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Mycoplasma pneumoniae detection causes excess antibiotic use in Norwegian general practice:

a retrospective case–control study

Abstract

Background
The 2011 *Mycoplasma pneumoniae* epidemic in Norway resulted in many GP consultations and significantly increased the prescription of macrolide antibiotics.

Aim
To investigate the signs, symptoms, course, and prescription patterns of antibiotics in patients positive for *M. pneumoniae* compared with patients negative for *M. pneumoniae*.

Design and setting
A retrospective case–control study using questionnaires collected from GPs in a county in Norway. A total of 212 *M. pneumoniae* positive and 202 control patients were included.

Method
Descriptive statistics and logistic regression analyses were performed on the reported findings.

Results
Forty-eight per cent of patients positive for *M. pneumoniae* received an antibiotic at first consultation. Another 45% in the same group received antibiotics after the polymerase chain reaction (PCR) result was known, although these patients were not clinically different from all other patients not receiving an antibiotic at first consultation. Logistic regression analysis to evaluate independent predictors for prescription of antibiotics at first consultation showed that the following factors were significantly associated: elevated C-reactive protein (CRP) level, temperature >38.0°C, pathological findings on pulmonary auscultation, and impaired general condition. Elevated CRP level, younger age, temperature >38.0°C, short duration of symptoms, and absence of rhinitis were found to be positive predictors for *M. pneumoniae* infection.

Conclusion
A positive PCR test for *M. pneumoniae* tends to trigger an antibiotic prescription, irrespective of the severity of the patient's condition at first consultation. New guidelines for treatment and possibly PCR testing should be established.

Keywords
antibiotics; epidemic; general practice; macrolide antibiotics; *Mycoplasma pneumoniae*; Norway; overprescription; prescribing.

INTRODUCTION

Acute respiratory tract infections are commonly seen in general practice and for decades have been the reason for many visits to the doctor's surgery.[1,2] *Mycoplasma pneumoniae* is recognised as an important respiratory tract pathogen,[3] and studies show that it is responsible for between 5% and 42% of all pneumonias,[4,5] and of other upper and lower respiratory tract infections.[1,6]

The bacterium *M. pneumoniae* has no cell wall, which renders it insensitive to β-lactam antibiotics.[7] It spreads by respiratory droplets with an incubation time that varies from 1 to 3 weeks.[8] It may cause respiratory disease such as upper respiratory tract infections, for example pharyngitits or tracheobronchitis,[3] and atypical pneumonias, as well as several extrapulmonary conditions.[3,6,8]

Little is known about how *M. pneumoniae* behaves in the community, because most studies are from hospital settings. Wang *et al*.[9] concluded in a Cochrane systematic review that more investigation is needed in this field. To the authors' knowledge, no major study of this subject has been made in general practice. Real-time polymerase chain reaction (PCR) has made it possible to detect *M. pneumoniae* faster and at an earlier phase of the infection than with serological tests,[10] mainly as a result of the higher sensitivity of the test (96–100%).[11]

In Norway, PCR on nasopharyngeal swabs is performed liberally by GPs when patients present with symptoms from the upper or lower airways, to search for bacterial and viral agents, and not exclusively *M. pneumoniae*. C-reactive protein (CRP) testing is also a widely used form of point-of-care testing in Norway, with a wide range of indications,[12] being available to most GPs.

