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Chlamydia species as a cause of community-acquired pneumonia in Canada

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Chlamydia *species as a cause of community-acquired pneumonia in Canada. T.J. Marrie, R.W. Peeling, T. Reid, E. De Carolis, and the Canadian Community-Acquired Pneumonia Investigators. ©ERS Journals Ltd 2003.*

ABSTRACT: *Chlamydia pneumoniae* has been implicated as a cause of community-acquired pneumonia (CAP) in several studies. However, there has been no comprehensive study of the role of *Chlamydia* species (*C. pneumoniae*, *C. psittaci* (avian and feline strains) and *C. pecorum*) as a cause of CAP. The aim of the present study was to determine the role of *C. pneumoniae*, *C. psittaci* and *C. pecorum* as causes of CAP.

A prospective cohort observational study of CAP was conducted at 15 teaching centres in eight Canadian provinces between January 1996–October 1997. Acute (n=539) and convalescent (n=272) serum samples were obtained for determination of antibody titres to *C. pneumoniae*, *C. psittaci*, *C. pecorum*, *C. trachomatis*, *Mycoplasma pneumoniae*, *Legionella pneumophila* serogroups I–VI, *Streptococcus pneumoniae* and various respiratory viruses.

Twelve of 539 (2.2%) patients had acute *C. pneumoniae* pneumonia and an additional 32 (5.9%) had possible acute infection. *C. pneumoniae* was the sole pathogen in 16 of 42 (38.1%) of these patients. The most common copathogens were *S. pneumoniae*, respiratory syncytial virus and influenza virus type A. *C. pneumoniae* pneumonia patients were older and more likely to show congestive heart failure compared to bacteraemic *S. pneumoniae* patients. The latter had a lower mean diastolic blood pressure, a higher white blood cell count and a lower arterial carbon dioxide tension. Two patients had antibody titres suggestive of recent infection with the feline strain of *C. psittaci*.

Although numerically *Chlamydia pneumoniae* is an important cause of community-acquired pneumonia, no distinctive clinical features associated with this pathogen were detected in the present study. Feline *Chlamydia psittaci* may cause a few cases of community-acquired pneumonia. Avian *Chlamydia psittaci* should be considered only if there is a compatible epidemiological history.

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There are four species within the genus Chlamydia, *C. pneumoniae*, *C. psittaci*, *C. pecorum* and *C. trachomatis* [1]. *C. psittaci* has been recognised as a cause of community-acquired pneumonia (CAP) following exposure to *C. psittaci*-infected parrots since 1879 [2]. In 1986, GRAYSTON and co-workers [3, 4] described a new species of Chlamydia, *C. pneumoniae*, as a cause of respiratory tract infections. Subsequent studies have shown that this microorganism is frequently implicated as a cause of CAP [5]. It is unclear whether *C. pecorum*, which was isolated from ruminants and named in 1992, is a human pathogen [6].

The purpose of the present study was to define the role of *C. pneumoniae*, *C. psittaci* (avian and feline strains) and *C. pecorum* as causes of CAP.

Methods

Patient population and study design

The present prospective study of CAP began on January 11, 1996 and was completed on October 31, 1997. It was conducted at 15 teaching hospitals in eight Canadian provinces. The study was approved by the local research ethics boards. All patients who were admitted to hospital with a diagnosis of pneumonia were screened by a study nurse.

Patients who met the following eligibility criteria were approached for enrolment in the study: 1) age $\geqslant$16 yrs; 2) evidence of a new pulmonary infiltrate on chest radiography not attributable to an aetiology other than that of pneumonia (*e.g.* congestive heart failure); 3) findings suggestive of bacterial pneumonia (chest pain, cough, rales, rhonchi and/or signs of consolidation) or an oral temperature of <36.5°C or >38.5°C; and 4) absence of hospitalisation for $\geqslant$14 days. Sputum production was not a requirement for study entry; however, every attempt was made to collect a sputum sample for Gram stain and culture.

Patients were excluded if they had nosocomial pneumonia.

