

## Acknowledgements

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## ORIGINAL ARTICLES

### Surveillance report

# DISSEMINATED AND CHRONIC LYME BORRELIOSIS IN NORWAY, 1995 – 2004

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Lyme borreliosis is the most common tickborne infection in Norway. All clinical manifestations of Lyme borreliosis other than erythema migrans are notifiable to Folkehelseinstituttet, the Norwegian Institute of Public Health. During the period 1995-2004 a total of 1506 cases of disseminated and chronic Lyme borreliosis were reported. Serological tests were the basis for laboratory diagnosis in almost all cases. The annual numbers of cases showed no clear trend over the period, but varied each year between 120 and 253 cases, with the highest number of cases reported in 2004. Seventy five per cent of cases with information on time of onset were in patients who fell ill during the months of June to October. There was marked geographical variation in reported incidence rates, with the highest rates reported from coastal counties in southern and central Norway. Fifty six per cent of the cases were in males and 44% in females. The highest incidence rate was found in children aged between 5 and 9 years. Neuroborreliosis was the most common clinical manifestation (71%), followed by arthritis/arthralgia (22%) and acrodermatitis chronica atrophicans (5%). Forty six per cent of patients were admitted to hospital. Prevention of borreliosis in Norway relies on measures to prevent tick bites, such as use of protective clothing and insect repellents, and early detection and removal of ticks. Antibiotics are generally not recommended for prophylaxis after tick bites in Norway.

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**Key words:** Lyme disease, borreliosis, tickborne, Norway

## Introduction

The incidence of Lyme borreliosis in different areas of Norway reflects the distribution of the tick vector, *Ixodes ricinus*. The prevalence of *Borrelia* sp. in *I. ricinus* has been investigated by phase contrast microscopy in many tick-infested locations along the Norwegian coast. Generally, the prevalence has been found to be 20%-30% in nymphs and 40%-60% in adult ticks [1]. No larvae examined were infected. Small rodents and birds are considered to be the main reservoir hosts in Europe [2].

The first description of erythema migrans with meningopolyradiculitis after tick-bite in Norway was published in

1955[3]. Cases of Lyme borreliosis were notified sporadically to the MSIS (Norwegian surveillance system for communicable diseases) from 1983, under the category 'other infectious diseases'. Since 1991 it has been a specified notifiable disease. In the early years of notification, all manifestations of Lyme borreliosis were notifiable, including erythema migrans. The case definition was revised with the implementation of the Infectious Disease Control Act in 1995, after which only disseminated and chronic manifestations remained notifiable, (that is, cases of erythema migrans were excluded).

In this article, we review surveillance data for disseminated and chronic Lyme borreliosis in Norway during the ten year period 1995-2004 in order to examine trends over time, geographical distribution, characteristics of patients and their clinical presentation.

## Materials and methods

The MSIS (Norwegian surveillance system for communicable diseases) is administered by the Department of Infectious Disease Epidemiology at Folkehelseinstituttet (the Norwegian Institute of Public Health, NIPH) in Oslo. Laboratories of clinical microbiology and clinicians are required by law to notify cases of certain infectious diseases to the MSIS central unit at NIPH. The reports from the laboratory and clinician are combined and registered as one case at NIPH.

We reviewed cases of disseminated and chronic Lyme borreliosis notified in Norway during the ten year period 1995 to 2004. The case definition for laboratory confirmed Lyme borreliosis was clinically suspected disseminated or chronic disease, like acrodermatitis chronica atrophicans (ACA), arthritis or neurological disease and demonstration of the bacteria *Borrelia burgdorferi* or definite antibody titres. Population data from Statistics Norway ([www.ssb.no](http://www.ssb.no)) were used to calculate annual incidence rates.

In order to study the geographical distribution of cases over time, we mapped the cases in the two years with the highest incidence rates. The maps were created as dot-density maps in ArcGIS 9, where one case was presented as one dot randomly placed within the border of the municipality of residence.

