

Vector-Borne Infection Research-Analysis-Strategy



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This is an example to show the type of simple research that could be done and is absolutely needed.

A Prospective Study of persisting or relapsing symptoms following treatment for Lyme borreliosis

Research question

What causes treatment failure in UK patients with Lyme borreliosis?

Description

Patients treated for Lyme borreliosis according to guidelines, but who remain symptomatic or relapse after a period of time require investigation into the causes of their illness. Three possible causes for the ongoing illness are: 1/ permanent or slow-to-recover harm caused by Lyme borreliosis or its treatment, 2/ Lyme bacteria infection persisting due to ineffective treatment, and 3/ untreated co-infection(s). It is possible to investigate these potential causes of persisting symptoms with laboratory testing of patients. Laboratory tests can detect the presence of persisting Lyme infection and co-infections. If laboratory tests for #2 and #3 are negative, this would add support to the theory of slow-to-recover or permanent harm and could direct further investigation into those areas.

Participant selection

Participants will be 18 years or older and have a past diagnosis of Lyme borreliosis, for which treatment was completed at least one year earlier, following which some symptoms did not significantly improve, or improved but later relapsed.

Design

Blood or plasma samples as required by testing laboratories, will be prepared in suitable aliquots at a phlebotomy clinic and sent to laboratories for tests to identify the presence of: 1/ evidence of persisting infection with borrelia spirochaetes, and: 2/ Common Lyme borreliosis co-infections including, babesiosis, bartonella, rickettsia, ehrlichiosis, etc.

Laboratory Measures

Whole Cell Sonicate and C6 ELISA's and Western blot (Innatoss)

Elispot test for Lyme borreliosis. PCR. (ArminLabs/Igenex)

Culture and identification of spirochaetes by darkfield microscopy, immunofluorescent anti-borrelia antibody and PCR (Advanced Laboratory Services)

Co-infection panel for co-infections (ArminLabs/Igenex)

All test results, test strips or copies with density readings, micrographs and data returned to the collating centre.

Symptom Measures

SF-36 Physical Function subscale

Burrascano Symptom Checklist (Lyme borreliosis)

Griffith Lyme and co-infection checklist

Analysis and Report

The presence or absence of Lyme borreliosis and/or various co-infections as reported by the laboratory test results, will be presented as data with statistical analysis, showing which of the following criteria each participant's laboratory results suggest:

- Infected with Lyme borreliosis spirochaetes
- Infected with one or more common Lyme borreliosis co-infections
- Infected with Lyme borreliosis spirochaetes and one or more common Lyme borreliosis co-infections
- None of the above

Secondary analysis

In order to refine generalisability of the results, data will be experimentally subdivided by additional criteria. This will provide information about the diversity of characteristics of the condition and could identify possible subsets within the overall description.

Criteria 1. Time post-treatment. Results will be divided into different post-treatment time periods of e.g.: relapse up to 3 years post-treatment or, more than 3 years post-treatment.

Criteria 2. Delay before treatment. Results will be divided into those who received treatment e.g.: within one year of symptom onset or, over one year after symptom onset.

Criteria 3. Post-treatment history. Participants will be subdivided into e.g.: those who improved little or not at all following treatment, and those who initially recovered or improved significantly but later relapsed.

Rationale

The USA Centres for Disease Control and Prevention (CDC) state: "Physicians sometimes describe patients who have non-specific symptoms (like fatigue, pain, and joint and muscle aches) after the treatment of Lyme disease as having post-treatment Lyme disease syndrome (PTLDS) or post Lyme disease syndrome (PLDS). The cause of PTLDS is not known." This vague explanation for a 'syndrome' which has no World Health Organisation ICD code, is not substantiated by any scientific research. Notwithstanding that it describes a common outcome which could affect around 20% of Lyme borreliosis cases, amounting to tens of thousands of patients every year worldwide.

The questions arising from this phenomenon could theoretically be very complex. They might involve aspects such as genetic predisposition, immune activation/suppression, medical history for predisposing illnesses etc, etc. But before considering these possibilities, it is rational that medical researchers should eliminate the simplest explanations for patients remaining ill, or relapsing following treatment for Lyme borreliosis.

The ticks which commonly transmit Lyme borreliosis are can harbour a large number of other infections, including bacteria and viruses. Some of these are transmissible to humans and can be serious infections in their own right. The treatment of Lyme borreliosis, might leave some patients infected with other infections that were not susceptible to the treatment given. Additionally, if the treatment for Lyme borreliosis was ineffective then the infection could relapse. Either of these scenarios could result in patients with 'non-specific symptoms' caused by potentially dangerous infections which require identification and treatment.

Several laboratories provide specialised testing for both Lyme borreliosis and co-infections. This makes the experiment straightforward to conduct. By testing participants for both Lyme borreliosis and common co-infections, it might be possible to identify those for whom treatment was inadequate or inappropriate. This research is essential because as a misdiagnosis, PTLDS could actually obstruct patients from getting necessary investigations, a correct diagnosis and proper treatment. Therefore, eliminating these possible explanations for Lyme borreliosis patients who do not recover following treatment, is an essential first step towards understanding the phenomenon.