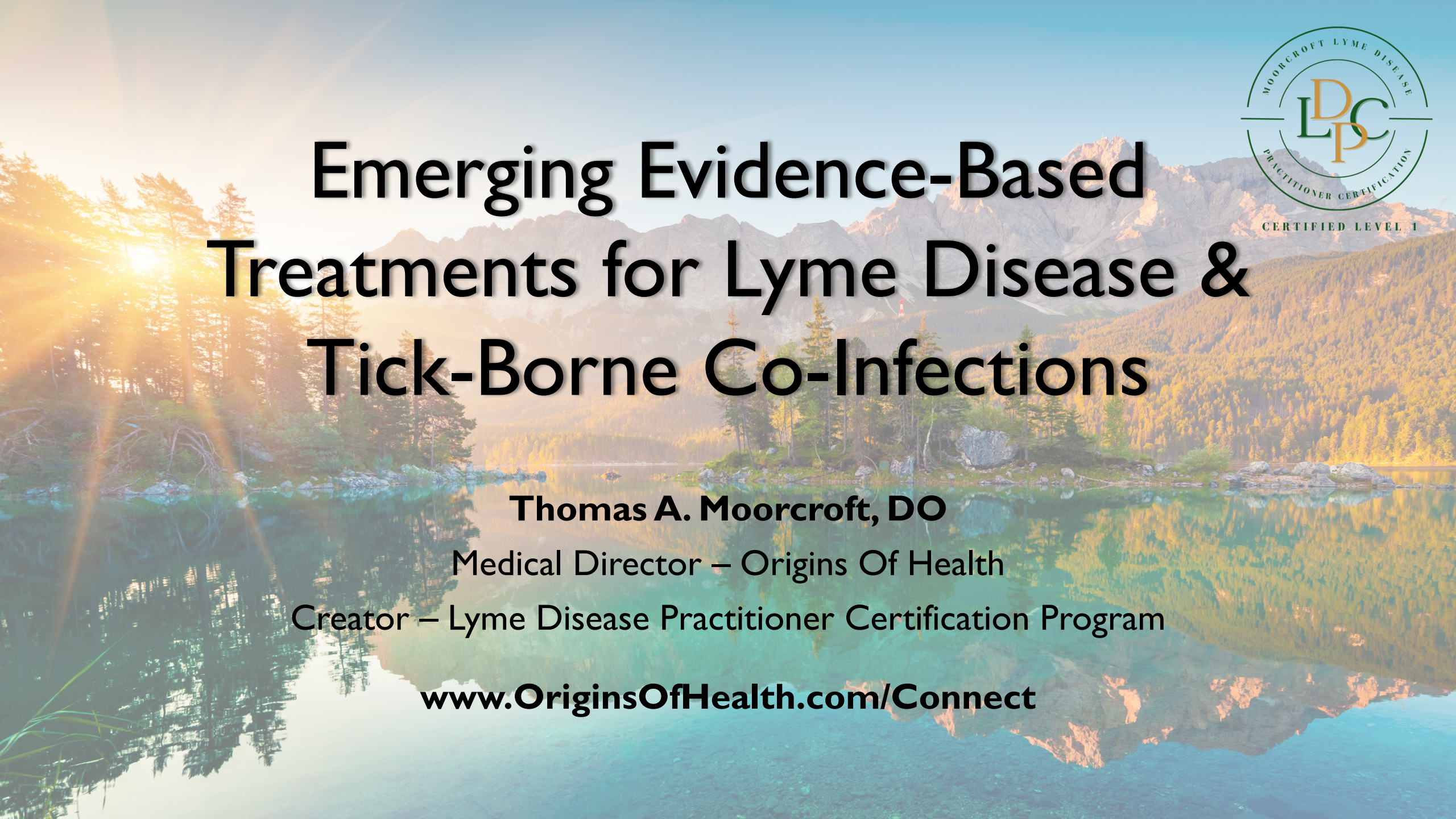

Emerging Evidence-Based Treatments for Lyme Disease & Tick-Borne Co-Infections

Thomas A. Moorcroft, DO

Medical Director – Origins Of Health

Creator – Lyme Disease Practitioner Certification Program

www.OriginsOfHealth.com/Connect

Learning Objectives

To develop an understanding of the frequency of tick-borne co-infection and the increased risk of patient co-infection from tick bite, including how this impacts presentation of symptoms and laboratory testing.

To develop an understanding of log and stationary bacterial growth as well as other bacterial persister forms and how each phase requires different treatment approaches.

To develop an understanding of the most up to date, evidence-based growing, stationary and persister co-infection treatments.

TickEncounter Resource Center **Ixodes scapularis (Blacklegged ticks or Deer ticks)**

Lyme disease, Babesiosis, Anaplasmosis, B. miyamotoi, Powassan virus

Contents lists available at ScienceDirect

Ticks and Tick-borne Diseases

journal homepage: www.elsevier.com/locate/ttbdis

Microbiome analysis of *Ixodes scapularis* ticks from New York and Connecticut

Rafal Tokarz[a,*], Teresa Tagliafierro[a], Stephen Sameroff[a], D. Moses Cucura[b], Alexandra Oleynik[a], Xiaoyu Che[a], Komal Jain[a], W. Ian Lipkin[a]

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[b] Division of Vector Control, Suffolk County Department of Public Works, Yaphank, NY, 11980, United States

ARTICLE INFO

Keywords:
Ticks
Metagenomics
High-throughput sequencing
Borrelia
Bartonella
Ixodes scapularis

ABSTRACT

We employed high throughput sequencing to survey the microbiomes of *Ixodes scapularis* collected in New York and Connecticut. We examined 197 individual *I. scapularis* adults and pools from 132 adults and 197 nymphs. We detected *Borrelia burgdorferi* sensu stricto in 56.3% of individual ticks, *Anaplasma phagocytophilum* in 10.6%, *Borrelia miyamotoi* in 5%, *Babesia microti* in 7.6%, and Powassan virus in 3.6%. We did not detect *Borrelia mayonii*, *Ehrlichia muris eauclairensis*, *Bartonella* spp. or pathogenic *Babesia* species other than *B. microti*. The most abundant bacterium (65%), and only rickettsial species identified, was the endosymbiont *Rickettsia buchneri*. A filarial nematode was found in 13.7% of adult ticks. Fourteen viruses were detected including South Bay virus (22%) and blacklegged tick phlebovirus 1 and 2 (73%). This study provides insight into the microbial diversity of *I. scapularis* in New York State and Connecticut.

Table 2
Prevalence of *I. scapularis*-associated microbes.

Agent	Prevalence (# of positive ticks)
Bacteria	
Anaplasma phagocytophilum	10.6% (21)
Borrelia burgdorferi s.s.	56.3% (111)
Borrelia miyamotoi	5.07% (10)
Rickettsia buchnerii	65.0% (128)
Invertebrate	
Babesia microti[*]	8.6% (17)
Babesia odocoilei[*]	8.6% (17)
Ixodes scapularis nematode	13.7% (27)
Virus	
Blacklegged tick phlebovirus	73.10% (144)
BLTV-associated virus 1	5.10% (10)
BLTV-associated virus 2	1% (2)
Powassan virus	3.60% (7)
South Bay virus	21.80% (43)
Suffolk virus	9.60% (19)

Tokarz 2019

ELSEVIER

Ticks and Tick-borne Diseases

Volume 10, Issue 2, February 2019, Pages 360-364

Original article

Regional prevalences of *Borrelia burgdorferi*, *Borrelia bissettiae*, and *Bartonella henselae* in *Ixodes affinis*, *Ixodes pacificus* and *Ixodes scapularis* in the USA

Borrelia burgdorferi – 13.9%
Bartonella henselae – 2.5%

N=929

In North Carolina (n=155)
Borrelia spp. - 63.2% and *B. henselae* - 10.3%

CERTIFIED LEVEL 1

Lyme Disease

Classic Presentation

Early Localized Disease (days-weeks)

– EM, Flu-like symptoms

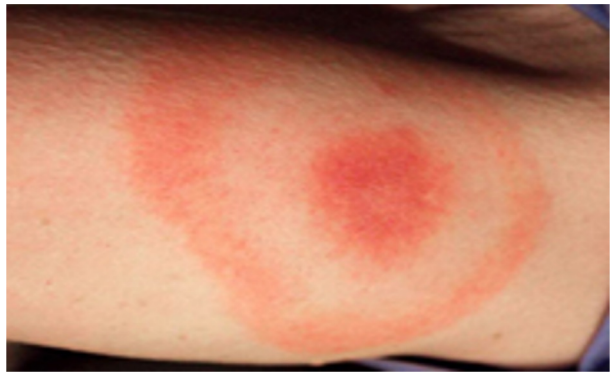
Early Disseminated Disease (days-weeks)

– Neurologic, Cardiac, Ocular symptoms

Late Disease (months-years)

– Arthritis, Neurologic

The EM Rash



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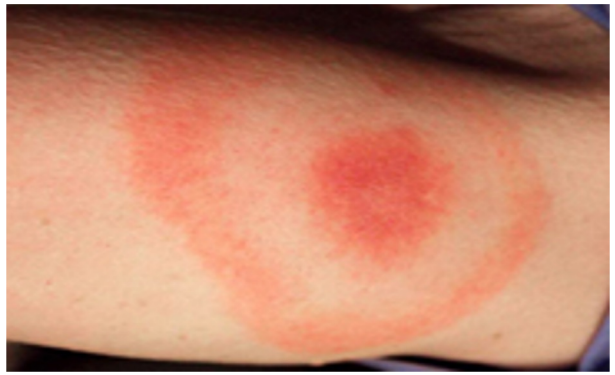

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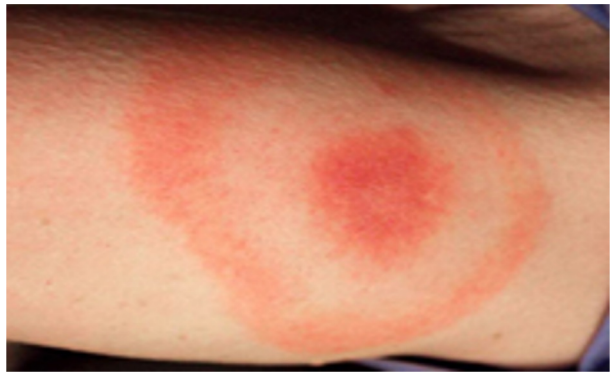

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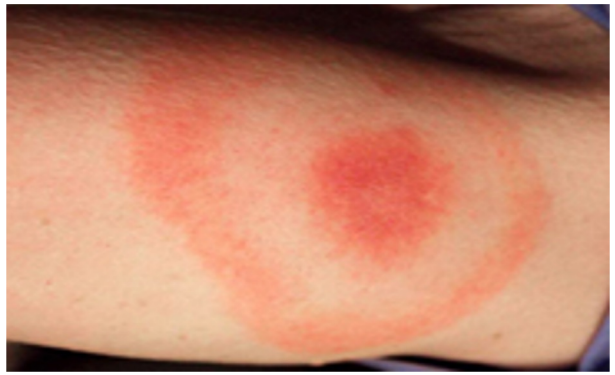

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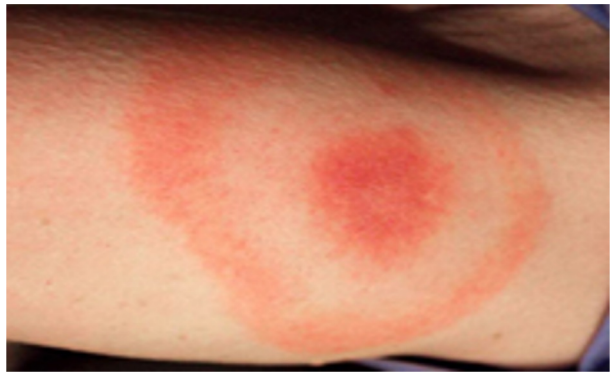

