

Applying common sense & lessons learned in Lyme Borreliosis Complex



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MAY 15, 2016

LIFTING THE VEIL: ACADEMY OF NUTRITIONAL MEDICINE, UK



Disclosure

Dr. Joseph G. Jemsek and the Jemsek Specialty Clinic have no financial relationship or any commercial interests related to the content of this presentation





23 Years background in HIV/ AIDS treatment through 2006

- Dr. Jemsek diagnosed the first cases of AIDS in North Carolina in 1983
- Fully dedicated treatment of tick-borne illness since 2001
- Destination practice
 - Patients from every state in America & over a dozen countries
- Over 10,000 Lyme Borreliosis Complex (LBC) patients seen by the practice & currently more than 3000 active patients
- 36 employees including 6 medical providers and researcher





- Uche R. Omabu, MD, MBA, JSC Researcher
- William Sweeney, VP Business Development, Danconia Media
- Kimberly B. Fogarty, PA-C, JSC
- ► Tara R. Fox, CPNP, JSC
- Rachel Markey, PA-C, JSC
- Lauren Shannon, FNP, JSC
- Kelly Lennon, AGNP-BC, JSC
- Leigh Kincer, special assistant, JSC
- Mark Pellin, journalist and media consultant
- John Allen, media consultant
- PJ Langhoff, Noted Author and Researcher



Thank you for this opportunity to address you today

"Everything I have learned... truly learned... in the practice of medicine, I have learned from my patients."

Joseph G. Jemsek MD, FACP





A life and journey in the profession of Medicine is a gift from God. Compassion for his fellow man and a lifetime dedicated to learning Medicine are the measure for the physician of His gift requited.

A physician's daily prayer will include thanks for the unique privilege to participate in a special intimacy and trust with the patient... which is a blessing from God and no other.

The good physician understands that humility, boundless curiosity, and an abiding respect for the complexity of the human condition, both in health and illness, are requisite traits for those who respect and honor His gift.

Joseph Jemsek, MD, FACP



Session I: 3:40pm - 4:25pm (45mins)

- Working Definition
- Persistence and Pathogenicity
- Evaluation of the LBC Patient
- Neuro-Functional Consideration

Break (04:25pm – 04:55pm) (25 mins)

Session II: 04:55pm – 05:40pm (45mins)

- Preparation for Treatment
- Selected Concepts in LBC Treatment
- Antibiotic Considerations
- Risk Factors for Poor Clinical Outcome
- Timeline Contributions



Definition

There is no accepted definition for "Lyme Disease"

"The beginning of Wisdom, is the definition of terms"

-Attributed to Socrates





"Chronic, relapsing, or otherwise 'unexplained' encephalopathy, arthritic symptoms, and neuropathy generally associated with tick-borne infections, spearheaded by *Borrelia burgdorferi* in combination with co-infecting organisms."

-Joseph G. Jemsek MD, FACP

"Lyme Borreliosis Complex" is a more appropriate term for persistent Lyme Disease. The definition should be distinct from Acute Borreliosis, aka 'Lyme disease'



Chronic, Relapsing, and Otherwise "Unexplained"

► I. ENCEPHALOPATHY

 Most common are decline in cognition and executive function, sleep disturbances, personality and mood alterations/disorders

► II. ARTHRITIC & PERIARTICULAR SYMPTOMS

- Periarticular symptoms include inflammatory and non-inflammatory enthesopathies
- Lyme arthritic symptoms are generally migratory and may overlap with several rheumatologic syndromes

► III. POLYNEUROPATHY / MONONEURITIS MULTIPLEX

• May include sensory (C-fiber) lesions; cord myelitis; ganglionitis/plexitis and motor neuron disease





Complex' reflects:

- Polymicrobial infection (Multiple co-pathogens, e.g. Bartonella spp., Babesia spp., HGE, HME)
- Multisystemic disease (Tropism)
- Multi-compartmental neurologic disease (Tropism)
- Immune-evasive and immunosuppressive (Unique survival mechanisms, including Bb capacity for altered life forms, biofilm issues, etc)
- Once an LBC pathogen is "IN" it's "IN"







https://upload.wikimedia.org/wikipedia/commons/7/70/Phylogenetic_tree.svg



The Spirochetal Groups





Borrelia *sensu lato complex*:

Collective name for all Borrelial species know to cause Lyme disease. They include:

- B. burgdorferi sensu stricto- Predominant specie in North America (also found in Europe)
- B. afzelli, B. garinii, B. andersonii, B. valaisiana, B. japonica, B. Lucitaniae, B. tanukii, B. tudae, B. americana, B. californienses, B.carolinesis etc.

Other Borrelial Species:

- B. recurrentis, B. miyamotoi, B. Dutonii (relapsing fever synd.)
- B. lonestari (Southern Tick Associated Rash Illness -STARI)

Emerging genospecies: Newly discovered and unclassified spp.

