Which test for which virus?

Nutritional Therapists of Ireland (NTOI)
Spotlight on Chronic Infections

Green Isle Hotel, Dublin, 13th April 2019

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ACADEMY of NUTRITIONAL MEDICINE

Agenda

The shortcomings of antibody testing

- CD3/CD57+
- EliSpot (Interferon Gamma Release Assay)

Specific viruses/associated conditions

- Herpes viruses: EBV, CMV, HSV 1/2, VZV, HHV6
- Enteroviruses: Coxsackie A&B, Echovirus
- Parvovirus

Checklists: Aid in test selection

Agenda

The shortcomings of antibody testing

Falling "between the cracks" with IgM and IgG testing

ENDOCRINOLOGY

Cytomegalovirus Ab(IgG)	183.0	AU/ml	
	< 6.0 AU/mL is considered non-reactive		
	>=6.0 AU/mL is considered reactive		
Cytomegalovirus Ab(IgM)	Negative		
Comment	Result suggestive of previous CMV infection.		

IMMUNOLOGY

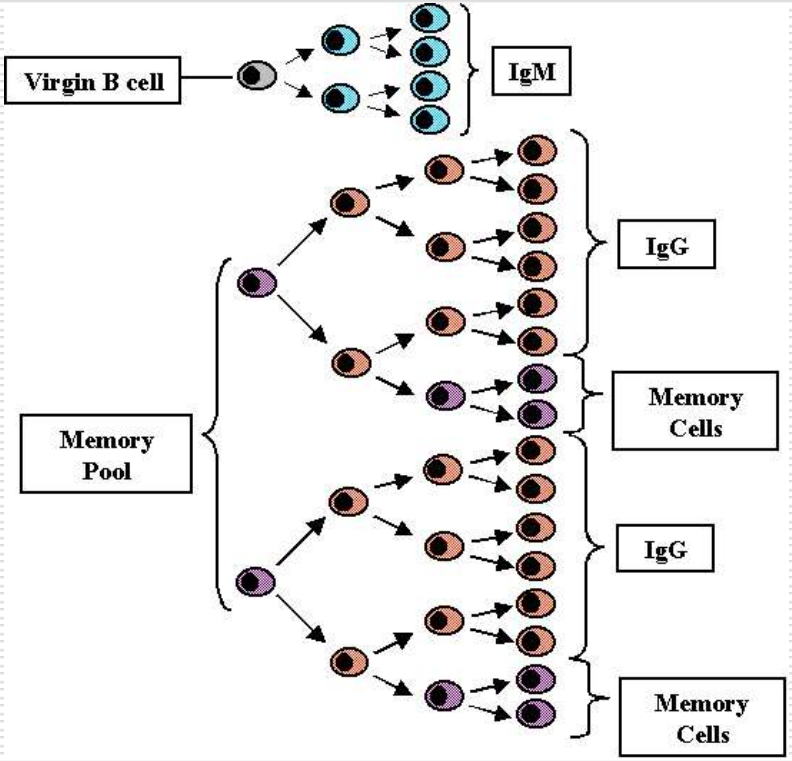
Epstein-Barr virus screen			
EBNA IgG antibody	* 36	U/ml	(< 5 U/ml Negative)
EBV Early Ag ab.(IgG)	<5	U/ml	(<10 U/ml Negative)
EBV VCA ab.(IgM)	<10	U/ml	(<20 U/ml Negative)
Comment	Results suggestive of past (latent) EBV infection.		

"IgG is produced in a delayed response to an infection and can be retained in the body for a long time …. Detection of IgG usually indicates a prior infection or vaccination."

Source: http://www.microbiologybook.org/mayer/Ab%20formation2000.htm

Falling between the cracks with IgM and IgG testing

In the primary response, the major class of antibody produced is IgM, whereas in the secondary response it is IgG (or IgA or IgE). The antibodies that persist in the secondary response are the IgG antibodies.



"Decline phase
The decline phase is not as rapid and antibodies may persist for months, years or even a lifetime."

Source: http://www.microbiologybook.org/mayer/Ab%20formation2000.htm; http://www.microbiologybook.org/mayer/ab1-8.jpg

Studies can be found using "at least fivefold rise" in IgG levels as a sign of viral reactivation – take max rr

Lupus. 2018 Jul;27(8):1271-1278. doi: 10.1177/0961203318770535. Epub 2018 Apr 18.

Longitudinal analysis of varicella-zoster virus-specific antibodies in systemic lupus erythematosus: No association with subclinical viral reactivations or lupus disease activity.

Rondaan C[1], van Leer CC[2], van Assen S[3], Bootsma H[1], de Leeuw K[1], Arends S[1], Bos NA[1], Westra J[1].

Author information

Abstract

Systemic lupus erythematosus (SLE) patients are at high risk of herpes zoster. Previously, we found increased immunoglobulin (Ig)G levels against varicella-zoster virus (VZV) in SLE patients compared to controls, while antibody levels against diphtheria and cellular immunity to VZV were decreased. We aimed to test our hypothesis tha
caused by stress because of lupus disease activity or imm
IgG and VZV-DNA were longitudinally determined in the se
polymerase chain reaction. Clinical data were retrieved fro
VZV-IgG or presence of VZV-IgM or VZV-DNA. Generalize
between antibody levels, lupus disease activity and medica
stranded DNA and complement levels were used as indicators of lupus disease activity. Results A VZV reactivation was determined in 11 patients (33%). In at least five of them, herpes zoster was clinically overt. No association between SLE disease activity or medication use and VZV-specific antibody levels was found. There was a weak association between total IgG and VZV-IgG. Conclusions Our results indicate that increased VZV-IgG levels in SLE do not result from frequent subclinical VZV reactivations, and are not associated with lupus disease activity. Increased VZV-IgG can only partially be explained by hypergammaglo

