Neuroborreliosis: Challenges and experiences from Norway

London 250315

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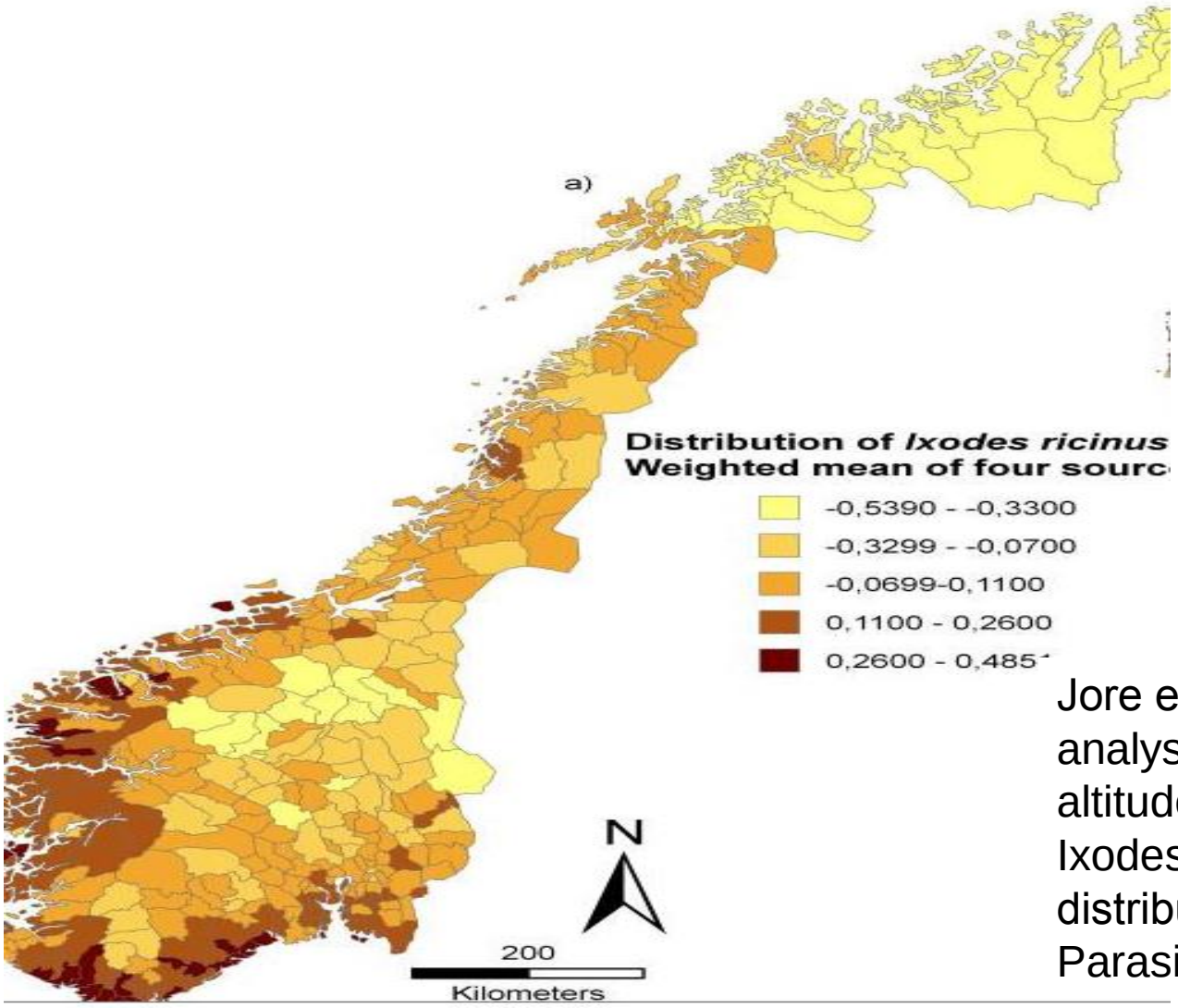
Distribution Ixodes *ricinus* in Norway

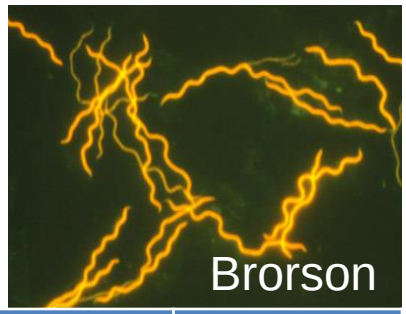


Jore et al. ”Multi- source analysis reveals latitude and altitude shifts in range of Ixodes ricinus at its northern distribution limit” Parasites & Vectors 2011

