Changing Epidemiology of Antimicrobial-Resistant *Streptococcus pneumoniae* in the United States, 2004–2005

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Background. The impact of pediatric 7-valent pneumococcal conjugate vaccination (PCV-7) on the population of *Streptococcus pneumoniae* in the United States was examined by determining the serotypes, antimicrobial resistance profiles, and genetic relatedness of isolates from patients with invasive and noninvasive infections during the 2004–2005 respiratory illness season.

Methods. Susceptibility testing, serotyping, and pulsed-field gel electrophoresis analysis were performed on 1647 *S. pneumoniae* isolates obtained from 41 US medical centers in 2004–2005 as part of a longitudinal antimicrobial resistance surveillance program. The results were compared with surveillance data from earlier periods.

Results. From the 1999–2000 to the 2004–2005 respiratory illness season, the prevalence of isolates with intermediate penicillin resistance (minimum inhibitory concentration, 0.1–1 μg/mL) increased from 12.7% to 17.9%, prevalence of penicillin-resistant isolates (minimum inhibitory concentration, ≥2 μg/mL) decreased from 21.5% to 14.6%, and prevalence of isolates resistant to erythromycin increased from 25.7% to 29.1% among *S. pneumoniae* isolates. The prevalence of multidrug resistance among isolates did not change (22.4% in 1999–2000 and 20.0% in 2004–2005). Sixty different serotypes were recognized among the isolates from 2004–2005; predominant serotypes were 19A (14.5%), 3 (11.2%), 6A (7.1%), 19F (7%), and 11A (6%). Serotypes that were included in PCV-7 accounted for 16.3% of isolates; 28.4% of strains isolated had PCV-7–related serotypes, and the remaining 55.3% of isolates had serotypes that were unrelated to PCV-7. The serotype distribution of the penicillin-resistant *S. pneumoniae* population changed from 1999–2000 to 2004–2005, with an increase in the prevalence of serotype 19A (1.5% to 35.4%) and serotype 35B (1.2% to 12.5%) and a decrease in the prevalence of most PCV-7 serotypes, including 23F (16.1% to 5%), 9V (16.1% to 4.2%), 6B (13.7% to 3.8%), and 14 (18.5% to 2.9%).

Conclusions. The penicillin-resistant *S. pneumoniae* population has changed; most isolates are now closely related to 2 Pneumococcal Molecular Epidemiology Network clones that increased in prevalence from 1999–2000 to 2004–2005 (Taiwan[19F]-14 [14.6% to 36.7%; 60% were serotype 19A] and Utah[35B]-24 [0.9% to 16.3%]).

Antimicrobial resistance with *Streptococcus pneumoniae* emerged during the 1990s in the United States [1, 2]. By the year 2000, >20% of pneumococcal isolates from patients with respiratory tract and invasive infections possessed a multidrug-resistant phenotype (i.e., were nonsusceptible to penicillin and ≥2 other non–β-lac-tam antimicrobial classes) [3]. As resistance rates have increased, therapeutic failures in patients with pneumococcal infections have occurred [4].

The 23-valent polysaccharide pneumococcal vaccine has been available since 1977 for individuals aged ≥2 years who have risk factors for serious pneumococcal disease. In February 2000, the heptavalent pneumococcal conjugate vaccine (PCV-7; Prevnar; Wyeth) was introduced in the United States for routine use in children aged <2 years. At the time of its introduction, 5 of the 7 serotypes included in PCV-7 (6B, 9V, 14, 19F, and 23F) accounted for 89% of the penicillin-resistant (MIC, ≥2 μg/mL) isolates of *S. pneumoniae* in the United States [5].

By 2004, 73% of children aged 19–35 months had received ≥3 of the 4 recommended PCV-7 doses [6].

Substantial decreases in the incidence of pneumococcal invasive disease were evident by 2001–2002 in all age groups [7–9]. Decreases in invasive disease due to antimicrobial-resistant pneumococci have also been attributed to PCV-7 [10, 11]. However, the increase in the rate of infections caused by non-vaccine "replacement" strains is an ongoing concern [9, 12–17].

Longitudinal surveillance of isolates that cause pneumococcal disease provides useful information for assessing the impact of current vaccines and establishes a basis to guide future vaccine development. Data derived from the characterization of isolates of S. pneumoniae recovered from patients with localized respiratory infections are limited [18]. In this article, we describe the antimicrobial susceptibility profiles, serotype distribution, and genetic relatedness of S. pneumoniae isolates that caused invasive and noninvasive infections in the United States during the 2004–2005 respiratory illness season. These data are compared with previous studies that we conducted during the 1994–1995 and 1999–2000 respiratory illness seasons, before the introduction and widespread application of PCV-7 [3, 5].

METHODS

A total of 1647 isolates of S. pneumoniae were characterized in this study. These organisms were recovered from patients in 41 US medical centers during the 2004–2005 respiratory illness season (1 November 2004 through 30 April 2005). Each laboratory was asked to submit 50 consecutive, clinically significant pneumococcal isolates from unique patients. On receipt in the central laboratory, organisms were stored at −70°C on beads.

The identification of isolates was confirmed using the AccuProbe S. pneumoniae culture identification test (Gen-Probe). Capsular serotypes were determined with type-specific antisera (Statens Serum Institut).

Antimicrobial susceptibility testing was performed using the Clinical and Laboratory Standards Institute broth microdilution method in Mueller-Hinton broth with 3% lysed horse blood at a final inoculum concentration of approximately 5×10^5 colony forming units per mL [19, 20]. Trays were incubated for 20–24 h in ambient air (air temperature, 35°C ± 2°C) before determining MICs. S. pneumoniae ATCC 49619 was used as a quality control strain. The multidrug resistance phenotype was defined as nonsusceptibility to penicillin (MIC, ≥0.12 μg/mL) and ≥2 other non–β-lactam antimicrobial classes.

In January 2008, the Clinical and Laboratory Standards Institute published new breakpoints for parenteral penicillin therapy of nonmeningitis (susceptible, ≤2 μg/mL; intermediate, 4 μg/mL; resistant, ≥8 μg/mL) and meningitis (susceptible, ≤0.06 μg/mL; resistant, ≥0.1 μg/mL) strains of S. pneumoniae, although the original breakpoints were retained for oral pen-

icillin therapy of nonmeningitis isolates (susceptible, ≤0.06 μg/mL; intermediate, 0.1–1 μg/mL; resistant, ≥2 μg/mL) [21]. For pneumococcal isolates recovered from specimens other than CSF, laboratories are advised to report meningitis and nonmeningitis interpretations. To avoid confusion, we applied the penicillin breakpoints that were used in previous studies and that were applicable during the surveillance periods (i.e., the current oral therapy nonmeningitis breakpoints) [21]. The penicillin nonsusceptible category is equivalent for oral nonmeningitis and parenteral meningitis isolates (≥0.1 μg/mL).

