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.

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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 to 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 isolate had 0–1 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 upturn 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).

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2491. Murine Typhus: a Common Cause of Acute Febrile Illness with Potential for Serious Complications

Zeezan Aziz, MD; Sundan Kallumadanda, MD; Feng Wang, MD; Vagish S. Hemmige, MD; and Daniel Musner, MD, FIDSA; Department of Family and Preventive Medicine, McAllen Family Medicine Residency Program, The University of Texas Rio Grande Valley, McAllen, Texas; Section of Infectious Diseases, Baylor College of Medicine, Houston, Texas; Baylor College of Medicine, Houston, Texas

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Background. Individual cases and outbreaks of murine typhus have been documented in South Texas. We report 90 cases from Hidalgo County, Texas, enumerating complications and comparing results in children and adults.

Methods. We reviewed records of 101 patients in three hospitals in Hidalgo County, Texas, who had positive typhus serology (IgG or IgM titer ≥1:128) during 3 years, 2014–2016 and were categorized as suspected, probable or confirmed murine typhus cases in accord with CDC definitions. We excluded 11 cases because a concurrent infection may have confounded our tabulation of manifestations or there was insufficient information to make a clinical diagnosis.

Results. The majority presented with typical typhus: fever, headache, myalgias and fatigue. Rash, thrombocytopenia and elevated hepatic transaminases were frequent (Table). Clinical complications in 25 cases (28%) caused a less typical syndrome, including bronchitis, pneumonia, pancreatitis, cholecytitis, mesenteric adenitis, myositis, rhabdomyolysis, meningitis and septic shock. Procalcitonin was >0.5 in 10 of 14 (71%) cases. Once the diagnosis was suspected, patients were treated with doxycycline with a rapid response in every case. Generally fever disappeared within 24–36 hours of the first dose.

Conclusion. Murine typhus is a common endemic infection in South Texas. Although most patients had a typical syndrome, the disease is multisystem, and complications appeared in 28% of cases. Procalcitonin was usually elevated. Rats and opossums are common reservoirs for Rickettsia typhi, and a search for cases of murine typhus may be warranted in other parts of the US as well, so that treatment with doxycycline can be begun promptly.

Disclosures. All authors: No reported disclosures.

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.

Tamaradilishvili, 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. Zandly, PhD9; Scott Snider, MS10; Lisa Miller, MD, MSPH11; Joan Baumbach, MD, MPH12; Bernard Beall, PhD13; and Cynthia Whitney, MD, MPH, FIDSA14; National Center for Immunizations and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia; 9Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia; 10Department of Medicine, Emory University School of Medicine and Atlanta VA Medical Center, Atlanta, Georgia; 11Vanderbilt University School of Medicine, Nashville, Tennessee; 12Oregon Public Health Division, Portland, Oregon; 13University of California - Berkeley, Berkeley, California; 14University of Pittsburgh, Pittsburgh, Pennsylvania; 15Minnesota Department of Health, St. Paul, Minnesota; 16New York State Department of Health, Albany, New York; 17Connecticut Emerging Infections Program, New Haven, Connecticut; 18Preventive Medicine Residency Program, University of Colorado School of Public Health, Aurora, Colorado; 19New Mexico Department of Health, Santa Fe, New Mexico; 20Centers for Disease Control and Prevention, Atlanta, Georgia

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Background. In February 2010, PCV13 was introduced for routine use among children < 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–June 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) before pe-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 35%-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 8% (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.

Table: Symptoms, signs, laboratory findings

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Age &lt; 18</th>
<th>Age &gt; 18</th>
<th>T value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever (temperature)</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>37/48 (80%)</td>
<td>60/78 (77%)</td>
</tr>
<tr>
<td>Rash</td>
<td>10/17 (59%)</td>
<td>22/29 (76%)</td>
<td>32/48 (70%)</td>
</tr>
<tr>
<td>AST &gt;50</td>
<td>12/59 (20%)</td>
<td>15/32 (47%)</td>
<td>23/36 (64%)</td>
</tr>
<tr>
<td>WBC count &gt;5 000</td>
<td>13/65 (20%)</td>
<td>15/50 (30%)</td>
<td>27/34 (80%)</td>
</tr>
<tr>
<td>Platelets &lt; 120 000</td>
<td>12/60 (20%)</td>
<td>15/30 (50%)</td>
<td>30/40 (75%)</td>
</tr>
<tr>
<td>Bilirubin &gt;1.5 mg/dl</td>
<td>3/61 (5%)</td>
<td>4/54 (8%)</td>
<td>27/32 (85%)</td>
</tr>
</tbody>
</table>

*Comparing pediatric vs. adult cases.
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; 1Pediatric Infectious Diseases, Boston University, Boston, Massachusetts and, 1Boston University Schools of Medicine and Public Health, Boston, Massachusetts

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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 by SR serotyped by Quellung reaction.

Results. Three-hundred thirty-seven IPD cases have been identified in MA children between 4 January 2010 and 33.31.2017(Figure). Thirty-six (10.4%) were in infants 1-6 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 6.8/103 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 9.6/103 (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 (50.5%) and CNS disease (66.6%). Children with at least one comorbidity were an increasing proportion of cases reaching 37.9% in 2016 (p = 0.004). The overall mortality rate was 4.5%. Isolates from 301 (90.1%) were available for serotyping; vaccine serotypes (VST) were identified in 101 (33.6%) cases [serotype 19A(49 cases), 7F(21 cases), 3(18 cases), 19F(7cases), 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). Serotypes 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 (from 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.

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