

Emergence of PCV13 nonvaccine-specific *Streptococcus pneumoniae* serogroups 15, 23, 33, and 35 isolated from children in Kansas City, Missouri

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ABSTRACT

Background: The 13-valent pneumococcal conjugate vaccine (PCV13) was licensed in February 2010 for the prevention of pneumococcal disease in children. This study examines the frequency of pneumococcal serotypes isolated from children ages 1 week to 19 years in our institution, with particular focus on emerging PCV13 nonvaccine-specific serotype strains. **Methods:** Active pneumococcal surveillance was conducted at Children's Mercy Hospital in Kansas City, MO from 2011 through 2015. All pneumococci isolated from clinical specimens were serotyped by the Quellung capsular swelling reaction. Patient demographic and clinical data were abstracted from medical chart reviews. Duplicate samples were not included in analysis. **Results:** From 2011 through 2015, 418 pneumococcal clinical isolates were evaluated: 118 (28%) invasive and 300 (72%) non-invasive strains. The most common non-PCV13 serogroups identified were 15 (10%), 23 (not F) (11%), 33 (5%), and 35 (9%). The most common PCV13-related serotypes were 3 (9%), 19A (9%), and 19F (8%). Except for serotypes 19A and 19F, the annual number of isolates with these serotypes/serogroups remained relatively stable. Serotype 19A decreased from 21 isolates (19% of the yearly total) in 2011 to 0 isolates in 2015. Surprisingly, the number of serotype 19F isolates increased from 5 (5%) in 2011 to 12 (15%) in 2015. Overall, 67% of non-invasive isolates and 76% of invasive disease isolates had capsule serotypes not included in PCV13. Serotypes 15, 19A, 23 and 35 were often penicillin nonsusceptible. The remaining serotype isolates were usually penicillin susceptible. Invasive pneumococcal disease was much less likely to occur in the third quartile compared to other yearly quartiles (p<0.01). **Conclusion:** PCV13 nonvaccine-specific *Streptococcus pneumoniae* serotypes cause a considerable number of infections in children, and continued surveillance of pneumococcal serotype distribution is important to guide the development of future pneumococcal vaccines.

BACKGROUND

- Streptococcus pneumoniae* is a common cause of invasive bacterial infections such as meningitis, bacteremia, and pneumonia in children. It is also an important etiology of local respiratory tract infections, such as acute otitis media and sinusitis.
- The heptavalent pneumococcal conjugate vaccine (PCV7) licensed in the USA in Feb 2000, and PCV13 licensed in Feb 2010, have resulted in decreased rates of pneumococcal invasive disease in children. However, nonvaccine serotypes have emerged.

OBJECTIVES

- Examine the frequency of pneumococcal serotypes isolated from patients at Children's Mercy Hospital, a 354-bed tertiary care pediatric medical center in Kansas City, Missouri
- Identify possible temporal changes in serotype distribution or antimicrobial susceptibility patterns

METHODS

- Active pneumococcal surveillance was conducted at Children's Mercy Hospital in Kansas City, MO from 2011 through 2015.
- All pneumococci isolated from clinical specimens were serotyped by the Quellung capsular swelling reaction and specific antisera (Statens Serum Institut, Denmark).
- Medical records of all patients were reviewed and demographic, clinical, and laboratory data were abstracted

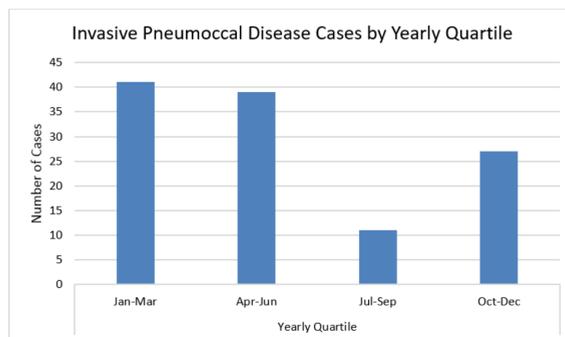
DEFINITIONS

- IPD (invasive pneumococcal disease): Isolation of *S. pneumoniae* from a normally sterile site; excluding middle ear fluid, uncomplicated sinusitis
- PCV13 serotypes: 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F
- Penicillin-resistant *S. pneumoniae*

	S	MIC (µg/mL)	I	R
Meningitis, IV penicillin	≤ 0.06	—	—	≥ 0.12
Non-meningitis, IV penicillin	< 2	—	4	> 8
Non-meningitis, oral penicillin	≤ 0.06	0.12-1	—	≥ 2

RESULTS

- 418 pneumococcal clinical isolates were evaluated
 - 118 (28%) invasive isolates and 300 (71%) noninvasive isolates
- Most common serotypes/serogroups identified (Figure 1)
 - Non-PCV13 serogroups: 15 (10%), 23 (not F) (11%), 33 (5%), and 35 (9%)
 - PCV13 serotypes: 3 (9%), 19A (9%), and 19F (8%)
 - Serotype 19A cases decreased from 21 isolates (19% of the yearly total) in 2011 to 0 isolated in 2015
 - Serotype 19F cases increased from 5 (5%) in 2011 to 12 (15%) in 2015
- Overall, 67% of noninvasive isolates and 76% of invasive disease isolates were non-PCV13 serotypes
- Serotypes/serogroups 15, 19A, 23, and 35 often had decreased penicillin susceptibility (Table 1).
- Invasive pneumococcal disease was much less likely to occur in the 3rd quartile compared to other yearly quartiles (p<0.01).



