2221. *Chlamydia pneumoniae* (Cpn) Induces IFN-γ Responses in Peripheral Blood Mononuclear Cells (PBMC) from Pediatric and Adult Asthma Patients: Effects of Age and Inhaled Corticosteroid Use

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Background. Chlamydia pneumoniae (Cpn) is unique in its ability to cause chronic infections, potentially triggering asthma exacerbations as well as subsequent asthma development. Th1-mediated immunity and IFN-γ are critical for clearing chlamydial infections. Persistent or recent Cpn infection may be identified in vitro by detecting T-helper cytokine IFN-γ produced by peripheral blood mononuclear cells (PBMC) stimulated by Cpn. Inhaled corticosteroids (ICS) may have an inhibitory effect on IFN-γ. Prior studies have shown increased Th2 responses upon in vitro Cpn stimulation with increased age. Our aim was to determine whether age and inhaled corticosteroid (ICS) use affect Cpn-induced PBMC produced IFN-γ levels.

Methods. Pediatric and adult subjects with (n = 23) and without (n = 10) asthma were enrolled. PBMC obtained from all subjects were stimulated with Cpn (MOI = 0.1 x48h) in vitro. IFN-γ levels in culture supernatants were determined by ELISA and reported as pg/mL. Nasopharyngeal (NP) swabs were tested for Cpn using Real-Time PCR. Statistical analysis for continuous variables was performed using the Mann–Whitney U test.

Results. None of the subjects were positive for Cpn by PCR on NP swab. Levels of IFN-γ produced by PBMC stimulated by Cpn were similar between asthmatic vs. control subjects (41.7 vs. 68.8, respectively; P = 0.72) and between pediatric and adult subjects with asthma (IFN-γ 54 vs. 20.1 respectively, P = 0.95). Pediatric subjects with asthma who received ICS had lower IFN-γ levels than those who did not (median IFN-γ 25.5 vs. 209; P = 0.003).

Conclusion. Our finding of lower IFN-γ levels among asthma patients on ICS compared with those not on ICS suggests that ICS use may dampen the systemic inflammatory response. While we did not find a statistically significant difference between pediatric and adult age groups in this pilot study, there was a trend to higher Cpn-induced IFN-γ levels among younger pediatric subjects. Future prospective studies should further define predictors of diminished IFN-γ responses in patients with asthma.

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2222. Impact of Empiric Aminoglycoside Usage on Outcomes in Bacterial Pneumonia

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Background. Although aminoglycosides are recommended as part of empiric combination therapy in selected patients with healthcare-associated pneumonia, their efficacy and safety remains unclear. The objectives of this study were to evaluate the impact of empiric aminoglycoside treatment on microbiologic cure, recurrent pneumonia and death, and acute kidney injury (AKI) among hospitalized patients treated for pneumonia who were clinically cured.

Methods. This was a nested cohort study including 441 hospitalized subjects with confirmed bacterial pneumonia who achieved clinical cure. All subjects had positive respiratory cultures at the beginning of therapy and also had cultures obtained at the time of antibiotic completion. Subjects with the same pathogen present at both the beginning of and at the end of treatment were categorized as microbiologic failure and all others were categorized as microbiologic cure. Serum creatinine was measured at both the beginning and end of therapy, with an absolute increase in serum creatinine of 0.5 mg/L or greater defined as AKI. Composite outcomes of 30- and 90-day recurrent pneumonia or death following the clinical cure of the index pneumonia were captured. Patients who received empiric aminoglycoside therapy were compared with patients who did not receive aminoglycoside therapy.

Results. Of 441 included subjects, 14.5% (N = 64) received aminoglycoside therapy and 85.5% (N = 377) did not. The mean age was 54.7 years, with 70.5% male and 78.2% white. Characteristics of the two groups (including Charlson Comorbidity Indices and APACHE II scores) were similar. Rates of microbiologic cure, death/recurrent pneumonia at 30- and 90-days and AKI and were similar in both groups (table). In subgroup analyses restricted to different pathogen groups these associations remained unchanged.

Conclusion. Among hospitalized patients with pneumonia who were clinically cured, empiric aminoglycoside therapy was not associated with an increased likelihood of microbiologic cure, death or recurrent pneumonia or AKI.

