MAJOR ARTICLE

Three-Year Surveillance of Community-Acquired *Staphylococcus aureus* Infections in Children

Sheldon L. Kaplan,[1,3] Kristina G. Hulten,[1,3] Blanca E. Gonzalez,[1,3] Wendy A. Hammerman,[1,3] Linda Lamberth,[3] James Versalovic,[2,3] and Edward O. Mason, Jr.[1,3]

Departments of [1]Pediatrics and [2]Pathology, Baylor College of Medicine, and [3]Texas Children's Hospital, Houston, Texas

Background. Methicillin-resistant *Staphylococcus aureus* (MRSA) isolates are increasingly frequent causes of skin and soft-tissue infections or invasive infections in many communities.

Methods. Prospective surveillance for community-acquired *S. aureus* infections at Texas Children's Hospital was initiated on 1 August 2001. Infections meeting the definition of community-acquired were identified. Demographic and clinical data were collected. Antibiotic susceptibilities, including inducible resistance to macrolide, lincosamide, and streptogramin B (MLS_B), were determined in the clinical microbiology laboratory with the methodology of the NCCLS. All data were entered into a computer database. Data were analyzed by χ^2 tests.

Results. From 1 August 2001 to 31 July 2004, the percentage of community-acquired *S. aureus* isolates that were methicillin resistant increased from 71.5% (551 of 771 isolates) in year 1 to 76.4% (1193 of 1562 isolates) in year 3 ($P = .008$). The number of both community-acquired MRSA (CA-MSRA) isolates and community-acquired methicillin-susceptible *S. aureus* (CA-MSSA) isolates increased yearly, but the rate of increase was greater for the CA-MRSA isolates. Among the CA-MRSA isolates, 2542 (95.6%) were obtained from children with skin and soft-tissue infections, and 117 (4.4%) were obtained from children with invasive infections. Overall, 62% of children with CA-MRSA isolates and 53% of children with CA-MSSA isolates were admitted to the hospital ($P = .0001$). The rate of clindamycin resistance increased significantly for both CA-MRSA isolates ($P = .003$) and CA-MSSA isolates ($P = .00003$) over the 3 years. MLS_B inducible resistance was found in 27 (44%) of 62 clindamycin-resistant CA-MSSA isolates, compared with 6 (4.5%) of 132 clindamycin-resistant CA-MRSA isolates ($P < .000001$).

Conclusions. CA-MRSA isolates account for an increasing percentage and number of infections at Texas Children's Hospital. Clindamycin resistance increased among community-acquired *S. aureus* isolates. Community surveillance of community-acquired *S. aureus* infections is critical to determine the appropriate empiric antibiotic treatment for either local or invasive infections.

Community-acquired methicillin-resistant *Staphylococcus aureus* (CA-MRSA) is now an established pathogen in many communities in the United States, as well as in the world [1–4]. In some areas, MRSA isolates account for the majority of *S. aureus* infections acquired in the community [5]. Skin and soft-tissue infections are the predominant types of CA-MRSA infections, but invasive and life-threatening infections are major concerns [5–7]. Although several clones of CA-MRSA have been described, one clone (USA300) is particularly common in many areas of the United States [8, 9].

Several investigators have reported their experience with CA-MRSA infection in children. We have primarily described invasive infections caused by CA-MRSA isolates in children at Texas Children's Hospital (TCH) (Houston) [10, 11]. In this report, we describe the overall experience with community-acquired *S. aureus* infections at TCH during a 3-year period from 1 August 2001 through 31 July 2004, to provide a more complete picture of CA-MRSA infection in children.

METHODS

Patients. Patients with community-acquired *S. aureus* infections and their corresponding isolates were prospectively identified and collected by a research nurse at TCH from 1 August 2001 to 31 July 2004. The Insti-

Received 3 December 2004; accepted 26 January 2005; electronically published 6 May 2005.

Reprints or correspondence: Dr. Sheldon L. Kaplan, Texas Children's Hospital, Feigin Center, Ste. 1150, MC 3-2371, 6621 Fannin, Houston, TX 77030 (skaplan@bcm.tmc.edu).

Clinical Infectious Diseases 2005; 40:1785–91

1058-4838/2005/4012-0012$15.00

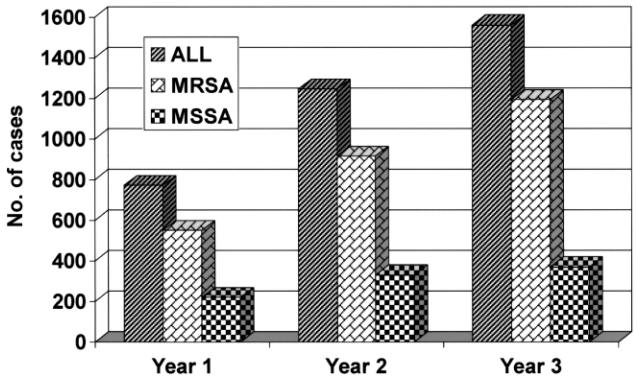

Figure 1. Annual number of cases of community-acquired *Staphylococcus aureus* infection in children admitted to Texas Children's Hospital from 1 August 2001 through 31 July 2004. $P = .008$, by χ^2 test for trend of yearly percentage of infections with community-acquired methicillin-resistant *S. aureus* isolates (MRSA). MSSA, methicillin-susceptible *S. aureus* isolates.

