DR KLINGHARDT WEEKLY DEBRIEF

FROM KLINGHARDT EDUCATION IN ASSOCIATION WITH SOPHIA HEALTH INSTITUTE

The Revolutionary Biological Approach to Treat Chronic Lyme Disease

Klinghardt Institute
The Heart Of Healing

Causes of Neuro-Inflammation

- Neurotoxins (endogenous, environmental)
- **Pathogens**
- Head trauma
- Autoimmunity
- Aging (eg. decline in melatonin)
- Vascular (eg. Microbleeds, etc.)
- **Exposure to Microwave (cellphone radiation)**

- 8 Najjar S, Pearlman DM, Alper K et al. *J Neuroinflammation* 2013; **10**: 43 PMID 23547920
- Hardeland R, Cardinali DP, Brown GM et al. *Prog Neurobiol* 2015; **127-128**: 46-63 PMID 25697044
- Stone J, Johnstone DM, Mitrofanis J et al. *J Alzheimers Dis* 2015; **44**(2): 355-373 PMID25318547
- Viviani B, Boraso M, Marchetti N et al. *Neurotoxicology* 2014; **43**: 10-20 PMID 24662010
- Marošová L, Neradil P, Zilka N. *Acta Virol* 2013; **57**(3): 273-281 PMID 24020754

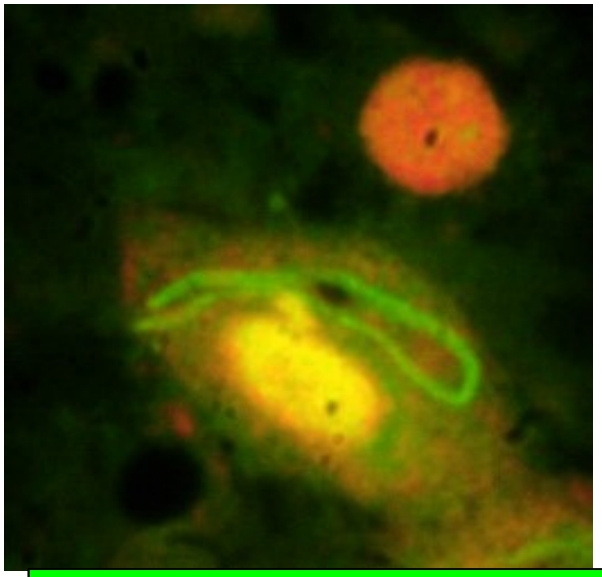
J Neuroinflammation. 2011 Aug 4;8(1):90

Alzheimer's disease - a neurospirochetosis.

Analysis of the evidence following Koch's and Hill's criteria. Miklossy J.

Abstract: It is established that chronic spirochetal infection can cause slowly progressive dementia, brain atrophy and amyloid deposition in late neurosyphilis. Recently it has been suggested that various types of spirochetes, in an analogous way to Treponema pallidum, could cause dementia and may be involved in the pathogenesis of Alzheimer's disease (AD). Here, we review all data available in the literature on the detection of spirochetes in AD and critically analyze the association and causal relationship between spirochetes and AD following established criteria of Koch and Hill. The results show a statistically significant association between spirochetes and AD (P = 1.5 x 10-17, OR = 20, 95% CI = 8-60, N = 247). When neutral techniques recognizing all types of spirochetes were used, or the highly prevalent periodontal pathogen Treponemas were analyzed, spirochetes were observed in the brain in more than 90% of AD cases. Borrelia burgdorferi was detected in the brain in 25.3% of AD cases analyzed and was 13 times more frequent in AD compared to controls. Periodontal pathogen Treponemas (T. pectinovorum, T. amylovorum, T. lecithinolyticum, T. maltophilum, T. medium, T.socranskii) and Borrelia burgdorferi were detected using species specific PCR and antibodies. Importantly, co-infection with several spirochetes occurs in AD. The pathological and biological hallmarks of AD were reproduced in vitro. The analysis of reviewed data following Koch's and Hill's postulates shows a probable causal relationship between **neurospirochetosis** and AD. Persisting inflammation and amyloid deposition initiated and sustained by chronic spirochetal infection form together with the various hypotheses suggested to play a role in the pathogenesis of AD a comprehensive entity. As suggested by Hill, once the probability of a causal relationship is established prompt action is needed. Support and attention should be given to this field of AD research**. Spirochetal infection occurs years or decades before the manifestation of dementia. As adequate antibiotic and anti-inflammatory therapies are available, as in syphilis, one might prevent and eradicate dementia.**

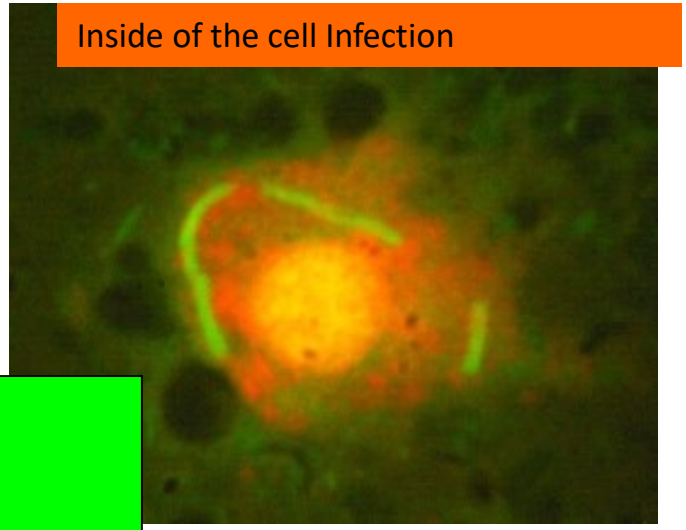
Borrelia to Tangles

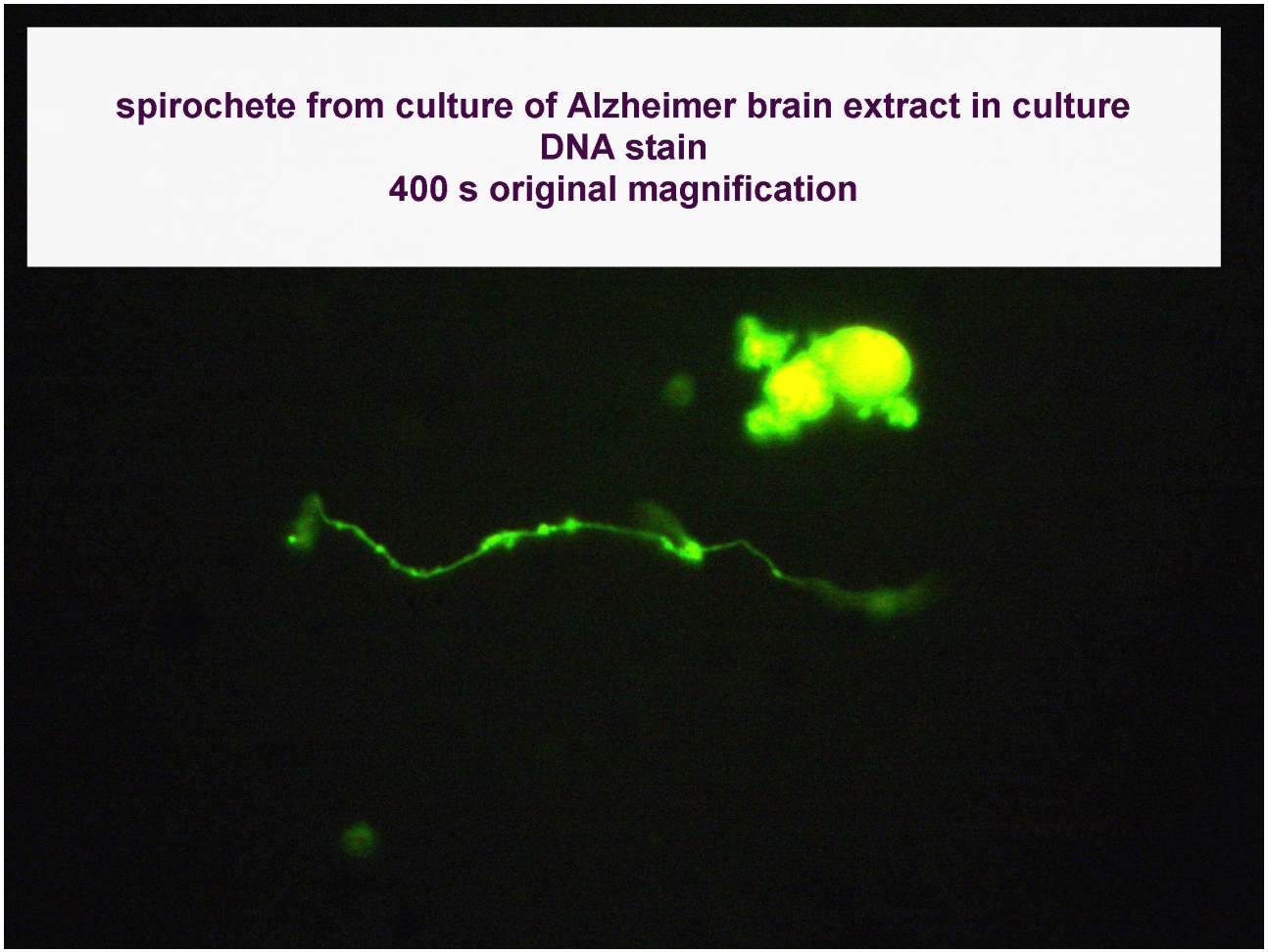


Borrelia spirochetes inside Hippocampal neurons in Alzheimer's disease

Infectious Agent Inside of the Nerve cell

Inside of the cell Infection




spirochete from culture of Alzheimer brain extract in culture
DNA stain
400 s original magnification

