Direct and Indirect Impact of 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Invasive Pneumococcal Disease (IPD) Among Children and Adults in the U.S.

Tamara Pilishvili, Centers for Disease Control and Prevention
Ryan Gierke, Centers for Disease Control and Prevention
Monica Farley, Emory University
William Schaffner, Emory University
Ann Thomas, Oregon Public Health Division
Arthur Reingold, University of California
Lee Harrison, University of Pittsburgh
Ruth Lynfield, Minnesota Department of Health
Shelley M. Zansky, New York State Department of Health
Susan Petit, Connecticut Emerging Infections Program

Only first 10 authors above; see publication for full author list.

Journal Title: Open Forum Infectious Diseases
Volume: Volume 4, Number suppl_1
Publisher: Oxford University Press (OUP) | 2017-10-04, Pages S66-S67
Type of Work: Article | Final Publisher PDF
Publisher DOI: 10.1093/ofid/ofx162.158
Permanent URL: https://pid.emory.edu/ark:/25593/s6f6c

Final published version: http://dx.doi.org/10.1093/ofid/ofx162.158

Copyright information:
© The Author 2017. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access work distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Accessed October 27, 2018 11:57 PM EDT
Bacteriology I, National Institute of Infectious Diseases, Tokyo, Japan; 2Department of Infection Control and Laboratory Diagnostics, Internal Medicine, Tokohu University Graduate School of Medicine, Sendai, Japan

Session: 277. Global Infections Saturday, October 7, 2017, 7:00 PM

**Background.** The proportion of enteric fever cases caused by *Salmonella enterica* subspecies *enterica* serovar Paratyphi A (S. Paratyphi A) has recently been increasing in Asian counties, which is a public health concern. In 2015, an unusual increase in S. Paratyphi A infection among Japanese travelers returning from Myanmar was noted, while there is little information on this uptrend in Myanmar.

**Methods.** Isolates from travelers who returned with enteric fever from 2005 to 2015 were analyzed in order to determine country-specific notification rates (epidemiological investigation). The notification rate was defined as cases returning from each country per 100,000 Japanese travelers who visited to the country. S. Paratyphi A isolates collected from 2001 to 2015 were analyzed by whole-genome sequencing (microbiological investigation).

**Results.** Yearly notification trends indicated that enteric fever was potentially endemic to Myanmar (5–16 cases/100,000 travelers); the trends were similar to those observed in India (4–21 cases/100,000 travelers). A rapid increase in S. Paratyphi A infection occurred from 2012–2014 (2–4 cases/100,000 travelers) to 2015 (13 cases/100,000 travelers). A phylogenetic tree, constructed based on analysis of 105 S. Paratyphi A isolates (33 and 30 related to Myanmar and Cambodia, and 42 controls), revealed that most Myanmar- and Cambodia-related isolates formed clusters in the same lineage (Figure 1). Additionally, Myanmar-related isolates from 2015 harbored identical plasmid type 1 and were genetically closely related (each isolates had 0–10 single-nucleotide polymorphisms (SNPs), mostly within 0–7 SNPs (Figure 2)), yielding a wider SNP range than outbreak-associated isolates from Cambodia in 2013 (within a SNP distance of 0–6).

**Conclusion.** Epidemiological trends and molecular subtyping suggested a possible outbreak of S. Paratyphi A infection occurred in Myanmar in 2015. The recent uptrend of S. Paratyphi A infection in Myanmar is important for travelers and clinicians since infection cannot be prevented by typhoid vaccination.

Figure 1. Polygenetic tree of 105 S. Paratyphi A isolates

Figure 2. SNP analyses of S. Paratyphi A isolates from Myanmar in 2015 (A) and Cambodia in 2013 (B).

