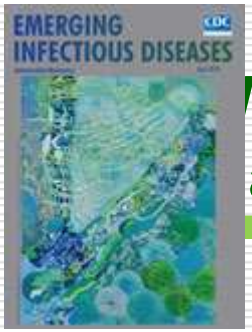
Infectious Pathogens and Cancer: The Emerging Evidence

Armin Schwarzbach MD PhD

Medical doctor and
Specialist for laboratory medicine
Augsburg, Germany

ArminLabs
Laboratory for tick-borne diseases

www.aonm.org



WHO, 1997: "Up to 84% of cases of some cancers are attributable to viruses, bacteria, and parasites"

"A growing body of research suggests that a number of viruses, bacteria, and parasites cause cancer in humans, thus providing new possibilities for treatment and prevention of cancer. **In 1997, the World Health Organization estimated that up to 84% of cases of some cancers are attributable to viruses, bacteria and parasites, and that more than 1.5 million (15%) new cases each year could be avoided by preventing the infectious disease associated with them.** … The pathogenic mechanisms by which infectious agents cause cancer have not been resolved but they appear to be diverse. … This finding not only suggests a causal role but that treatment of a bacterial infection can actually result in regression of cancer."

Cassell, GH. Infectious Causes of Chronic Inflammatory Diseases and Cancer Emerging Infectious Diseases. National Center for Infectious Diseases. Centers for Disease Control and Prevention, Atlanta, GA.

"… since the discovery of links between H. pylori and gastric lymphomas and adenocarcinomas, and HPV-induced neoplasias from mouth to anal domains, **chronic infections have provided a model to explain the transit of a benign cell into a malignant cell.**"

Alan B. MacDonald, M.D., Fellow, College of American Pathologists, January 2016

Source: Emerging Infectious Diseases Vol. 4 No. 2 / Jul. – Sept. 1998; ftp://ftp.cdc.gov/pub/eid/vol4no3/ascii/vol4no3.txt

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Infectious Pathogens and Cancer: The Emerging Evidence

1. Stealth bacteria involvement

2. Viral involvement

3. Indirect involvement

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Infectious Pathogens and Cancer: The Emerging Evidence

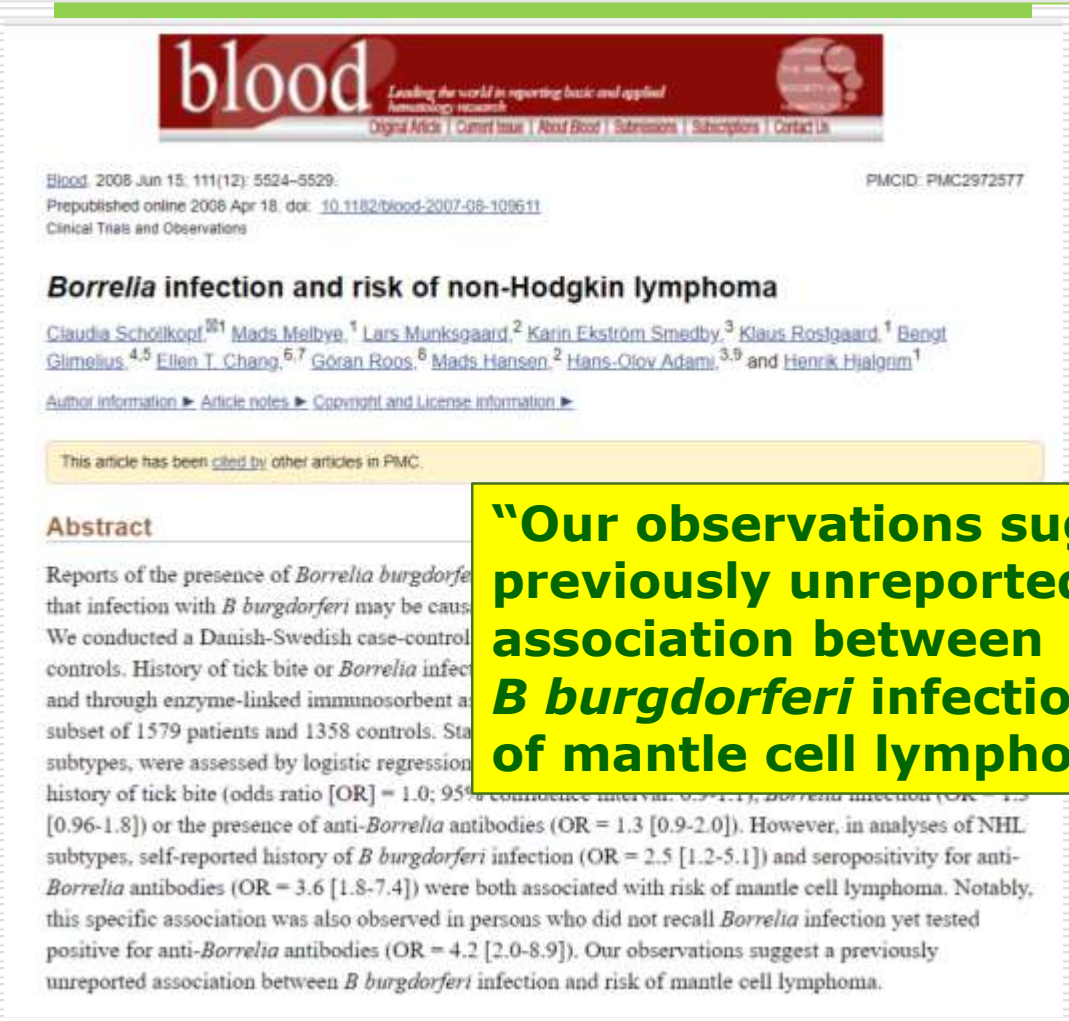
1. Stealth bacteria involvement

- Borrelia
- Bartonella
- Babesia
- Chlamydia pneumoniae
- Mycoplasma
- Chlamydia trachomatis
- Ehrlichia
- Toxoplasma

2. Viral involvement

3. Indirect involvement

Borrelia and non-Hodgkin/mantle cell lymphoma



blood
Leading the world in reporting basic and applied hematology research
Original Article | Current Issue | About Blood | Submissions | Subscriptions | Contact Us

Blood. 2008 Jun 15; 111(12): 5524–5529. PMCID: PMC2972577
Prepublished online 2008 Apr 18. doi: 10.1182/blood-2007-08-109611
Clinical Trials and Observations

Borrelia infection and risk of non-Hodgkin lymphoma

Claudia Schöllkopf,[*1] Mads Melbye,[1] Lars Munksgaard,[2] Karin Ekström Smedby,[3] Klaus Rostgaard,[1] Bengt Glimelius,[4,5] Ellen T. Chang,[6,7] Göran Roos,[8] Mads Hansen,[2] Hans-Olov Adami,[3,9] and Henrik Hjalgrim[1]

Author information ► Article notes ► Copyright and License information ►

Abstract

Reports of the presence of *Borrelia burgdorfe*
that infection with *B burgdorferi* may be caus
We conducted a Danish-Swedish case-control
controls. History of tick bite or *Borrelia* infec
and through enzyme-linked immunosorbent a
subset of 1579 patients and 1358 controls. Sta
subtypes, were assessed by logistic regression
history of tick bite (odds ratio [OR] = 1.0; 95%
[0.96-1.8]) or the presence of anti-*Borrelia* antibodies (OR = 1.3 [0.9-2.0]). However, in analyses of NHL subtypes, self-reported history of *B burgdorferi* infection (OR = 2.5 [1.2-5.1]) and seropositivity for anti-*Borrelia* antibodies (OR = 3.6 [1.8-7.4]) were both associated with risk of mantle cell lymphoma. Notably, this specific association was also observed in persons who did not recall *Borrelia* infection yet tested positive for anti-*Borrelia* antibodies (OR = 4.2 [2.0-8.9]). Our observations suggest a previously unreported association between *B burgdorferi* infection and risk of mantle cell lymphoma.

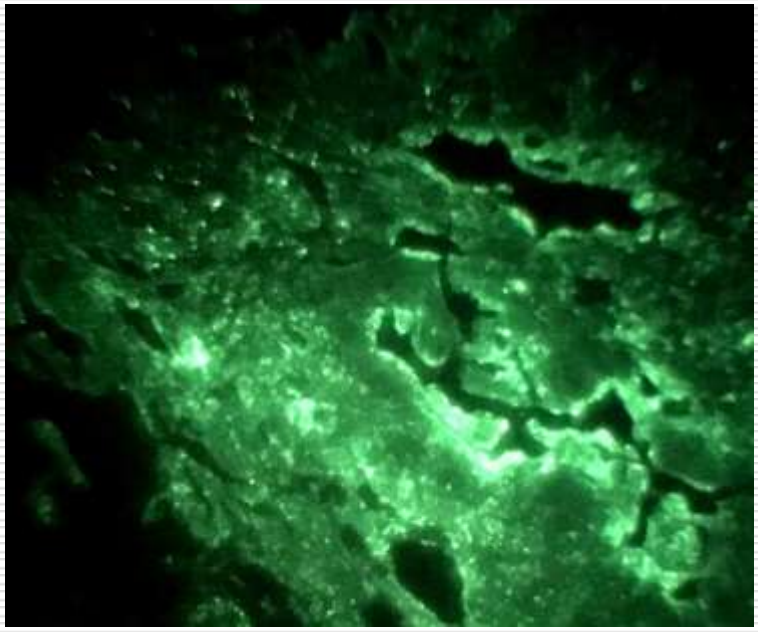
"Schoellkopf et al conducted a Danish-Swedish case-control study of 3,055 patients with non-Hodgkin's lymphoma and 3,187 population controls to evaluate the association of lymphoma subtypes with Borrelia burgdorferi. Self-reported history of B burgdorferi infection (OR = 2.5) and seropositivity for anti-Borrelia antibodies (OR – 3.6) were both found to increase the risk of mantle cell lymphoma"
Epidemiology of Chronic Disease: Global Perspectives (book), Randall E. Harris MD PhD, 2013.

"Our observations suggest a previously unreported association between *B burgdorferi* infection and risk of mantle cell lymphoma."

"Moreover, regression of lymphomas upon treatment of the Borrelia infection has also been reported"

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Borrelia in Glioblastoma Multiformae



Glioblastoma Multiformae Brain Biopsies - Formalin fixed- with Immunohistochemical Full Pam=nelPane Panel evaluation and Confirmation of Diagnosis by neuropathologist- --- Images (3 per case) of FISH DNA probe for detection of Burgdorferi Borrelia DNA with DNA probes specific for gene of Inner cell membrane of Burgdorferi Borrelia Gene bbo 0740- Validated DNA probe and all Controls acceptable

Alan MacDonald, M.D., FCAP, Copyright, year 2016 January, all rights reserved

"In the case of neurons, glial cells and Borrelia, there is evidence from co-incubation of cells in tissue culture with living Borrelia in pure cultures that Borrelia first binds to the tissue cultured cells, and then, stepwise, inserts the entire spirochete into the cytoplasm and then into the nucleus of glial cells. Liposomes from Borrelia's outer surface membrane contain DNA. Transmission electron micrographs have imaged the transit of Borrelia liposomes from the external cellular milieu, to penetrate the cytoplasm of eukaryotic cells, and next to penetrate the nucleus."

