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CLINICAL

Lyme borreliosis in Scotland during two peak periods

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ABSTRACT The epidemiology of Lyme borreliosis (LB) and climatic conditions in Scotland were studied. Questionnaire data from all new seropositive patients from July to September 2007 and 2008 were examined along with demographic data from seropositive patients, rainfall and temperature data for these years. There were significantly more samples, seropositive patients and seropositive patients per patients tested in July to September 2008 than 2007. The average annual incidence rate for 2007 and 2008 was estimated at 5.9/100,000 population for Scotland and 43.4/100,000 population for the Highlands of Scotland, increasing to 10.6 and 81.0/100,000 population respectively for the peak months July to September. January to April 2008 was significantly wetter and May to July 2008 significantly drier than in 2007. The number of cases of LB in Scotland is increasing annually as a result of many different factors including increased awareness, improved laboratory techniques and a complex relationship between climatic factors, tick behaviour and human behaviour.

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INTRODUCTION

The number of cases of Lyme borreliosis (LB) has been increasing in Europe[1] and in the USA.[2] We have found similar increases in Scotland, in particular the Scottish Highlands, the region where the highest population of ticks is found.[3,4] This increase may be due to improved laboratory diagnosis and heightened awareness of this condition among clinicians and the general public. However, increasing tick numbers due to climatic conditions and animal hosts, changing human behaviour and even other unknown factors may also contribute to the increase seen in LB.[5–7]

Lyme borreliosis in Scotland is most commonly diagnosed in the summer months, mainly after bites from infected *Ixodes ricinus* tick nymphs questing in late spring/early summer, and less commonly after bites from adult ticks in the cooler months.[6] A number of studies on the epidemiology of LB have been carried out throughout Europe and the USA.[1,2,4,7–12] Additional studies have also looked at the association of LB with weather conditions.[6,7] This paper examines the peak periods of LB (July to September) during 2007 and 2008.

MATERIALS AND METHODS

Serum samples from across Scotland are referred to the National Lyme Borreliosis Testing Laboratory at Raigmore Hospital in Inverness. Results from 2007 to 2008 were examined, especially the peak months of infection (July to September). Samples were tested by a two-step procedure as recommended by the Centers for Disease Control and Prevention.[13] They were initially screened by a *Borrelia burgdorferi* total antibody enzyme-linked immunosorbent assay (Zeus). All samples that were equivocal and positive, and any negative samples with a strong clinical suspicion of LB, were then confirmed by an in-house IgG Western blot method as described previously using an equal antigen mix from local *B. burgdorferi* sensu stricto and *B. afzelii* isolates.[14] For Western blot-negative patients potentially infected from areas outside Scotland, a second Western blot was performed using *B. burgdorferi* sensu stricto reference strain antigen.[14]

A questionnaire was sent to the referring laboratory/clinician for all new Western blot-positive patients (seropositive patients). The questionnaire had questions on clinical signs/symptoms (erythema migrans, rash, joint, neurological), their onset, tick bite (if any, and date and geographical location) and treatment (type, duration and success/failure). Lastly, the medical practitioner was asked to determine if the patient's symptoms were due to LB. General demographic data from all new *B. burgdorferi* seropositive patients from 2007 to 2008 were collated in conjunction with data from questionnaires returned for new seropositive patients detected from July to September each year. Statistical analysis was performed by chi-squared test. The monthly temperature and rainfall data for Scotland from January to July 2007 and January to July 2008 were sourced from the Meteorological Office[15] and analysed for any differences between the years.

