Lyme disease is a relatively well-described infectious disease with multisystem manifestations. Because of confusion over conflicting reports, anxiety related to vulnerability to disease, and sensationalized and inaccurate lay media coverage, a new syndrome, “chronic Lyme disease,” has become established. Chronic Lyme disease is the most recent in a continuing series of “medically unexplained symptoms” syndromes. These syndromes, such as fibromyalgia, chronic fatigue syndrome, and multiple chemical sensitivity, meet the need for a societally and morally acceptable explanation for ill-defined symptoms in the absence of objective physical and laboratory findings. We describe factors involved in the psychopathogenesis of chronic Lyme disease and focus on the confusion and insecurity these patients feel, which gives rise to an inability to adequately formulate and articulate their health concerns and to deal adequately with their medical needs, a state of disorganization termed aporia. Key words: aporia, chronic Lyme disease, Lyme disease, medically unexplained symptoms, misdiagnosis, psychological, psychopathogenesis.

It is human nature to seek to understand and remedy suffering. People process information from their environments and interactions through filters determined by their internal belief systems, thought processes, and experiences. The models thus produced, further shaped and molded by societal norms, are then used to interpret experiences (symptoms). Once people have a working model, they seek to understand the origins of their symptoms and to develop a plan of action intended to diminish or eliminate their suffering and anxiety.

In our society, fatigue, pain, weakness, and malaise are common complaints, often in people with no objective findings on physical examination or laboratory testing. Especially relevant to people with vague complaints is the fact that “objective diagnostic testing” is usually not “diagnostic.” Most serological tests have high rates of false positivity and a false positive result can be incorrectly interpreted as “proof” of diagnosis. This is all too common in rheumatology, where a weakly positive antinuclear antibody test is often interpreted as proof of systemic lupus erythematosus and a weakly positive rheumatoid factor as proof of rheumatoid arthritis. Evaluation by a competent rheumatologist is often sufficient to determine that the test and diagnosis are incorrect. No prior motive is ascribed to the disabusing clinician. The test and diagnosis are accepted as having been false alarms and the patient is reassured that she or he does not have one of these serious chronic illnesses. Patients who continue to suffer but are offered no diagnosis to fill the void left by the reversal of the incorrect diagnosis remain concerned, even frightened, but not necessarily angry.

Suffering, by its very nature visceral and preverbal, is amorphous. Specific manifestations and explanations of the suffering are often profoundly influenced by socially acceptable constructs. As pointed out by Shorter (1), there have been many examples of fatigue and other subjective complaints being formulated into a “specific” diagnosis, even without objective findings on examination or specific abnormalities in the laboratory. The “energy” of feeling as if one does not “fit” into societal expectations probably exists in all societies. The different manifestations (“packaging,” if you will) are defined by societal social norms and mores. The energy, like a vapor, expands to entirely fill and take on the shape and dimensions of the container offered. So it was for “myalgic encephalitis,” “atypical poliomyelitis,” “chronic brucellosis,” “the Candida connection/chronic candidiasis,” and “chronic Epstein-Barr virus infection.” Once these were debunked and discarded, one could confidently predict that another popular container would emerge.

Lyme Disease: The Rush to Diagnosis

In 1975, an epidemic of “juvenile rheumatoid arthritis” was identified in three small communities on the east bank of the Connecticut River (2). Through a series of epidemiologic studies, investigators determined that this outbreak was actually an inflammatory syndrome due to a tick-borne infection [spread by Ixodes scapularis, the deer tick, in the Northeast and Midwest and I. pacificus in the Pacific states (3)]. Ultimately the causative organism, Borrelia burgdorferi (3), was identified, serologic tests were developed, and the natural history of this zoonotic infection, in human and animal hosts, was understood. We now know that Lyme disease is the most common tick-borne infection in the United States (3), prevalent where there are ixodid ticks, as described above. The endemic area has been steadily growing, probably because the ticks that spread the infection are carried by the expanding (both numerically and geographically) deer population and by passerine birds during their migrations (4). In the Northeast there has been a remarkable change in ecology. Forest lands that were clear-cut and burned to make way for farms in the 17th and 18th centuries were abandoned with the westward migration of the 19th century and allowed to return to forest (4). At the end of the 20th century, suburban encroachment placed refugees from urban centers on land that now represented ecotones optimal for deer and mouse populations. With increases in these mammal populations comes a remarkable increase in the tick population. Thus, Lyme disease has become a public health problem because the development of more “environment at risk” has occurred at the very time

