Epidemiology and Clinical Features of Lyme Disease

Moderator: Loretta Jackson Brown

Presenter: Alison Hinckley, PhD

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Coordinator:

Welcome and thank you for standing by. At this time all participants are on a listen-only mode until the question-and-answer session of today's conference. At that time you may press star 1 if you'd like to ask a question. I'd like to inform all parties this call is being recorded. If you have any objections, you may disconnect at this time. I now would like to turn the call over to Ms. Loretta Jackson-Brown. You may begin, ma'am.

Loretta Jackson Brown:

Thank you, (Laurie). Good afternoon. I'm Loretta Jackson Brown, and I'm representing the Clinician Outreach and Communication Activity, COCA, with the Emergency Communication System at the Centers for Disease Control and Prevention. I am delighted to welcome you to today's COCA Webinar: "Epidemiology and Clinical Features of Lyme Disease.'We are pleased to have with us today Dr. Alison Hinckley. Here to review the epidemiology of lyme disease, early signs, treatment guidelines and prevention practices. You may participate in today's presentation by audio only via Webinar or you may download the slides if you are unable to access the Webinar. The PowerPoint slides set in the Webinar link can be found on our COCA Web page at emergency.cdc.gov/coca. Click on COCA Calls. The Webinar link and slides that can be found under the caller number and call pass codes.

At the conclusion of today's session, the participant will be able to describe populations at risk of contracting lyme disease in the United States, describe the early signs and symptoms of lyme disease, understand the appropriate use of serologic tests and advise patients on personal protective measures against tick bites.

Free continuing education credit is available for today's Webinar. Information on how to obtain free CEs will be provided at the conclusion of today's call. In compliance with continuing education requirements, all presenters must disclose any financial or other association with the manufacturers of commercial products, suppliers of commercial services or commercial supporters as well as any use of an unlabeled product or product under investigational use. CDC, our planner and the presenter for this presentation, do not have financial or other association with the manufacturers or commercial products, supplies of commercial services or commercial supporters. This presentation does not involve the unlabeled use of a product or products under investigational use. There was no commercial support for this activity.

Today's presenter Dr. Hinckley is an epidemiologist in the Division of Vector-Borne Diseases in the National Center for Emerging and Zoonotic Infectious Diseases at the Centers for Disease Control and Prevention. She holds a pH in environmental health from Colorado State University and completed post-doctoral fellow positions at Colorado State University's Environmental Health Advanced Systems Lab and CDC's Arboviral Diseases Branch. Since joining the Bacterial Diseases Branch in 2007, Dr. Hinckley has worked extensively to develop the TickNet Program. The ultimate goals of (Tick Net) are to foster greater

collaboration among CDC programs, working on tick-borne diseases, to enhance and integrate surveillance for tick-borne diseases in partnership with states and to facilitate applied research projects that address key public health questions regarding tick-borne diseases. In addition to serving as a Project Office - Officer for TickNet, Dr. Hinckley serves as a Lyme Disease Subject Matter Expert for CDC. She has authored or co-authored four manuscripts pertaining to lyme disease.

Following the presentation, you will have an opportunity to ask our presenter questions. For audio questions, dialing star 1 will put you into the queue for questions. You may submit questions via the Webinar system at any time using the Q&A tab at the top of your Webinar screen. At this time, please welcome Dr. Hinckley.

Dr. Alison Hinckley:

Thank you, Loretta, and good afternoon or good morning to you depending on where you are. I'm pleased today to give you-all an overview of lyme disease epidemiology and clinical features. You'll see on our next slide an overview. This talk is broken down into seven sections representing lyme disease background. That'll be background on the organism, vector, and factors affecting the emergence of the disease, the epidemiology of lyme disease in the United States including age, sex and geographic distributions, the clinical features of early- and late-stage disease, recommendation and performance of laboratory diagnostic tests for lyme disease, recommendations regarding antibiotic treatment, opportunities for prevention including prophylaxis following tick bites and last, but not least, resources for clinicians and health departments and ongoing efforts by CDC and others to combat the disease.

Now on to the background. In 1975 a group of concerned parents alerted the Connecticut State Health Department about an outbreak of inflammatory arthritis among children in and around Lyme Connecticut. Allen Steere and others conducted the first epidemiologic investigation by evaluating a cluster of juvenile and adult arthritis cases in the area. They soon recognized arthritis is a late manifestation of a multi-system disease associated with tick bites in the United States and in Europe. The most common early manifestation noted was a characteristic erythema migrans that's EM or the bull's-eye rash. This study identified lyme disease as a distinct disease. In 1981 Willy Burgdorfer and others identified spirochetes in the midgut of adult Ixodes ticks and cultured spirochetes from the blood and tissue of patient's presenting with these EM rashes. The spirochete was subsequently named Borrelia burgdorferi. Based on genotyping of isolates, Borrelia burgdorferi or B. burgdorferi was subsequently broken down into a number of genospecies that occur around the world. The strain infecting humans in the United States is called B. burgdorferi sensu stricto. It is shown here in a box. This strain also infects humans in Europe, although the two dominant genospecies there are B. garinii and B. afzellii. There is some newer evidence that B. spielmanii has been associated with the disease in Europe. In addition B. bissetii has been implicated only in Europe, although more information is needed to confirm this.