The brilliant work of pathologist A. Mac Donald – a true pioneer of our

Lyme spirochetes are present in AD brain tissue

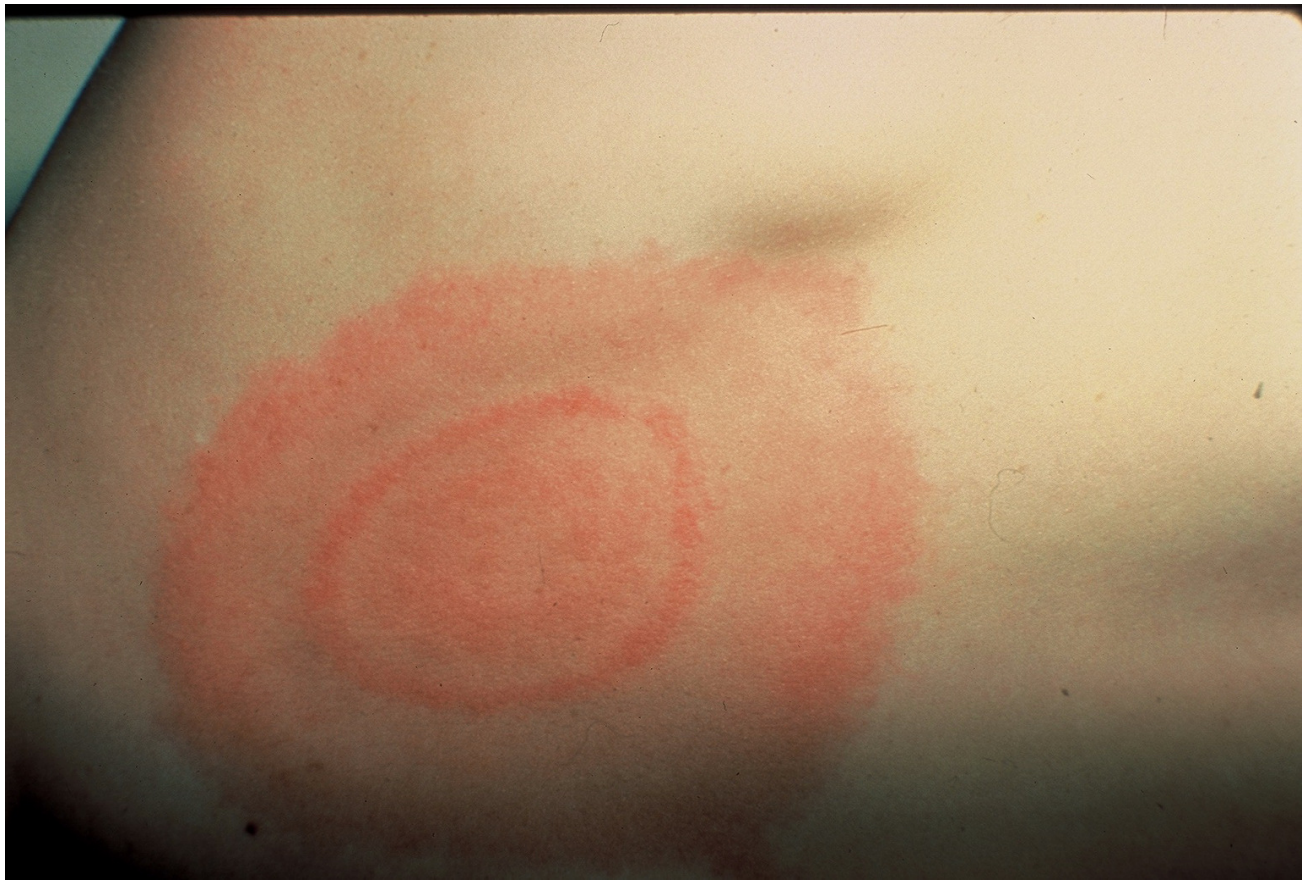
Borrelia in the brains of patients dying with dementia. JAMA. 1986 Oct 24-31;256(16):2195-6. MacDonald AB

AD Plaque is full of Lyme spirochetes!

Plaques of Alzheimer's disease originate from cysts of Borrelia burgdorferi, the Lyme disease spirochete. Med Hypotheses. 2006;67(3):592-600. Epub 2006 May 3. MacDonald AB

Spirochetes travel inside the neurons of the brain to conquer new territory!

Alzheimer's disease Braak Stage progressions: reexamined and redefined as Borrelia infection transmission through neural circuits. Med Hypotheses. 2007;68(5):1059-64. Epub 2006 Nov 17. MacDonald AB



Epidemiology

- Lyme disease is the most common vector borne disease in North America and Europe, with 300 000 new cases in the United States

  Kuehn BM. CDC estimates 300 000 US cases of Lyme disease annually. JAMA2013;310:1110.

- An estimated 100 000 new cases in Europe each year

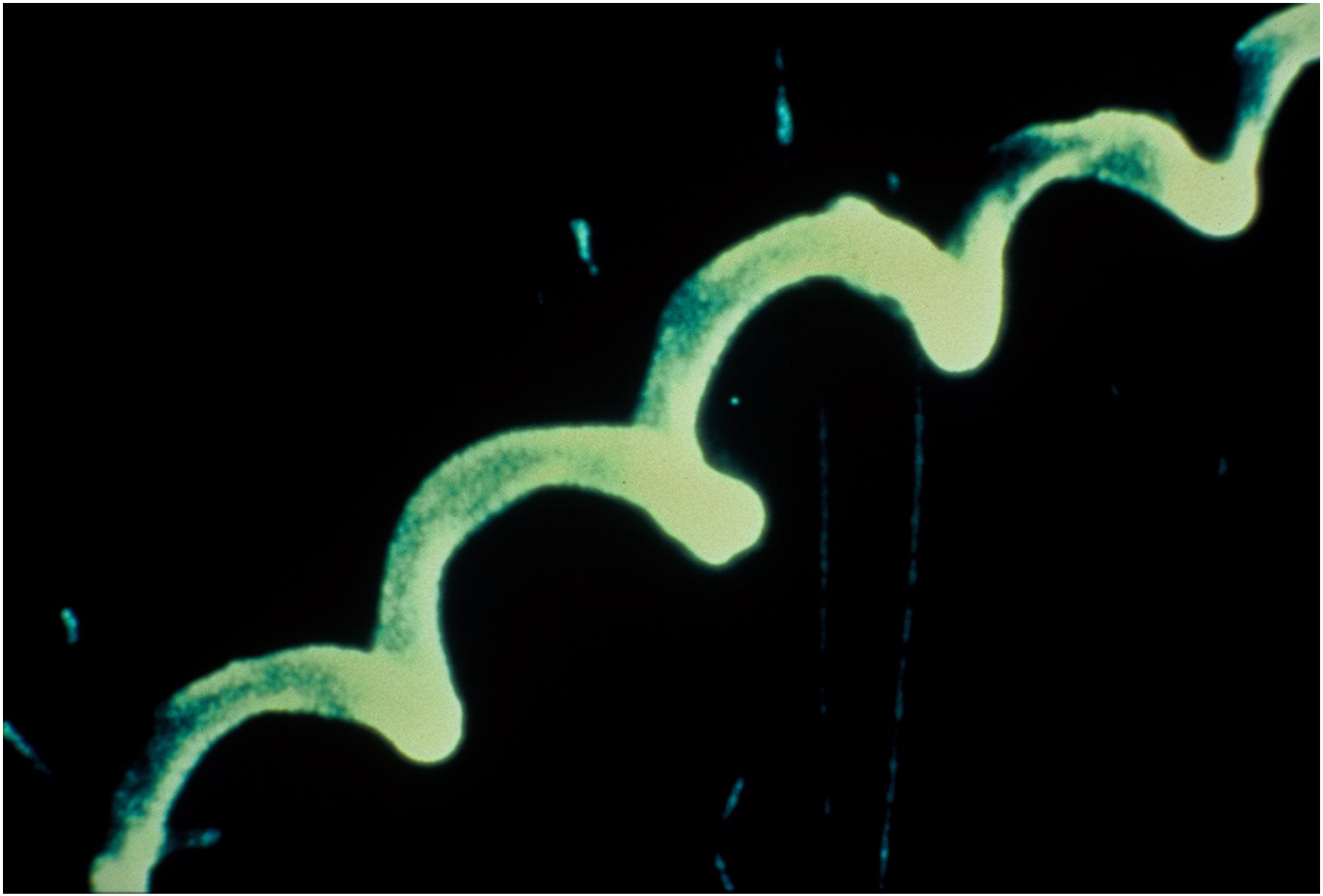
  Lindgren E, Jaenson T. Lyme borreliosis in Europe: influences and climate change, epidemiology, ecology and adaptation measures. World Health Organization Regional Office for Europe, 2006.

- These numbers are likely to be underestimated because case reporting is inconsistent

  Dubrey SW, Bhatia A, Woodham S, Rakowicz W. Lyme disease in the United Kingdom. Postgrad Med J2014;90:33-42.

- Many infections go undiagnosed

  Perronne C. Lyme and associated tick-borne diseases: global challenges in the context of a public health threat. Front Cell Infect Microbiol2014;4:74.



Dr. D. Klinghardt: Biologische Behandlung
der Lyme-Borreliose

What happens after antibiotics - up to 62% of the time?

- Thirty-four percent of a population-based, retrospective cohort were ill an average of 6.2 years after antibiotic treatment**.**

  Shadick NA, Phillips CB, Logigian EL, et al. The long-term clinical outcomes of Lyme disease. A population-based retrospective cohort study. Ann Intern Med 1994;121(8):560-7

- **Sixty-two percent of a retrospective evaluation** of 215 Lyme disease patients from Westchester County, NY**, remained ill an average of 3.2 years after antibiotic treatment**

  Asch ES, Bujak DI, Weiss M, et al. Lyme disease: an infectious and postinfectious syndrome. J Rheumatol1994;21(3):454-61

- A meta-analysis of **504 patients treated for Lyme disease found this group had more fatigue, musculoskeletal pain and neurocognitive difficulties than 530 controls**. Additionally, it demonstrated that persistent Lyme disease symptoms were a distinct set of symptoms, which differed from those of fibromyalgia, chronic fatigue syndrome and depression

  Cairns V, Godwin J. Post-Lyme borreliosis syndrome: a meta-analysis of reported symptoms. Int J Epidemiol2005;34(6):1340-5

Infect Drug Resist. 2011;4:97-113. doi: 10.2147/IDR.S19201. Epub 2011 May 3.

Evaluation of in-vitro antibiotic susceptibility of different morphological forms of Borrelia burgdorferi.

Sapi E[1], Kaur N, Anyanwu S, Luecke DF, Datar A, Patel S, Rossi M, Stricker RB.

Abstract

BACKGROUND:

Lyme disease is a tick-borne illness caused by the spirochete Borrelia burgdorferi. Although antibiotic therapy is usually effective early in the disease, relapse may occur when administration of antibiotics is discontinued. Studies have suggested that **resistance and recurrence of Lyme disease might be due to formation of different morphological forms of B. burgdorferi, namely round bodies (cysts) and biofilm-like colonies**. Better understanding of the effect of antibiotics on all morphological forms of B. burgdorferi is therefore crucial to provide effective therapy for Lyme disease.