Environmental Health Perspectives • VOLUME 110 | SUPPLEMENT 4 | AUGUST 2002

607
that large numbers of people are moving into these very areas. Lyme disease, either local or acquired on a visit to an endemic area, has become a reasonable consideration in many regions of the United States where it might not have been included in the appropriate differential diagnosis even a few years ago.

With a fuller appreciation of how *B. burgdorferi* and *I. scapularis* survive have come a number of efforts to control the disease, for example, deer population control, tick control by spraying properties, killing ticks on deer by use of deer feeding stations equipped with acaricide treatment stations, and deer enclosure fencing. Individuals have taken personal responsibility by clearing forest clutter and shrubbery to decrease the peri-domestic habitat conducive to tick population growth, doing tick checks at the end of days spent in high-risk areas, and using vaccine (5). Nonetheless, there has certainly been no remarkable decrease in the number of cases reported to the Centers for Disease Control and Prevention; these statistics are widely (and correctly) held to be an underestimate of the true number of cases. Adding to the difficulty in interpreting these statistics is the fact that they represent the county of report, not the county of acquisition of the disease.

The clinical spectrum of *B. burgdorferi* infection is now well known (3) and includes dermatologic, musculoskeletal, neurologic, and cardiac features occurring during three somewhat arbitrarily described different “stages”: early localized disease, early disseminated disease, and late disease. Early localized disease includes the classic erythema migrans rash occurring at the site of the tick bite. Many patients experience satellite lesions, due to hematogenous spread, and nonspecific symptoms similar to those of a “viral syndrome,” including arthralgias, myalgias, headache, and low-grade fever. Early disseminated disease includes neurologic damage (meningitis, cranial nerve palsy—most frequently facial nerve palsy—and peripheral neuropathies) and cardiac disease (usually conduction defect, which may be symptomatic). Ophthalmologic disease is uncommon. Late disease can include arthritis, at first migratory and then usually mono- or oligoarticular, and neurologic findings different from those of earlier disease, now including cognitive dysfunction and subtle polyradiculoneuropathies. The latter two “stages” may occur without antecedent erythema migrans or illness suggesting the onset of *B. burgdorferi* infection. There are other clinical problems ascribed to Lyme disease, often by dint of only serologic tests of dubious value—these linkages are often tenuous. Some features of early Lyme disease (e.g., high fever, liver function test abnormalities, cytopenias) are actually due to other tick-borne pathogens co-infected with *B. burgdorferi*.

There is often a rush to make the diagnosis of Lyme disease predicated on flimsy evidence, frequently based on a test rather than on clinical evidence (6,7). Serologic testing can help confirm the diagnosis of Lyme disease and, when used appropriately, can be quite helpful. However, these are not Lyme disease tests; they are merely tests that measure antibodies that bind to *B. burgdorferi* in an *in vitro* assay. These tests should never be used as screening tools; a positive test cannot inform a diagnosis in isolation. Nonetheless, weakly positive tests without immunoblot verification (crucial because the screening enzyme-linked immunosorbent assay (ELISA) is prone to false-positives) are often the sole evidence in favor of the diagnosis.

