Applying common sense & lessons learned in Lyme Borreliosis Complex

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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
Overview Lyme Borreliosis Complex (LBC)

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
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”
Phylogenic Tree of Life

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

- **Domain**: Bacteria
- **Phylum**: Spirochaetes
- **Class**: Spirochaetaceae
- **Order**: Brachyspiraceae
- **Family**: Leptospiraceae

**Genus**
- **Borrelia spp.**
- **Treponema spp.**
- **Leptospira spp.**

**Diseases**
- Lyme Disease/ LBC
- Relapsing fever
- STARI
- 1. Syphilis (STD)
- 2. Yaws
- 3. Bejel (Endemic Syphilis)
- 4. Pinta
- Leptospirosis (Field fever)
Many Species under Borrelia Genus

► Borrelia sensu lato complex:

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

- B. burgdorferi sensu stricto - Predominant species in North America (also found in Europe)
- B. afzelli, B. garinii, B. andersonii, B. valaisiana, B. japonica, B. Lucitaniae, B. tanukii, B. tuda, 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.
Spirochetal Cousins Cause: Lyme Disease & Syphilis

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

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“*Invasion of neural cells by *B. burgdorferi* provides putative mechanisms for the organism to avoid the host’s immune response while potentially causing functional damage to neural cells during infection of the CNS*”
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

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


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 pro-inflammatory constituent in the outer membrane of Gram-negative 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.
Lipoprotein: Fat Fly Protein Meanie

Image Courtesy of Jordan Jemsek
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.
Role of Co-Infections

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)

Vet Immunol Immunopathol. 2001 Dec;83(3-4):125-47
Vet Immunol Immunopathol. 2003 Aug 15;94(3-4):163-75
Infect Immun 2001; 69:3359–71

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.
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
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
Requisite Skills for Managing LBC

- **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

Reporting 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?
JSC Neuro-Functional Considerations in Tick-borne Illness

MAJOR CATEGORIES

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

CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
MAJOR CATEGORIES

1. Cognitive Dysfunction
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CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
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
- Dyssomonia
- Dyslexia
MAJOR CATEGORIES

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CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
The Limbic System
-the 'reptilian brain'-

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

**Column of fornix**

**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.

**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.

**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.

**Parahippocampal gyrus**
With other structures, this area helps modify the expression of emotions such as rage and fright.
This brain doesn’t think!
Hypothalamus-Pituitary Axis (HPA)
The brain, via the hypothalamus, controls endocrine functioning in the body.
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 pain-eliciting stimuli
Limbic System: Corpus Callosum

- 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”

http://www.wjh.harvard.edu/~mvaziri/Homepage/CV_files/split%20brain.pdf
http://www.ninds.nih.gov/disorders/agenesis/agenesis.htm
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
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
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 Alzheimer's disease, schizophrenia, heart failure, and sleep apnea. Damage also seen in thiamine deficiency due to alcohol abuse (Wernicke-Korsakoff syndrome).
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)
• Reticular activating system
• Thalamus
• Cortex
• Corpus Callosum

• Hippocampus
• Mammillary Bodies
• Cortical processing Temporal lobe (storage)

Working Memory (WM) ➔ Short-term Memory (STM) ➔ Long-term Memory (LTM)

Stimulus ➔ Attention ➔ Repetition

• Hippocampus (long term potentiation)
• Subiculum
• Basal ganglia (reward reinforcement/addiction)
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
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

CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
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

Distribution of ANS Innervations

Central Nervous System (CNS) → Preganglionic Nerve Fiber → Ganglion → Postganglionic Nerve Fiber → Target Organ

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
MAJOR CATEGORIES

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

CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
Mononeuritis Multiplex

- Peripheral nervous system (**motor and sensory components**): paresthesias, dysesthesias, radiculopathy, plexitis, fasciculations, twitching, tingling, balance issues

- Muscle weakness

- Atrophy
MAJOR CATEGORIES

1. Cognitive Dysfunction
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5. B Symptoms
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CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
‘B’ Symptoms

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

1. Cognitive Dysfunction
2. Limbic Irritability
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6. Energy level / Fatigue

CATEGORY RATING SYSTEM (on a scale of 1-10):
where 10 is individualized pre-morbid/highest functioning state
Energy level / Fatigue

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

Jemsek Specialty Clinic

The Netherlands

ENGLAND
FRANCE
GERMANY
ENGLAND
CANADA
AUSTRALIA
SWITZERLAND
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
Steps in Diagnosis and Treatment of LBC

1) Evaluation, interpretation, and prioritization of major pathological processes based on clinical and laboratory evaluations

2) Stabilization of faulty central life functions and reversal of stressors

3) Treatment

4) Healing process

5) Remission!
“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
The Key to Successful Outcomes

- 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:

