**Lyme Disease: Standards of Care**

For Disseminated Lyme, 43% treat for > 3 months
For Chronic Lyme, 57% treat for > 3 months


Two equally legitimate but divergent standards of care currently exist for the diagnosis and treatment of Lyme disease.

In Favor of Antibiotics for Chronic Lyme

ILADS Guidelines

“Refractory Lyme disease is a devastating condition that usually affects patients with persistent symptomatology and long-term disability. Prompt and aggressive institution of antibiotic therapy may be essential to prevent refractory disease. Increasing evidence shows that antibiotics have a beneficial effect on the course of refractory Lyme disease even in cases where the patient is intolerant of antibiotics or when a previous regimen has failed. Several months of therapy are often required to produce clear evidence of improvement.”
Against Antibiotics for Chronic Lyme

IDSA Guidelines

“To date, there is no convincing biologic evidence for the existence of symptomatic chronic B. burgdorferi infection among patients after receipt of recommended treatment regimens for Lyme disease. Antibiotic therapy has not proven to be useful and is not recommended for patients with chronic (6 months) subjective symptoms after administration of recommended treatment regimens for Lyme disease (E-I).”
Human Persistent *Bb* Infection Studies Cited by The Guidelines, but Pertinent Findings Omitted

"the detection of Osp A DNA in joint fluid indicates the presence of viable spirochetes"

<table>
<thead>
<tr>
<th>Patients</th>
<th>Treatment Received</th>
<th>SF PCR + After Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>&lt;1 month oral antibiotics</td>
<td>12 out of 12 (100%)</td>
</tr>
<tr>
<td>19</td>
<td>1-2 months oral antibiotics and/or IV antibiotics up to 3 weeks</td>
<td>7 out of 19 (37%)</td>
</tr>
<tr>
<td>10</td>
<td>“multiple courses of antibiotic therapy”</td>
<td>3 out of 10 (30%)</td>
</tr>
</tbody>
</table>

None of the above discussed in The Guidelines

Nocton J J; Dressler F; Rutledge B J; Rys P N; Persing D H; Steere A C. Detection of Borrelia burgdorferi DNA by polymerase chain reaction in synovial fluid from patients with Lyme arthritis N. Engl. J. Med. 1994 Jan, 330:4, 229-34.
Human Persistent *Bb* Infection Studies Cited by The Guidelines, but Pertinent Findings Omitted

38 treated Lyme patients—Long term outcomes

- 26% relapsed by 1 year and required re-treatment
- 34% had long term morbidity despite treatment

Patient #12 treated with 2 weeks IV penicillin
Despite treatment, severe neurologic illness
Re-treated--2 weeks IV ceftriaxone without effect

She died. On autopsy, brain tissue: Spirochetes demonstrated with mononuclear inflammation

None of the above discussed in The Guidelines
American patients, therefore sensu stricto

Human Studies Documenting Persistent *Bb* Infection, but NOT Cited by The Guidelines

- 12 Lyme patients failed antibiotics
- Spirochetes in synovium: 6 of 12 patients (50%)

“...the antigenic stimulus in Lyme arthritis would appear to be a small number of live spirochetes, demonstrated here by monoclonal antibodies, which may persist in the synovial lesion for years.”


- 67 yr old woman died—ARDS attributed to Lyme
  - Failed 2 weeks tetracycline, 10 days IV penicillin, & a 2nd course IV penicillin, duration unspecified

- Autopsy: Lymph nodes—Spirochetes consistent with *Bb*

Human Studies Documenting Persistent *Bb* Infection, but NOT Cited by The Guidelines

24 year old woman—EM after camping in PA

- Years later—arthritis, needed several surgeries
- Ultimately, seropositive Lyme arthritis diagnosed

- 2 courses IV penicillin, 3 of IV ceftriaxone, & 1 of IM penicillin all resulted in “dramatic reduction” of arthritis, but relapses after discontinuation of each
- Doxycycline for 13 months, sulfasalazine for 1 year, & arthroscopic synovectomy did not help

- Despite multiple antibiotic treatments, synovial tissue & synovial fluid silver stain revealed copious spirochetes; synovial fluid Lyme PCR positive

Human Studies Documenting Persistent *Bb* Infection, but NOT Cited by The Guidelines

- 7 Lyme patients with neurologic & urologic findings
- All treated with ceftriaxone, 3 wk mean
- 4 of 7 patients (57%) relapsed despite treatment
- Relapsers re-treated with ceftriaxone for 2-3 wks
- Antibiotics helpful in all, but 5 of 7 patients (71%) remained symptomatic