KEYWORDS: Systemic lupus erythematosus; herpes zoster; humoral immunity

"Reactivation of VZV was defined as an at least fivefold rise in VZV-IgG or presence of VZV-IgM or VZV DNA."[1]

"…reactivation of VZV (defined as a fivefold increase in the IgG antibody titer)"[2]

Source: 1. Rondaan, Christien & C van Leer, C & van Assen, S & Bootsma, H & de Leeuw, K & Arends, S & Bos, Nicolaas & Westra, J. (2018). Longitudinal analysis of varicella-zoster virus-specific antibodies in systemic lupus erythematosus: No association with subclinical viral reactivations or lupus disease activity. Lupus. 27. 2. http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.858.3795&rep=rep1&type=pdf;

Example: VZV reactivation

VZV IgG-/IgA-/IgM-antibodies

3	VZV IgG antibodies (ELISA)	positive	975,6 IE/l
	<80 IE/l	negative	
	>80 - < 110 IE/l	weak	
	>110 IE/l	positive	

Titers – a different perspective, also suspected reactivation

Analysis		Result	Units	Reference Range	Chart
HHV6-IgG-/IgM-antibodies					
4 **HHV6 IgG-antibodies (IFT)**	**+**	**1:1000**		**< 1:10**	**[..... *>**
4 HHV6 IgM-antibodies (IFT)		<1:10		< 1:10	[....*...]

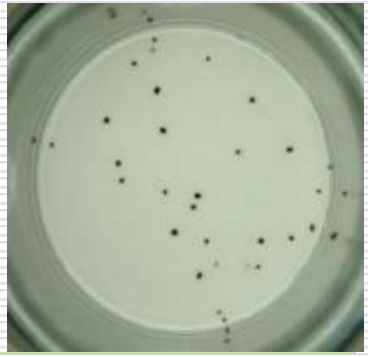
The specific Human Herpes Virus 6 (HHV6)-IgG-antibodies indicate humoral immune-response against Human Herpes Virus 6 (HHV6).

validated by
Dr.Armin Schwarzbach

EliSpot (Interferon-Gamma Release Assay)

Reflects the **current T-cellular activity** of bacteria and viruses

- **T-Cell-Spot/IGRA was approved by the FDA in May 2011 for M. tuberculosis**
- **"… A positive result suggests that an infection is likely, a negative result suggests that an infection is unlikely…."**
  "…Results can be available within 24 hours…"

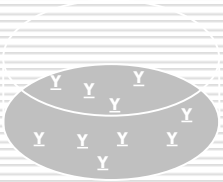


Laboratory tests for Cytomegalovirus

Using T-cells to show a cellular response against Lyme antigens is much more sensitive, and indicates active infection (in contrast to antibodies, which can remain for months or years long after an infection is gone). EliSpot (enzyme-linked immunosorbent spot) technology has long been used in Germany to do exactly this: it quantifies T-cells that secrete signature proteins (such as a given cytokine) against a specific antigen. The Borrelia EliSpot evaluates the number of spot-forming units using a stimulation index (SI) based on IGRA (Interferon Gamma Release Assay),

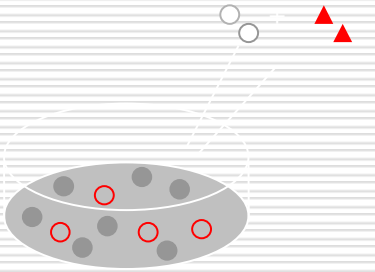
Source: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3856678/

Elispot LTT: The principle (I)



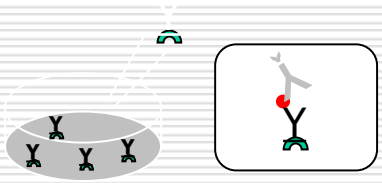
EliSpot well coated with monoclonal, cytokine-specific antibodies (IFNy, IL10, etc.)

Lymphocyte isolation

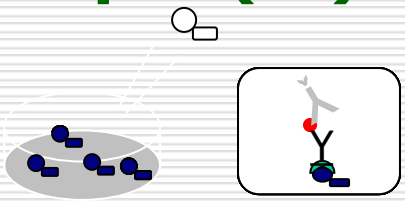


Incubation with cells and antigen: specific cells release cytokines

Elispot LTT: The principle (II)

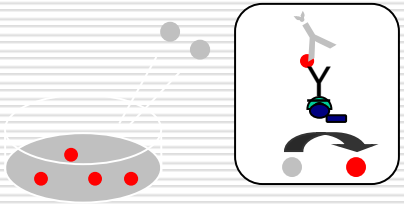


Add biotinylated secondary antibody complex: pr.AB/Cytokine/sec.AB



Add Streptavidin-enzyme conjugate

Analysis



Add substrate for colour development

The EliSpot (T-cell) test is currently available for:

- Borrelia burgdorferi (3 subspecies: B.b. sensu stricto + B.b. garinii + B.b. afzelii)
- Borrelia myamotoi
- Bartonella
- Babesia
- Chlamydia pneumoniae and trachomatis
- Mycoplasma pneumoniae
- Ehrlichia/Anaplasma
- Yersinia enterocolitica
- Epstein Barr Virus (EBV): lytic and latent
- Cytomegalovirus (CMV): lytic and latent
- Herpes Simplex Virus 1 / 2
- Varicella Zoster Virus (VZV)
- HHV-6, HHV-7, HHV-8

Also:
Candida
Aspergillus niger

Epstein Barr Virus (EBV)

Virus: Epstein Barr Virus, (obligate intracellular) double-stranded DNA virus, one of the Herpes viruses, also known as glandular fever, Mononucleosis/"Mono"

Transmission: "kissing disease", saliva, drinking from the same glass, toothbrush, blood, sex, blood transfusion, organ transplants

Symptoms (incubation period of several weeks): fatigue, fever, flu-like symptoms, nausea, loss of appetite, lymphadenitis (swollen lymph nodes in the neck), rash, sore throat, weakness, sore muscles

