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Incidence and antibiotic treatment of erythema migrans in Norway 2005–2009

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ABSTRACT

The first stage of Lyme borreliosis (LB) is mainly the typical skin lesion, erythema migrans (EM), which is estimated to comprise 80–90% of all LB cases. However, the reporting of, and the actual incidence of LB varies throughout Europe. Studies from Sweden and Holland have found EM incidences varying from 53 to 464 EM/100,000 inhabitants/year. Under-reporting of LB is common and a coefficient of three to reach a realistic estimate is suggested. In Norway, it is mandatory to report only the second and third LB stages to the National Institute of Public Health. To find the Norwegian incidence of EM, we extracted data from the electronic medical records of regular general practitioners and out-of-hours services in the four counties with the highest rates of registered LB in the 5 years from 2005 to 2009. We found an EM incidence of 448 EM/100,000 inhabitants/year in these counties, which yields a national incidence of 148 EM/100,000 inhabitants/year. Our findings show that solitary EMs comprised almost 96% of the total LB incidence in Norway. Older females have the highest rates of EM. Phenoxymethylpenicillin is the most commonly used drug to treat EM in Norway, which complies with the national guidelines for antibiotic use. Antibody tests are performed in 15% of cases. Less than 1% of patients are referred to secondary care. The study also shows a high number of patients seeking care for tick bites without signs of infection and there is an overuse of antibiotics in these patients.

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1. Introduction

Lyme borreliosis (LB)¹ is caused by the bacterium *Borrelia burgdorferi* sensu lato, which is transmitted through tick bites (TBs). LB can manifest with several different symptoms, which are traditionally divided into three disease stages. The first stage

is mainly the skin lesion, erythema migrans (EM), which is estimated to comprise 80–90% of all LB cases. However, little is known about its actual incidence (Rizzoli et al., 2011; Stanek et al., 2012; Vandenesch et al., 2014; Hofhuis et al., 2015). In Norway, it is not mandatory to report solitary EMs. Only disseminated LB cases, confirmed by antibody testing, culture confirmation or polymerase chain reaction (PCR)² analysis, are registered at the Norwegian Institute of Public Health. In Norway, the distribution of systemic manifestations in the study period (2005–2009) was 66.6% Lyme neuroborreliosis, 9.7% Lyme arthritis and 23.7% other or not specified manifestations, including Lyme carditis and multiple EMs (Personal communication, Myking S., Norwegian Institute of Public Health, 2016.06.02; MSIS, 2010).

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¹ Abbreviations: EM = erythema migrans, EMR = electronic medical record, LB = Lyme borreliosis, OOH = out-of-hours service, RGP = regular general practitioner, PCR = polymerase chain reaction, TB = tick bite

² PCR is a method to multiply and identify DNA from a tissue sample.

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According to the European Concerted Action on Lyme Borreliosis (EUCALB), the incidence of LB in European countries is increasing. In 2006, the World Health Organization (WHO) reported that the incidence of LB varied from 0.6/100,000/year in Ireland to 155/100,000/year in Slovenia (O'Connell, 1996; Lindgren and Jaenson, 2006; EUCALB, 2015). In this report, LB incidence in Norway was reported as 2.8/100,000/year, but increased to a peak of 7.3 LB/100,000/year in 2008. In the United States (US), the incidence of LB in 2005–2009 was on average 8.9/100,000 inhabitants/year (CDC, 2015). The US figures include EM cases (CDC, 2011). Hubalek (2009) performed a thorough overview of LB epidemiology, and found 85,500 LB cases worldwide annually, with 65,500 of these cases in Europe. However, under-reporting is common, and multiplying the reported incidence by three is suggested to reach a realistic estimate of the number of LB cases (Hubalek, 2009). In Sweden, it is not mandatory to report LB, but it is estimated to be 69/100,000/year, of which EM comprises 77% of all LB cases (Berglund et al., 1995; Public Health Agency of Sweden, 2013). However, Bennet et al. (2006) found a yearly incidence of 464 EM/100,000 inhabitants in an endemic county in Sweden. Studies of EM incidence in European countries are scarce (Smith and Takkinen, 2006), but in Holland, Hofhuis et al. (2015) found an incidence of general practitioner (GP) consultations for TBs and EM of 495 and 132 per 100,000 inhabitants/year, respectively.