The remaining genospecies are not known to be pathogenic to humans. The different pathogenic genospecies are associated with somewhat different disease expression. Arthritis occurs more commonly with B. burgdorferi sensu stricto. Neurologic manifestations are more often associated with B. garinii, and cutaneous manifestations are more common with B. afzellii. As I mentioned, B. burgdorferi is a spirochete, a modal spiral-chafed - spiral-shaped bacterium. It is made up of at least 30 different immunogenic proteins including three major outer surface proteins. These have roles in transmission and pathogenesis. Some are differentially expressed, and some, such as (VLLC), are highly immunogenic with at least one invariable region that is conserved across species. This means that diagnostic methods based on this lipoprotein can be used to identify responses to infections obtained in the U.S. and abroad. There will be more on this in the diagnostics section of the talk.

In the United States, lyme disease occurs in humans and animals following the bite of B. burgdorferi-infected ticks. The black-legged tick is the predominant vector in the U.S. It is depicted here in its different life stages. Humans are most often infected by the bite of nymphal ticks. Adults are much less likely than nymphs to transmit infection. This is because infected nymphs are out in large numbers in endemic areas

in the late spring and summer when people are most active and least covered. Nymphs are very small and hard to see, often compared to the size of a poppy seed. This means that they, unlike the adult ticks, may be less likely to be removed before transmission can occur. In most cases ticks must be attached for at least 48 hours for transmission. The proper name of the black-legged tick is Ixodes scapularis, and it exists in the yellow area of the top U.S. map on this slide. It transmits disease primarily in the northeastern United States from Virginias to the coastal Maine area and in the Midwestern U.S., primarily in Wisconsin and Minnesota. The western black-legged tick or the Ixodes pacificus tick in the bottom map is the vector in the western United States, predominately in California. Other species of ticks are not competent vectors.

As shown on the right of this slide, small rodents, especially the white-footed mouse, Peromyscus leucopus serve as the principal reservoir of B. burgdorferi infection for black-legged ticks in the Northeast and Midwestern states. As shown on the left in the West, B. burgdorferi is maintained in wood rats, Neotoma species by the Ixodes neotomae ticks. Ixodes pacificus ticks then pick up the infection from the wood rats and are able to spread to humans in subsequent feeds. Humans are incidental hosts of B. burgdorferi and do not contribute to its maintenance and nature. This figure illustrates the two-year life cycle of black-legged ticks. There are three stages of vector ticks: larva, nymph and adult. Each stage normally takes a single blood meal. Larvae acquire B. burgdorferi infection from small mammals in late summer and transmit to humans as nymphs in the following spring and summer, as shown in this diagram. As mentioned, the adult ticks can also transmit the infection, although their larger size makes it easier for them to be recognized and removed before transmission. Thus, the risk of human infection is greatest in late spring and summer, as shown in the big shaded area of this diagram and also in the box to the right. Transstadial transmission of B. burgdorferi from larvae to nymphs and from nymphs to adults helps maintain the infection cycle. And please note that deer, shown on the top of the slide, are immune to the spirochete but important to maintenance and transport of tick populations.

As shown on this Newsweek cover from 1989, lyme disease cases are reported from all over the U.S., although documented transmission of the disease is limited to specific areas of the U.S. Namely that is the Northeast, Midwest and select areas of the western states. On the next few slides, I'll explore the reasons for emergence in the areas and the potential for expansion into new areas. First and foremost, reasons for tick-borne disease emergence and increase as of late, can be linked to reforestation. This is very common in areas of the East that were over a century ago, cleared and used as agricultural lands. In the picture, note the stone wall in the background. Walls such as these marked the boundary of farms and fields and now can be found shaded by the growth of large forests in large areas of the Northeast. Lyme disease tick vectors thrive in high humidity areas such as by rivers and shaded damp forested and brushy areas with leaf litter, such as forests.

Reforestation is perhaps better illustrated on this slide. It depicts an area called Chipman Hill in Middlebury, Vermont over a 120-year time span. In the first slide on the left, we see an area that has relatively few trees and large land clearings. By the turn of the century, in the 1900s, a substantial increase in forested areas has occurred. By the 1980s, the slide on the right or the picture on the right, the forested areas thickly overlay the landscape of Chipman Hill. Increases in the abundance of tick host animals has also played a big role in the emergence and expansion of this disease. On this figure, we illustrate the increased numbers in thousands of deer in Connecticut between 1885 and 2005, essentially going from nothing to over 80,000 deer in 2005. You see a steady increase after 1945 and a more dramatic incline after the 1980s. These rises are related to many factors, such as reduction in natural predators and changes in land-use pattern. Since the mid-19 - or the mid-20th Century, there's been an expansion of suburban residential homes into forested areas. This suburbanization of reforested areas increases the opportunities for exposure to vector ticks.

