Paper

J R Coll Physicians Edinb 2015 45: 196–200
http://dx.doi.org/10.4997/JRCPE.2015.304

Distribution and presentation of Lyme borreliosis in Scotland – analysis of data from a national testing laboratory

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ABSTRACT This study examines the distribution of laboratory-confirmed cases of Lyme borreliosis in Scotland and the clinical spectrum of presentations within NHS Highland.
Methods General demographic data (age/sex/referring Health Board) from all cases of Lyme borreliosis serologically confirmed by the National Lyme Borreliosis Testing Laboratory from 1 January 2008 to 31 December 2013 were analysed. Clinical features of confirmed cases were ascertained from questionnaires sent to referring clinicians within NHS Highland during the study period.
Results The number of laboratory-confirmed cases of Lyme borreliosis in Scotland peaked at 440 in 2010. From 2008 to 2013 the estimated average annual incidence was 6.8 per 100,000 (44.1 per 100,000 in NHS Highland). Of 594 questionnaires from NHS Highland patients: 76% had clinically confirmed Lyme borreliosis; 48% erythema migrans; 17% rash, 25% joint, 15% neurological and 1% cardiac symptoms. Only 61% could recall a tick bite.
Conclusion The incidence of Lyme borreliosis may be stabilising in Scotland but NHS Highland remains an area of high incidence. Lyme borreliosis should be considered in symptomatic patients that have had exposure to ticks and not just those with a definite tick bite.

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KEYWORDS *Borrelia burgdorferi*, epidemiology, Lyme borreliosis, Scotland

DECLARATION OF INTERESTS No conflict of interest declared

INTRODUCTION

Lyme borreliosis (LB), a disease transmitted to humans via the bite of a tick infected with the bacteria *Borrelia burgdorferi*, is becoming increasingly prevalent in Scotland.[1] While some patients may remain asymptomatic or suffer only from a self-limiting erythema migrans (EM) rash around the site of a tick bite, LB can lead to debilitating disease with significant morbidity if left untreated.[2] As there is growing clinical, public, occupational and political interest in the burden of LB in Scotland it is essential that accurate data are collated.

The aim of this study was to examine the distribution of laboratory-confirmed cases of LB in Scotland and to study the clinical spectrum using questionnaire data on those cases from the Scottish Highlands.

METHODS

The number of serum samples referred to the National Lyme Borreliosis Testing laboratory (NLBTL), Raigmore Hospital, Inverness, from health boards throughout Scotland for serological testing from 1 January 1996 to 31 December 2014, and the corresponding number of new seropositive patients (laboratory-confirmed cases) was collated. In accordance with Centers for Disease Control and Prevention guidelines,[3] all sera referred to the laboratory were screened by enzyme-linked immunoassay (*B. burgdorferi* IgM/IgG, Zeus Scientific or Enzygnost Lyme link VlsE/IgG, Siemens) and confirmed by immunoblot. Sera that were weakly positive or positive by Western/Immuno-blot were classed as seropositive. Initially, an in-house Western blot incorporating reference strain *B. burgdorferi* sensu stricto was used,[4] followed by a local *B. burgdorferi* sensu stricto and *B. afzelii* antigen (50:50) mix[5,6] in June 2007. There was a significant change in testing protocols in July 2012. The in-house Western blot was replaced with CE marked commercial assays (EU Lyme IgG Western blot, Trinity biotech or Recomline Lyme IgG, Mikrogen) and in accordance with the British Infection Association position statement published in 2011,[7] samples from patients with: a clear recent history of a tick bite with EM; tick bite only; or no clinical details, were no longer routinely tested. Any such samples received were stored and only tested following discussion with the referring clinician.

General demographic data (age/sex/referring health board) from all cases of LB serologically confirmed by the NLBTL from 1 January 2008 to 31 December 2013

were analysed using descriptive statistics. Data (clinical symptoms/signs, details of any tick bites and if patient considered by medical practitioner to have LB) from questionnaires returned to the laboratory from all laboratory-confirmed cases within NHS Highland during this time period were also analysed.

RESULTS

The number of samples referred to the NLBTL for serological testing rose steadily from 869 in 1996 to 5,366 in 2011, then dipped to 4,630 in 2013 (Figure 1). The number of cases of LB confirmed by our laboratory remained low from 1996 (n=27) until 2003 (n=52) but then rose steadily to a peak of 440 cases in 2010 (Figure 1). The number of laboratory-confirmed cases then dramatically decreased to 175 in 2013 (Figure 1).

