Lyme Disease Investigation Guideline

Contents

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Revision History:

Date	Replaced	Comments
05/2018	01/2016	Updated case definition and updated Notification Section with requirements of new reporting regulations.
01/2016	09/2011	Updated Laboratory Analysis Section and Epidemiology More details added to Investigators Responsibilities and Data Management. Reformatted Standard Case Investigation section to assist with EpiTrax system data entry. Added information on PTLDS and when to close a case. Updated Notification, Investigator Responsibilities, and Data Management sections with disease surveillance indicator targets.
09/2011	04/2009	Minor formatting of investigation guideline. BEPHI replaced BSE throughout. Updated to 2011 CDC case definition.
02/2012	-	Removed references to KS-EDSS

Lyme Disease
Disease Management and Investigation Guidelines

CASE DEFINITION (CDC 2017)

Clinical Description for Public Health Surveillance:

A systemic, tick-borne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities. The most common clinical marker for the disease is erythema migrans (EM), the initial skin lesion that occurs in 60%-80% of patients.

For purposes of surveillance:

- EM is defined as a skin lesion that typically begins as a red macule or papule and expands over a period of days to weeks to form a large round lesion, often with partial central clearing. A single primary lesion must reach greater than or equal to 5 cm in size across its largest diameter. Secondary lesions also may occur. Annular erythematous lesions occurring within several hours of a tick bite represent hypersensitivity reactions and do not qualify as EM. For most patients, the expanding EM lesion is accompanied by other acute symptoms, particularly fatigue, fever, headache, mildly stiff neck, arthralgia, or myalgia. These symptoms are typically intermittent. The diagnosis of EM must be made by a physician. Laboratory confirmation is recommended for persons with no known exposure.

For purposes of surveillance, late manifestations include any of the following when an alternate explanation is not found:

- *Musculoskeletal system.* Recurrent, brief attacks (weeks or months) of objective joint swelling in one or a few joints, sometimes followed by chronic arthritis in one or a few joints. Manifestations not considered as criteria for diagnosis include chronic progressive arthritis not preceded by brief attacks and chronic symmetrical polyarthritis. Additionally, arthralgia, myalgia, or fibromyalgia syndromes alone are not criteria for musculoskeletal involvement.

- *Nervous system.* Any of the following, alone or in combination: lymphocytic meningitis; cranial neuritis, particularly facial palsy (may be bilateral); radiculoneuropathy; or, rarely, encephalomyelitis. Encephalomyelitis must be confirmed by demonstration of antibody production against *Borrelia burgdorferi* in the cerebrospinal fluid (CSF), evidenced by a higher titer of antibody in CSF than in serum. Headache, fatigue, paresthesia, or mildly stiff neck alone, are not criteria for neurologic involvement.

- *Cardiovascular system.* Acute onset of high-grade (2nd-degree or 3rd-degree) atrioventricular conduction defects that resolve in days to weeks and are sometimes associated with myocarditis. Palpitations, bradycardia, bundle branch block, or myocarditis alone are not criteria for cardiovascular involvement.

Laboratory Criteria for Case Classification:
For the purposes of surveillance, the definition of a qualified laboratory assay is:

- Positive Culture for *B. burgdorferi*, or
- Positive two-tier test. (This is defined as a positive or equivocal enzyme immunoassay (EIA) or immunofluorescent assay (IFA) followed by a positive Immunoglobulin M[1] (IgM) or Immunoglobulin G [2] (IgG) western immunoblot (WB) for Lyme disease)
- Positive single-tier IgG[2] WB test for Lyme disease[3].

[1] IgM WB is considered positive when at least two of the following three bands are present: 24 kilodalton (kDa) outer surface protein C (OspC)*, 39 kDa basic membrane protein A (BmpA), and 41 kDa (Fla). Disregard IgM results for specimens collected >30 days after symptom onset.

[2] IgG WB is considered positive when at least five of the following 10 bands are present: 18 kDa, 24 kDa (OspC)*, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa flagellin (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa.

[3] While a single IgG WB is adequate for surveillance purposes, a two-tier test is still recommended for patient diagnosis.

* Depending upon the assay, OspC could be indicated by a band of 21, 22, 23, 24 or 25 kDA

Exposure:
Exposure is defined as having been (less than or equal to 30 days before onset of EM) in wooded, brushy, or grassy areas (i.e., potential tick habitats) of Lyme disease vectors. A history of tick bite is not required.