• B. *bisetti*, B. *Spielmanii*, ... etc

INSTITUTE OF ARTHROPODOLOGY AND PARASITOLOGY U. S. NATIONAL TICK COLLECTION







Borrelia burgdorferi (Bb)

- Chromosome + 21 plasmids
- 132 lipoprotein genes
- More genetic material
- 90% genes unrelated to any other known bacteria
- Linear DNA





Treponema pallidum

- Only 22 lipoprotein genes
- Unlike Lyme, lives only in the human host, as it lacks the ability to thermally adapt
- Syphilis is Lyme's "dumb cousin"



Persistence and Pathogenicity of Bb

Multiple life forms of *B. burgdorferi*

- Spirochete
- Blebs and vesicles
- L-form
- Cyst
- May survive intracellularly, extracellularly, or in body fluids & tissues

Multisystemic, has been isolated from:

 Synovial Fluid, Skin, CSF, Brain, Blood, Muscle, Lymphatic tissues, Heart, Kidney, Splenic Tissues





spirochete ~

cyst



Available online at www.sciencedirect.com



Microbes and Infection 8 (2006) 2832-2840

Original article

Invasion of human neuronal and glial cells by an infectious strain of *Borrelia burgdorferi*

Jill A. Livengood, Robert D. Gilmore Jr.*

Centers for Disease Control and Prevention, Division of Vector-horne Infectious Diseases, 3150 Rampart Road, CSU Foothills Campus, Fort Collins, CO 80522, USA

Received 13 June 2006; accepted 30 August 2006

"In all neural cells tested, we observed B. burgdorferi in association with the cell"

pathogenesis of neuroborreliosis, we investigated the ability of *B. burgdorferi* to attach to and/or invade a panel of human neuroglial and cortical neuronal cells. In all neural cells tested, we observed *B. burgdorferi* in association with the cell by confocal microscopy. Further analysis by differential immunofluorescent staining of external and internal organisms, and a gentamicin protection assay demonstrated an intracellular localization of *B. burgdorferi*. A non-infectious strain of *B. burgdorferi* was attenuated in its ability to associate with these neural cells, suggesting that a specific borrelial factor related to cellular infectivity was responsible for the association. Cytopathic effects were not observed following infection of these cell lines with *B. burgdorferi*, and internalized spirochetes were found to be viable. Invasion of neural cells by *B. burgdorferi* provides a putative mechanism for the organism to avoid the host's immune response while potentially causing functional damage to neural cells during infection of the CNS.

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Keywords: Borrelia burgdorferi; Cell invasion; Neuroborreliosis

Microbes and Infection

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Keywords: Borrelia burgdorferi; Cell invasion; Neuroborreliosis



Worms In The Brain: Example of Tropism

- Lyme bacteria love all brain tissues!
- Neuroborreliosis
 - Memory loss
 - Severe mood disorders
 - Lack of concentration
 - Sleep disturbance
 - Anxiety
 - Difficulty with word retrieval
 - Headaches

Microbes Infect. 2006 Nov-Dec;8(14-15):2832-40. Emerg Infect Dis. 2006 Jul;12(7):1051-7. Infect. Immun. 2008 Jan;76(11):298-307. Epub 2007 Nov 5.







To fight, flee, or hide are the imperatives of long-term survival by an infectious microbe

- Active Immune Suppression
 - Complement Inhibition
 - Induction of anti-inflammatory cytokines

Immune Evasion /Induction of Immune Tolerance

- Phase and Antigenic Variation
- Immune Complexes

Physical Seclusion

- Intracellular seclusion
- Incursion into immune privileged sites

Microbes and Infection 6 (2004) 312–318 Ember E.M. et al.

Over 70+ papers between 1966 and 2009 which demonstrate persistence of Bb sp. in animal and human models

Compendium available upon request



- Bb and T. pallidum both lack lipopolysaccharides (LPS), the proinflammatory constituent in the outer membrane of Gramnegative bacteria
- But the virulence factors of Bb are its numerous lipoproteins of diverse functions (lipoprotein polymorphism)



Lipoprotein attaches to mammalian proteins, integrins, glycosaminoglycans, and glycoproteins to achieve tissue invasion and immune evasion

Herxheimer reactivity

 Reflects hyper-reactive immune response characteristic of lipoprotein exposure

Dr. Karl Herxheimer



Lipoprotein: Fat Fly Protein Meanie





Image Courtesy of Jordan Jemsek





Lipoprotein Reactivity

Herxheimer reactions were first described by dermatologists Adolf Jarisch and Karl Herxheimer in the late 1800s, when they observed febrile reactions in the treatment of syphilis with mercury compounds

In the Bb infection, the **die-off** of spirochetal organisms caused by antimicrobial therapy can result in **"maniacal inflammation**" aka the **'Herxheimer' Reaction**... due to release of the lipoprotein factor







Tick-Borne and Non-Tick-Borne Co-Infections lead to Immunosuppression through Synergism with Bb

- ▶ Babesia spp.
- Bartonella spp.
- Anaplasma phagocytophilum (HGE)
- Ehrlichia chaffeensis (HME)
- Mycoplasma fermentans
- Chlamydia pneumonia
- Herpesviruses (HHV-6, A/B)

Am J Trop Med Hyg. 2003 Apr;68(4):431-6 Vet Immunol Immunopathol. 2001 Dec;83(3-4):125-47 Vet Immunol Immunopathol. 2003 Aug 15;94(3-4):163-75 Clin Infect Dis. 1997 Jul;25 Suppl 1:S43-7 Infect Immun 2001; 69:3359–71 JAMA 1996; 275:1657–60.

Arch Virol Suppl. 2005;(19):147-56 Parasite Immunol 2000; 22:581–8. J Infect Dis 2002; 186:428–31. Arch Neurol 2001; 58: 1357–63. Transplantation. 2001 Jun 15;71(11):1678-80 Transpl Infect Dis. 2001 Mar;3(1):34-9



- Ticks are capable of transmitting all Borrelial species
- It is possible that other arachnids transmit Bb but the ticks are the most efficient
- Ticks harbor other pathogenic bacteria, viruses and protozoa
- More than one pathogen may be transmitted during bite; exception to the rule
- All the pathogen share and have in common long replication cycles...
- Possibility of sexual and vertical transmission (Syphilis as a case example)
 - between sex and ticks, most people are exposed or infected but without symptoms.