Thomas A. Moorcroft, DO

www.dermnet.com

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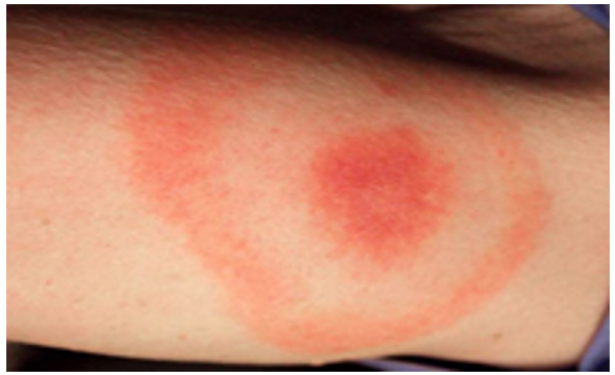


Clinical Presentation

Joint & muscle pains

Brain fog

Numbness & Tingling

Dizziness +/- syncope

Heart palpitations

Shortness of breath

Gastrointestinal distress

- Chronic gastritis, duodenitis, colitis
- Multiple food allergies, Leaky gut

Fried 2004
Fried 1996

Clinical Presentation

International Journal of General Medicine

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Empirical validation of the Horowitz Multiple Systemic Infectious Disease Syndrome Questionnaire for suspected Lyme disease

This article was published in the following Dove Press journal:
International Journal of General Medicine
4 September 2017
Number of times this article has been viewed

Maryalice Citera[1]
Phyllis R Freeman[2]
Richard I Horowitz[2]

[1]Department of Psychology, State University of New York at New Paltz, New Paltz, NY, [2]Hudson Valley Healing Arts Center, Hyde Park, NY, USA

Purpose: Lyme disease is spreading worldwide, with multiple *Borrelia* species causing a broad range of clinical symptoms that mimic other illnesses. A validated Lyme disease screening questionnaire would be clinically useful for both providers and patients. Three studies evaluated such a screening tool, namely the Horowitz Multiple Systemic Infectious Disease Syndrome (MSIDS) Questionnaire. The purpose was to see if the questionnaire could accurately distinguish between Lyme patients and healthy individuals.

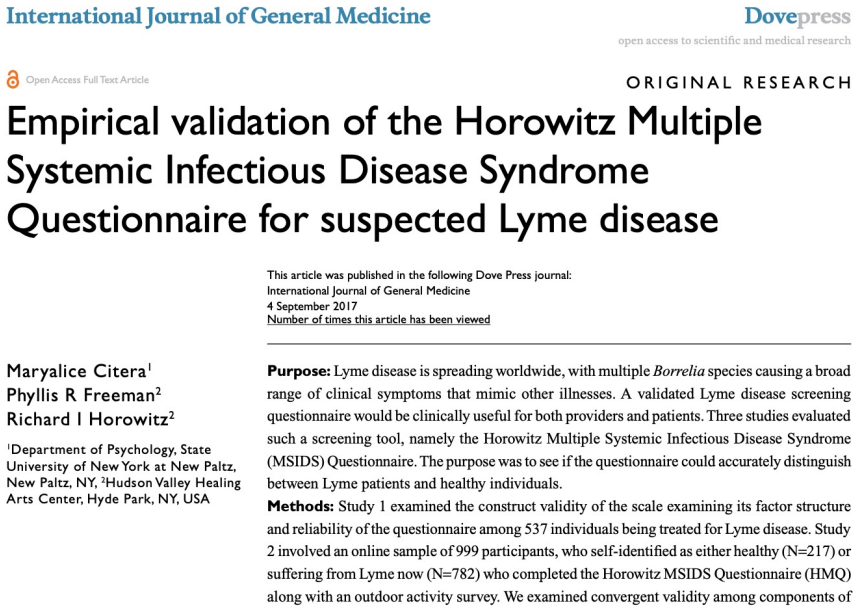
Methods: Study 1 examined the construct validity of the scale examining its factor structure and reliability of the questionnaire among 537 individuals being treated for Lyme disease. Study 2 involved an online sample of 999 participants, who self-identified as either healthy (N=217) or suffering from Lyme now (N=782) who completed the Horowitz MSIDS Questionnaire (HMQ) along with an outdoor activity survey. We examined convergent validity among components of

Key indicators of Lyme

Migratory joint pain

Migratory nerve pain/paresthesias

Clinical Presentation



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Key indicators of Lyme

Migratory joint pain

Migratory nerve pain/paresthesias

Differential of migratory pain includes:

- Crohn's/IBD
- Gonococcal arthritis
- Hepatitis A,B,C,D,E

Lyme in Children

About 50% presents as a GI complaint

- Isolated abdominal pain without clear etiology

Lyme in Children

About 50% presents as a GI complaint

- Isolated abdominal pain without clear etiology

Neuropsychiatric presentations

- Acute behavioral changes
- Regression
- Tics
- PANS/PANDAS

Treatment Viewpoints

Single Antibiotic

- Doxycycline
- Cefuroxime
- Amoxicillin

Duration

- 10-21 days

Single course of tx

Persistence of *Borrelia burgdorferi* in Rhesus Macaques following Antibiotic Treatment of Disseminated Infection

Monica E. Embers[1]*, Stephen W. Barthold[4], Juan T. Borda[2], Lisa Bowers[1], Lara Doyle[3], Emir Hodzic[4], Mary B. Jacobs[1], Nicole R. Hasenkampf[1], Dale S. Martin[1], Sukanya Narasimhan[5], Kathrine M. Phillippi-Falkenstein[3], Jeanette E. Purcell[3¤], Marion S. Ratterree[3], Mario T. Philipp[1]*

1 Divisions of Bacteriology & Parasitology, Tulane National Primate Research Center, Tulane University Health Sciences Center, Covington, Louisiana, United States of America, **2** Comparative Pathology, Tulane National Primate Research Center, Tulane University Health Sciences Center, Covington, Louisiana, United States of America, **3** Veterinary Medicine, Tulane National Primate Research Center, Tulane University Health Sciences Center, Covington, Louisiana, United States of America, **4** Center for Comparative Medicine, Schools of Medicine and Veterinary Medicine, University of California Davis, Davis, California, United States of America, **5** Section of Rheumatology, Department of Internal Medicine, Yale University School of Medicine, New Haven, Connecticut, United States of America

28 days oral = 0% cure

28 days IV + 56 days oral = 27% cure

Embers 2012

PLOS ONE

RESEARCH ARTICLE

Variable manifestations, diverse seroreactivity and post-treatment persistence in non-human primates exposed to *Borrelia burgdorferi* by tick feeding

Monica E. Embers[1]*, Nicole R. Hasenkampf[1], Mary B. Jacobs[1], Amanda C. Tardo[1], Lara A. Doyle-Meyers[2], Mario T. Philipp[1], Emir Hodzic[3]

Our results demonstrate **host-dependent signs of infection** and variation in antibody responses.

Persistence may not be reflected by maintenance of specific antibody production by the host

Evidence of **persistent, intact, metabolically-active B. burgdorferi after antibiotic treatment** of disseminated infection

Borrelia burgdorferi

Spirochete

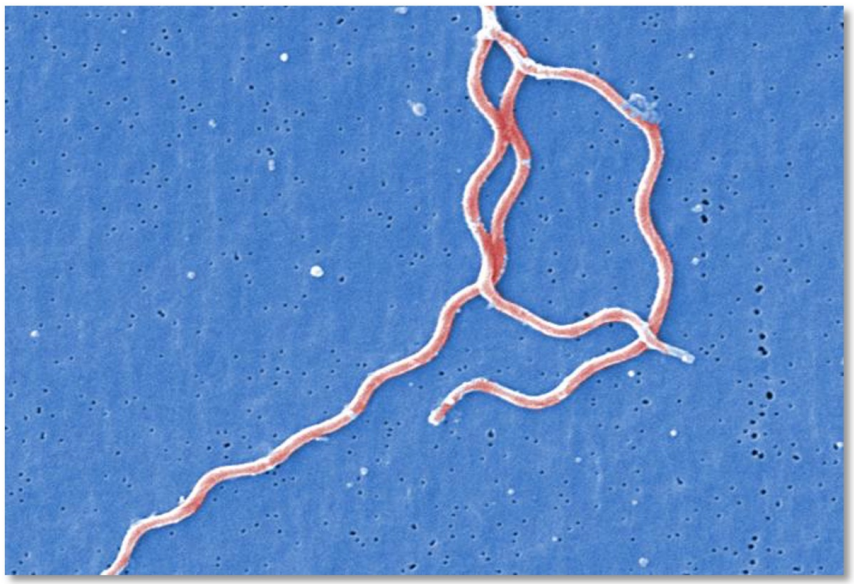

Image: CDC

Borrelia burgdorferi

Cell Wall Agent

Spirochete

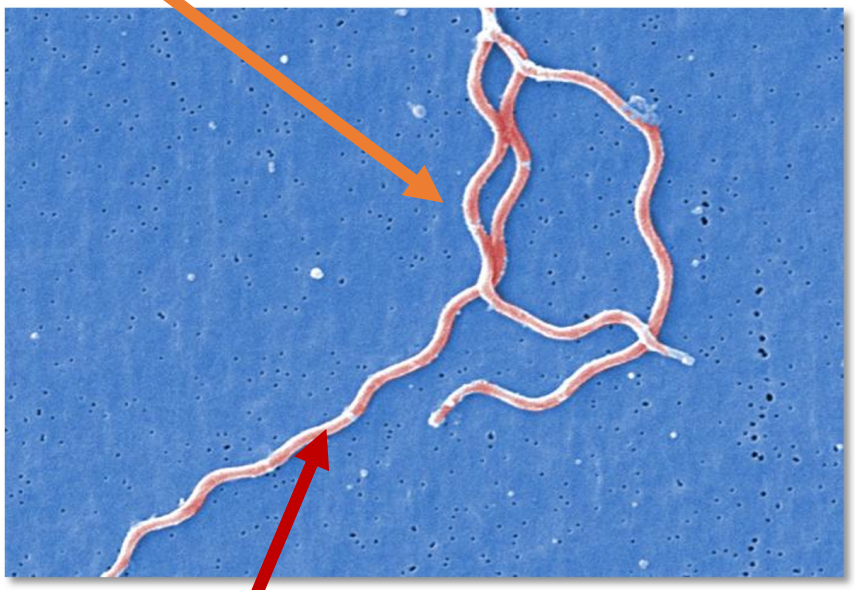

Image: CDC

Intracellular Agent

Treatment Viewpoints

Multiple Antibiotics

- Cell wall agents
  - Penicillins
  - Cephalosporins
- Intracellular
  - Tetracyclines
  - Macrolides

Duration

- 6 weeks or longer

May require multiple courses of tx

Role of natural tx

Antibiotics: Sites of Activity

Cell wall	Intracellular
Amoxicillin	Clarithromycin
Amoxicillin-clavulanate	Azithromycin
Penicillin G	Tetracycline
Benzathine PCN	Doxycycline
Cefuroxime	Minocycline
Cefuroxime	Tigecycline
Cefdinir	Fluoroquinolones
Ceftriaxone	TMP/SMZ
Cefotaxime	Rifampin
Ceftibuten	Other Rifamycins
Aminoglycosides	
Vancomycin	

Courtesy Maloney, Green, Szantyr, Moorcroft

How To Treat

Start Mono therapy and treat for 4 weeks, then reassess

Intracellular antibiotic + Probiotic

Minocycline + Probiotic

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WHY A TETRACYCLINE?