Based on information on clinical signs and symptoms as described by clinicians on the notification forms, patients were put into the following main categories: neuroborreliosis (including meningitis, facial paralysis and meningopolyradiculitis), arthritis, acrodermatitis chronica atrophicans (ACA), unknown and other. Cases with diagnosis based on analysis of cerebrospinal fluid (with or without confirmatory

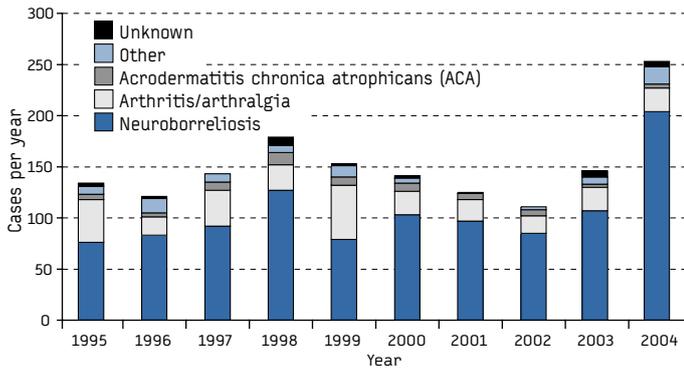
results from serum) were classified as neuroborreliosis regardless of information of other concomitant clinical manifestations.

**Results**

During the 10-year period 1995 to 2004, a total of 1506 cases of disseminated and chronic Lyme borreliosis were notified to NIPH. The number of cases varied between 120 and 253 annually, with the highest number of cases in 2004 [FIGURE 1].

**FIGURE 1**

**Number of cases of disseminated and chronic Lyme borreliosis notified in Norway by year of onset and main clinical symptoms, 1995-2004**

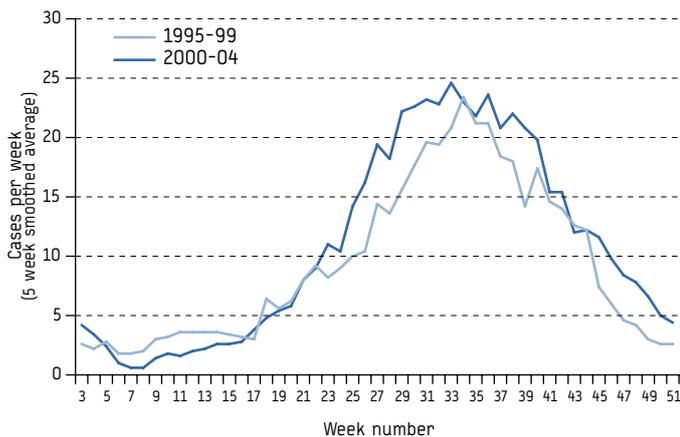


**Seasonality**

Date of symptom onset was available for 1014 cases. There was a clear seasonal pattern, with the number of cases starting to increase in week 20 (mid-May) and peaking in week 35 (August) [FIGURE 2]. Seventy five per cent (759/1014) of cases with information on time of onset fell ill during the months of June to October. The seasonal distribution of cases by onset remained similar during the ten year period [FIGURE 2].

**FIGURE 2**

**Seasonal distribution of disseminated and chronic Lyme borreliosis notified in Norway by week of onset by five-year period ; 5 week smoothed average**



**Geographical distribution**

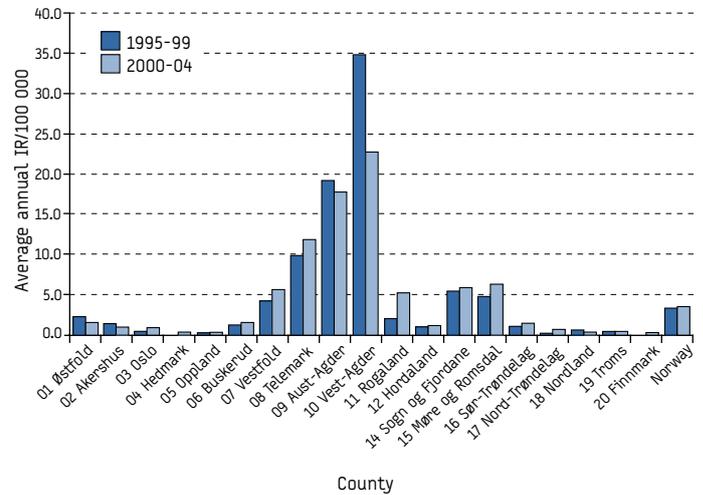
Of the 1506 cases reported, 1200 (79.7%) were reported as having been infected in Norway, 23 (1.5%) during travel abroad, and for 283 (18.8%) this information was missing.

