Neuro-psychiatric and Cognitive Impacts of Tickborne Disease

ILADS, Drexel University College of Medicine, and PA Lyme
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Disclosure Statement:

I do not have any financial arrangements or affiliations with any commercial entities whose products, research, or services may be discussed in these materials.
Outline

• Basic Questions
• Past and Present
• Pathophysiology: Inflammation, autoimmunity, sleep disturbances, biochemistry
• Clinical Presentations:
  – Multiple Psychiatric Symptoms
  – Intrusive Symptoms
  – Addiction
  – Dementia
  – Suicide and Violence
• Treatment
• Future Directions
• Conclusion
Basic Questions

• Does Lyme borreliosis cause mental illnesses?
• Why do some show no or minimal symptoms?
• Why is there such a variability in the clinical presentation?
• Can there be remissions and exacerbations?
• Are chronic Lyme and post treatment Lyme disease syndrome valid concepts?
Past

• When mental hospitals were filled with syphilis patients everyone recognized infections caused mental illness.
• After penicillin few physicians had capability in both infectious disease and psychiatry.
• Psychodynamic and neurochemical explanations became more dominant and widely accepted.
• But what caused neurochemical pathology?
Present

• Advances in evolutionary medicine, the microbiome, psychoimmunology, brain imaging and microarray testing expands our knowledge of the pathophysiology of mental illness.

• But limited multidisciplinary cooperation slows progress appreciating the association between microbes and mental illness.*

*Bransfield RC. Building Bridges Between Infectious Disease Physicians and Psychiatrists. Contagion Live. 2017 Nov 30
Variable Presentation

• Lyme borreliosis doesn’t benefit anyone. It may have no effect, be latent or cause a broad spectrum of multisystem symptoms.
• Most neuropsychiatric symptoms appear later in disease progression.
• Although there are general patterns, each patient has a unique presentation.
Disease Models

Most current disease models

- Acute infection
- Acute toxic exposure
- Genetic defect
- Trauma
- Cancer
- Degenerative disease

Fairly well understood pathophysiology

Well-defined diagnostic signs and symptoms

Model for complex disease with multiple variables

- Complex and multiple contributors: genetic and environmental (e.g., infections, toxins and deficiencies)

- Complex and multiple pathophysiological processes

- Complex and multiple clinical presentation with multiple signs and symptoms

• Predisposing & precipitating factors
• Infections
• immune & other reactions
• Pathophysiological processes
• Dysfunction
• Symptoms & Syndromes
• Ineffective Treatment
• Disease Progression
Multi-Systemic Disease Model

Disease Progression

Disease Recovery

Individual
Quantum Physics
Organic Molecule
Solar System
Inorganic Molecule
Galaxy
Universe
Subatomic Particle

Nervous System
Brain
Neural Network
Humanity
Family
Group

Nerve Cells
Genetic Code
Biosphere
Earth
Ecosystem

Inorganic Molecule
Atom

Subatomic Particle

Quantum Physics

Disease Progression

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Atom

Subatomic Particle

Quantum Physics
Categories of Disease Causation

- genetic (inherited alleles)
- parasitic
- noninfectious environmental (diet, lifestyle, chemicals, radiation)
Infectious Determinants of Mental Illness

• Clinicians and policymakers must recognize that many chronic diseases may indeed have infectious origins.[CDC]*
• NIH Human Microbiome Project recognizes bacterial cells outnumber human cells by 10 to 1. Humans depend on their microbiome and a person should really be considered a superorganism.
• Thousands of articles show a causal association between infections and mental illness (especially viral, venereal, vector-borne) and 400 articles support the causal association between tick-borne disease and mental illness.

*O’Connor SM. et al (CDC). Emerging Infectious Determinants of Chronic Diseases. Emerging Infectious Diseases. 2006;12(7):1051-7
Go round up the usual suspects...
Some microbes associated with mental symptoms & mental illness I

- **Spirochetes:**
  - *Borrelia afzelii* (Lyme disease in UK, Europe)
  - *Borrelia burgdorferi sensu stricto* (Lyme disease in USA, UK, Europe)
  - *Borrelia garinii* (Lyme disease in UK, Europe)
  - *Borrelia miyamotoi*
  - *Borrelia hermsii* (Relapsing Fever)
  - *Borrelia turicatae* (Relapsing Fever)
  - *Leptospira* (Leptospirosis)
  - *Treponema pallidum pallidum* (Syphilis)

- **Bacteria:**
  - *Anaplasmas phagocytophilum* (Human Granulocytic Ehrlichiosis)
  - *Bartonella henselae* (Cat scratch fever)
  - *Bartonella quintana* (Trench fever)
  - *Bartonella rochalimae* (Bartonellosis)
  - *Brucella* (Brucellosis)
  - *Chlamydophilia pneumoniae* (Chlamydia)
  - *Chlamydophila psittaci* (Chlamydia)
  - *Coxiella burnetti* (Q-Fever and "Post-Q Fever Fatigue Syndrome")
  - *Ehrlichia chaffeensis* (Human Monocytic Ehrlichiosis)
  - *Francisella tularensis* (Rabbit Fever or Tularemia)
  - *Haemophilus influenzae* (Haemophilus)
  - *Helicobacter pylori*
  - *Listeria*
  - *Meningococcus* (Meningococcal Meningitis)
  - *Mycoplasma fermentans*
  - *Mycoplasma pneumoniae*
  - *Mycobacterium tuberculosis* (Tuberculosis)
  - *Rickettsia akari* (Rickettsialpox)
  - *Rickettsia rickettsii* (Rocky Mountain Spotted Fever)
  - *Rickettsia species* (Eastern tick-borne Rickettsiosis)
  - *Shigella* (Shigellosis)
  - *Streptococcus pneumoniae* or *Pneumococcus* (Pneumonia)
  - *Streptococcus* (PANDAS, Sydenham’s Chorea, St Vitus Dance)
Some microbes associated with mental symptoms & mental illness II