Epidemics of *M. pneumoniae* occur in 5–7-year intervals in Norway.[13] During autumn 2011 there was an epidemic in Northern European countries, including Norway.[14]

About 85% of all antibiotic prescriptions in Norway are issued outside hospitals and nursing homes,[15] and above 50% are to treat respiratory tract infections.[16] According to Norwegian guidelines, pneumonia caused by *M. pneumoniae* should be treated with macrolides such as erythromycin in children and tetracyclines in adults.[17] However, there are no clear recommendations regarding antibiotic treatment for upper respiratory tract infections caused by *M. pneumoniae*. According to the Norwegian Institute of Public Health, about 10% of *M. pneumoniae* infections cause pneumonia.[18]

In 2011, the year of the epidemic, there was a 15% increase in the use of macrolides, streptogramins, and lincosamides in Norway compared with the previous year, with macrolides making up the majority of the increase.[15] Early in 2012 Norwegian pharmacies reported a shortage of erythromycin.[13] Macrolide use in Norway normally constitutes about 10% of the total use of antibiotics.[19]

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How this fits in

Mycoplasma pneumoniae epidemics occur in 5–7-year intervals in Norway, with the most recent occurring in the autumn of 2011. This study investigated the signs, symptoms, course, and prescription patterns in a group of patients who were treated in general practice in 2011. Short duration of symptoms before presenting at the doctor's surgery, young age, fever, elevated C-reactive protein, and the absence of rhinitis were found to be positive predictors for a *M. pneumoniae* infection. A positive PCR test for *M. pneumoniae* seems to trigger an antibiotics prescription irrespective of the severity of the patient's disease. This leads to a major over-prescription of macrolides and tetracyclines, therefore increasing the risk of developing antibiotic resistance to these agents.

The aim of this study was to analyse the effect of PCR results on antibiotic prescriptions made by GPs, and to compare the signs, symptoms, disease severity, and hospitalisation rates in patients with confirmed *M. pneumoniae* infections and in a control group with negative PCR tests.

METHOD

This case–control study was performed retrospectively at the end of the *M. pneumoniae* epidemic. The time frame was the last 6 months of 2011. The samples were taken as nasopharyngeal swabs and analysed by *M. pneumoniae* DNA PCR at the Department of Microbiology, Vestfold Hospital Trust, Tønsberg, Norway, using primers described by Raggam *et al*[10] with minor modifications. The result of the PCR analysis would normally reach the GP on day 3 after the first consultation.

The Vestfold Hospital Trust experienced an increase of 414% received swabs for PCR tests for *M. pneumoniae* compared with the same time frame the previous year. For practical reasons, because of the vast number of tests performed (9834), the GPs in the county of Vestfold with the highest number of *M. pneumoniae* PCR-positive patients in the relevant time period were invited to answer questionnaires concerning these patients. Questionnaires were distributed to the GPs in January 2012. Thirty-three of the county's 167 GPs participated in the study and 212 questionnaires were returned for outpatients with confirmed *M. pneumoniae*. The subsequent patient with a negative PCR taken by the same GP was used as the control, because this group was likely to present with comparable airway infections, and 202 control questionnaires were returned. The responses given on the questionnaires were based on the clinical notes made by the GPs at consultation and point-of-care testing, such as CRP. The GPs were aware of the result of the PCR test when answering the questionnaires.

The questionnaire encompassed patient history, signs, symptoms, ICPC-2 (International Classification of Primary Care) diagnosis, general condition of the patient, and previous history of pulmonary disease, as well as the laboratory tests performed, whether the patient was subjected to spirometry or chest X-ray, and whether the disease caused hospital admittance. Finally, the form requested details regarding antimicrobial treatment.

Statistical analyses involved the χ^2 test and the *t*-test, and were performed using SPSS (version 19). Logistic regression analyses were also performed to find independent predictors for *M. pneumoniae* PCR positivity and for antibiotic prescription at the initial consultation (prior to knowledge of the PCR test result). In both regression analyses, all factors with a *P*-value below 0.20 were included in the bivariate analysis. Missing data were excluded from the statistical analysis. To correct for clustering on the doctor level, a generalised estimation equation analysis was carried out.