RESULTS

Fig. 1 Most Common Serotypes/Serogroups Identified

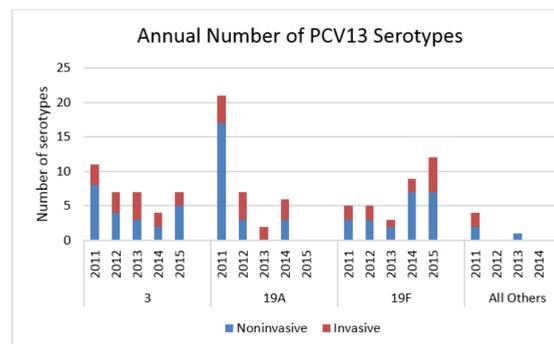
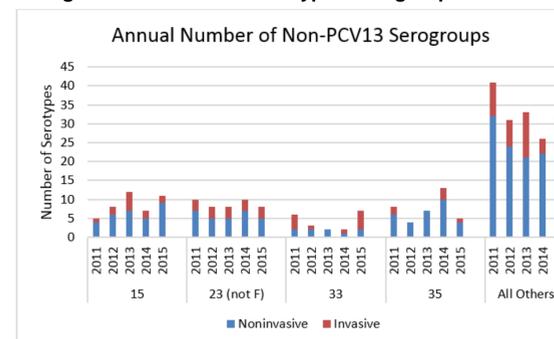


Table 1. Serotypes/Serogroups with Decreased Penicillin Susceptibility

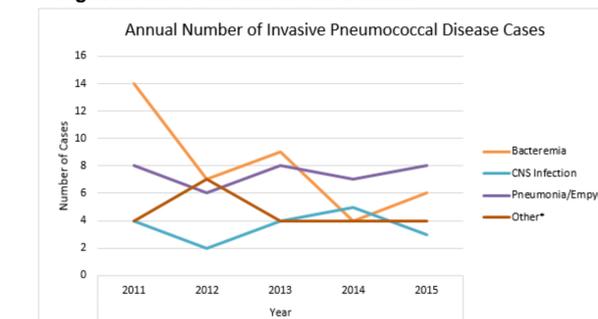
Serotype/Serogroup and Penicillin Susceptibility	Number (%) of Isolates per Year				
	2011	2012	2013	2014	2015
15					
total	5	8	12	7	11
Susceptible	5 (100%)	4 (50%)	4 (33%)	2 (29%)	3 (27%)
Intermediate resistance	0	4 (50%)	6 (50%)	4 (57%)	8 (73/5)
Resistance	0	0	2 (17%)	1 (14%)	0
19A					
total	21	7	2	6	0
Susceptible	1 (5%)	0	0	0	0
Intermediate resistance	4 (19%)	0	0	1 (17%)	0
Resistance	16 (77%)	7 (100%)	2 (100%)	5 (83%)	0
23 (not F)					
total	10	8	8	10	8
Susceptible	6 (60%)	3 (38%)	2 (25%)	5 (50%)	5 (63%)
Intermediate resistance	4 (40%)	4 (50%)	6 (75%)	5 (50%)	3 (37%)
Resistance	0	1 (13%)	0	0	0
35					
total	8	4	7	13	5
Susceptible	2 (25%)	2 (50%)	3 (42%)	3 (23%)	2 (40%)
Intermediate resistance	2 (25%)	0	2 (29%)	1 (8%)	0
Resistance	4 (50%)	2 (50%)	2 (29%)	9 (69%)	3 (60%)

RESULTS

Table 2. Vaccine History of Invasive Disease Cases with PCV13 Serotypes

Serotype	Cases
3	
total	14
PCV13 not received	10
PCV13 < 3 doses	1
PCV13 ≥ 3 doses	3
19A	
total	11
PCV13 not received	8
PCV13 < 3 doses	1
PCV13 ≥ 3 doses	2
19F	
total	12
PCV7 and PCV13 not received	4
PCV7 + PCV13 < 3 doses	2
PCV7 + PCV13 ≥ 3 doses	6

Fig. 2 Invasive Pneumococcal Disease



*Other includes musculoskeletal infections, tonsillar abscesses, orbital cellulitis, etc.

CONCLUSIONS

- PCV13 nonvaccine-specific *Streptococcus pneumoniae* serotypes/serogroups cause a considerable number of infections in children from the Kansas City area
- Penicillin non-susceptible IPD is less of a concern with the decline in 19A-related IPD cases
- IPD due to 19F strains appears to be on the rise, even in children vaccinated with at least the 3 primary doses of pneumococcal conjugate vaccine
- Continued surveillance of pneumococcal serotype distribution is important to guide the development of future pneumococcal vaccines.