Source: Alan MacDonald, M.D., FCAP, Copyright, Jan. 2016, https://durayresearch.files.wordpress.com/2016/01/report-for-gbm-cases-five-with-fish-probes.pdf; https://www.lymeneteurope.org/forum/viewtopic.php?t=6048

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Bartonella is able to produce tumours

Current Knowledge of *Bartonella* Species

M. Maurin, R. Birtles, D. Raoult*

Bartonella species are now considered emerging pathogens. Of the 11 currently recognized species, four have been implicated in human disease, although only two have been encountered in Europe. *Bartonella quintana* infections are now being diagnosed among the urban homeless and deprived, manifesting as trench fever, and *Bartonella henselae* has been shown to be the causative agent of cat scratch disease. Both species also cause a variety of HIV-associated infections, including bacillary angiomatosis. However, perhaps the most significant presentation of bartonellae infection is culture-negative endocarditis. The epidemiologies of *Bartonella* infections are poorly understood; most *Bartonella henselae* infections are probably acquired from infected cats, either directly by contact with a cat or indirectly via fleas. No animal reservoir has been implicated for *Bartonella quintana*; however, infection can be transmitted via the human body louse. Diagnosis of *Bartonella* infections can be made using histological or microbiological methods. The demonstration of specific antibodies may be useful in some instances, although certainly not in all. Cultivation of *Bartonella* is difficult, as the bacteria are extremely fastidious. Polymerase chain reaction-based or immunological methods for the detection of bartonellae in infected tissues have proven useful. Clinical relapse is often associated with *Bartonella* infections despite a wide range of prescribed regimens. Only aminoglycosides display in vitro bactericidal activity against intracellular *Bartonella* species; therefore, they are recommended for treatment of *Bartonella* infections.

Human infections due to *Bartonella* species are widely considered emerging diseases. They include long-recognized diseases such as Carrion's disease (classic bartonellosis), trench fever, and cat-scratch disease and newer clinical manifestations such as bacillary angiomatosis, peliosis hepatitis, septicemia, endocarditis, chronic lymphadenopathy, and neurologic disorders. New molecular biology techniques, mainly based on 16S rRNA gene amplification and analysis, have allowed recognition of the role of *Bartonella* (formerly *Rochalimaea* species in a number of these isms. The most striking pathological feature of *Bartonella* infection is the apparent ability of these bacteria to produce angioproliferative lesions in immunocompromised patients, such as those infected with HIV. Capillary and endothelial cell proliferations are characteristic histologic findings of bacillary angiomatosis, peliosis hepatitis, and classic bartonellosis. Bartonellae are the only known bacteria with the ability to produce angiogenic tumors in humans, although *Agrobacterium* species, which belong to the same phylogenic group as *Bartonella* species, produce tumors in plants.

"Bartonellae are the only known bacteria with the ability to produce angiogenic tumors in humans"

Source: Maurin, Max & Birtles, Richard & Raoult, D. (1997). Current knowledge of Bartonella species. European journal of clinical microbiology & infectious diseases

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Bartonella: angioproliferative lesions

Journal List › Infect Immun › v.72(12); 2004 Dec › PMC529148

Infection and Immunity

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

Infect Immun. 2004 Dec; 72(12): 7315–7317. PMCID: PMC529148
doi: 10.1128/IAI.72.12.7315-7317.2004

In Vitro Model of *Bartonella henselae*-Induced Angiogenesis

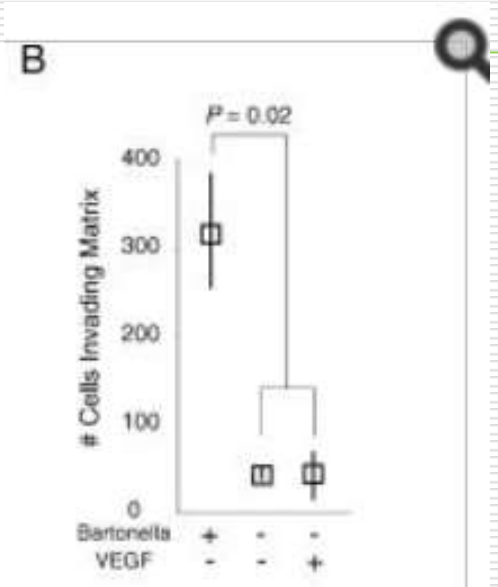
James E. Kirby*

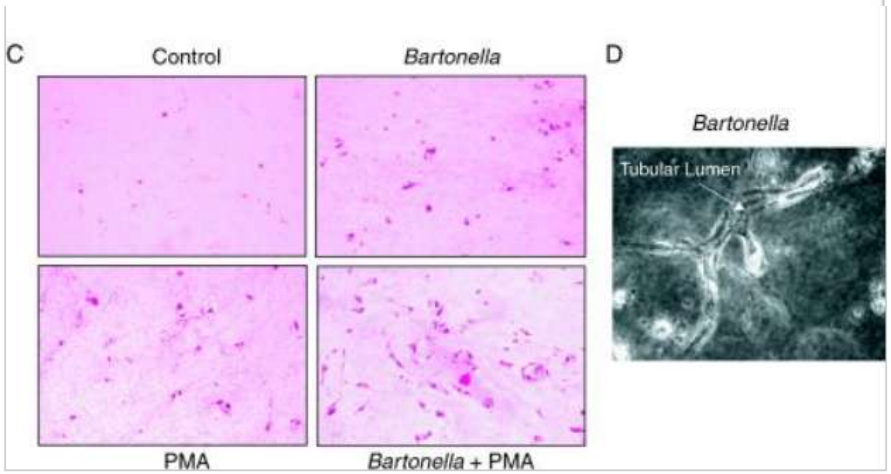
Author information ▶ Article notes ▶ Copyright and License information ▶

ABSTRACT Go to:

Bartonella henselae is a gram-negative pathogen that causes angiogenesis. Here, I establish in vitro models to study *Bartonella*-induced blood vessel formation. I found that *B. henselae* induces long-term endothelial survival and tubular differentiation within type I collagen matrix.

Bartonella henselae is an emerging bacterial pathogen that causes
disease), endocarditis, and angioproliferative lesions in AIDS patie
17). Angioproliferative lesions are the most unique and defining fe
of proliferating endothelial cells, these aggregates of immature vas
abnormal form of angiogenesis. They differ from the less exuberan
stimulation by vascular endothelial growth factor (VEGF), a critica
produced by tumors or introduced experimentally (18).





Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC529148/figure/f2/

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Bartonella and MGUS (Monoclonal Gammopathy of Undetermined Significance)

Am J Hematol. 2006 Feb;81(2):115-7.

Transient monoclonal gammopathy in a patient with Bartonella quintana endocarditis.

Sève P[1], Turner R, Stankovic K, Perard L, Broussolle C.

Author information

Abstract

Monoclonal gammopathy has been reported rarely in association with infectious diseases. Viral infection has been the most frequently reported. We report a case of Bartonella quintana endocarditis in a 45-year-old homeless male associated with a monoclonal IgG kappa gammopathy. The gammopathy disappeared after 8 months of antibiotics while the Bartonella antibody titre was decreasing. This correlation suggests a causative role for B. quintana for the monoclonal gammopathy. To the best of our knowledge, this the first report of monoclonal gammopathy in the course of B. quintana infection.

PMID: 16432867 DOI: 10.1002/ajh.20499

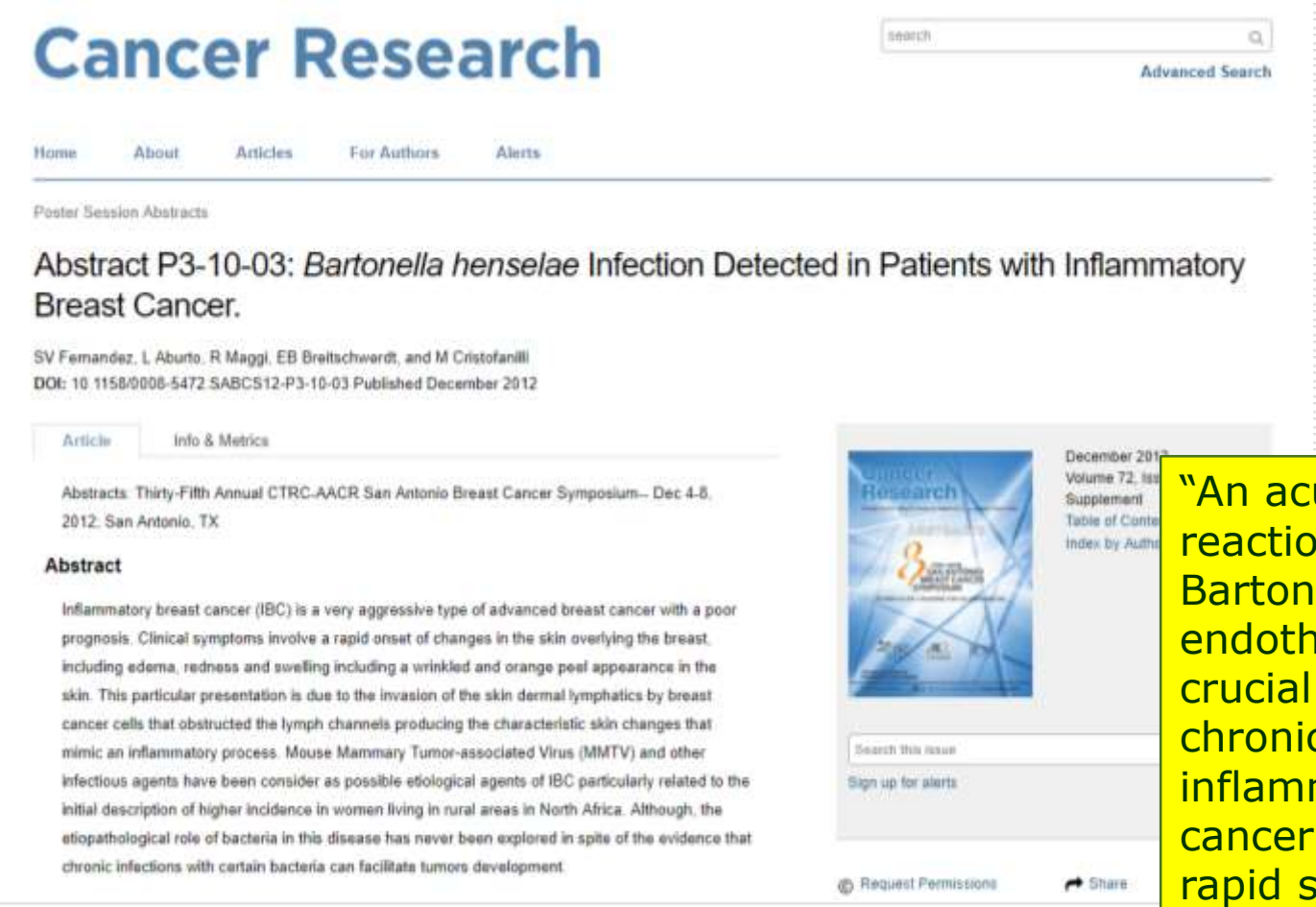
[Indexed for MEDLINE] Free full text

"This correlation suggests a causative role for B. quintana for the monoclonal gammopathy."

"The gammopathy disappeared after 8 months of antibiotics"

Source: Am J Hematol. 2006 Feb;81(2):115-7

Bartonella henselae in breast cancer



Cancer Research

search

Advanced Search

Home About Articles For Authors Alerts

Poster Session Abstracts

Abstract P3-10-03: *Bartonella henselae* Infection Detected in Patients with Inflammatory Breast Cancer.