And lastly, there are periodic changes in surveillance system in place to track cases. In this - there - in this example, again from Connecticut, we see how (methodoligic) changes to human lyme disease surveillance substantially impact documented case numbers. Surveillance is very time and resource intensive, and different approaches can affect the quality and reliability of the data. In Connecticut, lyme disease was passively reported by physicians until 1994 when enhanced lab reporting was added. Note

the increase in case numbers in the following years. Case numbers increased further when labs were required to report positive - required to report positive lab tests, and numbers fall back to almost the same level as the decade before when the state discontinued lab reporting in 2004. Without the background on inclusion of new methodology, it would look like lyme disease spiked upward sharply during the early 2000s. In fact, given the relative constancy of passive reporting over time, it is more likely that lyme disease is stable in Connecticut over this time period. I should note that since 2006, Connecticut has reinstated lab-based surveillance and reported cases have increased back to near 2002 levels.

To recap, here are the reasons for emergence or reemergence on - of lyme and other tick-borne diseases. The potential for expansion will continue to depend on these factors until we can enact an intervention that breaks the enzootic cycle of disease.

Now for the epidemiology of lyme disease. Lyme disease was made a nationally notifiable disease in 1990 with a uniform case definition adopted in 1991. Reporting is mandatory in all 50 states. In 2010, it was the 6th most commonly reported disease in the United States. It was the second most commonly reported disease in the northeastern states. Over the past 15 years from 1996 to 2010 shown here in this figure, the number of reported cases has risen substantially from over 15,000 to nearly 30,000 confirmed and probable cases.

Here's another way to look at the increasing burden of lyme disease. This map depicts the incidents rates of reported cases of lyme disease by county in endemic northeastern states in 1997 and 2005. In this figure, we can see by the increase in colored counties the geographic expansion of highly endemic areas to the north, west, and south. The increase in incidents is substantial in some already endemic counties that is depicted by color changes to orange or red, and this is shown predominately in the lower Hudson River Valley into eastern Pennsylvania.

This is a map of reported cases of lyme disease in the United States for 2010. You can more clearly see the geographic concentration of lyme disease in the Northeastern and Midwestern states. In fact, 12 states account for more than 95% of all reports made annually. Though lyme disease cases have been reported in nearly every state, cases are reported from the infected person's county of residence, not the place where they were necessarily infected. Thus, if a child from New Mexico spends part of his summer in Pennsylvania, when he becomes infected and develops lyme - where he becomes infected and develops lyme disease, his case report would be indicated on this map as a dot from north - from New Mexico. Lyme disease affects persons in all age groups, but the highest rates occur in children younger than 15 years of age and adults around 35 to 55 years. In the younger age groups, males are much more likely to become infected than females. This figure shows the month of onset for lyme disease cases in the United States. As is typical for vector-borne disease, the majority of illnesses begin in the summer months. Recall that this is when nymphal ticks are most active and people are more often outdoors. Adult black-legged ticks can also be active biters during the fall and winter questing - that is seeking a blood meal - on any given day provided temperature are at or above 50 degrees anecdotally.

Now for clinical features. Lyme disease is a multi-phase, multi-system disease that is characterized into early localized, early disseminated and late disseminated stages. The disease course is highly variable and evolves gradually over weeks: for acute disseminated two months, for the acute neurologic manifestations, acute arthritis and carditis, and even years for the late-stage arthritis and neurologic manifestations such as encephalopathy. This figure represents the breakdown of reported lyme disease cases from 2001 to 2010 by disease manifestation. The majority of reported cases represent the EM, erythema migrans rash. Other manifestations are less common, and some patients have more than one presentation.The characteristic EM occurs in approximately 60% to 80% of cases and is usually accompanied by mild constitutional symptoms and occasionally by regional lymphadenitis. An incubation period of 3 to 30 days with an average of 7 to 14 days occurs between the time of infection and onset of the rash. It is expanding, round, erythematous and can be warm to the touch, although is rarely painful. The EM rash can be distinguished from an allergic reaction by its relatively slower onset - allergic reactions should generally occur within hours of a tick bite - and its gradual expansion. Some lesions are atypical in appearance with central induration, fasciculation or ulceration or with a variation in color such

as a bluish hue. Here are a few pictures of more atypical forms. If left untreated, an early localized infection can disseminate over weeks to months. This most often presents as multiple EMs or Bell's palsy to the right, radicular neuropathy or carditis. Bell's palsy is one of the most common early disseminated forms. It would - due its early stage, it occurs most commonly during the summer, may be bilateral and may be accompanied by pleocytosis in the CSF. Arthritis can also be a presenting sign, but is more often considered a sign of late-stage disease. The typical acute arthritis attack is mono or oligoarticular and intermittent. After months to years of no or inadequate treatment, lyme disease can manifest as chronic arthritis or in neurologic forms such as mild encephalopathy or peripheral neuropathy.

