

Background. Parechovirus-A3 (PeV-A3) is an emerging pathogen causing sepsis and meningoenzephalitis in neonates and young infants. We previously reported that maternal antibodies against PeV-A3 are important to protect neonates and young infants from the infection. We showed that all neonates and infants who developed PeV-A3-related diseases had low neutralizing antibody titers (NATs) against PeV-A3 at the onset of disease, subsequently developed high NATs at 3 and 6 months of age. Subsequent changes in NATs against PeV-A3 in children who suffered from PeV-A3-related diseases are currently unknown. Additionally, their long-term neurological outcome is not well described in such population.

Methods. Subjects were PeV-A3-infected infants less than 4 months in Niigata, Japan during 2013–2014, and follow-up serum samples were obtained longitudinally from the patients at 3, 6 months, 1 and 3 years after the infection. NATs against PeV-A3 were measured using LLC-MK2 cells. Neurological outcomes of the patients were evaluated by their pediatricians at their study visits.

Results. We evaluated 45, 34, 33, 26, and 16 serum samples at onset, 3, 6 months, 1 and, 3 years after the infection, respectively. All 45 serum samples at onset had low NATs against PeV-A3 less than 1:32 which was regarded as a cutoff to prevent PeV-A3 infection. Subsequently, the NATs had elevated to the high level ($\geq 1:512$) after the infection in all patients. Three years after the infection, all patients except one achieved normal neurodevelopmental milestones. Only one patient who was diagnosed as severe status epilepticus due to meningoenzephalitis had developmental delay with difficulties in sitting and walking with support.

Conclusion. This study showed that NATs against PeV-A3 sustained high levels in patients who had severe PeV-A3-related diseases in their neonatal or young infantile periods. Neurological outcomes of the patients who suffered from PeV-A3-related diseases seem to be excellent, except for the case with complicated clinical course.

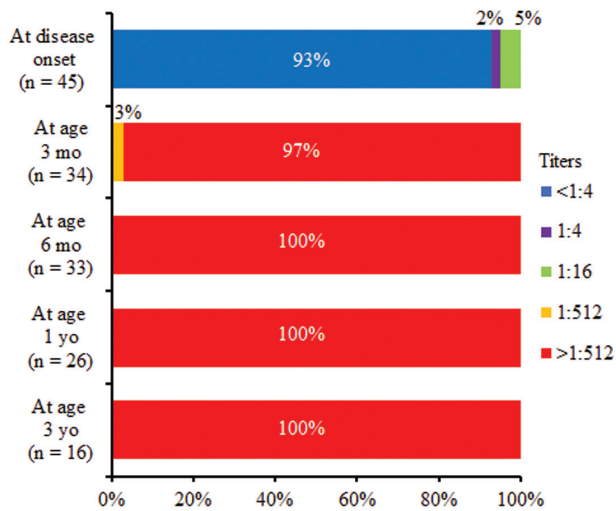


Figure Changes in neutralizing antibodies against parechovirus-A3 (PeV-A3) during the 3 years after the infection in neonatal or young infantile periods.

Disclosures. All authors: No reported disclosures.

2350. Parainfluenza Virus Infection Factors: 18 Years' Active Surveillance in a Pediatric Hospital

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Session: 248. Pediatric Viral Infections

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Background. Parainfluenza virus (PIV) is an important cause of acute lower respiratory tract infection (ALRI), hospitalization and mortality in children. The aims of this study were to describe the clinical-epidemiologic pattern and infection factors associated with PIV.

Methods. Prospective, cross-sectional study of patients admitted for ALRI 2000–2017, diagnosed with respiratory syncytial virus, adenovirus, influenza or parainfluenza by fluorescent antibody (FA) or real-time polymerase chain reaction (RT-PCR) assay of nasopharyngeal aspirates.

Results. From a total of 15,451 patients included, 13,033 were tested and 45% (5831) had positive samples; RSV was predominant (81.3%, 4738) all through the study period, followed by IF: 7.6% (440), PIF 6.9% (402) and AV: 4.3% (251). PIV followed a seasonal epidemic pattern predominantly during spring months

(September– October). The median age of cases was 8 months (IQR: 4–13 months); 54% of cases were males. The most frequent clinical presentation was bronchiolitis (61%); 53% had previous admissions for respiratory causes, 9% were readmissions. Comorbidity was found in 59.4%: recurrent respiratory disease (47.8%), congenital heart disease (5.7%), chronic neurological disease (6.5%); 8.5% were malnourished, 23% born preterm and 3.3% immunosuppressed; 23.5% had complications, 10.6% hospital-acquired infections. Lethality was 3.5% (14/396).

