Symptoms, Laboratory tests and Therapy options in Lyme disease and Co-Infections

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Borrelia: 15 million year old bacteria

WILD NATURE

Bacteria found in 15 million-year-old amber similar to Lyme disease

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Associated Press

GRANTS PASS, Ore. – Fossilized bacteria found inside a tick encased in 15 million-year-old amber indicates the bacteria that cause Lyme disease were likely around long before there were humans to get the disease.

George Poinar Jr. is professor emeritus of entomology at Oregon State University. He bought the amber about 30 years ago in the Dominican Republic, while researching the ancient origins of diseases spread by ticks and mosquitoes.

He did not find the tick until five years ago, and when he cracked open the amber, saw the tick was full of millions of fossilized bacteria.

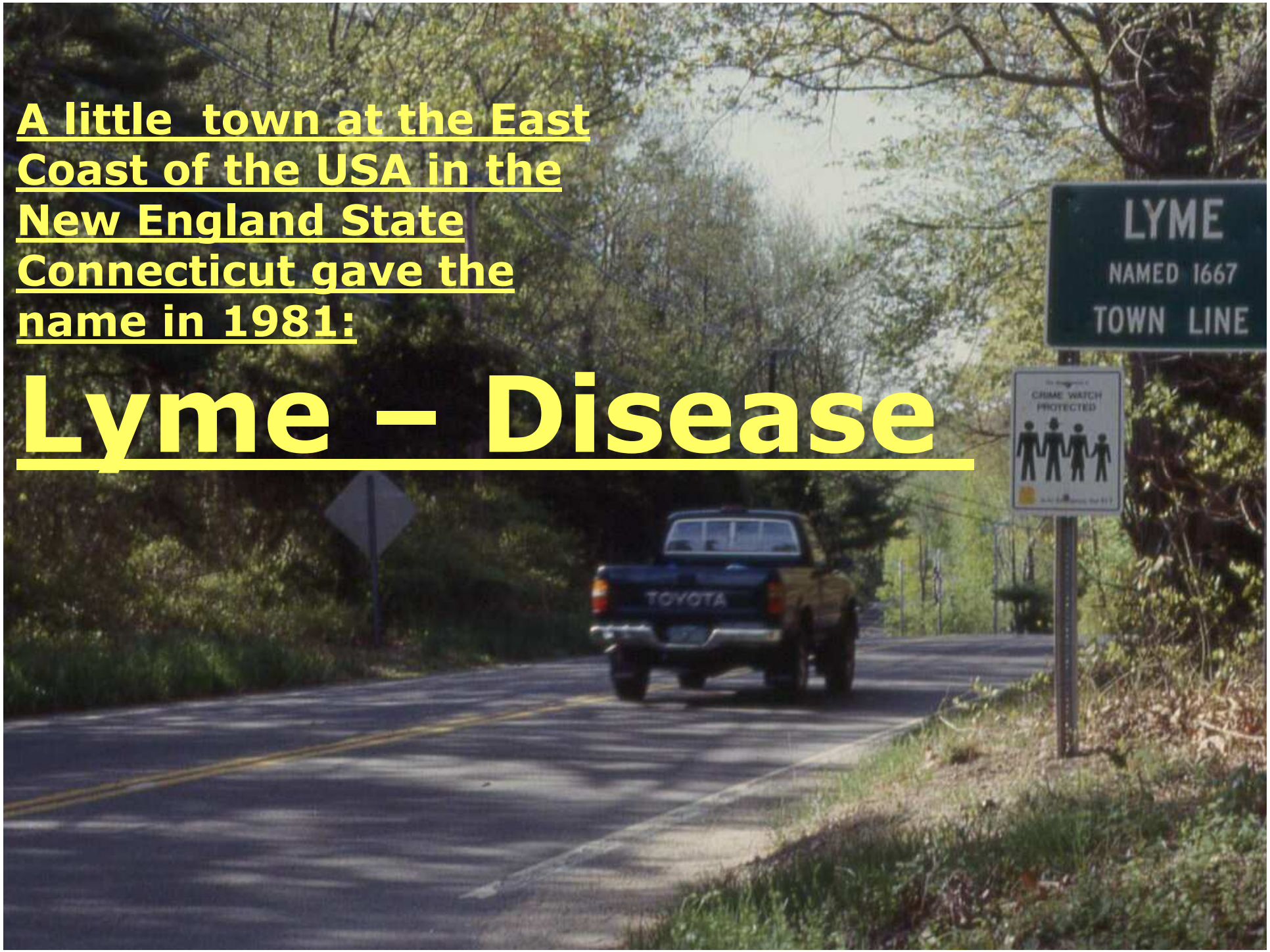
Poinar writes in the latest edition of the journal Historical Biology that the fossilized bacteria are similar in form to the bacteria causing Lyme disease.

The fossil record indicates homo sapiens has been around about 200,000 years.

Our oldiest patient 5300 years ago with Lyme disease: „Iceman“ Ötzi

Ötzis enemies: Ticks!

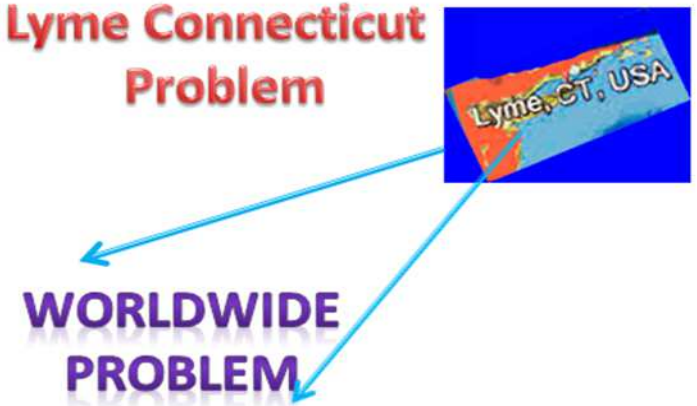
Ötzi's genome also hints at other health problems: Zink's team found almost two-thirds of the genome of *Borrelia borgdorferi*, a bacterium that causes Lyme disease. Zink found no other telltale signs of Lyme disease in Ötzi's preserved tissues, but he speculates that tattoos on the iceman's spine and ankles and behind his right knee could have been an attempt to treat the joint pain that occurs when the condition goes untreated.

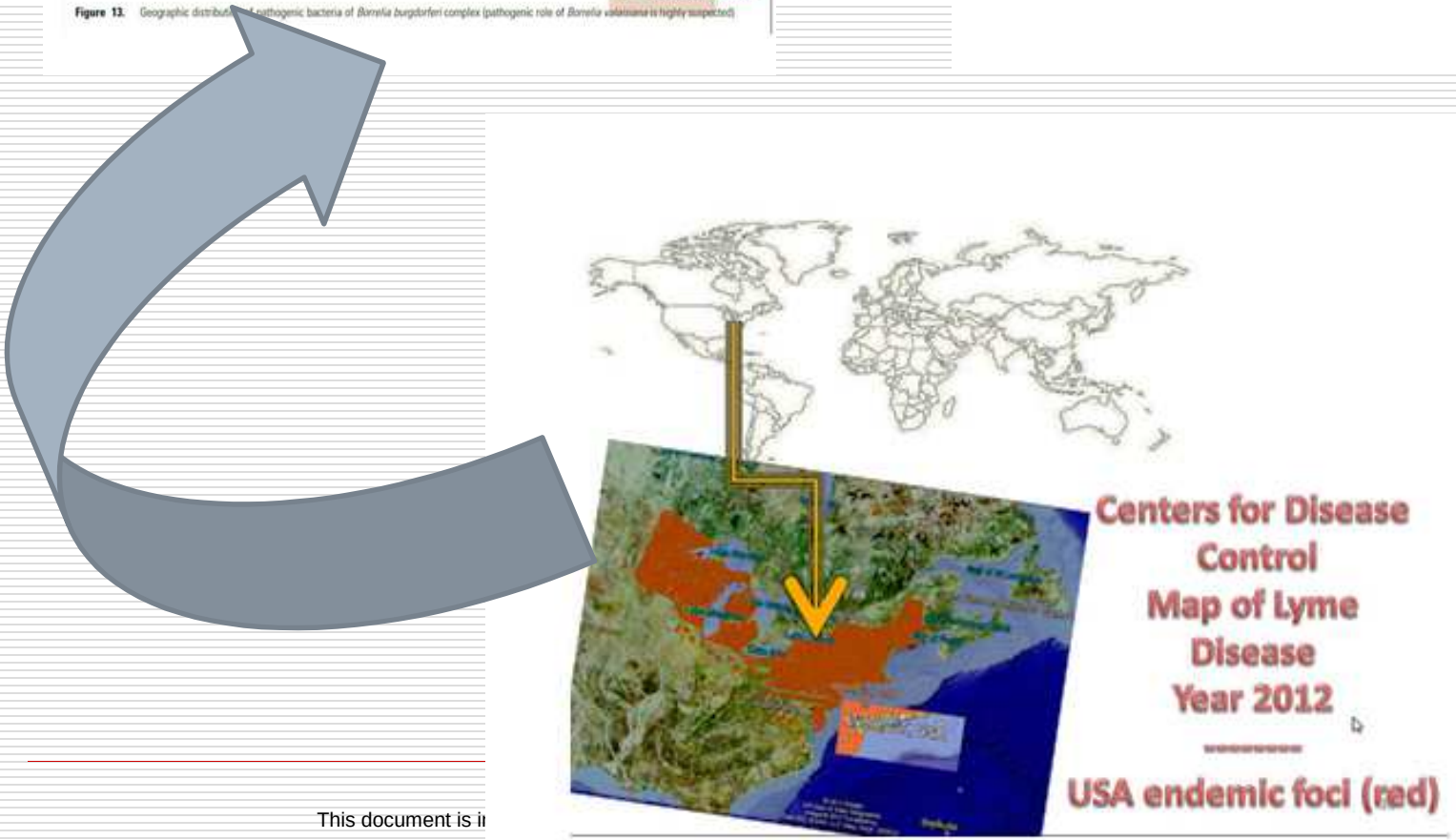


A little town at the East Coast of the USA in the New England State Connecticut gave the name in 1981:

