Integrative & Personalised Medicine 25

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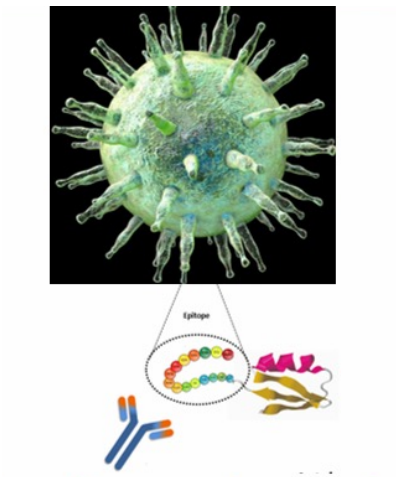

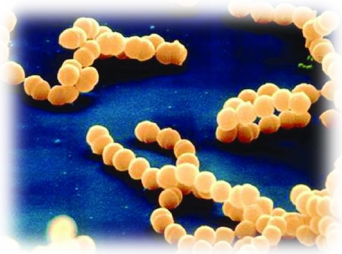

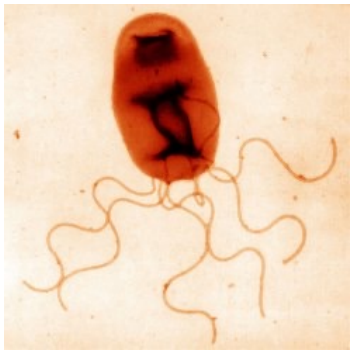

Autoimmunity, the viral/bacterial connection, and how testing can help

Armin Schwarzbach MD, PhD
Medical Doctor and Specialist for Laboratory Medicine

Gilian Crowther MA (Oxon), FBANT, CNHC reg.
AONM Director of Research

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He is a Medical Doctor qualified in Internal Medicine and Infectious Disease and also has many years of experience working in the department of infectious diseases at various renowned hospitals and clinics in Germany.

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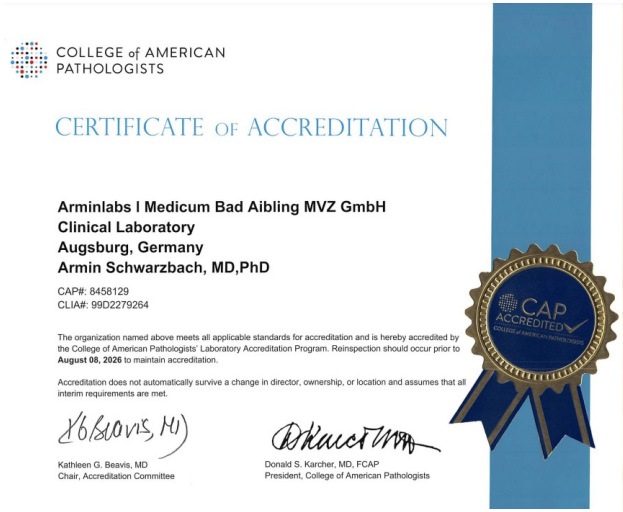
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augsburg 86154
GERMANY

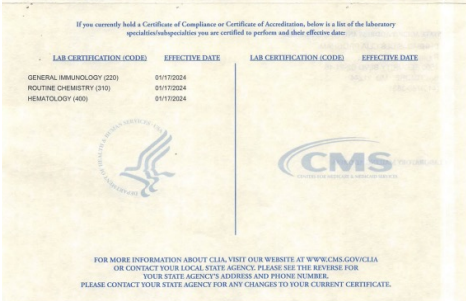
CLIA ID NUMBER
99D2279264

EFFECTIVE DATE
01/17/2024

LABORATORY DIRECTOR
ARMIN SCHWARZBACH M.D.

EXPIRATION DATE
01/16/2026

CMS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To whom it may concern

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(1) *When a CAB is accredited abroad and is operating with sites in UK (mainly in the case of an international company acting with different legal entities) it is advisable, to avoid market confusion, to make an explicit reference to the actual accredited CAB (e.g. including the full address in the foreign country).*

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F328 Issue: 3 based on Annex A of EA-INF/04:2016 Page 1 of 2

- UKAS Certificate of Equivalence
- Stating that the Recognition of the existing Accreditation meets the UKAS requirements

https://aonm.org/accreditation/

Agenda

- **Mechanisms by which viruses and bacteria can trigger autoimmunity**

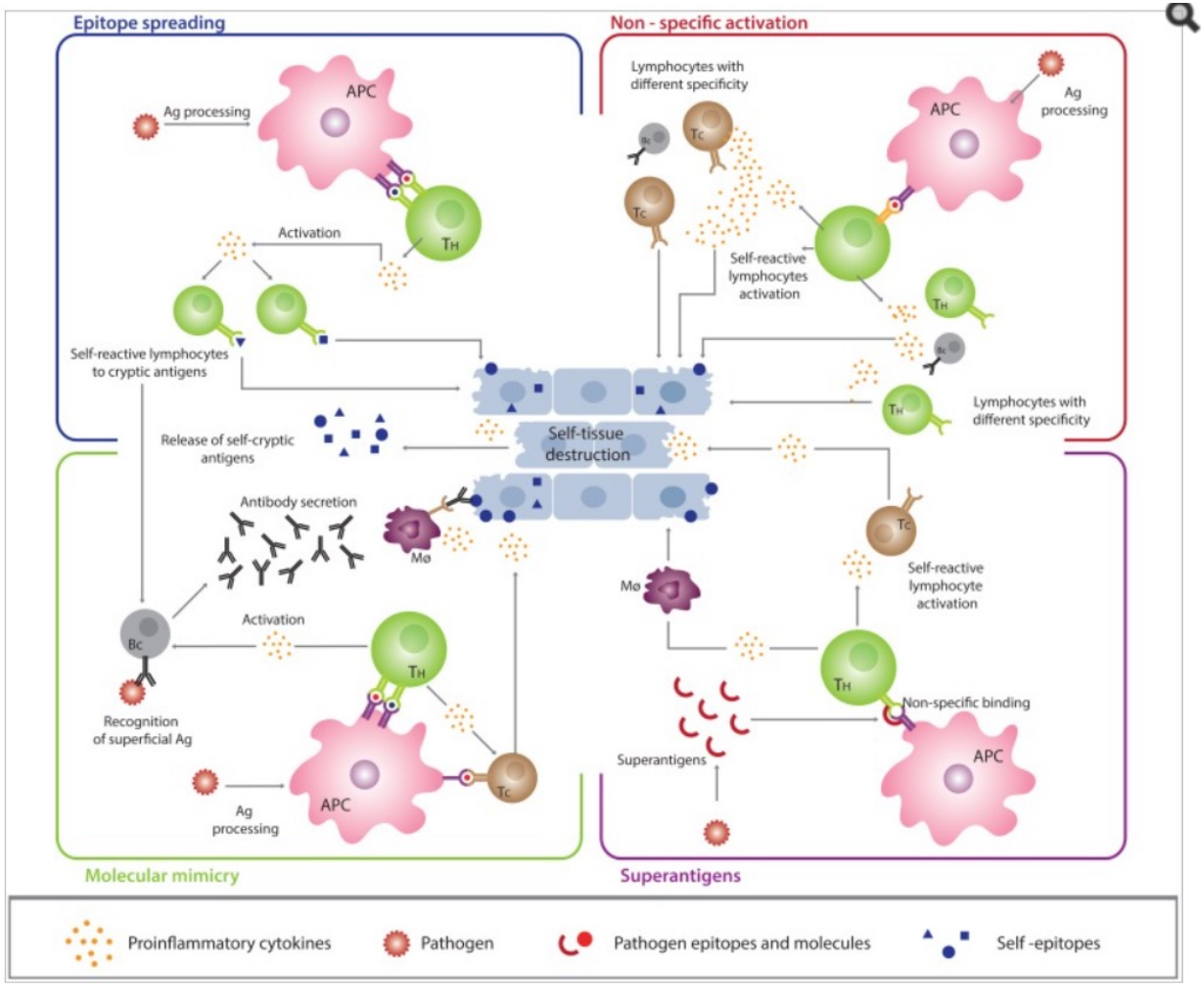
- Viral and bacterial involvement in specific autoimmune conditions (examples)
  - SARS CoV-2
  - Type 1 Diabetes and Autoimmune Diabetes insipidus
  - Multiple Sclerosis
  - Rheumatoid arthritis
  - Thyroid autoimmunity
  - IBD
  - PANS/PANDAS

- Methods of viral and bacterial testing
  - B cells: IgG, IgM, IgA
  - T cells: EliSpots

Illustration of the four key mechanisms by which infections can trigger autoimmunity

Epitope spreading

Molecular mimicry



Bystander activation

Super-antigens

Figure 2 Infectious mechanisms of autoimmune disease.

Source: https://www.ncbi.nlm.nih.gov/books/NBK459437/; Sfriso P, Ghirardello A, Botsios C, et al. Infections and autoimmunity: the multifaceted relationship. J Leukoc Biol. 2010;87:385–95.

Agenda

- Mechanisms by which viruses and bacteria can trigger autoimmunity
- **Viral and bacterial involvement in specific autoimmune conditions (examples)**
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  - B cells: IgG, IgM, IgA
  - T cells: EliSpots

SARS-CoV-2 involvement very significant: high risk of autoimmune disease found in many studies

SARS CoV-2

SARS-CoV-2 triggering autoimmune diseases

Leila Mobasheri [a], Mohammad Hossein Nasirpour [b], Elham Masoumi [c,d], Afsaneh Foolady Azarnaminy [e], Mozhdeh Jafari [f,g], Seyed-Alireza Esmaeili [f,g,*]

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[b] Department of Medical Genetics, Institute of Medical Biotechnology, National Institute of Genetic Engineering and Biotechnology (NIGE
[c] Department of Immunology, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran
[d] Student Research Committee, School of Medicine, Ilam University of Medical Sciences, Ilam, Iran
[e] Department of Anesthesiology, Social Security Organization Hospital, Ardabil, Iran
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ARTICLE INFO

Keywords:
SARS-CoV-2
Covid-19
Autoimmune disease
Autoimmunity
Cytokine

ABSTRACT

Autoimmunity, hyperstimulation of the immune system, can
thought to be important environmental elements that contribute to the development of autoimmune antibodies. It seems that viruses cause autoimmunity with mechanisms such as molecular mimicry, bystander activation of T cells, transient immunosuppression, and inflammation, which has also been seen in post-Covid-19 autoimmunity. Infection of respiratory epithelium by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) dysregulates the immune response, triggers both innate and acquired immunity that led to the immune system's hyperactivation, excessive cytokine secretion known as "cyto
syndrome (ARDS) associated with high mortality. Any factor
contribute to autoimmune disease, which has been docume
observed that some patients produce autoantibody and autore
self-tolerance. However, there is a scarcity of evidence defin
virus and the immune system to elicit autoreactivity. Here, w
findings in Covid-19 and the current reports of autoimmune

"We found that patients with COVID-19 exhibit marked increases in autoantibody reactivities as compared to uninfected individuals, and **show a high prevalence of auto-antibodies against immuno-modulatory proteins ..."[2]**

"Half of people hospitalized with COVID-19 had antibodies in their blood that could mistakenly attack the body's own proteins and tissues."[3]

Source: 1. Mobasheri L et al. SARS-CoV-2 triggering autoimmune diseases. Cytokine. 2022 Jun;154:155873.*2.* Wang EY et al. Diverse functional autoantibodies in patients with COVID-19. Nature. 2021 Jul;595(7866):283-288; 3. https://www.nih.gov/news-events/nih-research-matters/autoimmune-response-found-many-covid-19

Strong connection between Type 1 Diabetes and Covid

T1D

nature reviews endocrinology

Review Article | Published: 18 June 2024

The relationship between SARS-CoV-2 infection and type 1 diabetes mellitus

Cyril Debuysschere, Magloire Pandoua Nekoua, Enagnon Kazali Alidjinou & Didier Hober

Nature Reviews Endocrinology (2024) | Cite this article

643 Accesses | 687 Altmetric | Metrics

Abstract

Environmental factors, in particular viral infections, are thought to have an important role in the pathogenesis of type 1 diabetes mellitus (T1DM). The COVID-19 pandemic reinforced this hypothesis as many observational studies and meta-analyses reported a notable increase in the incidence of T1DM following infection with SARS-CoV-2 as well as an association between SARS-CoV-2 infection and the risk of new-onset T1DM. Experimental evidence suggests that human β-cells express SARS-CoV-2 receptors and that SARS-CoV-2 can infect and replicate in β-cells, resulting in structural or functional alterations of these cells. These alterations

"..human ß-cells express SARS-CoV-2 receptors … SARS-CoV-2 can infect and replicate in ß-cells, resulting in structural or functional alterations of these cells."