Complications: enlarged spleen, swollen liver, association with Non-Hodgkins Lymphoma, Multiple Sclerosis (MS)

EBV and SLE

Arthritis Research & Therapy

RESEARCH ARTICLE | OPEN ACCESS

Patients with systemic lupus erythematosus have abnormally elevated Epstein–Barr virus load in blood

Uk Yeol Moon[†], Su Jin Park[†], Sang Taek Oh, Wan-Uk Kim, Sung-Hwan Park, Sang-Heon Lee, Chul-Soo Cho, Ho-Youn Kim, Won-Keun Lee and Suk Kyeong Lee

[†] Contributed equally

Arthritis Res Ther 2004 **6**:R295 | **DOI:** 10.1186/ar1181

Received: 4 November 2003 | **Accepted:** 1 April 2004 | **Published:** 7 May 2004

Abstract

Various genetic and environmental factors appear to be involved in systemic lupus erythematosus (SLE). Epstein–Barr virus (EBV) is among the environmental factors that are suspected of predisposing to SLE, based

Epstein-Barr virus, cytomegalovirus, and multiple sclerosis susceptibility

"The consistency of EBNA-1 sero-positivity with MS across racial/ ethnic groups and between studies points to a strong biological link between EBV infection and MS risk."

A multiethnic study

1.Annette Langer-Gould, MD, PhD, Jun Wu, MD, MS, Robyn Lucas, PhD, Jessica Smith, MPH, Edlin Gonzale
MS, Lie Hong Chen, DrPH, Hong Quach, BA, Judith A. James, MD, Lisa F. Barcellos, PhD and Anny H. Xiang,

ABSTRACT

Objective: To determine whether Epstein-Barr virus (EBV) or cytomegalovirus (CMV) seropositivity is associated with multiple sclerosis (MS) in blacks and Hispanics and to what extent measures of the hygiene hypothesis or breastfeeding could explain these findings. EBV and CMV have been associated with MS risk in whites, and the timing and frequency of both viruses vary by factors implicated in the hygiene hypothesis.

Methods: Incident cases of MS or its precursor, clinically isolated syndrome (CIS), and matched controls (blacks, 111 cases/128 controls; Hispanics, 173/187; whites, 235/256) were recruited from the membership of Kaiser Permanente Southern California. Logistic regression models accounted for *HLA-DRB1*1501* status, smoking, socioeconomic status, age, sex, genetic ancestry, and country of birth.

Results: Epstein-Barr nuclear antigen-1 (EBNA-1) seropositivity was independently associated with an increased odds of MS/CIS in all 3 racial/ethnic groups ($p < 0.001$ for blacks and whites, $p = 0.02$ for Hispanics). In contrast, CMV seropositivity was associated with a lower risk of MS/CIS in Hispanics ($p = 0.004$) but not in blacks ($p = 0.95$) or whites ($p = 0.96$). Being born in a low/middle-income country was associated with a lower risk of MS in Hispanics ($p = 0.02$) but not after accounting for EBNA-1 seropositivity. Accounting for breastfeeding did not diminish the association between CMV and MS in Hispanics.

Conclusions: The consistency of EBNA-1 seropositivity with MS across racial/ethnic groups and between studies points to a strong biological link between EBV infection and MS risk. The association between past CMV infection and MS risk supports the broader hygiene hypothesis, but the inconsistency of this association across racial/ethnic groups implies noncausal associations.

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•Accepted in final form June 30, 2017.

Myasthenia Gravis and EBV

"Dysregulated EBV infection in the pathological thymus appears common in Myasthenia Gravis"

Ann Neurol. 2010 Jun;67(6):726-38. doi: 10.1002/ana.21902.

Epstein-Barr virus persistence and reactivation in myasthenia gravis thymus.

Cavalcante P[1], Serafini B, Rosicarelli B, Maggi L, Barberis M, Antozzi C, Berrih-Aknin S, Bernasconi P, Aloisi F, Manteqazza R.

⊕ Author information

Abstract

OBJECTIVE: Increasing evidence supports a link between Epstein-Barr virus (EBV), a ubiquitous B-lymphotropic human herpesvirus, and common B-cell-related autoimmune diseases. We sought evidence of EBV infection in thymuses from patients with myasthenia gravis (MG), an autoimmune disease characterized by intrathymic B-cell activation.

METHODS: Seventeen MG thymuses (6 follicular hyperplastic, 6 diffuse hyperplastic, 5 involuted) and 6 control thymuses were analyzed using in situ hybridization for EBV-encoded small RNAs (EBERs), immunohistochemistry for EBV latent and lytic proteins, and polymerase chain reaction for EBV DNA and mRNA.

RESULTS: All 17 MG thymuses showed evidence of active EBV infection, whereas none of the control thymuses were infected. Cells expressing EBERs (12 of 17) and EBV latency proteins (EBNA2, LMP1, and LMP2A) (16 of 17) were detected in medullary infiltrates and in germinal centers. Cells expressing early (BFRF1, BMRF1) and late (p160, gp350/220) lytic phase EBV proteins were present in 16 MG thymuses. Latency (EBNA1, LMP2A) or lytic (BZLF1) transcripts (often both) were present in all MG thymuses, and EBV DNA (LMP1 gene) was detected in 13 MG thymuses. We also found CD8+ T cells, CD56 + CD3-natural killer cells, and BDCA-2+ plasmacytoid dendritic cells in immune infiltrates of MG thymuses, but not germinal centers, suggesting an attempt of the immune system to counteract EBV infection.

INTERPRETATION: Dysregulated EBV infection in the pathological thymus appears common in MG and may contribute to the immunological alterations initiating and/or perpetuating the disease.

Graves' Disease and EBV

Viral Immunol. 2011 Apr;24(2):143-9. doi: 10.1089/vim.2010.0072.

The influence of Epstein-Barr virus reactivation in patients with Graves' disease.

