Fibromyalgia, ME, Degenerative Disorders, EDS, MCAS, PANS/PANDAS …: Tailored Testing Protocols

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Tailored testing protocols

- Fibromyalgia/Rheumatoid Arthritis
  - Correlations with Borrelia and coinfections
  - Testing suggestions
- Myalgic Encephalomyelitis (ME/CFS)
  - Correlations with Borrelia and coinfections
  - Testing suggestions
- Neurological Disease
- Dementia/Alzheimer‘s
- Osteoporosis
- Ehlers Danlos Syndrome
- Histadelia/MCAS/MCAD
- PANS/PANDAS

Fibromyalgia symptoms and Borrelia – clear associations

Richard Horowitz MD
Why Can't I Get Better?

Are Your Fibromyalgia Symptoms Due to Lyme Disease?

Tick-borne disorders often mimic chronic pain syndromes

Posted Dec 15, 2013

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Lyme disease is the number one vector borne spreading epidemic worldwide, and mimics common diseases such as Fibromyalgia (FM), Chronic Fatigue Syndrome (myalgic encephalomyelitis), autoimmune diseases like rheumatoid arthritis and MS, as well as psychiatric conditions such as depression and anxiety. The CDC recently released new statistics showing that ten times more individuals have been affected with Lyme than previously suspected. Since the blood tests for diagnosing Lyme disease have been shown to be unreliable, we would expect that a certain percentage of those diagnosed with FM are in fact suffering from Lyme disease. This has been my personal experience. In the last 26 years, I have seen over 12,000 chronically ill individuals with Lyme and associated tick-borne disorders, many of whom have been to 10-20 doctors looking for answers for their chronic fatigue and musculoskeletal pain. Lyme and associated tick-borne infections were often one of the underlying causes of their problem.

"Most fibromyalgia patients are Lyme positive."
(Rheum Dis Clin North Am. 1998 May;24 (2):323-51 & report of Lida Mattman,M.D.)

Source: https://www.psychologytoday.com/blog/why-can-t-i-get-better/201312/are-your-fibromyalgia-symptoms-due-lyme-disease

Numerous scientific references substantiate this

Berman, D.S. and Wenglin, B.D. *Complaints attributed to chronic Lyme disease: depression or fibromyalgia?* Am J Med. 1995 Oct; 99(4):440;
Fallon, B. *Neuropsychiatric Lyme disease: The new 'great imitator'.* Psychiatric Times. June 2004.
Nicolson, G., et al. *Mycoplasmal Infections and Fibromyalgia/Chronic Fatigue Illness (Gulf War Illness) Associated with Deployment to Operation Desert Storm.* Int Jnl Med 1998;1: 80-92.
Nicolson, G., et al. *Diagnosis and Integrative Treatment of Intracellular Bacterial Infections in Chronic Fatigue and Fibromyalgia Syndromes, Gulf War Illness, Rheumatoid Arthritis and other Chronic Illnesses.* Clin Prac of Alt Med 2000;1(2): 92-102
Pall M.L., *Common etiology of posttraumatic stress disorder, fibromyalgia, chronic fatigue syndrome and multiple chemical sensitivity via elevated nitric oxide/peroxynitrite.* Med Hypotheses, 2001; 57,139-145
Naziroglu M, et al. *Vitamins C and E treatment combined with exercise modulates oxidative stress markers in blood of patients with fibromyalgia: A controlled clinical pilot study.* Stress, November 2010; 13 (6): 498-505
Breeding, P.C., Nicolson, G.L. et al. *An integrative model of chronically activated immune-hormonal pathways important in the generation of fibromyalgia.* Brit. J. Med. Practit. 2012; 5(3): a524-a534
Russell IJ. *Neurochemical pathogenesis of fibromyalgia syndrome.* J Musculoskeletal Pain. 1996; 4:61-92
Clauw DJ, et al. *Chronic pain and fatigue syndromes: overlapping clinical and neuroendocrine features and potential pathogenic mechanisms.* Neuro immunomodulation, 1997; 4:134-153
Wallace DJ: *Is there a role for cytokine based therapies in fibromyalgia?* Curr Pharm Des 2006;12:17-22
Moldofsky H. *Sleep, neuroimmune and neuroendocrine functions in fibromyalgia and chronic fatigue syndrome.* Adv Neuroimmunol 1995;5:39-56
Staud R. *Autonomic dysfunction in fibromyalgia syndrome: postural orthostatic tachycardia.* Curr Rheumatol Rep. 2008 Dec; Vol 10 (6), pp 463-6

Fibromyalgia symptoms and Chlamydia pneumoniae (CPN)

Musculoskeletal Pain and Inflammation ■ Soft tissue infection by Chlamydia pneumoniae and subsequent inflammation. ■ Fibromyalgia Syndrome often starts after injury/accident. In the normal response to tissue repair, injured and inflamed areas attract macrophages. Chlamydia pneumoniae infected macrophages can leave Chlamydia pneumoniae behind in injured/inflamed area. Infection then becomes progressive gradually spreading from that area. As generalized inflammation increases (from free circulating cytokines) these sites are further infected by parasitized macrophages drawn to increasingly inflamed sites, etc. See http://www.cpnhelp.org/how_chlamydia_pneumoniae_ ■ Porphyrins blocking GABA receptors will also lower pain tolerance. ■ Generalized cytokine load

Chlamydial Endotoxins. Chlamydia pneumoniae contains a number of endotoxins in its structure, such as LPSi and HSPi-60. These endotoxins cause widespread inflammation (cytokine cascades) and a host of other metabolic disturbances. These are released chronically in small amounts in Chlamydia pneumoniae infection and in large amounts when Cpn cells are killed.

Source: http://www.prohealth.com/library/showarticle.cfm?libid=12763

Fibromyalgia and Mycoplasma

Diagnosis and Treatment of Chronic Mycoplasmal Infections in Fibromyalgia and Chronic Fatigue Syndromes: Relationship to Gulf War Illness

Garth L. Nicolson, Marwan Nasralla, Joerg Haier and Nancy L. Nicolson

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Huntington Beach, CA 92649

Summary

Mycoplasmal infections are associated with several acute and chronic illnesses, including Pneumonia, Asthma, Rheumatoid Arthritis, Immunosuppression Diseases such as AIDS, Genitourinary Infections and Gulf War Illness (GWI). Using forensic Polymerase Chain Reaction blood samples from 132 Chronic Fatigue Syndrome (CFS) (Myalgic Encephalomyelitis) and/or Fibromyalgia Syndrome (FMS) patients were investigated for the presence of mycoplasmal infections in blood leukocytes. CFS and FMS patients had completely overlapping signs and symptoms and were grouped for purposes of analysis. There was a significant difference between symptomatic CFS/ mycoplasmal infections (~63%) and healthy positive controls (~9%) (P incidence of *Mycoplasma fermentans* infections in these CFS/FMS pati (0%)(P<0.001). The prevalence of mycoplasmal infections in female an similar. Similar to GWI patients with mycoplasmal infections (~50%) a symptoms, mycoplasma-positive CFS/FMS patients respond to 6-week doxycycline, minocycline, ciprofloxacin, azithromycin and clarithromyci antibiotics plus nutritional support appear to be necessary for recovery.

"The identification of mycoplasma infections in the leukocyte blood fractions of a rather large subset of CFS, FMS and arthritis patients suggests that mycoplasmas, and probably other chronic infections as well, may be an important source of morbidity in these patients."

Fibromyalgia and Epstein Barr Virus/CMV

Journal of Neurology and Neuroscience

Evaluation of Antiviral Antibodies against Epstein-Barr Virus and Neurotransmitters in Patients with Fibromyalgia

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Citation: Reshkova V, Kalinova D, Milanov I. Evaluation of Antiviral Antibodies against Epstein-Barr Virus and Neurotransmitte
Patients with Fibromyalgia. J Neurol Neurosci. 2016, 6:3. doi: 10.21767/2171-6625.100035

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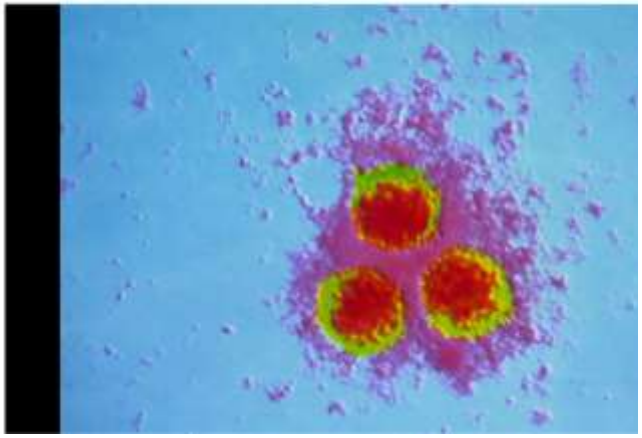
Abstract

Fibromyalgia (FM) is characterized by chronic widespread pain lasting for a minimum of three months, and pain at mechanical pressure in at least 11 of the 18 tender points. The cause of fibromyalgia is unknown. Several hypotheses have been developed including "central sensitization". This theory proposes that fibromyalgia patients have a lower threshold for pain because of increased reactivity of painsensitive neurons in the spinal cord or brain. Some researchers supposed that different

"The obtained results revealed that high EBV IgG concentrations in the serum of patients with FM correlated with pain intensity and associated clinical symptoms. This is consistent with the fact that FM is connected to the immune response to certain infectious agents (e.g. EBV, CMV)."

Fibromyalgia and Varicella Zoster Virus (VZV)

Varicella-zoster virus



Varicella Zoster Virus (VZV) - a highly contagious virus that spreads from person-to-person by coughing or sneezing, or through direct contact with the characteristic skin lesions it causes or fluids from blisters on an infected person.

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doi: 10.1007/82_2009_3

PMCID: PMC3076592
NIHMSID: NIHMS259279

Neurological Disease Produced by Varicella Zoster Virus Reactivation Without Rash

Don Gilden, Randall J. Cohrs, Ravi Mahalingam, and Maria A. Nagel

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Abstract

Reactivation of varicella zoster virus (VZV) from latently infected human ganglia usually produces herpes zoster (shingles), characterized by dermatomal distribution pain and rash. Zoster is often followed by chronic pain (postherpetic neuralgia or PHN) as well as meningitis or meningoencephalitis, cerebellitts, isolated cranial nerve palsies that produce ophthalmoplegia or the Ramsay Hunt syndrome, multiple cranial nerve palsies (polyneuritis cranialis), vasculopathy. myelopathy, and various inflammatory disorders of the eye. Importantly, VZV reactivation can produce chronic radicular pain without rash (zoster sine herpete), as well as all the neurological disorders listed above without rash. The protean neurological and ocular disorders produced by VZV in the absence of rash are a challenge to the practicing clinician. The

"Zoster is often followed by chronic pain (postherpetic neuralgia)"

Source: https://www.clinicaladvisor.com/varicella-zoster-virus/slideshow/377/

Consider Borrelia in the differential diagnosis of Rheumatoid Arthritis

Clinical and Vaccine Immunology
CVI Article | Journal Info. | Authors | Reviewers | Permissions | Journals.ASM.org

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Published online 2007 Sep 19. doi: 10.1128/CVI.00151-07
PMCID: PMC2168181

Serum Reactivity against *Borrelia burgdorferi* OspA in Patients with Rheumatoid Arthritis

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ABSTRACT

Go to:

Lyme arthritis and rheumatoid arthritis share common clinical features and synovial histology. It is unclear whether they also share similar pathogenesis. Previous studies have shown that the severity and duration of Lyme arthritis correlate directly with serum concentrations of antibody against outer surface protein A (OspA) of the causative pathogen *Borrelia burgdorferi*. We tested the sera of 68 subjects with rheumatoid arthritis, 147 subjects with other autoimmune diseases, and 44 healthy subjects who had never had Lyme

Detection of Mycoplasmal Infections in Blood of Patients with Rheumatoid Arthritis

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SUMMARY

Objectives: Mycoplasmal infections are associated with several acute and chronic illnesses. Some mycoplasmas can enter a variety of tissues and cells and cause system-wide or systemic signs and symptoms.

Methods: Patients (14 female, 14 male) diagnosed with Rheumatoid Arthritis (RA) were investigated for mycoplasmal infections in their blood leukocytes using a forensic Polymerase Chain Reaction (PCR) procedure. Amplification was performed with genus- and species-specific primers, and a specific radio-labeled internal probe was used for Southern hybridization with the PCR product. Patients were investigated for presence of *Mycoplasma spp.*, and positive cases were further tested for infections with the following species: *M. fermentans*, *M. hominis*, *M. pneumoniae* and *M*

Results: The *Mycoplasma spp.* sequence, which is not entirely specific for mycoplasmas, from the peripheral blood of 15/28 patients (53.6 %), and specific PCR products could not 13 patients (46.4 %). Significant differences ($p<0.001$) were found between patients and p controls in the genus-test (3/32) and in the specific tests (0/32). Moreover, the incidence o infections was similar in female and male patients. Using species-specific primers, we were infections of *M. fermentans* (8/28), *M. pneumoniae* (5/28), *M. hominis* (6/28) and *M. pene* RA patients. In 36% of the patients we observed more than one mycoplasma specie leukocytes. All multiple infections occurred as combinations of *M. fermentans* with other spe

Conclusions: The results suggest that a high percentage of RA patients have systemic mycoplasmal infections. Systemic mycoplasmal infections may be an important cofactor in the pathogenesis of RA, and their role needs to be further explored.

