

The Neuropsychiatric Manifestations of Lyme Borreliosis

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Lyme borreliosis (Lyme disease), a tick-borne spirochetal illness, has multi-systemic involvement and is rapidly increasing in certain areas of the United States. Although its neurologic manifestations are becoming increasingly well recognized, its psychiatric presentations are not well known. The first section of this paper will provide an overview of Lyme borreliosis and a review of the relevant neuropsychiatric literature. The second section will provide clinical descriptions of some common neuropsychiatric symptoms as well as a discussion of the problems typically faced by patients with this illness. Guidelines to assist the clinician in working with these patients will be presented.

Since the identification of the cause of syphilis in the early 1900s, psychiatrists have been aware that: (1) severe psychiatric disorders may be caused by a central nervous system infection; and (2) early antibiotic treatment may prevent permanent neurological damage. Syphilis was known as the "great imitator" because its multiple manifestations mimicked other known diseases. Today a new epidemic has emerged that has multiple manifestations and has been dubbed "the new great imitator"-Lyme Borreliosis (Lyme disease) (1). Because Lyme borreliosis, like syphilis, has neuropsychiatric manifestations, psychiatrists are being asked to see these patients-often before they are diagnosed. Incorrectly labeling these patients as having a functional psychiatric disorder may result in a delay in initiating antibiotic treatment. Such delay can lead to severe disability and, possibly, irreversible neurologic damage (2). Because of the epidemic of Lyme borreliosis in areas of New York State and its rapid spread nationwide (3), it behooves mental health professionals to be aware of its multiple typical and atypical presentations.

Part 1 of this paper consists of a general overview of Lyme disease and a review of its neuropsychiatric manifestations. Part 2 provides more detailed clinical descriptions of the neuropsychiatric aspects of Lyme borreliosis and suggests ways in which psychiatrists can be of help. The clinical vignettes will be based on data collected from approximately 200 patients with seropositive Lyme disease.

PART I. OVERVIEW (BRIAN A. FALLON)

Diagnosis

Lyme borreliosis caused by the spirochete *Borrelia burgdorferi*, is an infection commonly transmitted by the bite of an infected arthropod—primarily ticks. A tick feeding may take up to 3 days and disease transmission appears to take 12-24 hours. The clinical spectrum of the disease includes dermatologic, neurologic, ophthalmologic, cardiac, rheumatologic, and psychiatric manifestations (4).

The criteria for diagnosing Lyme disease vary depending upon the purpose. For surveillance studies (3), the diagnosis requires a history of exposure in an endemic area and either: (1) a physician-diagnosed erythema chronicum migrans rash, or, (2) serologic evidence of exposure to *Borrelia burgdorferi* and one of the following: (a) arthritic symptoms—recurrent brief attacks of joint swelling or joint pain; (b) neurologic symptoms—such as lymphocytic meningitis, cranial neuritis, radiculoneuropathy, and/or encephalomyelitis; or (c) cardiac conduction defects—second or third degree AV block.

This definition, while useful for research purposes, is unduly restrictive because about one-third of patients do not recall a rash and because current serologic testing is generally considered inadequate, producing false negatives and false positives (5). Thus, the diagnosis of Lyme disease at this point remains clinical not serologic.

Because Lyme borreliosis is multisystemic, the differential diagnosis has to be broad, including viral infections, aseptic meningitis, disseminated gonococcal infection, rheumatoid arthritis, late stage syphilis, multiple sclerosis, Guillian-Barre, AIDS, systemic lupus, subacute bacterial endocarditis, thyroiditis, Reiter's syndrome, fibromyalgia, chronic fatigue syndrome, and psychiatric disorders. If treated early, the disease may be limited to an asymptomatic rash or only a few days to a week of flu-like symptoms. In its later stages, patients may have multisystemic disease, leading to an inability to work for months to years. The simplest tasks may become insurmountable.

Distribution

Ticks infected with *borrelia burgdorferi* have been found across the United States and around the world (6). The number of United States cases has increased dramatically since record keeping started in 1980. Between 1985 and 1988, the number of states with reported cases of Lyme borreliosis rose from 8 to 46 (3). Although distributed nationwide, certain states carry the heaviest burden of illness. In 1988, for example, New York State accounted for more reports than any other state, contributing 56% of national Lyme case reports (3). Between 1986 and 1989, the annual incidence of Lyme disease in NYS (based on reported cases which met the surveillance definition) increased 7-fold. Many additional cases were reported which did not meet the surveillance case definition. These data indicate that Lyme disease is a steadily increasing national public health problem.

History

Although many people believe that Lyme disease was discovered in Lyme Connecticut in 1975, an illness very much like Lyme disease has been recognized in Europe for over 100 years. In 1883, a German physician described the rash common in the later forms of Lyme disease—*acrodermatitis atrophicans* (7). In 1909, a Swedish physician described the classic Lyme rash, known as erythema chronicum migrans (ECM), and linked it to a tick-borne infection (8). In 1922, Dr. Garin-Bujadoux described what is now recognized as a disseminated form of Lyme disease. His patient developed ECM after a tick bite, followed by a radiculopathy, peripheral paralysis of one arm, and meningitis (9). In 1941, Dr. Bannwarth described a similar neurologic syndrome and called it "chronic lymphocytic meningitis" (10). Principal signs were radicular pains, lymphocytic meningitis without meningeal signs, and involvement of the peripheral nervous system, particularly facial palsy. In Europe, Lyme disease with neurological manifestations has been described under many labels, including neuroborreliosis, the Garin-Bujadoux syndrome, and Bannwarth's syndrome. Lab studies often demonstrate an elevated ESR, an elevated spinal fluid IgM level, and pleocytosis in the spinal fluid, often with lymphocytic predominance. As will be discussed later, these

abnormal lab findings are not always present in the American form of neuroborreliosis.