There was marked geographical variation in reported incidence rates, with the highest incidence reported from coastal counties in southern and central parts of Norway [FIGURE 3]. Six counties in these areas accounted for 75% of the cases (these counties account for only 28% of the population in Norway). The highest annual

number of cases were reported in 1998 (n=179) and 2004 (n=253). The geographical distribution of cases was not markedly different in these years [FIGURE 4].

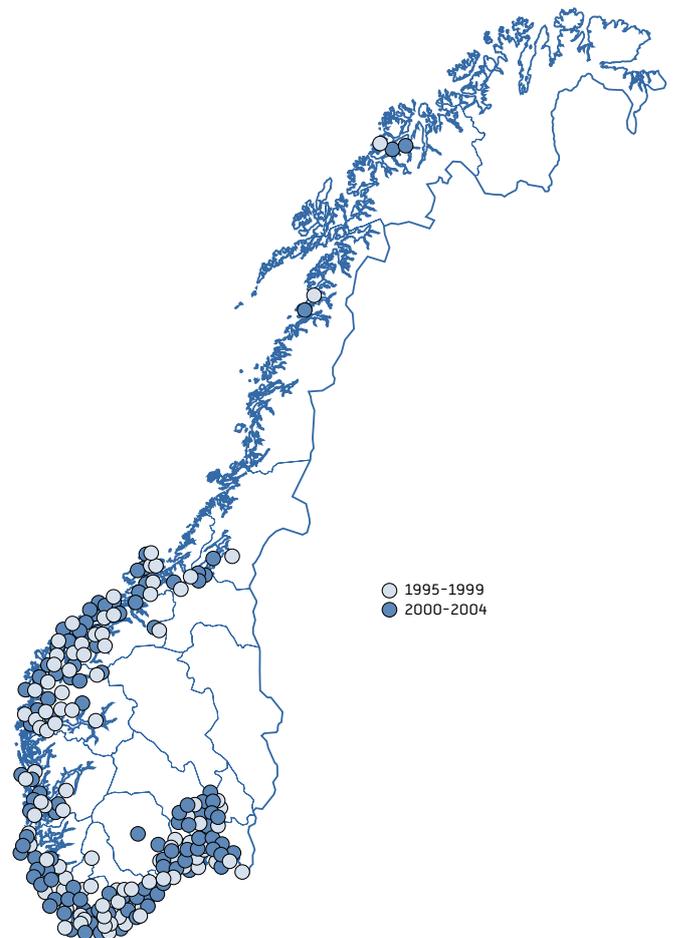
**FIGURE 3**

**Average annual incidence rate (IR) of disseminated and chronic Lyme borreliosis per 100 000 person-years by county, Norway 1995-2004**



**FIGURE 4**

**Distribution of cases of disseminated and chronic Lyme borreliosis notified in Norway 1995-2004**

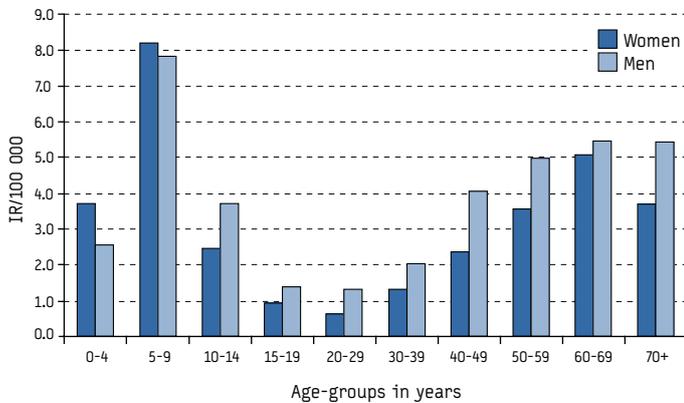


### Age and sex distribution

Fifty six per cent of the cases were in males and 44% in females. The highest incidence rate was found in children aged between 5 and 9 years (average annual IR 8.0/100 000) [FIGURE 5].

FIGURE 5

Age and sex specific average annual incidence rate (IR) per 100 000 disseminated and chronic Lyme borreliosis cases notified in Norway, 1995-2004



### Clinical symptoms and diagnosis

The most common clinical presentation in this study was neuroborreliosis, reported in 1070 of the patients (71.0%), with facial palsy as the most common reported presentation of neuroborreliosis (403 cases). Arthritis or athralgia was reported in 329 patients (21.8%), and acrodermatitis chronica atrophicans (ACA) in 75 patients (5.0%). For 65 patients (4.3%) more unspecific clinical symptoms were reported (e.g. fever, headache, myalgia, rash), and for 28 (1.9%) no clinical information was available. Ten cases (0.7%) had cardiac manifestations as a main or concomitant finding. For some cases, a combination of clinical manifestations were reported.

