm ET

During the live webinar, the presenter was unable to provide a reply to many of the questions because of the large number of questions received. After the webinar the presenter reviewed the questions, and has provided replies to questions received during the webinar. If you have a question concerning this document, please send an email to coca@cdc.gov

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Question: Please share your thoughts on IGENEX in terms of Lyme testing.

Question: Do you have a suggestion regarding "Southern Dot Blot" and other tests through IGeneX that are being reported to local health departments by local providers as positive Lyme?

Reply: A number of laboratories offer "in-house" testing for Lyme disease using their own assays or testing criteria. Such in-house assays do not require evaluation or approval by the Food and Drug Administration. Because of the potential for misleading results, CDC and FDA recommend against using in-house assays whose accuracy and clinical usefulness have not been adequately validated and published in the peer-reviewed scientific literature. Please see the following link regarding other types of Lyme disease testing:
http://www.cdc.gov/lyme/diagnosistreatment/LabTest/OtherLab/

Question: Have there been studies on decreasing the length of antibiotic treatment for Lyme disease?

Reply: PubMed lists the following recent paper (http://www.ncbi.nlm.nih.gov/pubmed/21342072):

Wormser GP, O'Connell S. Treatment of infection caused by *Borrelia burgdorferi* sensu lato. Expert Rev Anti Infect Ther. 2011 Feb;9(2):245-60.

Abstract
Borrelia burgdorferi sensu lato (Bbsl) infections, which are transmitted by Ixodes ticks, cause a wide variety of clinical manifestations and are of public health importance in parts of North America, Europe and Asia. A literature review of pertinent articles published up until July 6th 2010 was performed on the use of antimicrobials in the treatment and prevention of Bbsl infections. The clinical outcome with 10-28 days of antibiotic treatment is generally excellent, but in view of the experience with other infections, future studies might address whether the duration of antibiotic therapy could be shortened.

Question: Can you speak of surveillance for Ixodes ticks around the country (other than in endemic areas)?

Reply: CDC funded a recent entomologic survey of the Eastern United States through a cooperative agreement with research partners at Yale University (see Diuk-Wasser et al., 2012). However, most entomologic studies are done at the state and local level. Through the Epidemiologic and Laboratory Capacity (ELC) cooperative agreement with state health departments, CDC has also recently funded several states in non-endemic areas (e.g. North Dakota) to conduct surveillance for Ixodes ticks, as well as for the presence of *B. burgdorferi*.

Question: What, if any, are the recommendations for prophylaxis treatment for children< 8 yrs? John Jacocks Asked: Any thoughts about antibiotic prophylaxis for patients <8 years old?

Reply: The following statement is excerpted from Wormser et al, 2006:

Doxycycline is relatively contraindicated for women who are either pregnant or breast-feeding, as well as for children <8 years of age. In these patients, if chemoprophylaxis were to be used, an alternative antimicrobial, such as amoxicillin, would need to be considered. Amoxicillin is effective against B. burgdorferi both in vitro and in clinical trials of patients with Lyme disease, and it may be expected to be a useful prophylactic agent after a bite from an I. scapularis or I. pacificus tick. No cases of Lyme disease developed in 192 patients given 10 days of amoxicillin for prophylaxis after a bite from an I. scapularis tick in a randomized clinical trial, although failure of amoxicillin prophylaxis has been reported anecdotally from Europe. Amoxicillin has a shorter half-life than doxycycline, and a multiday regimen would likely be necessary for prophylaxis to be effective.

Practice guidelines for the treatment of Lyme disease. Infectious Diseases Society of America. Clin Infect Dis. 2006;43:1089-1134.

Question: Is Southern blot an acceptable diagnostic test with or without EIA or IFA?

New Reply: A number of laboratories offer "in-house" testing for Lyme disease using their own assays or testing criteria. Such in-house assays do not require evaluation or approval by the Food and Drug Administration. Because of the potential for misleading results, CDC and FDA recommend against using in-house assays whose accuracy and clinical usefulness have not been adequately validated and published in the peer-reviewed scientific literature. Please see the following link regarding other types of Lyme disease testing:
http://www.cdc.gov/lyme/diagnosistreatment/LabTest/OtherLab/

Question: What is the % of long term residuals after 22 years. Positive signs and incomplete IV treatment due to penicillin allergy? (22 years of symptoms due to incomplete treatment)

Reply: Many studies have demonstrated resolution of symptoms for the majority of patients treated for Lyme disease. With prompt treatment for early disease, the likelihood of continued symptoms at 6 months or even 1 year is low. Some patients do report minor symptoms at 1 year (such as fatigue, myalgias or arthralgias); however, many of the studies do

not use a comparable population to compare frequencies of these symptoms within the population at large (exception is the article by Cerar listed below). Patients with later manifestations of Lyme disease at the time of presentation can respond more slowly to therapy.

For further reading:

1) Marques A. Chronic Lyme Disease: A Review. Infect Dis Clin N Am 2008;22:341-60.

2) Seltzer EG. Long-term Outcomes of Persons With Lyme Disease. JAMA. 2000;283(5):609-616.

