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Session: 277. Global Infections
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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 countries, 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 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 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.

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 $\geq 1:128$) 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 bronchiolitis, pneumonia, pancreatitis, cholecystitis, 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.

Table: Symptoms, signs, laboratory findings

Symptoms	Number (%) abnormal			P value ^a
	Age < 18	Age >18	Total	
Fever (temperature >100.4)	36/36(100%)	53/54 (98%)	89/90 (99%)	1
Myalgia	15/20 (75%)	21/24 (88%)	36/44 (82%)	0.44
Headache	23/32 (72%)	37/46 (80%)	60/78 (77%)	0.38
Fatigue	10/17 (59%)	22/29 (76%)	32/46 (70%)	0.22
Signs				
Rash	18/36 (50%)	16/51(31%)	34/87 (39%)	0.12
Labs				
WBC count < 6,000	11/36(31%)	10/54(19%)	21/90(23%)	0.19
Platelets < 120,000	12/36(33%)	37/54(69%)	49/90(54%)	< 0.01
Bilirubin ≥ 1.5	3/36(8%)	14/54 (26%)	17/90(19%)	0.05
AST >50	25/36 (69%)	51/54 (94%)	76/90(84%)	< 0.01

^aComparing 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.

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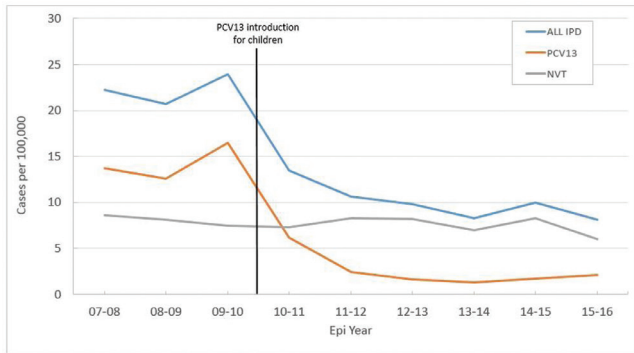
Background. In February 2010, PCV13 was introduced for routine use among children aged < 5 years. In June 2012, PCV13 was recommended for use in series with 23-valent polysaccharide vaccine (PPSV23) for adults ≥ 19 years with select medical conditions, and in August 2014, for all adults ≥ 65 years. We 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).

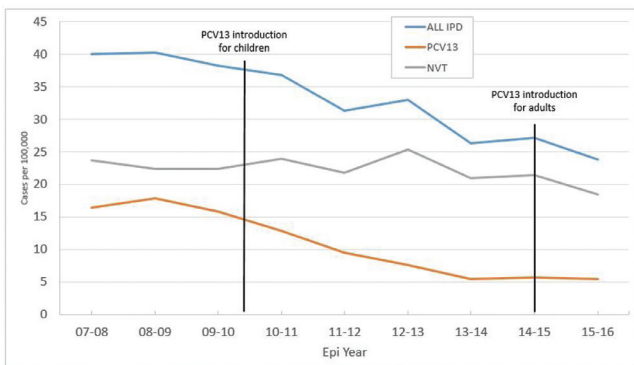
Results. ABCs identified 31,190 IPD cases between 2007 and 2015, with 2,750 cases among children <5 years and 10,930 among those ≥ 65 years. During the two post-PCV13 periods, overall IPD rates were 33%–62% lower relative to 2007–2009 among all age groups, including <5 years and ≥ 65 years (Figure). 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 7F. 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.

IPD rates among children < 5 years old, July 2007 - June 2016



IPD rates among adults ≥65 years old, July 2007 - June 2016



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; Seqirus: Consultant, Consulting fee; L. Harrison, GSK: Scientific Advisor, Consulting fee

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, serotyped 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 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 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; 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 15BC (13.5%), 33F (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.

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2494. Analysis of Invasive Pneumococcal Infections Due to 13-Pneumococcal Conjugate Vaccine Serotypes at 8 US Children's Hospitals During 2014 to 2016

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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. (Table) Of the 30 children with 0 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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ST	PCV13 Doses Prior to IPD ^a					Total Cases	Median age
	0	1	2	3	4		
3	8	5	3 (0)	8	10 (1)	34	54 months
19A	12 (5) ^b	1 (1)	2	2	7 (2)	24	25 months
19F	4	3 (2)	1	5 (1)	8 (2)	21	43 months
7F	4 (1)	0	0	0	0	4	
14	1	0	0	0	1 (1)	2	
18C	1	0	0	0	0	1	
23F	0	0	0	1 (1)	1 (1)	2	
Total	30	9	6	16	27	88	

^aPCV7 doses were included for ST 14, 18C, 19F, and 23F; PCV status of 2 patients was unknown.
^bnumber with underlying condition in ().

2495. Changes in Pneumonia Incidence and Infant Mortality 5 Years Following Introduction of the 13-valent Pneumococcal Conjugate Vaccine in a "3+0" Schedule in Nicaragua

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