Lyme – Disease

Figure 13. Geographic distribution of pathogenic bacteria of *Borrelia burgdorferi* complex (pathogenic role of *Borrelia valaisiana* is highly suspected)





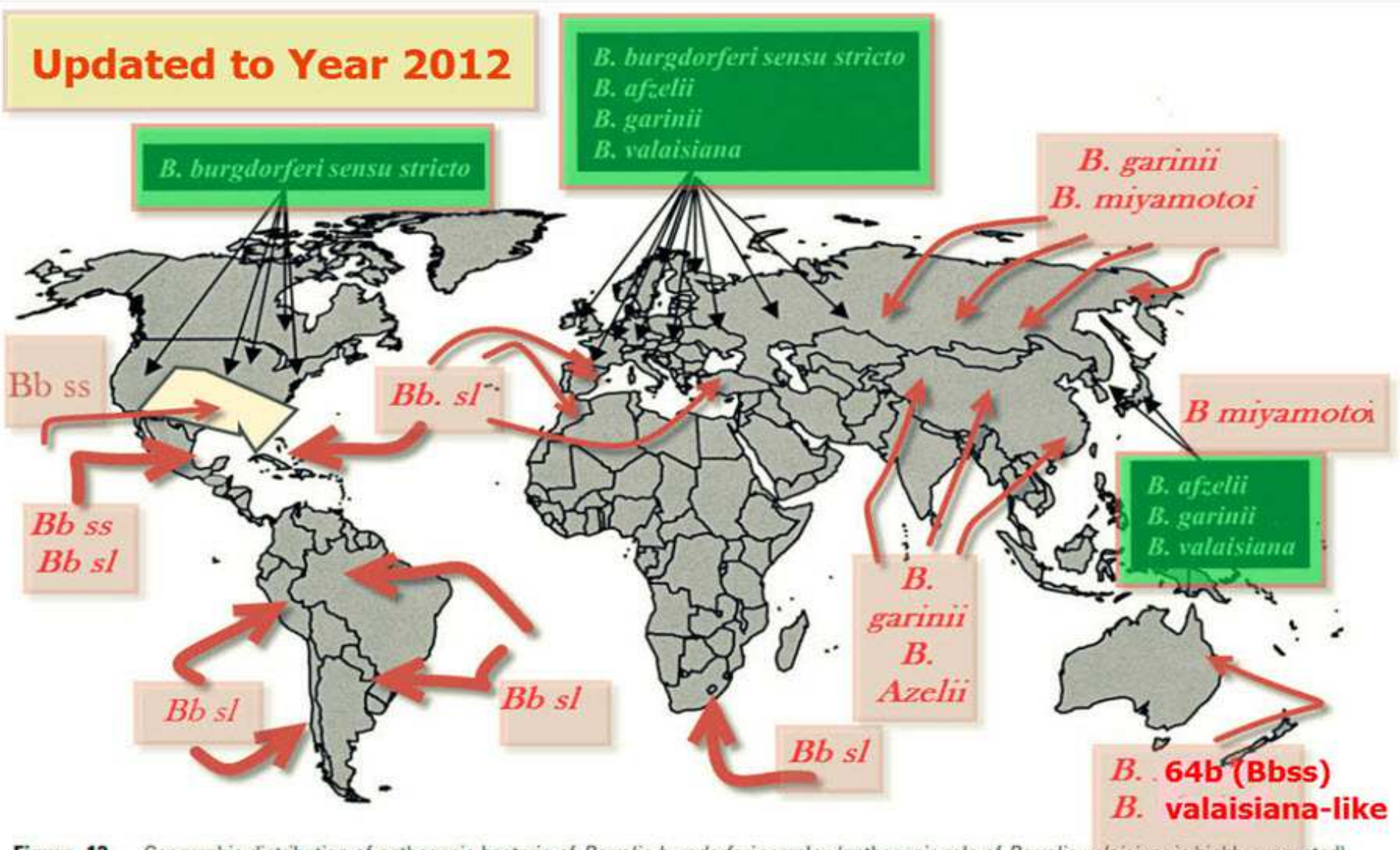
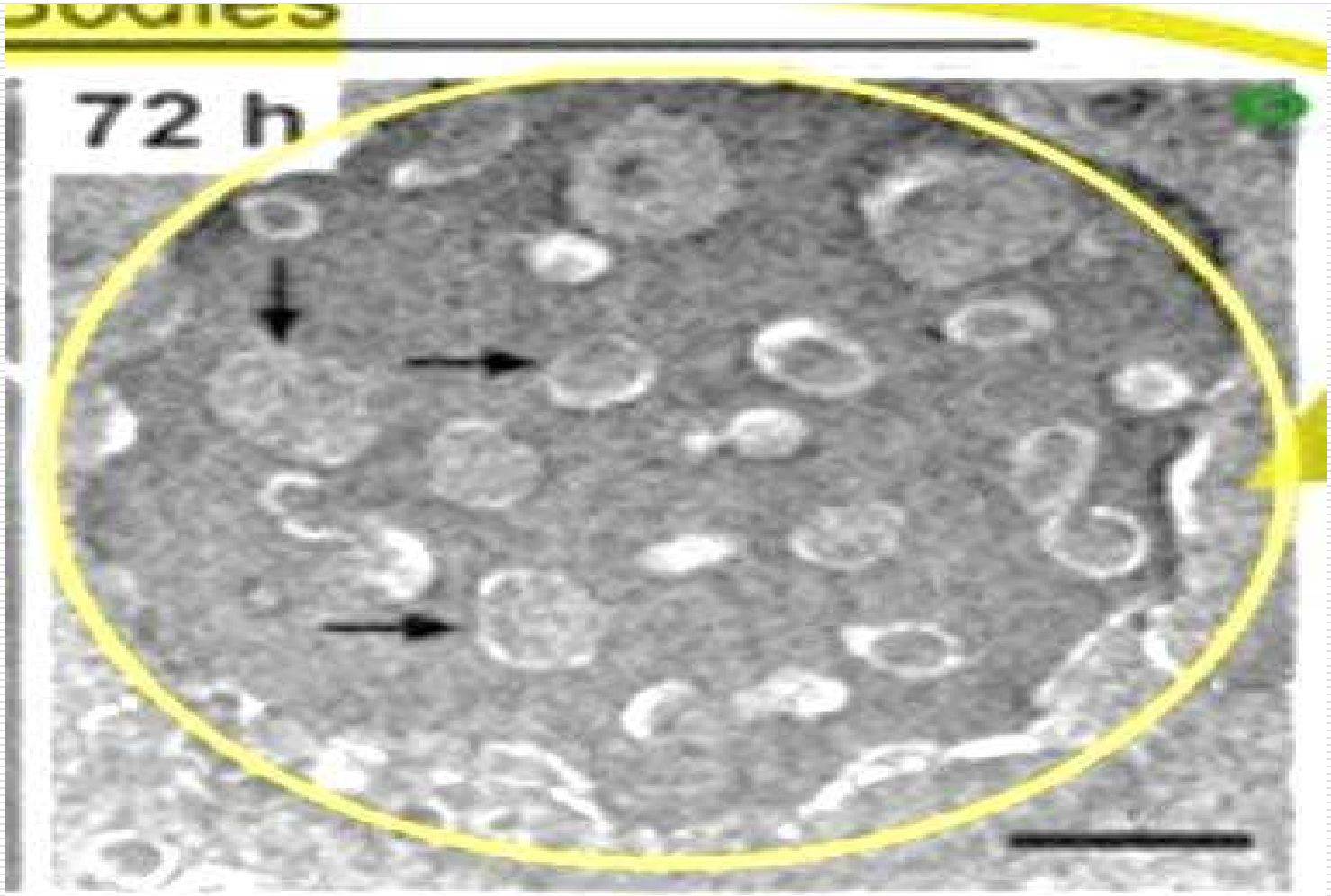
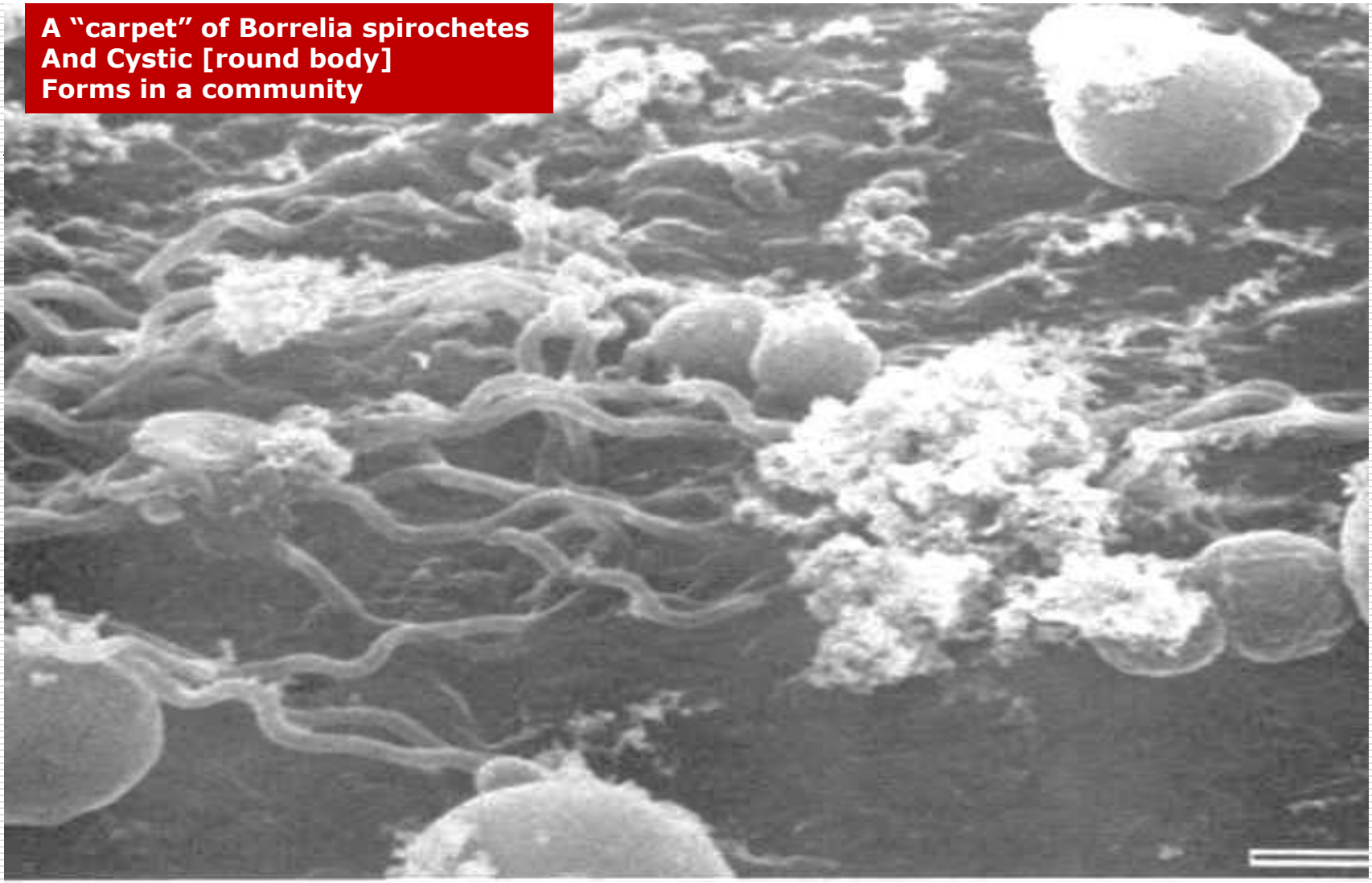