Borrelia in Ixodes Ricinus in Norway (PCR)

(Kjelland et al 2010)

- 1130 nymfs, 449 adults, 230 larva



Farsund	31 %
Mandal	25 %
Søgne	23 %
Tromøy	22 %

Bb Afselii	62 %
Bb Garinii	23 %
Bb sensu stricto	10 %
Mix	0.3 %

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MSIS- the Norwegian Surveillance System for Communicable Diseases : incidence of disseminated borreliosis

Disease	2009	2010	2011	2012	2013	2014
Disseminated borreliosis	273	288	248	256	315	321
Tick Born encephalitis	10	11	14	7	6	6

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Borreliosis clinical classification

Early localised	Early disseminated	Late disseminated
Erythema migrans Lymfocytoma	Neuroborreliosis	Late neuroborreliosis
	Arthritis	Chronic arthritis
	Carditis	Acrodermatitis chronica atropicans

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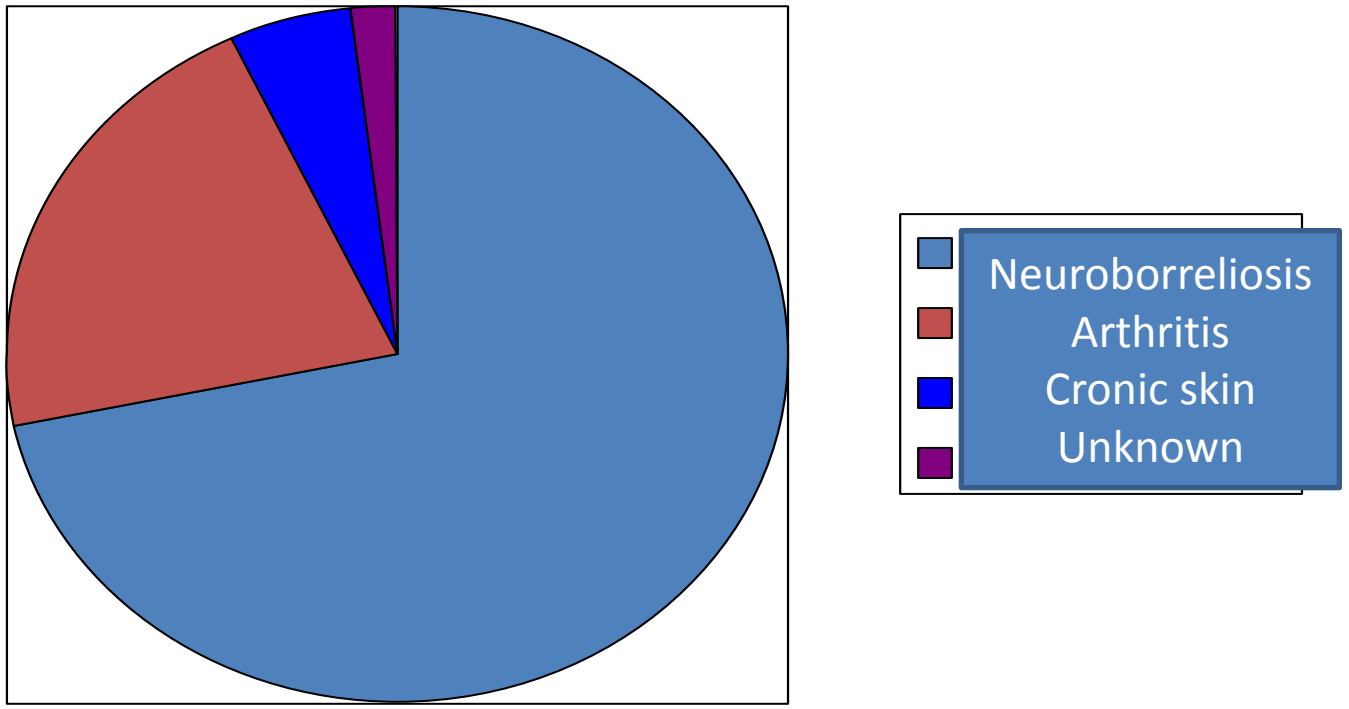
Norwegian distribution of disseminated borreliosis (MSIS)



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Risk of EM and disseminated disease after tick-bite in Norway and Sweden
STING study, EM study

Norway General practice: retrospective medical journal 2006-2007
4,67 EM/1000 inhabitants /year (Eliassen)
Sweden: 5 EM

Sting study 1546 ticks taken from bitten humans

428 carrying Borrelia
27 EM
2 neuroborreliosis
1 lymfocytoma

Low risk of developing Borrelia burgdorferi infection in the south-east of Sweden after being bitten by a Borrelia burgdorferi-infected tick. International Journal of Infectious Disease, 2011. Mars, vol 15. Fryland L, Wilhelmsson P, Lindgren PE, Nyman D, Ekerfelt C, **Forsberg P**.

