


Commentary: ‘What’s in a name? That which we call a rose by any other name would smell as sweet.’ Shakespeare W. Romeo and Juliet, II, ii(47–48)

Leonard H Sigal1–4* and Afton L Hassett1,5,6

The term ‘syndrome’ (from the Greek ‘concurrence’: a set of symptoms that occur together; the sum of signs of any morbid state) suggests, to many, that a collection of findings represents a disease *sui generis*. And so it is that ‘post-Lyme disease (borreliosis) syndrome (PLDS)’ a collection of non-specific symptoms, including fatigue, achiness, and cognitive dysfunction, with a marked paucity of objective clinical findings has taken on an identity, a life of its own in the USA and perhaps elsewhere.1 Of note, there are no unique, diagnostic, or even explicitly suggestive findings in PLDS; in fact, there are no objective clinical findings.1 In the hands of certain individuals, be they physicians or patients, such symptoms may be ascribed to ‘chronic Lyme disease (CLD)’—a chronic infection—based on little or no objective evidence of organ damage/dysfunction, evidence of ongoing infection, or even of proof of previous *Borrelia burgdorferi* infection. CLD is a purely hypothetical active, chronic, and refractory infection requiring extreme, in duration and intensity, antibiotic regimens, with untold consequences, physical, emotional, and ecological. As each therapeutic venture offers, at best, transient response, patients often descend into despair, even depression. Such patients experience ‘aporia’—the belief that there is no path to salvation,
no hope, and no way forward—"the fate of the symptomatic, anxious, and bewildered recipients upon receipt of equal parts new prescriptions and bad news.

Practitioners who seek to validate PLDS, similar to or identical with CLD, have found the term ‘symptoms suggestive of Lyme disease (LD)’ to be a useful guideline for diagnosis, although the symptoms are non-specific, either alone or in combination, and are unaccompanied by objective physical findings. No collection of these findings can be said to be explicitly suggestive of LD; the only pattern is the a priori bias in the thinking of committed ‘LD experts’. Findings elicited by consultation or testing are interpreted as ‘compatible with Lyme disease’ and taken as confirmatory, but in fact represent a circularity: any findings in a patient referred with a diagnosis of ‘PLDS or CLD’ and referred as part of the evaluation of PLDS or CLD must be due to LD. The report explicitly mentions LD and this is taken as definitive evidence, but these changes are neither specific for LD nor can they be differentiated from other illnesses in society. Ongoing symptoms then elicit longer durations and/or doses of ineffective antibiotics; lack of response leads to more antibiotics, not questioning of the diagnosis.

Cairns and Godwin performed a meta-analysis of studies looking at symptoms that occur or persist in patients long after the antibiotic treatment of their LD. The variety of symptoms reported sound very much like the complaints of patients we see in our regional Lyme Disease Center: fatigue, muscle/joint pain, muscle ache, swollen joints, memory problems, poor concentration, difficulty formulating ideas, and difficulty with word finding. Many of our patients have fibromyalgia syndrome (FMS); there is no substantive evidence of prior LD in many of these patients, but most have received antibiotics, many repeatedly. The assertion that the symptoms noted in this meta-analysis do not match with those of FMS, chronic fatigue syndrome, or depression, is quite a departure from our experience. The kinds of ‘soft’ neurocognitive problems described in the meta-analysis, mostly related to attention, are precisely what one sees in FMS. Of note, the excess of 5% symptoms in these patients is not remarkably greater than the prevalence of FMS in the American society.