Figure 13. Geographic distribution of pathogenic bacteria of *Borrelia burgdorferi* complex (pathogenic role of *Borrelia valaisiana* is highly suspected)

Cystic forms Borrelia burgdorferi = Cysts



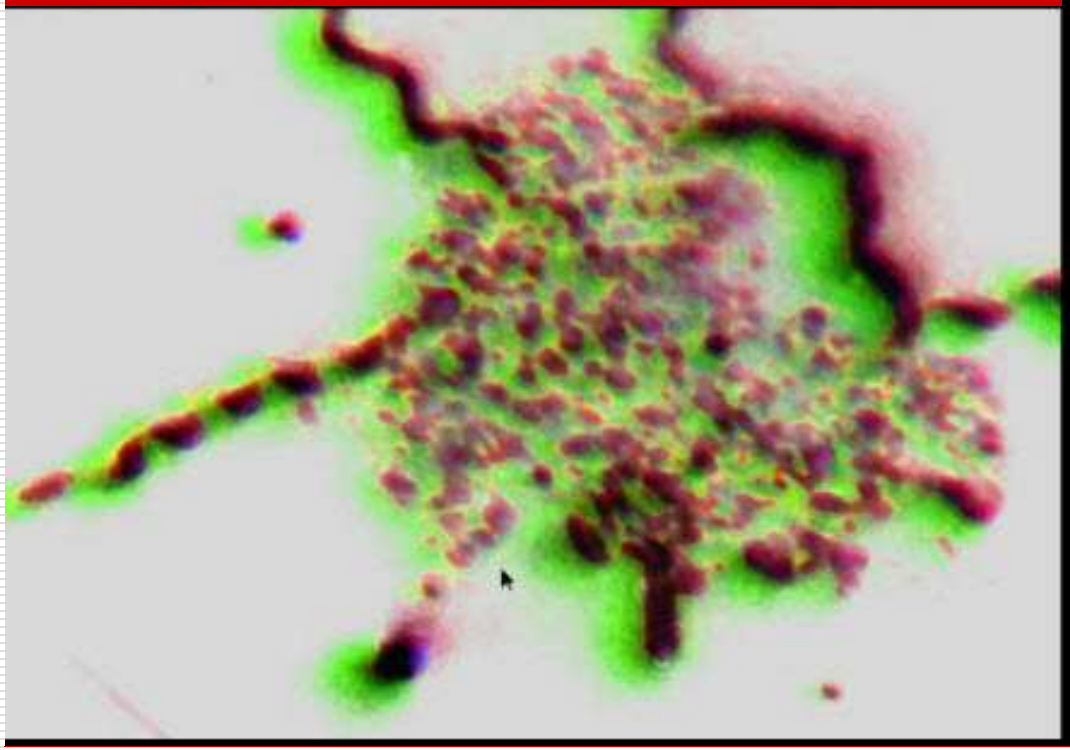
A "carpet" of Borrelia spirochetes And Cystic [round body] Forms in a community



ron microscope picture of *B. burgdorferi* spirochetes associated with the epithelium of the midgut
graph courtesy of D. Corwin, Rocky Mountain Laboratories.)

Borrelia burgdorferi In Vitro Biofilm community

Spiral Borrelia forms around the Edges of a biofilm Commnity. The specialized borrelia forms [granular forms] dominate the central regions of the Biofilm. Planktonic forms=Spiral :: Specialized forms are INSIDE the Community



Biofilm of Borrelia burgdorferi
Granular borrelia forms predominate in the bioflilm community
--Extracellular Matrix=green
Viable organisms=red--
Note: partial segmentation of spiral borrelia at 7 o'clock.
DNA segmentation is a precusrsor to the emergence of Granular (round/coccoid) Viable forms of borrelia burgdorferi
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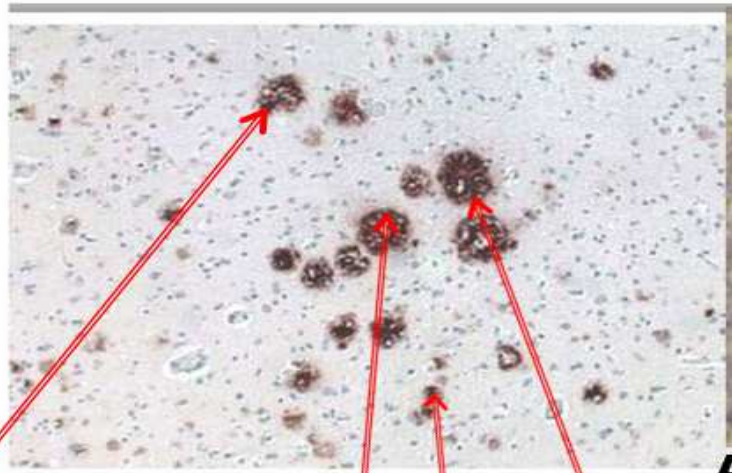
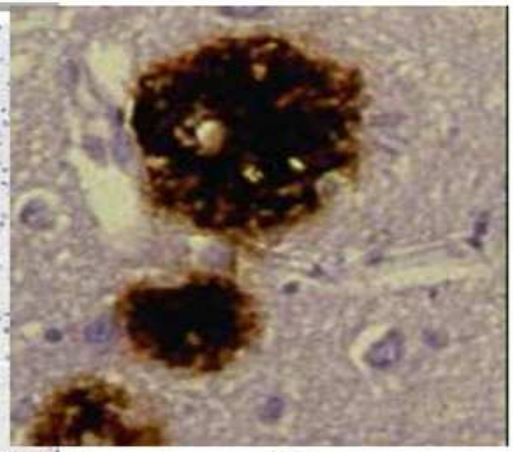
Alzheimer Plaques are Borrelia biofilms

