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ASM 2011

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Declining MRSA and Fluoroquinolone Resistance Rates Among *S. aureus* in the USA: Report from the SENTRY Antimicrobial Surveillance Program (2000-2009)

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SENTRY ANTIMICROBIAL SURVEILLANCE

ABSTRACT

Background: Antimicrobial resistance among staphylococci has generally been escalating in the past two decades especially MRSA and fluoroquinolone (FQ)-resistance rates. The SENTRY Antimicrobial Surveillance Program has monitored resistance worldwide and in this report, we analyze 46,450 staphylococcal isolates from the USA (2000-2009).

Methods: Several key antimicrobials (oxacillin [OXA], erythromycin [ER], clindamycin [CC], tetracycline [TC], trimethoprim/sulfamethoxazole [TMP/SMX], gentamicin [GT] and FQs [ciprofloxacin, levofloxacin]) were tested by CLSI reference methods (M07-A8) applying M100-S21 breakpoint criteria. A total of 38,806 SA (20,049 MRSA) and 7,644 coagulase-negative staphylococci (CoNS) were tabulated by year of isolation. Participating laboratories have remained consistent across the sampled years.

Results: The MRSA rates increased by year (38 to 57%) through 2008, but in 2009 the rate declined to only 51%. Among MRSA, the FQ-R rate was stable at 90-94% until 2003, then decreasing to 78% (2004) and further to 73% by 2009. This reduced resistance was associated with declines in resistance for CC (71 to 46%), GT (10 to 5%) and TMP/SMX (5 to 2%), while ER (95-96%)-resistant and TC (6-7%) resistance rates remained essentially unchanged. FQ-resistance in MSSA, however, increased from 5% in 2000 to 12% in 2009. Among tested CoNS, OXA-resistant (69-83%) and FQ-resistant (49-58%) rates were generally the same ($p > 0.05$) over the last decade.

	Rates (%) in SA			
Selected years*	MRSA	FQ-R in MRSA	FQ-R in MSSA	No. tested
1999-2000	39	91	5	5,915
2002-2003	46	92	10	4,630
2004-2005	50	76	9	6,473
2007-2008	57	73	13	11,721
2009	51	73	12	4,991

*Not all tabulated years are shown.

Conclusions: Two favorable trends in antimicrobial susceptibility results for staphylococci (MRSA) were noted by the SENTRY Program (USA): 1). Initial onset of a MRSA rate decline of 6% in one year (2009), and 2). decreases from 90 or more percent to 73-78% in FQ-R for 2004 onward, likely promoted by USA300 clonal dissemination and wide spread infection control interventions. Overall, multidrug-resistant *S. aureus* has decreased in prevalence in recent years.

INTRODUCTION

Antimicrobial resistance rates among staphylococci isolated in the United States (USA) have generally been recognized as escalating over the last three decades, particularly those of oxacillin (MRSA) and some more recently introduced classes such as the fluoroquinolones. Recently, the results from the SENTRY Antimicrobial Surveillance Program documented similar emerging resistances (particularly for ß-lactams) among *Streptococcus pneumoniae* through 2009. In contrast, resistance rates for pathogens isolated in Europe, Latin America and the Asia-Pacific region have varied, as presented by the SENTRY Program and local/regional-based surveys.

Since numerous interventions have been initiated worldwide to minimize resistance emergence and/or improve local infection control, we have utilized a 10-year sample of USA staphylococcal results for *Staphylococcus aureus* (38,806 strains; 2000-2009) and coagulase-negative species (7,644 strains; 2000-2009) to determine trends in key drug resistances and compare patterns among commonly used antimicrobials across three geographic regions (USA, Europe and Latin America). All testing was performed in a central reference laboratory design by Clinical and Laboratory Standards Institute (CLSI) methods.

MATERIALS AND METHODS

Organism populations: A total of 72,413 *S. aureus* strains were collected and tested for susceptibilities by the SENTRY Program from the USA (38,806 strains), Europe (23,154 strains) and Latin America (10,453 strains). These collections ranged from 4,876 to 8,830 strains per year. An additional 20,338 coagulase-negative staphylococci (CoNS) were sampled with 7,644, 9,017, and 3,677 strains derived from the USA, Europe and Latin America, respectively.

Susceptibility testing: Antimicrobial susceptibility tests were performed by the CLSI (2009) broth microdilution method with the quality control (QC) guidelines as published in M100-S21 (2011). Numerous antimicrobials were tested including: oxacillin, cefoxitin (for confirming MRSA strains), erythromycin, clindamycin, gentamicin, tetracycline, ciprofloxacin, levofloxacin and trimethoprim/sulfamethoxazole (TMP/SMX). Interpretations of susceptibility were those of the CLSI (2011) and fluoroquinolone resistance (FQR) was defined by the results from levofloxacin and ciprofloxacin breakpoints.

