

# Etiology of Community-Acquired Pneumonia in Hospitalized Patients in Northern Israel

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**ABSTRACT:** **Background:** Community-acquired pneumonia is a common infection and is associated with high rates of morbidity and mortality. Most patients with CAP are treated empirically. **Objectives:** To identify common pathogens causing CAP in hospitalized patients in northern Israel and to evaluate the correlation between etiology and disease severity. **Methods:** We conducted a prospective study of patients with CAP hospitalized at HaEmek Medical Center, Afula. We collected demographic, clinical and laboratory data (blood and sputum cultures, serology, pneumococcal urinary antigen test, and respiratory multiplex-polymerase chain reaction from nasopharyngeal swab). Radiologic evaluation was performed. **Results:** A total of 126 patients and 24 controls were enrolled. At least one pathogen was identified in 84 cases (66.7%), more than one in 43 patients (34.1%), and no pathogens in 42 (33.3%). Typical bacteria were found in 23 (18.3%), atypical bacteria in 66 (52.4%), and viruses in 42 (33.3%). The number (%) of patients with pathogens isolated was: *Chlamydomphila pneumoniae* 26 (20.6%), *Streptococcus pneumoniae* 23 (18.3%), *Mycoplasma pneumoniae* 23 (18.3%), influenza virus A-B 20 (15.9%), *Coxiella burnetti* 8 (6.3%), and parainfluenza and adenovirus 13 (10.3%) each. A correlation was found only between a high PORT score on admission and *S. pneumoniae*, although atypical pathogens did not show class predominance. **Conclusions:** *S. pneumoniae*, *M. pneumoniae* and *C. pneumoniae* were the most common pathogens isolated, while co-infection was very frequent. PORT score did not predict any of the pathogens involved. The choice of empiric antimicrobial treatment for CAP should be made according to local epidemiologic data.

IMAJ 2010; 12: 477–482

**KEY WORDS:** community-acquired pneumonia, pneumonia, epidemiology of CAP, etiology of pneumonia

Community-acquired pneumonia is a common and serious infectious disease associated with high morbidity and mortality rates. It is the sixth leading cause of death and the most common infectious cause of death worldwide [1]. Approximately 914,000 cases of CAP are diagnosed yearly in the United States, accounting for 2.8% of hospital admissions. Outpatients with CAP have a mortality rate below 5%, whereas in those hospitalized (20–25% of all CAP in the U.S. and 24–28% in Europe) the mortality rate rises to 12–25% and even higher in patients requiring mechanical ventilation or admission to intensive care units.

CAP also has an economic impact, leading to high consumption rates of antimicrobial agents in both community and hospital settings. Furthermore, the high frequency of respiratory infections and the excessive use of antimicrobials are major contributors to the development of resistant pathogens.

Although prior studies have described the clinical characteristics of patients with CAP and its microbiologic causes, the etiologic factors in outpatients and hospitalized patients with CAP have not been sufficiently evaluated. In general, recommendations for antibiotic treatment are based on local epidemiology, but almost all patients with CAP are treated empirically [2] because of the lack of diagnostic methods to rapidly identify the pathogen at an acceptable cost. Giving the right therapy at the right time is imperative for a better outcome. Knowing the local epidemiology of CAP, i.e., the most frequent pathogens according to demographic and clinical characteristics, is essential for prescribing appropriate empiric therapy. However, with the exception of one study conducted in southern Israel [3] more than 15 years ago on the etiology of hospitalized patients with CAP, there are no other data on this issue in the country. We therefore decided to conduct a study to identify respiratory pathogens causing CAP in patients hospitalized in a northern Israeli community hospital and to evaluate the clinical characteristics and severity of disease related to different pathogens.

## PATIENTS AND METHODS

The study was conducted at HaEmek Medical Center, Afula, a 500-bed community teaching hospital in northern Israel, with about 600 patients/year hospitalized with CAP. This prospective observational study, conducted between November 2006 and August 2007, was approved by the hospital's Helsinki Ethics Committee and registered at the American National Institutes of Health.

We recruited 127 patients diagnosed with CAP from four internal medicine departments after they signed an informed consent form. In addition, a control group was recruited, comprising 24 patients without infectious diseases who were hospitalized in the same departments during the same period. Due to budget limitations, the control group was recruited weekly in a 1:5 ratio (one control case for every 5 study cases), with matching gender and matching age  $\pm$  5 years. The investigators did not have any influence on the decision of the emergency room physicians with regard to hospitalization and initial antibiotic treatment.

