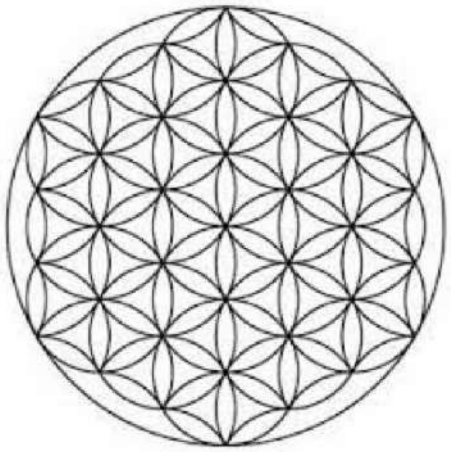
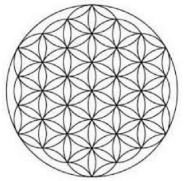
Tick-borne Disease Update

Julia Greenspan, ND



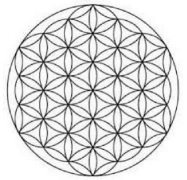
My Background

- Psychology undergraduate, social work in Portland Oregon in crisis management/Suicide prevention
- Licensed Naturopathic Doctor in NH since 2006
- ILADS member
- Tick borne disease focus for 10 years
- Over 4000 cases treated from patient population in New England and throughout the United States
- Practice energy healing modalities including Shamanism and Reiki
- No affiliations to claim



Conflict of interest

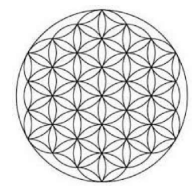
I have none



RISING ABOVE LYME DISEASE

A REVOLUTIONARY, HOLISTIC APPROACH TO MANAGING AND REVERSING THE SYMPTOMS OF LYME DISEASE— AND RECLAIMING YOUR LIFE

JULIA GREENSPAN, ND



Introducing Some of the Players

Lyme Borreliosis

Tick-borne Relapsing Fever

- Transmitted by soft-bodied ticks Ornithodoros, body lice
- Fast onset high fever, SOB, tachycardia/palpitations,
- Appears within seven days and relapses (hence forth the name)
- Headaches, myalgia, conjunctivitis, dry cough, N/V, hepatosplenomegaly, neuroinflammation, seizures, bells palsy, myocarditis
- Dx; serologic testing, blood smear with dark field microscopy

Lyme Borreliosis vs Relapsing Fever

- Relapsing Fever Clade within soft bodied ticks *Argasid* vector (detach in minutes)
  - Ticks lay low, stay with their hosts, protected from extreme temp variation, and have more genetic variability
- Host Range Expansion or “Host Switch” – expands diversity of “Borrelia experience”
  - Hosts can impose selective pressures while also spreading the pathogen geographically, the species it lives in over time while have impact on genetic variability – living in avians versus those who predominately are in mammals
  - The need for Borrelia to survive to be passed onto another host has adapted it to reside in current host for months to years evading the adaptive immunity

Oppler, et al. Evolutionary Genetics of *Borrelia*. Curr. Issues Mol. Biol. 42: 97-112. 2021

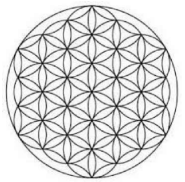
Lyme Borreliosis vs Relapsing Fever

- Lyme borreliosis clade within hard bodied ticks *Ixodes* vector (attach for days)
  - Less genetic variability even though they are in diverse hosts that cover more geographic range
- They have become skilled at adaptation with moving from vector to host "Selective pressure"
  - Weather may be driving force for they stand a better chance inside a being rather than out in the elements
  - Hard bodied ticks have harder time in high temps, Borrelia can withstand more temperature variations due to adaptations over time
  - Climate change may have significant impact on population of infected tick
  - *Borrelia burgdorferi sensu stricto* and *Babesia microti* co-infected in number beyond what would be by chance – reciprocal relationship
  - Equal amounts of spirochetes when there is single strain, then when there is multiple strains

Oppler, et al. Evolutionary Genetics of *Borrelia*. Curr. Issues Mol. Biol. 42: 97-112. 2021