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

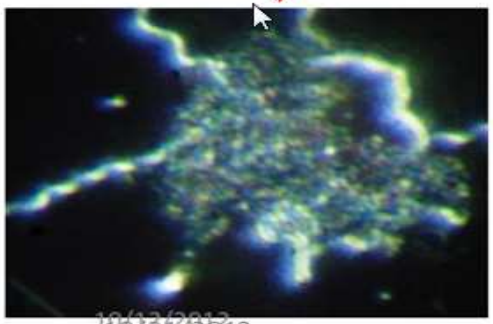


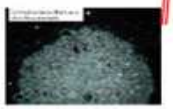
Alzheimer plaques - google

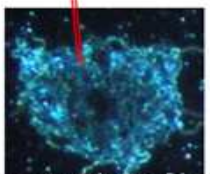


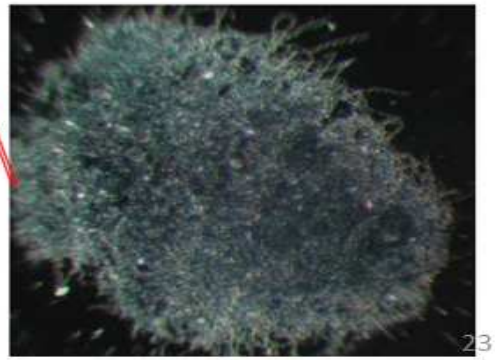
Alzheimer Plaques - Close Up

Borrelia Biofilm Units









Alzheimer Plaques resemble Biofilms of borrelia burgdorferi

Fresh infection with Borrelia burgdorferi: Bulls eye rash / Lymphocytoma

1. **Transmission of Borrelia during tick bites:** After 5 to 7 days, latest 7 to10 weeks development of a

   „Bulls eye rash" (Only 30-40 % of Lyme patients develop a „Bulls eye rash")

2. 20 % of infected patients develop a **feverish reaction** because of **penetration of Borrelia in the blood (only for a few days) („summer flu").**

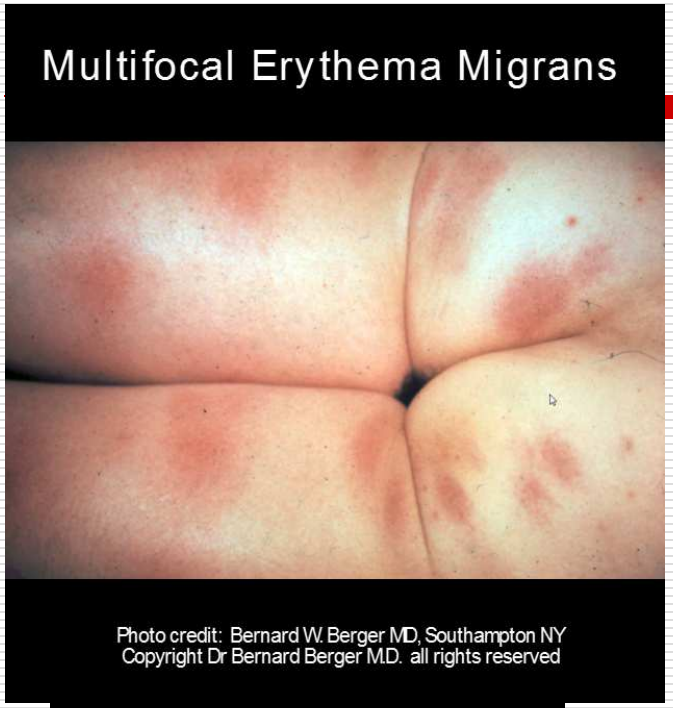
3. 90 % of the patients of stage I are be cured with or without any antibiotics, but 10 % not !

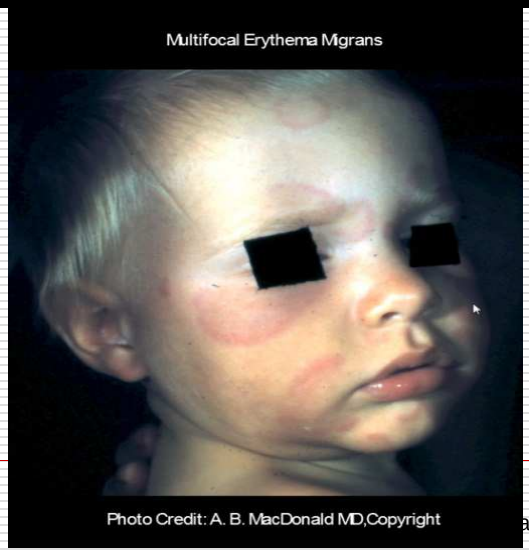
4. **Only 30-40 % of chronic Lyme patients remember a former tick-bite !!!**

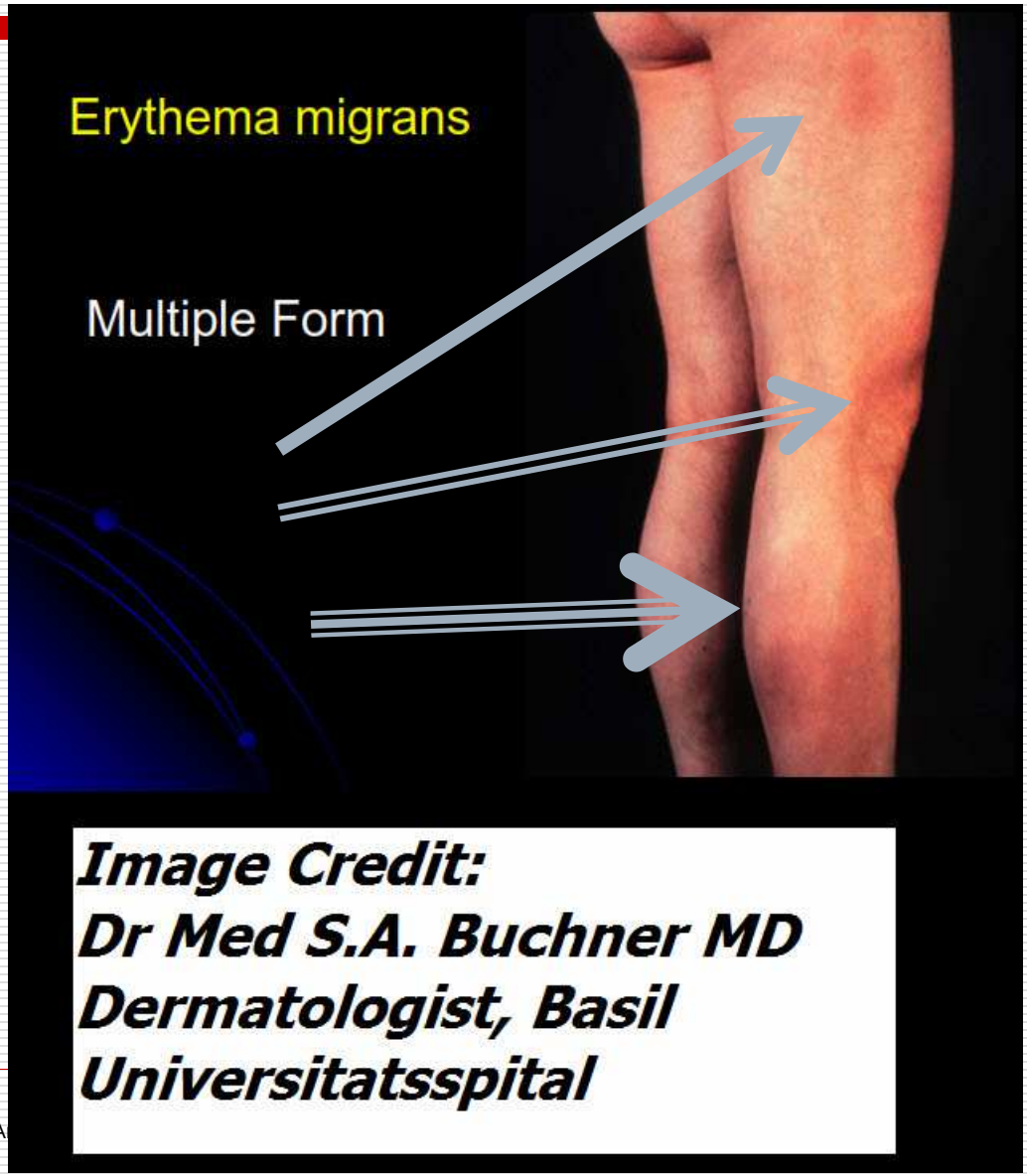
„Bulls eye rash“ (Stage I Lyme disease)