A study nurse completed the data collection forms and made daily visits to each patient (for a maximum of 7 days follow-up while in hospital) to record progress in terms of the progression of the pneumonia and any complications that may have occurred during the hospital stay. All data were verified against the original chart by a study monitor during a site visit.

Diagnostic work-up

Acute and 4–6-week convalescent serum samples were collected as part of the study protocol. In addition, a urine

For editorial comments see page 741.

sample from each patient was tested for *Legionella pneumophila* serogroup-I antigen.

Microbiological procedures

Blood, sputum and/or respiratory samples were processed for culture according to the methods in place at each centre's laboratory. All serum samples were tested for antibodies directed against *Mycoplasma pneumoniae*, influenza virus types A and B, parainfluenza virus types 1, 2 and 3, adenovirus, and respiratory syncytial virus using a standard complement fixation technique in microtitre plates. The adenovirus and respiratory syncytial virus antigens were purchased from Flow Laboratories (McLean, VA, USA); influenza virus types A and B, parainfluenza virus types 1, 2 and 3, and *M. pneumoniae* antigens were purchased from M.A. Bioproducts (Walkersville, MD, USA).

Acute phase serum samples from 539 patients and convalescent phase samples from 272 patients were tested for immunoglobulin (Ig)G and IgM directed against *C. pneumoniae* strain AR39; *C. psittaci* strains 6BC (avian), FP (feline pneumonitis), TT3 (turkey) and CP3 (pigeon); the *C. pecorum* ovine polyarthritis strain; and pooled antigens of *C. trachomatis* serovars BED, CJHI and FGK using a microimmunofluoresence assay [7].

Serum specimens were screened at 1:16 dilution for IgG and IgM directed against *C. pneumoniae* and titrated to end-point (some samples were tested for IgA); a four-fold rise in antibody titre between acute and convalescent serum samples or an IgM antibody titre of $\geqslant$1:16 was classified as indicating acute *C. pneumoniae* infection [5]. An IgG titre of $\geqslant$1:512 was indicative of possible acute infection [5]. Seropositive patients were defined as those with IgG titres of 1:16–1:256 and seronegative patients as those whose titres were <1:16. Seropositivity to other *Chlamydia* species was defined as a four-fold rise in antibody titre between acute and convalescent serum samples or a stable IgG titre of $\geqslant$1:64 [8].

Antibiotic therapy

Antibiotic therapy was categorised into three groups: monotherapy, concurrent combination therapy and sequential combination therapy. Monotherapy was defined as administration of one antibiotic class throughout the course of therapy regardless of method of administration or overlap in time of use. Concurrent combination therapy was defined as administration of two or more classes of antibiotic overlapping in time by $\geqslant$1 day. Sequential combination therapy constituted two or more drug classes administered sequentially with no overlap in time.

Statistical analysis

Differences between patient subpopulations were tested using the Pearson Chi-squared test for categorical variables and an unpaired t-test or one-way analysis of variance for continuous variables. Predictors of seropositivity to *C. pneumoniae* were tested in a logistic regression model using *C. pneumoniae* antibody status (negative or positive) as the dependent variable. Clinically relevant patient characteristics and factors found to be significantly associated with *C. pneumoniae* seropositivity on bivariate analysis were entered into the logistic model [9].

Table 1. – Seropositivity[#] to *Chlamydia pneumoniae* according to age

Age yrs	Subjects n	Seropositivity n (%)
$\leqslant$19	1	0 (0.0)
20–29	29	18 (62.1)
30–39	53	38 (71.7)
40–49	54	43 (79.6)
50–59	58	47 (81.0)
60–69	94	68 (72.3)
70–79	134	102 (76.1)
80–89	103	79 (76.7)
90–99	13	9 (69.2)

[#]: antibody titre $\geqslant$1:16.

Results

Antibodies directed against *C. pneumoniae* were present at a titre of $\geqslant$1:16 in 404 of 539 (75%) acute phase serum samples tested. Table 1 shows the seropositivity of the test population according to age in decades.