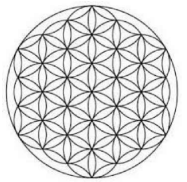
Babesiosis

- *Babesia duncani, Babesia microti, Babesia divergens* spread by ixodes scapularus ticks
- Malaria like infection that is a Piroplasm, parasitic within red blood cells
- 100 Babesia parasites identified, only a few pathogenic to humans
- Can be transmitted from mother to child and in blood banks
- N/V, Headache, Sweats, myalgia, depression/anxiety, no appetite, hepatosplenomegaly, intermittent fevers, eosinophilia, hiving, anemia, low platelets, elevated SED, elevated LDH, elevated billirubin
- Medication: Atovaquone, Malarone, Coartem, Ivermectin, Zithromax, Bactrim
- Testing: Antibody, blood smear, PCR



Bartonella

- Gram negative intracellular bacteria (Intraerythrocyctic parasitism, Lymphatic stage) – Ixodes ticks
- Evades innate immunity, triggers inflammatory cytokines
- Thought to use the lymphatic drainage system to avoid being brought to the lymphnode for elimination
- Evades with LPS structure with low endotoxin to remain undetected by phagocytes
- Transmitted by ticks, fleas, lice, flies, mites and spiders
- Endocarditis, various skin manifestations, central nervous system pathologies (eyes, encephalopathies)
- Tx: Rifampin, Rifabutin, Bactrim, Zithromax, more treatments listed later



Rocky Mountain Spotted Fever

- Head pain, N/V, myalgia, fever, cardiovascular, lethargy, confusion, petechial lesions, ataxic gait, paralysis, deafness, spasticity, aphasia, light sensitivity, respiratory system, myocarditis, pericarditis,
- Moves through lymphatic system and infects endothelial cells,
- Serology: hyponatremia, low platelets, WBC count impacted, elevated LFT's, PCR, IFA (IgG, IgM), elevated risk with low G6PD
- Doxycycline (age restrictions suspended) combined with Rifampin

Anaplasmosis – Human Granulocytic Anaplasmosis

- Colonizes in neutrophils, quick onset
- Neck pain, fevers, headaches, polyneuropathy, fascial palsy, chills, cough, rashes
- Within several tick species
- Clinical course related to Ehrlichiosis, but more CNS involvement
- Elevated LFT’s, thrombocytopenia, leukopenia
- Dx: Blood smear, PCR, IFA IgM, IgG

Ehrlichiosis (chaffeensis, ewingii)

- Lonestar tick vector
- Neck pain, fevers, headaches, polyneuropathy, fascial palsy, chills, cough, rashes, N/V
- Invades monocytes and macrophages, develop colonies
- Same symptoms seen with previous infections
- Dx: antibody testing, PCR, blood smear
- Tx Doxycycline, rifampin
- False positives can happen if there is Lyme disease, RMSF, Q fever

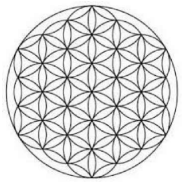
How can we best serve TBD patients?

Case History

Testing

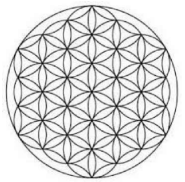
Treatment

Patience and Persistence…more patience



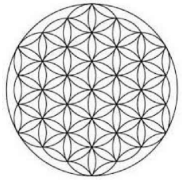
My Symptom FAQ's in Visit

- Head: Pain, hair loss, dizziness, lesions on the scalp
- Face: Abnormal sensations, fascial asymmetry, pain, rashes, difficulty with speech (comes and goes)
- Ears: tinnitus, pain in the ears
- Eyes: Floaters, light sensitivity, eye pain, droop, visual loss, diagnosis of optic neuritis
- Neck: pain, lymphadenopathy, sensations in the throat, head tremor
- Skin: **Rashes**, change in sensation, hives, shingles



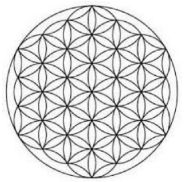
My Symptom FAQ's in Visit

- Cardiovascular: Heart palpitations, chest pain, syncope, **low**/high blood pressure
- Respiratory: Shortness of breath, sighing, post-nasal drip, rib pain,
- Digestive: change in bowel habit, any difficulties elimination, abdominal pain, ability to eat
- M/S: Pain in joints, muscles. Location, pattern of discomfort (migratory, stationary), swelling, burning
- Neurological: Memory, word recall, brain fog, gait, tremor, twitches,