The study group consisted of patients aged  $\geq$  18 years, hospitalized in an internal medicine department with a clinical diagnosis of an acute respiratory infection (fever, cough, dyspnea, tachypnea, pleuritic chest pain) and a new chest infiltrate on X-ray at admission compatible with CAP. Excluded were immunocompromised patients (i.e., those with an active malignancy or human immunodeficiency virus, or undergoing steroid or chemotherapy treatment), patients with aspiration pneumonia, nursing home residents, and pregnant women. CAP was defined as a diagnosis of pneumonia within 48 hours of admission in a patient who acquired the infection in the community. Both CAP and control group patients underwent the same evaluation, including:

- Demographic data (age, gender, smoking history, alcohol abuse)
- Underlying diseases (diabetes mellitus, arterial hypertension, chronic lung disease, congestive heart failure)
- Severity of disease: PORT score system [4]
- Outcome: hospital mortality rate and 30 day follow-up
- Antibiotic treatment before admission
- Laboratory tests directed at an etiologic diagnosis: at least two blood culture sets and one sputum culture obtained on admission. Blood cultures were processed by BACTEC 9000 technology and incubated for 7 days. Sputum cultures were categorized using the  $\geq$  25 white blood cells/ $<$  10 epithelial cell/field score, and further cultured using conventional methods. Pathogens were identified using VITEK cards (Bio-Merieux, France) and a VITEK-II system.

Two nasopharyngeal swabs (COPAN Cat # 503CS01) were collected on admission from each patient. The swab shafts were cut and the swab tips were placed in a tube containing poly-

merase chain reaction transport medium (Hy Laboratories, Rehovot, Israel) and stored at 2–8°C until processed. The following pathogens were investigated using two multiplex-PCRs (for RNA and DNA respectively): *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Legionella pneumophila*, adenovirus, influenza A virus, influenza B virus, respiratory syncytial virus, human metapneumovirus, and parainfluenza virus. DNA and RNA isolation were done with Genomic Extraction 100 reactions Bioneer (Cat.K-3032) and Pure Art Viral RNA QIAGEN (Ref: 90206-50 RNA) respectively.

Detection of DNA for *L. pneumophila*, *C. pneumoniae*, and *M. pneumoniae* was performed by a double amplification system nested method using Clonit AMS27-2/7, AMS25-2F, AMS26-2F respectively. Respiratory virus RNA (human adenovirus, influenza A virus, influenza B virus, human parainfluenza 1/2/3 virus, RSV A/B) were detected by DPO™ based multiplex PCR (Seegene, Cat. RV 2210 RV).

Antibodies for the following pathogens were investigated in two serum samples obtained on admission and after 14–21 days:

- *C. pneumoniae* immunoglobulin M, A and G using a micro-immunofluorescence assay (Chlamydia MIF, FOCUS Diagnostics, Cypress, CA, USA). Positive results were the presence of IgA or IgM, a twofold rise in IgG titer between acute and convalescent samples, or IgG titer  $\geq$  1:256.
- *M. pneumoniae* using an enzyme-linked immunosorbent assay: *Mycoplasma pneumoniae* ELISA (recombinant) IgM (Genzyme Virotech GmbH, Rüsselsheim, Germany). A positive result was the presence of IgM.
- *Coxiella burnetti* (Q fever) IgM using an ELISA test (*Coxiella burnetti* IgM ELISA, Panbio Diagnostics, Brisbane, Australia) and phase I and phase II antibodies using immunoblot test (ImmunoDOT™ *Coxiella burnetti*, Q fever; GenBio, San Diego, CA, USA). A positive result was the presence of IgM or IgG phase II.
- Adenovirus, influenza A-B virus, parainfluenza virus, and RSV using complement fixation test. A positive result was a fourfold rise in antibodies titer between acute and convalescent samples.
- Lastly, a urine sample was taken at admission and the presence of *S. pneumoniae* antigen was tested using the Binax NOW test (Binax NOW *S. pneumoniae* antigen test; Binax, Scarborough, ME, USA).

## STATISTICAL ANALYSIS

SPSS software was used for the analysis of the data. Qualitative variables were compared with the chi-square test. The level of significance was  $P \leq 0.05$ .

