recommendations, were prospectively enrolled through 45 general pediatric practice facilities in 30 municipalities in Greece. A single oropharyngeal sample was obtained from each subject in a standardized manner (questionnaire, procedure). Based on the time interval since the fourth dose of PCV13, the children sampled were grouped for analysis in 6 groups: 26 days to 11 months; 12–23 months; 24–35 months; 36–47 months; 48–59 months, and 60–71 months. Carriage and distribution of *Streptococcus pneumoniae* serotypes was detected by RT–PCR.

Results: A total of 1212 children aged 14–83 months were investigated. *S. pneumoniae* was identified in the pharyngeal swab of 617 children (50.9%); 172/617 (27.9%) children carried > 1 pneumococcal serotypes. As a consequence of co-colonization, a total number of 718 *S. pneumoniae* (belonging to 28 serotypes) was identified. The carriage rate of non-PCV13 serotypes escalated within 3 years after the fourth dose and plateaued during the fourth and fifth year. The carriage rate of PCV13 serotypes escalated during the 4 years after the fourth dose and declined thereafter. 22/305 children (7.2%) carried one or more PCV13 serotypes in the first year after the fourth vaccine dose, 27/201 (13.4%) in the second year, 34/207 (16.4%) in the third year, 48/224 (21.4%) in the fourth year, 40/191 (20.9%) in the fifth year and 13/84 (15.5%) in the sixth year ($P < 0.0001$) (Figure 1). The colonization frequency of serotypes 3 and 19A increased with the rise of the vaccination time interval (Figure 2). Changes in the frequency of other PCV13 serotypes were not significant. Serotypes 7F, 14 and 23F were not recovered.

Conclusion: Our study suggests that *S. pneumoniae* is present in the pharynx of children 26 days to 71 months after the completion of PCV13 vaccination, and that non-PCV13 serotypes predominate throughout this period. The carriage rate of PCV13 serotypes 3 and 19A increases significantly as the time interval from the fourth dose of PCV13 increases.

Figure 1:

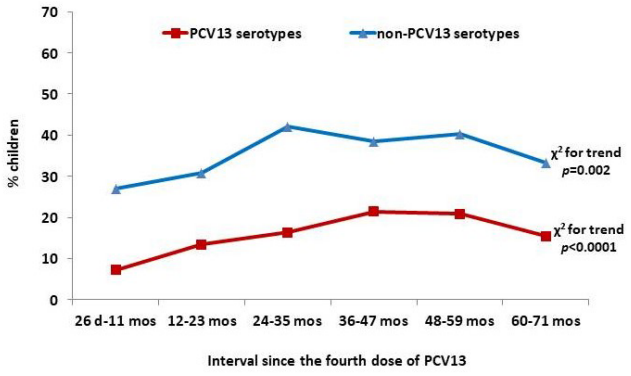
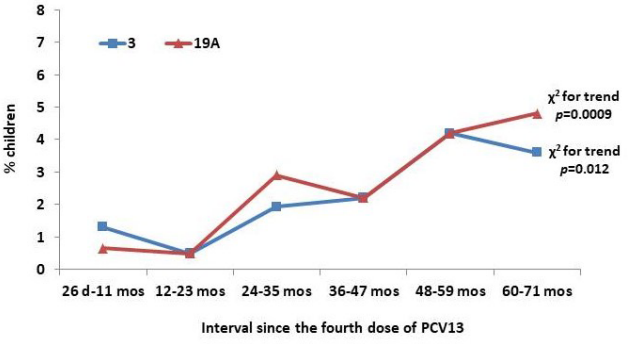


Figure 2:



Disclosures. **All authors:** No reported disclosures.

2704. Molecular Technology to Detect Pneumococcal Colonization in Young Children Reveals Increased Prevalence of Vaccine Serotypes as Compared with Enhanced Culture Methods

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Background: Human challenge studies demonstrate enhanced sensitivity of molecular technology for identification of vaccine serotype pneumococcal (SP) carriage in PCV13 immunized adults. We hypothesized that PCV13 immunized children would similarly harbor vaccine serotypes in their nasopharynx (NP) that could only be identified by molecular technology.

