I’ll have mine with a twist of Lyme: Lyme disease in the Dairy State.

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I have no financial disclosures relevant to this presentation.

I will reference non–FDA approved indications for medications during this presentation.
Case 1

- 16 year old male developed heart palpitations 4 days PTA.
- 1 day PTA felt fatigued and had mild chest pain, rash on shoulders
- Day of admission, lightheaded nearly to the point of fainting

- To ED: HR 63
Case 1

Photo: Parker Schimler

Google Maps
Case 1

- Lyme Elisa antibody screen – positive
- Confirmatory Western Blot
  - IgM – 3 of 3 bands (2 of 3 positive)
  - IgG – 9 of 10 bands (5 of 10 positive)

- Diagnosis – Lyme carditis with complete heart block

- Treatment – IV ceftriaxone 14 days
This map is based on the county of residence of confirmed cases. Some infections may have been acquired during travel to other areas.

Revised 04/28/2017  Data Source: Wisconsin Division of Public Health
Confirmed Lyme Disease Cases
Reported by Age Group – Wisconsin 2016 (n=1,491)

Source: Wis Div Health
Manifestations of Lyme Disease

- **Early Localized**
  - Erythema migrans
    - Single
  - Other symptoms
    - Fatigue – 54%
    - Anorexia – 26%
    - Neck Stiffness – 35%
    - Myalgias – 44%
    - Arthralgia – 44%
    - Adenopathy – 23%
    - Fever – 16%

- **Early Disseminated**
  - Multiple EM lesions
  - Cranial nerve VII palsy
  - Aseptic meningitis
  - Carditis
  - Ocular

- **Late**
  - Arthritis
    - Pauciarticular
    - Large joints (Knee!)
  - Neurologic disease

## Treatment of Lyme Disease

<table>
<thead>
<tr>
<th>Indication</th>
<th>Treatment</th>
<th>Duration, days (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tick bite in the United States</td>
<td>Doxycycline, 200 mg in a single dose, (4 mg/kg in children ≥8 years of age) and/or observation</td>
<td>...</td>
</tr>
<tr>
<td>Erythema migrans</td>
<td>Oral regimen</td>
<td>14 (14–21) e</td>
</tr>
<tr>
<td>Early neurologic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis or radiculopathy</td>
<td>Parenteral regimen</td>
<td>14 (10–28)</td>
</tr>
<tr>
<td>Cranial nerve palsy</td>
<td>Oral regimen</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Cardiac disease</td>
<td>Oral regimen or parenteral regimen</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Borreliotic lymphocytoma</td>
<td>Oral regimen</td>
<td>14 (14–21)</td>
</tr>
<tr>
<td>Late disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis without neurologic disease</td>
<td>Oral regimen</td>
<td>28</td>
</tr>
<tr>
<td>Recurrent arthritis after oral regimen</td>
<td>Oral regimen or parenteral regimen</td>
<td>14 (14–28)</td>
</tr>
<tr>
<td>Antibiotic-refractory arthritis</td>
<td>Symptomatic therapy</td>
<td>...</td>
</tr>
<tr>
<td>Central or peripheral nervous system disease</td>
<td>Parenteral regimen</td>
<td>14 (14–28)</td>
</tr>
<tr>
<td>Acrodermatitis chronica atrophicans</td>
<td>Oral regimen</td>
<td>21 (14–28)</td>
</tr>
<tr>
<td>Post-Lyme disease syndrome</td>
<td>Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy</td>
<td>...</td>
</tr>
</tbody>
</table>
Table 2. Recommended antimicrobial regimens for treatment of patients with Lyme disease.

