EmblemHealth

Lyme Disease Diagnosis and Treatment

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Definition

Lyme disease is caused by *Borrelia burgdorferi,* which is transmitted by the bite of the tick species *Ixodes scapularis* and *Ixodes pacificus.* Clinical manifestations most often involve the skin, joints, nervous system, and heart. Extracutaneous manifestations are less commonly seen than in earlier years. Early cutaneous infection with *B. burgdorferi* is called erythema migrans, which is the most common clinical manifestation of Lyme disease. *I. scapularis* may also be infected with and transmit *Anaplasma phagocytophilum* (previously referred to as *Ehrlichia phagocytophila*) and/or *Babesia microti,* the primary cause of babesiosis. Thus, a bite from an *I. scapularis* tick may lead to the development of Lyme disease, human granulocytic anaplasmosis (HGA, formerly known as human granulocytic ehrlichiosis), or babesiosis as a single infection or, less frequently, as a coinfection.

Diagnosis

Diagnosis is predicated upon clinical presentation that is consistent with signs and symptoms compatible with the disease and which is supported by a positive serologic/cerebrospinal fluid (CSF) titer by indirect immunofluorescence assay (IFA), Prevue Borrelia burgdorferi antibody detection assay or enzyme-linked immunosorbent assay (ELISA). (Serologic detection of active disease or previous infection involves a 2-test approach using a sensitive enzyme immunoassay (EIA) or IFA followed by a Western immunoblot. All specimens positive or equivocal by a sensitive EIA or IFA should be tested by a standardized Western immunoblot)

Guideline

I. Members with a confirmed Lyme disease diagnosis are eligible for an initial 4-week course of intravenous (IV) antibiotic therapy when the following criteria are met; **any**:

- **A.** Lyme arthritis that persists after failing to respond to a 4-week course of appropriate oral antibiotic therapy
- **B.** Lyme carditis —moderate to severe cardiac involvement as evidenced by any of the following:
  1. 1st-degree heart block with P-R interval ≥ 300 milliseconds
  2. Myopericarditis
  3. 2nd- or higher degree atrio-ventricular block
- **C.** Neurologic involvement of Lyme disease (neuroborreliosis) as evidenced by any of the following:
  1. Encephalomyelitis, based on MRI imaging, CSF pleocytosis, and no other cause found
  2. Meningitis confirmed by CSF analysis showing a lymphocytic pleocytosis
  3. Sensory/motor radiculoneuropathy or peripheral neuropathy (weakness and/or pain in the extremities or chest)
- **D.** All cases of Lyme disease in pregnant women who exhibit symptoms and signs of any of the following:
  1. Stage II Lyme disease with early dissemination documented by organ-specific manifestations of infection (arthritic, cardiac, or neurologic)
  2. Stage III late Lyme disease documented by findings of arthritis and/or neurologic complications, such as encephalomyelitis and subacute encephalitis

II. The following antibiotics constitute medically necessary IV therapy:
- **A.** Ceftriaxone (Rocephin®)
- **B.** Cefotaxime (Claforan®)
- **C.** Penicillin G
- **D.** Azithromycin (Zithromax®) — for members intolerant to b-lactam antibiotics

Limitations/Exclusions

I. Intravenous therapy with the following drugs is not considered medically necessary due to insufficient evidence of therapeutic value; **any**:
- **A.** Carbapenems (e.g., doripenem, ertapenem, imipenem, meropenem)
- **B.** First-generation cephalosporins (e.g., cefazolin)
- **C.** Azole antifungals
- **D.** Fluoroquinolones (e.g., levofloxacin, moxifloxacin)

II. One repeat 4-week course of outpatient IV therapy is considered medically necessary when the following criteria are met; **all**:
- **A.** The member has met the criteria for an initial course of intravenous antibiotic therapy, using lab results obtained within the past 3 months
- **B.** The member has completed an initial course of appropriate intravenous antibiotic therapy
- **C.** The member has objective evidence of either relapse of infection, progression of Lyme disease organ damage, and/or the finding of a new focus or type of organ damage

III. Intravenous therapy for the following indications is not considered medically necessary due to insufficient evidence of therapeutic value; **any**:
- **A.** Early Lyme disease
- **B.** Flu-like syndrome (fatigue, fever, headache, mildly stiff neck, arthralgias, and myalgias)

