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Surveillance status and recent data for *Mycoplasma pneumoniae* infections in the European Union and European Economic Area, January 2012

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In January 2012, the European Centre for Disease Prevention and Control (ECDC) conducted an email-based survey of European Union and European Economic Area countries to describe the existing surveillance activities for *Mycoplasma pneumoniae* infections, recent findings and existence of clinical guidelines for the treatment of *M. pneumoniae* infection. Of the 20 countries that participated in the survey, seven reported increases in *M. pneumoniae* infections observed during the autumn and winter of 2011.

In the first week of January 2012, the Norwegian Medicines Agency reported a likely shortage of erythromycin in the country following an unusually high number of mycoplasma infections [1]. Additional epidemic intelligence activities conducted at the European Centre for Disease Prevention and Control (ECDC) highlighted that similar increases in *M. pneumoniae* infections had been observed during the autumn of 2011 in various northern European countries, including Sweden, Denmark, Finland and the Netherlands [2-6].

With this epidemiological background and because *M. pneumoniae* infection is not notifiable at the European Union (EU) level, ECDC, in collaboration with EU and European Economic Area (EEA) Member States, conducted a brief survey among countries in order to verify whether unusual increases in reporting rates were recently observed, to describe existing *M. pneumoniae* surveillance activities and availability of guidelines for the treatment atypical pneumoniae which might include *M. pneumoniae* infections for clinicians in the country.

An email-based questionnaire was sent to EU/EEA Member States contact points (listed as Competent Bodies for Threat Detection) on 10 January 2012. Countries were asked to provide answers by the evening of 12 January 2012.

The questions asked in the email questionnaire are shown in the Box.

Disease background information

Mycoplasma pneumoniae, a bacterium lacking a cell wall, is a major cause of respiratory disease in humans. Infection can lead to prolonged carriage and therefore serve as a reservoir for the spread of the pathogen to others [7]. It is transmitted from person-to-person by respiratory droplets and its incubation period varies from one to three weeks, although it can be as short as four days [8]. *M. pneumoniae* infections tend to be endemic, punctuated by epidemics at four-to-seven-year intervals [9,10]. Climate, seasonality and geographical location are not thought to be of major importance, although in North America most epidemics usually begin during summer, peak in late autumn/

Box

Email questionnaire regarding *Mycoplasma pneumoniae* infection sent to EU/EEA countries, January 2012

1. Do you have MP surveillance ongoing in any form in your country?
2. If yes, please describe briefly which sources of information (including diagnostic tests, hospital-based/laboratory based, sentinel hospitals or standardised etc) are used by the ongoing surveillance in your country and whether there have been any major changes in the system in 2010 and 2011.
3. If you do have some form of MP surveillance, could you indicate whether you have seen any significant increases (or decreases) this autumn and winter or in previous years
4. Do you have existing national guidance for clinicians on the treatment atypical pneumonia, including infections with MP?
5. Do you have existing national guidance for handling outbreaks of atypical pneumonia, including with MP in institutional settings?

EEA: European Economic Area; EU: European Union; MP: *Mycoplasma pneumoniae*.

early winter and fade out during winter [8,11]. However, this pattern seems to differ between continents [8,11].

M. pneumoniae infects the upper and lower respiratory tracts in children and adults and is one of the aetiological agents of community-acquired pneumonia [11,12]. Studies have shown that it can cause up to 40% of community-acquired pneumonia and 18% of hospitalisations in children [13]. Most *M. pneumoniae* infections lead to overt clinical disease and although these infections are often self-limiting, 1–5% of cases may require hospitalisation. The most prominent symptoms are malaise, fever, headache and cough and in children aged less than five years, coryza and wheezing [13]. *M. pneumoniae* infection can also result in extrapulmonary manifestations, which can be present before, after or even in the absence of respiratory symptoms and have been reported with varying rates. Extrapulmonary manifestations of infection are rare, but when they occur can affect the central nervous system (including encephalitis and cranial nerve palsies) [11,14] and can also result in dermatological, haematological and cardiac manifestations [13].

Diagnostic testing for *M. pneumoniae* includes, among others, polymerase chain reaction (PCR) and serological assays, each with varying sensitivities and specificities and limited standardisation between testing protocols [15,16]. PCR is the preferred method in some countries [17]; however, no testing method has proven reliable in the context of an outbreak [14]. Surveillance data for *M. pneumoniae* infections are likely to be underestimates because of the challenges in diagnosis as well as the fact that in many cases, the infection is often subclinical and usually dealt with in outpatient settings.

National and international guidelines are available for the management of community-acquired pneumonia, including for those caused by *M. pneumoniae*. Therapeutic decision-making is up to the clinical judgement of the treating physician based on clinical presentation, co-morbidities, risk factors, assessment of pneumonia severity and the available evidence-based guidelines. Effective antibacterial agents for the treatment of *M. pneumoniae* include macrolides, tetracyclines and fluoroquinolones. Prudent use of antibiotics is urged for all cases of *M. pneumoniae* infection because of worldwide reports of macrolide resistance. Moreover, it is suggested that treating clinicians be vigilant when prescribing macrolides for suspected or confirmed cases, particularly in areas with high rates of macrolide resistance, as treatment might fail in patients infected with macrolide-resistant isolates.

Recent studies on previous outbreaks in both community and institutional settings have been published from Denmark [9], England and Wales [18], Finland [19], France [20], Italy [21], the Netherlands [7] and Scotland [22].

Survey findings

Of the 30 countries contacted, 20 replied to the questionnaire (response rate: 67%). Of those that replied, 13 reported having some type of surveillance activities providing data to monitor *M. pneumoniae* infections. Table 1 summarises the situation in 2011 and in previous seasons as well as surveillance activities. Seven countries had no available data that could be used to indicate changes in reporting rates for *M. pneumoniae* infections during 2011 compared with previous seasons. Of the 13 countries monitoring *M. pneumoniae*, seven indicated observing an increase compared with 2010 while six indicated no such increase (Belgium, Malta, Portugal, Slovakia, Slovenia and Spain). Of these six, Slovenia reported that reporting rates for *M. pneumoniae* infections were higher in the autumn of 2010 compared with the same period in 2011.

None of the responding countries reported major recent changes in the existing surveillance systems that would account for the observed increases. However, Sweden did highlight that awareness of *M. pneumoniae* among clinicians may be higher during this winter season, which may have resulted in more testing. Also, the widespread use of PCR for testing might have had an impact on current surveillance data.

With respect to which methods were used for laboratory diagnosis of *M. pneumoniae*, ten countries were able to provide some information. Five of these countries (the Netherlands, Norway, Spain, Sweden and the United Kingdom) reported using a mixture of serology and PCR. The Czech Republic and Portugal used mainly serological tests. Denmark and Slovenia reported data for samples confirmed by PCR and Finland reported using serology, PCR or culture for the diagnosis of *M. pneumoniae*.

A total of 15 countries reported some form of guidance available for clinicians for the treatment of atypical pneumonia, including *M. pneumoniae* infection; 10 countries have guidelines that are considered national (Table 2). Six reported the existence of guidelines that can be used in institutional outbreaks. Even though none are specific for *M. pneumoniae* infection, these guidelines would be applied in the occurrence of an outbreak of *M. pneumoniae* infection in institutional settings.

Limitations of the study

This survey was conducted as a part of epidemic intelligence activities conducted at the EU level. The questions included were not comprehensive enough to provide a complete and detailed overview of the functioning of the surveillance systems for *M. pneumoniae* infection in all countries. Details of diagnostic tests used, indicators for surveillance, frequency of surveillance, implicated stakeholders, etc. are therefore missing from this report. Furthermore, as clinical data and type of diagnostic test used for the diagnosis of each case were also not provided in the responses to

the survey, we have not been able to provide a direct comparison of such data between countries in this report. Additionally, given the short deadline, it may have been difficult for several countries to collect the relevant information in time.

Conclusion

As expected, surveillance for *M. pneumoniae* infections across responding EU/EEA countries is highly variable in terms of data collected and methods of laboratory detection of cases. For this reason, comparisons of surveillance data from different countries have limitations. However, information from predominantly northern European countries (Denmark, Finland, the Netherlands, Norway, Sweden, United Kingdom) and the Czech Republic does suggest that the autumn of 2011 had an increase of *M. pneumoniae* infections reported through the existing surveillance systems. Data from Denmark as presented earlier and in this issue [9,23] and Sweden [24] suggests that the epidemic wave started in 2010. With the results from our study, however, we cannot assess whether the reported increases fit into the expected four- to-seven-year epidemic waves even though this seems to be indicated by data from Finland, Norway and Denmark in this issue [23,25,26].

Available data seem to suggest that Member States from southern Europe are not yet facing an increase as important as that reported in the northern countries. Increasing awareness among healthcare providers in countries not yet heavily affected could strengthen surveillance activities and ensure timely diagnosis and appropriate treatment of the disease in affected patients. It would be interesting to analyse whether in the countries where increases in *M. pneumoniae* infection rates were reported, similar increases or concurrent decreases in reporting rates for other respiratory pathogens took place during the same time period. However, this was beyond the scope of this assessment.

For the responding countries for which information was available, it is clear that all treating clinicians

Table 1

Availability of surveillance data for *Mycoplasma pneumoniae* infection and comparison with 2010, EU/EEA countries, January 2012

Country	Data available on *M. pneumoniae* infections	Increase compared with 2010	Comments
Czech Republic	Yes	Yes	Numbers stable but percentage of positive samples 35% in 2011 compared with 21% during the same period in 2010.
Denmark	Yes	Yes	Almost twice as many samples were investigated in 2011 compared with 2010, but the proportion of *M. pneumoniae*-positive samples remained the same. An epidemic was also seen in 2010 [9].
Finland	Yes	Yes	Increase in *M. pneumoniae* infections reported since October 2010.
The Netherlands	Yes	Yes	Important increase in *M. pneumoniae* infection reports in autumn 2011, similar to previous epidemics in 2002 and 2005.
Norway	Yes	Yes	Increase in *M. pneumoniae*-positive samples since September 2011. Last epidemic reported in 2005/06 season.
Portugal	Yes	No	Retrospective data of discharged hospitalised cases, although underestimates, suggests a mean of 100 cases of *M. pneumoniae* infection per year based on laboratory results (serology), with no changes in the last 10 years.
Sweden	Yes	Yes	All time high in *M. pneumoniae* infection reports during autumn 2011.
United Kingdom[a]	Yes	Yes	Increase in *M. pneumoniae* infection reports since end of 2011, in line with reports during previous seasons.
Belgium	Yes	No	No observed increase.
Malta	Yes	No	No observed increase.
Slovakia	Yes	No	No observed increase.
Slovenia	Yes	No	Decrease compared with 2010.
Spain	Yes	No	No observed increase.
Cyprus	No	–	–
France	No	–	–
Greece	No	–	–
Hungary	No	–	–
Ireland	No	–	–
Poland	No	–	–
Romania	No	–	–

EEA: European Economic Area; EU: European Union.
a England, Wales and Scotland.

