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## Lyme/Lyme-like Disease

### **Overview** <sup>(3 - 5)</sup>

Lyme disease is the most common tick-borne disease in the United States. It was first seen in the mid-1970s in a cluster of children with arthritis in Lyme, Connecticut. In 1981, a tick-borne bacterium called *Borrelia burgdorferi* (*B. burgdorferi*) was found to be the cause of Lyme disease. Lyme bacteria are passed on to humans through the bite of infected blacklegged ticks.


The incubation period for Lyme disease is 3 to 30 days. In about 80% of Lyme disease patients, early symptoms include a “bull’s eye” skin rash, typically appearing at the site of a tick bite. This characteristic rash is also called “erythema migrans” (EM). Some patients with EM also have flu-like symptoms, which may include headache, fever, and fatigue. Patients treated with antibiotics in early *B. burgdorferi* infection usually recover rapidly and completely. If Lyme disease is not treated, infection can spread to joints, the heart, and the nervous system.

Most North American cases of Lyme disease occur in the northeastern, mid-Atlantic, and north-central U.S. Lyme bacteria have never been isolated from any of Missouri’s EM cases. Nevertheless, “bull’s eye” rashes similar to those caused by *B. burgdorferi* are diagnosed in Missouri and other south-central U.S. states. In contrast with true Lyme disease, “Lyme-like” rashes are not linked to any arthritic, neurological, or other long-term symptoms.

Some medical and scientific researchers call Missouri’s “Lyme-like” rashes the Southern Tick Associated Rash Illness or STARI. The condition also has been called Master’s disease, named after a southeast Missouri physician who first described the clinical presentation. Reports of EM from patients in Missouri and other south-central U.S. states have been associated with the bite of a lone star tick. Currently, “Lyme-like” rashes in Missouri have not been linked to any known pathogen.

Preventing Lyme or Lyme-like infection and other tick-borne diseases involves avoidance of tick-infested areas, wearing protective clothing, and application of insect repellents. Also critical to disease prevention is the prompt removal of ticks from the body – it usually takes several hours of tick attachment and feeding before tick-borne bacteria can be passed on to the host.

**Note:** Missouri patients who fulfill the Centers for Disease Control and Prevention (CDC) surveillance definition for Lyme disease are reported as such, although *Borrelia burgdorferi* has not yet been isolated from any of Missouri’s cases. The Missouri erythema migrans rashes are indistinguishable from those in other areas of the United States, but are referred to as erythema migrans-like by the CDC. The acute clinical syndrome appears similar to Lyme disease. **For the purposes of disease reporting in Missouri, it is called Lyme-like disease.** <sup>(1, 2)</sup>

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For a more complete description of Lyme disease, refer to the following texts:

- *Control of Communicable Diseases Manual (CCDM)*, American Public Health Association, 2004.
- American Academy of Pediatrics. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. 2006.

### **Case Definition** <sup>(5)</sup>

**Note:** *This surveillance case definition was developed for national reporting of Lyme disease; it is not intended to be used in clinical diagnosis.*

#### ***Clinical presentation***

A systemic, tick-borne disease with protean manifestations, including dermatologic, rheumatologic, neurologic, and cardiac abnormalities.

The best 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.

**A physician must make the diagnosis of EM.** 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.

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*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 evidence**

For the purposes of surveillance, the definition of a qualified laboratory assay is

- (1) A positive culture for *B. burgdorferi*, **or**
- (2) Two-tier testing interpreted using established criteria <sup>(7)</sup>, **or**
- (3) Single-tier IgG immunoblot seropositivity interpreted using established criteria <sup>(7-11)</sup>.

**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) in a county in which Lyme disease is endemic. **A history of tick bite is not required.**

**Disease endemic to county**

A county in which Lyme disease is endemic is one

- (1) In which at least two confirmed cases have been acquired in the county, or
- (2) In which established populations of a known tick vector are infected with *B. burgdorferi*.


**Detailed definitions for case classification**

*Confirmed:*

- a) A case of EM with a known exposure (as defined above), **or**
- b) A case of EM with laboratory evidence of infection (as defined above) and without a known exposure, **or**
- c) A case with at least one late manifestation that has laboratory evidence of infection.

