The Brain and Tick-Borne Diseases

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Holmdel High School Auditorium
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Outline

• Overview
• Tick-borne diseases causing chronic illness
• Symptoms & Evaluation
• Treatment
A Typical Patient: BC (Before Controversial Disease)

• A lover of life
• Healthy, active, proactive and enjoying outdoor activities
• Not psychosomatic
• Not malingering
A Typical Patient: AD (After the Disease)

• An onset of a worsening and fluctuating multitude of symptoms that are difficult to understand and impair many facets of life
• The validity of symptoms is questioned by family, friends, employer, physician and insurance companies
• The “unexplained symptoms” are considered of psychiatric origin—psychosomatic, malingering, etc, etc, etc.
Possible Disease Progression Over Time

- Tick bite, flu
- Musculoskeletal aches and pains
- Brain fog, sleepiness, fatigue, sleep disorder
- Increasing multisystemic symptoms
- Increasing subtle neurological symptoms
- Depression, anxiety, cognitive impairments
- Increasing pain, impairment, disability
- Increasing neuropsych symptoms, dementia
Lyme/TBD: Two Medical Views

- Rare, reliable immune testing; easily diagnosed and treated; never or very rarely chronic; never causing psychiatric symptoms, autism, etc; symptoms comparable to “the aches and pains of daily living”

- Common, unreliable immune testing, difficult to diagnose and treat; chronic; causing psychiatric symptoms, autism, etc [ILADS]; pain comparable to post surgical pain, fatigue comparable to MS, physical disability comparable to congestive heart failure [NIH]
As a psychiatrist I see the failures of our healthcare system

• If a patient’s symptoms are “medically unexplained” by current beliefs, the patient is considered to need a psychiatrist.

• Many patients are frustrated with the current system and need psychiatric assistance.

• In regard to Lyme disease, the late stage symptoms are mostly neuropsychiatric.

• I have seen thousands of patients with a broad spectrum of neurological, cognitive and psychiatric symptoms, including cases of suicide, violence, homicide, autism, developmental disabilities and dementia.
Mentally Ill Until Proven Otherwise

- Complex, poorly understood diseases are often considered to predominately have a psychological basis until proven otherwise. Tuberculosis, hypertension, and stomach ulcers were once considered to be psychosomatic.
- A failure to make a diagnosis based upon various so-called “objective tests” is not a basis for a psychiatric diagnosis.
- Many patients are given a psychiatric diagnosis as a result of an inadequate medical exam.
- Mental illness is always caused by something.
What obstructs forward progress?

• Dr Willie Burgdorfer, who discovered Borrelia burgdorferi, the spirochete causing Lyme, stated—“The controversy in the Lyme disease research is a shameful affair and I say this because the whole thing is politically tainted. Money goes to the same people who have for the last 30 years produced the same thing—nothing.”*

*Under Our Skin
This raises critical questions

- Has NIH and CDC Lyme disease research helped patients in the past 30 years?
- Could this disease have been improperly defined by a group of researchers to maintain the flow of research grant money to themselves, their institutions and their collaborators?
How Is Lyme Disease Defined?

- **Restrictive research definition**: A rigid and very narrow list of symptoms and a reliance upon poor quality immune testing.

- **Broad clinical definition**: A broad group of symptoms, pattern recognition, PCR (DNA testing) antigen testing, culturing the organism, complex clinical interpretation.

