**2701. The Impact of Infant 13-valent Conjugate Pneumococcal Vaccination Program on Invasive Pneumococcal Disease in Children in British Columbia, Canada**

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**Session:** 277. Vaccines: Bacterial
*Saturday, October 5, 2019: 12:15 PM*

***Background:*** A significant reduction in invasive pneumococcal disease (IPD) has been reported following implementation of the 7-valent pneumococcal conjugate vaccine (PCV7) infant immunization program, but not much has been reported after introduction of the 13-valent vaccine (PCV13). This study represents the effect of PCV13 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 children less than 17 years of age. 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 697 cases were reported over the 14 year period. The overall annual incidence decreased from 10.9 cases per 100,000 population in 2002 to 4.64 cases per 100,000 population in 2015. While overall decline of IPD was 59% (IRR 0.41; 95% CI: 0.35–0.51) compared with baseline, this reduction was greatest after introduction of PCV7 (IRR 0.44; 95% CI: 0.37–0.53); the incremental change after introduction of PCV13 was non-significant (IRR 0.94; 95% CI: 0.78–1.13). The greatest reduction in IPD was in children <2 years of age (PCV13 vs baseline: IRR 0.19; 95% CI: 0.14–0.25), followed by children 3–5 years of age (PCV13 vs baseline: IRR 0.34; 95% CI: 0.21–0.56); no significant change was observed in 6–17 year olds.

***Conclusion:*** While IPD rates have been significantly reduced since the introduction of the PCV vaccines, the impact of the additional 6 serotypes in the PCV13 vaccine is non-significant.

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

**2702. Infants Vaccinated with a Fully-Liquid DTaP-IPV-Hib-HepB Vaccine Are Protected During the High-Risk Period for *Haemophilus Influenzae* Type B Disease**

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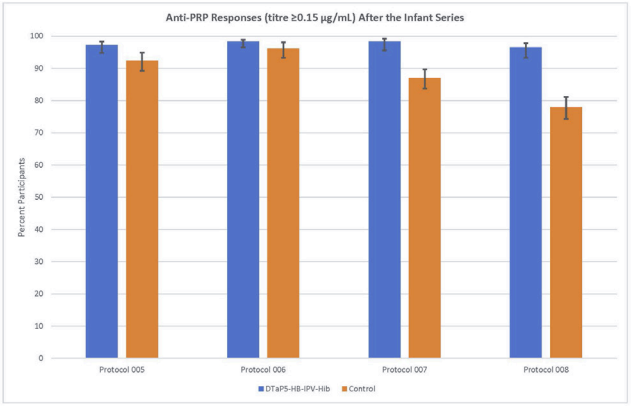
**Session:** 277. Vaccines: Bacterial
*Saturday, October 5, 2019: 12:15 PM*

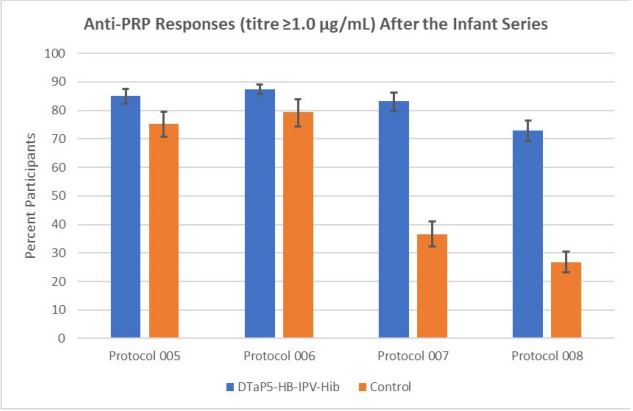
***Background:*** DTaP-IPV-Hib-HepB is a fully-liquid, combination vaccine (Vaxelis™) approved for vaccination in infants and toddlers against diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and *Haemophilus influenzae* type b (Hib). Safety and immunogenicity were evaluated in 4 Phase III, randomized, active-comparator controlled clinical trials (Protocols 005 and 006 in the US [Control: PENTACEL™] and Protocols 007 and 008 in the EU [Control: INFANRIX™ hexa]). The vaccine, studied in >6,800 children, has an acceptable safety profile generally similar to that of control vaccines (Xu, PIDJ, 2019; 38:439–43). DTaP-IPV-Hib-HepB includes polyribosylribitol phosphate (PRP) conjugated to outer membrane protein complex of *Neisseria meningitidis* (OMPC) that elicits a rapid response to Hib.