Although the first report of a tick-induced ECM rash was from Wisconsin in 1970 (11). Lyme disease first came to critical attention in the United States in 1975 when Dr. Alan Steere described what seemed to be a new illness after investigating an unusually high prevalence of presumed juvenile rheumatoid arthritis in Old Lyme Connecticut. Naming this outbreak after the town in which it occurred, he called this illness Lyme Arthritis (12). By the late 1970s it was recognized that the illness had systemic manifestations including neurologic, rheumatologic, dermatologic, and cardiac components and so the name of the illness was changed from Lyme arthritis to Lyme Disease. In 1982, the infectious agent *Borrelia burgdorferi* was identified (4). Soon thereafter, reports indicated that the European neuroborreliosis was caused by a similar if not identical organism (13). In acknowledgment of this infectious agent, Lyme disease is now referred to as Lyme borreliosis.

Clinical Profile

There are a wide variety of symptoms associated with Lyme borreliosis. Symptoms vary greatly, one or more systems may be involved, and new manifestations continue to be described. The progression of illness has generally been separated into early and late borreliosis.

The most identifiable early symptom of Lyme disease is the rash, erythema chronicum migrans, which may appear days to weeks after the bite. The rash typically is a bull's eye rash that may enlarge from its site of origin to 10cm or greater. Commonly the patient may experience flu like symptoms-fatigue and malaise, arthralgias, myalgias (backaches, stiff neck), fever, headaches. These symptoms however may be mild and therefore unremarkable.

The patient may not notice any symptoms until weeks or months after the original tick bite when late stage infection has already set in. Such late stage symptoms include neurologic, arthritic, ophthalmologic, psychiatric, dermatologic and/or cardiac symptoms. If untreated, the symptoms may last for months and years, sometimes punctuated by spontaneous remissions and recurrences. About 15 percent of infected patients develop objective neurologic abnormalities, most commonly displaying part of the triad of aseptic meningitis, cranial neuritis, and motor or sensory radiculitis.

Aseptic meningitis may begin with recurrent attacks of headaches, stiff neck, photophobia, nausea, and vomiting. The headaches may fluctuate from mild to severe. Spinal fluid abnormalities may include a pleocytosis or lymphocytosis, an increase in the synthesis rate, an elevated CSF protein, and oligoclonal immunoglobulins. The opening pressure may not be elevated (15). *Cranial neuritis*, such as Bell's palsy, may be unilateral or bilateral and may be seen in 5-10% of patients with neuroborreliosis (16). Other cranial nerves may be involved as well, especially the 3rd, 4th and 6th. The *radiculopathic syndromes* may also be unilateral or bilateral, with a predominance of motor over sensory symptoms. The most common dermatomes involved are the fifth cervical dermatome and T8 through T12 (14). Formal pain testing may show diminished or absent pain sensation in the affected dermatome. In Europe, the syndrome of meningitis and radiculitis was known as Bannwarth's syndrome.

The most common *cardiac problem* is an atrioventricular block (second or third degree) (17). Other cardiac problems may include acute myopericarditis, left ventricular dysfunction, and cardiomegaly. Although most cardiac symptoms tend to be brief, lasting from 3 days to 6 weeks, and rarely lead to residual dysfunction, increasing evidence suggests that Lyme disease carditis may be of long duration and lead to permanent heart damage (18).

Later into the disseminated phase of the illness, patients may develop arthritic, other neurologic, ophthalmologic, and other dermatologic symptoms. The timing may be variable, occurring within weeks of the early symptoms or after a gap of several years. The *arthritic symptoms* may begin as a migratory musculoskeletal discomfort (similar to fibromyalgia). In 60% of untreated patients, an inflammatory arthritis develops, typically affecting large joints, such as the knee. Subsequently a small portion of patients with arthritis develop a chronic synovitis. Arthritic attacks, lasting days to weeks, may recur or several years. *Ophthalmologic* manifestations in the early stage may include conjunctivitis, iritis, and uveitis while in late stage illness optic neuritis and optic atrophy may occur (4). The late *dermatologic* entity, known as acrodermatitis chronica atrophicans, is more common in Europe than in the United States (13).

The *late neurologic symptoms* consist primarily of a mild to severe *encephalopathy, a polyneuropathy, and profound fatigue*. This encephalopathy which is thought to occur in 9 of 10 patients with chronic neuroborreliosis is often characterized by subtle disturbances in mood, memory, and sleep (2). It is in ruling out subacute encephalopathy that psychiatrists will have their greatest diagnostic challenge, for these patients may be irritable, tearful, depressed, and have poor concentration and sleep. A diagnostic tip in favor of Lyme disease as the cause of the depression and irritability might be concomitant memory loss, word finding problems, or a concomitant polyneuropathy. The *polyneuropathies*, often demonstrable on electrophysiologic testing, include spinal or radicular pain, paresthesias, sensory loss, and/or lower motor neuron weakness.

A recent study (2) indicated that chronic neurologic abnormalities may emerge anywhere from 1 month to 14 years after infection. Like syphilis, therefore, Lyme borreliosis may remain latent and asymptomatic for a long period of time. Patients may have chronic neurologic symptoms for more than one year, with some patients suffering for 10 years or more despite having received antibiotic therapy.