RESULTS:

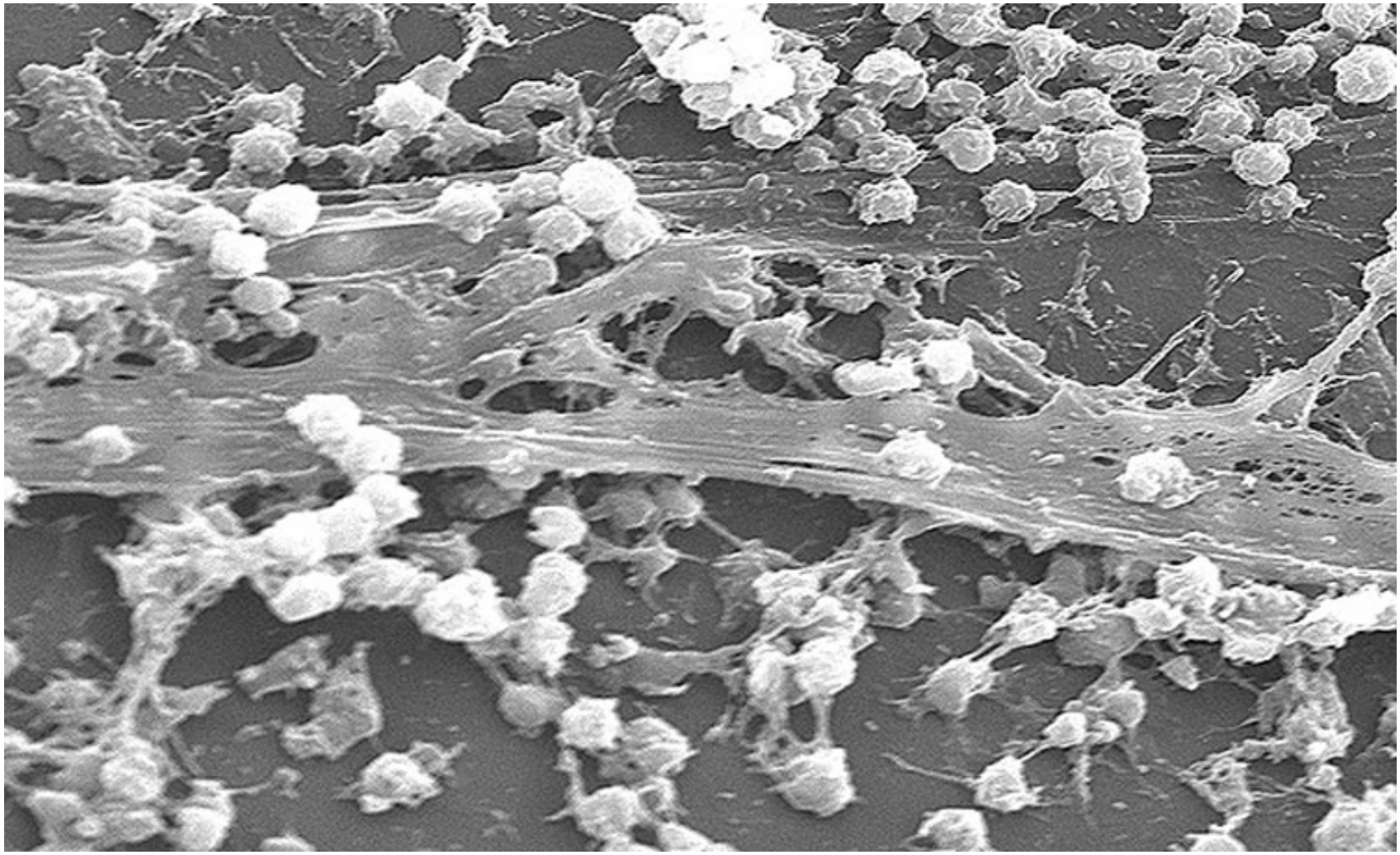
Doxycycline reduced spirochetal structures ~90% but **increased the number of round body forms about twofold**. Amoxicillin reduced spirochetal forms by ~85%-90% and round body forms by ~68%, while treatment with metronidazole led to reduction of spirochetal structures by ~90% and round body forms by ~80%. Tigecycline and tinidazole treatment reduced both spirochetal and round body forms by ~80%-90%. When quantitative effects on biofilm-like colonies were evaluated, the five antibiotics reduced formation of these colonies by only 30%-55%. In terms of qualitative effects, **only tinidazole reduced viable organisms by ~90%.** Following **treatment with the other antibiotics, viable organisms were detected in 70%-85% of the biofilm-like colonies.**

CONCLUSION:

Antibiotics have varying effects on the different morphological forms of B. burgdorferi. **Persistence of viable organisms in round body forms and biofilm-like colonies may explain treatment failure and persistent symptoms following antibiotic therapy of Lyme disease.**

Comment Dr.K: When Lyme is undertreated with Doxycycline only, there is a likely chance that permanent "round bodies" and biofilm are formed – being later the cause of autoimmune diseases (which rarely responds to treatment with antibiotics)

Biofilms on internal surfaces



Dr. D. Klinghardt: Biologische Behandlung
der Lyme-Borreliose

What does the persistent form of Lyme look like?

- **Schizoaffective d/o**
- **Multiple sclerosis**
- **Amylotrophic lateral sclerosis**
- **Alzheimers disease**
- **Parkinsons Disease**
- **Thyroid disease**
- **Hyperparathyroidism**
- **Hypothyroidism**
- **Insomnia**
- **Autism; ADHD; behavioral issues, learning differences**
- **Lupus**
- **Rheumatoid arthritis**
- **Polmyalgia rheumatica**
- **ME/CFIDS**
- **Fibromyalgia**
- **Multiple Chemical Sensitivity**
- **Bipolar d/o**
- **Addisons disease/adrenal fatigue**
- **Cancer (?)**

Differential Diagnosis

- Heavy metal toxicity: whole blood or rbc testing, hair analysis, urine challenge tests, Oligo scan
- Environmental illness (toxicity and allergy) and Electrosensitivity: by history, LDA/LDI testing, fat biopsy
- Mold / Mycotoxin exposure: history, elevated TGF beta 1, elevated C4a (Jewish hospital in Denver only), not C3a, urine mycotoxins. Home testing HERTSME
- Lyme disease, co- infection or other infection: provoked urine PCR testing, Western Blot, culture, low CD 57, both C4a and C3a elevated (R.Stricker, R.Shoemaker)

LYME BORRELIOSIS: Co-infections and opportunistic infections

Borrelia (bacteria)

Babesia and Protomyxzoa rheumatica FL1953 (Protozoa)

Ehrlichia

Rickettsia

Bartonella (bacteria)

Mycoplasma (L-form)

Viruses (esp. CMV,EBV)

<u>Opportunistic infections/infestations</u>

Parasites (lungworm V.Klapowi, helminths, protozoa)

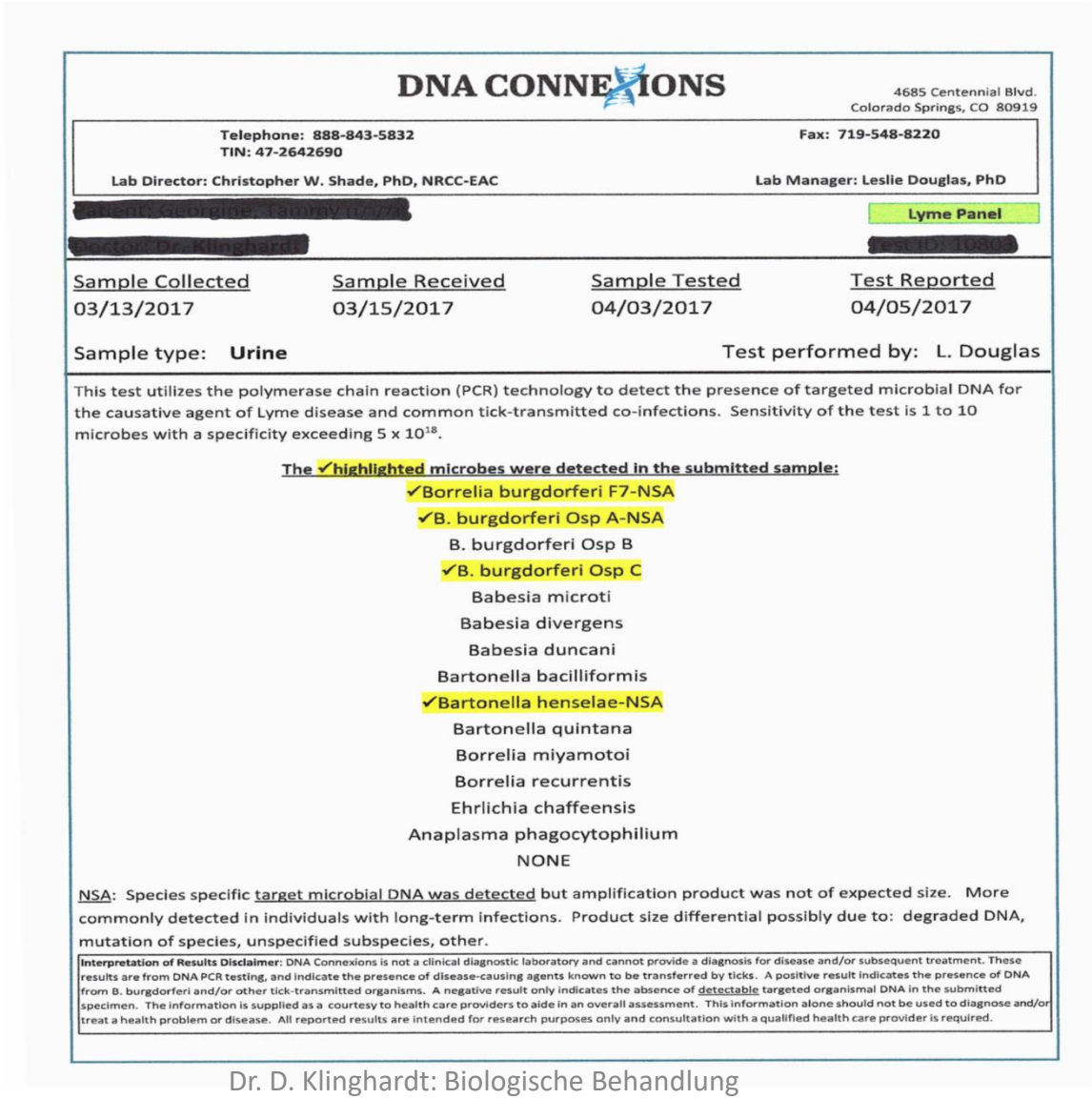
Mold (aspergillus sp., penicillum sp., cladysporium, etc.)