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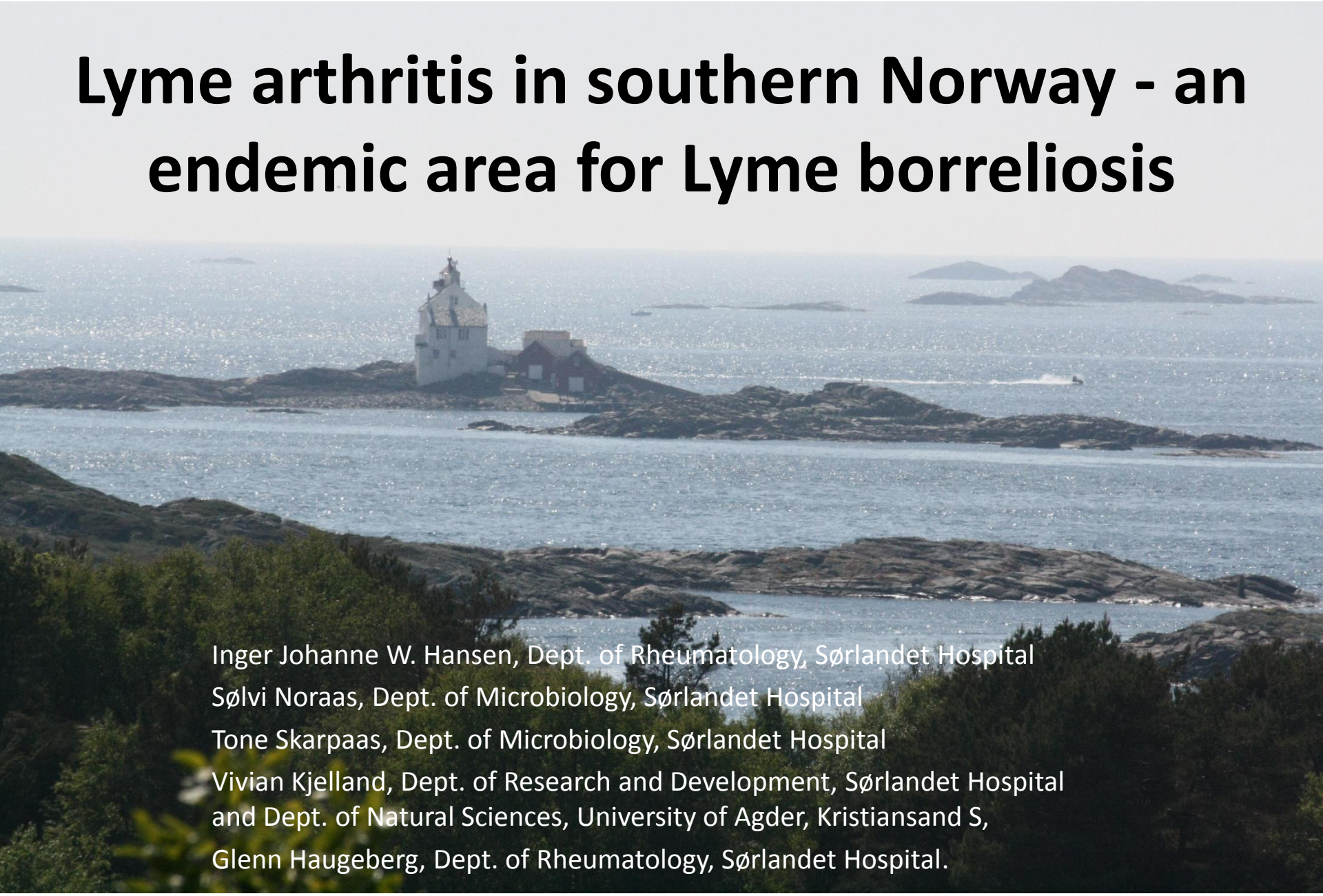
Lyme arthritis in southern Norway - an endemic area for Lyme borreliosis



Inger Johanne W. Hansen, Dept. of Rheumatology, Sørlandet Hospital

Sølvi Noraas, Dept. of Microbiology, Sørlandet Hospital

Tone Skarpaas, Dept. of Microbiology, Sørlandet Hospital

Vivian Kjelland, Dept. of Research and Development, Sørlandet Hospital and Dept. of Natural Sciences, University of Agder, Kristiansand S,

Glenn Haugeberg, Dept. of Rheumatology, Sørlandet Hospital.

