Chronic Pain and persistent infections – a new diagnostic and therapeutic concept

Dietrich Klinghardt MD, PhD

Fulda, April 2017

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Dr. med. Dietrich Klinghardt I Ariane Zappe

SophiaMed©
WEISHEIT WISSEN MEDIZIN

Die biologische Behandlung der Lyme-Borreliose

DIE PERSISTENZ VON ERREGERN ALS URSACHE CHRONISCHER ERKRANKUNGEN

Langjährige klinische Erfahrungen mit M. Alzheimer, Autismus, Multipler Sklerose, Amyotropher Lateralsklerose, M. Parkinson, Müdigkeit und Erschöpfung, Schlafstörungen, Schmerzzuständen und neurologischen Symptomen

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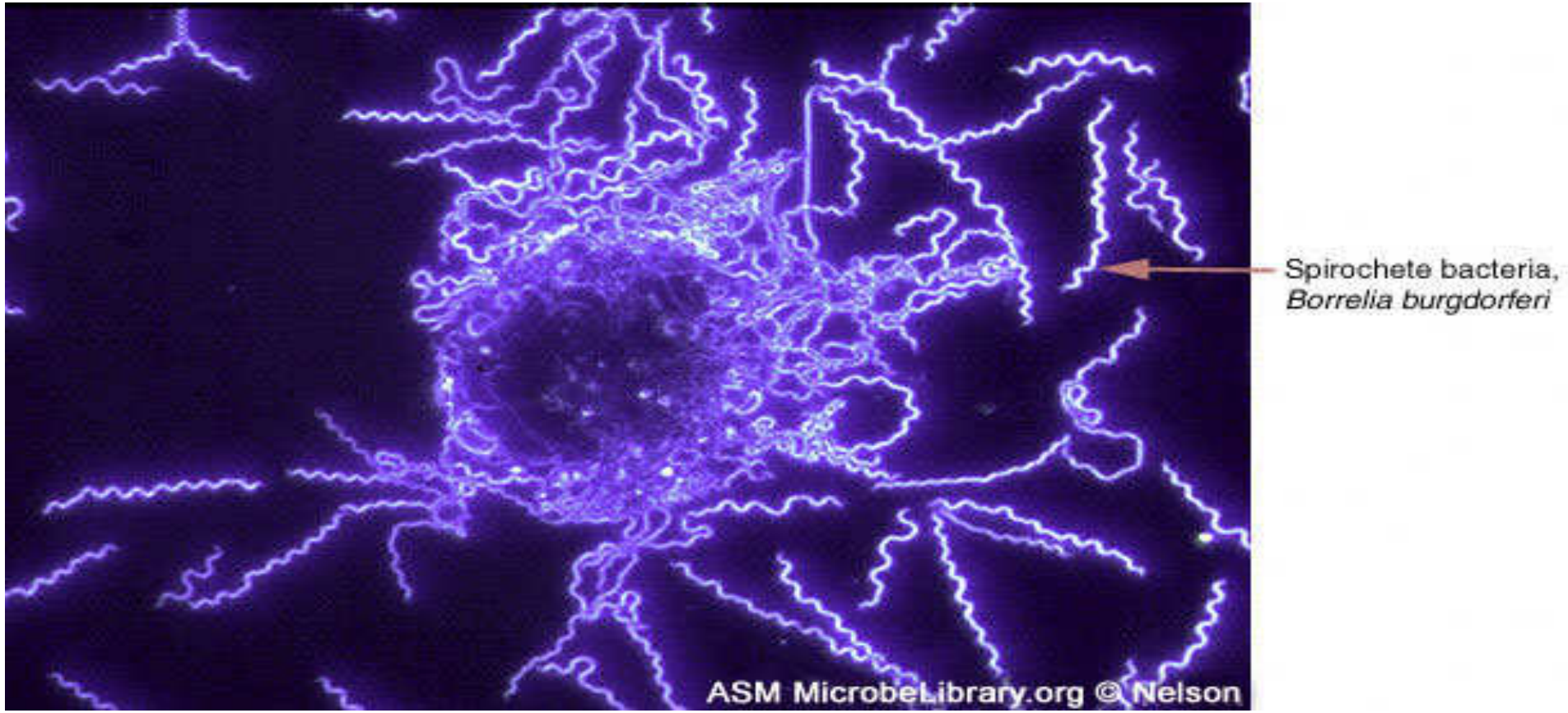
Personal experience

- When I worked as a physician in India (1979-82) I saw children and adults after horrible accidents. No matter what the long term deformity was, there was no pain after 6 weeks.
- I moved to the US: people had minor accidents, but pain that continuously increased after the initial event and grew over time, resulting in complete disability. The MRI was often completely normal right after the event, but showed several degenerated or ruptured discs after 1 year. What or who was eating the discs?
- Disc biopsies from these patients (I performed fluoroscopy-guided discography and intradiscal injections) showed the annulus fibrosus occupied by living Lyme spirochetes
- Question: is chronic pain the result of pathogens setting up their domicile and housekeeping in the injured area and the resulting immune reactions? (correct answer: yes!)



Morphology of Borrelia burgdorferi. Dark field image © Jeffrey Nelson, Rush University, Chicago, Illinois and The MicrobeLibrary

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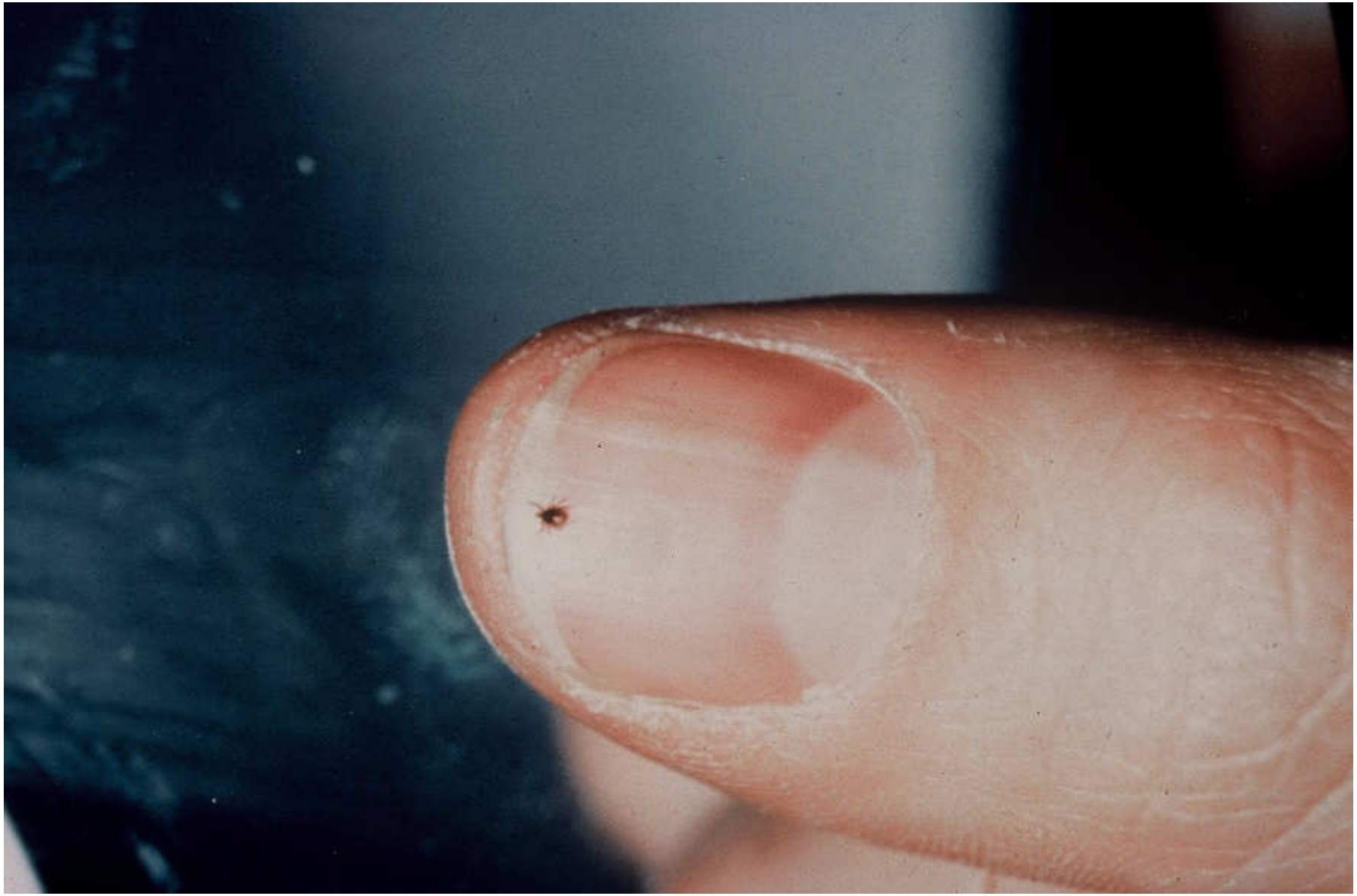