tutional Review Board of the Baylor College of Medicine (Houston, Texas) approved this study. Medical records of patients cared for at TCH who had a culture positive for *S. aureus* were reviewed. Information was gathered primarily from the central hospital information system. Patient data (e.g., demographics, underlying diseases, previous hospitalizations, primary diagnosis, and days of hospitalization) and isolate information (e.g., antimicrobial susceptibilities) were collected on a standardized form [10]. The patients and their respective isolates were classified according to 3 categories: (1) community-acquired isolates (2) nosocomial or hospital-acquired isolates, and (3) health-care associated, not hospital-acquired isolates in patients with frequent exposure to a health care facility because of an underlying condition, especially asthma or eczema. For this study, only community-acquired infections are being reported.

Definitions. Organisms were considered to be community-acquired if (1) the isolate was recovered within 48 h of hospitalization, (2) the isolate was obtained from an outpatient, with certain exceptions (see exclusion criteria below), or (3) the isolate was recovered after 48 h of hospitalization but clinical evidence clearly suggested that the infection was community-acquired (e.g., if a patient with no previous hospitalizations was admitted with osteomyelitis and, after 48 h of hospitalization, underwent surgical drainage, a specimen of which grew *S. aureus*). Exclusion criteria were (1) presence of any underlying illness possibly predisposing to frequent hospitalizations or frequent visits to medical facilities (e.g., immunodeficiency, cystic fibrosis, chronic renal failure, history of malignancy, asthma, or chronic skin illness); (2) the presence of indwelling catheters or percutaneous medical devices at the time specimens were obtained for culture, or any surgical site infection; and (3) hospitalization within the past year, excluding that of normal newborns. Invasive infections were defined as infections in the bloodstream, lymph nodes, mastoids, CNS, bones or joints, muscle, lungs, or pleural fluid, and superficial infections were defined as soft-tissue, wound, or skin infections.

Isolates. The clinical microbiology laboratory of TCH isolated *S. aureus* strains and determined antibiotic susceptibilities (to clindamycin, erythromycin, gentamicin, oxacillin, penicillin, trimethoprim-sulfamethoxazole, and vancomycin) by disk diffusion, using the methods and interpretation guidelines of the NCCLS. Testing for inducible macrolide, lincosamide, and streptogramin B (MLS_B) resistance was routinely performed [12]. The isolates were stored in horse blood at −80°C in the infectious disease laboratory until further use. Statistical analyses were performed using the χ^2 test or the χ^2 test for trend, for dichotomous variables, with the use of True Epistat (Epistat Services).

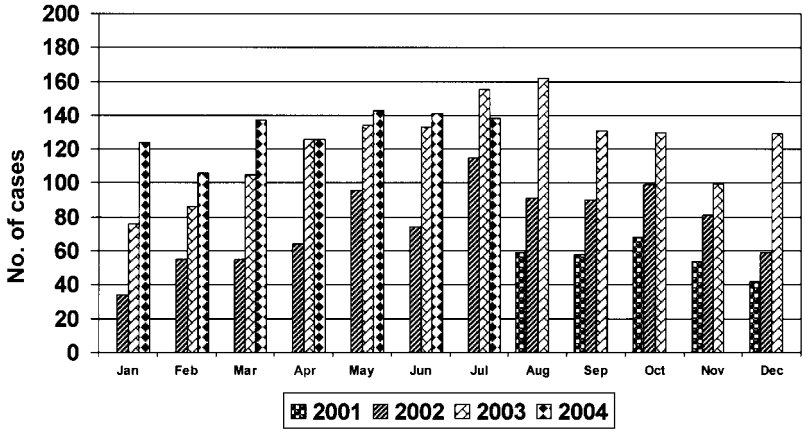

Figure 2. Monthly distribution of community-acquired *Staphylococcus aureus* infections in children at Texas Children's Hospital from 1 August 2001 through 31 July 2004.