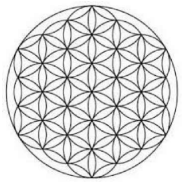
My Symptom FAQ's in Visit

- Urogenital/Hormone:
  - Female: cycles, bladder pain, pain with intercourse, uterine issues, pelvic pain, low libido
  - Male: prostate health, low libido
  - Other endocrine imbalance: thyroid, diabetes, immune dysfunction
- **Trauma history, physical, mental, emotional**
- **Current stressors**
- **Level of support in one's life**



Trauma Assessment

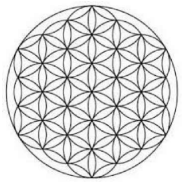
- Important to talk about their trauma history
- It’s a risk factor if they have a history of abuse with emotional, physical and/or sexual trauma
- Need to assess, I see trauma almost in all experiences with patients with severe debilitating Lyme disease, even if they down-play or initially deny it
- Fight-or-Flight with treatment experience, reactivation of victimization feelings
- Sympathetic dominance or the increased risk of having Autonomic Dysfunction due to low adrenal/neuro-hormone reserves with persistent trauma



Lyme disease is Multi-system Trauma

“Undigested” emotions potentially impacting course of recovery

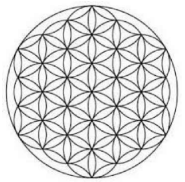
- Individual Trauma
- Trans-generational Trauma (miasma, family patterns)
- Medical System Trauma
  - Inability to trust the system



Lyme and Suicide Risk Factors

- Suicidal risk factors – most people who die of Lyme disease it's by their own hand.
- Took on average 8 years to find diagnosis
- Veterans and those with jobs outdoors
- 253 Charts reviewed with 68% being suicidal
- 10% had pre-existing depression, with 98% having depression after diagnosis
- Estimated 1200 suicides from Lyme disease per year

Robert C. Bransfield**. Suicide and Lyme and associated diseases.** Neuropsychiatr Dis Treat. 2017; 13: 1575–1587

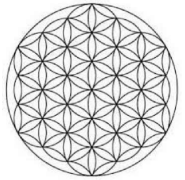


Herxing

- “Cytokine storm” impacting multiple systems as one time = **Suffering**
- Will trigger sympathetic nervous system and hormones of survival
- Old trauma memories or feelings will resurface
  - They will want escape but can’t from their own bodies, then suicidal ideation sets in
- Inability to complete treatment due to inflammation and panic/fear response

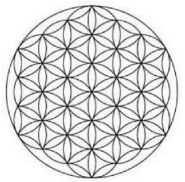
Biomagnetic Pair Therapy (Goiz) and Microbioenergetics (Miguel Ojeda-Rios, MD)

- The body is a biocomputer
  - Storing data from our current lift experiences into the now moment
  - This includes all data = transgenerational, archetypal, individual, collective
  - It speaks in 1's and 0's, yes or no (applied kinesiology, bioenergetics)
- This data holds a frequency that is resonate with health, disease, emotions, with microbes (beneficial and non-beneficial)
- When an illness is not resolving, we look deeper into resonate trauma, emotions, beliefs – this is data that can be collective, transgenerational or individual – **WE ASK THE BODY**



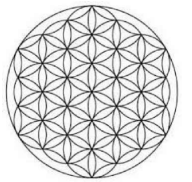
Biomagnetic Pair Therapy (Goiz) and Microbioenergetics (Miguel Ojeda Rios, MD)

- There is straight forward scan to check for magnetic pairs
- When treatment is failing to resolve symptoms (physical or energetic treatments), we ask the body if there is a program running that is in resonance with the infection
- These are imprints, emotions that are unconscious
- Once addressed there can be a rewrite of the code or belief that is in resonance with infection
- Release, resolution – can be immediate or may take time to unwind due to intensity



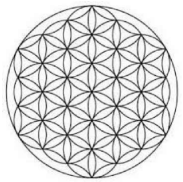
Emotional Code and Tick-borne Infection Miguel Ojeda Rios, MD

- Lyme disease – “Illness of the soul.” Bacteria that somatize transgenerational trauma/suffering. The loud soul.
- Babesia – I can no longer tolerate my circumstance
- Rocky Mountain Spotted Fever – confusion, delusion. What do I do? Where do I go?
- Bartonella – disillusionment
- Ehrlichiosis/Anaplasmosis – alienation
- Mycoplasma pneumonia – embarrassed by my personality, not enough
- Brucellosis – desperate desire for change