"The results suggest that a high percentage of RA patients have systemic mycoplasmal infections."

Rheumatoid arthritis and mycoplasma: Sources (extract)

- Hoffman RW, O'Sullivan FX, Schafermeyer KR et al. Mycoplasma infection and rheumatoid arthritis: analysis of their relationship using immunoblotting and an ultrasensitive polymerase chain reaction detection method. Arthritis Rheum. 1997; 40: 1219-1228
- Lee AH, Levinson AI, Schumacher HR Jr. Hypogammaglobulinemia and rheumatic disease. Semin. Arthritis Rheum. 1993; 22: 252-264 10.
- Clark HW, Coker-Vann MR, Bailey JS, Brown TM. Detection of mycoplasmal antigens in immune system complexes from rheumatoid arthritis synovial fluids. Ann. Allergy, 1988; 60: 394-398 11.
- Nicolson GL. Nasralla M, Haier J, Nicolson NL. Diagnosis and treatment of chronic mycoplasmal infections in fibromyalgia and chronic fatigue syndromes: Relationship to gulf war illness. Biomedical Therapy, 1998; 16: 266-271 12.
- Nicolson GL, Nicolson NL, Nasralla M. Mycoplasma infections and Chronic Fatigue Illness (Gulf War Illness) associated with deployment to Operation Desert storm. Intern. J. Med. 1998; 1: 80-92. 13.
- Nicolson GL, Nicolson NL. Diagnosis and treatment of mycoplasmal infections in Persian Gulf War IllnessCFIDS patients. Int. J. Occup. Med. Tox .1996; 5: 69-78. 14.
- Cimolai N, Malleson P, Thomas E, Middleton PJ. Mycoplasma pneumoniae associated arthropathy: confirmation of the association by determination of the antipolypeptide IgM response. J. Rheumatol. 1989; 16: 1150-1152 15.
- Barile MF, Yoshida H, Roth H. Rheumatoid arthritis: new findings on the failure to isolate or detect mycoplasmas by multiple cultivation or serological procedures and a review ot the literature. Rev. Infect. Dis. 1991; 13: 571- 582 16.
- Stephenson J. Studies suggest a darker side of 'benign' microbes. JAMA 1997; 278: 2051-2052 17.
- Schaeverbeke T, Gilroy CB, Bebear C, Dehais J, Taylor-Robinson D. Mycoplasma fermentans, but not M. penetrans, detected by PCR assays in synovium from patients with rheumatoid arthritis and other rheumatic disorders. J. Clin. Pathol. 1996; 49: 824-828 18.
- Taylor-Robinson D, Gilroy CB, Horowitz S, Horowitz J. Mycoplasma genitalium in the joints of two patients with arthritis. Eur. J. Clin. Microbiol. Infect. Dis. 1994; 13: 1066-1069 19.

Source: http://www.immed.org/autoimmune/06.16.12%20pdfs%20updates/Haier.etal.Rheumatol.pdf

Many symptoms of Yersinia overlap with those of fibromyalgia/rheumatoid arthritis

Table 7. Yersiniosis (Y. enterocolitica) Symptomatology

Stages	Symptoms
Early stage	Gradual development of gastroenteritis, pharyngitis, complications due to inflammation of the intestinal wall, mesenteric lymphadenopathy. Excretory for months after abatement of gastroenteritis
Late stage	Articular manifestations: Reactive arthritis in hip, knee, upper ankle, sacroiliac joints, arthralgias, ankylosing spondylitis, rheumatoid arthritis, sacroiliitis Erythema nodosum, iridocyclitis, conjunctivitis, gastrointestinal complaints, abdominal pain, diarrhea, ulcerative colitis, nephritis, insulin-dependent diabetes mellitus, hepatitis (ANA positive, rheumatoid factor positive), myocarditis (rare), central and peripheral nervous system manifestations, multisystem disease Disease progression in stages with intervals of fewer complaints Correlation with thyroiditis Positive LTT Oscillating serological findings (correlation with disease expression)

Source: Berghoff W. Chronic Lyme Disease and Co-infections: Differential Diagnosis. Open Neurol J. 2012; 6: 158–178

Fibromyalgia/Rheumatoid Arthritis: possible lab tests
(but use the checklist to tailor this to the patient)

1. Borrelia SeraSpot + Borrelia EliSpot + CD57-cells
2. Chl. pneumoniae IgG/IgA antibodies + Chl. pneumoniae EliSpot
3. Chl. trachomatis IgG/IgA antibodies + Chl. trachomatis EliSpot
4. Myco. pneumoniae IgG/IgA antibodies + Myco. pneumoniae Elispot
5. Ehrlichia/Anaplasma IgG/IgM antibodies + Ehrlichia/Anaplasma EliSpot
6. Rickettsia IgG/IgM antibodies
7. Bartonella IgG/IgM antibodies + Bartonella EliSpot
8. Coxsackie Virus IgG/IgA antibodies
9. EBV antibodies including Early Antigen + EBV EliSpot
10. CMV IgG/IgM antibodies + CMV EliSpot
11. VZV IgG/IgA/IgM antibodies + VZV EliSpot
12. HSV1/2 IgG/IgA/IgM antibodies + HSV1/2 EliSpot
13. Yersinia IgG/IgA antibodies + Yersinia EliSpot
14. HHV6 IgG/IgM antibodies
15. ANA (antinuclear antibodies) + CCP (cyclic citrullinated peptide) antibodies

ME and Lyme Borreliosis: connection recognized two decades ago

Chronic Fatigue Syndrome in Patients with Lyme Borreliosis

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Key Words
Lyme disease - Neuroborreliosis - Chronic fatigue syndrome

Abstract
Several authors have reported a chronic fatigue-like syndrome in patients that have suffered from Lyme borreliosis in the past. To further investigate this suspicion of an association without sample bias, we carried out a prospective, double-blind study and tested 1,156 healthy young males for Borrelia antibodies. Seropositive subjects who had never suffered from clinically manifest Lyme borreliosis or neuroborreliosis showed significantly more often chronic fatigue ($p = 0.02$) and malaise ($p = 0.01$) than seronegative recruits. Therefore we believe it is worth examining whether an antibiotic therapy should be considered in patients with chronic fatigue syndrome and positive Borrelia serology.

Introduction

Lyme borreliosis is the most common vector-borne infection in the northern hemisphere with an annual incidence of 69 cases per 100,000 inhabitants [1]. Although the clinical course of borreliosis has been well described, data supporting the existence of a syndrome of chronic fatigue following infection is only just emerging [2]. Symptoms of the postinfectious chronic fatigue syndrome include persistent headaches, neuropsychological deficits and general malaise which can occur months or even years after infection and successful treatment of borreliosis [3–5]. This has been reported by Shadick et al. [5] in a population-based, retrospective cohort study showing a significantly higher incidence of fatigue (26 vs. 9%; $p = 0.04$) and impaired ability to concentrate (16 vs. 2%; $p = 0.03$) in patients that had been diagnosed with Lyme borreliosis when compared with an uninfected control population. In addition, Benke et al. [3] studied patients several years after they had been treated for Lyme borreliosis and compared their scores on various neuropsychological tests against an age- and education-matched control group. These patients showed deficits in memory, mental flexibility and articulatory and phonematic skills that were limited to a few memory functions and did not appear to be linked to a general mental decline.

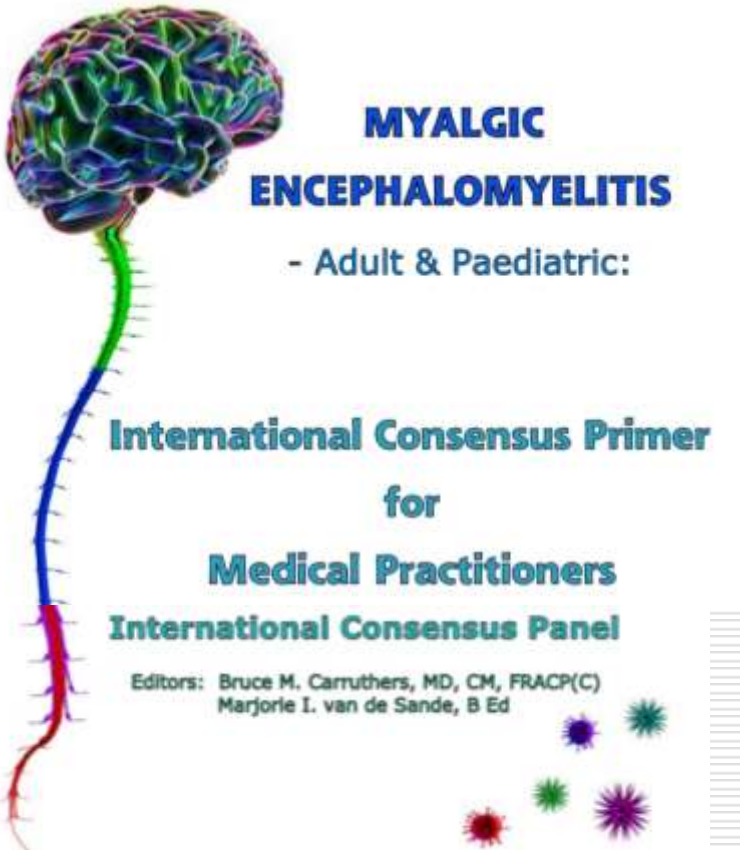
In a recent clinical and serological follow-up study, Treib et al. [6] observed a significant reduction of neurological deficits 4.2 years after antibiotic treatment. However, more than half of the patients reported unspecific complaints such as headache as well as memory and concentration problems, similar to a chronic fatigue syndrome.

The association between Lyme borreliosis and chronic fatigue remains uncertain, however. It is also unclear whether an infection with Borrelia can lead to isolated neuropsychological deficits that resemble a chronic fatigue syndrome without the patient manifesting any other clinical signs of borreliosis or neuroborreliosis.

This was almost two decades ago – in 2000: a large-cohort study, with 1,156 subjects. Conclusion:

"When encountering a patient with chronic fatigue syndrome one should consider Borreliosis as a possible cause"

The ME International Consensus Primer recommends considering Borrelia burgdorferi



Source: http://www.lymefiles.com/ME%20adult%20and%2

Immune: Tender lymphadenopathy: ☐ cervical, ☐ axillary, ☐ inguinal regions (more prominent in acute phase), ☐ flares with exertion; ☐ crimson crescents in the tonsillar fossa: ☐ demarcated along margins of both anterior and pharyngeal pillars, ☐ if patient has no tonsils, they assume a posterior position in the oropharynx; ☐ splenomegaly

GI: ☐ increased bowel sounds, ☐ abdominal bloating, ☐ abdominal tenderness: epigastrium (stomach), right lower quadrant (terminal ileum) and left lower quadrant (sigmoid colon) – *most patients have tenderness in 2-3/3 areas*

Cardiovascular & respiratory: ☐ arrhythmias: ☐ BP as above; ☐ mottling of extremities, ☐ extreme pallor, ☐ Raynaud's phenomenon, ☐ receded moons of finger nails (chronic phase) _____

Laboratory/Investigative Protocol: Diagnose by criteria. Confirm by laboratory and other investigations. A broad panel of tests provides a more robust basis to identify symptom patterns, abnormalities and orient treatment.