Table 2

Existence and details of clinical guidelines available in EU/EEA countries for treatment of *Mycoplasma pneumoniae* infection, January 2012

Country	Guidelines available	Details on available guidelines
Belgium	Yes	**Case treatment:** recommendations on treatment of lower respiratory infections from the Belgian Antibiotic Policy Coordination Committee (BAPCOC) [http://www.bapcoc.be/].
Czech Republic	Yes	**Case treatment:** (i) standards for the usage of antibiotics [http://www.cls.cz/dalsi-odborne-projekty]; (ii) specific guidelines for diagnostics and treatment of pneumonia in adults [http://www.pneumologie.cz].
Denmark	Yes	**Case treatment:** hospital-specific guidelines in addition to guidelines from Statens Serum Institut [http://www.ssi.dk].
Finland	Yes	**Case treatment:** national guidance for treatment of pneumonia, including *M. pneumoniae* infection and other atypical pneumonia.
France	Yes	**Case treatment:** recommendations on treatment of lower respiratory infections from the French Agency for the Safety of Health Products (Afssaps) [http://www.afssaps.fr/content/download/26334/348020/version/7/file/map-infections-respiratoires-basses-adultes.pdf]. **Institutional settings:** national recommendations for treatment of lower respiratory infections in homes for the elderly by the Ministry of Health [http://www.sante.gouv.fr].
Greece	Yes	**Case treatment:** national treatment guidelines exist on the management of community-acquired pneumonia, which include atypical pneumonia and infections with *M. pneumoniae* by the Hellenic Centre for Disease Control and Prevention (KEELPNO) and the Hellenic Society of Infectious Diseases [http://www.keelpno.gr]. **Institutional settings:** KEELPNO has guidance for handling airborne infections in institutional settings [http://www.keelpno.gr].
Hungary	Yes	**Case treatment:** national guidance exists, but does not address the newer diagnostic methods (e.g. PCR).
Ireland	Yes	**Case treatment:** Hospitals used their own guidelines for treatment of community-acquired pneumonia based on the latest guidelines from the British Thoracic Society, European Respiratory Society and the Infectious Disease Society of America. In children, the Paediatric Infectious Disease Society guidelines for community-acquired pneumonia in children are usually followed.
Malta	Yes	**Case treatment:** national guidelines have recently been published.
The Netherlands	Yes	**Case treatment:** (i) National Institute for Public Health and the Environment (RIVM): guideline specific for *M. pneumoniae* infection; (ii) Dutch College of General Practitioners: guideline for standard 'acute cough'. This includes case treatment of community-acquired pneumonia by general practitioners; (iii) Dutch Working Party on Antibiotic Policy (SWAB): guideline on the management of community-acquired pneumonia in adults [http://www.swab.nl/swab/cms3.nsf/uploads/6929745C8C9BE541C125794900720B77/$FILE/CAP_SWAB_Nov14-def.pdf]. **Institutional settings:** guidelines for infectious respiratory disease outbreak management, but not specific for M. pneumoniae.infection.
Norway	Yes	**Case treatment:** National guidelines on which antibiotics to use.
Portugal	Yes	**Case treatment:** recommendations of the National Society of Pneumologists for treatment of community-acquired pneumonia in hospitalised patients and outpatients covers infection with atypical microorganisms in all types of patients [http://www.sppneumologia.pt]
Romania	Yes	**Case treatment:** each infectious diseases clinic receives guidelines prepared by specialists from the Regional Academic Centre.
Slovakia	Yes	**Case treatment:** guidance on the management of *M. pneumoniae* infection is included in guidance of management atypical pneumonia, which has been prepared by a working group of experts from the Slovakian Pneumological Society.
Slovenia	Yes	**Case treatment:** national treatment guidelines exist [http://www.szd.si/user_files/vsebina/Zdravniski_Vestnik/2010/marec/245-64.pdf].
Spain	Yes	**Case treatment:** several national guidance documents for clinicians on treatment the atypical pneumonia prepared by scientific societies such as the Spanish Society of Infectious Diseases and Clinical Microbiology and Spanish Association of Paediatric Primary Care. **Institutional settings:** infection control guidance for institutional care settings and nosocomial outbreaks, including respiratory tract infections.
Sweden	Yes	**Case treatment:** STRAMA (Swedish strategic programme against antibiotic resistance) guidance on how to treat pneumonia in outpatient care.
United Kingdom	Yes	**Case treatment:** guidance on the management of community-acquired pneumonia by the British Thoracic Society, which includes consideration and treatment of, *M. pneumoniae* infection [http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Pneumonia/Guidelines/CAPGuideline-full.pdf]. **Institutional settings:** the Health Protection agency has guidance on the management of outbreaks of acute respiratory infection in institutional settings.
Cyprus	Data not available	–
Poland	Data not available	–

have access to guidance on how to treat *M. pneumoniae* infections even though it is a reality that the majority of these infections remain undetected and under-diagnosed.

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Increased incidence of *Mycoplasma pneumoniae* infection in Finland, 2010–2011

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The number of cases of *Mycoplasma pneumoniae* infection detected by laboratory-based surveillance increased in Finland in late 2010. During 2011, the number of cases was four times higher than during the previous epidemic in 2005. The 2011 epidemic affected mostly school-age children. The increased number of cases was probably not due to changes in laboratory procedures, but public interest may have had an effect, since the number of Google queries followed closely the epidemic curve.

The number of cases of *Mycoplasma pneumoniae* infection in Finland started to increase in October 2010 (222 cases; 4.1 per 100,000 population) and rose further during 2011 (in October, 1,242 cases; 23.1 cases per 100,000 population). Denmark, England and Wales also saw an increased incidence of *M. pneumoniae* infections in late 2010 [1,2]. Throughout 2011, the epidemic of *M. pneumoniae* infection in Finland attracted considerable public interest and media attention.

In order to assess the extent of this ongoing epidemic, we analysed the data on *M. pneumoniae* infection from laboratory-based surveillance. We also evaluated whether changes in laboratory methods and practices as well as public interest in the epidemic during 2011 were related to the size of the epidemic.

Background

M. pneumoniae causes mainly infection of the upper respiratory tract (tracheitis, bronchitis) and, in 3–10% of cases, pneumonia. Rare neurological symptoms such as meningitis and Guillain–Barré syndrome can be observed [3]. The bacterium is spread by respiratory droplets and direct contact with an infected person. The disease occurs in all age groups but is most common among children aged 7–16 years and young adults aged 17–25 years. Presumably due to lack of lifelong protective immunity and changes in circulating *M. pneumoniae* strains, epidemics typically occur in 3–5-year intervals [3], with seasonal peaks in autumn and winter.

National laboratory-based surveillance system

The laboratory-based surveillance system in Finland (population 5.4 million) covers 20 healthcare districts with catchment populations ranging from 68,000 to 1.4 million. Since 1995, all clinical microbiology laboratories mandatorily notify all positive findings of *M. pneumoniae* (culture, diagnostic rise in *M. pneumoniae*-specific IgG antibody titre, detection of *M. pneumoniae*-specific IgM antibodies and nucleic acid detection) to the National Infectious Disease Register, maintained by the National Institute for Health and Welfare. The following information is collected with each notification: date of birth, sex, unique national identity code, place of treatment, type of specimen and diagnostic method. Multiple notifications with the same national identity code are merged into one case, if reported within 12 months of each other. In this study, we analysed cases of *M. pneumoniae* infection notified to the National Infectious Disease Register from 1 January 1995 to 31 December 2011.

Study approach

To investigate whether there have been changes in laboratory methods or practices regarding *M. pneumoniae* diagnosis, we carried out an email survey of the five biggest laboratories in the country, located in Helsinki, Turku, Tampere and Kuopio, which notified 97.5% of all *M. pneumoniae* cases during 2010 and 2011. We asked about the total number of tests performed per month and the proportion of tests positive for *M. pneumoniae* per month in 2010 and 2011. In addition, we asked the laboratories which tests they used and whether there

had been changes in tests since the previous epidemic in 2005.

To investigate the extent of public interest in *M. pneumoniae*, we used Google Insight for Search beta and Google AdWords applications. We obtained the number of Google queries for 'mycoplasma' in Finland, during 2004 to 2011 by month.

Surveillance data

The number of cases of *M. pneumoniae* infection began to increase since October 2010 (Figure 1). The first peak was in March 2011 (n=838). The number of cases dropped between April and July 2011 and then started to increase again in September 2011 (n=667). The number of cases rose from 1,948 (36.2 per 100,000 population) in 2010 to 7,772 (145 per 100,000 population) in 2011. In 2011, the increase in the number of *M. pneumoniae* cases was detected in all healthcare districts but the incidence varied regionally (range by healthcare district: 55 per 100,000 population to 257 per 100,000 population).

During 1995 to 2011, a total of 22,835 cases were notified. Previous epidemics occurred in the winters of 2000–2002 and 2004–2006 with a peak in 2005 (1,881 cases; 36 per 100,000 population). These earlier epidemics lasted about two years, i.e. over two cold seasons.

The annual incidence during 1995 to 2011 was highest among children aged 5–14 years and lowest among elderly persons aged 65 years and older (Figure 2).

In 2011, the median age of the cases was 18 years (range: 0 –85) and 4,418 (57%) were female. During 2005 to 2011, the median age of the cases was also 18 years (range: 0–104) and 13,185 (58%) were female. The difference by sex was most prominent in persons aged 15–64 years, among whom the incidence was 1.8-fold higher in females than in males both during 1995 to 2010 and in 2011.

Most of the notifications were based on testing of serum or plasma (22,486; 98.5%), a few were from bronchoalveolar lavage (63; 0.3%), pharyngeal or nasopharyngeal swabs (94; 0.4%) or cerebrospinal fluid (35; 0.2%). In 98% of the notifications, the diagnostic method was detection of *M. pneumoniae*-specific antibodies; the rest were based on nucleic acid detection by PCR.