„Bulls eye rash“ (Stage I Lyme disease)

Multifocal Erythema Migrans

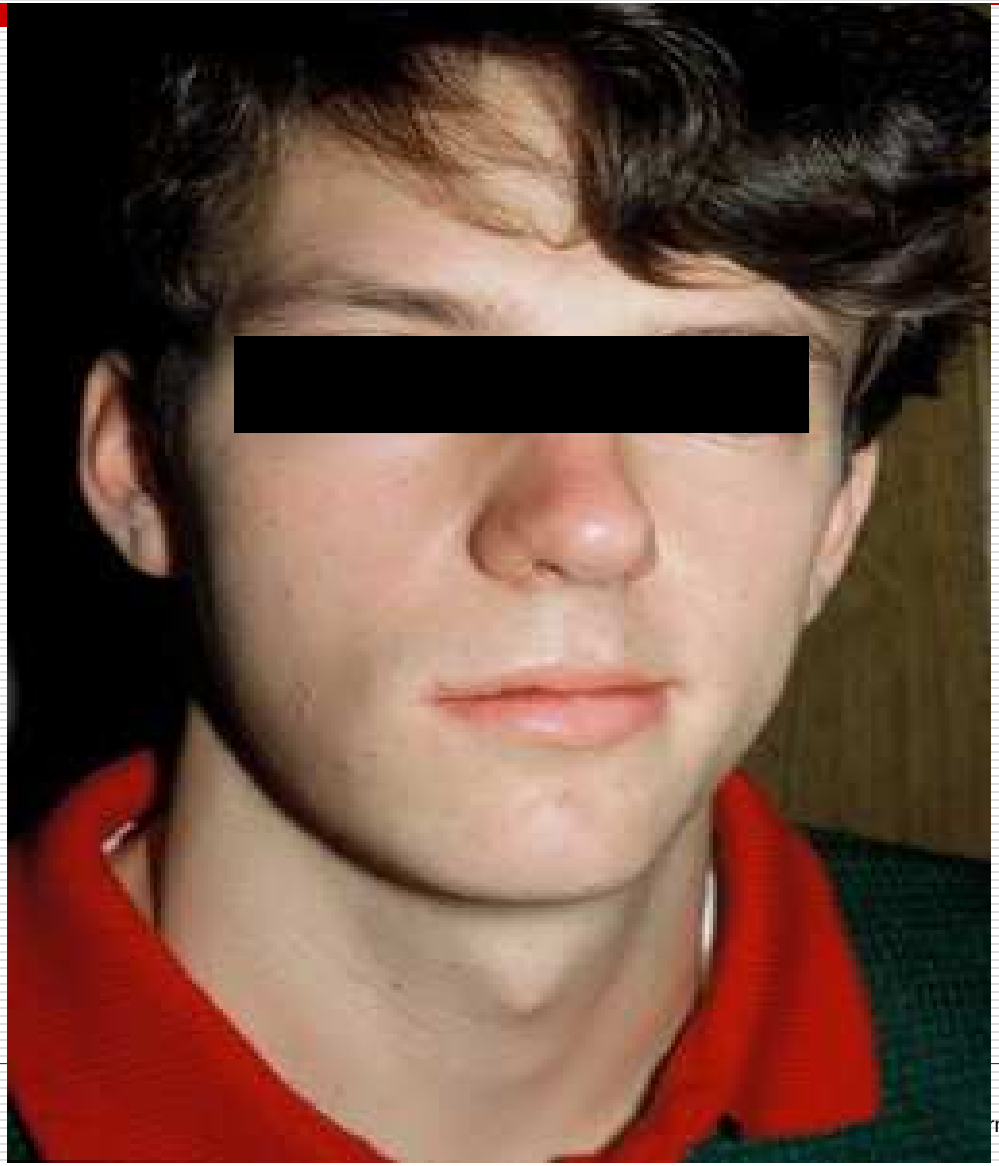






Stage I/II: Acute Neuroborreliosis:

„Bells palsy“ (right side)



Stage II/III (acute/chronic): Arthritis left knee (Very often without turgor)

Stage III: Acrodermatitis athrophicans Herxheimer

Chronic Lyme disease symptoms (stage III)

Power loss or reduction (mental/physical) at work, household, sport	>99 %
Fatigue/ Drowsiness/Listlessness	>99 %
Tingling/"Ants running"/Numbness/ „Needle burning" or „burning" skin-sensations	81 %
Neck pain/ neck stiffness	78 %
Shoulder pain	76 %
Headache/Dizziness	76 %
Changing, migrant joint pain (all joints are possible)	68 %
Changing, migrant muscle pain/"Rheumatism"/General weakness of the body	62 %
Feverish infection: in Stage I of Lyme disease as a sign for occurence of borrelia-bacteria in blood	≈20 %
Mental strain/Depressions/Schizophrenia/Psychosis	62 %
Back pain/Sciatic pain syndrome	58 %
Sleeplessness with partly sweating/urge to urinate mostly between 2 and 4 o´clock at night	47 %
Sore throat/Tendence for general infections/HSV or EBV-Infections	39 %
„Burning eyes"/Overproduciton of tears/Blurred vision/Double vision/Lightheadedness	28 %

New options for patient groups ?

What diseases can be caused by Borrelia ?

- Chronic fatigue syndrome ? CFS ? ME ?
- Multiple Sclerosis ? ALS ?
- Joint and muscle "Rheumatism" ? RA ?
- Arthrosis ?
- Fibromyalgia ?
- Parkinsonism ?
- Dementia ?
- Depression ?
- Autism (Germany: 145 000 autistic children) ?
- Thyroid and hormonal disorders ?
- Infertility ?
- Arrythmia, heart attacks, strokes ?
- Cancer ?

Can Borrelia (tick bites, insect bites) be the reason for it ?

LYME BORRELIOSIS: Great imitator

20-30% of autistic disorders could be caused by Borrelia and 58% by Mycoplasma (Bransfield et al.: Med Hypotheses.2008; 70(5):967-74)

Multiple Sclerosis, Myelopathies, Polyneuropathies, brain tumor, encephalopathy.
(Neurosurgery.1992May;30(5): 769-73)

Can cause meningitis, encephalitis, neuritis, mania, depression, schizophrenia, anorexia, dementia.
(Am J Psychiatry. 1994 Nov;151(11):1571-83)

90% of chronic fatigue patients are Lyme positive.
(Informal study by American Lyme Disease Alliance at www.lymealliance.org)

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

Borrelia can cause Parkinsonism
(Arch.of Path.& Lab.Med.127(9):1204-6)

Case report: Chronic Lyme disease stage III with T-cellular immune response

43-year-old patient, since May 2005 suffering from

- persistent paraesthesia of the left leg
- 80% blindness of the left eye
- progredient myalgia
- recurrent dizziness
- substantial loss of power during work (occupation disability)

Diagnosis by neurologists: MS !

Spinal fluid and laboratory tests were negative (No Borrelia antibody AI, no chronic IgG synthesis in form of oligoclonal bands in the spinal fluid)

Borrelia IgM/IgG-ELISA and immunoblot several different times negative

Therapy: Corticosteroides with increase of symptoms + bad side-effects

Case report: Initial findings Borrelia-LTT and CD57 count 26th Oct. 2005 before antibiotic treatment

Klinische Angaben: Diagnose unbek.
Material : EDTA, CPD Blut, CPD Blut, Heparinblut, Vollblut

Untersuchung		Ergebnis		Referenzbereich		
Leukozyten	↓	4.2	$x10^3/\mu l$	4.4 - 11.3		IMP
Erythrozyten		4.11	$x10^6/\mu l$	4.1 - 5.1		IMP
Hämoglobin		12.7	g/dl	12.3 - 15.3		PHO
Hämatokrit		37.6	%	36 - 47		RECH
MCV		91.5	fl	80 - 99		RECH
HBE (MCH)		30.9	pg	26 - 34		RECH
MCHC		33.8	g/dl	31 - 36		RECH
Thrombozyten		243	$x10^3/\mu l$	140 - 400		IMP
Differentialblutbild						
Neutrophile		46	%	45 - 75		IMP
Lymphozyten		43	%	20 - 45		IMP
Monozyten		9	%	2 - 13		IMP
Eosinophile	↓	1	%	2 - 4		IMP
Basophile		1	%	0 - 1		IMP
Sonstige Zellen		0	%			MIK
CD3- CD57+ Zellen	↓	3.6	%	5 - 20		[1]
(CD3-,CD57+ absolut)		65	/µl	60 - 360		RECH[1]
Eine Verminderung der Anzahl CD57+/CD3- Zellen kann für eine chronische Borreliose sprechen.						
Lymphozytentransformationstest						
Spontanaktivität		870	cpm	< 1000		LTT [1]
Ospc	↑	30.1	SI	< 2.0		LTT [1]
P18-Antigen	↑	4.8	SI	< 2.0		LTT [1]

B. burgdorferi-IgG-Blot	negativ	BLOT
B. burgdorferi-IgM-Blot	negativ	BLOT

Case report: Borrelia-LTT Jan 23rd 2006 after Ceftriaxon IV treatment (8 weeks after the end of therapy)

Ospc	↑ 2.2	SI	< 2.0	LTT 1
P18-Antigen	<1	SI	< 2.0	LTT 1
P100-Antigen	<1	SI	< 2.0	LTT 1

Significant decrease of the LTT (Lymphoycyte Transformation Test)

Lyme-Borreliose

B. burgdorferi-IgG-EIA	< 5	U/ml
B. burgdorferi-IgM-EIA	0.8	Index

Kein serologischer Hinweis auf Infektion mit B. burgdorferi.

