UVM ECHO Lyme and Tick-borne Illness: Early Disseminated Disease

Speaker:
Jean Dejace, MD
Early Disseminated Lyme

- Weeks to months after infection
- Typical presentations
  - Skin
  - Cardiac
  - Neurologic
Early Disseminated Lyme: Skin

Multiple rashes, disseminated infection

Photo Credit: Bernard Cohen

Description:
Early disseminated Lyme disease

[https://www.cdc.gov/lyme/signs_symptoms/rashes.html]
<table>
<thead>
<tr>
<th>Symptom Category</th>
<th>Number [Percent] Positive (95% C.I.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Two-Tier WCS ELISA&lt;sup&gt;a&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>All Lyme patient sera</td>
<td>293 [51.5%] (47.3, 55.7)</td>
</tr>
<tr>
<td>All Erythema Migrans</td>
<td>142 [35.2%] (30.6, 40.1)</td>
</tr>
<tr>
<td>Single Erythema Migrans</td>
<td>36 [27.1%] (19.7, 35.5)</td>
</tr>
<tr>
<td>Multiple Erythema Migrans</td>
<td>37 [63.8%] (50.1, 70.0)</td>
</tr>
<tr>
<td>Early Neurologic Lyme Disease-Acute</td>
<td>16 [80.0%] (56.3, 94.3)</td>
</tr>
</tbody>
</table>
Treatment of Early Disseminated Lyme

• Disseminated erythema migrans
  • Treatment is same as localized EM

• Treatment is PO

• 1 of 3 antibiotic regimens is recommended
  • Doxycycline 100mg BID
    • Note: doxycycline also treats anaplasma (others do not)
  • Amoxicillin 500mg TID
  • Cefuroxime 500mg BID

• Duration
  • 14-21 days (?10 days doxy)
Early Disseminated Lyme: Cardiac

Clinical Manifestations

Information on at least one defined clinical manifestation was available for 60.2% of confirmed cases from 35 states. Approximately three fourths (72.2%) of patients had erythema migrans; 27.5% had arthritis; and 1.5% had carditis.
Early Disseminated Lyme: Cardiac

• Presentation
  • Palpitations
  • Lightheadedness, syncope
  • Dyspnea, chest pain

• EKG: heart block
Early Disseminated Lyme: Cardiac

Lyme Carditis: Cardiac Abnormalities of Lyme Disease


We studied 20 patients, mostly young adult men, with cardiac involvement of Lyme disease. The commonest abnormality (18 patients) was fluctuating degrees of atrioventricular block; eight of them developed complete heart block. Thirteen patients had evidence of more diffuse cardiac involvement: electrocardiographic changes compatible with acute myopericarditis (11 patients), radionuclide evidence of mild left ventricular dysfunction (five of 12 patients tested), or frank cardiomegaly (one patient). Heart involvement was usually preceded by erythema chronicum migrans and sometimes accompanied by meningoencephalitis, facial palsy, arthritis, elevated serum IgM levels, or cryoglobulins containing IgM. The duration of cardiac involvement was usually brief (3 days to 6 weeks). The clinical picture in these patients has similarities to acute rheumatic fever; but in Lyme disease, complete heart block may be commoner, myopericardial involvement tends to be milder, and valves seem not to be affected.

Materials and Methods

Lyme disease was diagnosed in 19 of the 20 patients by the occurrence of erythema chronicum migrans. The lesion was defined by its gross appearance: a red macule or papule that expands to form a large annular lesion, usually with a bright red outer border and partial central clearing (2). Although one patient lacked this lesion, his remaining findings were like those of the other 19 patients.