Forty six per cent of patients were admitted to hospital. The hospitalisation rate was highest for patients with neurological symptoms (81%). The high proportion of neurological disease in children below 10 years of age with disseminated and chronic Lyme borreliosis (92.8%) explains the high rate of admission to hospital in children under ten years of age (79%).

Demonstration of Borrelia-specific antibodies was the basis of diagnosis in 1491 cases, microscopy in 2 cases, nucleic acid detection in 2 cases and unknown in 11 cases. Diagnosis was based on analysis of serum in 730 cases, cerebrospinal fluid (CSF) in 429 cases, blood and spinal fluid in 328 cases, synovial fluid in 5 cases, skin biopsy in one case and unknown in 12 cases. According to the notification forms, neuroborreliosis was laboratory confirmed by demonstration of antibodies in CSF in 429 cases, serum and CSF in 326 cases, only serum in 304 cases and was not reported for 7 cases.

### Discussion

Borrelia infection is the most common notifiable tickborne disease in Norway, and the annual number of cases of disseminated and chronic Lyme borreliosis in Norway has been fairly stable during the study period 1995 to 2004. However, in 2004 we observed an almost twofold increase of cases compared to mean annual cases during the last ten years. It is not yet known if this reflects a true increase in incidence or increased rates of detection or reporting. We have, however, no data that indicate any changes in diagnostic methods or reporting practices that could have caused the increase in number of notified cases we observed in 2004.

Erythema migrans is the most common clinical manifestation of Lyme disease. However, it is also the least severe presentation and the diagnosis cannot easily be confirmed by laboratory testing, as most patients do not demonstrate an antibody response at the time of diagnosis. For these reasons, Lyme disease with erythema migrans as the only manifestation has not been notifiable in Norway during

the study period 1995-2004. However, in 1993 and 1994, all clinical manifestations of Lyme borreliosis were notifiable, and at that time erythema migrans represented 43%-59% of notified cases where clinical information was available[4,5]. This is in accordance with routine passive surveillance data from other countries [6,7], but lower than reported in enhanced clinical surveillance[8] or community-based cohort studies[9]. In general there is probably a higher degree of underreporting when diagnosis is based on clinical symptoms alone, as is often the case with erythema migrans lesions.

Antibiotic treatment is recommended for erythema migrans and is generally believed to protect against disseminated and chronic manifestations. However, Norwegian surveillance data do not contain reliable information on the frequency of prior erythema migrans or noticed tick bites in patients with manifestations of disseminated and chronic disease. It is, however, well known that many, if not most, tick bites go unnoticed and that disseminated and chronic disease can develop without history of tick bite or erythema migrans.

Although Lyme borreliosis is most commonly diagnosed during the summer season, cases are reported throughout the year, probably because unspecific symptoms cause both doctor and patient delay, and also because of the long incubation period of some clinical manifestations. Clinicians should therefore consider disseminated or chronic Lyme borreliosis in their differential diagnosis during all months of the year in patients who live in or have travelled to endemic areas along the coast in southern and middle parts of Norway [FIGURE 4], particularly in patients with neurologic, rheumatic and dermatological signs and symptoms compatible with late onset Lyme disease.

Several tick species have been found in Norway. However the main vector for transmission of Lyme borreliosis to humans is the hard tick *I. ricinus*. The tick can be found in coastal areas with relatively mild winters in the southern and middle part of Norway [10], and this is also reflected in the geographical distribution of Lyme borreliosis cases [FIGURES 3,4].

In 1943 Tambs-Lyche published an extensive survey of the distribution of *I. ricinus* in Norway based on collections of ticks from domestic animals and information concerning the distribution of the tickborne disease babesiosis in cattle[11]. The survey found *I. ricinus* distributed in a narrow zone along the southern coast between the Oslofjord and Jæren, and along the western coast in a relatively wide zone including the innermost regions of most of the fjords and neighbouring valleys. Both ticks and babesiosis were absent from the treeless Jæren. Tambs-Lyche pointed out the importance of vegetation for tick distribution, since it has a modifying effect on the humidity of a habitat. Later, *I. ricinus* became established in those areas where trees had been planted or where bushes and trees had been established. In the periphery of its normal range in Norway, *I. ricinus* is found in scattered, suitable localities.