Significantly more males than females were seropositive (54.7 *versus* 45.3%, p=0.039) (table 2). A greater proportion of seropositive than seronegative patients were current smokers (32.1 *versus* 25.6%, p=0.005) and had a history of chronic obstructive pulmonary disease (COPD) (35.1 *versus* 22.2%, p=0.02). The mean body mass index (BMI) of the seropositive subjects was significantly higher than that of the seronegative subjects (26.0±6.4 *versus* 23.4±4.9, p=0.000). A significantly higher systolic and diastolic blood pressure was observed among seropositive subjects (p=0.024 and p=0.045, respectively).

The results of the logistic regression analysis for predictors of *C. pneumoniae* seropositivity are also presented in table 2. Significant risk factors included greater BMI, nonwhite race and current smoking status. No other significant associations were found between patient characteristics and risk of seropositivity.

Chlamydia pneumoniae *pneumonia*

Forty-two (7.8%) of the patients studied met the criteria for acute or possible acute *C. pneumoniae* infection. Eight of the 42 (19%) had an IgM titre of $\geqslant$1:16, four (9.5%) demonstrated a four-fold rise in antibody titre and 31 (73.8%) had a stable IgG titre of $\geqslant$1:512. No differences were found when the 12 patients with acute infection were compared with the 32 patients with possible acute infection. Multivariate analysis revealed no features predictive of acute infection. Twenty-two of the 42 (52%) patients with acute or possible acute *C. pneumoniae* infection who were tested for IgA had a titre of $\geqslant$1:64. Sixteen of the 42 (38%) patients with acute or possible acute *C. pneumoniae* pneumonia had no other pathogen identified as a cause of the pneumonia. Sixteen of the remaining 26 (61.5%) had one other pathogen identified and 10 (38.5%) had two or more pathogens implicated in the aetiology of the pneumonia. Table 3 details these copathogens. It is noteworthy that *S. pneumoniae*, influenza A and respiratory syncytial virus accounted for 33.0, 17.9 and 12.8% of the copathogens respectively.

In order to more clearly define the clinical manifestation of *C. pneumoniae* pneumonia, the 16 patients with *C. pneumoniae* as the sole pathogen were compared with the 26 patients who had *C. pneumoniae* plus copathogens (table 4).

Although this comparison is limited by the small sample

Table 2. – Clinical comparison of *Chlamydia pneumoniae*-seropositive and *C. pneumoniae*-seronegative patients

	Seropositive	Seronegative	p-value	Seropositivity odds ratio (95% CI)[#]
Male sex	221 (54.7)	60 (44.4)	0.039	
Age yrs	63.1±17.8	61.9±20.0	NS	
Body mass index	26.0±6.4	23.4±4.9	0.000	1.09 (1.04–1.15)
Race				
White	362 (89.6)	128 (94.8)	0.07	
Non-White	42 (10.3)	7 (5.2)		2.91 (1.04–8.12)
Smoking status				
Never smoker	78 (19.5)	44 (33.1)		
Past smoker	193 (48.4)	55 (41.4)		
Current smoker	128 (32.1)	34 (25.6)	0.005	2.24 (1.18–4.24)
COPD	142 (35.1)	30 (22.2)	0.02	
Systolic BP mmHg	133.1±27.1	126.8±29.1	0.024	
Diastolic BP mmHg	73.6±15.1	70.6±13.8	0.045	

Data are presented as n (%) or mean±SD. CI: confidence interval; COPD: chronic obstructive pulmonary disease; BP: blood pressure; NS: nonsignificant. [#]: logistic model included the following patient variables: sex, age, highest level of education achieved, body mass index, race (White *versus* non-White), admission (from home *versus* other), drinking status (nondrinker *versus* drinker), smoking status (never, past and current), history of underlying respiratory disease (no *versus* yes), history of predisposing medical factors (no *versus* yes) and time of immunoglobulin G screening (winter *versus* nonwinter months). Patients who had "never smoked" were used as the reference category for smoking status.

sizes, noteworthy illness-associated manifestations (between-group differences) emerged. The mean duration of symptoms (in days) prior to hospital admission among patients with *C. pneumoniae* as the sole pathogen was shorter at 4.6 *versus* 12.9 days. The overall mean duration of hospital stay was longer in the *C. pneumoniae* alone group than in the *C. pneumoniae* plus copathogens group (9.00±7.30 *versus* 7.58±3.49 days).