- The CDC states their restrictive epidemiological criteria is not to be used for diagnosis.
**Sensitivity/Specificity of Commercial Two-Tier Testing for Lyme Disease 46%***

<table>
<thead>
<tr>
<th>Study/Year</th>
<th>Location</th>
<th>Patients/Controls</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<td>Engstrom et al 1995</td>
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<td>USA</td>
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<td>Bacon et al 2003</td>
<td>USA</td>
<td>106/559</td>
<td>67%</td>
<td>99%</td>
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<tr>
<td>Binnicker et al 2008</td>
<td>USA</td>
<td>35/5</td>
<td>49%</td>
<td>100%</td>
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<tr>
<td>Steere et al 2008</td>
<td>USA</td>
<td>76/86††</td>
<td>18%</td>
<td>99%</td>
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<td><strong>TOTALS</strong></td>
<td>USA: 8</td>
<td>435/951</td>
<td>46%</td>
<td>99%</td>
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* Limited to studies from USA that included negative controls
† Non-commercial ELISA and Western blot
†† Non-commercial ELISA

Total allocation of funding for tick-borne disease studies by agency/organization, 2006-2010

- NIH-NIAID: $312,762,626 (85%)
- CDC: $27,865,186 (7%)
- NIH-NIAMS: $10,620,407 (3%)
- US Army Public Health Command: $475,500
- USDA-NWRC: $318,000
- NIH-NINDS: $2,593,865 (1%)
- NSF: $6,287,196 (2%)
- USDA-ARS: $7,181,000 (2%)
Total allocation of funding for tick-borne disease studies by study type, 2006-2010

- **Microbiological**: $210,393,439 (57%)
- **Prevention/Education**: $83,840,308 (23%)
- **Combination**: $47,278,120 (13%)
- **Environmental**: $5,864,235 (1%)
- **Treatment**: $17,168,281 (5%)
- **Surveillance**: $3,559,397 (1%)
The IDSA Lyme disease guidelines authors had:

- $92,000,000 in NIH & CDC Lyme grants
- $113,000,000 in NIH & CDC Lyme grants to their institutions & more to other collaborators
- 200 Lyme related patents (including Lyme ELISA)

[The IDSA Lyme disease guidelines review panel considered income of $10,000 from treating Lyme patients to be a conflict of interests.]
Who has the ELISA Patent?

- Barbara Johnson: CDC Fort Collins, advisor IDSA Lyme guidelines
- William T. Golde: seems to be with USDA and Plum Island.
- Dr. John T. Roehrig: chief of the Arbovirus Diseases Branch, Division of Vector-Borne Infectious Diseases, CDC.
- Tom Burkot, PhD: CDC Atlanta Division of Parasitic Diseases
- Joseph F. Piesman: CDC Ft. Collins DHHS Microbiology
- Leonard W. Mayers: CDC Atlanta Meningitis and Special Pathogens Branch, Division of Bacterial and Mycotic Diseases, National Center for Infectious Diseases
- Mark G. Keen: is/was with CDC Ft. Collins Division of Vector Borne Infectious Diseases.
- Ann R. Hunt: CDC Ft. Collins Division of Vector-Borne Infectious Diseases
Dr Fallon equates having Lyme disease to the Story of Job
The patients know more about their diseases than me. I must get faster modem, higher speed internet access than them.
The History of Mental Illness

• You’re possessed by demons & need punishment…
• Your mother caused it & you need psychoanalysis…
• Your serotonin is low & you need Prozac…
• Your genes are bad, you can’t change them…
• Your immune system & chronic infections contribute & you need antibiotics & immune treatments…
• Regardless patients with “medically unexplained symptoms” & doctors who treat them are possessed by demons & need punishment…
Tick-Borne Diseases Causing Chronic Illnesses
Categories of Disease Causation

- genetic (inherited alleles)
- parasitic
- noninfectious (diet, lifestyle, chemicals, radiation)
- environmental
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

Pathophysiology: Time & Space

• Time
  – Evolutionary concepts
  – The patient: disease progression over years and decades

• Space
  – A systems approach that considers multi-systemic contributors and deterrents to disease
Time

• Predisposing & precipitating factors
• Infections
• immune & other reactions
• Pathophysiological processes
• Dysfunction
• Symptoms & Syndromes
• Ineffective Treatment
• Disease Progression
NIH Human Microbiome Project