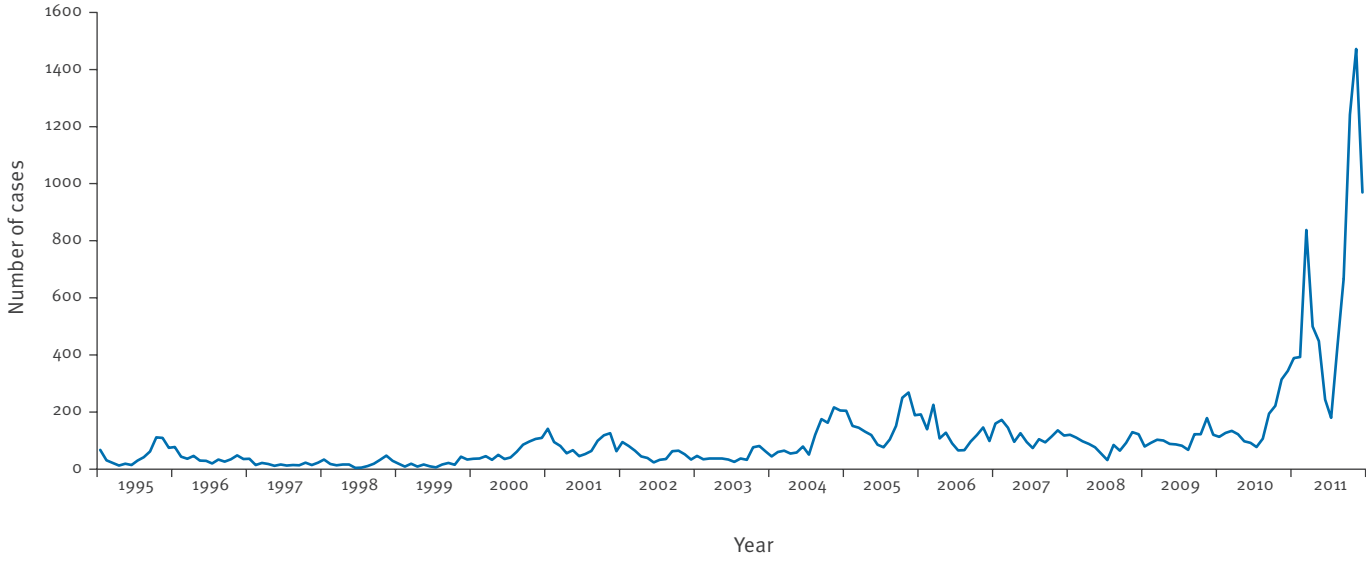
Laboratory survey

In the five laboratories taking part in the survey, detection of *M. pneumoniae* was mainly based on serological tests by enzyme immune assay (EIA). Diagnosis of infection required a diagnostic rise in *M. pneumoniae*-specific IgG antibody titre and/or detection of a *M. pneumoniae*-specific IgM. If necessary, the laboratory recommended collecting convalescent paired sera. Since the previous epidemic in 2005, there has been no change in diagnostic methods.

The number of serological tests performed for *M. pneumoniae* in the five laboratories was on average nearly four times higher in 2011 than in 2010 (range of increase by laboratory: 200–500%). The proportion of tests positive for *M. pneumoniae* during 2010 and 2011 varied between 8% and 17% in the five laboratories. There was also variation during 2010 and 2011 in four of the laboratories: in three the proportion of positive tests increased (from 8% to 9%, from 9% to 11%, from

Figure 1

Cases of *Mycoplasma pneumoniae* infection by month reported to the National Infectious Diseases Register, Finland, 1995–2011



Source: National Infectious Diseases Register, Finland.

11% to 17%); in one it decreased slightly (from 8.5% to 8.1%) and in one, it remained the same.

Public interest, assessed through Google queries

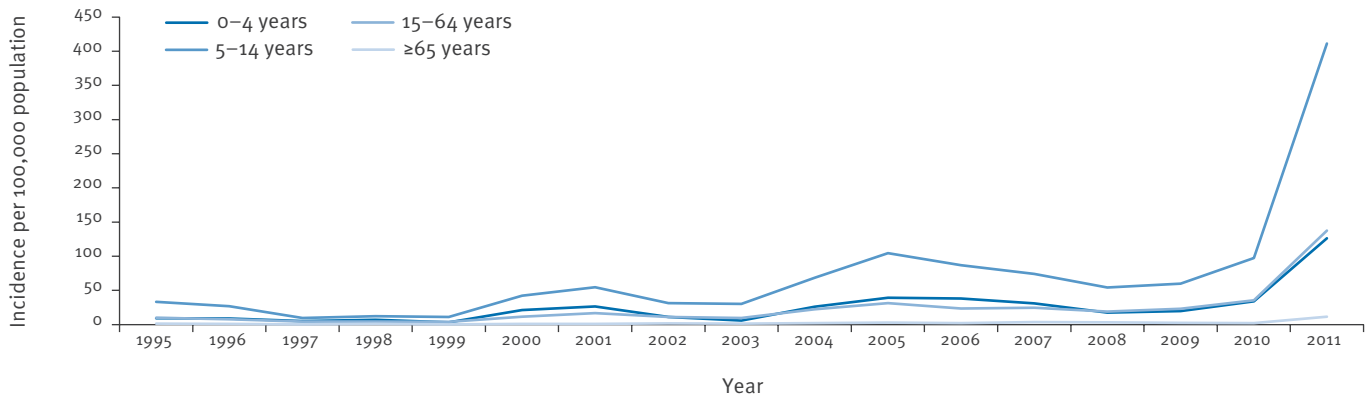
The first two peaks in the number of Google queries for 'mycoplasma' occurred during the epidemics in 2004–2005 and 2005–2006. After 2007, the number was stable. In October 2010, however, it rose again, peaking in March and November 2011 (Figure 3). As described in [4], the numbers of Google queries in Figure 3 reflect the number of searches per month for 'mycoplasma' relative to the total number of searches on Google between 2004 and 2011 in Finland. The data are normalised (data are divided by a common variable to cancel out the variable's effect on the data) and presented on a scale from 0 to 100. On the basis of data from Google AdWords, the approximate 12-month mean number of Google queries for 'mycoplasma' in Finland amounted to 7.3% of global searching for this term in 2011. Data on global and local searches in the previous years were not available.

Discussion

Our study based on nationwide laboratory data showed a fourfold increase in incidence and number of cases of *M. pneumoniae* infection in 2011 compared with the previous epidemic in 2005 – the highest in the history of our national surveillance. In Denmark, England and Wales, the previous epidemics were larger than their current ones (at the start of the current epidemics) [1,2]. There were no major changes in laboratory

Figure 2

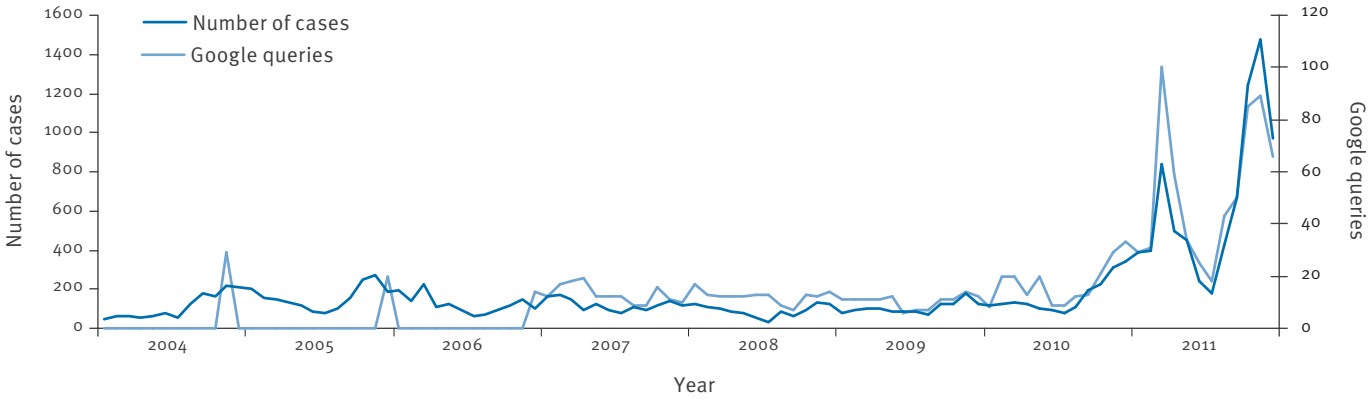
Annual incidence of *Mycoplasma pneumoniae* infection per 100,000 population by age group reported to the National Infectious Diseases Register, Finland, 1995–2011



Source: National Infectious Diseases Register, Finland.

Figure 3

Cases of *Mycoplasma pneumoniae* by month reported to the National Infectious Diseases Register and 'mycoplasma' queries in Google, Finland, 2004–2011



The Google queries shown in the graph do not represent absolute search volume numbers, because the data are normalised and scaled from 0 to 100. Normalisation means that data sets are divided by an unrelated, common Web search query. Data are scaled using the average search volume over the selected time period as a denominator.

Source: National Infectious Diseases Register, Google Insights for Search (Google data downloaded 21 December 2011).

diagnostics that could have contributed to the extent of the epidemic in Finland. However, data on the number of tests carried out from 2005 to 2006 were not available. As the number of tests performed may influence the rate of positive results, comparison of the heights of the epidemic peaks should therefore be made with caution.

Google is known to be a popular information source [5]. In Finland, Internet access is widespread: about 89% of the population aged 16–74 years used the Internet in the past three months [6]. On the basis of our results, we can assume that the high number of cases of *M. pneumoniae* infection – especially during the current epidemic – may partly reflect the intense public interest in and awareness of the disease. Patients with a prolonged cough may have been more active than in the past in seeking care and requesting testing for *Mycoplasma*, which may, in some instances, have lead to unnecessary antimicrobial treatment as prolonged cough after the acute phase of infection may not benefit from such treatment.

Diagnostic testing for *M. pneumoniae* also rose around fourfold in 2011, compared with 2010. The variation in proportion of tests positive for *M. pneumoniae* between laboratories (8–17%) could be related to differences in interpreting the serological results. This finding needs further evaluation, but highlights the importance of standardisation of laboratory methodology. It may also be a sign of regional differences in diagnostic activity and case ascertainment, since the sampling was not structured for epidemiological surveillance. Laboratory diagnosis of *M. pneumoniae* infection is not easy. High levels of *M. pneumoniae*-specifc IgM antibodies can persist for several weeks to up to one year after an acute infection [3,7,8]. Furthermore, *M. pneumoniae*-specifc IgG antibodies may remain elevated up to four years after illness [9]. In addition, it may be difficult for clinical microbiologists to interpret borderline results, since the date of symptom onset is rarely available in the laboratories.

Our survey found that PCR was not widely used in Finland for diagnosis of *M. pneumoniae* infection. PCR has been found to be superior to serology for the diagnosis of acute *M. pneumoniae* infection and has been shown to be highly sensitive, specific and rapid [10]. However, a positive PCR may be a sign of transient asymptomatic carriage of *M. pneumoniae* or the persistence of the pathogen after infection [9]. In Denmark, where PCR-based surveillance for *M. pneumoniae* infections is established, the proportion of tests positive for *M. pneumoniae* was approximately 3% since 2007 until it rose to 15% in September 2010 when the current epidemic started [1].