How To Treat

Start Mono therapy and treat for 4 weeks, then reassess

Intracellular antibiotic + Probiotic

Minocycline + Probiotic

ALWAYS ASSESS & REASSESS!

How To Treat

Start Combo therapy and treat for 4 weeks, then reassess

Cell Wall + Intracellular antibiotic + Probiotic

Cefuroxime + Minocycline + Probiotic

How To Treat

Start Combo therapy and treat for 4 weeks, then reassess

Cell Wall + Intracellular antibiotic + Probiotic

Cefuroxime + Minocycline + Probiotic

ALWAYS ASSESS & REASSESS!

Dosing

Standard dosing for most medications

Dosing

Standard dosing for most medications

Azithromycin & Amoxicillin

- Typically at upper end of dose range

DISCOVERY MEDICINE

Article Published in the Author Account of

Jie Feng

Stationary Phase Persister/Biofilm Microcolony of Borrelia burgdorferi Causes More Severe Disease in a Mouse Model of Lyme Arthritis: Implications for Understanding Persistence, Post-Treatment Lyme Disease Syndrome (PTLDS), and Treatment Failure

Borrelia Round Body or Cyst

Preac-Mursic 1996, Brorson 1997, Alban 2000, Brorson 1998, MacDonald 1988, MacDonald 2006

Borrelia burgdorferi

Cell Wall Agent

Spirochete

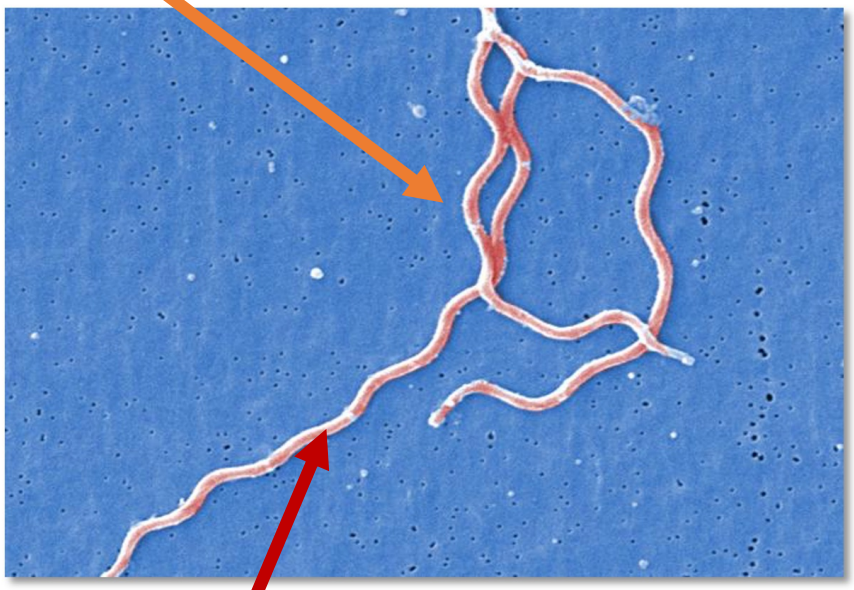

Image: CDC

Intracellular Agent

Cyst/Round Body

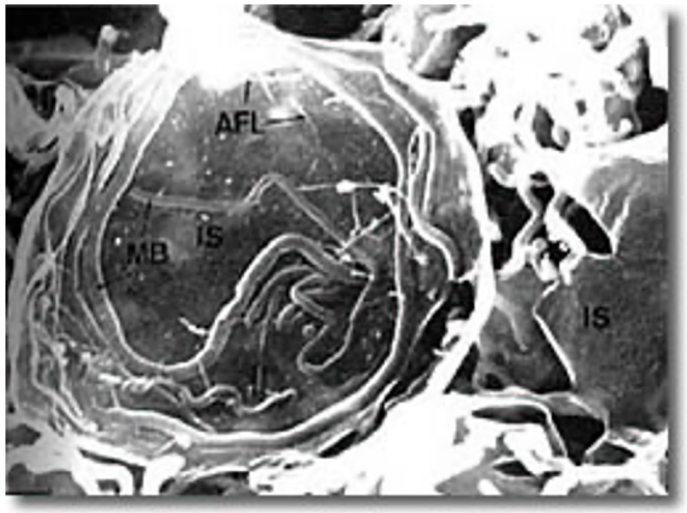

Image: Bradford 2004

Antibiotics: Sites of Activity

Cell wall	Intracellular	Cyst
Amoxicillin	Clarithromycin	Metronidazole
Amoxicillin-clavulanate	Azithromycin	Tinidazole
Penicillin G	Tetracycline	Hydroxychloroquine
Benzathine PCN	Doxycycline	Tigecycline
Cefuroxime	Minocycline	Daptomycin
Cefuroxime	Tigecycline	
Cefdinir	Fluoroquinolones	
Ceftriaxone	TMP/SMZ	
Cefotaxime	Rifampin	
Ceftibuten	Other Rifamycins	
Aminoglycosides		
Vancomycin		

Courtesy Maloney, Green, Szantyr, Moorcroft

Borrelia Round Body

Tinidazole 250mg BID x 3 consecutive days, 4 day break, repeat

- Can increase up to 750 TID prn
- I usually don't go above 500mg BID unless really making a difference

Borrelia Round Body

Tinidazole 250mg BID x 3 consecutive days, 4 day break, repeat

- Can increase up to 750 TID prn
- I usually don't go above 500mg BID unless really making a difference

- Bactericidal
- Inhibits DNA synthesis (first generation nitromidazole)
- No ETOH during or 3 days after – possible Disulfiram reaction
  - Recommend avoiding 3 days prior to starting also

- Possible peripheral neuropathy (? more in metronidazole)
  - B complex

Borrelia Round Body

Metronidazole 500mg BID x 3 consecutive days, 4 day break, repeat

- Can increase up to 750mg BID prn
- I generally don't go higher

Carcinogenic in mice and rats

- Bactericidal
- Inhibits nucleic acid synthesis (first generation nitromidazole)
- No ETOH during or **14 days after** – possible Disulfiram reaction
  - Recommend avoiding 3 days prior to starting also

- Possible peripheral neuropathy (? more in metronidazole)
  - B complex

Borrelia Round Body

Hydroxychloroquine 200mg BID

- ? Round body coverage
- Alkalinize intracellular compartment
  - ? Augment effects of intracellular antibiotics

Borrelia Round Body

Hydroxychloroquine 200mg BID

- ? Round body coverage
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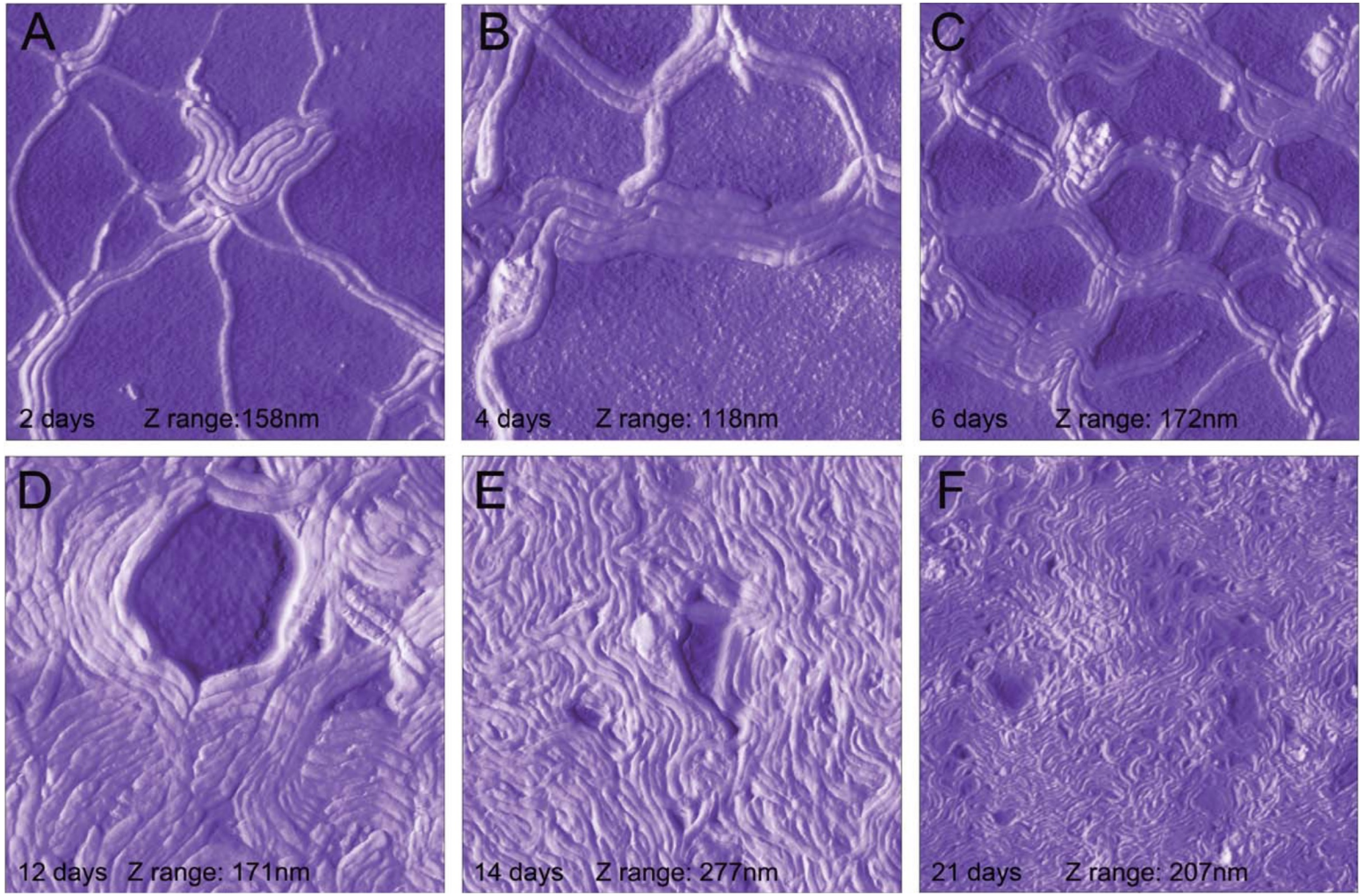
Grapefruit Seed Extract ???