Methods: We compared use of enhanced microbiologic culture vs. molecular technology to characterize SP colonization among NP swabs collected from 995 healthy or sick children <5 years old at Boston Medical Center from November 2015 to May 2017. NP specimens were broth enriched for 4 hours and cultured on selective blood agar. Specimens were evaluated for presence of SP using both routine microbiologic methods and RT–PCR. RT–PCR assays targeted the *lytA*, and *piaB* (SP membrane permease) genes, and 26 SP serotypes: all serotypes included in 13-valent pneumococcal conjugate vaccine and 13 prevalent non-vaccine serotypes

Results: A total of 162 (16.3%) NP specimens were positive for SP via enhanced culture, and an additional 163 (16.3%) were SP positive via *lytA*+ RT–PCR molecular technology. Prevalence of SP carriage was equivalent in children aged 0<2 years and 2≤5 years, but greater in children with respiratory tract infections (RTI) compared with children without RTI (26.5% vs. 9.6% among culture+ specimens only; and 43.2% vs. 25.8% among combined culture+ and molecular+ specimens). Using enhanced culture only, vaccine serotypes (VST) were identified in 4 (1%) of 450 children <2 years and 14 (2.6%) of 545 children 2 ≤5 years; adding molecular positive specimens increased the prevalence of VST to 2.9% in children <2 years and 4.6% in children 2 ≤5 years (table). Serotypes 3 and 19A were the two most commonly identified VST.

Conclusion: Combining molecular technology with enhanced culture reveals an increased prevalence of vaccine serotype colonization in young children. The ability of sensitive molecular methods to detect vaccine serotypes in culture-negative specimens suggests low-density vaccine serotype carriage persists in a highly immunized pediatric population. The importance of culture negative but RTPCR positive carriage for transmission requires further evaluation.

Table. Detection of vaccine serotype carriage by enhanced culture and molecular technology

Serotype	Children < 2 years				Children 2 ≤ 5 years			
	Culture positive	Molecular confirmation of culture positive	New molecular detection of culture negative	Combined prevalence of *S. pneumoniae*	Culture positive	Molecular confirmation of culture positive	New molecular detection of culture negative	Combined prevalence of *S. pneumoniae*
1	0	--	0	0	1	1/1	1	2
3	1	1/1	2	3	7	7/7	4	11
4	0	--	3	3	0	--	2	2
6B	0	--	0	0	1	0/1‡	0	1
9V	0	--	0	0	0	--	0	0
19A	1	1/1	3	4	3	2/3¥	4	7
19F	2	1/2†	1	3	2	2/2	0	2
Total VST isolates	4	3/4 (75%)	9	13	14	12/14 (86%)	11	25
Prevalence of VST in population	1%			2.9%	2.8%			4.6%

†1 isolate identified as 3 and 19A
‡1 isolate identified as 6C/D and 11A
¥1 isolate identified as 15A/F

Disclosures. **All authors:** No reported disclosures.

2705. Serotype Replacement Following Childhood Pneumococcal Conjugate Vaccination Programs in British Columbia, Canada

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Background: Pneumococcal conjugate vaccines have substantially reduced the incidence of invasive pneumococcal disease (IPD); however, the impact of the vaccine on non-vaccine serotypes (NVT) remains unclear. We evaluated the effect of PCV13 use in British Columbia, Canada.

Methods: The annual incidence following implementation of PCV7 (September 2004), and PCV13 (September 2010) was calculated using provincial laboratory surveillance data. We also compared incidence rate ratios (IRR) against pre-PCV13 (2004–10) and pre-PCV7 (2002–03) baselines using Poisson regression for non-conjugate vaccine type IPD.

