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TREATMENT OPTIONS FOR POST TREATMENT LYME DISEASE SYNDROME

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Abstract
With the high incidence of Lyme disease in the endemic areas of North America, it is important to appropriately diagnose and treat this condition to prevent post treatment Lyme disease syndrome (PTLDS). Background information regarding Lyme disease is given. The purpose of this research is to discuss the treatment options available for the patients that fit the case definition of PTLDS. A literature review was conducted using different electronic databases finding peer reviewed research articles pertaining to the treatment options available for PTLDS. Extended antibiotic use is shown to be not beneficial in most cases. Alternative treatment options listed on the internet are shown to not be evidence based. Therefore, symptomatic treatment options seem to be the best positive outcome-based option available for providers to use. These options are discussed in detail throughout this research. Though much more research is needed regarding the topic, this will give providers the information currently available that they will need to know when treating patients with PTLDS. Hopefully this will provide the patients with PTLDS the best outcome possible for improving their quality of life post Lyme disease.

Introduction
• Lyme disease is the most common vector borne illness in the USA (Rebman et al., 2017).
• Lyme disease is endemic in the Northeast and upper Midwest states but can also be found along the Pacific coast (Rebman et al., 2017).
• Presenting symptoms include erythema migrans, Lyme arthritis, and cranial nerve palsy which are treated with doxycycline. Hospitalization and IV ceftriaxone are often required for Lyme carditis and neurologic Lyme disease other than cranial nerve palsy (DynaMed Plus, Lyme disease., 2018).
• Misdiagnosis or inappropriate treatment lead to an increase in likelihood of developing PTLDS.

Statement of the Problem
Feng et al. (2017) have estimated that approximately 10%–20% of patients continue suffering from chronic symptoms described as PTLDS following the standard antibiotic treatment of early or late Lyme disease. The question remains that even if these symptoms are a direct or indirect consequence of Lyme disease, how can providers appropriately treat these patients.

Research Question
In patients who were treated appropriately for Lyme disease but develop PTLDS, does extended course antibiotic therapy versus symptomatic treatment versus alternative treatments help relieve PTLDS symptoms most effectively?

Literature Review
Evidence of PTLDS
• Infectious Diseases Society of America proposed a case definition for PTLDS in 2006 (Nemeth et al., 2016).
• Middelveen et al. (2018) confirms the presence of Borellia spirochetes with positive cultures in patients that were treated with antibiotics but remained symptomatic.

Treatment Options
Extended Antibiotic Use
• Studies going back to 2001 but most recently Berenste et al. (2016) have shown that extended use of antibiotics does not improve symptoms more than the placebo groups (p>0.001).

Based on Symptoms
Myalgic encephalomyelitis/chronic fatigue syndrome (CFS)
• Similarities between PTLDS and CFS suggest treatment of diet, exercise, counseling, acupuncture, and/or off-label use of methylphenidate may be beneficial (DynaMed Plus, chronic fatigue syndrome, 2018).

Lyme neuroborreliosis
• With triplicate data sets, Ramesh, Martinez, Martin, & Philipp (2017) showed that demethylase significantly reduced levels of Borrelia burgdorferi-induced inflammatory cytokines or chemokines over meloxicam (p<0.05; p<0.01; p<0.001).

Lyme arthritis
• Jowett, Gaudin, Banks, & Haddock (2017) show worse outcomes when corticosteroids and antivirals are used with antibiotics versus monotherapy of antibiotics alone.

Lyme arthralgia
• NSAIDs (ibuprofen or naproxen) and DMARDs (hydroxychloroquine or methotrexate) are shown to be effective after initial treatment (Arvicka & Steere, 2015)

Alternative Treatments
• Lantos et al. (2015) showed that oxygen therapy, energy and radiation, metal chelation, nutritional supplements and biological therapies found on the internet through Google did not substantiate any efficacy in treatment of Lyme disease.

Essential oils
• Oregano and cinnamon bark showed remarkable activity for complete eradication of the stationary phase of Borrelia burgdorferi in animals (Feng et al., 2017).

Supplements
• Nicolson, Settineri, & Ellthorpe (2012) showed a 30.7% reduction in fatigue within 60 days of using a daily ATP fuel supplement (p<0.001).

Discussion
• Rebman et al. (2017) found that 59% of participants in the study with PTLDS were either misdiagnosed or diagnosis was delayed. This stresses the importance of keeping Lyme disease in the differential diagnosis for typical symptoms occurring in endemic areas or those who have travelled to endemic areas.

• Further research needs to be done to develop more specific and sensitive lab tests so that concrete diagnoses can be made when clinical symptoms are not as straight forward as erythema migrans.

Applicability to Clinical Practice
• PTLDS case definition (Nemeth et al., 2016, Table 1): -An adult or child with a documented episode of early or late Lyme disease -Treatment with a generally accepted treatment regimen, with resolution of the objective manifestation

• Once PTLD is any of the following subjective symptoms within 6 months of the diagnosis and persistence of continuous or relapsing symptoms for at least 6 months after completion of antibiotic therapy:
• Fatigue, muscle and/or joint pain, complaints of cognitive difficulties, or subjective symptoms with such severity that, when present, they result in substantial reduction in previous levels of physical, occupational, educational, social or personal activities.

• Extended use of antibiotics should not be prescribed.

References
Hourihane, J. O., Bredin, S. P., & Nabulsi, A. (2017). Extended Antibiotic Use - In patients who were treated appropriately for Lyme disease but still develop PTLDS, does extended course antibiotic therapy versus symptomatic treatment versus alternative treatments help relieve PTLDS symptoms most effectively?

In patients who were treated appropriately for Lyme disease but still develop PTLDS, does extended course antibiotic therapy versus symptomatic treatment versus alternative treatments help relieve PTLDS symptoms most effectively?

• Numerous studies have shown that the use of extended antibiotics is not beneficial and increases the risk of adverse effects.

• There have been potential studies showing that alternative therapies may be something of use in the future. Further research needs to be done to establish the efficacy on humans.

• That leaves the only option currently available as assessing the best positive outcome with resolution of the objective manifestation

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• Alternative treatment options listed on the internet are shown to not be evidence based. Therefore, symptomatic treatment options seem to be the best positive outcome-based option available for providers to use. These options are discussed in detail throughout this research. Though much more research is needed regarding the topic, this will give providers the information currently available that they will need to know when treating patients with PTLDS. Hopefully this will provide the patients with PTLDS the best outcome possible for improving their quality of life post Lyme disease.

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Applicability to Clinical Practice
PTLDS case definition (Nemeth et al., 2016, Table 1):
• An adult or child with a documented episode of early or late Lyme disease
• Treatment with a generally accepted treatment regimen, with resolution of the objective manifestation
• Once PTLD is any of the following subjective symptoms within 6 months of the diagnosis and persistence of continuous or relapsing symptoms for at least 6 months after completion of antibiotic therapy:
• Fatigue, muscle and/or joint pain, complaints of cognitive difficulties, or subjective symptoms with such severity that, when present, they result in substantial reduction in previous levels of physical, occupational, educational, social or personal activities.
• Extended use of antibiotics should not be prescribed.

Patients must be warned that the efficacy of treatments listed on the internet are not evidence based and should be avoided. Treating the patients according to their symptoms and following the recommended guidelines for each is the most effective form of treatment for PTLDS as of now.