Biofilm



- Bb can co-exist in common biofilms with multiple other pathogens
- Most pathogens capable of producing biofilm – as many as 95% (personal communication with Dr. Alan MacDonald)
- Biofilm enables Bb to survive despite a stressful environment created via actions of the immune system and antibiotics
- One unique feature of Borrelia biofilm is the externalization of its DNA, which is incorporated into the matrix made by extracellular polymeric substances (EPS), giving the spirochetes a protective coat inside the host







- Resistance and recurrence are influenced by the formation of different morphological forms of Bb which can exist together in a matrix of different cell forms (cysts, spiral forms, granular, L-forms): all forms are capable of existing in biofilm
- Intelligent eradication of biofilm in terms of treatment is important in treatment of LBC
- Novel 'designer' drugs aim at destabilization of the biofilm will open up a new horizon in the treatment and cure of Lyme disease



Chronic Oxidative Stress



- Reactive oxygen species (ROS): Byproducts of normal metabolic reactions and aging process
- Oxidative stress occurs when ROS are produced beyond the capacity of the body's anti-oxidant mechanisms
- Oxidative stress either creates inappropriate excitatory responses OR reduces responses
- Oxidative stress retards or perturbs immunologic function and recovery as well as cellular function and recovery
- Chronic oxidative damage is a fundamental part of LBC & other chronic infection/inflammatory states: accelerates aging of the brain and body





In Summary, Bb and co-infections may cause vicious cycle of ongoing inflammation :

Characterized by :

- Multi-compartmental neuropathology
- Multisystemic involvement
- Immune evasion, immune exhaustion and immunosuppression
- Biofilm formation
- Lipoprotein as an engine for exaggerated immunoreactivity (Herxheimer effect) much occurring in the CNS and PNS
- Chronic oxidative stress via chronic inflammation





"The Meaning of Life is to Find your Gift, The Purpose of Life is to Give It Away."

-Pablo Picasso



"If you the physician fail to listen to the Patient who is your subject matter and the only reason you exist as a physician or as a profession, You will learn nothing as you 'practice' Medicine."

-Joseph G. Jemsek MD, FACP

Evaluation



- The average internist spends around 7 minutes with a patient. This is not nearly enough time to evaluate for chronic or complex illnesses such as LBC
- Physicians need to devote an appropriate amount of time to patient history and physical examination
- Thorough evaluation is crucial in determining extent of damage and subsequent therapeutic interventions



Thorough History & Physical Examination



History & Physical at Jemsek Specialty Clinic

1st Visit: 2 hrs minimum

2nd Visit: 45 mins to 1hr

Follow up visits: 30 mins



The Physician must commit to a thorough evaluation Listen to your patients!



- Modern physicians must learn to integrate multiple skills
- At JSC, we believe that the physician requires competencies in multiple disciplines:
 - Profound understanding of the role of the physician and the patient
 - Pain management
 - Pharmaceutical medicine: kinetics, drug distribution, routes of administration, drug-drug interactions, synergism, combination therapies to limit microbial resistance, pulsing therapies
 - Nutrition: use of supplements in dealing with the catabolic effects of oxidative stress




- Neuroendocrine issues: may be extensive; prioritize adrenal issues/ common confounding role of DI in sleep disorders
- Seizure management
- Vascular Health
- Sleep medicine
- Psychiatric management
- Gut health
- Mastering the concept of oxidative stress
- Understanding the paradigm of 'chronic stealth pathogen' infections as relates to drug Rx bioavailability;







Willie Sutton (1901 -1980) -Notorious Bank Robber -FBI Most Wanted List - 3 times prison escape - Sutton's Law





Reporter Mitch Ohnstad, "Willie, why do you rob banks?" Willie Sutton," Because that's where the money is."



Why does Jemsek Specialty Clinic study the Brain?



MAJOR CATEGORIES

- 1. Cognitive Dysfunction
- 2. Limbic Irritability
- 3. Dysautonomia
- 4. Mononeuritis Multiplex
- 5. **B** Symptoms
- 6. Energy level / Fatigue







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Cognitive Dysfunction



- Decline in mental processes involved in problem solving, decision making, reasoning, comprehension, production of language and memory
- Note and rate decline in executive functions (e.g. multi-tasking)
- Important to recognize the impact of major stressors



Cerebral Cortex & Associated Symptoms



Parietal Lobe

-Information processing

- -Spatial awareness
- -Vertigo
- Motion sickness

Occipital Lobe

-Visual snow

-Flashes

-Night blindness

-Diplopia

- -Convergence difficulty
- -Color distortions
- -Jumbling of images
- -Blurred vision
- -Fluctuating acuity
- -Residual shadows/images

Frontal Lobe

-Memory -Impulse control -ADD/ADHD -Personality changes -OCD

Temporal Lobe

-Auditory/ olfactory hallucinations

- -Tinnitus
- Dyssomnia
- -Dyslexia



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The Limbic System

-the 'reptilian brain'

Septum pellucidum A thin sheet of nervous tissue connects the fornix to the corpus

Cingulate gyrus

This area, together with the parahippocampal gyrus and the olfactory bulbs, comprises the limbic cortex, which modifies behavior and emotions.

