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 <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> -positive samples remained the same. An epidemic was also seen in 2010 [9].
Finland	Yes	Yes	Increase in <i>M. pneumoniae</i> infections reported since October 2010.
The Netherlands	Yes	Yes	Important increase in <i>M. pneumoniae</i> infection reports in autumn 2011, similar to previous epidemics in 2002 and 2005.
Norway	Yes	Yes	Increase in <i>M. pneumoniae</i> -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 <i>M. pneumoniae</i> infection per year based on laboratory results (serology), with no changes in the last 10 years.
Sweden	Yes	Yes	All time high in <i>M. pneumoniae</i> infection reports during autumn 2011.
United Kingdom ^a	Yes	Yes	Increase in <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> 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 <i>M. pneumoniae</i> 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/Zdravnicki_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, <i>M. pneumoniae</i> infection [http://www.brit-thoracic.org.uk/Portals/o/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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