

# Is Tayside becoming a Scottish hotspot for Lyme borreliosis?

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**ABSTRACT** The epidemiology of Lyme borreliosis (LB) in Tayside was studied and compared with Highland (an area of high endemicity) and the rest of Scotland. From April 2001 to March 2008 the incidence of LB in Tayside rose from an estimated 2.57 to 5.84 per 100,000 population. In 2008/09 the incidence of LB in Tayside increased further to an estimated 13.85 per 100,000 population. This rise was significant and, although numerically less than that in Highland (37.24 to 49.69 per 100,000 population), it was proportionally much larger (137% vs 33%) and confirmed that LB in Tayside has diverged from that in non-endemic Scottish regions. The dramatic rise of LB in Tayside cannot be accounted for by changes in laboratory protocol or changes in the number or demographics of patients tested. However, changes in climatic conditions and alterations in clinical presentations may have contributed to this significant rise.

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## INTRODUCTION

Lyme borreliosis (LB) is the most common vector-borne disease in Europe and the USA.<sup>1</sup> The causative agent, spirochaete *Borrelia burgdorferi* sensu lato, can be differentiated into at least 15 genospecies, seven of which are known to cause human disease.<sup>2</sup> The spirochaete is transmitted between vertebrate hosts by ixodid ticks as they take a blood meal. In Scotland the vector for LB is *Ixodes ricinus*, or sheep tick, which feeds on a range of mammals including birds, deer and sheep.<sup>3</sup> The majority of human cases occur in the summer months as human behaviour increases the risk of exposure and tick nymphs are questing.<sup>4</sup> Nymphs are much smaller than their adult counterparts and often go unnoticed, facilitating the transmission of the organism which requires the tick to have fed for 24–48 hours before transmission can occur.

The incidence of LB has been rising across the world, with foci of infection in the USA, Asia and Europe.<sup>1</sup> Rises in LB have been linked with improved diagnostics, raised awareness, changes in land use, increased tick density and burden of tick disease.<sup>5</sup> In Scotland the incidence of LB is highest in the Highlands, an area of high endemicity.<sup>6</sup> Scottish studies have therefore focused on this region and there is little information on the incidence and epidemiology of LB in other regions. There have been anecdotal reports that Tayside has experienced an increase in test requests for LB, and that an increased number of samples have been referred to the National LB Testing Laboratory (NLBTL) in recent years. This study was therefore carried out to identify any significant changes in the incidence of LB in Tayside.

## MATERIALS AND METHODS

### Patients' details

Samples submitted to the Medical Microbiology Department at Ninewells Hospital & Medical School in Dundee, representing infection in Tayside, and samples submitted to the NLBTL, Raigmore Hospital, Inverness, representing infection in Highland and the rest of Scotland, were studied. Archived data on patients' age, sex, month of sample submission, test request details and test results were collected and analysed for samples submitted from Tayside for *B. burgdorferi* testing from April 2001 to March 2010. Data were extracted from the local laboratory's computing system, LabCentre, and analysed in Excel. Archived data on samples submitted from Highland and the rest of Scotland for *B. burgdorferi* testing from April 2004 to March 2010 were extracted from the NLBTL computing system, Medipath, and analysed in Excel.

Tayside and Highland refer to health boards in Scotland. Tayside covers the city of Dundee and the counties of Angus and Perth & Kinross. Highland extends from Argyll & Bute in the south to Caithness and Sutherland in the north. The rest of Scotland refers to all other health boards in Scotland with the exception of Grampian.

### Laboratory tests

Throughout the study period, the two-step approach to laboratory testing was adopted in both centres.<sup>7</sup> Samples were screened locally using a *B. burgdorferi* immunoglobulin (IgM/IgG) enzyme-linked immunoassay (EIA) (Zeus Scientific) according to the manufacturer's instructions. Confirmatory testing of EIA equivocal/reactive samples was carried out by the NLBTL with an

**TABLE 1** Number of patients tested and new cases of Lyme borreliosis for Tayside and Highland from April 2001 to March 2010

Year (Apr–Mar)	Patients tested	New cases
<b>Tayside</b>		
2001/02	505	10 (1.98%)
2002/03	547	8 (1.46%)
2003/04	691	9 (1.30%)
2004/05	630	5 (0.79%)
2005/06	606	9 (1.49%)
2006/07	736	24 (3.26%)
2007/08	749	23 (3.07%)
2008/09	780	55 (7.05%)
2009/10	881	67 (7.60%)
<b>Highland</b>		
2004/05	n/a	56
2005/06	1,072	61 (5.69%)
2006/07	1,165	78 (6.70%)
2007/08	1,052	115 (10.93%)
2008/09	1,069	154 (14.41%)
2009/10	1,202	175 (14.56%)