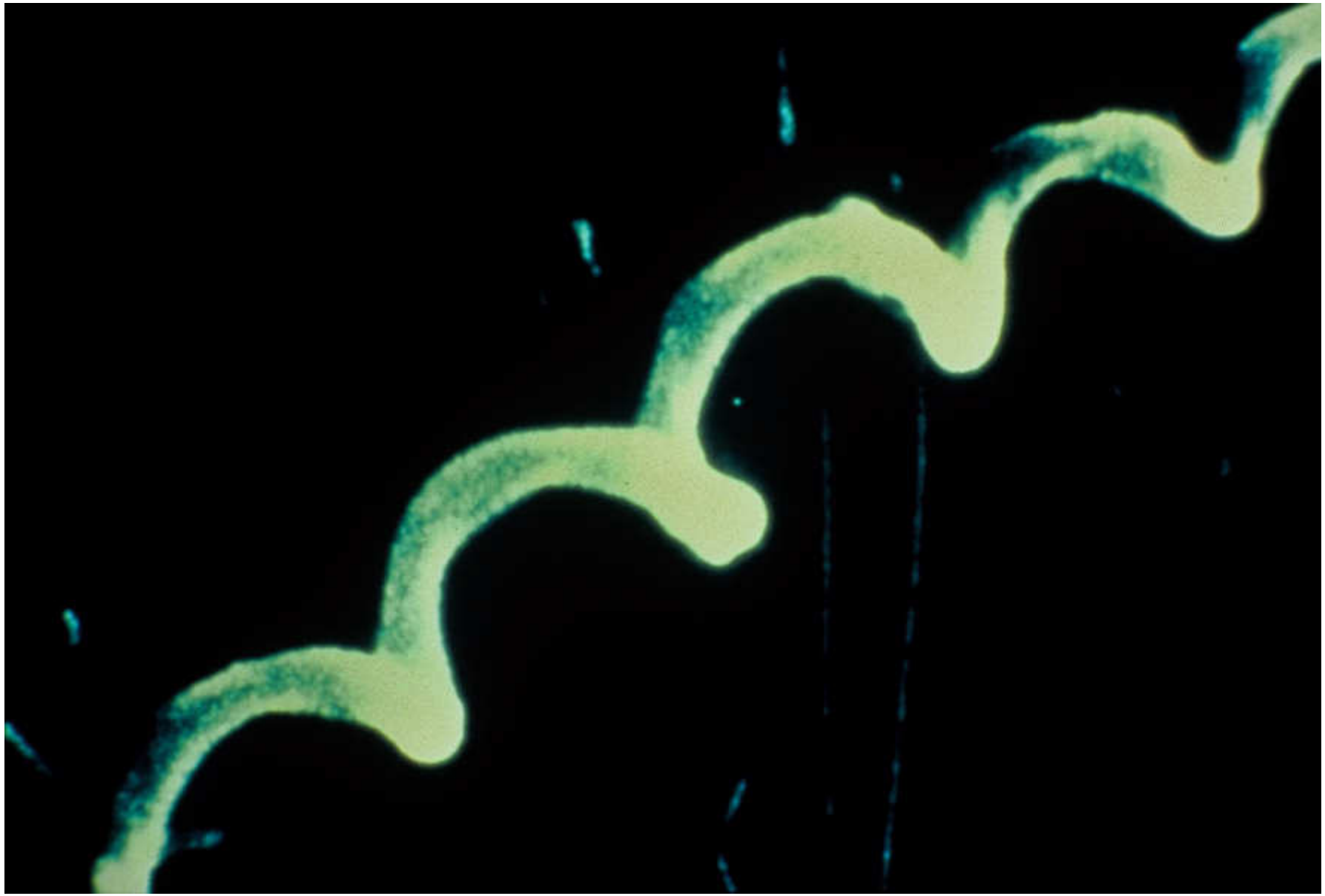

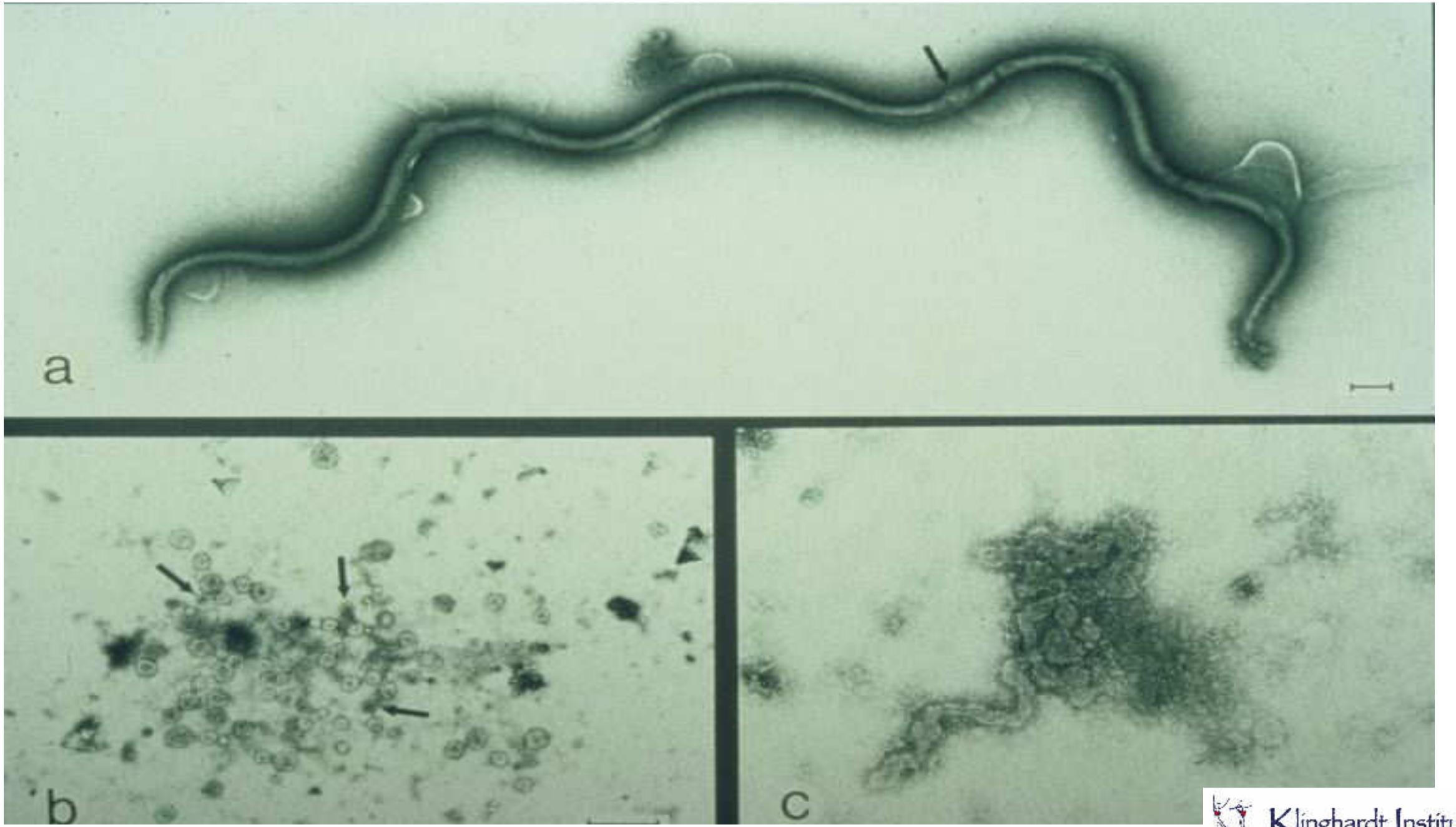

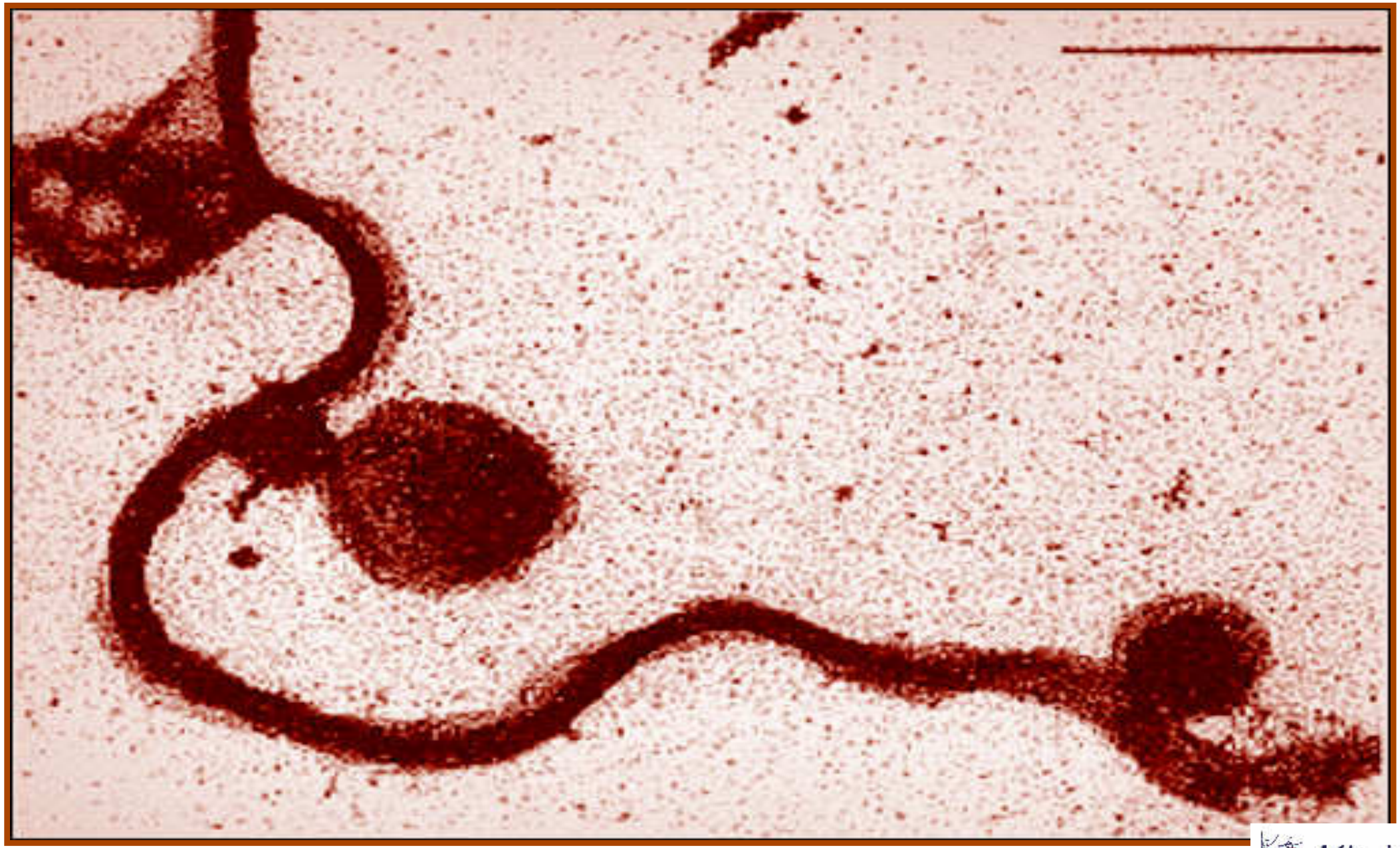

LYME BORRELIOSIS: TRANSMISSION

Mosquitos, lice, spiders, fleas

and ticks

Blood Transfusions

Sexual Intercourse

Trans-Placental to Fetus

Unpasteurized Milk

Breast Feeding

Food

The four most common pathogenic types of Lyme-Borrelia Spirochetes

- Borrelia garinii
- Borrelia afzelii
- Borrelia burgdorferi (Bb)

  Borrelia burgdorferi group: in-vitro antibiotic sensitivity: Orv Hetil, 2002 May 26; 143(21): 1195-8 (article in Hungarian), JP Henneberg, U Neubert –department of dermatology, Ludwig-Maximillian University, Munich, Germany

- Borrelia miyamotoi

  Human *Borrelia miyamotoi* Infection in the United States N Engl J Med 2013; 368:291-293 January 17, 2013 DOI: 10.1056/NEJMc1215469

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.)

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Borrelia Burgdorferi sensu strictu

- **Joint pain**
- Joint stiffness
- Joint swelling
- Gastrointestinal upset
- **Pelvic pain**
- **Fibromyalgia**
- Feeling of vibration in brain and spinal chord
- Myoclonus
- Fasciculations
- Dysuria
- Sciatica
- Chronic neck and low back pain
- Dysuria

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Babesia: Lyme patients with features of MS, ALS, PD, severe chronic depression have Babesia until proven otherwise (current test are not sufficient as proof of absence).

