

Increased reports of *Mycoplasma pneumoniae* from laboratories in Scotland in 2010 and 2011 – impact of the epidemic in infants

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In common with reports from other European countries, we describe a substantial increase in the number of laboratory reports of *Mycoplasma pneumoniae* in Scotland in 2010 and 2011. The highest number of reports came from those aged one year and younger. However, reports from young children were more likely to come from PCR testing than serological testing.

In light of the increasing incidence of *M. pneumoniae* in other parts of the United Kingdom (UK) and Europe in 2010 and 2011, we examined the numbers of *M. pneumoniae* laboratory reports in Scotland from January 2008 to December 2011. Here we describe the temporal distribution of reports and the age groups most affected.

Background

Mycoplasma pneumoniae causes upper and lower respiratory tract infection in all age groups. However, it is a particularly important bacterial cause of community-acquired pneumonia in children [1]. *M. pneumoniae* is endemic worldwide, but epidemics are common; historically in the UK, these usually occur once every four years [2]. The most recent increase in the incidence of *M. pneumoniae* was seen in England and Wales in 2010 and 2011 [3,4]. Similar increases have also been noted in many other countries in the same period, particularly in northern Europe [5-12].

Although the main burden of infection is typically found in school-age children [4,6,10], *M. pneumoniae* has also been noted as a significant cause of respiratory tract infection in children under the age of five [13-15]. As the possibility of *M. pneumoniae* infection may be overlooked in young children, recent UK clinical guidelines emphasise that *M. pneumoniae* is not uncommon in those aged one to five years [1]. However,

the local availability of different testing methodologies for *M. pneumoniae* may determine how frequently *M. pneumoniae* is diagnosed in particular age groups.

National laboratory-based surveillance and reporting

In Scotland, some diagnostic laboratories carry out PCR testing for *M. pneumoniae* as part of a multiplex real-time PCR screening approach for respiratory viruses [16]. Therefore, young children presenting with presumed respiratory viral infection to hospitals served by these laboratories also receive concomitant testing for *M. pneumoniae*. In hospitals served by other laboratories, serology is still the mainstay of *M. pneumoniae* diagnosis. However, serology is less convenient for diagnosis in young children, since obtaining a blood specimen from an infant is more difficult than obtaining an upper respiratory tract specimen.

Reports of *M. pneumoniae* from National Health Service (NHS) laboratories in Scotland are collated centrally by the national public health body Health Protection Scotland (HPS), via the Electronic Communication Of Surveillance in Scotland (ECOSS) non-mandatory reporting system. Reports from 1 January 2008 to 31 December 2011 inclusive were analysed in this study. Denominator testing data and clinical diagnosis were not recorded via ECOSS. Data were anonymised and analysed by week of year reported, age group (year of age was available in 2010 and 2011), sex, submitting laboratory and specimen type. Estimates of incidence were based on the most recent mid-year population estimate for Scotland [17]. Reports were submitted from all NHS microbiology laboratories in Scotland which carry out *M. pneumoniae* testing. These are based in hospitals in nine locations: Aberdeen, Ayr, Dundee, Dunfermline, Edinburgh, Fife, Glasgow, Inverness and

Lanarkshire. In the case of Glasgow, results from two laboratories in the city were combined. Respiratory specimens were tested by PCR and blood specimens by serology. Laboratories used a number of different commercial and in-house PCR and serological tests. Reports of positive serology were either from a diagnostic rise in *M. pneumoniae*-specific IgG antibodies or detection of *M. pneumoniae*-specific IgM.

Analysis of laboratory reports

Temporal distribution

During the study period, there were 1,232 laboratory reports of *M. pneumoniae* in Scotland; of these, 76 (6.2%) were from 2008, 125 (10.1%) from 2009, 290 (23.5%) from 2010 and 741 (60.1%) from 2011. The highest number of reports were found in the fourth quarter of 2011 (432 reports); this was nearly three times higher than in any other quarter in the study period. The number of reports began to rise from the autumn of 2010 through the winter of 2010/11, with a second and larger rise towards the end of 2011 (Figure 1). The peak reporting frequency was 48 reports in week 47 of 2011. The estimated national incidence of *M. pneumoniae* in 2011 was 14.2 per 100,000 population.

Laboratory testing

Reports of *M. pneumoniae* were issued from nine laboratories, with the two laboratories serving the largest populations (Edinburgh and Glasgow) issuing 77.0% of the reports. Testing methods differed across Scotland, with five laboratories using PCR only and four using serology only. Overall, 77.4% of reports were from respiratory specimens (PCR detection), 18.0% from serology, and the specimen type was not known in 4.6% of reports. Of the respiratory specimens, 92.1% were from the upper respiratory tract.