PFGE was performed using a simplified protocol for S. pneumoniae [22] with use of SmaI (250 U/mL) restriction endonuclease digestion of DNA. The CHEF-DR II (Bio-Rad) instrument was used for electrophoresis with conditions of 200 V at 14°C for 20 h (initial forward time, 1 s; final forward time, 20 s). Ethidium bromide–stained gels were analyzed using Bionumerics software (Applied Maths). The unweighted paired-group method with arithmetic averages and Dice's coefficient (optimization, 1.0%; position tolerance, 1.0%) was used for dendrogram construction. Isolates that differed by ≤3 bands (dendrogram similarity coefficient, ≥84%) were assigned to the same PFGE type [23]. PFGE profiles of 26 pneumococcal clones recognized by the Pneumococcal Molecular Epidemiology Network (PMEN) (Spain[23F]-1, Spain[6B]-2, Spain[9V]-3, Tennessee[23F]-4, Spain[14]-5, Hungary[19A]-6, South Africa[19A]-7, South Africa[6B]-8, England[14]-9, Slovakia [Czech Republic][14]-10, Slovakia [Czech Republic][19A]-11, Finland[6B]-12, South Africa[19A]-13, Taiwan[19F]-14, Taiwan[23F]-15, Poland[23F]-16, Maryland[6B]-17, Tennessee[14]-18, Colombia[5]-19, Poland[6B]-20, Portugal[19F]-21, Greece[6B]-22, North Carolina[6A]-23, Utah[35B]-24, Sweden[15A]-25, and Colombia[23F]-26) were included in the dendrogram for comparison with the surveillance isolates [24].

The relationship of isolate serotype to specimen type, patient age group, resistance profile, and PFGE type was examined. The serotype distribution and genetic relatedness of the penicillin-resistant S. pneumoniae (PRSP) population (MIC, ≥2 μg/mL) in 2004–2005 was compared with previously published results for PRSP isolates from 1994–1995 and 1999–2000 [3, 5]. Twenty-seven of the 41 laboratories in the 2004–2005 study also participated during the 1999–2000 surveillance period. Twenty-two of the 33 medical centers in the 1999–2000 study were part of the 1994–1995 surveillance project [3]. Fisher's 2-tailed exact test was used to assess the statistical significance of group proportion differences.

RESULTS

In 2004–2005, 32.5% of the pneumococcal isolates were nonsusceptible to penicillin (17.9% had an MIC 0.1–1 μg/mL; 14.6% had an MIC ≥2 μg/mL) (table 1). Rates of penicillin resistance varied by the specimen type from which isolates were obtained. Among isolates from blood specimens, 15.8% had

Table 1. MIC distributions for 1647 *Streptococcus pneumoniae* isolates obtained during the 2004–2005 respiratory illness season.

Antimicrobial agent	No. of isolates with MIC, µg/mL													MIC$_{50}$, µg/mL	MIC$_{90}$, µg/mL	I, %	R, %
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	64	>64				
Penicillin[a]	1023	89	109	74	41	71	123	108	9	...	...	...	...	0.03	2	17.9	14.6
Amoxicillin	1039	143	74	32	53	78	103	39	83	3	...	...	...	0.03	2	2.4	5.2
Ceftriaxone	828	323	70	71	89	169	69	21	7	...	...	...	...	0.03	1	10.3	5.9
Vancomycin	...	...	70[b]	756	821	...	...	...	...	...	...	...	...	0.25	0.5	...	...
Erythromycin	...	1159[c]	5	1	2	14	49	90	88	37	8	2	192	≤0.06	>128	0.1	29.1
Clindamycin	881	557	17	5	2	...	1	...	1	...	1	12	170	≤0.03	>64	0.1	11.2
Tetracycline	...	...	...	...	...	1360[d]	19	8	12	32	151	65[e]	...	≤1	32	0.5	15.8
TMP-SMX	9	44	434	597	115	56	46	118	175	46	7	...	...	0.25	8	6.2	21.0
Ciprofloxacin	2	2	6	11	679	653	259	17	3	3	9	2	1	1	2	1.0	1.1
Levofloxacin	3	5	...	12	377	1161	73	1	4	8	3	...	...	1	1	0.06	0.9
Moxifloxacin	15	145	1215	255	2	...	6	8	...	...	1	...	...	0.12	0.25	0.4	0.5
Chloramphenicol	...	...	...	...	...	251[d]	847	468	44	31	5	1[e]	...	2	4	...	4.9

NOTE. I, intermediate resistant; R, resistant, TMP-SMX, trimethoprim-sulfamethoxazole. MIC susceptibility categories for each antimicrobial agent are as follows: penicillin (I, 0.1–1 µg/mL; R, ≥2 µg/mL), amoxicillin (I, 4 µg/mL; R, ≥8 µg/mL), ceftriaxone (I, 1 µg/mL; R, ≥2 µg/mL), vancomycin (nonsusceptible, >1 µg/ml), erythromycin (I, 0.5 µg/mL; R, ≥1 µg/mL), clindamycin (I, 0.5 µg/mL; R, ≥1 µg/mL), tetracycline (I, 4 µg/mL; R, ≥8 µg/mL), TMP-SMX (I, 1/19–2/38 µg/ mL; R, ≥4/76 µg/mL), ciprofloxacin (I, 4 µg/mL; R, ≥8 µg/mL), levofloxacin (I, 4 µg/mL; R, ≥8 µg/mL), moxifloxacin (I, 2 µg/mL; R, ≥4 µg/mL), and chloramphenicol (R, ≥8 µg/mL).

[a] With use of the new 2008 Clinical and Laboratory Standards Institute breakpoints for oral penicillin (I, 0.1–1 µg/mL; R, ≥2 µg/mL), 17.9% of isolates had intermediate resistance and 14.6 were resistant; with use of the new parenteral penicillin therapy breakpoint for meningitis strains (R, ≥0.1 µg/mL), 32.5% were resistant; and with use of the new parenteral penicllin therapy breakpoints for nonmeningitis strains (I, 4 µg/mL; R, ≥8 µg/mL), 6.6% had intermediate resistance and 0.6% were resistant.

[b] ≤0.12 µg/mL.

[c] ≤0.06 µg/mL.

[d] ≤1 µg/mL.