The unusually long mean hospital stay was the result of four outliers with hospital stays of 39, 43, 93 and 172 days. All four outliers had a history of chronic illness and underlying respiratory disease. Only one of the four subjects had complications during the first 7 days of hospitalisation. However, three of the four outliers had their discharge delayed due to other medical conditions.

The *C. pneumoniae* alone group was more likely to exhibit asthma, nausea and vomiting and less likely to show COPD, purulent sputum and shaking chills. A higher respiratory frequency, pulse rate and systolic and diastolic blood pressure was more common among *C. pneumoniae* plus copathogen subjects.

In table 5, all patients with *C. pneumoniae* pneumonia are compared with those with bacteraemic pneumococcal pneumonia. The *C. pneumoniae* group was significantly older, had a lower pulse rate, a higher diastolic blood pressure and a higher arterial carbon dioxide tension. The white blood cell count was significantly higher in the bacteraemic *S. pneumoniae* group. The mortality rates were not significantly different at 4.9% for *C. pneumoniae* and 5.4% for the bacteraemic pneumococcal pneumonia group. The mortality rate of 9.4% for the remaining cohort (excluding the *C. pneumoniae* and bacteraemic *S. pneumoniae* patients) was also not significantly different from the mortality rates for the *C. pneumoniae* and the bacteraemic pneumococcal pneumonia patients.

Table 3. – Frequency of copathogens in acute or possible acute *Chlamydia pneumoniae* pneumonia[#]

Copathogen	n (%)
Streptococcus pneumoniae	13 (33)
Influenza virus type A	7 (17.9)
Respiratory syncytial virus	5 (12.8)
Mycoplasma pneumoniae	2 (5.1)
Legionella pneumophila	2 (5.1)
Pseudomonas aeruginosa	2 (5.1)
Parainfluenza virus type 3	1 (2.5)
Haemophilus influenzae	1 (2.5)
Legionella-like amoebal pathogen 4	1 (2.5)
Adenovirus	1 (2.5)
Methicillin-resistant *Staphylococcus aureus*	1 (2.5)
Bradford coccus[¶]	1 (2.5)
Escherichia coli	1 (2.5)
Mycobacterium tuberculosis	1 (2.5)

[#]: a total of 39 copathogens were identified from 26 patients; [¶]: described in [10].

Chlamydia psittaci *cases*

There were no cases of pneumonia due to *C. pecorum* or avian strains of *C. psittaci*. Two patients had IgG titres suggestive of pneumonia due to feline *C. psittaci*.

Patient 1 was a 77-yr-old female with shaking chills,

Table 4. – Clinical comparison of pneumonia patients with *Chlamydia pneumoniae* as sole pathogen and *C. pneumoniae* plus copathogens

	C. pneumoniae alone	*C. pneumoniae* plus copathogens
Male sex	8 (50.0)	17 (65.4)
Age yrs	70.6±19.2	65.1±13.7
6–15-yr-olds in household	0.0±0.0	0.2±0.4*
Smoking status		
Never smoker	5 (33.3)	2 (7.7)**
Past smoker	9 (60.0)	12 (46.2)**
Current smoker	1 (6.7)	12 (46.2)**
Hospital stay days[#]	9.00±7.30	7.58±3.49

Data are presented as n (%) or mean±SD. [#]: four outliers with hospital stays of 39, 43, 93 and 172 days were excluded. Three of the four patients had *C. pneumoniae* plus copathogens. All four outlier patients had other chronic illness and underlying respiratory disease, all had single lobar pneumonia based on chest radiography and two were admitted to the intensive care unit. Three of the four patients had their hospital discharge delayed due to other medical conditions. *: $p<0.05$ (unpaired t-test); **: $p<0.01$ (Pearson Chi-squared test).