*Probable:*

Any other case of physician-diagnosed Lyme disease that has laboratory evidence of infection (as defined above).

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*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).

**Note:** 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”.

**Status of Lyme Disease in Missouri**

There are currently no counties in Missouri that meet the Centers for Disease Control and Prevention’s (CDC) Lyme disease (infection with *Borrelia burgdorferi*) 2008 public health surveillance case definition for “**disease endemic to county**.” As of May 16, 2008, *B. burgdorferi* has not been isolated from any of the erythema migrans (EM) lesions from Missouri patients.

**Information Needed for Investigation**

- **Background on Lyme-like rashes**


Because the Lyme bacterium has not yet been isolated from any of Missouri’s EM cases, CDC and DHSS recommend that laboratory evidence of *B. burgdorferi* infection be obtained for EM lesion cases that have not traveled outside of Missouri during the incubation period.

- DHSS urges clinicians to consider submitting both acute-phase and convalescent-phase serum samples on their patients with suspect EM lesions for the purpose of diagnosing *B. burgdorferi* infection. A significant rise in IgG antibody titer between the acute and the convalescent sera is indicative of a recent infection with *B. burgdorferi*. For best results, the acute serum should be collected three weeks after onset and the convalescent serum should be collected five weeks after the acute specimen was collected. (See the **Laboratory Procedures** section below for information on submitting blood specimens to the Missouri State Public Health Laboratory for analysis.)
- Clinicians are also urged, when appropriate, to collect skin biopsy specimens from the EM lesion for culture.

- **Background on the Lyme disease two-tiered testing algorithm**

Laboratory evidence of *B. burgdorferi* infection is considered critical for late stage Lyme disease because the symptoms mimic many other common conditions<sup>(4, 12)</sup>. Without objective evidence of *B. burgdorferi* infection, case reports of people with other diseases will be counted erroneously as having Lyme disease.

For surveillance purposes, DHSS follows the CDC recommendation for two-tiered test criteria described below for establishing late manifestation of reportable Lyme disease. The criteria are based on reports generated during the 1994 Second National Conference on

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Serological Diagnosis of Lyme Disease. Following the conference, CDC published a special “Notice to Readers” in the August 11, 1995 issue of the MMWR, providing recommendations for Lyme disease test performance and interpretation <sup>(7)</sup>.

### The Two-tiered Algorithm for Serodiagnosis of Lyme disease

#### *First-Tier*

- First-tier testing is most often performed using a polyvalent ELISA, which measures IgM and IgG combined. This is a sensitive test and can yield false positives.
- Other acceptable first-tier, screening-level testing methods are the enzyme immunoassay (EIA) or immunofluorescent assay (IFA).

#### *Second-Tier*

- If the first-tier assay is negative, the specimen is not tested further.
- If the first-tier assay result is positive or equivocal, then the same serum specimen is retested by separate IgM and IgG immunoblots (“Western blot”).

Some commercial laboratories provide “reflex profile” testing for Lyme disease. A Lyme reflex profile begins with a screening test that automatically generates an order for IgM and/or IgG immunoblots according to the two-tiered algorithm.

- **Evaluate the laboratory evidence, clinical presentation, and exposure**

#### **Step 1. Follow-up with medical provider (confirm the diagnosis)**


Disease investigators must review laboratory evidence to determine whether there is sufficient evidence of *B. burgdorferi* infection to support follow-up with case’s medical provider.

Physician diagnosis of Lyme disease and the medical provider’s cooperation in completing the Lyme disease case report form is necessary for follow-up of:

- Report of an EM lesion of 5 centimeters or larger in diameter, **or**
- Positive culture, **or**
- Positive or equivocal ELISA/IFA/EIA result and a positive Western immunoblot, **or**
- Positive IgG Western immunoblot only.