Results: A total of 4,490 cases were reported over the 14 year period. The overall annual incidence increased from 5.73 cases per 100,000 population in 2002 to 7.90 cases per 100,000 population in 2015. Compared with baseline, PCV7 reduced VT-IPD (IRR: 0.49; 95% CI: 0.42–0.56), but the additional 6 serotypes in the PCV13 vaccine caused 214% increase in IPD (IRR: 2.65; 95% CI: 2.12–3.39). The majority of this increase is related to an increase in NVT disease (IRR: 3.17; 95% CI: 2.62–3.87) such as 23B, 23A, 9N, 20, 33F, 15C, 17F and 6C. IPD from PCV13 vaccine serotypes 19A and 7F which emerged after PCV7 continue to be high.

Conclusion: The introduction of PCV13 has a modest impact on IPD rates, due to inadequate control of serotypes 19A and 7F, and, of concern, IPD rates continue to escalate due to serotype replacement by non-vaccine serotypes.

Disclosures. **All authors:** No reported disclosures.

2706. Indirect Effects of Infant 13-valent Conjugate Pneumococcal Vaccination Program on Invasive Pneumococcal Disease in Adults in British Columbia, Canada

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Background: Many jurisdictions report a significant reduction in invasive pneumococcal disease (IPD) in adults following implementation of the pneumococcal conjugate vaccines, 7-valent (PCV7) and 13-valent (PCV13) in childhood immunization programs. This study evaluates the indirect effect of conjugate vaccines on IPD in British Columbia, Canada over a 14 year period (2002–2015).

Methods: Using provincial IPD laboratory surveillance data, we calculated the annual incidence following implementation of PCV7 (September 2004), and PCV13 (September 2010) in adults 18 years of age and older. We also compared incidence rate ratios (IRR) against pre-PCV13 (2004–2010) and pre-PCV7 (2002–2003) baselines for overall and age-specific IPD rates using Poisson regression.

Results: A total of 3793 cases were reported over the 14 year period. The overall annual incidence increased from 4.32 cases per 100,000 population in 2002 to 8.61 cases per 100,000 population in 2015. Overall, IPD has increased by 80% (IRR: 1.80; 95% CI: 1.59–2.04) compared with baseline, especially in adults ≥ 85 years of age (PCV13 vs baseline: IRR: 1.90; 95% CI: 1.25–03.05). This increase was the highest after introduction of PCV7 (IRR: 1.87; 95% CI: 1.65–2.11); the incremental change after introduction of PCV13 was non-significant (IRR 0.96; 95% CI: 0.90–1.03). While PCV7 type IPD plummeted by 76% (IRR 0.24; 95% CI: 0.18–0.31) since introduction of PCV7 compared with baseline, a modest decline in PCV13 type IPD of 20% was seen (IRR 0.80; 95% CI: 0.71–0.89) since introduction of PCV13.

Conclusion: Although PCV7-type IPD has decreased substantially, only a modest reduction in IPD from the additional 6 serotypes in the PCV13 vaccine was observed.

Disclosures. **All authors:** No reported disclosures.

2707. Non 13-Valent Pneumococcal Conjugate Vaccine Serotypes Predominate as Causes of Pneumococcal Otitis Media in Children

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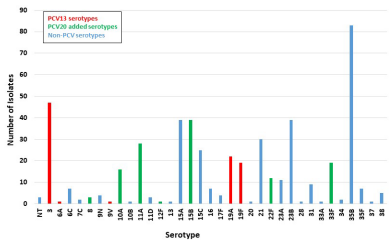
Background: Pneumococcal acute otitis media (AOM) in children due to vaccine-related serotypes (ST) has declined after the introduction of the 13-valent pneumococcal conjugate vaccine (PCV13), although some serotypes, such has 3, 19A and 19F have persisted. Among non-vaccine serotypes, 35B has been shown to contribute substantially to both OM and invasive infections. This study describes the current epidemiology of pneumococcal OM isolates obtained from the U S Pediatric Multicenter Pneumococcal Surveillance Group (USPMPSG).