A detailed travel history to verify whether exposure occurred in a high or low incidence state is needed. An exposure in a high-incidence state is defined as exposure in a state with an average Lyme disease incidence of at least 10 confirmed cases/ 100,000 for the previous three reporting years. A low-incidence state is defined as a state with a disease incidence of <10 confirmed cases/100,000 (*see* www.cdc.gov/lyme/stats/tables.html).

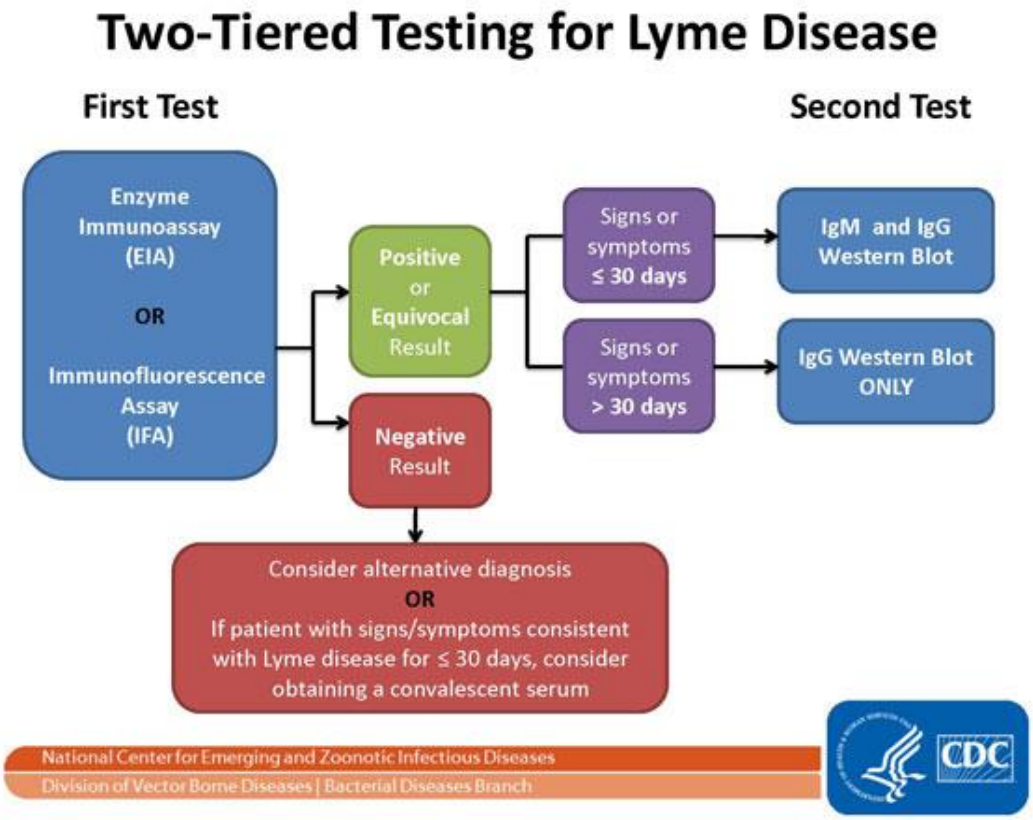
Case Classification:

- **Suspected:** a) a case of EM where there is no known exposure (as defined above) and no laboratory evidence of infection (as defined above), or b) a case with laboratory evidence of infection but no clinical information available (e.g. a laboratory report)
- **Probable**: Any other case of physician-diagnosed Lyme disease that has laboratory evidence of infection (as defined above).
- **Confirmed:** a) a case of EM with exposure in a high incidence state (as defined above), or b) a case of EM with laboratory evidence of infection and a known exposure in a low incidence state, or c) a case with at least one late manifestation that has laboratory evidence of infection.

Comment: Lyme disease reports will not be considered cases if the medical provider specifically states this is not a case of Lyme disease, or the only symptom listed is "tick bite" or "insect bite."

LABORATORY ANALYSIS:

- The State Public Health Laboratory sends all specimens to the CDC. *Warning:* Prior consultation required from the KDHE Epidemiology Program at 1-877-427-7317. CDC does not offer routine testing.
- Laboratory blood tests are helpful if used correctly.
- CDC currently recommends a two-step process when testing blood for evidence of antibodies against the Lyme disease bacteria.