RESULTS

Of a total of 414 patients, 186 (45%) were

Table 1. Antibiotic prescriptions in patients with and without *Mycoplasma pneumoniae*, case–control study in general practice in Vestfold, Norway, 2011

	M. pneumoniae positive	*M. pneumoniae* negative	Total	
Antibiotic or complications	***n*** **= 212 (%)**	***n*** **= 202 (%)**	***n*** **= 414 (%)**	***P*****-value**
Antibiotics at first consultation	101[a] (48)	54 (27)	155 (37)	<0.001
Beta-lactams	10 (5)	8 (4)	18 (4)	
Macrolides	75 (35)	32 (16)	107 (26)	
Tetracyclines	16 (8)	13 (6)	29 (7)	
Other antibiotics	0 (0)	1 (1)	1 (0)	
Antibiotics at a later consultation	107[a] (50)	18 (9)	125 (60)	<0.001
Beta-lactams	0 (0)	3 (2)	3 (1)	
Macrolides	83 (39)	13 (6)	96 (23)	
Tetracyclines	19 (9)	1 (1)	20 (5)	
Other antibiotics	5 (2)	1 (1)	6 (1)	
Antibiotics total	197 (93)	71 (35)	268 (65)	<0.001
Complications to treatment	11[b] (5)	4 (2)	15 (4)	NS

[a]The numbers add up to more than the total because some patients received antibiotics at both the first and at a later consultation. [b]The types of complications were most frequently absence of improvement and, in a few patients, reactions to treatment such as emesis and rashes.

male. The mean age was 19.2 years in the *M. pneumoniae* positive (MP+) group, and 33.8 years in the *M. pneumoniae* negative (MP–) group ($P<0.001$).

Of all 414 patients, 268 (65%) received an antibiotic at the first or at a subsequent consultation. Of the 212 MP+ patients, 101 (48%) received an antibiotic at the first consultation, before the PCR test result was available. In the MP– group, 54 (27%) of the 202 patients received an antibiotic at the first consultation. The types of antibiotics prescribed at first or later consultations are outlined in Table 1. Most patients in both groups received a prescription of a macrolide or a tetracycline antibiotic. At later consultations 107 (50%)of the MP+ patients received an antibiotic of any type. Some of these patients had also received an antibiotic at first consultation. Ninety-six (45%) of the MP+ patients received an antibiotic for the first time at a later consultation. In the MP– group only 18 (9%) received an antibiotic later than the initial consultation. A total of 197 (93%) of the MP+ group received antibiotics at either the first or a later consultation, compared with 71 (35%) of the MP– group. Delayed antibiotic prescribing was reported in nine of a total of 268 patients (3%) from both groups who received a prescription.

The mean time of symptoms before visiting the doctor's surgery was 8.3 days in the MP+ group, and 13.8 days in the MP– group ($P<0.001$).

Patient history data, signs, and symptoms are presented in Table 2. A temperature above 38°C was reported in 133 MP+ patients (63%) compared with 83 MP– patients (41%) ($P<0.001$). Rhinitis was described in 28 (13%) and 60 (30%) patients in the MP+ and MP– groups, respectively ($P<0.001$).

GPs were asked to categorise the patient's general condition on first consultation as normal, moderately decreased, or severely decreased. In the MP+ group, 109 (51%) patients had moderately or severely decreased general condition. In the control group there were 69 (34%) patients with moderately or severely decreased general conditions ($P = 0.002$).

Auscultation of the lungs presented pathological sounds in 59 (28%) and 33 (16%) patients in the MP+ and MP– groups, respectively ($P = 0.005$).

CRP was measured in 187 (88%) and 166 (82%) of the MP+ and MP– groups, respectively. The mean in the MP+ group was 28.8 mg/l, and 14.8 mg/l in the control group ($P<0.001$). All values below 8 mg/l were set to the value of 4 for statistical purposes.

In the MP+ group, 67 patients (32%) were diagnosed with pneumonia (ICPC-2) R81 (pneumonia) and R83 (other airway infections not specified including 'infections of the lower airways') at first consultation, and an additional 49 (23%) after the PCR results were known to the GPs, making a total of 116 patients (55%).