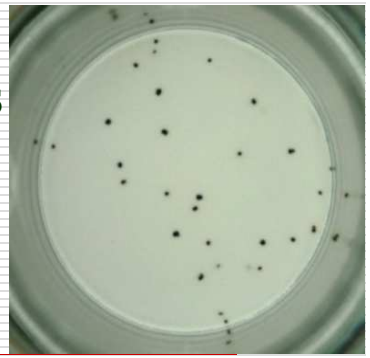
At Jan 23rd, 2006 patient is clinical symptom-free and capable of work!

Correct diagnosis: Chronic Neuroborreliosis with Multiple Sclerosis-like symptoms

Borrelia Elispot (LTT / T-Cell-Spot / IGRA: Interferon-Gamma-Release Assay /Lymphocyte Transformation Test)

1. Success control of an antibiotic therapy - **STAGING**:
   - About 2 months after the end of a therapy already significant reduction
   - Borrelia IgM-/IgG- titer reduction after 6-12- months !

2. Reflecting the **actual T-cellular activity** of Lyme disease:
   - Indication for an active Borrelia infection in cases of furthermore positive Elispot LTT after the end of therapies
   - **T-Cell-Spot/IGRA has been approved by the FDA in May 2011 for M. tuberculosis:**
   - **"… A positive result suggests that an infection is likely, a negative results suggests that an infection is unlikely…."**
     "…Results can be available within 24 hours…"



ELISPOT-LTT: New T-Cell Test a "Game Changer" for Lyme disease

… The sensitivity of ELISPOT is estimated at 84%, and the specificity is 94%...

… ELISPOT assays provide robust, highly reproducible data…

… ElISPOT can be retested for the acquisition of additional information in follow-up assays…

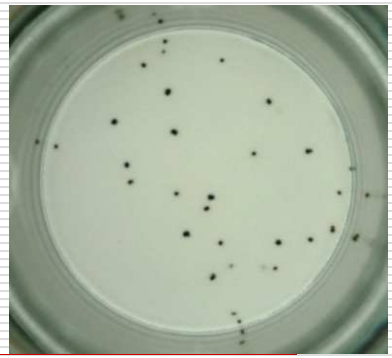
… the two assays systems (ELISPOT + CD57-cell count) compliment each other in the quest to understand T cell-mediated immunity in vivo….

Lehman PV et al.: Unique Strengths of ELISPOT for T Cell Diagnostics in: Kalyuzhny AE. Handbook of ELISPOT: Methods and Protocols, Methods in Molecular Biology, Vol. 792. 2nd Ed: Springer; 2012: 3-23

According this new studies:

82-100 % Specificity of Borrelia-Elispot-LTT

84 % Sensitivity of Borrelia Elispot-LTT



CD3-/CD57+ T-Lymphocytes

1. Subpopulation of the NK cells
2. Reduction indicates **chronic activity** of Lyme disease (symptoms > 1 year)
3. Reduction in untreated and inadequately treated Lyme disease
4. After the therapy end of chronic Lyme disease: normalization as an expression of therapeutical success

CD3-/CD57+ T-Lymphocytes

Reference range (mean/range)

Lyme patient:	46 /ul / 8 – 160 /ul
Healthy:	164 /ul / 60 – 354 /ul

Source: J.J.Burrascano JR., MD, R. Stricker, MD, 2006 ILADS, Crowne Plaza Hotel, Center City Philadelphia

Low CD57-count: Laboratory report

No serological evidence for an infection with Anaplasma.

CD 57 Flow Cytometry				
Leucocytes		3.31	/ul	2.6-10.0
Peripheral Lymphocytes		34.10	%	18.0-51.0
Lymphocytes		11.29	/µl	468-5100
Natural killer cells		17.98	%	6-29
Natural killer cells		203	/µl	60-700
CD 57 positive NK-cells		6.06	%	2-77
CD 57 positive NK-cells	-	68	/µl	100-360

The CD57-cell-count is an indication for a chronic immune-suppressive situation caused by Borrelia burgdorferi.

Blood Count				
Hemoglobin		14.8	g/dl	14-18
Erythrocytes		4.94	mill./ul	4.5-5.9
Hematocrit		44.0	%	40-54
MCH		30.0	pg	28-32
MCHC		33.6	g/dl	32-36
MCV		89.1	fl	80-98
Thrombocytes		222	tsd/ul	150-350
Leucocytes	-	3.31	tsd/ul	4-10

Differential Blood Count			
Basoph. Granulocytes	0.60	%	0-2
Eosin. Granulocytes	3.30	%	0-4
Neutroph. Granulocytes	49.6	%	40-70
Lymphocytes	34.1	%	25-40
Monocytes	12.4	%	2-14

What you should do: Basic diagnostic tests for chronic Borrelia infection

1. **Borrelia IgM- and IgG- antibodies by immunoblot-technique - NOT Elisa**
2. **Borrelia Elispot (LTT): actual Borrelia activity**
3. **CD3-/CD57+ T-Lymphocytes: chronic Borrelia activity**

Normalization 2 months after the end of therapies to verify a successful or not successful therapy.

Laboratory "STAGING" process

LYME BORRELIOSE and CO-INFECTIONS

Borrelia burgdorferi

+ Babesia

+ Bartonella

+ Ehrlichia/Anaplasma

+ Chlamydia

+ Rickettsia/Coxiella

+ Mycoplasma

+ Viruses (EBV, CMV, HSV)

Ehrlichia / Anaplasma

Bacteria: Ehrlichia chaffeensis, Anaplasma phagocytophilum (gram-negative, obligatory intracellular in granulocytes)

Vector: Ixodes ricinus

Spectrum of hosts: game (e.g. deer), domestic animals, humans

Symptoms (incubation time: days up to 4 weeks): rapid onset of beginning illness with fever, headache and prostration, headaches are "sharp, knife-like and often located behind the eyes", muscle pain, not joint pain, neurological symptoms (length: 1 up to 60 days) up to lethal ending, rarely diffuse vasculitic rash, including palms and soles (<10%)

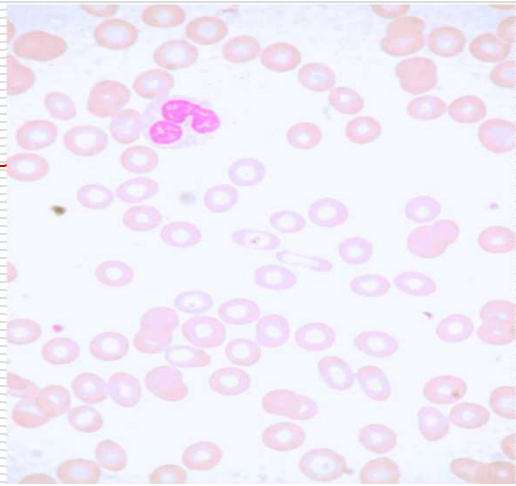
Risk factors: older people, severe basic illness, immune suppression (children)

Diagnosis Ehrlichia/ Anaplasma

Cellular activity test:
Ehrlichia/Anaplasma Elispot-LTT (Lymphocyte Transformation Test)

Antibodies: Ehrlichia-IgM and Ehrlichia-IgG

Babesia



Bacteria: Babesia microti, Babesia divergens, B. WA1

Vector/Transmission: Ixodes ricinus, blood transfusion

Hosts: game (e.g. deer), domestic animals, humans

Symptoms (incubation time 5 days – 9 weeks):

Rapid onset of beginning illness with severe fever, headache (can be severe-dull, global, involves the whole head, described like the head is in a vise), sweats (usually at night, but can be day sweats as well), fatigue (worse with exercise), "air-hunger", need to sigh and take a deep breath, dry cough without apparent reason, stiffness of neck, nausea, diminished appetite, tiredness, feeling of weakness, permanent exhaustion even worse during stress, dizziness, haemolytic anemia, hemoglobinuria, seldom hepatosplenomegalia, muscle pain, dizziness, mental dullness and slowing of reactions and responses, hypercoaguability, stomach pain, emotional lability, „mental dullness", kidney problems, dyspnoea, influenza like symptoms could be lethal!

Risk factors: Splenectomia, HIV, immune suppression (children), organ transplantation, older people

Human Babesiosis World map With Vector map

Alan MacDonald MD: Editorial Comment: Geographies with Endemic Babesiosis do not exist in a vacuum. Endemic Lyme borreliosis travels with Endemic human Babesiosis!!!!!.

