The Treatment of Tick-borne Illnesses
Clinical Observations and Recommendations During 20 Years of Neuropsychiatric/Functional Medicine

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“Disease is very old and nothing about it has changed. It is we who change as we learn to recognize what was formerly imperceptible.” – Jean Martin Charcot.

Twenty years ago, my practice was devoted to Integrative Medicine (with an emphasis on orthomolecular psychiatry and clinical ecology.) I could not predict, at that time, the far-reaching consequences of my decision to treat several patients with TBD (a school teacher with panic attacks, joint pain, and memory loss, a hunter with exhaustion, insomnia, and severe depression). I had no idea, that I had, indeed, joined a small group of like-minded physicians, (quite by accident), who also dealt with the same medical complexities (across medical specialties). They an insect borne disease, stemming from a reservoir of warm-blooded mammals harboring pathogenic bacteria, that had reached alarming endemic levels in their communities.

Later, I was to discover, that this complex microbial synergy of coexisting infections, extended far beyond our Connecticut borders, where it had first been designated as “Lyme disease.” In reality, it was not only localized in my state, but had as well, a national and international distribution.

CONTROVERSY IN DIAGNOSIS AND TREATMENT

I was also to ascertain, that the diagnosis and treatment of these TBD’s is extremely controversial in conventional medical circles. The TBD field is plagued with academic pronouncements, which do not mirror the clinical presentation of the TBD syndrome. There are in addition, unreasonable reporting CDC standards, which are misused and misinterpreted clinically. And finally there is unreliable testing information, based on the use of Borrelia species limited test kits (Western Blot IgG/M) which mislead the clinicians with “false negative” data. These critical problems have yet to be resolved. As a result, chronically infected individuals, are not recognized as being ill, and to their detriment, do not receive timely and appropriate treatment.

Syphilis, another ‘spirochete bacteria’ that is equally devastating, used to be ‘medicine’s great teacher.’ I had been taught in medical school “that to know syphilis was to know all internal medicine.” However, to know Borreliosis (Lyme disease) is not only to know internal medicine, but also to know neurology, psychiatry, immunology,
politics, economics, law, in all – a general systems hierarchy of many inter-related disciplines.

“Focused listening,” informs physicians of the human condition, both in sickness and in health. The hours spent at the bedside, in the examining room, and in the consulting office, transcend textbook learned data, or the latest scientific research published in peer-reviewed journals. A no better example of this medical axiom is our present day clinical understanding of TBD.

The treatment of TBD desperately needs more open-minded and seasoned doctors, across all specialties. These physicians will understand without bias, the confusing clinical presentation of TBD, and act against the prevailing dogma of myopic academia, and ‘reimbursement-limiting’ health insurance carriers. Even general consensus guidelines, or the woefully inadequate, present day standards of care, must inevitably be tempered by the physician’s own common sense. He must be aware at all times, of the presence of TBD in his differential diagnosis. This is particularly true of those patients who reside or vacation in known endemic areas.

My treatment of patients afflicted with TBD, has allowed me to witness exciting improvements in both their health and quality of life. Enthusiastic patient success stories are reported to me daily in my practice, and this has enriched my own professional life immeasurably.

A NEW MEDICAL SUBSPECIALTY?

I have come to understand that the treatment of TBD, for all practical purposes, has become a new medical subspecialty. Personally, I look upon this emerging field as a special challenge. I have the opportunity to provide care for a large and diverse group of neglected patients, in need of serious medical attention. Unfortunately, in too many instances, the larger medical community has taken a skeptical and dismissive approach to these people. However, with the application of correct treatment, many emotionally and physically exhausted individuals in my practice undergo a positive and dramatic change in their health. Their debilitating symptoms over time are significantly reduced. As a result, the patient’s condition is considerably improved, and they are able to return to their previously normal, expected routines, at work, at home and at play.
Tick-borne diseases, in addition to their difficult and mixed pathogenesis (making diagnosis and treatment extremely difficult), have another inherent problem for the patient and their physicians. They must overcome together, the medical dilemma inherent in the “mind/body” dichotomy. This is recognized as the ‘infamous’ split between our subjective ‘consciousness’ and the ‘material reality’ of our physical body.

Unfortunately, the concept of ‘mind’ or ‘consciousness’ has been treated independent of our physical ‘bodies’. Modern medicine has practically ignored, the critical relation of the “metaphysical” mind to the physical body. Instead it has concentrated mostly on the “physical brain”, as it relates to its physical body. Most of today’s specialists, consider the appearance of ‘mind’, as an interesting epiphenomenon. Its usefulness, by most current standards, is seen as being extremely limited, when applied to the area of clinical diagnosis and treatment. In fact most overworked physicians consider ‘mind’, or subjective symptoms, a liability in the management of their treatment protocols,( outside of psychiatry). For them, the fewer the ‘mind’ or subjective complaints that their patients have, the more compliant and cooperative their patients are considered to be. ‘Mind’, only becomes important when it is recognized as an extension of our ‘hardwired’ neurobiology.

This mysterious, vascularized, gray and white matter mass of spongy synapses has intrigued and captured the interest of research medicine today. As early as 1990, the Society for Neuroscience dedicated the subsequent ten years as the Decade of the Brain. Since that time the organization has grown from a handful of scientists to over 25,000 members.

Sophisticated neuro-imaging techniques (MRI, SPECT SCAN, PETSCAN), biochemical neurotransmitter analysis, genetic investigations of gene driven mental illness, brain peptide production and single cell evoked potential probes, have allowed researchers to better understand the brain’s previously inaccessible neurological secrets.

“Mind” or “consciousness” however, remains vaguely attached to the “brain” but
analyzed separately from the rest of the body. Gazzaniga determined with his elegant split brain studies, that the capacity for self-awareness appears limited only to the left brain. The right brain does not appear to have the capacity to process, a unified story of a ‘continuous self.’ It seems to process information directly and without interpretation. All that enters our consciousness, informing ourselves about ourselves, is primarily a leftbrain phenomenon. In the end, what we call an “I”, is a highly selective, personally censored, biased self-concept, carefully monitored by the vigilant left-brain!

THE CONSTANT SELF

Thus, unknown to us, and below the surface of awareness, we are engaged in our unconscious process of selection, interpretation, and above all “distortion” or selective memory bias to sustain a recognizable “self”. These psychological mechanisms are responsible for perpetuating our grand illusion of continuity. Our personalities appear to remain as an unchanging ‘constant’ for us, over the extended flow of “real lived time”. Our great neurological fiction, “the enduring self,” is perpetuated by our left brain, throughout our extended lives. Our sense of constancy, carefully edited, allows us to cope, in the strictest evolutionary sense, with the basic issues of daily survival. We spin a ‘fictitious self’ to allow ourselves to adapt to, and live safely in the ‘dangerous immediacy’ of our complex worlds.

MIND AND CONSCIOUSNESS

“Mind”, or the rich subjective world of personal “consciousness,” defines our humanity. It allows us to live as social and sentient humans, endowed with the privacy of our own subjective worlds. It provides the intricate mechanism for the expression of logical, rational thought, volition, and decision-making choices for our own basic survival. It brings us into contact with others in our society. Those persons with similar language, culture and customs, reinforce our highly selective world-view.

At the same time “mind” produces and directs our creative, intuitive artistic, mathematical and musical abilities. Finally, “mind” stretches the boundaries of our circumscribed selves, to bring us out beyond our closed world, and into contact with the mysterious quantum flux of the universe. This experience of awe and wonder connects us
to our beliefs in the existence of a “Higher Power”, or the religious experience of a “Loving God”.

All of our thoughts, feelings, and emotions, are as much a part of our conscious experience, as what we see and hear, in the outside world, with our own eyes and ears. Thus, our minds are nothing less than the expression of the reality of our core selves; they reflect our intricate signature personalities. Our minds are the sum total of all that we have experienced in our lifetimes. It also allows us to turn inward, so that we may experience our own sense of well-being. And yet, even with the new research information contributed to our scientific knowledge by the neurosciences, we are very far from understanding the exact nature of consciousness.

Searching for a “molecular” explanation of consciousness is a waste of time, since the physiological processes responsible for this wholly private experience, will be seen to degenerate into seemingly quite ordinary, workaday reactions, no more and no less fascinating that those that occur in, say, the liver.

MIND, EXCLUDED IN MEDICAL DIAGNOSIS

The mind/body split, in practical terms, must inevitably de-emphasize the “mind” and “whole patient medicine.” It follows logically, therefore, that there is a disproportionate physician emphasis on symptom relief, referral to specialists, expensive diagnostic procedures, and a misleading reliance on the interpretation of equivocal laboratory procedures. This comes at the expense of “face to face time” and the healing significance of the timely patient visit is all but lost.