Borrelia Arthritis, clinical appearance in Norway

21 cases in 5 years , incident rate of 2.7 in high endemic region:

Diagnose	N=21
Definite BA:	16
Possible BA:	5

Type artritt	N= 21
Monoarthrithis	20
Knee	18
Ankle	2
Polyarthritis	1

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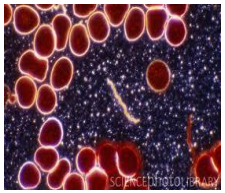
Neuroborreliosis definitions

- **Acute neuroborreliosis**: weeks to months after bite

- **Chronic neuroborreliosis**: More than 6 months after bite.



- ”**Post Lyme disease syndrome”** persistent symptoms after treated neuroborreliosis without signs of an active infection

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Diagnostic criteria neurobrreliosis

(Mygland et al. 2010 EFNS guidelines)

Definite neuroborreliosis

All 3 criteria fulfilled

1. Typical neurological symptoms
2. Pleocytosis CSF spinal fluid
3. Intrathecal anti-Borrelia antibody production

Acute nevroborreliose (NB) clinical appearance in Norway Bannwarth syndrome

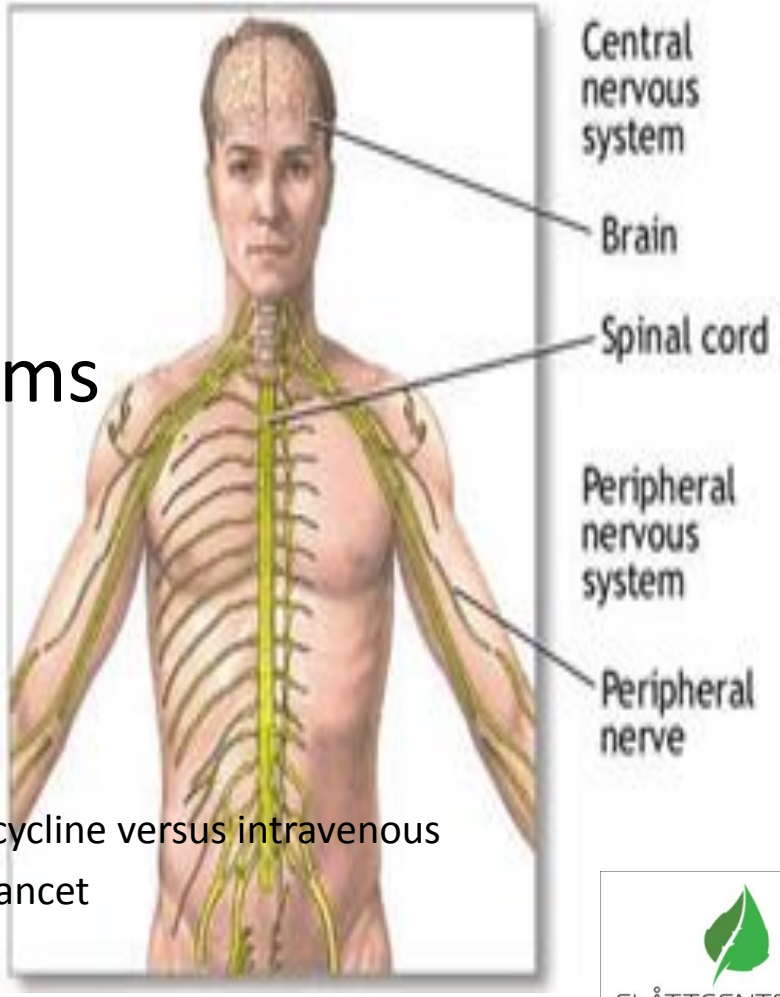
Meningitis

Radiating pain

Paresis and sensory symptoms

80% patients NB treatment

study



Ljøstad U, Skogvoll E, **Eikeland R**, Mygland A. Oral doxycycline versus intravenous ceftriaxone for European Lyme neuroborreliosis 2008 Lancet

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Exclusion of neuroborreliosis

Symptoms more than 3 months and two different ELISA negative antibody tests in blood and spinal tap