[e] ≥64 µg/mL.

intermediate resistance and 9.6% were resistant; from CSF or other sterile body fluid specimens, 33.3% had intermediate resistance and 13.3% were resistant; from ear specimens, 23.8% had intermediate resistance and 25.4% were resistant; from sinus specimens, 21.9% had intermediate resistance and 18.9% were resistant; from eye specimens, 29.8% had intermediate resistance and 6.4% were resistant; and from lower respiratory tract specimens, 16.8% had intermediate resistance and 14.7% were resistant. The prevalence of fluoroquinolone resistance was 0.5%–1.1%. Rates of erythromycin and multidrug resistance were 29.1% and 20.0%, respectively.

The 1647 *S. pneumoniae* isolates obtained in 2004–2005 comprised 60 different serotypes (table 2). The predominant serotypes were 19A (14.5% of isolates), 3 (11.2%), 6A (7.1%), 19F (7%), 11A (6.1%), 22F (4.7%), and 35B (4.4%). Serotypes included in PCV-7 accounted for 16.3% of strains; 28.4% of strains had PCV-7–related serotypes, and the remaining 55.3% of strains had serotypes unrelated to those included in PCV-7.

Of the 1647 isolates obtained, 53% were from lower respiratory tract specimens, 13% were from upper respiratory tract specimens, and 26% were from invasive specimens (blood, CSF, or other normally sterile body fluid specimens). Middle ear specimens yielded more PCV-7–related serotype isolates (40.5%; P = .003) and fewer PCV-7 serotypes (9.5%; P = .03) than did specimens from other sites (table 2). Compared with the proportions of isolates from other specimen sites, the proportions of serotype 19A (33.3%; P < .001), serotype 35B (8.7%; P = .02), serotype 21 (1.6%; P = .007), and serotype 29 (2.4%; P = .018) isolates were greater from middle ear specimens. The only significant difference between the serotype distribution of isolates recovered from sinus specimens, compared with other specimen types, was a greater prevalence of serotype 23A isolates (9.9%; P < .001). Specimens of CSF and other sterile body fluids yielded a greater proportion of serotype 23A isolates (13.3%; P = .009) and fewer PCV-7 serotype isolates (3.3%; P = .048) than did other sources. Cultures of blood specimens yielded more serotype 7F (4.4%; P < .001), 12F (5.9%; P < .001), 22F (6.7%; P = .04), and 4 (5.7%; P < .001) isolates than did cultures of other specimen types, but fewer serotype 3 (8.4%; P = .046), 11A (2.7%; P < .001), and 35B (1.2%; P < .001) isolates were recovered from blood cultures. Lower respiratory tract specimens yielded more serotype 11A (8.0%; P < .001) and nontypeable isolates (2.6%; P = .009) than did other specimen types.

Most of the isolates (60%) were from inpatients; 38% were from outpatients. Twenty percent of patients were aged ≤5 years, 8% were aged 6–20 years, 47% were aged 21–64 years, 21% were aged ≥65 years, and 4% were of an unknown age. The serotype distribution of isolates was similar among age groups, with a few exceptions (data not shown). For patients

Table 2. Serotype distribution of 1647 *Streptococcus pneumoniae* isolates from the 2004–2005 respiratory illness season, by specimen type.

Serotype	No. (%) of isolates						
	All specimens (n = 1647)	LRT (n = 870)	Blood (n = 406)	CSF/sterile BF (n = 30)	Ear (n = 126)	Sinus (n = 91)	Eye/other (n = 124)
PCV-7							
4[a]	34 (2.1)	10 (1.1)	23 (5.7)	…	…	1 (1.0)	…
6B[a]	35 (2.1)	22 (2.5)	7 (1.7)	…	2 (1.6)	3 (3.3)	1 (0.8)
9V[a]	21 (1.3)	11 (1.3)	9 (2.2)	…	…	…	1 (0.8)
14[a]	13 (0.8)	7 (0.8)	4 (1.0)	…	…	2 (2.2)	…
18C[a]	10 (0.6)	5 (0.6)	4 (1.0)	…	1 (0.8)	…	…
19F[a]	116 (7.0)	69 (7.9)	20 (4.9)	1 (3.3)	7 (5.6)	9 (9.9)	10 (8.1)
23F[a]	40 (2.4)	24 (2.8)	7 (1.7)	…	2 (1.6)	2 (2.2)	5 (4.0)
Total	269 (16.3)	148 (17.0)	74 (18.2)	1 (3.3)	12 (9.5)	17 (18.7)	17 (13.7)
PCV-7 related							
6A	117 (7.1)	59 (6.8)	28 (6.9)	4 (13.3)	5 (4.0)	10 (11.0)	11 (8.9)
9A	5 (0.3)	3 (0.3)	1 (0.2)	…	1 (0.8)	…	…
9L	5 (0.3)	4 (0.5)	1 (0.2)	…	…	…	…
9N[a]	14 (0.9)	9 (1.0)	2 (0.5)	…	1 (0.8)	…	2 (1.6)
18A	3 (0.2)	2 (0.2)	…	…	…	1 (1.0)	…
18B	5 (0.3)	4 (0.5)	…	…	…	…	1 (0.8)
18F	4 (0.2)	2 (0.2)	2 (0.5)	…	…	…	…
19A[a]	238 (14.5)	90 (10.3)	71 (17.5)	5 (16.7)	42 (33.3)	10 (11.0)	20 (16.1)
19B	3 (0.2)	…	3 (0.7)	…	…	…	…
19C	1 (0.1)	1 (0.1)	…	…	…	…	…
23A	47 (2.9)	22 (2.5)	6 (1.5)	4 (13.3)	1 (0.8)	9 (9.9)	5 (4.0)
23B	25 (1.5)	18 (2.1)	3 (0.7)	…	1 (0.8)	3 (3.3)	…
Total	467 (28.4)	214 (24.6)	117 (28.8)	13 (43.3)	51 (40.5)	33 (36.3)	39 (31.5)
Non–PCV-7							
1[a]	12 (0.7)	6 (0.7)	4 (1.0)	2 (6.7)	…	…	…
2[a]	1 (0.1)	1 (0.1)	…	…	…	…	…
3[a]	184 (11.2)	102 (11.7)	34 (8.4)	5 (16.7)	20 (15.9)	7 (7.7)	16 (12.9)
5[a]	2 (0.1)	…	…	…	1 (0.8)	1 (1.0)	…
7F[a]	29 (1.8)	7 (0.8)	18 (4.4)	…	1 (0.8)	1 (1.0)	2 (1.6)
7A	1 (0.1)	1 (0.1)	…	…	…	…	…
7C	8 (0.5)	4 (0.5)	3 (0.7)	…	1 (0.8)	…	…
8[a]	7 (0.4)	3 (0.3)	4 (1.0)	…	…	…	…
10F	1 (0.1)	…	1 (0.2)	…	…	…	…
10A[a]	23 (1.4)	14 (1.6)	6 (1.5)	…	…	1 (1.0)	2 (1.6)
11A[a]	101 (6.1)	70 (8.0)	11 (2.7)	1 (3.3)	6 (4.8)	7 (7.7)	6 (4.8)
11D	1 (0.1)	1 (0.1)	…	…	…	…	…
12F[a]	29 (1.8)	4 (0.5)	24 (5.9)	1 (3.3)	…	…	…
12B	2 (0.1)	1 (0.1)	1 (0.2)	…	…	…	…
13	5 (0.3)	2 (0.2)	2 (0.5)	…	1 (0.8)	…	…
15F	2 (0.1)	1 (0.1)	1 (0.2)	…	…	…	…
15A	44 (2.7)	29 (3.3)	8 (2.0)	2 (6.7)	1 (0.8)	3 (3.3)	1 (0.8)
15B[a]	38 (2.3)	20 (2.3)	10 (2.5)	1 (3.3)	4 (3.2)	1 (1.0)	2 (1.6)
15C	30 (1.8)	16 (1.8)	9 (2.2)	…	1 (0.8)	1 (1.0)	3 (2.4)
16F	38 (2.3)	23 (2.6)	10 (2.5)	1 (3.3)	…	4 (4.4)	…
16A	2 (0.1)	2 (0.2)	…	…	…	…	…
17F[a]	11 (0.7)	6 (0.7)	4 (1.0)	…	…	1 (1.0)	…
20[a]	7 (0.4)	4 (0.5)	3 (0.7)	…	…	…	…
21	6 (0.4)	2 (0.2)	…	…	2 (1.6)	…	2 (1.6)