3) Cerar D. Subjective Symptoms after Treatment of Early Lyme Disease. Am J Medicine 2010;123(1): 79–86.

Question: Why was the vaccine Lymerix discontinued and will another vaccine be developed?

Reply: A Lyme disease vaccine is no longer available. The vaccine manufacturer discontinued production in 2002, citing insufficient consumer demand. Protection provided by this vaccine diminishes over time. Therefore, if you received the Lyme disease vaccine before 2002, you are probably no longer protected against Lyme disease. Furthermore, previous Lyme disease infections do not confer future immunity.

A recent supplemental issue of Clinical Infectious Diseases, The Need for a New Lyme Disease Vaccine, Volume 52, Suppl 3, February 1, 2011 contains a number of articles and perspectives on the future of Lyme disease vaccine development.

Question: Will the EIA or Western blot ever be positive if we treat the patient with antibiotics?

Reply: It depends. Antibody responses can be abrogated in patients with early disease, who receive treatment (even inadequate treatment) very early. This means that a patient who receives a short course of antibiotics may not have a sufficient antibody response to be detected in standard tests.

However, repeat testing is also not recommended. Statistically speaking, anyone who is seronegative and tested multiple times is likely to have a positive result, by chance, at some point.

For an excellent explanation of this topic, see:

Halperin, J.J., Baker, P., and Wormser, G.P. In, "Lyme Disease: An Evidence-based Approach" (J.J. Halperin, Ed.), CAB International, 2011, pp.261-262.

This chapter can be downloaded here: http://www.aldf.com/pdf/Halperin_Book_Chapter_17.pdf.

Question: You described the EM as a characteristic lesion, but I think you should also mention that the EM is not Pathognomonic, correct?

Reply: Correct. The erythema migrans is not exclusively associated with a *B. burgdorferi* infection. Please see the presentation for discussion/slides of atypical EM, as well as Southern Tick Associated Rash Illness (STARI).

For an excellent explanation of this topic, see:

Tibbles CD and JA Edlow. Does This Patient Have Erythema Migrans? JAMA. 2007;297(23):2617-2627.

Question: In the Northeast where we normally have cold winters will this abnormally warm winter have an impact or bumper crop this year?

Reply: Tick populations are difficult to forecast. You may have heard that Dr. Richard Ostfeld is predicting a big tick year due to acorn masting in previous years; however this is a highly focal situation. The nymphal peak may depend on weather conditions in the early summer, but again, that is difficult to predict in advance.

Question: Can you please touch upon the importance of homeopathics being used in conjunction with antibiotics and why is this not recognized as an additional treatment form?

Reply: There are no known publications as to the efficacy of antibiotics with homeopathy for the treatment of Lyme disease.

Question: It is my understanding that due to the lack of specificity of laboratory tests, some patients will repeatedly test negative for Lyme. Also, due to the similarity between Lyme and STARI, if a patient repeatedly has negative results with Lyme testing, should a physician then consider STARI, especially if the patient is from or has visited the SE region? And what are the laboratory tests for STARI?

Reply: There is a lack of sensitivity for serologic testing in early Lyme disease. Antibodies may not be detectable for several weeks after onset of erythema migrans (see slides). This is why serologic testing is not considered necessary or useful for diagnosis of patients with erythema migrans.

In addition, antibody responses can be abrogated in patients with early disease who receive treatment (even inadequate treatment) very early. This means that a patient who receives a short course of antibiotics may not have a sufficient antibody response to be detected in standard tests. If the patient has no history or potential exposure to ticks from Lyme-endemic areas, a physician may certainly consider STARI. Please do recall that serologic testing for Lyme disease is very sensitive and specific for later stages of illness. It is only for these clinical stages, that Lyme disease serologic testing is recommended.

STARI is diagnosed on the basis of symptoms, geographic location, and possibility of tick bite. Because the cause of STARI is unknown, no diagnostic blood tests can be developed. Researchers once hypothesized that STARI was caused by the spirochete, Borrelia lonestari; however, further research did not support this idea.

Since the cause is unknown, it is also unknown whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians will often treat patients with oral antibiotics.

Additional information can be found here: http://www.cdc.gov/stari/disease/

Question: There have been recent publications on a mouse model for "chronic Lyme Disease". Has CDC evaluated these publications and/or developed talking points about them?

Reply: Contacted Ms. Kjemptrup directly. In addition, CDC's website has been updated to reflect the ongoing debate in the body of scientific literature that includes this paper.

Question: I live in Wisconsin and we are instructed to never use a tweezers to remove a tick! You run the risk of not getting the head out?! Is this something the CDC recommends for certain States? The recommended method is always by using your fingers. Can you elaborate? Margaret Regan Asked: A follow-up question about tick removal. If the head stays in the skin after removal should it be removed or can it be left in to come out on its own?

Reply: CDC recommends using tweezers for tick removal in all states. The reason why tweezers are recommended over fingers (or any other implement) is that they are likely to remove a tick quickly. The faster a tick is removed the less time it has to transmit *B. burgdorferi*. If the head is not removed initially, that is Ok. Once the body is removed, the tick will no longer be able to transmit the bacteria.