No respons of adequate treatment

Chronic Lyme; diagnostic and therapeutic challenges. Acta Neurol Scand Suppl. 2013 Ljøstad U, Mygland Å

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Nederland diagnostic and treatment guidelines on borreliosis 2013

- **Sensitivity of borrelia antibody tests:**
- Local infection: 50% sensitivity
- <6-8 weeks duration of symptoms of disseminated neuroborreliosis: 80% sensitivity
- > 8 weeks duration of symptoms of disseminated borreliosis: 98% sensitivity

(Hansen -81-91-92, Wilske -93, Goettner -05, Bacon-03)

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Treatment neuroborreliosis Norway:

- Before treatment study: Ceftriaxon 2 g iv 14 days
- After: Peroral Doxylin 200 mg for 14 days
- If suspected central nervous system infection Ceftriaxon

Ljøstad U, Skogvoll E, **Eikeland R**, Midgard R, Skarpaas T, Berg A, Mygland A. Oral doxycycline versus intravenous ceftriaxone for European Lyme neuroborreliosis: a multicentre, non-inferiority, double-blind, randomised trial. Lancet Neurol. 2008

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Long term consequences after Lyme Neuroborreliosis (LNB)?

- Antibiotics: good effect on acute symptoms
- Complaints exist in 10-50% after treatment*
- Muscular pain, fatigue and altered cognition
- Cause of long term complaints not known
- Prolonged and repeated antibiotic treatment does not seem to help**

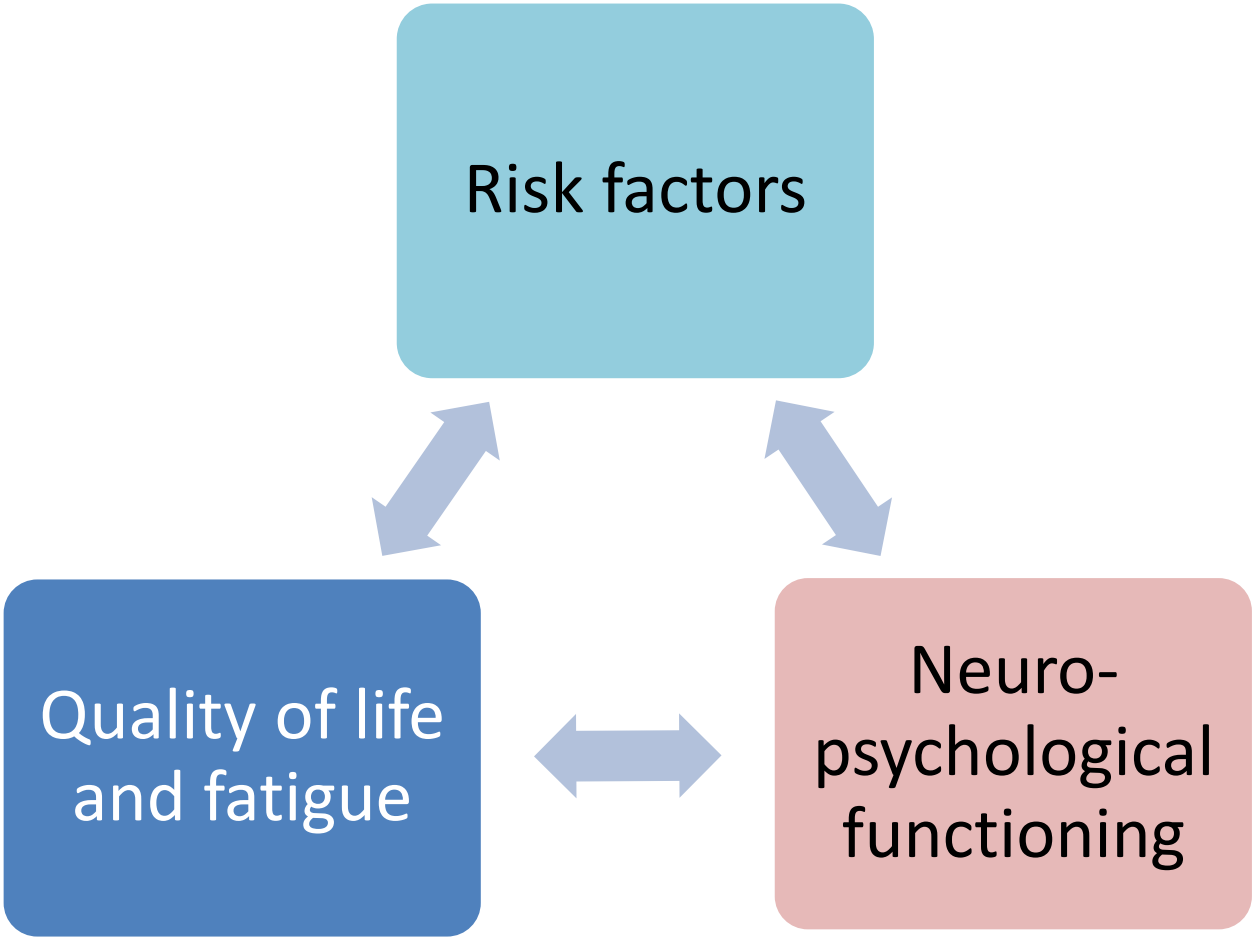
* Berglund 2002, Ljøstad 2009, Vretheim 2002