- Headaches and brain fog, memory loss**, migraines** and cluster headache
- **Night sweats**
- Dry cough
- dental problems: accelerated tooth decay and cavitation formation, TMJ problems
- Easy bruising
- Tinnitus
- epigastric pain, food malabsorption, weight loss and abdominal problems (GERD, Leaky Gut, Celiac plexus disease, constipation)
- Rage and Despair
- Vivid or violent dreams
- Buzzing in bottom of feet, fibromyalgia
- Psychic phenomena
- Severe neurological illnesses (Parkinson, MS, Alzheimer, Autism)
- Thirst/Polydipsia – pituitary problems, low or absent ADH
- Synergy with mold issues

Tx: Mepron + Azithromycin, **Artesunate i.v. or s.c., Artemisinin**, Noni, LDI

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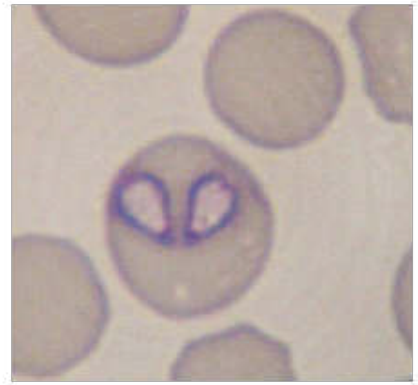
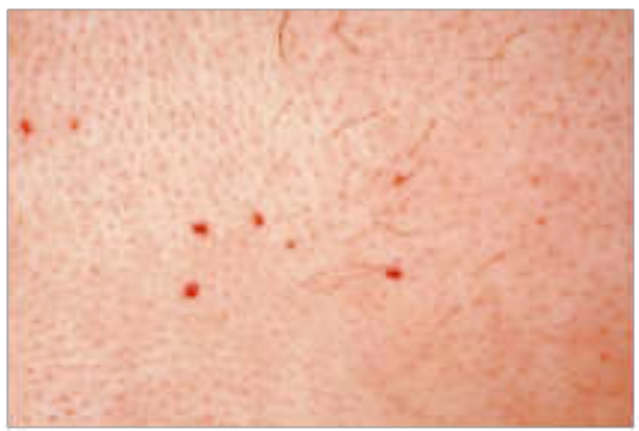
Babesien / FL1953



Unsere Messungen haben bestätigt, dass **mehr als 80 % der Borrelien-Träger auch mit Babesien infiziert sind.** Unserer Erfahrung nach leiden Lyme-Patienten mit der **Diagnose MS, ALS, M. Parkinson oder schwerer, chronischer Depression immer auch unter einer Infektion mit Babesien.**



Ein typischer Patient mit Babesien

Hauptsymptom der Babesien sind schwere Schweißausbrüche in der Nacht und Kirschangiome.

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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)

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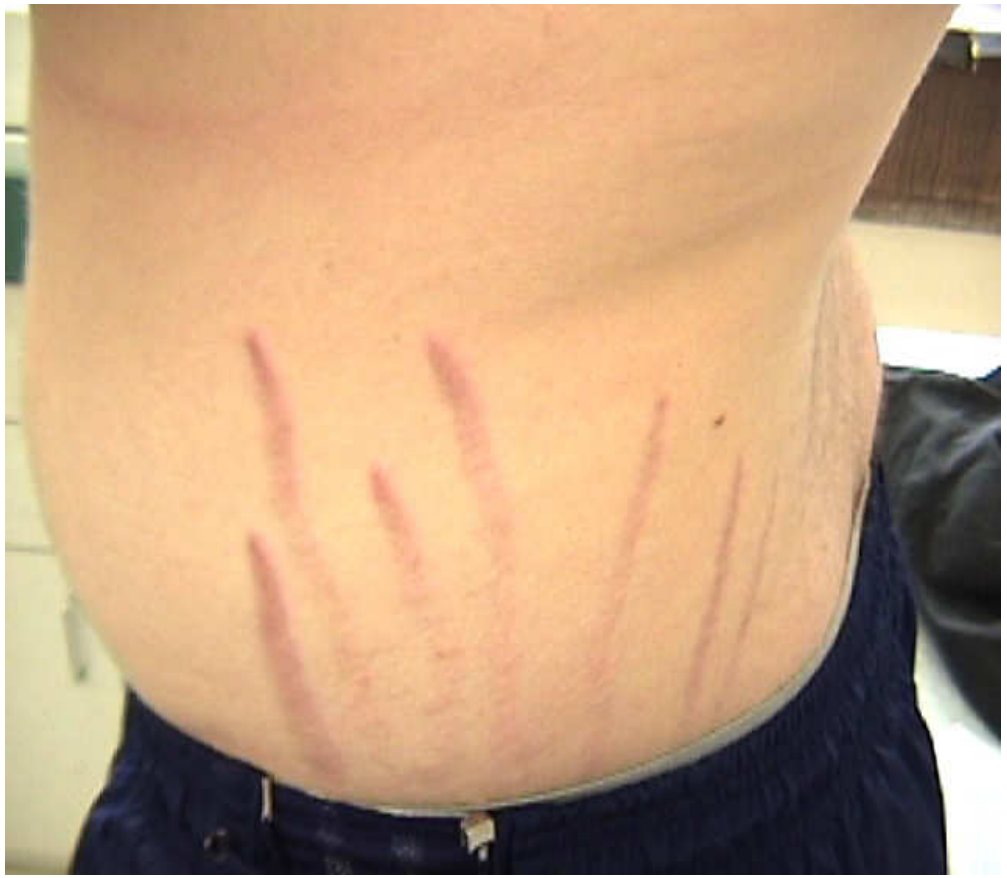
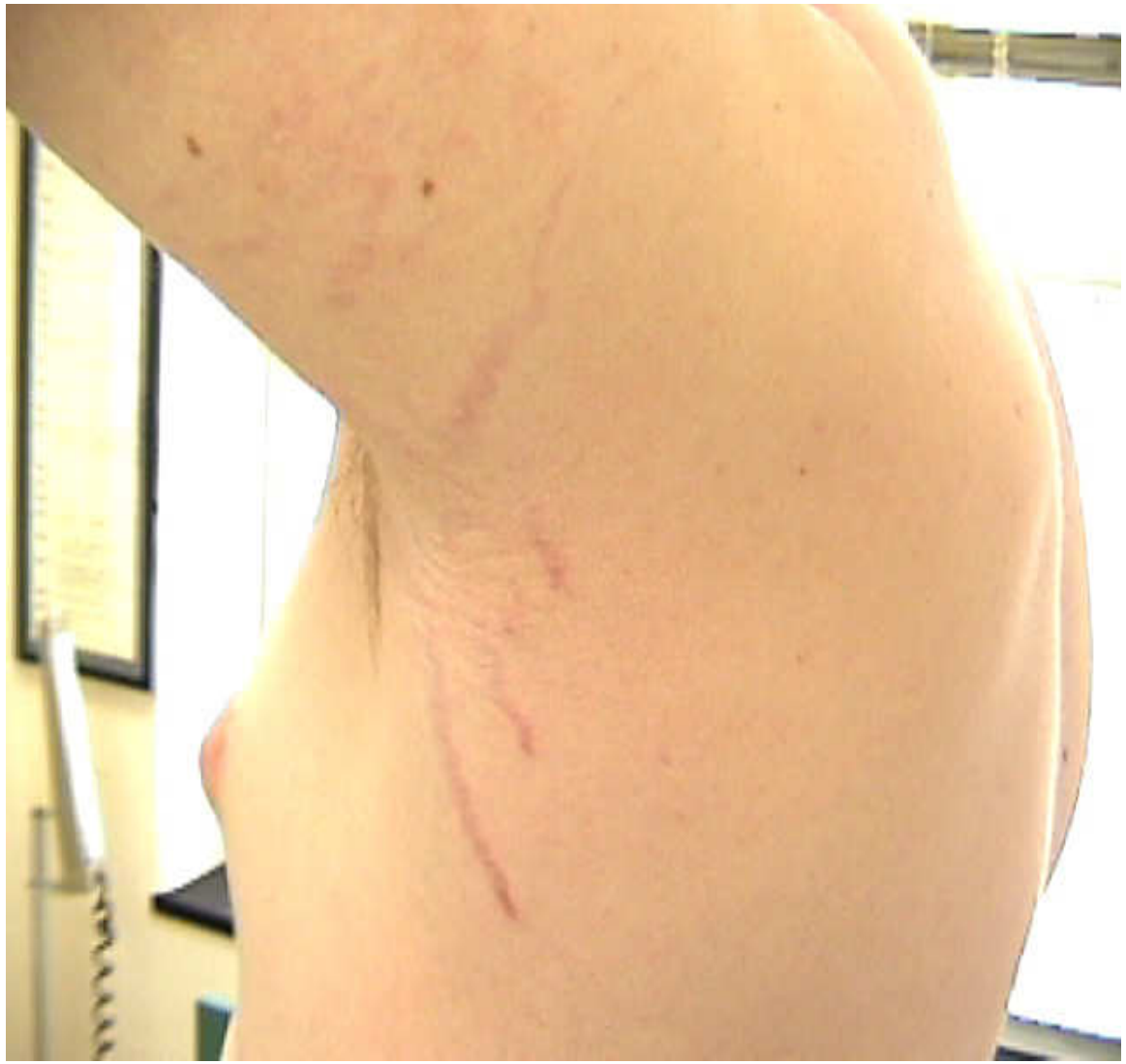
Bartonella Rashes