- **Viruses:**
  - Borna virus
  - Chikungunya virus
  - Coltivirus (Colorado Tick Fever)
  - Coronaviruses
  - Coxsackie virus
  - Cytomegalovirus
  - Enterovirus
  - Flaviviridae virus (Japanese B encephalitis & Tick-borne encephalitis virus)
  - Hepatitis C virus
  - Herpes virus family
  - Human endogenous retroviruses
  - Human herpesvirus 4 or Epstein-Barr virus
  - Human immunodeficiency virus
  - Human T-Cell Lymphotropic Virus Type 1 Influenza A virus subtype H3N2 (Hong Kong Flu)
  - Influenza virus
  - Pandemic Influenza of 1918
  - Papopavirus
  - Paramyxovirus (Measles virus)
  - Parvo B19
  - Poliovirus
  - Rabies virus
  - Rubella
  - Toga virus

- **Protozoa:**
  - Plasmodium (Malaria)
  - Babesia microti (Babesiosis)
  - Babesia duncani (Babesiosis)
  - Other Babesia species (Babesiosis)
  - Leishmania (Leishmaniasis)
  - Toxoplasma gondii (Toxoplasmosis)

- **Parasites:**
  - Blastocystis (Blastocystosis)
  - Strongyloides stercoralis (Strongyloidiasis)
  - Taenia solium (Neurocysticercosis or Cysticercosis)

- **Fungal:**
  - Cryptococcus
  - Coccidiomycosis
  - Histomycosis
  - Yeast:
    - Candida albicans (Candidiasis)
    - Candida dubliniensis
  - Prion
  - Variant Creutzfeldt-Jakob
Is Trauma from Infection from Infection or from the Host’s Immune Reaction?

**Parasite**
- Cell penetration
- Toxin release
- Incorporation of parasite genes into host genome

**Host**
- Cytokine release
- Antibodies
- Inflammation
- Other cellular response
Neuroinflammation

- The inflammatory response is an early, non-specific immune reaction to tissue damage or pathogen invasion. Inflammation of the central nervous system (CNS) is characterized by increased glial activation, pro-inflammatory cytokine concentration, blood-brain-barrier permeability, and leukocyte invasion.
Different immune reactions directly influence neuronal proliferation, differentiation, migration, and apoptosis. Microglia become activated after stress, trauma, or infection. They react with tissue repair or induction of immune responses: phagocytosis, secretion of cytokines, neuronal growth factors, and antigen presentation. Microglial activation may sustain chronic brain inflammation.\textsuperscript{2} NK, natural killer.
Are Mood and Anxiety Disorders Inflammatory Diseases?

• Studies demonstrate increases in inflammatory markers in:
  – Sleep deprivation: IL-6 [1]
  – Stress: IL-1 beta, TNF-alpha, IL-6 [2]
  – PTSD: IL-1 beta, IL-6, TNF-alpha [3]
  – Depression: IL-6, CRP, IL-1, TNF-alpha [3]
  – Bipolar: IL-6, TNF-alpha, CRP, sIL-2R, sIL-6R [3]
  – Schizophrenia: IL-6, IL-1 beta [4]
  – Autism: IL-6, autoimmune mechanisms [5]
  – Alzheimer’s: IL-6, TNF-, IL-1, TGF-, IL-12 and IL-18 [6]

Tick-borne Pathogens

- Borreliosis: *Borrelia burgdorferi* (multiple species and strains) also *B. americana, B. andersonii, B. bissettii, B. carolinensis, B. afzelii, B. garinii, B. spielmanii, B. lonestari, B. bissetti, B. kurtenbachii, B. chilensis, B. lusitaniae, B. valaisiana, B. sinica, B. bavariensis, B. finlandensis, B. japonica, B. miyamoti, B. Yangtze, B. tanukii, B. turdi
- Babesiosis: *Babesia microti, Babesia duncani, etc.*
- Other Piroplasm Diseases: Theileria and Cytauxzoon
- Ehrlichiosis: *Ehrlichia chaffeensis, Anaplasma phagocytophilum, and Ehrlichia ewingii.*
- Human Monocytic Ehrlichiosis: *Ehrlichia chaffeensis*
- Rocky Mountain Spotted Fever: *Rickettsia rickettsii*
- Tick-borne Relapsing Fever: *Borrelia turicatae, B. hermsi*
- Tularemia: *Francisella tularensis*
- Q Fever: *coxiella burnetii*
- Tick Paralysis (Tick Toxicosis): Unknown
- Powassan/Deer Tick Virus Encephalitis: Powassan and deer tick viruses
- Colorado Tick Fever: Colorado tick fever virus
- Southern Tick-Associated Rash Illness (STARI) or Master’s Disease
- Bartonellosis: *Bartonella species*
- Mycoplasmosis: *Mycoplasma species*
- Tick-borne Encephalitis: *Flavivirus*
- Maculatum Disease: *Rickettsia parkeri*
- Relapsing Fever: *Borrelia hermsii*
- *Rickettsia philipii*
- Bourbon virus
- Toxoplasma gondii
- Who knows what else?

Bransfield, Burrascano
Most, but Not All Tick-Borne Disease Symptoms Are Immune Mediated

Tick-Borne Infections → Immune Effects Th1 (Innate) & Th2 (Acquired) → Pathophysiology Causing Symptoms

Bransfield RC.
Tick-Borne Coinfections

• In addition other known and unknown tick-borne diseases such as *Babesia*,[1] *Bartonella*,[2] *Ehrlichia*,[3,4] *Mycoplasma*,[5] etc. have immune and metabolic effects that further add to the complexity of the pathophysiology of tick-borne infections.

Complex Interactive Infections:
An Interaction of Multiple Species
Immunosuppression and Co-pathogens

• Luc Montagnier, the Nobel laureate, says he has never seen AIDS without secondary (apparently causative) pathogens. And neither has he seen Lyme without pathogens other than *Borrelia*. The secondary causative pathogens reside in the tissue Microbiome, where 99.9% of species cannot be detected with PCR or culture.

• Because the suppression of some innate pathways in these diseases is so complete, the co-infections can be viewed a result of the disease process, rather than the cause.
Three Basic Types of *Borrelia burgdorferi* Infections

- Three basic types of *Borrelia burgdorferi* infections cause neuropsychiatric symptoms:
  - The **meningovascular form** associated with cerebrovascular infarcts.[1,2]
  - The **atrophic form** of Lyme meningoencephalitis, associated with cortical atrophy, gliosis and dementia.[1]
  - Infections outside the CNS causing effects within the CNS associated with neuropsychiatric symptoms. [3]

Figure 2: SERIAL IMAGES OF ONE NEURON WITH INTRACELLULAR SPIROCHETE
A Sequence of Brain Symptoms

• Early symptoms are mediated by proinflammatory cytokines and include brain fog and fatigue.

