"Lyme-Borreliosis is the most frequent TBD in Germany. Its incidence is estimated between 50-thousand and 100-thousand each year."

Wilske, Fingerle et al. on CD: "Lyme-Borreliose", version 1.0, Hoffmann-La-Roche AG, Nov. 2001

Incidence of Lyme-Disease in Germany:
50.000 - 60.000 / year
and in 150 -200 of TBE

Incidence of Lyme-Borreliosis in the region "Oder-Spree": 89,3 / 100 000
and in "Amt Scharmützelsee" 237 / 100 000
inhabitants
Talaska, Brandenburgisches Ärzteblatt 11 / 2002; 338-340

**PREVALENCE AND INCIDENCE OF LYME-BORRELIOSIS IN SOUTH AND EAST BAVARIA**

"We observed an incidence of Lyme-Disease of 1.5 % per year and 0.6 % of symptomless new infections per year."

Poster: B. Reimer1, A. Marschang1, V. Fingerle2, B. Wilske2, F. v. Sonnenburg1
1 Abteilung für Infektions- und Tropenmedizin, 2 Max-von-Pettenkofer Institut für Mikrobiologie, Universität München, 1999

"0.5% of the population are getting ill every year!"

"In the area examined by us, namely Kraichgau in Nord-Baden, about 17% of the population are seropositive. Most of these seropositive patients also have characteristic complaints. By prospective investigation of the cohort over nearly ten years we show that the annual rate of new illnesses (incidence) amounts to about 0.5% of the population."

http://www.dieterhassler.de/diagnostik_und_therapie.htm

"Every 5th inhabitant of Baden-Württemberg is infected with Borrelia burgdorferi. There are 40.000 new cases of infection every year according to bio-toxicologist Thomas Hartung at a workshop in the University of Konstanz. The danger of illness is particularly high in the large region of Konstanz, because an average of 35 percent - in individual areas up to 57 percent - of ticks are infected with Borrelia which they could pass on to humans."1

Comparison: in the area of Berlin-Brandenburg up to 60% of ticks are infected with Bb (Burmester) 2

1. Stuttgarter Zeitung v. 22. Februar 2001; S.7

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**Vectors / transmission of Borrelia burgdorferi**

**Mites** 1 “Work, which we completed this autumn, showed that mites feeding on Borrelia burgdorferi infected mice take up Borrelia. This puts mite-problems in a new light and requires epidemiological investigations ...”

1. http://www.meb.uni-bonn.de/parasitologie/wissensch.htm

**Mosquitoes** 2 Aedes vexans for B.afzelii
1. MMW 131 (1989) Nr. 18, S. 93
5. Magnarelli, J Clin Microbiol; Aug 1988; p 1482-1486 Ticks and Biting Insects with the Etiologic Agent of Lyme Disease, Borrelia burgdorferi.

**Tick species**

**Larvae (transovarial infection)**

**Nymphs**

**Adult ticks**

1. L. Gern, Schweiz; oral presentation, IPS-VI; Berlin 2001

Highly infectious ticks may carry more than 100 spirochetes 1
In spring-time Bb often is transmitted via ticks by cystic forms 2

3. L. Gern, Schweiz; oral presentation, IPS-VI; Berlin 2001

**Transmission of Bb during pregnancy and by blood-transfusion**

- Bb survives longer than treponema-pallidum in a refrigerator: 25 days at 4°C 1
- histological proof of foetal organs: mostly no inflammation, negative serology 2

1. Pantanowitz, Transfusion Medicine, 2002, 12, 85-106 (overview)

**It´s not always a tick: "biting flies" may be vectors of Borrelia burgdorferi as well as other insects**

1. MMW 131 (1989) Nr. 18, S. 93
5. Magnarelli, J Clin Microbiol; Aug 1988; p 1482-1486 Ticks and Biting Insects with the Etiologic Agent of Lyme Disease, Borrelia burgdorferi.
Pathomechanisms of Borrelia burgdorferi sensu lato and their implications for diagnostics, clinical appearance and treatment of Lyme-Disease

**Borrelia burgdorferi grows slowly**

Bb needs ca. 12-20 (8-35) hours for one generation-time
- cf E. coli needs ca. 20 min for one generation-time
- Bb sometimes needs 10 weeks for cultivating


**Borrelia burgdorferi sequester in tissue which is poorly vascularised**

- connective tissue (present in all organs) and which is
- poorly infiltrated by defence cells - the immune system


**Borrelia burgdorferi is able to invade human cells and persist there:**

e.g. blood-cells (macrophages), fibroblasts, endothelial, and synovial cells

Perhaps Bb can even survive in CNS-cells?


