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Susceptibility of *Staphylococcus aureus* Isolated from Skin and Wound Infections in the United States 2005-2007: Laboratory Based Surveillance Study

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ABSTRACT

Objectives: A study was conducted to describe the rates of antimicrobial susceptibility among *Staphylococcus aureus* reported from nine regions of the USA during 2005-2007, and to identify regional variation in patterns of resistance.

Methods: The Surveillance Network (TSN) comprises 296 laboratories across the nine census regions of the United States. TSN laboratories reported the susceptibility data for 6 antimicrobials by isolate with source and other relevant data. Antimicrobial susceptibility data were analyzed by individual drug resistance, multi-drug resistance, and geographical distribution of resistance phenotypes.

Results: There were over 380,000 isolates of *Staphylococcus aureus* tested and reported for the period 2005-2007. Methicillin resistance was observed in 57.8% in 2007 with little change from 2005. There was little difference in rates of methicillin resistance between community and hospital strains, although strains from intensive care units tended to be slightly more resistant overall. Resistance to other antimicrobials also was reported. Regional variation in resistance rates was noted with the highest rates in the Central states and lowest in New England and Mid-Atlantic regions. There was high activity observed with trimethoprim-sulfamethoxazole and gentamicin. Linezolid resistance was rare. Oxacillin resistance was similar among pediatric and elderly cohorts, while ciprofloxacin and clindamycin resistance was significantly (<0.01) more common in elderly patients compared with both pediatric and adult populations. Less than a third of all isolates (30.3%) showed no resistance mechanism. Three distinct resistance phenotypes accounted for 46% of all resistant strains. Overall there were more highly drug-resistant isolates from the ICU with 4, 5 or 6 drug-resistant phenotypes accounting for over a third of all strains.

Conclusions: Methicillin-resistant *S. aureus* has become prevalent in both the community and hospital setting however little change in incidence has been seen in past 3 years. Multi-resistant strains now are seen in all settings, but due to regional variation, empiric therapy should be guided by local susceptibility patterns. Currently, among the agents studied, only trimethoprim-sulfamethoxazole, gentamicin, and linezolid exhibit susceptibility rates >95%.

INTRODUCTION AND PURPOSE

Staphylococcus aureus has recently gained significant notoriety in both the medical and lay press and media principally through an apparent increase in the proportion of fatal infections, notably among children. The awareness of physicians and public alike has been elevated and changes in clinical practice may be driven by panic and concern. This brief report presents data from a large-scale laboratory-based surveillance program over the period 2005-2007 from almost 300 hospitals across the USA.

METHODS

Data from The Surveillance Network (TSN®) were analyzed in the current investigation. TSN is an electronic database of strain-specific, qualitative and quantitative antimicrobial susceptibility test data reported by clinical laboratories in United States that has been previously used to evaluate trends concerning antimicrobial susceptibility.[1,2] The TSN database contains over 120 million susceptibility results collected from 296 US institutions. Susceptibility was determined according to CLSI breakpoints that were current in the year of testing.[3-5]

This analysis focused specifically on *S. aureus* and used TSN to investigate *S. aureus* isolated from January 2005 to September 2007. The overall prevalence of *S. aureus* isolates taken from skin and wound specimen sources were studied according to patient location including inpatient, intensive-care unit (ICU) and outpatient. Strains of *S. aureus* isolated from skin or wound infections were used as the source most likely to yield the highest incidence of this species as per Styers *et al.*[6] MRSA rates for the study period were estimated by year. In addition, *S. aureus* and MRSA specifically were analyzed by US Bureau of Census region. Susceptibility to erythromycin, trimethoprim-sulfamethoxazole, and levofloxacin was examined as well as multi-drug resistant (MDR), defined as concurrent resistance ≥ 3 of the following agents: ciprofloxacin, clindamycin, erythromycin, gentamicin, oxacillin, and trimethoprim-sulfamethoxazole. Only strains tested simultaneously against each of these agents were included in the MDR analysis of prevalence and distribution of resistance. All incidence rates were compared statistically using chi-square analyses, with a p-value of <0.05 being significant.