Viruses (HSV 1 &2, CMV, EBV, HHV-6, XMRV, coxsackie, retroviruses, etc.)

Diagnosing Lyme

- By history? – mosquitoes, spiders, flees and lice carry it. Do you remember a flee bite 15 years ago?
- Clinical findings? - Lyme can mimic, cause or aggrevate any clinical symptom known to man
- IgeneX lab: sensitive Western Blot and appropriate tests for the co-infections (MediCare pays!)
- Armin labs: the LTT-Elispot is more sensitive than the Blot!
- Autonomic response testing
- Lyme culture (may take months)
- Less reliable tests: ELISA, CD 57, MELISA
- Bartonella: FryLabs
- Babesia : IgeneX FISH
- Best test: ultrasound provoked Co-infection urine PCR test

36 year old men with severe fatigue and brain fog. Western Blot negative for Lyme



DNA CONNEXIONS

4685 Centennial Blvd.
Colorado Springs, CO 80919

Telephone: 888-843-5832
TIN: 47-2642690

Fax: 719-548-8220

Lab Director: Christopher W. Shade, PhD, NRCC-EAC

Lab Manager: Leslie Douglas, PhD

[redacted]

Lyme Panel

[redacted]

[redacted]

Sample Collected	Sample Received	Sample Tested	Test Reported
03/13/2017	03/15/2017	04/03/2017	04/05/2017

Sample type: **Urine**

Test performed by: L. Douglas

This test utilizes the polymerase chain reaction (PCR) technology to detect the presence of targeted microbial DNA for the causative agent of Lyme disease and common tick-transmitted co-infections. Sensitivity of the test is 1 to 10 microbes with a specificity exceeding 5×10^{18}.

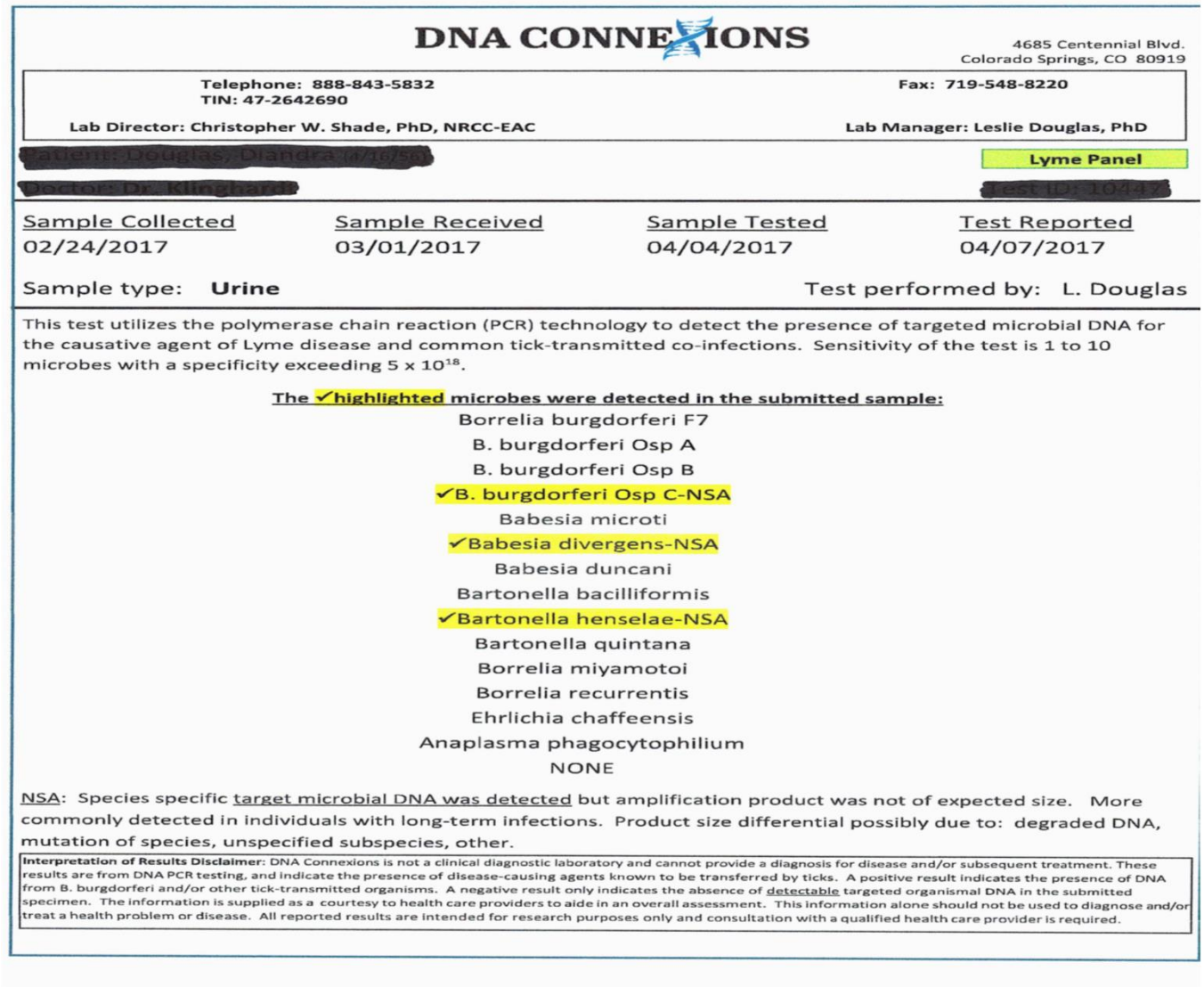
The ✓highlighted microbes were detected in the submitted sample:

✓Borrelia burgdorferi F7-NSA
✓B. burgdorferi Osp A-NSA
B. burgdorferi Osp B
✓B. burgdorferi Osp C
Babesia microti
Babesia divergens
Babesia duncani
Bartonella bacilliformis
✓Bartonella henselae-NSA
Bartonella quintana
Borrelia miyamotoi
Borrelia recurrentis
Ehrlichia chaffeensis
Anaplasma phagocytophilium
NONE

NSA: Species specific target microbial DNA was detected but amplification product was not of expected size. More commonly detected in individuals with long-term infections. Product size differential possibly due to: degraded DNA, mutation of species, unspecified subspecies, other.

Interpretation of Results Disclaimer: DNA Connexions is not a clinical diagnostic laboratory and cannot provide a diagnosis for disease and/or subsequent treatment. These results are from DNA PCR testing, and indicate the presence of disease-causing agents known to be transferred by ticks. A positive result indicates the presence of DNA from B. burgdorferi and/or other tick-transmitted organisms. A negative result only indicates the absence of detectable targeted organismal DNA in the submitted specimen. The information is supplied as a courtesy to health care providers to aide in an overall assessment. This information alone should not be used to diagnose and/or treat a health problem or disease. All reported results are intended for research purposes only and consultation with a qualified health care provider is required.

25 year old woman with POTS and severe fatigue and brain fog



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Sample Collected	Sample Received	Sample Tested	Test Reported
02/24/2017	03/01/2017	04/04/2017	04/07/2017

Sample type: **Urine**
Test performed by: L. Douglas

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B. burgdorferi Osp B
✓B. burgdorferi Osp C-NSA
Babesia microti
✓Babesia divergens-NSA
Babesia duncani
Bartonella bacilliformis
✓Bartonella henselae-NSA
Bartonella quintana
Borrelia miyamotoi
Borrelia recurrentis
Ehrlichia chaffeensis
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Helpful Tips From the Laboratory

- Abnormal lipid profile (**moderate LDL elevation**, elevated triglycerides. Late stage: low cholesterol)
- Insulin resistance (elevated fasting glucose and insulin)
- **Borderline low wbc** (below 5000), normal SED rate and CRP
- Low MSH, high TGF beta-1, high MMP-9, high C3a +C4a
- Low-normal thryroid hormone tests but positive Barnes test and excellent response to giving T3
- Phase 2 adrenal failure (high mid-night cortisol, low DHEA and testosterone, low progesterone, estrogen dominance)
- **Low-normal alkaline phosphatase** (indicating low zinc levels, usually from lyme associated kryptopyrole disorder)
- Decreased urine concentration

  (low specific gravity = often low ADH) – has to urinate at night

The Etiologic Agent of Lyme Disease in Deer Flies, Horse Flies, and Mosquitoes

Louis A. Magnarelli, John F. Anderson and Alan G. Barbour

The Journal of Infectious Diseases

Vol. 154, No. 2 (Aug., 1986), pp. 355-358

Flea and mosquito-borne diseases

King, M. Banfield Journal 2010 Vol. 6 No. 2 pp. 7-9, 12-14

http://mydigimag.rrd.com/publication/?i=37884

Abstract

This article discusses the flea- (**bartonellosis, *Haemobartonella*, rickettsial infections, yersiniosis** and feline viral infections) and mosquito- (heartworm disease) borne diseases, their transmission, clinical signs, and appropriate treatment in dogs and cats.

Lyme disease masquerading as brown recluse spider bite

Kevin C. Osterhoudt, Theoklis Zaoutis, Joseph J. Zorc

Ann Emerg Med. May 2002;39:558-561.

Abstract

We report a case of Lyme disease with clinical features resembling those described from brown recluse spider bites. The most striking manifestation was a necrotic skin wound. Brown recluse spider bites may be overdiagnosed in some geographic regions. Tick bite and infection with Borrelia burgdorferi should be considered in the differential diagnosis of necrotic arachnidism in regions endemic for Lyme disease

Medical Hypotheses
Volume 70, Issue 5, 2008, Pages 967–974 **The association between tick-borne infections, Lyme borreliosis and autism spectrum disorders**

Robert C. Bransfield, Jeffrey S. Wulfman, William T. Harvey, Anju I. Usman[d]

Summary

Chronic infectious diseases, including tick-borne infections such as *Borrelia burgdorferi* may have direct effects, promote other infections and create a weakened, sensitized and immunologically vulnerable state during fetal development and infancy leading to increased vulnerability for developing autism spectrum disorders. A dysfunctional synergism with other predisposing and contributing factors may contribute to autism spectrum disorders by provoking innate and adaptive immune reactions to cause and perpetuate effects in susceptible individuals that result in inflammation, molecular mimicry, kynurenine pathway changes, increased quinolinic acid and decreased serotonin, oxidative stress, mitochondrial dysfunction and excitotoxicity that impair the development of the amygdala and other neural structures and neural networks resulting in a partial Klüver–Bucy Syndrome and other deficits **resulting in autism spectrum disorders** and/or exacerbating autism spectrum disorders from other causes throughout life.