The following were independent predictors for PIF infection: recurrent respiratory disease odds ratio (OR): 1.65 (95% CI: 1.32–2.08); $P < 0.001$; readmissions, OR 1.95 (95% CI: 1.34–2.83); $P < 0.001$; born preterm, OR: 1.58 (95% CI: 1.19–2.10); $P = 0.001$.

Conclusion. Parainfluenza infection showed an epidemic seasonal pattern (September–October), with higher risk in children with recurrent respiratory disease, prematurity and previous admissions for respiratory causes.

Disclosures. A. Gentile, Sanofi Pasteur: Consultant, Speaker honorarium.

2351. Epidemiology and Clinical Characteristics of Parainfluenza Virus Type 4 in Korean Children, 2015–2017

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Session: 248. Pediatric Viral Infections

Saturday, October 6, 2018: 12:30 PM

Background. Human parainfluenza viruses (HPIVs) are one of common causes of respiratory tract infections in children. Among the four serotypes (HPIV-1–4), little is known about the epidemiology and clinical characteristics of HPIV-4. The aim of this study was to identify the epidemiology and the characteristics of HPIV-4 compared with HPIV-1–3 in Korean children.

Methods. We reviewed medical records of children with HPIV who had been admitted at Seoul National University Children's Hospital during 2015–2017. Detection of respiratory viruses in nasopharyngeal aspirates was performed using multiplex reverse transcription polymerase chain reaction. Patients who had underlying medical conditions such as chronic respiratory disease, immunodeficiency, congenital heart disease, or concurrent viral infections were excluded.

Results. Of 12,539 samples, 586 (8.1%) were positive for HPIV. By the exclusion criteria, 137 (23.4%) were finally included: 46 (33.6%) for HPIV-3, 34 (24.8%) for HPIV-1 and -4 respectively, 23 (16.8%) for HPIV-2. During the study period, two seasonal outbreaks were observed in each serotype. HPIV-1 was prevalent in September 2015 and August 2016, while HPIV-2 in August 2015 and July 2017. The peak of HPIV-3 infection occurred in July 2016 and May 2017. HPIV-4 was mostly infected from August to September in 2015 and in June 2017. Regardless of serotypes, HPIV was predominantly observed in boys and among children less than 5 years of age (70%); the median age in HPIV-4 was 3.1 (0–18) years. The most common clinical presentation was cough in all serotypes (78.7–88.2%). Sore throat was mainly presented in HPIV-4 infected patients compared with other serotypes (11.8%; $P = 0.029$). HPIV-4 infection was more often diagnosed as bronchiolitis (32.4%) compared with HPIV-1 (8.8%; $P = 0.016$) and -2 (8.7%; $P = 0.037$). Croup was most frequently diagnosed in children with HPIV-2 (21.7%), but no patients with HPIV-4 had croup ($P = 0.008$).

Conclusion. We observed seasonal peak in HPIV-4 from late spring to autumn. Lower respiratory tract infection was main clinical manifestation in HPIV-4 among hospitalized patients and HPIV-4 is a common respiratory pathogen causing significant morbidity in Korean children during 2015–2017.

Disclosures. All authors: No reported disclosures.

2352. Increased on Childhood Recurrent Wheezing and Asthma After Respiratory Syncytial Viral (RSV) Infection in Full-Term Infants

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Background. Studies suggest that RSV infection early in life is associated with the development of recurrent wheezing, yet, information on large population-based studies among US full-term healthy infants is incomplete. The objective of this study was to evaluate the risk of developing post-RSV recurrent wheezing/asthma during childhood among full-term infants in a US commercially insured population.