"Epidemiological studies and meta-analyses reported an increase in the incidence of type 1 diabetes mellitus during the COVID-19 pandemic as well as an association between SARS-CoV-2 infection and the risk of new-onset type 1 diabetes mellitus."

Source: Debuysschere C, Nekoua MP, Alidjinou EK, Hober D. The relationship between SARS-CoV-2 infection and type 1 diabetes mellitus. Nat Rev Endocrinol. 2024 Jun 18.

“The strongest evidence for an association with T1D points to Enterovirus infection, particularly to Coxsackieviruses B”, 2023

T1D

› Endocr Rev. 2023 Jul 11;44(4):737-751. doi: 10.1210/endrev/bnad007.

Coxsackievirus and Type 1 Diabetes: Diabetogenic Mechanisms and Implications for Prevention

Alexia Carré [1], Federica Vecchio [1], Malin Flodström-Tullberg [2], Sylvaine You [1], Roberto Mallone [1 3]

Affiliations + expand

PMID: 36884282 DOI: 10.1210/endrev/bnad007

Free article

Abstract

The evidence for an association between coxsackievirus B (CVB) infection, pancreatic islet autoimmunity, and clinical type 1 diabetes is increasing. Results from prospective cohorts and pancreas histopathology studies have provided a compelling case. However, the demonstration of a causal relationship is missing, and is likely to remain elusive until tested in humans by avoiding exposure to this candidate viral trigger. To this end, CVB vaccines have been developed and are entering clinical trials. However, the progress made in understanding the biology of the virus and in providing tools to address the long-standing question of causality contrasts with the scarcity of information about the antiviral immune responses triggered by infection. Beta-cell death may be primarily induced by CVB itself, possibly in the context of poor immune protection, or secondarily provoked by T-cell responses against CVB-infected beta cells. The possible involvement of epitope mimicry mechanisms skewing the physiological antiviral response toward autoimmunity has also been suggested. We here review the available evidence for each of these 3 non-mutually exclusive scenarios. Understanding which ones are at play is critical to maximize the odds of success of CVB vaccination, and to develop suitable tools to monitor the efficacy of immunization and its intermingling with autoimmune onset or prevention.

Key Findings of the Study:

- **Viruses as Triggers**: The Coxsackie B virus attacks the insulin-producing cells in the pancreas, leading to an autoimmune reaction where the immune system mistakenly attacks healthy cells.
- **Particularly Affected**: The infection is particularly common in young children, of whom a small but growing proportion later develop Type 1 diabetes.
- **Immune System Response**: Researchers found that the immune system of affected children shows only a limited defense response against the virus, which explains the persistent infection and the subsequent autoimmune process.

Source: Carré A, Vecchio F, Flodström-Tullberg M, You S, Mallone R. Coxsackievirus and Type 1 Diabetes: Diabetogenic Mechanisms and Implications for Prevention. Endocr Rev. 2023 Jul 11;44(4):737-751.

"CMV-positive diabetic patients significantly more likely to have autoantibodies than those who were CMV-negative"

T1D

THE LANCET

Submit Ar

RESEARCH ARTICLE VOLUME 332, ISSUE 8601, P1-4, JULY 02, 1988

ASSOCIATION OF CYTOMEGALOVIRUS INFECTION WITH AUTOIMMUNE TYPE 1 DIABETES

ChinY. Pak • RobertG. Mcarthur • Hyone-Myong Eun • Ji-Won Yoon

Published: July 02, 1988 • DOI: https://doi.org/10.1016/S0140-6736(88)92941-8

Abstract

Article info

Abstract

The lymphocytes from 59 newly diagnosed type 1 diabetic patie
of human cytomegalovirus (CMV) genome by molecular hybridis
genome was found in 13 (22%) of 59 diabetic patients, but in 1 (
antibody (ICA) and 41% had cytotoxic beta cell surface antibody
2·6% and 2·6% 62% and 69% of CMV genome-positive patients h
genome-negative patients. The single CMV genome-positive cor
CMV genome-negative control subjects had ICA. The strong corr
in diabetic patients suggests that persistent CMV infections may

"CMV has a lytic action on the β-cells of the islets of Langerhans responsible for insulin production"

SUMMARY AND COMMENT | GENERAL MEDICINE

July 29, 1988

CYTOMEGALOVIRUS ASSOCIATED WITH TYPE 1 DIABETES.

HGA, reviewing Pak C Y; Eun H M; McArthur R G; Yoon J W. Lancet 1988 Jul 2

Viral infections have long been suspected of causing the destruction of pancreatic beta cells, leading to diabetes. These investigators looked for the presence of human . . .

Viral infections have long been suspected of causing the destruction of pancreatic beta cells, leading to diabetes. These investigators looked for the presence of human cytomegalovirus (CMV) in the lymphocytes of 59 patients with newly diagnosed type 1 diabetes and 38 healthy controls. Serum levels of islet-cell antibody (ICA) and cytotoxic beta-cell surface antibody (CBSA) were measured in all subjects.

A CMV-specific genome was present in significantly more diabetics than controls (22 versus 2.6 percent), as was serum ICA (39 versus 2.6 percent). Diabetic patients who were CMV-positive were significantly more likely to have autoantibodies than those who were CMV-negative (62 versus 33 percent had ICA, and 69 versus 33 percent had CBSA). The single control subject who was CMV-positive did not have either autoantibody.

The authors conclude that the presence of both human CMV- specific viral genome in lymphocytes and islet-cell autoantibodies in serum from patients with type 1 diabetes suggests a possible link between diabetes and CMV infection. Persistent CMV infection may trigger beta-cell autoimmune disease.

Source: https://www.jwatch.org/jw198807290000007/1988/07/29/cytomegalovirus-associated-with-type-1-diabetes

T1D

Diabetes Type 1: Possible viral and bacterial lab tests

Viruses

1. Cytomegalovirus
2. Enteroviruses Coxsackie and Echovirus
3. SARS-CoV-2

Bacteria

1. Chlamydia pneumoniae
2. Yersinia
3. H pylori Blot IgG/IgA HLO-AK with CagA and VacA
   Please do a H pylori test that can detect the cytotoxin-associated gene A (CagA) and vacuolating cytotoxin A (VacA) – those are the genotypes of the most virulent strains

Borrelia, Chlamydia pneumoniae and H pylori all implicated in the etiology of MS

MS

NeuroSci

MDPI

Review

The Probable Infectious Origin of Multiple Sclerosis

Remi L. Landry [1,2] and Monica E. Embers [1,2,*]

[1] Department of Tropical Medicine, Tulane University School of Public Health and Tropical Medicine, New Orleans, LA 70112, USA; rlandry10@tulane.edu
[2] Division of Immunology, Tulane National Primate Research Center, Tulane University Health Science Covington, LA 70433, USA
* Correspondence: members@tulane.edu

Abstract: Multiple sclerosis (MS) is an immune inflammatory disease that causes demyelina the white matter of the central nervous system. It is generally accepted that the etiology of MS is factorial and believed to be a complex interplay between genetic susceptibility, environmental f and infectious agents. While the exact cause of MS is still unknown, increasing evidence su that disease development is the result of interactions between genetically susceptible individua the environment that lead to immune dysregulation and CNS inflammation. Genetic factors a sufficient on their own to cause MS, and environmental factors such as viral infections, smokin vitamin D deficiency also play important roles in disease development. Several pathogens hav implicated in the etiology of MS, including Epstein–Barr virus, human herpesvirus 6, varicella- virus, cytomegalovirus, *Helicobacter pylori*, *Chlamydia pneumoniae*, and *Borrelia burgdorferi*. Alt vastly different, viruses and bacteria can manipulate host gene expression, causing immune dy lation, myelin destruction, and neuroinflammation. This review emphasizes the pathogenic tr that should be considered in MS progression.

"**The association between spirochetes and MS dates back to 1925** when Adams et al. conducted an experiment in which rhesus monkeys (Macaca mulatta) were inoculated with material from MS cases [219]. Several months later, spirochetes were observed in the ventricular fluid of these monkeys. In 1952, Steiner reported the presence of spirochetes in plaques obtained from autopsied MS patients [220]. Additionally, in 1957, Ichelson successfully cultivated spirochetes from the spinal fluid of MS patients [221]. Newman et al. replicated Ichelson's culture method and detected spirochetes in the spinal fluid of MS patients, although in a lower percentage."

Source: Landry RL, Embers ME. The Probable Infectious Origin of Multiple Sclerosis. NeuroSci. 2023 Sep 7;4(3):211-234.

MS

Multiple sclerosis and Borrelia – research over 4 decades

medical hypotheses

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< Previous Article February 1988 Volume 25, Issue 2, Pages 89–92 Next Article >

Multiple Sclerosis is a chronic central nervous system infection by a spirochetal agent

Vincent Marshall
Animal Vaccine Laboratory, 255 Elliott Street, Council Bluffs, Iowa 51501 USA

PlumX Metrics

DOI: https://doi.org/10.1016/0306-9877(88)90023-0

Abstract References

Abstract

Multiple Sclerosis (MS) is a chronic central nervous system (CNS) infection similar to Lyme Disease (1) or Neurosyphilis in its latency period, pathogenesis, symptoms, histopathology and chronic CNS involvement. It does not have as yet a fully identified spirochetal etiological agent. Much research and clinical support for this hypothesis was published before 1954 and is based on silver staining of neural lesions, animal isolation of the etiologic agent and the characteristic symptoms and pathogenesis of the disease. If this hypothesis is correct, the disease should be treatable with antibacterial agents that penetrate the CNS (such as high dose antibiotics), diagnosible by specific immunological tests, and preventable by early treatment or by the use of vaccines in high risk populations.

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

Source: http://www.medical-hypotheses.com/article/0306-9877(88)90023-0/abstract

Infection with Bartonella also detected

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]

Author information ▶ Article notes ▶ Copyright and License information ▶

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

82% of MS patients tested positive for Chlamydia pneumoniae in oligoclonal antibodies in this study

MS

Chronic Bacterial and Viral Infections in Neurodegenerative and Neurobehavioral Diseases

Garth L. Nicolson, PhD

(Department of Molecular Pathology, The Institute for Molecular Medicine, Huntington Beach, CA)

DOI: 10.1309/96M3BWYP42L11BFU

Abstract

Often, patients with neurodegenerative or neurobehavioral diseases have chronic, neuropathic infections that could be important in disease inception, disease progression, or increasing the types or severities of signs and symptoms. Although controversial, the majority of patients with various neurodegenerative or neurobehavioral conditions, such as amyotrophic lateral sclerosis, multiple sclerosis, Alzheimer's disease, Parkinson's disease, and autistic spectrum disorders, show evidence of central nervous system or systemic bacterial and viral infections. For example, using serology or polymerase chain reaction evidence of *Chlamydia pneumoniae, Borrelia burgdorferi, Mycoplasma* species, human herpesvirus-1 and -6, and other bacterial and viral infections revealed high infection rates that were not found in control subjects. Although chronic infections were not found in some studies, and the specific role of chronic infections in neurological disease pathogenesis has not been determined or is inconclusive, the data suggest that chronic bacterial or viral infections could be common features of progressive neurodegenerative and neurobehavioral diseases.