**Essential Life Functions**
Secure the ELF

E → Essential
L → Life
F → Functions

Must gain control of the unruly elf!
Learn your POEMS

P → Pain
O → Others: Social Support / Co-morbidities
E → Endocrine/Metabolic
M → Mood/Psychiatric
S → Sleep
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
Classification of Nerve fibers

Erlanger & Gasser

A

α — Somatic Motor

Proprioception

β — Touch, Pressure

γ — Motor to Muscle Spindles

δ — Pain (fast), Cold, Touch

B — Preganglionic Sympathetic

Dorsal root — Pain, Hot, other receptors (mechano), reflex

C — Most Numerous

ANS — Postganglionic

Muscle Spindle — Ia

Golgi Tendon Organ — Ib

II

III

IV

Numerical

Simplified by DrAyushGoel @ www.MedicoNotebook.com
Other Considerations

(POEMS)

- Persisting co-morbid conditions
- Encouragement and support outside of clinical setting
  - Family and social support
Endocrine (POEMS)
Endocrine Dysfunctions in LBC

- 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
Mood & Neuropsychiatric Manifestations

- **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- bipolar 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
Activated by sunlight during daytime, SCN project inhibitory information to PVN in hypothalamus. The long axons of PVN then send nerve pulses down to the preganglionic sympathetic neurons of the spinal cord, which in turn modulate the activity of the superior cervical ganglia. The latter further project to the pineal gland to regulate the secretion of melatonin.

The circadian rhythm can be disrupted:
- Exposure to 400-500nm light at night
- Not receiving the light in the morning
- Jet lag – results in an imbalance of neurotransmitters and hormones
- Shift work where workers are exposed to visible light at night de-regulates a gene involved in controlling the circadian rhythm
- Exposure to light at abnormal times or due to change in location will either disrupt the clock gene function or cause activation of the ‘wake state’ of the circadian cycle at an abnormal time, such as in the evening.
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
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.
Beyond POEMS - Risk factors for poor clinical outcome

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
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.
Antibiotic therapy design based on these principles:

- 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
Antibiotic therapy design based on these principles:

- **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
Treatment of LBC is focused on Neuro-Immune Restoration and Cellular Recovery

- 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
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 neurtotropic 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 psychototropic 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... atovoquone (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
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 hepatosplenomegaly.

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.
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.
Methylation Defects

Spirochete Load

Co-Infections

Biofilm

Comorbidities

Oxidative Stress

MIN

MAX

Metabolic Derangements

POEMS
Methylation Defects
Co-Infections
Comorbidities
Spirochete Load
Oxidative Stress
MIN
MAX
Metabolic Derangements
POEMS
Methylation Defects

Comorbidities

Oxidative Stress

Spirochete Load
ELF, Maintenance and Healthy Lifestyle
Healthy Flight Pattern

SICK
+ Free Radicals

DETOX
+ Antioxidants
- Free Radicals
Healthy Flight Pattern

SICK
+ Free Radicals

DETOX
+ Antioxidants
- Free Radicals
Healthy Flight Pattern

SICK
+ Free Radicals

DETOX
+ Antioxidants
- Free Radicals
### Importance Of Treating Dysbiosis In Lyme Borreliosis

<table>
<thead>
<tr>
<th>EUBIOSIS</th>
<th>DYSBIOSIS</th>
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</thead>
<tbody>
<tr>
<td>Symbiotic coexistence of Host and Microflora</td>
<td>Harmful coexistence of Host &amp; Microflora</td>
</tr>
<tr>
<td>Protection of the intestinal mucosa against invading microorganisms</td>
<td>Damage to the intestinal epithelium- &gt;Gut wall thickening and reduced nutrient resorption</td>
</tr>
<tr>
<td>Contributes to immune system maturation and proper stimulation</td>
<td>Weakening of the Immune System</td>
</tr>
<tr>
<td>Antagonistic effect on undesired microbes</td>
<td>Unprocessed Antigen and Allergen exposure: Increases food sensitivity and non-specific immune reactions.</td>
</tr>
<tr>
<td>Nutrient Digestion</td>
<td>Increased gas production (H₂S, NH₃, CH₄, CO₂)</td>
</tr>
<tr>
<td>Vitamins, SCFA and protein synthesis</td>
<td>Acceleration of cell turnover – increased energy need</td>
</tr>
<tr>
<td>Better tolerance to antibiotic treatment</td>
<td>Vitamin deficiencies</td>
</tr>
</tbody>
</table>
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
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.
Functions of Methylation

- 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.
Applications of Methylation Cycle

- 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) & glutathione peroxidase (GPX1) perform the second step.

An excess in free radicals (oxidative stress) is damaging to cells and limits cellular recovery.
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.
Mitochondrial Oxidative Damage:

- Premature electron leakage to Oxygen generates Oxygen Radicals (Superoxides)

- Poorly functioning Mitochondria (ETC) increases superoxide production and results to increased Oxidative Stress
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.
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
FACTS and HYPOTHESES

- **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.
We should never underestimate the regenerative and compensatory power of the nervous system.
“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