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

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



Under the Arm



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Ehrlichiosis

Symptoms:

- Fever (only after initial infection, sometimes recurrent for years)
- Myalgia and arthralgia, tendon pain
- Headache (mild)
- Lycopenia and thrombocytopenia
- Hyponatremia
- Mental confusion
- Skin rashes, genital and oral ulcers
- Severe pain syndromes (sharp, shooting, disabling)
- Nausea and vomiting (acute flare-ups)
- Right upper quadrant pain
- **Lancinating sharp and unpredictable pains, unstable sciatica**

Diagnosis: IgG/IgM, provoked PCR

For tx think:

- Antibiotics (responds often to Doxycycline or Minocycline)
- **Rizoles and astragalus (elevates interferon gamma**)
- and colchicine (read papers by Michael Rask – not to be used during dental surgery or pregnancy) or colchicum drops, LDI

Making the diagnosis

- Symptoms and history
- Neurological/physical findings
- History of an insect bite or EM rash
- ART testing (*www.KlinghardtAcademy.com)*
- Direct microscopy and Flow Cytometry
- Detection of antibodies (ELISA, Western Blot, LTT Elispot, IgG/IgM)
- CD57 test: under 100 considered positive
- Lymphocyte proliferation tests (MELISA)
- Culture (J.Burrascano MD)
- Direct Microscopy (FryLabs)
- Indirect tests (FACT, different lab parameters
- Klinghardt: Ruggiero-Klinghardt protocol with “provoked urine PCR”

The Diagnostic Paradoxes

- Making the diagnosis dependent on the history of a tick bite represents poor logic: 22% of horse flies, deer flies and mosquitoes are infected with Borrelia and co-infections in endemic areas

- The etiologic agent of Lyme disease in deer flies, horse flies and mosquitoes, J Infect Dis 154 (1986), 355-358, LA Magnarelli, JF Anderson, AG Barbour,
- Klinik der Lyme-Borreliose: Hans Huber Verlag, Bern, CH (2002). 39-40, Norbert Satz

- Spirochetes can assume a cystic form which can lay “dormant” in tissues and escape detection from any of the above diagnostic methods

  Lyme disease, potential plague of the 21st century: R Bradford and H Allen, Townsend Letter for Doctors and Patients, Jan 2005, 70-79

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 cortisol, low DHEA and testosterone, low progesterone, estrogen dominance)
- Low alkaline phosphatase (indicating low zinc levels, usually from lyme associated kryptopyrole disorder)
- Decreased urine concentration (low specific gravity)

Differential Diagnosis

- Heavy metal toxicity: Melisa test, hair analysis, urine challenge tests
- Environmental illness (toxicity and allergy) and Electrosensitivity: by history, LDA testing at Breakspear Hospital
- Mold / Mycotoxin exposure: history, elevated TGF beta 1, elevated C4a (Jewish hospital in Denver only), not C3a
- Lyme disease, co- infection or other infection: positive Western Blot or pos. PCR, low CD 57, both C4a and C3a elevated (R.Stricker, R.Shoemaker)

PATIENT: KELLY, ROBERT
DOB: 01/01/29 SEX: M

SAMPLE ID: 101685

DIETRICH KLINGHARDT, MD

1200 112TH AV NE STE A100
BELLVUE, WA
98004

DRWN: 12/12/02
RCVD: 12/16/02
PRNT: 12/20/02

DIRECTOR: BOYD G. STEPHENS, M.

TEST NAME	RESULT	UNITS

LYME IgG WESTERN BLOT .....

The IgG WB is considered positive if two of the starred bands are present: 23-25, 31, 34, 39, 41, 93 kDa.

The IgG WB is considered equivocal if one of these bands are present: 23-25, 31, 34, 39, 93 kDa.

41 kDa, by itself, is negative.****REVISED 9/16/99

ASTPHLD/CDC recommendation: An IgG WB is positive if five of these bands are present: 18, 23-25, 28, 30, 39, 41, 45, 58, 66, 93kDa. New York State Department of Health considers Western Blots positive that conform to the ASTPHLD/CDC criteria.

BAND INTENSITY: Low +, Medium ++, High +++, Equiv +/-

LYME IGG WESTERN BLOT	POSITIVE
18 kDa	-
22 kDa	-
**23-25 kDa	++
28 kDa	++
30 kDa	++
**31 kDa	++++
**34 kDa	++
37 kDa	-
**39 kDa	+/-
**41 kDa	+++
45 kDa	+
58 kDa	+/-
66 kDa	+/-
73 kDa	-
83 kDa	-

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Borrelien-Elispot (LTT / T-Zell-Test)

1. Already 14 days after insect bite positiv
   (while IgM antibodies are still negative)

2. Therapy control /**STAGING**:
   - Already 6-8 weeks after successfull treatment significant decrease in LTT-positivity
   - IgM/IgG-titer decreases only after 6-12 Monaten!

3. Assessing activity of Borrelia in a recovering patient
   - If the Elispot/LTT remains positive and the titer stays up, the microbes are still active. You should consider another cycle of treatment

The Borrelia LTT-Elispot

Clinically symptomatic Borrelia patients –
before treatment with antibiotics

Specificity : 94 %

Sensitivity: 91 %

Quelle: V.von Baehr et al., J.Lab.Med.2007;31(3):149-158

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The Ruggiero-Klinghardt (RK) Protocol for the Diagnosis and Treatment of Chronic Conditions with Particular Focus on Lyme Disease

American Journal of Immunology

Dietrich Klinghardt and Marco Ruggiero

Received: 20-02-2017; Revised: 28-02-2017; Accepted: 08-03-2017

Abstract: Here we describe the Ruggiero-Klinghardt (RK) Protocol that is based on integration of Autonomic Response Testing (ART) with diagnostic ultrasonography and on application of therapeutic ultrasounds; the latter are used as a provocation tool and as an instrument to optimize drug uptake and utilization in specific areas of the body. This protocol consists of a precise sequence of diagnostic and therapeutic procedures with the ultimate goal of improving sensitivity and specificity of diagnosis at the same time evaluating and optimizing efficacy of treatments in chronic conditions including, but not limited to, persistent Lyme disease. The RK Protocol represents a paradigm shift in diagnostics and therapeutics: Thus, compartmentalized microbes, transformed cells, toxins and metabolites could be detected using a safe and non-invasive method. In addition, the RK Protocol allows optimization of efficacy of drugs and other therapeutic interventions. Although the RK Protocol was initially developed for persistent Lyme disease, it shows significant potential in conditions ranging from cancer to neurodegenerative diseases and autism. In oncology, the RK Protocol may serve to facilitate early diagnosis and to increase sensitivity of cancer cells to the killing effects of a variety of remedies ranging from conventional radio- and chemotherapy to more recent forms of immunotherapy. Thus, the 1st goal of the RK Protocol is diagnostic: That is, to make pathogens, toxins, transformed cells and cells infected by viruses that are inaccessible to conventional diagnostic and therapeutic tools, “visible” to the therapist who can detect them with laboratory methods and deal with them with appropriate interventions; and also to make them “visible” to the immune system that can fight them in a physiological manner. The 2nd goal is to optimize drug uptake and utilization in the organs and tissues studied and targeted with these procedures.