PCR = polymerase chain reaction

RSV = respiratory syncytial virus

Ig = immunoglobulin

ELISA = enzyme-linked immunosorbent assay

**RESULTS**

The study group comprised 127 hospitalized patients with CAP. One patient, included initially, was later diagnosed with lung cancer and therefore excluded from data analysis; 126 patients remained in the study group. Twenty-four patients without infectious diseases (age matched ± 5 years) were recruited as a control group. Significantly more patients in the study group were smokers and bedridden. Eighty-nine patients (70.6%) were evaluated 14–28 days after recruitment for a second serum sample. Demographic and clinical data are shown in Table 1.

At least one pathogen was found in 84 patients (66.7%) and two or more pathogens in 43 patients (34.1%). In 42 patients (33.3%) we failed to identify a respiratory pathogen [Table 2]. The distribution of isolates among the 84 patients with positive results was *S. pneumoniae* 18.3%, atypical pathogens 52.4% and viruses 45.2%. The most frequent isolates were *C. pneumoniae* (20.6%), influenza virus A or B (19.0%), *S. pneumoniae* (18.3%) and *M. pneumoniae* (18.3%). Analysis of pathogen distribution and clinical and laboratory characteristics of patients (age, gender, functional status, chronic obstructive pulmonary disease, smoking history, leukocytes, oxygen saturation) were not statistically significant.

Altogether, 144 samples carried respiratory pathogens in 84 patients. Seven blood cultures and one sputum sample grew *S. pneumoniae*. Eighteen patients had positive pneumococcal urinary antigen, one of them with positive sputum and three with positive blood culture. In addition, 90 blood tests and 45 positive PCR tests yielded positive results [Table 2]. *C. pneumoniae*

**Table 1.** Clinical and demographic characteristics of patients

	CAP group (n=126) (100%)	Control group (n=24) (100%)	P value
<b>Age (yrs)</b>			
Range	18-93	23-86	
Mean (SD)	58.3 (± 20.3)	56.3 (± 5.0)	
Median	62	58	
<b>Gender</b>			
Men	73 (57.9%)	9 (37.5%)	
Women	53 (42.1%)	15 (62.5%)	
<b>Functional status</b>			
Independent	109 (86.5%)	24 (100%)	0.04**
Non-institutionalized bedridden	17 (13.5%)	0 (0%)	0.07***
<b>Smoking (present or past)</b>	53 (42.1%)	4 (16.6%)	0.03*
<b>Comorbidities</b>			
Diabetes, COPD, hypertension, congestive heart failure, chronic renal failure	85 (67.5%)	14 (58.3%)	
<b>Mortality</b>	5 (3.96%)	0 (0%)	

\* Yates corrected test

\*\* Fisher exact test one-tailed P value

\*\*\* Fisher exact test two-tailed P value

COPD = chronic obstructive pulmonary disease

**Table 2.** Distribution of pathogens and diagnostic tests

Pathogen identified	Patients n (%)	Diagnostic test				
		PCR	Serology	Blood culture	Sputum culture	Pneumo-coccal urinary Ag
No pathogen	42 (33.3)	–	–	–	–	–
At least one pathogen	84 (66.7)					
Combined pathogens*	43 (34.1)					
<i>C. pneumoniae</i>	26 (20.6)	2	25	ND	0	ND
<i>S. pneumoniae</i>	23 (18.3)	ND	ND	7	1	18
<i>M. pneumoniae</i>	23 (18.3)	23	6	ND	0	ND
<i>L. pneumophila</i>	9 (7.1)	9	ND	ND	0	ND
<i>C. burnetti</i>	8 (6.3)	ND	8	ND	0	ND
Influenza A	13 (10.3)	4	13	ND	ND	ND
Influenza B	11 (8.7)	0	11	ND	ND	ND
Parainfluenza	13 (10.3)	1	13	ND	ND	ND
RSV	9 (7.1)	2	7	ND	ND	ND
Adenovirus	7 (5.5)	0	7	ND	ND	ND
HMPV	4 (3.2)	4	ND	ND	ND	ND
Total	126 (100)					

\*Combined pathology: more than 1 pathogen

RSV = respiratory syncytial virus, HMPV = human metapneumovirus

was identified in 25/26 cases by serology (96.15%) while PCR showed a low sensitivity (only two were positive, 7.69%).