Nagata K[1], Fukata S, Kanai K, Satoh Y, Segawa T, Kuwamoto S, Sugihara H, Kato M, Murakami I, Hayashi K, Sairenji T.

Author information

Abstract

In Graves' disease, the IgG class autoantibody against thyrotropin receptor (TRAb) is produced excessively and induces hyperthyroidism. Epstein-Barr virus (EBV) is one of the human herpesviruses that persists for life, mainly in B lymphocytes, and is occasionally reactivated. Therefore, EBV may affect the antibody production of B lymphocytes that would normally produce TRAb. The purpose of the present study was to evaluate the association of EBV reactivation with the etiology of Graves' disease. Serum levels of EBV antibodies and IgE were determined by ELISA. TRAb levels were determined by radioreceptor assay. We performed in-situ hybridization (ISH) of EBV-encoded small RNA (EBER)1 on the thyroid tissue of one of our patients. In Graves' disease patients with TRAb levels ≥ 10%, EA antibody levels, which indicate EBV reactivation, were moderately but significantly correlated with the levels of TRAb, and weakly but significantly correlated with IgE. EBER1-ISH revealed that one of our patients had EBV-infected lymphocytes infiltrating the thyroid gland. EBV re make TRAb, and this may contribute to or exacerbate the disease.

"In Graves' disease patients with TSH receptor antibodies (TRAb) levels ≥ 10%, EA antibody levels, which indicate EBV reactivation, were moderately but significantly correlated with the levels of TRAb"

Laboratory tests for Epstein Barr Virus (EBV)

Epstein Barr Virus IgG/IgM antibodies

Epstein Barr Virus Anti-EBNA antibodies

Epstein Barr Virus Early Antigen antibodies (reactivated or chronic)

Epstein Barr Virus Elispot

- EBV lytic antigen: sign of replication
- EBV latent antigen: sign of latency

Cytomegalovirus (CMV)

Virus: Cytomegalovirus (obligate intracellular organism), double-stranded DNA virus, one of the Herpes viruses

Transmission: body fluids (urine, saliva, breast milk, sexual transmission), organ transplantation, blood transfusion

Symptoms (incubation period several weeks): fatigue, fever, flu-like symptoms, lymphadenitis (swollen cervical lymph nodes), sore throat, splenomegaly

Complications: congenital infection with hearing loss, vision loss, seizures, mental disabilities, lack of coordination; immune suppressed patients: hepatitis, colitis, retinitis, pneumonitis, esophagitis, polyradiculopathy, transverse myelitis, subacute encephalitis; arterial hypertension, artheroscleroris, aortic aneurysms; association with Non-Hodgkins Lymphoma

Laboratory tests for Cytomegalovirus

CMV IgG/IgM antibodies

CMV Elispot – both lytic and latent

Herpes Simplex Virus 1/2 (HSV 1/2)

Virus: Herpes Simplex Virus (Human Herpes Virus HHV 1/2) (obligate intracellular organism), double-stranded DNA virus

Transmission: Saliva, sharing drinks, sexually transmitted

Symptoms (incubation time 2-20 days): Watery blisters on the skin or mucous membranes of the mouth, lips, genitals, anus, flu-like symptoms (fever, muscle aches, swollen lymph nodes, problems urinating, herpes keratitis (pain, light sensitivity, discharge)), fatique

Complications: Multiple Sclerosis (neurovirulent), loss of vision, encephalitis, latent infection; reactivation by organ transplantation or HIV: encephalitis, pneumonitis, bone marrow suppression

Laboratory tests for HSV 1/2

Herpes Simplex Virus 1/2 – IgG/IgA/IgM antibodies
(half-life time of localised IgA antibodies: 2 weeks)

Herpes Simplex Virus 1/2 - EliSpot

Varicella Zoster Virus (VZV)

Virus: Varicella Zoster Virus (Human Herpes Virus HHV 3) (obligate intracellular organism), double-stranded DNA virus

Transmission: airborne, touching shingles blisters

Symptoms (incubation time 10-21 days): "Chickenpox" in younger people, "Herpes Zoster" in adults: Watery blisters on the skin, fever, tiredness, loss of appetite, headache

Complications: Encephalitis, pneumonia, bronchitis, 10-20% reactivation from nerve ganglia (Herpes Zoster), post-herpatic neuralgia, Mollaret´s meningitis, Zoster multiplex, "Ramsay Hunt syndrome" (painful blisters on tongue/ear, facial weakness, hearing loss),

Inflammation of arteries (new study Journal of the American College of Cardiology, Vol. 70, Issue 2, July 2017, "Herpes Zoster increases risk of stroke and myocardial infarction" 23,233 patients had a higher risk of apoplectic stroke (35%) and myocardial infarction (59%) after Herpes Zoster

Laboratory tests for Varicella Zoster Virus (VZV)

Varicella Zoster Virus (VZV) – IgG/**IgA**/IgM antibodies
(half-life time of localised IgA antibodies: 2 weeks)