Cognitive impairments among patients with late Lyme disease may be subtle. Some patients may demonstrate initial abnormalities on neuropsychological testing, while others may not (2,19). Serial neuropsychological testing before and after antibiotic treatment may reveal significant improvement after treatment. In one study (19), improvement was noted on tests of memory (California Verbal Learning Test, Wechsler Memory Scale), attention and concentration (Symbol Digit Modalities), conceptual ability (Booklet Categories Test), and psychomotor and perceptual motor function (Block Design Subtest of the WAIS and Purdue Pegboard). Initial scores fell within normal range on some of these tests (eg. Wechsler Memory Scale) but nevertheless improved after treatment; this demonstrated that some patients with subjective memory loss that is not apparent on initial neuropsychological testing may nevertheless benefit from antibiotic treatment. Noteworthy is that many patients with cognitive deficits did not have clinical evidence of focal CNS disease. EEG's, CSF studies, and most other laboratory investigations were often normal. MRI scans were abnormal in many of the patients with moderate to severe memory impairment. The MRI abnormalities, which may be indistinguishable from those seen among patients with multiple sclerosis, indicated edema or inflammation suggesting that the Lyme disease patients may be suffering from a mild inflammatory encephalomyelitis. Finally, it should be noted that some patients even after a course of intravenous antibiotic treatment continue to have memory impairments demonstrable on neuropsychological testing (Selective Reminding Test) (20).

The course and severity of illness can vary. In most cases, Lyme disease if treated early is a transient illness with mild symptoms and no long-term sequelae. In a smaller portion of patients, the course may be chronic and severe. Case reports have linked a variety of neurologic syndromes to late Lyme disease, including blindness (21), progressive demyelinating-like syndromes (mimicking Multiple sclerosis (2) or Amyotrophic lateral sclerosis (22)), Guillian-Barre (23), progressive dementias (24), seizure disorders (25), strokes (26), and extrapyramidal disorders (27). Encephalomyelitis can be caused by *Borrelia burgdorferi* and is characterized by spastic paraparesis, ataxia, cognitive impairment, bladder dysfunction, and cranial neuropathy (28). Finally, although transplacental transmission of *Borrelia burgdorferi* does occur and only rarely leads to fetal injury, neonatal death has been linked with Lyme borreliosis based on culture positive frontal cortex specimens (29).

Laboratory Tests

Because *Borrelia burgdorferi* is difficult to culture, physicians are using indirect methods to detect the spirochetes. Antibody tests, such as indirect immunofluorescence and the enzyme-linked immunosorbent assay (ELISA), were initially thought to be dependable lab tests for the diagnosis of Lyme borreliosis. Now it is recognized that these tests give both false negative and false positive results (5). In addition, results from different laboratories on the same specimen may be highly variable, with one indicating no reactivity and another reporting significant antibody titers. Seronegative Lyme borreliosis, once a source of controversy, is now recognized as a diagnostic problem (30). Patients may have no detectable antibodies to *Borrelia burgdorferi* in either their serum or their CSF, but still have clinical disease. A recent report described 6 patients who were seronegative and CSF-antibody negative who were subsequently shown to have evidence of the spirochetes in the CSF based on a positive polymerase chain reaction assay (31).

The Western blot is often used to confirm positive results from an ELISA or IFA, although it too may be falsely

negative or falsely positive. When meningopolyneuritis or encephalomyelitis is suspected, intrathecal antibody determinations should be attempted. The spinal fluid may reveal a mononuclear pleocytosis and/or an elevated CSF IgG or IgM for *Borrelia burgdorferi*. CT and MRI findings may occur in the encephalitis cases, as well as EEG slowing and epileptic discharges. However, as previously noted, serologic and other objective abnormalities are not always found. Silver staining has been used for detecting spirochetes in tissues, but the yield is low. The polymerase chain reaction (31), which amplifies a target DNA sequence specific for Lyme disease, has promise as a sensitive and potentially specific means for identifying *Borrelia burgdorferi*. This test's commercial usefulness, given marked difficulties in avoiding contamination which cause false positives, remains to be determined.

Treatment

Lyme disease is treatable with antibiotics, however treatment may be less effective in the late stage of illness (32). Oral antibiotics, such as amoxicillin and doxycycline, are considered effective for the early stage of illness. When the central nervous system is involved, intravenous antibiotic treatment with third generation cephalosporins, such as ceftriaxone sodium and cefotaxime, is indicated for at least 10 days to 3 weeks. Recent reports now suggest that longer courses of treatment may be needed, as well as repeated courses if symptoms recur (2,33,42). Early during the antibiotic treatment patients may experience a sudden worsening of symptoms. This Jarisch-Herxheimer-like reaction is thought to be an inflammatory response to spirochetal lysis (33).

Patients given antibiotics early in illness tend not to have major late complications, although an unknown percentage of patients treated early still develop late complications. It is now thought that relapse is due to continued presence of spirochetes (2,42). Although most patients do improve with treatment, a subgroup of patients with late Lyme disease may not improve after a course of intravenous antibiotics (2).

Psychiatric Manifestations

A review of the world literature on the psychiatric manifestations of Lyme borreliosis suggests that psychiatric problems may be a prominent feature of Lyme borreliosis. The literature consists largely of case reports and small series and thus must be regarded as suggestive rather than definitive.

In 1930 a patient was described who three months after an ECM rash developed an encephalitis with psychotic symptoms and marked CSF abnormalities (34). More recently, a patient with Lyme borreliosis was described whose clinical picture was indistinguishable from an endogenous schizophrenia (35). The patient's paranoia and hallucinations remitted after one week of antibiotic treatment with ceftriazone, but afterwards the patient showed a mild organic brain syndrome.

In Europe, two recent review articles have stated that psychiatric symptoms can be a prominent feature of Lyme borreliosis, including agitated depression and psychosis (36,37). Kohler described a staging of psychiatric symptoms which parallel the neurologic ones. In stage I, fibromyalgia, painful muscular fasciculations, and mild depression may dominate the clinical picture. In stage II, a lymphocytic meningopolyneuritis may occur along with an organic psychiatric disorder, such as an organic affective syndrome or an organic personality syndrome. In stage III, chronic encephalitides and myelitides may be accompanied by severe psychiatric syndromes, such as organic psychoses, dementia, and anorexia nervosa. This staging was based on clinical observation not systematic studies.