Neurodegenerative diseases are chronic degenerative diseases of the central nervous system (CNS) that cause dementia. For the most part, the causes of these brain diseases remain largely unknown.[1] They are characterized by molecular and genetic changes in nerve cells that result in nerve cell degeneration and ultimately nerve dysfunction and death, resulting in neurological signs and symptoms and dementia.[1,2] In addition to neurodegenerative diseases, there are also neurobehavioral diseases that mainly, but not exclusively, appear in the young, such as autistic spectrum disorders (ASD) that encompass autism, attention deficit disorder, Asperger's syndrome, and other disorders.[3]

There appear to be genetic links to neurodegenerative and neurobehavioral diseases, but the genetic changes that occur and the changes in gene expression that have been found in these diseases are complex and not directly related to simple genetic alterations.[1,4] In addition, it is thought that nutritional deficiencies, environmental toxins, heavy metals, chronic bacterial and viral infections, autoimmune immunological responses, vascular diseases, head trauma and accumulation of fluid in the brain, changes in neurotransmitter concentrations, among others, are diseases.[12-14] Since they are usually systemic, such infections can affect the immune system and other organ systems, resulting in a variety of systemic signs and symptoms.[15-18]

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis (ALS) is an adult-onset, idopathic, progressive neurodegenerative disease affecting both central and peripheral motor neurons. Patients with ALS show gradual progressive weakness and paralysis of muscles due to destruction of upper motor neurons in the motor cortex and lower motor neurons in the brain stem and spinal cord, ultimately resulting in death, usually by respiratory failure.[19,20] The overall clinical picture of ALS can vary, depending on the location and progression of pathological changes found in nervous tissue.[21]

In ALS, the role of chronic infections has attracted attention with the finding of enterovirus sequences in a majority of spinal cord samples by polymerase chain reaction (PCR).[22,23] This finding is not without controversy, since others failed to

"Examination of MS patients for oligoclonal antibodies against *C. pneumoniae* revealed that 82% of MS patients were positive, whereas none of the control non-MS neurological patients had antibodies that were absorbed by *C. pneumoniae* elemental body antigens"

Source: Nicolson GL. Chronic Bacterial and Viral Infections in Neurodegenerative and Neurobehavioral Diseases. Lab Med. 2008 May;39(5):291–9; Yao S-Y, Stratton CW, Mitchell WM. CFS oligoclonal bands in MS include antibodies against Chamydophila antigens. Neurol 2001; 51: 1168-1176

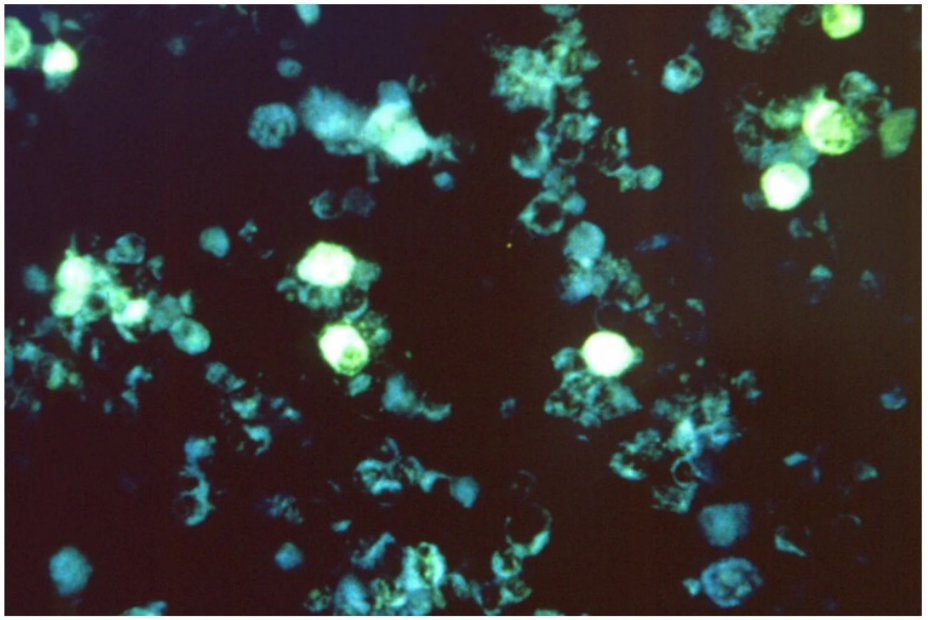
Harvard study published on 13th January 2022 in “Science”

MS

The Harvard Gazette

HEALTH & MEDICINE

Epstein-Barr virus may be leading cause of MS



Cells infected with Epstein-Barr, a common herpes virus that can cause mononucleosis and establishes a latent, lifelong infection of the host.

CDC

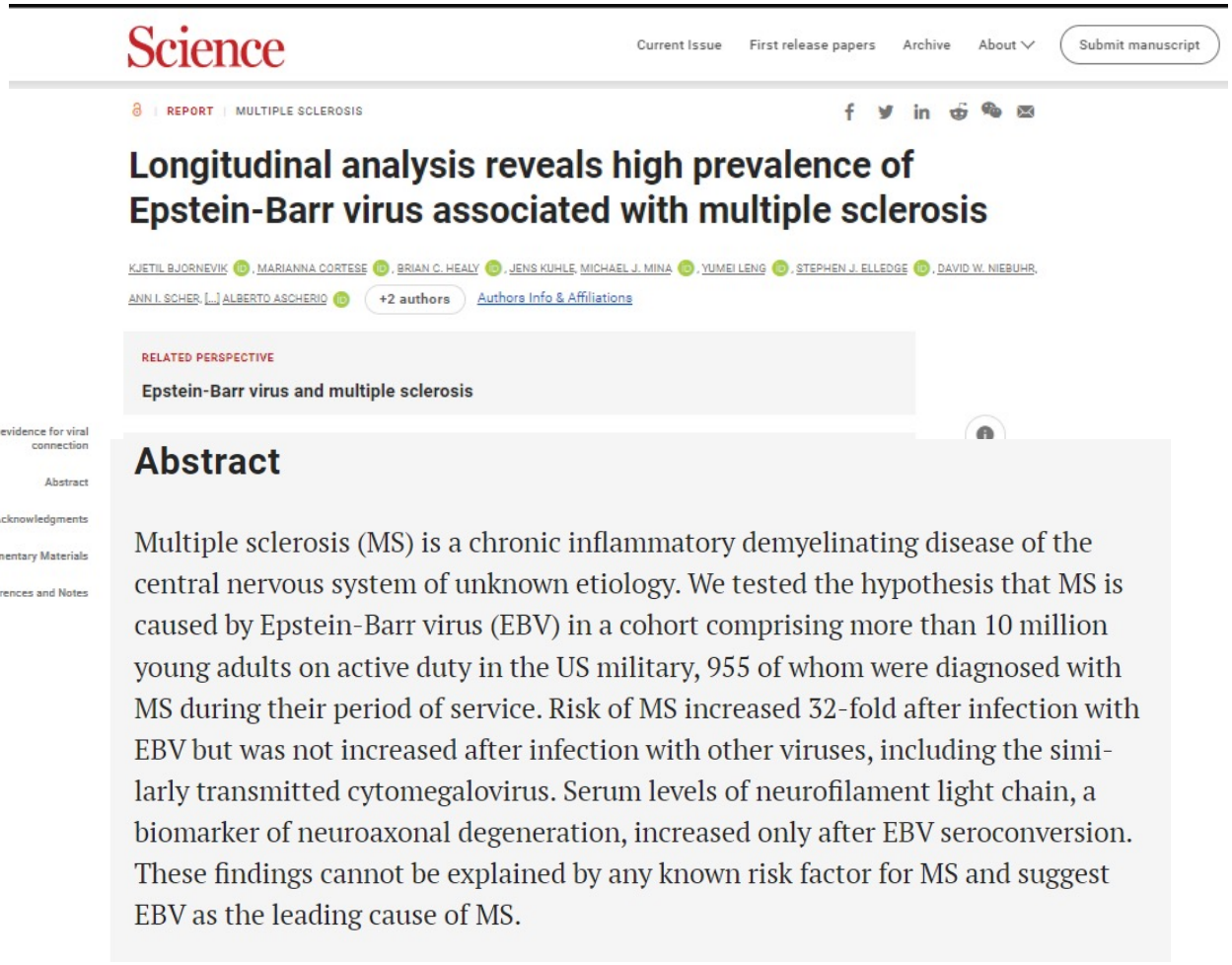
First study to provide 'compelling evidence of causality'

“The hypothesis that EBV causes MS has been investigated by our group and others for several years, but this is the first study providing compelling evidence of causality,” said Alberto Ascherio, professor of epidemiology and nutrition at Harvard Chan School and senior author of the study. “This is a big step because it suggests that most MS cases could be prevented by stopping EBV infection, and that targeting EBV could lead to the discovery of a cure for MS.”

Source: https://news.harvard.edu/gazette/story/2022/01/epstein-barr-virus-may-be-leading-cause-of-multiple-sclerosis/

The study found that the risk of developing MS increased 32-fold following EBV infection

MS



Science

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REPORT | MULTIPLE SCLEROSIS

Longitudinal analysis reveals high prevalence of Epstein-Barr virus associated with multiple sclerosis

KJETIL BJORNEVIK, MARIANNA CORTESE, BRIAN C. HEALY, JENS KUHLE, MICHAEL J. MINA, YUMEI LENG, STEPHEN J. ELLEDGE, DAVID W. NIEBUHR, ANN I. SCHER, [...] ALBERTO ASCHERIO +2 authors Authors Info & Affiliations

RELATED PERSPECTIVE

Epstein-Barr virus and multiple sclerosis

Stronger evidence for viral connection

Abstract

Acknowledgments

Supplementary Materials

References and Notes

Abstract

Multiple sclerosis (MS) is a chronic inflammatory demyelinating disease of the central nervous system of unknown etiology. We tested the hypothesis that MS is caused by Epstein-Barr virus (EBV) in a cohort comprising more than 10 million young adults on active duty in the US military, 955 of whom were diagnosed with MS during their period of service. Risk of MS increased 32-fold after infection with EBV but was not increased after infection with other viruses, including the similarly transmitted cytomegalovirus. Serum levels of neurofilament light chain, a biomarker of neuroaxonal degeneration, increased only after EBV seroconversion. These findings cannot be explained by any known risk factor for MS and suggest EBV as the leading cause of MS.

"Using data from more than ten million United States military recruits monitored over a 20-year period, 955 of whom were diagnosed with MS during their service, Kjetil Bjornevik *et al.* tested the hypothesis that MS is caused by EBV. They found that the risk of developing MS in individuals who were EBV-negative increased by 32-fold following EBV infection. "These findings," say the authors, "cannot be explained by any known risk factor and suggest EBV as the leading cause of MS."

Source: https://www.science.org/doi/10.1126/science.abj8222; https://www.eurekalert.org/news-releases/939665

Multiple Sclerosis: Possible viral and bacterial laboratory tests

MS

Bacteria

1. Borrelia EliSpot and TickPlex Basic
2. Bartonella Elispot
3. Chlamydia pneumoniae IgG/IgA and EliSpot
4. H pylori Blot IgG/IgA HLO-AK (CagA, VacA)

Viruses

1. EBV EliSpot
2. HHV6 EliSpot
3. SARS-CoV-2
4. Coxsackie Virus A & B IgG & IgA
5. Echovirus IgG, IgM & IgA

Need to consider Borrelia in the differential diagnosis of Rheumatoid Arthritis

RA

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

Clin Vaccine Immunol. 2007 Nov; 14(11): 1437–1441.
Published online 2007 Sep 19. doi: 10.1128/CVI.00151-07
PMCID: PMC2168181

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

Yu-Fan Hsieh,[1] Han-Wen Liu,[1] Tsai-Ching Hsu,[1] James C.-C. Wei,[2] Chien-Ming Shih,[3] Peter J. Krause,[4] and Gregory J. Tsay[1,2,*]

Author information ▶ Article notes ▶ Copyright and License information ▶

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

Source: Hsieh YF, Liu HW, Hsu TC, Wei JC, Shih CM, Krause PJ, Tsay GJ. Serum reactivity against Borrelia burgdorferi OspA in patients with rheumatoid arthritis. Clin Vaccine Immunol. 2007 Nov;14(11):1437-41.

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

Detection of Mycoplasmal Infections in Blood of Patients with Rheumatoid Arthritis

Jörg Haier[1], Marwan Nasralla[1], A. Robert Franco[2], and Garth L. Nicolson[1,3]

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[2]The Arthritis Center of Riverside, Riverside, CA 92501

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. penetrans*.

Results: The *Mycoplasma spp.* sequence, which is not entirely specific for mycoplasmas, was amplified from the peripheral blood of 15/28 patients (53.6 %), and specific PCR products could not be detected in 13 patients (46.4 %). Significant differences ($p<0.001$) were found between patients and positive healthy controls in the genus-test (3/32) and in the specific tests (0/32). Moreover, the incidence of mycoplasmal infections was similar in female and male patients. Using species-specific primers, we were able to detect infections of *M. fermentans* (8/28), *M. pneumoniae* (5/28), *M. hominis* (6/28) and *M. penetrans* (1/28) in RA patients. In 36% of the patients we observed more than one mycoplasma species in the blood leukocytes. All multiple infections occurred as combinations of *M. fermentans* with other species.

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.

"Systemic mycoplasmal infections may be an important cofactor in the pathogenesis of RA"

Source: Haier J, Nasralla M, Franco AR, Nicolson GL. Detection of mycoplasmal infections in blood of patients with rheumatoid arthritis. Rheumatology (Oxford). 1999 Jun;38(6):504-9.

