

Borrelia burgdorferi - Lyme Disease

Clinical Background

Lyme disease is the most common vector-borne disease in the U.S.

Epidemiology

- Incidence – increased 40% from 2001 to 2002
- Age – bimodal peaks
 - Pediatric 5-14 years
 - Elderly >60 years
- Sex – M:F, equal
 - M<F with acrodermatitis chronica atrophicans
- Transmission – infected *Ixodes* tick bite

Organism

- *Borrelia burgdorferi* is a member of the Spirochaetales family, which also includes *Treponema* and *Leptospira*

Risk Factors

- Exposure in regions where deer population is high during the spring or summer
- Northeast or Midwest geographic location
 - 12 U.S. states account for 95% of reported cases

Clinical Presentation

- Centers for Disease Control (CDC) clinical case epidemiologic surveillance criteria for defining Lyme disease
 - Erythema migrans (EM) ≥ 5 cm in diameter or
 - Laboratory confirmation of infection and at least 1 late manifestation
 - Musculoskeletal manifestation – recurrent, brief attacks of objective joint swelling in 1 or more joints
 - Neurological manifestations
 - All or part of a triad
 - Lymphocytic meningitis – cerebrospinal fluid (CSF) pleocytosis with higher number of monocytes
 - Cranial neuritis
 - Radiculoneuritis – termed Garin-Bujadoux-Bannwarth syndrome
 - Encephalomyelitis – requires demonstration of CSF antibody production
 - Cardiovascular manifestations – acute second or third-degree arteriovenous (AV) heart block
- Lyme disease stages
 - Stage 1 early localized
 - Occurs within hours to several weeks after infection
 - Characterized by EM or lymphocytoma (rare in U.S.)
 - Manifestations
 - Regional adenopathy and/or minor constitutional symptoms
 - Stage 2 early disseminated
 - Occurs weeks to months following the tick bite

- Characterized by neurologic and cardiac involvement (manifested in 15% and 8% of patients, respectively)
- Manifestations
 - Fever
 - Myalgias
 - Multiple EM lesions
 - Meningitis
 - Bells palsy
 - Guillain-Barré-like syndrome
 - Cardiac conduction abnormalities
 - Arthritis
- Stage 3 late disseminated
 - Occurs within a few weeks to 2 years following infection
 - Symptoms are more severe than early disseminated
 - Characterized by arthritis or central nervous system involvement
 - Occurs in 60% of individuals not effectively treated early in infection
 - Tends to be intermittent, lasting from several days to weeks
 - Manifestations
 - Memory loss
 - Fatigue
 - Neuropathy (often polyneuropathy)
- Initial symptoms usually appear in late spring/early summer, when ticks are active
- Late manifestations occur anytime

Treatment

- Lyme disease, caught early, is easily treated
 - Treatment prevents progression to chronic stage
 - Severe, long-term effects occur in <10% of untreated patients
- If known tick bite and EM present, proceed with treatment; testing is not necessary

Prevention

- Avoid exposure to ticks
- If exposure is unavoidable, use protective clothing and tick repellent (DEET); check for and remove ticks

Diagnosis

- Indications for testing
 - No testing necessary if patient presents with tick bite and erythema migrans
 - Patient at risk for Lyme disease with clinical symptoms
- Laboratory testing
 - Current CDC recommendations for serologic diagnosis of Lyme disease
 - Screen with a polyvalent ELISA test or C6 peptide antibodies
 - Confirm equivocal and positive results with Western Blot
 - <8 weeks after onset of disease – IgG-, IgM+
 - >8 weeks after onset of disease – IgG+
 - If testing is initially negative, consider other diseases; test convalescent sample
 - Serological testing
 - False-positive results from serologic tests may result from:

- Other spirochetal disease (syphilis, periodontitis)
- Autoimmune diseases (systemic lupus erythematosus, rheumatoid arthritis)
- Other infections (subacute bacterial endocarditis, HIV, acute EBV)
- Co- and triple-infections by parasites that cause babesiosis and granulocytic anaplasmosis (formerly known as human granulocytic ehrlichiosis) may occur
 - Serologic testing specific for these agents is recommended
 - If neurologic disease is present, test CSF for C6 antibodies or ELISA