(continued)

Table 2. *(Continued.)*

Serotype	No. (%) of isolates						
	All specimens (n = 1647)	LRT (n = 870)	Blood (n = 406)	CSF/sterile BF (n = 30)	Ear (n = 126)	Sinus (n = 91)	Eye/other (n = 124)
22F[a]	77 (4.7)	36 (4.1)	27 (6.7)	…	5 (4.0)	3 (3.3)	6 (4.8)
24F	1 (0.1)	1 (0.1)	…	…	…	…	…
25A	3 (0.2)	2 (0.2)	1 (0.2)	…	…	…	…
28A/28F	4 (0.2)	…	3 (0.7)	…	…	…	1 (0.8)
29	8 (0.5)	5 (0.6)	…	…	3 (2.4)	…	…
31	35 (2.1)	22 (2.5)	4 (1.0)	…	…	3 (3.3)	6 (4.8)
33F[a]	16 (1.0)	8 (0.9)	5 (1.2)	1 (3.3)	1 (0.8)	…	1 (0.8)
33A	6 (0.4)	1 (0.1)	4 (1.0)	…	1 (0.8)	…	…
34	11 (0.7)	7 (0.8)	1 (0.2)	1 (3.3)	…	…	2 (1.6)
35F	34 (2.1)	20 (2.3)	5 (1.2)	1 (3.3)	3 (2.4)	2 (2.2)	3 (2.4)
35A	15 (0.9)	8 (0.9)	…	…	1 (0.8)	1 (1.0)	5 (4.0)
35B	72 (4.4)	46 (5.3)	5 (1.2)	…	11 (8.7)	3 (3.3)	7 (5.6)
38	12 (0.7)	7 (0.8)	4 (1.0)	…	…	1 (1.0)	…
39/40/48	3 (0.2)	3 (0.3)	…	…	…	…	…
Nontypeable	30 (1.8)	23 (2.6)	3 (0.7)	…	…	1 (1.0)	3 (2.4)
Total	911 (55.3)	508 (58.4)	215 (53.0)	16 (50.0)	63 (50.0)	41 (45.1)	68 (54.8)

NOTE. BF, body fluid; LRT, lower respiratory tract; PCV-7, 7-valent pneumococcal vaccine.

[a] Included in the 23-valent polysaccharide pneumococcal vaccine.

aged 0–5 years, the percentage of isolates belonging to serotype 19A (25.3%; $P < .001$) and 35B (7.3%; $P = .006$) was significantly higher than that for other age groups, and the proportion of serotype 3 isolates was lower (7.0%; $P = .006$). Among the patients aged 21–64 years, the proportion of 19A isolates (11.1%; $P < .001$) was lower than that among other age groups. Isolates from patients aged ≥65 years included fewer serotype 19A (11.1%; $P = .049$) but more serotype 3 (14.3%; $P = .04$) and 22F (6.9%; $P = .04$) isolates, compared with isolates from patients in other age groups.

The serotype distribution of penicillin-nonsusceptible and multidrug-resistant isolates is presented in table 3. Fifty percent of the isolates with intermediate resistance to penicillin and 47.1% of the multidrug-resistant isolates expressed PCV-7–related serotypes (table 3). Serotypes 19A (33.1%), 19F (19.8%), 6A (11.6%), and 15A (10%) were predominant among multidrug-resistant isolates. Most PRSP (60%) and multidrug-resistant (53%) isolates were serotype 19A or 19F.

The 1647 isolates from 2004–2005 were assigned to 436 different PFGE types (table 4). Twenty-six PFGE types (A–Z) included ≥10 isolates. Nineteen PFGE types (a–t) included 6–9 isolates. PFGE types v1–9, w1–15, x1–23, and z1–67 represented PFGE patterns that included 5, 4, 3, and 2 isolates, respectively. There were 277 isolates with unique PFGE patterns (u1–277).

Eleven PFGE types identified among our isolates were closely related to PMEN clones. PFGE type C (83 isolates) was a single locus variant of Taiwan[19F]-14, type E (72) was related to Utah[35B]-24, type G (42) was related to Sweden[15A]-25, type N (21) was related to Tennessee[23F]-4, type S (15) was related to Spain[23F]-1,

type W (11) was related to Taiwan[19F]-14, type X (11) was related to Colombia[23F]-26, type a (9) was related to North Carolina[6A]-23, type e (8) was related to Spain[9V]-3, type g (7) was related to Spain[6B]-2, and type r (6) was related to England[14]-9. One unique multidrug-resistant isolate with a penicillin MIC of 4 μg/mL had a PFGE pattern similar to Maryland[6B]-17. Most of the 240 PRSP isolates (158 [65.8%]) and 329 multidrug-resistant isolates (168 [51.1%]) had PFGE types that were closely related to a PMEN clone. Only one-third of the 295 isolates with intermediate resistance to penicillin (98 [33.2%]) had PFGE profiles that were similar to PMEN clones.