One condition that complicates the diagnosis of lyme disease is called southern tick-associated rash illness or STARI. This condition is characterized by a rash that is indistinguishable from the lyme disease EM rash. It may also be, like lyme disease, accompanied by fatigue, fever, headache, muscle and joint pains, although it follows the bite of the lone star tick, amblyomma americanum. STARI is also known as Master's disease, named after its founder, Ed Masters, although unlike lyme disease, the cause of STARI is not known. One way to distinguish this disease from lyme disease is by identifying the attached tick. The lone star tick, shown in this picture, is somewhat larger than the black-legged tick and is recognizable by the characteristic white dot or markings on its back. Unlike the black-legged tick, the lone star tick predominately occurs in the southeastern United States and is an aggressive human biter. It is shown by this map, however - as shown by this map, however, there is some area of overlap between these two tick vectors in the mid- and northeastern area, and it complicates diagnosis of these two similar diseases. There are some clinical differences to these two diseases. Although STARI is hard to distinguish from the EM rash of early lyme disease when a single individual seeks medical care, we do notice these differences when a population is studied. This table illustrates the results of a study conducted by Gary Wormser and others to compare the characteristics of patients from a - from Missouri with STAR-I Missouri is where STAR-I was first observed - to patients in New York having lyme disease EM lesions. The results indicate that significant differences do exist. STARI patients are more likely to recognize a tick bite at the site of the lesion. The mean number of days to developing the EM is shorter for STARI patients, and in addition, significantly fewer STARI patients have multiple symptoms or lymphadenopathy as compared to lyme disease patients. Studies are ongoing to determine whether long-term effects are observed among STARI patients and whether antibiotics are helpful toward resolution of such symptoms.

Now for laboratory diagnosis. Serologic testing can provide additional diagnostic support to distinguish lyme disease from other causes of illness. CDC recommends a two-tiered approach to lyme disease serologic testing. This includes a positive or equivocal enzyme-linked immunosorbent assay or ELISA or immunofluorescence IFA assay shown here on the blue box in the left, followed by a confirmatory western block for IgG or IgM anti- Borrelia burgdorferi antibodies, shown on the right. Note: Both the IgM and IgG testing are recommended for serology on patients having symptoms less than 30 days due to the high potential for false positive IgM results. After 30 days, IgG is recommended. However, the sensitivity and specificity of this testing combination vary by stage of disease. It is relatively insensitive, that's less than 40% when used for testing of early stages of illness, particularly the EM rash. It is highly sensitive, nearly 90% and above, when used for diagnostic testing of late-stage of disseminated lyme disease. For this reason, CDC recommends this approach primarily for symptomatic patients having the potential for prolonged or disseminated disease. It is not necessarily helpful or generally useful for testing of EM patients.

It is also important to consider the likelihood of disease before performing laboratory testing for lyme disease. In this schematic, we illustrate how the validity of test results differ when testing specimens from people having a high likelihood on the left versus people having a low likelihood on the right. With regard to lyme disease, if we understand that a patient has a high likelihood, for example, they live in Dutchess County, New York, they have intermittent arthritis of the knee and a history of working outside in the summer, this would represent the left-side of the figure. We would then have good confidence that a positive result is a true positive. If, to contrast, we wish to test a patient having a low likelihood, representing the right-side of the slide, for example, they live in Central Florida, have no history of travel to lyme-endemic areas, and they have a clinical history of non-specific pain and fatigue with no previous EM rash, we would have low confidence in any positive result. A false positive may be more likely.

Please note, any of the numbers shown on this slide are not specific to lyme disease, but are instead a representation of limitations of any diagnostic test. Keeping that lesson in mind, I'd like to discuss several alternatives to standard two-tiered testing. The first two are ELISA test based on the antibody to the VLse antigen or a subcomponent, the C6 peptide. These are currently approved as first-tier assays in lieu of the standard wholesale sonicate or IFA test. However, the C6 is under evaluation as a standalone test. As a standalone, it offers several advantages over the standard ELISA. It has greater sensitivity for detecting earlier disease such as EM rash. It can detect non-U.S. strains. It is more objective and less labor-intensive, and given that the (tighter) may wane faster, it allows for easier distinction between current and previous infections.

Direct detection, that is culture or PCR of B. burgdorferi in clinical samples can aid in diagnosis during early infection. In particular, culture of B. burgdorferi spirochetes from skin biopsies can be useful when an EM rash is atypical or when patients have no recent history of being in lyme-endemic areas. In the United States, culture from skin is moderately sensitive, obtaining organisms in 60% to 86% of cases. Spirochetes may also be cultured from blood in the first two to three weeks of infection. Culture of spirochetes from CSF and synovial fluid has also been reported, although the sensitivity of this technique for these specimens is very low. Overall, culture is labor-intensive, slow and expensive. Its utility is also limited to untreated patients at the height of acute infection. Although PCR is a useful tool for many diseases, it is not generally useful for diagnosis of lyme disease, because there are so few organisms and they are only transiently present in select specimen. In the United States, it has shown to have very high specificity and moderate sensitivity for skin biopsies and moderate to high sensitivity for synovial fluid. The sensitivity of PCR testing, however, can be quite low for CSF and blood. Use of PCR for identification of B. burgdorferi DNA in urine has not been validated and is not recommended due to its questionable utility with regard to treatment decisions.