From 2008 to 2013 the average annual incidence of LB for Scotland was 6.8 cases per 100,000 population (Table 1), although this ranged from 1.7 in Lanarkshire to 44.1 in NHS Highland (Table 2).

During this time, more laboratory-confirmed cases were male (55%). The age of these patients followed a normal distribution, with a peak in the number of laboratory-confirmed cases in the 50–54 years age group (n=231), with few cases (less than 50 per 5 year age group) in those 75 years and older and younger than 20.

Patients referred from NHS Highland represented the majority of new cases of LB in Scotland from 2008–2013 (831/1865; 45%) (Table 2). Of the 804 questionnaires distributed to the referring clinician for all new cases from NHS Highland, 74% (594) were returned. Of these, 450 (76%) were deemed by the clinician to have LB, whereas 84 (14%) were not thought to have LB. Erythema migrans was recorded in only 285 (48%) of patients, and other rashes in a further 102 (17%); 149 (25%) had joint symptoms, 87 (15%) neurological features and 8 (1%) cardiac features. Only 362 of patients (61%) could recall having a tick bite.

TABLE 1 Total number of laboratory confirmed cases of Lyme borreliosis in Scotland and estimated annual incidence per 100,000 population, 2008–2013

	Total number of cases of LB	*Estimated annual incidence per 100,000 population
2008	339	7.8
2009	393	9.0
2010	440	9.8
2011	308	6.7
2012	210	4.1
2013	175	3.1
Total	**1865**	**6.8**

*As the case data were incomplete for Grampian and Forth Valley Health Boards during 2008–2013 they were not included in the incidence calculations.

DISCUSSION

The rise in laboratory-confirmed cases of LB from 2003 to 2010 may be due, in part, to the implementation of the NLBTL in May 2003, which actively encouraged nationwide testing for LB and led to the improvement of testing protocols. There is also heightened awareness of LB by both clinicians and the general public, which has undoubtedly increased demand for testing, and resulted in the detection of more cases.[8] However, the rise in LB

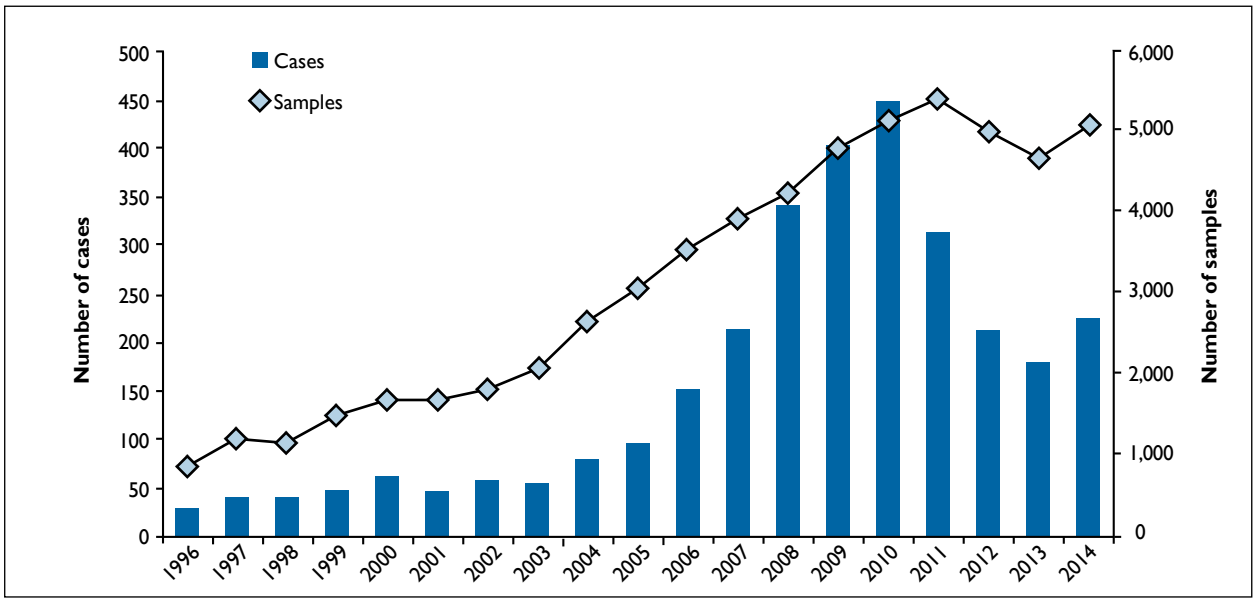

FIGURE 1 Laboratory samples and cases of Lyme borreliosis in Scotland 1996 to 2014