SV Fernandez, L Aburto, R Maggi, EB Breitschwerdt, and M Cristofanilli

DOI: 10.1158/0008-5472.SABCS12-P3-10-03 Published December 2012

Article Info & Metrics

Abstracts: Thirty-Fifth Annual CTRC-AACR San Antonio Breast Cancer Symposium-- Dec 4-8, 2012: San Antonio, TX

Abstract

Inflammatory breast cancer (IBC) is a very aggressive type of advanced breast cancer with a poor prognosis. Clinical symptoms involve a rapid onset of changes in the skin overlying the breast, including edema, redness and swelling including a wrinkled and orange peel appearance in the skin. This particular presentation is due to the invasion of the skin dermal lymphatics by breast cancer cells that obstructed the lymph channels producing the characteristic skin changes that mimic an inflammatory process. Mouse Mammary Tumor-associated Virus (MMTV) and other infectious agents have been consider as possible etiological agents of IBC particularly related to the initial description of higher incidence in women living in rural areas in North Africa. Although, the etiopathological role of bacteria in this disease has never been explored in spite of the evidence that chronic infections with certain bacteria can facilitate tumors development.

December 201

Volume 72, Iss

Supplement

Table of Conte

Index by Autho

Search this issue

Sign up for alerts

Request Permissions Share

"An acute inflammatory reaction triggered by the Bartonella infected endothelium may be crucial for initiating the chronic inflammation in inflammatory breast cancer patients and the rapid spread of tumor cells."

Source: Cancer Res 2012;72(24 Suppl):Abstract no. P3-10-03.

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Babesia and B-cell lymphoma

Infect Dis Clin North Am. Author manuscript; available in PMC 2014 Apr 24.
Published in final edited form as:
Infect Dis Clin North Am. 2008 Sep; 22(3): 469–ix.
doi: 10.1016/j.idc.2008.03.010

PMCID: PMC3998201
NIHMSID: NIHMS70263

Human Babesiosis

Edouard Vannier, PhD,[a] Benjamin E. Gewurz, MD, PhD,[b] and Peter J. Krause, MD[c,d]

Author information ► Article notes ► Copyright and License information ►

Introduction

Go to:

Human babesiosis is an emerging tick-borne infectious disease caused by protozoa of the genus *Babesia* that are obligate parasites of red blood cells. Long recognized as pathogens imposing a significant health burden on domesticated animals, *Babesia* spp. increasingly have been identified over the last 50 years as a cause of infection in people throughout the world.

The first reference to babesiosis is probably in Exodus 9:3, which describes the plague visited upon the cattle of Pharaoh Rameses II. Viktor Babes, a Hungarian pathologist wh... hemoglobinuria in cattle grazing in the Danube region of Romania, was... microorganism residing in red blood cells.[1] Shortly thereafter, Smith ... organism in Texas cattle.[2] Named *Pyrosoma bigeminum* after its pear... recognized as *Babesia bigemina*. The cattle tick, *Boophilus annulatus*, was identified as the vector for transmission of Texas cattle fever. By making this seminal observation, Smith and Kilborne established the concept that hematophagous arthropods can transmit an infectious agent to vertebrate hosts. More than 100 species of babesia subsequently have been identified in wild and domestic animals.[3]

"Interestingly, the majority of case patients in the study had underlying B-cell lymphoma"

Chlamydia pneumoniae associated with lung cancer

Cancer Epidemiology, Biomarkers & Prevention

Home About Articles For Authors Alerts

Chlamydia pneumoniae Infection and Risk for Lung Cancer

Anil K. Chaturvedi, Charlotte A. Gaydos, Patricia Agreda, Jeffrey P. Holden, Nilanjan Chatterjee, James J. Goedert, Neil E. Caporaso, and Eric A. Engels

DOI: 10.1158/1055-9965.EPI-09-1251 Published June 2010

Abstract

Background: We evaluated the relationship of *Chlamydia pneumoniae* infection with prospective lung cancer risk using traditional serologic markers [microimmunofluorescence (MIF) IgG and IgA antibodies] and *Chlamydia* heat shock protein-60 (CHSP-60) antibodies, a marker for chronic chlamydial infection.

Methods: We conducted a nested case-control study (593 lung cancers and 671 controls) within the screening arm of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial (NCT 77,464). Controls were matched to cases by age, sex, randomization year, follow-up time, and smoking (pack-years of smoking, time since quitting). We assessed *C. pneumoniae* seropositivity and endpoint antibody titers (IgG and IgA against *C. pneumoniae* elementary bodies and IgG against CHSP-60).

Results: *C. pneumoniae* seropositivity by microimmunofluorescence IgG or IgA antibodies was associated with lung cancer [odds ratio of 0.88 and 95% confidence interval (95% CI) of 0.65 for IgG; odds ratio of 0.98 and 95% CI of 0.76-1.27 for IgA]. In contrast, individuals seropositive for CHSP-60 IgG antibodies had significantly increased lung cancer risk (odds ratio, 1.30; 95% CI, 1.02-1.67), and risk increased with increasing antibody titers ($P_{trend} = 0.006$). CHSP-60-related risk did not differ significantly by lung cancer histology, follow-up time, or smoking. CHSP-60

"CHSP-60 seropositivity and elevated antibody titers were associated with significantly increased risk for subsequent lung cancer, supporting an etiologic role for C. pneumoniae infection in lung carcinogenesis."

Eur J Cancer. 2011 Mar;47(5):742-7. doi: 10.1016/j.ejca.2010.11.003. Epub 2010 Dec 29.

Chlamydia pneumoniae infection and lung cancer risk: a meta-analysis.

Zhan P[1], Suo LJ, Qian Q, Shen XK, Qiu LX, Yu LK, Song Y

Author information

Open/close author information list

Abstract

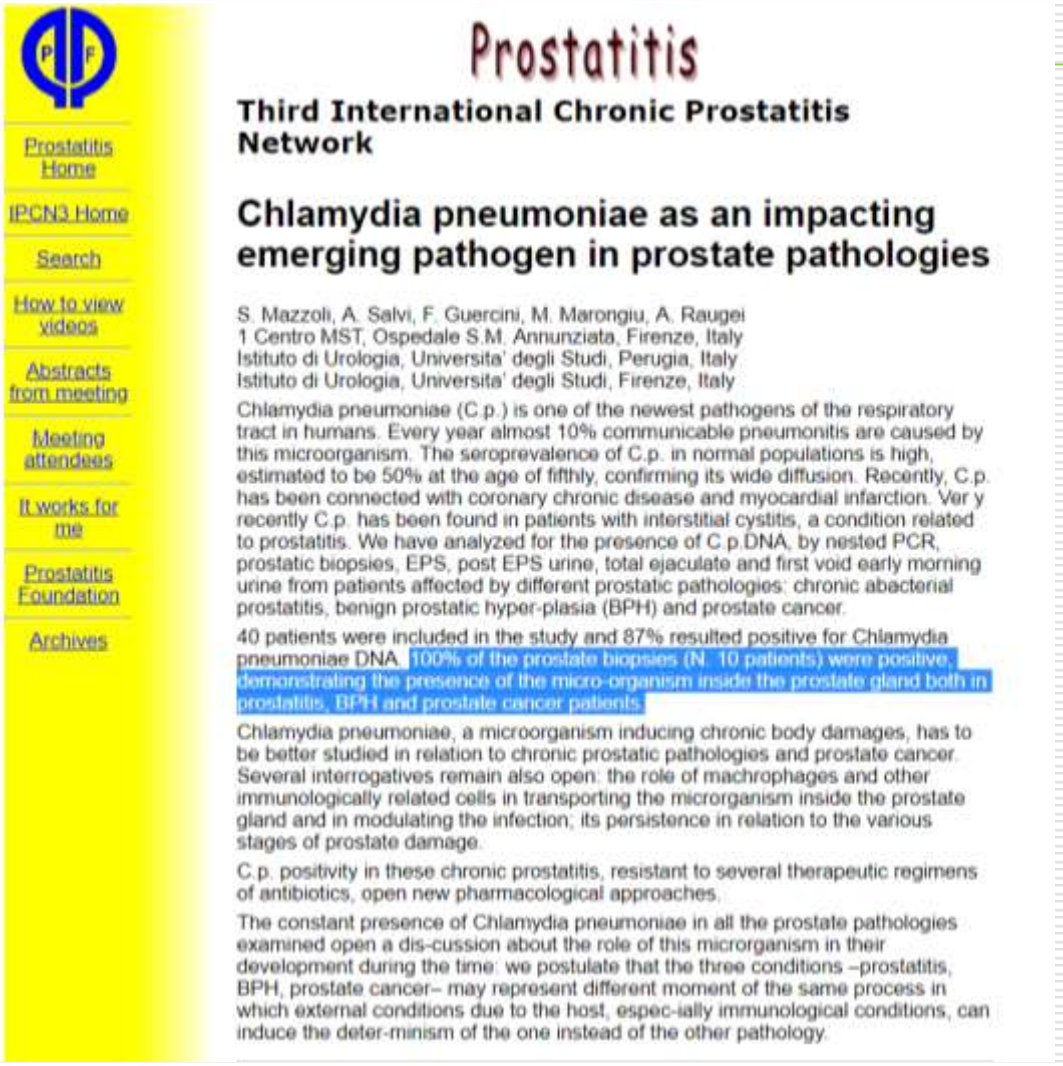
Chlamydia pneumoniae (C. pneumoniae) is a common cause of acute respiratory infection and has been hypothesised to cause several chronic diseases, including lung cancer. Numbers studies were conducted to analyse the association between C. pneumoniae infection and risk of lung cancer, but no clear consensus had been found. To assess this relationship more precisely, a meta-analysis was performed. The electronic databases PubMed, Embase, Web of Science and CNKI were searched. Data were extracted and analysed independently by two investigators. Ultimately, 12 studies, involving 2595 lung cancer cases and 2585 controls from four prospective studies and eight were included. Overall, people exposed to C. pneumoniae infection had an odds ratio (OR) of 1.48 (95% confidence 7) for lung cancer risk, relative to those not exposed. C. pneumoniae infection was clearly identified as a risk factor for rospective studies (OR, 1.16; 95% CI, 1.00-1.36) and retrospective studies (OR, 2.17; 95% CI, 1.79-2.63) and in both (OR, 1.22; 95% CI, 1.06-1.41) and the IgA ≥ 64 cutoff group (OR, 2.35; 95% CI, 1.88-2.93). In conclusion, C. pneumoniae infection is associated with an increased risk for lung cancer, higher titre may be a better predictor of lung cancer risk.

"Higher titre may be a better predictor of lung cancer risk"

Source: http://cebp.aacrjournals.org/content/19/6/1498.long; https://www.ncbi.nlm.nih.gov/pubmed/21194924

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Chlamydia pneumoniae in prostate cancer



Prostatitis Home
IPCN3 Home
Search
How to view videos
Abstracts from meeting
Meeting attendees
It works for me
Prostatitis Foundation
Archives

Prostatitis

Third International Chronic Prostatitis Network

Chlamydia pneumoniae as an impacting emerging pathogen in prostate pathologies

S. Mazzoli, A. Salvi, F. Guercini, M. Marongiu, A. Raugei
1 Centro MST, Ospedale S.M. Annunziata, Firenze, Italy
Istituto di Urologia, Universita' degli Studi, Perugia, Italy
Istituto di Urologia, Universita' degli Studi, Firenze, Italy

Chlamydia pneumoniae (C.p.) is one of the newest pathogens of the respiratory tract in humans. Every year almost 10% communicable pneumonitis are caused by this microorganism. The seroprevalence of C.p. in normal populations is high, estimated to be 50% at the age of fifthly, confirming its wide diffusion. Recently, C.p. has been connected with coronary chronic disease and myocardial infarction. Ver y recently C.p. has been found in patients with interstitial cystitis, a condition related to prostatitis. We have analyzed for the presence of C.p.DNA, by nested PCR, prostatic biopsies, EPS, post EPS urine, total ejaculate and first void early morning urine from patients affected by different prostatic pathologies: chronic abacterial prostatitis, benign prostatic hyper-plasia (BPH) and prostate cancer.