Testing

Casting Out a Wider Net



Detection of Spirochetes in CNS of 69 y/o women post-mortem

Gadila, et al. Frontiers in Neurology 10 May 2021 https://www.frontiersin.org/articles/10.3389/fneur.2021.628045/full

Diagnosed at at 54 y/o

Fever (104F), EM rash, headaches, joint pain

Pos ELISA, IgM, IgG – Lyme disease

10 days of treatment with Doxycycline initially

Detection of Spirochetes in the CNS of 69 y/o women post-mortem

- Treated with 6 weeks of ceftriaxone (no dose or frequency given) – 60% improvement in neurocognitive functioning
- Oral amoxicillin 500mg TID duration 6 mos post IV
- Says “initial improvement not sustained”
- Minocycline tried – “subsequent antibiotic therapy with minocycline tried was of no clear benefit.” - Omits dosage and duration tried
- At 62 y/o pos CSF for 4 bands IGG Lyme ab, all other markers in CSF neg for proteins or pathogen
- MRI showed “small vessel ischemia or demyelinating disorders like Lyme disease”, PET scan “diffuse Cortical hypometabolism worse in the posterior parietal and temporal lobes…sparing of the sensory motor cortex and visual cortex bilaterally – findings consistent with Alzeimers”

Detection of Spirochetes in the CNS of 69 y/o women post-mortem

- Two years later, sleep behavior disorder,
- Four years later, cognitive problems which worsened
- **Died 15 years after diagnosis of Lyme disease**
- Light sensitivity, paresthesia's, muscle fasciculations, and myoclonic jerks
- Neurocognitive testing showed deficits in executive functioning, visuospatial skills
- MRI showed mild atrophy, SPECT scan shows reduced blood perfusion in the right posterior parietal lobe and temporal lobes
- Only positive serological finding was IgG pos for Lyme at this time

Detection of Spirochetes in the CNS of 69 y/o women post-mortem

- Diagnosed with REM behavioral disorder with verbalization and movements and a neurodegenerative dementia
- Developed expressive aphasia, visual agnosia, anomia, deficits in executive functioning and calculation and mild memory problems.
- Developed oral dystonia – could not eat properly
- Personality changes, paranoia, REM sleep disorder, dememtia = Lewy body dememtia

Detection of Spirochetes in the CNS of 69 y/o women post-mortem

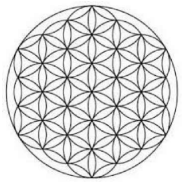
- Autopsy of brain:
- Mild enlargement of the lateral ventricle, temporal horn in particular
- Lewy bodies were present (nigral and corticol), with alpha-synuclein, neurofibrillary tangles, thickening of blood vessels,
- Moderate numbers of **activated microglial cells**
- **Large numbers of Macrophages**
- Amygdala and Spinal Cord pos DNA of Bb with nested PCR, pos IFA,

How can we apply this case in our practice?

- **Testing?** Pos for IGG AB for Bb. PCR was done for Bartonella henslae, Babesia microti, and Bb….all negative
- **How could medications such as antibiotics be used differently?** Mixing of drug classes, duration of treatment time
- Other factors present **elevated microglia**, **mast cell activation** with histamine response in the brain
- The ability of neurodegenerative disease to be concurrent with tick borne disease – throwing gas on the fire, brain inflammation support

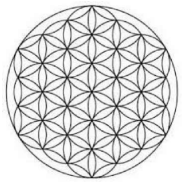
Testing: Casting Out a Wider Net

- Test for as many strains as you can for Borrelia, Tick-borne relapsing fevers, Bartonella (henslea, quintana, elizabethae, vinsonii), Babesia (duncani, microti), Rocky Mountain Spotted Fever, Francisella tulerensis, Q fever, Brucellosis, Mycoplasma pneumonia
- Check in with titers when you can. Example RMSF – this can go up and down throughout treatment, important to track this due to significance of the illness



Standard FOC Testing
(Quest, Labcorp, Hospital, Independent Labs)

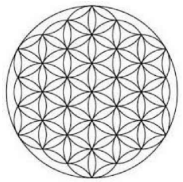
- Female/Male Hormones
- Adrenal hormones
- CMP/CBC
- Thyroid panel TSH, free T4, Free T3, antibodies, rev T3
- Vitamin D (ideal range 60-80)
- Viral panel with Herpes I/II, Epstein Barr, Parvovirus B19, CMV, HHV6
- ESR, SED, ANA, CRP, RF, CCP, Sjogrens Ab
- Anti-DNAse Strep B, Antistreptolysin O Ab