Sixteen patients (one with onset of the illness in 1975, one in 1976, three in 1977, two in 1978, and nine in 1979) were studied prospectively through December 1979 according to the protocol outlined previously (2, 10). Patients with high-degree atrioventricular (AV) block were admitted to the coronary care unit for monitoring; those with first-degree block were usually treated as outpatients. Electrocardiograms and chest roentgenograms were obtained on all patients; M-mode echocardiograms and first-pass radionuclide angiocardiograms were done by previously described techniques (13-15), primarily on inpatients. At each visit, in addition to blood tests done on patients with all
Early Disseminated Lyme: Cardiac

When heart disease was present, 15 patients still had skin lesions, and 10 were febrile (37.8 ° to 39 °C). Also, seven patients had meningoencephalitis

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Early Disseminated Lyme: Cardiac

<table>
<thead>
<tr>
<th>Variable</th>
<th>Molins et al. (CDC Lyme Repository) (14)</th>
<th>Wormser et al. (15)</th>
<th>Branda et al. (12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early Lyme disease with EM†</td>
<td>% Sensitivity (no. tested)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute phase</td>
<td>40 (40)</td>
<td>38 (298)</td>
<td>42 (114)</td>
</tr>
<tr>
<td>Convalescent phase</td>
<td>61 (38)</td>
<td>27 (105)</td>
<td>57 (63)#</td>
</tr>
<tr>
<td>Noncutaneous manifestations</td>
<td>96 (46)</td>
<td>94 (142)</td>
<td>87 (55)</td>
</tr>
<tr>
<td>Early disseminated Lyme disease</td>
<td>88 (17)</td>
<td>80 (20)</td>
<td>73 (26)</td>
</tr>
<tr>
<td>Late disseminated Lyme disease</td>
<td>100 (29)</td>
<td>96 (122)</td>
<td>100 (29)</td>
</tr>
</tbody>
</table>

Disseminated infection (Stage 2)

- Acute neurologic or cardiac involvement
d

11/13 (85) 11/13 (85) 13/13 (100)

Various manifestations of Lyme disease, 39 patients with other illnesses (with or without a history of Lyme disease), and 136 healthy subjects from areas of endemicity and areas in which the infection was not endemic.
Notes from the Field

Health care providers should consider Lyme disease as a cause of cardiac symptoms in patients who live in or have visited a high-incidence Lyme disease region, especially during summer and fall months and regardless of whether the patient reports erythema migrans. Additionally, health care providers should investigate the potential for cardiac involvement in patients who have other signs or symptoms of Lyme disease, particularly if they report chest pain, palpitations, lightheadedness, shortness of breath, or syncope.

Atis Muehlenbachs, MD, PhD\textsuperscript{12}, Jana Ritter, DVM\textsuperscript{12}, Jeanine Sanders\textsuperscript{12}, Sherif R. Zaki, MD, PhD\textsuperscript{12}, Claudia Molins, PhD\textsuperscript{2}, Martin Schriefer, PhD\textsuperscript{2}, Anna Perea, MSc\textsuperscript{2}, Kiersten Kugeler, PhD\textsuperscript{2}, Christina Nelson, MD\textsuperscript{2}, Alison Hinckley, PhD\textsuperscript{2}, Paul Mead, MD\textsuperscript{2}
This sounds scary.
Do I need an EKG in all Lyme patients?

**XVIII. Should all patients with early Lyme disease receive an electrocardiogram to screen for Lyme carditis?**

**Recommendation:**

1. We suggest performing an ECG **only in patients with signs or symptoms consistent with Lyme carditis** (*weak recommendation, low-quality evidence*). **Comment:** Symptoms of cardiac involvement in Lyme disease include dyspnea, edema, palpitations, lightheadedness, chest pain, and syncope.
Lyme Carditis Management

1. Hospitalize?

- symptomatic arrhythmia (e.g. syncope)
- signs of myopericarditis (dyspnea, edema)
- advanced heart block
- PR interval >300ms
Lyme Carditis Treatment

Mild cases can reasonably be treated outpatient w/ PO antibiotics.

Most inpatients get IV ceftriaxone, though there is no evidence to support superiority over PO.