Differential Diagnosis

- Neurologic
 - HIV
 - Acute meningitis
 - Acute encephalitis
 - Multiple sclerosis
 - Demyelinating disorder
 - Guillain Barré syndrome
- Musculoskeletal
 - *Neisseria gonorrhoea*
 - Parvovirus
 - Septic arthritis
 - Connective tissue diseases
 - Rheumatoid arthritis
 - Fibromyalgia
 - Rheumatic fever
 - Reactive arthritis trachomatis
 - Crystalline arthritis
- Acute febrile illness
 - *Ehrlichia chaffeensis*
 - *Rickettsia rickettsii*
 - *Babesia microti*
 - *Francisella tularensis*
 - Malaria
 - Colorado tick fever
- Heart block
 - Endocarditis
 - Sick sinus syndrome
 - Connective tissue disease
 - *Anaplasma phagocytophilum*

Lab Tests

Indications for Laboratory Testing

Tests generally appear in the order most useful for common clinical situations. For test-specific information, refer to the test number in the ARUP Laboratory Test Directory on the ARUP Web site at www.aruplab.com.

Test Name and Number	Recommended Use	Limitations	Follow Up
<p><i>Borrelia burgdorferi</i> Antibodies, Total by ELISA with Reflex to IgG & IgM by Western Blot (Early Disease) 0050267</p> <p>Method: Enzyme-Linked Immunosorbent Assay/Western Blot</p>	<p>Screen for Lyme disease <8 weeks after onset of disease</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features, combined with available laboratory tests</p>	
<p><i>Borrelia burgdorferi</i> C6 Peptide Antibodies, Total by ELISA with Reflex to IgG & IgM by Western Blot 0051043</p> <p>Method: Enzyme-Linked Immunosorbent Assay/Western Blot</p>	<p>Screen for Lyme disease <8 weeks after onset of disease</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	
<p><i>Borrelia burgdorferi</i> Antibodies, IgG & IgM by Western Blot 0050254</p> <p>Method: Western Blot</p>	<p>Confirm an equivocal or positive antibody test performed <8 weeks after appearance of erythema migrans</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	Retesting in 10-14 days may be helpful when serology test results are equivocal
<p><i>Borrelia burgdorferi</i> Antibody, IgG by Western Blot 0050255</p> <p>Method: Western Blot</p>	<p>Confirm an equivocal or positive antibody test performed >8 weeks after appearance of erythema migrans</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	

<p><i>Borrelia</i> species DNA Detection by PCR (Lyme Disease) 0055570</p> <p>Method: Polymerase Chain Reaction</p>	<p>Diagnose Lyme disease in patient with negative serologic results but disease still strongly suspected, or with immune deficiency</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p>	<p>Negative result does not rule out presence of PCR inhibitors or <i>B. burgdorferi</i> DNA concentrations below detection level of assay</p> <p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features, combined with available laboratory tests</p>	
<p><i>Borrelia burgdorferi</i> Antibody, IgG by Western Blot (CSF) 0055259</p> <p>Method: Western Blot</p>	<p>Adjunct test for neuroborreliosis in patient with neurological symptoms >8 weeks after onset of disease</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	<p>Detection of antibodies to <i>B. burgdorferi</i> in cerebrospinal fluid may indicate central nervous system infection</p> <p>Consider possible contamination by blood or transfer of serum antibodies across blood-brain barrier</p>
<p><i>Borrelia burgdorferi</i> C6 Peptide Antibodies, Total by ELISA (CSF) 0051046</p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Adjunct test for neuroborreliosis in patient with neurologic symptoms <8 weeks from onset of disease</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	<p>Detection of antibodies of <i>B. burgdorferi</i> in CSF may indicate central nervous system infection</p> <p>Consider possible contamination by blood or transfer of serum antibodies across blood-brain barrier</p> <p>For equivocal test results, repeat testing in 10-14 days may be helpful</p>

