Clinical Management and Outcomes of Lyme Disease in Wisconsin

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Marshfield, WI

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Background

• Lyme disease (LD)
  – Caused by spirochete *Borrelia burgdorferi*
  – Transmitted in US by *Ixodes scapularis* and *I. pacificus* ticks
  – Nationally-notifiable

• Wisconsin 7th highest LD incidence in US from 1992-1998
  – (9.5 cases/100,000)

• Little is known regarding LD management practices and outcomes in the midwestern United States
Objectives

- Describe LD serologic testing and treatment in WI
- Identify temporal changes in clinical management of LD
- Assess clinical outcomes
Marshfield and Mayo-Midelfort Clinic Network

• Marshfield Clinic
  – 450 physician multispecialty practice
  – regional centers in 31 central and northwest WI communities
  – fee-for-service and capitated care

• Mayo-Midelfort Clinic
  – multispecialty practice with >140 physicians
  – main campus in Eau Claire with regional centers in surrounding counties

• Representative of most ambulatory practice settings in WI
Methods: Case Ascertainment

- Clinical databases are linked between all outlying clinics and main clinic
- Databases include ICD-9 diagnoses on all patients
- Computerized search of diagnosis files between 1992-1998
- ICD-9 codes consistent with LD (088.81, 695.9, 066.9)
- Abstraction of corresponding medical charts
Medical Record Abstraction for LD-Related Illness

• Patient demographics
• Signs and symptoms
• Diagnostic testing
• Treatment
• Clinical outcomes
National LD Surveillance Case Definition

• Clinical criteria
  • Erythema migrans, or
  • At least one late manifestation and laboratory confirmation of infection

• Laboratory criteria for diagnosis
  • Isolation of *Borrelia burgdorferi* from clinical specimen, or
  • Demonstration of diagnostic levels of IgM or IgG antibodies to the spirochete in serum or CSF, or
  • A significant change in antibody levels in paired acute and convalescent serum samples
LD Case Classification

- **Probable (EM or Late LD)**
  - Met national surveillance case definition for EM or late LD

- **Possible (EM or Late LD)**
  - EM documented but size ≤ 5cm or unspecified
  - Positive LD serologic test with recurrent arthralgias or neurologic manifestations not meeting the probable case definition

- **Not LD**
  - Illness meeting neither of above criteria
Outcome Classification

- Medical record reviewed up to three years after initial visit to ascertain clinical outcome
  - ‘complete resolution’
    - No mention of LD at last clinic visit
  - ‘persistent LD symptoms’
    - LD mentioned at last clinic visit
  - ‘insufficient information’
    - No follow-up after initial clinic visit
Results: Patient Classification

N = 1,180

Not LD
569 (48%)

LD*
611 (52%)

Late LD
204 (33%)

EM
407 (67%)

Probable EM
300 (74%)

Possible EM
107 (26%)

Probable Late LD
68 (33%)

Possible Late
136 (67%)

*All LD patients: 56% male; median age = 37
Frequency of Serologic Testing Among Patients With EM

![Graph showing frequency of serologic testing among patients with EM.]

- Probable EM: 236/300 (79%) tested
- Possible EM: 73/107 (68%) tested
Frequency of Serologic Testing Among Patients With Late LD

Probable Late LD: 67/68 (99%) tested
Possible Late LD: 136/136 (100%) tested
Proportion of Patients with $\geq 4$ Serologic Tests

<table>
<thead>
<tr>
<th>Patient classification</th>
<th>Year of diagnosis</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1992-95</td>
<td>1996-98</td>
</tr>
<tr>
<td>Probable EM</td>
<td>12%</td>
<td>13%</td>
</tr>
<tr>
<td>Probable Late LD</td>
<td>52%</td>
<td>34%</td>
</tr>
<tr>
<td>Not LD</td>
<td>9%</td>
<td>22%</td>
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Antimicrobial Use

• The most frequently prescribed antimicrobials for initial therapy
  – Doxycycline
  – Amoxicillin
  – Ceftriaxone