We also found that culturing of *M. pneumoniae* was also scarce in Finland. It is known to be difficult, time-consuming and expensive, and therefore rarely routinely used in clinical practice [11]. Thus, information on the molecular epidemiology of circulating *M. pneumoniae* strains is lacking, and it is also not known whether the current epidemic strains are sensitive or resistant to macrolides, the antimicrobials commonly used in treatment [3].

Since our study was based on laboratory data only, we did not have information on clinical manifestation, severity of the disease or treatment. The burden of the *M. pneumoniae* epidemic in Finland remains unknown. Although people with *M. pneumoniae* infections are mainly seen as outpatients, a register-based linkage study between laboratory-confirmed cases and hospitalisation data or a time series of pneumonia-associated hospitalisation rates could give an insight into the burden and use of macrolides could be analysed.

Physicians and the public have been informed about the symptoms and treatment of *Mycoplasma* infections, as well as the difficulties in diagnosis.

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Increased incidence of *Mycoplasma pneumoniae* infection in Norway 2011

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Epidemics of *Mycoplasma pneumoniae* have recently been reported from England and Wales and from Denmark. A similar increase in *M. pneumoniae* infections was noted in Norway late autumn 2011.The epidemic has resulted in shortage of erythromycin and the use of alternative antibiotics has been recommended.

Background

Following reports of epidemics of *Mycoplasma pneumoniae* in Denmark and England and Wales [1,2], special attention has been paid by the Norwegian Institute of Public Health to detect any similar increase in Norway. Surveillance of *M. pneumoniae* infections in Norway is solely based on a voluntary laboratory-based reporting system, and the disease is not notifiable in the Norwegian Surveillance System for communicable diseases.

Surveillance of *M. pneumoniae* infections in Norway

A voluntary laboratory-based reporting system where a selection of laboratories report to the Norwegian Institute of Public Health the number of patients testing positive for all laboratory-confirmed virus diagnoses as well as for *M. pneumoniae* each month has been in place since 1975. The number of participating laboratories has varied over the years, but there have not been any major changes in the system during the last decades. At present, 16 of 21 diagnostic microbiological laboratories in Norway participate in this surveillance system. This covers more than 80% of the Norwegian population. A total of 12 laboratories, representing all regions of the country, submit data on the number of patients testing positive by serological or molecular tests for *M. pneumoniae*. There is no common case definition for reporting a positive result, and a positive serology may include a single high titre or a rise in *M. pneumoniae*-specific IgG antibody levels. Results obtained are indicative of the *M. pneumoniae* activity in Norway as a whole. Data on the total number of tests performed or age groups among patients with positive test results is not collected in this surveillance system. Monthly reports, available at Department of Virology, Norwegian Institute of Public Health, are submitted to all the participating laboratories, and to others who may be interested.

Since a consensus meeting of clinical microbiologists in Norway in 2003 [3], polymerase chain reaction (PCR) tests have been recommended as the most specific method of choice for laboratory diagnosis of suspected *M. pneumoniae* infection of less than four weeks duration [3]. Serology may add value to the diagnosis of long-standing infection, either by the detection of increasing antibody levels in paired serum samples, or by high antibody levels in samples drawn at least two weeks after onset of symptoms. Concurrently, the proportion of reported cases identified by PCR increased, while the proportion reported by serology decreased.

The yearly number of *M. pneumoniae*-positive tests reported to the Norwegian Institute of Public Health for the period January 1984 to December 2011 is shown in Figure 1. This figure demonstrates regular recurrent epidemics of *M. pneumoniae* in Norway, occurring with five- to seven-year intervals (2011/12, 2006, 2000, 1993 and possibly also in 1987). During the period from 2007 until August 2011 the number of reported cases remained low. From September 2011 a sharp increase in tests positive for *M. pneumoniae* was observed. PCR and serology were both used in equal measures as diagnostic methods until the epidemic was identified. Hereafter most cases were diagnosed by PCR (Figure 2).

Public health response

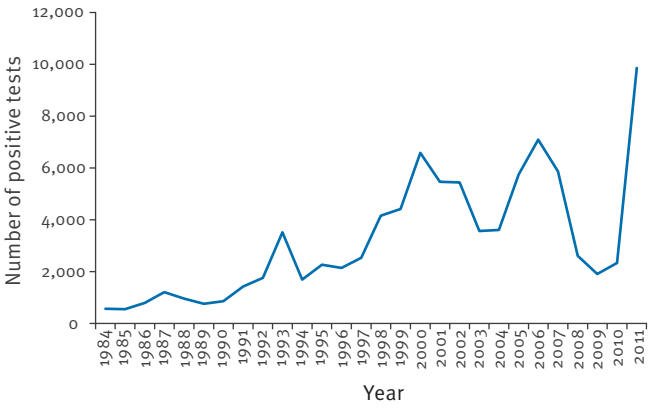
Following the observed increase of reported positive tests for *M. pneumoniae*, respective information was published on the website of the Norwegian Institute of Public Health on 25 October 2011 [4]. This website is the main communication platform to clinicians as well as to the media and the public with regards to activity of various infectious diseases in Norway. In addition, a message was posted on a closed communication platform among laboratories in Norway, This communication platform was also used to obtain detailed

descriptions of weekly numbers and proportions of *M. pneumoniae* cases from laboratories in all regions of the country in an ad hoc manner, adding to the surveillance by monthly reporting as described above.

Although most general practitioners and other clinicians are familiar with *M. pneumoniae* infections, these are not considered a well known disease among the general public. Little attention had been given to the last epidemic in 2006. In a new webposting on 7 December 2011 it was emphasised that not all suspected or confirmed cases of *M. pneumoniae* infection need antibiotic treatment [5], and if such treatment was indicated clinicians should chose antibiotics according to recommendations given in the national guidelines on the use of antibiotics in primary health care [6]. In these guidelines, erythromycin and doxycyclin are recommended as the drug of choice in the treatment of upper or lower respiratory infections caused by *M. pneumoniae*. Azithromycin is not recommended for the treatment of respiratory tract infections in Norway due risk of resistance development.

Figure 1

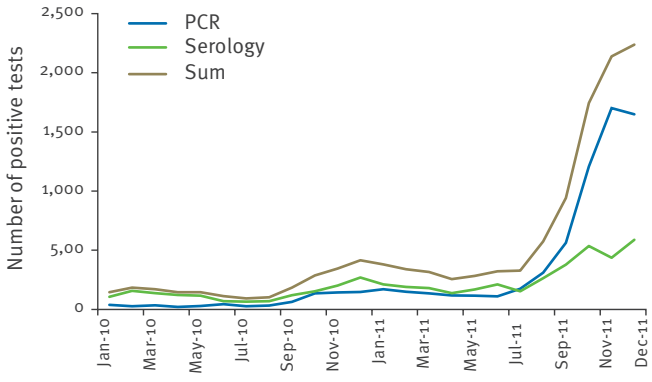
Number of laboratory-reported *Mycoplasma pneumoniae* infections by year, Norway January 1984 – December 2011



Source: Norwegian Institute of Public Health

Figure 2

Laboratory reports of *Mycoplasma pneumoniae* infection by diagnostic methods, Norway January 2010 – December 2011



PCR: Polymerase chain reaction

Source: Norwegian Institute of Public Health

Prescription of antibiotics

In the two months following publication, a two-fold increase in prescription of erythromycin was seen in Norway compared with the previous months and the same months in 2010. Monthly sales of erythromycin in the period from January 2010 to December 2011 are shown in Figure 3. The reason behind this increase is thought to be extensive treatment with erythromycin in respiratory tract infections suspected to be caused by *M. pneumoniae*. Awareness of the current mycoplasma epidemic might have influenced testing activity for pathogens causing respiratory tract infections, leading to an increase of positive tests.

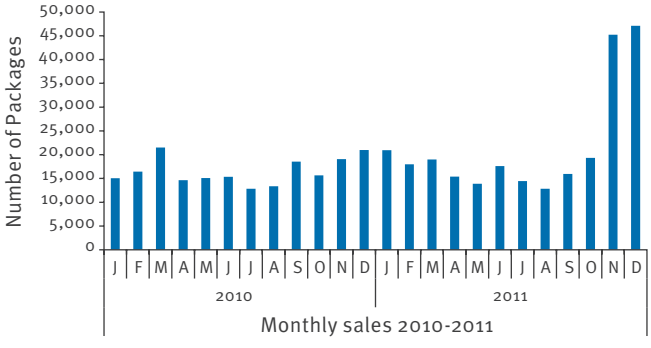
On 4 January 2012 the Norwegian Medicines Agency reported a shortage of erythromycin in the country expected to last until March–April 2012 [7]. Clarithromycin has been recommended as an alternative to erythromycin in the treatment of respiratory tract infections.

Discussion and conclusion

An epidemic of *M. pneumoniae* has been identified in Norway since September 2011 through voluntary laboratory-based surveillance reporting. The increase in erythromycin prescriptions seen since November 2011 is probably related to extensive and in many cases unnecessary antibiotic treatment of suspected or confirmed cases of *M. pneumoniae* infections. Awareness of the epidemic might have impacted both the laboratory testing rate and the prescription of antibiotics. The regularity in temporal timing of *M. pneumoniae* outbreaks may be used to foresee new epidemics in Norway. Unfortunately, the present reporting system of *M. pneumoniae* infections in Norway is not able to provide data on the overall testing activity for *M. pneumoniae* or other respiratory infections. A better

Figure 3

Monthly sales of erythromycin packages in Norway January 2010 – December 2011.



Source: Norwegian Medicines Agency

laboratory-based surveillance system for identifying increase in seasonal and recurrent non-notifiable diseases infections is under consideration.

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Department of Microbiology, Oslo University Hospital, Ullevål, Oslo; Department of Microbiology, Østfold Hospital, Fredrikstad; Department of Microbiology, Akershus University Hospital, Lørenskog; Department of Microbiology, Vestre Viken Hospital, Drammen; Department of Microbiology, Vestfold Hospital, Tønsberg ; Unilabs Telelab, Skien; Department of Microbiology, Sørlandet Hospital, Kristiansand; Department of Microbiology, Stavanger University Hospital, Stavanger; Department of Microbiology, Haukeland University Hospital, Bergen; Department of Microbiology, Molde Hospital, Molde; Department of Microbiology, St. Olav University Hospital, Trondheim; Department of Microbiology, Nordland Hospital, Bodø; Department of Microbiology, Tromsø University Hospital, Tromsø.

