Lessons from Lyme

Holly Ahern
Assoc. Prof. of Microbiology
SUNY Adirondack
ahernh@sunyacc.edu
518-743-2287
Lyme Disease STATS

- Only 1 in 10 Lyme disease cases are included in the statistics used for national and state disease surveillance. (cdc.gov)
- In 2015, there were nearly 400,000* NEW cases of Lyme disease in the US. (cdc.gov)
  - Syphilis ~ 56,482 (2013)
  - Hepatitis B ~ 3,050 (2013)
- A proportion of Lyme disease patients will develop a CHRONIC DISEASE as an outcome of infection.

* Incidence Ranking Based on Annual Cases:
The Societal Burden of Lyme disease (1, 43)

<table>
<thead>
<tr>
<th>Time of First Antibiotic Treatment</th>
<th>Cost of Treatment</th>
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<tbody>
<tr>
<td>At time of bite</td>
<td>$435</td>
</tr>
<tr>
<td>Diagnosed &lt; 6 weeks after bite</td>
<td>$2,238</td>
</tr>
<tr>
<td>Diagnosed &gt; 6 months after bite</td>
<td>$22,296</td>
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Rate of Lyme Disease in the US (cdc.gov)

| U.S. Population (2015 Census) | 324,000,000 |
| Annual Cases of Lyme disease (cdc.gov) | 380,690 |
| Rate                           | >1%         |

Lyme Disease Costs Up to $1.3 Billion Per Year to Treat, Study Finds

Research suggests prolonged impact of the tick-borne illness in some patients is greater and more widespread than previously understood.

Lyme disease, transmitted by a bite from a tick infected by the *Borrelia burgdorferi* bacteria, had long been considered easy to treat, usually requiring a single doctor’s visit and a few weeks of antibiotics for most people.

But new research from the Johns Hopkins Bloomberg School of Public Health suggests that a prolonged illness associated with the disease in some patients is more widespread and serious than previously understood. With an estimated 240,000 to 440,000 new cases of the tick-borne illness diagnosed every year, the researchers found that Lyme disease costs the U.S. health care system between $712 million and $1.3 billion a year — or nearly $3,000 per patient on average — in return doctor visits and testing, likely to investigate the cause of some patients’ lingering symptoms of fatigue, musculoskeletal pain and memory problems. These visits come after patients have finished their original course of antibiotics.
Lyme disease is only one form of BORRELIOSIS - diseases caused by spirochetes in the *Borrelia* genus. Other Borreliae cause the same clinical disease. (2-4)

- *B. miyamatoi*, *B. mayonii*, *B. bissetti*, two new unnamed genospecies., and the “relapsing fever” Borreliae.

All known Borreliae infect hosts with the intent to persist. They do this through evasion and suppression of the mammalian immune response. (5-7)

In humans, Borreliae subvert B-cell (antibody-mediated) immunity and incite T-cell mediated responses (inflammation). (8,9)

Natural form of human infection results in subclinical disease with “non-specific” symptoms. (10-12)

Borreliae in blood rapidly disseminate and invade cells and specific tissues including fibrocytes and lymphocytes, skin, synovium, cardiac tissue, nervous tissue. The various *Borrelia* genospecies prefer specific tissues. (13)

Once established in a tissue, Borreliae form protective biofilms. A proportion of the cells change gene expression to become dormant “persister” cells, capable of reactivating latent infections. (14-16)
Based on ~200 studies

- “Lyme Disease” is an acute infectious disease usually manifesting on the skin, although systemic disease may rarely occur.
- *Borrelia burgdorferi* is the sole cause of Lyme disease.
- Disease occurs in “Early” “Middle” and “Late” stages each with well defined signs and symptoms.
- “Early” disease is indicated 70-80% of the time by an unusual rash (EM), with is pathognomonic when present.
- In the absence of an EM and for people living in a few geographic regions, serologic tests should be performed to provide “evidence of infection” required for diagnosis and treatment.
- Lyme disease is preventable with a dose of doxycycline at the time of ticks bite, and is easily treatable with oral doxycycline at any stage of the infection.
- Treatment failure is rare.
- There is “no evidence” that treating patients with “longer-term” antibiotics results in discernable improvements in their quality of life.