Patient demographics

The male:female ratio was 1:0.94; there was no significant difference in the number of reports from males and females ($p=0.30$; chi-squared test). Approximately half of the reports (53%) were from children under the age of 15 years, with the age group of 0–4 year-olds accounting for 24.9% of all reports (Table). The

estimated incidence of *M. pneumoniae* in 2011 was highest in the 0–4 year-olds (67.5/100,000 population), declining to 52.2 per 100,000 in the 5–9 year-olds and 22.6 per 100,000 in the 10–14 year-olds.

Due to improvements in the quality of information provided from laboratories via ECOS, data on individual year of age were available from 2010 onwards. The mean age of patients was 20.0 years (standard deviation (SD) ± 19.8 years; range: <1 month to 89 years), however, 16.2% of the reports from 2010 and 2011 came from patients aged one year or younger (Figure 2).

Patient age and sample type

Between 2008 and 2011, *M. pneumoniae* reports from young children were more likely to come from PCR testing than serological testing: 28.8% of reports from respiratory specimens were from 0–4 year-old children, compared to 10.4% of serology specimens ($p<0.01$ Fisher's exact test) (Table).

An analysis of year of age data from 2010/11 demonstrated that the mean age for PCR reports was 18.6 years (SD ± 19.4 years; range: <1 month to 89 years). In contrast, the mean age for serology reports during the same period was 27.8 years (SD ± 19.9 years; range: 1 year to 88 years).

Macrolide resistance

A full analysis of the presence of mutations in the 23S rRNA gene associated with macrolide resistance is currently underway in PCR-positive specimens.

TABLE

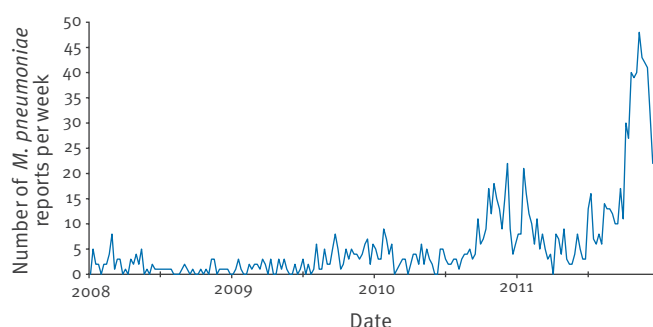
Mycoplasma pneumoniae reports by age group and specimen type, Scotland, 2008–2011 (n=1,232)

Age group (years)	Total <i>M. pneumoniae</i> reports (%) n=1,232	<i>M. pneumoniae</i> reports from respiratory specimens (%) n=954 ^a	<i>M. pneumoniae</i> reports from serology (%) n=222 ^a
0–4	307 (24.9)	275 (28.8)	23 (10.4)
5–9	218 (17.7)	173 (18.1)	40 (18.0)
10–14	128 (10.4)	97 (10.2)	28 (12.6)
15–19	67 (5.4)	45 (4.7)	14 (6.3)
20–24	60 (4.9)	41 (4.3)	15 (6.8)
25–29	55 (4.5)	45 (4.7)	6 (2.7)
30–34	75 (6.1)	55 (5.8)	20 (9.0)
35–39	75 (6.1)	59 (6.2)	12 (5.4)
40–44	73 (5.9)	45 (4.7)	22 (9.9)
45–49	43 (3.5)	31 (3.2)	8 (3.6)
50–54	39 (3.2)	24 (2.5)	11 (5.0)
55–59	26 (2.1)	19 (2.0)	6 (2.7)
60–64	17 (1.4)	12 (1.3)	4 (1.8)
≥65	49 (4.0)	33 (3.5)	13 (5.9)

^a 56 reports were from specimens of unknown type and are therefore excluded here.

FIGURE 1

Mycoplasma pneumoniae reports by week of year, Scotland 2008–2011 (n=1,232)



However, preliminary results indicate genotypic evidence of resistance in at least one specimen; a paediatric patient re-presenting to hospital with ongoing respiratory symptoms following first-line treatment with a macrolide for *M. pneumoniae* infection (data not shown).

Discussion

An examination of the current epidemiology of *M. pneumoniae* in Scotland was considered timely given the recent increasing incidence seen in other countries in the UK, Europe and elsewhere [3-12]. We found a substantial peak in the number of *M. pneumoniae* laboratory reports submitted to the national surveillance programme during the autumn/winter of 2011, following a smaller peak in the previous autumn/winter of 2010. The *M. pneumoniae* activity had been low from 2008 until the autumn of 2010. As expected, this picture is consistent with an increase in *M. pneumoniae* laboratory reports in England and Wales in the same period [3,4]. The estimated overall incidence of *M. pneumoniae* in Scotland in 2011 was around 10-fold lower than that reported in other northern European countries [8,10]. However, we found that the incidence was highest in the youngest age group, in contrast to a recent study in which incidence was highest in 5–14 year-olds [10]. Reporting of *M. pneumoniae* in the UK is not mandatory and reports only arise from the active microbiological investigation of patients with respiratory symptoms, mainly those presenting to hospitals. Therefore, our figures are likely to underestimate the true extent of the epidemic in Scotland, particularly in the community.