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Epidemic of *Mycoplasma pneumoniae* infection in Denmark, 2010 and 2011

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Denmark experienced two waves of *Mycoplasma pneumoniae* infection during autumn and early winter in 2010 and 2011, respectively. Both affected the whole country. The proportion of positive results was almost the same for both, indicating that the two waves were probably of equal size. High macrolide consumption during the epidemics did not seem to affect levels of macrolide resistance in *M. pneumoniae*, which remain low in Demark (1% to 3%).

Epidemics of *Mycoplasma pneumoniae* infection are normally seen at intervals of four to seven years [1,2]. In some cases, simultaneous epidemics are seen in more than one country. In 2010, Denmark [1], England and Wales [2], Sweden [3] and Finland [4] reported more cases of *M. pneumoniae* infection than normal. In autumn 2011, reports from Norway [5], Sweden [3], the Netherlands [6] and Finland [4] indicated an epidemic of *M. pneumoniae* infection in the northern part of Europe. In Denmark, we have also seen a rise in the number of *M. pneumoniae* cases during autumn 2011.

The surveillance of *M. pneumoniae* in Denmark has been described previously [1].The system is based on laboratory data from Statens Serum Institut (SSI). SSI receives samples (almost an equal number of blood/serum samples for serology and respiratory samples for PCR) from hospitals and general practitioners for routine diagnosis. The diagnosis and surveillance of *M. pneumoniae* infection used to be based on serology in the past, but since the beginning of the 1990s, PCR has been introduced as a routine test at SSI for rapid and early diagnosis of *M. pneumoniae*. A rise in the rate of PCR positive samples at SSI from < 5 % to 15% or more is considered as indicative of an epidemic [1]. During the last decade, the diagnosis of *M. pneumoniae* has been moved from SSI to local hospital laboratories which have also progressively introduced PCR as a routine diagnostic test for *M. pneumoniae* over the past years. In the beginning of October 2010, SSI saw an increase in the proportion of positive samples above the threshold (>15%) [7] (Figure 1). This tendency was confirmed by data from hospital laboratories in Denmark and in November 2010 Denmark reported a nation-wide increase in the number and proportion of *M. pneumoniae* PCR positive samples [1]. According to SSI laboratory data, the epidemic peaked in mid-December 2010, while the number decreased rapidly during the rest of December and in January 2011. The number of cases seemed to return to a normal level during spring and early summer 2011 (Figure 1). An increase was observed again in late summer and early autumn 2011 [8]. This prompted SSI to contact a selection of local laboratories all over the country, with a request to submit laboratory data on a weekly basis for *M. pneumoniae* PCR for 2011, to monitor if the rise could be confirmed and if it was nation-wide. The laboratories were selected to cover and represent most of the country, the eastern part (The Capital and Zeeland) the mid-south (Funen) and the north-western part (Northern Jutland).

Macrolide resistance in *M. pneumoniae* is a growing problem especially in East Asia, but it is also seen in the United States and Europe [9]. During an epidemic of *M. pneumoniae*, the macrolide consumption is known to increase considerably [10,11]. In December 2010, Denmark saw the highest consumption in a single month (3.9 defined daily doses (DDD)/1,000 population) compared to the consumption in December during the previous nine years (2.5 DDD/1,000 population on average). According to provisional data, the consumption in November 2011 was the highest for the month of November (3.6 DDD/1,000 population) compared to the last 10 years (2.4 DDD/1,000 population on average for November months between 2001 and 2010) personal communication, Maja Laursen, the Danish Medicines Agency, January 2012.

Laboratory investigation

SSI is situated in the Capital Region of Denmark and receives samples predominantly from the Capital Region and the Region Zealand. To further investigate if the rise in the absolute number and in the proportion of positive tests was seen all over the country, the institute received and analysed weekly data from four hospital laboratories (North Denmark Region, Region of Southern Denmark and two laboratories from the Capital Region).

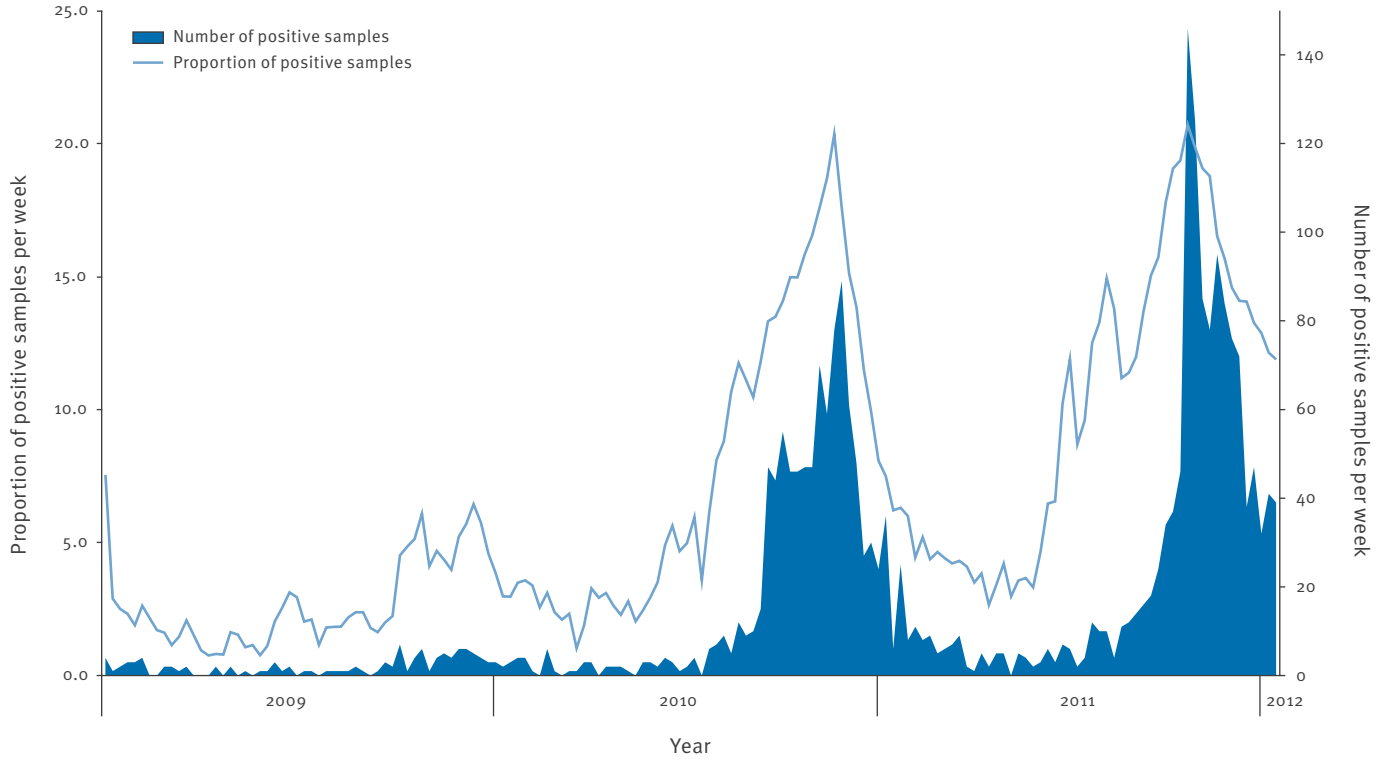
To compare the years 2009 (no epidemic) with the two epidemic years (2010 and 2011) SSI requested in January 2012 results for the period from 2009 to 2011. Data for the whole period were provided by two hospital laboratories (North and Capital 1) and by SSI. The South Denmark region laboratory provided data for 20 September 2010 (week 38) to 31 December 2011 (week 52) and Capital 2 laboratory provided data for 29 August 2011 (week 35) to 31 December 2011 (week 52). Capital 2 also provided data for the epidemic period in 2010 but only for eight weeks (25 October to 19 December 2010) and not on a weekly base but in an aggregated form (Table).The number of positive samples per week from each laboratory is presented in Figure 2. Both waves of the M. pneumonia epidemic were seen in the whole country almost simultaneously (Figure 2).

To compare the two epidemic periods, data for the same period (week 43 to week 50) for the two years from the five laboratories are presented in the table. The peak periods for both epidemic waves were within the selected eight weeks. Twice the number of positive samples (1.9 times) were detected in 2011 compared with 2010, but the number of samples investigated were also almost twice (1.8 times) as high in 2011 compared with 2010. The proportion of positive samples was in general equal during both waves (in average 15%–16.3%) but for North Denmark Region, the rate was higher in 2011 (17.3%) compared with 2010 (14.5%) despite the fact that more than a double number (2.6 times) of samples were tested (Table).

In 2010, the five laboratories diagnosed approximately 70% of all cases in Denmark; assuming that this also applies for 2011, it can be estimated that more than 4,600 cases were diagnosed in Denmark (the country's population counts 5.5 million inhabitants) during the eight-week period from 24 October to 18 December 2011. This corresponds to an incidence of approximately 10 new PCR diagnosed cases per 100,000 population per week in Denmark. In the North Denmark Region, one laboratory received all samples from the region for *M. pneumoniae* PCR. The population size of the region is 580,000 and 125 samples on average were positive per week (Table) giving an estimated incidence of more than 20 new cases per 100,000 population per week. In

Figure 1

Positive *Mycoplasma pneumoniae* PCR samples at Statens Serum Institut, Denmark, 1 January (week 1) 2009 to 29 January (week 4) 2012



The proportion of positive tests is the floating average of four weeks.

2010, the estimated incidence for this region was only eight per 100,000 population per week. The diagnostic activity for this region was almost 1 per 100 population during the eight-week period. The diagnostic activity for the whole country can be estimated from the figures in the table. If we consider the five laboratories representing 70% of the diagnostic activity, approximately five persons per 1,000 population were investigated during the eight weeks.