<p><i>Borrelia burgdorferi</i> Antibodies, Total by ELISA (CSF) 0099483</p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Screening test (confirmed by Western Blot) for neuroborreliosis in patient with neurologic symptoms <8 weeks from onset of disease</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	<p>Detection of antibodies to <i>B. burgdorferi</i> in cerebrospinal fluid may indicate central nervous system infection</p> <p>Consider possible contamination by blood or transfer of serum antibodies across blood-brain barrier</p> <p>Retesting in 10-14 days may be helpful when serology test results are equivocal</p>
<p><i>Borrelia burgdorferi</i> Antibodies, IgG & IgM by Western Blot (CSF) 0055260</p> <p>Method: Western Blot</p>	<p>Confirm positive test for CSF antibodies</p>	<p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>	<p>Detection of antibodies to <i>B. burgdorferi</i> in cerebrospinal fluid may indicate central nervous system infection</p> <p>Consider possible contamination by blood or transfer of serum antibodies across the blood-brain barrier</p>
<p><i>Babesia microti</i> Antibodies, IgG & IgM by IFA 0093048</p> <p>Method: Indirect Fluorescent Antibody</p>	<p>Consider for those who test negative for Lyme disease antibodies but who live in endemic areas and have compatible symptoms</p>		
<p><i>Anaplasma Phagocytophilum</i> (HGA) Antibodies, IgG & IgM 0097303</p> <p>Method: Indirect Fluorescent Antibody</p>	<p>Consider for those who test negative for Lyme disease antibodies but who live in endemic areas and have compatible symptoms</p>		

Additional Tests Available

Test Name and Number	Comments
<p><i>Borrelia burgdorferi</i> C6 Peptide Antibodies, Total by ELISA 0051044</p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	
<p><i>Borrelia burgdorferi</i> Antibody, IgM by Western Blot 0050253</p> <p>Method: Western Blot</p>	

<p><i>Borrelia burgdorferi</i> Total Antibodies, IgG and/or IgM by ELISA with Reflex to IgG by Western Blot (Late Disease) 0050268</p> <p>Method: Enzyme-Linked Immunosorbent Assay/Western Blot</p>	
<p><i>Borrelia burgdorferi</i> Antibody, IgM by Western Blot (CSF) 0055258</p> <p>Method: Western Blot</p>	
<p><i>Borrelia hermsii</i> Antibody Panel, IFA 0093170</p> <p>Method: Immunofluorescence Assay</p>	
<p>Lyme Antigen, Urine 0050219</p> <p>Method: Lyme Dot-Blot Assay</p>	
<p><i>Borrelia burgdorferi</i> Antibodies, Total by ELISA 0050216</p> <p>Method: Enzyme-Linked Immunosorbent Assay</p>	<p>Alternative first line screening test for Lyme disease</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p> <p>Up to 40% of patients with early disease are seronegative by ELISA at time they present with erythema migrans</p> <p>Serologic diagnosis often not established until advanced stage of disease</p> <p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p> <p>Retesting in 10-14 days may be helpful when serology test results are equivocal</p>
<p><i>Borrelia burgdorferi</i> C6 Peptide Antibodies, Total by ELISA with Reflex to IgG by Western Blot 0051045</p> <p>Method: Enzyme-Linked Immunosorbent Assay/Western Blot</p>	<p>Screen for Lyme disease >8 weeks after onset of disease</p> <p>If known tick bite and erythema migrans present, proceed with treatment – no testing necessary</p> <p>No objective tests for Lyme borreliosis exist that are 100% sensitive and 100% specific</p> <p>Diagnosis depends on clinical features combined with available laboratory tests</p>

Guidelines

Evidence-based guidelines for the management of Lyme disease. International Lyme and Associated Diseases Society - Disease Specific Society. 2004.

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General References

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Reviewed by

- Hillyard, David R., MD. Medical Director, Molecular Infectious Diseases at ARUP Laboratories; Professor of Pathology, University of Utah
- Litwin, Christine, MD. Medical Director, Immunology at ARUP; Professor of Pathology (Clinical), University of Utah

Diagnostic Algorithm(s)

PDF algorithm(s) available at www.arupconsult.com.

Lyme Disease Testing Algorithm

Related Content

- Babesia microti
- Dengue Fever Virus
- Francisella tularensis - Tularemia
- Meningitis, Acute

Parvovirus B19

Rickettsia rickettsii - Rocky Mountain Spotted Fever

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