Similarly at present, studies of PCR for evaluation of B. burgdorferi DNA in breast milk, semen or other specimen types have not been reported and are therefore not considered appropriate. PCR is to be used with caution. Even when testing appropriate specimens, skin, synovial fluid, for example, due to the potential for false-positive results. In areas where lyme disease in endemic, the predicted value of the EM rash sufficiently offsets the value of culture, PCR and histologic testing. Some laboratories offer lyme disease testing using assays whose accuracy and clinical usefulness have not been adequately established. Unvalidated tests available as of 2011, include the following list. At the top, although a single-tier IgG immunoblot test is considered acceptable as laboratory evidence of infection for surveillance purposes, according to the 2008 case definition for lyme disease, CDC does not recommend it as a standalone diagnostic test. The primary reason for this is that it is a highly subjective test with strong potential for interlab variability. Addition tests of questionable utility include capture assays for antigens in urine, culture immunofluorescence staining or self-sorting of cell wall deficient or statistic forms of B. burgdorferi, lymphocyte transformation tests, quantitative CD57 lymphocyte assays, reverse western blots, in-house criteria for interpretation of immunoblots and measurement of antibodies in joint fluid. More information regarding testing can be found on CDC's Web site, www.cdc.gov.

Now for treatment. The first two slides in the section are the recommendations regarding treatment for lyme disease from the Infectious Diseases Society of America. I'm including these tables for your quick reference should you choose to save or print this presentation. The first table presents treatment recommendations by disease manifestation. The second table specifies the recommended antimicrobial regimens for treatment of patients with lyme disease. In general, lyme disease is very treatable with antibiotics. Recommended regimens range from two to four weeks orally or intravenously depending on the stage of illness. In patients with persistent or recurrent joint swelling, retreatment with a second four-week course may be needed. As mentioned, most patients treated will - with antibiotics will have a very successful recovery. And some patients particularly those diagnosed with later stages of disease, may have persistent symptoms. These can be divided into two categories. Objective symptoms, an example would be facial paralysis following damage to the seventh cranial nerve. Arthritis is another example. Of subjective symptoms, they may include fatigue, muscle aches or reduced concentration. It is these subjective symptoms that pose more challenges clinically and politically.

In recent years, there has been great debate surrounding the persistent, subjective symptoms. This can be witnessed in all types of media, particularly online and even in the movies and magazines. There are two terms that have been used to describe patients with persistent subjective symptoms after recommended treatment. That's post-lyme disease syndrome, post-treatment lyme-disease syndrome, maybe, and chronic lyme disease. Terms - the question is not whether these symptoms are real, but instead, what is the cause of these symptoms and are additional antibiotics the best treatment for these persistent symptoms. Placebo-controlled studies have - there have been several, and they've found no sustained benefit to prolonged antibiotic treatment. Therefore, antibiotic treatment is not recommended. In fact, there have been several instances where people have instead been harmed by prolonged therapy. This slide illustrates one example of a 30-year-old woman who received 27 months of IV ceftriaxone via catheter. Ultimately, she died from a related infection, embolization of a large candida septic thrombus from the tip of her catheter. Upon review of her medical record, there was no substantive clinical or laboratory evidence that she had had an ongoing lyme disease infection. When treatment does not resolve symptoms following potential exposure to ticks that carry lyme disease, it also important to consider the possibility of co-infections. This may be more likely for patients and more apparent for patients having severe initial symptoms. Other tick-borne diseases transmitted by the black-legged tick include: anaplasmosis, babesiosis, deer tick virus, lineage - that is (polosen lineage II), I believe, and the newly identified ehrlichia muris-like agent, which was recently reported on, I think in the New England Journal of Medicine.

How do we prevent this disease? Well, there is prophylaxis against lyme disease. If you are bitten by a tick, a single dose of doxycycline may be offered to patients greater than 8 years to prevent lyme disease, provided the attached tick can be reliably identified as an adult or nymphal Ixodes scapularis tick, estimated to have been attached for greater than 36 hours based on the degree of engorgement of the tick or with certainty about the time of exposure to the tick. In addition, prophylaxis can be started within 72 hours of tick removal time, and much of the decision should be based upon ecologic information indicating that the local rate of infection of these ticks with Borrelia burgdorferi is equal to or greater than 20%. Please note that antibiotic treatment after a tick bite is not recommended as a means to prevent anaplasmosis, babesiosis, ehrlichiosis or Rocky Mountain spotted fever. Reducing exposure to ticks is the best defense against lyme disease. There are several steps an individual can take to prevent lyme disease. First, avoid tick habitat. Walk in the center of trails, not off in the bushy areas. Second, they can be told to use insect repellant. Options with greater than 20% deet have some efficacy with repelling ticks. Permethrin-treated clothing is also effective. We ask that people perform tick checks daily. Lastly, bathing or showering as soon as possible after coming indoors, preferably within two hours to wash off and more easily find ticks crawling on you can be one method of prevention. You can also do a great deal in your yard to prevent exposure to ticks. That method include clearing tall grasses and brush, creating a tick-safe zone, a barrier at the wood-lawn interface and mow the lawn frequently, remove leaf litter, wood and trash debris areas where ticks would thrive and quest, and also you can apply pesticides outdoors. It can be noted a single application of tick pesticide has been known to significantly reduce the number of ticks in a yard.

It is on this last point that CDC has decided to join forces with several state health department partners through a program called TickNet to conduct more targeted research for prevention of ticks. Among other studies, we are conducting the Lyme and Other Tick-Borne Diseases Prevention Study, LTDPS. It is placebo-controlled trial to evaluate the efficacy of a (caroside), that is tick pesticide, used to not only control ticks, but to prevent disease. Year 1 of the study took place in 2011 with over 1500 enrolled participants in Connecticut, Maryland, and New York, our partner states through the Emerging Infections Program, and recruitment began just a few weeks ago for Year 2 of the study. For information on this effort or other TickNet efforts, please visit the Web site listed at the bottom of the page.