Points to remember:

1. The immunoblot should not be run without first performing an EIA or IFA.
    - *If only immunoblot results are reported the investigator should contact the medical provider requesting any EIA or IFA results*.
2. The immunoblot should not be run if the EIA or IFA tests are negative.
3. A positive IgM immunoblot is only useful during the first 4 weeks of illness.
4. If you've been ill for longer than 4-6 weeks and the IgG immunoblot test is negative, it is unlikely that you have Lyme disease, even if the IgM is positive.

CDC recommends:

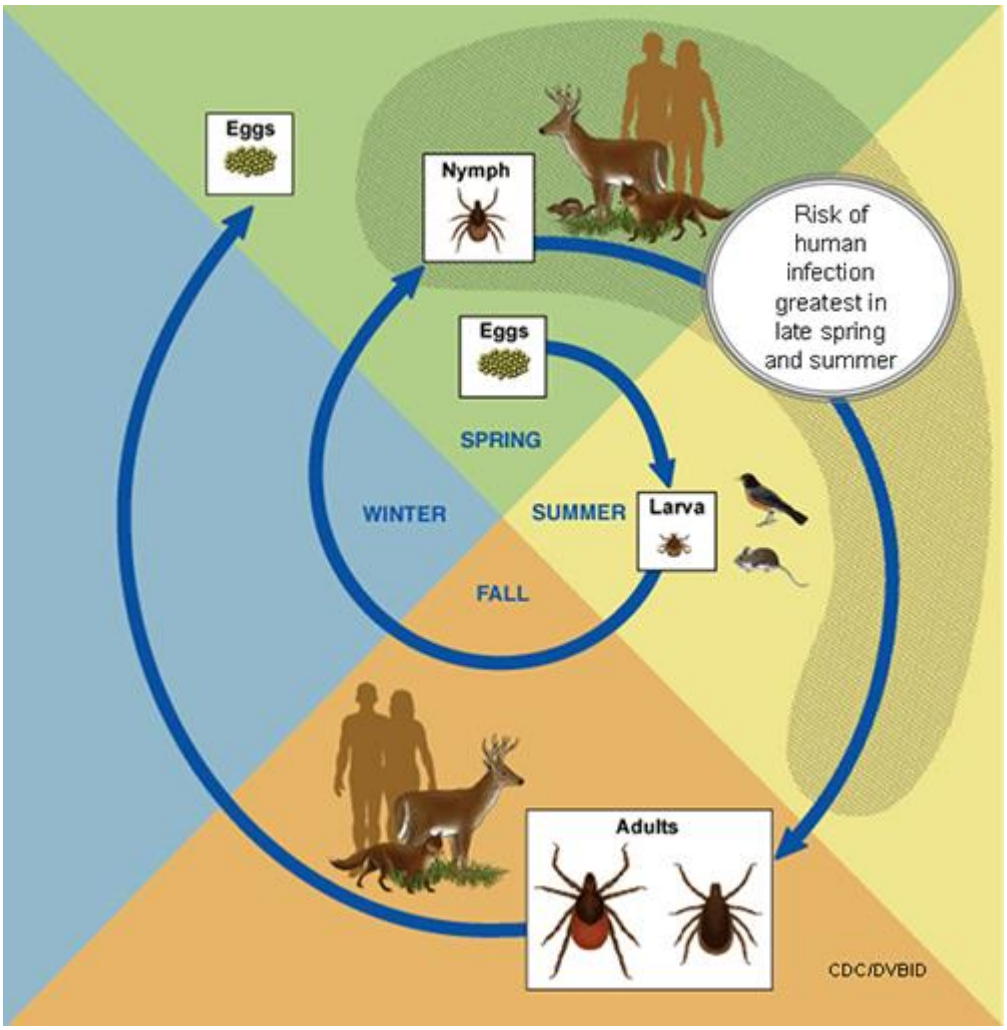
- IgM immunoblot be considered positive if two of the following three bands are present: 24 kDa (OspC) *, 39 kDa (BmpA), and 41 kDa (Fla).
- IgG immunoblot be considered positive if five of the following 10 bands are present: 18 kDa, 21 kDa (OspC) *, 28 kDa, 30 kDa, 39 kDa (BmpA), 41 kDa (Fla), 45 kDa, 58 kDa (not GroEL), 66 kDa, and 93 kDa.

* The molecular mass of OspC is dependent on the strain of *B. burgdorferi* being tested. The 24 kDa and 21 kDa proteins referred to are the same.