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosage for adults</th>
<th>Dosage for children</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Preferred oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>500 mg 3 times per day&lt;sup&gt;a&lt;/sup&gt;</td>
<td>50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose)&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>100 mg twice per day&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Not recommended for children aged &lt;8 years For children aged ≥8 years, 4 mg/kg per day in 2 divided doses (maximum, 100 mg per dose)</td>
</tr>
<tr>
<td>Cefuroxime axetil</td>
<td>500 mg twice per day</td>
<td>30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose)</td>
</tr>
<tr>
<td><strong>Alternative oral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selected macrolides&lt;sup&gt;c&lt;/sup&gt;</td>
<td>For recommended dosing regimens, see footnote d in table 3</td>
<td>For recommended dosing regimens, see footnote in table 3</td>
</tr>
<tr>
<td><strong>Preferred parenteral regimen</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ceftriaxone</td>
<td>2 g intravenously once per day</td>
<td>50–75 mg/kg intravenously per day in a single dose (maximum, 2 g)</td>
</tr>
<tr>
<td><strong>Alternative parenteral regimens</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cefotaxime</td>
<td>2 g intravenously every 8 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day)&lt;sup&gt;d&lt;/sup&gt;</td>
</tr>
<tr>
<td>Penicillin G</td>
<td>18–24 million U per day intravenously, divided every 4 h&lt;sup&gt;d&lt;/sup&gt;</td>
<td>200,000–400,000 U/kg per day divided every 4 h&lt;sup&gt;d&lt;/sup&gt; (not to exceed 18–24 million U per day)</td>
</tr>
</tbody>
</table>

<sup>a</sup> Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.

<sup>b</sup> Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.

<sup>c</sup> Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.

<sup>d</sup> Dosage should be reduced for patients with impaired renal function.
Antibiotic prophylaxis after tick bite

- Overall risk low - 1–3%
- Lack of data on amoxicillin
- Testing tick has poor predictability
- Most exposures do not require prophylaxis

IDSA Recommendations for single dose doxycycline
- Children ≥ 8 yrs
- *I. scapularis* tick
- Attached ≥ 36hrs
- Abx with 72 hr of removal
- ≥ 20% of ticks infected
- Doxy not contraindicated
Ixodes scapularis

Deer Tick
Bear Tick
Black Legged Tick

Diseases
- Borrelia burgdorferi
- Borrelia miyamotoi
- Borrelia mayonii
- Babesia microti
- Powassan virus
- Anaplasma phagocytophilum
- Ehrlichia muris

Slide courtesy of Dr. Alana Sterkel WSLH and Tick Encounter Resource center CDC
Dermacentor variabilis

- Wood Tick
- Dog Tick

Diseases
- Rocky mountain spotted fever
- Colorado tick fever
- Tularemia

Slide courtesy of Dr. Alana Sterkel WSLH. And Tick Encounter Resource center CDC
Lyme Caveats

- If first test ambiguous, repeat in ≥ 2 weeks
- False positive IgM common (2 bands)
- Do not test for vague, ill defined symptoms (fatigue, body aches)
- Most ticks are wood ticks
- Micro-epidemiology important
- Consider co-infection
- Doxycycline at any age >> amoxicillin
- Evidence is against long term abx (>30 days)
- Lyme not Lyme’s
Questions / Discussion
Wisconsin Ehrlichia/Anaplasma Annual Incidence
2016 (n=694)

Statewide Incidence = 12.03/100,000

Incidence per 100,000 (confirmed and probable cases)
- <1
- 1-15
- 16-30
- 31-60
- 61-90
- 91-120
- >120

This map is based on the county of residence. Some infections may have been acquired during travel to other areas.

Data Source: Wisconsin Division of Public Health

Revised 4/27/2017
Wisconsin Total Cases of Anaplasmosis/Ehrlichiosis Reported by Age 2008-2016 (n=4,378)

*Total Number of cases include confirmed and probable
Data Source: Wisconsin Division of Public Health
Revised 05/02/2017
Reported incidence rate* of *Ehrlichia chaffeensis* ehrlichiosis, by county — United States, 2000–2013
Reported incidence rate* of anaplasmosis, by county — United States, 2000–2013
Anaplasmosis/Ehrlichiosis

- Clinical manifestations
  - Fever
  - Headache
  - Malaise
  - Myalgia
  - Nausea/vomiting/diarrhea
  - Rash (Ehrlichia)
  - ARDS
  - Encephalopathy
  - Meningitis
  - DIC
  - Renal failure

- Lab/diagnosis
  - Leukopenia
  - Thrombocytopenia
  - Increased ALT/AST
  - PCR – serum/csf
  - Serology – acute and convalescent
  - Peripherial smear – morulae
Anaplasmosis/Ehrlichiosis

- **Doxycycline**
  - 4.4 mg/kg/day divided every 12 hours
  - Maximum/adult dose 100mg/dose
  - 7–14 days
  - If dx suspected should be used regardless of age
Babesiosis

- Agent: *Babesia microti*
  - Intraerythrocytic protozoa
  - “homegrown malaria”