(they are then switched to once they have improved)

Duration of therapy is same as other forms of early Lyme (2-3 weeks)
Early Disseminated Lyme: Neurologic

Approximately three fourths (72.2%) of patients had erythema migrans; 27.5% had arthritis; and 1.5% had carditis, defined for surveillance purposes as acute second- or third-degree atrioventricular block. Approximately 12.5% had a neurologic manifestation.
Neuroborreliosis: Diagnosis

• Most have positive serology (~80%)
• Consider LP to evaluate meningitis symptoms
  • CSF will show moderate lymphocytic pleocytosis
• In some cases of diagnostic uncertainty (e.g. previously positive serology) can consider:
  • CSF antibody index (must draw concurrent serum)
Neuroborreliosis: Management

The Clinical Assessment, Treatment, and Prevention of Lyme Disease, Human Granulocytic Anaplasmosis, and Babesiosis: Clinical Practice Guidelines by the Infectious Diseases Society of America

Gary P. Wormser,1 Raymond J. Dattwyler,2 Eugene D. Shapiro,5,6 John J. Halperin,3,4 Allen C. Steere,9 Mark S. Klempner,10 Peter J. Krause,8 Johan S. Bakken,11 Franc Strle,13 Gerold Stanek,14 Linda Bockenstedt,7 Durland Fish,6 J. Stephen Dumler,12 and Robert B. Nadelman1

Divisions of 1Infectious Diseases and 2Allergy, Immunology, and Rheumatology, Department of Medicine, New York Medical College, Valhalla, and 3New York University School of Medicine, New York, New York; 4Atlantic Neuroscience Institute, Summit, New Jersey; Departments of 5Pediatrics and 6Epidemiology and Public Health and 7Section of Rheumatology, Department of Medicine, Yale University School of Medicine, New Haven, and 8Department of Pediatrics, University of Connecticut School of Medicine and Connecticut Children’s Medical Center, Hartford; 9Division of Rheumatology, Allergy, and Immunology, Massachusetts General Hospital, Harvard Medical School, and 10Boston University School of Medicine and Boston Medical Center, Boston, Massachusetts; 11Section of Infectious Diseases, St. Luke’s Hospital, Duluth, Minnesota; 12Division of Medical Microbiology, Department of Pathology, The Johns Hopkins Medical Institutions, Baltimore, Maryland; 13Department of Infectious Diseases, University Medical Center, Ljubljana, Slovenia; and 14Medical University of Vienna, Vienna, Austria
Neuroborreliosis: Management

Lyme meningitis and other manifestations of early neurologic Lyme disease. The use of ceftriaxone (2 g once per day intravenously for 14 days; range, 10–28 days) in early Lyme disease is recommended for adult patients with acute neurologic disease manifested by meningitis or radiculopathy (B-I). Parenteral therapy with cefotaxime (2 g intravenously every 8 h) or penicillin G (18–24 million U per day for patients with normal renal function, divided into doses given every 4 h), may be a satisfactory alternative (B-I). For patients who are intolerant of β-lactam antibiotics, increasing evidence indicates that doxycycline (200–400 mg per day in 2 divided doses orally for 10–28) days may be adequate (B-I). Doxycycline is well absorbed orally; thus, intravenous administration should only rarely be needed.
Neuroborreliosis: Management

Lyme meningitis and other manifestations of early neuroborreliosis. There was agreement that lumbar puncture is indicated for those in whom there is strong clinical suspicion of CNS involvement (e.g., severe or prolonged headache or nuchal rigidity). Patients with normal CSF examination findings and those for whom CSF examination is deemed unnecessary because of lack of clinical signs of meningitis may be treated with a 14-day course (range, 14–21 days) of the same antibiotics used for patients with erythema migrans (see above) (B-III). Those with both clinical and laboratory evidence of CNS involvement should be treated with regimens effective for Lyme meningitis, as described above (B-III).