EPIDEMIOLOGY

The incidence of Lyme disease is associated with the density of infected tick vectors. While most cases in the United States have been reported in the Northeast, western states, and upper Midwest, nearly all states have reported cases. The incidence varies among states and counties and by season. Most cases occur between April and October with a peak in June and July, when the risk of contact with ticks is greatest.

The lifecycle of blacklegged ticks (*Ixodes scapularis* and *Ixodes pacificus*):



DISEASE OVERVIEW

A. Agent:
Lyme disease is caused by the corkscrew-shaped spirochete *Borrelia burgdorferi*.

B. Clinical Description:
While the chronology of signs and symptoms may vary significantly, there are three general stages in the clinical manifestation of Lyme disease: early localized, early disseminated, and late.

- *Early Localized*: Symptoms tend to be nonspecific and may include: fever, muscle aches, headache, mild neck stiffness, and joint pain. Erythema migrans (EM) occurs at the site of the tick bite in approximately 90% of cases. Typically, EM rashes are circular and grow to a diameter of 5-15 cm, although the shape can be triangular, oval, or irregular. EM frequently clears in the center, resulting in the classic "bull's-eye" presentation.
- *Early Disseminated*: In untreated persons, multiple EM rashes may appear within 3-5 weeks after the tick bite. These secondary lesions, indicative that the infection has spread into the blood, resemble the primary lesion but tend to be smaller. Common signs include: mild eye infections and paralysis of facial muscles (Bell's palsy). Additional symptoms may include: headache, fatigue, and muscle and joint pain. Disruptions of heart rhythm occur in <10% of cases.
- *Late*: Late disease is marked by recurrent arthritis in the knees and shoulders; other joints may also be involved. Neurological signs may include: impairment of mood, sleep disorders, memory difficulties, paralysis of facial muscles, pain or tingling sensations in the extremities and less commonly, meningitis and encephalitis. Late-stage symptoms can persist for several years and tend to resolve spontaneously.

C. Reservoirs:

- Certain ixodid ticks that can transmit transstadially (remain infected from one life stage cycle to the next).
- Wild rodents (i.e., including mice, pack rats squirrels, shrews, and other small vertebrates) help maintain an enzootic transmission cycle.
- Deer serve as important mammalian maintenance host for vector tick species.

D. Mode(s) of Transmission:

Tick-borne; in experimental animals, transmission by *I. scapularis* and *I. pacificus* does not occur until the tick has been attached for 24 hours or more; this may also be true in humans.

E. Incubation Period:

For EM, 3 to 32 days after tick exposure (mean 7 to 10 days); early stages may be inapparent and the patient may present only with late manifestations.

F. Period of Communicability:

Not communicable person-to-person.

G. Susceptibility and Resistance:

All persons are susceptible. Reinfection has occurred after treatment.

H. Treatment:

Amoxicillin is recommended for adults or children in early stages of disease. Doxycycline in adults and phenoxymethyl penicillin for children with early disease resolves illness and reduces the likelihood of later complications. Intravenous penicillin or ceftriaxone is effective for meningitis and late stage illness.

NOTIFICATION TO PUBLIC HEALTH AUTHORITIES

Suspected cases of Lyme disease shall be reported within 24 hours, except if the reporting period ends on a weekend or state-approved holiday, the report shall be made by 5:00 p.m. on the next business day after the 24-hour period:

1. Health care providers and hospitals: report to local public health.
2. Local public health jurisdiction: report to KDHE-BEPHI (see below).
3. Laboratories: report to KDHE-BEPHI (see below).

Kansas Department of Health and Environment (KDHE)
Bureau of Epidemiology and Public Health Informatics (BEPHI)
Phone: 1-877-427-7317
Fax: 1-877-427-7318.

Further responsibilities of state and local health departments to the CDC:

As a nationally notifiable condition, confirmed, probable, and suspect Lyme cases require ROUTINE report to the Center of Disease Control and Prevention (CDC).

1. ROUTINE reporting requires KDHE-BEPHI to file an electronic report for within the next reporting cycle.
2. **Local public health jurisdiction** will report information requested as soon as possible, ensuring that the electronic form is completed within 14 days of receiving a notification of a Lyme report.