Varicella Zoster Virus (VZV) - EliSpot

Coxsackie Virus

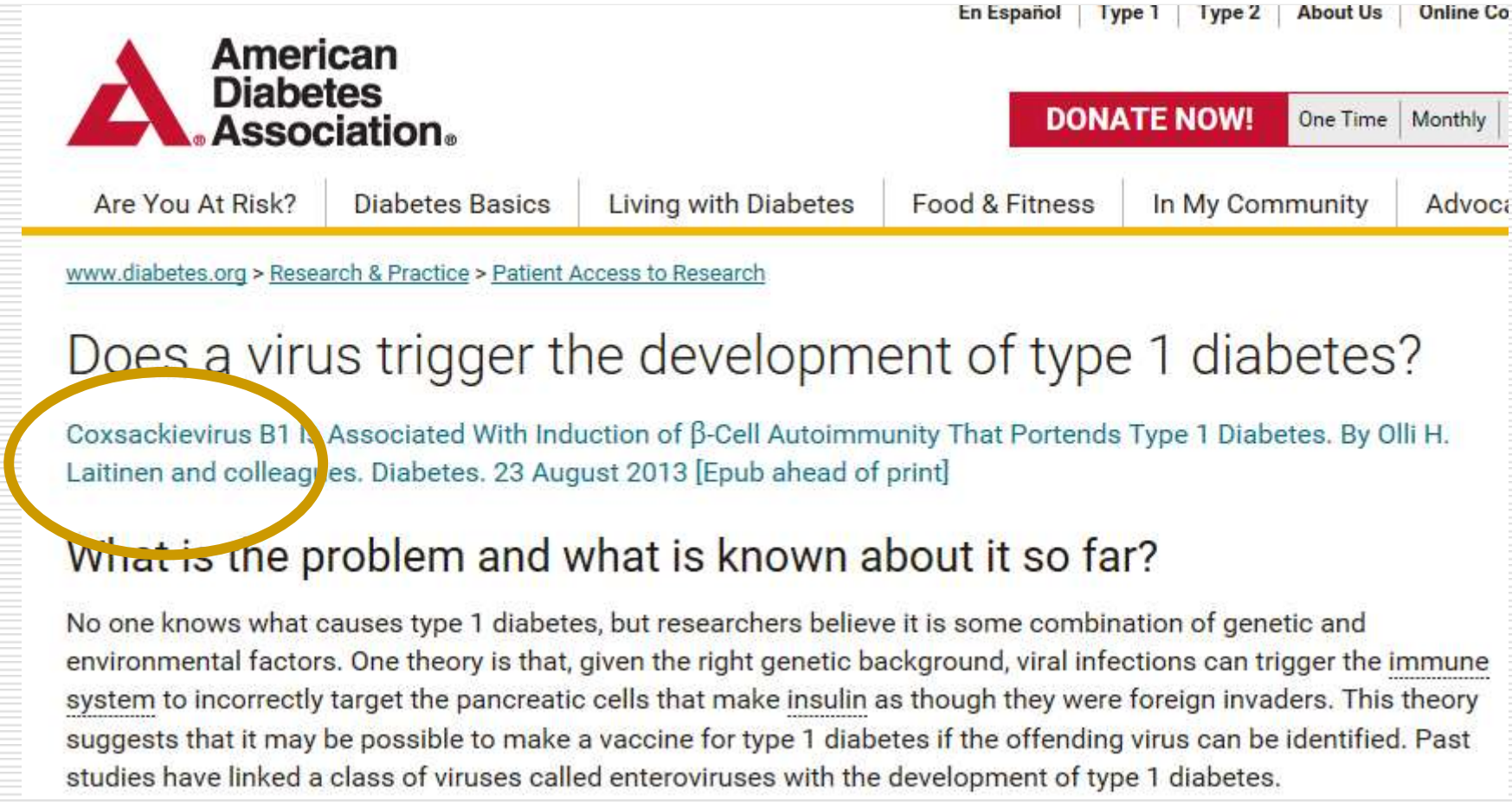
Virus: Coxsackie Virus (obligate intracellular), belongs to Picornaviridae/enterovirus family, is a single-stranded RNA virus divided into group A and group B

Transmission: fecal-oral contamination, droplets, body fluids, utensils, toys, nappy-changing table

Symptoms: Group A: Herpangina, AHC (acute hemorrhagic conjunctivitis, HFM (hand-foot-and-mouth disease), Group B: myocarditis, pericarditis, pleurodynia, hepatitis; Group A and B: fever, rashes, sore throat, diahorrea, cough, fatigue, conjunctivitis, loss of appetite, headache, night sweats, aseptic meningitis

Complications: CNS disease similar to poliomyelitis, systemic neonatal disease, IDDM (insulin-dependent diabetes mellitus), Group A: generalized myositis with flaccid paralysis, Group B: focal muscle injury, degeneration of neuronal tissue with spastic paralysis

Diabetes Type 1: B1 strain of Coxsackie B has antigens similar to those in pancreatic beta cells



Source: Kalish RA, Leong JM, Steere AC. Association of treatment-resistant chronic Lyme arthritis with HLA-DR4 and antibody reactivity to OspA and OspB of Borrelia burgdorferi. Infect Immun 1993; 61: 2774–2779; Gross DM, Forsthuber T, Tary-Lehmann M et al. Identification of LFA-1 as a candidate autoantigen in treatment-resistant Lyme arthritis. Science 1998; 281: 703–706.

Association with Cytomegalovirus …

Associations of cytomegalovirus with type I diabetes mellitus among children in Khartoum State

Eltayib Hassan Ahmad-Abakur[1,2]*, Mudathir A. Abdelkareem[1,3], Mohamed Ahmed Abrahim-Holi[1] and Ayman Ali[4]

[1]Department of Microbiology-Faculty of Medical Laboratory Sciences-Alzaeim Alazhari University, Sudan.
[2]Department of Microbiology-Dentistry & Oral Surgery Collage, Alasmaria Islamic University, Libya.
[3]Department of Microbiology-School of Medical Laboratory Sciences- SharqElneil College, Sudan.
[4]Department of Microbiology-Alribat University Hospital, Sudan.

Received 24 April, 2013; Accepted 24 March, 2014

Cytomegalovirus is one of the most common microorganisms that cause opportunistic infection that complicate the clinical care and progress of immunecompromised patients. The virus can cause severe diseases with multiple complications in[illegible] The present study is a case control study aimed at determining cy[illegible]ese children. Sera of eighty one (81) childre[illegible]the study group and 54 (66.7%) from appare[illegible]ted for IgG anti-cytomegalovirus using enzy[illegible]2%) of the total population of study were se[illegible]6%) were diabetic patients, the results indic[illegible]rus IgG antibodies with type I diabetes mell[illegible]lue 0.003) of cytomegalovirus IgG antibodies[illegible]

"the results indicate significant association (*P* value 0.025) of cytomegalovirus IgG antibodies with type I diabetes mellitus in children. The study reveals significant relation (*P* value 0.003) of cytomegalovirus IgG antibodies with type I diabetes mellitus in age group (5-9 years)."