In the United States, Pachner (38) presented two patients whose symptoms were largely psychiatric. A 12 year old boy with confirmed Lyme arthritis treated with oral antibiotics subsequently became depressed and anorectic. After being admitted to a psychiatric hospital with the diagnosis of anorexia nervosa, he was noted to have positive serologic tests for *Borrelia burgdorferi*. Treatment with a 14 day course of intravenous antibiotics led to a resolution of his depression and anorexia; this improvement was sustained on 3 year follow-up. A 21 year old man seropositive for *Borrelia burgdorferi* developed progressive confusion, agitation, disorientation, inappropriate laughter, and violent outbursts, a temporal lobe biopsy revealed spirochetes. Treatment with IV penicillin resulted in a return to normality within 3 months.

In one U.S. study of 27 patients with late neuroborreliosis, 33% were depressed based on their scores on the

Minnesota Multiphasic Personality Inventory (2). 89% of these 27 patients also had evidence of a mild encephalopathy, characterized by memory loss (81%), excessive daytime sleepiness (30%), extreme irritability (26%), and word finding difficulties (19%). Controlled studies indicate significantly more depression among patients with late Lyme borreliosis than among normal controls (20) and other chronically ill patients (39).

Confounding accurate diagnosis is the fact that many of the prominent symptoms of Lyme disease share features with depressive illness, including irritability, fatigue, emotional lability, poor concentration, memory problems, and impaired sleep (2). Ruling out Lyme disease as a cause of these depressive symptoms can be difficult because currently available serological tests are inadequate, a third of all patients do not recall a rash or tick bite, and a long quiescent period may precede the late symptoms. Even when the diagnosis of Lyme disease is clear, optimal treatment of these depressive symptoms is uncertain because in many patients the symptoms persist even after the standard 3 week course of antibiotics. Psychiatrists currently have no guidelines on how to treat these patients. While some doctors feel that depressive symptoms in the context of Lyme disease are evidence of continued disseminated infection, others believe that these represent a secondary emotional response to having a serious illness. Appropriate treatment if the former is true would consist of further antibiotics, while if the latter is true psychotherapy and/or antidepressant therapy would be the treatment of choice. Delayed additional antibiotic treatment due to an incorrect assessment of the disease process may enable an acute illness to develop into a chronic one (2).

In conclusion, further systematic study is clearly needed to better understand the prevalence and pathophysiology of psychiatric problems among patients with Lyme borreliosis and to identify optimal treatment. A critical review of the literature indicates that disturbances of mood, memory, and sleep are prominent features of this illness. Whether *Borrelia burgdorferi* also causes psychotic disorders and eating disorders remains an open question. Neurosyphilis, also caused by a spirochete, is known to be associated with memory problems, depression, mania, psychosis, and personality changes, such as irritability, emotional lability, and apathy (40). Given the remarkable similarities between syphilis and Lyme borreliosis, it is possible that the full range of psychiatric symptoms seen in neurosyphilis may also soon be recognized as features of Lyme borreliosis.

PART II. THE CLINICAL EXPERIENCE OF LYME DISEASE: PATIENT PERSPECTIVES AND THE PSYCHIATRIST'S ROLE (JENIFER A. NIELDS)

The purpose of this section is to better acquaint the clinician with some of the typical, often bizarre, neuropsychiatric symptoms seen in late-stage Lyme disease as well as with some of the psychological stresses that specific aspects of this illness and its treatment place on patients and their families. Psychiatrists should be alert to these clinical aspects of the disease in order not to miss the diagnosis of Lyme disease in patients who present with primarily psychiatric complaints and in order to render more effective care to patients with known disease. Accordingly, this section is descriptive; it is based on clinical interviews with adult and pediatric patients and their families as well as written descriptions from among approximately 200 seropositive patients who responded to a questionnaire regarding neuropsychiatric symptoms. Symptom frequencies drawn from an initial sample of 85 seropositive patients with clinical symptoms of late stage Lyme disease will be presented. A full description of this questionnaire and detailed results will be published elsewhere. The frequencies should not be considered representative of Lyme disease patients in general but rather of a subgroup with severe, long-standing and/or chronic disease.

PHENOMENOLOGY

Among the respondents to the questionnaire, some described syndromes indistinguishable from major depression, generalized anxiety disorder or panic attacks. Patients also described a variety of other neuropsychiatric symptoms, and the most prevalent and distinctive among such symptoms will be detailed here. (The arthritic, dermatologic, and cardiac symptoms will not be discussed.) Not all of the neuropsychiatric symptoms that follow are specific to Lyme borreliosis nor is the list comprehensive, but taken together they provide a clinical pattern typical of the cases in our study.

Fatigue and Memory Loss

Some of the most commonly reported symptoms in our sample were fatigue (94%) and memory problems (83%). Sometimes the fatigue is relatively mild, allowing the patient to continue working, perhaps in a diminished capacity. Sometimes, however, the symptoms may be quite severe, such that the patient may be bedridden due to intractable fatigue. Memory problems, too, can be mild or quite severe. One woman in our sample who had been a telephone switchboard operator for 20 years reported suddenly being unable to remember how to transfer calls. In this woman's case, the memory problems resolved completely following antibiotic treatment.

The differential diagnosis between fatigue and memory problems due to active Borrelial infection versus as part of another disorder, such as functional depression or chronic fatigue syndrome, is an important one. Patients with active borrelial infection who have prominent fatigue and memory symptoms may respond well to antibiotic treatment whereas for patients with a non-Lyme-related syndrome such treatment would be of no benefit. A history of tick exposure, positive serologies, erythema migrans, and other associated neurologic or arthritic symptoms may alert the clinician to the diagnosis of Lyme disease. If Lyme disease has been diagnosed and the patient has persistent symptoms despite having received a prior "adequate" course of antibiotics, some clinicians will recommend no further antibiotic treatment (based on the post-infectious autoimmune hypothesis) while others may recommend continued treatment until all symptoms remit (based on the persistent sequestered infection hypothesis). Treatment responses may be difficult to gauge both because fluctuations in symptomatology occur even in untreated Lyme disease, and because the clinical response to effective antibiotic treatment may be delayed in some cases.