Logistic regression analysis was performed to identify independent predictors of *M. pneumoniae* infection (Table 3). The following factors were found to be significantly associated: elevated CRP level, younger

Table 2. Signs and symptoms in patients with and without *Mycoplasma pneumoniae*, case–control study in Vestfold, Norway 2011

n = Number of reported results	*M. pneumoniae* positive *n* = 212 (%)	*M. pneumoniae* negative *n* = 202 (%)	Total *n* = 414 (%)	*P*-value
Sex, male (*n* = 414)	111 (52)	75 (37)	186 (45)	0.002
Mean age (95% CI) (*n* = 414)	19 (17 to 21)	34 (31 to 37)	26 (24 to 28)	<0.001
Symptoms				
Days of symptoms before first consultation (95% CI) (*n* = 388)	8 (7 to 9)	14 (12 to 16)	11 (10 to 12)	<0.001
Days of cough before first consultation (95% CI) (*n* = 261)	8 (7 to 9)	13 (10 to 15)	10 (9 to 11)	<0.001
Cough (*n* = 410)	209 (99)	189 (94)	398 (96)	0.030
Rhinitis (*n* = 256)	28 (13)	60 (30)	88 (21)	<0.001
Temperature >38°C (*n* = 332)	133 (63)	83 (41)	216 (52)	<0.001
Myalgia (*n* = 185)	18 (9)	21 (10)	39 (9)	NS
Sore throat (*n* = 285)	70 (33)	62 (31)	132 (32)	NS
Expectoration (*n* = 247)	54 (26)	56 (28)	110 (27)	NS
Signs				
Infected throat (*n* = 342)	45 (21)	40 (20)	85 (21)	NS
Lymphadenopathy (*n* = 208)	21 (10)	19 (9)	40 (10)	NS
Pulmonary findings (*n* = 393)	59 (28)	33 (16)	92 (22)	0.005
General condition (*n* = 178)				
General condition moderately decreased	100 (47)	68 (34)	168 (41)	0.040
General condition severely decreased	9 (4)	1 (1)	10 (2)	NS
General condition moderately + severely decreased	109 (51)	69 (34)	178 (43)	0.002
Additional tests				
Mean CRP (95% CI) (*n* = 353)	29 (25 to 33)	15 (11 to 19)	22 (19 to 25)	<0.001
Mean ESR (*n* = 12)	40	10	–	NS
Spirometry done (*n* = 7)	2 (1)	5 (3)	7 (2)	NS
Chest X-ray (*n* = 32), findings	10 (5)	2 (1)	12 (3)	NS
Other positive microbiological tests (*n* = 23)	10[a] (5)	13[b] (6)	23 (6)	NS
Other information				
Chronic pulmonary disease (*n* = 403)	22[c] (10)	31[d] (15)	53 (13)	NS
Admitted to hospital (*n* = 414)	6 (3)	1 (1)	7 (2)	NS
Other clinical findings (*n* = 31)	16[e] (8)	15 (7)	31 (7)	NS

[a]Bordetella pertussis = 4, B. parapertussis = 2, Group A Streptococcus = 2, Cytomegalovirus = 1, and Parainfluenza virus = 1. [b]B. parapertussis = 3, Group A Streptococcus = 3, Chlamydophila pneumoniae = 2, B. holmesii = 1, B. pertussis = 1, Human metapneumovirus = 1, Parainfluenza virus = 1, and coinfection by Haemophilus influenzae and Streptococcus pneumoniae = 1. [c]None of the patients were reported to have chronic obstructive pulmonary disease, 21 (10%) had asthma, and one patient had sarcoidosis. [d]22 (11%) had COPD, eight (4%) had asthma, and one patient had earlier experienced two incidences of pulmonary embolism. [e]Ear symptoms in five (2%), rashes in two (1%), and in nine (4%) miscellaneous small problems. CRP = C-reactive protein. ESR = erythrocyte sedimentation rate.