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

Provoked Urine PCR Test

Patient: **Hurusch, Evelyn** Doctor: **Dr. Klinghardt** **Lyme Panel**

Sample Collected	Sample Received	Sample Tested	Test Reported
12/08/2015	12/14/2015	01/06/2016	01/07/2016

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
B. burgdorferi Osp B-NSA
B. burgdorferi Osp C
Borrelia miyamotoi
Borrelia recurrentis
Anaplasma phagocytophilum
Babesia microti
Babesia divergens
Babesia duncani
Bartonella bacilliformis
Bartonella henselae-NSA
Bartonella quintana
Ehrlichia chaffeensis

NSA: Non-specific Amplification Product: Target DNA was detected that was not of expected size, possibly degraded DNA, mutation of species, unspecified subspecies, product smear, other.

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Interpretation of Results Disclaimer: Dental DNA is not a clinical diagnostic laboratory and cannot provide a diagnosis for disease and/or subsequent treatment

RESULTS:

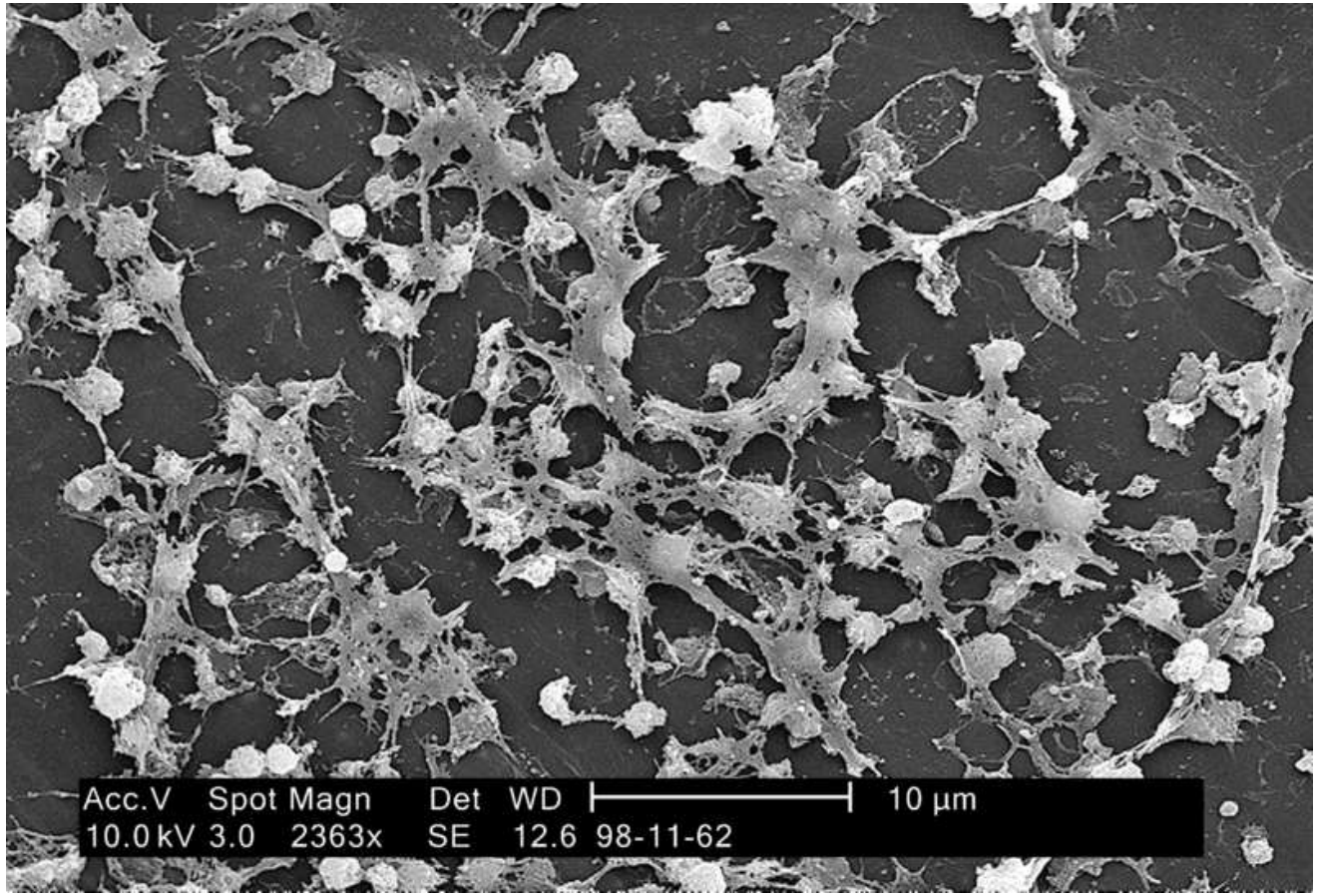
Doxycycline reduced spirochetal structures ~90% but **increased the number of round body forms about twofold**. Amoxicillin reduced spirochetal forms by ~85%-90% and round body forms by ~68%, while treatment with metronidazole led to reduction of spirochetal structures by ~90% and round body forms by ~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.**

Biofilme

- Sauerstoff aus dem Blut braucht 6 Minuten ins Bindegewebe statt 0,2 Sek
- körpereigenes Fibrin (Gerinnungsstoff)



Elektronenmikroskopische Aufnahme eines Staphylococcus aureus Biofilms
Quelle: www.wikipedia.de

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TIN: 84-1413291 CLIA#: 06D2019763

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

Patient: **Gannett, Kamille** Doctor: **Dr. Klinghardt** **Lyme Panel**

Sample Collected	Sample Received	Sample Tested	Test Reported
01/05/2016	01/07/2016	01/12/2016	01/13/2016

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

B. burgdorferi Osp B-NSA

B. burgdorferi Osp C-NSA

Borrelia miyamotoi

Borrelia recurrentis

Anaplasma phagocytophilum

Babesia microti

Babesia divergens

Babesia duncani

Bartonella bacilliformis

Bartonella henselae-NSA

Bartonella quintana

Ehrlichia chaffeensis-NSA

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Lab Director: Christopher W. Shade, Ph.D, NRCC-EAC Lab Manager: Robert C. Wheeler, BS, MS

PATIENT
Christine Mack

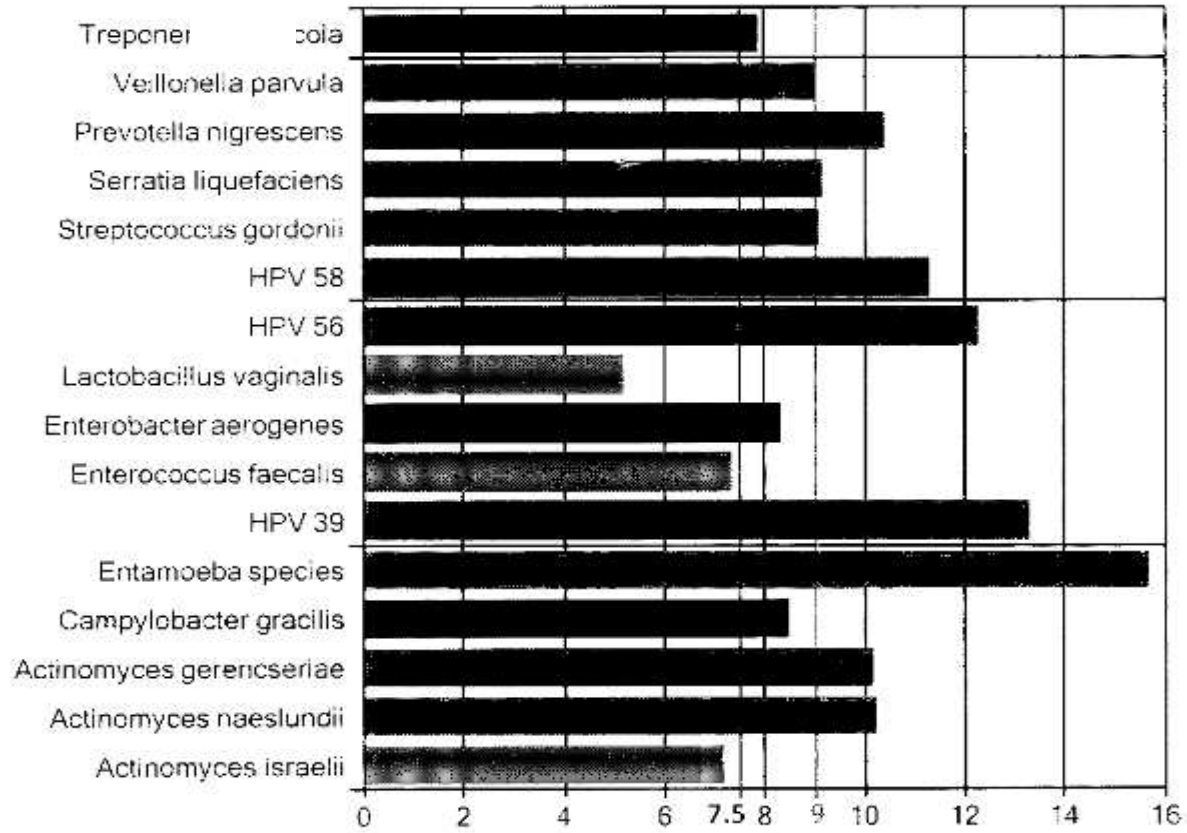
DOCTOR
DietrichKlinghardt

Test ID: 03174
Full View Test

Sample Collected	Sample Received	Sample Tested	Test Reported
	10/09/2015	10/14/2015	10/19/2015

