Clear evidence of a persistent disease pattern following Lyme disease

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There is considerable controversy regarding the disorder variously known as
"**post-LD syndrome**" or
"**chronic LD**" or
"**post-treatment chronic LD**"

- its existence
- its frequency
- its cause
- its treatment

"The clinical assessment, treatment, and prevention of Lyme disease, human granulocytic anaplasmosis and babesiosis: Clinical practice guidelines by the Infectious Diseases Society of America"

14 authors

Wormser et al., 2006
Clinical Infectious Diseases 43:1089-134

It appears that a non-committal, ambiguous approach is still being taken

Wormser et al, 2006:

"**To summarize**, it can be expected that a minority of patients with LD will be symptomatic following a recommended course of antibiotic treatment as a result of the **slow resolution of symptoms over the course of weeks to months**

or

as a result of a variety of other factors, such as the **high frequency of identical complaints in the general population**."

Wormser et al.:

"In many patients, posttreatment symptoms appear to be more related to the **aches and pains of daily living** rather than to either LD or a tickborne coinfection."

and

"Objective clinical manifestations are uncommon after treatment of patients with LD.

A much more likely scenario after treatment is the **persistence or development of subjective symptoms without any residual or new objective manifestation**."

and

"More often, patients categorized as having post-Lyme disease syndrome have **subjective symptoms alone**, such as musculoskeletal pains, cognitive complaints, and/or fatigue **without objective abnormalities on physical examination**."

and

"Previous studies of various infectious diseases have suggested that delayed convalescence can be related to the **emotional state of the patients before onset** of the illness …

One study of LD showed that poor outcome was associated with **prior traumatic events** and/or **past treatment with psychotropic medications**.

This is **an important consideration** for future investigations."

AND YET, to provide a framework for future research, Wormser et al. propose a definition of post-LD syndrome.
Briefly:

- Well-documented, confirmed diagnosis of LD
- Treatment with a generally accepted antibiotic regimen resulting in resolution or stabilization of objective manifestations
- No other disorders that may explain the symptoms

. . .

- Any of the following subjective symptoms occurring within 6 months of the LD diagnosis and lasting at least 6 months:

  - **fatigue**
  - **widespread musculoskeletal pain**
  - **complaints of cognitive difficulties**

  of such severity that they result in substantial reduction in previous levels of occupational, education, social, or personal activities

Jon Godwin and I performed a meta-analysis of 5 studies comparing symptoms in

- subjects who had had LD
  and
- randomly selected subjects from the general population

The meta-analysis provides very strong evidence of an increased prevalence of

- **fatigue,**
- **musculoskeletal pain, and**
- **cognitive difficulties**

in those who had had LD.

Cairns and Godwin, 2007
International Journal of Epidemiology 34:1340-5

Those who had had LD were **significantly more likely** to have the following symptoms:

- Fatigue
- Joint or muscle pain
- Muscle aches
- Swollen joints
- Memory problems
- Poor concentration
- Difficulties in formulating ideas
- Difficulties in word finding

Criticisms of the meta-analysis by Wormser et al:

"…the authors …chose to analyse certain early retrospective studies of patients principally diagnosed during the 1980's"	All available studies of that design were included in the meta-analysis – there was no special selection.
"A controlled, prospective study would be preferable to a meta-analysis for determination of whether the frequency of symptoms after treatment for LD exceeds that of similar symptoms in persons without LD."	I agree that a single, large, prospective study is generally better than a meta-analysis, but in this case it has not been done.

Criticisms of the meta-analysis, continued:

"… patients were included in these studies who were not treated with antibiotics at all, …"	Proportions of such patients were well below the differences in the prevalence of symptoms between patients and controls. This therefore does not explain the increased prevalence of symptoms in those who had had LD.
" … or who were treated with antibiotic regimens that are not currently recommended."	In 3 studies some patients received oral penicillin or i.v. oxacillin, which are no longer recommended. It is not clear whether this had any affect on the results of the meta-analysis.

Criticisms of the meta-analysis, continued:

"… included LD cases that were poorly characterized or were diagnosed on the basis of less reliable serologic testing methods than are currently recommended"	Proportion of misdiagnosed patients can be estimated in the older studies. The estimates are still clearly below the differences in the prevalence of symptoms between patients and controls. The pattern of a higher prevalence of symptoms in LD patients was also seen in the newer studies. This therefore does not explain the increased prevalence of symptoms in those who had had LD.

Criticisms of the meta-analysis, continued:

"Recall bias was also a potential limitation of the studies evaluated, given the possibility that a person with LD would be more likely to recall and/or to report subsequent symptoms..."	The earlier studies were performed before the extensive media reports on this topic. Furthermore, the available data from physical examinations and neurocognitive reports in these studies confirm the subjective reports.
"… patients were included in these studies … who were treated after a prolonged delay of months to years…"	This will affect the size of the difference in the prevalence of symptoms between LD subjects and controls, but not the basic question whether some LD patients have persistent symptoms.

Frequency of post-LD syndrome

This meta-analysis cannot provide a precise estimate of the current proportion of LD patients that will have symptoms persisting for years.

The proportion with persistent symptoms will vary from region to region and over time, depending on how well LD is recognized and the rapidity of diagnosis and treatment.

Many remaining questions

- Frequency, i.e. the proportion of LD patients with persistent symptoms
- Identification of the patients
- Duration of the disorder
- Detailed pattern of symptoms