#### **Step 2. Follow-up with patient**

- After contact with medical provider, if the reported case meets clinical and laboratory criteria for classification as a “confirmed,” investigators may need to contact the patient to evaluate exposure as defined in the case definition. According to the case definition, a “**county in which Lyme disease is endemic**” must have had:
  - At least two cases of EM (with laboratory evidence of *B. burgdorferi* infection) that were acquired in the county, **or**
  - Evidence of established populations of a known tick vector infected with *B. burgdorferi*

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### Step 3. Determining condition status (e.g., confirmed, probable, or suspected)

#### Confirmed Case:

- EM with potential exposure in a Lyme disease endemic county <30 days before illness, **or**
- EM with laboratory evidence of infection and without potential exposure in a Lyme disease endemic county <30 days before illness, **or**
- At least one physician diagnosed late manifestation with laboratory evidence of infection

#### Probable Case:

- Physician-diagnosed Lyme disease based on clinical presentations not described in the national surveillance case definition with laboratory evidence of infection.

#### Suspect Case:

- EM without potential exposure in a Lyme disease endemic county <30 days before illness and without any laboratory evidence of infection, **or**
- No clinical information but laboratory evidence of infection (i.e. a laboratory report only)

#### **“No Case” classification is indicated for:**

- A report of an EM lesion less than 5 centimeters, **or**
- A positive or equivocal ELISA/EIA/IFA result only, **or**
- A positive IgM Western immunoblot only.

**Step 4. Establish the extent of illness.** Are other people (e.g., family, friends) who might have shared the same exposure environment showing any signs of disease?


#### **Cautions Regarding Testing for Lyme disease**

Some private laboratories are providing tests for Lyme disease diagnosis using protocols that are not scientifically sound and have not been demonstrated to be valid in peer-reviewed scientific literature. Test methods such as urine antigen tests or blood microscopy for *Borrelia* species should not be used because their accuracy and clinical usefulness have not been adequately established.

In addition, to maintain the highest possible specificity, immunoblot interpretation should only be done in qualified laboratories that follow the CDC-recommended, evidence-based guidelines on immunoblot interpretation.

#### **Notification And Control Measures**

- Contact the [District Communicable Disease Coordinator](#) for assistance, if needed. The Missouri Department of Health and Senior Services Situation Room (DSR) is available (24/7) for assistance at (800) 392-0272.

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### **Prevention and Control Measures** *(For detailed information see)*


- *Control of Communicable Diseases Manual (CCDM)*, American Public Health Association, 2004, “Lyme Disease – Prevention”
- American Academy of Pediatrics. *Red Book: 2006 Report of the Committee on Infectious Diseases*. 27th ed. 2006, “Prevention of Tick-borne Infections”
- Antibiotic prophylaxis after a tick bite (in the absence of symptoms) is usually not recommended<sup>(12)</sup>. For this to be cost effective, the probability of *B. burgdorferi* infection would have to be abnormally high, which it is not in Missouri.
- **As of February 25, 2002 the manufacturer announced that the LYMERix™ Lyme disease vaccine would no longer be commercially available.** The efficacy of this vaccine against the Lyme-like disease seen in Missouri was never substantiated because the agent has not been positively identified and the vaccine had not been tested for efficacy against this disease.

### **Laboratory Procedures**

The Missouri State Public Health Laboratory (SPHL) does not perform testing for *B. burgdorferi*. However, the SPHL can arrange for testing of clinical specimens by the CDC’s and other laboratories. Information on laboratory procedures can be obtained from the Regional Communicable Disease Coordinator or from staff at the SPHL. The SPHL telephone number is 573-751-0633 and the web site is: <http://www.dhss.mo.gov/Lab/index.html>.(5/08)

- **Culture:** *B. burgdorferi* organisms have been readily isolated from the margins of erythema migrans lesions; however, the organisms have been isolated infrequently from blood, joints, and cerebrospinal fluid<sup>(12,13)</sup>. Contact the SPHL for assistance in locating a laboratory that will isolate *B. burgdorferi*.
- **Serology:** The SPHL can submit serological specimens for testing to the CDC Division of Vector Borne Infectious Diseases Laboratory, Fort Collins, Colorado. This laboratory offers an IgM antibody test on acute serum and an IgG antibody titer on paired serum. Positive or equivocal tests will be followed with a Western blot.
  - CDC will perform IgM antibody testing on acute serum if the serum is collected within four weeks of onset. For best results the acute serum should be collected three to four weeks after onset of symptoms. Test results on specimens collected before three weeks may give a false negative result.
  - CDC will perform IgG antibody testing on paired serum. For best results, the acute serum should be collected three weeks after onset and the convalescent serum should be collected five weeks after the acute specimen was collected. A significant rise in IgG antibody titer between the acute and the convalescent sera is indicative of a recent infection with *B. burgdorferi*.
  - All acute serum samples collected within the appropriate time frame will be sent to CDC for IgM testing and a request will be made at this time by the SPHL, to the submitter, for a convalescent specimen. Results of the IgM test will be sent to the submitter upon completion of testing. When the convalescent specimen arrives it will be sent to CDC for



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IgG testing. CDC will test both the acute and the convalescent specimens for IgG antibody. Upon completion of the IgG testing results will be sent to the submitter.