Standard FOC Testing

- Candida albicans
- Anti-Gliaden Antibodies, Tissue Trans-glutaminase, IgG, IgE food intolerance
- Histamine, Tryptase
- IgG subclass, IgE, IgA, IgM
- Iron, Ferritin
- Urine Mycotoxins
- Heavy metals

Treatment



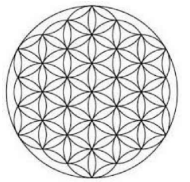
Biggest risk factor is delay in treatment

Acute Lyme disease is a tick-borne infection

Chronic Lyme disease is man made illness in majority of cases

Foundational Treatment Plan

- Reduction of inflammation and pain
- Treat the infections with a blend of complimentary medications
- Balance the hormone system with nutrients, herbs, and bio-identical hormones
- Improve detoxification pathways with supporting organs of elimination and greening life
- Boost immunity with herbal support, stress management, and proper nutrient balance
- Balance mood, clarity of thought and sleep regularity to improve sense of well-being
- Supporting a heathy digestive tract for safety and quality of life
- Improve strength and endurance with movement



Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?

- Sample size 3895 participants surveyed on MyLymeData patient registry from Lymedisease.org
- Non-responders to Treatment, Low Responders, High Responders (35%)
- Patient population were residents of US clinically diagnosed with Lyme disease
- Majority were late untreated Lyme disease when diagnosed
- All diagnosed by clinician
- 42% of remember being bit, 34% remember EM rash. 79% Pos labs. 68% co-infection is related

Johnson L, Shapiro M, Stricker RB, Vendrow J, Haddock J, Needell D. Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?. *Healthcare (Basel)*. 2020;8(4):383.

Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?

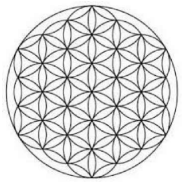
High treatment response was most closely associated with

(1) the use of antibiotics or a combination of antibiotics and alternative treatments

(2) longer duration of treatment

(3) oversight by a clinician whose practice focused on the treatment of tick-borne diseases.

Johnson L, Shapiro M, Stricker RB, Vendrow J, Haddock J, Needell D. Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?. *Healthcare (Basel)*. 2020;8(4):383.



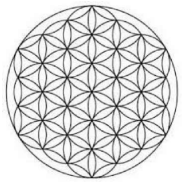
Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?

- 65% of high treatment responders were seeing a Lyme Literate ILADS associated practitioner for treatment
- 11% reported seeing an ID specialist
- “Compared to the general population and patients with other chronic diseases, CLD patients report significantly lower health quality status, more difficult mental and physical health days, a significant symptom disease burden, and greater activity limitations”
- “They also report impairment in their ability to work, increased utilization of healthcare services, and greater out-of-pocket medical costs, and they also report high rates of disability”

Johnson L, Shapiro M, Stricker RB, Vendrow J, Haddock J, Needell D. Antibiotic Treatment Response in Chronic Lyme Disease: Why Do Some Patients Improve While Others Do Not?. *Healthcare (Basel)*. 2020;8(4):383.

Treatment Duration

- There are many factors – patient tolerance, effectiveness of medication, PICC line maintenance, insurance coverage
- Most patients are on at least 3 months of IV's depending on the above factors
- Some…much longer
- We may switch classes depending on the infections present such as patient with RMSF, Babesia microti and Lyme disease
  - Start with IV doxycycline, then IV clindamycin (Doxy IV will do very well with Lyme disease without needing to use ceftriaxone)



Medication's that are used in similar cases

IV: Doxycycline 100mg-200mg per day (mostly 200mg per day) – **RMSF, Ehrlichiosis, Anaplasmosis** hard to get coverage unless these infections are present. **Insurance say no to coverage for Lyme, because oral is thought to be so well absorbed (Duel therapeutic effect of Doxycycline/Minocycline down reg NFKB – Bernardino, et al https://pubmed.ncbi.nlm.nih.gov/19301981/

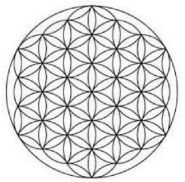
Zithromax 500mg per day – **Mycoplasma pneumonia, Bartonella** sp

Clindamycin 300-900mg twice per day **Babesia sp**

Used to use IV Rifampin 600mg daily more but tough due to being on backorder so often, **Bartonella, secondary medication for Ehrlichiosis, RMSF, Anaplasmosis**