- **C.** Initial treatment of Lyme arthritis without coexisting neurological symptoms (e.g., headache, stiff neck, and irritability [inclusive of isolated manifestations such as Bell's facial nerve palsy/paralysis)
- **D.** Non-specific subjective symptoms, such as persistent, chronically debilitating fatigue (chronic fatigue syndrome), difficulty in concentrating, musculoskeletal pain (fibromyalgia), and headache
- **E.** Pregnant woman presenting with localized Lyme disease manifested as a single lesion of erythema migrans without any other symptoms suggestive of disseminated disease
- **F.** Treatment of "post-Lyme disease" syndrome (i.e., persistent fatigue)
- **G.** Treatment of individuals with systemic symptoms without serologic or cerebrospinal fluid (CSF) studies confirming Lyme disease
- **H.** Prophylactic treatment of asymptomatic members when the sole evidence of Lyme disease is a positive immunologic test (ELISA, IFA, or Western blot)
- **I.** Treatment of persistent Lyme-associated arthritis after 2 prior courses of antibiotic therapy
- **J.** Mild cardiac involvement of Lyme disease as evidenced by any of the following:
    1. Transient ST-T depression, T-wave changes

IV. Repeat or prolonged courses of IV antibiotics (> 4 weeks) has not been shown to improve net health outcomes and are not considered medically necessary

V. Repeat diagnostic testing is not considered medically necessary

VI. The following diagnostic tests are not considered medically necessary due to insufficient evidence of therapeutic value:

- **A.** Antigen detection
- **B.** Borrelia burgdorferi antibody index testing
- **C.** Borrelia culture
- **D.** C6 peptide ELISA assay (using recombinant VlsE1 or peptide antigens of Borrelia burgdorferi)
- **E.** CD57+ lymphocyte counts
- **F.** Chemokine CXCL13
- **G.** Complement split products (e.g., C3a and C4a)
- **H.** Cyst formation
- **I.** Cytokine analysis
- **J.** Immune complexes
- **K.** iSpot Lyme assay
- **L.** Lymphocyte markers
- **M.** Lymphocyte transformation test
- **N.** Measurement of natural killer (NK) cells
- **O.** Microscope-based assays
- **P.** Neuroadrenal expanded panel (including histamine, serotonin, and hydroxyindoleacetic acid)
- **Q.** Polymerase chain reaction (PCR) for identification or quantification of Lyme disease (B. burgdorferi) spirochetal DNA or RNA
- **R.** Positron emission tomography (PET) scanning
- **S.** Provocative testing (testing for B. burgdorferi after antibiotic provocation)
- **T.** Serum borreliacidal assay
- **U.** SPECT scanning
- **V.** T-cell proliferation response assay

W. Urine antigen assay
X. Xenodiagnosis (using the natural tick vector, Ixodes scapularis)

VII. The following treatments are not considered medically necessary treatment for Lyme disease due to insufficient evidence of therapeutic value:
A. Chelation
B. Hyperbaric oxygen therapy
C. Singlet oxygen therapy
D. Intravenous ascorbic acid
E. Intravenous magnesium

Revision History

10/13/2017 — removed congestive heart failure from Lyme carditis indication sub-criteria list; clarified and simplified neurologic involvement sub- criteria; removed 1st degree heart block and left ventricular dysfunction from mild cardiac involvement sub-criteria list

Applicable Procedure Codes

96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96367	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); additional sequential infusion of a new drug/substance, up to 1 hour (List separately in addition to code for primary procedure)
96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); concurrent infusion (List separately in addition to code for primary procedure)
96369	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); initial, up to 1 hour, including pump set-up and establishment of subcutaneous infusion site(s)
96370	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); each additional hour (List separately in addition to code for primary procedure)
96371	Subcutaneous infusion for therapy or prophylaxis (specify substance or drug); additional pump set-up with establishment of new subcutaneous infusion site(s) (List separately in addition to code for primary procedure)
96374	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug
96375	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); each additional sequential intravenous push of a new substance/drug (List separately in addition to code for primary procedure)
93676	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); each additional sequential intravenous push of the same substance/drug provided in a facility (List separately in addition to code for primary procedure)
99601	Home infusion/specialty drug administration, per visit (up to 2 hours);
99602	Home infusion/specialty drug administration, per visit (up to 2 hours); each additional hour (List separately in addition to code for primary procedure)

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