The first aim of this study is to estimate the incidence of solitary EMs in Norway. The incidence of consultations for EMs in the four Norwegian counties having the highest reported incidence rates of systemic LB was registered to generate an estimate of the national incidence. The secondary aims of this study are to measure the compliance with national guidelines for antibiotic use, to assess the extent of referral to secondary care and antibody testing used. Doctor-seeking behaviour for mere TBs was also assessed.

2. Material and methods

2.1. Clinical setting

We performed our study in the four Norwegian counties with the highest reported incidence rates of systemic LB in Norway in 2008. With a reported incidence of LB cases of 18.9/100,000 inhabitants/year, these counties (Vestfold, Telemark, Aust-Agder and Vest-Agder) had almost three times the national rate of 7.3 LB/100,000 inhabitants/year. The total population of the study counties was 669,739, comprising 14.3% of Norway's total population in the study period (Statistics Norway, 2010).

In Norway, all citizens are assigned a regular GP (RGP) as their primary contact in the health-care system. Outside office hours, each municipality is obliged to have a GP on call in an out-of-hours service (OOH) (Morken et al., 2009). Except for acute admissions, patients need a referral from a GP to be admitted to the hospital. Therefore, we assumed that nearly all patients with a TB or an EM in need of medical care will visit either their RGP or an OOH.

2.2. Inclusion of physicians

We invited all RGPs and OOHs in the four study counties to participate in this study, which comprised 563 GPs and 25 OOHs. Limitations to the software used made it impossible to collect data from all different electronic medical record (EMR) systems (see Appendix). If the GP or OOH had an online server, data collection was not possible either. 407 GPs and 18 OOHs were able to participate and we obtained data from 213 (52%) and 14 (78%) of these participants, respectively (Fig. 1a). The number of patients on each GP's list was retrieved from the Norwegian Health Economics Administration for the mid-date of each GP's data collection period

(HELFO, 2016). For the OOHs, we used their catchment areas. The GPs had on average 1223 patients on their lists, and the 14 OOHs covered a population of 573,154 inhabitants.

2.3. Registration method

In Norway, both RGPs and OOHs use the International Classification of Primary Care (ICPC-2) diagnostic coding system (Classification Committee of the World Organization of Family Doctors, 2011). "Erythema migrans" and "Tick bite" are specific diagnoses in the ICPC-2, but are included in broader ICPC codes like *A78 Infectious disease* and *S73 Parasite infestation*. Because of this, we believed that we would not identify all of the relevant cases by limiting the search to these diagnoses. Therefore, we developed a computer program that could search through the full text of the EMRs (see Appendix).

2.4. Data collection

Data was collected in 2010 for the 5-year period from 1 January 2005 to 31 December 2009. The computer program identified 18 tick-related terms, including "erythema migrans" and "tick", but also abbreviations and local Norwegian names for ticks. Spelling failures were included, as were Danish and Swedish words for ticks because many doctors from other Nordic countries work in Norway (see Appendix).

When one or more of the search terms were matched, a dataset was extracted along with the full text of the journal note. The dataset included the following parameters: date of consultation, doctor's ID number in the health personnel register, patient's gender, age and postal code, diagnoses given and antibiotics prescribed. From the journal note, we found five additional parameters: whether the patient reported a recent or present TB, an EM, whether antibody testing had been performed, if the patient were referred to secondary care and whether the patient had been seen by another doctor prior to this consultation. We have only registered what the doctors documented, and have not interpreted clinical information to discern whether the diagnosis was correct or not.

2.5. Diagnostics and guidelines

In the following, an "erythema migrans" is defined as a consultation for a solitary EM either with or without a known TB. It is the clinical diagnosis given by the GP based on the appearance of the skin lesion together with patient information about a TB or time spent in a tick-infested area (Stanek et al., 2011). We have only registered solitary EMs because multiple EMs are regarded as a systemic LB infection and should be treated and reported differently. A "tick bite" is defined as a consultation for a TB without an EM. Multiple consultations within 3 months of each other were counted as single cases. If a patient was first seen with a TB, and then came back with an EM, this was counted as an EM case.

According to Norwegian guidelines, the antibiotic of choice for solitary EM is phenoxymethylpenicillin (PcV), with doxycycline and amoxicillin as alternatives. Antibiotic prophylaxis after TBs is not recommended in Norway (Norwegian Antibiotic Centre for Primary Care, 2015; Norwegian Directorate of Health, 2013; Nadelman et al., 2001).

From the text search, we have registered whether antibody tests were performed or not. We have not been able to register the results of the tests.

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