• Some symptoms are mediated by autoimmune processes and may include obsessiveness, tics, irritability and other symptoms.

• Some symptoms are associated with altered tryptophan catabolism, decreased serotonin, increased quinolinic acid, such as depression.

• Late stage symptoms are associated with brain inflammation and neurodegenerative changes.
Progressive Infection & Inflammation is Associated with Increasing Encephalopathy & Increasing Mental Symptoms

<table>
<thead>
<tr>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
</tr>
</thead>
<tbody>
<tr>
<td>Executive dysfunction</td>
<td>Increasing cognitive deficits</td>
<td>Dementia</td>
</tr>
<tr>
<td>Reduced frustration tolerance, irritability, dysthymia</td>
<td>Anxiety disorders, major depression, impulsivity, personality disorders</td>
<td>Major psychiatric disorders, psychosis, suicide, homicide</td>
</tr>
<tr>
<td>Insomnia, decreased appetite &amp; libido</td>
<td>Moderately impaired sleep, eating &amp; sexual functioning</td>
<td>Severely impaired sleep, eating &amp; sexual functioning</td>
</tr>
</tbody>
</table>

Increasing Neurological, Multisystem Symptoms & Fatigue
6 TBD Psychoimmunology Articles

The Psychoimmunology of Lyme/Tick-borne Diseases and its Association with Neuropsychiatric Symptoms I

- Immune mediated effects are a significant contributor to the pathophysiological processes and disease progression. These immune effects include persistent inflammation with cytokine effects and molecular mimicry and both of these mechanisms may be present at the same time in persistent infections. Pathophysiological changes have been associated with oxidative stress, excitotoxicity, changes in homocysteine metabolism, mitochondrial dysfunction and altered tryptophan catabolism.

The Psychoimmunology of Lyme/Tick-borne Diseases and its Association with Neuropsychiatric Symptoms II

- Lyme disease has been associated with the proinflammatory cytokines IL-6, IL-8, IL-12, IL-18 and interferon-gamma, the chemokines CXCL12 and CXCL13 and increased levels proinflammatory lipoproteins. Borrelia burgdorferi surface glycolipids and flagella antibodies appear to elicit anti-neuronal antibodies and anti-neuronal antibodies and Borrelia burgdorferi lipoproteins can disseminate from the periphery to inflame the brain.

No Adaptive Immunity with Some Infections

- Acute infections are usually associated with an early inflammatory reaction followed by adaptive immunity and a resolution of symptoms, but in some chronic infections that evade and suppress the immune system this progression does not always occur. Instead, inflammation can persist without adaptive immunity, autoimmune symptoms may occur, and reinfections are common.
Bb Induces IL-10 Mediated Immunosupression

- Bb enhances IL-10 production by macrophages and dendritic cells which impedes bacterial clearance, diminishes Bb uptake and trafficking by macrophages, suppresses ROS production, decreases production of proinflammatory mediators and co-stimulatory molecules, and suppress phagocytosis-associated events that are important for mediating both innate and adaptive immune responses.

The immune system cannot generate immunological memory during infection with *B. burgdorferi*

- “Our data demonstrate that *Bb* infection suppresses the development of long-lived antibody production and immunological memory formation and indicates that *Bb* may achieve this by suppressing the function and/or causing the rapid and global collapse of germinal centers.”

- “Antibodies disappear rapidly when infection is controlled by antibiotic treatment.”

Survival strategies of *Borrelia burgdorferi*, the etiologic agent of Lyme disease.
TBD Pathophysiology is a Failure to Shift from Inflammation to Adaptive Immunity

• Persisting immune activation causes the cytokine storm in chronic TBD. In these patients, the innate immune system is not turned off by a series of specific immune peptides. Specific genetic types are more prone to this phenomenon. Since reinfections are common, adaptive immunity may not occur. [1,2,3]

• Aberrant immune reactions are most likely the result of persistent infection causing persisting immune provocation.[4]

[1] Newell K.
Self Perpetuating Post Infection Immune Process?

• Some do not believe in chronic persistent infections and speculate that persistent and progressive symptoms following an infection are associated with a continuing self-perpetuating immune process post-infection.

• Does any evidence support this view?
Disease Precipitation vs. Disease Perpetuation & Disease Progression

• What precipitates a disease process may not be exactly the same as what causes the perpetuation and progression of the disease.

• Chronic stress and non-restorative sleep contribute to disease perpetuation & progression & are associated with:
  – Decreased regenerative functioning
  – Compromised immunity
  – Decreased resistance to infectious disease
  – Fatigue
Bidirectional Communication between the Brain and the Immune System: Implications for Physiological Sleep and Disorders with Disrupted Sleep

• Cytokines produced by cells of the immune and nervous systems regulate sleep.
• particularly interleukin-1beta and tumor necrosis factor-alpha, signal neuroendocrine, autonomic, limbic and cortical areas of the CNS to affect neural activity and modify behaviors (including sleep), hormone release and autonomic function.
• Sleep disorders are commonly associated with chronic inflammatory diseases and chronic age- or stress-related disorders. The best studied are rheumatoid arthritis, fibromyalgia and chronic fatigue syndromes.

Sleep Drives Metabolite Clearance from the Adult Brain

- Sleep is associated with a 60% increase in the interstitial space, resulting in a striking increase in convective exchange of cerebrospinal fluid with interstitial fluid which increases clearance of β-amyloid. The restorative function of sleep may be a consequence of the enhanced removal of potentially neurotoxic waste products that accumulate in the awake central nervous system.

Lyme Disease & Sleep Disorders

• Chronic sleep disturbances occur in 100% of Lyme disease patients. (1)

• Sleep restriction increases IL-6 and pain-related symptoms in healthy volunteers. (2)

• Impaired Sleep Correlates with Impaired Immune Functioning. (3)

• Growth hormone is dependent upon delta sleep & modulates immune response. (4)

• Increasing delta sleep is therapeutic.