Contrary to the examples noted above, denial of the diagnosis of Lyme disease often evinces anger and indignation from the patient. The frustration of having the chosen/accepted explanation for their suffering removed is almost intolerable (6–8). Having Lyme disease holds a certain appeal for patients searching for answers for a number of reasons. Like multiple chemical sensitivity syndrome, there is an identifiable environmental cause to which the patient fell victim. They are not to blame for their illness. The illness was obtained during healthy and societally acceptable activities such as gardening, hiking, and picnicking. Furthermore, Lyme disease has become a part of our culture. Media exposure has made Lyme disease, a relatively uncommon ailment, seem to be common to the public. Lyme disease is real, a curable illness with a well-established treatment, unlike the other medically unexplained symptoms (MUS), conditions such as fibromyalgia and chronic fatigue syndrome. Finally, Lyme disease *is not* fibromyalgia or chronic fatigue syndrome, which some medical practitioners have come to view with an unjustified disdain (9) as being “all in your head.”

Early in the process of clinical description, an unfortunate term was used in reference to Lyme disease: “the great imitator” (10). This term was originally used to describe syphilis, at its height a great mimic of other diseases. Mimicry by Lyme disease was raised as an issue in the days shortly after its description in order to raise the awareness of physicians in endemic areas. Unfortunately, the term took on a life of its own, and some advocacy groups and physicians accepted a premise that *B. burgdorferi* infection could perpetrate nearly any clinical deed (6,7). The claims mounted: *B. burgdorferi* could cause an illness that defied routine serologic tests, did not include antecedent or current features of Lyme disease, and was unrecognizable by the very scientists who first described Lyme disease. *B. burgdorferi* could cause an illness that persisted despite aggressive antibiotic therapy. *B. burgdorferi* could cause a progressive illness with features including fatigue, malaise, pain and cognitive dysfunction but no objective signs of tissue damage (6,8).

**Lyme Disease: The Latest “Cause” of Fatigue**

By the end of the 20th and start of the 21st century, Lyme disease has become a major public health issue in certain American communities, and unfortunately battle lines are being drawn. On the basis of scientific study, the physician-scientists and their supporters (the “rationalists”) are concerned about a tick-borne illness that can be diagnosed and treated, has a good prognosis, and can be prevented. However, there is also a “counterculture” of myth and speculation describing another “Lyme disease,” an “alternative reality” claiming that there is “chronic Lyme disease,” an incurable, irreversible, irretrievable illness, based on unproven premises. These “empiricists” are concerned about chronic Lyme disease, a clinical entity based on medical models often at odds with the scientifically corroborated features—clinical, microbiologic, and immunologic—of Lyme disease. Chronic Lyme disease has been used as the diagnosis to explain a variety of complaints. It is our premise that chronic Lyme disease is yet another in a long series of “containers” for ill-defined suffering (the energy or “vapor” alluded to above), giving it form and illusory “substance.” That these people are not well is not the proper focus of inquiry or debate—they are manifestly ill. The root cause and underlying mechanism of their illness should be the focus.

Some of these patients have, in fact, been diagnosed as having Lyme disease. Then why do they not improve with antibiotic therapy? A series of explanations for persistence of complaints despite antibiotic therapy that would be considered adequate was proposed in 1994 (11). Such explanations included:

1. **a** symptoms unrelated to Lyme disease—initial misdiagnosis;
2. **b** Slowly resolving Lyme disease;
3. **c** permanent tissue damage, not responsive to antibiotics;
4. **d** factors related to chronic illness;
5. **e** sterile infection caused by dead organism;
6. **f** post-Lyme disease syndromes, possible reactive phenomena; and
7. **g** true persisting infection with *B. burgdorferi*.

Initial misdiagnosis by others is commonly the reason for patients not improving in our practice; the rush to make this diagnosis often leaves logic and reason far behind. Many patients improve slowly after antibiotics, up to 50% having persisting nonspecific complaints that last 6 months or more. When the correct diagnosis of Lyme
Environmental Health Perspectives • VOLUME 110 • SUPPLEMENT 4 • AUGUST 2002