- Vector – deer tick (*Ixodes scapularis*)

- Reservoir – white footed mouse (not deer)
Babesiosis

- Malaise, fatigue, fever
- Chills/sweats, arthralgia, myalgia,
- Hypotension, respiratory distress, organomegally, jaundice
- Anemia, thrombocytopenia, DIC.
- Normal host or immunocompromised – esp asplenic
Babesiosis

- **Diagnosis**
  - Blood smear
  - Serology
  - Serum PCR

- **Treatment**
  - Clindmycin + quinine
  - Atovaquone + azithromycin

Image: US CDC
Reported Confirmed Babesiosis, Wisconsin 2000–2016

Source WI DHS
Confirmed Babesiosis, Wisconsin, 2012-2016
County of Likely Exposure (n=223)

Source WI DHS
Case 3

- 14 year old male 2 weeks prior sore throat and lump on neck
- 1 day later purple rash on palms, then arms and legs
- Fever to 103.5
- Seen in urgent care, RST, CBC normal
- 2 days later headache and bilateral red eyes
- NO significant travel or exposures
- Southcentral WI rural subdivision
Case 3

- Exam
  - Afebrile
  - Conjunctival injection bilateral
  - Rash on extremities
Case 3

- Started by PCP on doxycycline over concern for ricketsial infection
- Rocky Mountain Spotted fever serology: 1:160
- Completed 10 day course
Wisconsin Reported Total Cases of Rocky Mountain Spotted Fever 2009-2015 (n=63)

Data Source: Wisconsin Division of Public Health
FIGURE 1. Reported incidence rate\(^*\) of spotted fever rickettsiosis,\(^{†}\) by county — United States, 2000-2013

Source: MMWR CDC
Rocky Mountain Spotted Fever

- Cause: *Rickettsia rickettsii*
- Vector: Wood tick (*Dermacentor variabilis*)
- Diagnosis – serology
- Treatment: Doxycycline, early, regardless of age.
Case 4

- 9 yr old boy previously well, who presented late July with left frontal headache
- Felt warm temp to 101.3
- Brother with fever
- Fell on ground and had a generalized tonic–clonic seizure lasting 10 min
- Vomited after seizure
Case 4

- **Exam**
  - Febrile to 101
  - Alert and awakened
  - Right sided facial twitching and leftward eye deviation

- **MRI head**: gyriform restricted diffusion with superficial nodularity along the left cerebral convexity c/w atypical viral vs fungal infection
Case 4

- CSF
  - 118 nucleated cells – 9N/77L/11MP
  - 3 RBCs
  - Glucose 64
  - Protein 32
  - Gram stain and cx negative
Case 4

- Enteroviral PCR – neg
- HSV PCR – neg
- Serum IgM
  - Eastern Equine Encephalitis – neg
  - Lacrosse Encephalitis – POS (14.16)
  - West Nile Virus – neg
  - St. Louis Encephalitis – neg
  - Jamestown Canyon Virus – POS (3.87)
  - Powassan virus – neg
Encephalitis viruses – WI

- Mosquito borne
  - Lacrosse virus
  - Jamestown Canyon Virus
  - West Nile virus
  - Eastern Equine Encephalitis (very rare)

- Tick borne (*Ixodes scapularis* – deer tick)
  - Powassan virus (5 cases 2016)
LaCrosse Encephalitis

- Incubation 3–7 days
- Many infections are asymptomatic
- 90% of disease <15 yrs.
- Males > females
- Recovery is the rule, Mortality <1%
- Emotional lability 10%
- Epilepsy 6–10%
LaCrosse Encephalitis: Epidemiology

- **Vector**
  - *Aedes triseriatus*
  - “tree hole mosquito”
  - reproduces in stagnant water
  - tree holes/ old tires/ water containers
  - feed on viremic natural hosts

- **Natural Hosts**
  - chipmunks
  - squirrels
  - foxes
  - woodchucks
Wisconsin Total Cases of California Serogroup Viruses by Age
2008 - 2016 (n=74)
7 year old boy with persistent pneumonia
Seen by PCP 1 month earlier with 6 days of cough and nasal congestion.
CXR – LLL infiltrate
Placed on albuterol and azithromycin
No improvement after 5 days >>> cephalaxin
Fever continued at home
Cutaneous pustules
Admitted to local hospital IV ceftriaxone for 5 days
Fever continued >>> AFCH
Case 5