TABLE 2 Health Board distribution of laboratory confirmed cases of Lyme borreliosis in Scotland, 2008-2013

Health Board	Number of cases of Lyme borreliosis							Estimated average annual incidence/ 100,000
	2008	2009	2010	2011	2012	2013	Total	
Ayrshire & Arran	8	6	18	6	2	2	**42**	1.9
Tayside	51	59	49	36	15	13	**223**	9.2
Dumfries & Galloway	10	9	14	7	11	5	**56**	6.3
Lothian	40	40	41	21	10	11	**163**	3.3
Fife	10	8	9	12	4	2	**45**	2.1
Greater Glasgow & Clyde	53	70	105	46	28	18	**320**	4.5
Highland	147	169	717	152	108	84	**831**	44.1
Lanarkshire	13	22	14	8	2	0	**59**	1.7
Borders	2	5	6	3	2	3	**21**	3.1
Western Isles	5	5	3	6	2	1	**22**	13.8
*Forth Valley	-	-	10	11	5	0	**26**	-
*Grampian	-	-	-	-	21	36	**57**	-

*Samples not routinely referred to the NLBTL from 2008–2013

cases may also be attributed to changes in climate, land use and human behaviour, increasing tick survival rates, abundance and infection rates as well as human exposure to tick bites.[9] It is possible that the decreases in 2012 and 2013 may be as a result of a change in testing protocols in July 2012. The in-house WB was replaced with a slightly less sensitive but more specific CE marked commercial Immunoblot assay (unpublished data), and in accordance with the British Infection Association position statement,[7] clinicians were asked to treat EM empirically and not send sera for testing to reduce false negatives. These changes would not explain the earlier dramatic decrease in cases from 2010 to 2011 (440 to 308), especially as the number of samples tested by the laboratory peaked in this year at 5,366, and the subsequent rise in both samples and cases in 2014 (to 5,052 and 224, respectively) (Figure 1). Anecdotal evidence from local GPs suggests that the number of EM cases also rose significantly in 2014. It has been reported that the overall prevalence of LB may be stabilising even though its geographical distribution is increasing.[9] It is possible that the recent fluctuations in case numbers may be a reflection of other factors. For example, the winters of 2008/9, 2009/10 and 2010/11 were all colder and drier than average. With a mean temperature of 1.6°C (2.0°C below average), 2009/10 was the coldest winter since 1978/9 and the coldest on record for northern Scotland. That winter also had only 77% of the average winter rainfall.[10] These severe winters may have influenced tick numbers and infection rates in subsequent years.

The incidence of LB differs greatly between and within different countries. At 6.8 cases per 100,000 population during 2008–2013 (Table 1), the estimated annual incidence of LB for Scotland is much higher than that documented for England and Wales (1.7 per 100,000 population in 2011)[11] but comparable with Bulgaria (5.4 per 100,000 population, 1993–2005), Poland (9.3 per 100,000 population, 2000–2006) and France (8.2 per 100,000 population, 1999–2000).[12] Within Scotland the incidence of LB ranged from 1.7 to 44.1 per 100,000 population. Variations in incidence were also highlighted in a recent study in England where the study area of Winchester had an estimated annual incidence of 9.7 per 100,000, compared to the national average of 1.7.[13] In this study the incidence was highest within NHS Highland (44.1 per 100,000 population) (Table 1). While not as high as some European countries (Austria, Slovenia and Sweden), the incidence of LB in NHS Highland is comparable to Estonia, Germany and Lithuania[12] and many of the 13 states in the USA where LB is considered to be endemic (ranging from 12.4 to 111.2 per 100,000 population).