CRITICAL SUBJECTIVE SYMPTOMS IN TBD

Critical subjective symptoms (legitimate fabrications of “mind”) must be weighed with the same gravity as obvious physical symptoms. In the absence of obvious physical signs (and negative laboratory results) the ‘subjective-mind’ symptoms of the patient, assume even a greater importance. They must be given serious consideration when attempting to understand any disease process. “Mind” or subjective symptoms are particularly relevant markers in comprehending TBD’s. They are not unimportant incidentals to be discarded or to be minimized. They are often the keys to deciphering the
diagnostic mystery of the difficult patient

HIGHLY VARIABLE PATIENT SYMPTOM PRESENTATION IN TBD

The patient’s presentation of TBD disease is highly variable. A recognizable pattern of what appears to be clusters of unusual symptoms is not unfamiliar to the experienced clinician. There are many different ways in which TBD can present to the physician. Patients describe various degrees and intensities of pain, their sudden, inexplicable neurocognitive discrepancies, their blunted or exaggerated emotional response to the happenings of their daily life, their depleted energy level and experience of overwhelming fatigue, their extreme personality changes (including loss of libido, anxiety, depression), chronic sleep deficits in spite of extreme exhaustion, sleep apnoea, their persistent short-term memory difficulties, as well as focus and concentration problems especially with reading, writing, and speaking, problems in simultaneous, multiple tasking, their loss of a previously integrated knowable self, are all mainly “subjective or mind” symptoms. They are absolutely essential in making the clinical diagnosis of “encephalopathy” secondary to a TBD infection.

If these symptoms are labeled ‘non-specific,’ and dismissed out of hand, then the critical diagnosis of TBD encephalopathy is never made, and the unfortunate patient never recovers. An untreated ‘encephalopathy’, can progress over time. The end result can be an extremely disabling neuropsychiatric and/or neurocognitive condition, unrecognized even much later into the course of the illness. Borreliosis (Lyme disease) is a disease, which by its very nature exemplifies the mind/body split, since so many symptoms are “mind” symptoms. Subjective symptoms dominate the presentation of this illness. Therefore, the diagnosis and treatment of this illness, frequently drops through the cracks of specialty after specialty. Physical findings, except for the E.M. rash, and the hot, swollen monoarthritic joint, tend to be non-specific (ie. trigger points, tendonitis, costochondritis, floaters, cervical and lumbar pain, headaches, TMJ pain and tenderness, tooth pain, muscle soreness, eye twitching).

The disease further confounds the medical community, primarily because the (spirochete) bacteria, undergoes a chronic resting phase, an expression of microbiological “metamorphosis.” This in turn, ultimately gets expressed as the patient’s shifting,
subjective symptom. These adaptive, “immune evasive maneuvers” consistent with the Borrelia species, allow the spirochete to survive and persist in most tissues which it infects. The nervous system tissues, fascial/connective tissue, the vascular endothelial wall, and as recently discovered, the intracellular spaces of fibroblasts, macrophages, lymphocytes, and glial cells.

THE LOSS OF INDIVIDUAL-SPECIFIC TREATMENT PROTOCOLS

In addition, under the present day medical paradigm, there is a movement away from ‘individualized treatment programs’, which take into account the patient’s unique personal characteristics. Standards of care, although they serve as helpful guidelines, are often very conservative. They fail to take into account, the wide variations in patient diversity (i.e. age, sex, length of illness, co-infections, hormonal stage, immune response, GI absorption, medication tolerance, allergies, genetic background).

The stresses of modern practice can ruthlessly swallow a day, in a medical practice. Thus, time being limited; a physician can hardly know any of his patients in depth. Physicians are in danger of losing one of their most important assets; namely, their innate awareness of the ‘interconnected of things.’ The rush to ‘get through the day’, drains them of their medical curiosity and creativity. They must settle for consensus solutions, many of which do not reach the standards of “evidence-based medicine”. This is particularly true in TBD, where the patient presents as a diagnostic puzzle, and does not respond to conventional treatment.


Evidence-based medicine has aroused the legitimate fears of many clinicians. If it is considered to be the only scientifically valid method of medical diagnosis and treatment, it risks threatening the very foundation of medicine, namely the “art of patient care.” In fact, outcomes-oriented and evidence-based medicine, offers little help in the many grey zones of medical practice. This occurs when the evidence regarding options
can be incomplete or even contradictory. To develop criteria for assessing the appropriateness of clinical procedures, RAND has convened panels of clinical experts who rate hundreds of hypothetical cases on a risk-benefit scale. Many of the ratings for a substantial number of clinical scenarios cluster in the “uncertain” middle of the scale. For many clinical scenarios, there is a major disagreement among the expert panelists, which does not even allow for categorization.

If one actually demanded evidence from randomized controlled trials in support of each consensus indication, the grey zone would be much wider. Thus the boundaries of even the grey zones are themselves, uncertain again, varying with the evidence and its interpretation. Modern medicine seems to consist of a few things we know well, a few things we think we know pretty well, (but probably don’t), and lots of things we don’t know anything about at all.

Take any two technologies and they can be used in two different sequences; take five, and the number of possible sequences is one hundred and twenty and so on. Clinical strategies are usually tested alone, most always in separate studies. Rarely are the sequences of tests and treatment options studied together. The results therefore must obviously rest in the grey zone.

When strict evidence-based medicine by itself, is unable to guide most clinical decisions, some clinicians will espouse minimalism (i.e. short term treatment to T.B.D.). Other clinicians will favor a more aggressive series of interventions based on inference and experience. This conflict in treatment philosophies is nothing new. It is sobering to look back, and recognize how expert panels and guideline-setting bodies have misguided the profession. They failed to look ahead and ask how physicians can integrate information that arises from the scores of clinical trials published every month.

EVALUATIVE SCIENCES AND OLD ARTS.

In view of the limits of clinical research evidence, one might expect treatment indecisiveness, and in some cases, therapeutic paralysis, to be a much more common phenomenon in everyday practice. However, the human psyche is malleable, and clinicians rapidly become comfortable making decisions under conditions of evidence-based
uncertainty. Many treatments, in the grey zone, can be genuinely effective. Some diseases improve or remit, irrespective of the type of treatment. The doctor-patient relationship is often the most critical factor in “cure.” Patients can, and often do come into a practice with a puzzling array of “grey zone”, vague symptoms. Physicians have become comfortable over the years, relying on their educated guesswork. They can over the years, (through long hours and hard work), attain a special intuitive wisdom. More often than not, this medical magic yields surprisingly effective, pragmatic results. But it is easy to confuse personal opinion with strict scientific evidence, or worse, personal ignorance with genuine scientific uncertainty.

It does not help clarity matters when clinical-guideline-writers representing a supposed expert consensus, fails to distinguish “fact from fervor.” If clinical guidelines and other so-called trappings of evidence-based medicine are to be credible, they must unbiasedly and without pre-judgment analyze the best evidence and honestly acknowledge what we do and do not know about our present illness.

SICK OF BEING SICK!

Thus, the confused chronic TBD patient is confronted daily with a cluster of shifting, inconsistent symptoms never before experienced in their lifetime. A previously healthy individual, can slip into “permanent unwellness”, “I just want my life back,” or “I’m sick of being sick”, is the all too familiar lament of these chronically unhealthy individuals. Mislead by negative serology testing, and misunderstood CDC criterion, both the well-meaning doctor and their patient often end up being frustrated, and even at odds with one another.

An untreated “encephalopathy” can progresses to more disabling symptoms over time. As a result, both neurological and psychiatric symptoms may develop later in the course of the illness. No two patients display exactly the same evolution of symptoms. Paradoxically, there are many ways, in which the TBD disease symptoms can change over time, in the same patient. Different species of Borrelia or the complications of a coinfection is what makes the diagnosis of TBD so frustrating.
ANTIBIOTIC USE

The medical community, for the most part, has been cautioned to avoid “over diagnosis,” thinking, as well as dangerous, and costly, overuse of long-term antibiotics. Peer-reviewed journals, (JAMA, NEJM, LANCET) have warned against inappropriate antibiotic therapy. More importantly, the persistent kaleidoscopic TBD syndrome doesn’t make sense to a “cautious, conservative medical mind,” which prides itself on ‘scientific objectivity’. This is better known as ‘evidenced based medicine.’ “Borrelia with coinfection,” ‘blurs’ the boundaries between specialties. This complicates the initial diagnosis, and subsequent treatment recommendations for the patient.

DOUBLE REJECTION OF TBD PATIENT WITH PSYCHIATRIC SYMPTOMS

The TBD patients are a special class of “walking-wounded” sufferers, victims of their undiagnosed “invisible disability.” Their quality of life has been upended, and turned upside down. Their sense of self has been severely compromised by negative medical feedback. These individuals feel demoralized, and are often left without hope and even without family support. Unfortunately, neuropsychiatric Lyme patients are recipients of a “double rejection. They are in a class by themselves.

Because of the nature of their illness, and their general frustration with the medical profession, they can be insistent, demanding and difficult people. They push their doctor for an explanation of all the medical information they have researched. Some of the information is obviously of importance, obtained from journals or published articles in popular magazines. Some of the information is derived from association with other patients in self-help groups, and TBD anecdotes. Most of the time, the information is gleaned from the ubiquitous Internet. A large percentage of the information brought to the physician by the patient, is not very useful, and tends to be exaggerated or inaccurate.. An unyielding patient can produce legitimate physician frustration, when they insist that every symptom is directly related to Lyme disease. They will cling with absolute certainty, to the belief that they are unshakably correct, and will entertain no other diagnosis for their medical condition. And more times than not, they are right.

PSYCHIATRIC SYMPTOMS IN TBD PATIENTS
This behavior, unfortunately, can result, in the dismissal of a “too anxious patient” for persisting in their “Lyme obsession or delusion.” It is not uncommon for patients to be dropped from a practice, if they continue to argue and question their “nondiagnosis” of ‘Lyme disease,” even after supposedly negative serology. Other “encephalopathic” patients may exhibit classic psychiatric symptoms (i.e. OCD, instability, rage response, panic attack, and even bipolar episodes or frank psychotic symptoms.) They appear out of place in an internal medicine practice. They are quietly classified as mentally unstable, hypochondrial, or having personality disorder, and referred to a psychiatrist.