Ceftriaxone 2000mg daily (Day 1-4), Flagyl 500mg + Zithromax 500mg back- to-back - **recommend before bed or later in evening (Day 5-7) Lyme disease – treating multiple phases of infection

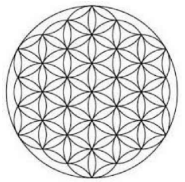
Ceftriaxone is not my favorite, have not seen someone fully recover often with this medication and the impact on the GB, already stressed can be difficult to manage



Ivermectin for Treatment of *Babesia microti*

- The fluorescence-based assay was used for evaluating the inhibitory effect of IVM on four *Babesia* species: ***B. bovis*, *B. bigemina*, *B. divergens*, *B. caballi*, and *Theileria equi***, the combination with diminazene aceturate (DA), clofazimine (CF), and atovaquone (AQ) on in vitro cultures, and on the multiplication of a ***B. microti*-infected** mouse model.
- This study shows validity in combination therapy, the most relevant for us is the evaluation of *B. microti, IN VIVO and IN VITRO*

Batiha GE, Beshbishy AM, Tayebwa DS, Adeyemi OS, Yokoyama N, Igarashi I. Evaluation of the inhibitory effect of ivermectin on the growth of *Babesia* and *Theileria* parasites in vitro and in vivo. *Trop Med Health*. 2019;47:42. Published 2019 Jul 11.



Ivermectin for Treatment of *Babesia microti*

- Used Ivermectin and Atovaquone over course of 45 days in the study, we know that treatment time is longer in humans, especially when chronic
- Dosing strategies Atovaquone 750mg/5ml (5-10 ml bid po) + Ivermectin 9-15mg QD dosing 5 days on, repeat cycles with two days off and retreat, I would repeat 4-6 times.
- There may be limitations in what you can get covered and being asked what it is used for.
- Having Peer reviewed literature can improve outcome with coverage

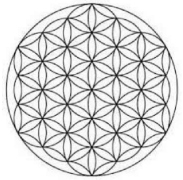
Batiha GE, Beshbishy AM, Tayebwa DS, Adeyemi OS, Yokoyama N, Igarashi I. Evaluation of the inhibitory effect of ivermectin on the growth of *Babesia* and *Theileria* parasites in vitro and in vivo. *Trop Med Health*. 2019;47:42. Published 2019 Jul 11.

Three Awesome Studies in 2020-21

Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani, (Zhang et al, 2020)

Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi (Feng J, et al, 2020)

Essential Oils with High Activity against Stationary Phase *Bartonella henselae* *(Ma X et al, 2019)*



Inhibitory Activity Against Babesia duncani

- *Cryptolepis sanguinolenta*
- *Artemisia annua*
- *Scutellaria baicalensis*

For comparison Clindamycin (37µM) and Quinine (10µM) were also used in the study

The herbs had a lower IC_{50} value than the antibiotics.

Zhang Y, Alvarez-Manzo H, Leone J, Schweig S, Zhang Y. Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani. *Front Cell Infect Microbiol*. 2021;11:624745. Published 2021 Mar 8. doi:10.3389/fcimb.2021.624745

Babesia – Cryptolepis sanguinolenta

- Active antiplasmodial components found in the root Isoquinoline alkaloids (antiviral, antifungal, antioxidant
- IC_{50} at 3.4µM compared to levels 10x's that amount for same effect with Clindamycin
- 90% Ethanol extract used
- *Cryptolepine*: was shown to impact the parasite at stages of division and growth Zhang Y, Alvarez-Manzo H, Leone J, Schweig S, Zhang Y. Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani. *Front Cell Infect Microbiol*. 2021;11:624745. Published 2021 Mar 8. doi:10.3389/fcimb.2021.624745
- Anti-neuroinflammatory: Impact LPS induced microglia targets NFkB
    - Abhijit Dey, Anuradha Mukherjee, in Discovery and Development of Neuroprotective Agents from Natural Products, 2018

Babesia duncani - Artemisia annua

- IC_{50} at 3.4µM
- 30% ethanol concentration
- Artesunate and Artemether, derived from Artemisinin showed more effective inhibitory value with *Babesia duncani*

Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of *B. burgdorferi*

- The active growers need no introduction, they are susceptible to treatment
- Stationary phase - atypical persister forms of Bb (round bodies, microcolonies, and biofilm)
- Daptomycin and Dapsone are most effective for persister cells but are difficult to get covered, more invasive with requiring IV's (Daptomycin), side effects of both (Dapsone/Daptomycin)