**Cell wall permeable antibiotics are required to treat intracellular Bb**

- Tetracycline, Doxycycline, Minocycline
- Macrolides: Roxithromycin, Azithromycin, Clarithromycin, - no Erythromycin!


**Borrelia burgdorferi can change its appearance**

- by "starvation" (antibiotics, CSF) Bb can change its appearance:
  - cyst, bleb, mesosom, granulum
- a "cyst" / L-form / spheroblast can later convert to living spirochetes again

2. Kestler, Antimicrobial Agents and Chemotherapy, May 1995; p.1127-1133; Effects of Penicillin, Ceftriaxone and Doxycycline on Morphology of Bb

**The slow growing of Bb means for the infected human being:**

- He / she can become ill a long time after infection (latency) 1
- treatment has to take a long time to reach as many generations as in treatment of fast-growing-bacteria (60 -100 x²)
- Consider using therapy-principles of other slow-growing-bacteria; e.g.: M. leprae, M. tuberculosis, T. pallidum
  - treatment of TBC: combi for at least 6 months;
  - similar to leprosy: ca. 2 years combi-therapy (E. Frekses, Borstel, Malta): before at least 10 years of Dapson 2

2. Hans Schadewaldt, Über die Rückkehr der Seuchen; VGS Köln 1994, S. 68; Robugen

"Considering an early germ-dissemination into CNS .. it seems being necessary to reach high antibiotic-levels in target-tissues like joint-synovia or CNS .. even in treatment of erythema migrans or Borrella-lymphozymosis."


**Decerin-binding-proteins (Dbp A, DbpB) are thought to be adhesion-molecules of Bb to collagen-associated extracellular matrix (decorin)**


**"Cysts" are resistant to the usual antibiotics**

- Metronidazole can be used against cysts
- CNS tissue is highly permeable to it
- Metronidazole can cause cancer or harm an embryo / foetus
- Possible to use other treatment options against cysts: Hydroxychloroquin (anti-malaria-drug); ranitidine bismuth citrate

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-1
  - arthritic complaints
  - 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 nerves

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

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 (cphalic) circulation of toxins
  - production of ectotoxins, Bbtox-1, (like Botulinus-toxin?)

1. pro NT: Zajkowska, Juchnowitz; Przegl Epidemiol 2002; 56 Suppl 1.37-50 (Abstract)
3. contra LPS: Takayama; 1987, Absence of LPS in Bb; Infect. Immun. 55, 2311-13

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


Heterogenity, antigenshift and antigendrift may lead to
- immunewasion
- difficulties in serological testing
- symptom-flares like relapsing-fever

2. Fang et al.: An Immune Evasion Mechanism for Spirochetal Persistence in Lyme Borreliosis; JEM Vol 195; No.4; Febr. 18, 2002 415-422

Heterogeneity, antigenshift and antigendrift may lead to
- immunewasion
- difficulties in serological testing
- symptom-flares like relapsing-fever

Parts of Bb cell wall protect Bb from the host defence system by manipulation of complement Systems (CRASPs)
- Factor H binding OspE


Borrelia burgdorferi may lead to immune-deficiency

BB suppresses inflammation (TNF-α, γ-interferon, G-CSF) –possibly no fever
- lack of : ESR, CRP, leucocytes-function

Trial: supplication of G-CSF (Hartung, Konstanz)

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."

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..."

Co-Infections with

Babesia
- ca. 5% seropositive, "healthy" adults

Ehrlichia

Bartonella
- cat-scratch-disease
- cases of death at Swedish "elite-crossrunners", eg myocarditis

Rickettsia
- spotted fever

FSME / TBE (Virus)

Other Borrelia-species
- relapsing fever


Uta Everth Jun 2003