- PMH: Shigella enteritis 3 months earlier after trip to Mexico (during WI outbreak)

- Social HX/ Exposures
  - Born in WI, lives in WI
  - Travel to Mexico x 4
  - No known raw dairy consumption
  - Dogs/cats/cows in Mexico
  - Parents immigrants
  - No know TB exposure
Case 5

- Fever continued despite vanco + ceftriaxone
Case 5

- Developed headache
- MRI numerous cerebral and cerebellar lesions c/w miliary disease
Case 5

- **CSF**
  - 1 Nucleated cell
  - Normal glucose and protein
  - *Blastomyces* antigen negative

- **Serum**
  - Quantiferon gold – negative
  - *Blastomyces* antigen – positive
  - *Histoplasma* antigen – negative

- **Urine**
  - *Blastomyces* antigen – positive
  - *Histoplasma* antigen – negative

- **BAL Culture** – *Blastomyces dermatitidis* day 21
Blastomycosis

- Persistent infiltrate despite anti-bacterials
- Fever
- Chills/shakes/night sweats
- Skin lesions
- Bone / osteomyelitis
- CNS disease
- Increased risk in immunocompromised
- Increased risk in WI Hmong population*
- Distinguish from TB / Histoplasmosis

*(Clin Infect Dis. 2013 Sep;)*
Blastomycosis

Diagnosis
- Antigen tests
  - Serum
  - CSF
  - Urine
- Antibody test
  - Serum
- Culture
  - Fungal media

Treatment
- Amphotericin liposomal – severe disease
- Itraconazole
- Duration 6–12 months
Emerging pathogens / vectors – WI

- **Pathogens**
  - Powassan virus – deer tick – encephalitis
  - *Borrelia mayonii* – deer tick – Lyme like illness
  - *Borrelia miyamotoi* – deer tick – relapsing fever
  - Jamestown Canyon virus – deer/mosquitos

- **Vectors**
  - Lone star tick
    - *Ehrlichia chafeensis*
    - *Ehrlichia ewingii*
    - Tularemia
    - Southern Tick–associated Rash Illness (STARI)
  - *Aedes albopictus* – tiger mosquito
    - zika virus
    - dengue virus
    - chikungunya virus
Amblyomma americanum

Lone Star tick

Diseases

- Ehrlichia
- Heartland virus
- STARI
- Francisella tularensis
Prevention

- Avoid woody areas with tall grass
- Long pants tucked into socks
- Long sleeves
- 20–30 % DEET
- Tick checks and removal
- Permethrin on clothing
- Mosquito /tick abatement
The Wisconsin State microbe is:

A. **Saccharomyces cerevisiae**
B. **Lactobacillus casei**
C. **Lactococcus lactis**
D. **Borellia burgdorferi**
Amblyomma americanum records in Wisconsin 2006-2013
Wisconsin Lyme Disease (*Borrelia mayonii*)
Total Confirmed Cases 2013 – 2016 (n=5)

This map is based on the county of residence of confirmed cases. Some infections may have been acquired during travel to other areas.

Revised 08/24/2016  Data Source: Wisconsin Division of Public Health
Lyme
Babesia
Anaplasma/ehrlichia
La crosse
Blasto
WNV
Zika?
Historical
Histo
RMSF
Powassan
Borrelia myomota
Distribution of Key Tickborne Diseases, United States, 2015

NOTE: Each dot represents one case. Cases are reported from the infected person's county of residence, not necessarily the place where they were infected.
ADD?

- TICK ID
Which of the following are dimorphic fungi that are endemic to Wisconsin?

- A) *Blastomyces dermatitidis*
- B) *Coccidioides immitis*
- C) *Histoplasma capsulatum*
- D) *Blastocystis hominis*
Which of the following are arthropod borne infections in which both the vector and the virus are endemic to Wisconsin?

- A) LaCrosse virus
- B) Dengue virus
- C) Zika virus
- D) West Nile virus
Prolonged or repeated course of antibiotics for Lyme disease:

- A) are routinely recommended by the IDSA for difficult cases.
- B) should only be prescribed by Lyme literate physicians.
- C) have resulted in deep venous thromboses, central line associated blood stream infections, *C. difficile* colitis and death.
- D) should be given if the patient responds to a course of antibiotics.