** Forsberg et al. SBU (Swedish Council on Technology Assessment) report 2013 Forsberg et al

The South Norwegian LNB cohort

- Aust- and Vest Agder county LNB treatment study 2004 -2008*
- 50 of them came to a follow-up 30 months after treatment
- Patients brought their own control person matched for age, gender and educational level without a history of LNB
- *Ljøstad U, Skogvoll E, Eikeland R et al. Oral doxycycline versus intravenous ceftriaxone for European Lyme neuroborreliosis: a multicentre, non-inferiority, double-blind, randomized trial. Lancet neurol 2008,7:609-5

Aim of the Long term prognosis after nevroborreliosis study



Neurological findings and subjective complaints

Neurological findings n=14 *	**Subjective symptoms alone n= 19****
Radiculopathy (n=6)	Fatigue (n=15)
Paresis arm/leg (n=4)	Memory loss (n=13)
Paresis face (n=3)	Attention problems (n=9)
Loss of sensation face (n=3)	Pain (n=7)
Tremor (n=2)	Paresthesias (n=7)
Reduced co-ordination (ataxia) (n=2)	Malaise (n=5)
Nystagmus(n=2)	
Reduced hearing (n=1)	
Anisocoria (n=1) *10 more than 1 finding	** 14 more than 1 symptome

Health related quality of life 30 months after treatment of LNB (SF-36)

Test (range)	Patients n=50 Mean (SD)	Controls n=50 Mean (SD)	P-level
Quality of life, physical component PCS (0-100)	44 (9)	52 (6)	**<0.001**
Quality of life, mental component MCS (0-100)	49(11)	54 (6)	**0.010**

Student t-test

Lyme neuroborreliosis reduces health related physical and mental quality of life 30 months after recommended treatment.

Fatigue and depression in LNB 30 months after treatment

Test (range)	Patients n=50 Mean (SD)	Controls n=50 Mean (SD)	P-level
Depression MADRS (0-60)	3.1 (4.9)	0.8 (1,8)	**0,003**
Fatigue FSS (0-7)	3,5 (1,9)	2.1 (1,2)	**<0,001**