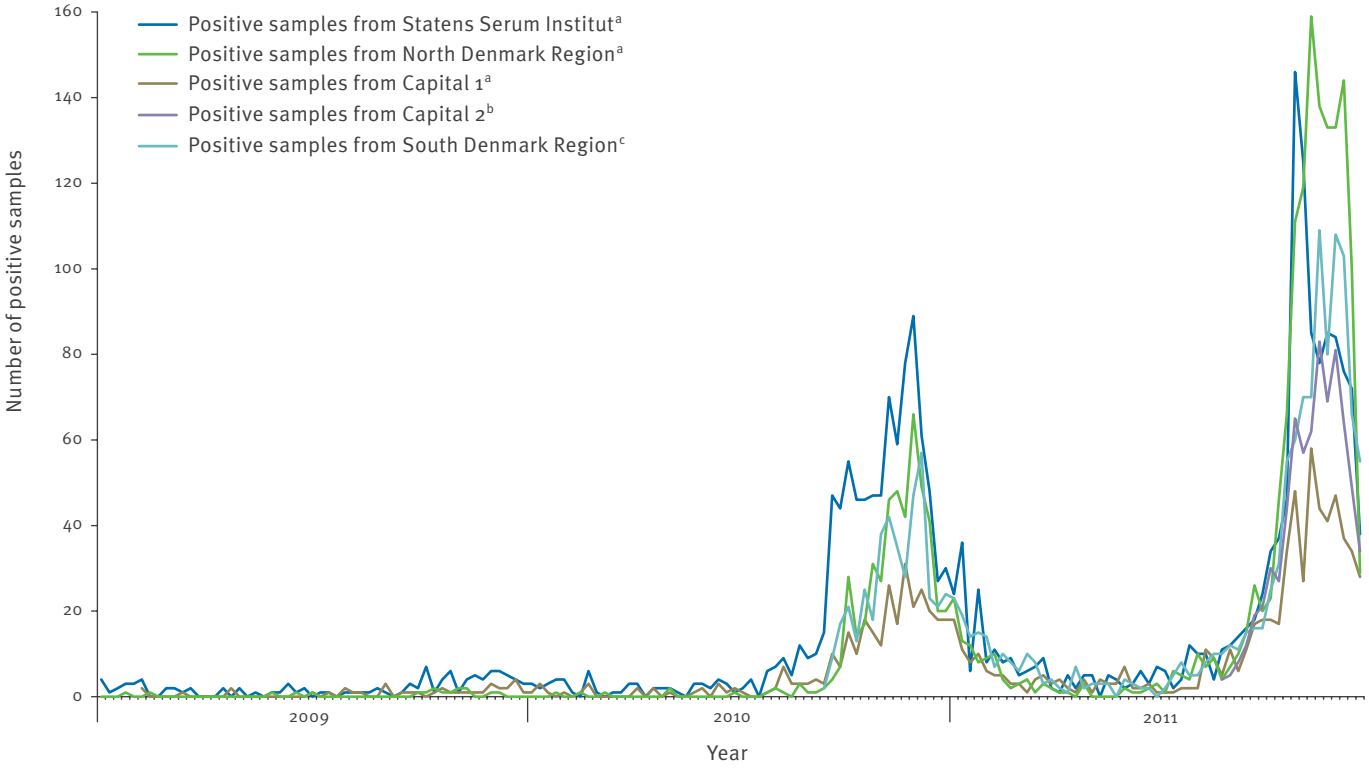
At SSI, we also investigated the prevalence of macrolide resistance for both 2010 and 2011. Macrolide resistance-associated mutations in the gene for the 23 sRNA were identified with a sequencing technique developed at SSI. The technique can be performed directly on DNA purified from PCR positive samples [12]. We did a survey on 140 PCR positive samples consecutively received at SSI during late September and early October 2010 (the beginning of the first wave) and on 108 PCR positive samples consecutively received in January 2011 (the end of the first wave). During the second wave in 2011 we investigated 117 PCR positive samples received in late October and in the beginning of November, representing the beginning of the 2011 wave. In the first wave we found two (1.4%) and three (2.9%) mutations, respectively, and in the second wave we only found one sample with a mutation (0.9%). Data for PCR positive samples from January 2012 (the end of the second wave) are currently unavailable.

Discussion and conclusions

In two successive years, Denmark experienced a high number of M. pneumonia infections during autumn and early winter. The situation can be characterised as one epidemic consisting of two waves. Epidemics spanning two autumn/winter seasons were also seen in Denmark in 1962 to 1964, in 1971 to 1973 and to some degree also in 2004 to 2006 [1]. The total number of PCR positive samples in 2011 was twice the number in 2010, but the number of investigated samples was also twice as high in 2011 compared with 2010 (Table). We are unable to determine whether this reflects a true increase in the number of cases from the 2010 wave to the 2011 wave or whether this reflects an increase in the awareness of the public and among physicians. However, as the proportion of positive samples was almost equal during the two periods, it is reasonable to assume that the two waves were of almost equal size, but the duration of the 2011/12 wave seems to be longer with a more gradual decline than the 2010 wave (Figure 1). However, it seems obvious that the 2011 wave was more extensive than the 2010 wave in the North Denmark Region, and it seems also likely that this region was more affected by the second wave than

Figure 2

Number of PCR positive samples from five selected laboratories in Denmark, 2009 to 2011



[a] Data were provided for the whole period (2009–2011).

[b] Data were provided for 25 October – 19 December 2010 and for 29 August – 31 December 2011.

[c] Data were provided for 20 September 2010 – 31 December 2011.

the rest of the country. Although there are differences between the regions, both waves hit the whole country almost simultaneously (Table and Figure 2). The incidence and diagnostic activity for the other regions cannot be estimated as we do not know the population base for the other laboratories. The diagnostic activity for the whole country (5 per 1,000 population) can only be estimated under the assumption that the five laboratories represent 70% of the diagnostic activity during the epidemic. However, a diagnostic activity of approximately 1 per 100 population in North Denmark Region during the eight-week period in 2011 can be considered as high.

The estimated average incidence of PCR diagnosed cases during the epidemic in 2011 was approximately 10 new cases per 100,000 population per week; this is probably a vast underestimation of the real number of cases of *M. pneumoniae* infection during this period, as many patients with mild symptoms will not consult their general practitioner, and only a fraction of patients who visit a practitioner will have samples collected for M. pneumonia PCR.

Although the consumption of macrolides is high during an epidemic of M. pneumonia it does not seem to influence the prevalence of macrolide resistance in *M. pneumoniae*. This is in contrast to other respiratory pathogens, such as *Streptococcus pneumoniae*, where resistance is closely linked to increased macrolide use [13]. This link was also observed following a previous Danish *M. pneumoniae* epidemic in 1998/99 [11]. However, we still need to investigate samples collected in January 2011 before any categorical statement on *M. pneumoniae* susceptibility to macrolides. Macrolide resistance in *M. pneumoniae* may be characterised as low in Denmark, as there is still no general problem, but in specific cases, macrolide resistance can lead to relapse and prolonged disease [12].

Table

Number and proportion of *Mycoplasma pneumoniae* samples tested by PCR at five laboratories, Denmark, 25 October (week 43) to 19 December (week 50) 2010 and 24 October (week 43) to 18 December (week 50) 2011

Laboratory (region)	Weeks 43–50 2010		Weeks 43–50 2011	
	Number of samples	Number of positive samples (%)	Number of samples	Number of positive samples (%)
SSI[a]	3,091	497 (16.1)	4,393	725 (16.5)
Capital 1	1,109	165 (14.9)	2,412	336 (13.9)
Capital 2	2,669	349 (13.1)	3,300	519 (15.7)
North	2,253	362 (14.5)	5,787	1,003 (17.3)
Southern	1,946	290 (14.9)	3,994	655 (16.4)
Total	**11,068**	**1,663 (15.0)**	**19,886**	**3,238 (16.3)**

[a] SSI: Statens Serum Institut.

We believe that it is important to have a national surveillance system for monitoring both the prevalence of the disease and the macrolide resistance in *M. pneumoniae*.

Acknowledgments

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Nationwide outbreak of *Salmonella enterica* serotype 4,[5],12:i:- infection associated with consumption of dried pork sausage, France, November to December 2011

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An outbreak of the monophasic variant of *Salmonella enterica* serotype 4,[5],12:i:- occurred in November and December 2011 in France. Epidemiological investigation and food investigation with the help of supermarket loyalty cards suggested dried pork sausage from one producer as the most likely source of the outbreak. Despite the absence of positive food samples, control measures including withdrawal and recall were implemented.

Outbreak description

On 7 December 2011, the National Reference Centre for *Salmonella* (NRC) alerted the French Public Health Institute (InVS) about a two-fold increase of *Salmonella enterica* serotype 4,[5],12:i:- since the first week of November. Between 31 October and 18 December (week 44 to week 50), a total of 337 cases were identified (Figure 1). The median age was 10 years (range: 0–90 years) with about 30% of children under five. A majority of women were affected (female to male sex ratio: 1.22). Cases were reported throughout France (Figure 2).

An epidemic of *Salmonella enterica* 4,[5],12:i:- was already observed about three months prior to this outbreak. Between 1 August and 9 October, 682 cases were reported (Figure 1), of whom 100 cases were interviewed at the time but no common vehicle of infection could be identified. In comparison, 212 cases with this serotype had been isolated during the same period in 2010.

These two consecutive outbreaks appeared in a context of emergence of monophasic variants of *Salmonella* Typhimurium all over Europe in humans, animals and food products [1,2]. Surveillance data from the French Agency for Food, Environmental and Occupational Health and Safety (Anses), showed that this 4,[5],12:i:- variant had been identified in multiple animal and food samples including pork and beef [3]. While this serotype was rarely identified before the mid-1990s, it is now among the most reported *Salmonella* serotype in the European Union [2,4-7, and personal communication, European Centre for Disease prevention and Control, 17 Jan 2011]. In France, serotype 4,[5],12:i:- ranks third among strains isolated from the pork industry (pork carcasses, pork meat and processed pork meat products ("charcuterie") in 2011.

An outbreak investigation team composed of experts from the InVS, NRC, Anses and the French Directorate General for Food (DGAL) was set up and launched simultaneously epidemiological, microbiological and food investigations to define the extend of the outbreak and identify the vehicle of transmission.

Epidemiological and microbiological investigations

Epidemiological investigation

A case was defined as a person resident in France, who had clinical sign of *Salmonella* infection and for whom monophasic *Salmonella enterica* serotype 4,[5],12:i:- was isolated from blood, stool or urine samples after week 44, i.e from 31 October to 18 December 2011 and received at the NRC.

In the defined period, 337 cases were identified. We interviewed 90 cases (or the parents for the children)

by telephone with a standardised semi-structured questionnaire. The interviews were conducted between 7 and 21 December 2011. Date of onset of these cases ranged from 25 September (week 38) to 8 December (week 49). The first 62 cases were interviewed with a trawling questionnaire covering travel history, contact with other diarrhoea cases and food consumption during the seven days prior to symptoms onset. From 14 December onwards, interviews of the 28 most recent cases were undertaken with a lighter version of the questionnaire focusing on consumption and place of purchase of pork delicatessen.

During the interviews of the first 62 cases, 53 cases (84%) reported eating cooked ham, 45 cases (73%) Emmental cheese, 42 cases (68%) dried pork sausages, 42 cases (68%) chicken, 38 cases (60%) minced beef and 38 cases (60%) eggs. Dried pork sausages were the only food item that appeared to have been consumed more frequently than expected. We compared this proportion with the consumption of controls who were interviewed during a case control study on the risk factors for *Campylobacter* infection: 46% of the controls had consumed such products (week 44 to 51, n=53, $p<10^{-3}$ [8]).