Routine laboratory investigation: ☐ CBC, ☐ ESR, ☐ CA, ☐ P, ☐ RBC Mg, ☐ vitamin D3, ☐ B12 & folate, ☐ ferritin, ☐ zinc, ☐ FBS, ☐ PC, ☐ Hb A1C, ☐ serum electrolytes, ☐ TSH, ☐ protein electrophoresis screen, ☐ CRP, ☐ creatinine, ☐ ECG (U+ T wave notching), ☐ CPK and liver function, ☐ rheumatoid factor, ☐ antinuclear antibodies, ☐ urinalysis, ☐ essential fatty acids, ☐ CoEnzyme Q10, ☐ immunoglobulins, ☐ diurnal cortisol levels, ☐ TTG, ☐ serotonin

Additional laboratory investigation: *(as indicated by symptoms, history, clinical evaluation, lab findings, risk factors)* ☐ 24 hour urine free cortisol, ☐ DHEA sulphate, ☐ ACTH, ☐ chest x-ray, ☐ hormones including free testosterone ☐ panoramic x-ray of dental roots, ☐ amino acid profile, ☐ abdominal ultra sound, ☐ lactose/fructose breath test

Further testing with specificity to ME, ***if and as indicated***. *Some tests are in the research stage but can identify abnormalities and focus treatment. Viral tests should be interpreted by a physician experienced in these infections.*

Pathogen	Tests	Pathogen	Tests
☐ Enterovirus	RT-PCR, serology, stomach biopsy	☐ mycoplasma	DNA-PCR, serology
☐ EBV, ☐ CMV, ☐ HHV-6	DNA-PCR, serology, antigenemia	☐ Borrelia burgdorferi	DNA-PCR, serology, Western Blot
☐ Clamydia pneumonia	DNA PCR, serology	☐ Parvovirus B19	DNA-PCR, IgG, IgM,

Immune system profiles: ☐ ***↓NK cell function & ↑ cytotoxicity**; ☐ B & T-cell function: ☐ IgG, ☐ IgG subclasses 1-4; ☐ IgA, ☐ IgM (shift from T1 to T2), ☐ cytokine/chemokine profile panel (94% accuracy): IL-8, IL-13, MIP-1β, MCP-1, IL4, ☐ flow cytometry for ↑ lymphocyte activity, ☐ ↑ 37 kDa 2-5A RNase L immunoassay – defect/ratio & bioactivity, ☐ food sensitivity panel, ☐ chemical sensitivities, ☐ stool for WCB - D-lactic acid bacteria balance, ova & parasites, ☐ autoimmune profile, **Intestinal dysbiosis:** ☐ IgA & IgM for intestinal aerobic bacteria in serum, ☐↑ leukocyte elastase activity in PBMCs, ☐ IgG food intolerance test, ☐ toxoplasmosis

Neurological & static testing: ☐ ***SPECT scan with contrast** - ↓ cortical/cerebellar region cerebral blood flow (rCBF) in the frontal, parietal, temporal and occipital & brain stem regions - *more brain involvement indicates increased illness severity,* ☐ **MRI of brain** – *(increased T2-weighted images in high white matter tracts & loss of GM volume) & rule out MS,* ☐ **MRI of spine** *(dynamic disc bulges/herniation , stenosis),* ☐ **sleep study** *(↓ stage 4 sleep, sleep pattern & rule out treatable sleep dysfunctions – upper airway resistance syndrome, sleep apnea, etc.)*

PENE: A 2 consecutive day comprehensive 8-12 minute cardiopulmonary exercise stress test (measuring heart, lung, and metabolic function) - only ME patients have significantly worse scores the second day & abnormal recovery from exertion.

* **Exercise tolerance test with expired gas exchange** - (2 consecutive days) – *measure cardiovascular, pulmonary &*

Editors: Carruthers & van de Sande 11

T & DIAGNOSTIC WORKSHEET

References for the Lyme Disease/ME connection (1/2)

Undiagnosed Lyme disease often called ME or CFS

Gustaw K. Chronic fatigue syndrome following tick-borne diseases.Neurol Neurochir Pol.2003;37:1211–21. 71% of ME/CFS cases had Lyme infection.

Chronic Fatigue Syndrome Patients Subsequently Diagnosed with Lyme Disease Borrelia burgdorferi: Evidence for Mycoplasma species Co-Infections Garth L. Nicolson, PhD, Nancy L. Nicolson, PhD and Joerg Haier, MD, PD, Journal of Chronic Fatigue Syndrome 2008; 14(4):5-17

Several Bacteria and ME / CFS scientific research papers at http://www.immed.org/fatigue_illness_research.html

RETROSPECTIVE ANALYSIS OF A COHORT OF INTERNATIONALLY CASE DEFINED CHRONIC FATIGUE SYNDROME PATIENTS IN A LYME ENDEMIC AREA.. Samuel Shor, MD, FACP

Treib, J., Grauer, M.T., Haas, A., Langenbach, J., Holzer, G.,Woessner, R. Chronic Fatigue Syndrome in patients with Lyme borreliosis Eur Neurol. 2000; 43(2): 107 - 9

Nicolson GL, and Nicolson NL. Chronic infections as a common etiology for many patients with chronic fatigue syndrome, fibromyalgia, and Gulf War Illness. Intern J Med. 1998; 1:42-6.

Taylor, S. Lyme disease (borreliosis). A plague of ignorance regarding the ignorance of a plague. http://www.autoimmunityresearch.org/lyme-disease/

In a presentation to the Edinburgh ME group in September 2005, Professor John Gow of Glasgow University stated that gene expression regulation in those with ME is identical to that seen in Lyme patients.

Relationship between Lyme Disease and CFS. Critical Needs and Gaps in Understanding Prevention, Amelioration, and Resolution of Lyme and Other Tick-Borne Diseases: The Short-Term and Long-Term Outcomes - Workshop Report. Released: April 20, 2011

Donta, S. Lyme disease as a model of Chronic Fatigue Syndrome. CFS Res Rev. 2002; 3(2): 1 - 4

Source: http://www.me-ireland.com/scientific/8.htm

References for the Lyme Disease/ME connection (2/2)

Goldenberg, D.L. Fibromyalgia, chronic fatigue syndrome, and myofascial pain syndrome. Curr Opin Rheumatol. 1995; 7(2): 127 - 35

Reponse to Dr. Ho-Yen in Scotland regarding Lyme and ME / CFS

News article at Lyme disease — a ticking timebomb that health authorities say does not exist

Evidence from Dr Samuel Shor, USA

See paper at RETROSPECTIVE ANALYSIS OF A COHORT OF INTERNATIONALLY CASE DEFINED CHRONIC FATIGUE SYNDROME PATIENTS IN A LYME ENDEMIC AREA

Results: Of the total 210 included in the analysis, 209 or 99% were felt to represent a high likelihood of "seronegative Lyme disease." Initiating various antimicrobial regimen, involved at least a 50% improvement in clinical status in 130 or 62%. Another 55 patients subjectively identified a beneficial clinical response to antimicrobials, representing a total of 188 or 88% of the total identified as having a high potential for seronegative Lyme disease.

Conclusions: A potentially substantial proportion of patients with what would otherwise be consistent with internationally case defined CFS in a Lyme endemic environment actually have a perpetuation of their symptoms driven by a persistent infection by Borrelia burgdorferi. By treating this cohort with appropriately directed antimicrobials, we have the ability to improve outcomes.

This is verified in another paper Lyme Disease Presenting as Chronic Fatigue Syndrome

Evidence from Dr Kenny de Meirleir, Belgium. The following evidence concerning the relationship between ME, CFS and undiagnosed lyme disease was presented by Dr. Kenny De Meirleir to the Belgian Senate in 2014 - ME, CFS, Lyme Presentation

A news report of this conference was provided on http://nelelijnen.be/index.php/lyme/300round-tafel-23-april-2014

Evidence presented by Dr. Richard Horowitz to the Belgian Parliament: The following presentation was made to the Belgian Parliament in June 2014 by Dr. Richard Horowitz, who has treated over 12,000 patients with Chronic Lyme, ME, and other infectious diseases

https://www.youtube.com/watch?v=JSx3KdFaupA&t=8m40s

Source: http://www.me-ireland.com/scientific/8.htm

ME and Chlamydia pneumoniae

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Editorials

Chronic fatigue syndrome or myalgic encephalomyelitis

BMJ 2007;335 doi:https://doi.org/10.1136/bmj.39316.472361.80 (Published 30 August 2007)
Cite this as: BMJ 2007;335:411

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Chlamydia pneumoniae infection a treatable cause of Chronic Fatigue Syndrome

The Editor
British Medical Journal

24 October 2007
John E Tovey
Consultant Pathologist

CHRONIC FATIGUE SYNDROME OR MYALGIC ENCEPHALOMYELITIS

In your Editorial (BMJ 2007; 335: 411-2), relating to the NICE clinical guidelines which appeared later in the Journal, you state "We remain unsure of the causes". In the guidelines also there is no mention of the possibility of an infective cause, or of the possible role of antibiotics in the treatment. NICE remarks that the attending physician

"Dr. Stratton's lab found that the majority (almost 100%) of CFS patients were PCR positive for CPN in blood samples.... Further, the majority also had either elevated IgM or IgG antibodies to CPN major outer membrane protein, cross-confirming the PCR-based findings."

Chronic *Chlamydia pneumoniae* Infection: A Treatable Cause of Chronic Fatigue Syndrome

Chronic fatigue syndrome (CFS), an elusive and controversial illness, has been a difficult management problem for clinicians. A number of infectious agents have been implicated as the cause of CFS, although consistent and compelling evidence is still lacking [1]. Few well-documented infections could cause persistent inflammatory reaction leading to the symptomatology of CFS [2, 3]. *Chlamydia pneumoniae* is a common cause of respiratory infection

Over the past 3 years, we encountered 10 of 171 patients with symptoms of chronic fatigue who had elevated titers of antibody to *C. pneumoniae* long after initial respiratory infection. Most patients had favorable clinical and serological responses to a 1- to 2-months course of azithromycin therapy, although relapse was common. The clinical symptoms of and titers of antibody to *C. pneumoniae* for our 10 patients over the course of treatment are summarized in table 1.

A 32-year-old female developed pharyngitis, cough, cervical lymphadenopathy, low-grade fevers, severe fatigue, and myalgia

Table 1. Clinical characteristics, titers of antibody to *Chlamydia pneumoniae* at the onset and during antibiotic therapy, and time to decrease in symptoms for patients with symptoms of CFS.

Patient no., age (y)/sex	Symptom(s) and sign(s)	Duration of symptoms (y)	Titer of antibody to *C. pneumoniae*						Time to improvement (w)
			Time of diagnosis	3 mo	6 mo	12 mo	18 mo	21–24 mo	
1, 32/F	CFS, cervical LN	3	≥1,024	512	128	<8	<8	32	<1
2, 72/F	Fatigue, dry cough, wheezing, sinus pain	1.5	≥1,024	. . .	32	8	256,* 512†	8	2
3, 28/F	Fatigue, cervical LN, arthralgia	1	256	128	512*	128*	8	32	1.5
4, 36/F	Pharyngitis, cough, fatigue, cervical LN	1	512	. . .	128	. . .	32	. . .	2
5, 54/F	Fatigue, otalgia, pharyngitis, right cervical LN	2	512	128	32	8	. . .	. . .	2
6, 75/F	Fatigue, dry cough, sinus pain	0.5	128	32	32	256*	. . .	. . .	1
7, 57/M	CFS, sinus pain and congestion	2.5	512	128	8	512*	. . .	. . .	2.5
8, 46/M	Fatigue, history of mastoiditis, myalgia	2	128	16	32	. . .	. . .	. . .	1
9, 70/M	Fevers, cough, severe fatigue	0.5	≥1,024†	16	32	32	. . .	. . .	2
10, 48/M	CFS, sinus pain, hoarseness, mild cough	3.5	≥1,024†	16	8	8	. . .	. . .	Undetermined

Source: Chia JKS, Chia LY. Chronic Chlamydia pneumoniae infection: a treatable cause of Chronic Fatigue Syndrome. Clin Infect Dis 1999; 29:452-453; http://www.prohealth.com/library/showarticle.cfm?libid=12763

ME and Chlamydia pneumoniae (CPN)

- **Fatigue:** ATP depletion from intracellular Chlamydia pneumoniae parasitism
- **Cardiac Insufficiency**: A recent paper found evidence of CPN throughout the myocardium. This is consistent with findings of cardiac insufficiency in CFS patients (see Peckerman).[1]
- **Tender Axillary or Cervical Lymph Nodes:** Lymph nodes are a major entry point for Cpn into the body via sinus infection, laryngitis, etc.[2]
- **Immune Deficiency**: CPN can infect the bone marrow
- **Gastrointestinal issues:** CPN infects endothelial tissues, as its preferred home, including the endothelial tissues of the gut.
- **Headaches:** CPN infects the vascular system leading to high blood pressure (from rigidified vascular walls) and inflammation of blood vessels (including in the brain), causing headaches

"No other single variable in the CFS literature even comes close to being found in near 100% of CFS patients."
(Trial conducted at Vanderbilt by leading ME clinical researchers Peterson, Cheney, Bell, and Stratton in late 1990s)[3]

Source: 1. "Persistent Chlamydia pneumoniae infection of cardiomyocytes is correlated with fatal myocardial infarction," by Spagnolie LG, et al. Cattedra di Anatomia ed Istologia Patologica, Dipartimento di Biopatologia e Diagnostica per Immagini, Universita di Roma Tor Vergata, Rome, Italy. [E-mail: spagnoli@uniroma2.it] Am J Pathol. 2007 Jan;170(1):33-42. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=17200180&dopt=Abstract; 2. "Phagocytes transmit Chlamydia pneumoniae from the lungs to the vasculature," Gieffers J, et al., Institute for Medical Microbiology and Hygiene, University of Lubeck, Lubeck Germany. Eur Respir J. 2004 Apr;23(4):506-10; 3. See http://www.prohealth.com/library/showarticle.cfm?libid=12763 for other references

ME and Mycoplasma

FEMS Immunol Med Microbiol. 2002 Nov 15;34(3):209-14.

High prevalence of Mycoplasma infections among European chronic fatigue syndrome patients. Examination of four Mycoplasma species in blood of chronic fatigue syndrome patients.

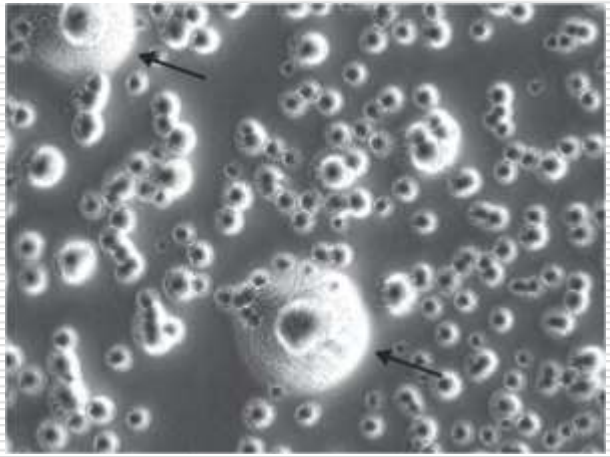
Nijs J[1], Nicolson GL, De Becker P, Coomans D, De Meirleir K.