… and with other enteroviruses: Echovirus (enteric cytopathic human orphan virus)

Autoimmunity. 2001;34(4):275-81.

Echovirus 4 and type 1 diabetes mellitus.

Díaz-Horta O[1], Bello M, Cabrera-Rode E, Suárez J, Más P, García I, Abalos I, Jofra R, Molina G, Díaz-Díaz O, Dimario U.

⊕ Author information

Abstract

AIMS/HYPOTHESIS: To determine the association between exposure to enteroviruses and Type 1 diabetes.

METHODS: We measured neutralizing antibodies to the following enteroviruses: Coxsackievirus CA9, CB1, CB2, CB3, CB4, CB5, CB6, and Echovirus E4, E6, E9, E11 in the sera of (1) Type 1 diabetic patients at diagnosis (n = 33), (2) healthy offspring of parents with Type 1 diabetes without islet cell antibodies (ICA) (n = 43) and (3) normal controls (n = 57). All subjects were less than 20 years old. We performed the neutralization test determining the cytopathogenic effect on Vero cells. HLA DR serotyping was also performed in Group 2.

RESULTS: Type 1 diabetic patients showed a higher frequency (21.2%, $p < 0.01$) of neutralizing antibodies to E4 in relation to controls (1.8%), although there were no differences comparing with offspring of Typ… 1 diabetes HLA DR susceptibility genes were also exposed to E4 (15.0%). High frequ… ound in the control group.

CONCLUSION: This study shows the association between Type 1… virus 4, suggesting the possible participation of this virus as an environmental trigger … ays high frequencies of exposure to enterovirus (including CB4) although th… tants).

"This study shows the association between Type 1 diabetes and the presence of neutralizing antibodies to Echovirus 4, suggesting the possible participation of this virus as an environmental trigger of this autoimmune disease."

Laboratory tests Coxsackie Virus / Echo Virus

Coxsackie Virus Type A7/B1 – IgG/IgA antibodies

Echo Virus – IgG/IgA antibodies

(half-life time of local-standing IgA antibodies: 2 weeks)

SLE: Parvovirus B19, CMV, HSV 1/2, VZV

Medicine (Baltimore). 2008 Nov;87(6):311-8. doi: 10.1097/MD.0b013e31818ec711.

Acute viral infections in patients with systemic lupus erythematosus: description of 23 cases and review of the literature.

Ramos-Casals M[1], Cuadrado MJ, Alba P, Sanna G, Brito-Zerón P, Bertolaccini L, Babini A, Moreno A, D'Cruz D, Khamashta MA.

Author information

Abstract

Few studies have evaluated the impact of viral infections on the daily management of patients with systemic lupus erythematosus (SLE). We analyzed the etiology and clinical features of acute viral infections arising in patients with SLE and their influence on the diagnosis, prognosis, and treatment of SLE. Cases occurring within the last 5 years were selected from the databases of 3 large teaching hospitals. Acute viral infections were confirmed by the identification of specific antiviral IgM antibodies and subsequent seroconversion with detection of specific IgG antibodies. In autopsy studies, macroscopic findings sugg sue samples. We performed a MEDLINE search for addit from our clinics and 65 from the literature review) of acute v SLE (fulfillment of the 1997 SLE criteria) associated with int us (EBV; n = 3), and hepatitis A virus (n = 1). The remain patients, symptoms related to infection mimicked a lu conditions, presented organ-specific viral infections (m tiorgan process similar to that described in catastrophic antiphospholipid syndrome-the final diagnosis was hemophagocytic syndrome in 5 cases and disseminated viral infection in 5. Twelve patients died due to infection caused by CMV (n = 5), herpes simplex virus (n = 4), EBV (n = 2), and varicella zoster virus (n = 1). Autopsies were performed in 9 patients and disclosed disseminated herpetic infection in 6 patients (caused by herpes simplex in 4 cases, varicella in 1, and CMV in 1) and hemophagocytic syndrome in 3. A higher frequency of renal failure (54% vs. 19%, p = 0.024), antiphospholipid syndrome (33% vs. 6%, p = 0.023), treatment with cyclophosphamide (82% vs. 37%, p = 0.008), and multisystemic involvement at presentation (58% vs. 8%, p < 0.001); and a lower frequency of antiviral therapy (18% vs. 76%, p < 0.001) were found in patients who died, compared with survivors. The most common viral infections in patients with SLE are parvovirus B19 (predominantly mimicking SLE presentation) and CMV (predominantly presenting in severely immunosuppressed patients). CMV infection may mimic a lupus flare or present with specific organ involvement such as gastrointestinal bleeding or pulmonary infiltrates. Other herpesviruses are common in immunosuppressed SLE patients and may produce a wide range of manifestations. Physicians should examine the pharynx, eyes, skin, and genitalia and should conduct serologic and molecular studies to improve early detection of viral infection in patients with SLE.

"The most common viral infections in patients with SLE are parvovirus B19 (predominantly mimicking SLE presentation) and CMV (predominantly presenting in severely immunosuppressed patients)."

EBV / CMV and SLE: Practical example

Untersuchung	Ergebnis	Einheit	Normbereich
Autoantikörper			
4 **Antinukl. Antikörper/ANA (IFT~+**	1:3200		< 1:100
4 ANA-Fluoreszenzmuster~	homogen		

Nachweis von antinukleären Autoantikörpern. Der positive ANA-Nachweis kann als e i n Diagnosekriterium für einen Systemischen Lupus Erythematodes herangezogen werden. Dieser Befund kann auch bei anderen Autoimmunerkrankungen (weitere Kollagenosen, chronische aktive Hepatitis, Rheumatoide Arthritis u.ä.) beobachtet werden.
Die Untersuchung auf Autoantikörper gegen dsDNS und ENA ist bei klinischem Kollagenoseverdacht angezeigt! Bei ANA mit homogenem Muster und V.a. Rheumatoide Arthritis ist die Bestimmung des Rheumafaktors und der CCP-Antikörper sinnvoll.