Table 3. Logistic regression analysis on predictors for a confirmed diagnosis of *Mycoplasma pneumoniae* corrected for multilevel (*n* = 176), case–control study in Vestfold, Norway, 2011

		Bivariate analysis		Multivariate analysis	
Factor	**Values (*n* in group)**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Age, years	>35 (ref) (*n* =140)	1		1	
	12–35 (*n* = 130)	3.3 (2.0 to 3.5)	<0.001	2.3 (0.96 to 5.35)	0.06
	<12 (*n* = 144)	6.3 (3.7 to 10.6)	<0.001	7.93 (2.9 to 21.7)	<0.001
Symptom days	>10 (ref) (*n* = 144)	1		1	
	7–10 (*n* = 125)	4.7 (2.7 to 8.1)	<0.001	2.95 (1.13 to 7.7)	0.03
	0–6 (*n* = 119)	2.7 (1.6 to 4.4)	<0.001	1.5 (0.59 to 3.8)	0.39
Rhinitis	No (ref) (*n* = 168)	1		1	
	Yes (*n* = 88)	0.34 (0.2 to 0.6)	<0.001	0.34 (0.1 to 0.95)	0.04
CRP value	<8 (ref) (*n* = 140)	1		1	
	8 to 22 (*n* = 96)	2.7 (1.6 to 4.5)	<0.001	2.05 (0.79 to 5.5)	0.14
	>22 (*n* = 116)	5.4 (3.2–9.3)	<0.001	4.0 (1.57 to 10.3)	0.01
Temperature >38.0°C	No (ref) (*n* = 116)	1		1	
	Yes (*n* = 216)	3.3 (2.0 to 5.3)	<0.001	3.0 (7.1 to 1.35)	0.008

The following symptoms were associated in the bivariate analysis but not in the multivariate: pathological sounds on pulmonary auscultation and impaired general condition. CRP = C-reactive protein. Ref = reference.

age, temperature >38.0°C, short duration of symptoms, and absence of rhinitis. The following symptoms were associated in the bivariate analysis but not in the multivariate: pathologic sounds on pulmonary auscultation and impaired general condition.

Furthermore, a logistic regression analysis was performed to evaluate which factors were independent predictors for prescription of antibiotics at the first consultation, before the PCR result was known to the GP (Table 4). The following factors were significantly associated: elevated CRP level, temperature >38.0°C, pathologic sounds on pulmonary auscultation, and impaired general condition. The following findings were associated in the bivariate analysis, but not significantly associated in the multivariate analysis: age and presence of cough.

Table 4. Logistic regression analysis on predictors for antibiotic prescription in patients with suspected *M. pneumoniae* corrected for multilevel (*n* = 176), case–control study in Vestfold, Norway, 2011

		Bivariate analysis		Multivariate analysis	
Factor	**(*n* in bivariate analysis)**	**OR (95% CI)**	***P*-value**	**OR (95% CI)**	***P*-value**
Pulmonary findings	Normal (ref) (*n* = 301)	1		1	
	Wheezing (*n* = 28)	0.5 (0.2 to 1.0)	0.053	0.5 (0.2 to 1.5)	0.23
	Crackles (*n* = 64)	6.2 (2.3 to 17.0)	<0.001	5.6 (1.2 to 25.4)	0.007
General condition	Good (ref) (*n* = 212)	1		1	
	Moderately affected (*n* = 168)	4.6 (2.9 to 7.1)	0.004	2.9 (1.6 to 5.1)	<0.001
	Severely affected (*n* = 10)	13.7 (2.8 to 66.5)	<0.001	6.3 (1.3 to 31.1)	0.023
CRP value	<8 (ref) (*n* = 140)	1		1	
	8–22 (*n* = 96)	1.8 (1.0 to 3.5)	0.04	0.7 (0.3 to 1.4)	0.3
	>22 (*n* = 116)	5.7 (3.3 to 9.9)	<0.001	2.4 (1.3 to 4.5)	0.007
Temperature >38.0°C	No (ref) (*n* = 116)	1		1	
	Yes (*n* = 216)	3.1 (2.6 to 6.1)	<0.001	2.7 (1.4 to 5.2)	0.005

The following findings were associated in the bivariate analysis, but not significantly associated in the multivariate analysis: age and presence of cough. CRP = C-reactive protein. Ref = reference.