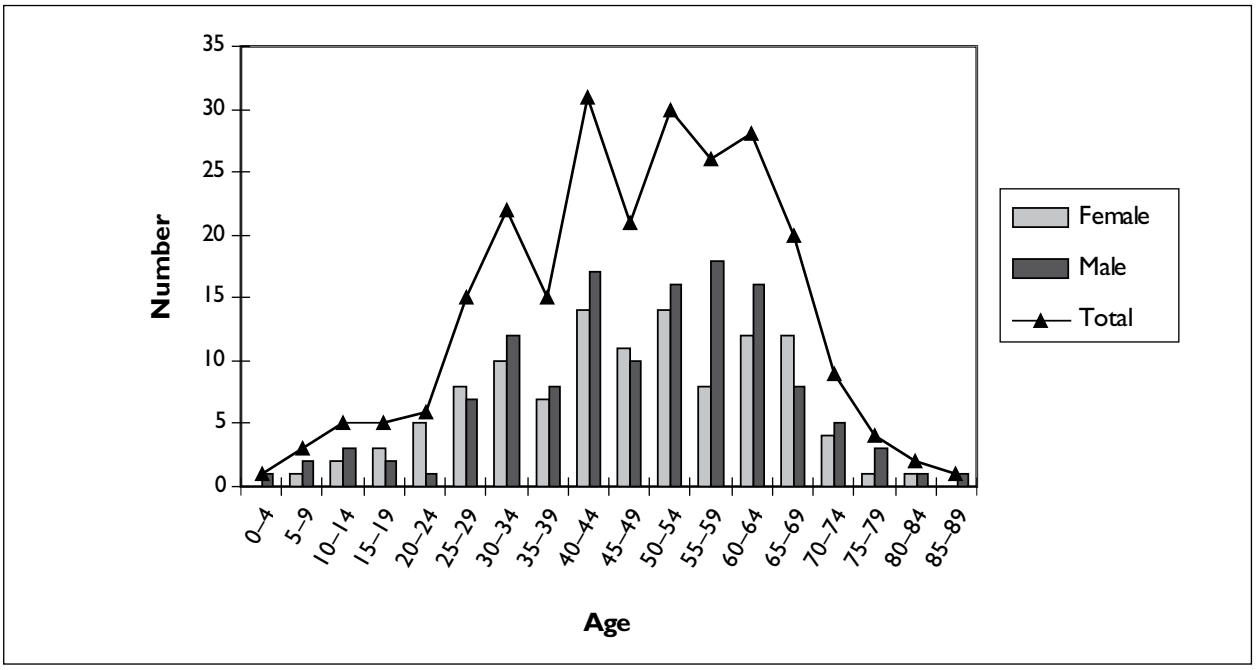

FIGURE 1 Age/sex distribution of seropositive patients for July to September 2007 and July to September 2008 combined.

RESULTS

The average annual incidence rate of LB in Scotland for 2007 and 2008 was estimated to be 5.9/100,000 population, and increased to 10.6/100,000 population for the periods from July to September. The average annual incidence rate in the Highlands of Scotland was higher at 43.4/100,000 population and increased to 81.0/100,000 population for the periods from July to September.

There were significantly more patients tested in July to September 2008 compared with the same period in 2007 (1,330 vs 1,097, χ^2=22.36, p<0.001), and significantly more seropositive patients (150 vs 94, χ^2=12.8, p<0.001). There was also a significantly higher proportion of seropositive patients per patients tested (150/1,330, 11% vs 94/1,097, 8.6%, χ^2=4.880, p<0.05).

Most seropositive patients were in the 40–64 years age group and there were very few seropositive patients below 25 and above 70 years of age (Figure 1).

When the weather data were examined (Figure 2) it was found that January to April 2008 was significantly wetter (χ^2=7.469, p<0.01), and May to July 2008 was significantly drier (χ^2=12.336, p<0.001) than the same months in 2007. May to July in 2008 was significantly drier than in 2007 due to the highly significant difference in rainfall in May (29.6 mm vs 128.9 mm, χ^2=62.22, p<0.001).

Analysis of returned questionnaires from July to September 2007 (65/94, 69.1%) and July to September 2008 (96/150, 64%) found that there was no significant difference in numbers between the two study periods with regard to sex, frequency of the specific signs/symptoms of LB, presentation of symptoms giving rise to suspicion of early LB, the presence of a tick bite, and whether treatment was given. However, there was a significantly higher proportion of patients considered by clinicians to have had LB in July to September 2007 than in July to September 2008 (56/65, 86.1% vs 67/96, 69.4%, χ^2=5.754, p<0.02). Using the returned questionnaire data from July to September 2007 and July to September 2008 combined (n=161), the percentage of patients with erythema migrans was 57.1%, arthritis 21.7%, rash 20.5%, neurological symptoms 7.5%, cardiac symptoms 2.5% and skin problems 0.6%. A considerable percentage of patients had symptoms giving rise to a clinical suspicion of early LB (83.9%), had a history of tick bite (59%), were treated (88.2%) or were clinically thought to have had LB (76.4%).

DISCUSSION

The number of cases of LB increased dramatically in Scotland from 2004 to 2006.[4] This study shows a further increase in both specimen numbers tested and seropositive cases from 2007 to 2008. It is reassuring that the proportion of seropositive cases increased with specimen numbers during the study period, as this assures us that the increased testing is justified. The estimated average annual incidence rates for 2007 and 2008 were higher than those previously documented for 2004 to 2006 (from 2.1 to 5.9/100,000 population for Scotland and from 28.0 to 43.4/100,000 population for the Highlands of Scotland).[4] The estimated average incidence rates of 10.6/100,000 population for Scotland and 81.0/100,000 population for the Highlands of Scotland for July to