40 patients were included in the study and 87% resulted positive for Chlamydia pneumoniae DNA. 100% of the prostate biopsies (N. 10 patients) were positive, demonstrating the presence of the micro-organism inside the prostate gland both in prostatitis, BPH and prostate cancer patients.

Chlamydia pneumoniae, a microorganism inducing chronic body damages, has to be better studied in relation to chronic prostatic pathologies and prostate cancer. Several interrogatives remain also open: the role of machrophages and other immunologically related cells in transporting the microrganism inside the prostate gland and in modulating the infection; its persistence in relation to the various stages of prostate damage.

C.p. positivity in these chronic prostatitis, resistant to several therapeutic regimens of antibiotics, open new pharmacological approaches.

The constant presence of Chlamydia pneumoniae in all the prostate pathologies examined open a dis-cussion about the role of this microrganism in their development during the time: we postulate that the three conditions –prostatitis, BPH, prostate cancer– may represent different moment of the same process in which external conditions due to the host, espec-ially immunological conditions, can induce the deter-minism of the one instead of the other pathology.

"100% of the prostate biopsies (N. 10 patients) **were positive**, **demonstrating the presence of the micro-organism inside the prostate** gland both **in** prostatitis, benign prostate hyperplasia and **prostate cancer patients**."

Source: https://www.prostatitis.org/a212000.html

High level of Mycoplasma in various cancers

World Journal of Gastroenterology

World J Gastroenterol. 2001 Apr 15; 7(2): 266–269
Published online 2001 Apr 15. doi: 10.3748/wjg.v7.i2.266
PMCID: PMC4723534

Mycoplasma infections and different human carcinomas

Su Huang, Ji-You Li, Jian Wu, Lin Meng, and Cheng-Chao Shou

Abstract

AIM: To explore relationships between human carcinomas and mycoplasma infection.

METHODS: Monoclonal antibody PD4, which specifically recognizes a distinct protein from mycoplasma hyorhinis, was used to detect mycoplasma infection in different paraffin embedded carcinoma tissues with immunohistochemistry. PCR was applied to amplify the mycoplasma DNA from the positive samples for confirming immunohistochemistry.

RESULTS: Fifty of 90 cases (56%) of gastric carcinoma were positive for mycoplasma hyorhinis. In other gastric diseases, the mycoplasma infection ratio was 28% (18/49) in chronic superficial gastritis, 30% (14/46) in gastric ulcer and 37% (18/49) in intestinal metaplasia. The difference is significant with gastric cancer ($\chi^2 = 12.06$, $P < 0.05$). In colon carcinoma, the mycoplasma infection ratio was 55.1% (32/58),but it was 20.9% (10/49) in adenomatous polyp ($\chi^2 = 13.46$, $P < 0.005$). Gastric and colon cancers with high differentiation had a higher mycoplasma infection ratio than those with low differentiation ($P < 0.05$).

Table 1 Mycoplasma infection in different grades of gastric carcinoma.

Grades of differentiation	Total number of cases	Infection of mycoplasma: Negative cases (-)	Positive cases (+)	Positive cases (++)	Total positive cases	Ratio of positive (%)
I-II	23	3	12	8	20	87
II-III	18	7	9	2	11	61
III	49	30	14	5	17	39
Total	90	40	35	14	50	56

Table 3 Mycoplasma infection in different grades of colon carcinoma.

Grades of differentiation	Total number of cases	Infection of mycoplasma: Negative cases (-)	Positive cases (+)	Positive cases (++)	Total positive cases	Ratio of positive (%)
I-II	42	15	15	12	27	64
II-III	8	5	2	1	3	37
III	8	6	2	0	2	30
Total	58	26	19	13	32	55 (mean)

Table 4 Mycoplasma infection in other carcinoma tissues.

Types of carcinoma	Total number of cases	Infection of mycoplasma: Negative cases (-)	Positive cases (+)	Positive cases (++)	Total positive cases	Ratio of positive (%)
Esophagus	53	26	21	6	27	50.9
Lung	59	28	23	8	31	52.6
Breast	63	38	17	8	25	39.7
Glioma	91	53	27	11	38	41.0
Total	266	145	88	33	121	45.5

"There was high correlation between mycoplasma infection and different cancers, which suggests the possibility of an association between the two."

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4723534/

Strong link with prostate cancer …

Journal List › Oncotarget › v.2(4); 2011 Apr › PMC3248169

Oncotarget
Open Access Impact Journal

Oncotarget. 2011 Apr; 2(4): 289–297. PMCID: PMC3248169
Published online 2011 Apr 4. doi: 10.18632/oncotarget.256

Association of *Mycoplasma hominis* infection with prostate cancer

Yulia A. Barykova,[1] Denis Yu. Logunov,[1] Maxim M. Shmarov,[1] Andrei Z. Vinarov,[2] Dmitry N. Fiev,[2] Natalia A. Vinarova,[2] Irina V. Rakovskaya,[1] Patricia Stanhope Baker,[3] Inna Shyshynova,[3,5] Andrew J. Stephenson,[4] Eric A. Klein,[4] Boris S. Naroditsky,[1] Alexander L. Gintsburg,[1] and Andrei V. Gudkov[3,5]

Author information ▶ Article notes ▶ Copyright and License information ▶

See commentary "Mycoplasma and cancer: in search of the link" on page 271.
See commentary "The "Infectious" Nature of Human Prostate Cancer: A Cautionary Note" on page 281.

This article has been cited by other articles in PMC.

Abstract

Go to:

The origin of chronic inflammation preceding the development of prostate cancer (PCa) remains unknown. We investigated possible involvement of mycoplasma infection in PCa by screening prostate biopsies from two groups of Russian men undergoing PCa diagnosis. *M. hominis* was detected by standard PCR in 15% of the 125 patients in the first group and by quantitative real-time PCR in 37.4% of the 123 men in the second group. In both groups, stratification of patients according to diagnosis showed that *M. hominis* was present at three times higher frequency in patients with PCa than in those with benign prostatic hyperplasia. No *M. hominis* was detected in the prostates of 27 men without detectable prostate disease. In addition, PCa-positive men had higher titers of antibodies against *M. hominis* and average PSA levels were higher in *M. hominis*-positive men. These data, together with previous observations linking mycoplasma infection with cell transformation, genomic instability and resistance to apoptosis, suggest that *M. hominis* infection may be involved in PCa development and may, therefore, be a potential PCa marker and/or target for improved prevention and treatment of this disease.

"This study by Barykova *et al*. [7] is the latest of several that indicate **a strong link between mycoplasma species and prostate cancer**"

Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3248167/

arminlabs
DIAGNOSING TICK-BORNE DISEASES

… and lung cancer

Format: Abstract Send to

J Cell Biochem. 2008 May 15;104(2):580-94.

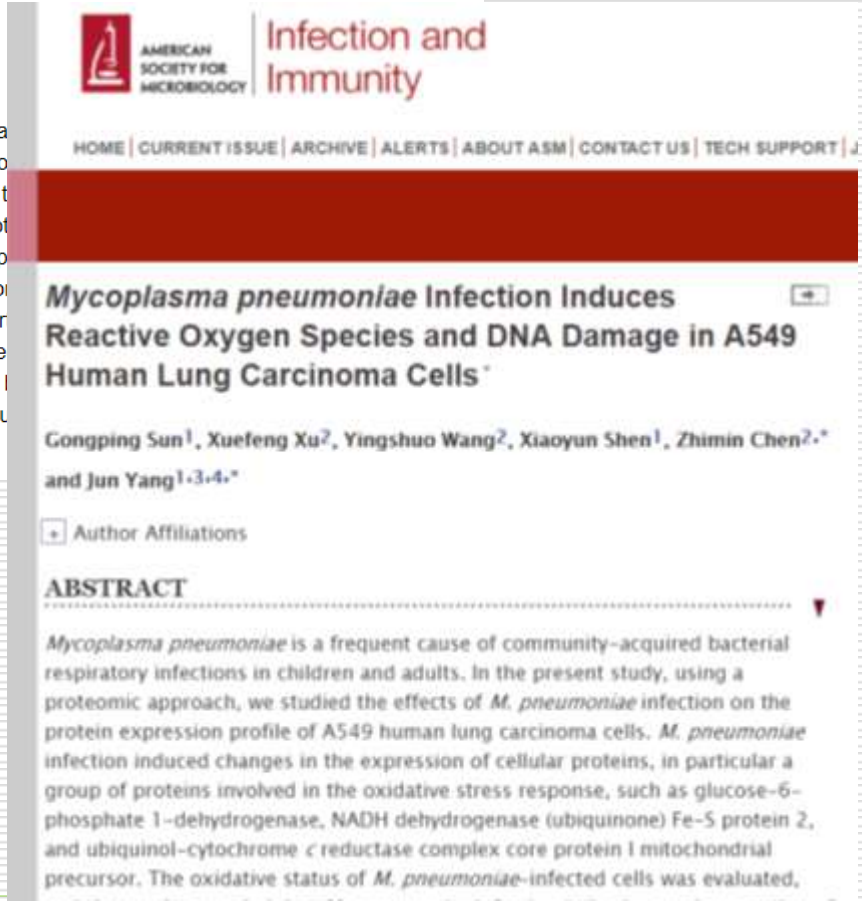
Mycoplasma infection transforms normal lung cells and induces bone morphogenetic protein 2 expression by post-transcriptional mechanisms.

Jiang S[1], Zhang S, Langenfeld J, Lo SC, Rogers MB.

Author information

Abstract

Bone morphogenetic protein 2 (BMP2) is an essential growth factor and morphogen, whose pa
influences development and physiology. We present the novel finding that mycoplasma infectio
lines of diverse types (mesenchymal, epithelial, and myeloid). Mycoplasma infection triggered t
protein in BEAS-2B cells (immortalized human bronchial epithelial cells), which normally do not
production in A549 cells (lung adenocarcinoma cells). Indeed, mycoplasma is as strong an exp
and retinoic acid. Second, we showed that post-transcriptional mechanisms including regulatio
mechanisms, contributed to the increased BMP2 expression in mycoplasma-infected cells. Fur
AS1411 that binds the post-transcriptional regulator nucleolin induced BMP2 exclusively in infe
proliferation in BEAS-2B cells transformed by chronic mycoplasma infection, as demonstrated
These findings have important implications regarding the effects of mycoplasma on BMP2-regu
differentiation, and apoptosis.



AMERICAN SOCIETY FOR MICROBIOLOGY | Infection and Immunity

HOME | CURRENT ISSUE | ARCHIVE | ALERTS | ABOUT ASM | CONTACT US | TECH SUPPORT

***Mycoplasma pneumoniae* Infection Induces Reactive Oxygen Species and DNA Damage in A549 Human Lung Carcinoma Cells**

Gongping Sun[1], Xuefeng Xu[2], Yingshuo Wang[2], Xiaoyun Shen[1], Zhimin Chen[2,*] and Jun Yang[1,3,4,*]

Author Affiliations

ABSTRACT

Mycoplasma pneumoniae is a frequent cause of community-acquired bacterial respiratory infections in children and adults. In the present study, using a proteomic approach, we studied the effects of *M. pneumoniae* infection on the protein expression profile of A549 human lung carcinoma cells. *M. pneumoniae* infection induced changes in the expression of cellular proteins, in particular a group of proteins involved in the oxidative stress response, such as glucose-6-phosphate 1-dehydrogenase, NADH dehydrogenase (ubiquinone) Fe-S protein 2, and ubiquinol-cytochrome *c* reductase complex core protein I mitochondrial precursor. The oxidative status of *M. pneumoniae*-infected cells was evaluated,

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Mycoplasma in metastases

Biochem Biophys Res Commun. 2014 Apr 4;446(2):620-5. doi: 10.1016/j.bbrc.2014.03.024. Epub 2014 Mar 15.