Fornix

The fornix is a pathway of nerve fibers that transmits information from the hippocampus and other limbic areas to the mamillary body.

Column of fornix

callosum.

Mamillary body.

This tiny nucleus acts as a relay station, transmitting information to and from the fornix and thalamus.

Olfactory bulbs

The connection of these structures with the limbic system helps explain why the sense of smell evokes long-forgotten memories and emotions.

Amygdala __

This structure influences behavior and activities so that they are appropriate for meeting the body's internal needs. These include feeding, sexual interest, and emotional reactions such as anger.

Parahippocampal gyrus With other structures, this area helps modify the expression of emotions such as rage and fright.

_ Midbrain

The limbic areas influence physical activity via the basal ganglia, the large clusters of nerve cell bodies below the cortex. Limbic midbrain areas also connect to the cortex and the thalamus.

Pons

Hippocampus

This curved band of gray matter is involved with learning and memory, the recognition of novelty, and the recollection of spatial relationships.





This brain doesn't think!

DUNCE





Limbic System: Hypothalamus and Pituitary Gland



Hypothalamus-Pituitary Axis (HPA)

The brain, via the hypothalamus, controls endocrine functioning in the body.



Limbic System: Thalamus

The thalamus acts as the relay station for all sensory information entering the brain (save for smell)

Damage to the thalamus causes misinterpretation of this incoming sensory information, causing amplification of a stimulus that would normally not elicit a pain response (examples: photophobia and phonophobia)

Dejerine-Roussy Syndrome (also known as central pain syndrome): recognized by lesions in the thalamus as a result of stroke. Patients initially develop numbness, and then develop severe pain out of proportion with paineliciting stimuli





- Largest white matter structure in the brain
- Connects & synchronizes the left
 & right cerebral hemisphere
 communications
- Location-based attention selection; assists in tactile localization & matching of visual patterns
- Maintaining balance of attention and arousal







Damage results in "Split Brain Effect"



Limbic System: Basal Ganglia



Involved in voluntary motor control & procedural learning Also largely involved with inhibition (**GABA**) and reward (Dopamine) Lesions usually associated with involuntary tremors and Movement Disorders

It is made up of the:

- 1. Nucleus accumbens: reward circuit and pleasure experiences
- 2. Substantia nigra: Striatal input of dopaminergic neurons
- 3. Globus pallidus: direct & indirect inhibitory pathways modulate movement
- 4. Putamen: Automatic performance of previously learned movements





Primary roles:

- Modulation of emotions
- Processing and memory of emotional reactions
- Regulation of aggression, sexual behavior, and sleep regulation

Kluver-Bucy Syndrome: Damage to the amygdala that produces placid behavior, visual agnosia, oral tendencies (hyperorality) and hypersexuality

Amygdala "Devil Gland"

Limbic System: Hippocampus



- Primary function is consolidation of information from short-term to long-term memory and spatial navigation (GPS of the brain)
- Anterograde amnesia: inability to form or retain new memory; due to hippocampal lesion
- The hippocampus is also significantly affected in Alzheimer's disease
- Hippocampal neurons shrink in response to prolonged stress





Limbic System: Mammilliary Bodies

- Connects the amygdalae and the hippocampi to the thalamus via the mamillo-thalamic tract
- Important in recollective memory
- Damage to this area results in impaired memory especially anterograde amnesia
- Mammillary body atrophy seen in Alzheimers disease, schizophrenia heart failure, and sleep apnea. Damage also seen in thiamine deficiency due to alcohol abuse (Wernicke-Korsakoff syndrome)



The brain as viewed from the underside and front. The thalamus and Corpus Striatum (Putamen, caudate and amygdala) have been splayed out to show detail.



Circuit of Papez: Memory formation

- Involved in spatial and episodic memory formation
- All disease processes affecting a component of the Circuit of Papez affects memory function (e.g. Alzheimer's, PD, Semantic Dementia, Korsakoff Syndrome, transient global Amnesia)



Koeppen & Stanton: Berne and Levy Physiology, 6th Edition. Copyright O 2008 by Mosby, an imprint of Elsevier, Inc. All rights reserved



Memory







The limbic system is the center of the LBC storm
 Think White Matter!



- Heightened startle response
- Unprovoked crying/giggling-('gelastic seizures')
- Uncharacteristic
- personality changes
- Rage, paranoia
- Hypervigilance
- Emotional lability
- Insomnia, dysomnia

- Pain
- Cravings
- ADD/ADHD
- Tremor
- Bruxism
- Photophobia, phonophobia, osmophobia
- Vibrations
- Hallucinations

'Komodo Syndrome'

When the limbic system is inflamed by infectious elements, the patient's clinical picture may be characterized by marked neuropsychiatric instability, intolerance of sensory input, and inability to interact with one's environment

CDC SAYS 30 DAYS OF MEDS



MAJOR CATEGORIES

- 1. Cognitive Dysfunction
- 2. Limbic Irritability

3. Dysautonomia

- 4. Mononeuritis Multiplex
- 5. B Symptoms
- 6. Energy level / Fatigue







Autonomic Nervous System (ANS)

- Motor innervation of smooth muscle, cardiac muscle & glands
- Composed of two divisions:
 - Sympathetic ("Fight or Flight")
 - Parasympathetic ("Rest and Digest")
- Impacted by Limbic System, Brainstem, and Peripheral nerves



Post ganglionic neurons travel on C- Fibers which are polymodal and have slow conduction velocity. An important information for effective pain management.