RESULTS

- Consistent participant laboratories contributed to the sampled collection across all years and regions (2000-2009).
- In the sampled *S. aureus,* MRSA rates increased in the USA (40 to 57%) over the initial 9 years, but dramatically declined in 2009 (51%). In Europe, MRSA rates were stable or decreasing (25-33%), and in Latin American nations a 7% increase in MRSA occurred over the 10 years (Table 1).
- FQR *S. aureus* rates generally stayed the same for the decade with 2009 occurrences across the regions ranging from 29 to 44%. However, significant FQR rate changes (decreases) among the MRSA populations in the USA and Latin America emerged in 2004 and 2007, respectively. FQR rates in MSSA strains were low (range for 2009, 6 to 12%) and without significant trending (Table 1).
- Figure 1 illustrates the concurrent decreases in resistance for six monitored antimicrobials among USA MRSA strains, most evident for levofloxacin and clindamycin in 2004. Gradual decreases of erythromycin, gentamicin, tetracycline and TMP/SMX resistance rates were noted over the entire decade.
- Table 2 shows the antimicrobial resistance trends for CoNS where the most striking changes were noted in Latin America (2006). FQR markedly increase (+18%) especially among MR-FQR (+23%). All other regions and analysis subgroups showed very modest increases (+1 to 8%) or no rate change for the monitored period.

Figure 1. Trends in erythromycin, levofloxacin, clindamycin, gentamicin, tetracycline, and TMP/SMX resistance rates among 20,049 MRSA in USA (2000-2009, SENTRY Antimicrobial Surveillance Program).

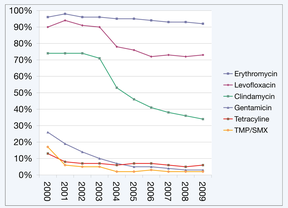

Table 1. Ten-year resistance trends for fluoroquinolones (ciprofloxacin and levofloxacin) among *S. aureus* isolated in the USA, Europe and Latin America (SENTRY Antimicrobial Surveillance Program, 2000-2009; 72,413 strains).

	USA (% occurrence)[a]				Europe (% occurrences)				Latin America (% occurrences)			
Study year	MRSA	FQR	MRSA + FQR	MSSA + FQR	MRSA	FQR	MRSA + FQR	MSSA + FQR	MRSA	FQR	MRSA + FQR	MSSA + FQR
(no. tested)	(38,806)				(23,154)				(10,453)			
2000	40	40	90	5	33	34	94	4	34	33	93	2
2001	48	50	94	10	33	34	92	6	44	41	89	4
2002	46	47	92	10	31	34	94	8	37	36	92	4
2003	46	47	91	10	28	30	91	6	37	38	94	5
2004	49	43	78[b]	8	25	27	91	6	42	41	94	3
2005	51	44	77	9	29	32	93	7	35	34	92	3
2006	56	47	73	12	28	32	94	8	40	40	91	6
2007	56	46	73	11	29	31	90	7	43	38	83[b]	5
2008	57	48	73	14	27	30	87	8	43	40	85	6
2009	51[c]	44	74	12	26	29	91	7	41	35	78	6
(10-year % variance)	(+11)	(+4)	(-16)	(+7)	(-7)	(-5)	(-3)	(+3)	(+7)	(+2)	(-15)	(+4)

a. Susceptibilities determined by CLSI (2011) criteria.
b. Significant one-year decline in resistance.
c. Decline in resistance contrasts to prior 9 years of experience.

Table 2. Ten-year resistance trends for fluoroquinolone (ciprofloxacin and levofloxacin) among coagulase-negative staphylococcal (CoNS) isolates from the USA, Europe and Latin America (SENTRY Antimicrobial Surveillance Program, 2000-2009; 20,338 strains).

	USA (% occurrence)[a]				Europe (% occurrences)				Latin America (% occurrences)			
Study year	MR	FQR	MR + FQR	MS + FQR	MR	FQR	MR + FQR	MS + FQR	MR	FQR	MR + FQR	MS + FQR
(no. tested)	(7,644)				(9,017)				(3,677)			
2000	77	54	66	14	78	52	65	6	76	44	53	4
2001	77	56	66	23	77	53	65	12	80	48	59	0
2002	78	59	70	20	79	56	68	10	78	50	63	6
2003	83	58	67	17	76	54	68	10	81	45	54[b]	7
2004	82	50	56	24	77	55	69	8	77	48	61	4
2005	82	61	71	14	72	55	72	13	77	52	66	5
2006	75[b]	59	71	22	77	61	76	10	85[b]	59[b]	68	11
2007	74	58	71	20	76	58	73	11	82	58	71	0
2008	71	56	69	22	77	58	73	7	81	61	74	9
2009	73	54	67	19	81	60	72	13	80	62	76	8
(10-year % variance)	(-4)	(0)	(+1)	(+5)	(+3)	(+8)	(+7)	(+7)	(+4)	(+18)[c]	(+23)[c]	(+4)

a. Susceptibilities determined by CLSI (2011) criteria
b. Significant one-year decline or increase in resistance.
c. Significant all-year increase/trend.

CONCLUSIONS

- Significant changes in antimicrobial agent susceptibility patterns were demonstrated for *S. aureus* (72,413 strains) monitored by the SENTRY Program in 2000-2009:
  - Decrease in MRSA rate for the USA in 2009.
  - Decreases in resistance for six drugs (Figure 1) among USA MRSA over the last 10 years, markedly decreasing in 2004 for levofloxacin and clindamycin (USA300 phenotype).
  - A similar decrease for FQR-MRSA in Latin America was noted, beginning in 2007.
- CoNS susceptibility patterns were more stable with the most significant changes being escalating FQR (usually among MR-CoNS) in Latin American strains.
- Overall, the results for a 10-year sample of SENTRY Program isolates yields encouraging evidence of declining resistances in MRSA driven by clonal expansion of USA300, occurring in the USA and possibly in Latin America. Also, CoNS resistances were stable in the USA and Europe, but FQR rates have recently increased (+23%, usually among MR-CoNS).

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