Tick Borne Diseases in Wisconsin: Clinical Update and Practice Pearls

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Objectives

• Appropriately recognize and diagnose Lyme disease

• Recognize common and uncommon clinical manifestations of Anaplasmosis

• Recognize at-risk patients and clinical manifestations of Babesiosis
A Turkey Hunter with a Fever
Tickborne Infections as a Cause of Nonspecific Febrile Illness in Wisconsin

Edward A. Belongia,¹ Kurt D. Reed,¹ Paul D. Mitchell,¹ Nancy Mueller-Rizner,¹ Mary Vandermause,¹ Michael F. Finkel,² and James J. Kazmierczak³

¹Marshfield Medical Research Foundation and Marshfield Clinic, Marshfield, ²Mayo-Midelfort Clinic, Eau Claire, and ³Wisconsin Division of Public Health, Madison, Wisconsin

• 27% of patients seen in urgent care with a Spring/Summer non-specific febrile illness in northwest Wisconsin had lab evidence of a tick-borne infection

CID 2001;32:1434
Lyme (aka Medford???) Disease
Lyme Disease in North America was First Described in Wisconsin!

- Dr. Rudolph Scrimenti, dermatologist, Milwaukee, published a case in 1970
- 57-year-old physician with erythema migrans was successfully treated with Penicillin G in Milwaukee in 1969
Reported Cases of Lyme Disease -- United States, 2001

1 dot placed randomly within county of residence for each reported case

Reported Cases of Lyme Disease -- United States, 2003

1 dot placed randomly within county of residence for each reported case

Reported Cases of Lyme Disease -- United States, 2005

Reported Cases of Lyme Disease -- United States, 2010

1 dot placed randomly within county of residence for each confirmed case

Lyme Disease Pearl: Most EM rashes are not a classic “target” rash
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Early Disseminated Lyme Facial Palsy
If it seems like severe zoster neuropathy, but no rash: Consider Lyme disease

- 61-year-old male with severe abdominal flank pain: Dx: CT negative diverticulitis/zoster sine zoster
- 36-year-old teacher with fever & severe abdominal pain: Dx: Appendicitis (pathology normal)
- 59-year-old admitted to the hospital for suspected “abdominal catastrophe”

- “Bannwarth’s syndrome”
- Acute Lyme radiculitis
- Pain may be severe!
- Hard to diagnose, because not considered
- Keys: Exposure history, serologic testing (acute and convalescent)
Early Disseminated Lyme Carditis
Late Lyme Arthritis
Late Lyme Arthritis
Know how to use Lyme serologic testing!

- 6/17/12: Fever, headache, oval rash with punctum. Lyme screening assay negative
- 7/8/12: Disseminated ECM: Doxycycline for 21 days
- 8/11/12: Sore throat. Lyme screen positive, Lyme Western blot positive for IgM. Retreated and ID consult
Serologic testing is poor for early disease but very good for early disseminated and late disease.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Proportion (% of patients with positive result, by test(s)</th>
<th>Sonicate 2-test approach</th>
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<tbody>
<tr>
<td></td>
<td>VlsE C6 peptide ELISA</td>
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<td>Patients with Lyme disease</td>
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<tr>
<td>Erythema migrans without evidence of disseminated disease</td>
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<td></td>
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<tr>
<td>Acute</td>
<td>7/36 (19)</td>
<td>4/36 (11)(^{a})</td>
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<tr>
<td>Convalescent, after antibiotics</td>
<td>17/36 (47)</td>
<td>14/36 (39)(^{a})</td>
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<td>Erythema migrans with evidence of disseminated disease(^c)</td>
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<td></td>
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<tr>
<td>Acute phase</td>
<td>15/40 (38)</td>
<td>15/40 (38)(^{a})</td>
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<tr>
<td>Convalescent phase (after receipt of antibiotics)</td>
<td>25/40 (63)</td>
<td>28/40 (70)(^{a})</td>
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<tr>
<td>Disseminated infection (stage 2)</td>
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<td></td>
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<tr>
<td>Acute neurologic or cardiac involvement(^d)</td>
<td>13/13 (100)</td>
<td>11/13 (85)</td>
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<tr>
<td>Persistent infection (stage 3)</td>
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<td></td>
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<td>Arthritis or chronic neurologic involvement(^e)</td>
<td>31/31 (100)</td>
<td>7/31 (23)</td>
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Clinical Infectious Diseases 2008;47:188–195
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Lyme serology screens have a specific and somewhat limited role!

- Do not use if patient has EM rash (adds nothing but confusion)
- Do not use to routinely follow-up on positive tests
- Do not use to test patients with years of chronic subjective musculoskeletal complaints
- Do not use just because patient requests it
DO use Lyme serologic testing for at risk patients...