The NEW ENGLAND JOURNAL of MEDICINE

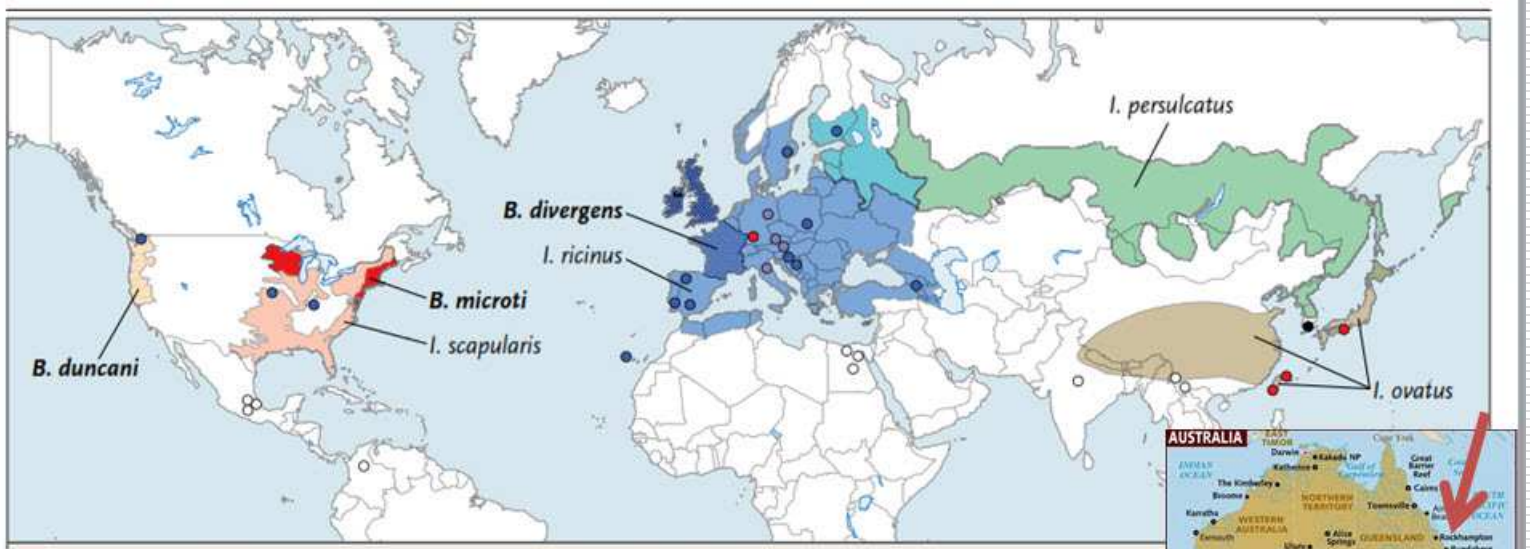


Figure 1. Geographic Areas Where Human Babesiosis and Ixodes Tick Vectors Are Endemic.

IMAGE Credit: New England Journal of Medicine: Vannier,E., and Krause, P., 2012, 366:2397-2401 (Modified to Include Australian endemic Human babesiosis)

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Babesia: Diagnosis

Babesia-DNS-PCR/FISH in blood

Antibodies: Babesia-IgM and Babesia-IgG

Bartonella (cat scratch fever)

Bacteria: Bartonella henselae (gram-negative, optional intracellular in endothel-cells / erythrocytes) and/or BLO = Bartonella like organisms

Vector/Transmission: cat-scratch surface wounds, Ixodes ricinus (Germany/Europe: up to 40% contaminated ticks)

Symptoms (incubation time 3 – 38 days): headache (80%), tiredness (100%), amyostasia, muscle twitches, tremors, seizures, fever in the mornings (30%, in thrusts up to 6 weeks, otherwise 1 – 3 weeks), swollen lymphnodes, arthralgia (often), myalgia, insomnia, depression, agitation, severe mood swings, amentia, lack of concentration and alertness, dizziness, anxiety, outbursts, antisocial behaviour, restlessness, gastritis, intestinal symptoms, sore soles (especially in the morning), tender subcutaneous nodules along the extremities, occasional lymphadenopathy and light sweats; Complications: endocarditis, retinitis, epilepsy, aseptic meningitis, hepatosplenomegalia

BLO: No or only minimal musculoskeletal symptoms (according to JJ. Burrascano)!

Risk factors: immune suppression (children)

Bartonella: Diagnosis

Antibodies Bartonella henselae/quintana-IgM and Bartonella henselae/quintana-IgG

Elevated vascular endothelial growth factor (VEGF) seldom increased, but in such cases activity marker for monitoring

Rickettsia

Bacteria: Rickettsia conorii, R. rickettsii, R. helvetica, R. slovaca, R. prowazekii (not gram-stainable, obligatory intracellular in endothel cells)

Vector/hosts: rodent, dogs, humans, Ixodes ricinus

Symptoms (incubation period 5 - 7 days): fever, lymphadenitis, exanthema

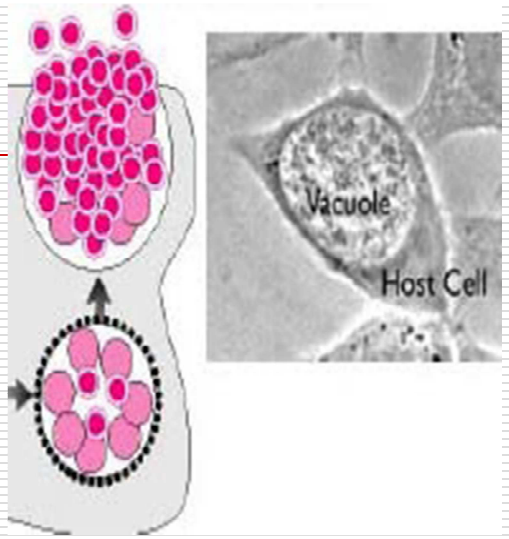
Complications (app. 13%): peri-/myocarditis, kidney insufficiency, pneumonia, encephalitis, gastrointestinal bleedings, anemia, hepatitis, myalgia

Rickettsia: Diagnosis

PCR Rickettsia in blood (EDTA-blood)

Antibodies Rickettsia-IgM and -IgG

Chlamydia pneumoniae infection



Bacteria: Chlamydophila pneumoniae (gram-negative, intracellular)

Vector/Transmission: airborne infection, human

to human, ticks ? Or reactivated in Lyme disease

(horses, koalas, frogs are infected)

Symptoms: **cough, slight throat pain, hoarseness,**

sinusitis, atypical pneumonia, meningoencephalitis, bronchiolitis obliterans, myocarditis, Guillain-Barre-Syndrom

after infection (4-6 weeks): arthritis, tendovaginitis

Associations: e.g. Morbus Alzheimer, Multiple Sclerosis, Depressions, Fibromyalgia, Chronic Fatigue Syndrome (CFS), heart attacks, acute ischemic stroke (AIS), arteriosclerosis, Autism, Parkinsonism, Rheumatoid Arthritis

Risk factors: immune suppression (children/older people)

Chlamydia pneumoniae: Laboratory tests

T-Cellular activity test:

Chlamydia pneumoniae Elispot-LTT (Lymphocyte Transformation Test)

Antibodies for Chlamydia pneumoniae-IgA and Chlamydia pneumoniae-IgG: indirect detection, half-life time of local-standing IgA-antibodies: 2 weeks

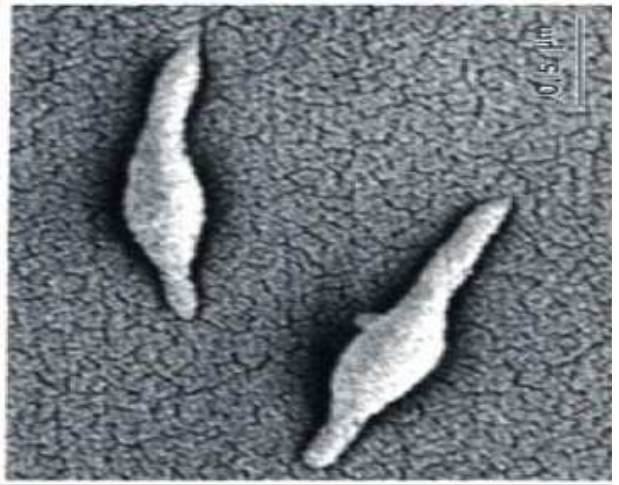
New study IgA in AIS: 60.8 %

"Chlamydia pneumoniae seropositivity in adults with acute ischemic stroke: A case-control study", NK Rai et al., Official Journal of Indian Academy of Neurology, 14, 2011 p. 93-97)

Chlamydia pneumoniae: Therapy

- Macrolides (**Azithromycin, Clarythromycin**)
- **Doxycyclin/Minocyclin**
- Levofloxacin
- **Metronidazole**

Mycoplasma infection

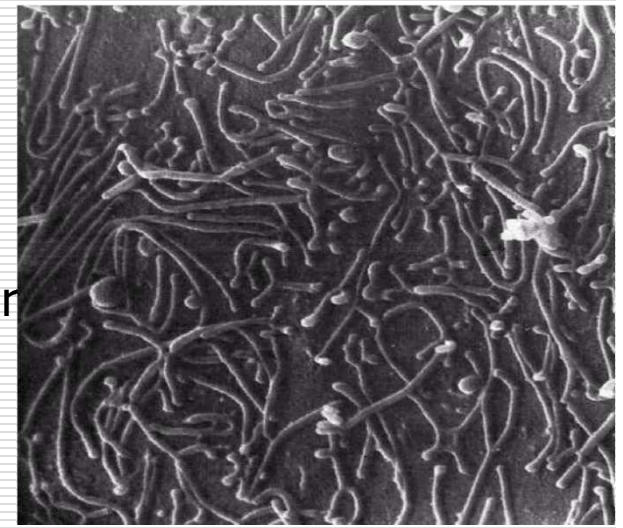


Bacteria: Mycoplasma pneumoniae/fermentans (gram-positive, intracellular)

Transmission: airborne infection (aerogen),

human to human, ticks ?