• A study researching all of the various microbes that live in people. The project has already established that the bacteria in the human microbiome collectively possess at least 100 times as many genes as the 20,000 or so in the human genome.
• Bacterial cells outnumber human cells by 10 to 1.
• Humans depend on their microbiome for essential functions, including digestion, leading microbiologists to conclude that a person should really be considered a superorganism.

http://nihroadmap.nih.gov/hmp
PubMed Citations

- Tick borne diseases: 20,000
- Lyme disease: 8,200
- Borrelia burgdorferi: 6,250
- Mycoplasma: 18,000
- Babesia: 2,900
- Bartonella: 1,900
- Ehrlichia: 1,900
- Anaplasma: 1,500
- Masters Disease or Stari: 700
Research & Clinical Observation: Microbes & TBD Cause Mental Illness

- Thousands of peer-reviewed journal articles demonstrate the causal association between infections and mental illness.
- 250 peer reviewed scientific articles demonstrate the causal association between Lyme/tick-borne disease and mental illness.
- Clinical observation by front line physicians also supports this view.
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 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)
  - *Chlamydomphila pneumoniae* (Chlamydia)
  - *Chlamydomphila 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
  - Coltiviruse (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
  - Varicella zoster virus (Chicken Pox)
  - Viral meningitis
  - West Nile 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:**
  - Cryptococccus
  - Coccidiomycosis
  - Histomycosis
  - Yeast:
    - Candida albicans (Candidiasis)
    - Candida dubliniensis
- **Prion**
  - Variant Creutzfeldt-Jakob

Infections Present in Tick-Borne Disease Patients

- **Bacteria**: Lyme disease, Ehrlichiosis, Bartonella, Mycoplasma, Chlamydia, RMSF, Typhus, Tularemia, Q-Fever,
- **Parasites**: Babesiosis and other piroplasms, filariasis, amebiasis, giardiasis...
- **Viruses**: EBV, HHV-6, HHV-8, CMV, St Louis Encephalitis, W Nile, Powassan encephalitis and other viral encephalopathies
- **Candida** and other fungi
Cousins: Lyme Disease & Syphilis

**Lyme disease**
- Chromosome + **21 plasmids**
- **132 genes**
- More genetic material
- 90% genes unrelated to any other known bacteria
- Perhaps the most complex bacteria known

**Syphilis**
- Only **22 genes**

*Syphilis is the dumb cousin*

Jemsek J
Figure 2: SERIAL IMAGES OF ONE NEURON WITH INTRACELLULAR SPIROCHETE
CO-EXISTENT FUNGAL INFECTION OFTEN MASKS THE SPIROCHETE. PHOTO SHOWS MANY SPIROCHETES EMBEDDED IN FUNGAL GROWTH. BLOOD CULTURE OF LYME PAT.
Direct or Immune Effects Causing Pathophysiology?

- Infection or Complex Interactive Infections
- Immune Effects Th1 & Th2
- Pathophysiology Causing Symptoms
Hepatitis C & Interferon Treatment

• A good model for inflammation mediated mental symptoms
• Symptoms include depression, anxiety, mania, irritability, impulsiveness, hostility, relapse of substance abuse & lassitude.[1]
• Cognitive impairments
• Irritability, aggression, anger, emotional lability, anxiety attacks, panic attacks, and insomnia. [2]
• Psychosis in Patients with Comorbid Hepatitis C and HIV [3]

1 Henry, Castera, Demotes-Mainard
3 Rosalind et. al. Psychosomatics 44:5, September-October 2003
Cytokine Activation Causes Psychiatric Symptoms

• Interleukin-6 Is Elevated in the Cerebrospinal Fluid of Suicide Attempters and Related to Symptom Severity (1)
• Interluken-1Beta & Self-Inflicted Aggressive Behavior (2)
• IL-1Beta Causes Fatigue (3)

Sickness Syndrome

(Mediated by Proinflammatory Cytokines IL-1, IL-6, and TNF)

