Dynamics of colonization of *Streptococcus pneumoniae* strains in healthy Peruvian children before and after PCV7 introduction

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Background

- ✓ *Streptococcus pneumoniae* (*Spn*) causes severe bacterial pneumonia, otitis media, bacteremia, and meningitis in young children.
- ✓ Typically, colonization is asymptomatic, but bacterial acquisition is the first step in pathogenesis.
- ✓ Little is known about the effects of pneumococcal conjugate vaccine introduction on complex carriage dynamics, including the order and frequency of *Spn* serotype colonization.
- ✓ In Peru, the 7-valent pneumococcal vaccine (PCV7) was introduced into the national immunization program in July 2009.

Goal

Assess *Spn* carriage dynamics before and after vaccine introduction among children in the Peruvian Andes

Methods

- ✓ Prospective, household-based study (RESPIRA-PERU) of young children conducted in San Marcos, Cajamarca, Peru
- ✓ Eligible children were less than three years of age at time of enrollment and anticipated remaining in the study area for at least one year.
- ✓ Children were followed until three years of age or until the end of the study, which lasted from May 2009 to September 2011.
- ✓ Additional newborns were added to the cohort to replace children leaving or aging out of the cohort.
- ✓ Nasopharyngeal (NP) samples were collected monthly. DNA was extracted from NP samples and bacterial density was quantified by *lytA*-based qPCR.
- ✓ *S. pneumoniae* strains were serotyped by Quellung reactions (2011) and multiplex PCR (2009).

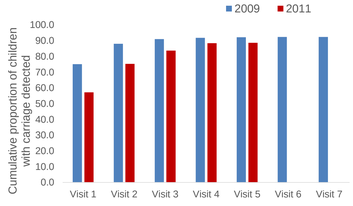
Statistical Analyses

- ✓ Proportion of children with *Spn* colonization during the two years of the study period
- ✓ Distribution of serotypes detected in 2009 and 2011
- ✓ Identify 'persister' strains: strains present at both the first and last NP swab
- ✓ Identify 'recolonizer' strains: strains that replaced a different, earlier strain and were detected at the last NP swab
- ✓ Differences in bacterial density between PCV7 and non-PCV7 types, as well as between first and last detected colonizing strains
- ✓ Seasonal trends in the carriage of PCV7 and non-PCV7 types

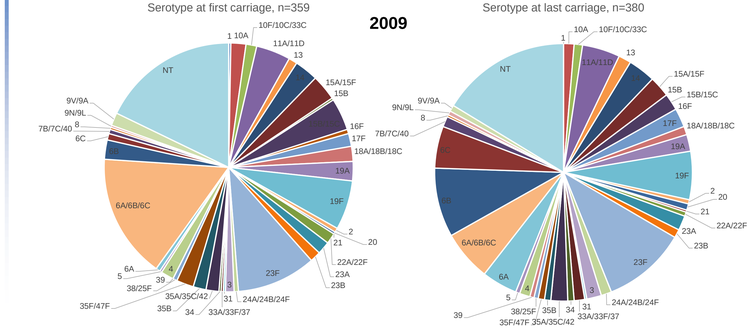
Results

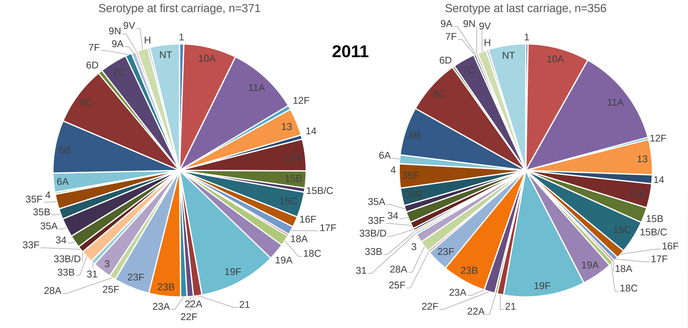
I. High rates of *Spn* carriage in Peruvian children

	2009 (n=510)	2011 (n=509)
Median age at cohort entry, months (IQR)	14.1 (18.1)	9.1 (51.2)
Male sex (%)	53	50
Mean number of study visits with NP swab collected	4.3	3.5
Average days from first to last NP swab collected	86	76
Spn carriage detected at least once	92% (471/510)	89% (451/509)
Median length of carriage, days (IQR)	63 (41,125)	56 (35,91)