The 8 predominant PFGE patterns (A-H) included 40.6% of the isolates from 2004–2005. Most of the isolates of each PFGE type expressed a common serotype and antibiogram profile. The distribution of specimen types that yielded PFGE A and PFGE G isolates was similar to that of the overall isolate population. The distribution of isolates that were obtained from culture of blood specimens varied between the major PFGE types; more isolates were obtained from blood specimens among PFGE B (33%; $P = .04$), PFGE F (36.4%; $P = .03$), and PFGE H isolates (65.6%; $P < .001$) than that among the overall isolate population, and fewer isolates were from blood culture specimens among PFGE C (10.8%; $P = .002$), PFGE D (10.5%; $P = .003$), and PFGE E isolates (11.1%; $P = .005$). The prevalence of isolates from lower respiratory tract specimens was higher among PFGE D isolates (64.5%; $P = .04$) and lower among PFGE H isolates (28.1%; $P = .007$) than that among the general isolate population. The proportion of isolates from middle ear specimens was higher among PFGE C (20.5%;

Table 3. Serotype distribution of 1647 *Streptococcus pneumoniae* isolates from the 2004–2005 respiratory illness season, by susceptibility profile.

Serotype	No. (%) of isolates Penicillin S (n = 1112)	Penicillin I (n = 295)	Penicillin R (n = 240)	MDR (n = 329)
PCV-7				
4[a]	32 (2.9)	1 (0.3)	1 (0.4)	2 (0.6)
6B[a]	13 (1.2)	13 (4.4)	9 (3.8)	13 (4.0)
9V[a]	3 (0.3)	8 (2.7)	10 (4.2)	11 (3.3)
14[a]	4 (0.4)	2 (0.7)	7 (2.9)	8 (2.4)
18C[a]	10 (0.9)	...	...	...
19F[a]	48 (4.3)	10 (3.4)	58 (24.2)	65 (19.8)
23F[a]	21 (1.9)	7 (2.4)	12 (5.0)	12 (3.6)
Total	131 (11.8)	41 (13.9)	97 (40.4)	111 (33.7)
PCV-7 related				
6A	53 (4.8)	57 (19.3)	7 (2.9)	38 (11.6)
9A	1 (0.1)	1 (0.3)	3 (1.3)	1 (0.3)
9L/9N[a]/18F/18A	26 (2.3)	...	...	...
18B	4 (0.4)	1 (0.3)	...	1 (0.3)
19A[a]	84 (7.5)	69 (23.4)	85 (35.4)	109 (33.1)
19B	2 (0.2)	...	1 (0.4)	1 (0.3)
19C	...	...	1 (0.4)	
23A	30 (2.7)	16 (5.4)	1 (0.4)	5 (1.5)
23B	20 (1.8)	5 (1.7)	...	...
Total	220 (19.8)	149 (50.5)	98 (40.8)	155 (47.1)
Non–PCV-7				
1[a]	11 (1.0)	1 (0.3)	...	1 (0.3)
3[a]	178 (16.0)	3 (1.0)	3 (1.3)	2 (0.6)
11A[a]	95 (8.5)	5 (1.7)	1 (0.4)	4 (1.2)
15F	1 (0.1)	1 (0.3)	...	1 (0.3)
15A	10 (0.9)	34 (11.5)	...	33 (10.0)
15B[a]	37 (3.3)	...	1 (0.4)	1 (0.3)
15C	27 (2.4)	3 (1.0)	...	2 (0.6)
16F	37 (3.3)	1 (0.3)	...	...
20[a]	6 (0.5)	1 (0.3)	...	...
21	5 (0.4)	1 (0.3)	...	...
22F[a]	76 (6.8)	1 (0.3)	...	1 (0.3)
29	...	5 (1.7)	3 (1.3)	
31	34 (3.1)	1 (0.3)	...	1 (0.3)
33F[a]	15 (1.3)	...	1 (0.4)	...
35F	32 (2.9)	2 (0.7)	...	
35A	6 (0.5)	5 (1.7)	4 (1.7)	5 (1.5)
35B	12 (1.1)	30 (10.2)	30 (12.5)	3 (0.9)
39	...	...	1 (0.4)	
48	...	1 (0.3)	...	1 (0.3)
Nontypeable	19 (1.7)	10 (3.4)	1 (0.4)	8 (2.4)
Other[b]	160 (14.4)	...	...	...
Total	761 (68.4)	105 (35.6)	45 (18.8)	63 (19.1)

NOTE. I, intermediate resistant (penicillin MIC, 0.1–1 μg/mL); MDR, multidrug resistant (Penicillin I or R and resistant to $\geqslant$2 other classes of antimicrobials); R, resistant (penicillin MIC, $\geqslant$2 μg/mL); S, susceptible (penicillin MIC, $\leqslant$0.06 μg/mL).

[a] Included in the 23-valent polysaccharide pneumococcal vaccine.

[b] Other nonvaccine serotypes that included only penicillin-susceptible isolates and no MDR isolates were serotype 2, 5, 7F, 7A, 7C, 8, 10F, 10A, 11D, 12F, 12B, 13, 16A, 17F, 24F, 25A, 28F, 28A, 33A, 34, 38, and 40; of these, serotypes 2, 5, 7F, 8, 10A, 12F, and 17F are included in the 23-valent polysaccharide pneumococcal vaccine.

$P < .001$) and PFGE E isolates (18%; $P = .002$), and the fraction of isolates from sinus specimens was higher among PFGE C isolates (12%; $P = .02$) and lower among PFGE B isolates (1%; $P = .04$), compared with the overall isolate population.

The age distribution of patients from whom isolates were obtained among the predominant 8 PFGE types was similar to the overall isolate population, with a few exceptions. There was a greater proportion of isolates from patients aged 0–5 years among PFGE type C (34.9%; $P = .001$) and type E isolates (37.5%; $P < .001$) than among the overall isolate population. Among patients aged 21–64 years, there were more PFGE H (81.3%; $P < .001$) and fewer PFGE E isolates (34.7%; $P = .04$), compared with the distribution of isolates overall. A greater proportion of PFGE F isolates were from patients aged $\geqslant$65 years (34.8%; $P = .009$) than that among the overall isolate population.

Among the centers that submitted isolates, 28.5% of isolates were from the Northeast, 24.5% were from the Midwest, 17.1% were from the Southeast, 16.1% were from the Southwest, and 13.8% were from the West. Variation in the geographic distribution of isolates among the predominant 8 PFGE types was noted for PFGE C (increased proportion of isolates from Southeast, 26.5%; $P = .02$) and PFGE G (increased proportion of isolates from Northeast, 47.6%; $P = .009$; decreased proportion of isolates from the Midwest, 9.5%; $P = .03$).