The best test for the diagnosis of *M. pneumoniae* was PCR, which detected all 23 cases (6 were detected also by serology). *L. pneumophila* was found in nasopharyngeal swabs by PCR in nine patients (7.1%); unfortunately we were not able to check urinary antigen for this pathogen. The majority of viruses and *C. burnetti* were identified by serology; PCR showed a low sensitivity for these pathogens.

The most frequent combinations of pathogens were *S. pneumoniae* with *C. pneumoniae* (5 patients), parainfluenza (n=5) and influenza B (n=4); parainfluenza with influenza A (n=5) and B (n=7); *M. pneumoniae* with *C. pneumoniae* (n=4); and *C. pneumoniae* with influenza B (n=4) [Table 3].

All blood cultures, sputum cultures and PCR were negative in the control group, but five control patients tested positive by serologic methods for *C. pneumoniae* (20.8%), three (12.5%) for single or combined viral pathogens (adenovirus, RSV, influenza A-B, parainfluenza), and one (4.1%) for pneumococcal antigen in urine.

Of the 126 patients 96 (76.2%) did not receive antimicrobials before admission; in 62 of them (64.5%) a respiratory pathogen was found. Despite the fact that 30 patients received antimicrobials before recruitment, the use of multiple diagnostic methods enabled the identification of respiratory pathogens in 22 of them (73.3%, not significant).

**Table 3.** Number of patients presenting combination of pathogens

	CP	SP	MP	LP	CB	IA	IB	PI	RSV	AV	HMPV
<i>C. pneumoniae</i> (CP)	–	5	4	2	3	3	4	3	2	3	1
<i>S. pneumoniae</i> (SP)	5	–	1	2	1	2	4	5	0	0	
<i>M. pneumoniae</i> (MP)	4	1	–	1	2	2	3	3	0		
<i>L. pneumoniae</i> (LP)	2	2	1	–	2	0	0	0			
<i>C. burnetti</i> (CB)	3	1	2	2	–	0	0				
Influenza A (IA)	3	2	2	0	0	–					
Influenza B (IB)	4	4	3	0	0						
Parainfluenza (PI)	3	5	3	0							
RSV	2	0	0								
Adenovirus (AV)	3	0									
HMPV	1										

RSV = respiratory syncytial virus, HMPV = human metapneumovirus

**Table 4.** Correlation between respiratory pathogen and severity of CAP by PORT score class

Pathogen isolated	PORT Score Class		
	Mild CAP I-II n = 74 (58.7%)	Moderate CAP III n = 31 (24.6%)	Severe CAP IV-V n = 21 (16.7%)
<i>C. pneumoniae</i>	17 (22.9)	6 (19.3)	3 (14.2)
<i>S. pneumoniae</i>	12 (16.2)**	3 (9.6)*	8 (38.0)
<i>M. pneumoniae</i>	17 (22.9)	4 (12.9)	2 (9.5)
<i>L. pneumophila</i>	6 (8.1)	2 (6.5)	1 (4.7)
<i>C. burnetti</i>	8 (10.8)	0	0
Influenza A	7 (9.4)	3 (9.6)	2 (9.5)
Influenza B	8 (10.8)	1 (3.2)	2 (9.5)
Parainfluenza	8 (10.8)	3 (9.6)	2 (9.5)
RSV	5 (6.7)	3 (9.6)	1 (4.7)
Adenovirus	6 (8.1)	1 (3.2)	0
HMPV	2 (2.7)	0	2 (9.5)
No pathogen	15 (20.2)	18 (58.0)	9 (42.8)
<b>Total</b>	<b>74 (100)</b>	<b>31 (100)</b>	<b>21 (100)</b>

Values are presented as no. (%)

\* $P = 0.03$  between moderate and severe CAP\*\* $P = 0.02$  between mild and severe CAP

RSV = respiratory syncytial virus, HMPV = human metapneumovirus

The correlation between respiratory pathogens and PORT score was explored. The PORT score [4] was calculated for every patient to assess the severity of disease and to determine whether there was a correlation between severity class and the identified respiratory pathogen. Most patients (58.8%) belonged to the mild CAP category (class I: 39, 31%; class II: 35, 27.8%). Moderate CAP (class III) was diagnosed in 31 patients (24.6%) and severe CAP in only 16.6% (class IV: 12, 9.5%; class V: 9, 7.1%) [Table 4]. The most frequent pathogens identified

in mild CAP were *C. pneumoniae* and *M. pneumoniae* (22.9% each), and *S. pneumoniae* (16.2%); in moderate CAP the most frequent were *C. pneumoniae* and *M. pneumoniae* (19.3% and 12.9% respectively). Patients with *S. pneumoniae* were more frequently diagnosed when CAP was severe than when the disease was moderate or mild (38.0% vs. 9.6% and 16.2%,  $P = 0.03$  and  $P = 0.02$  respectively) [Table 4]. In general, there was a wide distribution of pathogens in all severity risk classes: *S. pneumoniae* was found in 16% of mild CAP, while 'atypical pathogens' were also seen in severe CAP.