Symptoms associated with ANS dysfunction:



Dysautonomia

POTS/NMH Temperature intolerance Nausea, motion sickness **Air hunger Flushing and chills** Gastroparesis Hyper/hypotensive crises **Barometric sensitivities CRPS/RSD Raynaud's phenomenon** "Power down" atonic episodes



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- Peripheral nervous system (motor and sensory components): paresthesisas, dysesthesias, radiculopathy, plexitis, fasciculations, twitching, tingling, balance issues
- Muscle weakness
- Atrophy



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'B' Symptoms

- Arthralgia
- Myalgia
- Enthesopathies
- Arthritis
- Arthritic syndrome secondary to immune reconstitution



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Energy level / Fatigue

- Chronic Oxidative Stress
- Mitochondrial damage
- Neural Insult
- Malabsorption
- Malnutrition
- Substrate deficiencies
- Drug effects





Erythema chronicum migrans (ECM)



- While bulls eye morphology is considered "classic," it is the exception. Variability occurs with linear, punctuate, arcuate, bluish coloration, occasionally necrosis, central vesiculation morphology.
- Pain, itching, or scaling is not characteristic.
- Can recur , often in the same site, both without and with antibiotic therapy (especially intensive antimicrobial therapy): "Dermal Herxheimer"







- 2003 study by Salazar et al (J Immun) examined fluid from blisters created using epidermal suction blister technique over EM rash of sample patients
- Immune components found in fluid included neutrophils, activated macrophages, mono- and plasmacytoid dendritic cells, and memory cells (CD27) and effector T cells
- Findings indicate that EM infiltrates have components of both innate AND adaptive immunity
- Therefore may conclude that EM rash may not only demonstrate current infection, but also show evidence of past exposure to Borrelia





"Life is like a game of cards. The hand that is dealt you represents determinism; the way you play is your free will."

-Jawaharlal Nehru, 1889-1964







Break

Refer to Handout

71



"LBC has no peer nor precedent in human illness because of its unique ability to routinely and efficiently disassemble the human nervous system and therefore create a major disconnect from life and reality."

-Joseph Jemsek, MD, FACP

72

ENGLAND

CANADA

FRANCE

Emerging Pandemic







-

Regierung RKI und NRZ

SWITZERAND

ENGLAND

NEATHERLANDS

he

ITALY


Increased human susceptibility due to the following theories:

- Adverse confluence of reservoir, vectors and hosts
- Natural or environmentally induced microbial mutations
- Microbial genetic manipulations
 - Bioengineering for Profit
 - Bioengineering for biological warfare
- Therefore Immunocompetence decline associated with genetic susceptibility



Exacerbating Social Factors

- Distancing between physician-patient relationship
- Bayh-Dole Act Patent/ Trademark Act Amendment
- Diagnosis based on criteria determined by patent and trademark holders i.e. CDC/ IDSA Conflict of Interest.
- HMO, NHS practicing medicine without a license
- Therefore patients denied Insurance and physicians treatment decisions restricted



JF_JSC Patient



Steps in Diagnosis and Treatment of LBC







"To have quality IN life, You must have quality OF life"

"Borreliosis Complex is a thief devolving all of us to a more primitive and less human state; we need to pull the alarm before it is too late. It is up to us."

-Joseph Jemsek, MD, FACP





- Preparation of the Complex Patient for the Treatment "Journey" is the Key to Successful Outcomes
- The goal of treatment is the simultaneous reduction of infection load and enhancement of immunologic capital
- Treatment of infection load is highly complementary to immunologic strengthening and control
- Consistent reduction of oxidative stress in the treatment period facilitates the 'Journey' to immunologic recovery







Most important aspect in preparation for treatment is to stabilize and restore:





Secure the ELF



E → Essential L → Life F → Functions



Must gain control of the unruly elf!

81



Learn your POEMS





 $P \rightarrow Pain$

- **○** → Others: Social Support / Co-morbidities
- E → Endocrine/Metabolic
- $M \rightarrow Mood/Psychiatric$
- $S \rightarrow Sleep$



PAIN and Immune Function

Pain (POEMS)

- Affects the innate immune system (resulting in inflammation)
- May recruit T-cells, even resulting in production of anti-neuronal antibodies
- Mediators released by immune cells, such as cytokines, sensitize nociceptive signaling in the peripheral and central nervous systems







Other Considerations

(POEMS)

- Persisting co-morbid conditions
- Encouragement and support outside of clinical setting
 - Family and social support









Endocrine disorders are a common finding in LBC patients, presumably due to high levels of infection/inflammation in Hypothalamic Pituitary Axis (HPA) which is highly vascular

Infection may affect neuroendocrine cells by

- Direct lesion/inflammation
- Oxidative stress
- Feedback effect of chronic inflammatory state
- Pain, Sleep disruption and psychological distress
- All resulting to elevation or suppression of hormonal secretion







Failure of Inhibition

- Heightened startle reflex
- Rage, aggression, impulsiveness, mania
- Hypervigilence & paranoia

Failure of Stimulation

• Apathy, anhedonia

Depression & Anxiety Disorders

- Generalized Anxiety Disorder, Panic Disorder, OCD, Anorexia nervosa/bulimia
- Emotional lability- biopolar disorder etc.
- Hallucinations- auditory, visual, olfactory, tactile
- Sexual dysfunction- hypo or hypersexuality

(POEMS)



Sleep Disorders

Dyssomnias

- Parasomnias
- Hyponogogic seizures/paralysis
- Nocturia
- Dysautonomia
- Epileptiform Seizures most common in REM sleep