Based on ~10,000 studies

- Skin manifestations of borreliosis occur in <40% of cases. When rash does appear, classic bulls-eye appearance is <10%. (42)
- Lyme disease is one form of borreliosis, and other Borreliae besides *B. burgdorferi* cause the same clinical disease not called Lyme disease.
- Concept of “disease stages” is completely inconsistent with the biology of the disease agent. The “stages” correlate to Borreliae tissue tropisms (i.e., skin is called “Early” while nervous or cardiac tissue is called “Late”)
- Serology is specific, but VERY INSENSITIVE (<50%) for all (so-called) stages of the disease. (23-26)
- Lyme disease is not “preventable” with a single dose of doxycycline and no form of Lyme disease is “easily treatable” with oral doxycycline. (17-22, 40)
- Treatment failure is common but dismissed because symptoms are “non-specific.”
- There is likewise NO EVIDENCE that longer-term antibiotics DO NOT result in discernable improvements in patients’ QOL. (41)
Consequences of NO DIAGNOSIS or MISDIAGNOSIS
A Case Study

Ineffective or delayed antibiotic treatment enables the bacteria to disseminate to joints, nervous system, or cardiac tissue where they establish treatment resistant biofilms, driving both local and systemic inflammatory reactions and causing “non-specific” disease symptoms. (27-38)

Associated Costs:

• Visits to Hospital Emergency Room and Emergent Care to deal with rapid escalation of symptoms (cranial neuritis, encephalopathy, arrhythmias, and whole body pain).

• Additional clinical testing including CT scans, MRI scans, referrals to other medical specialty areas (neurology, cardiology, rheumatology, endocrinology) with associated laboratory testing.

• Prescriptions for potentially LIFE-LONG medications for Lyme disease misdiagnosed as psychiatric or “autoimmune” chronic diseases; including psychiatric medications, pain medications, immune system modulators (steroids, biologics).
The DOMINANT MEDICAL GUIDELINES for Lyme disease are based on 40 year old science and do not reflect the disease as experienced by patients. These guidelines:

• **ASSUME** the skin tropism (EM rash) develops in nearly all cases of Lyme disease and is therefore pathognomonic for all forms of Lyme borreliosis.

• **EXCLUDE** from diagnosis (and therefore treatment) the majority of Lyme disease cases (40-90%), in people who are infected with Borreliae but do not develop the EM rash.

• Favor a diagnostic test with a low rate of false positive **BUT A HIGH RATE OF FALSE NEGATIVES**.

• **EXCLUDE** from diagnosis (and therefore treatment) patients with **FALSE NEGATIVE** serologic tests (>50%).

• Recommend treatments based on clinical studies which **EXCLUDE** subjects without an EM or positive serology.

• **MISCONCEIVE** lack of timely diagnosis or treatment failure as a “post-treatment” syndrome of psychiatric origin. (12, 39)

• **PROVIDE NO MEDICAL OPTIONS** for patients not meeting the above specifications, other than referral to other specialists.
Setting Goals

- **Improve the quality of life for Lyme disease patients**

- **Lower the cost burden of Lyme disease for patients, employers, insurers, and society.**

**Goal 1**

- Recognize and acknowledge the excessive limitations, particularly related to diagnosis, in the dominant medical guidelines for Lyme disease.

- Give equal weight to ALL evidence-based, peer reviewed, patient centered medical guidelines that MEET THE CRITERIA OF THE NGC*.

**Goal 2**

- Proactively educate physicians to end the practice of “two-pill” prophylaxis, which INCREASES PATIENT RISK OF DISSEMINATED DISEASE.

- Proactively educate insurance companies reimbursement for EVIDENCE-BASED MODALITIES to manage symptoms and improve QOL for Lyme disease patients.

*NGC – National Guidelines Clearinghouse