LYME DISEASE:
UPDATE AND RECENT CONTROVERSIES

Dr. Paul Frankish
SJRHEM Rounds
January 10th, 2017
ACKNOWLEDGMENTS

• Thank you to Dr. Stephen Robinson for his help in creating and researching this presentation
OBJECTIVES

- Transmission
- Clinical Manifestations
- Serologic Testing
- Prophylaxis and Treatment
- Pediatric Considerations
- “Chronic Lyme Disease”
- Take Home Points
Not currently the time of year, but spring is around the corner. Seems to be in the news every other week. Task forces being formed. Elizabeth May has been a big proponent. Avril Lavigne has come forward regarding her battle with Chronic Lyme. I do not disagree that we need to look into this further, but I am not a fan of how the media is painting physicians to be in their articles. We are portrayed as ignorant and uncaring, forcing patients to spend much of their hard earned money to seek diagnosis and treatment elsewhere. For a deeper look I suggest the documentary Under Our Skin.

INTRODUCTION

- Extensive media coverage regarding difficulties in diagnosing and treating
- Federal government initiatives into research
- Celebrities coming forward with their own horror stories and stigma
- Most of this actually stems from the controversy of “Chronic Lyme Disease”
Discovered in Lyme, Connecticut by Dr. Burgdorfer, investigating an abnormal cluster of juvenile RA. Other common tick-borne illnesses are transmitted through the lone star tick (*Amblyomma americanum*) and the American dog tick (*Dermacentor variabilis*) that transmit ehrlichiosis and Rocky Mountain spotted fever, respectively. The ticks serve as the vector between the animal population and humans. Deer are the preferred host for ticks, and the tick population is highest when deer are present, but the actually pick up the Borrelia from small mammals mostly.
Nymphs cause the majority of infections and are most efficient at transmitting the bacteria. Since they are small, they can feed longer and go undetected.
Millidgeville and North Head are the two listed Endemic areas on healthycanadians.gc.ca for New Brunswick. Nymphs may not have a well developed scutum and can be very small. Best to send all ticks for identification.
A) is an Argasid (soft tick, *Ornithodoros turicata*)
B) has a scutum, long body but short mouth parts (dog tick, *Dermacentor variabilis*)
C) is *Ixodes scapularis* (!)
D) has a scutum, but has a short and stout body – it also has a “lone star” on its body (lone star tick, *Amblyomma americanum*)
Usual tick is about 3 mm in size, engorged tick can approach the size of a dime.
Majority of serology is negative in early stage, predominantly IgM if positive. Testing is not recommended at this point, just treat! The beef with our testing and not diagnosing early doesn’t hold much weight, as antibody related testing is expected to be negative. In fact some patients if treated early will never sero convert at all (ie. no objective evidence of past infection).
ERYTHEMA MIGRANS PEARLS

- Often just a macule with no central clearing (20-30%)
- Classically 1-2 weeks from time of tick bite, but anywhere from 3-30 days
- Some patients may either not have it or notice it
- May have multiple lesions
- Rashes within 2 days are usually an immune reaction to tick saliva²
Lots of variations, but all uniformly are large erythematous macules.
Serologic testing is universally positive at this point (>90%). Bilateral 7th Cranial nerve palsies are practically diagnostic of Lyme disease. Think about Lyme disease and ask about tick exposure in patients with CN VII palsy, subacute meningitis, AV block or large joint effusions.
Serology remains positive for years, but will be IgG at this point.
Again the issues raised Lyme Advocacy groups only hold weight if you are using the tests inappropriately (ie. either in early acute phase when you should be treating (FN), or in vague chronic symptoms with no hx of a tick bite/exposure (FP)).
The medias talk of the inadequacies of our tests are largely due to misunderstanding about how an antibody test works. They will quote up to 50% of cases missed, but this is in early stage, and not where this test is designed to be used.
**If patient has travelled to another country with endemic Lyme disease caused by an alternate Borrelia species, just specify this when submitting the test and they can perform specific testing for B. afzelii/garinii.

**

STEP 2

- Western Blot is highly specific
- Only performed in the setting of a positive Step 1
- Only applies to North American Lyme disease
- Specific CDC criteria for interpretation
This scenario is unlikely, as by 4 weeks most have converted to a largely IgG response, IgM suggests active infection and would likely be there in isolation at 4 weeks or later. Consider testing if EM rash with no clear exposure, or initial negative Step 1 test with ongoing symptoms consistent with Lyme disease. Sensitivity goes up in convalescent phase.
5. From *Branda, J* et. al. (2010) in *Clinical Infectious Disease*. Canadian test uses C6 assay (C6 protein on conserved part of the Spirochete) in the Tier 1 test (CID 2008: 47: 188-195). Again this test is specific so its not churning out false positives in the early going. It becomes sensitive in later stages.  