Four patients (3.2%) were transferred to another hospital, and five died during hospitalization (mortality rate 3.96%) [Table 1]. Four of the five patients who died were diagnosed with *S. pneumoniae*, but no pathogen was found in the last patient. All of them belonged to a high risk class according to PORT score.

## DISCUSSION

This is the first study conducted in northern Israel and the second one in the country to identify respiratory pathogens in patients hospitalized due to CAP. The previous study was carried out in southern Israel 15 years ago [3]. No data are available from many areas of the world. Although *S. pneumoniae* is a leading cause of CAP worldwide, the incidence of other pathogens depends on geographic and population factors [5].

Comparing our study to the previous one, two important factors should be considered: the different laboratory tests used for pathogen identification, and the variation of epidemiology over time [5]. The two Israeli studies differ in several aspects [3]. The southern study included 346 cases, almost three times more than ours, and identified etiologic agents in 80.6% of their patients, a rate higher than ours (66.7%). Similar rates of combined etiologic agents were found in both: 38.4% in the southern study vs. 34.1% in ours. *C. pneumoniae*, *S. pneumoniae* and *M. pneumoniae* were the most common respiratory pathogens in both studies, but most pathogens showed significant differences in their distribution: *S. pneumoniae* was detected in 42.8% vs. 18.3%, *M. pneumoniae* in 29.2% vs. 18.3%, *C. pneumoniae* 17.9% vs. 20.6%, *L. pneumophila* 16.2% vs. 7.1%, *Coxiella burnetti* 5.8% vs. 6%, and viral pathogens 10.1% vs. 45.2% (the southern vs. our study respectively) [3]. *L. pneumophila* showed a very low prevalence in our sample compared to previous Israeli data, perhaps because the urinary antigen test was not performed; on the other hand, the higher rates of viral pathogens that we found as a single or combined agent can probably be attributed to the new laboratory tests that were used (PCR of nasopharyngeal swab).

The rate of pathogen detection (66.7%) and pathogen distribution in our study is in accordance with epidemiologic

studies worldwide, which identified respiratory pathogens in 50–70% of CAP cases, and found *C. pneumoniae*, *S. pneumoniae* and *M. pneumoniae* to be the most common respiratory pathogens [2,5–10]. *S. pneumoniae* is still the single most common defined pathogen in nearly all studies of hospitalized patients with CAP. Other bacteria commonly isolated in sputum cultures are *Haemophilus influenzae*, *Staphylococcus aureus* and Gram-negative bacilli, but their role is often disputed. The diagnostic value of Gram stain and sputum culture has been debated for two decades [1,11,12]. Common problems are that 10–30% of CAP patients have a non-productive cough, 15–30% receive antimicrobials before hospital admission, and negative results are reported in 30–65% of sputum samples. In general, blood and sputum cultures have a high specificity but low sensitivity for identification of respiratory pathogens [13], and the use of pneumococcal urinary antigen test (sensitivity 70–90%, specificity 80–100%) [8,13] improves the rate of etiologic diagnosis. *S. pneumoniae* was diagnosed in our study in 23 patients (18.3%), which is in the lower scale of the range of 12–76% reported in the literature [1–3,8,10]. The decrease in the relative frequency of identified pneumococcal cases of CAP has been described elsewhere, although the reasons for this decrease are not clear [14,15]; possibilities include pneumococcal vaccination (not evaluated in our study), preadmission treatment with antibiotics (urinary antigen may reduce this factor), and low severity index of CAP [13].

In our study, *S. pneumoniae* was distributed through all the class groups but was more significant in severe CAP, where it was responsible for the death of four patients. The best diagnostic test for *C. pneumoniae* in our study was serology (25 positive tests, 19.8%). The rate of *C. pneumoniae* that we found was similar to previous reports [1–3]. It is noteworthy that five patients (20.8%) in the control group also had a positive serologic test, which could indicate present or past infection, or respiratory mucosal colonization. The value of PCR for respiratory samples should not be underestimated: in 73.3% of the patients treated by antimicrobials before enrollment we successfully identified an etiologic agent.