Feng, J., Leone, J., Schweig, S., & Zhang, Y. (2020). Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of *B. burgdorferi*. *Frontiers in medicine*, *7*, 6. https://doi.org/10.3389/fmed.2020.00006

Borrelia persisters

"The new definition of persisters can be as follows: persisters refer to genetically **drug susceptible** quiescent (non-growing or slow growing) organisms that survive exposure to a given cidal antibiotic or drug and have the capacity to revive (regrow or resuscitate and grow) under highly specific conditions" Zhang Y. Persisters, persistent infections and the Yin-Yang model. *Emerg Microbes Infect*. 2014;3(1):e3. doi:10.1038/emi.2014.

Persisters are tolerant to antibiotic therapy without becoming resistant
This is not inherited through cell lines – resistant versus persistent (stable inherited drug resistant behaviors)

Rudenko, N., Golovchenko, M., Kybicova, K. *et al.* Metamorphoses of Lyme disease spirochetes: phenomenon of *Borrelia* persisters. *Parasites Vectors* **12,** 237 (2019). https://doi.org/10.1186/s13071-019-3495-7

Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of *B. burgdorferi*

Cryptolepis sanguinolenta and ***Polygonum cuspidatum***, showed **strong** activity against both growing B. burgdorferi and non-growing stationary phase B. burgdorferi.

Effective against stationary phase compared to doxycycline and cefuroxime

Cryptolepis sanguinolenta

***Juglans nigra* (Black walnut)**

***Polygonum cuspidatum* (Japanese knotweed)**

Artemisia annua (Sweet wormwood)

Uncaria tomentosa (Cat's claw)

Cistus incanus

Scutellaria baicalensis (Chinese skullcap)

Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020;7:6. Published 2020 Feb 21. doi:10.3389/fmed.2020.00006

Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi

Those not effective with non-growing:

Stevia rebaudiana, Andrographis paniculata, **Grapefruit seed extract**, **colloidal silver**, **monolaurin,** and **antimicrobial peptide LL37** had little or no activity against stationary phase *B. burgdorferi*.

Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020;7:6. Published 2020 Feb 21. doi:10.3389/fmed.2020.00006

Cryptolepis sanguinolenta

- Antimalarial – have historically used Cryptolepis for Babesia infections Bb – treats GROWING and NON-GROWING stationary phase Bb
- Anti-tuberculinic
- Anti-fungal
- Anti-parasitic
- **Cryptolepine – most well researched active component**
  - Change cellular morphology of the pathogenic cells, cellular breakdown
  - They do not know the MOA due to lack of in-depth research

Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020;7:6. Published 2020 Feb 21. doi:10.3389/fmed.2020.00006

Juglans nigra

- Bacteriostatic activity against log phase spirochetes of *B. burgdorferi* and *B. garinii* and bactericidal activity against *Borrelia* round bodies (Goc, et al 2016)

Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020;7:6. Published 2020 Feb 21. doi:10.3389/fmed.2020.00006

Baca

Polygonum cuspidatum

- anti-tumor, antimicrobial, anti-inflammatory, neuroprotective, and cardioprotective effects, with the polyphenol resveratrol being one of the main active constituents.
- *In vitro* testing shows resveratrol exhibited activity against log phase spirochetes of *Borrelia burgdorferi* and *Borrelia garinii*, minimal activity against borrelia round bodies, and no significant activity against borrelia associated biofilms
- Active ingredient Polydatin
- Cardioprotective, neuroprotective, anti-inflammatory, immunoregulatory, lung and liver protective
  - Qiao-Hui Du, Cheng Peng & Hong Zhang (2013) Polydatin: A review of pharmacology and pharmacokinetics, Pharmaceutical Biology, 51:11, 1347-1354, DOI: 10.3109/13880209.2013.792849

Feng J, Leone J, Schweig S, Zhang Y. Evaluation of Natural and Botanical Medicines for Activity Against Growing and Non-growing Forms of B. burgdorferi. Front Med (Lausanne). 2020;7:6. Published 2020 Feb 21. doi:10.3389/fmed.2020.00006