Finally, a subgroup analysis was made of the patients who did not receive antibiotics at the first consultation. Logistic regression analysis was performed to evaluate independent predictors for antibiotics later in the course of the illness.

The presence of *M. pneumoniae* positive PCR and the following clinical features registered on first consultation were analysed as independent factors: pulmonary findings, impaired general condition, temperature >38.0°C, and elevated CRP level. In this analysis the presence of *M. pneumoniae* was the dominating factor with an odds ratio (OR) of 75.6 (95% confidence intervals [CI] = 27.7 to 206.3), and the only other factor associated was elevated temperature with an OR of 3.6 (95% CI = 1.4 to 9.4).

DISCUSSION

Summary

Antibiotic usage. A main finding of this study is the extensive use of antibiotics. This was probably due to an increased awareness among GPs and the public of the *M. pneumoniae* epidemic in the area, which lowered the threshold for prescribing macrolides and tetracyclines. The Norwegian Institute of Public Health also advised on its website that antibiotics could be prescribed empirically, before or without PCR testing.[20]

It may seem that a positive PCR test automatically released an antibiotic prescription because only 48% of the MP+ patients were deemed to be in need of antibiotics at first consultation, and 45% received antibiotics later. The general condition was evaluated by the GPs as similar in the MP+ and MP– patients who did not receive antibiotics at first consultation. CRP values were relatively low in the MP+ group not receiving antibiotics. Also, because GPs received the PCR result, at the latest, 3 days after the initial consultation, it is likely that the GPs knew the *M. pneumoniae* status of the patients at most of the sequential consultations. This makes it plausible that positive PCR results were the main cause for the prescription, rather than the patient's health condition, resulting in an over-prescription of antibiotics. This is further underlined by the gap between

the number of patients diagnosed with pneumonia (ICPC-2) at first consultation and the total number receiving antibiotic treatment. The change in diagnosis may reflect the need of GPs to legitimate their antibiotic prescription. The situation is also complicated by the knowledge that the *M. pneumoniae* bacteria can persist in the nasopharynx for variable periods after resolution of symptoms.[21]

Another cause for the increased prescription rate after confirmed presence of *M. pneumoniae* may be that GPs were attempting to prevent the disease from spreading. This may be a valid argument in some cases, but in a number of cases the duration of symptoms before consultation was so long-lasting that antibiotic treatment would probably not affect the clinical course or prevent spread. However, this is a critical question that should be addressed in future research and guidelines, also taking the incubation time and possible spread at this time into consideration.

The following factors were significantly associated with antibiotic prescribing regardless of *M. pneumoniae* PCR status: elevated CRP level, temperature >38.0°C, pathological sounds on pulmonary auscultation, and impaired general condition. This demonstrates what the GPs had emphasised in their evaluation.

Norwegian guidelines describe the treatment of pneumonia caused by *M. pneumoniae*, but there is a lack of guidelines when it comes to the treatment of upper respiratory tract infections in which *M. pneumoniae* is suspected or confirmed. The rate of antibiotic use probably should have been significantly lower, because macrolide-resistant strains of *M. pneumoniae* are increasing in frequency worldwide,[9,22] although not yet in Scandinavia.[14] This coincides with lower levels of antibiotic resistance in the Scandinavian countries in general,[23] probably as a result of more restrictive prescription patterns. It is likely that there would be a benefit in decreasing the use of macrolides during *M. pneumoniae* epidemics to prevent the emergence of resistant strains. Delayed antibiotic prescribing may be a useful tool to achieve decreased consumption of antibiotics.[15]