Unexplained Symptoms • Psychopathogenesis of chronic Lyme disease

disease is delayed (or, rarely, when the course of the disease is aggressive), damage may have occurred that cannot resolve even when the infection is eradicated. This has been the case in a few patients with permanent heart block or facial palsies that have not totally resolved. We have seen many patients with complaints referable to poor sleep, poor physical conditioning, anxiety, depression, or muscle atrophy. In these cases, no active infection was identified, often the initial diagnosis was in error, and nonantibiotic therapy was warranted. Inflammation and organ dysfunction may persist even after B. burgdorferi is killed by host defenses and antibiotics, with residual debris acting as a persisting focus of inflammation (12). Until the organism is cleared from the site of infection, there may be active “disease” without active infection. “Post-Lyme disease syndrome” has been the subject of much debate, but no immunopathogenic process has been identified (12). There has been speculation that immunologic cross-reactivity between the organism and a host component may drive inflammation, but this has not been proven (12). Many patients with post-Lyme disease syndrome actually have fibromyalgia, a phenomenon first identified by our group (13,14) and corroborated by others (15). Finally, there is the theoretical possibility that the organism may survive antibiotics and cause ongoing inflammation. This is unproven and implausible in the setting of ongoing seronegativity and the absence of any physical findings of inflammation or objective tissue damage.

Any of these may be the true explanation for the patient’s ongoing suffering, but none save the last represents ongoing infection, nor will they respond to further antibiotic therapy. Many sufferers have taken antibiotics for many months and years, obtaining no lasting relief. Oral and intravenous antibiotics, in combinations or sequential cycles, even self-induced malaria (for a pyrexia-induced cure as was used many years ago for neurophilis) have been tried. A recent trial of long-term antibiotics funded by the National Institutes of Health was closed because it failed to show any effect on the ongoing complaints of patients with chronic Lyme disease (16). And yet these patients cleave to the diagnosis of chronic Lyme disease, often demanding more antibiotics that do not offer a surcease to their suffering. There is reason to seek alternative explanations for these refractory cases. The antibiotics used have toxicities often worse than the patient’s original problems—avoidance of further iatrogenic damage is important (8,17). If the diagnosis of Lyme disease is in error, another process is not being dealt with. Correct treatment is not being given for the real illness. If antibiotics have not worked, there is scant hope for the future. There is need to give the patient a cause for optimism.

Although providing care for these patients can be exceptionally frustrating (18), it is imperative that they not be dismissed. The illness is not “all in their heads.” Lessons we have learned from our experiences with patients with fibromyalgia are applicable to patients with chronic Lyme disease. We must address their pain, fatigue, and cognitive symptoms, as well as the psychological and behavioral processes that contribute to their suffering. With further study we may understand the psychological predispositions to this syndrome.

**Lyme Disease, Medically Unexplained Syndromes, and the Anxious Patient**

As many as half the patients presenting to Lyme disease specialty clinics are depressed and/or suffering from excessive stress (19). Excessive stress and depression may be due to having a chronic illness; alternatively, it is possible that depression and high levels of stress may have preceded the initial infection and are symptomatic of an underlying vulnerability, which predisposes to chronic, nonspecific symptoms and complaints. In the only study assessing psychological factors that predict the course of Lyme disease, a strong association between a history of prior psychological trauma and chronic physical symptoms was found (20). It is possible that antecedent traumatic psychological experiences may play an etiologic role in the persistence of symptoms after the infection has been adequately treated (20). This relationship has been demonstrated in other MUS conditions, including multiple chemical sensitivity (21), chronic fatigue syndrome, (22), irritable bowel syndrome (23–26), chronic pelvic pain (27), and fibromyalgia (28–30).

These findings and our own clinical observations have led us to speculate that the symptoms of a disproportionate number of chronic Lyme disease patients may be the product of chronic psychological stress and resultant neuropsychological changes stemming from chronic early stress states predisposes one to experiencing excessive levels of psychological stress because of a negative bias in information processing (32). For example, not only are benign events viewed as threatening, but also there is a perceived inability to cope effectively with these threatening events. Further, in dealing with symptoms of unclear cause or treatment, such patients may be uniquely vulnerable to a “fear of the unknown,” an all-encompassing poorly defined anxiety based on a lack of clear understanding of the perceived threat to self.