Children, whose TBD illness is not understood, can on rare occasions have become further victimized. Persistent and anxious parents continually confront their frustrated pediatricians with their infected children. In extreme cases these parents have been unfairly diagnosed as “Munchausen’s By Proxy” parents. The egregious result is that their children are “not treated, for their medical condition.” Instead an even worst-case scenario can follow. Their child can be removed in error, from a loving family, by a misguided Protective Services agency. The psychological impact and emotional consequences, for all family members concerned, are obviously devastating.

THE PSYCHIATRIST’S ROLE IN TBD

The term “empathy,” comes for the German “einfühlung”, which literally means “in-feeling”, or “feeling into.” The precondition for the “empathic dialogue”, is a searching attitude of simultaneously ‘knowing’ and ‘not knowing.’ Martin Buber, the great Jewish philosopher referred to authentic dialogue as the “I-Thou experience.” This phenomenon pertained to all forms of human contact, ‘including professional relations with a physician.

Psychiatrists, with their training and listening skills, their comfort level with the importance of subjective symptoms, their longer sessions, their understanding of stress situations as it affects the immune and the neuroendocrine system, their emphasis on complex psychological connectedness, their understanding of the evolution of disease over time, make them an excellent physician-advocate for diagnosis and treatment of
A SAFE AND SECURE PLACE

The work of ‘healing’ can only begin for most traditional psychiatrists in what Leston Havens MD has described as a “safe place”. The bewildered TBD patient needs the same consideration from the other specialists with whom he consults. Just as in the very best hospital experience, the TBD patient needs a “safe and nurturing place”, in which to “de-stress” and be understood. In this context, they can elaborate their complicated medical narrative without interruption or premature dismissal.

Hopefully, the clinical observations which I have gleaned over a fifteen year period, treating TBD exclusively (over 2500 cases) will help clarify some of the contentious issues for both the patient and his/her physician.

NECESSARY CHANGES IN CDC, NIH, AND STATE DEPARTMENT OF HEALTH:

From the perspective of 15 years’ direct clinical experience with more than 2500 successfully treated cases of tick-borne illnesses, I am convinced that there needs to be a serious and non prejudicial re-evaluation of this enigmatic disease state. The changes must begin with the National Institute of Health and Centers for Disease Control at the highest level of governmental responsibility. This same information must be communicated to the Department of Health (i.e. Connecticut, New York, New Jersey) at the state level and to all major insurance carriers, especially in the Northeast, Midwest and California. Both the diagnosis and the treatment of what “informed practitioners” (Lyme literate) around the country, have designated as “chronic” or “persistent” Lyme Disease (with/without co-infection), needs to be recognized, rather than being dismissed out of hand. This possible multi-organism condition, often from an unsuspected tick-bite, at some unknown time, is a complex and potentially serious illness.

ACUTE LYME DISEASE AND CONVENTIONAL MEDICINE

Bare in mind, this is not the “well described” and commonly known syndrome of ‘acute Lyme Disease.’ This well documented clinical picture, of embedded tick bite, rash (erythema migrans,) flu, fever, fatigue, mild arthritis and transient neurological
symptoms, most alert physicians in Lyme-endemic areas generally able to recognize. They are able to treat the condition conservatively (3-6 weeks of oral antibiotic therapy) and for the most part, successfully.

Unfortunately, more than half the rashes are not typical and can present with many different dermatological patterns. More often than not, this causes diagnostic problems for the unsuspecting physician. Patients who have never seen, or ever developed a rash, may develop serious symptoms many months or even years later. Or they may remain completely asymptomatic; with no outward evidence of infection.

**CHRONIC, PERSISTENT LYME AND TBD**

The identification of chronic or persistent Lyme is very unlikely (with coinfection) in today’s medical climate, unless the physician is properly educated in identifying this syndrome. Chronic TBD is invariably excluded from the patient’s differential diagnosis, particularly if the serology produces negative results. Indeed, the presentation of the ‘acute phase of the illness’ is really the only utilized definition for Lyme disease proper. This definition in actual practice recognizes almost exclusively, the dermatological and rheumatological symptoms.

The offerings of the patient’s “mind” are dismissed as inconsequential, unless the individual is severely disturbed. (Psychosis, panic attack, manic-depression). The subjective description of a “self” in distress is not accepted as helpful or useful diagnostic information. For that reason, the neurological, neuroendocrine, neuropsychiatric and neurocognitive sequelae of “chronic, persistent Lyme” are almost always overlooked. To repeat, they are overlooked, because they do not appear to be included in most physicians’ diagnostic understanding of this complicated phase of the disease. Ask most doctors what constitutes “chronic Lyme”, namely, how is it diagnosed and how is it treated, and the answer almost always comes back, “chronic Lyme” does not exist!!

**CO-INFECTIONS**

The equally serious consequences, of number co-infections, residing in the same patient are also not likely to be considered. A confusing array of symptoms (*including*
chronic joint and muscle pain, sleeplessness, crushing headache, overwhelming fatigue, mood and personality changes) can be present continuously or intermittently at one time or another. Often in frustration, the unsuspecting physician wishing to put diagnostic closure, on those diverse symptoms will attach various descriptive labels to fit the unwell patient: Fibromyalgia, chronic fatigue syndrome, chronic viral syndrome, depression, stress or seasonal disorder with migraine headaches.

SERIOUS NEUROLOGICAL DISORDERS

Much more serious disorders are also considered in the diagnosis. Atypical multiple sclerosis, systemic lupus, early Parkinson’s disease or early ALS, these are but a few of the labels which, have stuck to patients in their search for answers. And of course, what is the inevitable result? The chronic phase of Borreliosis is left untreated, or the treatment is directed toward at the wrong diagnosis!

STANDARD OF CARE

Surprisingly, the standard of care, earnestly followed by most of the well-meaning physicians in the community, is unproven, beyond the acute phase of the illness. It fails to take into account the sophisticated avoidance mechanisms of the bacteria. The incomplete science, upon which these guidelines rest, are in the final analysis simply “speculative hypothesis” - spun into treatment recommendations. They ignore the critical medical problem of ‘advanced Borreliosis’ (IDSA vs. ILADS).

In such a state, the infected patients often find themselves, on a slow, inexorable, slide to “chronic un-wellness,” and a significantly diminished quality of life. In many of the severe cases, the patient may have visited a merry-go-round, of no less than half a dozen or more unsuspecting physicians and specialists, before they were finally diagnosed and properly treated, if at all!

FEMALE vs. MALE

Women, in my practice, as collaborated by other physicians, appear to be more affected than men – approximately at 2:1 or as high as 3:1 ratio. Some CNS neural cells appear to harbor estrogen and progesterone receptors. Men appear to have a more speedy
and complete recovery as compared to women.

Higher levels of testosterone, appears to protect males. Men, with low testosterone and low libido appear to have a more difficult time in recovering from the illness. The female menstrual cycle is associated with exacerbation of “Borrelia symptoms” which can, in turn, exacerbate “menstrual symptoms” and contribute to gynecological problems, including worsening of endometriosis and increased risk of miscarriage.

STRESSORS AS ACTIVATORS OF LYME

Some symptomic or previously asymptomatic patients may reactivate their infection following stressors of various kinds. Trauma, surgery, pregnancy, an intercurrent illness, the flu, taking an antibiotic for an unrelated reason like sinusitis, severe psychological stress (a death in the family, a divorce) or having received the infamous Lyme vaccine. All these factors have been involved adversely in my practice, leading to reactivation of the infection.

As a result of these general observations, I will offer a number of recommendations which can reduce some of the confusion about the disease, faced by physicians in our community. My hope is, that my clinical experience (and that of other “like-minded” colleagues), will serve to clarify some of the more contentious issues, as well as some of the general misconceptions, pertaining to this subject matter. Frankly, if one has studied in detail, the microbiology of Borrelia, has experienced its clinical diversity and one has followed patients in treatment, through this elusive condition – there would be no misconceptions.

BIOLOGY AND PATHOGENESIS

There is a wealth of proven biological data, essential to understanding the Borrelia bacteria spirochete and its pathogenesis upon which, diagnostic and treatment considerations must be based.

PREDILECTION FOR SPECIFIC SYSTEMS

1. It has been known for many years, that this organism has a predilection for
articulacr, vascular, muscular nervous system tissue and can penetrate almost any tissue
and reside for months or years extracellularly as well as intracellularly. This includes the
cerebro-endothelial wall of arterioles and capillaries of the brain. The myelin of myelin
sheath of peripheral nerves, the sensorial cells of joints, the fibrocytes of muscles and T
and B cells as well as macrophages of the immune system, to none but a few tissues.

**PENETRATION OF CELLS**

2. Burgdorfer (the researcher after whom the (Lyme) Borrelia organisms is
named) showed that the bacteria had the capability to penetrate cell walls. In his studies,
he demonstrated that it invaded the tick gut’s wall and spread via the hemolymph to the
salivary glands.

**BINDS PLASMINOGEN**

3. The B.b. binds human plasminogen to surface proteins. It is then converted to
plasmin to provide the mechanism where by B.b. can digest the extracellular matrix and
penetrate cell walls using the host’s own enzymes.