TABLE 1 Epidemiological and clinical patterns of Lyme borreliosis

Study	Sex ratio	Age group incidence	Clinical pattern
France 1989–1997[9]	55% Male	Bimodal Working age normal distribution	Neurological 45.9%, arthritis 20%, tick bite 46%
Portugal 1990–2004[12]	53.5% Female	n/a	Neurological 23.2%, arthritis 9.6%
Norway 1995–2004[11]	56% Male	n/a	Neurological 71%, arthritis 22%
Sweden 1997–2003[7]	54.4% Female	n/a	n/a
Bulgaria 1999–2002[10]	64.3% Female	Bimodal Working age normal distribution	Neurological 19%, arthritis 8%, erythema migrans 69.1%, tick bite 78%
Germany 2002–3[1]	55% Female	Bimodal Working age normal distribution	2002: Erythema migrans 89.3% 2003: Erythema migrans 86.7%
France 2003[8]	n/a	n/a	Neurological 30%, tick bite 69%
USA 2003–2005[2]	54% Male	Bimodal	Neurological 11%, arthritis 30%
Scotland 2004–2006[4]	55.1% Male	Peak 40–64	n/a
Current study Jul–Sept 2007/8	53.7% Male	Peak 40–64	Neurological 7.5%, arthritis 21.7%, erythema migrans 57.1%, tick bite 59%

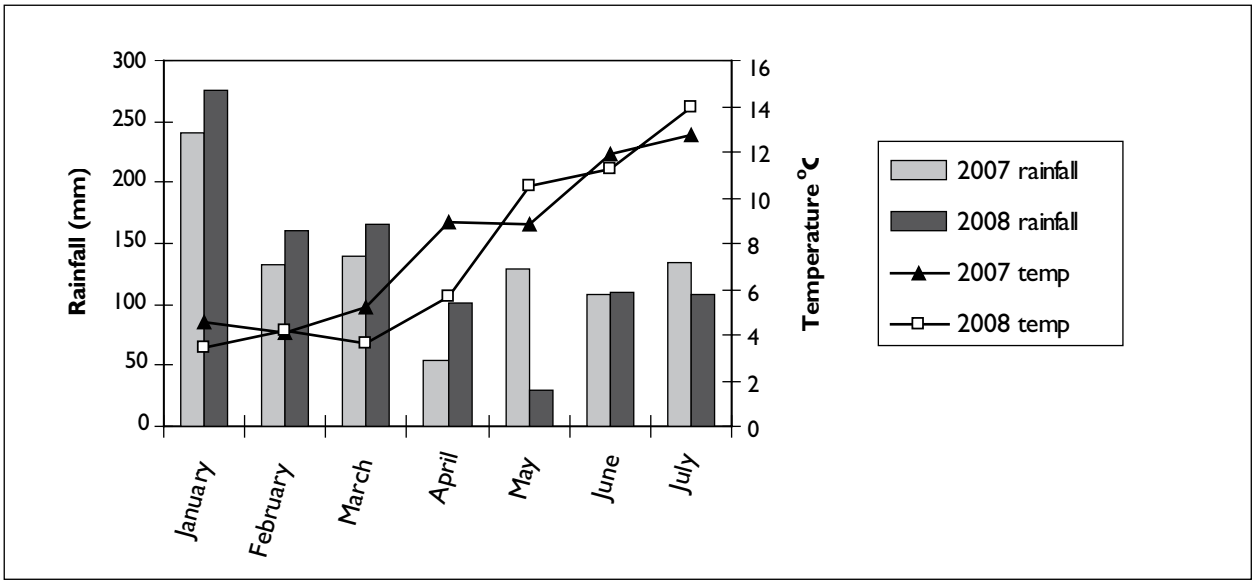

FIGURE 2 Temperature and rainfall data for Scotland, January to July 2007 and January to July 2008.

September 2007 and 2008 combined are the peak incidence rates we would expect for these regions and reflect the risk of LB infection in the summer months. There is no doubt that part of the explanation of these increases is a greater recognition of LB by clinicians and the general public.

The epidemiology of LB varies considerably throughout the world and we have previously shown some differences in clinical presentation in Scotland.[16] A summary of a review undertaken to compare our study to others in Europe and in the USA is shown in Table 1. The ratio of male to female seropositive cases found in this study (53.7% vs 46.3%) is consistent with what we found in a study in 2004 to 2006, where the percentages were 55.1% vs 44.9%.[4] A predominance of male over female cases has been reported in the USA,[2] France[9] and Norway,[11] but studies in Germany,[1] Sweden,[7] Bulgaria[10] and Portugal[12] have reported a female preponderance. In many studies in the USA and Europe there is a bimodal age incidence pattern, including a peak in the 5–15 years age group,[1,2,9,10] as well as a peak in the older age ranges (40–65 years) that we do not see in Scotland. The general normal distribution of seropositive cases seen in the working age groups is comparable to other reports.[1,9,10] Similar to our 2004–2006 study,[4] most of the seropositive cases were again found in the 40–64 years age range. Only 59% of seropositive patients could recollect having a tick bite, which puts this finding in the mid-range of other studies where 46–78% of patients reported tick bites.[8–10]