**Submission of Blood Specimens:** The following forms must accompany specimens sent to the SPHL:

- Syphilis test results by the RPR or MHA-TP test, **or**
- A completed syphilis test request form, if the specimen is to be tested by the SPHL (this is to rule out syphilis, which is a spirochete, as is *B. burgdorferi*); **and,**
- CDC Specimen Submission Form 50.34; in this Section or at:  
[http://www.cdc.gov/ncidod/dybid/misc/CDC50\\_34.pdf](http://www.cdc.gov/ncidod/dybid/misc/CDC50_34.pdf) (5/08), or call the Missouri State Public Health Laboratory at (573) 751-0633

**NOTE: CDC testing will not be initiated without the inclusion of:**


- a. Type of specimen
- b. Suspected etiology
- c. Date of onset of symptoms
- d. Brief clinical description
- e. Date of specimen collection
- f. Pertinent travel history
- g. Antibiotic treatment received and date

For information on shipping, specimen types and amount, or for further assistance Additional information on rickettsial detection can be obtained from the Virology Unit at the SPHL (573) 751-0633.

### **Reporting Requirements**


Lyme disease is a Category II disease and shall be reported to the local health authority or to the Missouri Department of Health and Senior Services (DHSS) within three days of first knowledge or suspicion by telephone, facsimile or other rapid communication.

1. For all cases, complete a “[Disease Case Report](#)” (CD-1).
2. For all cases, complete a “[Lyme Disease Case Report](#)” (MO580-1807).
3. Entry of the completed CD-1 into MOHSIS negates the need for the paper CD-1 to be forwarded to the [District Health Office](#).
4. Send the completed secondary investigation form to the District Health Office.
5. All outbreaks or “suspected” outbreaks must be reported as soon as possible (by phone, fax, or e-mail) to the Regional Communicable Disease Coordinator. This can be accomplished by completing the [Missouri Outbreak Surveillance Report](#) (CD-51).
6. Within 90 days of the conclusion of an outbreak, submit the final outbreak report to the Regional Communicable Disease Coordinator.

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### **Web Resources and Information**

1. Free tick-borne disease prevention posters and bookmarks from the Missouri Department of Health and Senior Services (DHSS website)  
<http://www.dhss.mo.gov/TicksCarryDisease/Publications.html> (5/08)
2. Downloadable tick-check promotion radio public service announcements (DHSS website—spots require .mp3 player such as Windows Media Player or Real Player)  
<http://www.dhss.mo.gov/TicksCarryDisease/Prevention.html> (5/08)
3. University of Missouri Outreach and Extension Home and Garden Guide "Ticks," (University of Missouri Extension website)  
<http://muextension.missouri.edu/explore/agguides/pests/g07382.htm> (5/08)
4. Centers for Disease Control and Prevention - Protect Yourself from Ticks and Lyme Disease,  
<http://www.cdc.gov/nasd/docs/d000901-d001000/d000961/d000961.html> (5/08)
5. Centers for Disease Control and Prevention - Lyme Disease Home page,  
<http://www.cdc.gov/ncidod/dvbid/lyme/index.htm> (5/08)
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[http://www.cdc.gov/ncidod/dvbid/lyme/lyme\\_brochure.pdf](http://www.cdc.gov/ncidod/dvbid/lyme/lyme_brochure.pdf) (5/08)
7. American Lyme Disease Foundation, Inc., <http://www.aldf.com> (5/08)
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[http://www.acponline.org/clinical\\_information/resources/lyme\\_disease/patient/index.html](http://www.acponline.org/clinical_information/resources/lyme_disease/patient/index.html) (5/08)
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### **Lyme/Lyme-like Disease Physician Education Materials**

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