In addition, we hypothesize that neurobiological changes stemming from chronic early stress states predisposes one to physiological manifestations of psychological distress (33). Once vulnerable, environmental stressors may then act as triggers for these stress-related syndromes. In addition, in post-Lyme disease syndrome, the trigger might be the infection with B. burgdorferi, whereas in other psychophysiological disorders the trigger could be a severe emotional stressor such as a loss (death, divorce, loss of employment) or traumatic event (spousal abuse, automobile accident, surgery). In pain (emotional and physical), literally millions of these patients present to physicians in search of medical explanations for their emotional distress and related physical symptoms. By training, most physicians look for medical explanations, whereas lack of training and time constraints explain their hesitancy to explore the psychological aspects of their patients’ illnesses. Especially in the case of chronic Lyme disease, “medicalization” takes root in what is a very fertile environment, leading patients to adopt a permanent sick role in light of their firmly entrenched belief that they have an incurable disease. One cannot approach such patients...
using a purely “biomedical model” of disease; rather, one must use a “biopsychosocial” or “illness behavior” model of illness if one is to understand and help these patients.

The acceptance of the sick role by many of these patients is perhaps the most damaging scar left by chronic Lyme disease. These are people in search of an explanation. When they listen to the media, they hear only poor outcomes and horror stories of denial and betrayal by physicians and insurance companies. The media reports “David vs. Goliath” stories and puts a sensationalist spin on stories as is needed to attract listeners/readers—the media are there to entertain and titillate, not educate. When patients look at the medical literature, often without the assistance of a physician, what they see is explanations couched in shades of gray. After therapy, symptoms of Lyme disease may increase, decrease, disappear, or persist. Serologic reactivity, by ELISA or Western blot, may increase, decrease, or remain at a constant level. Similarly, the immunologic repertoire, as judged by the number of bands, may expand, contract, or persist. This lack of certainty and predictability can yield confusion and anxiety. It also plays on their fears and enhances their personal hypervigilance, identifying and focusing on new physiological aberrations and experiences (e.g., tachycardia after exertion, lightheadedness when arising rapidly, minor forgetfulness in times of detail overload) and turning them into symptoms of a disease. These people chronically monitor their symptoms, often documenting changes in detailed diaries that focus on even the most subtle changes in their apparent health status. In this way the overanxious “worried well” can evolve into patients with MUS conditions, in this example, chronic Lyme disease.

People living in Lyme disease–endemic areas want explanations for their complaints, their ills. The suburban splendor of their dreams has been turned into a land of hidden perils and risks. The risk is the tiny deer tick, mice, and deer that come out of the wilderness at their backyards. An invisible threat from the wilderness strikes a primal “fear of the unknown” into the heart of the urbanized human, an animal totally dependent on vision to identify and avoid threats. Thus, tick-borne infection may evoke a visceral fear that we in the medical community have not understood or dealt with well. The response is an outwardly directed hypervigilance, often leading to extreme actions taken to avoid Lyme disease, including excessive use of acaricides and tick repellants and exaggerated modifications of their peridomestic properties, for example, paving over their backyards.

The stressed residents of endemic areas represent an avid market for a somatic diagnosis and a potentially very energetic advocacy group on behalf of their chosen diagnosis. We, as academic physicians and researchers, do not have the access to the media or politicians to compete. But this is the influence that has caused state legislators in New Jersey and Connecticut to determine the minimum duration of intravenous antibiotics for Lyme disease that insurance companies must cover and the criteria to determine when further antibiotic courses are necessary. Most of these people are functional, with varying degrees of (sometimes exaggerated) concerns about a real public health risk. The lack of a response from the authorities, coupled with what many in this group believe is the medical community not taking these concerns seriously, has often evoked hostility and anger.