**BLOOD-BRAIN BARRIER**

4. Brain microvascular endothelial cells (BMEC) are essential to the blood brain
barrier due to their high electric resistance. Borrelia can traverse this barrier by the
addition of plasminogen, which is localized to the site of spirochete-endothelial cell
interaction, leading to a transient breakdown of the blood brain barrier and facilitating the
invasion of B. Burgdorferi in the C.N.S. It is evident the B.b. is resourceful, if not
extremely clever. It has the advantage of millions of years of evolutionary practice, and
the necessary equipment to penetrate most cell-types.

**INTRACELLULAR SURVIVAL**

5. Once inside, it can survive within the cytoplasm, safe from immune detection.
This would explain one of the possible mechanism by which the organism escapes the
immune system of the ‘host’ and persists during the later stages of the disease.
INSIDE MACROPHAGES

6. Also as stated, persistence of B.b. has been shown to exist within migrating macrophages. This provides a possible pathogenic mechanism for recurrent Borrellosis.

CHANGES SURFACE ANTIGENS

7. The organism can also evade immune detection by changing what is known as “surface antigens,” a complex protein sequence on its outer coat and even alter the lipoproteins within its cytoplasm, giving it a survival advantage.

CYSTIC FORM

8. Electron microscopy has revealed that B. Burgdorferi appears to metamorphose from an active, motile, spiral, flagellar form, to a dormant resting cystic form, particularly in the C.S.F. Under special circumstances, it can then reverse itself from the dormant cystic form, back to the active motile form, producing a whole new generation of spirochete bacteria (without a re-infection from a tick-bite). Present testing methods, under these circumstances, would be unable to detect the presence of the bacteria in the C.S.F.

9. Elegant photo microscopy demonstrated that the bacteria can penetrate a T or B cell (Lymphocyte) and camouflage itself with the cytoplasmic contents (much the same as wearing a rain coat) to escape immune detection.

10. Untreated Borreliosis in most cases (along with possible co-infection) will eventually become a chronic spirochetal infection, following the example of other bacteria of the same genus: (syphilis, relapsing fever, and leptosporosis). The cork-screw, mature, B. Burgdorferi bacteria, besides exhibiting intracellularly, has been shown in a number of studies to change to a cystic cell wall deficient phase or non-motile spherical starvation stress form, seeming to occur when the host environment becomes hostile, (i.e. decreased source of fatty acids and lipids.) Remarkably in this state, the bacteria can persist and evade immunologic detection.

11. Under times of physical or psychological stress for the patient, the bacteria can produce a new generation of spirochetes. They metamorphose from the cell wall deficient form or the (NMSSS form), back to the mature spiral form. If the live B.
Burgdorferi as well as its plasmid structure, or its fragments, (flagellar protein) persists in the body, it can still continue to induce tissue injury (chronic inflammation and R.O.S. (reactive oxygen species)).

**IL-8 AND INFLAMMATION**

12. Borrelia bacteria promotes inflammation by stimulating endothelial cells (cell walls of capillaries) to cause white cells (leukocytes) to adhere to them and produce a soluble agent, IL-8, that attracts neutrophils, causing persistent inflammation or more specifically, vasculitis.

**LIPO PROTEINS AND CYTOKINE STIMULATORY PROPERTIES**

13. Studies have demonstrated that outer surface lipo-proteins of Borrelia possess cytokine stimulatory properties co-related with the severity of the disease. OSpa was found to be a potent stimulator of a nuclear factor – detectable within 15 minutes, also upregulating IL-6 cytokine, and the chemokine IL-6, as well as, adhesive molecule Eselectin, which in turned cause enhanced binding of neutrophils. The cytokine IL-6 is known as an important pain modulator and can produce hyperalgesia, fatigue, depression, and neuro-immune modulation.

14. Production of IL-8 promotes serious sympathetic nervous system pain.

15. A recent study of pediatric patients, afflicted with persistent Lyme on arthritis and whose symptoms continued, despite what is considered adequate treatment demonstrated a population of rapidly dividing cells of mesenchymal origin, which continue to remain activated and show cytokine secretion in culture.

**MOLECULAR MIMICRY**

16. ‘Molecular mimicry’ with auto-immune like pathology or the production of a neurotoxin, (not yet isolated) liberated by the bacteria, has both been suggested as possible pathogenic mechanisms. Chronic, debilitating, neurological deficits may take months or even years to develop (a creeping un-wellness). This chronic, persistent, infection over time increases the possibility of an auto-immune-type reaction (“a classic immune cascade with release of lymphocyte cytokines and interleukin-2/6). The CNS
appears to be particularly susceptible to this type of process. (Encephalopathy) Other illnesses such as M.S., ALS or systemic lupus, have on more than one occasion, been suspected of being the result of an underlying Borrelia infection. These are only a small sample, of the basic biological facts, relating to the pathogenesis of Borrelia. These facts must be taken into consideration, when treatment program guidelines are recommended, most notably for the chronically infected patient. This issue is far too important to be co-opted by a small handful of IDSA academic physicians.

**DIAGNOSTIC REPORTING**

After almost 25 years, physicians in endemic areas do not yet have accurate methods to make an exclusive laboratory diagnosis of this disease. The CDC reporting criteria were never intended for clinical diagnostic purposes. They are restrictive guidelines for reporting numbers.

The CDC acknowledges in their own publications, that their guidelines are statistical and epidemiological. The average physician, by following only these rules, has no other standard on which to base an accurate serum interpretation. Let me repeat: For the present, the prevailing conditions in medicine are such that the diagnosis is an “either/or” proposition. Simply put, “you are, or you’re not positive”. “You have Lyme disease or you don’t have it!” There is no middle ground. There is no other serological, interpretation on which to base a reasoned judgment. Moreover, the CDC standard says nothing about the co-infection.

There are at least 11 Babesia forms found in ticks, but we can only test for B. Microti and WA-1 form. Blood smear are useful after the first 2 weeks only. The same with Ehrlichia, more species are known, than can be tested for. Bartonella symptoms are almost impossible to separate from Lyme and again, hard to diagnose under the present circumstance, test are at best minimally helpful. A physician, can only use, the limited reporting criteria, as set forth by the CDC to confirm his clinical diagnosis. Insurance companies, despite 20 years of data to the contrary, continue to insist on CDC criteria to validate a physician’s “clinical” diagnosis. (See medical policy reference manual – Blue Cross Blue Shield of CT)

Three Northeast states; Rhode Island, Connecticut and New Jersey, have
introduced legislation to safeguard the rights of patients to obtain minimal treatment for Borrelia, stressing the importance of the physician’s judgment over the less accurate serological confirmation. Neither is the physician to be harassed by the State Medical Boards for this approach. Without these laws, I fear that unfair insurance denials for services and witch-hunts against physicians would continue to plague those patients and, those doctors who strive to treat it conscientiously, afflicted with “Lyme disease.” Even the prestigious New England Governor’s conference unanimously passed Resolution 166, concerning Lyme disease and other tick borne illnesses. (See Rhode Island Resolution Chap. 159 enacted 06/25/02.)

LABORATORY ACCURACY

After analyzing thousands of serum specimens over 15 years, I have found the laboratory results for Borrelia and other tick borne illnesses, as tested by the large laboratories (Quest, Smith Kline, LabCorp), to be inconsistent, with the positive clinical evidence of Borreliosis. These labs, possibly because of their volume, cannot be relied upon to provide serological confirmation in most cases. Inter-lab reliability can also be frustratingly inconsistent. The commercial “testing kits” which these labs all purchase from the same sources are restricted in their antigenicity as it applies to the Borrelia subspecies.

Other smaller, specialty, laboratories are, on the other hand, more accurate and more consistent in their result. They deal almost exclusively with virology, bacteriology, and tick borne infections (Igenex, Medical Diagnostic Lab, and Immunosciences.)

FOLLOW-UP TESTING

Follow-up testing methods for treatment “in progress” would also, be of estimable in value, but at this time, they have not yet been developed or marketed and therefore are not yet commercially available. This leaves the physician in a quandary. Without the serological confirmation of patient improvement, only the physician’s clinical judgment, and the patient’s regular reporting of symptoms (improved or worsening), can determine treatment outcome. Follow up visits, and close monitoring (i.e. patient keeping a journal), spaced no more than a month to a month and a half apart, is critical to care and the only
tool that the physician has, to render a judgment about treatment. Namely, frequency of reproduction cycles of the organism, appearance of co-infection symptoms, Jarish-Herxheimer reactions, sensitivity to medications, dosage changes, antibiotic changes, route of administration changes, referred to specialists for 2nd opinion (neurology; cardiology.)

FAMILY CO-INFECTION SYNDROME

Physicians must recognize the effects of this illness on vulnerable family members. In my practice, is not unusual to have 10-15 patients on the same street, from half a dozen families become infected. Family members have become ill with T.B.D., both at the same and at different times (presumably from the same deer, white footed mouse and tick reservoir.) Their symptoms can vary from neurological, to rheumatological. They often have a confusing array, of temporary intermittent, shifting complaints. No one is spared, neither, the young nor the old. Father, mother and all of the children, in the same family (including the pets and nanny) may have at one time, or another, been exposed to, and made ill by, infected ticks.