Low levels of macrolide resistance have been reported in Europe [11,18] but not from other countries in the UK [3,4]. In a preliminary analysis as part of the present study we found one genotypically resistant isolate, however, a full assessment of the level of macrolide resistance in Scotland is required and is now underway.

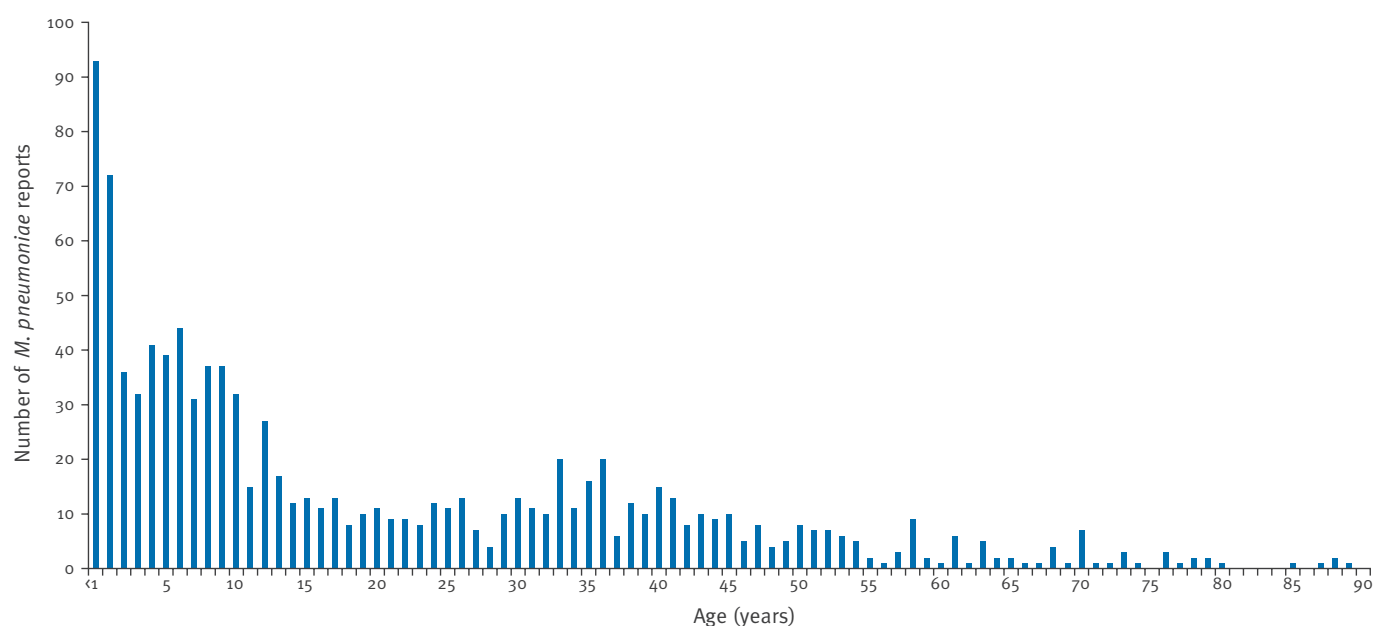
As we were able to differentiate reports into narrow age bands, it was clear that in Scotland, *M. pneumoniae* was most frequently reported in the youngest children, particularly those one year and younger. The incidence was also highest in the age group of 0–4 year-olds, with 67.5 per 100,000. A limitation of this study is that denominator testing data is not currently captured by the surveillance programme, so we are unable to determine if the proportion of *M. pneumoniae*-positive children in this age group was less than that in older age groups, as found in other studies [4,6,10]. Numerically however, we have found a significant burden in infants, which has previously been under-appreciated. A study examining the clinical course, treatment and outcomes of *M. pneumoniae* infection in infants is now underway.

We also found significantly fewer *M. pneumoniae* reports from serology compared to respiratory specimens in children aged 0–4 years. This may be due to the ease of obtaining upper respiratory tract specimens for PCR, compared to blood specimens for serology, in the youngest patients. Therefore, in hospitals where only serological testing is available, *M. pneumoniae* infections in young children may be under-diagnosed.

The majority of *M. pneumoniae* reports in Scotland originated from two large laboratories which test almost exclusively by PCR as part of in-house multiplex

FIGURE 2

Mycoplasma pneumoniae reports by year of age, Scotland, 2010–2011 (n=1,031)



real-time PCR screens for respiratory pathogens. In the future, as this molecular syndromic screening approach becomes more widespread, more infants are likely to be tested for *M. pneumoniae*, and more infections found. During *M. pneumoniae* epidemics, there may be a requirement to change empirical prescribing for community-acquired pneumonia from beta-lactam antibiotics to macrolides in the most affected age groups. However, further work is required to determine the clinical consequences of *M. pneumoniae* infection in infants and the need for antibiotic treatment.

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