Support for this hypothesis includes multiple cases of mothers with Lyme disease and children with autism spectrum disorders; fetal neurological abnormalities associated with tick-borne diseases; similarities between tick-borne diseases and autism spectrum disorder regarding symptoms, pathophysiology, immune reactivity, temporal lobe pathology, and brain imaging data; positive reactivity in several studies with autistic spectrum disorder patients for*Borrelia burgdorferi* (22%, 26% and 20–30%) and 58% for mycoplasma; similar geographic distribution and improvement in autistic symptoms from antibiotic treatment. It is imperative to research these and all possible causes of autism spectrum disorders in order to prevent every preventable case and treat every treatable case until this disease has been eliminated from humanity.

Medical Hypotheses; May 2012, Vol 78, Issue 5, 606-615

"Long term antibiotic therapy may be an effective treatment for children co-morbid with Lyme disease and Autism Spectrum Disorder" Kuhn, M, S.Grave, R.Bransfield, S.Harris

Patients diagnosed with Lyme disease share many of the same physical manifestations as those diagnosed with an Autism Spectrum Disorder (ASD). In this study four male children (ages 26–55 months) who have an ASD diagnosis and one male child (age 18 months) who displayed behaviors consistent with an ASD, were assessed using the SCERTS Assessment Process Observation (SAP-O) form. The SAP-O meets state and federal requirements for providing a comprehensive, ongoing assessment of a child with an ASD [33] . The SAP-O form measures children's abilities using observational, authentic assessment procedures in the domains of joint attention, symbol use, mutual regulation, and self regulation via observations of specific behaviors in familiar settings [33] . The five children tested positive for Lyme disease and their SAP-O score was evaluated before and after 6 months of antibiotic therapy. Each child was prescribed 200 mg of amoxicillin three times per day and three of the five children were prescribed an additional 50 mg of Azithromycin once per day.

All of the children's scores on the SAP-O assessment improved after 6 months of antibiotic therapy. The assessors also reported anecdotal data of improved speech, eye contact, sleep behaviors, and a reduction of repetitive behaviors.

Liegner, K. B. (2019). Disulfiram (Tetraethylthiuram Disulfide) in the treatment of lyme disease and babesiosis: report of experience in three cases. *Antibiotics*, *8*(2), 72.

Abstract

Three patients, each of whom had required intensive open-ended antimicrobial therapy for control of the symptoms of chronic relapsing neurological Lyme disease and relapsing babesiosis, were able to discontinue treatment and remain clinically well for periods of observation of 6–23 months following the completion of a finite course of treatment solely with disulfiram. One patient relapsed at six months and is being re-treated with disulfiram.

Potula, Hari-Hara, et al. "Repurposing **disulfiram** (Tetraethylthiuram Disulfide) as a potential drug candidate against Borrelia burgdorferi in vitro and in vivo." *bioRxiv* (2019): 842286.

ABSTRACT: Lyme disease caused by the *Borrelia burgdorferi* (*Bb or B. burgdorferi*) is a most common vector-borne, multi-systemic disease in USA. Although, most Lyme disease patients can be cured with a course of antibiotic treatment, a significant percent of patient population fail to be disease-free post-treatment, necessitating the development of more effective therapeutics. We previously found several drugs including disulfiram having with good activity against *B. burgdorferi*. In current study, we evaluated the potential of repurposing the FDA approved disulfiram drug for its *borrelia*cidal activity. Our *in vitro* results indicate disulfiram shows excellent *borrelia*cidal activity against both the log and stationary phase *B. burgdorferi*. Subsequent mice studies have determined that the disulfiram eliminated *B. burgdorferi* completely from hearts and urinary bladder by day 28 post infection, demonstrating the practical application and efficacy of disulfiram against *B. burgdorferi in vivo*. Moreover, disulfiram treated mice showed reduced expression of inflammatory markers and protected against histopathology and organ damage. Furthermore, disulfiram treated mice showed significantly lower amounts of total antibody titers (IgM and IgG) at day 21 and total IgG2b at day 28 post infection. Mechanistically, cellular analysis of lymph nodes revealed a decrease in percentage of CD19+ B cells and increase in total percentage of CD3+ T cells, CD3+ CD4+ T helpers, and naïve and effector memory cells in disulfiram-treated mice.

Together, we demonstrate that disulfiram has the potential and could be repurposed as an effective antibiotic for treating Lyme disease in near future.

Younger, David S., and Beverley F. Murphy. "Antabuse for Lyme Disease: The Way Forward." *World Journal of Neuroscience* 10.01 (2019): 1.

Abstract: Despite leadership by dedicated lay organization and patient-based advocacy groups, the way forward for prospective candidates for disulfiram treatment has been difficult. This article provides the background, overview of disulfiram, in particular its intended use in post-treatment Lyme disease syndrome after a standard of care course of antibiotics fails to alleviate symptoms of tick borne disease. A series of recommendations are offered to guide patients and clinicians.

1) Awaiting the results of clinical trials, individuals with PTLDS should consider treatment with disulfiram as an adjunct to conventional antibiotics but not a replacement.
2) Physician prescribed treatment with disulfiram should be carried out employing standard doses of 250 mg (or fractions thereof).
3) Safety monitoring should include blood studies for systemic complications, and avoidance of contact with alcohol in toiletries, foods, beverages, medications, and other sources of inadvertent alcohol exposure.
4) A **starting dose as low as 62.5 mg** can be slowly increased to the target dose depending upon tolerability and side effects.
5) Common side effects that may limit achievement of full doses include fatigue, body pain, nausea, headaches, peripheral neuropathy and neuropsychiatric disturbances.
6) The duration of treatment should be carefully determined among all individuals in keeping with empiric therapy to avoid inadvertent toxicity or prolonged use of disulfiram.
7) Peripheral neuropathy is not an absolute exclusion for consideration of disulfiram. Such cases should be carefully examined at baseline and monitored in the course of therapy.
8) Cases of painful small fiber sensory polyneuropathy may be monitored with IENF analysis in a punch skin biopsy of the calf and thigh.
9) **IVIg may be initiated before disulfiram in existing cases of peripheral neuropathy** as an effective treatment, or in the course of therapy for those with emergent neuropathy of either large or small fiber caliber, or exacerbation of either pre-existing disease.
10) Emergency or exacerbation of neuropsychiatric disturbances should lead to discontinuation of medication.

Bartonella and Bartonella-like Organisms (BLOs)

Symptoms:

- Brainfog, headache (“ice pick”), photophobia
- swollen lymph glands and/or swollen joints
- **OCD behavior, anxiety**
- Rapid relapse when antibiotics are stopped or no response to antibiotics
- endocardits
- hepatitis
- neovacularization
- fatigue
- low grade fever
- jaw bone cavitations, devitalized teeth
- often co-infection in ALS
- fibromyalgia and joint pain
- Transverse myelitis, spinal stenosis and arachnoiditis

Fried, J Schairer, G Madigan, A Bal - J Pediatr Gastroenterol Nutr, 2002: “*Bartonella henselae* is associated with heartburn, abdominal pain, skin rash, mesenteric adenitis, gastritis and duodentis in children and adolescents”.

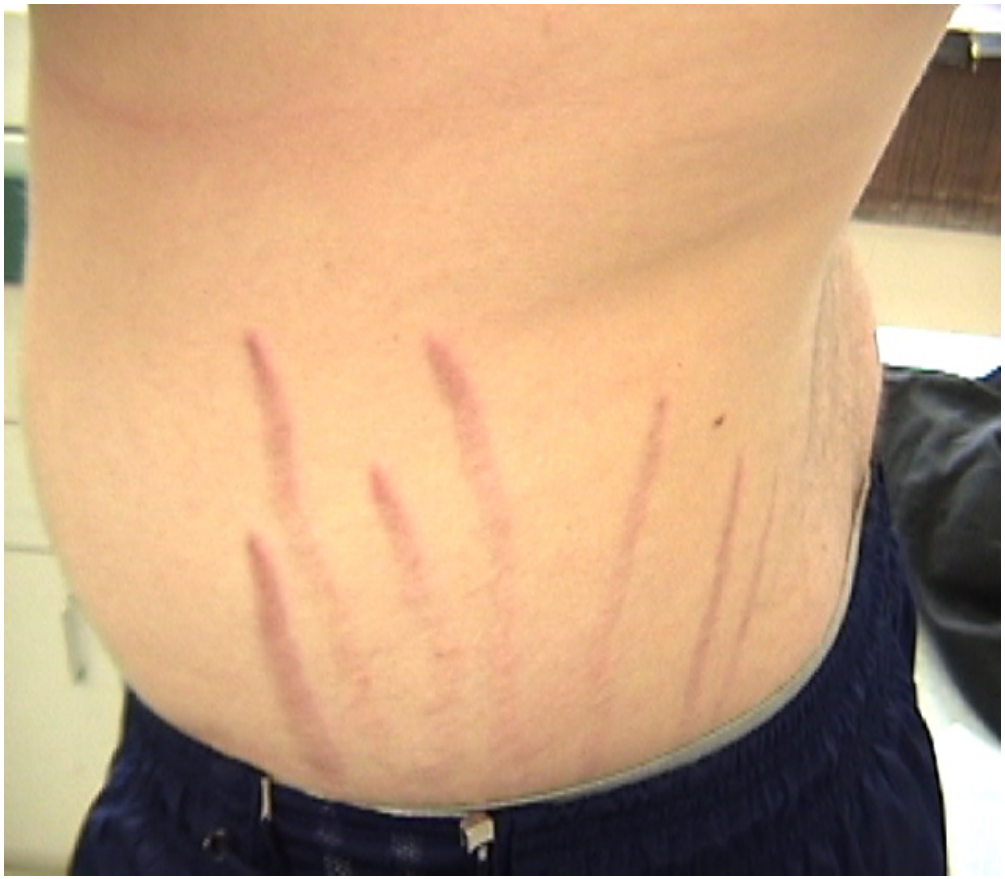
Diagnosis: provoked PCR, IgG/IgM or smear+stain (FryLabs)

Drug of choice in patients over 18: Cipro or Levofloxacin (Cave: possible longterm adverse effects), otherwise **Azithromycin 250 mg b.i.d**., **Doxycycline 100 mg b.i.d**. and **Rifampin** 300 mg b.i.d. together or: Polygonum and Stephania root (BioPure “Cocktail”) + propolis +calendula, ozonated plant oils (Rizol Gamma), ozone joint injections, LDI