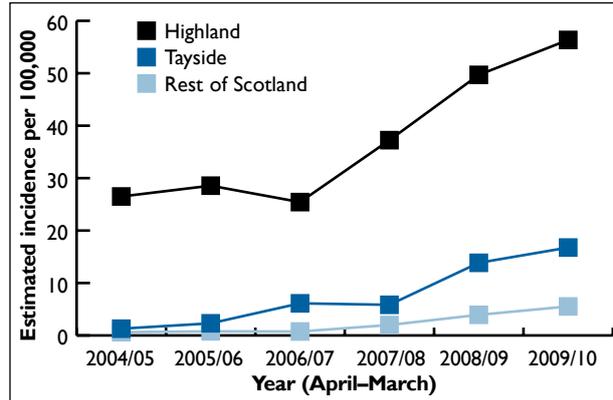
in-house IgG Western blot. Enzyme-linked immunoassay-negative samples with strong clinical suspicion of LB were also submitted for Western blot testing. The Western blot was performed as previously described.<sup>8</sup> However, the antigen used and interpretation criteria were revised in April 2004,<sup>9</sup> June 2007<sup>10</sup> and October 2008.<sup>5</sup> In this study, all patients with a weak positive or positive Western blot result were classed as seropositive.

To further investigate LB in Tayside, patient demographics and test request details for samples submitted between March 2006 and April 2010 were studied. To improve sample size, data from 2006/07 were combined with 2007/08, and data from 2008/09 combined with 2009/10. There was good correlation in the age/sex structure of patients tested and no significant differences in the number of new cases in the combined study years.

Meteorological Office data on monthly rainfall for the north of Scotland (Highland) and east of Scotland (Grampian, Tayside, Perthshire, Fife, Lothian and Borders) were sourced from the Meteorological Office website.<sup>11</sup> Data were analysed for differences between areas and years and significance determined using the chi-squared ( $\chi^2$ ) test. Mid-year population estimates were gathered from the General Register Office for Scotland.<sup>12</sup>

## RESULTS

In Tayside there has been a significant rise in the number of patients tested for LB rising from 505 in 2001/02 to 881 in 2009/10 ( $\chi^2=168.6$ ,  $p<0.001$ ) (Table 1). The incidence of LB in Tayside has also significantly risen in this

**FIGURE 1** Incidence of Lyme borreliosis for Tayside, Highland and rest of Scotland from April 2004 to March 2010.

time, from an estimated 2.57/100,000 population in 2001/02 to 16.76/100,000 population in 2009/10 ( $\chi^2=42.1$ ,  $p<0.001$ ) (Figure 1). This rise can be attributed to significant increases in the number of cases of LB in 2006/07 ( $\chi^2=6.8$ ,  $p<0.01$ ) and 2008/09 ( $\chi^2=13.1$ ,  $p<0.001$ ) (Table 1). Despite fluctuations in the number of patients tested in recent years (Table 1), the estimated incidence of LB in Highland has risen significantly each year since 2006/07, rising from 25.43/100,000 population in 2006/07 to 56.35/100,000 population in 2009/10 ( $\chi^2=36.0$ ,  $p<0.001$ ) (Figure 1). In comparison, incidence for the rest of Scotland remained very low at 0.78 and 0.75/100,000 population in 2005/06 and 2006/07, rising steadily to 5.53/100,000 population in 2009/10 (Figure 1).

### Tayside patient demographics

There were no significant differences in the proportion of male and female patients tested in Tayside in 2006/08 (49.2% male, 50.8% female) and 2008/10 (47.5% male, 52.5% female). Moreover, there was good correlation between the age/sex structure of patients tested in Tayside in 2006/08 with those tested in 2008/10 ( $r^2=0.95/0.83$  for males/females respectively). Additionally, the ratio of male to female LB cases in Tayside did not change significantly, with 27 male (57.4%) and 20 female (42.6%) cases in 2006/08 and 61 male (50.0%) and 61 female (50.0%) cases in 2008/10. There were also no significant differences in the proportion of cases in patients aged less than 40 years, 40–64 years or over 64 years in 2006/08 versus 2008/10, with the majority of cases in those of working age.