Lastly, but not least, resources for clinicians and health departments. Most notably, over the past few years CDC has taken care to make more resources available to clinicians to help with lyme disease, which can at times be a very frustrating and complicated disease for patients and providers. An example of available resources include: continuing medical education courses or CMEs like this, clarified diagnosis, treatment and testing info through CDC's Web site but also through venues like Medscape,

which went live with the new lyme disease diagnostics video just yesterday. We have up-to-date maps and statistics, frequently asked questions. Later this spring, we're going to have a”Physician's Guide to Tick-Borne Diseases” available for free on the Internet. It's really quite fantastic. We also have talking points on the Web site to help providers with - discuss with patients having ongoing symptoms, and of course, whenever you have a question of any kind, there is CDC-Info. This is an inquiry line that allows you to email or call CDC with your questions. We've also developed numerous fact sheets, public service announcements, et cetera to aid in communication to high-risk groups. Our efforts to educate and better communicate with front-line healthcare providers is among our highest program priorities in this and upcoming years.

So as I conclude this talk, I'd like to ask you to make recommendations to us on how we could better serve you. What resources for lyme disease would make a difference in your practice or your health department? How can we better distribute information to you or your colleagues? To help us with these efforts, though, we need your feedback. Thank you.I'll hand it over to Loretta.

Loretta Jackson Brown:

Thank you, Dr. Hinckley. We will now open up the lines for the question-and-answer session. And remember, you can submit questions through the Webinar by clicking on the Q&A tab and typing your question there.

Coordinator:

We'll now begin the question-and-answer session. If you'd like to ask a question, please press star 1. Please record your name. Your name is required to introduce your question. To withdraw a request, you press star 2. One moment while we wait for our first question.

Loretta Jackson Brown:

And while we're waiting for a question from the phone, Dr. Hinckley, I have a question through the Webinar system.

Dr. Alison Hinckley:

Okay.

Loretta Jackson Brown:

And the question is: Have there been studies on decreasing the length of antibiotic treatment for lyme disease?

Dr. Alison Hinckley:

I am unfamiliar with any studies that have to do with decreasing the amount of antibiotics for lyme disease. As I mentioned, most infections are successfully treated with two or three weeks of - between two and four weeks of antibiotics. I wouldn't personally know if that's effective at any level less, and I think I would be concerned about the potential for inadequate treatment at lower length of - lower durations of treatment. However, I'm not a clinician, so I will check into that and can post the question at a later time – the answer at a later time.

Loretta Jackson Brown:

Okay. (Laurie), do we have any questions on the phone?

Coordinator:

I have a question from Dr. (Castile). Go ahead. Your line's open.

Dr. (Castile):

Thank you. I was wondering why it takes so long for - after the tick is attached to transmit the organism?

Dr. Alison Hinckley:

there's - that's a great question. There are a number of things that happen within the tick in order to initiate transmission of the organism from the midgut through the salivary gland and into the skin. Those tick times - there are some protein shifts associated with making the organism pathogenic that occur inside the tick. One of these that is often discussed is the tick developing or being able to create OspC, which allows transmission of the organism into the skin, and that's noted in very early disease in human expression.

Dr. (Castile):

Okay. And how do you recommend removing a tick?

Dr. Alison Hinckley:

Oh, I'm glad you asked that. We have recommendations on the CDC Internet page for how to remove a tick. In general, it's as you would expect, take the - take forceps or tweezers, make sure to grab very closely next to the skin so that you can hope to get as much of the tick head as possible, and with a quick, sharp move directly pull the tick out. We don't endorse any anecdotal removal therapies. I know there are things such as painting nail polish on a tick or using a match to remove a tick, and those are both somewhat hazardous but also not known to be effective.

Dr. (Castile):

Okay. The one I've heard is using dishwashing detergent.

Dr. Alison Hinckley:

I have not heard dishwashing detergent, but I think given that a lot of people have tweezers somewhat nearby, I think it would be a good and safe alternative.

Dr. (Castile):

Okay, thank you.

Coordinator:

I have no questions at this time. Again, if you'd like to ask a question, press star 1 and record your name.

Loretta Jackson Brown:

Okay, we've gotten several questions through the Webinar system, and I thought it'd be a great idea if we kind of share them with the group. So Dr. Hinckley, you have a couple of questions related to prophylaxis.

Dr. Alison Hinckley:

Okay

Loretta Jackson Brown:

Some folks want to know are you giving doxy at 100 milligrams and also they want to know about prophylaxis for those 8 years and younger.

Dr. Alison Hinckley:

That's a good question. There is no recommendation for prophylaxis of children, as shown in the IDSA Guidelines. We recommend - you can see on the slide with the IDSA Guidelines, for the top line on the first slide of the IDSA Guidelines, is for tick bite in the United States. Can we scroll back to that?

Loretta Jackson-Brown:

I think...