Student t-test

Spinal fluid findings 30 months after LNB treatment

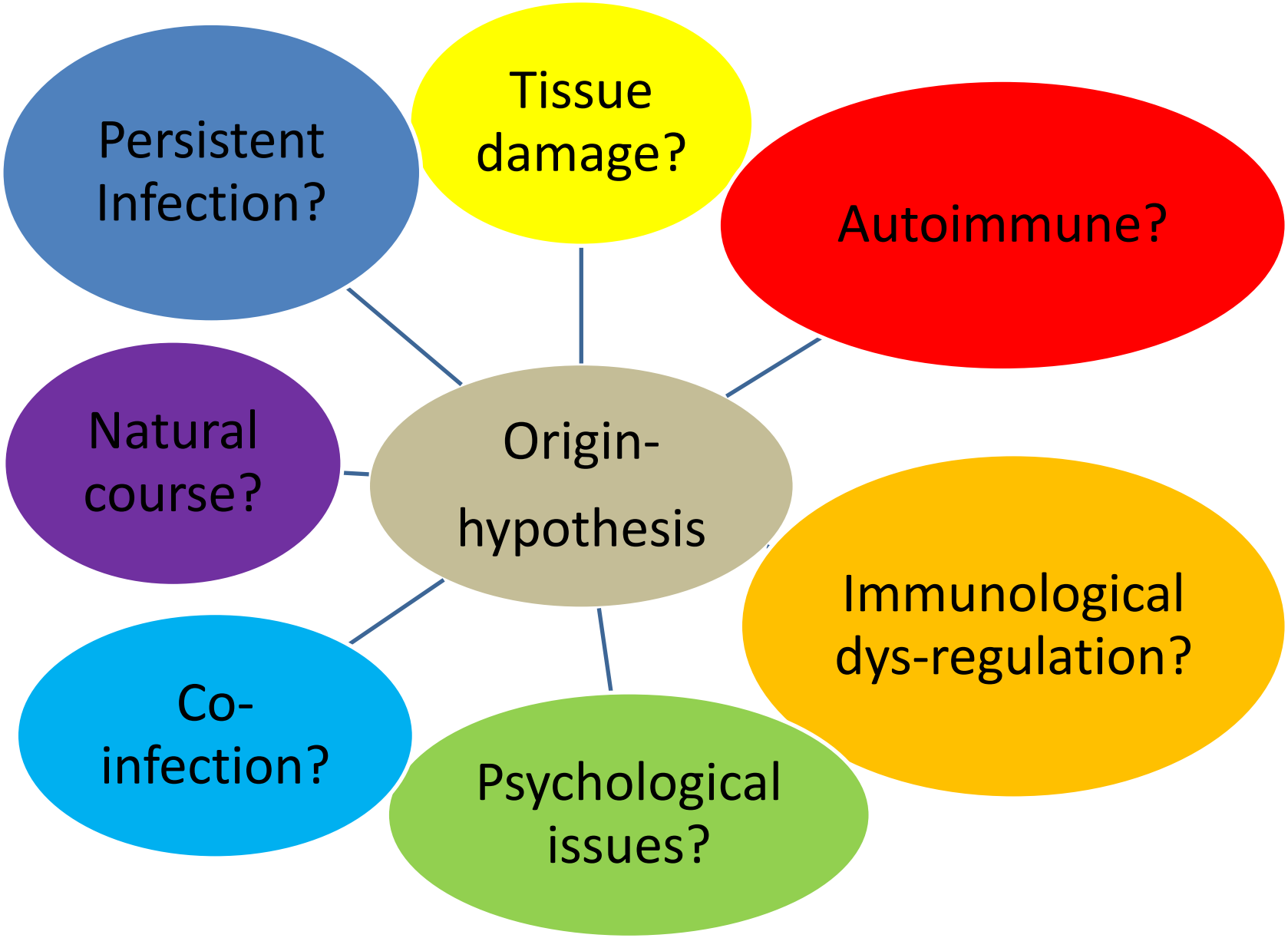
- Raised cell count:10% (one person 6, one 7 and one 66 cells , normal less than 5-6 cells)
- High protein level: 28%
- Borrelia anti- body production: 61%
- Oligoclonal bands: 43%

No signs of persistent infection

Conclusions

- Most patients recover after treated Lyme neuroborreliosis, long term complaints exist
- Reduced quality of life, fatigue and cognitive deficits
- Risk factors: Symptoms >6 weeks before treatment, more severe disease before treatment and non-recovery at 4 months
- No signs of active infection at 30 months
- Pain and depression are not the course

Course of long term complaints?



Why a national advisory unit for tick-borne diseases?

- Fear of serious consequences after tick-bite is common
- Poor knowledge and confusion about pathogens, diagnostics, treatment, prognoses among health professionals, politicians, media, patients
- Growing incidence of ticks and tick-born diseases

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Norwegian National Advisory Unit on Tick-borne Diseases

