

The human body may confuse *Borrelia burgdorferi* with its own tissue

- LYMERix, the US-Bb-vaccine on Osp-A-basis, has been recalled because of side-effects (Feb. 2002)
- Some of side-effects may be caused by "molecular mimicry" of Osp-A with hLFA-1²
 - arthritic complaints
 - o possibly impaired leucocyte-funktion
- Part of the side-effect can be induced (in this way) without vaccination
- Cross-reactivity of 41kD with myelin of peripheral nerves¹

1. Aberer, Ann Neurol 26, 1989, 732-737: Molecular Mimicry and Lyme Borreliosis: A Shared Antigenic Determinant Between *Borrelia burgdorferi* and Human Tissue
2. Steere AC, Gross D, Meyer AL, Huber BT; J Autoimmun 2001 May;16(3):263-8; Autoimmune mechanisms in antibiotic treatment-resistant Lyme arthritis

Quorum sensing - Bacterial interactions: What's that ?

Why are micro-organisms simultaneously active?
How do they communicate?
Do we find this phenomenon at Bb ?
LuxS

Possible implications for LD:

- "up-regulation" of erp / OspE (CRASPs)
- "flares" - symptoms can be active at different points of the body

Stevenson B, Babb K.; Infect Immun 2002 Aug;70(8):4099-105; LuxS-mediated quorum sensing in *Borrelia burgdorferi*, the Lyme disease spirochete.

Parts of Bb cell wall protect Bb from the host defence system

by manipulation of complement Systems (CRASPs)
Factor H binding
OspE

1. The Journal of Immunology, 2002, 169: 3847-3853. Complement Inhibitor Factor H Binding to Lyme Disease Spirochetes Is Mediated by Inducible Expression of Multiple Plasmid-Encoded Outer Surface Protein E Paralogs, Alitalo et al.
2. Brade, Kraiczy: Immunevasion of Bb: Insufficient killing of the pathogens by complement and antibody; Int.J.Med.Microbiol.291; Suppl.33; 141-146 (2002)

Co-Infections with

Babesia

- ca. 5% seropositive, "healthy" adults¹

Ehrlichia

Bartonella

- cat-scratch-disease
- cases of death at Swedish "elite-cross-runners", eg myocarditis²

Rickettsia

- spotted fever³

FSME / TBE (Virus)

Other *Borrelia*-species

- relapsing fever⁴

1. Hunfeld KP et al. Wien Klin Wochenschr, 1998; 110: 901-8
2. McGill S et al. Scand J Infect Dis, 2001; 3: 423-8
3. Appl Environ Microbiol 2002 Sep;68(9):4559-66 *Rickettsia monacensis* sp. nov., a Spotted Fever Group Rickettsia, from Ticks (*Ixodes ricinus*) Collected in a European City Park. Simser JA, Palmer AT, Fingerle V, Wilske B, Kurti TJ, Munderloh UG.
4. Richter D, Schlee DB, Matuschka F-R. Relapsing fever-like spirochetes infecting European vector tick of Lyme disease agent; Emerg Infect Dis 2003 June; Vol. 9, No. 6; <http://www.cdc.gov/ncidod/EID/vol9no6/02-0459.htm>

Borrelia burgdorferi-debris can make you ill

Lysis of Bb, e.g by taking antibiotics, may release cell wall pieces

- acute: Herxheimer-reaction
It's estimated that parts of Bb cell wall of gram negative bacteria) are responsible for a severe course of illness (Lyme-encephalopathy)
- ca. 3% dry-weight of Bb are LPS
 - Perhaps colestyramine inhibits the entero-hepatic (cephalic) circulation of toxins
 - ? production of ectotoxins, Bbtox-1, (like *Botulinus*.-toxin?)

1. pro NT: Zajkowska, Juchnowitz; Przegł Epidemiol 2002; 56 Suppl 1:37-50 (Abstract)
2. Beck; Inf. Dis 152 (1985), 108-117, Chemical and biological characterization..
3. contra LPS: Takayama; 1987, Absence of LPS in Bb; Infect.Immun, 55, 2311-13

Heterogeneity, antigenshift and antigendrift may lead to

- immunevasion
- difficulties in serological testing
- symptom-flares like relapsing-fever

1. Onishi et al.; Antigenic and genetic heterogeneity of Bb populations transmitted by ticks; Proc.Natl.Acad.Sci. USA 2001;January 16; 98 (2): 670-675
2. Fang et al.: An Immune Evasion Mechanism for Spirochetal Persistence in Lyme Borreliosis; JEM Vol 195; No.4; Febr. 18, 2002 415-422
3. Hefty et al.: Changes in Temporal and Spatial Patterns of Outer Surface Lipoprotein Expression Generate Population Heterogeneity and Antigenic Diversity in the Lyme-DiseaseSpirochete, *Borrelia burgdorferi*: Infection and Immunity July 2002; p. 3468-3478
4. Wilske et al.:Impact of Strain Heterogeneity on Lyme Disease Serology in Europe:Comparison of Enzyme-Linked Immunosorbent Assays Using Different Species of *Borrelia burgdorferi* sensu lato; JCM Febr. 1998, 427-436

Borrelia burgdorferi may lead to immune-deficiency

Bb suppresses inflammation (TNF- α , γ -interferon, G-CSF)
-possibly no fever
-lack of : ESR, CRP, leucocytes-funktion
Trial: supplication of G-CSF (Hartung, Konstanz)

1. Diterich,Hartung; Modulation of Cytokine Release in Ex Vivo-Stimulated Blood from Borreliosis Patients, Infection and Immunity, Febr. 2001, p.687-694
2. Current study of Universität Konstanz about antibiotics plus Neutropen for the treatment of LD
3. Immunology Volume 107 Issue 1 Page 46 - September 2002 ; Cytokines in Lyme borreliosis: lack of early tumour necrosis factor-alpha and transforming growth factor-beta1 responses are associated with chronic neuroborreliosis, Mona Widhe

"When diagnosed early, borreliosis can be treated successfully with antibiotics. If the infection is not diagnosed, diagnosed too late or treated with an inadequate or overly short course of antibiotics, a chronic course of the disease may develop affecting the nervous system, joints and heart which is difficult or even impossible to treat."

1. BgVV, IPS VI, Berlin 2001, press release 15/2001, 27. April 2001;
2. D.T. Dennis, CDC; oral presentation, IPS VI, Berlin 2001 - "...sometimes it's severe or disabling, in particularly, when the diagnosis is missed early..."