### Clinical category

In 2008/10, a significantly reduced proportion of LB cases in Tayside had clinical details suggestive of early LB ( $\chi^2=11.7$ ,  $p<0.001$ ) (Table 2). There was also a significant rise in the proportion of cases with neurological or joint symptoms, from five (10.6%) in 2006/08 to 37 (30.3%) in 2008/10 ( $\chi^2=7.0$ ,  $p<0.01$ ). A rise in the proportion of cases with clinical details classified as 'other' in 2008/10 was not significant.

**TABLE 2** Clinical classification of test request details for Tayside cases of Lyme borreliosis

Test request details	2006/08	2008/10
Early Lyme borreliosis*	39 (83.0%)	70 (57.4%)
Neurological	5 (10.6%)	31 (25.4%)
Joint symptoms	0	6 (4.9%)
Other	2 (4.3%)	6 (4.9%)
Not stated	1 (2.1%)	9 (7.4%)
Total	47	122

\*Includes erythema migrans/rash/tick bite/flu-like illness.

### Weather data

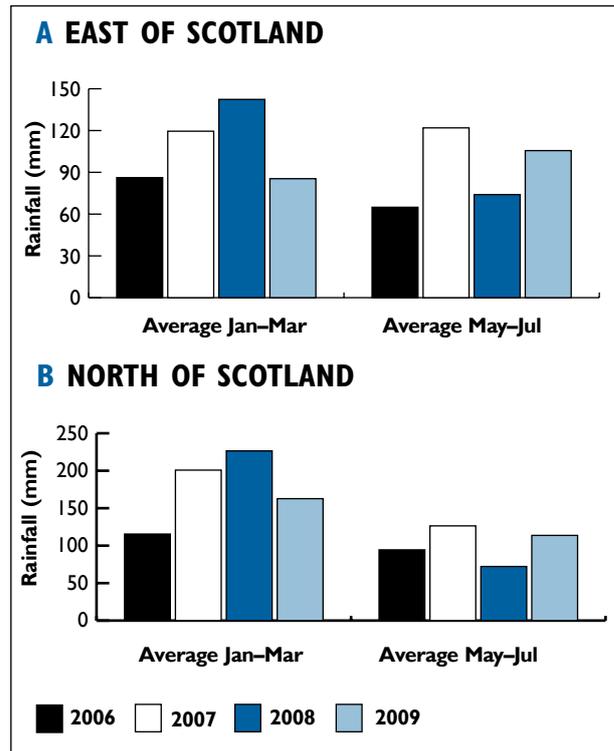
Weather data for the north and east of Scotland from 2006 to 2009 were analysed. The east of Scotland had a significant rise in average monthly rainfall in January–March 2007 ( $\chi^2=5.4$ ,  $p<0.025$ ). This was followed by a smaller rise in 2008 and a significant fall in 2009 ( $\chi^2=14.2$ ,  $p<0.001$ ) (Figure 2A). This pattern was mirrored in the north of Scotland, which also had a significant rise in average monthly rainfall in January–March 2007 ( $\chi^2=23.02$ ,  $p<0.001$ ), followed by a smaller rise in 2008 and a significant fall in 2009 ( $\chi^2=10.4$ ,  $p<0.002$ ) (Figure 2B).

In the east of Scotland May–July 2007 and 2009 were significantly wetter than the same period in 2006 ( $\chi^2=17.39$ ,  $p<0.001$  and  $\chi^2=9.70$ ,  $p<0.002$ , respectively) or 2008 ( $\chi^2=11.73$ ,  $p<0.001$  and  $\chi^2=5.56$ ,  $p<0.02$ , respectively) (Figure 2A). May–July 2007 was also significantly wetter in the north of Scotland than in 2006 or 2008 ( $\chi^2=4.63$ ,  $p<0.05$ ;  $\chi^2=14.79$ ,  $p<0.001$ ; and  $\chi^2=9.48$ ,  $p<0.003$  respectively). In 2009 May–July was significantly wetter than 2008 but not 2006 (Figure 2B).