Photophobia

As in various other infections and/or CNS disturbances (e.g. meningitis, migraine, psittacosis, typhus, Rocky Mountain Spotted Fever), photophobia may be a prominent feature. In our sample, 70% of respondents reported photophobia. The severity of this symptom can be quite striking, and there may be variants, including idiosyncratic responses to particular kinds of light. Patients may need to wear sunglasses or glacier glasses, even indoors, even at night. Several patients reported feeling "faint" or "dizzy" in particular when exposed to fluorescent lights, making it difficult to go to supermarkets or other public places. Of note: such a patient might be referred to a psychiatrist because of what seemed like agoraphobia. Some patients have developed panic-attacks that seemed to be triggered by sound or light stimulation-especially bright lights that flicker, such as fluorescent lights-and which resolved following antibiotic treatment. others have developed nausea in response, again, to lights that flicker: fluorescent lights, TV or computer screens, strobe lights during EEG testing or the headlights of cars moving in the opposite line of traffic. The hyper-sensitivity to light can be incapacitating or merely uncomfortable. It may preclude driving at night or going outdoors during the day or it may make what are normally routine or even pleasurable activities seem noxious.

Sound Sensitivity

A more distinctive, somewhat less common but often very intense symptom, reported in 48% of our sample, is hypersensitivity to and/or idiosyncratic responses to sound stimulation. One boy developed sound sensitivity so severe that ordinary conversation was deafening to him; he wore headphones and put pillows over his head to block out the sound. To one woman even the sound of another person's breathing seemed unbearably loud. In her case, the sound sensitivity also included vertigo, nausea and nystagmus in response to sounds. Any sudden sound, like the phone ringing, and certain household sounds, like the running of tap water, could cause her to fall or retch. This peculiar short-circuiting of the inner ear's auditory and vestibular functions is known as the Tullio phenomenon. This phenomenon has been deemed pathognomonic for syphilis (43) but, as it appears, can occur in Lyme disease as well (41), and thus provides one more example of the "new great imitator," Lyme disease, imitating the old "great imitator," syphilis (1).

Sensory Hyperacusis

As previously reported in illnesses caused by other species of borrelia (44), hypersensitivity can occur in other

sensory modalities as well: touch, taste and smell. Abnormalities of taste and smell occurred in 33% and 25% of our sample, respectively. Foods may taste abnormally sour or bitter, smells may seem overly intense and noxious. Alterations in the perception or processing of other kinds of sensory stimulation occur also. One patient, before she realized she was ill with Lyme disease, noticed one day that her car was vibrating with unusual violence. She took the car emergently in to a mechanic, thinking that the shock absorbers were shot or the ball bearings loose and that it would be dangerous to continue to drive the car in that condition. As it turned out, there was nothing wrong with the car. The problem was in the patient who had suddenly and unwittingly developed a heightened sensitivity to vibrations. She subsequently became alert to this heightened vibration sense in other contexts as well. When the diagnosis of Lyme disease was finally made, this symptom, along with other, more common symptoms of Lyme disease, resolved with antibiotic treatment.

Extreme Irritability and/or Emotional Lability

Many patients reported mood and behavioral changes during the course of their illness. In our sample, 64% of patients reported increased irritability and/or emotional lability in association with symptoms suggestive of meningeal irritation: neck stiffness and headache. The mood and behavior changes are often so severe and pervasive as to constitute a personality change. Sudden, intense irritability is most often triggered by sensory stimulation in patients who are acutely sensitive to sound, touch or light but may also occur unprovoked and seemingly inexplicably. One man, acutely sensitive to sound, was so intensely bothered by the noise his three-year-old son was making that he picked him up and shook him in a sudden and unprecedented fit of violence. His wife was shocked and alarmed by this behavior, as was the patient himself. A woman, typically reserved and eager to please, became uncontrollably irritable one day at work and found herself yelling at her boss in a most uncharacteristic fashion. Others have found themselves bursting into tears, sometimes several times a day, on what seems like very little provocation.

Word Reversals When Speaking and/or Letter Reversals When Writing

These odd, idiosyncratic but quite common symptoms were reported in 69% of our sample. Patients with no prior history of dyslexia have found themselves writing letters backwards, reversing numbers or routinely reversing the first and second letters of a word. One patient recalls also switching her shoes: putting the left shoe on the right foot and the right shoe on the left foot before she realized her mistake. This patient also experienced what might be understood as reversals in temporal sequencing: for instance, saying the word "tomorrow" when she meant "yesterday" and vice versa.

Spatial Disorientation

Reported in 57% of our sample. A not uncommon scenario is of a patient who, recalling no rash or flu-like symptoms, had experienced some aches and pains and/or memory problems but had not paid much attention to these symptoms until he found himself, on two consecutive days, lost in his own neighborhood, on his way home from work. Such a scenario suggests a disorder of topographic orientation and geographic memory such as may be seen among patients with parietal lobe dysfunction (45). Patients have reported other behaviors as well which seem to relate to disturbances of the body-environmental schemata. A young woman described repeatedly bumping into things on the left side of her body, dropping things from her left hand despite having no weakness in that hand and occasionally placing objects, such as a milk carton, several inches short of a table edge with the result that they would fall to the floor. These difficulties remitted completely following adequate antibiotic treatment.