Each individual, in the same family, can display a puzzling array of different clinical symptoms, which are different in intensity, duration, and the system or systems infected. These conditions may represent only Borreliosis, or can be the combined result of a co-infection syndrome (CIS). Up to four or more pathological organisms may all interact at the same time (Babesia, Bartonella, Mycoplasma and Ehrlichia.) This coinfection syndrome is obviously difficult, for the physician to diagnose, if he is not familiar either with its existence or its presentation in a patient.

It can impact directly, on the emotional well being of marriages (separation and divorce), on economic well being (job loss, loss of insurance coverage, exorbitant costs of correct or incorrect medical treatment), or partial and total disability (chronic illness). Children of these families have their own special problems. Characteristic, or uncharacteristic, academic under-achievement (poor grades from a previously good student, failures, school absences, missing up to 1-2 years and social isolation from peers), seriously delayed development, ranging from failure to thrive, to childhood autism, (sometimes, stemming from post-natal Lyme.)
If both the parents and the children, are infected at the same time, (which is not unusual), the stress on the family becomes almost intolerable. I have seen what I call “family co-infection syndrome” severely disrupt the quality of family life. It can diminish personal self esteem, cause loss of identity, and permanently destroy previously, affectionate, and loving interpersonal relationships.

The family system can have a direct impact on the compliance of the infected patient. The designated Lyme patient can in turn, directly impact the family system. A general systems approach to the problem of TBD expands the field, and those factors which improve or inhibit the outcome.

In an acute health crisis or emergency (that those resolve in days, weeks, or even months) –“good technical biomedical” care takes priority. There is almost always a predictable time frame, with a more or less predictable outcome. Patients endure the inevitable hardships for a defined period of time. The family members usually are supportive in the crisis (i.e. emergency room visits for kidney stones, bronchial pneumonia, broken bones or appendicitis.)

**CHRONIC CONDITIONS**

In chronic conditions (cancer, heart disease, diabetes), uncertainties and ambiguities of diagnosis and prognosis often extend well into the distant future. With these more serious illnesses, there is often the family expectation that the patient’s condition will worsen, and result in complete disability, dependency, and in terminal cases, death.

**FAMILY CARE GIVING SYSTEM**

The individual is not considered in isolation, but rather is seen as an integral part of a dynamic “family care giving system.” The total family system and not just the individual patient in isolation, becomes the central focus in a chronic tick-borne illness.

One of the questions, often asked by family members with TBD patient is - what is normal family coping? And how should we as family members adapt to living with TBD? What can we expect, over time and well into the future? Is the patient able to be cured? What is a remission? What is a relapse?
BELIEF SYSTEMS

The patient’s own belief systems about health and illness are equally critical to the treatment outcome. For discussion purposes, I view TBD, as not just localized in one organ or even multiple organ systems that belongs to a solitary, infected patient. The useful working disease definition should be understood as a “TB-family illness system.” The physician really joins the “family illness system” to create a therapeutic alliance in the best interest of the patient.

Naturally the processes of the disease strongly influence the patient’s and family’s response: early, chronic persistent, relapsing, and disability-dependency.

Chronic, persistent, and relapsing TBD asserts itself into family life with a vengeance. It not only impacts the life of the individual infected patient, but other members of the family as well must adapt continually to radical changes in the person. The age of the patient, the developmental tasks appropriate for that person, and the stage of the family life cycle, all contribute to defining the strengths and weaknesses of the family support system.

DISRUPTION OF ORDERLY STAGES

The TBD disrupts the orderly stages of the family life-cycle. We like to believe that we plan our lives and that we have some reasonable control over its outcome. We have the expectation that it will unfold with an expectable beginning, middle, and a noble end (with gentle transitional periods leading to each next important stage). We welcome birth and anticipate all as part of the natural order of the family life cycle. TBD can play havoc with both the individual life cycle and the family life cycle.

INDIVIDUAL LIFE CYCLE:
• Childhood / Adolescence
• Early / middle / late adulthood
• Senior adulthood / old age – autumn years

Individuals shift from the responsibilities of nurturing / cohesion / family reliance needs / autonomy / independence / self reliance needs.
FAMILY LIFE CYCLE:

1. unattached young adult
2. newly married couple (dyad)
3. family and young children (triad)
4. family with adolescence in high school
5. launching late adolescent children (college)
6. family/extended family/grandchildren

The above family life cycle periods, coincide with specific developmental tasks. There are swings between tasks which emphasize “bonding with cohesion” (early child raising), and tasks that emphasize personal identity and autonomy (adolescence/young adulthood). For example, birth, which brings the addition of a new family member, leads to a long period of dependency and socialization with children. Cohesion, nurturing, intense bonding, and constant family activity in this circumstance, is the healthy norm.

AN UNWELCOME FAMILY MEMBER

In a somewhat analogous way, the appearance of chronic TBD in a family, partially resembles the addition of a new, but unwelcome, family member, which also requires high cohesion and maintenance. If the illness coincides with the “autonomous” stage family life, it can cause serious problems. The “sickness” demands of Borreliosis (Lyme) for “cohesion” and nurturing are in conflict with the high energy demands of autonomy and independence. For example, when a parent develops a chronic TBD condition, during the child-rearing phase of care taking, the family is severely taxed.

Each family life cycle stage is unique. A wage earner father, who is seriously compromised, and out of work, impacts the family system differently, than a mother who is ill, exhausted, and cannot run a household, nurture her children and be a companion, wife and a sexually active partner.

Children, of course, present their own heart breaking problems depending on their degree of dysfunction and their age (early childhood, school age, adolescent). Not only does a single child impact the whole family system, shifting its priorities, but some families are faced with the overwhelming burden, of having more than one child infected with TBD at the same time. During this extended period of time (sometimes more than
five years), when a single child or multiple children are chronically ill (physical, emotional, or cognitively handicapped) in the same family, the family unit suffers disproportionately and the culture of illness becomes the norm.

The extent to which a “chronically ill family system” is either supported by or divided by their extended family system, obviously impacts the outcome and the stress experienced by all members of the family-illness system.

**LYME AND PREGNANCY**

There is a growing body of case-study literature which cautions prospective mother as to the hazards of pregnancy suffering from a concurrent active Lyme or TBD exposure. Clinical evidence has demonstrated the presence of active Borrelia organism in utero, found in umbilical blood, uterine muscle, placenta and the growing fetus.

Congenital birth defects have been documented, along with stillbirths. Prenatal conditions include: pyloric stenosis, serious developmental delays, failure to thrive, chronic immune deficits with increased susceptibility to infection. Gastro-intestinal symptoms including: projectile vomiting, mal-absorption and severe stomach pain. Behavioral symptoms include: OCD, serious speech delays, excessive temper tantrum, persistent headaches, childhood schizophrenia, and autism.

Borrelia organisms and DNA have been isolated from the breast milk of the mother. Antibiotic therapy for the mother and the infant should be utilized as soon as possible.

**GUIDELINES - IDSA VS. ILADS**

The complicated pathogenesis, as demonstrated by the unusual immunologic presentation of the B. Burgdorferi (with co-infection) therefore, necessitates a cautious, but open-minded and informed approach to proper diagnosis and treatment. A rigid suspicious, uncompromising, skeptical attitude mounted by certain physicians toward the infected, chronically un-well patient, is unacceptable practice.

The great Canadian physician Sir William Osler, (my countryman, trained at my medical school, University of Toronto and then McGill) was the father of bedside, clinical teaching at John Hopkins in the early 1900’s. He stated:
Let not your conception of misfortunes of disease
Come from work heard. Learn to see, learn to hear,
Learn to feel. And then know by practice alone
Can you become experts.

SUCCESSFUL TREATMENT PROGRAMS

The usual treatment recommendations therefore, are for the most part, extremely limited. Only minimal selections of oral antibiotics are prescribed: (Penicillin G, tetracycline, doxycycline and amoxicillin). In addition, the “duration” of treatment is curtailed long before, the presenting ‘symptoms,’ have resolved. Frustrating relapses are a common occurrence after what is considered sufficient treatment. Often the harried physician, who believes he has treated the patient appropriately, can offer nothing but incomplete symptom relief for persistent symptoms, with other prescribed medications. Intravenous therapy, when initiated, usually consists of 3-6 weeks of Rocephin. Insurance carriers have strict rules governing longer term treatment, and often refuse to cover these essential requests.

Alternative oral medications may well be a more effective option clinically in patients who have failed to improve on the more commonly prescribed regimens (amoxicillin, doxycycline).

These new antibiotics include (Ceftin, Cedax, Suprax, Biaxin, Zithromax, Dynabac, Cipro, and Levaquin). The anti-parasitic medications (Plaquetnil, Lariam, Malarone, Mepron, Flagyl, and Tinidazole) are not considered in the IDSA guidelines. They can be effective in counteracting the effects of chronic, relapsing Borreliosis.

KAFKA SCENARIO

An untreated or partially treated Lyme patient is reminiscent of a disoriented train traveler in a Kafka-like scenario. The traveler wishes to board a train on the East Coast with the intention of reaching the West Coast. However, once arrived at the train station, the traveler can’t find the “right boarding track.” The information given to him concerning “schedules and time” is hopelessly “outdated” and inaccurate. In addition, the “information booth” official continues to direct him to the wrong gate. The conductor on
the platform denies the existence of such a train ever traveling to the West Coast. The traveler, hopelessly confused, finally boards the correct train that appears to head to the West Coast. Halfway through the journey, he is told that his destination has been reached. He is instructed to get off the train. Little wonder, the “traveler” is disoriented, feels crazy, and begins to doubt the reality of his/her own senses. After all, if the supposed successful course of treatment does not improve, the patient’s symptoms are no better off at the end than he was at the beginning.