Table 5. – Clinical comparison of *Chlamydia pneumoniae* pneumonia and bacteraemic *Streptococcus pneumoniae* pneumonia patients

	C. pneumoniae	*S. pneumoniae*	p-value
Male sex	24 (57.1)	31 (54.4)	NS
Age yrs	67.4±15.7	55.6±19.1	0.001
Pulse rate beats·min^{-1}	97.3±22.2	108.4±22.1	0.016
WBCs 10^9 cells·L^{-1}	13.6±5.5	17.4±8.6	0.011
PMNs %	82.7±16.3	66.1±28.9	0.003
P_{a,CO_2}	37.0±6.6	33.3±7.2	0.034
Mortality %	2 (4.9)	3 (5.4)	NS

Data are presented as n (%) or mean±SD. WBC: white blood cell; PMN: polymorphonuclear neutrophil; P_{a,CO_2}: arterial carbon dioxide tension; NS: nonsignificant.

nausea, vomiting, chest pain and a cough productive of yellow sputum. The oral temperature was 39°C, and crackles and wheezes were present on bilateral auscultation. The chest radiograph revealed bilateral interstitial basilar opacities. The patient was treated intravenously with cefuroxime (750 mg *t.i.d.*) and erythromycin (500 mg *q.i.d.*) for 4 days followed by cefuroxime axetil (500 mg *b.i.d.*) for 11 days and made an uneventful recovery. Acute and convalescent serum samples had IgG titres of 1:256 directed against *C. psittaci* strain FP and titres of 1:64 directed against strain CP3. Unfortunately data on pet exposure were not collected as part of the present study.

Patient 2 was a 60-yr-old female who had received cefuroxime axetil (500 mg *b.i.d.*) at home for 4 days prior to being admitted with cough, pleuritic chest pain, and shortness of breath. The oral temperature was 38.2°C, crackles and wheezes were present on auscultation over the right lung and chest radiography showed patchy opacities involving the right lung. Cefuroxime (750 mg *t.i.d.*) and erythromycin (500 mg *q.i.d.*) were administered intravenously for 2 days, followed by clarithromycin (500 mg *b.i.d.*) orally for 13 days, which led to a complete recovery. An acute phase serum sample had an IgG titre of 1:1024 directed against strain FP and 1:256 against CP3 and *C. pneumoniae*. The IgA titre directed against strain FP was 1:256 and against CP3 1:128.

Discussion

The present study highlights several features of *C. pneumoniae* seroepidemiology and pneumonia due to this microorganism. WANG and GRAYSTON [11], using a titre of 1:32 as significant or positive, found that antibody directed against *C. pneumoniae* was rare in young children but increased considerably in the 15–19-yr-old age group in Seattle and amongst 10–14-yr-olds in Denmark. The rates continued to rise until age 30–39 yrs and remained high into old age. Because of the difference in criteria for a positive test, these data are not directly comparable with the present data; however, the same general trend in seropositivity is shown in the present study.

O'NEILL *et al.* [12] tested 400 serum samples from 400 randomly selected adults in Northern Ireland using the microimmunofluoresence assay at a single dilution of 1:64. They found that 70% of patients had IgG directed against *C. pneumoniae*. Using a cut-off of ⩾1:16 it was found that 75% of the Canadian adults in the present study had IgG directed against *C. pneumoniae*, whereas 57.3% were positive if a cut-off of ⩾1:64 was used, and 67.8% if a cut-off of ⩾1:32 was used.

SAIKKU [13] tested 16,328 patients with respiratory symptoms at the University of Helsinki between 1986–1991. Using a cut-off of 1:32 as positive, it was found that seropositivity continues to increase with age up to age 90 yrs. The rate among males was higher than that among females after age 40 yrs. In this study, by the age of 90 yrs, 90% of the males and 75% of the females were seropositive. Others have also reported higher seropositivity rates in males [14–16].

In one study, seropositivity was unrelated to sex, age or smoking, but there was an inverse trend between infection and socioeconomic status, as measured by educational level achieved [12]. In contrast, in the present study of adults with CAP, current tobacco smoking, nonwhite race and higher BMI were significantly associated with *C. pneumoniae* seropositivity. Non-White subjects had a risk of 2.91 (95% confidence interval (CI) 1.04–8.12) relative to White subjects. Furthermore, subjects with a higher BMI had a risk of 1.09 (95% CI 1.04–1.15). O'NEILL *et al.* [12] also found that seropositive subjects weighed more than seronegative ones. Increased body mass is a known risk factor for coronary artery disease and recent seroepidemiological studies have associated coronary artery disease and atherosclerosis with antibody to *C. pneumoniae* [17].