Detection of mycoplasma infection in circulating tumor cells in patients with hepatocellular carcinoma.

Choi HS[1], Lee HM[1], Kim WT[1], Kim MK[1], Chang HJ[2], Lee HR[3], Joh JW[4], Kim DS[5], Ryu CJ[6].

Author information

Abstract

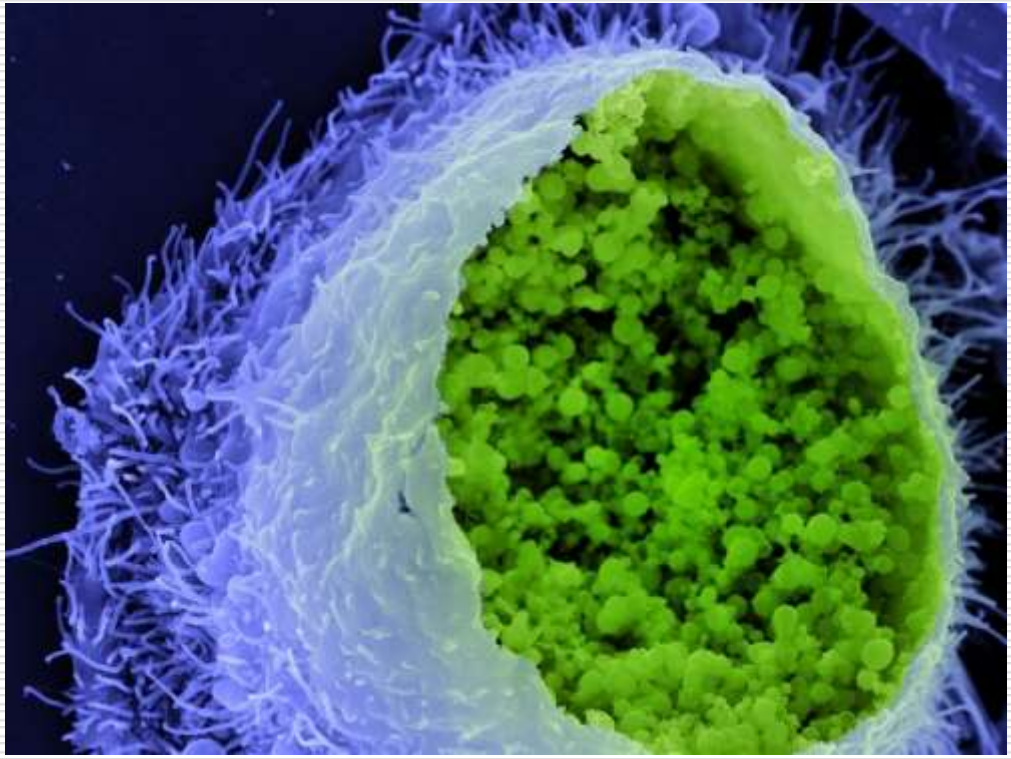
Many studies have shown that persistent infections of bacteria promote carcinogenesis and metastasis. Infectious agents and their products can modulate cancer progression through the induction of host inflammatory and immune responses. The presence of circulating tumor cells (CTCs) is considered as an important indicator in the metastatic cascade. We unintentionally produced a monoclonal antibody (MAb) CA27 against the mycoplasmal p37 protein in mycoplasma-infected cancer cells during the searching process of novel surface markers of CTCs. Mycoplasma-infected cells were enriched by CA27-conjugated magnetic beads in the peripheral blood mononuclear cells in patients with hepatocellular carcinoma (HCC) and analyzed by confocal microscopy with anti-CD45 and CA27 antibodies. CD45-negative and CA27-positive cells were readily detected in three out of seven patients (range 12-30/8.5 ml blood), indicating that they are mycoplasma-infected circulating epithelial cells. CA27-positive cells had larger size than CD45-positive hematological lineage cells, high nuclear to cytoplasmic ratios and irregular nuclear morphology, which identified them as CTCs. The results show for the first time the existence of mycoplasma-infected CTCs in patients with HCC and suggest a possible correlation between mycoplasma infection and the development of cancer metastasis.

KEYWORDS: Circulating tumor cell; Hepatocellular carcinoma; Metastasis; Monoclon

"The results show for the first time the existence of mycoplasma-infected CTCs in patients with HCC and suggest a possible correlation between mycoplasma infection and the development of cancer metastasis."

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Chlamydia trachomatis blocks apoptosis by destroying the p53 tumour suppressor gene



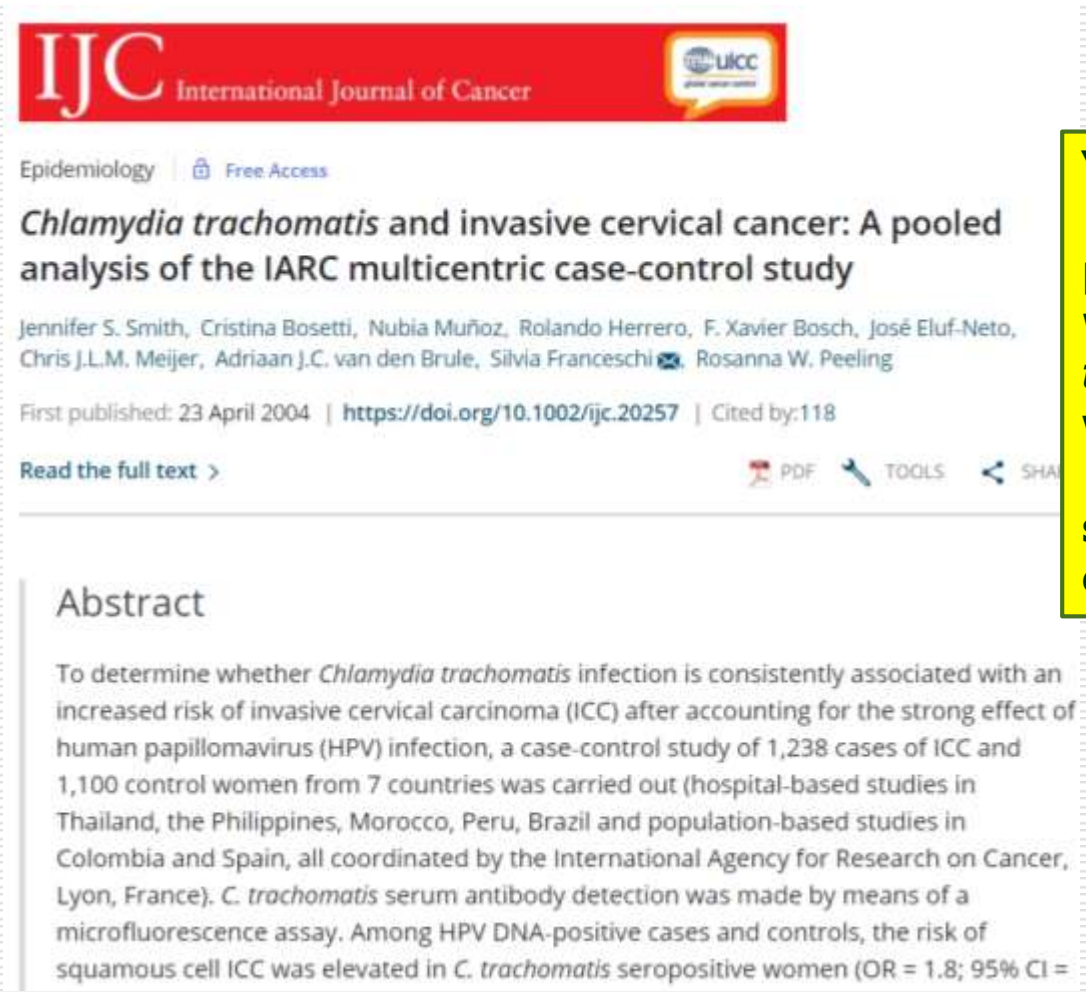
A research team at the Max Planck Institute for Infection Biology in Berlin has now observed the breakdown of an important endogenous protective factor in the course of chlamydial infection. **By activating the destruction of p53 protein, the bacterium blocks a key protective mechanism of infected cells, the initiation of programmed cell death. This protective function of p53 is also impaired in many forms of cancer.**

Chlamydia infection promotes host DNA damage and proliferation but impairs the DNA damage response.
Chumduri et al. Cell host & microbe, Vol: 13, Issue: 6, Page: 746-58, 2013

Source: http://www.cell.com/cell-host-microbe/pdf/S1931-3128(13)00193-5.pdf

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Chlamydia trachomatis is associated with a greater risk of invasive cervical cancer



IJC International Journal of Cancer

Epidemiology | Free Access

Chlamydia trachomatis and invasive cervical cancer: A pooled analysis of the IARC multicentric case-control study

Jennifer S. Smith, Cristina Bosetti, Nubia Muñoz, Rolando Herrero, F. Xavier Bosch, José Eluf-Neto, Chris J.L.M. Meijer, Adriaan J.C. van den Brule, Silvia Franceschi, Rosanna W. Peeling

First published: 23 April 2004 | https://doi.org/10.1002/ijc.20257 | Cited by:118

Read the full text > PDF TOOLS SHA

Abstract

To determine whether *Chlamydia trachomatis* infection is consistently associated with an increased risk of invasive cervical carcinoma (ICC) after accounting for the strong effect of human papillomavirus (HPV) infection, a case-control study of 1,238 cases of ICC and 1,100 control women from 7 countries was carried out (hospital-based studies in Thailand, the Philippines, Morocco, Peru, Brazil and population-based studies in Colombia and Spain, all coordinated by the International Agency for Research on Cancer, Lyon, France). *C. trachomatis* serum antibody detection was made by means of a microfluorescence assay. Among HPV DNA-positive cases and controls, the risk of squamous cell ICC was elevated in *C. trachomatis* seropositive women (OR = 1.8; 95% CI =

"This study, based on data from 1,238 case and 1,100 control participants in 7 countries worldwide, shows that ***C. trachomatis*** **serum antibodies were associated with a 1.8-fold increased risk of squamous cell invasive cervical cancer**."

Source: https://onlinelibrary.wiley.com/doi/abs/10.1002/ijc.20257

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Ehrlichia associated with myelodysplastic disease and leukaemia

ELSEVIER

Medical Hypotheses

Volume 85, Issue 6, December 2015, Pages 891-893

Could ehrlichial infection cause some of the changes associated with leukemia, myelodysplastic diseases and autoimmune disorders, and offer antibiotic treatment options?

Charles A. Kallick[a], Daniel A. Friedman[b], Mramba B.A. Nyindo[c]

Show more

https://doi.org/10.1016/j.mehy.2015.09.015

Abstract

We hypothesize that a large group of medical conditions of unknown etiology including leukemia, multiple myeloma, myelodysplastic and autoimmune disorders, may be associated with or caused by an obscure group of intracellular obligate parasitic bacteria named Ehrlichia/Anaplasma (EA). Ensconced in the stem cells of the bone marrow, EA may disrupt the normal development and function of many of the cells of immunity, manifesting itself as different syndromes. Recent studies of the activity of EA suggest direct effects on the immune system consistent with the manifestations of leukemia. We reference here three leukemia patients with direct or indirect evidence of EA infection. Moreover, EA have been

"Recent studies of the activity of EA [Ehrlichia/Anaplasma] suggest direct effects on the immune system consistent with the manifestations of leukemia"

"It is further hypothesized, moreover, that treatment of leukemia with antibiotics effective against EA would also result in beneficial impact. This has been tried. The results, cited below, hint at proof of EA infection as a cause of leukemia as well as a potentially important course of treatment."