DISCUSSION

Longitudinal surveillance of pneumococci in the United States from the 1994–1995 to the 1999–2000 respiratory illness season demonstrated an increase in PRSP isolates (9.5% to 21.5%; $P < .001$) and a stable rate of isolates with intermediate resistance to penicillin (14.1% to 12.7%) [3]. The more recent increase in the number of isolates with intermediate resistance to penicillin (12.7% to 17.9%; $P < .001$) and decrease in the prevalence of PRSP isolates (21.5% to 14.6%; $P < .001$) from the 1999–2000 to the 2004–2005 respiratory illness season may be a direct effect of PCV-7 introduction in 2000, because the vaccine targeted major PRSP serotypes. From 1999–2000 to 2004–2005, the prevalence of erythromycin-resistant isolates increased from 25.7% to 29.1% of isolates ($P = .03$), and the number of multidrug-resistant isolates was stable (22.4% to 20.0%; $P = .1$).

Active Bacterial Core surveillance of invasive pneumococcal disease in 8 metropolitan areas reported a decrease in the rate of penicillin-nonsusceptible isolates from 25.8% to 21.6% from 1999 to 2004 [10]. The higher (but stable) 2004–2005 rate of penicillin-nonsusceptible isolates (32.5%) in the current study can be partially explained by higher resistance rates among noninvasive (18.2% intermediate resistant and 16.1% resistant) isolates, but resistance rates for invasive isolates (17.0% intermediate resistant and 9.9% resistant) were also higher than those reported in the Active Bacterial Core study.

Although 60 different serotypes were represented by the 1647 pneumococcal isolates collected in 2004–2005, most PRSP and multidrug-resistant strains were serotype 19A (35% of PRSP

Table 4. PFGE type distribution of 1647 *Streptococcus pneumoniae* isolates from the 2004–2005 respiratory illness season, by susceptibility profile.

PFGE type	No. (%) of isolates — Total ($n = 1647$)	Penicillin I ($n = 295$)	Penicillin R ($n = 240$)	MDR ($n = 329$)	Serotype(s) (no. of isolates) or PFGE type distribution
A	145 (8.8)	1 (0.3)	1 (0.4)	1 (0.3)	3 (141), 15F (1), 11A (1), 19A (1), and 19F (1)
B	103 (6.3)	32 (10.8)	6 (2.5)	10 (3.0)	19A (76), 15B (11), 15C (8), NT (3), 19F (2), 3 (1), 7F (1), and 6B (1)
C (Taiwan[19F]-14)[a]	83 (5.0)	…	78 (32.5)	77 (23.4)	19F (32), 19A (48), 16F (1), NT (1), and 15B (1)
D	76 (4.6)	3 (1.0)	…	3 (0.9)	11A (70), 15B (2), 19F (1), 19A (1), 33A (1), and 35A (1)
E (Utah[35B]-24)	72 (4.4)	31 (10.5)	39 (16.3)	4 (1.2)	35B (48), 35A (4), 35F (1), 33F (1), 19A (3), 6B (2), 6A (1), 29 (7), 39 (1), 3 (1), 23F (2), and 7F (1)
F	66 (4.0)	2 (0.7)	…	2 (0.6)	22F (62), 19F (1), 6A (1), 2(1), and 31 (1)
G (Sweden[15A]-25)	42 (2.6)	38 (12.9)	…	37 (11.2)	15A (37), 19F (2), 11A (1), 19A (1), and 6A (1)
H	32 (1.9)	1 (0.3)	…	1 (0.3)	4(26), 19A (3), 31 (1), 19B (1), and 15C (1)
I	25 (1.5)	3 (1.0)	…	…	15C (10), 15B (10), 19A (4), and 3(1)
J	24 (1.5)	…	…	…	7F (22) and 19F (2)
K	23 (1.4)	…	…	…	31 (22) and NT (1)
L	22 (1.3)	…	…	…	33F (10), 33A (5), 10A (1), 18C (1), 11A (1), 1 (1), 3 (1), 15A (1), and 19F (1)
M	22 (1.3)	…	…	…	12F (21) and 12B (1)
N (Tennessee[23F]-4)	21 (1.3)	3 (1.0)	2 (0.8)	2 (0.6)	23F (8), 23A (9), 23B (3), and 19F (1)
O	20 (1.2)	13 (4.4)	…	13 (4.0)	6A (18), 48 (1), and 18B (1)
P	20 (1.2)	…	…	…	35F (18) and 10A (2)
Q	18 (1.1)	…	…	…	6A (18)
R	16 (1.0)	…	…	…	19F (14), 23A (1), and 11A (1)
S (Spain[23F]-1)[b]	15 (0.9)	2 (0.7)	13 (5.4)	15 (4.6)	19F (8), 23F (4), 23A (1), 3 (1), and 15B (1)
T	14 (0.9)	14 (4.7)	…	1 (0.3)	6A (14)
U	14 (0.9)	…	…	…	23A (12), 28A (1), and 15C (1)
V	13 (0.8)	…	…	…	3 (13)
W (Taiwan[19F]-14)	11 (0.7)	1 (0.3)	10 (4.2)	11 (3.3)	19A (7) and 19F (4)
X (Colombia[23F]-26)	11 (0.7)	11 (3.7)	…	…	23A (10) and 23B (1)
Y	10 (0.6)	…	…	…	23F (8), 23A (1), and 18C (1)
Z	10 (0.6)	…	…	…	38 (8) and 25A (2)
a (North Carolina[6A]-23)	9 (0.5)	5 (1.7)	4 (1.7)	9 (2.7)	6A (8) and 19A (1)
b	8 (0.5)	…	…	…	10A (8)
c	8 (0.5)	…	…	…	9N (7) and 9L (1)
d	8 (0.5)	…	…	…	10A (7) and 35B (1)
e (Spain[9V]-3)[c]	8 (0.5)	4 (1.4)	3 (1.3)	2 (0.6)	9V (7) and 9A (1)
f	8 (0.5)	2 (0.7)	…	1 (0.3)	7C (5), 19A (2), and 24F (1)
g (Spain[6B]-2)	7 (0.4)	2 (0.7)	5 (2.1)	7 (2.1)	6B (6) and 6A (1)
h	7 (0.4)	…	…	…	6A (5), 19B (1), and 23F (1)
i	7 (0.4)	…	…	…	8 (6) and 3 (1)
j	7 (0.4)	…	…	…	34 (4) and 35F (3)
k	7 (0.4)	2 (0.7)	…	1 (0.3)	35F (3), 35A (2), 35B (1), and NT (1)