**INTRAVENOUS ANTIBIOTICS**

The usual recommended intravenous medications, as set forth in the guidelines, include only Rocephin, Penicillin G and sometimes Claforan. Other options (IV Zithromax, Merrem, IV Doxycycline, and Vancomycin) are not utilized but in practice, can be critical in treating the condition. Combinations of oral medications (i.e. the cephalosporin and/or macrolide antibiotic group combined with an ant parasitic) or antimalarial medication (though not listed in the guidelines) are extremely helpful against the disease.

Obviously, extended IV treatment programs, ranging from three to six months, sometimes, up to 1 year, are never considered – and yet, it is clear that without these long term programs, some patients would be seriously compromised; remain untreated, and relapse quickly.

**MAINTENANCE THERAPY**

Maintenance antibiotic therapy is not discussed in the guidelines. A virtually important part of any treatment program after IV treatment. Almost all extended treatment methods, are continually referred to as “unproven or not medically necessary” by most of the larger insurance companies, aided in no small measure by the consultant specialists whose writings they quote and who they employ to “support” their frequent denials for care. I must, however, “give the devil his due.” In my practice, although denials are commonplace, the greater majority of patients have been approved for 12-16 weeks of I.V. antibiotic therapy, based on my letter of medical necessity.
ANTIBIOTIC CHOICES

ORAL THERAPY

Always check blood levels when using agents marked with an asterisk (*), and adjust dose to achieve a peak level in the mid-teens and a trough greater than five. Because of this, the doses listed below may have to be raised. Consider Doxycycline first due to concern for Ehrlichia.

*Amoxicillin

- Adults: 1g q8h plus probenecid 500mg q8h; doses up to 6 grams daily are often needed
- Pregnancy: 1g q6h and adjust
- Children: 50 mg/kg/day divided into q8h doses
- Adults: 100 mg qid with food; doses of up to 600 mg daily are often needed, as doxycycline is only effective at high blood levels.

*Doxycycline

- Not for children or in pregnancy.
- If levels are too low at tolerated doses, give parenterally.
Cefuroxime axetil

Oral alternative that may be effective in amoxicillin and doxycycline failures.

*Useful in EM rashes co-infected with common skin pathogens.

Adults and pregnancy: 1g q12h and adjust.
Children: 125 to 500 mg q12h based on weight.

Tetracycline

Adults only, and not in pregnancy. 500 mg tid to qid

Erythromycin

Poor response and not recommended.
Adults: 500 to 1000 mg q12h. Add hydroxychloroquine, 200–400 mg/d or amantadine 100–200 mg/d.

Clarithromycin

Cannot be used in pregnancy or in younger children
Adults: 500 to 1200 mg/d.
Adolescents: 250 to 500 mg/d.
Add hydroxychloroquine, 200–400 mg/d, or amantadine 100–200 mg/d

Azithromycin

Cannot be used in pregnancy.
Oral azithromycin is not as effective as clarithromycin.

Augmentin

Cannot exceed three tablets daily due to the clavulanate, thus is given with amoxicillin. This combination can be effective when Bb beta lactamase is felt to be present.

Chloramphenicol

Not recommended as not proven and potentially toxic.
500 to 1500 mg daily in divided doses.

Metronidazole
Adults only.
(see text)

**PARENTERAL THERAPY**

Risk of biliary sludging can be minimized with intermittent breaks in therapy (i.e.: infuse five or less days in a row per week).

**Ceftriaxone**
Adults and pregnancy: 2g q12h, four days in a row each week.
Children: 75 mg/kg/day up to 2g/day
Comparable efficacy to ceftriaxone; no biliary complications.
Adults and pregnancy: 2g q8h; may dose as high as 12g daily. Suggest a continuous infusion.
Children: 90 to 180 mg/kg/day dosed q6h (preferred) or q8h, not to exceed 12 g daily.

**Cefotaxime**
**Doxycycline**
Requires central line as is caustic.
Surprisingly effective, probably because higher overall, and spiked blood levels when given parenterally.

Always measure blood levels.
Adults: 400 mg q24h and adjust based on levels.
Cannot be used in pregnancy or in younger children.

**Azithromycin**
Requires central line as is caustic.
Dose: 500 to 1000 mg daily in adolescents and adults.

**Penicillin G**
IV penicillin G is minimally effective and not recommended.
Surprisingly effective IM alternative to oral therapy.
May need to begin at lower doses as strong, prolonged (6 or more week) Herxheimer-like reactions have been observed.

**Benzathine penicillin**
Adults: 1.2 million U three times per week (higher doses with large body habitus)
Adolescents: 300,000 to 2.4 million U weekly.
May be used in pregnancy.

Poorly studied but anecdotally effective
Vancomycin Observed to be one of the best drugs in treating Lyme, but potential toxicity limits its use. It is a perfect candidate for pulse therapy to minimize these concerns. Use standard doses and confirm levels.

Imipenim and Unisyn Similar in efficacy to cefotaxime, but often works when cephalosporins have failed. Must be given q6 to q8 hours.

Cefuroxime Useful but not demonstrably better than ceftriaxone or cefotaxime.

Ampicillin IV More effective than penicillin G. Must be given q6 hours.

TREATMENT CATEGORIES

**PROPHYLAXIS** of high risk groups — education and preventive measures. Antibiotics are not given.

**TICK BITES** — Embedded Deer Tick With No Signs or Symptoms of Lyme (see appendix)

Decide to treat based on the type of tick, whether it came from an endemic area and percent infected, how it was removed, and length of attachment (nymphs: at least one day; adults: anecdotally, as little as four hours). The risk of transmission is greater if the tick is engorged, or if it was removed improperly allowing the tick's contents to spill into the bite wound. High risk bites are treated as follows (remember the possibility of coinfection!):
1. Adults: Oral therapy for 21 days.
2. Pregnancy: Amoxicillin 1000 mg q6h for 6 weeks. Test for Babesia, Bartonella and Ehrlichia. Alternative: Cefuroxime axetil 1000 mg q12h for 6 weeks.
3. Young Children: Oral therapy for 21 days.

**EARLY LOCALIZED** — Single erythema migrans with no constitutional symptoms:

1. Adults: oral therapy for 6 weeks.
2. Pregnancy: 1st and 2nd trimesters: IV X 21 days then oral X 6 weeks
   3rd trimester: Oral therapy X 6 weeks.
   Any trimester — test for Babesia, Bartonella, and Ehrlichia

**DISSEMINATED DISEASE** — Multiple lesions, constitutional symptoms, lymphadenopathy, or any other manifestations of dissemination.

**EARLY DISSEMINATED** — Milder symptoms present for less than one year and not complicated by immune deficiency or prior immunosuppressive treatment:

1. Adults: Oral therapy until no active disease for 4 weeks (4–6 months typical)
2. Pregnancy: As in localized disease, but duration as above. Treat throughout pregnancy, and do not breast feed.

**PARENTERAL ALTERNATIVES** for more ill patients and those unresponsive to or intolerant of oral medications:

1. Adults and children: IV therapy for at least 6 weeks (until clearly improved). Follow with oral therapy or IM benzathine penicillin until no active disease
for 6–8 weeks. IV may have to be resumed if oral or IM therapy fails.

2. Pregnancy: IV then oral therapy as above.

LATE DISSEMINATED — Present greater than one year, more severely ill patients, and those with prior significant steroid therapy or any other cause of impaired immunity:

1. Adults and pregnancy: Extended IV therapy (10 or more weeks), then oral or IM, if effective, to same endpoint.
2. Children: IV therapy for 6 or more weeks, then oral or IM follow up as above.

CHRONIC LYME DISEASE

By definition, this category consists of patients with active infection, of a more prolonged duration, and most likely have higher spirochete loads, weaker defense mechanisms, possibly more virulent or resistant strains, and probably are significantly co-infected. Neurotoxins may also be significant in these patients. Search for and treat concurrent illnesses including viruses, Chlamydia, and Mycoplasma. These patients require a full evaluation for all of these problems, and each abnormality must be addressed.

This group will most likely need parenteral therapy, especially high dose, pulsed therapy, and antibiotic combinations, including metronidazole. Antibiotic therapy will need to continue for many months, and the antibiotics may have to be changed periodically to break plateaus in recovery. Be vigilant for treatment-related problems such as antibiotic-associated colitis, yeast overgrowth, intravenous catheter complications, and abnormalities in blood counts and chemistries.

If treatment can be continued long term, then a remarkable degree of recovery is possible. However, attention must be paid to all treatment modalities for such a recovery — not only antibiotics, but rehab programs, nutritional supplements, enforced rest, low carbohydrate, high fiber diets, attention to food sensitivities, avoidance of stress,
abstinence from caffeine and alcohol, and absolutely no immunosuppressants, even local doses of steroids (intra articular injections, for example).

Unfortunately, not all patients with chronic Lyme disease will fully recover and treatment may not eradicate the active Borrelia infection. Such individuals may have to be maintained on open-ended, ongoing antibiotic therapy, for they repeatedly relapse after antibiotics are stopped. Maintenance antibiotic therapy is thus mandatory.