EBV EliSpot (lytisch+latent)			
1 **EBV-lytischer Peptidmix**	!	2	SI

0-1 = negativ
2-3 = grenzwertig
ab 4 = positiv

1 **EBV-latenter Peptidmix**	!	9	SI

0-1 = negativ
2-3 = grenzwertig
ab 4 = positiv

Mittels EliSpot finden sich aktuell positive T-Zell-Reaktionen gegen Epstein Barr Virus (EBV).

Erläuterung EBV-Antigene:
EBV lytisches Antigen: Hinweis auf EBV-Replikation
EBV latentes Antigen: Hinweis auf EBV-Latenz

Achtung: Ab 01.08.2016 geänderte Nachweisgrenze!

CMV EliSpot			
1 **CMV Peptidmix**	!	21	SI

0-1 = negativ
2-3 = grenzwertig
ab 4 = positiv

Ulcerative colitis: CMV, HSV and EBV

World J Gastroenterol. 2016 Feb 14; 22(6): 2030–2045.
Published online 2016 Feb 14. doi: 10.3748/wjg.v22.i6.2030
PMCID: PMC4726676

Cytomegalovirus and ulcerative colitis: Place of antiviral therapy

Sylvie Pillet, Bruno Pozzetto, and Xavier Roblin

Author information ▶ Article notes ▶ Copyright and License informa

This article has been cited by other articles in PMC.

Dig Liver Dis. 2001 Oct;33(7):551-8.

Evidence of Epstein-Barr virus infection in ulcerative colitis.

Bertalot G[1], Villanacci V, Gramegna M, Orvieto E, Negrini R, Saleri A, Terraroli C, Ravelli P, Cestari R, Viale G.

Abstract

Go to:

The link between cytomegalovirus (CMV) infection and inflammatory bowel diseases remains an important subject of debate. CMV infection is frequent in ulcerative colitis (UC) and has been shown to be potentially harmful. CMV reactivation needs to be diagnosed using methods that include *in situ* detection of viral markers by immunol
the density of infection using
particularly important. Altho
flare-ups of refractory UC, a
situation. The presence of co
other immunosuppressive ag
to favor CMV reactivation, v
drugs. According to these fir
presence of CMV reactivatic
ganciclovir in cases of high v

Gene Cell Tissue. 2015 October; 2(4): e32846. doi: 10.17795/gct-32846
Published online 2015 October 28. Letter

Investigation of Ulcerative Colitis for Herpes Simplex Virus and Cytomegalovirus Genomic Sequences by the Polymerase Chain Reaction

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"….the importance of herpes virus, as an exacerbating factor of UC, has been neglected by many clinicians."