Toxoplasma may increase the risk of brain cancer

THE ROYAL SOCIETY PUBLISHING | BIOLOGY LETTERS

ABOUT ▸ BROWSE BY SUBJECT ▸ ALERTS ▸ FREE TRIAL ▸

Biol Lett. 2012 Feb 23; 8(1): 101–103. PMCID: PMC325
Published online 2011 Jul 27. doi: 10.1098/rsbl.2011.0588

Incidence of adult brain cancers is higher in countries where the protozoan parasite *Toxoplasma gondii* is common

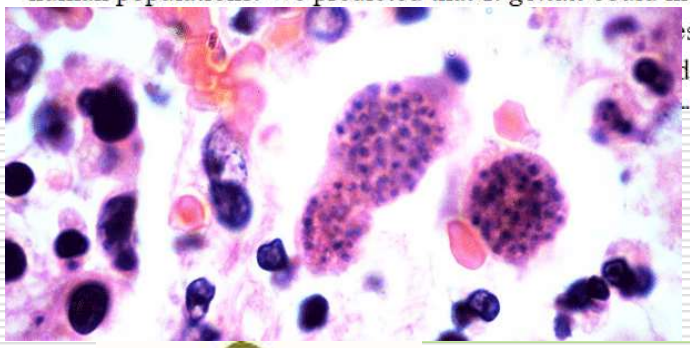
Frédéric Thomas,[1,*†] Kevin D. Lafferty,[2,†] Jacques Brodeur,[3] Eric Elguero,[1] Michel Gauthier-Clerc,[4] and Dorothé Missé[1]

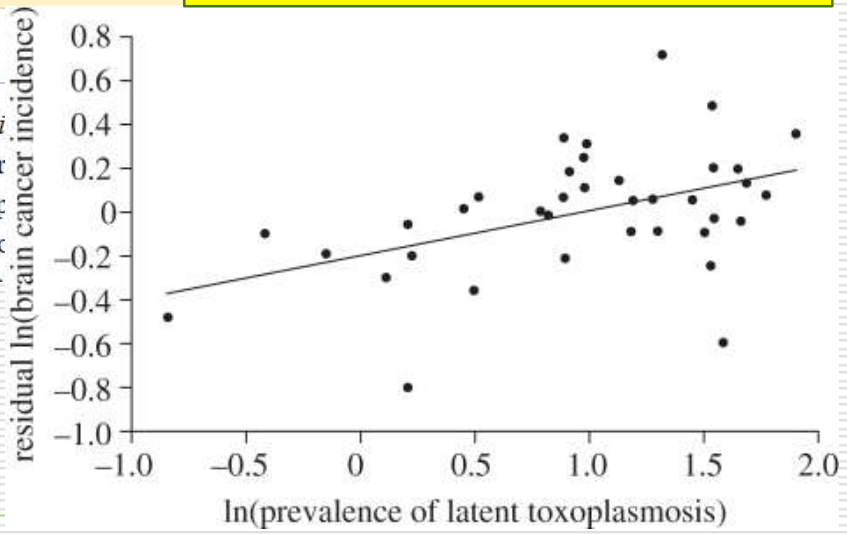
Author information ▸ Article notes ▸ Copyright and License information ▸

ABSTRACT

We explored associations between the common protozoan parasite *Toxoplasma gondii* human populations. We predicted that *T. gondii* could increase the risk of brain cancer s inflammation and inhibits ap dence of brain cancers and serc

"We predicted that T. gondii could increase the risk of brain cancer because it is a long-lived parasite that encysts in the brain, where it provokes inflammation and inhibits apoptosis. …
Infection with T. gondii was associated with a 1.8-fold increase in the risk of brain cancers across the range of T. gondii prevalence in our dataset (4-67%)."





arminlabs
DIAGNOSING TICK-BORNE DISEASES

Toxoplasmosis higher in patients with solid organ tumours

Toxoplasmosis: an overlooked infection in cancer patients

R.M. Wassef, R.R. Abdel Malek, E.M. Rizk, A.M. Boghdady

Annals of Oncology, Volume 27, Issue suppl_6, 1 October 2016, 1383P,
https://doi.org/10.1093/annonc/mdw387.20
Published: 11 October 2016

Background: Toxoplasmosis is a widespread disease caused by the Apicomplexan, coccidian protozoan *Toxoplasma gondii* (*T. gondii*). Human prevalence rates for toxoplasmosis vary greatly in different parts of the world ranging from 0% in North Alaska and Canada to 94% in Costa Rica and Guatemala. Once the host acquires the infection by ingestion, *T. gondii* crosses the intestinal epithelium, disseminates into the deep tissues and traverses biological barriers to reach sites where it causes severe pathology. Normally, the immune response efficiently prevents the dissemination of the parasite. In immunocompromised hosts, however, such reactivation may be more frequent, leading to a massive and potentially fatal recrudescence. Studies of prevalence of Toxoplasmosis in patients with neoplasms are scarce. This report represents the first prevalence study of Toxoplasmosis in cancer patients in Egypt.

Methods: Blood samples were collected from 150 immunocompromised patients having different types of malignancies as well as 50 immunocompetent individuals as a control group, to assess the seroprevalence of anti-*T.gondii* antibodies. The "CTK biotech Onsite Toxo IgG/IgM Rapid Test Cassettes" was used according to the manufacturer's enclosed manual for the detection of infection.

"Among cancer patients, prevalence of *T.gondii* was significantly higher (20% & 4% for IgG and IgM respectively) compared with controls (8% and 2%) (p = 0.003). **Toxoplasmosis was higher in patients having solid organ tumors (24%) than in patients with haematological malignancies (12%)** (p = 0.06)."

Source: Annals of Oncology (2016) 27 (6): 474-482. 10.1093/annonc/mdw387

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Which bacterial tests to consider, in which cancers?

Type of cancer	Bacterial tests to consider
Lymphoma	Borrelia (Elispot/Seraspot), Babesia (Elispot), Ehrlichia/Anaplasma (Elispot/IgG, IgM)
Monoclonal gammopathy	Bartonella (Elispot)
Leukaemia	Ehrlichia/Anaplasma (Elispot/ IgG, IgM) Coxiella (Q fever) (IgG, IgM)
Glioma/brain cancers	Borrelia (Elispot/Seraspot) Mycoplasma (Elispot/IgG, IgA) Toxoplasma (IgG, IgM)
Angiogenic tumours	Bartonella (Elispot)
Lung cancer	Chlamydia pneumoniae (Elispot/IgG, IgA), Mycoplasma (Elispot/IgG, IgA)
Prostate cancer	Chlamydia pneumoniae (Elispot/IgG, IgA), Mycoplasma (Elispot/IgG, IgA)
Oesophageal	Mycoplasma (Elispot/IgG, IgA)
Breast	Mycoplasma (Elispot/IgG, IgA) Bartonella (Elispot)
Metastases	Mycoplasma (Elispot/IgG, IgA)
Cervical cancer, downregulation of p53	Chlamydia trachomatis (Elispot/IgG, IgA)
Solid tumours (if cat owner/contact with cats)	Toxoplasma
General	CD3/CD57+

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Infectious Pathogens and Cancer: The Emerging Evidence

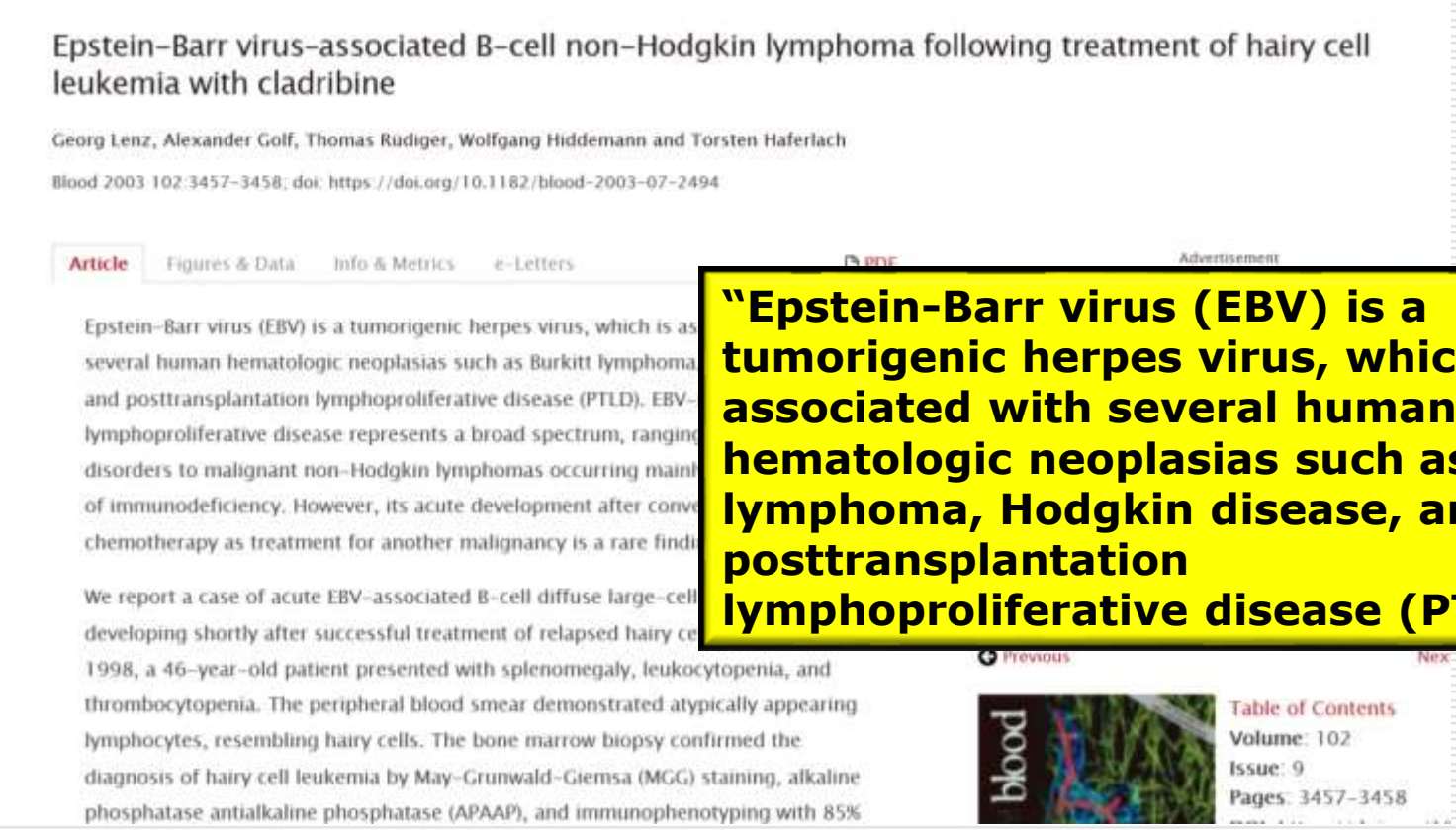
1. Stealth bacteria involvement

2. Viral involvement

- ▶Epstein Barr Virus
- ▶Cytomegalovirus
- ▶HHV6
- ▶Herpes Simplex Virus 1 & 2

3. Indirect involvement

Epstein Barr virus



Epstein–Barr virus–associated B–cell non–Hodgkin lymphoma following treatment of hairy cell leukemia with cladribine

Georg Lenz, Alexander Golf, Thomas Rüdiger, Wolfgang Hiddemann and Torsten Haferlach

Blood 2003 102:3457–3458; doi: https://doi.org/10.1182/blood-2003-07-2494

Article Figures & Data Info & Metrics e-Letters

Epstein–Barr virus (EBV) is a tumorigenic herpes virus, which is as
several human hematologic neoplasias such as Burkitt lymphoma
and posttransplantation lymphoproliferative disease (PTLD). EBV–
lymphoproliferative disease represents a broad spectrum, ranging
disorders to malignant non–Hodgkin lymphomas occurring mainl
of immunodeficiency. However, its acute development after conv
chemotherapy as treatment for another malignancy is a rare findi