INVESTIGATOR RESPONSIBILITIES

1) Report all cases to the KDHE-BEPHI.
   - Initiate the case investigation within 3 days of notification of a report.
   - Complete the investigation within 14 days of the notification.
2) Contact medical provider to collect additional information and confirm diagnosis using current case definition.
   - Collect all information requested in Step 1 of case investigation.
   - Ensure that case/proxy is aware of the diagnosis.
3) Conduct a case investigation to determine the individual's at-risk activities and potential geographical location of exposure.
4) Record data, collected during the investigation, in the KS EpiTrax system under the data's associated [tab] in the case morbidity report (CMR).
5) As appropriate, use the disease fact sheet to notify the case, contacts and other individuals or groups.

STANDARD CASE INVESTIGATION AND CONTROL METHODS

Case Investigation

1) Contact the medical provider who ordered testing of the case and obtain the following information; including medical records for hospitalized patients.
   - Did the physician diagnosis Lyme disease? [Investigation – Symptoms]
     - If the physician, specifically states it is not a case of Lyme disease – the investigator should document this and close the case.

- Was erythema migrans (EM) diagnosed by a physician? [Investigation – Symptoms]
  - EM is a skin lesion that begins as a red macule/papule and expands over a period of days or weeks to form a large round lesion (often with partial central clearing). The size must reach at least 5 cm.
  - If there was EM diagnosed, invest time and effort to identify the most likely location of exposure (Step 2). [Investigation – Exposure]
- Obtain information on any laboratory tests performed.
  - Results of EIA/IFA testing, IgM and IgG or Total (1st tier).
  - Results of Western Blot, IgM and IgG (2nd tier).
  - Results of culture, if done.
- Record onset date of first symptoms associated to this episode [Clinical]
  - Non-confirmatory symptoms, including arthralgias, bundle branch block, cognitive impairment, encephalopathy, fatigue, fever/sweat/chills, headaches, myalgias, myocarditis, neck pain, rash other than EM, palpitations, paresthesias, peripheral neuropathy, visual/auditory impairment. [Investigation – Symptoms]
  - Confirmatory symptoms: Arthritis (characterized by brief attacks of joint swelling), Bell's Palsy or other cranial neuritis, radiculoneuropathy, lymphocytic meningitis, encephalomyelitis, 2nd/3rd degree atrioventricular block. [Investigation – Complications]
- Collect patient's demographics (address, birth date, gender, race/ethnicity, primary language, and phone number(s)). [Demographic]
- Record treatment: type of antibiotic and number of days prescribed.
- Record hospitalizations: location and duration of stay. [Clinical]
- Record outcomes: survived or date of death. [Clinical]
- Record pregnancy status for women. [Clinical]

2) Establish if illness is compatible to Lyme based on labs and symptoms.
   - A case of EM diagnosed by a medical provider who does not specifically state it is not a case of Lyme should always be investigated.
   - If any of the following situations are present without EM the investigation can be closed as 'Not a Case':
     - The medical provider states it is not a case of Lyme disease.
     - A positive IgM result was collected >30 days from the onset of illness when the IgG result is negative or unknown.
     - A serology specimen that was positive for IgM by immunoblot that did not first have an EIA/IFA performed that was 'equivocal' or 'positive' for IgM or total antibody.
3) If a continued investigation is needed and the patient charts do not provide information on the following risk factors or travel, interview the case to determine risk factors and transmission. [Investigation – Exposure]
   - Thirty days prior to patient's illness onset, was there any exposure to wooded or brushy areas or exposure to animals that may have been in a wooded/brushy area.
   - Where were the wooded or brushy areas located that were associated to direct or indirect exposure during the 30 days prior to illness onset.
     - Travel to other Kansas counties? (If yes, City/County and dates)

  - Was there travel outside of Kansas?
    - Travel in the U.S.? (If yes, City/State and dates)
    - Travel internationally? (If yes, City/Country and dates)
- Record patient's occupation [Epidemiologic]

4) Examining the epidemiological information, record where the infection was most likely imported from. (Indigenous or out-of-county, state, or U.S.) [Epidemiologic]; also record the county, state, and country that was the most likely exposure [Investigation – Exposure].

Contact Investigation

Not usually required, these diseases cannot be transmitted from person-to-person, but an individual living in the same household, travel companions, co-workers, and anyone else who might be exposed to infected ticks is potentially at risk.

Isolation, Work and Daycare Restrictions

None.

Case Management

Not required, but some patients may report "Chronic Lyme disease". Please read the talking points below on "Chronic Lyme" or Post-treatment Lyme disease.