Sample Type: Knee Joint Fluid

The following bacteria were detected in the sample that was submitted for testing:



9 or greater indicates a serious risk

Greater than 7.5 but less than 9 indicates a moderate risk

Total Risk Factor, as reported on the chart above, is the sum of the Pathogen Risk Factor and Measured Risk Factor. Total Risk Factor equal to or greater than 9 is considered a serious risk. Total Risk Factor between 7.5 and 9 is considered of moderate risk

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Treatment Basics (Sophia Health Institute Lyme/chronic pain resolution)

- Reduce electromagnetic stressors (switching off fuses, no WiFi/WLAN, etc.)
- Detox (aluminium, mercury, lead and glyphosate)
- Ketogenic diet + moderate exercise
- ART food intolerance testing and modification of diet
- Anti-parasitic interventions (Gubarev enema protocols, oral herbal and medical antihelmintics)
- Anti-Mold strategies (home testing, ozonated plant oils etc.)
- Microbiome inoculation (Bravo orally and rectally), FMT
- Rerum (005-0.01 ml s.c starting dose once every 5 days; slowly increase to 0.5. Reduce and increase dose according to symptoms (over-or understimulation of immunity)
- Rugiero ultrasound mobilization and drug-uptake technique
- Klinghardt Herbal Co-Infection cocktail and specific pain interventions (see following slides)

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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

“Lymphadenopathy during Lyme Borreliosis Is Caused by Spirochete Migration-Induced Specific B Cell Activation”

PLOS one; Published: May 26, 2011

S.Tunev, C.Hastey, E.Hodzic, S.Feng, S. Barthold, N. Baumgarth

DOI: 10.1371/journal.ppat.1002066

Author Summary

Acute Lyme Disease is one of the most important emerging diseases in the US. People with acute Lyme disease often develop swollen lymph nodes, or lymphadenopathy, but we do not know why this happens or what effect it has on the course of the disease. We show here that when mice are infected with live*Borrelia burgdorferi* spirochetes (the bacteria that cause Lyme disease), live spirochetes collect in the lymph nodes. These **lymph nodes** then swell up and **start producing large numbers of antibody-producing cells**. Although many of these antibodies can recognize the bacteria**, they apparently lack the quality to clear the infection**. We hypothesize that by moving into the lymph node, usually a site in which strong immune responses are induced, **Borrelia evades the immune response**: it goes to the lymph nodes and **tricks the immune system into making a very strong but inadequate response**.

Rugiero/Klinghardt: Lymphnodes can be accessed with ultrasound and pathogens can be chased away. Targetet remedies can be concentrated in the lymphnodes with ultrasound

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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.

Klinghardt: when Lyme is not visible to the immune system, it is also not visible in the conventional lab

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

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

Effectiveness of Stevia Rebaudiana Whole Leaf Extract Against the Various Morphological Forms of Borrelia Burgdorferi in Vitro

Eur J Microbiol Immunol (Bp). 2015 Dec ;5(4):268-80. Epub 2015 Nov 12

P A S Theophilus, M J Victoria, K M Socarras, K R Filush, K Gupta, D F Luecke, E Sapi

Abstract:

Lyme disease is a tick-borne multisystemic disease caused by Borrelia burgdorferi. Administering antibiotics is the primary treatment for this disease; however, relapse often occurs when antibiotic treatment is discontinued. The reason for relapse remains unknown, but recent studies suggested the possibilities of the presence of antibiotic resistant Borrelia persister cells and biofilms. In this study, we evaluated the effectiveness of whole leaf Stevia extract against B. burgdorferi spirochetes, persisters, and biofilm forms in vitro. The susceptibility of the different forms was evaluated by various quantitative techniques in addition to different microscopy methods. The effectiveness of Stevia was compared to doxycycline, cefoperazone, daptomycin, and their combinations. Our results demonstrated that Stevia had significant effect in eliminating B. burgdorferi spirochetes and persisters. Subculture experiments with Stevia and antibiotics treated cells were established for 7 and 14 days yielding, no and 10% viable cells, respectively compared to the above-mentioned antibiotics and antibiotic combination. **When Stevia and the three antibiotics were tested against attached biofilms, Stevia significantly reduced B. burgdorferi forms. Results from this study suggest that a natural product such as Stevia leaf extract could be considered as an effective agent against B. burgdorferi.**

Biological Lyme and Co-Infection protocol (KiScience.com, SophiaMed.com)

- Biofilm breaking. Anti-spirochetal activity. Prevention of further tick and insect bites: **Cistus incanus** tincture (Mediterranean Rockrose): 2 pipettes 3 times/day or 4-6 cups of the tea
- To tease microbes from hiding places/ joint pain: Hyaluronic acid: 4 pipettes 2 times/day sublingually
- Binders: to absorb and excrete mobilized biotoxins and "roadkill": **chlorella** 3 grams 3times/ day and **Zeolite**: knifetip (1 gram) 3 times/day
- Lyme cocktail (KiScience.com)
- Liposomal herbal tinctures: **Artemisia annua, Astragalus, Smilax, Jap.Knotweed, Red Root, Cilantro, Andrographis, whole leaf Stevia (brown/green liquid)** and **Propolis**. Start with 2 drops twice daily. Keep in mouth for 2-3 minutes before swallowing. Increase dose every 3 days. As soon as aggrevation of symptoms is noticed, go back to the last tolerated dose, stay there for 3 days, then increase again. If improvement is noticed, stay at that dose for 10-14 days or until nothing more seems to happen, then increase again. Maximum dose: 3 dropperful 3 times/day (rarely needed)
- To increase strength of the cocktail and to enhance penetration: MicroSilver: 2 tablespoon twice daily away from all other things, not diluted with water (take like homeopathic)
- Supportive measures: colonics, lymphatic drainage, psychological counselling, exercise only to tolerance

American Journal of Immunology

Clinical Procedures

The Ruggiero-Klinghardt (RK) Protocol for the Diagnosis and Treatment of Chronic Conditions with Particular Focus on Lyme Disease

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Dietrich Klinghardt and Marco Ruggiero / American Journal of Immunology 2017, ■■ (■): ■■■.■■■
DOI: 10.3844/ajisp.2017.■■■.■■■

Table 1. The Ruggiero-Klinghardt (RK) Protocol steps of diagnostic and therapeutic procedures

Step 1.	First comprehensive Autonomic Response Testing (ART).
Step 2.	Total-body diagnostic ultrasonography that has the role of further refining the diagnostic hypotheses put forward by ART.
Step 3.	Application of therapeutic ultrasounds with particular focus on the areas identified as "abnormal" with the previous steps.
Step 4.	Second ART performed after application of therapeutic ultrasounds: Comparison of the results with those obtained with the first ART of Step 1.
Step 5.	Collection of midstream urine in a sterile container that is then shipped to the laboratory. Alternatively, the presence of microbes, toxins, circulating cancer cells or other pathogenic noxae is investigated in other biological matrixes such as stools, blood or serum or breath that are appropriately collected.
Step 6.	Pharmacological treatment with remedies specific for the identified pathogens.
Step 7.	Daily application of therapeutic ultrasounds targeted to the areas identified with the previous steps.

Follow-up at 3-4 month intervals to evaluate the effectiveness of treatment and to assess the treatment end-point.

Borrelienschmerz und spezifiche Interventionen

- Borrelia Burgdorferi selbst verursacht unspezifische Schmerzen, die heute meist als Fibromyalgie fehlgedeutet warden
- Ehrlichia verursacht scharfe einschiessende Schmerzen (Kopf, Ischias, Finger, Nacken usw.)
- Babesia fuehrt zu Migraine und schwer behandelbaren Kopf-Symptomen, fast immer verbunden mit Schmerzen oder Dysfunktion in der Gegend vom Ggl. Coeliacum, Verstopfung
- Bartonella fuehrt zu Laehmungen, MS, ALS, lokalisierten Gelenkproblemen aber eher selten zu systemischen Schmerzerkrankungen

1. Neural Therapy with 5% Dextrose

- Die lokale Infiltration von 5%iger Dextrose blockiert TRPV-1. Dadurch werden anti-entzuendliche Peptid Hormone freigesetzt (Galanin, Somatostatin. John Lyftogt, New Zealand)
- TRPV1 Protonen Channel: stimuliert den Release von Substance P und Calcitonin-Gene-Related Peptid
- Führt zu oft sofortiger Reduktion oder Elimination von Schmerz und Entzündung und resultiert in Heilung des betroffenen Gewebes mit erstaunlichen Langzeiterfolgen

Borrelienschmerz: 5%ige Dextrose

- Technik: die Schmerzgegend wird mit nicht-toxischem Stift markiert
- Die Gegend wird subkutan infiltriert mit 5%iger Dextrose (ohne Prokain)
- Menge: Körpergewicht in kg mal 2 = ml der Dextrose, die pro Behandlung verwendet wird (70 kg Person =140 ml)
- Nadel: 5-8 cm, G27. Nadelführung ganz eng unter der Haut, aber subkutan
- Häufigkeit: oft reicht eine Behandlung. Der ganze Effekt ist nach 48 Stunden erreicht. Wenn öfter behandelt wird: 1 mal/ Woche. Wenn nach der ersten Behandlung keine Verbesserung eintritt, Triggerpunkt Therapie mit DMPS oder Artesunat (siehe unten)