Borrelia Biofilms



Sapi 2012, Sapi 2008, Costerton 1999

Biofilms

Liposomal treatments

- Liposomal Artemisinin
- Liposomal Botanical combination

Systemic Enzymes

- Nattokinase 100mg (2,000 FU) 1-2 capsules BID, away from food & other meds/supps
- Lumbrokinase 32mg (300,000 IU) 1-2 capsules BID, away from food & other meds/supps
- Serrapeptase 60,000 SPU 1-2 capsules BID, away from food & other meds/supps
- Combination enzymes

Biofilms

?? Stevia – Dr. Shapi – yes, Dr. Zhang - no

??Monolaurin – Goc 2015 – yes, Dr. Zhang - no

Essential oil study

- ?? Oil of Oregano
- ??Cinnamon
- ??Clove

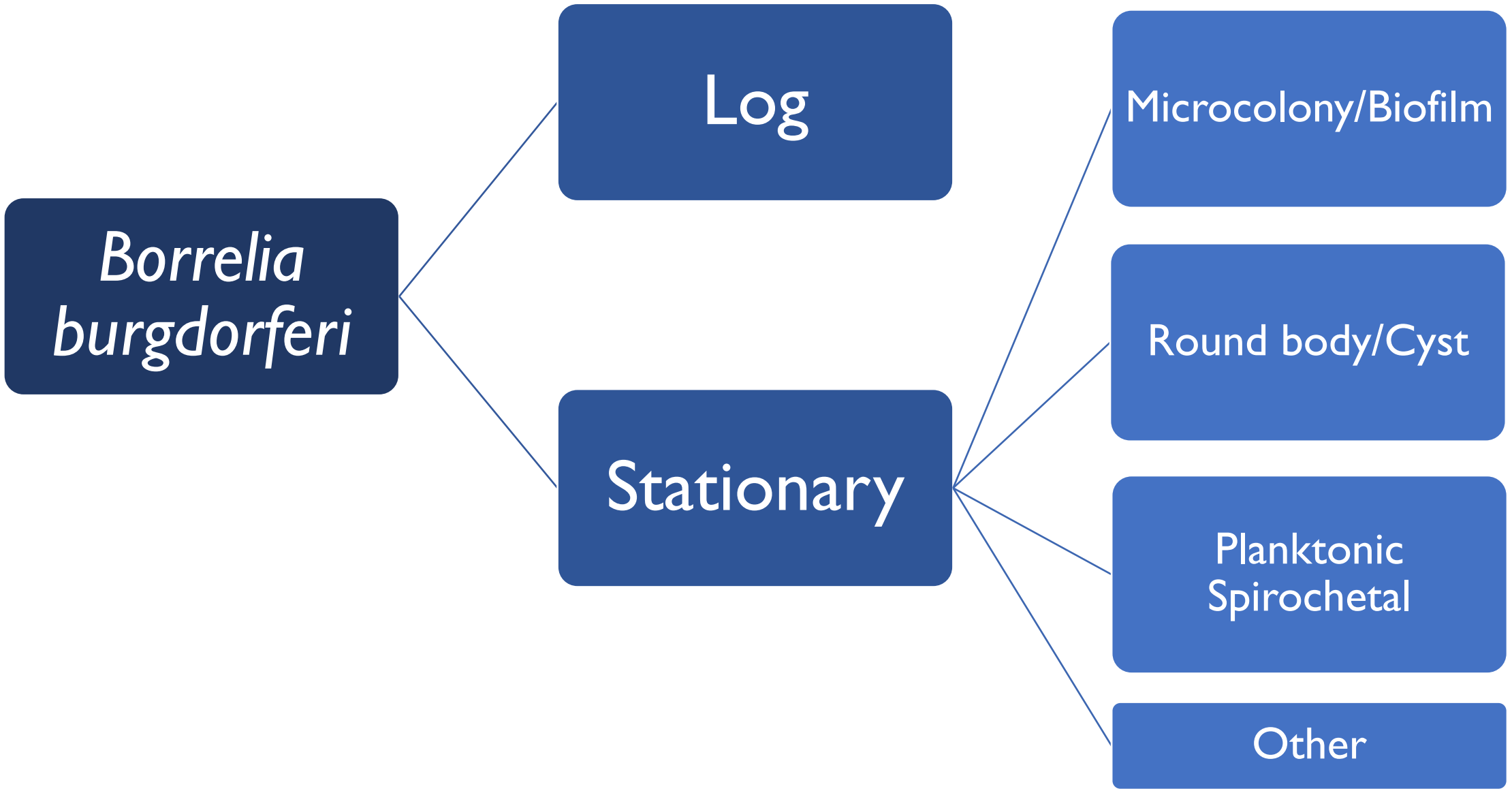
Biofilms

Dapsone

Daptomycin IV

?? Disulfiram

??Azlocillin IV



Stationary Forms - Lyme

frontiers in Medicine

ORIGINAL RESEARCH
published: 21 February 2020
doi: 10.3389/fmed.2020.00006

Check for updates

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

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Cryptolepis sanguinolenta**

Polygonum cuspidatum

Scutellaria baicalensis

Juglans nigra **(Stationary, Not Growing)**

Artemisia annua **(Stationary, Not Growing)**

Uncaria tomentosa **(Stationary, Not Growing)**

Cryptolepis is only herb or medication tested to eradicate B. burgdorferi stationary forms in subculture

Feng 2020

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All of these herbs outperformed Doxycycline & Cefuroxime

Cryptolepis is only herb or medication tested to eradicate B. burgdorferi stationary forms in subculture

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<u>Little or NO Activity</u>

Stevia rebaudiana

Andrographis paniculata

Grapefruit seed extract

Colloidal silver

Monolaurin

Antimicrobial peptide LL37

Feng 2020

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<u>Not Good for Growing *Borrelia*</u>

Artemisia annua

Juglans nigra

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<u>Not Good for Growing *Borrelia*</u>

Artemisia annua

Juglans nigra

Uncaria tomentosa

Good for Stationary

Feng 2020

Disulfiram

- inhibits aldehyde dehydrogenase
- able to form disulfides with other thiol-bearing molecules
- "**Potentially** causes the **inhibition of *B. burgdorferi* metabolism** as the formation of mixed disulfides with metal ions would compete for the zinc and manganese cofactors that are crucial to the survival of *B. burgdorferi*"

Gao 2020

Disulfiram

Initially, Goal dose: 500mg daily x 6-12 weeks

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Start at 250mg ½ tablet daily and increase every 1-2 weeks as able

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May need to go as low as 25mg every other day and titrate

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Some patients benefit from enteric coating

Disulfiram

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Start at 250mg ½ tablet daily and increase every 1-2 weeks as able

May need to go as low as 25mg every other day and titrate

Some patients benefit from enteric coating

More recent clinical experience shows:

- Likely don't need more than 250mg daily
- Doses as low as 25mg a few times a week can be effective

Disulfiram

No ETOH

Check LFTs regularly

- At least every 2 weeks initially
- More frequently prn

Liver support

- Liver support combinations
- RLA/ALA
- NAC

Disulfiram

Neuropathy

Disulfiram

Neuropathy

Monitor it closely

- If it starts, stop
- If it's full blown, stop
- B complex and GSH may help decrease risk

Disulfiram

Neuropathy

Monitor it closely

- If it starts, stop
- If it's full blown, stop
- B complex and GSH may help decrease risk

May take 1-2 months, rarely longer to recover

Dapsone

Anti-leprosy agent found to have anti-Borrelial activity

- including biofilms

Horowitz 2020

Dapsone

Anti-leprosy agent found to have anti-Borrelial activity

- including biofilms

Protocol - Dapsone, Doxycycline, Rifampin, Methylene Blue,

Leucovorin, L-5-MTHF, liposomal glutathione, Probiotics.

Dapsone

Week 1 - Dapsone 25 mg 1 one time a day

Week 2 - Dapsone 25 mg 1 two times a day

Week 3 - Dapsone 25mg 2 in AM and 1 in PM

Week 4 - Dapsone 25mg 2 in AM and 2 in PM

Weeks 5-12 - Dapsone 100mg 1 two times a day

Dapsone

Week 1 - Dapsone 25 mg 1 one time a day

Week 2 - Dapsone 25 mg 1 two times a day

Week 3 - Dapsone 25mg 2 in AM and 1 in PM

Week 4 - Dapsone 25mg 2 in AM and 2 in PM

Weeks 5-12 - Dapsone 100mg 1 two times a day

I find the need to continue titrating and protocol at least 4 months

Horowitz 2020

Dapsone

Check for G-6PD deficiency

Will lead to folate deficiency anemia

- Leucovorin & methylated folate in very high doses required
- **Below methylated folate 30mg daily & leucovorin 25mg BID** I see severe anemia

Frequently leads to methemoglobinemia

- Weekly CBCs & methemoglobin levels
- Methylene blue helps, but it still happens

Horowitz 2020

Borrelia miyamotoi

B. miyamotoi

EM Rash

Meningoencephalitis

Hearing loss

Horowitz 2020

B. miyamotoi

EM Rash

Meningoencephalitis

Hearing loss

Looks like Lyme + Anaplasma and/or Babesia

Horowitz 2020

B. miyamotoi

EM Rash

Meningoencephalitis

Hearing loss

Looks like Lyme + Anaplasma and/or Babesia

Treatment?

- Like Lyme??

Horowitz 2020

CERTIFIED LEVEL 1

Babesia

Babesiosis Symptoms

Fevers, chills

Sweats: day or night

Shortness of Breath

Air hunger

Rib pain

Sharp, shooting pains

Bone pain

Headache, especially **Head Pressure**

Hatcher 2001
Reubush 1977
Vannier 2012
White 199

Babesiosis Symptoms

Myalgias, Arthralgia

Encephalopathy/Brain fog

Numbness & Tingling

Fatigue

Depression & Anxiety

Insomnia

Dysautonomia

Gastrointestinal symptoms

Hatcher 2001
Reubush 1977
Vannier 2012
White 199

Babesiosis Treatment

Atovaquone + Azithromycin +/- TMP/SMZ

Atovaquone/Proguanil +/- macrolide

Clindamycin +/- Quinine

Babesiosis Treatment

Evidence of possible resistance in *Babesia*

- Should be using at minimum two drugs
- Possible role for triple drug protocols

Duration

- ? 4-5+ months

B. duncani Treatment

J Biol Chem. 2018 Dec 28;293(52):19974-19981. doi: 10.1074/jbc.AC118.005771. Epub 2018 Nov 21.

Establishment of a continuous *in vitro* culture of *Babesia duncani* in human erythrocytes reveals unusually high tolerance to recommended therapies.

Abraham A[1], Brasov I[2], Thekkiniath J[1], Kilian N[1], Lawres L[1], Gao R[1], DeBus K[1], He L[3], Yu X[4], Zhu G[4], Graham MM[5], Liu X[5], Molestina R[2], Ben Mamoun C[6].

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Abstract

Human babesiosis is an emerging tick-borne disease caused by apicomplexan parasites of the genus *Babesia* Clinical cases caused by *Babesia duncani* have been associated with high parasite burden, severe pathology, and death. In both mice and hamsters, the parasite causes uncontrolled fulminant infections, which ultimately lead to death. Resolving these infections requires knowledge of *B. duncani* biology

"These data suggest that current practices are of limited effect in treating the disease"

Abraham 2018

B. duncani Treatment

frontiers in Cellular and Infection Microbiology

ORIGINAL RESEARCH
published: 08 March 2021
doi: 10.3389/fcimb.2021.624745

Botanical Medicines Cryptolepis sanguinolenta, Artemisia annua, Scutellaria baicalensis, Polygonum cuspidatum, and Alchornea cordifolia Demonstrate Inhibitory Activity Against Babesia duncani

*Yumin Zhang[1], Hector Alvarez-Manzo[1], Jacob Leone[2], Sunjya Schweig[3] and Ying Zhang[4]**

[1] Department of Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Johns Hopkins University, Baltimore, MD, United States, [2] FOCUS Health Group, Naturopathic, Novato, CA, United States, [3] California Center for Functional Medicine, Kensington, CA, United States, [4] State Key Laboratory for the Diagnosis and Treatment of Infectious Diseases, National Clinical Research Center for Infectious Diseases, The First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, China

Zhang 2021

B. duncani Treatment

TABLE 1 | Evaluation of a panel of 46 herbal medicines at 0.01% (v/v) for inhibitory activity against *B. duncani* after 3 days of incubation.

