

# Distribution of *Streptococcus pneumoniae* serotypes among non-sterile isolates from adults 18 years and older in Europe and the United States, 2014-2015

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## Background

- Worldwide, *Streptococcus pneumoniae* represents a leading cause of mortality and morbidity in children and adults.
- A 7-valent pneumococcal conjugate vaccine (PCV7) was introduced in the infant immunization program in United States (US) and European Union (EU) in 2000 and 2001, respectively, followed by a 13-valent (PCV13) vaccine in 2010 and 2009.
- As pneumococcal disease risk is increased in older adults and in those with certain chronic medical conditions, it is important to monitor both the burden of adult pneumococcal disease and changing serotype specific epidemiology in the setting of pneumococcal vaccination programs.

## Objective

The objective of this study was to determine the serotypes and antibiotic susceptibilities of a convenience sample of 732 *S. pneumoniae* non-sterile isolates collected from adults 18 years and older in 19 European countries and the US through the Tigecycline Evaluation Surveillance Trial, (TEST) from 2014-2015.

## Methods

- Investigators enrolled in the TEST program collect clinically relevant causative agents from a variety of body sites.
- Only one isolate per patient is accepted. Individual sites are requested to collect and ship a total of 15 *S. pneumoniae* isolates per year to International Health Management Associates (IHMA).
- Susceptibility testing is performed using supplied panels and standard Clinical and Laboratory Standards Institute (CLSI) broth microdilution methodology by the local laboratories and by IHMA.
- A total of 732 isolates of *S. pneumoniae* were collected from non-sterile respiratory specimens from adults  $\geq 18$  years of age between 2014-2015.
- Isolates were collected from sputum (n = 531; 72.5%), trachea (n = 108; 14.8%), head/ears/nose/throat (n = 61; 8.3%), and unspecified respiratory sites (n = 32; 4.4%).
- Isolates from 2014-2015 were from the US (n=195) and Europe (n=537). 72% of European isolates were collected among 5 countries (Spain [n=124], Germany [n=86], France [n=68], Belgium [n=64], Italy [n=47]), with the remaining 28% of isolates collected among 14 countries (n=1-24 isolates each) [Table 1].
- Serotypes were determined by PCR
  - Isolates non-typeable by PCR were serotyped by the Quellung reaction.
  - Minimum inhibitory concentrations (MIC) were determined by both microdilution and interpreted using CLSI guidelines (erythromycin,  $\leq 0.25$  mg/L, susceptible; penicillin,  $\leq 2$  mg/L, susceptible [parenteral nonmeningitis breakpoint]) [1].

- From the total number of isolates, 326 were from adults  $\geq 65$  years of age and 406 were from those 18-64 years of age.
- The prevalence of serotypes and susceptibility to penicillin and erythromycin for the ten most common serotypes in non-sterile respiratory specimens collected in Europe and the US are shown in Table 2. Serotype prevalence differed among age groups and regions.
- Serotype 3 was most prevalent among isolates collected in Europe from all adults (14.7-16.6%) [Table 3] and in the US among adults 18 to 64 years of age (16.4%), and was the second most prevalent among adults  $\geq 65$  years of age from the US (9.0%) [Table 4]. Serotype 19A was most prevalent among adults  $\geq 65$  years of age from the US (11.9%) [Table 4].
- Serotype 11A was more common among adults from Europe than the US, whereas serotype 19A was more common in the US [Tables 2-4]. Serotype 19A was more prevalent among individuals  $\geq 65$  years of age than younger adults in both regions (US, 11.9% versus 6.3%; Europe, 7.3% versus 3.6%) [Tables 3-4].
- Decreased susceptibility to penicillin was most often found in serotypes 19A, 17F, 19F, and 16F. Decreased susceptibility to erythromycin was most commonly seen in serotypes 15A, 19A, 6C, and 19F and was more prevalent than penicillin non-susceptibility [Figure 1].