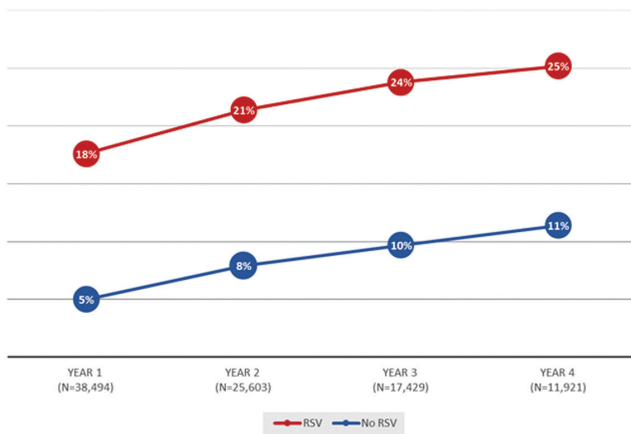
Methods. Retrospective, observational study used data from Truven MarketScan Commercial Claims and Encounters Database (January 1,

2000–December 31, 2016) to identify full-term infants with and without a RSV diagnosis in the first year of life (RSV and non-RSV cohorts respectively). Infants were excluded if they had any of the following: prematurity (<37 weeks' gestation), low birth weight, small for gestational age, congenital heart or chronic lung disease, asthma or wheezing; or had received palivizumab. At least 2 years' continuous follow-up post birth was required throughout the ≤5-year follow-up period. RSV/non-RSV infants were 1:1 matched for gender, region and health plan type. Cumulative incidence of recurrent wheezing or asthma was identified by ICD-9/10 codes, through 1, 2, 3 and 4 years (Y) post-index (1 year after birth) follow-up, and analyzed using conditional logistic regression.

Results. Matched RSV/non-RSV pairs totaled 38,494 (Y1), 25,603 (Y2), 17,429 (Y3), and 11,921 (Y4) for the years' follow-up. Demographic characteristics, birth year and month were evenly represented between cohorts. Other infections during the perinatal period were more common in the RSV vs. the non-RSV cohort (5.4% vs. 3.2%; $P < 0.0001$), as were other respiratory conditions (5.8% vs. 2.6%; $P < 0.0001$), and antibiotic use (76.7% vs. 44.7%; $P < 0.0001$). Rates of influenza and pneumococcal vaccinations were comparable between cohorts. Cumulative incidence of recurrent wheezing or asthma in the RSV cohort was more than two-fold higher compared with the non-RSV cohort for each follow-up period ($P < 0.001$) (Figure 1).

Conclusion. Healthy, full-term, commercially insured children infected with RSV during the first year of life had from 2.2- to 3.6-fold increased risk of developing recurrent wheezing or asthma in the next 1–4 years. This reveals an important medical need for interventions targeting RSV infection in infants.

Figure 1.



Disclosures. A. Mejias, Janssen: Grant Investigator and Scientific Advisor, Consulting fee and Research grant. Abbvie: CME talks, Speaker honorarium. B. Wu, Janssen Scientific Affairs, LLC: Employee and Shareholder, Salary. N. Tandon, Janssen Scientific Affairs: Employee and Shareholder, Salary and stocks. W. Chow, Janssen Scientific Affairs, LLC: Employee and Shareholder, Salary and stocks. N. Connolly, Janssen Scientific Affairs, LLC: Employee and Shareholder, Salary and Stocks. S. Lakhota, Janssen Scientific Affairs, LLC: Research Contractor, Fee for service. E. Franco, Janssen Scientific Affairs, LLC: Employee and Shareholder, Salary and stocks. O. Ramilo, Janssen Scientific Affairs, LLC: Consultant, Consulting fee.

2353. Respiratory Syncytial Virus (RSV) in Preterm Infants: Epidemiology, Clinical Pattern, and Risk Factors in a Pediatric Hospital in Argentina

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Session: 248. Pediatric Viral Infections
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Background. RSV is the main agent that causes Acute Lower Respiratory Tract Infection(ALRI) in children. Preterm infants(PT) have a higher risk of hospitalization and complications associated with RSV infection. The aim of this study was to describe epidemiology, clinical pattern and risk factors associated to RSV infection in PT infants.

Methods. Prospective, Cross-sectional study of patients admitted for ALRI, 2000–2017. Virological diagnosis was made by fluorescent antibody assay of nasopharyngeal aspirates or RT-PCR. We compared epidemiological and clinical features, complications and lethality between full term(FT) and PT infants. Logistic regression was performed to establish lethality risk factors in PT.