"Our study showed H. pylori infection was associated with the development of rheumatoid arthritis"

RA

Article | Open access | Published: 13 September 2023

Influence of *Helicobacter pylori* infection on risk of rheumatoid arthritis: a nationwide population-based study

Tzu-Hsuan Lee, Meng-Che Wu, Ming-Hung Lee, Pei-Lun Liao, Chieh-Chung Lin & James Cheng-Chung Wei

Scientific Reports **13**, Article number: 15125 (2023) | Cite this article

3871 Accesses | **5** Citations | **20** Altmetric | Metrics

Abstract

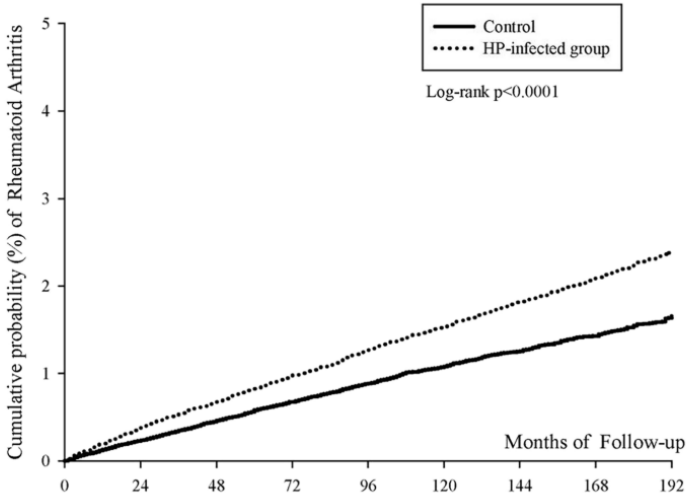
The relationship between *Helicobacter pylori* infection and rheumatoid arthritis has been investigated, but the results remain controversial. This study aims to determine the association between the two diseases via a 17-year retrospective cohort study. Using the National Health Insurance Research Database, a nationwide population based in Taiwan, we ic individuals with *H. pylori* infection and matched controls between 2000 and 2 propensity score matching at a 1:1 ratio. The adjusted hazard ratio of rheuma determined by multiple Cox regression. The incidence rate of rheumatoid arth 10,000 person-months in the *H. pylori* cohort, with a higher risk compared to group. In the < 30 years old subgroup, the risk was highest, especially in wom with *H. pylori* infection. Patients with < 1 year follow-up showed 1.58 times hi susceptibility to rheumatoid arthritis. Individuals with follow-ups of 1–5 years demonstrated 1.43 and 1.44 times higher risks of rheumatoid arthritis, respec showed *H. pylori* infection was associated with the development of rheumato Clinicians should note higher risk, especially < 30 years old. More research ne understand underlying mechanism.

2 million individuals, 2000 - 2017

"In the < 30 years old subgroup, the risk was highest, especially in women < 30 years old with H. pylori infection."

Figure 2

From: Influence of *Helicobacter pylori* infection on risk of rheumatoid arthritis: a nationwide population-based study



n at risk

Control	97533	92866	84704	753381	65354	53966	42043	27745	10460
HP-infected group	97533	93627	86301	77497	67644	56397	44150	29273	11246

Kaplan–Meier curves of cumulative probability of RA in study groups. HP, *Helicobacter pylori*.

"H. pylori CagA-positive patients develop more severe RA."

Source: Lee TH, Wu MC, Lee MH, Liao PL, Lin CC, Wei JC. Influence of Helicobacter pylori infection on risk of rheumatoid arthritis: a nationwide population-based study. Sci Rep. 2023 Sep 13;13(1):15125.

RA

Rheumatoid Arthritis: Possible lab tests

Bacterial tests

1. Borrelia
2. Mycoplasma
3. Chlamydia pneumoniae/trachomatis
4. H pylori Blot IgG/IgA HLO-AK (CagA, VacA)
5. Yersinia enterocolitica

Viral tests

1. EBV antibodies including Early Antigen + EBV EliSpot
2. CMV EliSpot
3. HSV1/2 IgG/IgA/IgM antibodies + HSV1/2 EliSpot
4. SARS-CoV-2

Homology of HLA-DR molecules and T-cell receptors from human thyroid autoantigens and Yersina/Borrelia

Hashimoto's/ Grave's

THYROID
Volume 16, Number 3, 2006

Human Thyroid Autoantigens and Proteins of *Yersinia* and *Borrelia* Share Amino Acid Sequence Homology That Includes Binding Motifs to HLA-DR Molecules and T-Cell Receptor

Salvatore Benvenga,[1–3] Libero Santarpia,[1] Francesco Trimarchi,[1] and Fabrizio Guarneri[4]

We previously reported that the spirochete *Borrelia burgdorferi* could trigger autoimmune thyroid diseases (AITD). Subsequently, we showed local amino acid sequence homology between all human thyroid autoantigens (human thyrotropin receptor [hTSH-R], human thyroglobulin [hTg], human thyroperoxidase [hTPO], human sodium iodide symporter [hNIS]) and *Borrelia* proteins ($n = 6606$), and between hTSH-R and *Yersinia enterocolitica* ($n = 1153$). We have now updated our search of homology with *Borrelia* ($n = 11,198$ proteins) and extended our search on *Yersinia* to the entire species ($n = 40,964$ proteins). We also searched the homologous human and microbial sequences for peptide-binding motifs of HLA-DR molecules, because a number of these class II major histocompatibility complex (MHC) molecules (DR3, DR4, DR5, DR8, and DR9) are associated with AITD. Significant homologies were found for only 16 *Borrelia* proteins (5 with hTSH-R, 2 with hTg, 3 with hTPO, and 6 with hNIS) and only 19 *Yersinia* proteins (4 with hTSH-R, 2 with hTg, 2 with hTPO, and 11 with hNIS). Noteworthy, segments of thyroid autoantigens homologous to these microbial proteins are known to be autoantigenic. Also, the hTSH-R homologus region of one *Borrelia* protein (OspA) contains an immunodominant epitope that others have found to be homologous to hLFA-1. This is of interest, as the hLFA-1/ICAM-1 ligand/receptor pair is aberrantly expressed in the follicular cells of thyroids affected by Hashimoto's thyroiditis. A computer-assisted search detected antigenic pept
in AITD. In conclusion, our *in silico* data do not directly de
AITD but suggest that a restricted number of them might h
HLA-DR alleles.

1

"Data from this study suggests that a restricted number of Borrelia and Yersinia proteins might have the potential to trigger AITD n persons with certain HLA-DR alleles"[1]

"… in some genetically predisposed subjects, Borrelia infection can be the trigger of Hashimoto's thyroiditis and/or lichen sclerosus"[2]

Source: Benvenga S, Santarpia L, Trimarchi F, Guarneri F. Human Thyroid Autoantigens and Proteins of Yersinia and Borrelia Share Amino Acid Sequence Homology That Includes Binding Motifs to HLA-DR Molecules and T-Cell Recpetor. Thyroid. 2006;16:225–236; 2. Guarneri F, Guarneri C. Molecular mimicry in cutaneous autoimmune diseases. World J Dermatol 2013; 2(4): 36-43

High Yersinia titres found in thyroid disorders

Hashimoto's/Grave's

ORIGINAL ARTICLE

Prevalence of *Yersinia* plasmid-encoded outer protein (Yop) class-specific antibodies in patients with Hashimoto's thyroiditis

S. Chatzipanagiotou[1], J. N. Legakis[2], F. Boufidou[1], V. Petroyianni[3] and C. Nicolaou[1]

[1]Department of Clinical Microbiology, Aeginition Hospital, Medical School, [2]3rd Department of Medicine, Sotiria Hospital, Medical School and [3]Laboratory of Medical Biopathology and Molecular Diagnosis, Medical School, National University of Athens, Athens, Greece

Objective To investigate the prevalence of class-specific antibodies (IgG, IgA) to *Yersinia enterocolitica* plasmid-encoded outer proteins (Yops) in patients with diagnosed Hashimoto's thyroiditis.

Methods Seventy-one patients with Hashimoto's disease, 464 healthy blood donors and 250 patients with non-postinfectious rheumatic disorders (matched controls) were tested for class-specific antibodies to Yops. Anti-Yop antibodies were determined by ELISA and Western blot.

Results The prevalence of class-specific antibodies to Yops as determined by ELISA was 14-fold higher (20 of 71; 28.2%) in people with Hashimoto's thyroiditis than in the two control groups. These results were confirmed by the Western blot, with 16 positive sera, three equivocal and one negative.

Conclusions There is strong clinical and seroepidemiologic evidence for an immunopathologic causative relationship between *Yersinia enterocolitica* infection and Hashimoto's thyroiditis. Further investigation concerning the mechanisms involved and the possible effects of antibacterial chemotherapy on the outcome of Hashimoto's disease is warranted.

Keywords *Yersinia enterocolitica*, *Yersinia* outer proteins (Yops), Hashimoto's thyroiditis

Accepted 5 December 2000

Clin Microbiol Infect 2001; 7: 138–143

"75% of patients with thyroid disorders have been found to have high Yersinia titres, especially in Hashimoto's as well as Grave's disease, because molecular mimicry can cause it to cross-react with the thyroid gland."

Source: Chatzipanagiotou, Stylianos & Legakis, Ioannis & Boufidou, Fotini & Petroyianni, V & Nicolaou, C. (2001). Prevalence of Yersinia plasmid-encoded outer protein (YOP) class-specific antibodies in patients with Hashimoto's thyroiditis. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 7. 138-43. 10.1046/j.1469-0691.2001.00221.x.

Incidence of Hashimoto's/Graves' Disease increases with SARS-CoV-2 infections

Hashimoto's/Graves'

Review > J Med Virol. 2023 Aug;95(8):e29001. doi: 10.1002/jmv.29001.

COVID-19-induced autoimmune thyroiditis: Exploring molecular mechanisms

Bita Mohammadi [1 2], Kamal Dua [3 4 5], Mohammadreza Saghafi [1 2], Sachin Kumar Singh [4 6], Zahra Heydarifard [7 8], Milad Zandi [9]

Affiliations + expand

PMID: 37515444 DOI: 10.1002/jmv.29001

Abstract

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) damages multiple organs, including the thyroid, by direct invasion and cell entry via angiotensin-converting enzyme 2 or indirectly by promoting excessive inflammation in the body. The immune system is a critical factor in antiviral immunity and disease progression. In the context of SARS-CoV-2 infection, the immune system may become overly activated, resulting in a shift from regulatory to effector responses, which may subsequently promote the development and progression of autoimmune diseases. The incidence of autoimmune thyroid diseases, such as subacute thyroiditis, Graves' disease, and Hashimoto's thyroiditis, increases in individuals with COVID-19 infection. This phenomenon may be attributed to aberrant responses of T-cell subtypes, the presence of autoantibodies, impaired regulatory cell function, and excessive production of inflammatory cytokines, namely interleukin (IL)-6, IL-1β, interferon-γ, and tumor necrosis factor-α. Therefore, insights into the immune responses involved in the development of autoimmune thyroid disease according to COVID-19 can help identify potential therapeutic approaches and guide the development of effective interventions to alleviate patients' symptoms.

Keywords: ACE2; COVID-19; SARS-CoV-2; autoimmune thyroiditis; immune response.

Hashimoto's/Graves': Possible viral laboratory tests

Bacteria

1. Borrelia
2. Yersinia

Viruses

Hashimoto's

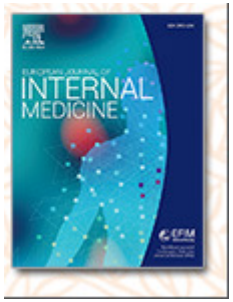
1. EBV EliSpot
2. HSV 1 & 2 IgG & IgA
3. CMV EliSpot
4. Parvovirus B19 IgG & IgM
5. SARS-CoV-2

Graves'

1. SARS-CoV-2
2. Possibly the Herpes viruses

"The present study supports the concept of the Yersinia enterocolitica infection as a trigger of chronic IBD"

IBD



ELSEVIER

European Journal of Internal Medicine 16 (2005) 176 – 182

EUROPEAN JOURNAL OF INTERNAL MEDICINE

www.elsevier.com/locate/ejim

Original article

Inflammatory bowel disease associated with *Yersinia enterocolitica* O:3 infection☆

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Received 24 May 2004; received in revised form 18 October 2004; accepted 4 November 2004

Abstract

Background: Certain microorganisms may be associated with the development of inflammatory bowel disease (IBD). These pathogens may possess such properties as immunological capability or tissue invasiveness. An association between *Yersinia enterocolitica* infection and ulcerative colitis (UC) was suggested 30 years ago, and a connection with Crohn's disease (CD) may also exist. The aim of this study was to further elucidate the association between *Y. enterocolitica* O:3 infection and IBD.
Methods: During the period 1990–1997, antibody response against *Y. enterocolitica* was estimated in 1588 patients by tube agglutination. Forty-one patients with *Y. enterocolitica* infection (titer = 320) constituted the study group; 1041 patients without antibody response constituted the control group. The study was completed in 2003, after 6–13 years.
Results: At diagnosis of *Y. enterocolitica* infection, UC of acute onset was demonstrated in three males; another suffered from CD. At follow-up, two additional patients had developed UC and two CD. In the control group, 32 patients were diagnosed as having UC and 10 CD. This difference in IBD prevalence is significant (8/41>42/1041, $p=0.00035$), as were the differences in prevalence of UC and CD separately ($p=0.006$; viz. $p<0.015$).
Conclusion: The present study supports the concept of the *Y. enterocolitica* infection as a trigger of chronic IBD.