Diagnosis of *M. pneumoniae* can be done by serology (agglutination, complement fixation and ELISA) but is often confounded by interspecies cross-reaction [16]. PCR has been recommended for *M. pneumoniae* detection because of its high sensitivity, specificity and rapid results. *M. pneumoniae* is not part of the normal flora and its presence is frequently associated with infection [1,3,5,7,10,17], and in asymptomatic cases suggests colonization rather than infection [17]. Because at present there are no standardized diagnostic methods [18], a combination of serology and PCR of nasopharyngeal swabs is recommended for the reliable diagnosis of *M. pneumoniae* [17]. The best diagnostic tools for the detection of *L. pneumophila* are the combination

of PCR of nasopharyngeal swabs together with the urinary antigen test [17,19]. One of the limitations of our study was the lack of urinary test for *L. pneumophila* antigen. We found a prevalence of 7.1% by PCR of nasopharyngeal swabs, which was lower than the earlier Israeli study. *L. pneumophila* DNA PCR of nasopharyngeal swab is a good diagnostic test [13], but its sensitivity decreases within 3 days and turns negative after 4–6 days of antimicrobial therapy [19]. The fact that 23.8% of the patients in our study received antibiotics before admission at least partially explains our findings. Moreover, the prevalence of causative pathogens may vary geographically and over time, a point that few studies have investigated [1,2,5,10]. We believe that the prevalence of *L. pneumophila* in Israel needs to be reevaluated to clarify whether there is a geographic or time frame variation, or if we missed cases because of the omission of the urinary test [13].

The prevalence of *C. burnetti* was stable along time: 5.8% in 1991–92 [3] to 6.3% in 2006–07 – which was notably higher than reported in some European countries, hinting at endemic status in our region [3,5,9,20]. This finding is important, suggesting that empiric antimicrobial treatment be considered.

More than half of our patients were classified as mild CAP. Why were these patients hospitalized? It is widely recognized that severity indexes are based mainly on the risk of death among older people and may underestimate the severity of disease in young patients [14]. Thus, the fact that the majority of our patients were young (mean age 58.3, range 18–93) can explain the low score index and low mortality rate: zero in class I–III and 5/21 patients (23.8%) in class IV–V. The overall mortality in study patients was 3.96%, but does not preclude the need for admission for treatment [4,14].

The correlation between respiratory pathogens and severity of disease is a relevant but unresolved issue. We found that *C. pneumoniae* and *M. pneumoniae* were more frequent but not exclusive of mild CAP (22.9% each, not significant); furthermore, more patients with *S. pneumoniae* were diagnosed as severe CAP than as mild to moderate CAP (38% vs. 16.2%,  $P = 0.02$ ) (38% vs. 9.6%,  $P = 0.02$ ). Moreover, all the pathogens were identified in each CAP severity class, but in our sample we could not predict an etiologic agent by PORT class.

To the best of our knowledge the present study is the second to evaluate the etiology of CAP in Israel [3] and the first after 15 years using novel diagnostic tools for the identification of CAP etiology. Nonetheless, we are aware of several limitations. First, the small number of patients recruited may not be representative of the entire population, even on a regional scale. Other limitations are the low severity index of CAP patients in the sample, the lack of urinary antigen test for *L. pneumophila*, and the high prevalence of positive serology to *C. pneumoniae* in the control group, similar to the prevalence in CAP patients.

This probably indicates an old infection in both groups and should be considered as a suspected, presumptive, or possible cause of the current infection.

In conclusion, despite the limitations in our study we found respiratory pathogens in two-thirds of CAP patients in northern Israel, using varied and modern diagnostic tests. Our findings provide primary care physicians and emergency room teams with knowledge of the local epidemiologic patterns, emphasizing the role of atypical bacterial and viral pathogens as etiologic agents of CAP, together with higher rates of *S. pneumoniae* in severe CAP. Periodic surveys are also required in other areas of the country to assess the regional variability in the epidemiology of CAP so that preventive measures can be taken and therapeutic approaches implemented.

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#### Acknowledgments:

The study was funded by Theravance Inc (USA) (Dr. Michael Kitt) and the Rochlein Fund, HaEmek Medical Center.

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