There is another population concerned with Lyme disease. They are chronically ill and suffering and have accepted the diagnosis of chronic Lyme disease as the explanation for their woes, often despite compelling objective evidence to the contrary. Some may have once had the disease but have been treated with antibiotics in a manner usually deemed “sufficient,” whereas others may have had no prior illness to suggest Lyme disease. Some of the latter group may have had the diagnosis of Lyme disease made solely on the basis of test results: valid tests with equivocal results, tests with results misread or misinterpreted, novel tests whose results cannot be interpreted, or tests whose results are known to be invalid. Regardless, technology trumps common sense and clinical skills, and a diagnosis is made and accepted. Many of these patients have become true believers in the phenomenon of chronic Lyme disease, fiercely devoted to the concept and vociferous members of support and advocacy groups. They may become avid proselytizers and tireless protesters. Often there are local physicians or advocate “gurus”; frequently, these leaders accuse the medical establishment of blindness and misdeeds, claiming that the establishment is interfering with their ability to properly care for their many patients by imposing rules and targeting with investigations. If their chosen physicians, the first to properly identify their chronic Lyme disease when so many practitioners before were unable to do so, are taken away from them, many patients become more agitated and energized.

Acceptance of the diagnosis of chronic Lyme disease provides a number of benefits for these sufferers. It legitimizes the pain, suffering, and disability. It provides a structure by which to understand a very frightening experience. It produces a community with which to identify and from which to draw strength and comfort. It gives the sufferer a means by which to address the suffering on personal and societal levels. Perhaps most important, the diagnosis of Lyme disease denies a psychiatric diagnosis—“this is NOT in my head, doctor.” Mention of psychosomatics, stress, anxiety, or depression is met with scornful rejection by the patients. They often claim their stress is in fact due to the denial of the diagnosis by insurance companies and non—“Lyme-literate” physicians. Believers respond to skepticism about chronic Lyme disease by spreading this new gospel with even more fervor. They issue jeremiads directed at the greedy denying insurance companies, the blind academic “nonbelievers,” the nefarious government “cover-up,” and the confused, doubtful local physician. Any attempt to deny these people their diagnosis or access to their chosen physician or their chosen modes of therapy is met with anger, vengeful resentment, and active protest.

**Psychoneuroimmunologic Changes in Chronic Lyme Disease: Exhaustion and Aporia**

A paradigm shift might hold the greatest promise for effective care. Integrative conceptualizations of chronic Lyme disease and other MUS syndromes will guide treatment that addresses psychophysiological disorders beyond the symptomatic, palliative level. Elucidating neurobiological mechanisms such as hypothalamic–pituitary–adrenal axis dysfunction, pain transmission system dysfunction, or dysautonomia (34) may dictate psychophysiological approaches to treatment, including respiratory sinus arrhythmia biofeedback (35) and/or trials of novel mediations, perhaps those with noradrenergic and dopaminergic effects. Similarly, psychotherapeutic interventions will include, but move beyond, relaxation and coping skills training. We propose that a more in-depth cognitive behavioral therapy approach may alter the underlying maladaptive belief systems that drive stress-evoking thoughts, self-defeating behavior, and negative affective processes (32). All these interventions must be subjected to empirical evaluation, and once they are validated, we look forward to testing them in other MUS syndromes. All interventions must be offered with great caution because most of these patients will resist the implied stigma of a “psychological” diagnosis. We believe the MUS syndromes represent a prime example of how psycho-neuro-endocrino-immunology drives disease and illness.