"Among other microorganisms, Shigella dysenteriae, Salmonella species, Campylobacter jejuni, and Yersinia enterocolitica have been implicated as possible causative agents of UC. An acute intestinal infection sometimes precedes the first attack. Y. enterocolitica, Mycobacterium paratuberculosis, Listeria monocytogenes, and paramyxovirus (measles) have been studied in association with CD."

Source: Saebo A, Vik E, Lange OJ, Matuszkiewicz L. Inflammatory bowel disease associated with Yersinia enterocolitica O:3 infection. Eur J Intern Med. 2005 Jun;16(3):176-182.

History of gastroenteritis caused by Salmonella or Campylobacter is associated with increased risk of developing IBD

IBD

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Research Highlight | Published: October 2009

IBD

Risk of IBD increases after *Salmonella* or *Campylobacter* gastroenteritis

Ezzie Hutchinson

Nature Reviews Gastroenterology & Hepatology **6**, 561 (2009) | Cite this article

3256 Accesses | **3** Altmetric | Metrics

Gradel, K. O. *et al*. Increased short- and long-term risk of inflammatory bowel disease after *Salmonella* or *Campylobacter* gastroenteritis. *Gastroenterology* **137**, 495–501 (2009).

The pathogenesis of IBD involves many genetic and environmental factors, including enteric bacteria that may trigger or exacerbate the disease. Few human studies of IBD have focused on pathogenic bacteria that cause gastroenteritis other than *Mycobacterium paratuberculosis* and adherent-invasive *Escherichia coli*, even though adhesion of bacteria and increased permeability of the intestinal mucosa in this illness is important in the pathogenesis of IBD. A population-based cohort long-term follow-up study now shows that gastroenteritis caused by infection with nontyphoid *Salmonella* or thermophilic *Campylobacter* increases the risk of developing IBD. "The potential consequences of foodborne bacterial infections may not be as

A 2009 study in Nature Reviews Gastroenterology & Hepatology found that **individuals exposed to Salmonella or Campylobacter had a significantly higher likelihood of being diagnosed with IBD** compared to those who were not exposed. The increased risk was similar for both Salmonella and Campylobacter infection

"A population-based cohort long-term follow-up study now shows that gastroenteritis caused by infection with nontyphoid Salmonella or thermophilic Campylobacter increases the risk of developing IBD."

Source: Hutchinson, E. Risk of IBD increases after *Salmonella* or *Campylobacter* gastroenteritis. *Nat Rev Gastroenterol Hepatol* **6**, 561 (2009). https://doi.org/10.1038/nrgastro.2009.152

It is possible that CJI alters the natural course of UC by activating an abnormal mucosal immune response

IBD

OXFORD

Gastroenterology Report, 4(4), 2016, 287–292

doi: 10.1093/gastro/gov029
Advance Access Publication Date: 8 July 2015
Original article

ORIGINAL ARTICLE

Risk factors and clinical implication of superimposed *Campylobacter jejuni* infection in patients with underlying ulcerative colitis

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Abstract

Background and aims: Superimposed *Campylobacter jejuni* infection (CJI) has been described in patients with ulcerative colitis (UC). Its risk factors and impact on the disease course of UC are not known. Our aims were to evaluate the risk factors for CJI in UC patients and the impact of the bacterial infection on outcomes of UC.

Methods: Out of a total of 918 UC patients tested, 21 (2.3%) of patients were found to be positive for CJI (the study group). The control group comprised 84 age-matched UC patients who had tested negative for CJI. Risk factors for CJI and UC-related outcomes at 1 year after diagnosis of CJI were compared between the two groups.

Results: Ten patients (47.6%) with CJI required hospital admission at the time of diagnosis, including eight for the management of "UC flare". Treatment with antibiotics resulted in improvement in symptoms in 13 patients (61.9%). On multivariate analysis, hospital admission in the preceding year was found to be an independent risk factor for CJI [odds ratio (OR): 3.9; 95% confidence interval (CI): 1.1–14.1] and there was a trend for chronic liver disease as a strong risk factor (OR: 5.0; 95% CI: 0.9–28.3). At 1-year follow up, there was a trend for higher rates of UC-related colectomy (28.8% *vs.* 14.3%; $P = 0.11$), and mortality (9.5% *vs.* 1.2%; $P = 0.096$) in the study group.

Conclusion: Recent hospitalization within 1 year was found to be associated with increased risk for CJI in UC patients. There was a trend for worse clinical outcomes of UC with in patients with superimposed CJI, which was frequently associated with UC flare requiring hospital admission.

"It is possible that CJI alters the natural course of UC by activating abnormal mucosal immune response, thus leading to more inflammation and more severe disease that result in worse outcomes."[1]

"Furthermore, an increase of Campylobacterota along with a decline of Bacteroidota in the colon was previously associated with increased risk for IBD."[2]

Source: 1.Arora Z, Mukewar S, Wu X, Shen B. Risk factors and clinical implication of superimposed Campylobacter jejuni infection in patients with underlying ulcerative colitis. Gastroenterol Rep (Oxf). 2016 Nov;4(4):287-292; 2. Hutchinson, E. Risk of IBD increases after *Salmonella* or *Campylobacter* gastroenteritis. *Nat Rev Gastroenterol Hepatol* **6**, 561 (2009)

All children with Crohn's disease that were examined had a commonly occurring virus -- an enterovirus -- in their intestines[1]

IBD

Citation: Clinical and Translational Gastroenterology (2013) 4, e38; doi:10.1038/ctg.2013.7
 2155-384X/13
www.nature.com/ctg

Human Enterovirus Species B in Ileocecal Crohn's Disease

Niklas Nyström, MD[1], Tove Berg, PhD[2], Elin Lundin[3], Oskar Skog, PhD[3], Inga Hansson, PhD[3], Gun Frisk, PhD[3], Ivana Juko-Pecirep[3], Mats Nilsson, PhD[3], Ulf Gyllensten, PhD[3], Yigael Finkel, MD, PhD[4], Jonas Fuxe, PhD[2,5] and Alkwin Wanders, MD, PhD[3,5]

OBJECTIVES: Advanced ileocecal Crohn's disease (ICD) is characterized by strictures, inflammation in the enteric nervous system (myenteric plexitis), and a high frequency of *NOD2* mutations. Recent findings implicate a role of *NOD2* and another CD susceptibility gene, *ATG16L1*, in the host response against single-stranded RNA (ssRNA) viruses. However, the role of viruses in CD is unknown. We hypothesized that human enterovirus species B (HEV-B), which are ssRNA viruses with dual tropism both for the intestinal epithelium and the nervous system, could play a role in ICD.
METHODS: We used immunohistochemistry and *in situ* hybridization to study the general presence of HEV-B and the presence of the two HEV-B subspecies, Coxsackie B virus (CBV) and Echovirus, in ileocecal resections from 9 children with advanced, stricturing ICD and 6 patients with volvulus, and in intestinal biopsies from 15 CD patients at the time of diagnosis.
RESULTS: All patients with ICD had disease-associated polymorphisms in *NOD2* or *ATG16L1*. Positive staining for HEV-B was detected both in the mucosa and in myenteric nerve ganglia in all ICD patients, but in none of the volvulus patients. Expression of the cellular receptor for CBV, CAR, was detected in nerve cell ganglia.
CONCLUSIONS: The common presence of HEV-B in the mucosa and enteric nervous system of ICD patients in this small cohort is a novel finding that warrants further investigation to analyze whether HEV-B has a role in disease onset or progress. The presence of CAR in myenteric nerve cell ganglia provides a possible route of entry for CBV into the enteric nervous system.
Clinical and Translational Gastroenterology (2013) **4**, e38; doi:10.1038/ctg.2013.7; published online 27 June 2013
Subject Category: Inflammatory Bowel Disease

INTRODUCTION

Crohn's disease (CD) is a chronic inflammatory bowel disease characterized by segmental, transmural inflammation, and fissuring abscesses. On the basis of clinical features, such as age of diagnosis, location of disease, and stricturing/penetrating behavior, CD is subclassified in several clinical phenotypes.[1,2]

Ileocecal CD (ICD) is a distinctive phenotype, which is characterized by its localization in the ileocecal region of the intestine, and by the fact that it more often than other CD phenotypes leads to strictures, stenosis, perforation, and

The etiology of CD is unknown but it is considered a polygenic disease, which develops in a complex interplay between environmental factors and aberrant immune responses in a genetically susceptible host. In support of this, a majority of CD susceptibility genes that have been identified, including *NOD2* and *ATG16L1*, have known immune cell functions.[8–10] Recently, these genes were shown to have important roles in the immune response against single-stranded RNA (ssRNA) viruses[11–15] and the ATG16L1 pathway, also a prerequisite for Coxsackie virus replication.[16] NOD2 was shown to act as an intracellular pattern recognizing receptor for ssRNA

"The results showed significant amounts of enteroviruses in the intestines of all of the children with Crohn´s disease, whereas the control group had no or only minimal amounts of enteroviruses in their intestines."

Source: 1. https://www.sciencedaily.com/releases/2013/06/130627102827.htm; Niklas Nyström, Tove Berg, Elin Lundin, Oskar Skog, Inga Hansson, Gun Frisk, Ivana Juko-Pecirep, Mats Nilsson, Ulf Gyllensten, Yigael Finkel, Jonas Fuxe, Alkwin Wanders. **Human Enterovirus Species B in Ileocecal Crohn's Disease**. *Clinical and Translational Gastroenterology*, 2013; 4 (6): e38

IBD: possible viral and bacterial involvement

Viruses

1. Enteroviruses Coxsackievirus and Echovirus
2. Norovirus
3. EBV EliSpot
4. CMV EliSpot
5. VZV IgG, IgM & IgA

Bacteria

1. Campylobacter jejuni
2. Salmonella
3. Yersinia enterocolitica
4. Shigella
5. Listeria

Multiple bacteria have potential psychiatric manifestations – and can act as a trigger for PANS/PANDAS

PANS/ PANDAS

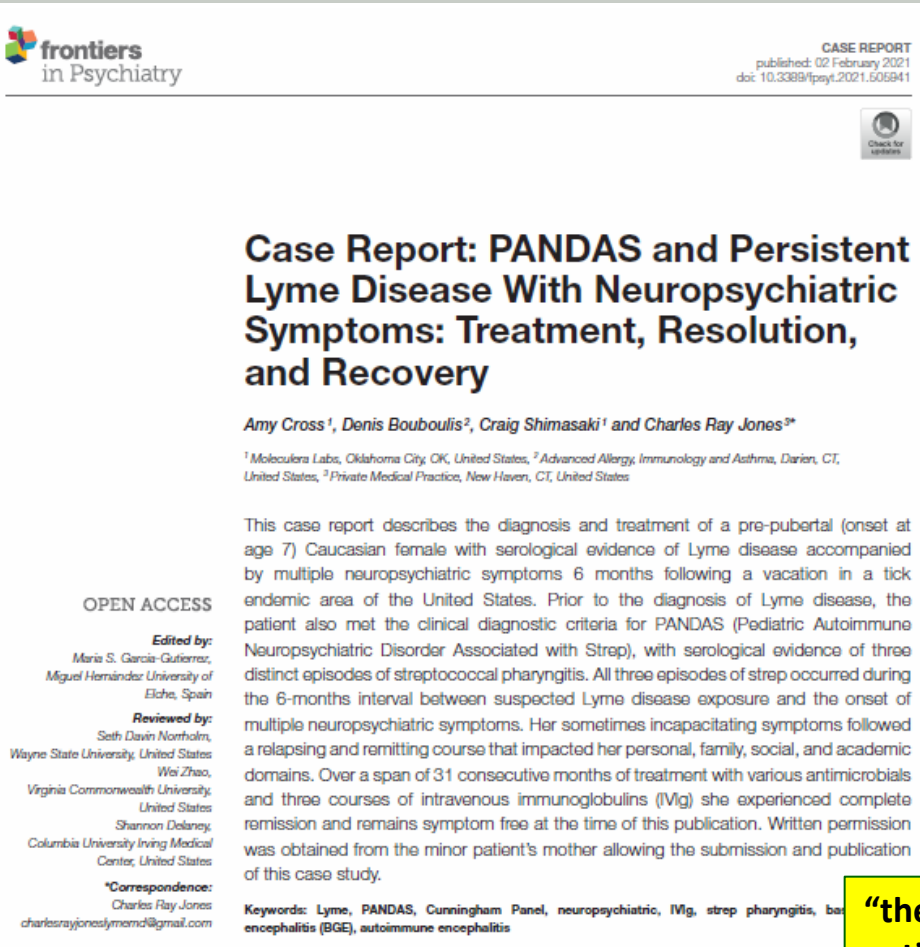
Table 1. Infectious agents with potential psychiatric manifestations.