RESULTS

- Overall MRSA rates in the USA showed little change between 2005 and 2006 but there was a significant difference in oxacillin resistance between 2006 and 2007, p<0.05 (**Table 1**).
- In 2007, the lowest rates of MRSA were observed in the New England region (48.1 %) and the Mid-Atlantic region (48.9 %) compared with the highest rates observed in the East South Central region (67.3%) and the West South Central region (67.0%) (Figure 1); these differences were statistically significant, p<0.05.
- The lowest resistance rates were seen with trimethoprim-sulfamethoxazole (1.6-2%) and vancomycin (no resistance detected). Linezolid resistance was reported in 13 of 80,527 isolates in 2007 (**Table 1**), although these have not been confirmed.
- Among MDR isolates the most common observed resistances were to erythromycin (99.4%), oxacillin (95.1%), and ciprofloxacin (95.6 %), while resistance to gentamicin and trimethoprim-sulfamethoxazole was seen in 5.7% and 3.9% of MDR isolates, respectively (**Table 2**).
- Susceptibility varied for certain agents by age group with notably less resistance for ciprofloxacin and clindamycin among isolates from patients aged ≤17 years (**Table 2**).
- In 2007, less than a third (30.3%) of all *S. aureus* strains were pan-susceptible, while 11.6% expressed a single resistance phenotype (data not shown). Overall, MDR was noted in 32% of isolates from skin or wound infections. The prevalence of various phenotypes varied according to patient location (**Table 3**).

RESULTS

Figure 1: Resistance Rates Among *S. aureus* from Skin and Wound Specimen Sources in the USA According to Region: TSN Database 2007

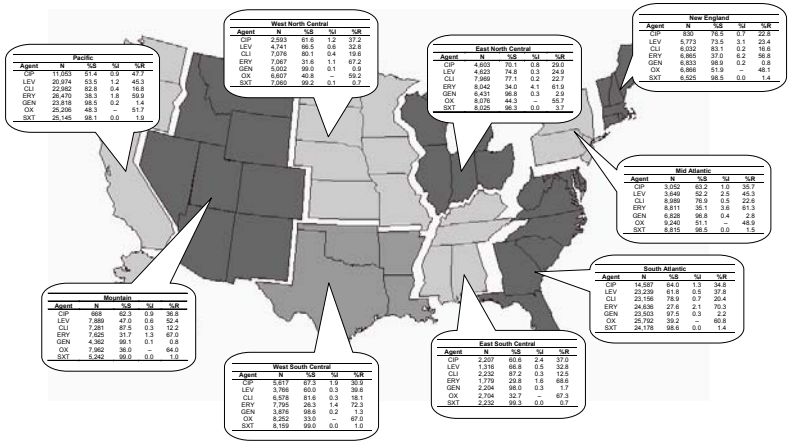

Table 1: Overall Resistance Rates among *S. aureus* from Skin and Wound Specimen Sources in the USA: TSN Database 2005-2007

Agent	Year of Isolation[a]	Total N	Susceptible %	Intermediate %	Resistant %
Ciprofloxacin	2005	43,919	64.0	4.0	31.9
	2006	55,667	63.7	1.6	34.7
	2007	45,210	61.8	1.2	37.0
Levofloxacin	2005	102,936	61.3	1.6	37.1
	2006	102,598	60.9	1.6	37.5
	2007	75,970	59.5	1.0	39.5
Clindamycin	2005	132,106	78.6	0.5	20.9
	2006	130,110	80.4	0.4	19.2
	2007	92,295	81.0	0.4	18.6
Erythromycin	2005	133,157	33.4	2.4	64.2
	2006	139,276	32.7	2.4	64.9
	2007	99,090	32.8	2.4	64.8
Gentamicin	2005	105,198	97.6	0.3	2.1
	2006	114,345	97.9	0.3	1.8
	2007	82,857	98.0	0.2	1.8
Linezolid[b]	2005	95,843	>99.9	–	–
	2006	107,776	>99.9	–	–
	2007	80,527	>99.9	–	–
Oxacillin	2005	140,640	42.1	–	57.8
	2006	143,130	42.4	–	57.6
	2007	100,705	43.0	–	57.0
Trimeth/sulfa[c]	2005	118,615	97.9	0.1	2.0
	2006	130,159	98.4	0.0	1.6
	2007	95,381	98.4	0.0	1.6

[a] 2007 included data from January to September.
[b] Some *S. aureus* isolates were non-susceptible to linezolid.
[c] Trimeth/sulfa = trimethoprim/sulfamethoxazole.

Table 2: Resistance Rates among *S. aureus* Tested Concurrently against Ciprofloxacin, Clindamycin, Erythromycin, Gentamicin, Oxacillin, and Trimethoprim/sulfamethoxazole from Skin and Wound Sources by Patient Age: TSN Database 2007