(continued)

Table 4. *(Continued.)*

| PFGE type | No. (%) of isolates | | | | Serotype(s) (no. of isolates) or PFGE type distribution |
	Total (*n* = 1647)	Penicillin I (*n* = 295)	Penicillin R (*n* = 240)	MDR (*n* = 329)	
m	7 (0.4)	…	…	…	12F (7)
n	7 (0.4)	…	…	…	11A (7)
o	6 (0.4)	…	…	…	18F (3), 18C (2), and 18A (1)
p	6 (0.4)	2 (0.7)	1 (0.4)	3 (0.9)	19A (3), 19F (1), 9A (1), and 9V (1)
q	6 (0.4)	4 (1.4)	2 (0.8)	6 (1.8)	19A (4) and 9V (2)
r (England[14]–9)	6 (0.4)	1 (0.3)	3 (1.3)	3 (0.9)	14 (4) and 19F (2)
s	6 (0.4)	…	…	…	35B (6)
t	6 (0.4)	…	…	…	31 (5) and 20 (1)
v 1–9	45 (2.7)	9 (3.1)	…	3 (0.9)	9 PFGE types, 5 isolates each
w 1–15	60 (3.6)	18 (6.1)	1 (0.4)	4 (1.2)	15 PFGE types, 4 isolates each
x 1–23	69 (4.2)	11 (3.7)	17 (7.1)	20 (6.1)	23 PFGE types, 3 isolates each
z 1–67	134 (8.1)	26 (8.8)	17 (7.1)	26 (7.9)	67 PFGE types, 2 isolates each
u 1–277	277 (16.8)	54 (18.3)	38 (15.8)	67 (20.4)	277 PFGE types, 1 isolate each

NOTE.I, intermediate resistant (penicillin MIC, 0.1–1 μg/mL); MDR, multidrug resistant (Penicillin I or R and resistant to ≥2 other classes of antimicrobials); NT, nontypeable; R, resistant (penicillin MIC, ≥2 μg/mL). There were 436 different PFGE patterns detected among all isolates.

[a] Ranked third in prevalence among penicillin R isolates from 1999–2000 [5]. According to multilocus sequence type of representative isolate, this is a single locus variant of Taiwan[19F]-14.

[b] Isolates in this PFGE type (closely related to Spain[23F]-1) ranked second in prevalence among penicillin R isolates from 1999–2000 [5].

[c] Isolates in this PFGE type (closely related to Spain[9V]-3) ranked first in prevalence among penicillin R isolates from 1999–2000 [5].

strains and 33% of multidrug-resistant strains) or 19F (24% of PRSP strains and 20% of multidrug-resistant strains) (table 3). The distribution of PRSP serotypes in the current study is compared with that distribution in the 1994–1995 and 1999–2000 surveillance periods in table 5 [5]. From 1999–2000 to 2004–2005, a significant decrease (*P* < .001) was noted in the percentage of PCV-7 serotypes among PRSP serotypes (overall, 89.4% to 40.4%; 6B, 13.7% to 3.8%; 9V, 16.1% to 4.2%; 14, 18.5% to 2.9%; 23F, 16.1% to 5.0%). There was an increase in the prevalence of serotype 19F isolates from 1994–1995 (13.6%) to 1999–2000 (24.3%), followed by no change in the prevalence of serotype 19F after vaccine introduction. This reduced effect of PCV-7 against serotype 19F in relation to other vaccine serotypes has been reported elsewhere [25].

An increase in the prevalence of PRSP isolates with serotypes related to PCV-7 from 1999–2000 to 2004–2005 (6.1% to 40.8%; *P* < .001) was primarily attributable to an increase in the prevalence of serotype 19A (1.5% to 35.4%; *P* < .001). The Active Bacterial Core surveillance system reported an increase in invasive pneumococcal disease caused by serotype 19A penicillin-resistant strains from 1998 to 2005 (6.7% to 35%) [26]. In our study, the increase in the prevalence of nonvaccine serotypes from 4.6% to 18.8% (*P* < .001) from 1999–2000 to 2004–2005 among the PRSP isolates was primarily attributable to serotype 35B (1.2% to 12.5%; *P* < .001) strains.

Similar trends of increased serotype 19A prevalence among pneumococci causing invasive disease have been reported by other investigators [10, 12, 15–18]. PCV-7 introduction in 2000 may have provided selective pressure for the change from 1999–2000 to 2004–2005, but the decrease in the proportion of serotype 6B (23.1% to 13.7%; *P* = .016) and serotype 23F (32.7 to 16.1%; *P* < .001) isolates among PRSP isolates from 1994–1995 to 1999–2000—before the introduction of PCV-7—suggests that other factors must be considered (table 5).

The genetic diversity of the 1647 isolates from the 2004–2005 respiratory illness season—with a distribution among 436 different PFGE types (table 4)—is similar to that observed in a multilocus sequence typing analysis of carriage and invasive disease isolates (590 isolates comprised 143 sequence types) [25]. The smaller number of PRSP isolates from 2004–2005 (table 4) were more diverse (240 isolates; 73 PFGE types) than the 329 PRSP isolates from 1999–2000 (65 PFGE types) [5]. The distribution of PRSP strains among major PFGE types (i.e., those types including ≥5 isolates) has fluctuated during the study periods. In 1999–2000, 10 major PFGE types accounted for 78.4% of the PRSP population [5]. In 2004–2005, only 62.9% of the PRSP strains were included in 6 major PFGE types. This overall change from 1999–2000 to 2004–2005 reflects the emergence of 2 dominant clones in a background of increasing genetic diversity because of multiple factors. Separating the effect of vaccines from the natural evolution of the pneumococcal population is difficult.

The PRSP clones with the greatest decrease in prevalence over time were Spain[23F]-1 and Spain[9V]-3. Isolates closely related to Spain[23F]-1 comprised the largest percentage (23%) of PRSP isolates in 1994–1995, 14% of PRSP isolates in 1999–2000 [5],

Table 5. Change in the prevalence of penicillin-resistant *Streptococcus pneumoniae* isolate serotypes between the 1994–1995, 1999-2000, and 2004–2005 respiratory illness seasons.