Symptoms: tiredness (100%), fever, joint pain, swelling of joints, muscle pain, headache, insomnia, anxiety, emotional lability, lack of concentration, memory loss, Autism



Risk factors: immune suppression (children/older people), Chronic Fatigue Syndrome (CFS), „Gulf War I syndrome"

Mycoplasma: Laboratory tests

Antibodies: Mycoplasma pneumoniae-IgA and Mycoplasma pneumoniae-IgG: indirect detection (half-life time of local-standing IgA-antibodies: 2 weeks)

Mycoplasma: Therapy

- Macrolides (**Azithromycin, Clarythromycin**)
- **Doxycyclin/Minocyclin**
- **Metronidazole**
- Levofloxacin, Ciprofloxacin

Other complicating / reactivated viruses or bacteria

- ☑ Yersinia enterocolitica
- ☑ Herpes simplex Virus Typ I/II
- ☑ Cytomegalie-Virus
- ☑ Toxoplasma
- ☑ Epstein-Barr-Virus
- ☑ Borna-Virus
- ☑ Hepatitis C-Virus
- ☑ Coxsackie-Virus

Coinfections-Checklist: Patient 1

B.C.
Name, First name

15th Oct. 2010
Date

►	**Symptoms - Please tick the appropriate symptoms** (to be filled in by the patient)	X	**Score-Points** (to be filled in by the physician)	**Ran-king**
01	Stomach-ache	X	Ehrlichia: **5**	**4**
02	Anaemia		Babesia: **5**	**4**
03	Diarhoea		Rickettsia: **5**	**4**
04	Fever or feverish feeling	X	Bartonella: **6**	**3**
05	Lack of concentration, memory disturbance, forgetfulness	X	Chl.pneumoniae: **8**	**1**
06	Encephalitis (Inflammation of the brain)		Chl.trachomatis: **3**	**6**
07	Yellowish colour of the skin (Jaundice)	X	Yersinia: **4**	**5**
08	Painful joints	X	Mykoplasma: **7**	**2**
09	General aches and pains	X	Coxsackie-Virus: **7**	**2**
10	Flu-like symptoms	X	EBV: **6**	**3**
11	Rash			
12	Petechiae			
13	Heart-problems	X		
14	Cough			
15	Headache	X		
16	Impaired liver function/ liver parameters			
17	Pneumonia			
18	Swollen or inflamed lymph nodes			
19	Tonsilitis			
20	Enlargement of the spleen (Splenomegaly)			
21	Fatigue / exhaustion	X		
22	Muscle pain	X		
23	Shivering	X		
24	Blurred vision			
25	Nausea, vomiting	X		
26	Dark urine	X		
27	Painful or ichty urinating			

Laboratory test results: Patient 1

		Results	Unit	Reference range
Borrelia burgdorferi antibodies (ELISA)				
Borrelia-IgG-antibodies (ELISA)	+	**71.9**	RU/ml	< 16=neg. > 22.0=pos.
Borrelia-IgM-antibodies (ELISA)		4.72	RU/ml	< 16=neg. > 22.0=pos.
Borrelia burgdorferi antibodies (immunoblot)				
Borrelia-Blot-IgG-antibodies	+	**positive**		negative
		Bands: OspC (+),p41 +, VlsE-Bb +		
Borrelia-Blot-IgM-antibodies		negative		negative
Borrelia burgdorferi Elispot LTT				
Borrelia burgd. Fully Antigen	+	**4**	SI	< 2
Borrelia OSP-Mix (OSPA/OSPC/DbpA)	+	**3**	SI	< 2
Borrelia LFA-1		1	SI	< 2
Yersinia antibodies				
Yersinia-IgG-antibodies (EIA)	+	**1.9**	Ratio	<0.8=neg.; >1.1=pos.
Yersinia-IgA-antibodies (EIA)	+	**8.6**	Ratio	<0.8=neg.; >1.1=pos.

Laboratory test results: Patient 1

		Results	Unit	Reference range
Yersinia Elispot LTT				
Yersinia-Elispot LTT	+	**20**	SI	< 2
Chlamydia pneumoniae antibodies				
Chlam.pneum.-IgG-antibodies (ELISA)	+	**1.2**	Ratio	<0.8=neg.;>1.1=pos.
Chlam.pneum.-IgA-antibodies (ELISA)	+	**3.5**	Ratio	<0.8=neg.;>1.1=pos.
Chlamydia pneumoniae Elispot LTT				
Chlamydia pneumoniae-Elispot LTT	+	**18**	SI	< 2
Mycoplasma pneumoniae antibodies				
Mycoplasma pneumoniae-IgG (EIA)	+	**1.1**	Ratio	< 0.8 = neg.; >1.1 = pos.
Mycoplasma pneumoniae-IgM (EIA)		0.3	Ratio	< 0.8 = neg.; >1.1 = pos.
Mycoplasma pneumoniae IgA (EIA)	+	**2.0**	Ratio	< 0.8 = neg.; >1.1 = pos.
Cytomegalo-Virus				
Cytomegalo-Virus-IgG-antibodies (EIA)	+	**3.7**	Ratio	<0.8=neg.;>1.1=pos.
Cytomegalo-Virus-IgM-antibodies (EIA)		0.3	Ratio	<0.8=neg.;>1.1=pos.
Cytomegalo Virus Elispot LTT				
CMV-Elispot LTT	+	**4**	SI	<2

Laboratory test results: Patient 1

		Results	Unit	Reference range
Coxsackie-Virus antibodies				
Coxsackie-Virus-IgG Type B1 (IFT)	+	**1:400**	Titer	< 1:100
Coxsackie-Virus-IgA Type B1 (IFT)	+	**1:100**	Titer	< 1:10
Rickettsia antibodies				
Rickettsia rickettsii IgG-antibodies	+	**1:256**	Titer	< 1:64
Rickettsia typhi IgG-antibodies		< 1:64	Titer	< 1:64
Epstein-Barr-Virus antibodies				
EBV-CA-IgG-antibodies (EIA)	+	**7.1**	Ratio	< 0.8=neg; >1.1=pos
EBV-EBNA-antibodies (EIA)	+	**4.2**	Ratio	< 0.8=neg; >1.1=pos
EBV-CA-IgM-antibodies (EIA)		0.4	Ratio	< 0.8=neg; >1.1=pos
Epstein-Barr-Virus Elispot LTT				
EBV-Elispot-LTT (lytic)	+	**17**	SI	< 2
EBV-Elispot-LTT (latent)	+	**8**	SI	< 2
CD 57 Flow Cytometry				
CD 57 positive NK-cells	-	**37**	/µl	100-360

Summary Patient 1 (Spanish patient)

Coinfections-checklist (symptoms):

Multiple infection with

Borrelia burgdorferi + Chlamydia pneumoniae + Mycoplasma pneumoniae + Coxsackie-Virus + Epstein Barr Virus + Rickettsia + Yersinia

Laboratory test results:

Multiple infection with

Borrelia burgdorferi + Chlamydia pneumoniae + Mycoplasma pneumoniae + Coxsackie-Virus + Epstein Barr Virus + Rickettsia rickettsii + Yersinia + Cytomegalo Virus

5 bacteria + 3 viruses !

What is the therapeutical consequence ?

Antibiotics for Borrelia, Chlamydia and Mycoplasma:

- Macrolides (Azithromycin, Clarythromycin)
- Doxycyclin/Minocyclin
- Metronidazol

Intracellular working remedies:

- Hydroxychloroquin (Plaquenil)
- Artemisia annua / Artemisinin

What is the therapeutical consequence ?

Viruses (EBV, CMV, Coxsackie etc.)

- Dimepranolacedoben/Inosin 50 mg/kg body weight daily(Delimmun)
- Immunmodulation (viamins etc.)
- Herbal products / Alternative pathways

Biofilms

- Serrapeptase
- Lumbrocinase

Other/additonal therapy options

1. **Probiotics (No antibiotics without probiotics)**
2. **Minerals**
3. **Patients with musculoskeletal symptoms need pain therapy (f.e. LDN?)**

Thank you very much for your attention !

Armin Schwarzbach M.D. Ph.D.
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