## DISCUSSION

There has been an increasing rise in LB in Tayside. From April 2001 to March 2006 there were up to ten new cases of LB confirmed in Tayside each year (Table 1). However, in 2006/07 this rose significantly to 24 ( $\chi^2=6.8$ ,  $p<0.01$ ) and the estimated incidence of LB in Tayside was significantly higher than that for the rest of Scotland, excluding Highland (6.12 vs 0.75/100,000,  $\chi^2=83.2$ ,  $p<0.001$ ) (Figure 1). This rise was maintained and in 2008/09 the incidence of LB in Tayside increased significantly to 13.85/100,000 population ( $\chi^2=36.13$ ,  $p<0.001$ ). Although this rise was numerically lower than that seen in the endemic region of Highland, it was proportionally much greater (137% vs 33.4%) and confirmed that the incidence of LB in Tayside is diverging from the rest of Scotland, excluding Highland (Figure 1).

There has also been a significant increase in testing in Tayside (Table 1), demonstrating the increased awareness of the general and medical population of Tayside. However, as there was a significant increase in the proportion of



**FIGURE 2** Average monthly rainfall for January–March and May–July in the east (A) and north (B) of Scotland.

patients that were positive in 2006/07 (9/606 vs 24/736,  $p=0.0499$ , Fisher's exact test) and again in 2008/09 (23/749 vs 55/780  $p=0.0004$ , Fisher's exact test), this suggests that the rise of LB in Tayside cannot be accounted for by increased testing. There were also no significant changes in the demographics of patients tested or of LB cases, despite the proportion of male LB cases declining from 57.4% in 2006/08 to 50% in 2008/10.

Scotland appears unusual in having more male than female cases as a large number of European countries, including Germany and Portugal, report a female preponderance.<sup>13,14</sup> Age distribution of LB can also vary between studies. Some show a bimodal distribution with a peak of cases in five–15 year-olds and a peak in the older age group.<sup>13,15,16</sup> However, reports from Scotland show a broad peak in those of working age.<sup>6,17</sup> This corresponds to that seen in this study, where the majority of cases occurred in 30–64 year-olds, with very few cases in patients aged less than 25 or over 70 years.

Although there were no significant changes in the demographics of LB cases in Tayside, there was a significant rise in the proportion of LB cases with neurological or joint symptoms recorded on test request forms in 2008/10 compared with 2006/08 (Table 2).

There was also a rise in the number of cases with test request details classified as 'other', indicating that the clinical pattern of LB in Tayside is changing, with a more diverse spectrum of symptoms than previously seen. We

speculate this may be linked to a change in *B. burgdorferi* genospecies within the local tick population as certain genospecies are associated with differing clinical presentations. For example, *B. afzelii* has been associated with acrodermatitis chronica atrophicans, while *B. burgdorferi* sensu stricto is strongly associated with arthritic symptoms and *B. garinii* with neurological presentations.<sup>18,19</sup> However, there is little information on the prevalence and distribution of *B. burgdorferi* genospecies in the UK. A small study sampling two sites in the Scottish Highlands isolated *B. afzelii* and *B. burgdorferi* sensu stricto, while other UK studies have isolated *B. garinii* and *B. valaisiana*.<sup>20–22</sup> Changes in the distribution of *B. burgdorferi* genospecies may therefore have led to a change in the clinical presentation of LB in Tayside, but this may not explain the dramatic and sustained rise of LB in 2008/10.

Tick population densities are influenced by a number of interconnected factors, including host availability, habitat and climate conditions. It has been reported that a wet January–March may aid tick survival and that there is an association between tick establishment and LB endemicity in ticks.<sup>4,23</sup> Moreover, it has been reported that infection rates in ticks correlate with disease frequency in humans.<sup>23</sup> In the east of Scotland, January–March rainfall peaked in 2008, coinciding with the dramatic rise of LB

in Tayside (Figure 2A). That year also had a dry summer, potentially leading to increased human exposure. However, winter rainfall fell in 2009, which also had a wet summer; yet the incidence of LB in Tayside remained high in 2009/10. Moreover, a similar rainfall pattern was observed in the north of Scotland (Figure 2B) and, although a significant rise of LB was detected in Highland in 2008/09, this rise was of a similar size to the previous year, suggesting rainfall pattern alone cannot account for the rise of LB in Tayside (Table 1).

When LB in Scotland has been examined, Highland has consistently been shown to be an endemic region. However, this study has shown that the incidence of LB in Tayside is also rising. Medical practitioners should therefore be aware of the increased risk to patients who visit or reside in these areas and the wide spectrum of clinical symptoms associated with LB. It appears that Tayside is in the early stages of becoming a 'hot spot' for LB, diverging from the pattern seen in the rest of Scotland and developing into an area of endemicity similar to Highland.

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