Dr. Alison Hinckley:

We're going back. It indicates doxycycline 200 milligrams in a single dose, 4 milligrams per kilogram in children greater than 8 years of age. If you go back to treatment. One more. So the top line of this slide is the prophylaxis treatment. And again, I mean it's important to be very clear that you have Ixodes - an engorged Ixodes scapularis tick. Because there are still risks with taking even a single dose of doxycycline.

Loretta Jackson-Brown:

Okay great. Other questions are related to the vaccine, Lymerix, and they want to know why was it discontinued and will another vaccine be developed?

Dr. Alison Hinckley:

So Lymerix was discontinued, I think in 2002 due to poor marketability. There were also some political issues surrounding it. I know of no currently or near currently available vaccine in the United States. There are some efforts to develop vaccines for lyme disease in Europe. There are ongoing research studies to attempt another vaccine, although it is not a difficult vaccine to make or to market to a small area of the country. So marketability may continue to be an issue.

Loretta Jackson Brown:

Okay excellent. Other questions related to diagnostic testing. Is southern blot an acceptable diagnostic test with or without EIA or ISA?

Dr. Alison Hinckley:

Southern blot is not one of the recommended tests. We are recommending western blot be used in conjunction with EIA, preferably the two-tiered testing. ELISA being run first is ideal and necessary. Western blot is the recommended second tier for positive or equivocal ELISAs.

Loretta Jackson Brown:

Okay excellent. Operator, do we have any questions from the phone?

Coordinator:

I do have some questions. Just as a reminder, if you have your mute feature pressed, you might want to deactivate it so we can get your name. I need your name to introduce your question. Our next question comes from Dr. (Dale Schwab). Go ahead.

Dr. (Dale Schwab):

Hi, thank you. I might have missed this, but I was wondering for patients that are infected in Europe, do you expect to see the similar western blot pattern for positives? I've heard back-and-forth on that.

Dr. Alison Hinckley:

I'm not clear on the - I'm sorry. I'm not clear on the western blot or the use...

Dr. (Dale Schwab):

of a patient that's infected with a tick - a different species in Europe than the one found...

Dr. Alison Hinckley:

Uh huh. I think the recommendation for the first tier test for that would be important. C6 would be one that would valuably identify other strains outside the U.S. If that's positive, is that what I should assume based upon.

Dr. (Dale Schwab):

Right, right, then would you gone on to the reflex testing?

Dr. Alison Hinckley:

For western...

Dr. (Dale Schwab):

(Unintelligible).

Dr. Alison Hinckley:

blot?

Dr. (Dale Schwab):

Right.

Dr. Alison Hinckley:

I will have to verify that. I know some of the proteins are specific to the U.S. strain. So if you could email that question, I would be happy to get the answer back to you.

Dr. (Dale Schwab):

Okay, I'll be happy to do that.

Dr. Alison Hinckley:

Thank you.

Dr. (Dale Schwab):

Thank you.

Loretta Jackson-Brown:

Right, if you would, email the question to COCA at coca@cdc.gov, and we are - we have a number of questions that I - I'm sure we're not going to have time to get each one of them. And so, what we'll be able to do is we will include the - a Q&A session from this presentation in the transcript, and we will have that posted to our COCA Web site in the next few days. But we're welcome to continue questions until we reach the top of the hour. So, operator, do you have any more questions?

Coordinator:

I have two at this time. Our next question comes from (Marie Larson). Your line's open.

(Marie Larson):

Yes, my question is: What about those patients who were diagnosed in 1990, early 1990s on the West Coast? What type of long-term residuals or percentage of residuals would you expect? And one, for example, had very positive signs but incomplete IV treatment due the penicillin allergy.

Dr. Alison Hinckley:

So patients on the West Coast are - we recommend the patients be treated in the same manner that patients on the East Coast are. It's the same organism, although the tick that transmits it is somewhat different. On the West Coast, you might also need to be aware of the possibility for cross-reactivity with something - with Borrelia hermsii, which is tick-borne relapsing fever, if that's a possibility in the area. If there is no resolution with a typical course of antibiotic treatments, and you are - and you feel secure in the diagnosis of lyme disease, there's a couple of avenues for patients, and I would recommend not long-term antibiotic therapy as one of those avenues. But instead, since we can feel fairly confident that the organism is going to be treated effectively, some of the damage that ensues following the infection and if the infection was not identified quickly enough, you know, there could be some long-term damage that would need other types of therapy like occupational therapy or certainly some sort of support for ongoing symptoms that a person is going - psychiatric support would be one that we might recommend for a person who is experiencing long-term symptoms or reduction of capabilities.

(Marie Larson):

Thank you.

Coordinator:

Just as a reminder, if you'd like to ask a question, please press star 1 and record your name. Our last question at this time comes from (Jake Pry). Your line's open.

(Jake Pry):

Yes, I just had a question. You had mentioned that deer is resistant to the disease. Is any research being done on why they're not infected by the same we are?

Dr. Alison Hinckley:

I'm not aware of any research being done on why deer might be resistant. However, there's a great many studies being done on the role that deer play in increasing tick populations in the East Coast and the Midwest. I think there's still some differing opinions on whether reduction - large reductions in deer will make a big impact in the overall tick numbers, and therefore, affect lyme disease. So that's an area I'm familiar with. I'm not familiar with deer bactericidal properties.