The present study demonstrates that current smokers have a risk of 2.24 (95% CI 1.18–4.24) relative to patients who have never smoked. COPD was associated with *C. pneumoniae* seropositivity in the present study; however, it was not considered as a confounding factor. Two studies have found higher seropositivity rates in smokers [15, 18], whereas MENDALL *et al.* [19] did not.

In an outbreak of C. *pneumoniae* pneumonia in a nursing home, there was no difference in incidence between smokers and nonsmokers but the smokers showed an earlier onset of illness [20]. Among smokers, the median day of onset of illness after the index case resident was 16 days compared with 22 days for nonsmokers. In a population-based study, ALMIRALL *et al.* [21] found that smoking any type of tobacco had an odds ratio for CAP of 1.00 for never smokers and 1.88 for current smokers. Since the present authors studied a population of patients with pneumonia, the effect of current smoking on the rate of *C. pneumoniae* seropositivity may be confounded by the increased risk of pneumonia in this population.

Twelve of 539 (2.2%) patients had acute *C. pneumoniae* pneumonia and an additional 32 (5.9%) had possible acute infection. No differences between the two groups were found and multivariate analysis did not suggest features predictive of *C. pneumoniae* infection.

Thirty-eight per cent (16 of 42) of the present patients with acute or possible acute *C. pneumoniae* pneumonia had this microorganism as the sole infecting pathogen. This is similar to the 30.6% reported by LIEBERMAN *et al.* [22]. The copathogens in the study of LIEBERMAN *et al.* [22] and in the present study were also similar. In both studies, *S. pneumoniae* was the most common copathogen. In the present study, influenza virus type A and respiratory syncytial virus were the second and third most common copathogens, whereas, in the study of LIEBERMAN *et al.* [22], they were *M. pneumoniae* and *Legionella* sp. MCCONNELL *et al.* [23], in a study of 62 patients with *C. pneumoniae* pneumonia, divided the patients into those with primary infection (n=17) and those with recurrent infection (n=38). Seven (41%) with primary infection had a second respiratory pathogen present and seven (18%) in the recurrent infection group also had more than one respiratory pathogen present. *S. pneumoniae* and *Haemophilus influenzae* were most commonly implicated. ALMIRALL *et al.* [24] studied 105 patients with CAP and found that 16 had *C. pneumoniae* pneumonia. Seven of the 16 had a copathogen demonstrated, adenovirus in three, parainfluenza virus in two, *L. pneumophila* in one and respiratory syncytial

virus in one. FILE *et al.* [25] found that 21 of 47 (44.6%) patients with *C. pneumoniae* pneumonia had a copathogen. The consistency of these reports leaves little doubt that, in most instances, *C. pneumoniae* infection is accompanied by a copathogen.

The observation that *C. pneumoniae* induces ciliostasis in human ciliated bronchial epithelial cells suggests that this pathogen impairs normal clearance mechanisms in the respiratory tract and hence makes the host more susceptible to infection by other, more virulent, pathogens [26].

In a recent meta-analysis of *C. pneumoniae* pneumonia, mortality was 9% and associated with underlying factors or secondary infections [27]. *C. pneumoniae* mortality in the present study was low at 4.9% but this was not significantly different from the 5.4% in the bacteraemic pneumococcal pneumonia group and the 9.4% for the remainder of the cohort.

In a comparison of *C. pneumoniae* with *M. pneumoniae* and viral infections as a cause of acute respiratory disease in a university student health clinic population, THOM *et al.* [28] found that the mean number of days from onset of symptoms until enrolment was longer in patients with *C. pneumoniae* infections than in the other two groups (12.8 *versus* 7.9 and 7.3 days respectively).