SAFETY

Nearly two decades of experience in treating thousands of patients with Lyme has proven that therapy as described above, although intense, is generally well tolerated. The most common adverse reaction seen is allergy to probenecid. In addition, yeast superinfections are seen, but these are generally easily recognized and managed. The induction of Clostridium difficile toxin production is seen most commonly with ceftriaxone, but can occur with any of the antibiotic regimens mentioned in this document. However, pulsed dose therapy and regular use of the lactobacillus preparations seems to be helpful in controlling yeast and antibiotic related colitis, as the number of cases of C. difficile in Lyme patients is low when these guidelines are followed.

When using central intravenous lines including PICC lines (peripherally inserted central catheters), if ANY line problems arise, it is recommended that the line be pulled for patient safety. Salvage attempts (urokinase, repairing holes) are often ineffective and may not be safe.

Please advise all patients who take the tetracyclines of skin and eye sensitivity to sunlight and the proper precautions, and advise birth control if appropriate. When doxycycline is given parenterally, do not refreeze the solution prior to use!

Remember, years of experience with chronic antibiotic therapy in other conditions, including rheumatic fever, acne, gingivitis, recurrent otitis, recurrent cystitis, COPD,
bronchiectasis, and others have not revealed any consistent dire consequences as a result of such medication use. Indeed, the very real consequences of untreated, chronic persistent infection by B. burgdorferi can be far worse than the potential consequences of this treatment.

CO-INFECTIONS IN LYME

PIROPLASMOsis (Babesiosis)

GENERAL INFORMATION

Piroplasms are not bacteria, they are protozoan. Therefore, they will not be eradicated by any of the currently used Lyme treatment regimens. Therein lies the significance of co-infections — if a Lyme patient has been extensively treated yet is still ill, suspect a coinfection.

Babesia infection is becoming more commonly recognized, especially in patients who already have Lyme Disease. It has been published that as many as 66% of Lyme patients show evidence of co-infection with Babesia. It has also been reported that Babesia infections can range in severity from mild, subclinical infection, to fulminate, potentially life-threatening illness. The more severe presentations are more likely to be seen in immunocompromised and elderly patients. Milder infections are often missed because the symptoms are incorrectly ascribed to Lyme. Babesia infections, even mild ones, may recrudesce and cause severe illness. This phenomenon has been reported to occur at any time, even up to several years after the initial infection. Furthermore, asymptomatic carriers pose risks: to the blood supply as this infection has been reported to be passed on by blood transfusion and to the unborn child from an infected mother as it can be transmitted in utero. Some quotes from the literature:

Krause, PJ. Spielman, A, Telford, SR et.al. Persistent parasitemia after acute Babesiosis
“The clinical spectrum of human Babesiosis ranges from an apparently silent infection to a fulminant malaria-like disease.”
“When left untreated, silent Babesial infection may persist for months to years.”
“Silent infections, which occur in about a third of infected people, may recrudesce.”
“Babesial infection may recrudesce after many months of asymptomatic parasitemia.”
“Although parasites were initially detected microscopically in the blood of two of the untreated subjects, and all of the treated subjects, none could be found a week after the onset of illness.”
“Persistent symptoms of Babesiosis accompanied persistent blood-borne Babesial DNA.”
“The persistence of seroreactivity increasingly correlated with the persistence of Babesial DNA.”
“In those with only subtle symptoms, Babesiosis often remains undiagnosed.”
“Furthermore, physicians tend not to recognize Babesial infection in those who are coinfecte
with the agent of Lyme Disease, because Babesial symptoms tend to be ascribed to Lyme Disease.”
“Physicians caring for patients with moderate to severe Lyme disease should consider
obtaining diagnostic tests for Babesiosis and possibly other tick-borne pathogens... especially in patients experiencing "atypical Lyme disease” or patients in whom the response to antibiotic treatment is delayed or absent.”


“Subjects with evidence of both infections reported a greater array of symptoms than those infected by the spirochete or piroplasm alone.”
“Co-infection generally results in more intense acute illness and a more prolonged convalescence than accompany either infection alone.”
“Spirochete DNA was evident more often and remained in the circulation longer in coinfecte
subjects than in those experiencing either infection alone.”
“Co-infection might also synergize spirochete-induced lesions in human joints, heart and 34 nerves.”
“Babesial infections may impair human host defense mechanisms”
“The possibility of concomitant Babesial infection should be considered when moderate to severe Lyme Disease has been diagnosed.”

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SIDE EFFECTS OF MEDICATION V.S. DIRECT EFFECTS OF THE DISEASE

There has been a disproportionate emphasis on the hazards of extended antibiotic treatment for the persistent Borreliosis. I personally have encountered few, if any serious problems except for Candida overgrowth with GI upsets; gall bladder stones with I.V. Rocephin; (sometimes necessitating surgery), and PICC line inflammation with roughly 6-8 cases out of hundreds being an actual line infection. **Serious life threatening complications have not been my experience in 15 years of treating chronic Borreliosis with co-infections.** I do not question, the sincerity of responsible physicians, who are uncertain about the risks vs. benefits to the patient if longer, more aggressive courses of antibiotics are prescribed. However, almost all of my colleagues in ILADS (more than 125 physicians) who treat Borreliosis on a regular basis, have had positive results, with minimal negative side effects using extended treatment. We believe that the real concern is not the long-term hazardous “side effects” of these medications although they must be administered appropriately, and with responsible monitoring by the physician. In my mind, the serious health problems; are in fact, associated with “early termination of treatment.” The risks of relapse or persistence of symptoms increases when treatment is aborted prematurely. The guidelines ‘triumph’ but the patient’s condition remains unstable, unchanged, or soon to relapse.

I.D.S.A.: Infectious Disease Society of America

According to IDSA (Infectious Disease Society of America), recommendations,
extended treatment, utilizing oral and IV antibiotic therapy, is not considered “medically necessary, except in the most extreme, intractable cases.” The clinical reality of relapsing, persistent Borreliosis is dismissed as the “rare, exceptional, case.” Its occurrence is not considered common or widespread in endemic areas.

Moreover, there are dire warnings, by some of the IDSA “members” as well as others in the medical community that pertain to the issue of ‘over diagnosis/over treatment’. Chronic Borreliosis, they claim is an ‘imagined and unproven condition.’ These same physicians caution, that “potentially” serious consequences could arise, from extended courses of antibiotic therapy. The ‘under diagnosis/under-treatment’ side of the debate, (the side on which I, and other ILADS treating physicians stand) cautions that serious consequences can arise from ignoring the persistent, debilitating symptoms of Borreliosis (with or without co-infection.)

This particular group of entrenched IDSA physicians; would have us believe, that chronic Borreliosis, is mostly a fiction. The majority of practicing physicians naturally are influenced by what they read, and it is understandable, how they could be mislead into forming negative conclusions about the field, the patients, and the physicians who treat them.

The treatment of Borreliosis, advocated in the IDSA unproven guidelines, are simplistic and out of touch with clinical reality. I call these “disinformation” guidelines. Physicians in endemic areas, such as ours, are woefully, misinformed, and in spite of their best efforts, chronic or persistent Borreliosis, (in many patients) goes untreated. Programs that could make a significant difference in a patient’s recovery, are not considered or prescribed, because of the ‘disinformation guidelines.’

The logical question is, why has the field of tick-borne infectious illnesses been so slow to adapt to new information? Why has it clung to its outmoded guidelines? Guidelines, that flies in the face of current knowledge and clinical evidence? Why, because, a select group of medical academics from five or six universities (possibly no more than 20 leading individuals and their associates in all) have long dominated the field. They call themselves impressively, the Infectious Disease Society of America (IDSA). Through research published in respected journals, (NEMJ, Lancet, etc. (peerreviewed)), this small group of academic physicians, claim to be experts, more
informed than most practicing physicians in the field. Many other equally as
knowledgeable, and similarly credentialed, scientists and clinicians, (not only practicing
in the U.S. but also in Europe, where the problem of T.B.D. is equally as serious) remain
largely at a disadvantage. They have not had their research, nor their ideas published as
widely.

Members of the IDSA appear to be absent from most yearly open conferences
(L.D.F.) Instead, they organize and attend exclusive ‘conferences,’ which are not open to
the public or other learned physicians or scientists. They extend invitations, only to the
like minded! As a consequence, there is no ‘open,’ free exchange of ideas. The
unresolved question, of persistent, relapsing Borreliosis with extended treatment remains
an unexplored problem, and more often than not, a problem whose solution has already
been prejudged in favor of restrictive I.D.S.A. guidelines.

Quoting from the IDSA guidelines:
Randomized controlled studies of treatment of patients who remain unwell after standard
courses of antibiotic therapy for Lyme disease are in progress.
To date there are no convincing published data showing that repeated or prolonged
courses of oral or IV anti-microbial therapy are effective for such patients. The
consensus of the IDSA expert-panel members is that there is insufficient evidence to
regard chronic Lyme disease as a separate diagnostic entity.

Late Lyme disease:
The response to treatment of late manifestations (arthritis/ oligoarticular) irritability,
memory deficit, and (somnolence) neuropathy (distal paraesthesias or radicular pain) is
typically slow and improvement or resolution of symptoms may take weeks or months.
However, appropriate antibiotic treatment results in eventual recovery in most patients.

So again, the question, why would a group of respected researchers continue to
hold fast to their obviously rigid position? What have they to gain by influencing the field
of research and the public debate in such a one-sided way. The reason, I believe, is not
too difficult to understand. It has nothing to do with research and science; or the public
good. It has everything to do with medical politics, money for legal consultant fees,
government and pharmaceutical grants, insurance company collusion or hubris.