In total, 87 of 90 of the cases reported eating pork delicatessen and the most common items consumed were cooked ham (74 cases, 82%) and dried pork sausage (58 cases, 65%). In addition, 42 interviewed cases (47%) reported buying pork delicatessen at supermarket chain A, and 18 cases (22%), 16 cases (18%), and 14 (16%) at supermarket chain B, C and D, respectively. These results are not exclusive as about 33% of the supermarket chain B's clients are also clients of supermarket chain A.

Health authorities of the European Union were first alerted on the 9 December and regularly updated through the Epidemic Intelligence Information System (EPIS) and the Early Warning Response System (EWRS) of the European Centre of Disease Prevention and Control (ECDC). As of 16 January 2012, no other European country has reported an excess of *Salmonella enterica* serotype 4,[5],12:i:- in November and December 2011.

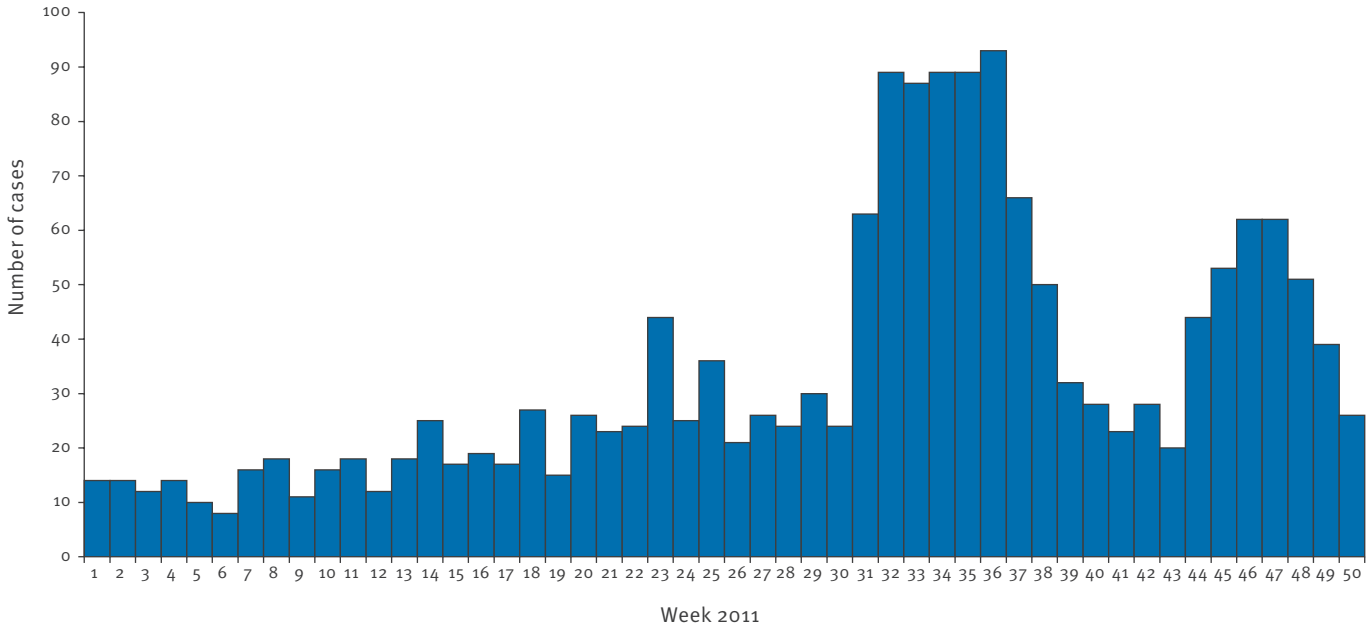
Microbiological investigation

The NRC performed subtyping on a selection of 129 monophasic variants with serotype 4,[5],12:i:- isolated from cases between 2 November and 5 December 2011.

PulseNet-standardised *Xba*I pulsed-field gel electrophoresis (PFGE) [9] multilocus variable number of tandem repeats analysis (MLVA) subtyping [10] and molecular typing based on the CRISPR polymorphisms (Crispol subtyping) [11] revealed a major profile among the epidemic isolates. It was characterised by a XTYM-159 PFGE pattern (found on 12 of 13 tested strains), a 3-13-9-NA-211 MLVA profile (9 of 9 tested strains) and a Crispol type 1 (87 of 129 tested strains). The antibiotic resistance ASSulTe (resistance to ampicillin, streptomycin, sulphonamide and tetracycline) was found on all 33 tested strains. Those profiles are currently predominant in France, and it was therefore not possible to distinguish with certainty between epidemic and non-epidemic cases.

Figure 1

Salmonella enterica 4,[5],12:i:- cases reported by the National Reference Centre, by week of isolation at the primary laboratory, France, 2011 (n=1,721)



Food investigation and trace-back

Loyalty cards

Epidemiological investigations pointed to a dried pork sausage purchased principally at supermarket chain A and consumed after week 44 2011. Therefore purchases of pork delicatessen at supermarkets A and B up to four weeks prior to symptom onset were investigated by the DGAL using data recorded through supermarket loyalty cards.

Among the 90 interviewed cases, 39 provided the number of their loyalty card for supermarket chain A during the interview. For 17 cases no purchases of dried pork sausage could be found. Of the 22 cases with documented purchase of dried pork sausage, 15 had bought sausage from a French producer X and the remaining seven cases bought sausages of seven different brands and origins from other producers. Dried pork sausages from producer X represented less than 3% of supermarket chain A's sales for this type of food item.

Eleven loyalty cards from supermarket chain B were collected. However, the supermarkets of chain B buy products individually rather than centrally for the whole chain, and the products are therefore not coded in the central database and cannot be traced through the loyalty card data.

Investigation at producer X

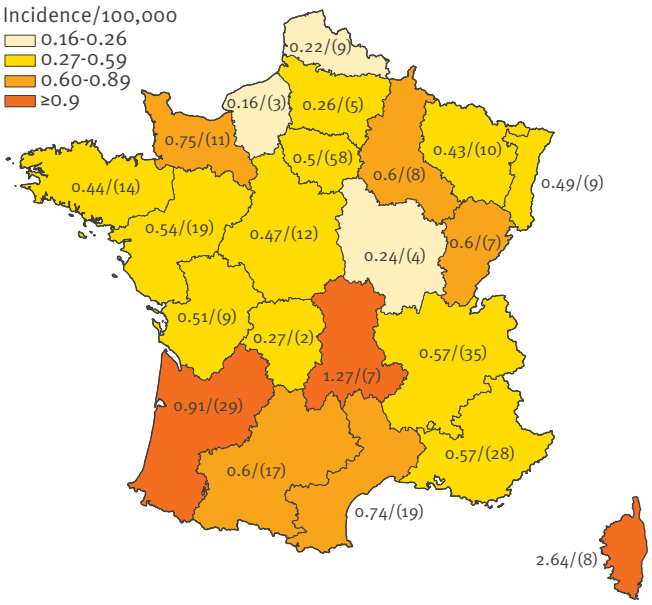
Forty-five lots of the pork sausage (one lot=8,000 sausages) had been produced between 1 September and 15 December 2011. Between 1 October and 15 December, 80 to 100% of the sausages were distributed to supermarket chain A. The remaining lots were distributed to other supermarket chains including chain B and others used by the cases.

As of 15 December, the producer's own checks on raw materials and final products as well as food inspection done during the outbreak investigation of 43 samples (25 g per sausage per lot) of dried pork sausages produced between 24 August and 21 November resulted negative for *Salmonella*.

The sausages had been distributed nationwide in metropolitan France, the French department of La Reunion, the French overseas territories of Saint Pierre and Miquelon and French Polynesia, and also in Maurice Island. In addition, there was secondary distribution by supermarket chain A to Poland, Portugal and Slovenia.

Figure 2

Incidence rate, per 100,000 inhabitants and per region, of *Salmonella enterica* 4,[5],12:i:- cases isolated by the National Reference Centre, 31 October to 18 December 2011, France (n=337)



Discussion

We describe a nationwide outbreak of salmonellosis involving 337 identified cases of infection with the *Salmonella enterica* serotype 4,[5],12:i:- between 31 October and 18 December 2011. The investigation indicated dried pork sausage from producer X as being the most likely source of the outbreak.

The incrimination of the dried sausage was supported by the following findings: Firstly, an unusually high proportion of the interviewed cases reported having eaten dried sausage. Secondly, the proportion of cases that had bought pork delicatessen in supermarket chain A was much higher than the market share of this supermarket chain among the different supermarket chains in France. Thirdly, according to loyalty card records from supermarket chain A, around 68% of the cases' purchases of sausages were sausages from producer X. However producer X's sausages represent less than 3% of the sausages market share at supermarket chain A. This discrepancy makes it likely that the vehicle of infection was dried pork sausage from producer X. Finally, the fact that more than half of the production of producer X is sold through supermarket chain A explains the high proportion of cases that purchased dried pork sausage at supermarket chain A.

Public health measures were implemented on 16 December 2011: The DGAL ordered a withdrawal and a recall with a press release and posters, which applied to all supermarkets distributing the incriminated sausage. As accurate identification of suspect lots was not possible, the withdrawal/recall applied to all lots put on the market between 1 October and 15 December, considering the three months of shelf life of the product. To be released on the market, newly produced lots had to pass a reinforced sampling plan and a clearance monitoring. Countries that received those sausages from producer X or via the supermarket chains were informed on 20 and 23 December through the Rapid Alert System for Food and Feed (RASFF).

The use of the loyalty card from supermarket chain A was important to identify the vehicle of infection and

the local producer involved in this outbreak. These cards are used more and more and prove helpful in the investigation of food-related outbreaks. Nevertheless we should keep in mind that they do not necessarily reflect the consumption of cases perfectly. For instance, the card may not be used systematically, the household can purchase foods in additional shops and markets for which they have no loyalty cards, many food products are consumed outside the household and not recorded on the card, and the central database of the supermarket does not always contain data on all foods sold such as foods directly purchased by the retailers. For these reasons the data have to be interpreted together with the results from epidemiological and microbiological investigations.

That the producer and microbiological analysis did not find *Salmonella* does not exclude contamination. The limited number of samples and the processing of the food (especially salting and drying) reduce the likelihood of isolating the bacteria. Implementing checks earlier in the process (before salting and drying) and using additional methods of testing such as polymerase chain reaction (PCR) should be considered.

The outbreak strain was the most common genotype of *Salmonella enterica* serotype 4,[5],12:i:-. The low diversity of genotypes among this serotype did not allow a more specific case definition with the techniques used.

In this investigation we focused efforts on descriptive epidemiology and detailed trace-back data from loyalty cards. A case control study was not performed because such a study may have shown an association with sausage, but would not have contributed to the identification of the brand name necessary to take control measures.