Product Names	*Plants*	Inhibition (%)
Chinese Skullcap (90% EE)	*Scutellaria baicalensis*	84
Cryptolepis (90% EE)	*Cryptolepis sanguinolenta*	80
Cryptolepis (60% EE)	*Cryptolepis sanguinolenta*	70
Chinese Skullcap (60% EE)	*Scutellaria baicalensis*	68
Japanese knotweed (60% EE)	*Polygonum cuspidatum*	59
Sweet wormwood (30% EE)	*Artemisia annua*	58
Alchornea	*Alchornea cordifolia*	54
Japanese knotweed (90% EE)	*Polygonum cuspidatum*	42
Andrographis (90% EE)	*Andrographis paniculata*	37
Andrographis (60% EE)	*Andrographis paniculata*	36
Sweet wormwood (60% EE)	*Artemisia annua*	35
Andrographis (30% EE)	*Andrographis paniculata*	34
Cistus	*Cistus incanus*	34
Ashwagandha (30% EE)	*Withania somnifera*	33
Hemp oil	*Cannabis sativa*	26

Control - ethanol carrier at 30%, 60%, and 90%, did not show obvious inhibitory effect at up to 1% concentration.

Zhang 2021

Emerging Approaches To *Babesia* Tx

1. Atovaquone or Atovaquone/Proguanil
2. Artemisinin
3. Tafenoquine or Primaquine
4. Azithromycin
5. Systemic enzymes

Emerging Approaches To *Babesia* Tx

Atovaquone 750mg/5ml

- 5ml BID
- May start as low as 1.5ml BID in very ill patients
- Take with fat to increase absorption from low 20% to high 40%

Atovaquone/Proguanil 250mg/100mg

- 1 tablet BID
- May work up to 3 tablets BID

Emerging Approaches To *Babesia* Tx

Whole leaf artemisinin – 800-1000mg daily in divided doses

Liposomal artemisinin – 50mg capsules 2 BID 5 days/wk, 3wks/mo

- Studies revealing 4-5x increased absorbability

Emerging Approaches To *Babesia* Tx

Whole leaf artemisinin – 800-1000mg daily in divided doses

Liposomal artemisinin – 50mg capsules 2 BID 5 days/wk, 3wks/mo

- Studies revealing 4-5x increased absorbability

Artesunate

- Availability
- Cost

Emerging Approaches To *Babesia* Tx

Tafenoquine 150mg

- inhibits hematin polymerization, leading to parasite death
- 2 tablets once a week
- May need to start at ¼ of 1 tablet
- Reaches peak blood levels in 12 weeks (reportedly)

Emerging Approaches To *Babesia* Tx

Tafenoquine 150mg

- inhibits hematin polymerization, leading to parasite death
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- Some clinicians increase to 3-4 tablets weekly to bi-weekly**

Emerging Approaches To *Babesia* Tx

Tafenoquine 150mg

- inhibits hematin polymerization, leading to parasite death
- 2 tablets once a week
- May need to start at ¼ of 1 tablet
- Reaches peak blood levels in 12 weeks (reportedly)
- Some clinicians increase to 3-4 tablets weekly to bi-weekly**

- Some clinicians have been using a loading dose of 1 tablet daily x 3 days then 1 tablet weekly

Emerging Approaches To *Babesia* Tx

Primaquine 26.3mg

- exact mechanism of action unknown; binds to and alters DNA
- Start 1 tablet daily, increase to 3 tablets daily over weeks
- Can be used but much more frequent dosing (shorter half-life)

Emerging Approaches To *Babesia* Tx

Both have dose related methemoglobinemia

- Over 30mg daily of primaquine
- Over 300 mg of tafenoquine

Recommended to be on methylene blue when on higher doses**

Emerging Approaches To *Babesia* Tx

Both should not be used in patients with G6PD deficiency with <70% activity

- Technically, Primaquine can be used in those with 30-70% activity and monitored very closely for hemolysis, though the risk-benefit likely isn't worth it.
- *Tafenoquine for the radical cure and prevention of malaria: the importance of testing for G6PD deficiency*
  - https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7064913/

Emerging Approaches To *Babesia* Tx

Then add:

- Azithromycin
- Systemic enzymes

Emerging Approaches To *Babesia* Tx

Then add:

- Azithromycin
- Systemic enzymes

Emerging Approaches To *Babesia* Tx

Then add:

- Azithromycin
- Systemic enzymes

OR

Is there a better order?

Clofazimine

Plus Atovaquone to treat *B. microti*

Clofazimine

Plus Atovaquone to treat *B. microti*

Binds to mycobacterial DNA, inhibiting growth

Dosing based upon Leprosy experience

Clofazimine

300mg qMonth plus 50mg daily x 6-12 months

vs

100-200mg daily until controlled, then 100mg daily

CERTIFIED LEVEL 1

Bartonella

Bartonella Symptoms

Myalgias, Arthralgias

Headache

Fatigue, Decreased stamina

Tremors, Transient focal muscle fasciculation

Migratory peripheral neuropathy

Foot/Heel pain

Alcohol intolerance

Breitschwerdt 2010
Eskow 2001
Maggi 2012

Bartonella Symptoms

Mild Anxiety/Depression

OCD-type symptoms

Rage

Acute changes in personality or Regression

- Especially in kids

Unilateral symptoms

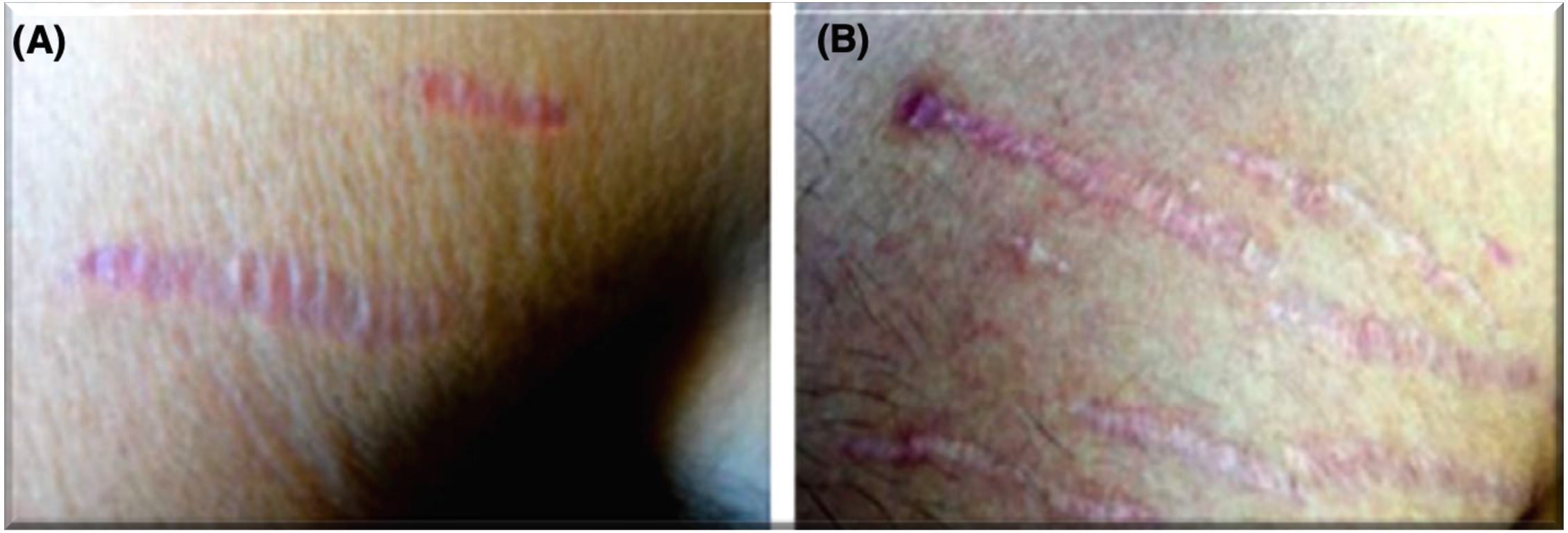
Oddities

- Tic disorders

PANS/ PANDAS

Breitschwerdt 2012
Schaller 2007
Charles Ray Jones – PC 2015
Ann Corson – PC 2015

Bartonella Striae?



Maluki 2019

Bartonella Pearls

Things we see, but to date have not been scientifically confirmed

Bartonella striae should blanch

- Other striae should not

Lymph nodes swollen

- Lyme has lymphadenitis without swelling

Subcutaneous nodules

- Inner forearm, lateral thigh

Bartonella Treatment

Azithromycin 500 mg on day one, then 250 mg for four days

- Under 45.5 kg: 10 mg/kg on day one, then 5 mg/kg for four days

Uptodate Accessed 8/26/20

Alternative 7-10 day courses

Clarithromycin 500 mg BID

- If under 45.5 kg, 15 to 20 mg/kg divided in two doses

Rifampin 300 mg BID

- In children, 10 mg/kg BID

Trimethoprim-sulfamethoxazole DS one tablet BID

- In children, trimethoprim 8 mg/kg per day, sulfamethoxazole 40 mg/kg per day, divided in two doses

Ciprofloxacin 500 mg BID if age >17 years

Uptodate Accessed 8/26/20

Bartonella Treatment

- In vitro sensitivities do not correlate well with in vivo
- Critical to use 2 antibiotics in serious infections
- "Our findings…could explain relapses observed using azithromycin [alone] for the treatment of *B. henselae* infections"

Biswas 2010
Rolain 2004

Bartonella Treatment

- In vitro sensitivities do not correlate well with in vivo
- Critical to use 2 antibiotics in serious infections
- "Our findings…could explain relapses observed using azithromycin [alone] for the treatment of *B. henselae* infections"

Double or Triple Intracellular agents

Biswas 2010
Rolain 2004

Bartonella Treatment

Duration of treatment is unclear

- High relapse rate if less than 15 days
- Recommend 3-4 months
  - If HIV + and bacillary angiomatosis or bacillary peliosis

Biswas 2006

Bartonella Treatment

Treat until symptom free, and then…

Reassess

- Resolved with treatment, returned after discontinuing
  - Unlikely "post-whatever syndrome"
  - Very unlikely to be completely new, unrelated illness