(1) Greenberg HE; Ney G; Scharf SM; Ravdin L; Hilton E. Sleep, 18(10):912-6 1995
(2) M. Haack, E et al. J Pain; April 2004, Supplement 1 • Volume 5 • Number 3
Circadian Rhythms

Healthy

Alertness

Deep Sleep

Chronic Stress

Alertness

Deep Sleep

AM

AM
Variability in Sleep Patterns in a Normal Adult vs a Patient With Major Depression


Please see important safety information on accompanying slides and full prescribing information.
Disease Progression

Non-Restorative Sleep

Fatigue
Cognitive Impairments
Emotional Impairments
Pain Sensitivity
Immune Dysfunction
IDO and interferon--induced depressive symptoms: a shift in hypothesis from tryptophan depletion to neurotoxicity

• The enzyme indoleamine 2,3-dioxygenase (IDO), which converts tryptophan (TRP) into kynurenine (KYN) and which is stimulated by proinflammatory cytokines, may be implicated in the development of IFN--induced depressive symptoms, first by decreasing the TRP availability to the brain and second by the induction of the KYN pathway resulting in the production of neurotoxic metabolites.

• This study does support a role for IDO activity in the pathophysiology of IFN--induced depressive symptoms, through its induction of neurotoxic KYN metabolites.
IDO shifts tryptophan metabolism from serotonin to quinolinic acid.
**Bb and Quinolinic Acid**

- CSF quinolinic acid is significantly elevated in *Bb* infection--dramatically in patients with CNS inflammation, less in encephalopathy and correlates with the severity of CNS symptoms, including depression.

- The presence of this known agonist of NMDA synaptic function--a receptor involved in learning, memory, and synaptic plasticity--may contribute to the neurologic and cognitive deficits seen in many Lyme disease patients.


Bransfield *Psychiatric Annals*. 42(9):337-341. September 2012
Clinical Presentations
Lyme Disease: a Neuropsychiatric Illness

• Up to 40% of patients with Lyme disease develop neurologic involvement of either the peripheral or central nervous system. Like syphilis, Lyme disease may have a latency period of months to years before symptoms of late infection emerge. A broad range of psychiatric reactions have been associated with Lyme disease including paranoia, dementia, schizophrenia, bipolar disorder, panic attacks, major depression, anorexia nervosa, and obsessive-compulsive disorder.

Neuropsychiatric Symptoms

- The neuropsychiatric manifestations of Lyme Borreliosis may progress over time and may include:
  - Cognitive: hyperacusis, dyslexia-like symptoms, slow processing, executive functioning impairments and other symptoms.
  - Emotional: low frustration tolerance, anhedonia, anxiety disorders, panic attacks, depression, suicidality and other symptoms.
  - Vegetative: impairments of sleep, appetite, sexual functioning and temperature.
  - Behavioral: anger, declining productivity, social withdrawal, substance use and other symptoms.
Tick Borne Disease & Mental Symptoms

• Encephalopathy 89%, Memory Loss 81%, Fatigue 74%, Depression 37%, Extreme irritability, 26% [Logigian EL et al. 1990]
• Attention/Concentration, 77%, Memory Complaints 65%, Mental Fatigue 70%, Depression 37%, Anger/Irritability 53%, Rages/Explosive Behavior 25%, Anxiety/Panic Attacks 54% [Shea 2013]
• Cognitive impairment 92%, fatigue 94%, sleep impairment 92%, depression 64%, [Johnson L, Wilcox S, Mankoff J, Stricker RB. 2014]
• Memory loss 63%, Poor concentration 60%, Difficulty finding words 46%, Confusion 44%, Inattention 44%, Fatigue 88%, Sleep disturbances 66%, Mood swings 47%, Irritability 47%. [Lobraico J et al. 2014]
• Impairments of reasoning (93%), memory (92%) and attention (91%), with speaking (75%), listening (73%), reading and/or writing (79%) [Molrine CJ 2015]
• Memory impairments (76%), processing impairments (78%), depression (76%), panic attacks (50%), mood swings (66%) explosive anger (52%) [Bransfield 2018]
Association of Lyme Disease and Schizoaffective Disorder, Bipolar Type: Is it Inflammation Mediated?

• Borrelia burgdorferi (Bb) can present with symptoms similar to schizophrenia and bipolar disorder. It has been suggested that inflammation incurred during the Bb infection leads to neurodegenerative changes that result in schizophrenia-like presentations. We report a case of a 41-year-old male with a past history of Bb infection who presents with psychosis. Later in the course of his hospitalization, he developed mood symptoms and was diagnosed with schizoaffective disorder, bipolar type. This case highlights the diagnosis and treatment of a patient with the unique presentation of schizoaffective disorder, bipolar type in the setting of previous Bb infection.

Geographical correlation of schizophrenia to *Ixodes* ticks and Lyme disease in the USA

- The epidemiological correlation between *Ixodes* ticks and schizophrenia originally published by Brown has been adjusted according to the more recent epidemiological data on the risk of Lyme disease including zooprophylaxis.
Intrusive Symptoms

• “Frightening, stabbing, horrific images - usually of death, dying or pain and suffering. Often gory and unreal as in a horror story. Faces mostly with blood or terror exaggerated awful expressions. Visions of stabbing or killing often of those close to you or familiar. Episodic, not continuous. Fleeting faces most usually of the worse possible situation Helpless stumped bodies perhaps close to death. These images don’t seem to necessarily be associated with a particular occasion, place or time, but come and invade the privacy of my mind.”
Lyme/TBD & Intrusive Symptoms

• 131 cases with a history of *Borrelia, Babesia, Bartonella, Anaplasma, Ehrlichia* and other pathogens demonstrates 45 (34%) acquired intrusive symptoms (89% aggressive, 18% sexual and altered sexual imagery, 40% other--bizarre, horrific, etc.). Within these 45 cases other symptoms included cognitive 100%, neurological 98%, musculoskeletal 89%, obsessiveness 89%, depersonalization 87%, depression 80%, low frustration tolerance 80%, fatigue 76%, explosive anger 73%, suicidal 69%, social isolation 67%, anhedonia 62%, disinhibition 62%, paranoia 49%, hallucinations 42%, homicidal 31%, OCD 29%, PTSD 13%.*


*Bransfield R. Neurology Psychiatry & Brain Research. Vol 22(2016).*
Some Lyme disease patients self-medicate psychiatric symptoms and pain, become dependent and engage in drug-seeking behavior with benzodiazepines, hypnotics, alcohol, pain medication and marijuana.