Serotype	No. (%) of penicillin resistant isolates			P^a	P^b
	1994–1995 (*n* = 147)	1999–2000 (*n* = 329)	2004–2005 (*n* = 240)		
PCV-7					
4[c]	…	1 (0.3)	1 (0.4)		
6B[c]	34 (23.1)	45 (13.7)	9 (3.8)	.016	<.001
9V[c]	15 (10.2)	53 (16.1)	10 (4.2)		<.001
14[c]	14 (9.5)	61 (18.5)	7 (2.9)	.014	<.001
18C[c]	…	1 (0.3)	…		
19F[c]	20 (13.6)	80 (24.3)	58 (24.2)	.008	
23F[c]	48 (32.7)	53 (16.1)	12 (5.0)	<.001	<.001
Total	131 (89.1)	294 (89.4)	97 (40.4)		<.001
PCV-7 related					
6A	2 (1.4)	15 (4.6)	7 (2.9)		
9A	…	…	3 (1.3)		
19A[c]	…	5 (1.5)	85 (35.4)		<.001
19B	…	…	1 (0.4)		
19C	…	…	1 (0.4)		
23A	…	…	1 (0.4)		
Total	2 (1.4)	20 (6.1)	98 (40.8)	.03	<.001
Non–PCV-7					
3[c]	…	…	3 (1.3)		
11A[c]	…	…	1 (0.4)		
15B[c]	…	…	1 (0.4)		
22F[c]	…	1 (0.3)	…		
29	…	…	3 (1.3)		
33F[c]	…	…	1 (0.4)		
35A	…	…	4 (1.7)		
35B	9 (6.1)	4 (1.2)	30 (12.5)	.005	<.001
39	…	…	1 (0.4)		
Nontypeable	5 (3.4)	10 (3.0)	1 (0.4)		
Total	14 (9.5)	15 (4.6)	45 (18.8)		<.001

NOTE. Penicillin resistant isolates had an MIC ⩾2 μg/mL.

[a] *P* value comparing the change in the number of isolates from 1994–1995 to 1999–2000 (only *P* values <.05 are shown; Fisher's exact test).

[b] *P* value comparing the change in the number of isolates from 1999–2000 to 2004–2005 (only *P* values <.05 are shown; Fisher's exact test).

[c] Included in the 23-valent polysaccharide pneumococcal vaccine.

and only 5.4% of PRSP isolates in 2004–2005 (table 4). Isolates closely related to Spain[9V]-3 were predominant among the 1994–1995 and 1999–2000 PRSP isolate populations (12.2% and 16.1%, respectively) [5] but decreased to represent only 1.3% of the 2004–2005 PRSP isolates.

PRSP clones that have emerged over time are Taiwan[19F]-14 and Utah[35B]-24. Isolates closely related to Utah[35B]-24 (PFGE type E) decreased from 6.1% of the PRSP population in 1994–1995 to 0.9% of the PRSP population in 1999–2000 (*P* = .002) [5] and then increased to 16.3% of the PRSP population in 2004–2005. The lower proportion of the Utah[35B]-24–related strains that were recovered from blood culture (11%) explains

its limited recognition by surveillance programs that focused on only invasive isolates [27]. The low prevalence of multidrug resistance (5.6%) among Utah[35B]-24 strains is reassuring. However, the overall predominance of this nonvaccine clone (fifth most common PFGE type)—43% of isolates have intermediate resistance to penicillin and 54% are resistant—suggests that serotype 35B should be considered for future vaccines. Another nonvaccine strain of concern is Sweden[15A]-25 (PFGE type G; 42 isolates); 90.5% of isolates had intermediate resistance to penicillin and 88.1% were multidrug resistant.

Isolates with PFGE patterns most closely related to Taiwan[19F]-14 (PFGE type W; multilocus sequence type 236) increased

slightly from 1.5% of the PRSP population in 1999–2000 [5] to 4.2% of the PRSP population in 2004–2005. PFGE type C isolates (>3 bands different by PFGE but related by multilocus sequence typing analysis [multilocus sequence type 271] to Taiwan[19F]-14 [6 of 7 common alleles]) increased from 4.8% of the PRSP population in 1994–1995 to 13.1% of the PRSP population in 1999–2000 ($P = .003$) [5] and increased again to 32.5% of the PRSP population in 2004–2005 (table 4). The prevalence of serotype 19A expression by PRSP isolates closely related to Taiwan[19F]-14 (PFGE types C and W) increased from only 3.9% of isolates in 1994–2000 to 60.2% of isolates in 2004–2005, whereas serotype 19F expression decreased from 93.4% to 37.5% for the same time periods.

The Active Bacterial Core surveillance program analyzed 151 penicillin-resistant 19A strains causing invasive disease in 2005 and found most (73.5%) to be closely related to Taiwan[19F]-14 [26]. Of the 85 PRSP serotype 19A isolates in our study, 53 (62.4%) were closely related to Taiwan[19F]-14 (PFGE types C and W) and were multidrug resistant. PCV-7 may have provided the selective pressure for the Taiwan[19F]-14 clone to switch from serotype 19F to 19A. The predominance of the Taiwan[19F]-14 clone indicates that there are additional virulence factors beyond serotype. However, the diversity of the serotype 19A isolates in the 2004–2005 collection indicates a serotype advantage. The second most common PFGE type (PFGE type B, 103 isolates) includes the largest number of serotype 19A isolates (76 isolates) but a small portion of penicillin-nonsusceptible and multidrug-resistant phenotypes. Longitudinal monitoring of resistance in this fairly drug-susceptible serotype 19A clone will be of interest.

It is notable that only the prevalence of serotype 19A increased among the PCV-7–related serotypes. This finding appears to be a consequence of limited vaccine activity against serotype 19F. The prevalence of serotype 6A isolates among PRSP was stable (4.6% in 1999–2000 to 2.9% in 2004–2005; $P = .4$), and the prevalence of PRSP isolates closely related to the North Carolina[6A]-23 clone decreased from 5.2% in 1999–2000 to 1.7% in 2004–2005 ($P = .04$) [5] (table 4). Isolates of PCV-7–related serotypes 9A, 19B, 19C, and 23A were only detected among the PRSP population in 2004–2005 and only in small numbers. The 3 serotype 9A PRSP isolates detected in 2004–2005 were not related; 2 had unique PFGE patterns and the third isolate was closely related to the Spain[9V]-3 clone.

In conclusion, this 2004–2005 surveillance study of pneumococci causing respiratory and invasive disease revealed a lower rate of high-level penicillin resistance but higher erythromycin and intermediate penicillin resistance rates than that detected in 1999–2000. The prevalence of penicillin-resistant isolates expressing serotypes 19A and 35B isolates increased, whereas the prevalence of isolates with serotypes included in PCV-7 (23F, 9V, 6B, and 14) decreased. The PRSP population after the introduction of PCV-7 continues to be clonal, but the predominant strains have changed, with 37% closely related to Taiwan[19F]-14 (most expressing serotype 19A) and 16% related to Utah[35B]-24.

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