(Jake Pry):

Thank you.

Coordinator:

I have no further questions at this time.

Loretta Jackson Brown:

Hey, Dr. Hinckley. We have, again, a great number of questions on the Webinar, and I'm going to summarize as best I can. This question has to do with specificity related to laboratory tests. With patients who repeatedly test negative for lyme, so due to the similarity between lyme and STAR-I, if a patient repeatedly has a negative result with the lyme test, should a provider consider STAR-I, especially if the patient is from or has visited the southeast region, and what are the lab tests for STAR-I?

Dr. Alison Hinckley:

That is a good question. There are a couple of things to note, I think, with this question. If a person develops a characteristic EM rash and is treated very promptly, there's a good possibility that they will not go on to develop the antibodies that you would pick up in a test either within t2 weeks or within, you know, 12 weeks of disease. They're not going to develop the antibodies. So it'll aggregate the response. If the person has a history of tick bites that we think are potentially responsible for the disease. I assume it's an EM, because you're talking about STARI. There's a good potential that STARI could be the diagnosis if they were in an area with amblyomma ticks within 3 to 30 days of onset of the disease. Although, as I mentioned for STAR-I, it's a little bit sooner. Currently there are no antibiotics recommended for STARI, because we are not aware of the cause of STARI. We don't know if there's etiologic agent responsible. I can tell you, anecdotally physicians often choose to treat STAR-I as if it's lyme disease, but the CDC has no recommendations regarding treatment for that disease.

Loretta Jackson Brown:

Thank you. Also there's several questions for clarification on tick removal. In particular, - someone states that they live in Wisconsin, and that their practice is to not use tweezers, because you run the risk of not getting the head out. And also if you do - if the head does stay in the skin after removal, should it be removed or can it be left in for it to maybe come out later?

Dr. Alison Hinckley:

This was a good question. I believe - I think that's a really common question. The head is often left whenever the tweezers are used. However, I understand that once the majority of the tick is removed, transmission is not likely to occur. The midgut is removed where the actual organism is. It would be best if you could go ahead and remove the tick and the mouthparts later after you remove the full tick, but again, I think a better description of this is not in the words that I'm saying, but on the Web site. And there's a good figure that helps navigate through tick removal.

Loretta Jackson Brown:

Excellent. Thank you.

Dr. Alison Hinckley:

Yes. I'm sorry I'm not a better wordsmith.

Loretta Jackson Brown:

That's okay. And we have these additional resources on our COCA Web page, and that link is provided on our slide set. But in general if you go to emergency.cdc.gov/coca. You click on COCA Calls, the call information is available on our call page. The recording of this call will be archived and available to you in a few days. The PowerPoints are currently up on the page as

well as additional resources related to lyme disease.

Okay, we still have a few minutes for questions, and I'll share this one with you. They would like you to discuss the difference between arthralgia and arthritis with respect to lyme disease.

Dr. Alison Hinckley:

Oh, there it is. You know, I'm not a clinician. I think somebody would do a better job, but I can tell you that arthritis for lyme disease is generally intermittent. Like I said, it's generally in a single joint or another - I could have - actually a clinician speak to you on that real quick, if you were ready to do it.

(Christina Nelson):

Hi, this is (Christina Nelson). I'm a Medical Officer, and I work with Dr. Hinckley. Basically it's semantics. So arthralgia means there's pain. Arthritis, the ending -itis means there is evidence of inflammation, so there's going to be redness, swelling, and it could have pain along with it. Does that answer your question?

Loretta Jackson Brown:

Thank you. It came through the Webinar system, so we don't get feedback on that one.

(Christina Nelson):

Okay.

Loretta Jackson Brown:

Excellent.

(Christina Nelson):

We'll get a clarification if they have further questions.

Loretta Jackson Brown:

Yes, right. Okay. (Laurie), do we have any more questions on the phone?

Coordinator:

I have no further questions.

Loretta Jackson Brown:

Okay. Well, thank you. Again, we have a number of questions through our Webinar system. We will include them in our transcript. We'll do a Q&A. We will send those to Dr. Hinckley and her staff, and they'll be able to provide a reply to you. So please check the COCA Web site in a few days.

And so with that, on behalf of COCA, I would like to thank everyone for joining us today with a special thank you to our presenter, Dr. Hinckley. If you have additional questions for today's presenter, please email us at coca@cdc.gov. Put "Dr. Hinckley" in the subject line of your email, and we will ensure that your question is forwarded to her for a response. Again, the email address is coca@cdc.gov.

The recording of this call and the transcript will be posted to the COCA Web site at emergency.cdc.gov/coca within the next few days. Free continuing education credits are available for today's call. Those who participated in today's COCA conference call and would like to receive continuing education credits should complete the online evaluation by April 5th, 2012 using Course Code EC1648. For those who will complete the online evaluation between April 6th, 2012 and March 5th, 2013, use course code WB1648. All continuing education credits for COCA calls are awarded through CDC's Continuing Education Center online system at www.2a.cdc.gov/tceonline .

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Thank you again for being a part of today's COCA Webinar. Have a great day.

Coordinator:

This concludes today's conference. We thank you for your participation. You may disconnect your lines at this time. Have a great day. One moment.

END