Better outcomes and reduced overdoses are associated with early diagnosis, effective treatment and awareness of potential substance abuse that can exacerbate symptoms.
Dementia

• Because CNS \textit{B. burgdorferi} infections are associated with CNS inflammation and systemic TBD are also associated with low-grade inflammatory processes, it supports clinical observations that rapidly progressive dementia can be associated with CNS infection and that slowly progressive dementia can be associated with systemic infection.

Rapidly progressive frontal-type dementia associated with Lyme disease

• The authors report a case of fatal neuropsychiatric Lyme disease (LD) that was expressed clinically by progressive frontal lobe dementia and pathologically by severe subcortical degeneration. Antibiotic treatment resulted in transient improvement, but the patient relapsed after the antibiotics were discontinued. LD must be considered even in cases with purely psychiatric presentation, and prolonged antibiotic therapy may be necessary.

Violence
Suicide and Lyme and Associated Diseases

• Suicidality seen in LAD contributes to causing a significant number of previously unexplained suicides and is associated with immune-mediated and metabolic changes resulting in psychiatric and other symptoms which are possibly intensified by negative attitudes about LAD from others. Some LAD suicides are associated with being overwhelmed by multiple debilitating symptoms, and others are impulsive, bizarre, and unpredictable.

• Negative attitudes about LAD from family, friends, doctors, and the health care system may also contribute to suicide risk. By indirect calculations, it is estimated there are possibly over 1,200 LAD suicides in the US per year.

The Death Formula

Lyme & associated diseases infection →
Persistent proinflammatory cytokines →
Dysregulation of tryptophan metabolism →
Quinolinic acid → NMDA receptor agonism →
Glutamate dysregulation →
Neural circuit dysfunction →
Psychiatric dysfunction →
Suicidal, sometimes also homicidal
Contributors vs. Deterrents of Violence

Violence Contributors
- Individual
- Nervous System
- Family
- Group
- Humanity
- Ecosystem
- Biosphere
- Earth
- Solar System
- Galaxy
- Universe
- Quantum Physics
- Organic Molecule
- Inorganic Molecule
- Subatomic Particle
- Atom

Violence Deterrents
- Individual
- Nervous System
- Family
- Group
- Humanity
- Ecosystem
- Biosphere
- Earth
- Solar System
- Galaxy
- Universe
- Quantum Physics
- Organic Molecule
- Inorganic Molecule
- Subatomic Particle
- Atom
Violence

Contributors

Failed Deterrents

Acute Triggers
<table>
<thead>
<tr>
<th>Findings</th>
<th>Homicidal group</th>
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<th>Non-homicidal group</th>
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<tbody>
<tr>
<td></td>
<td>Pre-infection (95% CI)</td>
<td>Post-infection (95% CI)</td>
<td>Pre-infection (95% CI)</td>
<td>Post-infection (95% CI)</td>
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<tr>
<td><strong>Psychiatric symptoms</strong></td>
<td></td>
<td></td>
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<tr>
<td>Suicidal</td>
<td>2% (0% - 6%)</td>
<td>98% (94% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>46% (32% - 60%)</td>
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<tr>
<td>Sudden abrupt mood swings</td>
<td>4% (0% - 9%)</td>
<td>94% (87% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>66% (53% - 79%)</td>
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<tr>
<td>Explosive anger</td>
<td>4% (0% - 9%)</td>
<td>91% (83% - 99%)</td>
<td>0% (0% - 0%)</td>
<td>52% (38% - 66%)</td>
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<td>Paranoia</td>
<td>0% (0% - 0%)</td>
<td>88% (79% - 97%)</td>
<td>0% (0% - 0%)</td>
<td>36% (23% - 49%)</td>
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<tr>
<td>Ahedonia</td>
<td>2% (0% - 6%)</td>
<td>86% (76% - 96%)</td>
<td>0% (0% - 0%)</td>
<td>56% (42% - 70%)</td>
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<tr>
<td>Hypervigilance</td>
<td>2% (0% - 6%)</td>
<td>84% (74% - 94%)</td>
<td>0% (0% - 0%)</td>
<td>54% (40% - 68%)</td>
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<td>Exaggerated startle</td>
<td>2% (0% - 6%)</td>
<td>84% (74% - 94%)</td>
<td>0% (0% - 0%)</td>
<td>66% (53% - 79%)</td>
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<td>Disinhibition</td>
<td>2% (0% - 6%)</td>
<td>84% (74% - 94%)</td>
<td>0% (0% - 0%)</td>
<td>32% (19% - 45%)</td>
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<td>Nightmares</td>
<td>2% (0% - 6%)</td>
<td>82% (71% - 93%)</td>
<td>0% (0% - 0%)</td>
<td>58% (44% - 72%)</td>
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<td>Depersonalization</td>
<td>0% (0% - 0%)</td>
<td>71% (58% - 84%)</td>
<td>0% (0% - 0%)</td>
<td>52% (38% - 66%)</td>
</tr>
<tr>
<td>Intrusive images aggressive</td>
<td>4% (0% - 9%)</td>
<td>62% (49% - 75%)</td>
<td>0% (0% - 0%)</td>
<td>16% (6% - 26%)</td>
</tr>
<tr>
<td>Hallucinations</td>
<td>2% (0% - 6%)</td>
<td>47% (33% - 61%)</td>
<td>0% (0% - 0%)</td>
<td>42% (28% - 56%)</td>
</tr>
<tr>
<td>Dissociative episodes</td>
<td>0% (0% - 0%)</td>
<td>38% (25% - 51%)</td>
<td>0% (0% - 0%)</td>
<td>12% (3% - 21%)</td>
</tr>
<tr>
<td>Derealization</td>
<td>0% (0% - 0%)</td>
<td>37% (24% - 50%)</td>
<td>0% (0% - 0%)</td>
<td>24% (12% - 36%)</td>
</tr>
<tr>
<td>Intrusive images sexual</td>
<td>2% (0% - 6%)</td>
<td>26% (14% - 38%)</td>
<td>0% (0% - 0%)</td>
<td>6% (0% - 13%)</td>
</tr>
<tr>
<td><strong>Behavioral symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marital/family problems</td>
<td>0% (0% - 0%)</td>
<td>80% (69% - 91%)</td>
<td>0% (0% - 0%)</td>
<td>48% (34% - 62%)</td>
</tr>
<tr>
<td>Legal problems</td>
<td>0% (0% - 0%)</td>
<td>42% (28% - 56%)</td>
<td>0% (0% - 0%)</td>
<td>4% (0% - 9%)</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>6% (0% - 13%)</td>
<td>33% (20% - 46%)</td>
<td>0% (0% - 0%)</td>
<td>10% (2% - 18%)</td>
</tr>
<tr>
<td><strong>Psychiatric syndromes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depression</td>
<td>6% (0% - 13%)</td>
<td>98% (94% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>76% (64% - 88%)</td>
</tr>
<tr>
<td>Panic disorder</td>
<td>2% (0% - 6%)</td>
<td>82% (71% - 93%)</td>
<td>2% (0% - 5.9%)</td>
<td>50% (36% - 64%)</td>
</tr>
<tr>
<td>Social anxiety disorder</td>
<td>4% (0% - 9%)</td>
<td>66% (53% - 79%)</td>
<td>4% (0% - 9.4%)</td>
<td>70% (57% - 83%)</td>
</tr>
<tr>
<td>OCD</td>
<td>2% (0% - 6%)</td>
<td>51% (37% - 65%)</td>
<td>2% (0% - 5.9%)</td>
<td>32% (19% - 45%)</td>
</tr>
<tr>
<td>PTSD</td>
<td>6% (0% - 13%)</td>
<td>36% (23% - 49%)</td>
<td>2% (0% - 5.9%)</td>
<td>24% (12% - 36%)</td>
</tr>
<tr>
<td>Rapid bipolar</td>
<td>0% (0% - 0%)</td>
<td>28% (10% - 40%)</td>
<td>0% (0% - 0%)</td>
<td>10% (2% - 18%)</td>
</tr>
<tr>
<td><strong>Cognitive symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Memory impairments</td>
<td>0% (0% - 0%)</td>
<td>98% (94% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>76% (64% - 88%)</td>
</tr>
<tr>
<td>Processing impairments</td>
<td>0% (0% - 0%)</td>
<td>94% (87% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>78% (67% - 89%)</td>
</tr>
<tr>
<td>Dyslexia symptoms</td>
<td>4% (0% - 9%)</td>
<td>78% (67% - 89%)</td>
<td>0% (0% - 0%)</td>
<td>68% (55% - 81%)</td>
</tr>
<tr>
<td><strong>Neurological symptoms</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neuropathy</td>
<td>0% (0% - 0%)</td>
<td>92% (84% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>70% (57% - 83%)</td>
</tr>
<tr>
<td>Cranial nerve symptoms</td>
<td>0% (0% - 0%)</td>
<td>92% (84% - 100%)</td>
<td>0% (0% - 0%)</td>
<td>66% (53% - 79%)</td>
</tr>
<tr>
<td>Seizures</td>
<td>0% (0% - 0%)</td>
<td>20% (9% - 31%)</td>
<td>0% (0% - 0%)</td>
<td>24% (12% - 36%)</td>
</tr>
<tr>
<td><strong>Urogenital</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Decreased libido</td>
<td>0% (0% - 0%)</td>
<td>80% (69% - 91%)</td>
<td>4% (0% - 9.4%)</td>
<td>44% (30% - 58%)</td>
</tr>
<tr>
<td>Irritable bladder</td>
<td>4% (0% - 9%)</td>
<td>56% (42% - 70%)</td>
<td>2% (0% - 5.9%)</td>
<td>44% (30% - 58%)</td>
</tr>
<tr>
<td>Intolerance to alcohol</td>
<td>0% (0% - 0%)</td>
<td>44% (30% - 58%)</td>
<td>0% (0% - 0%)</td>
<td>24% (12% - 36%)</td>
</tr>
<tr>
<td>Incontinence</td>
<td>2% (0% - 6%)</td>
<td>38% (25% - 51%)</td>
<td>2% (0% - 5.9%)</td>
<td>18% (7% - 29%)</td>
</tr>
<tr>
<td>Genital pain</td>
<td>0% (0% - 0%)</td>
<td>32% (19% - 45%)</td>
<td>0% (0% - 0%)</td>
<td>24% (12% - 36%)</td>
</tr>
</tbody>
</table>
Psychiatric symptoms