Methods: From the USPMPSG database, we collected data from patients <18 years of age with pneumococcal OM isolates from 2014 to 2018. Analysis included demographics, immunization status, antimicrobial susceptibility data and serotype. Statistical comparisons included Fisher's exact and Wilcoxon rank-sum tests.

Results: A total of 494 patients with isolates were identified within the time period from 5 children's hospitals. Median age was 1.7 years (range 0–17.6) and 299 (60.5%) were male; 176 (35.7%) had an underlying condition. Thirty-two patients had received no dose of either PCV7 or PCV13. Thirty-five serotypes were identified (3 isolates were non-typeable), of which 6 serotypes [35B (16.8%), 3 (9.5%), 15A (7.9%), 15B (7.9%), 23B (7.9%) and 21 (6.1%)] caused more than half of the total OM infections (figure). Ninety (18.2%) isolates were of PCV13 serotypes. Twenty-five of 476 (5.3%) isolates had a penicillin MIC>2 µg/mL. These were of serotypes 11A, 15A/C, 19A/F, 35B and NT; 10/455 (2.2%) isolates had ceftriaxone MIC>1 µg/mL and were of ST 3, 15A, 19A/F and 35B.

Conclusion: Most pneumococcal OM were caused by non-PCV13 serotypes. Serotype 35B remained the most common serotype among pneumococcal isolates recovered from ear drainage or middle ear cultures. The low proportion of penicillin-resistant isolates along with the increasing proportion of AOM cases being due to non-pneumococcal isolates supports the consideration to switch routine antibiotic treatment for AOM to standard dose amoxicillin-clavulanate from high dose amoxicillin in PCV13 immunized children (*Pediatr Infect Dis J* 2018;37:1255–1257).

Figure. Pneumococcal Serotypes Causing Otitis Media, 2014-2018



Disclosures. **All authors:** No reported disclosures.

2708. Genetic Structure of *Streptococcus pneumoniae* Isolated from Invasive Disease in Korea, 2014–2016

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Background: The extended-valency pneumococcal conjugate vaccines (PCVs) were implemented into Korean national immunization program in 2014. This study investigated the change in genetic structures of *Streptococcus pneumoniae* causing invasive pneumococcal disease (IPD) in Korean children after 10- and 13-valent conjugate vaccine (PCV10 and PCV13, respectively) use.

Methods: Between January 2014 and December 2016, invasive isolates were collected from 23 hospitals throughout Korea. Cases of IPD were defined by isolating pneumococci from normally sterile sites. Each pneumococcal isolate was identified using standard microbiological techniques and serotyped by Quellung reaction. The multi-locus sequence typing (MLST) was analyzed for randomly selected isolates.

Results: A total of 91 pneumococcal isolates were analyzed. Common serotypes were 10A (18.7%), 12F (11.0%), 15A (9.9%), 19A (9.9%), 15B/C (7.7%), 23A (6.6%), 35B (5.5%), and 23B (4.4%). The isolates belonged to 38 sequence types (STs), including 4 newly discovered STs. Of the 4 clonal complexes (CCs), 3 clonal complexes were antibiotic-resistant international clones. CC166 (11.9%) were associated with non-vaccine serotypes (NVTs; 11A, 15B/C, 23A, and 13). Serotypes of CC320 (10.9%) comprised of serotype 19A and 19F. The main serotypes responsible for CC81 (10.9%) were serogroup 15. New serotype-ST combinations were observed, especially in serotype 13 and serogroup 15. Also, a possibility of capsular switch event was noted between serogroup 6 and serogroup 15A.).

Conclusion: The introduction of extended-valency PCVs has resulted in the change of the genetic structure of pneumococcal isolates in Korean children. This study demonstrates that selective pressure from PCV10/13 caused predominant serotypes to be NVTs and genetic changes such as capsular switch events.

Disclosures. **All authors:** No reported disclosures.