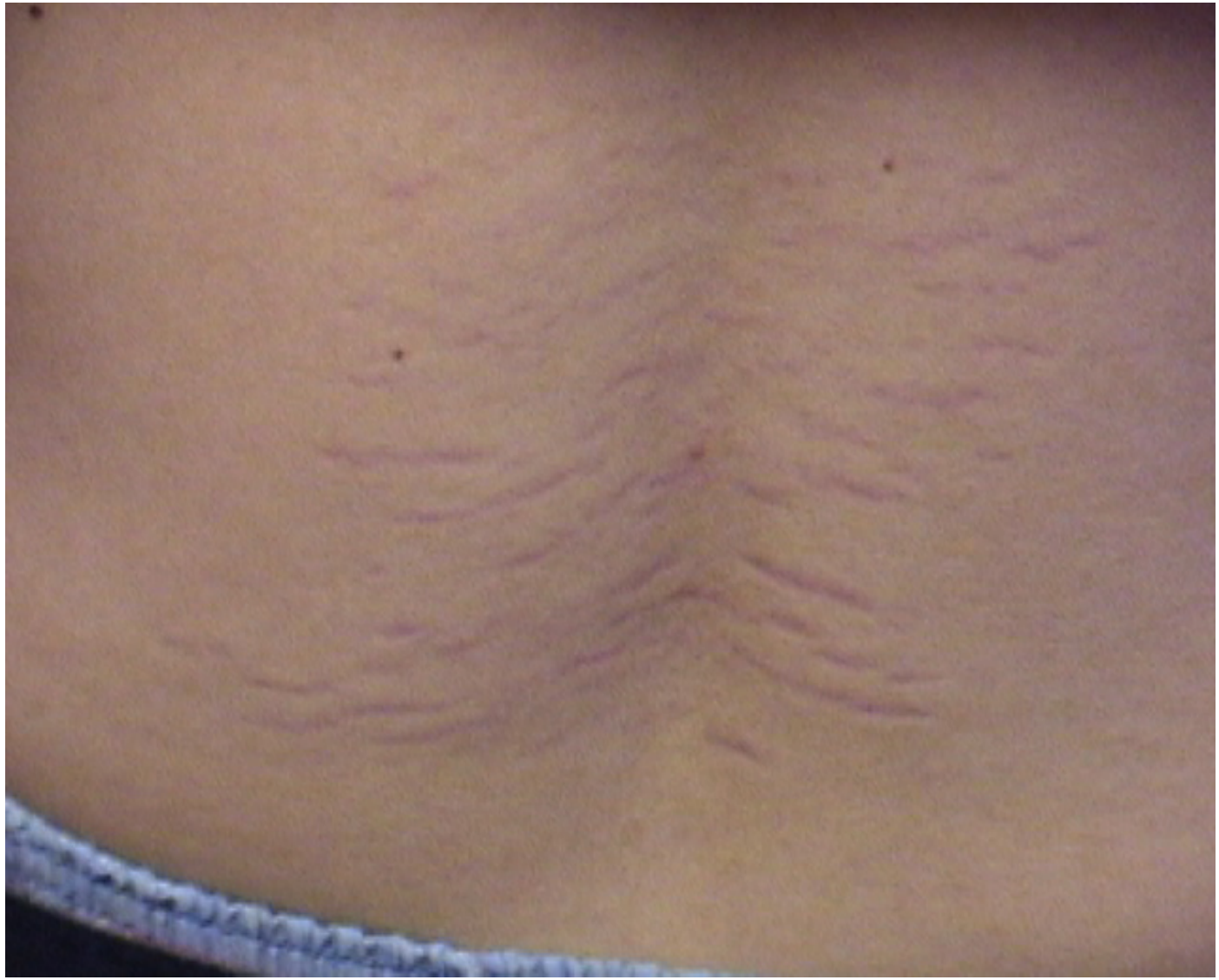
Bartonella Rashes

Linear rashes- look like stretch marks, clinically associated with gastritis

Photos taken by Dr. Martin Fried, with thanks to the Lyme Disease Association



Lower Back



Dr. D. Klinghardt: Biologische Behandlung
der Lyme-Borreliose

Rolain, J. M., Brouqui, P., Koehler, J. E., Maguina, C., Dolan, M. J., & Raoult, D. (2004). Recommendations for treatment of human infections caused by **Bartonella** species. *Antimicrobial Agents and Chemotherapy*, *48*(6), 1921-1933.

With a recently established erythrocyte coculture model, it was found that most of the antibiotics tested (i.e., **doxycycline, fluoroquinolone compounds, and beta-lactams) were not bactericidal** against *Bartonella* (90). Gentamicin was **bactericidal at 4 µg/ml, as was rifampin**. At this concentration, gentamicin was shown to enter erythrocytes slowly and to reach a peak level of 0.26 µg/ml after 24 h. However, when the ability of gentamicin to kill extraerythrocytic *B. quintana* at the concentration of 0.26 µg/ml achieved in the erythrocyte was tested, it was found that gentamicin was not bactericidal, even after 96 h of incubation (90). We hypothesize that erythrocytes may be a reservoir for *B. quintana* and that the bactericidal activity of gentamicin that was observed occurs mainly when the bacteria emerge from the erythrocytes and are found extracellularly.

The only prospective treatment trial, a double-blind, placebo-controlled study of azithromycin treatment of immunocompetent patients with uncomplicated CSD, was reported by Bass et al. (8). **An 80% decrease in the initial lymph node volume was documented in 7 of 14 azithromycin-treated patients** but in only 1 of 15 placebo-treated controls during the first 30 days of observation ($P = 0.026$) (8). There was no difference in any clinical outcome measurement except for the rate and degree of decrease of total lymph node volume as determined by sonographic documentation. At 30 days, patients treated with azithromycin had a significantly greater reduction in the total lymph node volume, as demonstrated by sonography, in comparison to the total lymph node volume of the placebo group (8). The investigators did not demonstrate any efficacy of azithromycin for the treatment of disseminated CSD, either for prevention of the evolution of localized CSD to disseminated disease or for prevention of complications such as encephalitis or endocarditis. Thus, a recommendation to treat immunocompetent CSD patients with azithromycin remains very premature at present.

Zheng, X., Ma, X., Li, T., Shi, W., & Zhang, Y. (2020). Effect of different drugs and drug combinations on killing stationary phase and biofilms recovered cells of Bartonella henselae in vitro. *BMC microbiology*, *20*, 1-9.

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

Goo, Y. K., Terkawi, M. A., Jia, H., Aboge, G. O., Ooka, H., Nelson, B., ... & Nishikawa, Y. (2010). **Artesunate, a potential drug for treatment of Babesia infection.** *Parasitology international*, *59*(3), 481-486.

Abstract

The effects of artesunate, a water-soluble artemisinin derivative, against *Babesia* species, including *Babesia bovis*, *Babesia gibsoni* and *Babesia microti* were studied. Cultures of *B. bovis* and *B. gibsoni* were treated with 0.26, 2.6, 26 and 260 μM artesunate, showing inhibition of parasite growth at concentrations equal to and greater than 2.6 μM artesunate by days 3 post-treatment for *B. gibsoni* and *B. bovis* in a dose-dependent manner. Consistent with *in vitro* experiments, artesunate was effective in the treatment of mice infected with *B. microti* at doses equal to and greater than 10 mg/kg of body weight on days 8–10 post-infection. Taken together, these results suggest that artesunate could be a potential drug against *Babesia* infection.

D.The Klinghardt Approach

Wormwood: **Artemisia annua,** Artemisinin and Artesunate

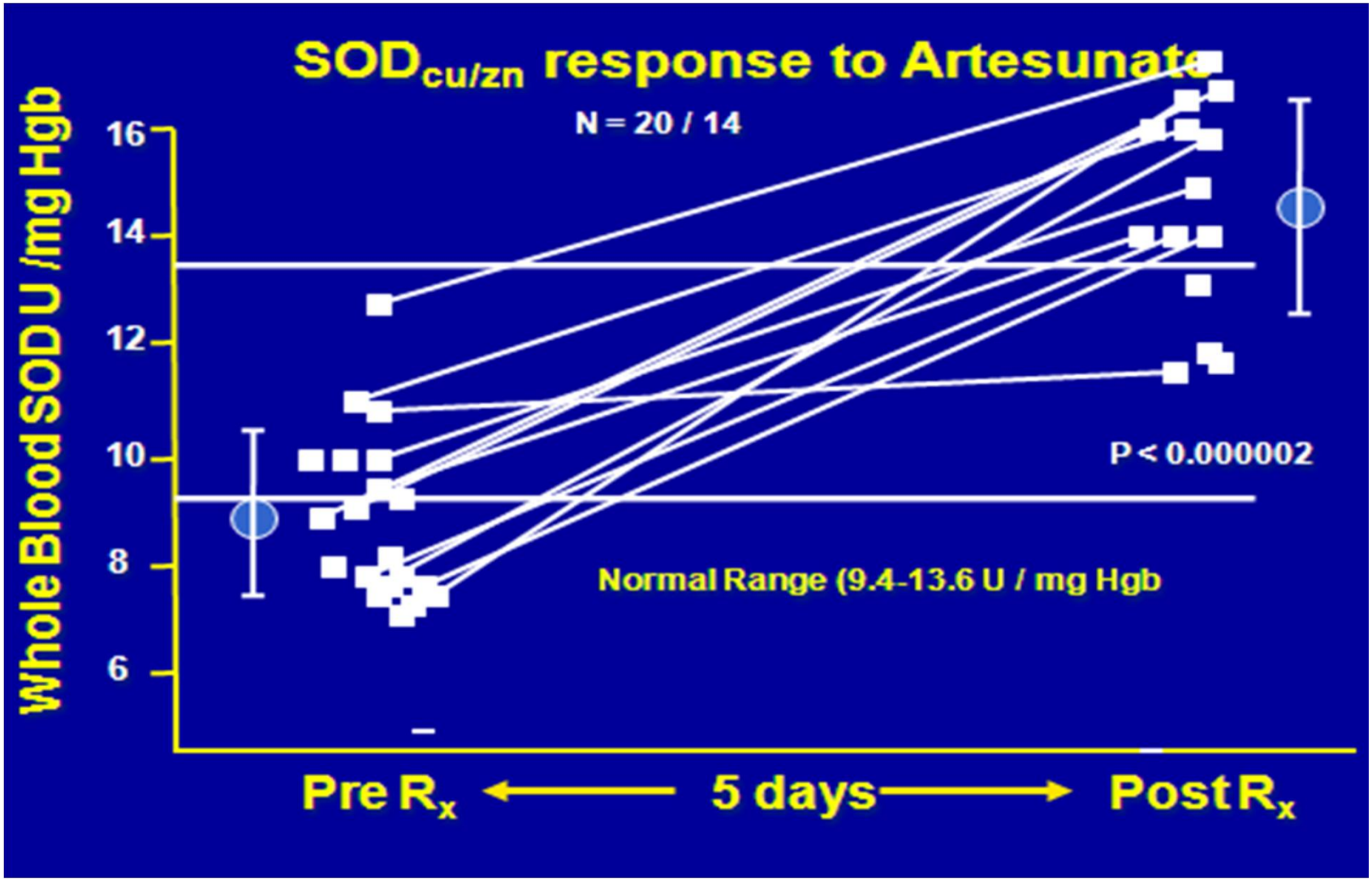
Trends In Parasitology; Volume 31, Issue 12, December 2015, Pages 605–607