- Non-homicidal group (Mean = 41%)
- Homicidal group (Mean = 71%)

- Suicidal
- Sudden abrupt mood swings
- Explosive anger
- Paranoia
- Ahedonia
- Exaggerated startle
- Hypervigilance
- Disinhibition
- Nightmares
- Depersonalization
- Intrusive images aggressive
- Hallucinations
- Dissociative episodes
- Derealization
- Intrusive images sexual

0% 20% 40% 60% 80% 100%
## Violence in Lyme Disease

### Contributors to Violence
- Suicidality
- Sudden abrupt mood swings
- Explosive anger
- Paranoia
- Anhedonia
- Hypervigilance
- Exaggerated startle
- Disinhibition
- Nightmares
- Depersonalization
- Intrusive aggressive images
- Dissociative episodes
- Derealization
- Intrusive sexual images
- Marital/family problems
- Legal problems
- Substance abuse
- Depression
- Panic Disorder
- Memory impairments
- Neuropathy
- Cranial nerve symptoms
- Decreased libido

### Failed Deterrents to Violence
- Cognitive capacities, executive functioning
- Capacity to process interpersonal cues
- Capacity for impulse control
- Psychosocial maturation
- Higher level coping skills
- Empathy
- Social connections

### Acute Triggers
- Frustration
- Acute stress
- Intrusive symptoms
- Hallucinations
- Delusions
- Auditory and other stimulation
- Perceived threat or injury
- Jarisch-Herxheimer reactions
Aggressiveness, Violence, Homicidality, Homicide and Lyme Disease

• Most aggression with LD was impulsive, sometimes provoked by intrusive symptoms, sensory stimulation or frustration and was invariably bizarre and senseless.

• Post infection findings associated with homicidality that separated from the non-homicidal group within the 95% confidence interval included suicidality, sudden abrupt mood swings, explosive anger, paranoia, anhedonia, hypervigilance, exaggerated startle, disinhibition, nightmares, depersonalization, intrusive aggressive images, dissociative episodes, derealization, intrusive sexual images, marital/family problems, legal problems, substance abuse, Depression, Panic Disorder, memory impairments, neuropathy, cranial nerve symptoms and decreased libido.

• Seven LD homicides included predatory aggression, poor impulse control and psychosis.