- with a systemic febrile illness (**BUT EXAMINE SKIN FIRST!**)
- with objective evidence of early disseminated or late disease (heart block, aseptic meningitis, facial palsy, etc.)
- 3 weeks after a negative acute test in patients with a reasonable chance of having acute Lyme disease
Lyme disease: Undertreated early, over-treated late?
Lyme Disease Treatment

• **Prevention**: Doxycycline 200 mg x 1 after bite by an *Ixodes scapularis* tick

• **Early Disease (EM)**: Doxycycline 100 mg twice daily x 10 days

• **Early Disseminated Disease**: (Facial Palsy, Carditis, Disseminated EM, etc): Doxycycline x 14-21 days
Lyme Disease Treatment

• **Late Disease (arthritis):** Doxycycline x 28 days
  – Ceftriaxone for severe/persistent

• **Neurologic disease:** Doxycycline 100-200 mg twice daily vs. Ceftriaxone 2 G IV depending on severity

• **Doxycycline intolerant:** Amoxicillin or Cefuroxime >>> Azithromycin

Oral Antibiotics Are Effective For Lyme Facial Nerve Palsy

Lyme Facial Nerve Palsy
Matched Cohort

IDSA Annual Meeting, Vancouver, 10/2010
“Treatment failure” is Exceedingly Rare

![Graph showing treatment failure-free survival](image-url)

*P* = .660

- **Solid line**: 3 to 10 days
- **Dashed line**: 11 to 15 days
- **Dotted line**: Greater than 15 days

*Clinical Infectious Diseases 2010;50:512–520*
Culture-Confirmed Infection and Reinfection with *Borrelia burgdorferi*

John Nowakowski, MD; Ira Schwartz, PhD; Robert B. Nadelman, MD; Dionysios Liveris, PhD; Maria Aguero-Rosenfeld, MD; and Gary P. Wormser, MD

Re-infection, not “relapse”, commonly occurs in endemic areas
A Word on “Chronic Lyme Disease”

• Some clinicians utilize alternative diagnostic and treatment paradigms for Lyme disease
• “Lyme literate” MDs
• Int’l Lyme and Associated Diseases Society (ILADS) are the public face of this group
• Advocate for an entity called “chronic Lyme disease” in the absence of objective findings
• Prescribe prolonged courses of oral and IV antibiotics to treat “chronic Lyme disease”
Dispute spreads on how to treat Lyme disease

SHAWN DOHERTY | The Capital Times | sdoheraty@madison.com | (25) Comments | Posted: Wednesday, June 30, 2010 7:10 am

When she first got sick, Della Haugen figured she was just tired. It was spring 2008 and she’d been working overtime as a photojournalist for WISC-TV/Channel 3 in Madison, covering flooding in the Wisconsin Dells. But then her symptoms got worse — much worse. Joint pain. Dizziness. Headaches. Muscle weakness. Night sweats so bad, she had to change her sheets. And weird bruises all over her body. Her doctor told her she had the flu.

One sleepless night, Haugen, 36, found a hitchhiker in her bed: a tiny tick. She flushed it down the toilet, realizing too late that she may have destroyed key evidence. Haugen visited her doctor, who diagnosed her with Lyme disease.
The Problem: Missed Diagnoses

- Juvenile rheumatoid arthritis (Still’s disease)
- Bipolar disorder
- Polymyalgia rheumatica/Temporal arteritis
- Paraneoplastic polyneuropathy from lung cancer
- Rheumatoid arthritis
The Problem: Ecologic Costs

Antibiotics: Will they work when you really need them?
The Problem: Cost

<table>
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<th>Antibiotic Therapy</th>
<th>Outpatient Cost</th>
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<tr>
<td>Doxycycline 100 mg orally 2X daily x 4 weeks</td>
<td>$6</td>
</tr>
<tr>
<td>Ceftriaxone 2 G IV daily x 4 weeks</td>
<td>$5528</td>
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The Problem: Direct Treatment Associated Adverse Events
The Problem: Direct Treatment Associated Adverse Events

Death Due to Community-Associated *Clostridium difficile* in a Woman Receiving Prolonged Antibiotic Therapy for Suspected Lyme Disease

To the Editor—*Clostridium difficile* infections can occur outside the hospital in association with antibiotic use and can result in fulminant colitis and death. In December 2009, the Minnesota Department of Health investigated a death due to *C. difficile* of a 52-year-old woman with no recent hospitalizations.
Final Report of the Lyme Disease Review Panel of the Infectious Diseases Society of America (IDSA)

• Review Panel whose task was to determine whether the 2006 IDSA Lyme guidelines were based on sound medical/scientific evidence and whether these guidelines required change
• 8 unbiased medical reviewers were chosen to serve
Final Report of the Lyme Disease Review Panel of the Infectious Diseases Society of America (IDSA)

- Process was conducted over 14 months
- Hearings held 7/30/2009
- 65 page final report issued April, 2010
- 1025 references (not inclusive of all of the sources reviewed)
The Verdict

- **OVERWHELMING** endorsement of IDSA guideline recommendations
- 535 votes to endorse vs. 1 vote of dissent
- Only high quality prospective clinical trials demonstrating both benefit and safety of prolonged antibiotic therapy will be sufficient to change the guidelines
A Turkey Hunter with a Fever
Identification of a Granulocytotropic *Ehrlichia* Species as the Etiologic Agent of Human Disease