Fluctuations in Symptoms

This can be one of the most frustrating and perplexing aspects of the illness. A patient with late-stage Lyme disease might feel totally drained one day, the next day be able to function almost normally and the day after experience such mental confusion as to be unable to focus on even the simplest of tasks. Sometimes the fluctuations may be brought on by exertion or stress or exposure to sensory stimuli or by the initiation of antibiotic treatment, but sometimes no explanation can be found. The fluctuations make it impossible for patients to make plans, and may make it seem to friends, teachers, family members or even the patients themselves as if the symptoms were

somehow under voluntary control or as if they were hysterical in origin. Of course psychological factors, too, can influence symptomatology, but fluctuations are typical regardless of mental state.

Such vicissitudes raise a particular problem in children who may experience fluctuating cognitive impairments: short-term memory problems, word-finding difficulties, dyslexia, problems with calculations or inability to concentrate. School systems are by and large unaware of the cognitive aspects of late-stage Lyme disease and, in particular, of the ways in which cognitive impairments may fluctuate from day to day in a given child. Teachers may assume the child is just moody or uncooperative. Family dynamics, too, may be complicated by confused expectations of the sick member, and resentments may build when a person's functional status, mood and ability to participate in family life seem inexplicably erratic. Patients and family members alike find it difficult to have their hopes raised repeatedly by a transient clinical improvement, only to be slapped down again by a recrudescence of debilitating symptoms. Even with treatment, recovery from late-stage Lyme disease is most often a lengthy process involving significant fluctuations in symptoms even in the context of overall improvement.

Worsening of Symptoms During Antibiotic Treatment

Nearly half of the patients in our sample reported a transient worsening of neuropsychiatric symptoms during the first few days of antibiotic treatment. The worsening of symptoms during initiation of antibiotic treatment is thought to be a variant of the Herxheimer reaction as seen in the treatment of syphilis (33). In Lyme disease, however, this Herxheimer-like reaction can be quite prolonged-lasting a few days or longer-and can be frightening to patients who are expecting a resolution, not a worsening, of their symptoms. The reaction can sometimes be difficult to distinguish from an allergic reaction to the medicine, a distinction with obvious and crucial treatment implications.

This Herxheimer-like reaction may be experienced as a worsening of psychiatric symptoms: some patients in our sample experienced panic attacks for the first and only time when starting on antibiotics. Others have reported an intensification of depressive symptoms, suicidality or anxiety. Many reported an increased startle response and photophobia during the first few days of antibiotic treatment.

Uncertainty as to Diagnosis and Treatment

A great deal is unknown about Lyme disease at this point in time, and experts disagree regarding its diagnosis and management. Some patients remain seronegative, for a variety of reasons (some known, some unknown) (30) and therefore remain undiagnosed and untreated for long periods of time. The medical literature now documents that some patients, even following what has been presumed to be adequate treatment, go on to develop late-stage symptoms, sometimes months or years later (2). Even now, some doctors think that so-called seronegative Lyme disease is fairly common and others that it is virtually nonexistent. Some doctors believe that prolonged antibiotic treatment may be necessary in late Lyme disease (33,46), and others, emphasizing the less specific symptoms of late Lyme disease (similar to fibromyalgia or chronic fatigue syndrome), consider such treatment in many cases to be excessive and unreasonable (47). Patients may be told that Lyme disease is easily curable with antibiotics and that further concern about it is a matter of "Lyme anxiety" (48); from other sources, they may learn that Lyme infection in some cases may lead to a chronic, severely debilitating, perhaps irreversible disease (2). Such manifold uncertainties as to diagnosis, treatment and prognosis at this stage in the history of Lyme disease put the patient in a difficult position. The patient may get conflicting advice from reputable sources and not know what to do. He may be told that his symptoms are not related to Lyme disease. He may be told there is no medical cause for his complaints and be referred to a psychiatrist. And, especially since Lyme disease may in fact involve the brain and manifest as depression or confusion or irritability, it may be hard not only for the clinician, but also for the patient himself to recognize the effects of the disease as against his emotional reactions to it. Some patients, who have subsequently been effectively treated, have said that, prior to being diagnosed, they had feared they were just going crazy.

HOW CAN THE PSYCHIATRIST BE OF HELP?

It is important to make a clear diagnostic assessment of the range of problems a patient brings. In cases where the diagnosis is unknown or uncertain or where the psychiatric picture is atypical, aspects of the medical history, such as

living in an endemic area, hiking, tick exposure, neck pain or a past history of a swollen knee might alert the clinician to the possibility of Lyme disease. If Lyme disease is suspected, a thorough medical evaluation is essential.

Among patients presenting to a psychiatrist with a known diagnosis of Lyme disease, some complaints, such as irritability or depression with sleep disturbance or hypersensitivity to sensory stimuli, may be directly related to the disease process. Other problems, such as depressed mood, feelings of inadequacy, bitterness or guilt may be secondary effects of having a severe chronic illness. Such problems may result from alterations in functional status, loss of social relationships or problematic family dynamics precipitated by the illness. The psychiatrist may help patients to address these problems, for instance, by a process of mourning and acceptance, by cognitive reframing or by occupational adjustment and a redistribution of family responsibilities. Psychotropic medications may be helpful as an adjunct to medical treatments for Lyme disease. Most commonly used are anxiolytics, low-dose antidepressants for pain and sleep and higher dose antidepressants for major depression. Given that Lyme disease can cause conduction abnormalities, it is of particular importance to obtain an EKG before starting treatment with tricyclic antidepressants. When patients suffer from irritability related to sensory hyperacusis, as described earlier, it may be useful to help such patients identify the triggers and avoid them if possible. It may also be quite helpful just to explain to patients and/or to family members that such irritability and the resultant behavior changes can indeed be a function of the disease. One man developed extreme irritability related to auditory hyperacusis. His wife recalls thinking: "This is not the man I married." She doubted that she could continue to live with him if this personality change were to persist. Even after he had been treated and returned to normal, both husband and wife remained uneasy until they found an explanation for the change: that it had to do with an illness, and was not some inexplicable, inextricable newly emergent part of the man himself.