2709. Immune Response After Diphtheria and Tetanus Toxoid Booster in Patients with Adult-Onset Immunodeficiency with Anti-interferon-γ Autoantibody

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Background: Immunization were the key of prevention in tetanus and diphtherial disease. Nevertheless, in previous observational study, low seroprotection rate of both diphtheria and tetanus were observed in Thai healthy population. Reduced-dose diphtheria and tetanus toxoid vaccine (dT) was recommended to all adult patients regardless of immunologic status. However, data on vaccine efficacy in interferon gamma (IFN-γ) autoantibody were limited. We therefore conducted clinical study to evaluate efficacy and safety of one dose of dT in IFN-γ autoantibody patient compared with healthy individuals at 4 weeks after vaccination.

Methods: Study was conducted from February to April 2019. Total 18 patients with confirmed IFN-γ autoantibody were enrolled. Baseline tetanus and diphtheria serologic study and 4 weeks after vaccination were examined. Antibody levels were measured with a solid-phase IgG-specific ELISAs (EUROIMMUN, Germany). Geometric mean titers (GMTs) were calculated using the log transformation of serological titers and from taking the antilog mean of the transformed values.

Results: Seroprevalence of tetanus was 94.5% in healthy population compared with 60.1% in IFN-γ autoantibody patients. While, seroprevalence of diphtheria was 27.8% and 77.8%, respectively. After vaccination, all healthy adults had reached seroprotection level in both diphtheria and tetanus. For patients with IFN-γ autoantibody, 88.9% and 94.4% had anti-tetanus toxin IgG and anti-diphtheria toxin IgG level above 0.1 IU/mL, respectively. These results indicated seroconversion rate of 71% for tetanus and 75% for diphtheria after dT vaccination. (Table 2). In the subgroup analysis, unboosted IFN-γ autoantibody patient had lower tetanus seroconversion rate compared with previously boosted patient (50% vs 100%). Active infection was also associated with lower immune response after tetanus vaccination. There was no severe adverse event in both group.

Conclusion: This is the first study on immune response after dT vaccination in IFN-γ autoantibody patient. Seroconversion rate of dT vaccine in IFN-γ autoantibody patient were slightly lower than healthy adults. Active infection and previously unboosted patient provided lower immune response of tetanus.

Baseline characteristics	IFN-γ autoantibody (n=18)	healthy adult (n=18)	p-value
Age	54.22 ± 14.03	44.11 ± 13.37	0.034*
Gender Male	16 (88.9%)	8 (44.4%)	0.005*
Childhood vaccination	15 (83.3%)	17 (94.4%)	0.229
Residence			
Central (Bangkok and adjacent province)	7 (38.9%)	14 (77.8%)	0.018*
Rural	11 (61.1%)	4 (22.2%)	
History of tetanus booster	12 (66.7%)	11 (61.1%)	0.729
History of diphtheria booster	1 (5.6%)	5 (27.8%)	0.287
Comorbidity			
Diabetes mellitus	1 (5.6%)	2 (11.1%)	1
Hypertension	3 (16.7%)	1 (5.6%)	0.603
Dyslipidaemia	3 (16.7%)	2 (11.1%)	1
Other autoimmune disease	3 (16.7%)	0 (0%)	0.229
Chronic kidney disease	5 (27.8%)	0 (0%)	0.045*
Cerebrovascular disease	2 (11.1%)	0 (0%)	0.486
Prednisolone use	2 (11.1%)	0 (0%)	0.486
Hb	12.69 ± 4.92	13.12 ± 1.83	0.736
WBC	11136.11 ± 7280.64	6894.44 ± 1300.48	0.026*
Absolute neutrophil count	7658.89 ± 6156.7	3786.28 ± 1016.14	0.017*
Absolute lymphocyte count	2127.22 ± 549.24	2504.44 ± 621.1	0.062
Absolute eosinophil count	809.44 ± 950.04	194.44 ± 171.16	0.015*

Table 1: Baseline characteristics between patients with IFN- γ autoantibody and healthy adults