1) It is not uncommon for patients treated for Lyme disease with a recommended 2 to 4 week course of antibiotics to have lingering symptoms of fatigue, pain, or joint and muscle aches at the time they finish treatment.
2) In a small percentage of cases, these symptoms can last for more than 6 months. Although sometimes called "chronic Lyme disease," this condition is properly known as "Post-treatment Lyme Disease Syndrome" (PTLDS).
3) The cause of PTLDS is not known, but additional antibiotic treatment may not be the best course of action.
   - Studies have not shown that patients who received prolonged courses of antibiotics do better in the long run than patients treated with placebo.
   - Long-term antibiotic treatment for Lyme disease has been associated with serious complications.
   - Patients with PTLDS almost always get better with time; but it can take months to feel completely well.

For a patient who feels they are suffering from PTLDS, instruct them:

1) Check with your doctor to make sure that Lyme disease is not the only thing affecting your health.
2) Become well-informed. A lot of inaccurate information is available, especially on the internet. Learn how to sort through this maze.
3) Track your symptoms. It can be helpful to keep a diary of your symptoms, sleep patterns, diet, and exercise to see the influence on your well-being.
4) Maintain a healthy diet and get plenty of rest.
5) Share your feelings. If your family and friends can't provide the support you need, talk with a counselor who can help you find ways of managing your life during this difficult time.

Additional resources are at: www.cdc.gov/lyme/postlds/index.html

Contact Management

1) Preventive treatment is generally not recommended after a recognized tick bite. However, in areas that are highly endemic for Lyme disease, a single dose of doxycycline may be offered to adult patient who are not pregnant and to children older than 8 years of age when ALL of the following circumstances are met:
   - Doxycycline is not contraindicated.
   - The attached tick can be identified as an adult or nymphal *I. scapularis*.
   - Estimated time of attachment is ≥36 hours based on the degree of tick engorgement or likely time of exposure.
   - Prophylaxis can be started within 72 hours of tick removal.
   - Lyme disease is common in the county or state where the patient lives or has recently traveled.
2) Instruct those exposed to a tick to monitor themselves for symptoms. Treatment is necessary only if symptoms develop.
3) Those who exhibit any signs or symptoms compatible with tick-borne illness should be referred to their medical provider for evaluation.

Environmental Measures

Veterinary tick control in domestic animals:

1) Domestic animals may become infected with Lyme disease bacteria and some (dogs, for instance) may develop arthritis.
2) Domestic animals can carry infected ticks into areas where people live.
3) Veterinary tick control products may help to reduce tick presence on pets.

Community-based integrated tick management strategies:

1) May reduce the incidence of tick-borne infections, but limiting exposure to ticks is the most effective method of prevention
2) Strategies to reduce vector tick densities through area-wide application of an acaricide (i.e., chemicals that kill ticks and mites) and control of tick habitats (e.g., leaf litter and brush) have been effective in small-scale trials.
3) New methods under development include applying acaricide to rodents and deer by using baited tubes, boxes and deer feeding stations in areas where these pathogens are endemic.
4) Biological control with fungi, parasitic nematodes, and parasitic wasps may play important roles in integrated tick control efforts.

Additional measures that can assist with determining risk include:

- Entomologic surveys: Inventory and mapping of tick populations sometimes with limited testing for Borrelia burgdorferi. This can occur as part of special studies and through monitoring at deer.
- Reports of increased Lyme morbidity in animals in the area.
- Tick identification: Contact your local K-state extension office or the Insect Diagnostician with the K-State Department of Entomology.

Education

As opportunities allow, the following general messages should be distributed:

1) In tick-infested areas, the highest risk of bites is occurs from March-July.
2) The use of protective clothing, including light-colored garments, long pants tucked into socks, long-sleeved shirts, hats, as well as tick repellents, may reduce risk.
3) Outdoor activities in tick-infested areas present opportunities for exposure.
4) Keep yards clear of excessive leaves, brush, and tall grasses. Walk in the center of trails to avoid contact with tall grasses and brush.
5) When camping, sleep in screened tents.
6) Hunters should be aware of tick infestations on mammals, especially deer, and check for tick attachments after handling carcasses.
7) Keep pets free of ticks.
8) Transmission requires a long attachment. Check for ticks at regular intervals while outdoors and after spending time outdoors in tick infested areas.
9) Remove attached ticks intact, do not leave embedded head parts. Use gentle, direct traction with tweezers or hemostat. Other methods, such as application of a hot match or petroleum products to the tick, are less reliable. Do not crush ticks as this may result in direct inoculation of spirochetes.