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

---

**Table: Symptoms, signs, laboratory findings**

| Symptoms | Age < 18 | Age > 18 | P value*
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (temperature &lt; 100.4)</td>
<td>36/36 (100%)</td>
<td>53/54 (98%)</td>
<td>89/90 (99%)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>15/20 (75%)</td>
<td>21/24 (88%)</td>
<td>36/44 (82%)</td>
</tr>
<tr>
<td>Headache</td>
<td>23/32 (72%)</td>
<td>37/46 (80%)</td>
<td>60/78 (77%)</td>
</tr>
<tr>
<td>Rash</td>
<td>10/17 (59%)</td>
<td>22/29 (76%)</td>
<td>32/46 (70%)</td>
</tr>
<tr>
<td>Signs</td>
<td>18/36 (50%)</td>
<td>16/51 (31%)</td>
<td>34/87 (39%)</td>
</tr>
<tr>
<td>Labs</td>
<td>WBC count &lt; 6,000</td>
<td>11/36 (31%)</td>
<td>10/54 (19%)</td>
</tr>
<tr>
<td>Platelets &lt; 120,000</td>
<td>12/36 (33%)</td>
<td>37/46 (80%)</td>
<td>49/90 (54%)</td>
</tr>
<tr>
<td>Bilirubin ≤ 1.5</td>
<td>3/36 (8%)</td>
<td>14/45 (26%)</td>
<td>17/90 (19%)</td>
</tr>
<tr>
<td>AST &gt; 50</td>
<td>25/36 (69%)</td>
<td>51/64 (84%)</td>
<td>70/90 (84%)</td>
</tr>
</tbody>
</table>

*Comparing pediatric vs. adult cases.

---

2492. *Direct and Indirect Impact of 13-valent Pneumococcal Conjugate Vaccine (PCV13) on Invasive Pneumococcal Disease (IPD) Among Children and Adults in the U.S.*

Tamar Piliulski, MPH1; Ryan Gierke, MPH2; Monica Farley, MD, FIDSA3; William Schaffner, MD, FIDSA, FSHEA4; Ann Thomas, MD, MPH5; Arthur Reingold, MD, FIDSA6; Lee Harrison, MD7; Ruth Lynfield, MD, FIDSA8; Shelley M. Zandek, PhD9; Steve Soccol, MD MPH10; Lisa Miller, MD, MS11; Joa Baumbach, MD, MPH12, MS13; Bernard Beall, PhD14 and Cynthia Whitney, MD, MPH, FIDSA15; 1National Center for Immunizations and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; 2Georgia Department of Medicine, Emory University School of Medicine and Atlanta VA Medical Center, Atlanta, Georgia; 3Vanderbilt University School of Medicine, Nashville, Tennessee; 4Oregon Public Health Division, Portland, Oregon; 5University of California - Berkeley, Berkeley, California; 6University of Pittsburgh, Pittsburgh, Pennsylvania; 7Minnesota Department of Health, St. Paul, Minnesota; 8New York State Department of Health, Albany, New York; 9Connecticut Emerging Infections Program, New Haven, Connecticut; 10Preventive Medicine Residency Program, University of Colorado School of Public Health, Aurora, Colorado; 11New Mexico Department of Health, Santa Fe, New Mexico; 12Centers for Disease Control and Prevention, Atlanta, Georgia

Session: 278. Pneumococcal and Pertussis Vaccines Saturday, October 7, 2017, 7:00 PM

**Background.** In February 2010, PCV13 was introduced for routine use among children aged <5 years. In June 2012, PCV13 was recommended for use in series with 23-valent polysaccharide vaccine (PPSV23) for adults ≥19 years with select medical conditions, and in August 2014, for all adults ≥65 years. We evaluated the direct and indirect effects of PCV13 6 years post-introduction on invasive pneumococcal disease (IPD).

**Methods.** IPD cases (isolation of pneumococcus from sterile sites) were identified among residents of Active Bacterial Core surveillance (ABCs) sites during July 2007–2016. Isolates were serotyped by Quelling, PCR, or whole genome sequencing and classified as PCV13 or non-vaccine type (NVT). Incidence changes were estimated as percent changes (one minus rate ratio) and 95% confidence intervals (95% CI) between pre-PCV13 (2007–2009) and two post-PCV13 periods (July 2014–June 2015 and July 2015–June 2016).

**Results.** ABCs identified 31,190 IPD cases between 2007 and 2015, with 2,750 cases among children <5 years and 10,930 among those ≥65 years. During the two post-PCV13 periods, overall IPD rates were 33%-62% lower relative to 2007–2009 among all age groups, including <5 years and ≥65 years (Figure). Significant reductions in PCV13-type IPD incidence were observed for all age groups during both post-PCV13 periods, with incidence 84% (95% CI 78, 88%) and 68% (95% CI 63, 73%) lower in 2015–2016 among children <5 years and adults ≥65 years, respectively. PCV13-type IPD reductions were driven by serotypes 19A and 7E IPD due to non-vaccine types also declined significantly among children <5 years (<27%, 95% CI –42, -9%) and adults ≥65 years (24%, 95% CI –34, –14%). PCV13-type IPD incidence did not differ significantly between the two post-PCV13 periods.