**Table 1. Geographic distribution of serotyped non-sterile *S. pneumoniae* isolates (n=732)**

Region	Country	No. of isolates	Age range		
			18 to 64 years	$\geq 65$ years	Total
Total		732	406	326	
Europe		537	278	259	
	Belgium	64	24	40	
	Croatia	9	7	2	
	Czech Republic	7	4	3	
	Denmark	10	4	6	
	Finland	1	1	--	
	France	68	37	31	
	Germany	86	54	32	
	Greece	16	7	9	
	Hungary	5	2	3	
	Ireland	11	7	4	
	Italy	47	28	19	
	Netherlands	10	6	4	
	Poland	9	7	2	
	Portugal	18	10	8	
	Romania	1	--	1	
	Spain	124	54	70	
	Sweden	8	6	2	
	Switzerland	24	11	13	
	United Kingdom	19	9	10	
North America		195	128	67	
	United States	195	128	67	

## Results

**Table 2. Prevalence and susceptibility to penicillin and erythromycin of the ten most common serotypes, by region**

Europe (n=537)					United States (n=195)				
Serotype	n	PEN-S (n (%))	ERY-S (n (%))		Serotype	n	PEN-S (n (%))	ERY-S (n (%))	
3 <sup>A</sup>	84	83 (98.8)	73 (86.9)		3 <sup>A</sup>	27	27 (100)	21 (77.8)	
11A <sup>A</sup>	46	44 (95.7)	38 (82.6)		19A <sup>AA</sup>	16	10 (62.5)	3 (18.8)	
19A <sup>AA</sup>	29	20 (69.0)	13 (44.8)		22F <sup>A</sup>	15	15 (100)	10 (66.7)	
23B	28	28 (100)	27 (96.4)		23A	14	14 (100)	11 (78.6)	
23A	26	26 (100)	21 (80.8)		6C	13	13 (100)	7 (53.8)	
35B	24	24 (100)	21 (87.5)		11A <sup>A</sup>	12	12 (100)	5 (41.7)	
22F <sup>A</sup>	22	22 (100)	21 (95.5)		23B	11	11 (100)	6 (54.5)	
6C	22	22 (100)	10 (45.5)		35B	10	10 (100)	2 (20.0)	
15A	21	21 (100)	7 (33.3)		16F	9	9 (100)	9 (100)	
19F <sup>AA</sup>	20	18 (90.0)	9 (45.0)		19F <sup>AA</sup>	8	8 (100)	6 (75.0)	

<sup>A</sup>Contained in PCV13; <sup>AA</sup>Contained in PPV23.  
n, number of isolates; PEN-S, penicillin-susceptible; ERY-S, erythromycin-susceptible.

**Table 3. Prevalence and susceptibility to penicillin and erythromycin of the ten most common serotypes identified in adults from Europe (n=537), by age group**

18 to 64 years (n=278)					$\geq 65$ years (n=259)				
Serotype	n	PEN-S (n (%))	ERY-S (n (%))		Serotype	n	PEN-S (n (%))	ERY-S (n (%))	
3 <sup>A</sup>	41	40 (97.6)	34 (82.9)		3 <sup>A</sup>	43	43 (100)	39 (90.7)	
11A <sup>A</sup>	26	25 (96.2)	22 (84.6)		11A <sup>A</sup>	20	19 (95.0)	16 (80.0)	
23A	16	16 (100)	12 (75.0)		19A <sup>AA</sup>	19	12 (63.2)	8 (42.1)	
22F <sup>A</sup>	15	15 (100)	15 (100)		23B	13	13 (100)	12 (92.3)	
23B	15	15 (100)	15 (100)		15A	12	12 (100)	4 (33.3)	
35B	15	15 (100)	14 (93.3)		9N <sup>A</sup>	11	11 (100)	10 (90.9)	
6C	13	13 (100)	4 (30.8)		23A	10	10 (100)	9 (90.0)	
19F <sup>AA</sup>	12	10 (83.3)	4 (33.3)		35B	9	9 (100)	7 (77.8)	
19A <sup>AA</sup>	10	8 (80.0)	5 (50.0)		6C	9	9 (100)	6 (66.7)	
15A	9	9 (100)	3 (33.3)		19F <sup>AA</sup>	8	8 (100)	5 (62.5)	