Diniz 2009

Bartonella Treatment

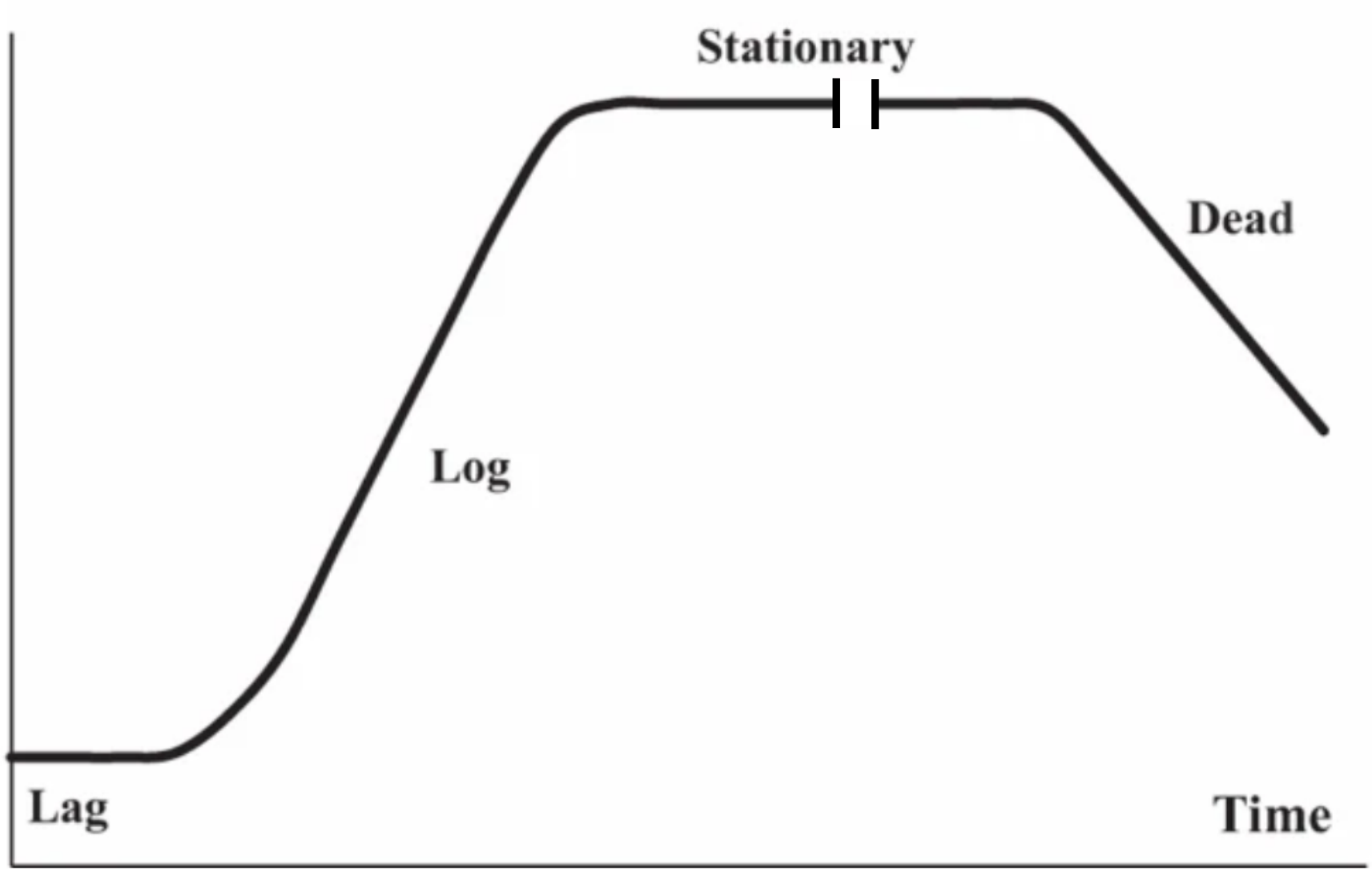
Treat until symptom free, and then…

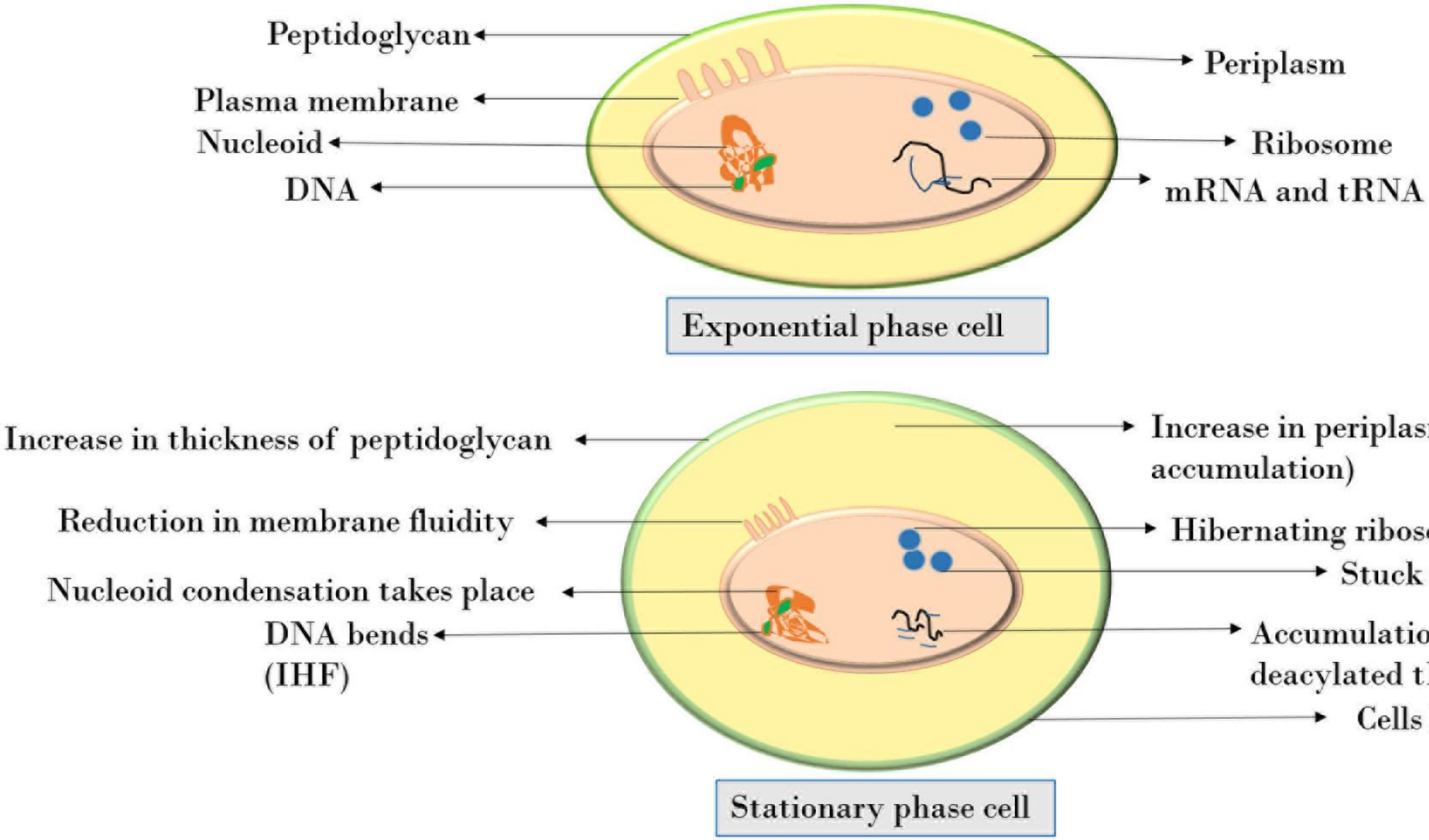
Reassess

- Resolved with treatment, returned after discontinuing
  - Unlikely "post-whatever syndrome"
  - Very unlikely to be completely new, unrelated illness

Relapse is known to occur after treatment withdrawal

- Retreatment is often necessary





Jaishankar 2017

antibiotics

MDPI

Article

Identification of FDA-Approved Drugs with Activity against Stationary Phase *Bartonella henselae*

Tingting Li [1,2], Jie Feng [1,3], Shuzhen Xiao [1,4], Wanliang Shi [1], David Sullivan [1] and Ying Zhang [1,*]

Table 3. Evaluation of select drug candidates against a 5-day old stationary phase *B. henselae* culture at their respective maximum drug concentration in serum (C_{max}) values.

Antimicrobial Agents	Con. of Drug Exposure (μg/mL)	CFU per mL after Drug Exposure	
		1 Day	3 Day
Control *	0	$3.67 \pm 2.08 \times 10^7$	$1.33 \pm 0.11 \times 10^6$
Rifampin	10	$2.10 \pm 0.85 \times 10^5$	$8.67 \pm 0.46 \times 10^3$
Azithromycin	2	$3.00 \pm 1.00 \times 10^6$	$5.33 \pm 2.31 \times 10^5$
Doxycycline	5	$5.33 \pm 1.53 \times 10^6$	$1.00 \pm 0.40 \times 10^6$
Erythromycin	1	$3.00 \pm 1.00 \times 10^6$	$1.00 \pm 0.20 \times 10^6$
Ciprofloxacin	5	$1.77 \pm 0.45 \times 10^6$	$2.60 \pm 1.40 \times 10^5$
Gentamicin	10	$1.00 \pm 0.17 \times 10^4$	0
Streptomycin	25	$7.33 \pm 2.08 \times 10^4$	0
Amikacin	100	$2.00 \pm 1.73 \times 10^3$	0
Methylene blue	5	0	0
Daptomycin	60	0	0
Pyrvinium pamoate	5	0	0
Clotrimazole	25	$2.00 \pm 1.73 \times 10^3$	0
Nitroxoline	5	$3.47 \pm 0.31 \times 10^6$	$2.00 \pm 0.00 \times 10^2$
Nitrofurantoin	1	$3.00 \pm 0.00 \times 10^5$	$9.33 \pm 1.15 \times 10^3$
Clinafloxacin	5	$9.00 \pm 1.00 \times 10^5$	$5.33 \pm 3.06 \times 10^4$
Clofoctol	35	$2.20 \pm 0.72 \times 10^6$	$1.00 \pm 0.53 \times 10^5$
Miconazole	6	$2.07 \pm 0.38 \times 10^6$	$2.13 \pm 0.31 \times 10^5$
Pentamidine	0.5	$2.00 \pm 1.00 \times 10^6$	$2.00 \pm 0.00 \times 10^5$
Aprepitant	2	$1.20 \pm 0.17 \times 10^7$	$9.00 \pm 2.65 \times 10^5$
Colistin	2	$7.33 \pm 1.15 \times 10^6$	$6.67 \pm 3.06 \times 10^5$
Amifostine	15	$3.00 \pm 1.00 \times 10^6$	$5.33 \pm 2.23 \times 10^5$
Berberine	1	$3.40 \pm 0.27 \times 10^6$	$1.00 \pm 0.00 \times 10^6$

* The beginning CFU for the 5-day old stationary phase *B. henselae* culture was about 2×10^8 CFU/mL.

Zheng *et al. BMC Microbiology* (2020) 20:87
https://doi.org/10.1186/s12866-020-01777-9

BMC Microbiology

RESEARCH ARTICLE Open Access

Effect of different drugs and drug combinations on killing stationary phase and biofilms recovered cells of *Bartonella henselae* in vitro

Xiaoyan Zheng[1,2], Xiao Ma[2], Tingting Li[2], Wanliang Shi[2] and Ying Zhang[2*]

Abstract

Background: *Bartonella henselae* is a Gram-negative bacterium transmitted to humans by a scratch from cat in the presence of ectoparasites. Humans infected with *B. henselae* can result in various clinical diseases including local lymphadenopathy and more serious systemic disease such as persistent bacteremia and endocarditis. The current treatment of persistent *B. henselae* infections is not very effective and remains a challenge. To find more effective treatments for persistent and biofilm *Bartonella* infections, in this study, we evaluated a panel of drugs and drug combinations based on the current treatment and also promising hits identified from a recent drug screen against stationary phase and biofilm recovered cells of *B. henselae*.

Results: We evaluated 14 antibiotics and 25 antibiotic combinations for activity against stationary phase *B. henselae* (all antibiotics were at 5 μg/ml) and found that ciprofloxacin, gentamicin, and nitrofurantoin were the most active agents, while clofazimine and miconazole had poor activity. Drug combinations azithromycin/ciprofloxacin, azithromycin/methylene blue, rifampin/ciprofloxacin, and rifampin/methylene blue could rapidly kill stationary phase *B. henselae* with no detectable CFU after 1-day exposure. Methylene blue and rifampin were the most active agents against the biofilm *B. henselae* after 6 days of drug exposure. Antibiotic combinations (azithromycin/ciprofloxacin, azithromycin/methylene blue, rifampin/ciprofloxacin, rifampin/methylene blue) completely eradicated the biofilm *B. henselae* after treatment for 6 days.

Conclusions: These findings may facilitate development of more effective treatment of persistent *Bartonella* infections in the future.