The high incidence of LB in NHS Highland raises the question of antibiotic prophylaxis as it has been suggested that it should be considered in LB endemic areas,[14] even though prophylaxis for LB does not seem to be widely advocated in Europe. In the USA, prophylaxis is not recommended unless: an adult or nymphal *I. scapularis* tick has been attached for more than 36 hr; prophylaxis can be started within 72 hr of removal; tick bite was in a hyperendemic area (i.e. *B. burgdorferi* infection rate is more than 20%, such as in parts of New England, mid-Atlantic States, Minnesota and Wisconsin), and doxycycline is not contraindicated.[15]

Although NHS Highland has a high incidence there are insufficient data to determine tick infection rates and assess if it is a hyperendemic area where prophylaxis should be considered. A small study by our laboratory

found that 20.7% of ticks in an area near Inverness were infected with *Borrelia*, but only 5.7% were infected in another area a few miles away. Both of these areas had been sampled 16 years previously and were found to have 9.4% and 9.1% infected ticks, respectively. These data show how infection rates can fluctuate markedly between geographical areas and with time, making estimates of tick infection rates for a whole country or geographical area very difficult.[16]

Introducing the concept of antibiotic prophylaxis for LB at a time when the current emphasis is on restricting antibiotic prescribing is challenging. It may be more prudent to focus on prevention with emphasis on: wearing suitable clothing in tick areas; increased vigilance checking for tick bites; and prompt tick removal as well as increasing the awareness of the need to check for the presence of any rashes and ensuring prompt, appropriate antibiotic treatment.

To gain a more comprehensive picture of the clinical signs and symptoms and tick bite histories from LB patients, the NLBTL began distributing questionnaires to the referring clinicians for all new seropositive patients in NHS Highland from June 2007. The low number of patients with EM (48%) was surprising and is much lower than that documented in other studies (69.1 to 89.3%).[17-19] While the results may reflect the unwillingness of clinicians to diagnose a rash as EM, of which there are many different presentations (non-EM rash recorded in a further 17%), it is more likely to reflect the clinical awareness in NHS Highland, with most cases of EM treated empirically without laboratory confirmation, as recommended.[7] It is likely therefore that the majority of samples sent to the laboratory by NHS Highland clinicians are those from patients with a more complex clinical picture. This may be confirmed by the fact that 14% of our seropositive patients were deemed not to have LB by the referring clinician. Many patients present with non-specific symptoms and are tested for LB as part of the differential diagnosis or, in some cases, because of patient anxiety or pressure. Patients can remain seropositive for years following an infection (even if subclinical) and current serological tests for LB cannot distinguish between current and past infection. This means that a positive result may be misleading as it could be due to past infection and that LB is not the cause of the patient's symptoms at the time of testing. Interestingly, only 61% of patients could recall having a tick bite. This information is important for clinicians as LB should be considered not just in those patients with a definite history of a tick bite, but in those that have potentially been exposed to ticks.

Currently, laboratory data are the only way to ascertain the burden of LB in Scotland but it is recognised that there are deficiencies in this approach to defining the epidemiology of infection.[2] While a few seropositive patients may be incorrectly recorded as new cases, we believe the burden of LB is much higher than recorded by laboratory reports. Many patients with EM (clinically diagnostic of LB) are not recorded as cases as they are yet to seroconvert, or they are not referred for laboratory confirmation (as recommended).[7] Anecdotal reports from some GPs in the Highlands indicate that perhaps only 20% of cases are referred for laboratory testing. Prior to 2010, LB was a notifiable disease in Scotland and although the NLBTL reported all laboratory confirmed cases, the data published by Health Protection Scotland (HPS) varied and the reporting of clinical cases by medical practitioners was limited.[20] This means that published data, which has been quoted by numerous European studies, are not a fair reflection on the burden of LB in Scotland. However, the NLBTL is currently working with Health Protection Scotland to improve the data collated, which will now include reporting all seronegative patients with EM. We believe that mandatory reporting of all clinical cases, including those with EM, would provide the best estimate of the burden of LB in Scotland, although it is recognised that there will still be limitations with this approach

CONCLUSION

The incidence of LB may be stabilising in Scotland but NHS Highland remains an area of high incidence. Laboratory figures are likely to considerably underestimate the extent of the disease. We feel that mandatory reporting of all clinical cases is required to give a more accurate understanding of the burden of LB in Scotland and this will allow preventative measures, including the need for antibiotic prophylaxis, to be fully assessed and better targeted within Scotland.

ACKNOWLEDGEMENTS

We would like to thank all our users for their continued support of the testing service. We would also like to thank the staff within the Microbiology department at Raigmore Hospital for their technical expertise and Arwyn Schumacher for her excellent data entry skills. Dr James Douglas provided invaluable clinical advice.

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