Author information

Abstract

Prevalence of Mycoplasma species infections in chronic fatigue syndrome (CFS) has been extensively reported in the scientific literature. However, all previous reports highlighted the presence of Mycoplasmas in American patients. In this prospective study, the presence of Mycoplasma fermentans, M. penetrans, M. pneumoniae and M. hominis in the blood of 261 European CFS patients and 36 healthy volunteers was examined using forensic polymerase chain reaction. One hundred and seventy-nine (68.6%) patients were infected by at least one species of Mycoplasma, compared to two out of 36 (5.6%) in the control sample (P<0.001). Among Mycoplasma-infected patients, M. hominis was the most frequently observed infection (n=96; 36.8% of the overall sample), followed by M. pneumoniae and M. fermentans infections (equal frequencies; n=67; 25.7%). M. penetrans infections were not found. Multiple mycoplasmal infections were detected in 45 patients (17.2%). Compared to American CFS patients (M. pneumoniae>M. hominis>M. penetrans), a slightly different pattern of mycoplasmal infections was found in European CFS patients (M. hominis>M. pneumoniae, M. fermentansz Gt;M. penetrans).

Professor Nicolson found that 70% of a cohort of ME patients were infected with at least one strain of Mycoplasma. It generally prefers low-oxygen environments, and stimulates reactive oxygen species (ROS), which cause damage to cell and mitochondrial membranes – membrane potential is lost. Which means the mitochondrial ATP production is hugely impaired.

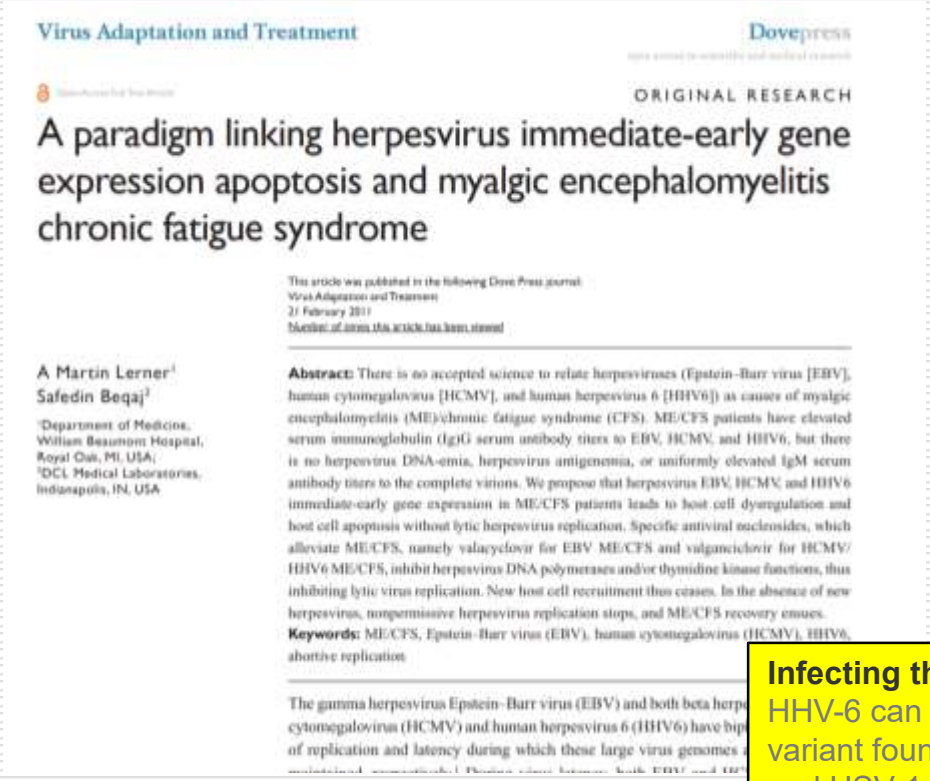


Source: Nicolson GL et al. Chronic Fatigue Syndrome Patients Subsequently Diagnosed with Lyme Disease Borrelia burgdorferi: Evidence for Mycoplasma Species Coinfections. Journal of Chronic Fatigue Syndrome, Volume 14, 2007 - Issue 4

ME and Mycoplasma: Sources (extract)

- Endresen GK. Mycoplasma blood infection in chronic fatigue and fibromyalgia syndromes. Rheumatol Int. 2003 Sep;23(5):211-5. PMID: 12879275
- Mycoplasma blood infection has been detected in about 50% of patients with CFS and/or FMS. Most patients with CFS/FMS who have mycoplasma infection appear to recover and reach their pre-illness state after long-term antibiotic therapy with doxycycline.
- Nijs J, Nicolson GL, De Becker P, Coomans D, De Meirleir K. High prevalence of Mycoplasma infections among European chronic fatigue syndrome patients. Examination of four Mycoplasma species in blood of chronic fatigue syndrome patients. FEMS Immunol Med Microbiol. 2002 Nov 15;34(3):209-14. PMID: 12423773
- Compared to American CFS patients (M. pneumoniae>M. hominis>M. penetrans), a slightly different pattern of mycoplasmal infections was found in European CFS patients (M. hominis> M. pneumoniae, M. fermentansz.Gt;M. penetrans).
- Nasralla M, Haier J, Nicolson GL. Multiple mycoplasmal infections detected in blood of patients with chronic fatigue syndrome and/or fibromyalgia syndrome. Eur J Clin Microbiol Infect Dis. 1999 Dec;18(12):859-65. PMID:10691196
- Nasralla M, Haier J, Nicolson GL. Multiple mycoplasmal infections detected in blood of patients with chronic fatigue syndrome and/or fibromyalgia syndrome. Eur J Clin Microbiol Infect Dis. 1999 Dec;18(12):859-65. PMID:10691196

In patients with a central nervous system component, think herpes viruses (EBV, HSV, CMV, VZV, HHV6)



Virus Adaptation and Treatment

Dovepress

ORIGINAL RESEARCH

A paradigm linking herpesvirus immediate-early gene expression apoptosis and myalgic encephalomyelitis chronic fatigue syndrome

This article was published in the following Dove Press journal:
Virus Adaptation and Treatment
21 February 2011

A Martin Lerner[1]
Safedin Beqaj[2]

[1]Department of Medicine, William Beaumont Hospital, Royal Oak, MI, USA; [2]DCL Medical Laboratories, Indianapolis, IN, USA

Abstract: There is no accepted science to relate herpesviruses (Epstein–Barr virus [EBV], human cytomegalovirus [HCMV], and human herpesvirus 6 [HHV6]) as causes of myalgic encephalomyelitis (ME)/chronic fatigue syndrome (CFS). ME/CFS patients have elevated serum immunoglobulin (Ig)G serum antibody titers to EBV, HCMV, and HHV6, but there is no herpesvirus DNA-emia, herpesvirus antigenemia, or uniformly elevated IgM serum antibody titers to the complete virions. We propose that herpesvirus EBV, HCMV, and HHV6 immediate-early gene expression in ME/CFS patients leads to host cell dysregulation and host cell apoptosis without lytic herpesvirus replication. Specific antiviral nucleosides, which alleviate ME/CFS, namely valacyclovir for EBV ME/CFS and valganciclovir for HCMV/HHV6 ME/CFS, inhibit herpesvirus DNA polymerases and/or thymidine kinase functions, thus inhibiting lytic virus replication. New host cell recruitment thus ceases. In the absence of new herpesvirus, nonpermissive herpesvirus replication stops, and ME/CFS recovery ensues.

Keywords: ME/CFS, Epstein–Barr virus (EBV), human cytomegalovirus (HCMV), HHV6, abortive replication

The gamma herpesvirus Epstein–Barr virus (EBV) and both beta herpe
cytomegalovirus (HCMV) and human herpesvirus 6 (HHV6) have bip
of replication and latency during which these large virus genomes

"We propose that herpesvirus EBV, HCMV, and HHV6 immediate-early gene expression in ME/CFS patients leads to host cell dysregulation and host cell apoptosis without lytic herpesvirus replication. Specific antiviral nucleosides, which alleviate ME/CFS, namely valacyclovir for EBV ME/CFS and valganciclovir for HCMV/ HHV6 ME/CFS, inhibit herpesvirus DNA polymerases and/or thymidine kinase functions, thus inhibiting lytic virus replication. New host cell recruitment thus ceases. In the absence of new herpesvirus, nonpermissive herpesvirus replication stops, and ME/CFS recovery ensues."

Infecting the brain via the Olfactory Nerve, Limbic Encephalitis

HHV-6 can travel to the brain through the nose, and is also the dominant variant found in the sensory ganglia (Hufner 2007). Like HHV-6, measles and HSV-1 tend to affect the limbic system as well as the hippocampus (Harberts 2011). There have been a number of abnormalities found in CFS patients in the hippocampus: reduced concentration of N-acetylaspartate, (Brooks 2000), hippocampal atrophy and 5-HT1A receptor binding in the hippocampus (Cleare 2005).[1]

Source: 1. https://hhv-6foundation.org/associated-conditions/hhv-6-and-chronic-fatigue-syndrome

Coxsackie frequently found in ME – especially B1

"L. Postviral Fatigue Syndrome - also known as myalgic encephalomyelitis (ME), it occurs as both sporadic and epidemic cases. It is a poorly characterized illness, the cardinal feature being excess fatiguability of the skeletal muscles. Other symptoms that may be present include muscle pain, headache, inability to concentrate, paraesthesiae, impairment of short term memory and poor visual accommodation. Focal neurological signs are rare. Evidence of myopericarditis may be present occasionally. There may be a history of a nonspecific viral illness and some lymphadenopathy may be present. Routine laboratory investigations are usually normal. Recovery usually takes place within a few weeks or months but the illness may persists in some patients with periods of remission and relapse.

The aetiology is uncertain but it is thought that there is a substantial functional component as well as a viral component in many cases. ME occasionally follows confirmed virus infections such as varicella/zoster, influenza A and IM. It may follow some bacterial infections such as toxoplasma gondii and leptospira. In the majority of cases though, the initiating infection cannot be diagnosed specifically. **There is now substantial evidence for a persistent enterovirus infection, particularly coxsackie B viruses in many cases of ME. Patients with ME appears to have a higher prevalence of antibodies against coxsackie B viruses than matched controls. Furthermore, coxsackie B viruses may occasionally be isolated from the faeces as well as skeletal muscle biopsies in patients with ME."**

Source: http://virology-online.com/viruses/Enteroviruses5.htm

ME (Myalgic Encephalomyelitis), often called CFS in the UK *(but do the checklist to tailor this further)*

1. Borrelia SeraSpot + Borrelia EliSpot + CD57 cells
2. Chlamydia pneumoniae IgG/IgA antibodies + Chlamydia pneumoniae EliSpot
3. Mycoplasma pneumoniae IgG/IgA antibodies
4. Bartonella IgG/IgM antibodies
5. Parvovirus B19 IgG/IgM antibodies
6. Echovirus IgG/IgM antibodies
7. Coxsackie Virus IgG/IgA antibodies
8. EBV EliSpot
9. CMV EliSpot
10. Herpes Simplex Virus 1/2 IgG/IgA/IgM antibodies + Herpes simplex Virus EliSpot
11. HHV 6-IgG/IgM antibodies

Multiple Sclerosis: references (sample)

Multiple Sclerosis, myelopathies, polyneuropathies, brain tumours,
encephalopathy. (Neurosurgery.1992May;30(5): 769-73)

1986 (USA): Relapsing fever/Lyme disease – Multiple sclerosis. Medical Hypotheses, volume 21, issue 3, pages 335-343

2000 (Poland): Lyme borreliosis and Multiple sclerosis: Any Connection? A Seroepidemic study. Ann Agric Environ Med. issue 7, 141-143

2001 (Norway): Association between Multiple sclerosis and Cystic Structures in Cerebrospinal Fluid. Infect 29:315

2004 (Switzerland): Chronic Lyme borreliosis at the root of Multiple sclerosis – is a cure with antibiotics attainable?

MS and Borrelia – research over 4 decades

Dr. Vincent Marshall's exhaustive research from the 80's showed spirochetes on the axons of nerves of MS patient autopsies in Europe.

Source: https://www.ncbi.nlm.nih.gov/pubmed/15617845; http://www.medical-hypotheses.com/article/0306-9877(88)90023-0/abstract

MS and Chlamydia pneumoniae

Empirical antibacterial treatment of infection with *Chlamydophila pneumoniae* in Multiple Sclerosis

David Wheldon MB FRCPath

After much controversy there is now powerful evidence for the respiratory pathogen *Chlamydophila (Chlamydia) pneumoniae* being a causal factor in some variants of the neurological illness multiple sclerosis. A series of remarkable studies finds:

- **the presence of *C. pneumoniae* gene sequences in the cerebrospinal fluid of patients who have the disease, and culture of the organism when sensitive cultural methods are used** [Sriram S, Stratton CW, Yao S, Tharp A, Ding L, Bannan JD, Mitchell WM. *Chlamydia pneumoniae* infection of the central nervous system in multiple sclerosis. Ann Neurol. 1999 Jul;46(1):6-14.]