Clinical findings. As expected, the mean age was lower for the MP+ group (19.2 years) than the MP– group (33.8 years). This fits with the age spectrum that *M. pneumoniae* is known to affect: children and young adults, and a subset of adults, mostly females, possibly because mothers and grandmothers are often in closer contact with affected children.[15] It may also reflect the fact that females visit the doctor's surgery more frequently than males for a variety of conditions, including respiratory tract infections.[24]

The logistic regression analysis showed that the following factors were significantly associated with a *M. pneumoniae* PCR positivity: elevated CRP level, younger age, temperature >38.0°C, short duration of symptoms, and absence of symptoms of rhinitis. To the authors' knowledge, no such analysis has previously been performed in a general practice setting. The finding of rhinitis as a negative predictor of *M. pneumoniae* infection is an interesting parallel to what has been found in the diagnosis of group A β-haemolytic streptococcus (GAS) in sore throat. Rhinitis and cough have been shown to be negative predictors for the presence of GAS.[25]

Almost all MP+ patients had a cough: 209 (99%). There was no significant difference between the two groups concerning the rate of expectorations, which is noteworthy because *M. pneumoniae* is known to cause a predominantly dry cough.

Few (six [3%]) MP+ patients were admitted to hospital and the rate of reported complications was low. This confirms that infections by *M. pneumoniae* mostly cause low-grade disease that can be treated safely in general practice without hospitalisation.

Strengths and limitations

An advantage of this study is that most studies on this topic have examined hospital populations. The present study is one of few with a sizeable population of *M. pneumoniae* PCR positive patients derived from general practice.

A weakness of the study is that the GPs made their reports based on what may have been insufficient notes in the patients' electronic medical records. This is underlined by the lack of reported data at some of the key questions, such as the presence of rhinitis. The same kind of bias is also relevant for GPs' reporting of the patients' general condition. There is also a discrepancy regarding the ICPC-2 diagnosis the GPs gave the patients at consultation and the severity reported in the questionnaires.

Comparison with existing literature

The existing literature on the clinical signs and symptoms of *M. pneumoniae* infections in children and adolescents was systematically reviewed by the Cochrane collaboration in 2012;[9] however, this was based only on information from hospitals.

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Ethical approval

The study was approved by the Norwegian regional ethical committee (Reference 2011/2583A).

Provenance

Freely submitted; externally peer reviewed.

Competing interests

Mats Foshaug reports grants from Allmennmedisinsk forskningsutvalg (General Practice Research Committee). The other authors declare no competing interests.

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The review concluded that chest pain and possibly crepitations were positive predictors for the presence of *M. pneumoniae* infection, with wheeze as a negative predictor. Coryza and cough were concluded not to be useful diagnostic indicators of *M. pneumoniae*. In the present study, the presence of rhinitis was a strong negative predictive factor, while fever, young age, and short duration of symptoms were positive predictors. In medical encyclopaedias the absence of rhinitis has not been mentioned as a predictor for *M. pneumoniae* infection.[8]

Implications for research and practice

As antibiotic prescriptions seem to be governed by the mere existence of a positive *M. pneumoniae* PCR, it may be beneficial to establish guidelines regarding the indications for performing this test.

There should be discussion about whether *M. pneumoniae* infections not considered pneumonias should be treated with antibiotics, or if a 'wait-and-see' approach is equally sound. The possibility that antibiotics may shorten the time of symptoms and spread of disease should be taken into consideration when this question is addressed. However, up to 13.5% of the population are found to be healthy carriers of *M. pneumoniae* during epidemics,[26] possibly demolishing the indication of antibiotics as a means of preventing spread.

Finally, it is advisable that a new prospective study into the signs and symptoms of *M. pneumoniae* infections seen in general practice is performed, preferably at the next opportunity. Such a study could use questionnaires similar to the one used in this study, possibly with antibiotic-treated groups and placebo groups in a double-blind study.

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