Conclusion

Considering the epidemiological investigation and trace back results suggesting a link between *Salmonella enterica* 4,[5],12:i:- infection and consumption of dried pork sausages from producer X, and despite the absence of positive sampling results on the sausages, control measures including withdrawal/recall were implemented. The epidemic peak has passed and the number of cases has been at the usual level since week 52 2011.

Monophasic *Salmonella enterica* variants are becoming predominant in the European Union [2,4-7 and personal communication, European Centre for Disease prevention and Control, 17 Jan 2011] and are increasingly reported in humans, animals and food samples. This is the second described outbreak in France involving dried pork sausage, and indicates that this food item might be a likely vehicle of infection and further outbreaks in humans may be expected [12].

Given the limitations to detect *Salmonella* in dried sausages, the ability of the standard reference method to detect of monophasic variant strains in dried sausages is questionable. Additional methods should be explored in order to improve monitoring protocols.

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* Erratum: The name of V Vaillant was erroneously left out of the list of authors at the time of publication of this article. This mistake was corrected on 3 February 2012. We apologise to the authors.

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Outbreak of cryptosporidiosis in a child day-care centre in Gipuzkoa, Spain, October to December 2011

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From October to December 2011, an outbreak of 26 cases of cryptosporidiosis occurred in a day-care centre in Gipuzkoa, Spain. The infection spread from person to person and affected 24 children under two years of age (attack rate: 38%) and two caregivers. *Cryptosporidium* oocysts were observed in 10 of 15 samples. During 2010, only four cases of *cryptosporidium* were detected in Gipuzkoa, and 27 overall in Spain.

On 24 November 2011, a paediatrician notified the epidemiological surveillance service of Gipuzkoa (Basque Country, northern Spain) of a child with diarrhoea in whose stools oocysts of *Cryptosporidium* had been isolated, as well as of an unusually large number of children with diarrhoea who attended the same day-care centre as the first child. All were tested for *Cryptosporidium* because our laboratory has a policy of testing for this microorganism in samples from children under the age of five years. In this paper, we present the epidemiological, environmental and parasitological research undertaken to study the outbreak and report the measures taken to control it.

Background

Cryptosporidium is a coccidian parasite. Its infectious forms, oocysts, are excreted in the host's faeces. The principal zoonotic reservoirs are humans, cattle and other domestic animals. It is transmitted by the faecal-oral route: person-to-person or from animal to person, as well as by ingestion of contaminated water or food. Extensive outbreaks have been reported to be associated with transmission through drinking water or related to swimming pools [1,2]. On the other hand, transmission between humans has resulted in outbreaks in day-care centres with incidence rates of 30–60% [3-7]. Given that oocysts are resistant to chlorine, it is essential that properly functioning filtration systems are used for the safety of public water supplies [8].

The median incubation period in humans is seven days (range: 2–14 days). Oocysts are found in stools an average of seven days after the end of signs and symptoms, and in most cases they stop being excreted two weeks after symptoms have resolved. The most common signs and symptoms include watery diarrhoea, abdominal pain, vomiting and fever. In immunocompetent patients, the infection is self-limiting, lasting for up to 20 days (mean of 10 days) [7].

During 2010 and the first 25 weeks of 2011, 46 cases of cryptosporidiosis were notified to the Spanish National Microbiology Surveillance System. Thirty-one of these cases were children aged between one and four years, followed by nine children aged five to nine years [9]. Data from other countries in Europe are diverse and notification rates during 2009 vary considerably between countries, with 10 per 100,000 in Ireland, 4.37 per 100,000 in Belgium and 1.35 per 100,000 in Germany [10].

Outbreak investigation

An active search for cases in the day-care centre was undertaken, by three primary care paediatricians and the Microbiology Unit of the referral hospital. A case was defined as a child or staff of the day-care centre who presented between 1 October and 20 December 2011 with frequent, non-bloody, watery diarrhoea, and/or in whose stool *Cryptosporidium* oocysts had been isolated. The following variables were recorded for the detected cases: sex, age, date of onset, clinical signs and symptoms, diarrhoea in people living in the same household, and complications.

Samples were taken for microbiological and parasitological analysis. *Cryptosporidium* oocysts were detected by extension on microscope slides, drying, Auramine O staining and observation at 400x magnification in an epifluorescence microscope. The samples were also investigated for the following

microorganisms: *Salmonella, Shigella, Campylobacter, Aeromonas* and *Yersinia enterocoliticus*. The laboratory does not look systematically for viruses until the number of suspected cases increases in the population. Cases went up in our community in the last week of December 2011.

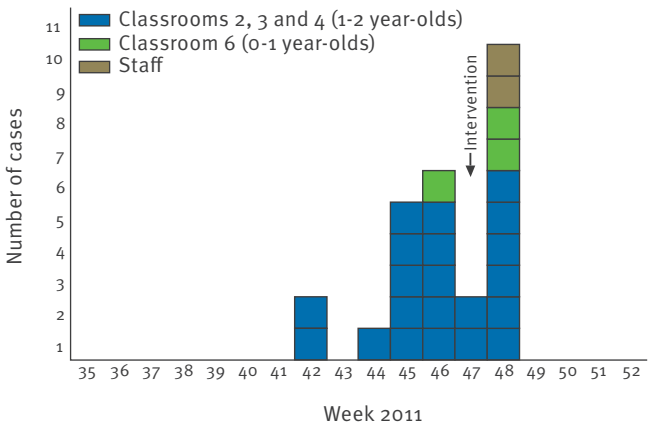
The epidemic curve confirmed that an outbreak was ongoing and showed a person-to-person pattern of transmission (Figure). Twenty-six individuals fulfilled the case definition, with onset of symptoms on 14 October in the first case and on 6 December in the last. All those affected presented with diarrhoea and the duration of illness was five to 30 days, with irregular occurrence of symptoms. All except two of the children were seen by a paediatrician and none received drug treatment. The day-care centre occupies a three-story building, with two classrooms on each floor.

At the time of the study, 63 children between 0 and two years of age attended the day-care, as well as the staff that consisted of six caregivers. There were 39 1–2-year-olds in classroom 2 (ground floor) and classrooms 3 and 4 (first floor), 13 in each. In classroom 1 (ground floor) and classrooms 5 and 6 (second floor), there were 24 0–1-year-olds, eight in each. A total of 24 children fell ill (attack rate: 38.1%), and only three of them were in the group of 0–1-year-olds. Children shared some activities by age group. The Table lists the number of children affected and the attack rates in each classroom. Two caregivers also fell ill.

Three household contacts reported diarrhoea during the outbreak period, but their aetiology was not determined. There were no complications except in a pair of two siblings who both lost weight. In the microscopic analysis, *Cryptosporidium* spp. oocysts were isolated in 10 of 15 stool samples, and no other enteropathogen was found in any of the samples studied.

Figure

Cases of diarrhoea caused by *Cryptosporidium* spp. in a day-care centre, Gipuzkoa, Spain, October-December 2011 (n=26)



Environmental investigation and control measures

In addition, an environmental investigation was also undertaken by the local public health technicians. Information on hygiene practices and water usage was collected. The investigation detected deficiencies in hygiene procedures in the day-care centre. Single use paper towels were not available in any of the risk areas. Besides, the hot water system was damaged during the period of the outbreak and only cold water was available.

As soon as the outbreak was confirmed, strengthening of hygiene measures was recommended to the staff of the day-care centre, and they were asked to advise taking children to their paediatrician in the event of more cases. The recommended measures involved correcting the above-mentioned deficiencies, improving compliance with universal hygiene rules and, given the characteristics of the microorganism (resistance to chlorine), cleaning surfaces with 3% hydrogen peroxide [8]. All measures recommended were implemented within 24-48 hours.

A letter was sent to the parents informing them of the outbreak and advising good hygiene practices. In addition, they were told that those with diarrhoea must not to use public swimming pools or other recreational water facilities for the duration of the outbreak [7,8].

Discussion

Although it is assumed that the most common transmission is through water [11], water was not considered in the outbreak described here because no additional cases were detected in the local population, the children did not engage in water activities and they only drank bottled water. The epidemiological curve shows that the first two cases occurred in October 2011 in the same classroom (ages 1–2 years), and that it was transmitted to other children that shared the same classroom and/or activities. In the classrooms of the 0–1-year-olds, only three cases occurred; it is important to note that the index case was a relative of a case

Table

Number of cryptosporidiosis cases and attack rate in each classroom of a day-care centre, Gipuzkoa, Spain, October–December 2011 (n=24)

Classroom	Age (years)	Number of exposed	Number of cases	Attack rate
Ground floor				
Classroom 1	0–1	8	0	0%
Classroom 2	1–2	13	4	31%
First floor				
Classroom 3	1–2	13	10	77%
Classroom 4	1–2	13	7	54%
Second floor				
Classroom 5	0–1	8	0	0%
Classroom 6	0–1	8	3	37.5%
Total		**63**	**24**	**38.1%**

in the classrooms of the 1–2-year-olds. Consistent with descriptions in the literature [7,12], the illness in this *Cryptosporidium* outbreak was mild and self-limiting with a relatively long duration.

It is known that the infective dose for *Cryptosporidium* is relatively low (one to 10 oocysts) and affected individuals excrete a large number of oocysts (up to 10^8)* [12]. In our reference hospital, which covers a population of 75,000 inhabitants, four positive *Cryptosporidium* cases were detected during 2010, and 17 in 2011. Of these 17 cases, 10 were children in the studied day-care centre.

Further, though routine laboratory tests to determine whether stool samples contain parasites and/or eggs do not identify species of *Cryptosporidium*. On this occasion, the fact that our laboratory has a policy of testing for this microorganism in under-fives made it possible to identify the aetiology of the outbreak. Although national coverage is not guaranteed, 27 cases were notified to the surveillance system in Spain during 2010. Our laboratory, which covers 0.15% of the Spanish population, notified four cases. This strongly suggests that cryptosporidiosis is an underdiagnosed disease in Spain.

Once the outbreak was declared, efforts were made to detect and remedy problems, as well as the application of stringent hygiene by caregivers as described above, and seemed to be effective in stopping the spread of the infection. Depletion of susceptible hosts could also be considered as a possible reason that stopped the outbreak. Nevertheless, probably thanks to the implemented measures, children under the age of one year were practically not affected, except for those who had close contact with one of the older cases. The Food and Drug Administration (FDA) approved the usage of nitazoxanide as first choice drug against Cryptosporidiosis [8]. However, in this case the drug was not prescribed as it was not readily available and all cases recovered naturally. The possibility of excluding affected children from the centre was considered, but discarded due to the lack of consensus in the literature on its effectivity, as well as the high social cost [3,13-15].

*Erratum: The number 108 was corrected on 3 February 2012.

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