SHENG-MIN CHEN,¹ J. STEPHEN DUMLER,² JOHAN S. BAKKEN,³ AND DAVID H. WALKER¹*

*Department of Pathology, University of Texas Medical Branch, Galveston, Texas 77555¹; Department of Pathology, University of Maryland School of Medicine, Baltimore, Maryland 21201²; and Duluth Clinic, Duluth, Minnesota 55805³*

Received 21 October 1993/Returned for modification 9 November 1993/Accepted 24 November 1993

- Human Granulocytic Ehrlichiosis was first described in a patient from NW WI in 1990
- Renamed Human Granulocytic Anaplasmosis, caused by Anaplasma phagocytophila
Expansion of the Midwestern Focus for Human Granulocytic Anaplasmosis into the Region Surrounding La Crosse, Wisconsin

Steven D. Lovrich,¹ Dean A. Jobe,¹ Todd J. Kowalski,² Seema M. Policepatil,³ and Steven M. Callister¹,2*
Ehrlichia/Anaplasma Disease Incidence, WI 2007
Cases per 100,000 population

Annual Incidence per 100,000
Total number represents confirmed and probable cases

County shading represents 2007 incidence rate among county residents

Wisconsin River
Anaplasmosis

- Carried by the same tick vector (Ixodes species)
- Leukopenia with a left shift (≈40%)
- Thrombocytopenia (≈66%)
- Liver transaminitis (≈50%)
- If clinical and lab profile fits, TREAT!
Anaplasmosis: Diagnostic Challenges

• May see on peripheral smear (<50% sensitive)
• PCR to diagnose if symptoms <7 days (≈60-70% sensitive?)
• Serology to diagnose if symptoms >7 days
• If clinical and lab profile fits, TREAT!
“Typical” Anaplasmosis Patient

- Tick exposure
- Fever, headache, myalgias
- Suggestive lab findings
- RAPID and APPRECIATED response to doxycycline (10 day course recommended)
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- If clinical and lab profile fits, TREAT!
“Atypical” Anaplasmosis Patients

• GI predominant illness
• Pneumonia/pulmonary infiltrates
• Sepsis syndrome
• Sub-acute febrile illness lasting weeks

Severe Human Granulocytic Anaplasmosis Transmitted by Blood Transfusion

Matjaz Jereb, Blaz Pecaver, Janez Tomazic, Igor Muzlovič, Tatjana Avsic-Zupanc, Tanja Premru-Srsen, Snežna Levicnik-Stezinar, Primoz Karner, and Franc Strle

A 36-year-old woman acquired severe human granulocytic anaplasmosis after blood transfusion following a cesarean section. Although intensive treatment with mechanical ventilation was needed, the patient had an excellent recovery. Disease caused by Anaplasma phagocytophilum infection was confirmed in 1 blood donor and in the transfusion recipient.
Emergence of a New Pathogenic Ehrlichia Species, Wisconsin and Minnesota, 2009

Ehrlichia-muris-Like strain

• 2.4% of Ixodes ticks infected with E. muris-like strain in this study conducted in Minnesota and Wisconsin (near Eau Claire)

• 4 patients described with apparent infection (2 were immunosuppressed)
  – Responded to doxycycline therapy

• E. muris also reported from Ixodes ticks near Spooner in 1990s
Prevalence of pathogenic microbes in *Ixodes* ticks near La Crosse, WI

- *Borrelia burgdorferii* 39%
- *Anaplasma phagocytophila* 14%
- *Babesia microti* 5%
- *Ehrlichia muris-like agent* 1.5%
Fever in an Asplenic Turkey Hunter
Reported Confirmed Babesiosis, Wisconsin 2000–2011

(N=93)

Year of Onset

Cases


Babesiosis made notifiable in WI - 2001

www.dhs.wisconsin.gov/communicable/.../BabesiosisMorbidityData.pdf
Confirmed babesiosis cases by county of likely exposure, Wisconsin 2007–2011 (n=93)

Unknown = 52
Babesiosis: A Potentially Fatal Disease

- *Babesia microti* is the primary agent of disease in US
- Protozoan RBC parasite
- Systemic febrile illness with hemolytic anemia
- At risk patients:
  - Asplenic patients
  - Immune-compromised patients
  - Elderly
Babesiosis Diagnosis: Smear or PCR
Complications of Severe Babesiosis

- ARDS
- Renal failure
- DIC
- Congestive heart failure
- Splenic rupture
Babesiosis: Treatment

- **NOT** Doxycycline!
- Atovaquone/Azithromycin or Clindamycin/Quinine
- For severe disease: consider RBC exchange
Transfusion-Associated Babesiosis: Shouldn’t We Be Ticked Off?
Conclusions

• Wisconsin is a historically important hotbed of tick-borne diseases

• Treat ECM and variant ECM, and be aware of the pitfalls of serologic diagnoses of Lyme disease

• Consider anaplasmosis and babesiosis in the work-up of febrile patients during the tick season in Wisconsin
Thank-you!