FDA Approved Tx Stationary Phase Bartonella henselae

- Transmitted by ticks, fleas, sandflies, mosquitos gram neg bacteria
- Can persist in the blood as “intra-erythrocytic parasitism”
- Can take shelter in RBC, evading human immune system & ABX exposure
- Hard to grow in medium which makes it hard to research, just like Bb
- The first-line antibiotics for treatment of Bartonella infections include **doxycycline, erythromycin, azithromycin, tetracyclines, gentamicin, rifampin, ciprofloxacin, and sulfa drugs**

Li T, Feng J, Xiao S, Shi W, Sullivan D, Zhang Y. Identification of FDA-Approved Drugs with Activity against Stationary Phase Bartonella henselae. Antibiotics (Basel). 2019;8(2):50. Published 2019 Apr 29. doi:10.3390/antibiotics8020050

Bartonella henselae and Biofilm

- *"B. henselae* is able to adhere to host cells and form a biofilm"
- "The ability of a microbe to make biofilm linked to chronic disease"
- "Biofilm regulation in *B. henselae* consists of a complex gene regulatory system that allows the bacteria to survive in different phases of the lifecycle, resist antibiotic treatment, and persist in the human host"
- "susceptible to minocycline and macrolide antibiotics such as erythromycin, clarithromycin, azithromycin, and fluoroquinolone"
- Article recommends Aminoglycosides, for endocarditis added with another ABX

Citation: Okaro, U.; George, S.; Anderson, B. What Is in a Cat Scratch? Growth of *Bartonella henselae* in a Biofilm. Microorganisms 2021, 9, 835. https://doi.org/10.3390/ microorganisms9040835

FDA Approved Tx Stationary Phase Bartonella henselae

- Azole drugs (sulconazole, econazole, oxiconazole, butoconazole, clotrimazole, bifonazole, and miconazole), daptomycin, methylene blue, amifostine (Ethyol), Lopinavir/ritonavir, colistin, amikacin, nitroxoline, berberine, verteporfin, pentamidine, aprepitant, clinafloxacin, and clofoctol
- **Rifampin** most effective inhibiting growing *B. henselae* with the lowest MIC, **did not kill** all stationary phase *B. henselae* cells
- Same thing with Doxycycline, Zithromax – best for active phase

Li T, Feng J, Xiao S, Shi W, Sullivan D, Zhang Y. Identification of FDA-Approved Drugs with Activity against Stationary Phase Bartonella henselae. Antibiotics (Basel). 2019;8(2):50. Published 2019 Apr 29. doi:10.3390/antibiotics8020050

FDA Approved Tx Stationary Phase Bartonella henselae

- ***Gentamicin*** does not enter RBC's very easily which means that the infection harboring in the RBC's is hidden from Gentamicin
- ***Methylene blue*** works well for stationary *B. henslae* well documented effects on stationary Bb, antimalarial as well (Borrelia + Bartonella + Babesia)
- ***Daptomycin*** did well, but has high MIC value, is usually only helpful for gram-positive bacteria, this is the first proof of it showing activity against gram neg bacteria (**Borrelia + Bart)**
- ***Pyrvinium*** impact on stationary Bartonella good but not well absorbed in human body

Essential Oils for TBD

- Suntres ZE, Coccimiglio J, Alipour M. The bioactivity and toxicological actions of carvacrol. Crit Rev Food Sci Nutr. 2015;55(3):304-18. doi: 10.1080/10408398.2011.653458. PMID: 24915411
- Feng J, Zhang S, Shi W, Zubcevik N, Miklossy J, Zhang Y. Selective Essential Oils from Spice or Culinary Herbs Have High Activity against Stationary Phase and Biofilm *Borrelia burgdorferi*. *Front Med (Lausanne)*. 2017;4:169. Published 2017 Oct 11. doi:10.3389/fmed.2017.00169

Essential oils – Antimicrobial/Biofilm

- Feng et al. **Selective Essential Oils from Spice or Culinary Herbs Have High Activity against Stationary Phase and Biofilm *Borrelia burgdorferi. Frontiers in Medicine, October 2017***
- Oregano, Cinnamon, Clove oil greatest antimicrobial activity at lowest concentration
- Oregano oil was the most potent with active ingredient Carvacol
  - Cell membrane disruptor, biofilm disruption
- Bergamot (Citrus family) – most effective on stationary phase Borrelia
- Apply topically – locally with carrier like coconut oil, olive oil, almond oil
- We do not advocate for internal use unless being medically managed
- We also use as needed for pain, sleep, cognition

Tick-borne Disease Update

Julia Greenspan, ND