TABLE 1. Rates of microbiologic cure, death and recurrent pneumonia and acute kidney injury among hospitalized patients treated with and without empiric aminoglycosides for pneumonia.[£]

All patients	**No empiric aminoglycoside (N=377)**	**Empiric aminoglycoside (N=64)**	**p-value**
Microbiologic Cure, No (%)	203 (53.9)	34 (53.1)	1.00
30-day death and/or recurrent pneumonia, No (%)	140 (37.1)	25 (39.1)	0.78
90-day death and/or recurrent pneumonia, No (%)	164 (43.5)	30 (46.9)	0.68
AKI, No (%)	54 (14.3)	10 (15.6)	0.85
S. aureus	**No empiric aminoglycoside (N=131)**	**Empiric aminoglycoside (N=16)**	
Microbiologic Cure, No (%)	63 (48.1)	11 (68.8)	0.18
30-day death and/or recurrent pneumonia, No (%)	49 (37.5)	4 (25.0)	0.42
90-day death and/or recurrent pneumonia, No (%)	56 (42.8)	6 (37.5)	0.79
AKI, No (%)	14 (10.7)	3 (18.8)	0.40
Nonfermenting gram-negative bacilli*	**No empiric aminoglycoside (N=113)**	**Empiric aminoglycoside (N=26)**	
Microbiologic Cure, No (%)	31 (27.4)	9 (34.6)	0.49
30-day death and/or recurrent pneumonia, No (%)	42 (37.2)	11 (42.3)	0.66
90-day death and/or recurrent pneumonia, No (%)	48 (42.5)	13 (50.0)	0.52
AKI, No (%)	24 (21.2)	5 (19.2)	1.00
Enterobacteriaceae**	**No empiric aminoglycosides (N=124)**	**Empiric aminoglycosides (N=24)**	
Microbiologic Cure, No (%)	76 (61.3)	10 (41.7)	0.11
30-day death and/or recurrent pneumonia, No (%)	58 (46.8)	13 (54.2)	0.66
90-day death and/or recurrent pneumonia, No (%)	69 (55.7)	14 (58.3)	1.00
AKI, No (%)	16 (12.9)	4 (16.7)	0.74

[£]Aminoglycosides include IV tobramycin, IV gentamicin and IV amikacin.

*Nonfermenting gram-negative bacilli defined as *Pseudomonas aeruginosa, Acinetobacter baumannii, Stenotrophomonas maltophilia*.

***Enterobacteriaceae defined as *E. coli, Proteus spp., Klebsiella spp., Enterobacter spp., Citrobacter spp. and Serratia spp.).*

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2223. Real-time Prediction of Respiratory Pathogen Infection Based on Machine Learning Decision Support Tool

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Background. Respiratory pathogens are a common cause of disease. Currently there is not a practical tool to predict the putative etiology of each case with an inexpensive, fast point-of-care assay. Here, we describe a decision support tool that enables the prediction of both bacterial and viral respiratory pathogen infections in a single patient, using a Machine Learning model.

Methods. The data were obtained from the Hadassah-Hebrew University Medical Center during a period of 10 years beginning from 2007 and contained more than 40,000 patients from a 1,000,000-population community for whom specimens were tested by either PCR or culture. The pathogens included were, *H. influenzae*; *M. catarrhalis*; *S. pneumoniae*; *M. pneumoniae*; Adenovirus; Human metapneumovirus; Influenza H1N1, A, B; parainfluenza 1,2 and 3; and RSV. We then created a Machine-Learning algorithm to simulate the spread of infection in the entire Jerusalem area. We defined transmission areas based on geographical distances of patients' home-addresses. Then we prospectively tested the tool accuracy over a 4-month period, in addition to real-time improvement of the model.

Results. Initial model was created based on gender, age, home addresses and the diagnostics test results. We then reconstructed a putative spread pattern for each of the pathogens that can be correlated to potential "transmission routes." The initial prediction tool had an AUC for most pathogens around 0.85. It ranged from 0.75 to 0.8 for the bacterial and 0.82 to 0.89 for the viral pathogens. In almost all pathogens the NPV was 0.98–0.99. We then tested the decision support tool prospectively over four consecutive months (January to April 2019—1,700 patients with respiratory complaints from whom samples were sent to the lab). While the AUC in the prospective cohort was 0.81 on average, the NPV remained high on 0.98.

Conclusion. The implementation of the decision support tool on respiratory pathogen diagnostics enables better prediction of patients not infected with either viral or bacterial pathogens. The use of such a tool can save more than 50% of diagnostic tests expenses as well as real-time mapping of disease spread. Improvement of the Machine Learning protocol may further promote the optimization of positive predictive values.

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