We report a case of acute EBV–associated B–cell diffuse large–cell
developing shortly after successful treatment of relapsed hairy ce
1998, a 46–year–old patient presented with splenomegaly, leukocytopenia, and
thrombocytopenia. The peripheral blood smear demonstrated atypically appearing
lymphocytes, resembling hairy cells. The bone marrow biopsy confirmed the
diagnosis of hairy cell leukemia by May–Grunwald–Giemsa (MGG) staining, alkaline
phosphatase antialkaline phosphatase (APAAP), and immunophenotyping with 85%

Advertisement

Previous Nex

blood

Table of Contents
Volume: 102
Issue: 9
Pages: 3457–3458

"Epstein-Barr virus (EBV) is a tumorigenic herpes virus, which is associated with several human hematologic neoplasias such as Burkitt lymphoma, Hodgkin disease, and posttransplantation lymphoproliferative disease (PTLD)"

*Source: * Ramesh G et al. Interaction of the Lyme Disease Spirochete Borrelia burgdorferi with Brain Parenchyma Elicits Inflammatory Mediators from Glial Cells as Well as Glial and Neuronal Apoptosis. Am J Pathol. 2008 Nov; 173(5): 1415–1427*

arminlabs
DIAGNOSING TICK-BORNE DISEASES

B-Cell Non-Hodgkin's Lymphoma: EBV/CMV

- **Epstein Barr Virus-associated Non-Hodgkin's lymphoma of B-cell origin, Hodgkin's disease, acute leukemia, and systemic lupus erythematosus: a serologic and molecular analysis, Mitarnun W, Pradutkanchana J, Takao S, Saechan V, Suwiwat S, Ishida T** http://www.ncbi.nlm.nih.gov/pubmed/12188384
- **EBV-Associated Lymphoproliferative Disorders: Classification and Treatment, Carbone A, Annunziata G, Dotti, G, The oncologist** 1083-7159/2008
- **Cytomegalovirus infection in patients with lymphoma: an important cause of morbidity and mortality. Torres HA, Kontoyiannis DP, Aguilera EA, Younes A, Luna MA, Tarrand JJ, Nogueras GM, Raad II, Chemaly RF. Clin. Lymphoma Myeloma, 2006 Mar;6(5): 393-8**

History of the discovery of EBV points to its tumorigenic origin

(1932). They attempted to define the specificity of this observation by examining control sera. One of these showed a very high titer of such agglutinins, and was found to be from an IM patient. This led to the discovery of the so-called "heterophile antibodies (HA)," which evolved into a diagnostic test for IM. Attempts to transmit the disease to other humans or animals were inconsistently successful and further advances had to wait several decades.

In 1946, a British colonial surgeon, Denis Burkitt, was assigned to a post in Uganda, where he took care of a population of 250,000 people. In 1957, he was asked to see a child with a peculiar mass in the jaw, which rendered him "totally baffled." He saw other such cases and reviewed the hospital records for other cases. These showed that the tumor, a lymphoma, often affected the internal organs and the nervous system, rather than lymph nodes. He sent questionnaires to clinics around the continent using mails, and was able to establish the geographic distribution of this tumor, and noted that it overlapped the distribution of malaria and yellow fever, as well as an epidemic of o'nyong nyong fever. The fact that the geographical distribution of Burkitt's lymphoma (BL) overlapped that of several mosquito-borne diseases suggested the possibility that the disease was transmittable. Burkitt gave several talks about his findings on a visit to London, and Anthony Epstein, a virologist interested in tumor viruses, was present. He had Burkitt send him samples of the tumors and was able to detect a herpes-like virus by electron microscopy. However, the virus could not be cultured. For more accurate characterization of the virus, samples were sent to the laboratory of Werner and Gertrude Henle. They were able to show that antibodies to the Epstein–Barr virus (EBV) were present not only in pediatric oncology patients, but also were common in the general population. The first connection between EBV and a specific disease was made when a technician in

Epstein–Barr Virus and Cytomegalovirus Infections 25

the Henles' laboratory, who was seronegative, developed IM. Her serum, previously used as a negative control, became strongly seropositive (Henle et al. 1968). This observation provided the impetus for the studies of college students by Niederman et al. (1968) in which the etiologic role of EBV in IM was established. The role of EBV was then established in a number of tumors. This includes BL, a number of B

"The fact that the geographical distribution of Burkitt's lymphoma (BL) overlapped that of several mosquito-borne diseases suggested the possibility that the disease was transmittable. Burkitt gave several talks about his findings on a visit to London, and Anthony Epstein, a virologist interested in tumor viruses, was present. He had Burkitt send him samples of the tumors and was able to detect a herpes-like virus by electron microscopy."

Source: Epstein-Barr Virus and Cytomegalovirus infections Alex Tselis

EBV/CMV and tumours

(1932). They attempted to define the specificity of this observation by examining control sera. One of these showed a very high titer of such agglutinins, and was found to be from an IM patient. This led to the discovery of the so-called "heterophile antibodies (HA)," which evolved into a diagnostic test for IM. Attempts to transmit the disease to other humans or animals were inconsistently successful and further advances had to wait several decades.

In 1946, a British colonial surgeon, Denis Burkitt, was assigned to a post in Uganda, where he took care of a population of 250,000 people. In 1957, he was asked to see a child with a peculiar mass in the jaw, which rendered him "totally baffled." He saw other such cases and reviewed the hospital records for other cases. These showed that the tumor, a lymphoma, often affected the internal organs and the nervous system, rather than lymph nodes. He sent questionnaires to clinics around the continent using mails, and was able to establish the geographic distribution of this tumor, and noted that it overlapped the distribution of malaria and yellow fever, as well as an epidemic of o'nyong nyong fever. The fact that the geographical distribution of Burkitt's lymphoma (BL) overlapped that of several mosquito-borne diseases suggested the possibility that the disease was transmittable. Burkitt gave several talks about his findings on a visit to London, and Anthony Epstein, a virologist interested in tumor viruses, was present. He had Burkitt send him samples of the tumors and was able to detect a herpes-like virus by electron microscopy. However, the virus could not be cultured. For more accurate characterization of the virus, samples were sent to the laboratory of Werner and Gertrude Henle. They were able to show that antibodies to the Epstein–Barr virus (EBV) were present not only in pediatric oncology patients, but also were common in the general population. The first connection between EBV and a specific disease was made when a technician in

the Henles' laboratory, who was seronegative, developed IM. Her serum, previously used as a negative control, became strongly seropositive (Henle et al. 1968). This observation provided the impetus for the studies of college students by Niederman et al. (1968) in which the etiologic role of EBV in IM was established. The role of EBV was then established in a number of tumors. This includes BL, a number of B

"The role of EBV was then established in a number of tumors"

Source: Epstein-Barr Virus and Cytomegalovirus infections Alex Tselis

EBV: Latency antigens associated with various types of cancer

Table 1 Latency antigens and types

Latency type	Latency antigens						
	EBER	EBNA-1	EBNA-2	EBNA-3	LMP-1	LMP-2	BARTs
1	+	+	–	–	–	–	+
2	+	+	–	–	+	+	+
3	+	+	+	+	+	+	+
Other	+	+/–	–	–	–	+	+/–

Latency types	
Latency 1	Burkitt's lymphoma
Latency 2	Nasopharyngeal carcinoma, Hodgkin's disease
Latency 3	Infectious mononucleosis, lymphoproliferative disease
Other	Perpheral blood B lymphocytes

EBER Epstein–Barr virus-encoded RNA, *EBNA* Epstein–Barr nuclear antigen, *LMP* Latent membrane protein, *BART* BamHI A rightward transcripts

The pathogenesis of encephalitis (or meningitis or hepatitis or other focal visceral involvement) is not completely clear and there are several possibilities, which are not mutually exclusive. First, EBV may affect neurons (or other neural cells or endothelium) directly (Jones et al. 1995). There have been a few scattered reports of neurons and glial cells staining with EBV antigens, although there is not much detail (Biebl et al. 2009). In some patients with EBV encephalitis, as well as some with primary CNS lymphoma, lytic EBV mRNA was detected in the CSF, suggesting lytic replication of EBV in the brain in addition to latent replication (Weinberg et al. 2002a). Secondly, EBV-infected B cells are in an activated state and elaborate several proinflammatory cytokines, which can cause injury of the surrounding parenchyma (Foss et al. 1994). This injury is not necessarily irreversible. Third, EBV-infected B cells are actively attacked by EBV-specific cytotoxic T cells, and this can also injure the surrounding parenchyma. Finally, an acute disseminated encephalomyelitis can be triggered as in other viral infections.

Normally, EBV-infected B cells are suppressed (though not eliminated) by the immune system and lymphoproliferation can result during immunosuppression. In tissue culture in which T cells have been eliminated, B cells are immortalized and proliferate. In vivo, the B cell lymphoproliferation proceeds sequentially from polyclonal to oligoclonal to monoclonal, and evolves into a lymphoma. This can occur under circumstances of immunosuppression in transplant, chemotherapy, and AIDS patients as mentioned above. The lymphoproliferation can be accompanied by the elaboration of various cytokines, and a severe systemic illness resembling

Different latencies associated with Burkitt's lymphoma, nasopharyngeal carcinoma, Hodgkin's disease, lymphoproliferative disease

Source: Epstein-Barr Virus and Cytomegalovirus infections Alex Tselis

"How EBV causes blood cancer", study, University of Sussex - report November 2016

Scientists reveal how a common virus triggers blood cancer

Scientists at the University of Sussex, trying to uncover how the common Epstein-Barr virus causes blood cancer in adults and children, have discovered how the virus takes control of two genes involved in cancer development so it can switch them on or off.

The research team, led by Professor Michelle West, set out to determine how the Epstein-Barr virus controls two genes; *MYC*, a gene known to drive cancer development when it is altered or switched on at high level and *BCL2L11*, a gene which normally triggers cell death to prevent cancer, but can be turned off by the virus.

With thanks to funding from the blood cancer charity Bloodwise, the scientists discovered that the virus controls the *MYC* and *BCL2L11* genes by hijacking 'enhancer' DNA regions which are situated far away from the genes. These enhancers act as 'control centres' and are able to contact and control genes from long distances by the looping out of the intervening stretches of DNA.

Professor Michelle West

Professor West's team found that Epstein-Barr virus turns on the *MYC* gene by increasing contacts between a specific set of enhancers and the gene. The scientists believe this may explain how the virus causes the changes to the *MYC* gene that are found in Burkitt's lymphoma.

The team also discovered new enhancers which control the *BCL2L11* gene. In this case, they found that Epstein-Barr virus stops these control centres from contacting the gene. Encouragingly the team have discovered that this blocking effect can be reversed by using a specific drug - paving the way for new treatments.

Professor West said: "This is a key step towards uncovering how this common virus which, affects thousands of people every year, causes blood cancer.

"It is now important to carry out further studies to c ... tell us more about how the virus drives lymphoma developmen ... ugs."

Dr Alasdair Rankin, Research Director at Bloodwis ... a, but we were never sure of the exact mechanisms. These ... e behaviour of genes that control cancer growth.

Professor West said: "This is a key step towards uncovering how this common virus which, affects thousands of people every year, causes blood cancer."

"By mapping out the complex genetic interactions that help lymphoma cells grow and survive, this research can guide the design of new treatments to target the disease. It may also help to identify those drugs currently used to treat other diseases that could be effective in treating these types of lymphoma."