Cytokines Induce Sickness Behavior

- Anhedonia
- Malaise
- Hypersomnia
- Anorexia
- Social Withdrawal
- Poor Concentration
- Weakness

Body Infections: Brain Symptoms

- Infections in the body can have immune effects upon the brain that cause mental symptoms.
- Cognitive and psychiatric symptoms can be present in tick-borne diseases when there is no infection in the brain.
A Sequence of Brain Symptoms

- Early symptoms are mediated by proinflammatory cytokines and include brain fog and fatigue.
- Another wave of symptoms are mediated by autoimmune processes and may include obsessive symptoms, tics, irritability and other symptoms.
- The next group of symptoms are associated with altered tryptophan metabolism, decreased serotonin, increased quinolinic acid and are associated with depression.
- Late stage symptoms are associated with brain inflammation and neurodegenerative changes.
Progressive Infection & Inflammation is Associated with Increasing Encephalopathy & Increasing Mental Symptoms

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<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
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<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, depression, impulsivity, personality disorders</td>
<td>Major psychiatric disorders, psychosis, suicide, homicide</td>
</tr>
</tbody>
</table>

Increasing Neurological, Multisystemic Symptoms & Fatigue
Lyme Disease and Autism

Geographical Patterns

• Of the twenty states that reported the highest occurrence of Autistic Disorder per 10,000 people; fifteen reported a higher than average number of Lyme disease cases. Conversely, of the twenty states that reported the lowest incidence of Autistic Disorder per 10,000 people; zero reported a higher than average number of Lyme disease cases.

Kuhn M, Grave S, Bransfield R, Harris S.
Top twenty five states for prevalence of Autism Disorder and prevalence of Lyme disease in those states in 2009 (Kuhn et al.)

Reported Cases 2009

- Autism per 10,000
- Lyme Disease per 100,000

Top 25 States / Prevalence of Autism

- GA
- TX
- IL
- MO
- NC
- CA
- OH
- MI
- NY
- NH
- DE
- NV
- MD
- IN
- VA
- RI
- WI
- VT
- NJ
- MA
- PA
- OR
- CT
- ME
- MN

Top 25 States / Prevalence of Autism Disorder
Bottom twenty five states for prevalence of Autism Disorder and prevalence of Lyme disease in those states in 2009 (Kuhn et al.)
Lyme and Dementia I

Lyme and Dementia II

Lyme/TBD/Infections & Violence

• It is hypothesized parasites can alter host behavior by altering aggressiveness and sexual aggressiveness.

• Infections fostered by poor hygiene and warfare environments can cause impairments that contribute to violence, which can be particularly significant when affecting large groups and powerful and influential individuals. Throughout history, regions of the world with a higher burden of infections and vector borne disease have a higher association with violence.

• Human history is also a history of violence. Microbes and psychoimmunology are a part of both history and the future.

Bransfield RC. Neurology, Psychiatry and Brain Research. Gunzburg, Germany 2012
Symptoms & Evaluation
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 Lyme/TBD.
• Pattern recognition, differential diagnosis
• Lab: (no test can rule out LYD/TBD)
• Medical judgment
Consider Neuropsychiatric LYD/TBD with:

- An acquired case of attention deficit disorder
- Regressive autism with childhood bipolar
- Panic attacks that last more than ½ hour
- An onset of bipolar illness later in life
- Progressive white matter cognitive impairments with anxiety and depression
- Progressively declining mental state
- Psych symptoms but no musculoskeletal symptoms with prior partial treatment
Comorbidity: Psychosomatic, Somatopsychic or Multi-systemic?

• **Psychosomatic**: Mental distress results in somatic symptoms.

• **Somatopsychic**: Somatic distress results in mental symptoms.

