

## Supplementary S1

### Peer-Reviewed Evidence of Lyme Borreliosis/Tick-Borne Disease Associated with Psychiatric Symptoms

The following is a list of peer-reviewed articles that support the evidence of Lyme and other tick-borne diseases associated with neuropsychiatric illness. It is organized into two different categories— neuropsychiatric symptoms and dementia.

#### Lyme/Tick-Borne Diseases and Neuropsychiatric Symptoms

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Persistent *Bartonella henselae* infection in a Child. *Parasit Vectors*. 2016;9:e254

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


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## Supplementary S2

### Lyme Disease Screening Assessment

Based upon: Bransfield RC, Aidlen DM, Cook MJ, Javia S. A Clinical Diagnostic System for Late-Stage Neuropsychiatric Lyme Borreliosis Based upon an Analysis of 100 Patients. *Healthcare*. 2020; 8(1):13.

<https://doi.org/10.3390/healthcare8010013>

\_\_\_\_\_ Do you live, vacation, or engage in occupational or other activities in areas that may expose you to ticks?

\_\_\_\_\_ Have family members, neighbors, or the family dog been infected?

\_\_\_\_\_ Is there a history of a tick bite, possibly with a flu-like illness and/or a bull's-eye or other rash?

\_\_\_\_\_ Is there a point at which your health declined, followed by a fluctuating progression and development of multi-systemic symptoms, including cognitive, psychiatric, neurological, and somatic symptoms adversely impacting school, social life, family life?

\_\_\_\_\_ Have you ever been treated for Lyme disease, suspected you had Lyme disease but was told it was ruled out?

\_\_\_\_\_ Have antibiotics ever caused a sudden worsening followed by an improvement of symptoms?"



## Supplementary S3

### Coinfection Screen: Sorting out Lyme and Associated Coinfections<sup>1</sup> (Check if yes)

#### *Classic Lyme (Bb infection)*

Gradual onset of initial (viral-like) symptoms—this often makes it difficult to pinpoint when the infection began. Also, as in the case with Bb infection, laboratory tests for them are often insensitive. Thus, there is a need to sort it all out clinically to provide guidance in testing and treatment. Here are some clues:

1. \_\_\_\_ Multisystem—almost always, in disseminated stages, involves more than one part or system (i.e., joint pain plus cognitive dysfunction).
2. \_\_\_\_ Migratory—first a knee will hurt, then over time this may lessen, and the elbow or shoulder acts up, and later the joints calm down, but headaches worsen.
3. \_\_\_\_ Stiff joints and loud joint crepitus, especially the neck (“Lyme shrug”).
4. \_\_\_\_ Headaches are often nuchal and associated with stiff, painful, and crepitant neck.
5. \_\_\_\_ Afternoon fevers, often unnoticed—most Lyme patients have subnormal temperatures in the morning but rise to 99+ by early to mid-afternoon. No obvious sweats.
6. \_\_\_\_ Tiredness and limited stamina—often is a strong need to rest or even nap in the afternoon, especially when the flushed face and elevated temperature appears.
7. \_\_\_\_ Four-week cycles—Bb activity, and thus symptoms, wax and wane in a cycle that repeats roughly every four weeks. This cycle, if clear, can guide your treatments.
8. \_\_\_\_ Slow response to treatment, with an initial symptom flare in most (“Herxheimer-like reaction”), then improvement over weeks, punctuated by the monthly symptom flares. Likewise, if treatment is ended too soon, an initial period of well-being will gradually be replaced by a return of symptoms over a few weeks.
9. \_\_\_\_ EM rash in 25% to 50% of patients.

#### *Bartonella and “Bartonella-Like Organisms”*

1. \_\_\_\_ Gradual onset of initial illness.
2. \_\_\_\_ Central nervous system symptoms are out of proportion to the musculoskeletal ones and can include muscle twitches, tremors, insomnia, seizures, agitation, anxiety, severe mood swings, outbursts, and antisocial behavior.
3. \_\_\_\_ Gastrointestinal involvement may present as gastritis or abdominal pain (mesenteric adenitis).
4. \_\_\_\_ Sore soles, especially in the morning.
5. \_\_\_\_ Tender subcutaneous nodules along the extremities, especially outer thigh, shins, and occasionally along the triceps.
6. \_\_\_\_ Occasional lymphadenopathy.
7. \_\_\_\_ Morning fevers, usually around 99; occasionally light sweats are noted.
8. \_\_\_\_ Elevated vascular endothelial growth factor (VEGF) occurs in a minority, but the degree of elevation correlates with activity of the infection and may be used to monitor treatment.
9. \_\_\_\_ Rapid response to treatment changes—often symptoms improve within days after antibiotics are begun, but relapses occur also within days if medication is withdrawn early.
10. \_\_\_\_ May have papular or linear red rashes (like stretch marks that do not always follow skin planes), especially in those with GI involvement.

#### *Babesia Species*

1. \_\_\_\_ Rapid onset of initial illness, often with sudden onset of high fever, severe headaches, sweats, and fatigue; thus, it is easy to know when infection began.
2. \_\_\_\_ Obvious sweats, usually at night, but can be day sweats as well.

3. \_\_\_\_ Air hunger, the need to sigh and take a deep breath; dry cough without apparent reason.
4. \_\_\_\_ Headaches can be severe–dull, global (involves the whole head, described like the head is in a vise).
5. \_\_\_\_ Fatigue is prominent, does not clear with rest, and is made worse with exercise.
6. \_\_\_\_ Mental dullness and slowing of reactions and responses.
7. \_\_\_\_ Dizziness–more like a tippy feeling, and not vertigo or purely orthostasis.
8. \_\_\_\_ Symptoms cycle rapidly, with flares every four to six days.
9. \_\_\_\_ Hypercoagulation is often associated with Babesia infections.
10. \_\_\_\_ Rarely, splenomegaly.
11. \_\_\_\_ Very severe Lyme disease can be a clue to Babesia infection, as it will make Lyme symptoms worse and Lyme treatments less effective.

#### ***Ehrlichia/Anaplasma***

1. \_\_\_\_ Rapid onset of initial illness with fever, headache, prostration.
2. \_\_\_\_ Headaches are sharp, knife-like, and often behind the eyes.
3. \_\_\_\_ Muscle pain, not joint pain, and can be mild or severe.
4. \_\_\_\_ Low WBC, low platelet count, elevated liver enzymes, and (rarely) inclusions seen in the WBCs.
5. \_\_\_\_ Rarely see diffuse vasculitic rash, including palms and soles (less than 10%).
6. \_\_\_\_ Rapid response to treatment.

#### ***DNA Viruses (HHV-6, EBV, CMV)***

1. \_\_\_\_ Persistent fatigue made worse with exercise.
2. \_\_\_\_ Sore throat, lymphadenopathy, and other viral-like complaints.
3. \_\_\_\_ May see elevated liver enzymes and low WBCs.

#### ***Mycoplasma***

1. \_\_\_\_ Gradual onset.
2. \_\_\_\_ May be light night sweats.
3. \_\_\_\_ Symptoms are made worse with exercise.
4. \_\_\_\_ Major fatigue and neurological dysfunction, especially autonomic neuropathies.
5. \_\_\_\_ Metabolic disturbances, immune damage, very low CD57 count (less than 20).
6. \_\_\_\_ Found in the sickest and most poorly responding Lyme patients (CFIDS-like).

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<sup>1</sup> Burrascano JJ. The Burrascano Checklist of Current Symptoms. Available online: <http://www.lymenet.org/BurrGuide200810.pdf> (accessed on 9 November 2019).