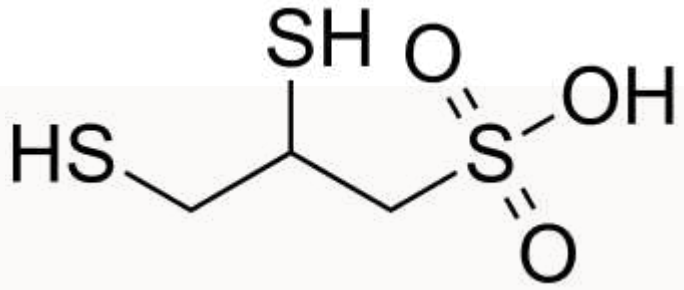
2. Neural Therapy with DMPS and/or DMSO

- Im Jahr 1992 berichtete ich ueber meine Forschungsergebnisse mit der DMPS-unterstuetzten Neuraltherapie bei der Behandlung der chronischen Fibromyalgie (Fakultaet der Universitaet Utah/Salt Lake City)
- Seither habe ich ueber 5000 Patienten mit chronischen Therapie-resistenten Schmerzen mit dieser Methode behandelt, oft erfolgreich
- Mischung: 1-2 ml DMPS (50-100 mg) plus 8-9 ml 1%iges Prokain
- Technik: Triggerpunkt Technik wie beschrieben bei J.Travel (Triggerpoint Manual Vol.I). Alle Ganglien und der Beckenboden sollten neuraltherapeutisch mitbehandelt warden (gleiche Mischung).
- Gold Standard: paravertebrale Injektion 2.5 cm lateral der Mittellinie naher der Facettengelenke im 2 cm Takt
- Gesamtmenge: 250 mg DMPS +entsprechende Menge Prokain
- Nadel: G27, 4 cm
- Verlauf: meist Verbesserung innerhalb 48 Stunden, meist anhaltend. Haeufigkeit: 1-2 mal pro Woche bis schmerzfrei, dann sooft wie noetig.
- Literatur: Robert Kidd Lehrbuch: “Neural therapy”

DMPS und DMSA

Dimercaptopropansulfonsäure

$C_3H_8O_3S_3$



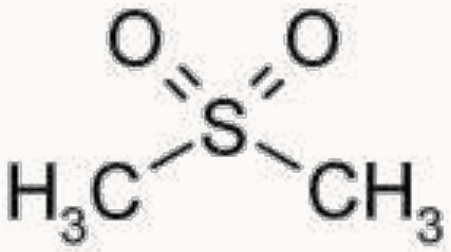
Phase 2:
Entgiftung

DMPS
MSM

Neuraltherapie

Dimethylsulfon

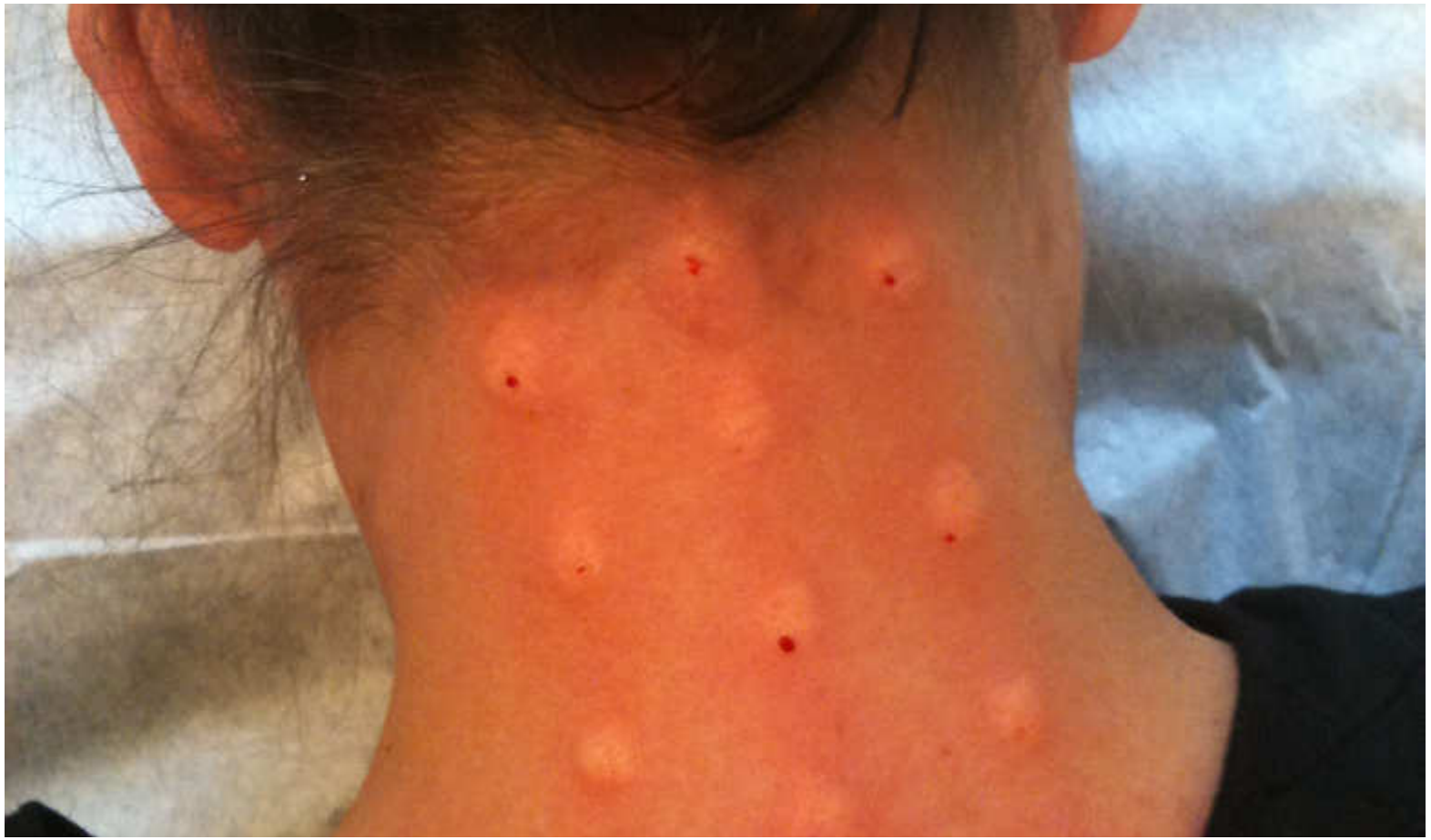
$C_2H_6O_2S_3$



3. Neural Therapy with Bee Venom

- Bienengift hat einen nachgewiesenen direkten anti-Borrelien Effekt, aber auch positive Wirkung auf Hypothalamus, Hypophyse und Epiphyse
- Chronische Schmerzerkrankungen koennen mit der Bienengift Therapie (Apitherapie) oft bleibend schmerzfrei werden und bleiben
- Nebenwirkung: lebensverlaengernd, heilt chronische Depression, erhoeht Dopamin und Serotonin Spiegel, normalisiert alle Neurotransmitter und Hormone, verbessert Verdauung, Intelligenz
- Technik: langsam ansteigende Dosis. Nomenklatur BV 20= 20 Bienenstiche in 1 ml). Beginn: 0.05 ml (=1 Bienenstich) immer zusammen mit 2 ml Prokain. Zieldosis fuer 70kg Person: 0.5 ml (=10 Bienenstiche). Auch bei 0.5 ml Bienengift nur 2 ml 1%iges Prokain
- Anfangs 3 mal/Woche. Bei Therapieerfolg (geht oft 3-4 Monate) 2 mal/ Woche
- Technik: Schmerzgegend Quaddeln mit G30 1/2cm Nadel. Nie tief spritzen, nie in die Gelenke

Segmental Therapy: Cervical Spine



Mellitin and Lyme

- (5) Lubke, L.L., and Garon, C.F.: The Antimicrobial Agent Melittin Exhibits Powerful In Vitro Inhibitory Effects on the Lyme Disease Spirochete. Clinical Infectious Diseases, 1997;25(Suppl 1):S48-51

  From the Bacterial Pathogenesis Section, Rocky Mountain Laboratories Microscopy Branch, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Hamilton, Montana, USA

  Abstract
  Borrelia burgdorferi has demonstrated a capacity to resist the in vitro effects of powerful eukaryotic and prokaryotic metabolic inhibitors. However, treatment of laboratory cultures on Barbour-Stoenner-Kelly medium with melittin, a 26-amino acid peptide contained in honeybee venom, showed **immediate and profound inhibitory effects** when they were monitored by dark-field microscopy, field emission scanning electron microscopy, and optical density measurements.
  Furthermore, at melittin concentrations as low as 100 microg/mL, virtually all spirochete motility ceased within seconds of inhibitor addition. Ultrastructural examination of these spirochetes by scanning electron microscopy revealed obvious alterations in the surface envelope of the spirochetes.

"Bee Venom Therapy for Chronic Pain", Dietrich K. Klinghardt, MD, PhD, FAANaOS-C, FABPMS-C, Board Certified Diplomate Pain Management Specialties, Neurological and Orthopaedic Medicine

The Journal of Neurological & Orthopaedic Medicine & Surgery, ISSN 0890-6599/90-1103, Volume 11, Issue 3, **October 1990**, Editorial Offices 2320 Rancho Drive, Suite 108, Las Vegas, Nevada 89102-4592, pages 195-197.