Recent studies from Sweden have concluded that one of the main reasons for the observed increase in the density and geographical ranges of *I. ricinus* is relatively mild winters, and that this is a possible explanation for the increase in both TBE and Lyme borreliosis cases[12,13]. Other factors such as human behaviour and host animal populations may also have played a part, and these may also be partly related to climate. However, the effect of climate has been disputed by others [14,15]. If climate affects the density and geographic distribution of ticks, it would be expected to also affect the incidence of both Lyme borreliosis and TBE.

More recent studies of ticks in Norway [1,16] do not show any expansion of the range of *I. ricinus* since 1940. On the other hand, there is a marked rise in the density of the tick population in many parts of its range, especially on islands, due to changes in animal husbandry practices, in vegetation, and in the distribution and population densities of host animals such as the roe deer and the European elk.

Increased tick populations may lead to an increased annual spreading of ticks by birds within a country. More than 4000 migratory birds have been investigated for ticks, and the transport of ticks on migrating birds to Norway is well documented [17]. Climatic and

environmental factors may explain why tick populations have not so far become established outside their previous endemic areas.

There is no available vaccine for Lyme borreliosis. Prevention relies on measures to prevent tick bites, such as use of protective clothing and insect repellents, and early detection and removal of ticks. Antibiotics are generally not recommended for prophylaxis after tick bites in Norway.

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## ORIGINAL ARTICLES

### Surveillance report

# EPIDEMIOLOGY OF INVASIVE MENINGOCOCCAL DISEASE IN FRANCE IN 2003

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National surveillance of invasive meningococcal disease (IMD) is based on mandatory reporting. The case definition for surveillance notification was changed in mid-2002 to include cases without microbiological confirmation. The IMD alert detection system was enhanced in 2003 with daily reporting and weekly analysis by district, serogroup, and age. Evaluation of the exhaustivity of the surveillance with capture-recapture analysis allowed correcting for underreporting.

In 2003, 803 cases were reported. After correction for underreporting, the estimated incidence was 1.78 / 100 000. After excluding 'new' cases reported with new definition criteria, the 2002-2003 increase was 4%. Incidence decreased with age, with the highest values in infants less than 1 year (20/100 000), children aged between 1 and 2 years (11/100 000) and in teenagers of 17 years old (7/100 000). The overall case fatality rate was 12%. Fifty nine per cent of cases were due to serogroup B, 32% to C, 5% to W135, and 4% to Y and non-groupable meningococci. Patients with *purpura fulminans* treated with intravenous antibiotics before admission to hospital were shown to have lower fatality rates than those not treated.

In 2001-2003, 5 situations required particular attention: two clusters of serogroup B IMD had set off mass prophylaxis, one outbreak due to a specific B IMD clonal complex with high case fatality rate, and two districts crossed the alert threshold for serogroup C IMD, 2/100 000, and mass vaccination was recommended.

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#### Introduction

Invasive meningococcal disease (IMD) is a rare but serious infectious disease responsible for high case fatality and sequela rates, that affects mainly children and young adults. France, with an incidence below 2/ 100 000 inhabitants, is among those European countries with low incidence [1]. This article presents the characteristics of the IMD surveillance in France in 2003, and the recent epidemiological trends.

#### Methods

In France, IMD is a mandatory notifiable disease. When a new case is reported to the district health authorities, the patient's close contacts in the household and in the community during the 10 previous days of admission are traced, in accordance with the national recommendations [2]. All close contacts are requested to intake chemoprophylaxis and vaccination if appropriate. The notifying clinician or microbiologist fills in a notification form which is sent to the district health authorities, and then to the Institut de Veille Sanitaire (InVS) for national surveillance. Serogrouping of the strains is done at the hospital either after isolation of the strain or using polymerase chain reaction (PCR). Pathogen strains are sent to the National Reference Centre for Meningococci (CNRM) for phenotyping and genotyping analysis. The case definition used for national surveillance was expanded in mid-July 2002 from laboratory confirmed cases with *N. meningitidis* culture or positive antigen

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Epidemiology of invasive meningococcal disease in France in 2003