Unfortunately, any attempt to deny the diagnosis or to offer an alternative explanation and treatment is dismissed with anger and animosity. Physicians who present alternative explanations are accused of being in the hip pockets of insurance companies and are demonized—“how can such a physician have any motive aside from personal profit?” Academicians are charged with trying to diminish the import of Lyme disease—why
they should do this and thereby decrease the likelihood of obtaining research funding is not made clear. The venom of the critics suggests that the denial of this diagnosis is striking close to the heart of a dearly held belief or value. These patients are experiencing “aporia”, defined in The Random House Dictionary of the English Language (36) as “the expression of a simulated or real doubt, as about where to begin or what to do or say” (in rhetoric) or “a difficulty encountered in establishing the theoretical truth of a proposition created by the presence of evidence both for and against it” (in logic or philosophy). For our purposes, aporia is a state of confusion, self-doubt, and exhaustion! This manifests in patients as an inability to adequately formulate and articulate their complaints, their fears of unknown threats/disease, and their elusive sense of anguish. They are “stuck” and thoroughly unable to deal effectively with their health care needs. Defensive anger stems from the threat of removing their diagnosis; illness behavior in their experience of chronic Lyme disease has become their only fundamentally acceptable “language” for expression of their distress; to borrow a term from the psychology literature, it is their “ego-syntonic” language.

In the final analysis there is a struggle over who defines a new and emerging disease: patients, their chosen clinicians and advocacy groups, or the biomedical establishment’s scientists and physicians. It is clear that the scientific community faces a formidable challenge. Unexplained suffering and fear of the unknown are far greater than fear of even the worst, incurable disease and drive these patients to extreme measures. Dealing with the phenomenon of chronic Lyme disease, a new constituent of the MUS syndromes complex, requires an appreciation of its complex psychopathogenesis. We need to appreciate and study the aporia of MUS conditions—to describe and heal the sense of being lost, hopeless, and vulnerable.