The same IDSA academic group, in the name of protecting patients in their
guidelines, state that there “is no convincing published data,” to support either the existence or the further treatment of persistent Borreliosis and co-infection once standard (short-term treatment) is completed. (See IDSA statement.)

But exactly what studies are they referring to? What ‘convincing’ published data does not convince them? If they mean studies, in which there are, a double blinded crossover, placebo, controlled pharmaceutical paradigm then they may be technically correct. They are, after all, primarily researchers and not clinicians. So, perhaps this group is not convinced.

In this vein, what ever happened to the individual clinical trial, the individual case history, or treating a patient until there is complete symptom reduction?

Whatever happened to extended maintenance therapy? Isn’t that the usual prescribing practice, routinely in all specialties of medicine (i.e. Cholesterol-lowering drugs, anti-hypertensive drugs, cardiac medications, anti-histamines, oral hypoglycemics for diabetes (type 1), anti-depressants, acne and long term tetracyclines; antipsychotics, aids with anti-virals, anti-tuberculosis antibiotics, etc., etc.) What makes Borreliosis so different?

Why is there such hostile prejudice against the recognition and treatment of this particular illness? Why is it singled out to be excluded from everyday common sense medicine?

Whatever happened to the simple gracious “art of medicine,” and the healing encounter? Since when did we overlook, the fact, that which makes us human, is our unique, genetic, and biological variability? Why have we overlooked the fact, in the T.B.D., that each of us has different, immune responses? Each of us, presents as a biochemically distinct individual, at different life stages and different ages? When did we stop taking into account all these essential factors and restrictively limit ourselves to one-size fits all medicine

ILADS GUIDELINES
WHAT SHOULD BE DONE

Clearly, as they now stand, the clinical and laboratory guidelines for the diagnosis of Lyme disease are out-modeled and can be dangerously misleading.

The old recommended two tier approach potentially misses up to 40% of the patients. For patients who have been infected for more than twelve months, the incidence of false negative results may well be over 50%. ELISA assays have been found in some studies to be as high as 56% false negative (depending on the kit) when compared to clinical diagnosis. One, out of two patients, if this system is employed, are not diagnosed and eliminated from treatment. One must also, be mindful, of the antigenic variability as it relates to different Borrelia species subtypes. These subtypes are not included in standard lab commercial test kits. The acceptable, reportable KDA bands (antibodies) as advised by the CDC, for determination of Borreliosis, are far too restrictive. It does not match up with the symptom and the clinical diagnosis (i.e. 31 KDA a critical band is not reportable).

REVERSE REPORTING FOR A POSITIVE TEST

The first, recommended change, therefore; is to revise the reporting criteria for a positive laboratory test. Unless this occurs, the misleading differences, between “statistical reporting” and “clinical validation” by the Western Blot will persist. Consider a map of Connecticut, being used to understand the state of Texas, or an unwitting traveler, trying to navigate his way around the state, using the wrong map. The interpretation of Western Blot results, and relating them to the clinical picture, is much like the above example. Confusion reigns! Patients are, too often, denied the critical treatment they absolutely need, by ‘seronegative Lyme’ results. Physicians who treat, as well as insurance providers, must be alerted to the fact that the ELISA and Western Blot tests taken individually or together whether, positive or negative, do not necessarily confirm or exclude the diagnosis of Borreliosis. In short the history and “clinical symptoms” confirm the diagnosis, and not the serology.

Other helpful studies, other than antibody assays, have been used to aid in the diagnosis of Lyme disease. Sophisticated neuropsychological evaluation can reveal areas of basic brain function and integration which may be surprisingly abnormal
(Encephalopathy.) Frequently, one finds auditory processing deficits, short term memory deficits, decreased processing speed: concentration and attention deficient issues, and diminished I.Q. (as compared to previous test scores), in cognitively challenged individuals.

**MRI & SPECT SCAN**

The MRI and in particular the SPECT SCAN, are both neuro-radiological diagnostic tools which, can evidence underlying organic brain pathology. Demyelinating plague formation demonstrated, in the MRI, and the vasculitis and hypofusion in the frontal, pre-frontal, parietal lobes, and temporal lobes, visualized on a SPECT scan may help delineate the possible extent of the neuropathology. In some instances, of Lyme encephalopathy, where diseases like M.S. or ALS are considered, a lumbar puncture and examination of C.S.F. can be helpful in difficult cases.

**REVISED CLINICAL DEFINITION**

Secondly, the misleading and absurdly narrow “clinical definition” of Borreliosis must also be drastically revised. It fails to take into account, the wide range of patient complaints. Even though the symptoms are multi-systemic, and can often appear to mimic other conditions, there are numerous common patterns and clusters which, occurs over and over. A seminal paper “When to suspect Lyme Disease” written in 1994 by John D. Bleiweiss, M.D. from Trenton, New Jersey, should be required reading by any physician living and working in an endemic area. Rarely, in my 40 years of medicine, have I read anything so clinically relevant and informative as this seminal paper. Recently, I re-read the article, and found it as timely, and as relevant as it was almost a decade ago. Let me quote just one small section.

**JOHN D. BLEIWEISS – WHEN TO SUSPECT LYME DISEASE**

“Symptoms vary stereotypically during the day. Joint stiffness and “brain fog” are often reported on rising in the a.m. (but not solely in the a.m.) Fatigue can be unrelieved by sleep, or develop between noon and 4pm, whereupon a short nap provides refreshment. “Madman Syndrome” (explosive irritability) may appear toward
the end of a stressful work period or late in the evening. A “mad face” (scowl) can herald imminent detonation.

On cursory inspection, many patients with LD appear deceptively well but in fact feel awful. Don’t be fooled. The mien of a Lyme patient ranges from phlegmatic, sullen, staring off into space, to one of agitated anxiety and hyperkineticism. Their oral and written recitations similarly vary from cryptic to being overinclusive and circumstantial. Stuttering was reported by several patients to coincide with the onset of their LD and often reversible. Patients most frequently report fatigue that varies from mild to debilitating. Usually, there is a loss of interest and initiative so that lounging around becomes habitual. This derives not from laziness, but results from lassitude. There is a tendency to nap, sleep that is not rejuvenating, and hypersomnia at inopportune moments, i.e. in the classroom or during a favorite past times. Paradoxically, at usual bedtimes, patients often experience insomnia or frequent awakenings. Sleep does not always provide respite, as ferocious or vivid nightmares can occur. Cold hands and feet, even in warm environments, occur, and some patients have Raynaud’s phenomenon. Potentially contributing to this vasoconstriction are excessive levels of vasoconstricting hormones, magnesium and potassium deficiency, limbic or hypothalamic dysfunction due to CNS infection, local inflammation of capillary sphincters or hypothyroidism.”

The treatment of this disease is much more than antibiotic alone. Issues of sleep deficit medication for insomnia, pain relief for central and peripheral nervous system, neuropsychiatric difficulties (depression, anxiety), neurocognitive difficulties, endocrine problems, (thyroid, adrenal), arthritis, muscular spasms with trigger points (fibromyalgia), weight problems, yeast over growth, dietary restrictions, nutritional supplementation for immune-support (a whole complex field in itself and vital to healing), physical therapy prescription, family support are some of the therapeutic interventions that must be considered while treating a T.B.D. patient.

**INSURANCE REIMBURSEMENT**

Insurance companies must be responsible to their beneficiaries for coverage of
long term care. Restrictions, on the amount, type, and the duration of antibiotics or any other important medication for the T.B.D. syndrome, must not be controlled by the insurance company or a distant medical consultant. Extended treatment, must follow the course of clinical improvement and decisions about care, must be at the discretion of the doctor responsible for the case. Extra paper work, lengthy interrogatories, withholding of payment, and general all around “stonewalling” has to be eliminated. Some insurance companies are more sympathetic than others and seem to understand the illness. They appear willing to support the patient and their care.

CHILDREN – A UNIQUE PROBLEM

Children present a unique problem. The public school system must be made to understand and accommodate to the chronically ill child. School children need a supportive and compassionate environment. A severely, compromised, “Borreliachallenged” child makes a “poor student.” They are exhausted, volatile, memory impaired, attention deficit, angry, depressed sometimes even suicidal. They are full of somatic complaints: headaches, GI symptoms, constant muscle pain, arthritis, blurred vision, etc.

SCHOOLS AND STATE INFORMATION

The state of Connecticut must issue a directive to all public school superintendents. They must be informed and kept up-to-date as to how Borreliosis can affect their student population, particularly, children at risk in endemic areas. At least once a year, a special PTA (parent teacher association) meeting must be organized at all school levels. These meetings ought to be led by knowledgeable physicians (or their informed staff) who treat the complications of the disease in their practices. Special funding for home tutors, extra classes and neuropsychological testing should be budgeted for these children.

Pediatricians, neurologists, psychiatrists, infectious disease specialists and family practitioners, are among those physicians, who especially need more up to date and clinically relevant information.

Physicians should be alerted to the new state legislation extending treatment
protocols and expanding “Standard of Care” options (ILADS GUIDELINES) need to be considered as a legitimate source for informed decision working by the patient.

Finally, more stringent legislation by the state assemblies needs to be enacted to endure that the patients and their treating physician, are not harassed by insurance companies, practice lawyers, and state medical boards for aggressively treating chronic, persistent, relapsing Borreliosis and co-infection. (Rhode Island)
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