Impact of Pneumococcal Immunization on Antibiotic Resistance - Results of the German Colonization Study

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Background: Over 100 countries have introduced pneumococcal conjugate vaccines (PCVs) into their childhood immunization schedules. Data documenting the impact of PCVs on antimicrobial-nonsusceptible pneumococci are of high interest. In 2006, German health authorities recommended universal PCV immunization for infants, starting with PCV7 and later substituted by PCV10 or PCV13. Epidemiological data show that PCV-serotypes often carry antibiotic resistance.

Methods: Multicenter prospective epidemiological trial: 242 healthy infants (age 2-4 months) recruited from eight pediatric offices distributed over Germany were followed-up until age five and had nasopharyngeal swabs taken according to WHO Working Group Standards: Visit 1 (V1) before the first PCV-immunization (age 2-4 mo.), V2 after completed primary immunization (age 9-12 mo.), V3 after booster (age 17-19 mo.), V4 at 59-61 mo., **figure 1**).

Streptococcus pneumoniae (Spn) serotyping was done using the Neufeld Quellung reaction and antibiotic susceptibility testing was performed for routine anti-infectives (i.e., erythromycin, penicillin, clindamycin, tetracycline).

Results 1: Of our initially included subjects, 65.3% were followed-up to age five, all of them completely immunized against pneumococci.

Pneumococcal colonization increased from 14.7% at V1 over 31.5% (V2), 34.8% (V3) to 42.2% at V4. At age 5, no PCV7- or PCV10 serotypes could be detected anymore, and only six PCV13-serotypes (3&19A).

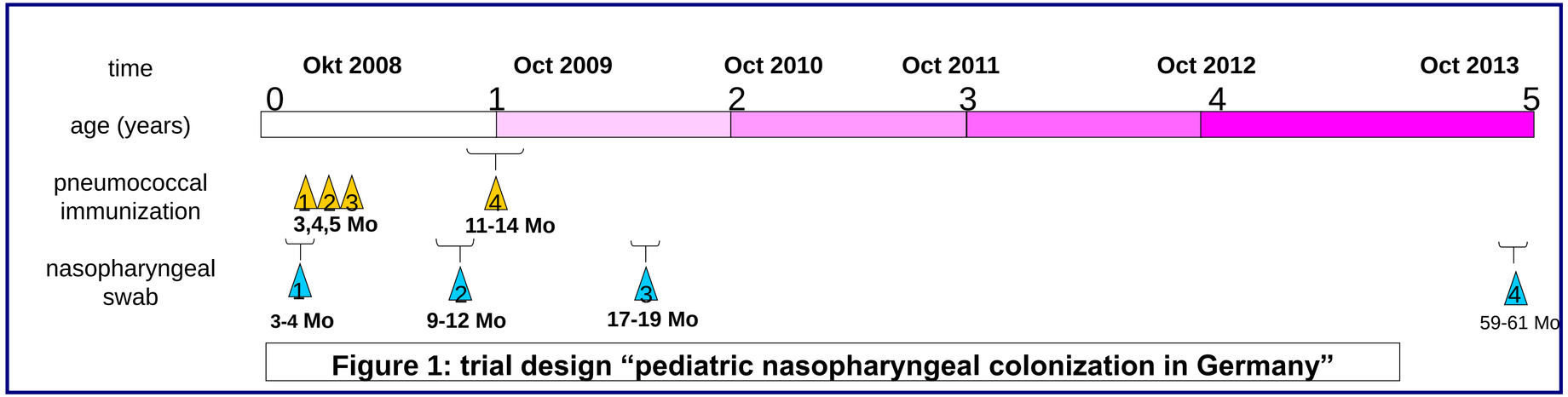


Figure 1: trial design "pediatric nasopharyngeal colonization in Germany"

	Visite 1		Visite 2		Visite 3		Visite 4	
	total (N=236)		total (N=217)		total (N=203)		total (N=155)	
Age [months]	n	%	n	%	n	%	n	%
median	2.3		11.8		18.6		60.4	
minimum	1.9		8.6		16.4		59.0	
maximum	4.9		14.9		26.1		68.0	
Siblings								
yes	119	50.4	114	52.5	112	55.2	117	75.5
no	117	49.6	103	47.5	91	44.8	38	24.5
Siblings' age [years]	total (N=173)		total (N=163)		total (N=159)		total (N=166)	
median	5.0		5.0		6.0		8.0	
minimum	0.0		1.0		0.0		0.0	
maximum	18.0		19.0		20.0		17	
Day-care								
yes	1	0.4	5	2.3	25	12.3	151	97.4
no	235	99.6	212	97.7	178	87.7	4	2.6
Siblings in day-care								
yes	97	41.1	102	47.0	102	50.3	101	65.2
no	117	49.6	104	47.5	91	44.8	38	24.5
unknown	22	9.3	12	5.5	10	4.9	16	10.3
Tobacco-smoke exposure								
yes	76	32.2	65	30.0	61	30.0	44	28.4
no	160	67.8	152	70.0	142	70.0	111	71.6

Results 2: In parallel with mucosal decolonization, a decrease of antibiotic-resistant pneumococci was observed, especially for macrolides (24% at V1, 11% at V4) and clindamycin (from 13% to 5%). For tetracyclines, which are more important in older age groups, a decrease from a maximum of 13% to 5% was found.

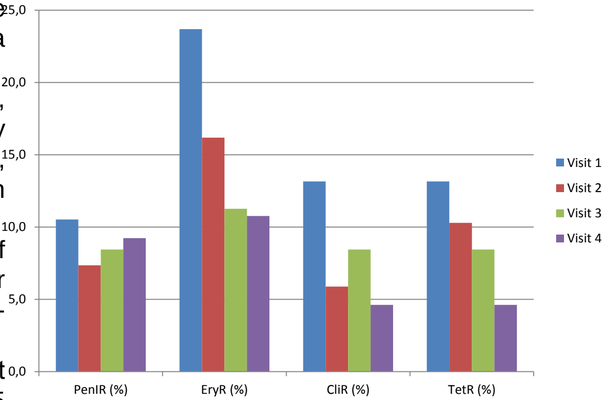
Discussion 1: In the USA (2009-2013), antimicro-bial-nonsusceptible IPD caused by exclusive PCV13 serotypes (1, 3, 5, 7F, 19A), and multi-drug-nonsusceptible IPD decreased in all age groups.

In South Africa, PCV9 induced a decrease of penicillin-resistant IPD by 67%. In Brazil, under the impact of PCV10, resistancies solely decreased against β-lactam-antibiotics.

Data from Israel also showed a significant reduction of isolates with penicillin MICs of 0.125 g/ml (26.2% to 16.4%), accompanied by increasing non-vaccine-type strains with penicillin MICs of 2 g/ml (mainly serotype 19A).

Our data are in line with observations from other countries with PCV immunization programs, where strains carrying antibiotic resistance were mainly PCV13 serotypes. International surveillance data demonstrate that targeting prevalent capsular serotypes with PCVs is effective in reducing resistant infections.

Discussion 2: Overall, continued surveillance is needed to document the effects of PCV13 on serotype distribution, antimicrobial resistance, and replacement.



Conclusion: Our surveillance-study shows a continuous decrease of resistance against important antibiotics, confirming effective decolonization also in clinical practice.

In times of globally increasing antibiotic resistance, a positive 'side effect' of PCV-immunization is a subsequent decrease of antibiotic resistant-pneumococci. Nonetheless, resistant non-vaccine-serotype clones continue to emerge and expand.

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