- **an association of new *C. pneumoniae* respiratory infections with episodes of clinical relapse** [Buljevac D, Verkooyen RP, Jacobs BC, Hop W, van der Zwaan LA, van Doorn PA, Hintzen RQ. *Chlamydia pneumoniae* and the risk for exacerbation in multiple sclerosis patients. *Ann Neurol.* 2003 Dec;54(6):828-31.]

- **a statistically significant elevation of *C. pneumoniae*-specific serum antibody levels when the disease shifts into the progressive form** [Munger KL, Peeling RW, Hernán MA, Chasan-Taber L, Olek MJ, Hankinson SE, Hunter D, Ascherio A. Infection with *Chlamydia pneumoniae* and risk of multiple sclerosis. *Epidemiology* 2003 14:2 141-147]

- **antibodies to *C. pneumoniae* in the cerebrospinal fluid of patients with the disease** [**(1.)** Yao, S., Stratton, C.W., Mitchell, W.M., Sriram, S. (2001). CSF oligoclonal bands in multiple sclerosis represent antibodies against Chlamydophila. *Neurology* 56, 1168-76. **(2.)** Fainardi, E., Castellazzi, M., Casetta, I. et al. (2004). Intrathecal production of *Chlamydia pneumoniae*-specific high-affinity antibodies is significantly associated with a subset of multiple sclerosis patients with progressive forms. *Journal of the Neurological Sciences* 217, 181-8.]

- **evidence of active *C. pneumoniae* protein synthesis in the central nervous system, with production of a bacterial protein evoking an**

"... there is now powerful evidence for the respiratory pathogen *Chlamydophila (Chlamydia)pneumoniae* being a causal factor in some variants of the neurological illness multiple sclerosis."

Source: http://www.davidwheldon.co.uk/ms-treatment1.html

Bartonella-induced MS?

Journal of Clinical Microbiology

JCM Article | Journal Info. | Authors | Reviewers | Permissions | Journals.ASM.org

J Clin Microbiol. 2008 Sep; 46(9): 2856–2861. PMCID: PMC2546763
Published online 2008 Jul 16. doi: 10.1128/JCM.00832-08

***Bartonella* sp. Bacteremia in Patients with Neurological and Neurocognitive Dysfunction**

E. B. Breitschwerdt,[1,*] R. G. Maggi,[1] W. L. Nicholson,[2] N. A. Cherry,[1] and C. W. Woods[3]

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ABSTRACT Go to:

We detected infection with a *Bartonella* species (*B. henselae* or *B. vinsonii* subsp. *berkhoffii*) in blood samples from six immunocompetent patients who presented with a chronic neurological or neurocognitive syndrome including seizures, ataxia, memory loss, and/or tremors. Each of these patients had substantial animal contact or recent arthropod exposure as a potential risk factor for *Bartonella* infection. Additional studies should be performed to clarify the potential role of *Bartonella* spp. as a cause of chronic neurological and neurocognitive dysfunction.

Bartonella henselae causes a prototypical illness characterized by fever and regional lymphadenopathy following a cat scratch or bite (8, 9). Cat scratch disease (CSD) is usually self-limited, and antibiotic

"Of the six research subjects, including Barnes, that Breitschwerdt used in his study, two were veterinarians who reported frequent bites from cats, dogs, pocket pets and other animals, one reported a severe scratch from a cat, one had frequent arthropod exposure and had been bitten by a pig and pecked frequently by various fowl, another owned a horse farm and had frequent arthropod exposure and cat scratches, and the sixth was a teenager who developed severe debilitating migraine headaches after a tick was removed from his ankle."

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2546763/, https://www.lymeneteurope.org/forum/viewtopic.php?t=2445

Multiple Sclerosis: Laboratory tests suggested

1. Borrelia SeraSpot + Borrelia EliSpot + CD57-cells
2. Chlamydia pneumoniae EliSpot, and Chlamydia pneumonia IgG/IgA antibodies
3. Mycoplasma pneumoniae Elispot, and IgG/IgA antibodies
4. Bartonella Elispot
5. Coxsackie Virus IgG/IgA antibodies
6. EBV EliSpot
7. CMV EliSpot
8. HHV6 IgG/IgM antibodies

Parkinson's: Cases of Lyme-associated Parkinsonism in medical literature

Journal List › Am J Pathol › v.173(5); 2008 Nov › PMC2570132

The American Journal of PATHOLOGY
Cellular and Molecular Biology of Disease
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Am J Pathol. 2008 Nov; 173(5): 1415–1427.
doi: 10.2353/ajpath.2008.080483
PMCID: PMC2570132

Interaction of the Lyme Disease Spirochete *Borrelia burgdorferi* with Brain Parenchyma Elicits Inflammatory Mediators from Glial Cells as Well as Glial and Neuronal Apoptosis

Geeta Ramesh,* Juan T. Borda,† Jason Dufour,‡ Deepak Kaushal,* Ramesh Ramamoorthy,* Andrew A. Lackner,† and Mario T. Philipp*

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Abstract

Go to:

Lyme neuroborreliosis, caused by the spirochete ***Borrelia burgdorferi***, often manifests by causing neurocognitive deficits. As a possible mechanism for Lyme neuroborreliosis, we hypothesized that ***B. burgdorferi*** induces the production of inflammatory mediators in the central nervous system with concomitant neuronal and/or glial apoptosis. To test our hypothesis, we constructed an ***ex vivo*** model that consisted of freshly collected slices from brain cortex of a rhesus macaque and allowed live ***B. burgdorferi*** to penetrate the tissue. Numerous transcripts of genes that regulate inflammation as well as oligodendrocyte and neuronal apoptosis were significantly altered as assessed by DNA microarray analysis. Transcription level increases of 7.43-fold ($P = 0.005$) for the cytokine tumor necrosis factor-α and 2.31-fold ($P = 0.016$) for the chemokine interleukin (IL)-8 were also detected by real-time-polymerase chain reaction array analysis. The immune mediators IL-6, IL-8, IL-1β, COX-2, and CXCL13 were visualized in glial cells ***in situ*** by immunofluorescence staining and confocal microscopy. Concomitantly,

"The transcript of the embryonic lethal, abnormal vision, Drosophila-like 4 gene (NCBI NM_021952), which is associated with inflammation and neuronal death and is up-regulated in Parkinson's disease, was upregulated in spirochete-stimulated tissues by 9.98-fold."

Link between Parkinsonism and Mycoplasma also evidenced

Movement Disorders

Brief Report

Reversible parkinsonism and dystonia following probable mycoplasma pneumoniae infection

Dr. Jong S. Kim, Il S. Choi, Myoung C. Lee

First published: July 1995

DOI: 10.1002/mds.870100419

Cited by (CrossRef): 13 articles

View issue TOC
Volume 10, Issue 4
July 1995
Pages 510–512

Journal of Child Neurology

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Transient Parkinsonism Following *Mycoplasma pneumoniae* Infection With Normal Brain Magnetic Resonance Imaging (MRI)

Chee Geap Tay, MMed (Paed), Choong Yi Fong, FRCPCH, Lai Choo Ong, MRCP

First Published December 5, 2013 | Research Article

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Abstract

Parkinsonism caused by infection is uncommon in children. We report 2 previously healthy children with acute self-limiting parkinsonism following *Mycoplasma pneumoniae* infection, with normal brain magnetic resonance imaging (MRI). Our case report expands the phenotype of parkinsonism associated with *M pneumoniae* infection. We recommend that children with acute parkinsonism preceded by a period of febrile illness, even with a normal brain MRI, should be investigated for *M pneumoniae* infection.

"We recommend that children with acute Parkinsonism preceded by a period of febrile illness, even with a normal brain MRI, should be investigated for *M pneumoniae* infection."

Parkinsonism

1. Borrelia SeraSpot + Borrelia EliSpot + CD57 cells
2. Mycoplasma pneumoniae Elispot, and IgG/IgA antibodies
3. Bartonella Elispot
4. Coxsackie Virus IgG/IgA antibodies
5. EBV EliSpot
6. CMV EliSpot

Alzheimer's Disease

J Alzheimers Dis. 2014;41(4):1087-93. doi: 10.3233/JAD-130446.

Lyme neuroborreliosis and dementia.

Blanc F[1], Philippi N[1], Cretin B[1], Kleitz C[2], Berly L[2], Jung B[1], Kremer S[3], Namer IJ[4], Sellal F[5], Jaulhac B[6], de Seze J[7].

Author information

Abstract

INTRODUCTION: Descriptions of Lyme disease and dementia are rare.

OBJECTIVE: To describe patients with dementia and a positive "intrathecal anti-Borrelia antibody index" (AI), specific for neuroborreliosis.

METHODS: Among 1,594 patients seen for dementia, we prospectively identified and studied 20 patients (1.25%) with dementia and a positive AI. Patients underwent a battery of neuropsychological tests brain, MRI, FDG-PET, and cerebrospinal fluid (CSF) analysis. An etiological diagnosis of the dementia was made at the end of the follow-up of

RESULTS: We found two groups of patients with dementia, the first (n = 7, 0.4 improvement of dementia after treatment by antibiotics and the second (n = 1 antibiotics. In the second group, the final diagnoses were Alzheimer's disease = 1), FTLD (n = 3), hippocampal sclerosis (n = 1), and vascular dementia (n = between the two patient groups at baseline. Brain MRI showed more focal atr second group. Tau, p-tau, and Aβ42 concentrations in the CSF were normal i second.

CONCLUSION: Pure Lyme dementia exists and has a good outcome after antibiotics. It is advisable to do Lyme serology in demented patients, and if serology is positive, to do CSF analysis with AI. Neurodegenerative dementia associated with positive AI also exists, which may have been revealed by the involvement of Borrelia in the CNS.

KEYWORDS: Alzheimer's disease; Lewy body dementia; Lewy body disease; Lyme disease; Lyme neuroborreliosis; dementia; frontotemporal lobe dementia; hippocampal sclerosis; intrathecal anti-Borrelia antibody index; vascular dementia

"Pure Lyme dementia exists and has a good outcome after antibiotics. It is advisible to do Lyme serology in demented patients"

Source: Blank et al.: Journal of Alzheimer´s disease, Volume 4/2014, 1087-1093

2016 editorial, Journal of Alzheimer's Disease, 31 authors: "incontrovertible evidence of a microbial component"

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doi: 10.3233/JAD-160152

PMCID: P
NIHMSID: NI

Microbes and Alzheimer's Disease

Ruth F. Itzhaki,[a,*] Richard Lathe,[b,*] Brian J. Balin,[c] Melvyn J. Ball,[d] Elaine L. Bearer,[e] Heiko Braak,[f] Maria J. Chris Carter,[h] Mario Clerici,[i] S. Louise Cosby,[j] Kelly Del Tredici,[f] Hugh Field,[k] Tamas Fulop,[l] Claudio Grassi, Griffin,[n] Jürgen Haas,[b] Alan P. Hudson,[o] Angela R. Kamer,[p] Douglas B. Kell,[q] Federico Licastro,[r] Luc Lefenr Lövheim,[t] Roberta Mancuso,[u] Judith Miklossy,[v] Carola Otth,[w] Anna Teresa Palamara,[x] George Perry,[y] Chris Preston,[z] Etheresia Pretorius,[aa] Timo Strandberg,[bb] Naji Tabet,[cc] Simon D. Taylor-Robinson,[dd] and Judith A. Hudson[ee]

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We are researchers and clinicians working on Alzheimer's disease (AD) or related topics, and we write express our concern that one particular aspect of the disease has been neglected, even though treatment based on it might slow or arrest AD progression. We refer to the many studies, mainly on humans, implicating specific microbes in the elderly brain, notably herpes simplex virus type 1 (HSV1), *Chlam pneumoniae*, and several types of spirochaete, in the etiology of AD [1–4]. Fungal infection of AD bra 6] has also been described, as well as abnormal microbiota in AD patient blood [7]. The first observati of HSV1 in AD brain were reported almost three decades ago [8]. The ever-increasing number of these studies (now about 100 on HSV1 alone) warrants re-evaluation of the infection and AD concept.