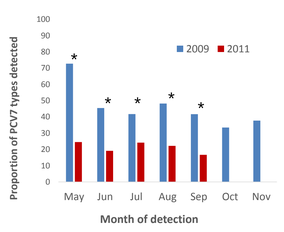


II. Similar distributions of first and last strain detected in both years





III. In 2009, non-PCV7 types increase relative to vaccine types in Sep-Nov; in 2011, non-PCV7 types dominate



Most common Serotypes*, 2009	Frequency (% of all samples)	Most common Serotypes, 2011	Frequency (% of all samples)
6A/B/C	131 (12.1)	11A	102 (10.6)
23F	105 (9.7)	19F	96 (10.0)
19F	64 (5.9)	6C	75 (7.8)
6B	62 (5.7)	10A	72 (7.5)
11A/D	51 (4.7)	6B	52 (5.4)
6C	39 (3.6)	23B	42 (4.4)
14	36 (3.3)	13	39 (4.1)
6A	29 (2.7)	15C	38 (4.0)
19A	27 (2.5)	19A	36 (3.7)
15A/F	22 (2.0)	23F	34 (3.5)
15B/C	22 (2.0)	35F	27 (2.8)
17F	19 (1.8)	7C	27 (2.8)

*Statistically significant difference in vaccine types by year, chi-square

*PCV7 types in red

IV. Persisting vs. re-colonizing strains

	2009	2011	
Persisters*	11A/D (57%, n=14)	6B (71%, n=24)	10A (76%, n=21)
	19F (53%, n=19)	10A (76%, n=21)	11A (80%, n=30)
	23F (63%, n=33)	19F (60%, n=32)	6C (59%, n=22)
		7C (64%, n=11)	
Re-colonizers**	6A (87%, n=15)	13 (58%, n=13)	15A (55%, n=11)
	6B (73%, n=30)	15C (60%, n=15)	19A (73%, n=11)
	6C (94%, n=16)	23B (60%, n=15)	35F (55%, n=11)

PCV7 types in red

* only includes serotypes with more than 10 carriage events recorded

V. Most common strains, a. 2009

First serotype*, 2009	Last serotype*					
	11A/ 11D	14	19F	23F	6A/6B/ 6C	Total
11A/11D	8	0	1	2	0	14
14	0	4	0	0	0	11
19F	0	0	10	0	1	19
23F	0	1	2	21	0	33
6A/6B/6C	2	2	1	1	18	51
Total	14	10	20	34	20	
% Persisting	57.1	40.0	50.0	61.8	90.0	
% Recolonizing	42.9	60.0	50.0	38.2	10.0	

b. 2011

First serotype*, 2011	Last serotype*								
	10A	11A	15A	15C	19F	23B	6B	6C	Total
10A	16	0	0	0	1	1	0	0	21
11A	1	24	0	1	0	0	0	1	30
15A	0	1	5	0	2	0	0	1	11
15C	0	1	0	6	1	0	0	0	10
19F	0	1	0	0	19	0	0	1	32
23B	1	1	0	0	2	6	0	0	13
6B	1	0	1	0	0	0	17	1	24
6C	1	0	0	3	2	0	0	13	22
Total	25	35	11	15	33	15	19	25	
% Persisting	64.0	68.6	45.5	40.0	57.6	40.0	89.5	52.0	
% Recolonizing	36.0	31.4	54.5	60.0	42.4	60.0	10.5	48.0	

*PCV7 types in red

Limitations

- ✓ Only the dominant serotypes in NP samples were detected, so the prevalence and effect of co-colonization is not known.
- ✓ Serotyping for 2009 and 2011 isolates was performed using two different methods (multiplex PCR and Quellung reactions, respectively), so we cannot directly compare serotype distributions.
- ✓ The 2011 cohort was younger, due to the recruiting of infants to replace older children, which may affect serotype distribution in 2011 as compared to 2009.

Conclusions

- ✓ Nearly all children in 2009 and 2011 (>89%) carried *S. pneumo*.
- ✓ Half were recolonized by a different serotype, with strains of serogroup 6 most likely to recolonize children in 2009 and serotypes 19A, 23B, and 15C most likely to recolonize children in 2011.

Ethical approval

The RESPIRA-PERU study was approved by the Ethical Review Board (ERB) of the Instituto de Investigación Nutricional, and the Institutional Review Boards (IRB) of Vanderbilt University and Emory University. An ERB/IRB-approved written informed consent form was obtained from one parent of participating subjects at enrollment. The study was also approved by the local health authorities and by community leaders.

Acknowledgements

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