REFERENCES AND NOTES

1. Shorter E. From Paralysis to Fatigue. A History of Psychosomatic illness in the Modern Era. New York:Free Press, 1992.
2. Steere AC, Malaviya SE, Snydman DR, Shope RE, Andiman WA, Ross MR, Steele FM. Lyme arthritis. An epidemic of oligoarticular arthritis in children and adults in three Connecticut communities. Arthritis Rheumatism 20:7–17 (1977).
3. Steere AC. Medical progress: Lyme disease. N Engl J Med 345:115–125 (2001).
4. Cronin W. Changes in the Land. New York:W.W. Norton, 1983.
5. Sigal LH. Lyme disease: a clinical update. Hosp Pract 26:31–48 (2001).
6. Sigal LH. Pityfall in the diagnosis and management of Lyme disease. Arthritis Rheumatism 41:195–204 (1998).
7. Steere AC. Deck of Taylor E, McHugh GL, Logigian EL. The over-diagnosis of Lyme disease. JAMA 269:1812–1816 (1993).
8. Sigal L. The Lyme disease controversy: the social and financial costs of the mismanagement of Lyme disease. Arch Int Med 156:1493–1500 (1996).
9. Bohr TW. Fibromyalgia syndrome and myocardial pain syndrome. Do they exist? Neurol Clin 13(2):365–384 (1995).
10. Pachner A. Borrelia burgdorferi in the nervous system: the new “great imitator.” Ann NY Acad Sci 539:56–64 (1988).
11. Sigal L. Persisting complaints of Lyme disease: a conceptual review. Am J Med 96:385–374 (1994).
12. Sigal LH, the immunology and potential mechanisms of immunopathogenesis of Lyme disease. Annu Rev Immunol 15:63–92 (1997).
13. Hsu V, Patelia S, Sigal L. “Chronic Lyme disease” as the incorrect diagnosis in patients with fibromyalgia. Arthritis Rheumatism 36:1493–1500 (1993).
14. Sigal L, Patelia SJ. Lyme arthritis as the incorrect diagnosis in children and adolescents. Pediatrics 90:523–528 (1992).
15. Dineenman H, Steere A. Lyme disease: associated with fibromyalgia. Ann Intern Med 117:261–265 (1993).
16. Klemperer MS, Hu LT, Evans J, Schmid CH, Johnson GM, Trevino RP, Norton D, Levy L, Wall D, McCall J, et al. Two controlled trials of antibiotic treatment in patients with persistent symptoms and a history of Lyme disease. N Engl J Med 345:85–92 (2001).
17. Sigal L. Editorial: Lyme disease: primus non nocere. J Infect Dis 171:423–424 (1995).
18. Walker EA, Katon WJ, Keegan D, Gardner G, Sullivan M. Predictors of physician frustration in the care of patients with rheumatological complaints. Gen Hosp Psychiatry 19:315–323 (1997).
19. Reid MC, Schoon RT, Evans J, Rosenberg JC, Horvait RJ. The consequences of overdiagnosis and overtreatment of Lyme disease: an observational study. Ann Intern Med 120:354–362 (1998).
20. Solomon SP, Hilton E, Weinschel ES, Pollock S, Grinrich E. Psychological factors in the prediction of Lyme disease course. Arthritis Care Res 11:419–426 (1998).
21. Bell IR, Baldwin CM, Russek LSS, Schwartz GER, Hardin EE. Early life stress, negative paternal relationships and chemical intolerance in middle-aged women: support for a neural sensitization model. J Womens Health 7:1135–1147 (1998).
22. Sali E. Precipitating factors for the chronic fatigue syndrome. J Psychiatric Res 31:59–65 (1997).
23. Walker EA, Gelfand AN, Gelfand MD, Katon WJ. Psychiatric diagnoses, sexual and physical victimization, and disability in patients with irritable bowel syndrome or inflammatory bowel disease. Psychol Med 25:1259–1267 (1995).
24. Walker EA, Katon WJ, Roy-Byrne PP, Jamekia RP, Russo JR. Histories of sexual victimization in patients with irritable bowel syndrome or inflammatory bowel disease. Am J Psychiatry 150:1502–1506 (1993).
25. Irwin C, Falsetti SA, Lydiard RB, Ballenger JC, Brock DD, Brenner W. Comorbidity of posttraumatic stress disorder and irritable bowel syndrome. J Clin Psychiatry 57:576–578 (1996).
26. Reilly J, Baker GA, Rhodes J, Salomon P. The association of sexual and physical abuse with somatization: characteristics of patients presenting with irritable bowel syndrome and non-epileptic attack disorder. Psychiatry 29:399–406 (1999).
27. Heim C, Ehlers U, Harker JP, Heilhammer DH. Abuse-related posttraumatic stress disorder and alterations of the hypothalamic-pituitary-adrenal axis in women with chronic pelvic pain. Psychosom Med 60:308–316 (1998).
28. Alexander RW, Bradley LA, Alarcon GS, Tran-A Alexander M, Aaron LA, Alberts KR, Martin MY, Stewart KE. Sexual and physical abuse in women with fibromyalgia: association with outpatient health care utilization and pain medication usage. Arthritis Care Res 11:102–115 (1998).
29. Taylor ML, Trotter DR, Cuuka ME. The prevalence of sexual abuse in women with fibromyalgia. Arthritis Rheumatism 22:229–234 (1989).
30. Walker EA, Keegan D, Gardner G, Sullivan M, Bernstein D, Katon WJ. Psychosocial factors in fibromyalgia compared with rheumatoid arthritis. II: Sexual, physical, and emotional abuse and neglect. Psychosom Med 59:572–577 (1997).
31. Winfield JB. Pain in fibromyalgia. Rheum Dis Clin North Am 25:55–79 (1999).
32. Young JS. Cognitive Therapy for Personality Disorders. A Schema-Based Approach. 3rd ed. Sarasota, FL: Professional Resource Press, 1999.
33. Sternberg EM. The Balance Within. The Science Connecting Health and Emotions. New York:WH Freeman and Company, 2000.
34. Clouw DJ, Chrousos GP. Chronic pain and fatigue syndromes: overlapping clinical and neuroendocrine features and potential pathogenic mechanisms. Neuroimmunology 41:34–153 (1997).
35. Lehrer PM, Vaschillo E, Vaschillo B. Resonant frequency biofeedback training to increase cardiac variability: ratio nale and manual for training. Appl Psychophysiol Biofeedback 25:171–191 (2000).
36. Flexner SB, Hauk LC, eds. The Random House Dictionary of the English Language, 2nd ed. New York:Random House, 1987.