Additional education materials are available at:

- www.cdc.gov/lyme/toolkit/index.html
- www.cdc.gov/ticks/index.html

MANAGING SPECIAL SITUATIONS

A. Outbreak Investigation:

- There are no formal outbreak definitions; however, the investigator may consider the possibility of an outbreak when there is an unusual clustering of cases in time and/or space.
- Notify KDHE immediately, 1-877-427-7317.
  - Active case finding will be an important part of any investigation.

DATA MANAGEMENT AND REPORTING TO THE KDHE

A. Accept the case assigned to the LHD and record the date the LHD investigation was started on the [Administrative] tab.

B. Organize and collect data, using appropriate data collection tools including:
- The Lyme Disease Form can be used to collect information.
- Alternatively, investigators can collect and enter all required information directly into EpiTrax [Investigation], [Clinical], [Demographics], [Epidemiological] tabs.
- During outbreak investigations, refer to guidance from a KDHE epidemiologist for appropriate collection tools.

C. Report data collected during the course of the investigation via EpiTrax**.**
- Verify that all data requested on the Lyme Disease Form has been recorded on an appropriate EpiTrax [tab], or that actions are completed for a case lost to follow-up as outlined below.
- Some data that cannot be reported on an EpiTrax [tab] may need to be recorded in [Notes] or scanned and attached to the record.
- Paper report forms do not need to be sent to KDHE after the information is recorded and/or attached in EpiTrax. The forms should be handled as directed by local administrative practices.

D. If a case is lost to follow-up, after the appropriate attempts to contact the case have been made:
- Indicate 'lost to follow-up' on the [Investigation] tab with the number of attempts to contact the case recorded.
- Record at least the information that was collected from the initial reporter.
- Record a reason for 'lost to follow-up' in [Notes].

E. Once the investigation is completed, the LHD investigator will record the date the investigation was completed on the [Administrative] tab and click the "Complete" button. This will trigger an alert to the LHD Administrator so they can review the case before sending to the state.
- The LHD Administrator will then "Approve" or "Reject" the CMR.
- Once a case is "Approved" by the LHD Administrator, BEPHI staff will review and close the case after ensuring it is complete and that the case is assigned to the correct event, based on the reported symptoms reported.

  (Review the EpiTrax User Guide, Case Routing for further guidance.)

ADDITIONAL INFORMATION / REFERENCES

A. Treatment / Differential Diagnosis: Red Book: 2015 Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2015.

B. Epidemiology, Investigation and Control: Heymann. D., ed., Control of Communicable Diseases Manual (CCDM), 20th Edition. Washington, DC, American Public Health Association, 2015.

C. Case Definitions: CDC Division of Public Health Surveillance and Informatics, Available at: wwwn.cdc.gov/nndss/

D. Kansas Regulations/Statutes Related to Infectious Disease: www.kdheks.gov/epi/regulations.htm

E. CDC References on Established Criteria for Interpreting Testing:

- Centers for Disease Control and Prevention. Recommendations for test performance and interpretation from the Second National Conference on Serologic Diagnosis of Lyme Disease. MMWR MMWR Morb Mortal Wkly Rep 1995; 44:590–1. Accessed at: www.cdc.gov/mmwr/preview/mmwrhtml/00038469.htm
- Dressler F, Whalen JA, Reinhardt BN, Steere AC. Western blotting in the serodiagnosis of Lyme disease. J Infect Dis 1993; 167:392–400.
- Engstrom SM, Shoop E, Johnson RC. Immunoblot interpretation criteria for serodiagnosis of early Lyme disease. J Clin Microbiol 1995; 33:419–27.
- Centers for Disease Control and Prevention. Notice to readers: caution regarding testing for Lyme disease. MMWR Morb Mortal Wkly Rep 2005; 54:125–6. Accessed at: www.cdc.gov/mmwr/preview/mmwrhtml/mm5405a6.htm

F. Surveillance for Lyme Disease --- United States, 1992—2006 (CDC,2008): www.cdc.gov/mmwr/preview/mmwrhtml/ss5710a1.htm

G. Tickborne Diseases of the United States: A Reference Manual for Health Care Providers: www.cdc.gov/lyme/resources/TickborneDiseases.pdf

H. Additional Information (CDC): www.cdc.gov/health/default.htm