**Conclusion.** IPD incidence declined among children and adults in the U.S. following PCV13 introduction among children. The lack of difference in PCV13 rates between 2014–2015 and 2015–2016 suggests no measurable early impact of PCV13 introduction among adults ≥65 years. To date, we found no evidence of significant replacement disease with non-PCV13 types. Further work is needed to explain reductions in non-vaccine type disease observed in the post-PCV13 era.
Disclosures. W. Schaffner, Pfizer: Scientific Advisor, Consulting fee; Merck: Scientific Advisor, Consulting fee; Novavax: Consultant, Consulting fee; Dynavax: Consultant, Consulting fee; Sanofi Pasteur: Consultant, Consulting fee; GSK: Consultant, Consulting fee; Sequirus: Consultant, Consulting fee; L. Harrison, GSK: Scientific Advisor, Consulting fee.

2493. Invasive Pneumococcal Disease in Massachusetts Children 6 Years Following Introduction of PCV13
Inci Yildirim, MD MSc1; Brent Little, PhD2; Stephen I. Pelton, MD3; Pediatric Infectious Diseases, Emory University, Atlanta, Georgia; 3Pediatric Infectious Diseases, Boston University, Boston, Massachusetts and, 2Boston University Schools of Medicine and Public Health, Boston, Massachusetts

Session: 278. Pneumococcal and Pertussis Vaccines
Saturday, October 7, 2017: 2:00 PM

Background. A second generation 13-valent pneumococcal conjugate vaccine (PCV13) replaced PCV7 in the childhood immunization schedule in Massachusetts (MA) beginning in April 2010.

Methods. Cases of invasive pneumococcal disease (IPD) in children <18 years of age were detected through an enhanced surveillance system in MA since 2001. All cases in children and Streptococcus pneumoniae (SP) isolates, when available, are submitted to Department of Public Health (MDPH) and parents/physicians are interviewed for confirmation of demographic and clinical data. All available isolates are confirmed as IP, serotyped by Quellung reaction.

Results. Three-hundred thirty-seven IPD cases have been identified in MA children between 4 January 2010 and 31 March 2017 (Figure). Thirty-five (10.4%) were in infants <6 months; 41 (12.2%) in children between 6 and 12 months; 60 (17.8%) in toddlers 12 to 24 months; 100 (29.7%) in children between 2 and 5 years of age and 101 (29.9%) were in children >5 years old. Among children under 2; incidence of IPD declined to 6.8/105 children (95% CI 2.6–11.1) in 2015/16 period which represents a 72.1% decline compared with 2010/11; however in 2016/17 IPD incidence increased by 41.2% to 9.6/105 (95% CI 4.6–14.6) for the first time since the implementation of PCV13. Bacteremia was the most common clinical presentation (62.9%) followed by pneumonia (30.5%) and CNS disease (6.6%). Children with at least one comorbidity are counted if IPD occurred >2 weeks after a dose.

Results. PCV13 ST accounted for 19.7% (27/137), 26.8% (30/112) and 26% (33/127) of IPD cases in 2014, 2015 and 2016, respectively. ST 3, 19A and 19F accounted for 90% of the PCV13 ST IPD cases. >50% of the children had received ≤2 doses of PCV13 prior to IPD. Of the 30 children with ≥2 doses of PCV15, 15 were an increasing proportion of cases reaching 37.9% in 2016 (p < 0.004). The overall mortality rate was 4.3%. Isolates from 301 (90.1%) were available for serotyping; vaccinocine serotypes (VST) were identified in 101 (33.6%) cases [serotype 19A (49 cases), 7F (21 cases), 3 (18 cases), 19F (7 cases), 6A (3 cases), serotypes 14, 18C and 5 (1 case each)]. The proportion of VST disease declined to 24.1% from 59.2% over 6 years after PCV13 (p < 0.001). Serotype 15B (13.5%), 3F (12.5%) and 22F (12.5%) were the most common nonvaccine serotypes (NVST).