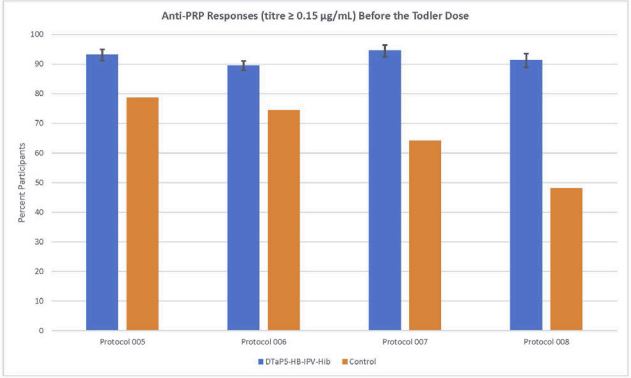
***Methods:*** Data from these studies provide a summary of the anti-PRP responses of DTaP-IPV-Hib-HepB compared with Control.

***Results:*** After the infant series, the percentage of participants who achieved short-term and long-term protective antibody thresholds for PRP (i.e., anti-PRP titer ≥0.15 µg/mL and ≥1.0 µg/mL, respectively) were higher in DTaP-IPV-Hib-HepB recipients compared with Control. A high level of protective responses (96.6% ≥0.15 µg/mL and 72.9% ≥1.0 µg/mL) were seen after the second dose in the 008 study of the 2 infant series followed by toddler dose hexavalent vaccination schedule (2 + 1). Across all 4 studies, anti-PRP titers were higher in DTaP-IPV-Hib-HepB recipients (91.4% ≥0.15 µg/mL and 46.8% ≥1.0 µg/mL) when compared with Control (63.4% ≥0.15 µg/mL and 17.1% ≥1.0 µg/mL) at the pre-Toddler dose (i.e., prior to the administration of the Toddler dose in the second year of life, between 11–15 months of age). One month after the toddler dose, high levels of anti-PRP titers were achieved in both DTaP-IPV-Hib-HepB recipients (99.8% ≥0.15 µg/mL and 96.6% ≥1.0 µg/mL) and Control (99.5% ≥0.15 µg/mL and 94.9% ≥1.0 µg/mL).

***Conclusion:*** These results support that DTaP-IPV-Hib-HepB induces an early Hib response in the first 6 months of life that is sustained until the booster dose is administered in the second year of life. Thus, a high percentage of infants vaccinated with DTaP-IPV-Hib-HepB are protected during the high-risk period for Hib disease.




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

**2703. Pneumococcal Carriage of 13-Valent Pneumococcal Conjugate Vaccine (PCV13) and Non-PCV13 Serotypes among Greek Children Vaccinated with PCV13 in a 3 + 1 Schedule During the First 6 years after the Fourth Dose of PCV13**

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**Session:** 277. Vaccines: Bacterial
*Saturday, October 5, 2019: 12:15 PM*

***Background:*** We evaluated the long-term impact of full PCV13 vaccination in a 3 + 1 schedule on pneumococcal colonization patterns of children in order to clarify PCV13 serotype persistence/enhancement and re-colonization.

***Methods:*** From January 18 to August 29, 2017, consecutive children who had received the 4-dose course of PCV13, as per the National Immunization Program

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:**

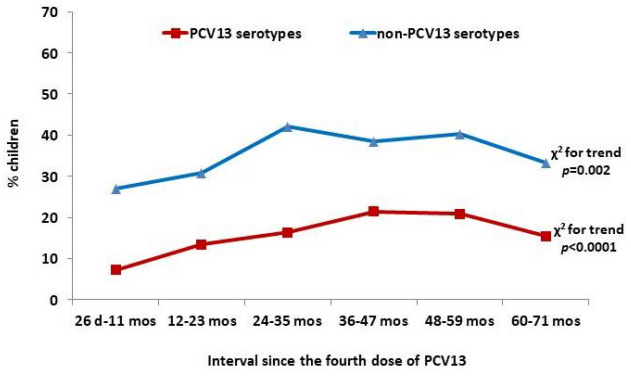
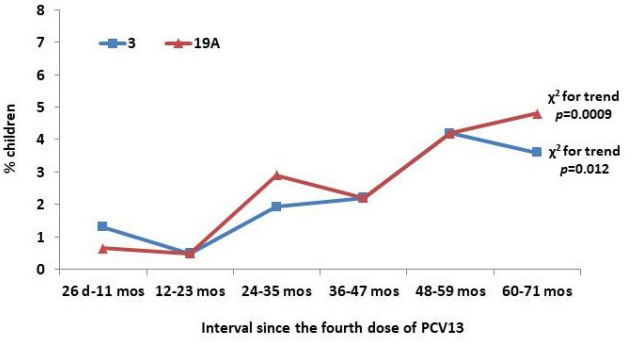



**Figure 2:**




***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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**Session:** 277. Vaccines: Bacterial
*Saturday, October 5, 2019: 12:15 PM*

***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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**Session:** 277. Vaccines: Bacterial
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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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