• Patients without LD
  – 94% received antimicrobials
  – 29% received multiple courses

• No temporal changes in proportion of patients receiving multiple courses of antimicrobials
Limitations

• Study based on medical record abstraction
  – Visits possibly missed due to patients seeking care in other systems
  – Inconsistent documentation of signs and symptoms in medical records
  – Variation in scheduled patient follow-up
  – Temporal changes in accepted testing methods
Conclusions

• Serologic testing was common among patients with EM
  – empiric therapy recommended (Ann Int Med 1997; 127, 1106-1108)

• There was a temporal increase in patients without LD who had ≥4 serologic tests
  – Decreasing number of tests for patients with late LD

• Recommended drugs are used for LD therapy (Clin Inf Dis 2000; 31, Supp. 1, S1-S14)
  – but they are often given to patients without LD

• The majority of patients have complete resolution of LD symptoms
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Acknowledgements

- Marshfield Clinic
  - Catherine Grimm
  - Nita Herr
  - Deborah Hilgemann
  - Deborah Kempf
  - Donna Wittman
  - Sonia Weigel
  - Lorelle Ziegelbauer

- Mayo-Midelfort Clinic
  - Londa Dahnke
  - Peggy Munden
  - Robert Noyce, MD
## Patient Demographic Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Not LD</th>
<th>EM</th>
<th>Late LD</th>
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<tbody>
<tr>
<td>Age (median)</td>
<td>41 years</td>
<td>36 years</td>
<td>41 years</td>
</tr>
<tr>
<td>% Male</td>
<td>51%</td>
<td>56%</td>
<td>60%</td>
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### Multiple-course (≥2) Antimicrobial Therapy: Temporal Analysis

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<tbody>
<tr>
<td></td>
<td>1992-95</td>
<td>1996-98</td>
<td>p</td>
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<tr>
<td>Probable EM</td>
<td>19%</td>
<td>13%</td>
<td>0.16</td>
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<tr>
<td>All EM</td>
<td>21%</td>
<td>14%</td>
<td>0.10</td>
</tr>
<tr>
<td>Probable Late LD</td>
<td>63%</td>
<td>57%</td>
<td>0.65</td>
</tr>
<tr>
<td>All Late LD</td>
<td>53%</td>
<td>56%</td>
<td>0.55</td>
</tr>
<tr>
<td>Not LD</td>
<td>28%</td>
<td>31%</td>
<td>0.51</td>
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Late manifestations of LD

• Musculoskeletal System: Recurrent, brief attacks of objective joint swelling in or a few joints.
• Nervous System: Lymphocytic meningitis, cranial neuritis (especially facial palsy), radiculoneuropathy or, rarely encephalomyelitis alone or in combination
• Cardiovascular System: Acute onset, high grade (2\textsuperscript{nd} or 3\textsuperscript{rd} degree) atrioventricular defects that resolve in days or weeks and are sometimes associated with myocarditis
Comparision of Results With Other Studies

- Published studies from other endemic settings
  - MC Reid et.al., 1998: New England
  - LH Sigal et.al., 1990: Mid-Atlantic
Reported Cases of Lyme Disease - United States, 1982-2000

Cases (thousands)

- 1982: 0.5
- 1984: 1.0
- 1986: 1.5
- 1988: 2.0
- 1990: 2.5
- 1992: 3.0
- 1994: 4.0
- 1996: 5.0
- 1998: 6.0
- 2000: 18.0

CDC
Demographic Characteristics of Patients with EM

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Demographic Characteristics of Patients with Late LD

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<tr>
<td>% Male</td>
<td>40%</td>
<td>52%</td>
<td>48%</td>
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Serologic Tests Performed for Patients With Late LD
(n = 404 tests)
Proportion of Patients Receiving Any Antimicrobial Therapy

<table>
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<th>Proportion</th>
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<tbody>
<tr>
<td>All EM (n=407)</td>
<td>99%</td>
</tr>
<tr>
<td>All Late LD (n=204)</td>
<td>99%</td>
</tr>
<tr>
<td>Not LD (n=569)</td>
<td>94%</td>
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