Agent	Age Phenotype	≤16 years			17-64 years			≥65 years		
		Total n	%S	%R	Total n	%S	%R	Total n	%S	%R
Ciprofloxacin	All	4,552	79.1	19.4	16,567	64.0	34.7	5,891	49.9	49.2
	MDR	829	10.9	89.0	5,183	4.5	95.3	2,597	1.7	98.3
	non-MDR	3,723	94.3	3.9	11,384	91.1	7.1	3,294	87.9	10.5
	OX R	2,392	65.1	32.9	9,363	44.2	54.5	3,021	17.4	81.9
	OX S	2,160	94.5	4.5	7,204	89.7	9.1	2,870	84.1	14.8
Clindamycin	All	4,552	90.6	8.9	16,567	83.9	15.7	5,891	65.5	33.8
	MDR	829	71.5	28.1	5,183	57.9	41.8	2,597	27.8	71.4
	non-MDR	3,723	94.8	4.6	11,384	95.7	3.9	3,294	95.2	4.2
	OX R	2,392	90.7	8.9	9,363	78.5	21.2	3,021	44.1	54.9
	OX S	2,160	90.4	8.9	7,204	90.8	8.7	2,870	88.0	11.6
Erythromycin	All	4,552	37.5	60.5	16,567	33.8	64.2	5,891	36.2	60.6
	MDR	829	0.2	99.5	5,183	0.5	99.3	2,597	0.3	99.5
	non-MDR	3,723	45.8	51.8	11,384	49.0	48.2	3,294	64.4	30.0
	OX R	2,392	10.8	88.1	9,363	8.3	90.5	3,021	6.0	92.2
	OX S	2,160	67.1	30.0	7,204	67.0	30.0	2,870	67.9	27.4
Gentamicin	All	4,552	98.6	1.3	16,567	97.9	1.8	5,891	95.9	3.6
	MDR	829	94.2	5.2	5,183	94.6	5.0	2,597	91.7	7.7
	non-MDR	3,723	99.6	0.4	11,384	99.5	0.4	3,294	99.1	0.5
	OX R	2,392	98.4	1.5	9,363	97.2	2.5	3,021	93.5	5.9
	OX S	2,160	98.8	1.0	7,204	98.9	0.9	2,870	98.3	1.3
Oxacillin	All	4,552	47.5	52.5	16,567	43.5	56.5	5,891	48.7	51.3
	MDR	829	2.8	97.2	5,183	3.9	96.1	2,597	7.9	92.1
	non-MDR	3,723	57.4	42.6	11,384	61.5	38.5	3,294	80.9	19.1
	OX R	2,392	0	100	9,363	0	100	3,021	0	100
	OX S	2,160	100	0	7,204	100	0	2,870	100	0
Trimeth/sulfa	All	4,552	98.8	1.2	16,567	98.4	1.6	5,891	98.0	2.0
	MDR	829	96.0	4.0	5,183	96.0	4.0	2,597	96.3	3.7
	non-MDR	3,723	99.4	0.6	11,384	99.5	0.5	3,294	99.4	0.6
	OX R	2,392	98.9	1.1	9,363	98.2	1.8	3,021	97.2	2.8
	OX S	2,160	98.7	1.3	7,204	98.6	1.4	2,870	98.9	1.1

Table 3: Predominant Resistance (%) Phenotype among *S. aureus* from Skin and Wound Specimens by Source: TSN database 2007

Phenotype	Out-patient N = 19,183		In-patient N = 7,789		ICU N = 538	
	Non-MDR	MDR	Non-MDR	MDR	Non-MDR	MDR
No resistance	31.3	–	28.2	–	28.3	-
ERY, OX	21.3	–	15.2	–	6.1	-
CLI, ERY	2.8	–	1.9	–	3.2	-
CIP OX	1.9	–	2.5	–	1.3	-
CIP, ERY, OX	–	15.6	–	15.7	-	11.3
CIP, CLI, ERY	–	1.1	–	1.6	-	2.0
CIP, CLI, ERY, OX	–	8.9	–	16.9	-	27.7
CIP, CLI, ERY, GEN, OX	–	0.5	–	1.5	-	3.3
CIP, CLI, ERY, GEN, OX, SXT	–	0.3	–	0.7	-	3.5

CIP = ciprofloxacin; CLI = clindamycin; ERY = erythromycin;
GEN = gentamicin; OXA = oxacillin; SXT = trimethoprim/sulfamethoxazole;
MDR = multi-drug resistant.

CONCLUSIONS

- The overall rate of methicillin resistance did not alter markedly over the 3 year study period, with almost two-thirds of all skin and wound *S. aureus* being resistant to methicillin (and macrolides).
- Clear inter-regional differences in staphylococcal resistance were evident; the New England and Mid-Atlantic regions generally had the lowest resistance rates; while the Central regions usually showed higher resistance rates.
- There was a higher incidence of MDR phenotypes in both inpatient and ICU isolates compared with outpatient strains.
- There was little variation in methicillin resistance among pediatric, adult, and elderly populations.
- The local application of TSN data may help improve the management of these infections most recently highlighted in both medical and lay media, as variability among resistance profiles has been found to exist on a regional basis.
- Prospective and more expansive surveillance including isolates from infections not previously examined, such as impetigo, minor abrasions, or simple wounds is needed to continue to guide empirical management and therapy.

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