How to Remove a Tick

1. Use fine-tipped tweezers to grasp the tick as close to the skin's surface as possible.
2. Pull upward with steady, even pressure. Don't twist or jerk the tick; this can cause the mouth-parts to break off and remain in the skin. If this happens, remove the mouth-parts with tweezers. If you are unable to remove the mouth easily with clean tweezers, leave it alone and let the skin heal.
3. After removing the tick, thoroughly clean the bite area and your hands with rubbing alcohol, an iodine scrub, or soap and water.

Note: Avoid folklore remedies such as "painting" the tick with nail polish or petroleum jelly, or using heat to make the tick detach from the skin. Your goal is to remove the tick as quickly as possible--not waiting for it to detach. From: http://www.cdc.gov/ticks/removing_a_tick.html

If tweezers are not available, you may use your fingers to remove the tick, being careful not to crush or squeeze the body. The overriding goal is to remove the tick before it can transmit disease.

Question: When doing tick surveillance are ticks tested in pools like mosquitoes or as individuals in determining positive rates during sampling surveillance. Thanks.

Reply: At CDC, we do not pool ticks when testing for the presence of *B. burgdorferi* because infection rates in the northeastern U.S. are so high (25% nymphs, 50% adults) that all pools would be positive.

Question: For the >20% ticks positive for prophalaxis, is that for a broad areas? What if you only have specific areas >20%?

Reply: According to the IDSA Treatment Guidelines, "Infection of ≥20% of ticks with *B. burgdorferi* generally occurs in parts of New England, in parts of the mid-Atlantic States, and in parts of Minnesota and Wisconsin, but not in most other locations of the United States." Further, "Prophylaxis after I. pacificus bites is generally not necessary because of low infection rates with B. burgdorferi in almost the entire region in which this tick is endemic. However, if a higher infection rate (≥20%) were documented in specific local areas, prophylaxis with single-dose doxycycline would be justified if the other criteria above are met." Clinical judgment should be exercised depending on the available information regarding the rates of tick infection and the location where the patient was infected. Generally speaking, along the eastern seaboard from Maryland to Maine, you will have infectivity rates exceeding 20%.

Question: Can you discuss the difference in arthralgia (not sufficient for clinical compatibility) and arthritis with respect to Lyme disease?

Reply: Arthralgias can be symptomatic of early disseminated Lyme disease, along with erythema migrans, fever, myalgias, headache, etc. In contrast, Lyme arthritis is a sign of late disseminated Lyme disease, characterized by recurrent attacks or persisting objective joint swelling in one or more large joints (most commonly the knee, but also may occur in the hip, elbow, ankle, and wrist). Two-tiered serologic testing is very sensitive and specific for this clinical manifestation of Lyme disease.

Question: Are people who had three doses of the vaccine still immune?

Reply: No, their immunity has waned. They should take protective measures to prevent infection.

Question: I had a patient who had an initial negative Lyme test despite a single EM rash. She then developed multiple EM rashes, was retested again and was negative and again a week or so after the multiple rashes developed and finally +. Why would that happen?

Reply: Like blood tests for many other infectious diseases, the test for Lyme disease measures antibodies made by white blood cells in response to infection. It can take several weeks after infection for the body to produce sufficient antibodies to be detected. Therefore, patients tested during the first few weeks of illness will often test negative. In

contrast, patients who have had Lyme disease for longer than 4-6 weeks, especially those with later stages of illness involving the brain or the joints, will almost always test positive. A patient who has been ill for months or years and has a negative test almost certainly does not have Lyme disease as the cause of their symptoms. Serologic testing is generally not useful or recommended for patients with single EM rashes. For this manifestation, a clinical diagnosis (alone) is recommended.

Question: In the charts, there are black-legged ticks in the Midwest. However, there are very few people who have Lyme disease. Why is that?

Reply: The upper Midwest is certainly endemic for Lyme disease. In areas such as Iowa and Illinois, Lyme disease is emerging. Typically, the *Ixodes scapularis* ticks move into an area, then over time acquire the spirochete and Lyme disease becomes more problematic. You can view cases of Lyme disease by state from 2000-2010 at: http://www.cdc.gov/lyme/stats/chartstables/reportedcases_statelocality.html

Question: Some labs are using a multiplex PCR test that are designed to detect genomic and plasmid DNA from Borrelia burgdorferi. What is the usefulness and sensitivity of this test?

Reply: A number of laboratories offer "in-house" testing for Lyme disease using their own assays or testing criteria. Such in-house assays do not require evaluation or approval by the Food and Drug Administration. Because of the potential for misleading results, CDC and FDA recommend against using in-house assays whose accuracy and clinical usefulness have not been adequately validated and published in the peer-reviewed scientific literature. Please see the following link regarding other types of Lyme disease testing: http://www.cdc.gov/lyme/diagnosistreatment/LabTest/OtherLab/

For more information about Lyme disease testing, see:

Aguero-Rosenfeld ME, Wang G, Schwartz I, Wormser GP. Diagnosis of lyme borreliosis. Clin Microbiol Rev. 2005 Jul;18(3):484-509.