Ministry of Health

↓

The South-Eastern Norway Regional Health Authority

↓

Sørlandet Hospital Board

↓

Medical quality and safety department

↓

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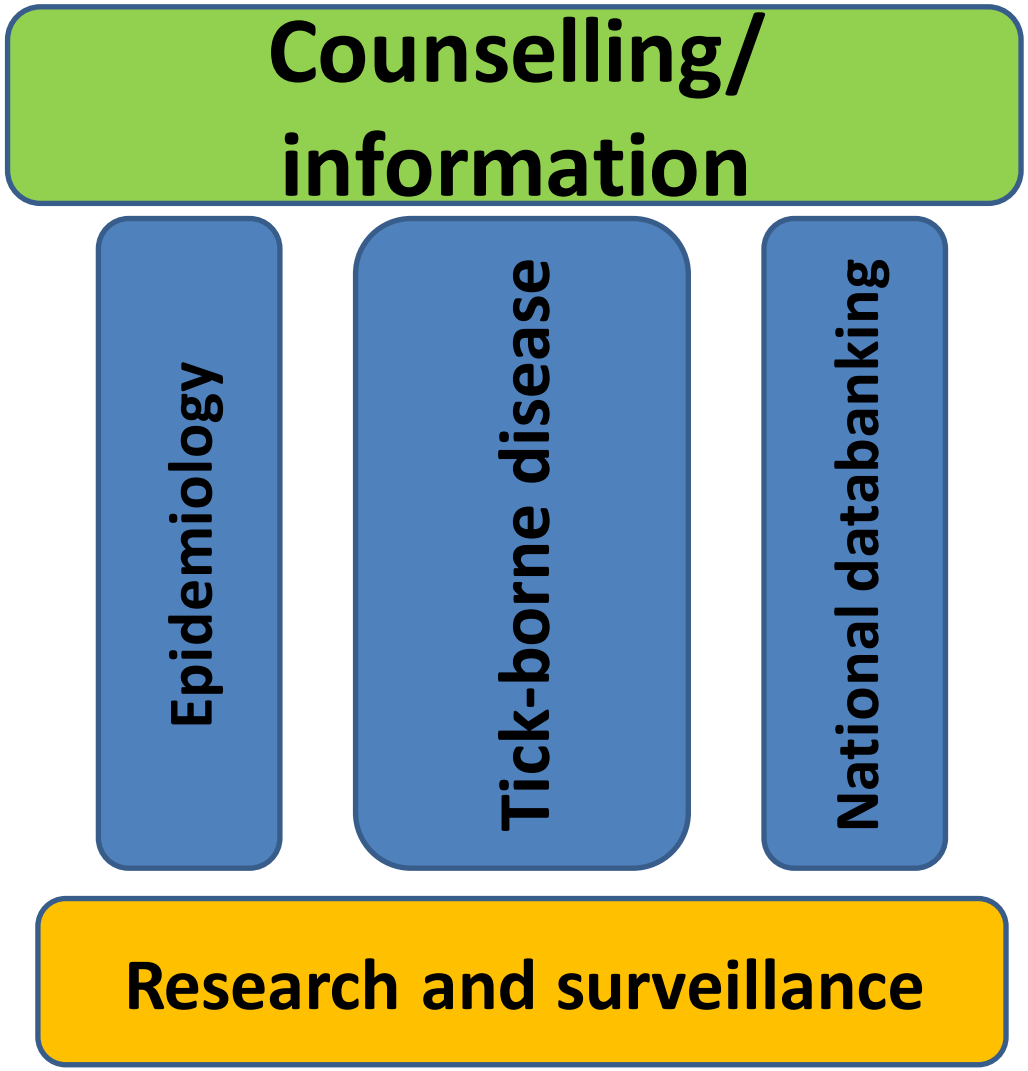

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Groups of interest

- People suffering from acute tick-borne disease and people with persisting complaints after tick-borne diseases
- Healthcare professionals
- Politicians
- Media
- Norwegian population in general

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Employees NKFS 2015

- Randi Eikeland (PhD, specialized in neurology)
- Harald Reiso (PhD, specialized in general medicine)
- Yvonne Kerlefsen (MSc in Biology)

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National reference group NKFS

- Leader: Ingeborg Aaberge: Norwegian institute of public health, Immunology/microbiology
- Dag Tveitnes: Western Norway Regional Health Authority, Pediatrics
- Dag Hvidsten: Northern Norway Regional Health Authority, Microbiology/pediatrics
- Hilde Gran: General medicine
- Elling Ulvestad:The university of Bergen, Immunology/microbiology
- Rune Midgard: Central Norway Regional Health Authority, Neurology
- Vivian Kjelland: University of Agder, Molecular biology
- Carl Erik Semb: Norsk Lyme Borreliose-Forening
- Dag Berild: South-Eastern Norway Regional Health Authority/University of Oslo, Infectious diseases
- Randi Eikeland: NKFS, Neurology
- Yvonne Kerlefsen. Harald Reiso. NKFS

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Counselling/ information

- To Systemize and distribute knowledge about tick-borne diseases
- To help to establish Clinical guidelines
- To organize symposia and teaching courses for health care professionals, patients, general public
- To Supervise and consult health care professionals, politicians, media and patients
- www.sshf.no/flått
- Flaattsenteret@sshf.no

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Research and surveillance

- Establish and attend local/national/international research networks on tick-borne diseases
- Promote research and PhD candidates
- Supervision, literature services, contacts
- Contribute to the establishment of a national registry and bio-bank for Borrelia-serology
- Project leader of multi centre study on tick-born diseases BorrSci 2015-2020 (2 million £ founding)

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My thesis is free for down loading at:

http://hdl.handle.net/1956/5870

Thank you for your attention!

Picture: NRK Sørlandet