Conclusion. In the post-PCV13 era, IPD is primarily due to NVSTs and disproportionately observed in children with comorbid conditions. In the most recent year (4.1.2016 through 3.31.2017) an increase in incidence was observed in MA children after six years of declining cases following implementation of PCV13.

Disclosures. S. I. Pelton, Pfizer: Board Member and Grant Investigator, Consulting fee, Research grant and Speaker honorarium; Merck: Board Member, Consulting fee and Speaker honorarium; GSK: Board Member, Consulting fee and Speaker honorarium; Seqirus: Board Member, Consulting fee and Speaker honorarium.

2494. Analysis of Invasive Pneumococcal Infections Due to 13-Pneumococcal Conjugate Vaccine Serotypes at 8 US Children's Hospitals During 2014 to 2016
Sheldon L. Kaplan, MD, FIDSA1; William J. Barson, MD, FPID1; Philana Ling Lim, MD2; Jose Romero, MD3; John S. Bradley, MD, FIDSA, FPID3; Tanja, MD, FIDSA4; Laurence B. Girvin, MD5; Jill Hoffman, MD6; Kristina Hulten, PhD7 and Edward O. Mason Jr, PhD, FIDSA8; Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, Texas; 2 Nationwide Children's Hospital and The Ohio State University College of Medicine, Columbus, Ohio; Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania; 3University of Arkansas for Medical Sciences, Little Rock, Arkansas; 4Pediatric Infectious Diseases, University of California at San Diego School of Medicine, San Diego, California; 5 Northwestern University Feinberg School of Medicine, Chicago, Illinois; 6 Wake Forest University School of Medicine, Winston-Salem, North Carolina; 7Children's Hospital, Los Angeles, Los Angeles, California; 8Baylor College of Medicine and Texas Children's Hospital, Houston, Texas

Session: 278. Pneumococcal and Pertussis Vaccines
Saturday, October 7, 2017: 2:00 PM

Background. The 13-valent Pneumococcal Conjugate Vaccine (PCV13) was licensed in 2010 and is directed against serotypes (ST) 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F. Details of cases of invasive pneumococcal disease (IPD) due to PCV13 ST since 2010 in the US are sparse. We describe IPD cases due to PCV13 ST seen at 8 US children's hospitals over years 2014 to 2016 which may aid in understanding why some IPD cases due to these ST have persisted.

Methods. Children with IPD have been prospectively identified at 8 children's hospitals in the US since 1993. Data from 2014 through 2016 were analyzed. Demographic, clinical data and number and dates of PCV doses were collected on case report forms and isolates were sent to a central laboratory for serotyping. PCV doses are counted if IPD occurred >2 weeks after a dose.

Results. PCV13 ST accounted for 19.7% (27/137), 26.8% (30/112) and 26% (33/127) of IPD cases in 2014, 2015 and 2016, respectively. ST 3, 19A and 19F accounted for 90% of the PCV13 ST IPD cases. >50% of the children had received ≤2 doses of PCV13 prior to IPD. Of the 30 children with ≥2 doses of PCV15, 15 were of an age at diagnosis for which ≥2 doses of PCV was recommended. An underlying condition was noted in 18. For PCV13 ST, the types of IPD were pneumonia (n = 39), mastoiditis (n = 15), bacteremia (n = 15), meningitis (n = 12) and other sites of infection (n = 9). Whereas the numbers of yearly cases were similar for ST3 (12, 10, 13) and ST19A (8, 16, 6), the numbers for 19F increased slightly (3, 8, 10).

Conclusion. Four to 6 years after PCV13 was introduced, PCV13 ST (especially ST 3, 19A and 19F) accounted for about 25% of IPD in children. For all of the PCV13 ST, over half of these IPD cases occurred in children who had received ≥2 doses of the recommended PCV schedule; 25% of cases occurred in children who had not received any doses but were of the age at diagnosis that at least 2 PCV doses should have been received. Additional PCV3 ST IPD cases may be preventable if the PCV13 schedule is followed as recommended.

Disclosures. S. L. Kaplan, Pfizer: Grant Investigator and Speaker at PCV13 Launch Meeting in China, Research grant and Speaker honorarium; J. S. Bradley, Merck & Co., Inc.: Investigator, Research support.

OFID 2017:4 (Suppl 1) • Oral Abstracts • S67