(POEMS)

- Disposition to Mood Disorders
- Hallucination, Vivid & Intrusive Dreams
- Myotonic activities
- Pain



Hastings MH, Brancaccio M, Maywood ES (2014)



Health Effects of Sleep Deprivation

Neurologic

- Sympathetic Overdrive
- Poor Cognitive function and impaired decision making
- Slow motor function and response
- Poor memory consolidation
- Worsens mood disorders
- Decreases Pain Threshold
- Fatigue

Cardiovascular

- Hypertension
- Atherosclerotic cardiovascular disease (ASVAD)
- Arrhythmias- atrial fibrillation



Health Effects of Sleep Deprivation

Immunologic

- Decrease cellular repair and maintenance
- Sleep deprivation associated with decreased NK cell activity, decreased lymphocyte (T cells), decreased IgG and IL-4

Metabolic/Endocrine

- Increased Insulin Secretion
- Increase Cortisol
- Decreased Leptin (suppresses appetite)
- Increase Ghrelin (increases appetite)
- Decreased Glucose Metabolism Efficiency





EEG Sleep Waves

The brain remains active in REM Sleep while the body muscles rest is atonia. The function of the REM sleep therefore is to rest the body. In Non-REM, the brain activity and metabolism significantly decreases (>50% especially in deep sleep characterized by Delta waves while muscles regain tone.

Therefore the function of the Non-REM is to rest the brain... This is immuno-restorative.





Stages of Sleep







Recognize possible presence of

- Gut Dysbioisis
- Methylation Pathways Defects
- Mitochondrial Defects
- Subacute cholecystitis
- Refractory POEMS
- Biofilm/CCSVI
- Polymicrobial Complex

- Other Infections
- Paradoxical Drug Reactions
- Heavy Metal Toxicity, GMOs and Other Environmental Neurotoxins
- Motor Neuron Predominant Presentation (ALS Equivalence)
- Peri-menstrual Volatility
- Unresolved Comorbidities



96



- Supportive therapy and exogenous antioxidants are no longer able to maintain homeostasis due to degree of immune dysfunction and oxidative stress
- Antibiotics reliably reduce spirochetal and co-infections load
- Steady and progressive killing of the pathogen gradually expands expressive clonal T-cells functions
- Use of antibiotics does not preclude strict application of healthy life style
- Goal is to limit use of antimicrobials which occasional be may not necessary





- Bb has multiple strains, life forms & locations
- Synergizing co-infections ALWAYS present in LBC
- Highly genomically replete microbial pathogens capable of immune evasion, immunosuppression and antimicrobial resistance
- No practical retrieval and strain/species definition of pathogens, and no practical or reliable antimicrobial sensitivity testing
- Slow replication characteristics of all targeted pathogens (allows for pulse approach in therapy)
- Combination Rx limits resistance
- Combination treatment based theoretical models and physician's experience
- Rest periods or treatment holidays allows for cellular repair and detoxification





Route of Antibiotic Administration determined by multiple factors-

- Formulation (IV vs. Oral)
- Tolerance
- Drug-drug Interaction
- Optimal route for bioavailability to diseased tissue (CSF penetration, Limited GI absorption issues etc.)
- Assist floundering, dysfunctional immune system
 - Effectively levels the "playing field"
- Important to continue to manage stressors during Treatment...e.g. nutritional, psychiatric, hormonal, life adjustments on Rx, sleep, pain, seizures
 - "We don't treat many chronic illnesses with one drug" JGJ '07



ELF/POEMS

- Antibiotic/Antimicrobial Therapy
- Metabolic and methylation pathway optimization
- Reduction of Oxidative Stress and Inflammatory Radicals
- Mitochondrial Support
- Restoration of cellular membrane Integrity
- Neuronal Remyelination and Repair



Tree of Life: The Mighty Oak Winter

INFIRMITIES

Structural: many diseased branches Infections: Scale (insects), Lecanium (fungal), Phytophthora (fungal) Root disease: Root Stem Canker

Crown: Hypoxylon Canker (fungus)

REMEDIES

Assessment and Prioritization Gentle pruning of diseased branches (lower infection load)



Stabilization and Treatment Induction

Evaluation, Diagnosis and Initial Plan

General detoxification instructions

• Gluten free, supplements, salt baths, etc.

Correct laboratory outliers

Most resulting from 'spin down' effect of chronic oxidative stress

Address POEMS

- Pain- Neuropathic, regional (C-fiber) and musculoskeletal (A-fiber)
 - Use of combination neurotropic meds, eg.
 Lamotrigine/gabapentin/pregabalin, etc.
 - Use of THC (Marinol), CBDs, as indicated, NSAIDs occasional use
- **Other** Social support, address uncontrolled co-morbidities





- Endocrine High incidence Hashimoto's disease, free T3 most critical value
 - Prioritize for adrenal disorders (life threatening), diabetes insipidus (sleep disruption d/t nocturia)
- Mood Detoxification will stabilize much of the mood and sleep disturbance,
 - learn general concepts of psychotropic meds and
 - Consult with psychiatric colleagues beneficial
- **Sleep** Initiation with least habituating program (herbals, etc) but use benzodiazapine meds as needed, tolerate hypersomnelence,
 - employ delta wave promoting ancillary meds only (Trazadone, Seroquel, gabapentin, etc),
 - R/O sleep apnea as indicated, recognize restless leg syndrome





