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

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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 from Myanmar was noted, while there is little information on this uprend 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 phage 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 uprend 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 distance and phylogenetic tree of S. Paratyphi A isolates from Myanmar in 2015 (A) and Cambodia in 2013 (B).

Disclosures. All authors: No reported disclosures.

2491. Murine Typhus: a Common Cause of Acute Febrile Illness with Potential for Serious Complications
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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 2013–2016 and were categorized as suspected, probable or confirmed murine typhus cases in accord with CDC definitions. We excluded 11 cases because a confirmed diagnosis was not made in a timely fashion. 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 phage 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 uprend 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
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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–June 2016. Isolates were serotyped by Quellung, 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 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 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.
2493. Invasive Pneumococcal Disease in Massachusetts Children 6 Years Following Introduction of PCV13

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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 as SP by Quellung reaction.

Results. Three-hundred-thirty-seven IPD cases have been identified in MA children between 4.January 4, 2010 and 03.31.2017 (Figure). Thirty-five (10.4%) were in children between 4 and 6 years of age; 41(12.2%) in children between 6 and 12 months; 60 (17.8%) in children aged ≥2 years; 100 (29.7%) in children between 2 and 5 years of age and 301 (90.1%) were available for serotyping; vaccination status of 2 doses was included for ST 14, 18C, 19A 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 some IPD cases due to these ST why they persist.

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. (Table) Of the 30 children with ≥2 doses of PCV, 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, 10, 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 PCV13 ST IPD cases may be preventable if the PCV13 schedule is followed as recommended.

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