Family therapy may be indicated especially where a sick child is concerned. Siblings may feel shortchanged because of a relative lack of attention while the sick child may envy-and resent-his or her siblings for their capabilities and lack of physical suffering.

Couples therapy may be indicated in some cases. Most patients report a significant loss of libido. This can lead to frustration, alienation and anger in the spouse, and may in any case make it difficult for some couples to maintain intimacy. There may be a diffuse sense of loss on both sides which is then displaced and experienced as anger or resentment against the spouse. Defenses that have served the partners well throughout most of their marriage may be overwhelmed by the manifold adjustments the illness demands; couples may need help in finding alternative ways of coping and interacting.

Many patients have felt abandoned by their medical doctors when the diagnosis was uncertain or the treatment not fully curative. Others have had to see many different doctors before one was able to put together the diversity of their symptoms and come up with a diagnosis. Several patients have said that the hardest thing to bear-even more than the pain and disability-had been the feeling that they were somehow inexplicably altered, in their emotions and personality and ability to function, without hope of finding a cause or a cure, and without a doctor who would honor their difficulty, whether or not he or she could solve it. For some patients, then, the ambiguities surrounding diagnosis and treatment and the consequent sense of abandonment by medical professionals were among the most distressing aspects of the illness experience. The psychiatrist can be of help by lending respectful support to such patients: by listening and by helping them to clarify their options.

CONCLUSION

In most cases, Lyme disease, when treated early, is a mild illness with no long-term sequelae. When first identified in its later stages, however, some of the symptoms of the illness may be less responsive to antibiotic treatment, resulting in a disabling, chronic disorder. From the foregoing clinical vignettes, it should be clear that Lyme disease, particularly when it involves the central nervous system, can in some patients be an extremely debilitating, bizarre, terrifying and perplexing disease. It can present in a great variety of ways, and the symptoms can fluctuate dramatically and unpredictably. At the same time, there are patterns to its emergence that can suggest the diagnosis in cases where laboratory indices are inconclusive. Much uncertainty surrounds the diagnosis and treatment of Lyme disease at this stage in its history, and such uncertainty adds to the distress that the illness causes for patients. Lyme disease is aptly called the "new great imitator," and it can imitate psychiatric disorders no less than medical ones. Psychiatrists working in endemic areas are well-advised, then, to keep Lyme disease in mind as part of their

differential diagnosis for a broad range of disorders including, for instance, panic attacks, somatization disorder, depression, and dementia, especially in cases that are atypical or otherwise suggestive of systemic disease. It should be borne in mind also that new clinical manifestations of Lyme disease are still being discovered and described. In cases of known Lyme disease, it is important for psychiatrists to take a comprehensive approach to treatment as so many aspects of the patient's life-physical, emotional, cognitive, familial, sexual, social and occupational-may be significantly affected by the illness.

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REFERENCES

1. Pachner AR. **Borrelia burgdorferi in the Nervous System: the New "Great Imitator."** In Lyme Disease and Related Disorders. Annals New York Academy of Sciences 539: 56-64, 1988.
2. [Logigian EL, Kaplan RF, Steere AC. Chronic neurologic manifestations of Lyme disease. NEJM 323: 1438-1444, 1990.](#)
3. [White DJ, Chang HG, Benach JL, et al. The geographic spread and temporal increase of the Lyme disease epidemic. JAMA 266: 1230-1236.1991.](#)
4. [Burgdorfer W. Lyme borreliosis: ten years after discovery of the etiologic agent, Borrelia burgdorferi. Infection 19: 257-262.1991.](#)
5. [Magnarelli LA. Laboratory Diagnosis of Lyme disease. Rheumatic Disease Clinics of North America. 15: 735-745, 1989.](#)
6. Schmid GP. **The global distribution of Lyme disease.** Rev Infect Dis 7:41-50, 1986.
7. Weber K, et al. **Erythema Migrans Disease and related disorders.** Yale J Biol Med 57: 13-21, 1984.
8. Afzelius A. **Erythema Chronicum Migrans.** Acta Derm Venereol 2: 120-125, 1921.
9. Garin, Bujadoux: **Paralysie par les tiques.** J Med Lyon 71: 765-767.1922.
10. Bannwarth A: **Chronische lymphocytare meningitis, entzündliche polyneuritis and "rheumtisumes."** Arch Psychiatr Nervenkr 113: 284-376, 1941.
11. Scrimenti RJ. **Erythema chronicum migrans.** Arch Dermatol 102: 104-105, 1970.
12. [Steere AC, Malawista SE, Hardin JA. et al: Erythema chronicum migrans and Lyme arthritis. Ann Int Med 86: 685-698.1977.](#)
13. [Asbrink B, Hovmark A, Hederstedt B. The spirochetal etiology of acrodermatitis chronica atrophicans Herxheimer. Acta Derm Venereol 64: 506-512, 1984.](#)
14. [Pachner AR, Steere AC. The triad of neurologic manifestations of Lyme disease: meningitis, cranial](#)