<table>
<thead>
<tr>
<th>Stage</th>
<th>Sens (%)</th>
<th>Spec (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Early</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute</td>
<td>17</td>
<td>98</td>
</tr>
<tr>
<td>Convalescent</td>
<td>53</td>
<td>98</td>
</tr>
<tr>
<td>Early disseminated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple EM lesions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Acute</td>
<td>43</td>
<td>98</td>
</tr>
<tr>
<td>- Convalescent</td>
<td>75</td>
<td>98</td>
</tr>
<tr>
<td>Cardiac/Neuro</td>
<td>100</td>
<td>98</td>
</tr>
<tr>
<td>Late</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthritis/Neuro</td>
<td>100</td>
<td>98</td>
</tr>
</tbody>
</table>

SPIN (better at ruling in)    SNOUT (better at ruling out)
CDC Algorithm for using the 2 Tier test.
IDSA guideline. Species identification not as useful, as generally they don’t bring it in, or its mangled. I couldn’t find a true infection rate for Millidgeville, and since we only have 10-12 confirmed cases per year in the whole province it may be hard to say. As its listed as an endemic area I have been practicing under the assumption that it is greater than 20%.
PROPHYLAXIS

- Single dose of Doxycycline 200 mg or 4mg/kg for children greater than 8 years old
- Not sufficient evidence to recommend any other regimes
- A “watch and wait” approach is recommended in these cases
Duration of 10-14 days is recommended.
TREATMENT

• IV Regimens:
  • Ceftriaxone 2 grams IV Q24H
  • Cefotaxime 2 grams IV Q8H
  • Pen G 4 million units IV Q4H
General idea, oral for less severe, IV for more severe. 2 weeks for EM, up to 4 weeks for others.
PEDIATRIC CONSIDERATIONS

• Essentially treated the same as with adults!
• Peak incidence at 5-9 years old
• Diagnostic criteria, testing, prophylaxis, and treatment are the same

CPS guidelines on Lyme Disease.
Cefotaxime is not listed in the CPS guidelines. Macrolides have poor efficacy against B. burgdorferi. Duration of treatment is essentially the same, 2-4 weeks depending on mild to severe manifestations, and IV for more severe disease.
“CHRONIC LYME DISEASE”

- “If Lyme disease is not diagnosed and treated early, the spirochetes can spread and may go into hiding in different parts of the body. Weeks, months or even years later, patients may develop problems with the brain and nervous system, muscles and joints, heart and circulation, digestion, reproductive system, and skin. Symptoms may disappear even without treatment and different symptoms may appear at different times.”

Excerpt from lymedisease.org initial explanation of chronic lyme disease. This is a similar to what you will read in CanLyme and most other patient advocate or support websites.
PTLDS is an accepted subset of patients (10-20%), that have persistent fatigue, MSK pain, and subjective neuro symptoms for months to years after treatment with antibiotics. The consensus in the medical community is that they eventually get better with time and that the symptoms are attributable to auto-immune dysfunction. About 2% of the general population also has symptoms similar to PTLDS (ie. CFS or Fibromyalgia).
The IDSA vs ILADS has spawned the “Lyme Wars”. 2014 Guidelines released by ILADS have made recommendations such as treating every tick bite patient regardless of attachment or endemic Lyme rates, with 3 weeks of antibiotics, using 3 weeks of treatment as a minimum duration, and retreating with 4-6 weeks of oral or possibly IV antibiotics for any return of symptoms, whether that be weeks/months/or years later. They also list such a myriad of symptoms, that you could attribute almost any constellation of symptoms to chronic Lyme.
“CHRONIC LYME DISEASE”

- Multiple RCT’s have been unable to demonstrate any benefit to long term antibiotic courses in Lyme Disease:
  - *Klempner et. al* (NEJM 2001), 78 and 51 patients, 90 day course
  - *Krupp et. al.* (Neurology 2003), 55 patients, 28 day course
  - *Fallon et. al.* (Neurology 2008), 37 patients, 70 day course
  - *Berende et. al.* (NEJM 2016), 281 patients, 84 day course

Klempner – 30 days Ceftriaxone, then 60 days Doxy, in both seropositive and negative patients previously treated for Lyme.
Krupp – 28 days of Ceftriaxone, improvement in only fatigue, but with significant adverse effects (3 hospitalizations).
Fallon – 10 weeks of Ceftriaxone, objective improvement at 12 weeks, no improvement at 24 weeks.
Berende – 2 weeks Ceftriaxone for all, then 12 weeks Doxy, Azithro, or placebo, no difference between 2 weeks or longer in symptoms.
Its very important we understand how our 2 Tier testing works in Canada, so that we are able to “talk the talk” with these patients. Most patients with EM will have negative serologic tests, and this shouldn't be viewed as a weakness of our test, it's not designed for early Lyme Disease with Erythema migrans. If they have erythema migrans, just treat them.
We need to approach these patients with an open, respectful, and caring dialogue. Stick to your principles about what you believe is best practice, but also take the time to listen to them, legitimize their symptoms, and try to help if you can (referrals, follow up, etc). If you go into these rooms with obvious preconceptions and attitude, they will sense it, and you will get no where with them.

“CHRONIC LYME DISEASE”

- These are sick patients with severely debilitating symptoms
- They are highly suspicious and feel abandoned by the medical community
- In my experience, they can provoke similar counter-transference to that seen with Borderline Personality disorder
There is some human and animal studies suggestive that chronic spirochete infection may exist, albeit mostly DNA fragments in tissue or urine, and how best to treat this and whether its linked to Chronic Lyme disease has not been studied, but we still need to keep an open mind.

“CHRONIC LYME DISEASE”

• Although the deck is stacked heavily against “Chronic Lyme”, we have all learned things in medical school that have now been disproven

• We need to practice with the best available guidelines, but also be prepared to the possibility that persistent infection might truly exist"12-14
False positives are highly likely in patients with low pre-test probability.
If a patient presents a positive test from a private lab, only look at the CDC criteria interpretation.


RESOURCES


RESOURCES


RESOURCES