Bransfield RC. Aggressiveness, Violence, Homicidality, Homicide and Lyme Disease
Conclusion: LD and the immune, biochemical, neurotransmitter, and neural circuit reactions to them can cause impairments associated with violence. Many LD patients have no aggressiveness tendencies or only mild degrees of low frustration tolerance and irritability and pose no danger, however, a lesser number experience explosive anger, a lesser number experience homicidal thoughts and impulses and much lesser number commit homicides. Since such large numbers are affected, this very small percent of can be highly significant. Much of the violence associated with LD can be avoided with better prevention, diagnosis and treatment of LD.
Did Infections Caused by World War I Contribute to Causing World War II?

- Learning from history might help individuals to better understand some of the causes of violence, which, in turn, could help reduce current conflicts to ultimately prevent future wars. There were many infections during and after WWI which may have resulted in many residual neuropsychiatric impairments in those who had been infected; these include impairments associated with violence in the general population and leaders. Violent tendencies resulting from these infections occurring in a critical mass of individuals as well as influential individuals could have been one of the many contributors to WWII.

Bransfield RC. Contagion Live. Jan 5, 2018
Did Infections Caused by World War I Contribute to Causing World War II?

• It is possible that current war zones endemic to violence may follow a similar pattern in which there is a repetitive cycle of infection, brain impairments contributory to violence, and thus, resulting violence. To break such a cycle, a public health approach and a cross-disciplinary scientific effort made by psychiatrists, infectious disease physicians, psychoimmunologists, and neuroscientists to better understand and prevent the causes of violence may eventually be more effective in reducing violence than military or punitive interventions.

Bransfield RC. Contagion Live. Jan 5, 2018
Could a Pandemic Causing Mental Dysfunction Contribute to Global Instability?

• If a pandemic occurs that causes the mental impairments which increase the risk of violence, it could result in global social instability. Lyme and associated diseases is one of the infections that can cause violence. In an era with advanced weapon technology, greater safeguards are needed to prevent the mental impairments that can cause violence and one of the many causes of these impairments includes infections and the immune impairments associated with these infections. Greater attention to hygiene and prevention, diagnosis and treatment of infectious diseases can help prevent violence on both a regional and global level.
Lyme Fatalities

• Suicide, drug overdoses, homicides.
• Other neuropsych: congenital Lyme infections, Lyme meningitis, symptomatic late Lyme neuroborreliosis, late Lyme neuritis or neuropathy, meningovascular and neuroborreliosis with cerebral infarcts, intracranial aneurysm, late Lyme encephalitis, late Lyme meningo-encephalitis or meningomyelo encephalitis, atrophic form of Lyme meningo-encephalitis with dementia & subacute presenile dementia.*

*Global Network on Institutional Discrimination and Ad Hoc Committee for Health Equity in ICD11 Borreliosis Codes. 2017
Assessment
Assessment

• Like other illnesses, Lyme Borreliosis is diagnosed by a comprehensive clinical exam with a thorough history, mental status exam, review of systems, neurological exam, physical exam, a knowledgeable interpretation of laboratory findings, pattern recognition and clinical judgment.
Clinical Assessment

- In depth history, review of systems
- Thorough exam relevant to patient’s complaints and findings
- Are there relapsing progressive multi-systemic symptoms, including cognitive, psychiatric, neurological, and somatic?
- The greater the comorbidity, the greater the likelihood of a complex infectious disease.
- Pattern recognition, differential diagnosis
- Lab: (no test can rule out Lyme disease)
- Medical judgment
### Common Neuropsychiatric Symptoms

<table>
<thead>
<tr>
<th>Poor attention span</th>
<th>Poor short term memory</th>
<th>Dyslexia symptoms</th>
<th>Slow processing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Distracted by frustration</td>
<td>Sensory hyperacusis causing flooding</td>
<td>Executive dysfunction</td>
<td>Depersonalization</td>
</tr>
<tr>
<td>Sensory hyperacusis causing flooding</td>
<td>Poor time management</td>
<td>Intrusive images &amp; thoughts</td>
<td>Low frustration tolerance</td>
</tr>
<tr>
<td>Poor short term memory</td>
<td>Dyslexia symptoms</td>
<td>Executive dysfunction</td>
<td>Impulsivity</td>
</tr>
<tr>
<td>Slow processing</td>
<td>Executive dysfunction</td>
<td>Intrusive images &amp; thoughts</td>
<td>Abrupt mood swings</td>
</tr>
<tr>
<td>Executive dysfunction</td>
<td>Poor time management</td>
<td>Intrusive images &amp; thoughts</td>
<td>Anhedonia</td>
</tr>
<tr>
<td>Poor time management</td>
<td>Depersonalization</td>
<td>Intrusive images &amp; thoughts</td>
<td>Decreased productivity</td>
</tr>
<tr>
<td>Depersonalization</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Depression</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Panic attacks (long duration)</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Social anxiety</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Generalized anxiety</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Obsessiveness</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Non-restorative sleep</td>
</tr>
<tr>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Intrusive images &amp; thoughts</td>
<td>Appetite disturbances</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Intrusive images &amp; thoughts</td>
<td>Decreased libido</td>
</tr>
<tr>
<td>Abrupt mood swings</td>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Headaches</td>
</tr>
<tr>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Impulsivity</td>
<td>Cranial nerve symptoms</td>
</tr>
<tr>
<td>Abrupt mood swings</td>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Neuropathy</td>
</tr>
<tr>
<td>Abrupt mood swings</td>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Fatigue</td>
</tr>
<tr>
<td>Abrupt mood swings</td>
<td>Impulsivity</td>
<td>Abrupt mood swings</td>
<td>Chronic pain</td>
</tr>
<tr>
<td>Suicidal</td>
<td>Abrupt mood swings</td>
<td>Suicidal</td>
<td>Alcohol intolerance</td>
</tr>
</tbody>
</table>
Comprehensive Multi-System Assessment

- **Cognitive:** Attention, sensory hyperacusis, working & short term memory, sequential memory, geographical memory, word finding, speech fluency, neologisms, comprehension, auditory & visual processing, processing speed, writing skills, math skills, dyslexia-like symptoms, imagery, executive functioning, “brain fog.”