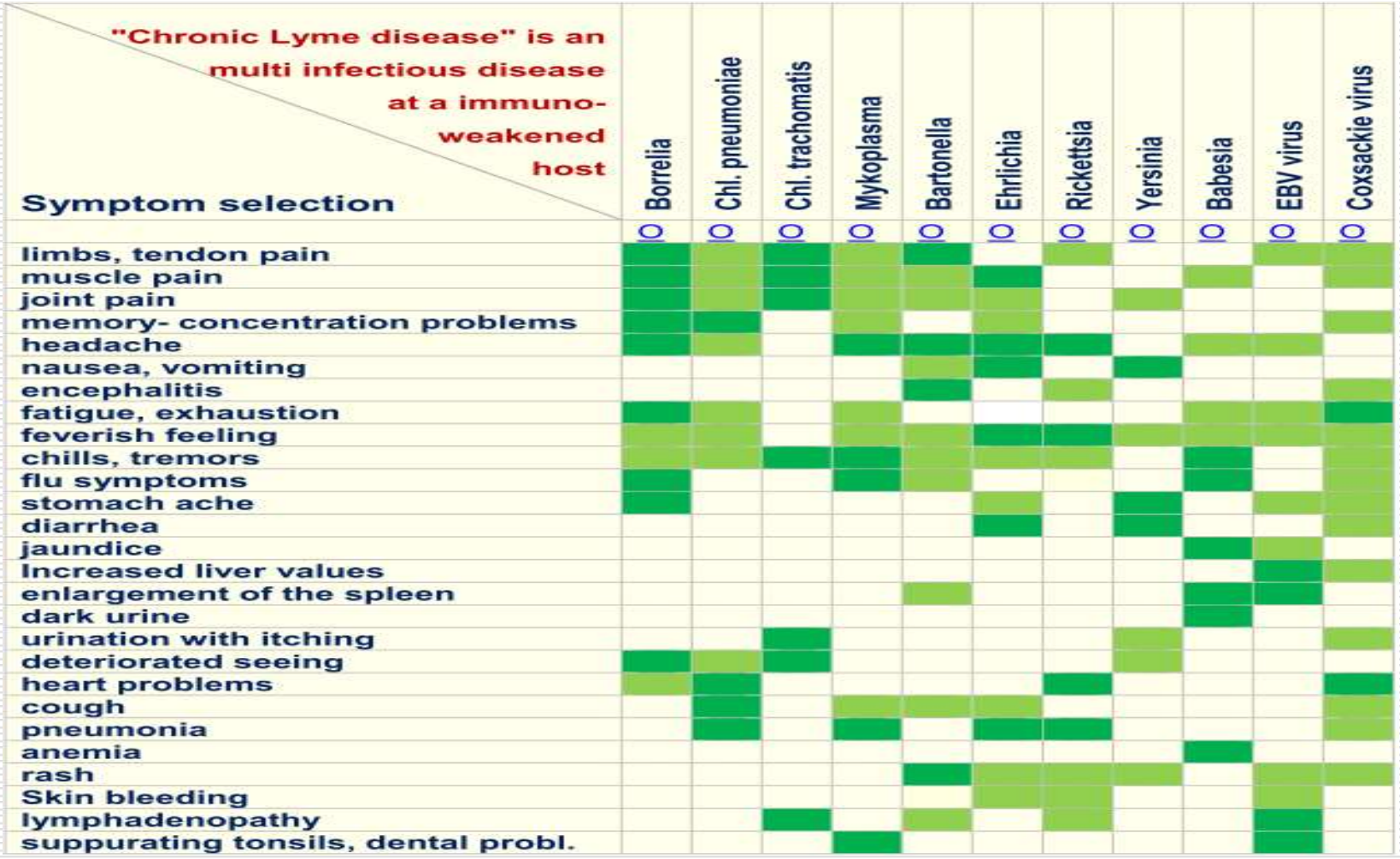
Sarcoidosis: EBV, CMV, HSV …

Box 1 Suspected Causes of Sarcoidosis	
Infectious	**Noninfectious**
Mycobacteria	Dusts
Tuberculous	Clay
Nontuberculous*	Pine
Cell-wall deficient (L-forms)*	Pollen
Bacteria	Talc
Corynebacterium spp.	Mixed*
*Propionibacterium acnes**	Metals
Tropheryma whippleii	Aluminum
Others	Beryllium‡
Fungi	Zirconium
Cryptococcus spp.	
Endemic fungi	
Viruses	
Cytomegalovirus	
Epstein-Barr virus	
Herpes simplex virus	
Others	

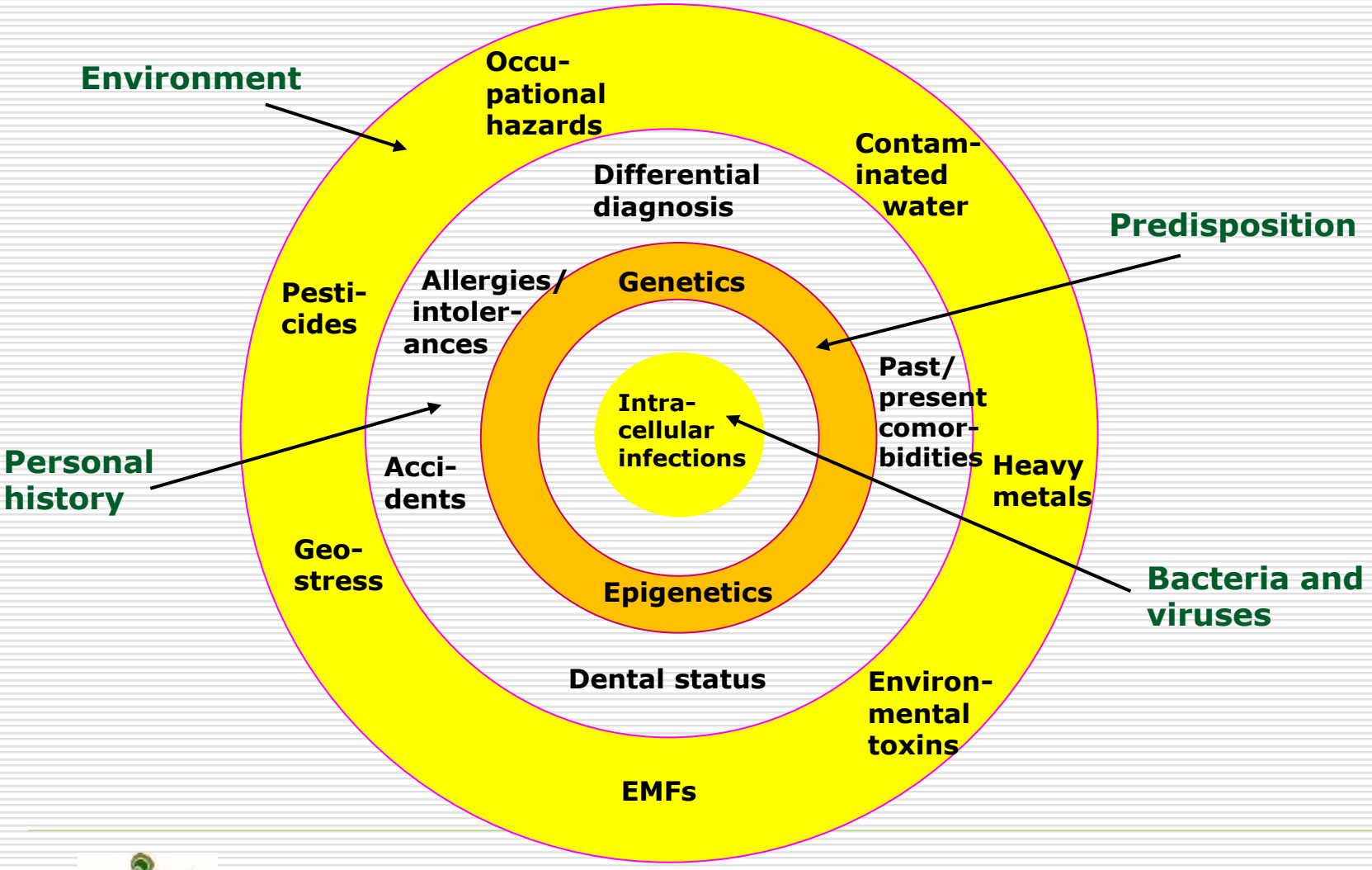
*These organisms have been the focus of most recent studies, but no single agent is confirmed. It is very possible that several disparate agents induce similar reactions leading to sarcoidosis.

Source: http://www.clevelandclinicmeded.com/medicalpubs/diseasemanagement/pulmonary/sarcoidosis/

MULTIPLE SYMPTOMS = MULTIPLE INFECTIONS



Model: "Peeling the onion"



Thank you very much for your attention!

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DIAGNOSING TICK-BORNE DISEASES

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or call the AONM helpline on 0333 121 0305