As the percentage of patients in this study clinically thought to have early LB was high (83.9%), it highlights that tick bites are often going unnoticed. The considerable number of questionnaires returned to the laboratory

highlights the clinical interest in LB in Scotland. It was surprising therefore that the number of clinicians who thought their patients had LB significantly dropped in the second year studied, in spite of the increased number of seropositive cases diagnosed. It may be that some clinicians were cautious as to whether the laboratory result was significant; nevertheless some of these patients had been successfully treated with antibiotics, and some had erythema migrans which, in itself, is diagnostic of LB.

We have reported previously that a warm, wet January to March (aiding tick survival) followed by a dry April to July (increasing human exposure) can account for an increase in incidence of LB in Scotland.[6] Further to this, a significantly wetter January to April and drier May to July in 2008 may be a contributing factor for the increase in LB in 2008, in particular the unusually dry May. Tick questing in Scotland begins in April and May when air temperatures increase,[17] and this, paired with a presumed increase in human outdoor activity as a result of the dry weather, would undoubtedly have led to increased human exposure. Nevertheless, we believe increased tick surveillance and the relationships between tick activity and environmental conditions are needed before predictions of future trends are possible.

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REFERENCES

1 Mehnert WH, Krause G. Surveillance of Lyme borreliosis in Germany, 2002 and 2003. *Euro Surveill* 2005; 10:83–5.
2 Bacon RM, Kugeler KJ, Griffith KS et al. Lyme disease – United States 2003–2005. *Morb Mortal Wkly Rep* 2007; 56:573–6.
3 Ho-Yen DO, Davidson MM, Chisholm SM et al. How prevalent is Lyme disease in Scotland? *SCIEH Weekly Report* 1999; 33:214–5.
4 Ho-Yen DO, Mavin S, Hopkins PC et al. Lyme borreliosis: differences between the patients who are tested and those with the infection. *HPS Weekly Report* 2008; 42:441–3.
5 Edlow JA. Lyme disease and related tick-borne illnesses. *Ann Emerg Med* 1999; 33: 680–93.
6 Mavin S, Joss AWL, Ho-Yen DO. Incidence of Scottish Lyme disease appears to be related to the effects of weather on tick survival and human behaviour. *J R Coll Physicians Edinb* 2005; 35:112–5.
7 Bennett L, Halling A, Berglund J. Increased incidence of Lyme borreliosis in southern Sweden following mild winters and during warm, humid summers. *Eur J Clin Microbiol Infect Dis* 2006; 25:426–32.
8 Trombert-Paolantoni S, Ferquel E, Postic D. Retrospective study of Lyme borreliosis positive serologies in 2003. *Pathologie Biologie* 2005; 53: 522–6.
9 Dhote R, Basse-Guerineau AL, Beaumesnil V et al. Full spectrum of clinical, serological, and epidemiological features of complicated forms of Lyme borreliosis in the Paris, France, area. *Eur J Clin Microbiol Infect Dis* 2000; 19:809–15.
10 Christova I, Komitova R. Clinical and epidemiological features of Lyme borreliosis in Bulgaria. *Wien Klin Wochenschr* 2004; 116: 42–6.
11 Nygard K, Brock Brantsaeter A, Mehl R. Disseminated and chronic Lyme borreliosis in Norway, 1995–2004. *Euro Surveill* 2005; 10:235–8.
12 Lopes de Carvalho I, Núncio MS. Laboratory diagnosis of Lyme borreliosis at the Portuguese National Institute of Health (1990–2004). *Euro Surveill* 2006; 11:257–60.
13 Centers for Disease Control and Prevention. Recommendations for test performance and interpretation from the 2nd National Conference on serologic diagnosis of Lyme disease. *Morb Mortal Wkly Rep* 1995; 44:590–1.
14 Mavin S, Evans R, Milner RM et al. Local *Borrelia burgdorferi* sensu stricto and *Borrelia afzelii* strains in a single mixed antigen improves Western blot sensitivity. *J Clin Pathol* 2009; 62: 552–4.
15 Met Office. UK climate and weather statistics. Available from http://www.metoffice.com/climate/uk
16 Milner RM, Mavin S, Ho-Yen DO. Lyme borreliosis in Scotland is different. *J Infect* 2009; 59:146–7.
17 Hendry G, Ho-Yen D, Blackwell A. *Ticks: your pets, your family and you*. 2nd ed. Edinburgh: Mercat Press; 2006. p. 25.