• Or a **multi-systemic** process adversely affecting the brain and body causing both psychiatric and somatic symptoms.
Multisystemic 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 life long conditions which 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.
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.
Psychiatric Assessment
www.MentalHealthandIllness.com

- Cognitive
- Emotional
- Vegetative
- Behavioral
- Psychiatric syndromes
- Neurological
- Somatic
Treatment
Risk of Disease vs. Treatment

• If Lyme disease is benign, the risk of the disease may not outweigh the risk of treatment.

• If Lyme disease is serious, the risk of the disease may outweigh the risk of treatment.
Symptom Priority

- A TBD patent may have over 100 different symptoms.
- After completing an assessment, prioritize which symptoms are most severe and contribute the most towards perpetuating chronic illness.
- Treat the high priority symptoms first and work your way down the list.
What Symptoms Perpetuate TBD Disease?

- Sleep disorders
- Fatigue
- Cognitive impairments
- Depression
- Anxiety
- Pain
- Headaches
- Others
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.
Symptomatic Treatment

• Regardless of whether chronic Lyme disease is active infection or something else, symptomatic treatment is beneficial and can prevent and sometimes reverse progression of illness.

• Symptomatic treatment improves:
  – Functioning
  – Immune functioning
  – Resistance to infection
Basic Treatment Strategies

• Three commonly associated symptoms are non-restorative sleep, fatigue and cognitive impairments

• Increase deep sleep

• Normalize circadian rhythm, improve cognitive functioning, stress reduction, pain management as well as traditional psychotropic interventions for depression, anxiety, psychosis, etc.
Delta Sleep and Lyme Disease

- Chronic fatigue & sleep disturbances are prevalent in Lyme disease. (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. Sanchez, J. Broussard, M. Regan, J. Mullington J Pain; April 2004, Supplement 1 • Volume 5 • Number 3
Circadian Rhythms

Alertness
Deep Sleep

Healthy

Alertness
Deep Sleep

Chronic Stress
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
Psychotropics

- Antidepressants were developed from TB drugs that had mood lifting side effects
- All psychotropics may be used when needed
- Psychotropics effect neurotransmitters &:
  - Are sometimes antimicrobial
  - Can be immune modulators
  - May alter CNS gene expression
  - Can be neuroprotective
  - Can increase neurogenesis and brain derived neurotropic factor
Psychotropics are also Antimicrobial & Immune Modulating

- Antidepressants modulate cytokine functioning (1)
- The immunostimulating and antimicrobial properties of lithium and antidepressants (2)
- Immunomodulatory effect of SSRIs on human T lymphocyte function and gene expression (3)
- Antiviral & immunomodulatory effect of lithium

2 Lieb J. J Infect. 2004 Aug;49(2):88-93
3 Taler, et al. European Neuropsychopharmacology
4 Rybakowski JK. Pharmacopsychiatry. 2000 Sep;33(5):159-64.
Neuropsychiatric Herxheimer Reaction

- Treating Lyme/tick-borne disease patients with antibiotics may cause a Jarisch-Herxheimer reaction
- This reaction may exacerbate any symptom caused by the infection
- A sudden appearance of depression, suicide attempts, agitation & violence may be a part of this reaction. “You can’t bear to live. It is beyond the imagination.”
- Slowly starting the antibiotic, close observation & psychotropics are helpful
Adjusting to Lyme Disease

• Individuals who acquire Lyme disease are often more active than the average and invariably have great difficulty adapting to the impairments and limitations caused by this disease.

• Due to the multi-systemic nature of the disease, it is difficult to do anything that isn’t adversely affected by this disease.
Social & Family Dynamics

- Patients also have difficulty because Lyme disease, like any other *invisible disability*, is difficult for family, employers, physicians, insurers, government and others to understand and acknowledge.

- Often multiple family members have Lyme disease which can result in a further decline in family stability and increased conflicts.
Recovery is a marathon with many twists and turns
Website

Mental Health and Illness .com
www.mentalhealthandillness.com

International Lyme and Associated Diseases Society www.ILADS.org