The present authors found that patients with *C. pneumoniae* pneumonia were older, had a lower white blood cell count and were more likely to have congestive heart failure than patients with *S. pneumoniae* pneumonia. Furthermore, the *C. pneumoniae* pneumonia patients exhibited a higher diastolic blood pressure and arterial carbon dioxide tension than the comparison group. There were no differences in the radiographic patterns of the pneumonia or outcomes such as admission to intensive care and mortality. However, the bacteraemic *S. pneumoniae* pneumonia subjects had a shorter duration from onset of symptoms to admission and a significantly higher pulse rate and white blood cell count on admission.

FILE *et al.* [25] compared seven patients with *C. pneumoniae* primary infection (IgM-positive) with 18 reinfected patients. The mean age of those with primary infection was significantly less and mean temperature was higher for those with primary infection than for those with reinfection.

No cases of avian psittacosis were found and only two patients with possible feline *C. psittaci* pneumonia. The present data suggest that a diagnostic work-up for these pathogens should be limited to patients with epidemiological data that suggest such an infection.

The strengths of the present study are the large sample size, inclusion of patients with various underlying factors, comprehensiveness of the serological diagnostic work-up, prevalence of key CAP pathogens and identification of clinical manifestations, observation of the clinical course of CAP infection while hospitalised and the multiple-centre Canadian sites.

Some limitations exist to this study. First, the requirements for informed consent and follow-up of serological studies curtailed enrolment. Secondly, the study was performed exclusively in Canada, which may limit the general applicability of the findings. Another limitation of the study was reliance on serological techniques alone for the diagnosis of *C. pneumoniae* infection.

It is concluded that *Chlamydia pneumoniae* is an important pathogen in community-acquired pneumonia. Coinfection with other respiratory pathogens is common in patients with *Chlamydia pneumoniae* pneumonia. Avian and feline *Chlamydia psittaci* are uncommon causes of community-acquired pneumonia and should only be considered in the appropriate epidemiological setting.

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References

1. Schachter J, Stamm WE. Chlamydia. *In*: Murray PR, Baron EJ, Pfaller MA, Tenover FC, Yolken RH, eds. Manual of Clinical Microbiology. 7th Edn. Washington, DC, American Society of Microbiology, 1999; pp. 795–806.
2. Harris RL, Williams TW. Contribution to the question of pneumotyphus: a discussion of the original article by J. Ritter in 1880. *Rev Infect Dis* 1985; 7: 119–122.
3. Grayston JT, Kuo C-C, Wang S-P, Altman J. A new *Chlamydia psittaci* strain, TWAR, isolated in acute respiratory tract infections. *N Engl J Med* 1986; 315: 161–168.
4. Grayston JT, Kuo C-C, Campbell LA, *et al. Chlamydia pneumoniae* sp. nov. for *Chlamydia* sp. strain TWAR. *Int J Syst Bacteriol* 1989; 39: 88–90.
5. Dowell SF, Peeling RW, Boman J, *et al.* Standardizing *Chlamydia pneumoniae* assays: recommendations from the Centers for Disease Control and Prevention (USA) and the