HHV6 and Hodgkin's disease

Human herpesvirus-6 (HHV-6) in Hodgkin's disease: Cellular expression of viral antigens as compared to oncogenes met and fes, tumor suppressor gene product p53, and interleukins 2 and 6

Article in In vivo (Athens, Greece) 8(4):501-16 · July 1994 with 9 Reads
Source: PubMed

Gerhard Richard Krueger
43.68 · University of Texas Health Science Center at Houston

R Knuefermann

+ 5

"Patients with Hodgkin's disease (HD) frequently show elevated serum titers against human herpersvirus-6 (HHV-6) and their tissues contain significantly increased numbers of cells with HHV-6 DNA."

Abstract

Patients with Hodgkin's disease (HD) frequently show elevated serum titers against human herpersvirus-6 (HHV-6) and their tissues contain significantly increased numbers of cells with HHV-6 DNA. This may coincide with similar data of Epstein-Barr virus (EBV) infections. According to in vitro studies, Hodgkin- and Reed-Sternberg (RS) cells can be infected by HHV-6 and may be coinfected by HHV-6 and EBV. Both viruses are potentially oncogenic and also may interfere with the production of various cytokines. We now demonstrate by using immunohistological methods that HHV-6 antigens are present in 77.3% of the HD lymphomas, 37% of which contain the replication-associated p41 "early-late" antigen and 63% the late membrane antigen complex gp116/64/54. Monocytic cell populations including HD and RS cells are most frequently antigen-positive, while lymphoid cells are less frequently. These cells also express IL-6 and IL-6 receptors as well as the IL-2 receptor a chain (CD25), while only occasionally the IL-2 receptor beta chain (p70). IL-6 receptors are significantly more frequently expressed than IL-6 itself. HD and RS cells constitute a significant pool of proliferating cells as reflected by their 95% positivity for PCNA, yet tumor suppressor genes are found in only 21% and the proto-oncogenes fes and met are expressed in various types of cells. The data may indicate that both viruses possibly contribute to the course of the disease through polyclonal stimulations of cell proliferation and coincident dysregulation of the cytokine network control of cell function and proliferation. A direct oncogenic effect of EBV and HHV-6 in HD appears less probable.

Source: Krueger et al. Human herpesvirus-6 (HHV-6) in Hodgkin's disease: cellular expression of viral antigens as compared to oncogenes met and fes, tumor suppressor gene product p53, and interleukins 2 and 6. In Vivo. 1994 Jul-Aug;8(4):501-16

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Herpes viruses and blood cancers: tests suggested

1. EBV EliSpot
2. EBV IgG/IgM, anti-EBNA antibodies and early antigen
3. CMV IgG/IgM
4. CMV EliSpot
5. HHV6 IgG/IgM
6. CD3/CD57+ cells

Link between HSV1 and oral cancer well established; HSV2 and cervical cancer more equivocal

J Clin Diagn Res. 2016 Aug;10(8):ZC14-7. doi: 10.7860/JCDR/2016/18593.8229. Epub 2016 Aug 1.

Assesment of Correlation of Herpes Simplex Virus-1 with Oral Cancer and Precancer- A Comparative Study.

Jain M[1]

Author information

Abstract

INTRODUCTION: Most common malignant neop... enhance the development of oral carcinoma in ... and cigarette smoking and so must be consider...

AIM: To assess and compare the correlation of ...

MATERIALS AND METHODS: The study compr... group. Their blood samples were collected and ...

RESULTS: There was statistically insignificant difference between the HSV-1 IgG level in cancer and precancer but statistically sign... difference was found between the HSV-1 IgG level among control group and cancer/precancer.

CONCLUSION: The present study clearly indicates that quantitative estimation of IgG antibody against HSV-1 in cancer/precancer ... will give the clue in the etiology of cancer or precancer. However, further studies with a large sample size should be carried out to d... the role of HSV-1 in etiology of oral cancer and precancer.

"The present study clearly indicates that quantitative estimation of IgG antibody against HSV-1 in cancer/precancer patients will give the clue in the etiology of cancer or precancer."

News > Medscape Medical News

HSV-2 Infection Increases Risk of Invasive Cervical Carcinoma

Laurie Barclay, MD

November 06, 2002

Nov. 6, 2002 — Herpes simplex virus 2 (HSV-2) can be a cofactor with the human papillomavirus (HPV) in the development of cervical carcinoma, according to a pooling of case-control studies reported in the Nov. 6 issue of the *Journal of the National Cancer Institute*. The editorialist agrees and sheds additional light on the association of sexually transmitted diseases and cancer.

"Although HSV-2 infection may act in conjunction with HPV infection to increase the risk of invasive cervical cancer, the effect of HSV-2 infection on invasive cervical cancer risk is modest compared with the strong effect of HPV infection on invasive cervical cancer risk," write Jennifer S. Smith, PhD, and colleagues from the International Agency for Research on Cancer (IARC) Multicentric Cervical Cancer Study Group.

Using blood and cervical specimens from 1,263 women with cervical cancer and 1,117 women without cervical cancer, the investigators detected HSV-2 antibodies in the blood of 44.4% of women with squamous-cell carcinoma (95% confidence interval [CI], 41.5%-47.3%), 43.8% of women with adenocarcinoma

Herpes Simplex Virus Type II (HSV-2) is not a Cofa... Papillomavirus in Cancer of the Uterine Cervix

Article in American Journal of Obstetrics and Gynecology 188(1):129-34 · February 2003 with 141 Reads

DOI: 10.1067/mob.2003.86 · Source: PubMed

Cite this publication

Abstract

Cells that were cotransfected with herpes simplex virus-16 and the herpes simplex virus type 2 Xho -2 DNA induce tumors in nude mice. In a cross-sectional study, we investigated the role of herpes simplex virus type 2 as a cofactor to human papillomavirus in cervical cancer. Cervical cells that were obtained with an endocervical Cytobrush brush (Medscand) from 439 women (50 women with cancer lesions, 65 women with high-grade squamous intraepithelial lesions, 80 women with low-grade squamous intraepithelial lesions, 244 healthy subjects) and DNA that was extracted from 150 cervical cancer biopsy specimens were analyzed with polymerase chain reaction for herpes simplex virus type 2 Xho -2 and Bgl IIC transforming DNA sequences. All 439 cervical samples and 150 cervical cancer biopsy specimens tested negative for herpes simplex virus type 2 Xho -2 and Bgl IIC DNA by polymerase chain reaction. Overall, none of 200 samples (0%) from women with invasive cervical cancer contained herpes simplex virus type 2 Xho -2 or Bgl IIC DNA (95% CI, 0.0-1.8). Although herpes simplex virus type 2 Bgl IIN transforms epithelial cells in vitro, it was not detected in cervical cancer specimens.

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Infectious Pathogens and Cancer: The Emerging Evidence

1. Bacterial involvement

2. Viral involvement

3. Indirect involvement:

…. these stealth pathogens indirectly cause a conducive environment to multiple diseases, including cancer …

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Borrelia – and other intracellular bacterial/viral infections – cause mitochondrial dysfunction

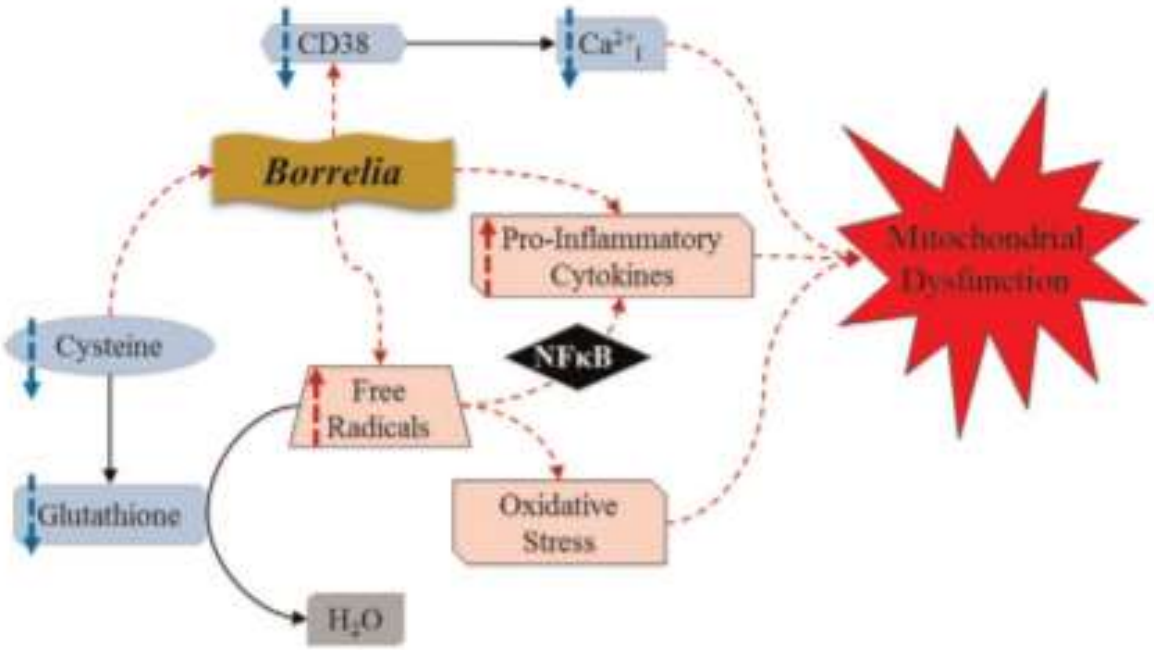


Fig. 3. Proposed scheme of the effect of *Borrelia* infection on metabolic and signaling pathways within host cells. This scheme shows the cells normal processes (solid arrows) used to scavenge free radicals and maintain calcium homeostasis. The proposed effect of *Borrelia* infection is shown (dashed arrows) by the induced state of oxidative stress, disrupted calcium homeostasis, increased pro-inflammatory cytokines, and ultimately, mitochondrial dysfunction.

"The results suggest that oxidative stress and interrupted intracellular communication may ultimately contribute to a condition of mitochondrial dysfunction in the immune cells of Lyme borreliosis patients." …

… potentially contributing to cancer, as we have heard from other speakers today

Source: Peacock BN et al. New insights into Lyme disease. Redox Biology. 2015;5:66-70.

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Indirect links: unfortunately a perfect physiological storm

Borrelia	**Oxidative stress causes damage to DNA, proteins and lipids** **Utilises host purines (ATP)** **Depletes cell and mitochondrial membranes** **Upregulates mitochondrial superoxide levels** **This together can cause huge inflammation**
Babesia	Infects erythrocytes = can cause **haemolysis** and intravascular coagulation = **hypoxia** thrombocytopenia = **immunosuppression**
Bartonella	Parasitised erythrocytes sequestered by the spleen = immunosuppression
Mycoplasma	Prefers low-oxygen environments, stimulates ROS, which causes **damage to cell membranes – membrane potential is lost**
Ehrlichia	Infects leukocytes = immunosuppression
Anaplasma	Infects granulocytes = immunosuppression
All these steath pathogens …	… cause inflammation, as inflammation breaks down tissues and allows the bacteria to gain access to the host's resources Interfere with/disable the host's immune system, **upregulate cytokines**, **trigger ROS/RNS** … **shift host's immune response from Th1 (intracellular) towards Th2 (extracellular)** to distract attention from their location – **but Th2 is conducive to cancer**

Sources: All available on request

arminlabs
DIAGNOSING TICK-BORNE DISEASES

Thank you very much for your attention!

arminlabs
DIAGNOSING TICK-BORNE DISEASES

AONM
ACADEMY OF NUTRITIONAL MEDICINE

For tests, please go to
www.aonm.org
https://aonm.org/arminlabs

or call the AONM helpline
on 0333 121 0305