Bee Venom Therapy: Biochemical Analysis		
Fraction:	**Action:**	**Effect on Pain/Painful Joint:**
Hyaluronidase & Isoenzymes	Depolymerizes hyaluronic acid (the "glue" of the body)	Allows other components of Bee Venom to penetrate deep into tissues, inside cells, inside joint
Compound X (W. Shipman)	Lowers surface tension of all fluids (Surfactant)	"Wets" cell walls with Bee Venom, allows better penetration
Phospholipase A	Converts lecithin (cell wall) into lyso-lecithin. Lyso-lecithin acts as emulsifier, causes hemolysis in high doses. Most toxic component of Bee Venom	Emulsifies debris within joint and other tissues, increases local pain (for 10-15 minutes): counter-irritant
Melittin	Stimulates ACTH-secretion in the pituitary (Cortisol). Protects lysosomal membranes. Powerful antibacterial agent. Causes lysis of mast cells. Strongly kationic.	Strong anti-inflammatory effect (long acting). Short-acting histamine effects: increased capillary permeability, edema, temperature elevation, itching pain, increased vitality and sense of well-being; forces Bee Venom to attach to negatively charged cell wall.
Apamin	Stimulates central secretion of serotonin and dopamine. Blocks neurosynaptic processes in periphery	Increases central and peripheral pain threshold; decreased pain, increased sense of well-being
Mast cell degenerating protein (Haberman)	Strong anti-inflammatory action (approximately 100 times more than hydrocortisone)	Reduces inflammation and pain through local action on tissues inflammation
Other components: Acid phosphatase, alpha-glucosidase, phospholipase B, several peptides	Inhibition of: complement, kinines proteases, substance "P", and other effects	Anti-inflammatory, pain reducing

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BEE VENOM THERAPY RESULTS						
Diagnosis	**# of Patients**	**Worse**	**Unchanged**	**Mildly Better**	**Good Results**	**Excellent Results**
Gout	5					5*
Rheumatoid Arthritis (seropositive)	10	1	1		6	2
Rheumatoid Arthritis (seronegative)	5				4	1
Fibromyalgia (with elevated ESR)	7		1		2	4
Sprain/Strain Cerv. Spine	21			1*	4*	16*
Sprain/Strain Lumbar Spine	22		4*	2*	5*	11*
Disc Injury, Neck	8			1*	4*	16*
Disc Injury, Lumbar	13		2*	3*	4*	4*
Post-Laminectomy Pain	6		1	1	3	1
Arthritis Small Joints Hand	9		1	2	2	4
Painful Bunion	6			1		5
Post-Herpetic Neuralgia	4				1	3
Fracture Nonunion Navicular	1					1
Intractable Pain from Large Burn Wound (after skin grafting)	1					1
Osteoarthritis Knee	2				2	
Ankylosing Spondylitis	2				2	
Vertigo	5				3*	2*
Multiple Sclerosis	1				1	
Footnote: Asterisk (*) indicates that those patients had other significant treatment modalities.						

Mellitin (a polypeptide also consisting of 26 amino acids which represents 40-60% of the bee venom)

- antibacterial
- antifungal
- anti-lyme disease (in vitro experiment)
- antitumoural
- central nervous system inhibitory;
- block nerve muscle and ganglial synapses
- contraction of the striated and smooth muscles
- histamine releasing
- mastocytololysic
- radio protecting (against X-irradiation; study on mice, Shipman and Cole, 1967)
- vascular permeability increasing
- haemolysis
- lowers blood pressure
- anti-inflammatory
- mellitin (which represents 40-60 % from the B.V. substances) has no antigenic properties (Orlov); otherwise, according to Artemov, the bee enemies would have gotten a specific immunity
- stimulate the pituitary - adrenal axis to release both cathecolamines and cortisol (Brooks *et al.*)
- increase plasma cortisol levels
- acts on biological membranes
- Presently, it is one of the most potent anti-inflammatory agents known, and it can be useful in treating arthritis and rheumatism

4. Neural Therapy with Artesunate

- Artesunat ist ein sehr effektives Malariamittel, dass immer haeufiger eingesetzt wird bei der Behandlung der chronischen Borreliose, insbesondere bei der Ko-Infektion Babesia microti.
- Die Ampulle enthaelt 100 oder 250 mg Trockenpulver, dass mit NaCL rekonstituiert wird
- Technik: Triggerpunkt Technik nach J.Travel
- Mischung: 30 -60 mg Artesunat in 10 ml Spritze mit Prokain (cave: Artesunate is diluted in 8.4% Bicarb. Has to be diluted at least 1:4 for local injections)
- Besonders effektiv: paravertebrale Injektion, Anspritzen des Ggl. Sphenopalatinum und des Beckens
- Haeufigkeit: 1-2 mal pro Woche bis schmerzfrei
- Innerhalb von 24-48 Stunden danach unbedingt DMPS segmental ueber der Niere und i.v. wegen starker Schwermetall Mobilisation

Klinghardt Institute
The Heart Of Healing

Herbal Drugs: Ethnomedicine to Modern Medicine 2009, pp 173-194

Artemisinin A Versatile Weapon from Traditional Chinese Medicine

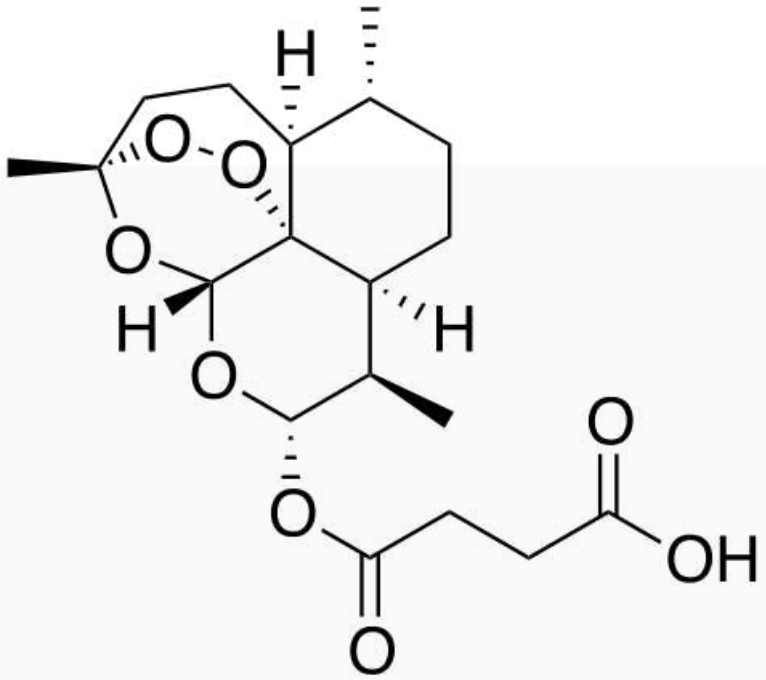
Thomas Efferth, German Cancer Research Center, Heidelberg, Germany

Abstract
Traditional Chinese medicine (TCM) commands a unique position among all traditional medicines because of its 5000 years of tradition. Our own interest in natural products from TCM was triggered in the 1990s by sesquiterpene lactones of the artemisinin type from *Artemisia annua* L. The first description of the Chinese herb *Artemisia annua* L. (*qinghao*, Sweet wormwood) dates back to 168 B.C.E. Artemisinin (*qinghaosu*) was identified in 1972 as the active antimalarial constituent of*Artemisia annua* L. Artemisinin and its derivatives are used for the treatment of malaria. As shown in recent years, this class of compounds also shows activity against cancer cells, schistosomiasis, and certain viruses, i.e., human cytomegalovirus, hepatitis B anc C virus, and bovine viral diarrhea virus. Interestingly, the bioactivity of artemisinin seems to be even broader and also includes the inhibition of other protozaons such as *Leishmania, Trypanosoma*, and *Toxoplasma gondii*, as well as some trematodes, fungi, yeast, and bacteria. The analysis of its complete profile of pharmacological activities, as well as the elucidation of molecular modes of action and the performance of clinical trials, will further elucidate the full potential of this versatile weapon from nature against diseases.
(400fache Kraft der Artemisia-anna-Pflanze)

Neuraltherapie mit Artesunat

Artesunat

$C_{19}H_{28}O_8$



Artesunat

5. Neural Therapy with Ozone

- Ozone is ideal for triggerpoint injections (10 Gamma) or joint injections (20-30 Gamma)
- Ozone has the least side effects and works well in closed spaces (joints, ganglia)
- It has both anti-microbial and detoxification effects, leads to hormesis effects: anti-oxidative/anti-inflammatory response
- Ozone injections are safe and often have long lasting pain relieving effects not seen with Procaine alone in chronic Lyme

6. Neural Therapy with Rerum

- Rerum injections are not only used in - or near - infected body compartments, but also as a neuro-regenerative intervention in autonomic ganglia, nerve plexi, the vagus nerve, the epidural space and celiac plexus
- The SophiaMed technique also uses Rerum injections directly into lymph nodes, tumours and dental foci (intraosseous neural therapy)
- We also use Rerum as a proliferative agent in facet joints, ligament insertions, tendons and in non-resolving skin conditions/areas
- Technique: 0.1- 1 ml Rerum is drawn into a 10 ml syringe filled with 1% preservative free Procaine and the content is used in the standard neural therapy fashion, using the recommended fluid amounts documented in the textbooks