- Patient #2, despite 3 weeks ceftriaxone:
  Relapsed — *Bb* demonstrated in bladder biopsy, confirmed with monoclonal antibodies

58 year old woman, no history of tick bite or EM; neurologic manifestations

Seronegative, CSF Lyme antibody negative

CSF intermittently positive for *Bb* immune complexes, Osp A free antigen, and PCR

3 out of 7 LP’s, (43%) were negative by CSF PCR

Patient treated anyway and improved from treatment

7 rounds of IV antibiotics & 3 years continuous oral

Severe Herxheimer reactions upon re-initiation of each antibiotic therapy, followed by improvements

Human Studies Documenting Persistent *Bb* Infection, but NOT Cited by The Guidelines

3 CNS Lyme patients—brain biopsy proven persistent infection after antibiotics

Patient #1
- Seronegative, CSF antibody negative, no pleocytosis
- CSF cultured positive for *Bb* sensu lato

Treated with 3 wks ceftriaxone, partial improvement
Treated with 8 months doxy, patient relapsed, Lyme PCR positive in both plasma & bone marrow

Ceftriaxone re-started, but patient died. On autopsy, brain tissue was Lyme PCR positive

Patient #2

- Initially IgM seropositive, IgG seronegative, then both seronegative despite disease progression
- CSF repeatedly negative for Lyme antibodies & PCR
- Brain biopsy PCR positive in 3 separate samples

Failure of 7 weeks ceftriaxone & almost 9 months of various, often high dose oral antibiotics

After stopping antibiotics, multiple relapses with recurrent brain lesions & a positive plasma Lyme PCR

After another 100 days ceftriaxone, all brain lesions resolved. Patient remained well. MRI and PCR negative on long term follow up.

Human Studies Documenting Persistent *Bb* Infection, but NOT Cited by The Guidelines

- 165 patients, all initially met CDC case definition
  - Antibiotics—Median duration of 16 weeks
- Despite antibiotics 32 of 165 (19%) relapsed
  - 13 of 32 (41%) positive by culture, PCR, or both; 85% having received ceftriaxone as well as oral antibiotics
  - 3 patients were culture positive
- All 13 patients re-treated—After at least 4 to 6 weeks IV ceftriaxone, 69% improved.

- One of the 3 cultures was *Bb* sensu stricto

Persistent *Bb* infection despite:

- **Recommended and/or long term antibiotic therapy;**

Confirmed by culture, and/or PCR & Immuno-electron microscopy

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Human Persistence Data NOT Cited by IDSA &
New Data Published After IDSA Guidelines

Persistent *Bb* infection despite:

- Recommended and/or long term antibiotic therapy;
- Confirmed by culture, and/or PCR & Immuno-electron microscopy

Antibiotic Re-Treatment of Chronic Lyme Patients: Studies Demonstrating Benefits

**Randomized Controlled Trials**


**Open Label Trials**


Review of the 4 NIH Sponsored Chronic Lyme Re-tx Randomized Controlled Trials


Review of the 4 NIH Sponsored Chronic Lyme Re-tx Randomized Controlled Trials


Unrealistic Design Assumptions to Assess Primary Outcomes

Trials Were Underpowered to Detect Clinically Meaningful Treatment Effects

Inappropriate Minimum Clinically Important Difference—Improvement to a level of health which was a full standard deviation superior to that of the general population to detect a treatment effect

Review of the 4 NIH Sponsored Chronic Lyme Re-tx Randomized Controlled Trials


Design Assumptions to Assess 2 Primary Outcomes Were Unrealistic
Trial Was Underpowered to Detect Clinically Meaningful Treatment Effects

Design Assumption & Analysis Appropriate for the 3rd Primary Outcome: Fatigue
Demonstrated Benefits to Fatigue After Treatment
No Evidence of Unblinding

Review of the 4 NIH Sponsored Chronic Lyme Re-tx Randomized Controlled Trials


Design Assumption & Analysis Appropriate for Cognitive Function
Demonstrated Benefits to Cognitive Function After Treatment
Relapse of Cognitive Dysfunction on Stopping Antibiotics

Benefits Also Demonstrated for Fatigue and Body Pain After Antibiotic Therapy by subgroup analysis

There is convincing biologic evidence for the existence of symptomatic chronic *B. burgdorferi* infection among patients after the receipt of recommended antibiotic treatment regimens for Lyme disease.

In my opinion, there are egregious oversights in the IDSA Guidelines, in that they have not included volumes of published data which documents persistent infection after antibiotic therapy, inclusive of the IDSA Guidelines authors’ own published works.
For More Information Visit
ILADS.ORG