- **Psychiatric:** Disinhibition, low frustration tolerance, irritability, hypervigilance, exaggerated startle, explosive anger, suicidal, aggressiveness, paranoia, hallucinations, depression, rapid cycling bipolar, panic disorder, obsessive compulsive disorder, intrusive symptoms, posttraumatic stress disorder, social anxiety, generalized anxiety, phobias, depersonalization, self mutilation, psychosis, decreased social & school functioning, accident prone, etc.

- **Vegetative:** Sleep, eating, sexual functioning, thermal dysregulation, fatigue.

- **Neurological:** Headaches (multiple types), cranial nerve neuritis & neuralgia, eye findings, migratory polyneuropathy, spinal cord signs, transverse myelitis, radiculopathy, peripheral neuropathies, motor neuropathies, movement disorders, tics, gait, balance, ataxia, seizures, white matter lesions,

- **Autonomic Nervous System:** POTS, nausea, orthostatic hypotension, anhydrosis, etc.

- **Musculoskeletal:** Migratory arthralgias, arthritis, crepitations, periostitis, fibro, stiffness, neck and back discomfort.

- **GU:** Spastic bladder, testicular pain/pelvic pain, menstrual irregularity, sexual dysfunction, decreased libido.

- **Cardiac/Pulmonary:** Chest pain, shortness of breath, palpitations, heart block, murmur.

- **Gastrointestinal:** GERD, irritable gut, reduced GI motility (gastro-paresis, ileus, etc.).

- **Immune:** Fevers, sweats or chills, lymphadenopathy.

Bransfield RC. Neuropsychiatric Lyme Disease: Pathophysiology, Assessment & Treatment. ILADS European Meeting. Augsburg, Germany. 28 May, 2011.
Initial SPECT scan shows extensive hypoperfusion, predominantly in the frontal and temporal lobes and to a lesser degree in the parietal and occipital lobes. After treatment, there is marked improvement of the hypoperfusion pattern in the temporal, frontal, and parietal lobes; only small areas of the hypoperfusion pattern remain.

SPECT, single photon emission CT.

Lyme Neuroborreliosis: Magnetic Resonance Imaging

Common Differential LYD/TBD Diagnosis

- Chronic fatigue not associated with LYD/TBD
- Fibromyalgia not associated with LYD/TBD
- Epstein-Barr not associated with LYD/TBD
- Multiple Sclerosis not associated with LYD/TBD
- Lupus
- Posttraumatic stress disorder
- Hypochondriasis
- “Somatization disorder” or psychosomatic


Multisystem vs. Psychosomatic

• A person is reasonably healthy throughout most of their life, and then there is a point in time where a multitude of symptoms progressively appear. The number and complexity of these symptoms may be overwhelming and illness may be labeled hypochondriasis, somatization disorder, or psychosomatic. However, both hypochondriasis and psychosomatic illnesses begin in childhood and are lifelong conditions with a psychodynamic explanation and vary in intensity depending upon life stressors. If a complex illness with both mental and physical components begins in adulthood, the likelihood that this is psychosomatic is very remote.
Treatment
Antibiotics or Psychotropics or Other Treatments?

- When a patient has been treated with just antibiotics and has not adequately responded, consider psychotropics.
- When a patient has been treated with just psychotropics and has not adequately responded, consider antibiotics.
- When a patient is treatment resistant consider both &/or other treatments.
A Few Key Points

• What causes a condition may be different from what perpetuates a condition.
• A complex, chronic, TBD patient may have over 100 different symptoms.
• How do the symptoms interact with each other?
• Make a list with the patient ranking which symptoms are the most severe and most impede recovery. This will determine treatment strategy.
What Symptoms Impede Recovery?

- Non-restorative sleep, fatigue, cognitive impairments (the terrible triad).
- Emotional symptoms: depression, anxiety, depersonalization, mood swings, psychosis
- Chronic pain: headaches, neuropathy, radiculopathy, musculoskeletal
- Somatopsychic symptoms: GI, GU, dysautonomia
- Addiction
Symptomatic Treatment

• Regardless of the debate treating psychiatric symptoms with psychotropics can prevent and sometimes reverse progression of illness.

• Symptomatic treatment improves:
  – Functioning
  – Immune functioning
  – Resistance to infection
How Much Treatment is Enough?

- Successful psychiatric management can sometimes result in reduction of infection.
- Successful reduction of infection can sometimes result in reducing psychotropics.
- Our current technological limitations prevents us from being sure all tick-borne infections have been eradicated.
- After stabilization constant vigilance is needed to prevent relapse.
Treatment

• When the symptoms are caused by persistent infection, antibiotic treatment late in the course of the illness may prevent some further neuropsychiatric disease progression, but may be unable to reverse all the previously established neuropsychiatric impairments.
“Post-treatment Lyme Disease”

• How do you know if treatment was adequate and post-infection or not?
• Further clarification is needed
• Post-treatment with persistent infection
  – With disease progression
  – Without disease progression (latent)
• Post-treatment without persistent infection?
  – With disease progression
  – Without disease progression
Future Directions

• The future is promising with the development of DNA based rapid diagnostic systems of parasites and immune responses which would help to better identify the causative pathogens, better clarify the pathophysiology and help to facilitate earlier more effective treatment.
Microsoft partners with Adaptive Biotech on AI-driven blood test to diagnose dozens of diseases at once

• A project to build a universal blood test that can screen for multiple diseases at a time by decoding the information in the immune system.

• Adaptive uses technology called next-generation sequencing will read the genes of the T-cells and B-cells of those cells and create an immune profile made up of billions of data points.

• The project will connect the dots between the genetic markers on immune cells and diseases.

Conclusion I

- Infections, Tick-borne infections and persistent complex interactive infections with immune evasion and suppression provoke persistent immune reactions, biochemical changes & sleep disorders resulting in disease progression of psychiatric symptoms. Chronic inflammation in the body can cause chronic inflammation in the brain, resulting in deleterious effect upon brain functioning that contribute to causing mental illness.

- Cross disciplinary research, prevention, diagnosis & effective treatment can help prevent mental illness and violence.
Conclusion II

• Current approaches reduce symptoms that contribute to disease progression (sleep disorders, fatigue, cognitive impairments, depression anxiety disorders, chronic pain) in combination with antimicrobial and other treatments.

• The future is promising with the development of DNA based rapid diagnostic systems of parasites and immune responses which would help to better identify the causative pathogens, better clarify the pathophysiology and help to facilitate earlier more effective treatment.
Thanks for your attention and your commitment to our patients

Questions?