AD is associated with neuronal loss and progressive synaptic dysfunction, accompanied by the deposition

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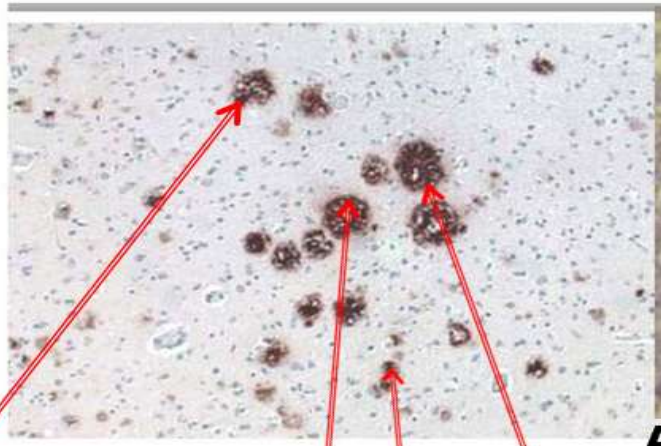
"There is incontrovertible evidence that Alzheimer's Disease has a dormant microbial component. We can't keep ignoring all of the evidence"

Professor Douglas Kell,
Manchester University

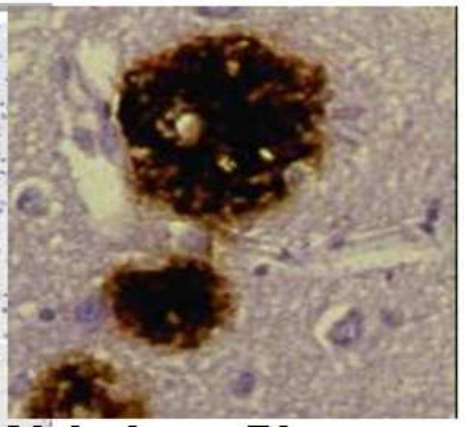
"We refer to the many studies, mainly on humans, implicating specific microbes in the elderly brain, **notably herpes simplex virus type 1 (HSV1), *Chlamydia pneumoniae*, and several types of spirochaete**, in the etiology of AD [1–4]."

Alzheimer Plaques can be Borrelia biofilms

Dr Alois Alzheimer – with Morphing of Alzheimer plaques on his portrait

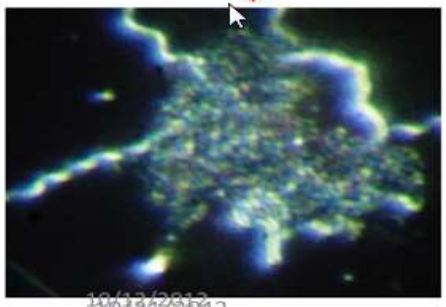


Alzheimer plaques - google

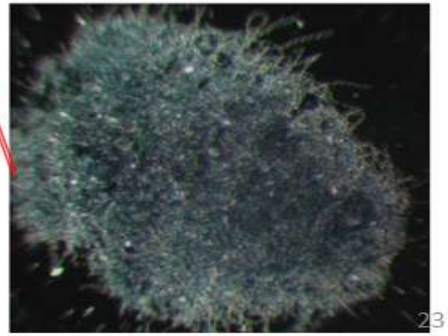


Alzheimer Plaques - Close Up

Borrelia Biofilm Units



Alzheimer Plaques resemble Biofilms of borrelia burgdorferi



Amyloid plaques in Alzheimer's Disease: Protection against microbial infection?

"When you look in the plaques, each one had a single bacterium in it," says Tanzi. "A single bacterium can induce an entire plaque overnight."

"Our findings raise the intriguing possibility that Alzheimer's pathology may arise when the brain perceives itself to be under attack from invading pathogens"

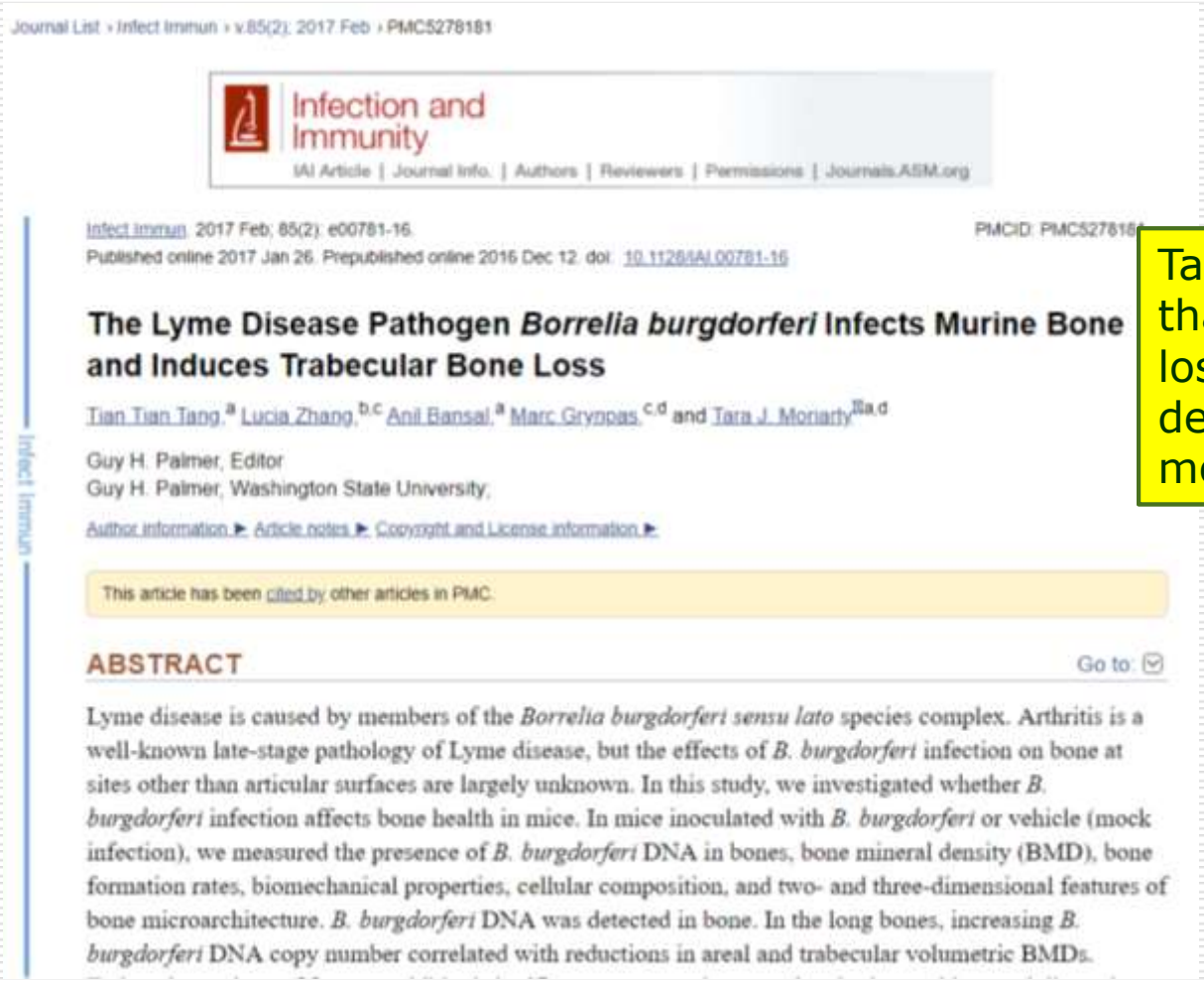
Alzheimers / Dementia

1. Borrelia SeraSpot + Borrelia-EliSpot + CD57 cells
2. Chlamydia pneumoniae IgG/IgA antibodies + Chlamydia pneumoniae EliSpot
3. Mycoplasma pneumoniae Elispot and IgG/IgA antibodies
4. Coxsackie Virus IgG/IgA antibodies
5. Herpes simplex virus 1 / 2 IgG/IgA/IgM antibodies + Herpes simplex virus EliSpot
6. EBV EliSpot
7. CMV EliSpot

Osteoporosis/osteopenia as a result of Lyme Disease?: Ötzi a case in point

- Mitochondrial DNA analysis has shown that the **bacteria responsible for Lyme disease resided deep in Ötzi's bones**. Though he didn't die from complications of the disease, work from a team of scientists at the University of Toronto's Faculty of Dentistry now suggests that the 5,000-year-old man might have suffered from **bone loss as a result of his infection**.
- While scientists have long established a link between advanced Lyme disease and the development of osteoarthritis, until now **no one has systematically studied the effects of this disease on bones**.
- The bacteria were not only detectable in the bones of mice, **they were seen to cause significant bone loss in the longer bones, mere weeks after infection**.
- **In fact, the bone loss developed at a rapid rate, taking just four weeks to advance to osteopenia, a forerunner to the more severe form of bone loss disease, osteoporosis. The study found that the amount of bone loss directly correlated to the bacterial load found in the bones.** The more bacteria present, the greater the rate of bone loss.
- **The findings suggest that monitoring bone loss in human Lyme disease patients may be warranted, especially because bone loss is a significant risk factor for fractures later in life.**
- **"One of our main focuses right now is on the mechanism that induces the bone loss,"** said Tian Cornelia Tang, **Faculty of Dentistry**.
- **Cellular studies are currently underway to determine just how the bacteria interact with the bone building cells of the body, osteoblasts**, with the hope of finding new drug targets to combat not just the bacteria, but the newly discovered associated bone loss.
- **"We need to know how long the osteopenia lasts after bacterial infection, and whether it progresses to osteoporosis,"** added Moriarty.

Borrelia infects bone and induces bone loss



Journal List › Infect Immun › v.85(2); 2017 Feb › PMC5278181

Infection and Immunity

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Infect Immun. 2017 Feb; 85(2): e00781-16. PMCID: PMC5278181

Published online 2017 Jan 26. Prepublished online 2016 Dec 12. doi: 10.1128/IAI.00781-16

The Lyme Disease Pathogen *Borrelia burgdorferi* Infects Murine Bone and Induces Trabecular Bone Loss

Tian Tian Tang,[a] Lucia Zhang,[b,c] Anil Bansal,[a] Marc Grynpas,[c,d] and Tara J. Moriarty[a,d]

Guy H. Palmer, Editor

Guy H. Palmer, Washington State University,

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ABSTRACT

Go to:

Lyme disease is caused by members of the *Borrelia burgdorferi sensu lato* species complex. Arthritis is a well-known late-stage pathology of Lyme disease, but the effects of *B. burgdorferi* infection on bone at sites other than articular surfaces are largely unknown. In this study, we investigated whether *B. burgdorferi* infection affects bone health in mice. In mice inoculated with *B. burgdorferi* or vehicle (mock infection), we measured the presence of *B. burgdorferi* DNA in bones, bone mineral density (BMD), bone formation rates, biomechanical properties, cellular composition, and two- and three-dimensional features of bone microarchitecture. *B. burgdorferi* DNA was detected in bone. In the long bones, increasing *B. burgdorferi* DNA copy number correlated with reductions in areal and trabecular volumetric BMDs.

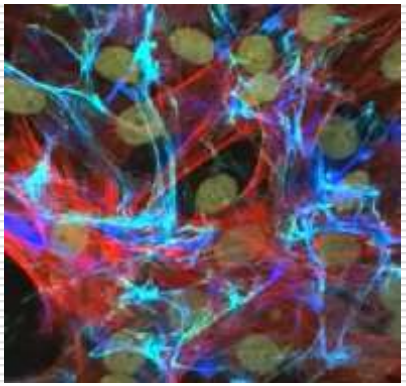
Tang *et al.* found that *Borrelia* causes a loss of bone mineral density in a mouse model of the disease.

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5278181/

Tests for Osteoporosis/Osteopenia

1. Borrelia SeraSpot
2. Borrelia EliSpot
3. CD57+ cells

Ehlers Danlos Syndrome and Borrelia?: Bb hides in connective tissue and damages collagen



Open Neurol J. 2012; 6: 179–186.
Published online 2012 Dec 31. doi: 10.2174/1874205X01206010179
Suppl 1

How Lyme Disease Hides in Connective Tissue

Lyme Disease is caused by Borrelia burgdorferi a corkscrew shaped bacterium with an affinity for connective tissue[2]. Connective tissue is the most widely distributed, varied type of tissue found in the human body. It includes: loose connective tissue (epithelia, fascia, pleura, pericardial sac, esophagus, and the outer covering of blood vessels, nerves, and brain.); fat (adipose tissue); dense irregular connective tissue (skin, capsules around organs and fibrous sheath around bones); dense regular connective tissue (tendons and ligaments); cartilage (ear, larynx, joints, between ribs, intervertebral discs); bone (skeleton); and blood (erythrocytes, leukocytes, and platelets).

Borrelia is known to spread to the Lymphatic system within the first 24 hours after infection.[3] During inflammation the lymphatic channels will maintain in an open position not only increasing flow of protein and lymphatics but also inadvertently spreading infectious agents. From the lymphatic system Borrelia will move to collagen rich areas of the body. Collagen is a type of connective tissue found in skin, bone, tendon, cartilage, synovium, the walls of blood vessels and the outer covering of nerves. (see my prior post on Decorin and Collagen)

Damage of Collagen and Elastic Fibres by Borrelia Burgdorferi – Known and New Clinical and Histopathological Aspects

Kurt E Müller*

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Abstract

Go to

Lyme Borreliosis, or Lyme's disease, manifests itself in numerous skin conditions. Therapeutic intervention should be initiated as soon as a clinical diagnosis of erythema migrans is made. The histopathology of some of the skin conditions associated with Lyme Borreliosis is characterised by structural changes to collagen, and sometimes also elastic fibres. These conditions include morphea, lichen sclerosus et atrophicus and acrodermatitis chronica atrophicans. More recently, further skin conditions have been identified by the new microscopic investigation technique of focus floating microscopy: granuloma annulare, necrobiosis lipoidica, necrobiotic xanthogranuloma, erythema annulare centrifugum, interstitial

Borrelia has an affinity to connective tissue, and is known to damage collagen and elastic fibres. How it does that is explained on the next page

Source: http://tenaciouspt.blogspot.co.uk/2016/10/histamine-intolerance-may-be-affecting.html

It cleaves aggrecan, which destroys joints and connective tissue

Journal List › Front Cell Infect Microbiol › v.3; 2013 › PMC3743303

frontiers in Cellular and Infection Microbiology

Front Cell Infect Microbiol. 2013; 3: 40.
Published online 2013 Aug 14. doi: 10.3389/fcimb.2013.00040

PMCID: PMC3743303

Borrelia burgdorferi aggrecanase activity: more evidence for persistent infection in Lyme disease

Raphael B. Stricker* and Lorraine Johnson

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Abstract

Lyme disease is the most common tickborne illness in the world today. A recent study describes for the first time an enzyme produced by the spirochetal agent of Lyme disease, *Borrelia burgdorferi*, that clea aggrecan, a proteoglycan found in joints and connective tissue. Discovery of the spirochetal aggrecanas raises many questions about the pathogenesis of Lyme arthritis and lends support to the concept of persistent *B. burgdorferi* infection in patients with chronic Lyme disease symptoms.