There remains the possibility that patients with prior LD and symptoms thought to represent PLDS could have a chronic ongoing infection or a post-infectious phenomenon, analogous with reactive arthritis. The former has been described in rare individual cases, but certainly no scientific study has ever supported the contention that B. burgdorferi can become refractory or resistant to standard antibiotics, or evade the immune system by ‘hiding’. A post-infectious process has been proposed: cross-reactivity between human LFA-1 and an articular antigen has been suggested and cross-reactivity between B. burgdorferi’s flagellin and an epitope of human heat shock protein 60 expressed only in neural cells has been demonstrated. However, in neither system has an immunopathogenetic linkage been established. The truth may not lie in immunopathogenesis, but rather in psychopathogenesis. We are not suggesting that our patients are psychopathic or that this is ‘all in their heads’—far from it. However, it is apparent that psychological variables are involved. In our patient population, drawn mostly from Eastern USA, there has often been misattribution of vague symptoms to PLDS/CLD, often a post hoc ergo propter hoc fallacy. Understandably, people want a medical (not psychological) explanation for their physical symptoms; preferably one that is treatable and has a good prognosis. However, the acceptance of the conventional wisdom about PLDS/CLD has led to anxiety, fear, hopelessness, and deep confusion (aporia). This could be called a ‘contaminated milieu phenomenon’—errors in judgment by both clinicians and patients, misleading media reports, self-serving support groups and organizations leading to misattribution, poor clinical outcomes, and iatropathogenesis.

Cairns and Godwin state that ‘...ongoing infection has not been excluded’, which is of course true, but how can you prove the absence of a phenomenon that has never been demonstrated? We hope that misinterpretation of their report will not exacerbate the anxiety and misattribution that are probably at the root of much of the PLDS/CLD predominantly limited to females in the North-east.

What is needed now is a prospective study conducted in an area endemic for PLDS/CLD, to explore the likelihood and determinants of progression from proven LD to PLDS/CLD. Such a study is currently underway at our Lyme Disease Center; we estimate that in ~2 years we will have reportable data. We are also conducting a study of patients with self-described (often physician diagnosed) PLDS/CLD. Preliminary findings from our study indicate that 43 of our first 100 study patients at no time met CDC criteria for LD. Yet, almost 90% of the patients without prior B. burgdorferi infection received at least one course of antibiotics before our evaluation and 21% had been treated with intravenous antibiotics (described below). All of these patients reported musculoskeletal pain, 95% reported fatigue, and most reported sleep disturbance (76.7%) and neurocognitive impairment (81.4%); 46.5% were diagnosed with FMS or a fibromyalgia-like disorder. However, our most striking finding was that 83.7% of these patients met criteria for at least one Axis I clinical disorder (e.g. depression or anxiety) and/or Axis II personality disorder. In findings not yet published, 59.1% of our ‘PLDS’ group (patients who at one time met criteria for LD and report persistent symptoms) met criteria for at least one clinical disorder like anxiety or depression. We are certainly not suggesting that patients with PLDS/CLD have underlying psychiatric disturbances or that their complaints should be dismissed or devalued. We are, however, suggesting that chronic pain, anxiety, fear, and aporia do have consequences and that the ‘diagnosis’ of PLDS/CLD is improper and dangerous and seemingly a ‘diagnosis of exclusion’ in many practices. We remain concerned that many patients are being ‘dismissed’—not by being ushered out of the office or being ignored but by being swept along into an incorrect diagnosis with resulting incorrect treatment.

The fact that these patients are not well and not functioning adequately mandates that we ask certain questions, most notably ‘who is at risk for developing these symptoms?’ and ‘what is the mechanism?’ It is increasingly clear that some people in society are predisposed to developing FMS or related syndromes. The trigger for this phenomenon may be an infectious illness. However, many of our patients never had LD; they might have had another febrile illness, physical trauma, or emotional stressor that caused the evolution of FMS. The claim of antecedent LD may be false; however, the patient is still not well. To condemn such patients to illusory treatments and a future of debility, frustration, and despair is universally
unacceptable. Proper prospective studies, preferably in a less ‘contaminated’ informational and emotional setting, are our best means of correcting the mistakes of the past.

Acknowledgements

Studies noted were funded by National Institutes of Health 1 K08 MH65360-1 (‘The Role of Co-Morbid Mental Disorders in Lyme Disease).

References