LYME DISEASE

AGENT: *Borrelia burgdorferi, B. mayonii*

WHERE FOUND
Lyme disease is most frequently reported from the Upper Midwestern and northeastern United States. Some cases are also reported in northern California, Oregon, and Washington. In 2015, 95% of Lyme disease cases were reported from 14 states: Connecticut, Delaware, Maine, Maryland, Massachusetts, Minnesota, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, Vermont, Virginia, and Wisconsin.

INCUBATION PERIOD
3–30 days

SIGNS AND SYMPTOMS

LOCALIZED STAGE*
- Erythema migrans (EM)—red ring-like or homogenous expanding rash; classic rash not present in all cases. See examples on following pages.
- Flu-like symptoms—malaise, headache, fever, myalgia, arthralgia
- Lymphadenopathy

*During the localized (early) stage of illness, Lyme disease may be diagnosed clinically in patients who present with an EM rash. Serologic tests may be insensitive at this stage. During disseminated disease, however, serologic tests should be positive.

DISSEMINATED STAGE
- Multiple secondary annular rashes
- Flu-like symptoms
- Lymphadenopathy

Rheumatologic Manifestations
- Transient, migratory arthritis and effusion in one or multiple joints
- Migratory pain in tendons, bursae, muscle, and bones
- Baker's cyst
- If untreated, arthritis may recur in same or different joints

Cardiac Manifestations
- Conduction abnormalities, e.g., atrioventricular node block
- Myocarditis, pericarditis

Neurologic Manifestations
- Bell’s palsy or other cranial neuropathy
- Meningitis
- Motor and sensory radiculoneuropathy, mononeuritis multiplex
- Subtle cognitive difficulties
- Encephalitis, encephalomyelitis, subtle encephalopathy, pseudotumor cerebri (all rare)

Additional Manifestations
- Conjunctivitis, keratitis, uveitis
- Mild hepatitis
- Splenomegaly
LYME DISEASE OR STARI?

An erythema migrans-like rash has also been described in humans following bites of the lone star tick, *Amblyomma americanum*. This condition has been named Southern Tick-Associated Rash Illness (STARI). Although the rash may be accompanied by flu-like symptoms, long-term sequelae have not been reported. Because the cause of STARI is unknown, diagnostic blood tests are not available.

Lone star ticks can be found from central Texas and Oklahoma eastward across the southern states and along the Atlantic Coast as far north as Maine.

It is not known whether antibiotic treatment is necessary or beneficial for patients with STARI. Nevertheless, because STARI resembles early Lyme disease, physicians often treat patients with the same antibiotics recommended for Lyme disease.

GENERAL LABORATORY FINDINGS

- Elevated erythrocyte sedimentation rate
- Mildly elevated hepatic transaminases
- Microscopic hematuria or proteinuria
- In Lyme meningitis, CSF typically shows lymphocytic pleocytosis, slightly elevated protein, and normal glucose.

LABORATORY DIAGNOSIS

- Demonstration of diagnostic IgM or IgG antibodies in serum. A two-tier testing protocol is recommended—EIA or IFA should be performed first; if positive or equivocal, it is followed by a Western blot.
- Isolation of organism from a clinical specimen
- In suspected Lyme meningitis, testing for intrathecal IgM or IgG antibodies may be helpful.

NOTES ON SEROLOGIC TESTS FOR LYME DISEASE

- Serologic tests are insensitive during the first few weeks of infection. During this stage, patients with an EM rash may be diagnosed clinically. While not necessary, acute and convalescent titers may be helpful in some cases.
- In persons with illness > 1 month, only IgG testing should be performed (not IgM). A positive IgM test alone is not sufficient to diagnose current disease.
- Due to antibody persistence, single positive serologic test results cannot distinguish between active and past infection.
- Serologic tests cannot be used to measure treatment response.
- Enzyme immunoassay (EIA) and immunofluorescence assay (IFA) tests have low specificity and may yield false-positive results. They may cross-react with antibodies to commensal or pathogenic spirochetes, some viral infections (e.g., varicella, Epstein-Barr virus), or certain autoimmune diseases (e.g., lupus).