Results. A total of 15,451 patients included, 13,033 were tested and 45% (5,831) had positive samples; RSV was predominant (81.3%, 4,738) all through the study period showing a seasonal epidemic pattern (May–July); 14% (655) were PT.

	PT	FT	OR	IC 95%	Two-tailed P
Gender	58.47%	56.19%	1.1	0.9, 1.3	0.274
Age (median)	7 (4–13)	7 (3–12)			0.001
Bronchiolitis	60.15%	61.39%	0.9	0.8, 1.1	0.548
Comorbidities	56.34%	38.75%	2.0	1.7, 2.4	0.000
Perinatal respiratory history	46.56%	5.46%	15.1	12.3, 18.5	0.000
Cardiopathy	8.09%	5.60%	1.5	1.1, 2.0	0.012
Malnourishment	10.09%	3.74%	2.9	2.1, 3.9	0.000
Chronic respiratory disease	41.37%	28.96%	1.7	1.5, 2.1	0.000
Bronchopulmonary dysplasia	5.95%	0.05%	128.8	31.0, 534.9	0.000
Immunosuppression	1.07%	1.97%	0.5	0.2, 1.2	0.114
Previous hospitalization (ALRI)	41.74%	23.94%	2.3	1.9, 2.7	0.000
Chronic neurological disease	7.48%	3.66%	2.1	1.5, 3.0	0.000
Re-admission	4.74%	3.00%	1.6	1.1, 2.4	0.020
Length of stay (median)	7 (5–10)	8 (5–11)			0.000
ICU requirement	10.84%	7.55%	1.5	1.1, 2.0	0.004
Nosocomial infection	7.86%	6.01%	1.3	1.0, 1.8	0.074
Lethality	3.09%	1.54%	2.0	1.2, 3.4	0.005

Congenital cardiopathy OR = 3.41(1.12–10.3), $P = 0.003$ and perinatal respiratory history OR = 3.1(1.6–6.1), $P < 0.001$ were the independent predictors for VSR lethality in PT.

Conclusion. RSV showed an epidemic pattern (May–July) and affected PT with certain comorbidities, with more severe disease, more complications during hospitalization and higher lethality than FT. RSV lethality in PT was more associated with congenital cardiopathy and perinatal respiratory history.

Disclosures. A. Gentile, Sanofi Pasteur: Consultant, Speaker honorarium.

2354. Performance of Novel Clinical Case Definitions for Respiratory Syncytial Virus Infections in Young Infants: A Latent Class Analysis

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Session: 248. Pediatric Viral Infections
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Background. Respiratory syncytial virus (RSV) is a major cause of pediatric morbidity and mortality worldwide. Appropriate case definitions are needed to accurately assess disease burden and evaluate novel RSV therapeutics and vaccines. Limited data exist on performance of RSV case definitions among young infants or in high-resource settings.

Methods. We used data collected on infants <6 months of age tested for RSV as part of routine clinical care at Children's Healthcare of Atlanta between January 2010 and December 2015. We evaluated sensitivity, specificity, positive (PPV), and negative predictive values (NPV) of clinical features, existing case definitions used by the World Health Organization (WHO), and alternative definitions we constructed using latent class analyses (LCA) to detect laboratory-confirmed RSV infection.

Results. Among 565 infants tested for RSV, 161 (28.5%) had laboratory-confirmed RSV infection. Among all case definitions evaluated, WHO-acute respiratory infection (ARI) ("cough or sore throat or shortness of breath or coryza, and a clinician's judgment that illness is due to infection") was the most sensitive [98.1%, 95% confidence interval (CI), 96.1–100.0, NPV 96.3%, 95% CI 92.2–100.0. The definition developed through LCA (cough and shortness of breath and coryza and wheeze and poor feeding and chest in-drawing) was the most specific (95.8%, 95% CI 93.8–97.8; PPV 51.4%, 95% CI 34.9–68.0).

Conclusion. The WHO ARI definition was the most sensitive for detecting laboratory-confirmed RSV infections among infants aged <6 months. However, alternative case definitions can confer higher specificity. Appropriate case definitions will vary depending on the content and setting in which they are utilized.