After 'stabilization' period (several weeks or as long as necessary),

- gentle 'pruning' with basic antimicrobials given on pulse basis, e.g. combination of beta-lactam (amoxacillin, cefuroxime), long acting tetracycline, azithromycin
- Rx example M,W,F two weeks on, one week off...
- Add metronidazole day 4/5 week two only
- Safety labs each of 3-5 cycles
- Primary objectives of the Induction Program is compliance, provocation, manageability

Tree of Life: The Mighty Oak Early to Mid-Spring

INFIRMITIES

Structural: better, continue pruning

Soil Preparation: cautious aeration/amendments

Infection, Root disease, Crown: unchanged

REMEDIES

Infections: Anti-scale spray and coating for insects

Antifungal spray for fungal infestations

Phosphites for Root Stem Canker (hardens roots/more impervious to infection)

Fertilizer application



'Babesia Oriented' Program

- Proceed only if patient stable enough to withstand more rigorous therapy
- Using combination anti-malaria Rx... atoyoquone (e.g. Mepron), Artemisia product, Enula (Elecampane) and Coartem and continuing Rx of Bb with limited Bartonella coverage
- Rx based on assumptions of long life cycle for Babesia sp in RBC life cycle of 100 days; anticipate (4-6) 4 week cycles (2 to 2 ½ wks on, 1 ½ to 2 weeks off)





Babesia and other 'stealth pathogens in LBC live in biofilm

- After first cycle initiate and ramp up biofilm treatment i.e. lactoferrin and xylitol in first few days of Rx cycle... 'must kill what you release'
- The pathogen from the biofilms are now 'planktonic' i.e. free living easier to phagocytose and susceptible to antimicrobial
- When biofilm Rx starts, adjustment of 'pulsing program'. Wk 2 becomes 'kill zone' with daily therapy
- 'Blue sky days' slowly ensue with reduction of infection loads and expansion of clonal T-Cells

Traction typically occurs and patient begins to see 'blue sky' days...

The Tree of Life becomes substantially unburdened of disease but much Rx remains and much healing remains to occur

Tree of Life: The Mighty Oak Mid-Spring to Early Summer

INFIRMITIES

Structural: much better/strengthened

Infection, Root disease, Crown: Much better... Surveillance for 'opportunistic infections' such as Boring Insects, Caterpillars

Crown: Hypoxylon Canker (fungus)

REMEDIES

Opportunistic Infections: appropriate treatments Soil analysis for optimal amendments/fertilizer



Pyrimethamine based Program

- At Babesia program conclusion patient experiencing progressively more extended periods of relief or 'blue sky days' which often run consecutively for up to 2 weeks.
- A strong clinical correlate is the resolution of hepatospenomegaly.

Expectations and Observations:

- Non-physiologic sweating, may persist (persistent dysautonomia)autonomic nervous system is slow to heal
- Difficulty sustaining remission on the 'off cycles' or 'Holiday' suggests confounding issues, e.g. persistent 'leaky gut', absorption issues, unrequited pain or life stressors
- Improvement gradual as the nervous system and body heals, and oxidative stress is reduced.


- Immune reconstitution may give rise to temporary symptom reemergence or emergence of new symptoms e.g. immune reconstitution arthralgia syndrome.
- Increased immunologic focus coupled with strengthening as the Tree of Life establishes health and yields new growth.
- After 12-15 months of intermittent therapy averaging less than 10 days/month, the patient will go to a maintenance program consisting of 3 days in one Rx week/month...
- The Tree of Life now just requires normal maintenance to remain healthy.



Tree of Life: The Mighty Oak Outcomes

Once the Mighty Oak, our Tree of Life has been 'mended' and nourished in a sensible sequence of actions, our Tree will sprout vibrant new growth (focus) from its crown and other healthy branches which will further enhances health through the release of beneficial phenols and carbohydrates

Our Tree will be able to optimize reserves and will have resilience for future challenges as it is set to live a long and healthy life





























EUBIOSIS

- Symbiotic coexistence of Host and Microflora
- Protection of the intestinal mucosa against invading microorganisms
- Contributes to immune system maturation and proper stimulation
- Antagonistic effect on undesired microbes
- Nutrient Digestion
- Vitamins, SCFA and protein synthesis
- Better tolerance to antibiotic treatment

DYSBIOSIS

- Harmful coexistence of Host & Microflora
- Damage to the intestinal epithelium->Gut wall thickening and reduced nutrient resorption
- Weakening of the Immune System
- Unprocessed Antigen and Allergen exposure: Increases food sensitivity and non-specific immune reactions.
- Increased gas production (H₂S, NH₃, CH₄, CO₂)
- Acceleration of cell turnover increased energy need
- Vitamin deficiencies







Restoring Eubiosis

- Identify Aggravating Factors
- Remove/control offending agents including yeast overgrowth
- Reinoculate the gut with beneficial microbes
 - Probiotics/Kefir with beneficial Strains e.g. L. *rhamnosus*
- Repair mucosal lining
 - Glutamine/SCFA



Nutrigenomics and Methylation



- The transfer of a methyl group on a substrate usually catalyzed by an enzyme.
- Defects in methylation pathways may affect the severity of illness, medication tolerance and response to therapy







- Regulation of Gene Expression
- Regulation of Enzyme/Protein Function
- RNA Processing
- Inactivation of toxins
- Modification of Heavy Metal
- Substrates production for many important biochemical pathways

Methyl Cycle abnormalities predisposes to ill health and impacts on ability of cells to repair