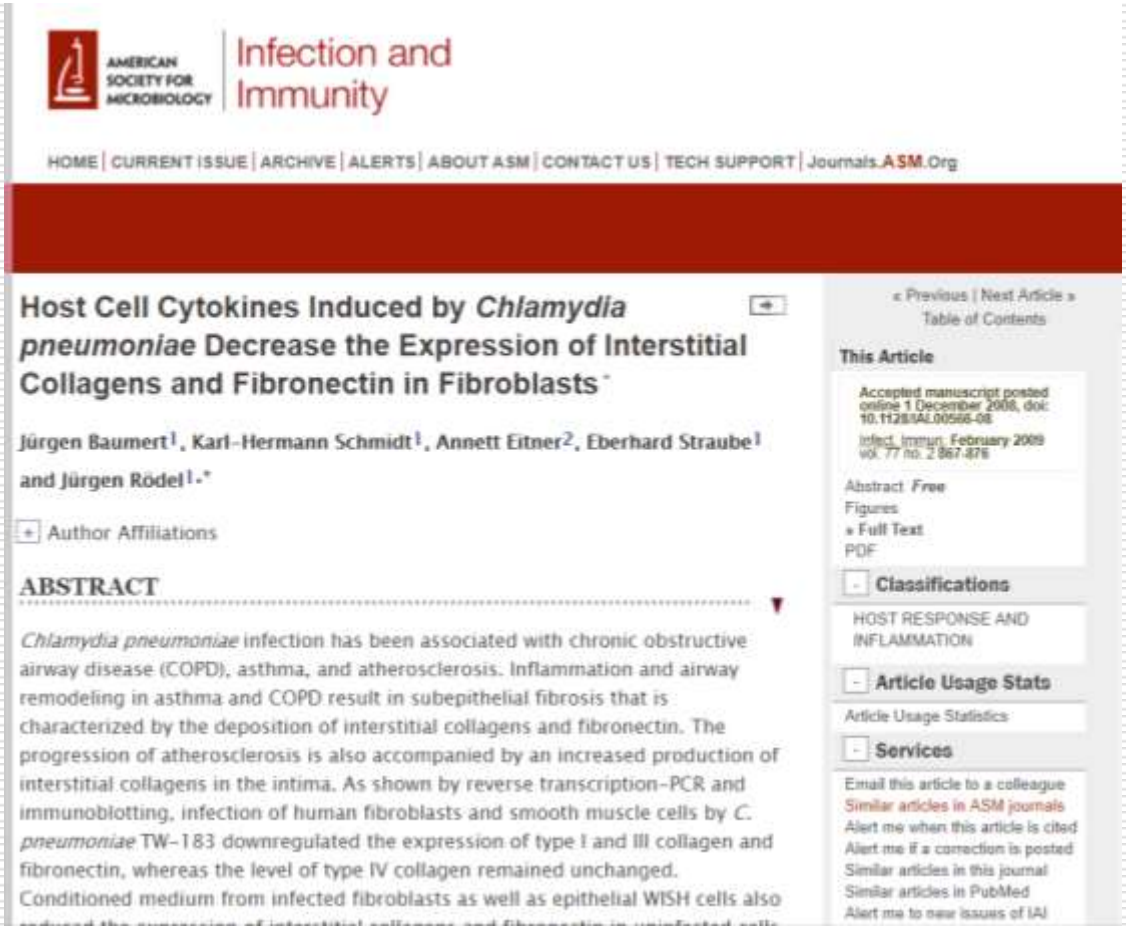
Keywords: Lyme disease, *Borrelia burgdorferi*, aggrecanase, arthritis, BbHtrA

Lyme disease is the most common tickborne illness in the world today (Stricker and Johnson, 2011). As of July 2013, the Medline database lists more than 25,000 published peer-reviewed articles about tickborne diseases. Despite this plethora of scientific information, however, the pathogenetic mechanisms of

"*Borrelia burgdorferi* cleaves aggrecan, a proteoglycan found in joints and connective tissue …. The spirochetal aggrecanase, called BbHtrA, was identified in the three major species of *B. burgdorferi*, was expressed on the spirochete surface, and was shown to cleave aggrecan at a site that destroys the function of the proteoglycan."

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3743303/

EDS: Collagen and fibronectin expression are downregulated by Chlamydia pneumoniae



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Host Cell Cytokines Induced by *Chlamydia pneumoniae* Decrease the Expression of Interstitial Collagens and Fibronectin in Fibroblasts

Jürgen Baumert[1], Karl-Hermann Schmidt[1], Annett Eitner[2], Eberhard Straube[1] and Jürgen Rödel[1,*]

Author Affiliations

ABSTRACT

Chlamydia pneumoniae infection has been associated with chronic obstructive airway disease (COPD), asthma, and atherosclerosis. Inflammation and airway remodeling in asthma and COPD result in subepithelial fibrosis that is characterized by the deposition of interstitial collagens and fibronectin. The progression of atherosclerosis is also accompanied by an increased production of interstitial collagens in the intima. As shown by reverse transcription–PCR and immunoblotting, infection of human fibroblasts and smooth muscle cells by *C. pneumoniae* TW-183 downregulated the expression of type I and III collagen and fibronectin, whereas the level of type IV collagen remained unchanged. Conditioned medium from infected fibroblasts as well as epithelial WISH cells also

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This Article

Accepted manuscript posted online 1 December 2008, doi: 10.1128/IAI.00566-08
Infect. Immun. February 2009 vol. 77 no. 2 867-876

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"Infection of human fibroblasts and smooth muscle cells by *C. pneumoniae* .. downregulated the expression of type I and III collagen and fibronectin"

Source: http://iai.asm.org/content/77/2/867.full

Testing protocol for involvement of infections in connective tissue disorders/Ehlers Danlos Syndrome

1. Borrelia SeraSpot
2. Borrelia EliSpot
3. CD57+ cells
4. Chlamydia pneumoniae EliSpot
5. Chlamydia pneumoniae IgG/IgA antibodies

Borrelia and Mast Cell Activation Syndrome/Disease (MCAS/MCAD)

Journal List › Infect Immun › v.67(3); 1999 Mar › PMC96436

Infection and Immunity

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Infect Immun. 1999 Mar; 67(3): 1107–1115. PMCID: PMC96436

Borrelia burgdorferi Spirochetes Induce Mast Cell Activation and Cytokine Release

Jeffrey Talkington and Steven P. Nickell*

Editor: J. R. McGhee

Author information ▶ Article notes ▶ Copyright and License information ▶

ABSTRACT

Go to:

The Lyme disease spirochete, *Borrelia burgdorferi*, is introduced into human hosts via tick bites. Among the cell types present in the skin which may initially contact spirochetes are mast cells. Since spirochetes are known to activate a variety of cell types in vitro, we tested whether *B. burgdorferi* spirochetes could activate mast cells. We report here that freshly isolated rat peritoneal mast cells or mouse MC/9 mast cells cultured in vitro with live or freeze-thawed *B. burgdorferi* spirochetes undergo low but detectable degranulation, as measured by [5-^{3}H] hydroxytryptamine release, and they synthesize and secrete the proinflammatory cytokine tumor necrosis factor alpha (TNF-α). In contrast to findings in previous studies, where *B. burgdorferi*-associated activity was shown to be dependent upon protein lipidation, mast cell TNF-α release was not induced by either lipidated or unlipidated recombinant OspA. This activity was additionally shown to be protease sensitive and surface expressed. Finally, comparisons of TNF-α-inducing activity in known low-, intermediate-, and high-passage *B. burgdorferi* B31 isolates demonstrated passage-dependent loss of activity, indicating that the activity is probably plasmid encoded. These findings

Borrelia and Mast Cell Activation Syndrome/Disease (MCAS/MCAD)

Format: Abstract ▾ Send to ▾

Parasit Vectors. 2017 Jun 27;10(1):313. doi: 10.1186/s13071-017-2243-0.

Interaction of primary mast cells with Borrelia burgdorferi (sensu stricto): role in transmission and dissemination in C57BL/6 mice.

Bernard Q[1,2], Wang Z[3], Di Nardo A[3], Boulanger N[4,5].

⊕ Author information

Abstract

BACKGROUND: Borrelia burgdorferi (sensu lato), the causative agent of Lyme borreliosis is a bacterium transmitted by hard ticks, Ixodes spp. Bacteria are injected into the host skin during the tick blood meal with tick saliva. There, Borrelia and saliva interact together with skin cells such as keratinocytes, fibroblasts, mast cells and other specific immune cells before disseminating to target organs.

METHODS: To study the role of mast cells in the transmission of Lyme borreliosis, we isolated mouse primary mast cells from bone marrow and incubated them in the presence of Borrelia burgdorferi (sensu stricto) and tick salivary gland extract. We further analyzed their potential role in vivo, in a mouse model of deficient in mast cells (Kit $^{wsh-/-}$ mice).

RESULTS: To our knowledge, we report here for the first time the bacteria ability to induce the inflammatory response of mouse primary mast cells. We show that OspC, a major surface lipoprotein involved in the early transmission of Borrelia, induces the degranulation of primary mast cells but has a limited effect on the overall inflammatory response of these cells. In contrast, whole bacteria have an opposite effect. We also show that mast cell activation is significantly inhibited by tick salivary gland extract. Finally, we demonstrate that mast cells are likely not the only host cells involved in the early transmission and dissemination of Borrelia since the use of mast cell deficient Kit $^{wsh-/-}$ mice shows a limited impact on these two processes in the context of this mouse genetic background.

CONCLUSIONS: The absence of mast cells did not change the replication rate of Borrelia in the skin. However, in the absence of mast cells, Borrelia dissemination to the joints was faster. Mast cells do not control skin bacterial proliferation during primary infection and the establishment of the primary infection, as shown in the C57BL/6 mouse model studied. Nevertheless, the Borrelia induced cytotokine modulation on mast cells might be involved in long term and/or repeated infections and protect from Lyme borreliosis due to the development of a hypersensitivity to tick saliva.

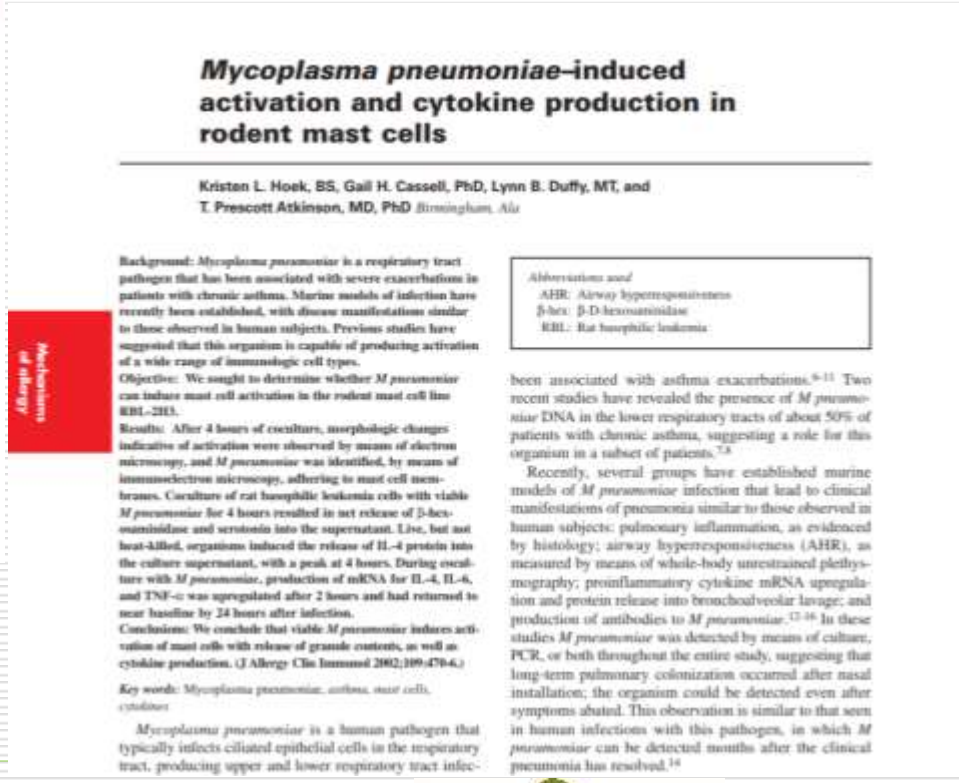
KEYWORDS: Borrelia; Ixodes tick; Kit wsh−/− mouse; Mast cells; Pathogen transmission; Tick saliva

PMID: 28655322 PMCID: PMC5488306 DOI: 10.1186/s13071-017-2243-0

"We report here for the first time the bacteria ability to induce the inflammatory response of mouse primary mast cells. We show that OspC, a major surface lipoprotein involved in the early transmission of Borrelia, induces the degranulation of primary mast cells …"

Mast Cells and Mycoplasma

Mycoplasma pneumoniae induces mast cell activation and degranulation



Mechanisms of allergy

Mycoplasma pneumoniae–induced activation and cytokine production in rodent mast cells

Kristen L. Hoek, BS, Gail H. Cassell, PhD, Lynn B. Duffy, MT, and T. Prescott Atkinson, MD, PhD *Birmingham, Ala*

Background: *Mycoplasma pneumoniae* is a respiratory tract pathogen that has been associated with severe exacerbations in patients with chronic asthma. Murine models of infection have recently been established, with disease manifestations similar to those observed in human subjects. Previous studies have suggested that this organism is capable of producing activation of a wide range of immunologic cell types.