Science & Society

Reflections on the Nobel Prize for Medicine 2015 – The Public Health Legacy and Impact of Avermectin and Artemisinin

David H. Molyneux, Steve A. Ward

The award of the Nobel Prize to Dr Bill Campbell and Professor Satoshi Ōmura for their role in the discovery of avermectin and Professor Youyou Tu for her work on the development of artemisinin has been universally welcomed by the International Health community for what the Nobel Committee described as 'The discoveries of Avermectin and Artemisinin have revolutionized therapy for patients suffering from devastating parasitic diseases. Campbell, Ōmura and Tu have transformed the treatment of parasitic diseases. The global impact of their discoveries and the resulting benefit to mankind are immeasurable'.

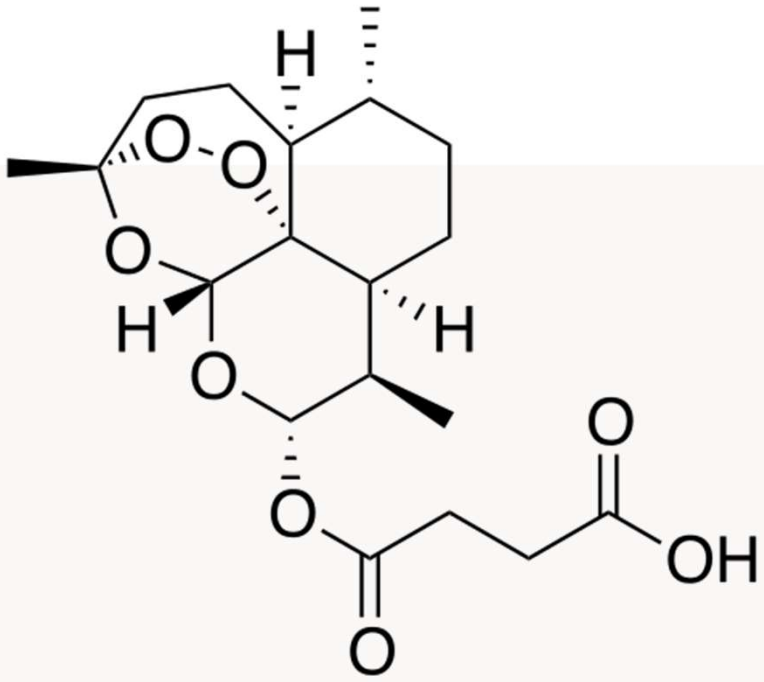

SOD cu/zn response to Artesunate
N = 20 / 14
Whole Blood SOD U /mg Hgb
16
14
12
10
8
6
P < 0.000002
Normal Range (9.4-13.6 U / mg Hgb
Pre Rx
5 days
Post Rx

Artesunate, artemisinin and Artemisia have not been studied for Lyme and co-infections, but clinical experience is strongly suggesting their use as a potent and safe treatment

From the literature: Lyme treatment with wormwood, andrographis and Japanese knotweed

- Spring 2014 Journal of the New Zealand Association of Medical Herbalists AVENA, Vol14, issue 3, Sara Mertens
- Artemisia annua and artemisinin for treatment of Babesia: “Bell’s Palsy of the Gut and other GI manifestations of Lyme and associated diseases” Virginia T. Sherr, M.D., DLFAPA; in: PRACTICAL GASTROENTEROLOGY • APRIL 2006, pg 88
- ”Herbs with Anti-Lyme Potential” Townsend letter, James Duke PhD, April 2007, pg 114-117
- “Lyme disease: A Look Beyond Antibiotics” Dietrich K.Klinghardt, MD, PhD; Explor Infect Dis, 2005
- “The Use of the Herb Artemisinin for Babesia, Malaria, and Cancer” www.amazon.com J.Schaller - 2006 - Florida: Hope Academic Press
- Oxford Textbook of Infectious Diseases, 2000: several references for the use of artemisinin for Babesia, Lyme, Bartonella

Artesunate
$C_{19}H_{28}O_8$



Phase 4:
Reduces
pathogen load

Artesunate

Neural therapy

Aluminum potentizes Lyme

Occurrence of Severe Destructive Lyme Arthritis in Hamsters Vaccinated with Outer Surface Protein A and Challenged with *Borrelia burgdorferi*

Infect. Immun. February 2000 **vol. 68 no. 2** 658-663 Cindy L. Croke1,2, Erik L. Munson1,2, Steven D. Lovrich3,John A. Christopherson1,2, Monica C. Remington1,2,Douglas M England4,5, Steven M. Callister3,6 and Ronald F. Schell1,2,7,*

ABSTRACT

Arthritis is a frequent and major complication of infection with *Borrelia burgdorferi* sensu stricto. The antigens responsible for the induction of arthritis are unknown. Here we provide direct evidence that a major surface protein, outer surface protein A (OspA), can induce arthritis. Hamsters were vaccinated with 30, 60, or 120 μg of recombinant OspA (rOspA) in aluminum hydroxide and challenged with *B. burgdorferi* sensu stricto isolate 297 or C-1-11. Swelling of the hind paws was detected in 100, 100, and 50% of hamsters vaccinated with 30, 60, or 120 μg of rOspA, respectively. In addition, arthritis developed in 57% of hamsters vaccinated with a canine rOspA vaccine after infection with *B. burgdorferi*sensu stricto. **When the canine rOspA vaccine was combined with aluminum hydroxide, all vaccinated hamsters developed arthritis** after challenge with *B. burgdorferi* sensu stricto. Histopathologic examination confirmed the development of severe destructive arthritis in rOspA-vaccinated hamsters challenged with *B. burgdorferi*sensu stricto. These findings suggest that rOspA vaccines should be modified to eliminate epitopes of OspA responsible for the induction of arthritis. Our results are important because an rOspA vaccine in aluminum hydroxide was approved by the Food and Drug Administration for use in humans

Most if not all patients are high in aluminum

Dietrich Klinghardt
In den Engematten 5

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Tél.:+49 7684 9088360

[redacted]

Date: 2017/03/08
Female 20 years
Date of Birth: [redacted]
Blood group: [redacted]
Weight: 113 lb
Size: 4 ft 7 in

Heavy Metal Test Report

		Result	Normal	High -	High +	Excess
Aluminium		0.01347				
Antimony	Sb	0.00193				
Silver		0.01003				
Arsenic	As	0.00386				
Barium		0.00582				
Beryllium	Be	0.00421				
Bismuth		0.00739				
Cadmium		0.00838				
Mercury	Hg	0.00306				
Nickel	Ni	0.00308				
Platinum	Pt	0.00228				
Lead		0.00656				
Thallium	Tl	0.00141				
Thorium	Th	0.00087				

Heavy Metals Intoxication

Overall Intoxication — unsatisfactory: 69%

Suspicion of the blockage for the elimination of heavy metals due to the possible lack of sulfur conjugation: 75%

Immune Modulation: use LDI/LDA

Homeopathy (2010) 99, 156e166;

doi:10.1016/j.homp.2010.05.009, available online at http://www.sciencedirect.com

ORIGINAL PAPER

Large-scale application of highly-diluted bacteria for Leptospirosis epidemic control

Gustavo Bracho1,*, Enrique Varela2, Rolando Ferna´ndez3, Barbara Ordaz3, Natalia Marzoa3, Jorge Mene´ndez4, Luis Garcı´a5, Esperanza Gilling6, Richard Leyva7, Reynaldo Rufı´n8, Rube´n de la Torre9, Rosa L Solis10, Niurka Batista5, Reinier Borrero5 and Concepcio´n Campa

Background: Leptospirosis is a zoonotic disease of major importance in the tropics where the incidence peaks in rainy seasons. Natural disasters represent a big challenge to Leptospirosis prevention strategies especially in endemic regions. Vaccination is an effective option but of reduced effectiveness in emergency situations. Homeoprophylactic interventions might help to control epidemics by using highly-diluted pathogens to induce protection in a short time scale. We report the results of a very large-scale homeoprophylaxis (HP) intervention against Leptospirosis in a dangerous epidemic situation in three provinces of Cuba in 2007.

Methods: Forecast models were used to estimate possible trends of disease incidence. A homeoprophylactic formulation was prepared from dilutions of four circulating strains of Leptospirosis. **This formulation was administered orally to 2.3 million persons** at high risk in an epidemic in a region affected by natural disasters. The data from surveillance were used to measure the impact of the intervention by comparing with historical trends and non-intervention regions.

Results: After the homeoprophylactic intervention a significant decrease of the disease incidence was observed in the intervention regions. No such modifications were observed in non-intervention regions. In the intervention region the incidence of Leptospirosis fell below the historic median. This observation was independent of rainfall.

Conclusions**: The homeoprophylactic approach was associated with a large reduction of disease incidence and control of the epidemic**. The results suggest the use of HP as a feasible tool for epidemic control, further research is warranted. Homeopathy (2010) 99, 156e166.

Keywords: Homeoprophylaxis; Prevention; Leptospirosis; Epidemics; Cuba

PLoS One. 2015 Mar 25;10(3):e0117207. doi: 10.1371/journal.pone.0117207. eCollection 2015.

Drug combinations against Borrelia burgdorferi persisters in vitro: eradication achieved by using daptomycin, cefoperazone and doxycycline.

Feng J[1], Auwaerter PG[2], Zhang Y[1].