NOTE: Coinfection with *B. microti* and/or *A. phagocytophilum* should be considered in patients who present with initial symptoms that are more severe than are commonly observed with Lyme disease alone, especially in those who have high-grade fever for more than 48 hours despite appropriate antibiotic therapy or who have unexplained leukopenia, thrombocytopenia, or anemia. Coinfection should also be considered in patients whose erythema migrans skin lesion has resolved but have persistent flu-like symptoms.
### TREATMENT

Treatment regimens listed in the following table are for localized (early) Lyme disease. See references for treatment of patients with disseminated (late) Lyme disease. These regimens are guidelines only and may need to be adjusted depending on a person’s age, medical history, underlying health conditions, pregnancy status, or allergies. Consult an infectious disease specialist for the most current treatment guidelines or for individual patient treatment decisions.

<table>
<thead>
<tr>
<th>AGE CATEGORY</th>
<th>DRUG</th>
<th>DOSAGE</th>
<th>MAXIMUM</th>
<th>DURATION (DAYS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adults</td>
<td>Doxycycline</td>
<td>100 mg twice per day, orally</td>
<td>N/A</td>
<td>10-21*</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime axetil</td>
<td>500 mg twice per day orally</td>
<td>N/A</td>
<td>14-21</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin</td>
<td>500 mg three times per day orally</td>
<td>N/A</td>
<td>14-21</td>
</tr>
<tr>
<td>Children</td>
<td>Amoxicillin</td>
<td>50 mg/kg per day orally, divided into 3 doses</td>
<td>500 mg per dose</td>
<td>14-21</td>
</tr>
<tr>
<td></td>
<td>Doxycycline</td>
<td>4 mg/kg per day orally, divided into 2 doses</td>
<td>100 mg per dose</td>
<td>10-21*</td>
</tr>
<tr>
<td></td>
<td>Cefuroxime axetil</td>
<td>30 mg/kg per day orally, divided into 2 doses</td>
<td>500 mg per dose</td>
<td>14-21</td>
</tr>
</tbody>
</table>

* Recent publications suggest the efficacy of shorter courses of treatment for early Lyme disease.

**NOTE:** For patients intolerant of amoxicillin, doxycycline, and cefuroxime axetil, the macrolides azithromycin, clarithromycin, or erythromycin may be used, although they have a lower efficacy. Patients treated with macrolides should be closely observed to ensure resolution of clinical manifestations.
REFERENCES


LYME DISEASE

ERYTHEMA MIGRANS RASHES

The erythema migrans (EM) rash occurs in 70–80% of patients with Lyme disease. EM rashes expand slowly over a few days after which they may develop a “bull’s-eye” appearance consisting of a red ring with central clearing. However, EM may take alternate forms—solid lesions, blue-purple hues, and crusted or blistering lesions have all been documented. The rash is not painful or pruritic, but it may be warm to the touch. If early localized Lyme disease is not treated, patients may develop multiple secondary circular rashes as spirochetes disseminate throughout the body.

CLASSIC EM—CIRCULAR RED RASH WITH CENTRAL CLEARING THAT SLOWLY EXPANDS

Photo courtesy of Taryn Holman.

BLUISH HUE WITHOUT CENTRAL CLEARING

Photo courtesy of Yevgeniy Balagula.

RED, EXPANDING LESION WITH CENTRAL CRUST

Photo courtesy of Bernard Cohen.
RED, OVAL-SHAPED PLAQUE ON TRUNK
Photo courtesy of Alison Young.

PURPLE LESION ON BACK OF KNEE
Photo courtesy of New York State Department of Health.

EARLY DISSEMINATED LYME DISEASE—MULTIPLE RED LESIONS WITH DUSKY CENTERS
Photo courtesy of Bernard Cohen.

TICK BITE WITH MILD ALLERGIC REACTION
Not an erythema migrans. Allergic reactions typically appear within the first 48 hours of tick attachment and are usually <5 cm in diameter.

Special thanks to DermAtlas for providing many photographs.