Objective: We sought to determine whether *M pneumoniae* can induce mast cell activation in the rodent mast cell line RBL-2H3.

Results: After 4 hours of coculture, morphologic changes indicative of activation were observed by means of electron microscopy, and *M pneumoniae* was identified, by means of immunoelectron microscopy, adhering to mast cell membranes. Coculture of rat basophilic leukemia cells with viable *M pneumoniae* for 4 hours resulted in net release of β-hexosaminidase and serotonin into the supernatant. Live, but not heat-killed, organisms induced the release of IL-4 protein into the culture supernatant, with a peak at 4 hours. During coculture with *M pneumoniae*, production of mRNA for IL-4, IL-6, and TNF-α was upregulated after 2 hours and had returned to near baseline by 24 hours after infection.

Conclusions: We conclude that viable *M pneumoniae* induces activation of mast cells with release of granule contents, as well as cytokine production. (J Allergy Clin Immunol 2002;109:670-6.)

Key words: *Mycoplasma pneumoniae*, asthma, mast cells, cytokines

Abbreviations used
AHR: Airway hyperresponsiveness
β-hex: β-D-hexosaminidase
RBL: Rat basophilic leukemia

Mycoplasma pneumoniae is a human pathogen that typically infects ciliated epithelial cells in the respiratory tract, producing upper and lower respiratory tract infec- been associated with asthma exacerbations.[9-11] Two recent studies have revealed the presence of *M pneumoniae* DNA in the lower respiratory tracts of about 50% of patients with chronic asthma, suggesting a role for this organism in a subset of patients.[7,8]

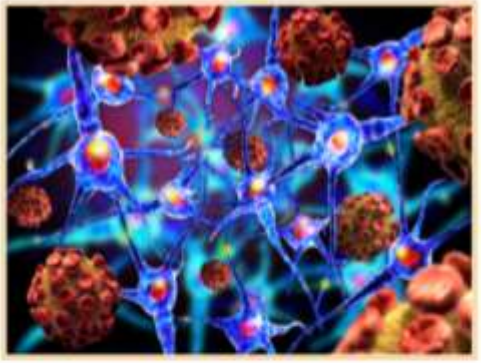
Recently, several groups have established murine models of *M pneumoniae* infection that lead to clinical manifestations of pneumonia similar to those observed in human subjects: pulmonary inflammation, as evidenced by histology; airway hyperresponsiveness (AHR), as measured by means of whole-body unrestrained plethysmography; proinflammatory cytokine mRNA upregulation and protein release into bronchoalveolar lavage; and production of antibodies to *M pneumoniae*.[12-16] In these studies *M pneumoniae* was detected by means of culture, PCR, or both throughout the entire study, suggesting that long-term pulmonary colonization occurred after nasal installation; the organism could be detected even after symptoms abated. This observation is similar to that seen in human infections with this pathogen, in which *M pneumoniae* can be detected months after the clinical pneumonia has resolved.[14]

Testing protocol for histadelia/MCAS/MCAD

1. Borrelia SeraSpot
2. Borrelia EliSpot
3. CD57+ cells
4. Chlamydia pneumoniae EliSpot
5. Chlamydia pneumoniae IgG/IgA antibodies
6. Mycoplasma pneumoniae Elispot and IgG/IgA antibodies

PANS (Paediatric Acute-onset Neuropsychiatric Syndrome)/ PANDAS (Paediatric Autoimmune Disorders Associated with Strep) and infectious triggers

Molecular Mimicry in PANS and PANDAS



Both PANS and PANDAS are associated with infection-triggered autoimmune responses known as "molecular mimicry". This occurs when our immune system mistakenly attacks normal body tissues because of the structural similarities between a particular molecule on an infectious agent and the molecules in our own body tissues. Rheumatic Fever is one example of molecular mimicry where the immune system is triggered to attack the heart valves in certain individuals after experiencing a strep infection. In PANS and PANDAS, it is believed that something similar occurs where antibodies are triggered to attack a part of the brain called the Basal Ganglia, which is understood to be responsible for movement and behavior.

When some patients are exposed to certain bacteria, viruses or germs, their immune system may go awry, producing autoantibodies that attack not only the invading germs but healthy "receptors" and other targets in the brain. This misguided reaction can result in inflammation in the brain, triggering an abrupt onset of symptoms.

Children with PANS and PANDAS are often Misdiagnosed

All too often, children with PANS and PANDAS are misdiagnosed as having a psychiatric illness and may be treated solely with psychotropic drugs to manage their symptoms. Unfortunately, for PANS and PANDAS patients this does not address the root cause of the symptoms, which is an infection-

Source: http://www.moleculeralabs.com/

Much evidence for the connection beween PANS/PANDAS and Lyme/coinfections

Journal List › Int J Gen Med › v.5; 2012 › PMC3292400

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Int J Gen Med. 2012; 5: 163–174.
Published online 2012 Feb 22. doi: 10.2147/IJGM.S24212

PMCID: PMC3292400

Lyme disease and pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS): an overview

Hanna Rhee[1] and Daniel J Cameron[2]

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This article has been cited by other articles in PMC.

Pavone P, Parano E, Rizzo R, Trifiletti RR. J Child Neurol. 2006 Sep; 21(9):727-36.

Abstract

Lyme disease (LD) is a complex, multisystemic illness. As the most common vector- borne disease in the United States, LD is caused by bacterial spirochete *Borrelia burgdorferi* sensu stricto, with potential coinfections from agents of anaplasmosis, babesiosis, and ehrlichiosis. Persistent symptoms and clinical signs reflect multiorgan involvement with episodes of active disease and periods of remission, not sparing the coveted central nervous system. The capability of microorganisms to cause and exacerbate various neuropsychiatric pathology is also seen in pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), a recently described disorder attributed to bacterium *Streptococcus pyogenes* of group A beta-hemolytic streptococcus in which neurologic tics and obsessive-compulsive disorders are sequelae of the infection. In the current overview, LD and PANDAS are juxtaposed through a review of their respective infections etiologies, clinical presentations, mechanisms of disease development, ture directions related to immunoneuropsychiatry are also

bmed/16970875

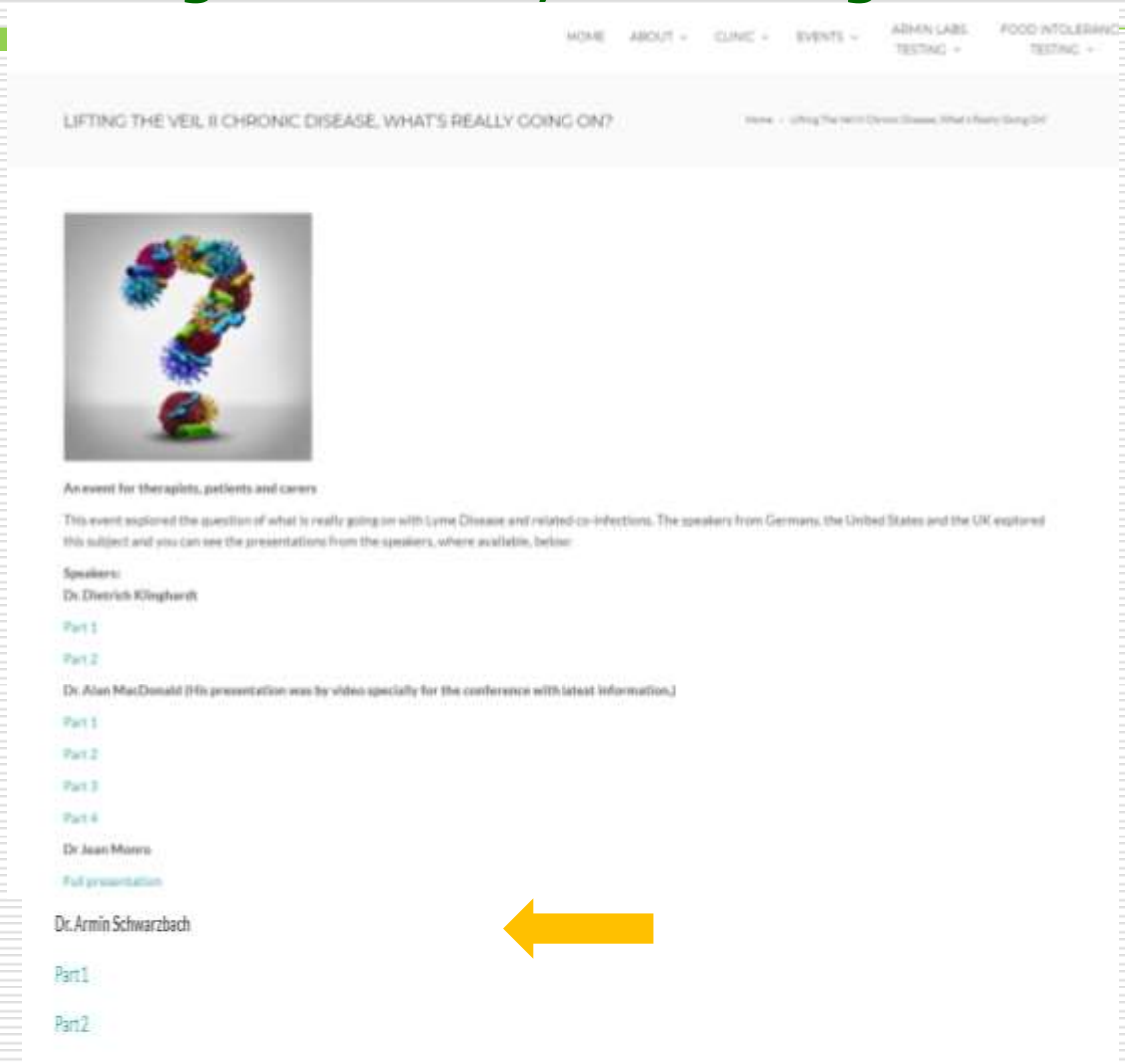
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3292400/

Possible testing protocol for PANS (Paediatric Acute-onset Neuropsychiatric Syndrome/PANDAS (Paediatric Autoimmune Disorders Associated with Strep)

1. Borrelia SeraSpot + Borrelia EliSpot
2. Mycoplasma pneumoniae Elispot and IgG/IgA antibodies
3. Coxsackie Virus IgG/IgA antibodies
4. Babesia Elispot
5. Bartonella Elispot
6. HHV6
7. Influenza

Source: Conversation with Professor Craig Shimasaki, Moleculera Laboratories, 20th February 2018

Downloadable "Tailored testing protocols" Mark 1 in "Lifting the Veil II," including for Autism



Lyme Disease and Viruses: Their Role in Degenerative & Autoimmune Conditions

Armin Schwarzbach MD PhD

Specialist for laboratory medicine

ArminLabs
Laboratory for tick-borne diseases
Tel. 0049 821 2182879
info@arminlabs.com

www.arminlabs.com

www.aonm.org

In that presentation: multiple autoimmune conditions

- Rheumatic fever, reactive arthritis, rheumatoid arthritis – all can potentially be forms of Lyme arthritis
- Molecular mimicry in neuroborreliosis
- Neuropathy
- Vasculitis
- Autoimmune thyroid disease/Hashimoto's
- Multiple sclerosis
- .....

Viral involvement in autoimmunity is also well documented

- Examples:
  - SLE (Lupus)
  - Ulcerative colitis
  - Sarcoidosis
  - Grave´s disease

Tick-borne diseases and viruses in cancer and unexplained syndromes

Armin Schwarzbach PhD

Medical doctor and

Specialist for laboratory medicine

Augsburg

In that presentation: What cancers are tick-borne diseases associated with?

Haematologic disorders that can develop into malignancies

- Myelodysplastic syndromes
- Leukaemia
- Monoclonal Gammopathy of Undetermined Significance (MGUS)
- Lymphomas/Non-Hodgkin's Lymphoma
- ... and others

The body of knowledge on involvement of bacteria/viruses in patient pathology is huge

- Please always ask if you would like to know whether a bacterial or viral infection could be associated with your patient's condition. We'll do the research and get back to you!

Thank you very much for your attention!

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