Spirochetes
Borrelia burgdorferi sensu lato (new genus name *Borreliella*) [9–13,15–17] (Supplementary S1)
Borrelia burgdorferi sensu stricto (Lyme disease in USA, Europe)
Borrelia afzelii (Lyme disease mostly in Europe, Asia)
Borrelia garinii (Lyme disease mostly in Europe, Asia)
Relapsing fever group (also known as relapsing fever group *Borrelia*) [18]
Leptospira species (leptospirosis) [19]
Treponema pallidum (syphilis) [20–23]
Other bacteria
Actinomyces [24]
Bartonella henselae and other species (cat scratch disease, bartonellosis) [25–28]
Brucella species (brucellosis) [29]
Chlamydia species [30,31]
Coxiella burnetii (Q Fever and "Post-Q Fever Fatigue Syndrome") [32]
Ehrlichia chaffeensis (human monocytic ehrlichiosis) [33,34]
Helicobacter pylori [35]
Mycoplasma pneumoniae and other species [36–38]
Rickettsia species (spotted fever, scrub typhus, African tick bite fever) [39–43]
Streptococcus pyogenes (group A beta hemolytic strep, PANDAS, Sydenham's Chorea, St Vitus Dance) [44]
Tropheryma whipplei (Whipple's disease) [45,46]

Source: Bransfield RC, Mao C, Greenberg R. Microbes and Mental Illness: Past, Present, and Future. Healthcare (Basel). 2023 Dec 29;12(1):83.

"… recent reports suggest a causal connection between Lyme disease and PANS"

PANS/ PANDAS



frontiers in Psychiatry

CASE REPORT
published: 02 February 2021
doi: 10.3389/fpsyt.2021.505941

Case Report: PANDAS and Persistent Lyme Disease With Neuropsychiatric Symptoms: Treatment, Resolution, and Recovery

*Amy Cross[1], Denis Bouboulis[2], Craig Shimasaki[1] and Charles Ray Jones[3]**

[1] Moleculera Labs, Oklahoma City, OK, United States, [2] Advanced Allergy, Immunology and Asthma, Darien, CT, United States, [3] Private Medical Practice, New Haven, CT, United States

This case report describes the diagnosis and treatment of a pre-pubertal (onset at age 7) Caucasian female with serological evidence of Lyme disease accompanied by multiple neuropsychiatric symptoms 6 months following a vacation in a tick endemic area of the United States. Prior to the diagnosis of Lyme disease, the patient also met the clinical diagnostic criteria for PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Strep), with serological evidence of three distinct episodes of streptococcal pharyngitis. All three episodes of strep occurred during the 6-months interval between suspected Lyme disease exposure and the onset of multiple neuropsychiatric symptoms. Her sometimes incapacitating symptoms followed a relapsing and remitting course that impacted her personal, family, social, and academic domains. Over a span of 31 consecutive months of treatment with various antimicrobials and three courses of intravenous immunoglobulins (IVIg) she experienced complete remission and remains symptom free at the time of this publication. Written permission was obtained from the minor patient's mother allowing the submission and publication of this case study.

Keywords: Lyme, PANDAS, Cunningham Panel, neuropsychiatric, IVIg, strep pharyngitis, ba… encephalitis (BGE), autoimmune encephalitis

OPEN ACCESS

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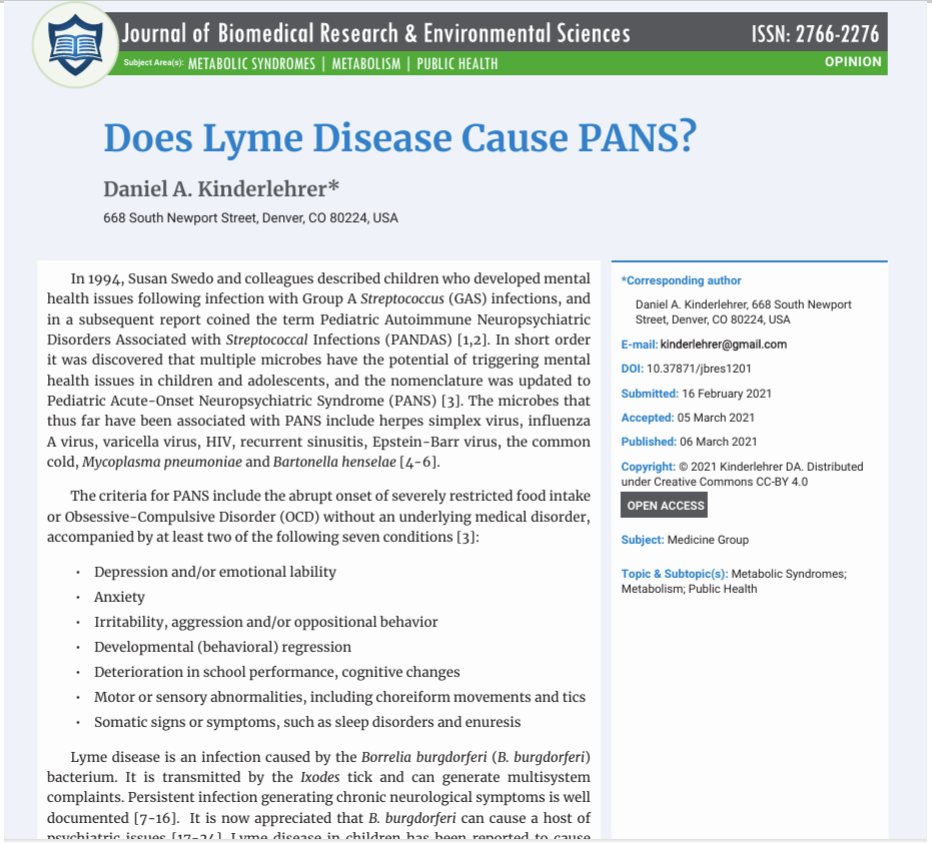

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OPINION

Does Lyme Disease Cause PANS?

Daniel A. Kinderlehrer*
668 South Newport Street, Denver, CO 80224, USA

In 1994, Susan Swedo and colleagues described children who developed mental health issues following infection with Group A *Streptococcus* (GAS) infections, and in a subsequent report coined the term Pediatric Autoimmune Neuropsychiatric Disorders Associated with *Streptococcal* Infections (PANDAS) [1,2]. In short order it was discovered that multiple microbes have the potential of triggering mental health issues in children and adolescents, and the nomenclature was updated to Pediatric Acute-Onset Neuropsychiatric Syndrome (PANS) [3]. The microbes that thus far have been associated with PANS include herpes simplex virus, influenza A virus, varicella virus, HIV, recurrent sinusitis, Epstein-Barr virus, the common cold, *Mycoplasma pneumoniae* and *Bartonella henselae* [4-6].

The criteria for PANS include the abrupt onset of severely restricted food intake or Obsessive-Compulsive Disorder (OCD) without an underlying medical disorder, accompanied by at least two of the following seven conditions [3]:

- Depression and/or emotional lability
- Anxiety
- Irritability, aggression and/or oppositional behavior
- Developmental (behavioral) regression
- Deterioration in school performance, cognitive changes
- Motor or sensory abnormalities, including choreiform movements and tics
- Somatic signs or symptoms, such as sleep disorders and enuresis

Lyme disease is an infection caused by the *Borrelia burgdorferi* (*B. burgdorferi*) bacterium. It is transmitted by the *Ixodes* tick and can generate multisystem complaints. Persistent infection generating chronic neurological symptoms is well documented [7-16]. It is now appreciated that *B. burgdorferi* can cause a host of

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Subject: Medicine Group
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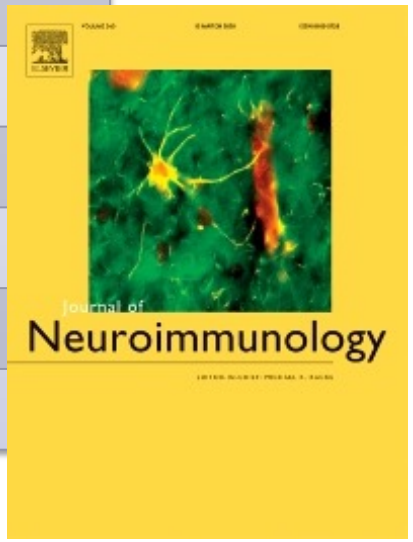
"the clear association of an elevation of antineuronal antibodies and CaMKII activation, i.e., abnormal Cunningham Panels, in patients with a history of Lyme disease suggests the capacity of *B. burgdorferi* to trigger PANS."

Source: Cross A, Bouboulis D, Shimasaki C, Jones CR. Case Report: PANDAS and Persistent Lyme Disease With Neuropsychiatric Symptoms: Treatment, Resolution, and Recovery. Front Psychiatry. 2021 Feb 2;12:505941; Kinderlehrer DA. Does Lyme Disease Cause PANS? J Biomed Res Environ Sci. 2021;2(3):126-131; Fallon BA et al. Anti-lysoganglioside and other anti-neuronal antibodies in post-treatment Lyme disease and erythema migrans after repeat infection. Brain Behav Immun. 2020;2: 100015.

Almost all patients have multiple coinfections: many bacterial

PANS/ PANDAS

Streptococcus	Ehrlichiosis
Borrelia Burgdorferi (Lyme)	Parainfluenza
Ehrlichiosis	MERSA
Epstein Barr Virus (EBV)	Herpes Zoster
Parvovirus	Staphylococcus
Human Herpes Virus-6 (HHV-6)	Candida
Herpes Simplex Virus-1 (HSV-1)	Rickettsia
Bartonella	Tularemia
Clostridium Difficile	Mycoplasma
Klebsiella	



= bacterial

Source: Shimasaki C, Frye RE, Trifiletti R, Cooperstock M, Kaplan G, Melamed I, Greenberg R, Katz A, Fier E, Kem D, Traver D, Dempsey T, Latimer ME, Cross A, Dunn JP, Bentley R, Alvarez K, Reim S, Appleman J. Evaluation of the Cunningham Panel™ in pediatric autoimmune neuropsychiatric disorder associated with streptococcal infection (PANDAS) and pediatric acute-onset neuropsychiatric syndrome (PANS): Changes in antineuronal antibody titers parallel changes in patient symptoms. J Neuroimmunol. 2020 Feb 15;339:577138, https://www.sciencedirect.com/science/article/pii/S0165572819303522

Various other neurotropic infections can be culprits, too: Bartonella, Toxoplasma

PANS/ PANDAS

Case Reports > J Cent Nerv Syst Dis. 2019 Mar 18;11:1179573519832014.
doi: 10.1177/1179573519832014. eCollection 2019.

Bartonella henselae Bloodstream Infection in a Boy With Pediatric Acute-Onset Neuropsychiatric Syndrome

Edward B Breitschwerdt [1], Rosalie Greenberg [2], Ricardo G Maggi [1], B Robert Mozayeni [3], Allen Lewis [4], Julie M Bradley [1]

Affiliations + expand

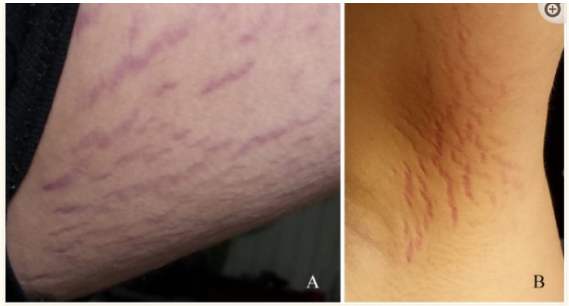
PMID: 30911227 PMCID: PMC6423671 DOI: 10.1177/1179573519832014
Free PMC article

Abstract

Background: With the advent of more sensitive culture and molecular diagnostic testing modalities, *Bartonella* spp. infections have been documented in blood and/or cerebrospinal fluid specimens from patients with diverse neurological symptoms. Pediatric acute-onset neuropsychiatric syndrome (PANS) is characterized by an unusually abrupt onset of cognitive, behavioral, or neurological symptoms. Between October 2015 and January 2017, a 14-year-old boy underwent evaluation by multiple specialists for sudden-onset psychotic behavior (hallucinations, delusions, suicidal and homicidal ideation).

Methods: In March 2017, *Bartonella* spp. serology (indirect fluorescent antibody assays) and polymerase chain reaction (PCR) amplification, DNA sequencing, and *Bartonella* enrichment blood culture were used on a research basis to assess *Bartonella* spp. exposure and bloodstream infection, respectively. PCR assays targeting other vector-borne infections were performed to assess potential co-infections.