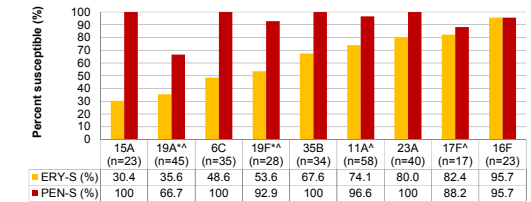
<sup>A</sup>Contained in PCV13; <sup>AA</sup>Contained in PPV23.  
n, number of isolates; PEN-S, penicillin-susceptible; ERY-S, erythromycin-susceptible.

**Table 4. Prevalence and susceptibility to penicillin and erythromycin of the nine to ten most common serotypes identified in adults from the United States (n=195), by age group**

18 to 64 years (n=128)					$\geq 65$ years (n=67)				
Serotype	n	PEN-S (n (%))	ERY-S (n (%))		Serotype	n	PEN-S (n (%))	ERY-S (n (%))	
3 <sup>A</sup>	21	21 (100)	17 (81.0)		19A <sup>AA</sup>	8	6 (75.0)	1 (12.5)	
22F <sup>A</sup>	10	10 (100)	7 (70.0)		23A	6	6 (100)	4 (66.7)	
6C	9	9 (100)	5 (55.6)		3 <sup>A</sup>	6	6 (100)	4 (66.7)	
11A <sup>A</sup>	8	8 (100)	4 (50.0)		22F <sup>A</sup>	5	5 (100)	3 (60.0)	
19A <sup>AA</sup>	8	4 (50.0)	2 (25.0)		23B	5	5 (100)	3 (60.0)	
23A	8	8 (100)	7 (87.5)		35B	5	5 (100)	1 (20.0)	
16F	7	7 (100)	7 (100)		11A <sup>A</sup>	4	4 (100)	1 (25.0)	
17F <sup>A</sup>	6	5 (83.3)	4 (66.7)		6C	4	4 (100)	2 (50.0)	
19F <sup>AA</sup>	6	6 (100)	4 (66.7)		7C	3	3 (100)	3 (100)	
23B	6	6 (100)	3 (50.0)						

<sup>A</sup>Contained in PCV13; <sup>AA</sup>Contained in PPV23.  
n, number of isolates; PEN-S, penicillin-susceptible; ERY-S, erythromycin-susceptible.

**Figure 1. Serotypes with the lowest percentages of erythromycin-susceptible and penicillin-susceptible isolates collected from non-sterile respiratory specimens, all ages and regions.**



<sup>A</sup>Contained in PCV13; <sup>AA</sup>Contained in PPV23.  
n, number of isolates; ERY-S, erythromycin-susceptible (MIC values  $\leq 0.25$  mg/L); PEN-S, penicillin-susceptible (MIC values  $\leq 2$  mg/L) [1].

## Study Limitations

- This dataset is a convenience sample of clinical isolates and cannot be considered representative.
- The vaccine uptake for the vaccines examined in this study is not known.
- This study only analyses the role of vaccine use in driving pneumococcal serotype evolution. It does not take into account differences in antibiotic prescription patterns among patient populations and regions, which also exert selective pressure on serotype evolution.

## Conclusions

- These data, although limited in numbers, suggest a persistent burden of pneumococcal disease in adults, including disease caused by PCV13 serotypes 3, 19A, and 19F, and was observed in countries with established pediatric PCV13 immunization programs, such as the United States.
- Direct vaccination of adults with PCV13 may be useful in reducing disease caused by these serotypes in adults.
- The association between pneumococcal serotypes and antibiotic resistance highlights the need for ongoing monitoring of the serotype epidemiology of this important pathogen.

## References

- Clinical and Laboratory Standards Institute. 2017. M100-S27. Performance standards for antimicrobial susceptibility testing, 27th informational supplement. Clinical and Laboratory Standards Institute, Wayne, PA.