Keywords: *Bartonella henselae*, Stationary phase, Biofilm, Antimicrobial activity, Drug combination

Most Active Single Agents

Ciprofloxacin

Gentamicin

Nitrofurantoin

Table 2 Effect of drugs or drug combinations on survival of stationary phase *B. henselae*

Drugs (5 μg/ml)	CFU per mL after drug exposure
Drug free control	$2.8 \pm 0.4 \times 10^{10}$
Amikacin	$8.0 \pm 0.2 \times 10^{4}$
Azithromycin	$6.5 \pm 0.4 \times 10^{5}$
Cefuroxime	$2.2 \pm 0.2 \times 10^{5}$
Ciprofloxacin	$6.0 \pm 0.1 \times 10^{2}$
Clofazimine	$1.6 \pm 0.2 \times 10^{10}$
Daptomycin	$5.0 \pm 0.2 \times 10^{7}$
Disulfiram	$1.0 \pm 0.2 \times 10^{7}$
Doxycycline	$8.0 \pm 0.3 \times 10^{6}$
Gentamicin	$5.0 \pm 0.2 \times 10^{2}$
Methylene blue	$3.2 \pm 0.4 \times 10^{4}$
Miconazole	$1.5 \pm 0.1 \times 10^{10}$
Nitrofurantoin	$2.8 \pm 0.1 \times 10^{2}$
Rifampin	$6.0 \pm 0.3 \times 10^{5}$
SXT	$3.5 \pm 0.2 \times 10^{6}$

Zheng 2020

Most Active Single Agents

Ciprofloxacin

Gentamicin

Nitrofurantoin

Table 2 Effect of drugs or drug combinations on survival of stationary phase *B. henselae* [a]

Drugs (5 μg/ml)	CFU per mL after drug exposure
Drug free control	$2.8 \pm 0.4 \times 10^{10}$
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SXT	$3.5 \pm 0.2 \times 10^{6}$

Zheng 2020

Most Active Combos – Stationary Forms

Azithromycin+Amikacin	$4.3 \pm 0.3 \times 10^5$
Azithromycin+Rifampin	$2.0 \pm 0.2 \times 10^5$
Azithromycin+Cefuroxime	$5.2 \pm 0.2 \times 10^5$
Azithromycin+Ciprofloxacin	0
Azithromycin+Clofazimine	$2.2 \pm 0.3 \times 10^6$
Azithromycin+Daptomycin	$1.8 \pm 0.1 \times 10^5$
Azithromycin+Disulfiram	$1.4 \pm 0.2 \times 10^5$
Azithromycin+Doxycycline	$1.2 \pm 0.3 \times 10^6$
Azithromycin+Gentamicin	$5.1 \pm 0.3 \times 10^4$
Azithromycin+Methylene blue	0
Azithromycin+Miconazole	$1.3 \pm 0.2 \times 10^5$
Azithromycin+Nitrofurantoin	$4.0 \pm 0.3 \times 10^5$
Azithromycin+SXT	$8.5 \pm 0.1 \times 10^6$

Rifampin+ Amikacin	$1.6 \pm 0.1 \times 10^5$
Rifampin+Cefuroxime	$2.2 \pm 0.1 \times 10^4$
Rifampin+Ciprofloxacin	0
Rifampin+Clofazimine	$2.8 \pm 0.1 \times 10^5$
Rifampin+Daptomycin	$1.2 \pm 0.1 \times 10^6$
Rifampin+Disulfiram	$8.5 \pm 0.2 \times 10^5$
Rifampin+Doxycycline	$1.2 \pm 0.1 \times 10^6$
Rifampin+Gentamicin	$1.6 \pm 0.1 \times 10^4$
Rifampin+Methylene blue	0
Rifampin+ Miconazole	$8.0 \pm 0.3 \times 10^5$
Rifampin+Nitrofurantoin	$1.2 \pm 0.1 \times 10^5$
Rifampin+SXT	$1.6 \pm 0.1 \times 10^5$

Zheng 2020

Most Active Combos – Stationary Forms

Azithromycin+Amikacin	$4.3 \pm 0.3 \times 10^5$
Azithromycin+Rifampin	$2.0 \pm 0.2 \times 10^5$
Azithromycin+Cefuroxime	$5.2 \pm 0.2 \times 10^5$
Azithromycin+Ciprofloxacin	0
Azithromycin+Clofazimine	$2.2 \pm 0.3 \times 10^6$
Azithromycin+Daptomycin	$1.8 \pm 0.1 \times 10^5$
Azithromycin+Disulfiram	$1.4 \pm 0.2 \times 10^5$
Azithromycin+Doxycycline	$1.2 \pm 0.3 \times 10^6$
Azithromycin+Gentamicin	$5.1 \pm 0.3 \times 10^4$
Azithromycin+Methylene blue	0
Azithromycin+Miconazole	$1.3 \pm 0.2 \times 10^5$
Azithromycin+Nitrofurantoin	$4.0 \pm 0.3 \times 10^5$
Azithromycin+SXT	$8.5 \pm 0.1 \times 10^6$

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Rifampin+Cefuroxime	$2.2 \pm 0.1 \times 10^4$
Rifampin+Ciprofloxacin	0
Rifampin+Clofazimine	$2.8 \pm 0.1 \times 10^5$
Rifampin+Daptomycin	$1.2 \pm 0.1 \times 10^6$
Rifampin+Disulfiram	$8.5 \pm 0.2 \times 10^5$
Rifampin+Doxycycline	$1.2 \pm 0.1 \times 10^6$
Rifampin+Gentamicin	$1.6 \pm 0.1 \times 10^4$
Rifampin+Methylene blue	0
Rifampin+ Miconazole	$8.0 \pm 0.3 \times 10^5$
Rifampin+Nitrofurantoin	$1.2 \pm 0.1 \times 10^5$
Rifampin+SXT	$1.6 \pm 0.1 \times 10^5$

Zheng 2020

Most Active Single Agents - Biofilms

Table 3 Evaluation of select drug candidates against *B. henselae* biofilm-recovered cells after drug exposure at different times

Drugs (5 μg/ml)	CFU per mL after drug exposure		
	2 day	4 day	6 day
Drug free control	$1.3 \pm 0.2 \times 10^{10}$	$1.8 \pm 0.2 \times 10^{10}$	$2.6 \pm 0.3 \times 10^{10}$
Azithromycin	$4.5 \pm 0.3 \times 10^{9}$	$5.2 \pm 0.3 \times 10^{9}$	$9.3 \pm 0.2 \times 10^{5}$
Cefuroxime	$5.6 \pm 0.3 \times 10^{9}$	$2.3 \pm 0.2 \times 10^{9}$	$1.7 \pm 0.1 \times 10^{6}$
Ciprofloxacin	$3.2 \pm 0.3 \times 10^{8}$	$2.5 \pm 0.3 \times 10^{8}$	$5.1 \pm 0.3 \times 10^{2}$
Daptomycin	$9.8 \pm 0.2 \times 10^{9}$	$3.4 \pm 0.3 \times 10^{9}$	$2.7 \pm 0.2 \times 10^{6}$
Disulfiram	$6.1 \pm 0.3 \times 10^{9}$	$4.6 \pm 0.3 \times 10^{9}$	$3.8 \pm 0.3 \times 10^{7}$
Doxycycline	$5.3 \pm 0.3 \times 10^{9}$	$3.8 \pm 0.1 \times 10^{9}$	$6.2 \pm 0.3 \times 10^{5}$
Gentamicin	$6.2 \pm 0.3 \times 10^{9}$	$5.8 \pm 0.2 \times 10^{9}$	$8.1 \pm 0.3 \times 10^{2}$
Methylene blue	$8.9 \pm 0.4 \times 10^{9}$	$6.8 \pm 0.2 \times 10^{9}$	$2.3 \pm 0.2 \times 10^{2}$
Miconazole	$9.8 \pm 0.3 \times 10^{9}$	$2.2 \pm 0.1 \times 10^{10}$	$1.6 \pm 0.1 \times 10^{10}$
Nitrofurantoin	$4.3 \pm 0.1 \times 10^{9}$	$3.6 \pm 0.2 \times 10^{9}$	$2.8 \pm 0.2 \times 10^{9}$
Rifampin	$5.6 \pm 0.2 \times 10^{9}$	$4.8 \pm 0.3 \times 10^{9}$	$3.2 \pm 0.2 \times 10^{2}$
SXT	$7.8 \pm 0.3 \times 10^{9}$	$6.4 \pm 0.3 \times 10^{9}$	$2.7 \pm 0.2 \times 10^{9}$
Azithromycin+Ciprofloxacin	$4.1 \pm 0.2 \times 10^{9}$	$5.8 \pm 0.3 \times 10^{6}$	0
Azithromycin+Methylene blue	$6.8 \pm 0.2 \times 10^{9}$	$5.2 \pm 0.3 \times 10^{5}$	0
Rifampin+Ciprofloxacin	$7.6 \pm 0.2 \times 10^{9}$	$4.7 \pm 0.2 \times 10^{9}$	0
Rifampin+Methylene blue	$5.9 \pm 0.1 \times 10^{9}$	$4.8 \pm 0.2 \times 10^{9}$	0

Zheng 2020

Most Active Combos - Biofilms

Table 3 Evaluation of select drug candidates against *B. henselae* biofilm-recovered cells after drug exposure at different times

Drugs (5 μg/ml)	CFU per mL after drug exposure		
	2 day	4 day	6 day
Drug free control	$1.3 \pm 0.2 \times 10^{10}$	$1.8 \pm 0.2 \times 10^{10}$	$2.6 \pm 0.3 \times 10^{10}$
Azithromycin	$4.5 \pm 0.3 \times 10^{9}$	$5.2 \pm 0.3 \times 10^{9}$	$9.3 \pm 0.2 \times 10^{5}$
Cefuroxime	$5.6 \pm 0.3 \times 10^{9}$	$2.3 \pm 0.2 \times 10^{9}$	$1.7 \pm 0.1 \times 10^{6}$
Ciprofloxacin	$3.2 \pm 0.3 \times 10^{8}$	$2.5 \pm 0.3 \times 10^{8}$	$5.1 \pm 0.3 \times 10^{2}$
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Rifampin+Ciprofloxacin	$7.6 \pm 0.2 \times 10^{9}$	$4.7 \pm 0.2 \times 10^{9}$	0
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Zheng 2020

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Rifampin+Methylene blue	$5.9 \pm 0.1 \times 10^{9}$	$4.8 \pm 0.2 \times 10^{9}$	0

Zheng 2020

Methylene Blue

Dosing:

- 25-50mg BID
- Benefits at 4-8mg daily
- No need for liposomal

Methylene Blue

MAO-I

- Haven't seen Serotonin Syndrome with oral
  - Reported with IV dosing

Caution combining with amphetamines – Risk of hypertensive crisis

Blue urine

- Stains toilet if not on top of it
- Dysuria, particularly in males

Methylene Blue

Where it shines:

Cognitive issues

Air hunger

Clotrimazole

Oral

Adults

- 10mg four times a day
- 20mg sustained release capsule BID

Children

- Liquid 10mg three times a day
- 10mg three times a day
- 10-15mg sustained release capsule BID