Results: For 18 months, the boy remained psychotic despite 4 hospitalizations, therapeutic trials involving multiple psychiatric medication combinations, and immunosuppressive treatment for autoimmune encephalitis. Neurobartonellosis was diagnosed after cutaneous lesions developed. Subsequently, despite nearly 2 consecutive months of doxycycline administration, *Bartonella henselae* DNA was PCR amplified and sequenced from the patient's blood, and from *Bartonella* alphaproteobacteria growth medium enrichment blood cultures. *B henselae* serology was negative. During treatment with combination antimicrobial chemotherapy, he experienced a gradual progressive decrease in neuropsychiatric symptoms, cessation of psychiatric drugs, resolution of *Bartonella*-associated cutaneous lesions, and a return to all pre-illness activities.



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Toxoplasma on the Brain: Understanding Host-Pathogen Interactions in Chronic CNS Infection

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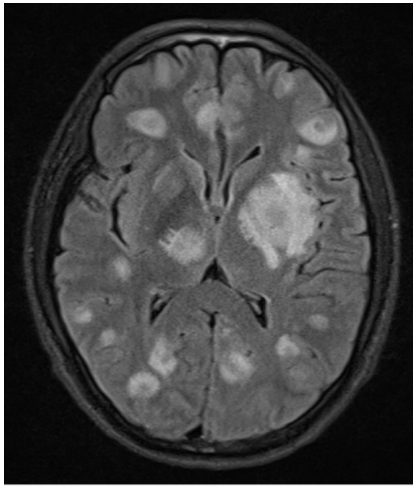
Toxoplasma gondii is a prevalent obligate intracellular parasite which chronically infects more than a third of the world's population. Key to parasite prevalence is its ability to form chronic and nonimmunogenic bradyzoite cysts, which typically form in the brain and muscle cells of infected mammals, including humans. While acute clinical infection typically involves neurological and/or ocular damage, chronic infection has been more recently linked to behavioral changes. Establishment and maintenance of chronic infection involves a balance between the host immunity and parasite evasion of the immune response. Here, we outline the known cellular interplay between *Toxoplasma gondii* and cells of the central nervous system and review the reported effects of *Toxoplasma gondii* on behavior and neurological disease. Finally, we review new technologies which will allow us to more fully understand host-pathogen interactions.



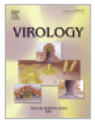
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6423671/; https://aonm.org/wp-content/uploads/2018/11/Dr.-Schwarzbach-Presentation-AONM-Conference-November-2018.pdf

Enteroviruses linked to autoimmune conditions of the CNS – Coxsackie, Echovirus, etc.

ELSEVIER

Virology

Volume 411, Issue 2, 15 March 2011, Pages 288-305



Review

Enterovirus infections of the central nervous system

Ross E. Rhoades, Jenna M. Tabor-Godwin, Ginger Tsueng, Ralph Feuer

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https://doi.org/10.1016/j.virol.2010.12.014

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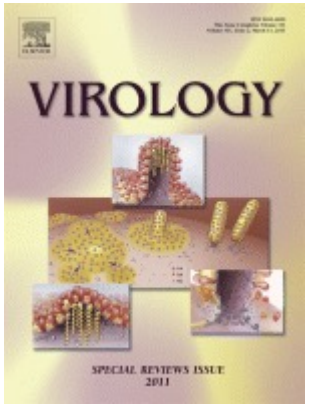
Abstract

Enteroviruses (EV) frequently infect the central nervous system (CNS) and induce neurological diseases. Although the CNS is composed of many different cell types, the spectrum of tropism for each EV is considerable. These viruses have the ability to completely shut down host translational machinery and are considered highly cytolytic, thereby causing cytopathic effects. Hence, CNS dysfunction following EV infection of neuronal or glial cells might be expected. Perhaps unexpectedly given their cytolytic nature, EVs may establish a persistent infection within the CNS, and the lasting effects on the host might be significant with unanticipated consequences. This review will describe the clinical aspects of EV-mediated disease, mechanisms of disease, determinants of tropism, immune activation within the CNS, and potential treatment regimes.



"‥ EVs have been linked to autoimmune-like diseases, including diabetes, chronic inflammatory myopathy, and chronic myocarditis, perhaps in part due to the long-term presence of viral material. Therefore, EVs may be able to persist within the CNS potentially causing lasting neuropathology."

Source: Rhoades RE, Tabor-Godwin JM, Tsueng G, Feuer R. Enterovirus infections of the central nervous system. Virology. 2011 Mar 15;411(2):288-305.

PANS/PANDAS: possible viral lab tests

PP

Difficult to say – best to do a really good history, checking infections of family members, and do the co-infection checklist. All the Herpes viruses are neurotropic, and the Enteroviruses, and SARS-CoV-2 involvement is now well established.

Agenda

- Mechanisms by which viruses and bacteria can trigger autoimmunity
- Viral and bacterial involvement in specific autoimmune conditions (examples)
  - SARS CoV-2
  - Type 1 Diabetes and Autoimmune Diabetes insipidus
  - Multiple Sclerosis
  - Rheumatoid arthritis
  - Thyroid autoimmunity
  - IBD
  - PANS/PANDAS
- **Methods of viral and bacterial testing**
  - B cells: IgG, IgM, IgA
  - T cells: EliSpots

The most useful antibody in a chronic infection is Immunoglobulin A …

Antibodies

IgA is an excellent immunoglobulin as it indicates current, ongoing or very recent infection, as well as chronic persistent infection, reactivation or reinfection

"IgA antibody is the most abundant antibody class in human serum and has a unique role in mediating immunity. IgA is a polyvalent antibody that is translocated to mucosal surfaces as the first line of defense against infections. Most of the secreted IgA lines the mucosal surfaces including respiratory, digestive and genitorurinary tracts to protect against pathogens while maintaining gut homeostasis."

The persistence of IgA antibodies in Coxsackie, as an example →

Humoral immunity against viral antigens in type 1 diabetes: altered IgA-class immune response against Coxsackie B4 virus

H Hyöty, T Huupponen, L Kotola, P Leinikki

PMID: 2426921 DOI: 10.1111/j.1699-0463.1986.tb02094.x

Abstract

A group of 210 pediatric Type 1 diabetic patients with long duration of illness and their matched controls (age range 2-19 years) were analysed for Coxsackie B4 antibodies in IgG-, IgM- and IgA-antibody classes by enzyme-linked immunosorbent assay (ELISA). About 60% of both patients and controls were seropositive. However, patients had higher prevalence and mean levels of IgA-class antibodies compared to controls. No such difference was found in IgG- or IgM-antibody classes. The elevation of IgA-class antibody levels was evident early after the Coxsackie B4 infection and seemed to persist for several years. IgA-class antibody levels did not differ between sexes in either patients or controls. The elevated levels of IgA-antibodies against Coxsackie B4 virus did not correlate with the elevated IgA antibodies against mumps virus, which served as control antigens. Thus it seems that in IDDM patients the abnormal IgA response against both Coxsackie B4 and mumps virus is antigen-specific.

Source: https://www.genscript.com/IgA-antibody.html; Granfors K, Viljanen M, Tiilikainen A, Toivanen A. Persistence of IgM, IgG, and IgA antibodies to Yersinia in yersinia arthritis. J Infect Dis. 1980 Apr;141(4):424-9; *Mucosal Immunity, Stephen P. James, in Encyclopedia of Immunology (Second Edition), 1998, https://www.sciencedirect.com/topics/neuroscience/immunoglobulin-a; Hanson, L., Andersson, B., Carlsson, B. et al. Infection (1985) 13(Suppl 2): S166.;* Hyöty H et al. Humoral immunity against viral antigens in type 1 diabetes: altered IgA-class immune response against Coxsackie B4 virus. Acta Pathol Microbiol Immunol Scand C. 1986 Apr;94(2):83-8.

... Indicates likely continuing infection along the mucosal membranes

Antibodies

VZV IgG-/IgA-/IgM-antibodies

4 VZV IgG antibodies (ELISA) positive
4643,8 IE/l

<80 IE/l negative
>80 - < 110 IE/l weak
>110 IE/l positive

4 VZV IgA antibodies (ELISA) positive
1,287 Ratio

Ratio < 0,8 = negative
Ratio 0,8 - 1,1 = weak
Ratio >= 1,1 = positive

4 VZV IgM antibodies (ELISA) negative
0,306 Ratio

Ratio < 0,8 = negative
Ratio 0,8 - 1,1 = weak
Ratio >= 1,1 = positive

Analysis		Result Units	Reference Range	Chart
Coxsackie IgG-/IgA-antibodies				
4 Coxsackie-IgG Typ A7 (IFT)	+	1:100	< 1:100	[..... *>
4 Coxsackie-IgG Typ B1 (IFT)	+	1:1000	< 1:100	[..... *>
4 Coxsackie-IgA Typ A7 (IFT)	+	1:100	< 1:10	[..... *>
4 Coxsackie-IgA Typ B1 (IFT)	+	1:10	< 1:10	[..... *>

The specific positive Coxsackie-Virus Type A7/B1-IgG-/IgA-antibodies indicate current humoral immune responses against Coxsackie-Virus Type A7 and Coxsackie-Virus Type B1 (recent infection with Coxsackie-Virus Type A7/B1?).

Analysis		Result Units	Reference Range	Chart
7 ECHO IgG-antibodies (IFT)	+	1:1000	< 1:100	[..... *>
7 ECHO IgA-antibodies (IFT)	+	1:10	< 1:10	[..... *>

The specific positive ECHO-virus-IgG/IgA-antibodies indicate current humoral immune responses against ECHO-virus (recent infection with ECHO-virus?).

SARS-CoV-2 tests also still very helpful to know where the patient stands

Antibodies

Analysis	Result	Units	Reference Range
SARS-CoV2 virus IgG/IgA Ab			
3 SARS CoV2 IgG-Ab	**positive**		**negative**
	! 5,021	**Ratio**	
Ratio < 0,8	= negative		
Ratio 0,8 - 1,1	= weak		
Ratio >= 1,1	= positive		
3 SARS CoV2 IgA-Ab	**positive**		**negative**
	! 1,140	**Ratio**	
Ratio < 0,8	= negative		
Ratio 0,8 - 1,1	= weak		
Ratio >= 1,1	= positive		

Analysis	Result	Units	Reference Range
SARS-CoV2 virus IgG/IgA Ab			
3 SARS CoV2 IgG-Ab	**positiv**		**negativ**
	! 51,650	**BAU/ml**	
<25,6 BAU/ml:	negative		
25,6 bis 35,2 BAU/ml:	weak		
>35,2 BAU/ml:	: positive		
Attention! changed reference range!			
please note!			
3 SARS CoV2 IgA-Ab	negative		negative
	0,647	Ratio	
Ratio < 0,8	= negative		
Ratio 0,8 - 1,1	= weak		
Ratio >= 1,1	= positive		

Sign of good immunity to the virus (IgG), but no current infection (IgA)

Antibodies

Immunoglobulin A is not available when the infection does not live in the mucosal membranes, e.g. EBV

An immunoarray exists for EBV, but needs to have the full array of markers – useful for determining possible reactivation

9 markers including viral capsid antigen (VCA), early antigen (EA), & Epstein-Barr Nuclear Antigen (EBNA)

Epstein-Barr-Virus Immuno-Array

EBV VCA p18 IgG	+	positive	negative
EBV VCA p23 IgG	+	positive	negative
EBV EA p54 IgG		negative	negative
EBV EA p138	+	positive	negative
EBV EBNA-1 IgG	+	positive	negative
EBV VCA p18 IgM		negative	negative
EBV VCA p23 IgM		negative	negative
EBV EA p54 IgM	+	positive	negative
EBV EA p138 IgM		negative	negative

The specific EBV-IgG/IgM-, EBV-Early Antigen-antibodies and EBV-EBNA-antibodies indicate humoral immune response against Epstein Barr Virus (former or reactivated or EBV-infection in convalescence?).

The other arm of the immune system showing a cellular response – T cells

T-cells

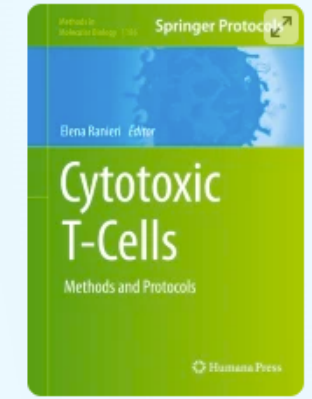
So how to test chronic infection in infections where there is no IgA available?

There is another arm to the immune system that can be tested, too: not just B cells, but T cells. Tests of cellular T-cell immunity are called EliSpots (enzyme-linked immunosorbent spot). This is a lymphocyte transformation test using an Interferon Gamma Release Assay.