Laboratory Centre for Disease Control (Canada). *Clin Infect Dis* 2001; 33: 492–503.
6. Fukushi H, Hirai K. Proposal of *Chlamydia pecorum* sp. nov. for *Chlamydia* strains derived from ruminants. *Int J Syst Bacteriol* 1992; 42: 306–308.
7. Wang S-P, Kuo C-C, Grayston JT. Formalized *Chlamydia trachomatis* organisms as antigens in the microimmunofluorescence test. *J Clin Microbiol* 1979; 10: 259–261.
8. Schachter J, Dawson CR. Human chlamydial infections. *In*: Schachter J, Dawson CR, eds. Human Chlamydial Infections. Littleton, MA, PSG Publishing, 1978; pp. 24–62.
9. Norusis MJ. SPSS 8.0. Guide to Data Analysis. Upper Saddle City, NJ, Prentice Hall, 1998.
10. Marrie TJ, Raoult D, La Scola B, Birtles RJ, de Carolis E and the Canadian Community-Acquired Pneumonia Study Group. Legionella-like and other amoebal pathogens as agents of community-acquired pneumonia. *Emerg Infect Dis* 2001; 7: 880–883.
11. Wang SP, Grayston JT. Microimmunofluorescence serological studies with the TWAR organism. *In*: Oriel D, Ridgway G, Schachter J, Taylor-Robinson D, Ward M, eds. Chlamydial Infections. Proceedings of the Sixth International Symposium on Human Chlamydial Infections. London, Cambridge University Press, 1986; pp. 329–332.
12. O′Neill C, Murray LJ, Ong GML, O′Reilly DP, Evans AE, Bamford KB. Epidemiology of *Chlamydia pneumoniae* infection in a randomly selected population in a developed country. *Epidemiol Infect* 1999; 122: 111–116.
13. Saikku P. The epidemiology and significance of *Chlamydia pneumoniae. J Infect* 1992; 25: Suppl. 1, 27–34.
14. Paltiel O, Kark JD, Leinonen M, Saikku P. High prevalence of antibodies to *Chlamydia pneumoniae*: determinants of IgG seropositivity among Jerusalem residents. *Epidemiol Infect* 1995; 114: 465–473.
15. Freidank HM, Brauer D. Prevalence of antibodies to *C. pneumoniae* TWAR in a group of German medical students. *J Infect* 1993; 27: 89–93.
16. Thom DH, Grayston JT, Siscovick DS, Wang SP, Weiss NS, Daling JR. Association of prior infection with *Chlamydia pneumoniae* and angiographically demonstrated coronary heart disease. *JAMA* 1992; 268: 68–72.
17. Grayston JT, Kuo C-C, Campbell LA, Benditt EP. *Chlamydia pneumoniae*, strain TWAR and atherosclerosis. *Eur Heart J* 1993; 14: 66–71.
18. Saikku P, Leinonen M, Tenkanen L, *et al.* Chronic *Chlamydia pneumoniae* infection as a risk factor for coronary heart disease in the Helsinki Heart Study. *Ann Intern Med* 1992; 116: 273–278.
19. Mendall M, Carrington D, Strachan D, *et al. Chlamydia pneumoniae*: risk factors for seropositivity and association with coronary heart disease. *J Infect* 1995; 30: 121–128.
20. Troy CJ, Peeling RW, Ellis AG, *et al. Chlamydia pneumoniae* as a new source of infectious outbreaks in nursing homes. *JAMA* 1997; 277: 1214–1218.
21. Almirall J, Gonzalez CA, Balanzo X, Bolibar I. Proportion of community-acquired pneumonia cases attributable to tobacco smoking. *Chest* 1999; 116: 375–379.
22. Lieberman D, Ben-Yaakov M, Lazarovich Z, *et al. Chlamydia pneumoniae* community-acquired pneumonia: a review of 62 hospitalized adult patients. *Infection* 1996; 24: 109–114.
23. McConnell CT Jr, Plouffe JF, File TM, *et al.* Radiographic appearance of *Chlamydia pneumoniae* (TWAR strain) respiratory infections. *Radiology* 1994; 192: 819–824.
24. Almirall J, Morato I, Riera F, *et al.* Incidence of community-acquired pneumonia and *Chlamydia pneumoniae* infection: a prospective multicentre study. *Eur Respir J* 1993; 6: 14–18.
25. File TM, Plouffe JF, Breiman RF, *et al.* Clinical characteristics of *Chlamydia pneumoniae* infection as the sole cause of community-acquired pneumonia. *Clin Infect Dis* 1999; 29: 426–428.
26. Shemer-Avni Y, Lieberman D. *Chlamydia pneumoniae* induced ciliostasis in ciliated bronchial epithelial cells. *J Infect Dis* 1995; 171: 1274–1278.
27. Fine MJ, Smith MA, Carson CA, *et al.* Prognosis and outcome of patients with community-acquired pneumonia: a meta-analysis. *JAMA* 1996; 275: 134–141.
28. Thom DH, Grayston JT, Wang S-P, Kuo CC, Altman J. *Chlamydia pneumoniae* strain TWAR, *Mycoplasma pneumoniae*, and viral infections in acute respiratory disease in a university student health clinic population. *Am J Epidemiol* 1990; 132: 248–256.