*Division of Medicine, New York School of Medicine, Valhalla, NY; \(^{17}\)Division of Medicine, University of Vermont, Burlington, VT*
Oral doxycycline versus intravenous ceftriaxone for European Lyme neuroborreliosis: a multicentre, non-inferiority, double-blind, randomised trial

Unn Ljøstad, Eirik Skogvoll, Randi Eikeland, Rune Midgard, Tone Skarpaas, Åse Berg, Åse Mygland

Summary

Background Use of intravenous penicillin and ceftriaxone to treat Lyme neuroborreliosis is well documented, although oral doxycycline could be a cost-effective alternative. We aimed to compare the efficacy of oral doxycycline with intravenous ceftriaxone for the treatment of Lyme neuroborreliosis.

Methods From April, 2004, to October, 2007, we recruited consecutive adult patients from nine hospitals in southern Norway into a non-inferiority trial. Inclusion criteria were neurological symptoms suggestive of Lyme neuroborreliosis without other obvious causes, and presence of any of the following: a CSF white-cell count of more than five per mL; intrathecal production of specific Borrelia burgdorferi antibodies; or acrodermatitis chronica atrophicans. Patients were randomly allocated to receive 200 mg oral doxycycline or 2 g intravenous ceftriaxone once per day for 14 days, in a double-blind, double-dummy design. A composite clinical score (range 0 to 64, 0=best) was based on standardised interviews and clinical neurological examination. The primary outcome was reduction in clinical score at 4 months after the start of treatment. Analysis was per protocol. This trial is registered with ClinicalTrials.gov, number NCT00138801.
XIV. What are the preferred antibiotic regimens for the treatment of acute neurologic manifestations of Lyme disease without parenchymal involvement of the brain or spinal cord?

Recommendation:

Since the recommended treatment for neuroborreliosis may be the same whether meningitis is present or not, the decision to perform a CSF examination must be individualized.

Penicillin, or oral doxycycline, over other antimicrobials (strong recommendation, moderate-quality evidence).

IDSA/AAN/ACR 2019 Draft Lyme Disease Guidelines
Draft - Do Not Distribute
Steroids In Facial Palsy?

Steroid Use in Lyme Disease-Associated Facial Palsy Is Associated With Worse Long-Term Outcomes

Nate Jowett, MD; Robert A. Gaudin, MD; Caroline A. Banks, MD; Tessa A. Hadlock, MD

Objective: The purpose of this study was to determine whether differences in long-term facial function outcomes following acute Lyme disease-associated facial palsy (LDFP) exist between patients who received antibiotic monotherapy (MT); dual therapy (DT) with antibiotics and corticosteroids; and triple therapy (TT) with antibiotics, corticosteroids, and antivirals.

Study Design: Retrospective cohort.

Methods: All patients with a prior diagnosis of unilateral LDFP who presented to our center between 2002 and 2015 were retrospectively assessed for inclusion. Two blinded experts graded static, dynamic, and synkinesis parameters of facial functions using standardized video documentation of facial function.

Results: Fifty-one patients were included. The mean time of assessment following LDFP onset was 15.1 months (range 0.3–84 months). Significantly worse facial outcomes were seen among those who received DT and TT as compared to those who received MT, most pronounced among those assessed 12 months or later following onset of LDFP (Dynamic—$P = 0.031$, post hoc MT vs. TT: mean difference [MD], 15.83; 95% confidence interval [CI], 1.54–30.13; $P = 0.030$. Synkinesis—$P = 0.026$, post hoc MT vs. DT: MD, 21.50; 95% CI, 0.68–42.32; $P = 0.043$, post hoc MT vs. TT: MD, 19.22; 95% CI, 2.23–36.22; $P = 0.027$).

Conclusion: An association between corticosteroid use in acute LDFP and worse long-term facial function outcomes has been demonstrated. Care should be taken in differentiating viral or idiopathic facial palsy (e.g., Bell palsy) from LDFP.

Key Words: Corticosteroids, Lyme disease, facial paralysis, synkinesis, outcomes, glucocorticoids, prednisone, neuroborreliosis, facial palsy, facial nerve, Borrelia burgdorferi, facial spasm, nerve regeneration.

Level of Evidence: 4.

Laryngoscope, 127:1451–1458, 2017