- [neuritis. and radiculoneuritis. Neurology 35: 47-53. 1985.](#)
15. [Finkel MF. Lyme disease and its neurologic complications. Arch Neurol 45: 99-104, 1988](#)
 16. [Halperin JJ. Nervous System Manifestations of Lyme Disease. Rheumatic Disease Clinics of North America. 15: 635-647, 1989.](#)
 17. [Reznick JW, Braunstein DB, Walsh RI, Smith Cr, Wolfson PM, Gierke IW, Gorelkin I, Chandler RW. Lyme carditis. Electrophysiologic and histopathologic study. Am J Med 5: 923-927, 1986.](#)
 18. [Stanek G, Klein J, Bittner R, Glogar D. Isolation of Borrelia burgdorferi from the myocardium of a patient with long-standing cardiomyopathy. NEJM 322: 249-252, 1990.](#)
 19. [Halperin JJ, Pass HL, Anand AK, Luft BJ, Volkman DJ, Dattwyler RJ. Nervous system abnormalities in Lyme disease. Annals NY Acad Sciences 539: 24-34, 1988.](#)
 20. [Krupp LB, Masur D, Schwartz J, Coyle PK, Langenbach LJ, Fernquist SK, Jandorf L, Halperin JJ. Cognitive functioning in late Lyme borreliosis. Arch Neurol 48: 1125-1129, 1991.](#)
 21. [Steere AC, Duray PH, Danny JH, et al: Unilateral blindness caused by infection with Lyme disease spirochete, Borrelia burgdorferi. Ann Int Med 103: 382-384, 1985.](#)
 22. [Halperin JJ, Kaplan GP, Brazinsky S et al: Immunologic reactivity against Borrelia burgdorferi in patients with motor neuron disease. Arch Neurol 47: 686-594.1990.](#)
 23. [Clavelou P, Beytout J, Vernay D, et al: Neurologic manifestations of Lyme disease in the northern part of the Auvergne. Neurol 39 \(suppl 1\): 350, 1989.](#)
 24. [MacDonald AB, Miranda JM. Concurrent neocortical borreliosis and Alzheimer's disease. Human Pathology 18: 750-761, 1987.](#)
 25. [Reik L, Smith L, Khan A. et al. Demyelinating encephalopathy in Lyme disease. Neurology 35: 267-269, 1985.](#)
 26. [Kohler J, Kern U., Kaper J, Rhese-Kupper B, Thoden U. Chronic central nervous system involvement in Lyme borreliosis. Neurology 863-867, 1988.](#)
 27. [Kohlhepp W, Kuhn W, Kruger H. Extrapyrarnidal features in central Lyme borreliosis. Eur Neurol 29: 150-155, 1989.](#)
 28. [Ackerman R, Rhese-Kupper B, Gollmer E, Schmidt R. Chronic neurologic manifestations of Erythema migrans borreliosis. In Lyme Disease and Related Disorders. Annals NY Acad Science. 539: 16-23, 1988.](#)
 29. [Lavoie PE, Lattner BP, Duray PH, Malawista SE, Barbour AG, Johnson RC. Culture positive, seronegative, tranepalcental Lyme borreliosis infant mortality. IV Int. Conf. Lyme borreliosis 1990 \(abstract\).](#)
 30. [Dattwyler RJ, Volman DJ, Luft BJ, et al. Seronegative Lyme disease. NEJM 319:1441-1446, 1988.](#)
 31. [Keller TL, Halperin JJ, Whitman M. PCR detection of Borrelia burgdorferi DNA in cerebrospinal fluid of Lyme neuroborreliosis patients. Neurology 42: 32-42, 1992.](#)
 32. [Rahn DW, Malawista SE. Lyme disease: recommendations for diagnosis and treatment. Ann Intern Med 114: 472-481, 1991.](#)
 33. [Burrascano J. Late-stage Lyme: treatment options and guidelines. Int Med 10:102-10, 1989.](#)

34. Hellerstron M. **Erythema chronicum migrans Afzelii**. Acta Derm Venereol (Stockh) 11:305-321, 1930. (referenced in Kohler et al: Neurology 38: 863-867, 1988)
35. [Barnett W, Sigmund D, Roelcke U, Mundt C. **Endogenous paranoid-hallucinatory syndrome caused by Borrelia encephalitis**. Nervenarzt 62: 446-7, 1991.](#)
36. [Omasits M, Seiser A, Brainin M. **Recurrent and relapsing borreliosis of the nervous system**. Wiener klinische wochenschrift 102: 4-12, 1990.](#)
37. [Kohler VJ. **Lyme disease in neurology and psychiatry**. Fortchr 108:191-194, 1991.](#)
38. [Pachner AR. **Central Nervous System Manifestations of Lyme Disease**. Arch Neurol 46:790-795, 1989.](#)
39. Fallon BA, Nields JA, DelBene D, Saoud J, Wilson K, Liebowitz MR. **Depression and Lyme disease: a controlled survey**. American Psychiatric Association. 145 Meeting, 1992. (Abstract).
40. [Rundell JR, Wise MG. **Neurosyphilis: a psychiatric perspective**. Psychosomatics 26: 287-295, 1985.](#)
41. [Nields JA, Kveton JF. **Tullio phenomenon and seronegative Lyme borreliosis**. Lancet 338:128-129, 1991.](#)
42. [Preac-Mrusic V, Weber K, Pfister W, et al. **Survival of Borrelia burgdorferi in antibioticly treated persons with Lyme borreliosis**. Infection 17:355, 1989.](#)
43. Schuknecht HF. **Pathology of the Ear**. Harvard University Press, Cambridge: p 133. 1974.
44. Felsenfeld O. Borrelia. Warren Green Press, St. Louis: p. 105, 1971. Adams RD, Victor M. **Principles of Neurology**. 4th Edition. McGraw Hill, NY: p362-366, 1989.
45. Lavoie PE. **Lyme Disease (Lyme Borreliosis)**. In Conn's Current Therapy 1991.
46. Rakel RE, ed. WB Saunders: 1991.
47. [Sigal LH. **Summary of the first 100 patients seen at a Lyme disease referral center**. Amer J Med 88: 577-581, 1990.](#)
48. Lettau L. **Lime vs Lyme Disease**. Ann Int Med 115: 157, 1991.