Abstract

Although most Lyme disease patients can be cured with antibiotics doxycycline or amoxicillin using 2-4 week treatment durations, some patients suffer from persistent arthritis or post-treatment Lyme disease syndrome. Why these phenomena occur is unclear, but possibilities include host responses, antigenic debris, or B. burgdorferi organisms remaining despite antibiotic therapy. In vitro, B. burgdorferi developed increasing antibiotic tolerance as morphology changed from typical spirochetal form in log phase growth to variant round body and microcolony forms in stationary phase. B. burgdorferi appeared to have higher persister frequencies than E. coli as a control as measured by SYBR Green I/propidium iodide (PI) viability stain and microscope counting. To more effectively eradicate the different persister forms tolerant to doxycycline or amoxicillin, drug combinations were studied using previously identified drugs from an FDA-approved drug library with high activity against such persisters. Using a SYBR Green/PI viability assay, daptomycin-containing drug combinations were the most effective. Of studied drugs, daptomycin was the common element in the most active regimens when combined with doxycycline plus either beta-lactams (cefoperazone or carbenicillin) or an energy inhibitor (clofazimine).

Daptomycin plus doxycycline and cefoperazone eradicated the most resistant microcolony form of B. burgdorferi persisters and did not yield viable spirochetes upon subculturing, suggesting durable killing that was not achieved by any other two or three drug combinations. These findings may have implications for improved treatment of Lyme disease, if persistent organisms or detritus are responsible for symptoms that do not resolve with conventional therapy. Further studies are needed to validate whether such combination antimicrobial approaches are useful in animal models and human infection.

PMID: 25806811

Alvarez-Manzo, H. S., Zhang, Y., Shi, W., & Zhang, Y. (2020). Evaluation of Disulfiram Drug Combinations and Identification of Other More Effective Combinations against Stationary Phase Borrelia burgdorferi. *Antibiotics*, *9*(9), 542.

Abstract: Lyme disease, caused by *Borrelia burgdorferi*, is the most common vector-borne disease in USA, and 10–20% of patients will develop persistent symptoms despite treatment ("post-treatment Lyme disease syndrome"). *B. burgdorferi* persisters, which are not killed by the current antibiotics for Lyme disease, are considered one possible cause. Disulfiram has shown to be active against *B. burgdorferi*, but its activity against persistent forms is not well characterized. We assessed disulfiram as single drug and in combinations against stationary-phase *B. burgdorferi* culture enriched with persisters. Disulfiram was not very effective in the drug exposure experiment (survival rate (SR) 46.3%) or in combinations. Clarithromycin (SR 41.1%) and nitroxoline (SR 37.5%) were equally effective when compared to the current Lyme antibiotic cefuroxime (SR 36.8%) and more active than disulfiram. **Cefuroxime + clarithromycin** (SR 25.9%) and cefuroxime + nitroxoline (SR 27.5%) **were significantly more active than cefuroxime + disulfiram** (SR 41.7%). When replacing disulfiram with clarithromycin or nitroxoline in three-drug combinations, bacterial viability decreased significantly and subculture studies showed that combinations with these two drugs (cefuroxime + clarithromycin/nitroxoline + furazolidone/nitazoxanide) inhibited the regrowth, while disulfiram combinations did not (cefuroxime + disulfiram + furazolidone/nitazoxanide). Thus, clarithromycin and nitroxoline should be further assessed to determine their role as potential treatment alternatives in the future.

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.

Lyme disease is the most common vector-borne disease in the US and Europe. Although the current recommended Lyme antibiotic treatment is effective for the majority of Lyme disease patients, about 10–20% of patients continue to suffer from persisting symptoms. There have been various anecdotal reports on the use of herbal extracts for treating patients with persisting symptoms with varying degree of improvements. However, it is unclear whether the effect of the herb products is due to their direct antimicrobial activity or their effect on host immune system. In the present study, we investigated the antimicrobial effects of 12 commonly used botanical medicines and three other natural antimicrobial agents for potential anti-Borrelia burgdorferi activity in vitro. Among them, 7 natural product extracts at 1% were found to have good activity against the stationary phase B. burgdorferi culture compared to the control antibiotics doxycycline and cefuroxime. **These active botanicals include Cryptolepis sanguinolenta, Juglans nigra (Black walnut), Polygonum cuspidatum (Japanese knotweed), Artemisia annua (Sweet wormwood), Uncaria tomentosa (Cat's claw), Cistus incanus, and Scutellaria baicalensis (Chinese skullcap).** In contrast, Stevia rebaudiana, Andrographis paniculata, Grapefruit seed extract, colloidal silver, monolaurin, and antimicrobial peptide LL37 had little or no activity against stationary phase B. burgdorferi. The minimum inhibitory concentration (MIC) values of Artemisia annua, Juglans nigra, and Uncaria tomentosa were quite high for growing B. burgdorferi, despite their strong activity against the non-growing stationary phase B. burgdorferi. On the other hand, the top two active herbs, **Cryptolepis sanguinolenta and Polygonum cuspidatum**, showed strong activity against both growing B. burgdorferi (MIC = 0.03–0.06% and 0.25–0.5%, respectively) and non-growing stationary phase B. burgdorferi.

Cistus tea (prevention of tick bites, biofilm- dissolving, borreliocidal, anti-retroviral) Start with 1/2 cup per day, slowly increase to 8 cups per day – according to tolerance. Re-brew the tea-leaves once to get the benefit from sequential release of additional polyphenols and other healing agents. Add **Galaktose** as sweetener for its immune modulating effect (anti-autoimmunity). Once the full dose has been reached, add **Cistus Incanus tincture** 1/2 dropperful to each cup. The tincture concentrates the essential oils from the plant. Source: Biopure.eu, BioPureUS.com and KiScience.com

Rauwald, H. W., et al. "On the **antispirochaetal activity** of manoyloxides and carvacrol from the oleoresin labdanum of Cistus creticus L." Planta Medica 79.13 (2013): PN53.

Binders: when the treatment awakens the immune system, mild to moderate Herxheimer reactions are to be expected, also the release of toxins that were entrapped before. Progress can be facilitated or symptoms can be minimalized by using colonics, lymph drainage and the oral use of agents that bind mobilized toxins and prevent re-absorption.

- **Zeolite**: 1/2 tsp 2-3 times daily between meals and/or at bedtime
- **Chlorella**: 8-16 tablets (250 mg each) 3 times per day 30 min before meals or at bedtime Source: BioPureUS

KiVita (German speaking countries: **LKC** in the US: "**Cocktail**" from BioPureUS.com): **Polygonum cuspidatum (Jap.knotweed), Andrographis, Astragalus, Artemisia annua, Scutalaria, Propolis, Cilantro, Smilax, Ribes nigrum:** 2-3 dropperful 3 times/day As soon as any improvement is noticed, stay with that dose without further increase. If a die-off effect or worsening occurs, go back to the last tolerated dose

Lyme is intelligent.
With the help of ART we have found substantial missing ingredients:

Aluminium detox should be an essential part of treatintg Lyme:

- A. Citric acid – apple cider vinegar (or half lemon) in 250-500 ml water in the morning
- B. Malic acid: use magnesium malate up to 600 mg with dinner
- C. AluLu (UK: Polmolo, US: AluTox) herbal mix to provide bio available silica
- D. Ionic foot/handbath: platinum electrode only. 30 min 4 times/week (www.biopure.eu and www.kiscience.com)

Bait/"Lockmittel": to tease the pathogens to come out of hiding (biofilm, intracellular). We use sublingual hyaluronic acid 2 dropperful 4 times/day

EMR: Pathogens thrive in high microwave environments. Reduce exposure. Consider radioprotective clothing, protective rosemary, propolis and gingko extracts

Retroviruses: Insect bites commonly transmit retroviruses which are the cause of many "Lyme" symptoms: use RetroV powder (2 tsp twice daily) and RetroBai (Baikalin) 2 capsules 2-3 times/day (Biopure.eu)

- **Mold**: many Lyme patients suffer from mould illness as well. The Cistus tea has phenomenal anti-fungal properties, chlorella and zeolite are excellent toxin binders. Consider adding **O3-Oil Gamma (Rizol Gamma)** to the mix: 10 drops 3 times a day. Rizol Kappa and Lambda often test for Bartonella (same dose). Do not use longer than 3 weeks before pausing for 2 weeks, then repeat. In children we prefer the use of Sporanox 100-200 mg twice daily, for up to 9 months. The **home** has to be mould free, as well as the body. We use several strategies in addition to the home mold mitigation:
  - **propolair** propolis evaporation in the home
  - Spraying the home with **HOCL**
  - Spraying the home with **EM**
- The dosages recommended above are for a 160 lb person. Adjust the individual doses accordingly. Other suppliers can be used as long as the products are sourced carefully and meet the sensitive exclusion criteria. Herbs may have the same name but may not have the same amount of biological activity.
- During the initial active treatment phase antioxidant vitamins have been shown to be an obstacle rather than helpful.
- **Biophysics**: at SHI we use sauna, acupuncture, **neural therapy, microcurrent**, sound and **light therapy (K-Scan, PhotonWave)**, pulsating magnetic fields, homeopathy, massage and **ultrasound to enhance remedy uptake** and recovery of the autonomic nervous system. But clearly neural therapy stands out in its effectiveness, simplicity and versatility.
- Most chronic Lyme patients start feeling better after 3-4 months on this protocol and reach a profound level of recovery after 18 months.
- Some patients who were severely ill for many years and have taken antibiotics for more than 3 years may need a safe, simple, inexpensive and well tolerated maintenance dose of some of these liposomal herbs for the rest of their life.

Other helpful anti-microbial treatment options

- **Artesunate** injections: in Europe we use injectable Artesunate (60 mg vials) for the refractory treatment of Lyme and co-infections. The patient also learns to self-inject into the subcutaneous tissue. Dosage: slowly increase to 120 mg twice weekly – always together with the oral program. Artesunate can also be used i.v. or diluted with Procaine and injected into trigger points, glands and autonomic ganglia (neuraltherapy Klinghardt system).
- **i.v.ozone** therapy (Dr.Frank Schallenberger MD, Robert Rowen MD), also for joint and trigger point injections
- We have excellent experience sending clients to www.SwissBioHealth.com for successful cavitation surgery and placement of zirconium oxide implants when needed
- Hyperthermia (has disappointed on its own, but helpful while giving i.v. antibiotics)
- Hypothermia
- Intravenous **Desferal** (Iron overload, aluminium toxicity)and **DMPS** (sulfhydryl affinitive toxins) have a significant place in the treatment of chronic Lyme
- Dr.Klinghardt liposomal herbal Lyme cocktail (BioPure.eu, KlinghardtInstitute.com)
- High dose **Melatonin** to modulate the inflammasome
- Bee venom therapy

Dietrich K.Klinghardt MD, PhD

www.INK.ag

www.KlinghardtInstitute.com

Sophia Health Institute in Woodinville, WA