“Accuracy, sensitivity, reproducibility, and robustness – a gold standard”

T-cells

“Enzyme-linked immune absorbent spot (Elispot) is a quantitative method for measuring relevant parameters of T cell activation. The sensitivity of Elispot allows the detection of low-frequency antigen-specific T cells that secrete cytokines and effector molecules, such as granzyme B and perforin. Cytotoxic T cell (CTL) studies have taken advantage with this high-throughput technology by providing insights into quantity and immune kinetics. Accuracy, sensitivity, reproducibility, and robustness of Elispot resulted in a wide range of applications in research as well as in the diagnostic field. Actually, CTL monitoring by Elispot is a gold standard for the evaluation of antigen-specific T cell immunity in clinical trials and vaccine candidates where the ability to detect rare antigen-specific T cells is of relevance for immune diagnostic.”



Source: Ranieri E, Popescu I, Gigante M. CTL ELISPOT assay. *Methods Mol Biol.* 2014;1186:75-86.

New "Springer Protocols" book (2024) with a chapter on EliSpots

T-cells

Book | © 2024

Chapter 6

Adaptive Immune Response Investigation in Lyme Borreliosis

Mihail Pruteanu, Armin Schwarzbach, and Markus Berger

Abstract

To diagnose Lyme Borreliosis, it is advised to use an enzyme-linked immunosorbent test to check for serum antibodies specific for Lyme and all tests with positive or ambiguous enzyme-linked immunosorbent assay (ELISA) results being confirmed by immunoblot. This method of measuring the humoral immunity in human fluids (e.g., by ELISA) has provided robust and reproducible results for decades and similar assays have been validated for monitoring of B cell immunity. These immunological tests that detect antibodies to *Borrelia burgdorferi* are useful in the diagnosis of Borreliosis on a routine basis. The variety of different *Borrelia* species and their different geographic distributions are the main reasons why standards and recommendations are not identical across all geographic regions of the world. In contrast to humoral immunity, the T cell reaction or cellular immunity to the *Borrelia* infection has not been well elucidated, but over time with more studies a novel T cell-based assay (EliSpot) has been developed and validated for the sensitive detection of antigen-specific T cell responses to *B. burgdorferi*. The EliSpot Lyme assay can be used to study the T cell response elicited by *Borrelia* infections, which bridges the gap between the ability to detect humoral immunity and cellular immunity in Lyme disease. In addition, detecting cellular immunity may be a helpful laboratory diagnostic test for Lyme disease, especially for seronegative Lyme patients. Since serodiagnostic methods of the *Borrelia* infection frequently provide false positive and negative results, this T cell-based diagnostic test (cellular assay) may help in confirming a Lyme diagnosis. Many clinical laboratories are convinced that the cellular assay is superior to the Western Blot assay in terms of sensitivity for detecting the underlying *Borrelia* infection. Research also suggests that there is a dissociation between the magnitude of the humoral and the T cell-mediated cellular immune responses in the *Borrelia* infection. Lastly, the data implies that the EliSpot Lyme assay may be helpful to identify *Borrelia* infected individuals when the serology-based diagnostic fails to do so. Here in this chapter the pairing of humoral and cellular immunity is employed to evaluate the adaptive response in patients.

"The EliSpot Lyme assay can be used to study the T cell response elicited by Borrelia infections, which bridges the gap between the ability to detect humoral immunity and cellular immunity in Lyme disease. **Many clinical laboratories are convinced that the cellular assay is superior to the Western Blot assay in terms of sensitivity for detecting the underlying Borrelia infection..** Research also suggests that there is a dissociation between the magnitude of the humoral and the T cell-mediated cellular immune responses in the Borrelia infection."

Examples: Borrelia burgdorferi/Mycoplasma

Borrelia burgdorferi Elispot

Borrelia burgdorferi Full Antigen	+	32	SI
Borrelia b. OSP-Mix (OSPA/OSPC/DbpA)	+	29	SI
Borrelia burgdorferi LFA-1	(+)	2	SI

>3 = positive

2-3 = weak positive

<2 = negative

The results of the EliSpot-Tests indicate current cellular activity against Borrelia burgdorferi.

Mycoplasma pneum.EliSpot

1 Mycoplasma pneum. EliSpot ! 7 SI

SI = Stimulation Index
0-1 = negative
2-3 = weak positive
> 3 = positive

The result of the EliSpot test indicates current cellular activity against Mycoplasma pneumoniae.

Exhaustive references available for correlations between different diagnoses and Borrelia, other bacteria, and viruses

- SARS-CoV-2
- Type 1 Diabetes
- Multiple Sclerosis
- Rheumatoid arthritis
- Hashimoto‘s/Graves
- IBD
- Sjögren’s Syndrome
- Myasthenia Gravis
- Guillain Barré Syndrome
- Antiphospholipid syndrome
- PANS/PANDAS
- Fibromyalgia
- M.E./CFS
- Parkinsonism
- Autism
- Alzheimer‘s/Dementia
- ALS/Motor Neurone Disease
- ....

Please just ask: we have done extensive research

ArminLabs has evidence-based questionnaires/checklists to home in on the most likely coinfections

Short Symptom Checklist for Lyme Borreliosis

Name, first name ..... Date: .....

►	Actual and former symptoms: Please mark with a cross	X
1	Former or recent tick bite	
2	Former or recent bull´s eye rash	
3	Summer flu after tick bite	
4	Fatique/Malaise/Lethargy	
5	Loss of physical/mental capacity, general weakness	
6	Neck-pain, neck stiffness	
7	Headache	
8	Painful joints, swollen joints	
9	General aches and pains, tendon problems	
10	Muscle pain, muscle weakness	
11	Fever, feverish feeling, shivering	
12	Ears: intermittent red, swollen earlap	
13	Heart problems, disturbance of cardiac rhythm	
14	Cough, expectoration, breathlessness	
15	Night sweat	
16	Sleeplessness, waking up around ..... p.m.	
17	Tinnitus	
18	Swollen lymph nodes	
19	Numbness of the skin	
20	"Burning" or "pins and needles" skin sensations, painful sole or f	
21	Back pain, back stiffness	
22	Occasional muscle twitching in the face, arms, legs	
23	Shivering, chill	
24	Blurred, foggy, cloudy, flickering, double vision	
25	Aggressiveness, drowsiness, panic attacks, anxiety, mood swings	
26	Concentration problems, short-term memory loss, forgetfulness	
27	Skin partly thin, paper-like, transparent, dry	
	Total number of symptoms	

Antibiotics? When? Which one(s)? How long?

.....

Coinfections-Checklist

Name, first name ..... Date (DD/MM/YYYY) .....

	Actual and former symptoms Please mark with a cross	X	Score-Points (filled in by physician/naturopath)	Ranking
1	Stomach ache, gut problems	☒	Ehrlichia&Anaplasma: 5	4
2	Anaemia	☐	Babesia: 4	5
3	Diarhoea intermittent	☐	Rickettsia: 4	5
4	Fever or feverish feeling	☒	Bartonella: 7	2
5	Lack of concentration, memory disturbance, forgetfulness	☒	Chl.pneumoniae: 6	3
6	Encephalitis/Inflammation of the brain (NMR)	☐	Chl.trachomatis: 2	7
7	Yellowish colour of the skin/eyes	☐	Yersinia: 3	6
8	Painful joints, swollen joints	☐	Mycoplasma: 5	4
9	General aches and pains, tendon problems	☐	Coxsackie-/Echo-Virus: 8	1
10	Flu-like symptoms intermittent	☒	EBV/CMV/HSV/VZV: 8	1
11	Rash(es)	☒		
12	Small red/purple spots of the skin	☐		
13	Heart problems, disturbance of cardiac rhythm	☒		
14	Cough, expectoration	☐		
15	Headache	☒		
16	Impaired liver function/ liver laboratory values	☒		
17	Pneumonia, bronchitis	☐		
18	Swollen lymph nodes	☒		
19	Tonsilitis	☒		
20	Enlargement of the spleen	☐		

The autofill checklists help decide which other infections to test for, as Lyme rarely occurs alone

Multiple Infection Checklist

arminlabs

Name, first name ..... Date (DD/MM/YYYY) .....

	Your current and former symptoms Please click on the boxes next to the symptoms that you suffer from	X
1	Stomach ache, gut problems	☐
2	Anaemia	☐
3	Diarhoea intermittent, intestinal crampings/pain	☐
4	Fever or feverish feeling	☐
5	Lack of concentration, memory loss, forgetfulness	☐
6	Encephalitis/Inflammation of the brain	☐
7	Yellowish colour of the skin/eyes	☐
8	Painful joints or swollen joints	☐
9	General aches and pains, tendon problems	☐
10	Flu-like symptoms	☐
11	Rash(es), striae, exanthema	☐
12	Small red/purple spots of the skin	☐
13	Heart problems, disturbed cardiac rhythm	☐
14	Cough, expectoration, "air-hunger"	☐
15	Headache, dizziness	☐
16	Impaired liver function/ liver laboratory values	☐
17	Pneumonia, bronchitis	☐
18	Swollen lymph nodes	☐
19	Enlargement of the spleen	☐
20	Fatigue / exhaustion, intermittent or chronic CFS	☐
21	Muscle pain, muscle weakness	☐
22	Shivering, chill	☐
23	Blurred, foggy, cloudy, flickering, double vision	☐
24	Nausea, vomiting	☐
25	Dark urine	☐
26	Itching or pain when urinating	☐
27	Tingling, numbness, "burning" sensations	☐
28	Neck pain, neck stiffness	☐
29	Shoulder pain	☐

Ranked in order of priority:
CPn, Mycoplasma and the Herpesviruses draw for
first place here ↓

Below you'll find the number of the symptoms for each of the infections that we test for and the ranking, in which order you should test for them

Ranking of the infections	No. of symptoms	Rank
Chlamydia pneumoniae	4	1
Mycoplasma pneumoniae	4	1
Yersinia	2	3
Campylobacter	2	3
HSV 1/2	4	1
EBV	4	1
CMV	4	1
VZV	3	2
HHV 6	4	1
Parvovirus	3	2
Coxsackie-Virus	3	2
Echovirus	2	3

Links to many more detailed Arminlabs presentations and webinars on the AONM website …

https://aonm.org/view-past-webinars/

DR. ARMIN SCHWARZBACH

DR. SARAH MYHILL

PROFESSOR LEONA GILBERT

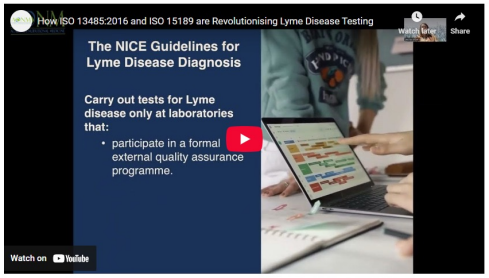
ZHANETA MISHO

GILIAN CROWTHER MA

DECEMEBER ROUNDTABLE – DELVING DEEPER ON TESTING, THERAPIES AND MANAGEMENT STRATEGIES FOR CHRONIC INFECTIONS

PROF. LEONA GILBERT

HOW ISO 13485:2016 AND ISO 15189 ARE REVOLUTIONISING LYME DISEASE TESTING



https://aonm.org/past_events/

Schizophrenia, Bipolar, ASD/Autism, Anxiety/Panic Attacks, OCD/Tourette's, PANS/PANDAS … : Tailored Testing Protocols

Holiday Inn Regents Park, 18th November 2018, London, UK

Armin Schwarzbach MD PhD

Specialist for Laboratory Medicine

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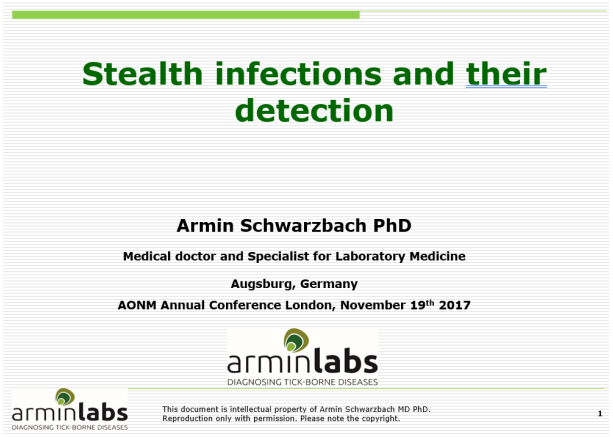

Stealth infections and their detection

Armin Schwarzbach PhD

Medical doctor and Specialist for Laboratory Medicine

Augsburg, Germany

AONM Annual Conference London, November 19th 2017

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Thank you very much!
Q&A/Discussion

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CERTIFICATE OF ACCREDITATION

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