Clotrimazole

Elevated transaminases

Clotrimazole

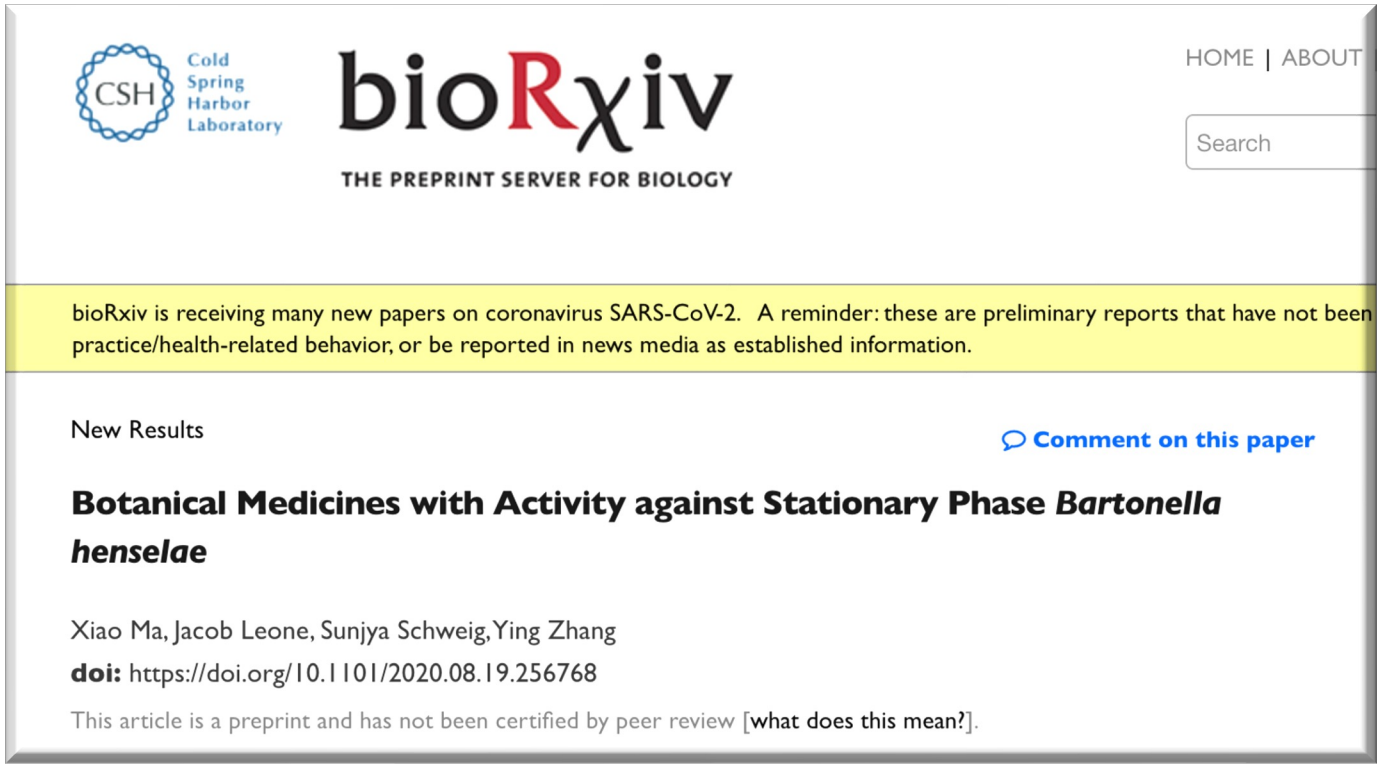
Where it shines:

Yeast

Aflatoxins

PANS

Stationary Forms & Biofilms



Cold Spring Harbor Laboratory

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bioRxiv is receiving many new papers on coronavirus SARS-CoV-2. A reminder: these are preliminary reports that have not been practice/health-related behavior, or be reported in news media as established information.

New Results

Comment on this paper

Botanical Medicines with Activity against Stationary Phase *Bartonella henselae*

Xiao Ma, Jacob Leone, Sunjya Schweig, Ying Zhang

doi: https://doi.org/10.1101/2020.08.19.256768

This article is a preprint and has not been certified by peer review [what does this mean?].

Cryptolepis sanguinolenta

Juglans nigra

Polygonum cuspidatum

Scutellaria baicalensis

Scutellaria barbata

Putting It Together

Medications

Cefuroxime

Minocycline

Tinidazole

Hydroxychloroquine ?

Borrelia burgdorferi

Spirochete

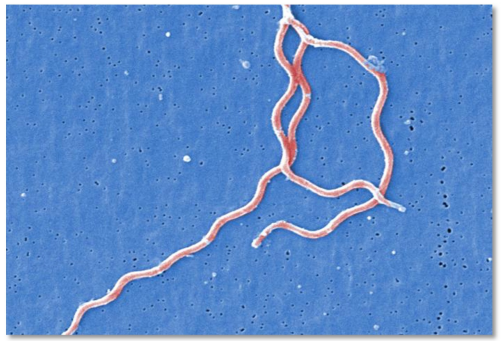

Image: CDC

Cyst/Round Body

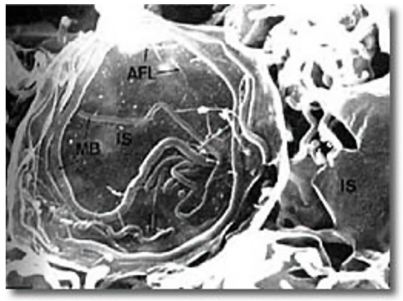

Image: Bradford 2004

Biofilm

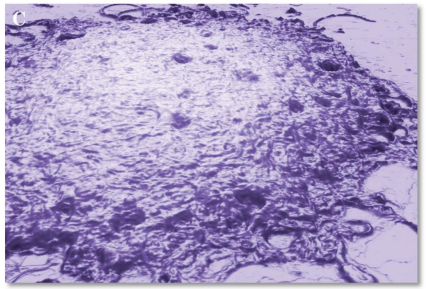

Image: Shapi 2012

Thomas A. Moorcroft, DO

Herbs

Cryptolepis

Polygonum cuspidatum

Scutellaria baicalensis

Biofilm

Evidence-based herbals

Liposomal botanicals

Liposomal Artemisinin

Enzymes

Putting It Together

What about if *Babesia microti*?

- Consider Atovaquone, azithromycin, artemisinin, tafenoquine
- Think about this in the beginning
    - Inform your choice between a tetracycline and a macrolide

Putting It Together

What about if Babesia duncani?

- Medications???
- Focus on herbals
- Maybe add azithromycin and atovaquone/proguanil

Putting It Together

What about if *Babesia odecoilei*?

- Research??
- Clinical experience consider
  - Atovaquone, artemisia annua or derivative, tafenoquine, azithromycin

Putting It Together

What about other *Babesia spp?*

- Evidence-based herbals seem to help across the board
- AND, more infections appear to also need antibiotic and Rx anti-parasitic treatments

Putting It Together

What about if *Bartonella henselae*?

- Think double intracellular coverage
  - What about other pathogens?
    - *Borrelia burgdorferi* or *miyamotoi, Babesia* spp., *Mycoplasma, Chlamydiphilia* etc

Putting It Together

What about if *Bartonella henselae*?

- Think double intracellular coverage
  - What about other pathogens?
    - *Borrelia burgdorferi* or *miyamotoi, Babesia* spp., *Mycoplasma, Chlamydiphilia* etc
- Think evidence-based herbals

Putting It Together

What about if *Bartonella henselae*?

- Think double intracellular coverage
  - What about other pathogens?
    - *Borrelia burgdorferi* or *miyamotoi, Babesia* spp., *Mycoplasma, Chlamydiphilia* etc
- Think evidence-based herbals
- Stationary forms
  - Methylene blue
  - Clotrimazole
    - especially if concurrent aflatoxins or other mycotoxins

Putting It Together

What about if *Bartonella henselae*?

- Evidence-based herbals
- Nitrofurantoin?

Putting It Together

What about if *Bartonella henselae*?

- Evidence-based herbals
- Nitrofurantoin?

What about if another *Bartonella*?

- Clinical judgement

Putting It Together

In the end, Treat the patient in front of you

Putting It Together

In the end, Treat the patient in front of you

Follow the evidence as much as it is clinically useful

Putting It Together

In the end, Treat the patient in front of you

Follow the evidence as much as it is clinically useful

Innovate clinically based upon experience and new research

Putting It Together

In the end, Treat the patient in front of you

Follow the evidence as much as it is clinically useful

Innovate clinically based upon experience and new research

Always assess and reassess

- Not only the patient

Putting It Together

In the end, Treat the patient in front of you

Follow the evidence as much as it is clinically useful

Innovate clinically based upon experience and new research

Always assess and reassess

- Not only the patient
- But your diagnosis

Herbs & Pathogens

	Borrelia burgdorferi	Babesia microti	Babesia duncani	Bartonella henselae
Cryptolepis sanguinolenta	**G/S**	**G**	**G**	**S**
Scutellaria baicalensis	**G/S**	**?**	**G**	**S**
Polygonum cuspidatum	**G/S**	**?**	**+/--**	**S**
Uncaria tomentosa	**S**	**?***	**-**	**+/--**
Artemisia annua	**S**	**G**	**+/--**	**+/---**
Juglans nigra	**S/? G**	**?**	**-**	**S**

G = Growing form. S = Stationary or non-growing form, including round bodies and biofilms

*effective against divergens, but not tested in other human Babesias

- Significant discrepancy exists in herbal research results
- Many commonly used herbs don't do in vitro what many claim they do
- Inhibition of less than 60% not included
- For *B. henselae* stationary forms, herbs listed did better than commonly used antibiotics
- *Cryptolepis* – No regrowth of *B. burgdorferi* or *B. duncani*

Batiha 2020, Feng 2020, Goo 2010, Ma 2020, Zhang 2021

Summary

Tick-borne co-infections are frequent and the increased risk of patient co-infection from tick bite

- This impacts presentation of symptoms and laboratory testing.

An understanding of log and stationary bacterial growth as well as other bacterial persister forms is critical in treating patients

- Each phase requires different treatment approaches

Most up to date, evidence-based growing, stationary and persister co-infection treatments


MOORCROFT LYME DISEASE
LDPC
PRACTITIONER CERTIFICATION
CERTIFIED LEVEL 1

Resources

Herbal Dosing

Cryptolepis sanguinolenta

- Tincture (1:5 extract) - Start with 5 drops three times a day, slowly work up to 40 drops three times a day

Scutellaria baicalensis

- 1 capsule (459mg) three times a day
- Tincture (1:5 extract) - Start with 5 drops three times a day, slowly work up to 40 drops three times a day

Ma 2020
Feng 2020
Zhang 2021

Herbal Dosing

Artemisia annua

- Artemisinin (liposomal) - 50mg 2 capsules BID
- Whole herb – 1 capsule (300mg) TID
- ? 5 days per week, 3 weeks per month vs continuous

Polygonum cuspidatum (Japanese knotweed root)

- Whole herb (capsules) - 1500mg daily
- Tincture (1:5 extract) - Start with 5 drops three times a day, slowly work up to 40 drops three times a day

Herbal Dosing

Uncaria tomentosa (Cat's claw inner bark)

- Capsules: 1500mg daily
- Tincture (1:5 extract) - Start with 5 drops three times a day, slowly work up to 40 drops three times a day

Houttuynia cordata

- Tincture (1:5 extract) - Start with 5 drops three times a day, slowly work up to 40 drops three times a day

Children's Herbal Dosing

$$\frac{\text{Child's Weight}}{150 \text{ lbs.}} = \frac{\text{Child's dose}}{\text{total \# drops or mg (of the adult dose)}}$$

TickEncounter Resource Center

Amblyomma americanum (Lone Star ticks)

Ehrlichiosis, Rocky Mountain Spotted Fever, Q fever, STARI borreliosis

Thomas A. Moorcroft, DO

TickEncounter Resource Center

Dermacentor variabilis (American Dog ticks)

Rocky Mountain Spotted Fever, Tularemia

www.LymePractitionerCertification.com

Top 5 Herbs for Tx Lyme
www.OriginsOfHealth.com/Connect