- Identify Single Nucleotide Polymorphisms in genes which may affect enzyme functions in Methylation Pathways
- SNPs can remain unexpressed or its effects compensated for in good health and or with adequate nutrition
- Important in determining effective supplement need for health maintenance and recovery





Methionine (Methylation) Cycle

- Energy production
- Gene expression (activation/deactivation) through methylation of DNA, RNA, proteins and lipids
- Vitamin B12 resynthesis and functions

Folate Cycle

- DNA & RNA synthesis
- Neural regeneration and other folate dependent processes







Neurotransmitter Cycle

- Pathway for Serotonin, Dopamine, NorEpi and Epinephrine production and degradation
- Knowledge of enzyme mutations and activity level is useful in developing the most effective individualized regimen and safety profile for sleep, pain and mood control
- Also function in Estradiol inactivation and selected drug metabolisms







Urea Cycle

- Normal vascular endothelial function and Nitric Oxide cytokine production
- Poor enzyme function here leads to poor Ammonia detoxification superoxides and peroxinitrites which cause neuronal damage.

Transulfuration Cycle

- Homocysteine metabolism
- Certain enzyme polymorphisms here can result to high sulfites and ammonia level.







Predict Risk of Metabolic Substrates and Vitamin Deficiencies

Determine Dose and Appropriate Multivitamin Supplementation

- Methylcobalamin / Hydroxycobalamin / Cyanocobalamin
- MethylFolate/ Folate / Folinic Acid
- Phosphatidylcholine / Cytidine diphosphate choline (CDP) / PS
- Predict tolerance for different classes of antidepressants
- Determine Antioxidant Potential
- Determine Oxidative Stress susceptibility





- Integrity of mitochondrial enzymes involved in oxidative stress and inflammation affects recovery.
- Superoxide dimutases (SOD1, SOD2, SOD3) perform the first step in activating free oxidative radicals
- Catalase (CAT) & glatathione peroxidase (GPX1) perform the second step
- An excess in free radicals (oxidative stress) is damaging to cells and limits cellular recovery



Mitochondrial Electron Transport Chain







- The majority of Oxygen required in a tissue is consumed in the Electron transport Chain
- Its function is to accept electron at the end of the chain and water formed is added to cellular water





- Premature electron leakage to Oxygen generates Oxygen Radicals (Superoxides)
- Poorly functioning Mitochondria (ETC) increases superoxide production and results to increased Oxidative Stress





Mitochondrial Oxidative Damage:

- The common pathogenesis for cellular and neurological damage
- Persistent fatigue
- Persistent neuronal insult
- Target mitochondrial antioxidant enzyme support limits superoxides, peroxides and peroxinitrite damages and give a chance to cellular recovery.





JSC Treatment contributions

- Coined the term Lyme Borreliosis Complex
- Use of combination neurotropics to control C-Fiber pain (Classic Neuropathic pain)
- Importance of Stabilization of Life functions- Limbic excitation, mood, pain and sleep (POEMS)
- Recognition of Significant T & B immune cell depletion CD4, CD8 in LBC
- Recognition of arthritic syndrome resurgence secondary to immune reconstitution
- Biofilm Eradication using Xylitol and Lactoferrin





- Role of Non-Hepatic Hyperammonemia, NO and other noxious metabolites in inflammation
- Routine use of combination anti-infective medications for Borrelial and Co-infections
- Recognition of important harbingers of illness in childhood history
- Consistent use of pulsed antibiotic therapy in LBC
- Extrapolation of LBC to numerous chronic diseases of unknown etiology





Fact: Borrelia burgdorferi (Bb) is a genetically endowed higher-order bacterium with multiple life forms, constituted by multiple genospecies and multiple strains, none of which have been adequately characterized and correlated with the expression of human illness

• **Hypothesis:** Human genetic and immunologic risk factors for disease expression play a role in disease susceptibility and expression of LBC

Fact: Bb is often associated with other tick borne pathogens in a 'Lyme picture'

 Hypothesis: There is a pandemic of 'Lyme disease' or LBC as a result of the 'folding in' of other persistent pathogens in combination with Bb, with the dramatic effect of more profound clinical expression of chronic illness and associated immunosuppression







Fact: Bb has nefarious and very broad tropisms; that is, Bb is capable of invading multiple cell lines which include all order of neurologic cell lines, endothelial cells, fibroblasts, immunologic T cell lines, etc. Other co-pathogens do or may do the same, e.g. Bartonella sp, Mycoplasma, Chlamydiae

 Hypothesis: Tropism by various Bb species/ strains and other pathogens play a role in the expression of strain specific clinical illness



- Hypothesis: Bb and other pathogens have 'hijacked' the human biome, creating chaos thru their devastating tropism for neurologic and other tissues and exerting an inexorable immunosuppressive effect; thereby disrupting what had been a peaceful symbiotic relationship between 500 trillion microorganisms and a human host with 50 trillion cells...
- Hypothesis: The human biome has never had to contend with a set of chronic infections with this combination of virulence, persistence, and survivability, i.e. a polymicrobial infection syndrome with marked avidity for critical neuronal structures, amongst other systems, which places the human biome at high risk for severe limitations in human capacities and normal relationships with their environment





Neuroplasticity



We should never underestimate the regenerative and compensatory power of the nervous system



NH_JSC Patient





"The greatest enemy of knowledge, is not ignorance but the illusion of knowledge"

Stephen Hawking

"The greatest obstacle to discovery, is not ignorance but the illusion of knowledge"

Daniel J. Boorstin







Thank You for Attending