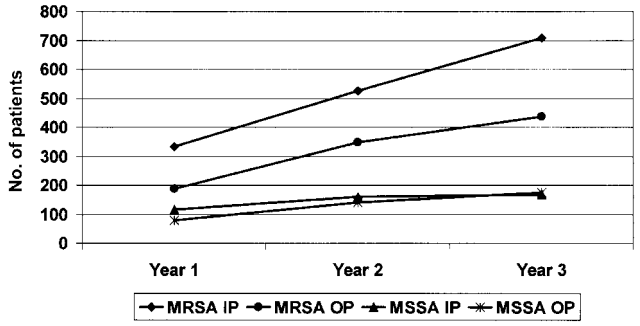

Figure 3. The number of inpatients (IP) and outpatients (OP) at Texas Children's Hospital with skin and soft-tissue infections caused by community-acquired *Staphylococcus aureus* isolates per study year from 1 August 2001 through 31 July 2004. For community-acquired methicillin-resistant *S. aureus* isolates (MRSA) versus methicillin-susceptible *S. aureus* isolates (MSSA), $P = .0001$ for IP and $P = .05$ for OP by χ^2 test for trend.

RESULTS

During the 3 years of the study, 3578 *S. aureus* isolates were associated with community-acquired infections; 2659 (74%) of the isolates were MRSA. The percentage of community-acquired *S. aureus* isolates that were methicillin resistant was 71.5% (551 of 771 isolates) in year 1, 73.5% (915 of 1245 isolates) in year 2, and 76.4% (1193 of 1562 isolates) in year 3 ($P = .008$) (figure 1). The number of both CA-MRSA and CA-MSSA isolates increased yearly, but the increase was greater for the CA-MRSA isolates (2.2-fold vs. 1.7-fold increase). The monthly distribution of community-acquired *S. aureus* isolates during the 3 study years demonstrated increased numbers of isolates among corresponding months from year to year, as well as similar seasonal peaks in the number of cases each year during the summer months (figure 2).

Of the CA-MRSA isolates, 2542 (95.6%) were recovered from children with skin and soft-tissue infections, and 117 (4.4%) were obtained from children with invasive infections. Of the CA-MSSA isolates, 853 (91.8%) were associated with skin and soft-tissue infections, and 76 (8.2%) were associated with invasive infections. CA-MSSA isolates were significantly more likely than CA-MRSA isolates to be associated with invasive infections ($P = .00002$).

Overall, among children with skin and soft-tissue infections, 62% of those with CA-MRSA isolates and 53% of those with CA-MSSA isolates were admitted to the hospital ($P = .0002$). The number of children admitted to TCH per year with skin and soft-tissue infections caused by CA-MRSA or CA-MSSA isolates has increased, particularly for the CA-MRSA group (figure 3). Over the 3 years of the study, the number of skin and soft-tissue infections caused by CA-MRSA isolates showed a significantly greater increase for both inpatients ($P = .0001$) and outpatients ($P = .05$), compared with the number caused by CA-MSSA isolates. The mean duration of hospitalization for children with skin and soft-tissue infections was 4.0 days (median, 3 days) for the CA-MRSA group and 4.4 days (median, 4.0 days) for the CA-MSSA group.

Age and race/ethnicity. The age distribution for the children with CA-MRSA and CA-MSSA infections over the 3 study years is shown in table 1. The 2 isolate groups did not differ with respect to age distribution overall, or when analyzed for systemic infection versus skin or soft-tissue infection. Furthermore, the age distribution over the 3-year period did not change, because the number of cases increased yearly for all age groups (figure 4).

The racial/ethnic distribution for children with CA-MRSA and CA-MSSA infections is shown in table 2. The number of cases increased yearly for all the major racial/ethnic groups. The distribution of racial groups differed significantly between the 2 isolate groups ($P < .000001$); overall, 39.3% and 27.1% of children were African American in the CA-MRSA and CA-MSSA groups, respectively.

Sites and types of invasive infection. The number of cases of invasive infection caused by CA-MRSA isolates in years 1, 2, and 3 was 30, 40, and 47, respectively, and the number caused by CA-MSSA isolates was 24, 29, 23, respectively. Although the number of cases of invasive infection appeared to be increasing more for the CA-MRSA isolates than for the CA-MSSA isolates,

Table 1. Age distribution of children with community-acquired *Staphylococcus aureus* infections at Texas Children's Hospital from 1 August 2001 through 31 July 2004.

Isolate, patient age in years	No. of infected children			
	Study year 1	Study year 2	Study year 3	Total, no. (%)
MRSA				
<1	81	134	204	419 (15.8)
1	121	195	265	581 (21.9)
2	72	116	136	324 (12.2)
3	43	60	84	187 (7.0)
4–9	100	190	199	489 (18.4)
⩾10	134	220	305	659 (24.8)
All	551	915	1193	2659 (100)
MSSA				
<1	41	63	55	159 (18.1)
1	37	30	69	96 (10.9)
2	26	28	29	83 (9.4)
3	13	29	24	66 (7.5)
4–9	49	87	100	236 (26.8)
⩾10	54	93	92	239 (27.2)
All	220	330	369	879 (100)

NOTE. MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

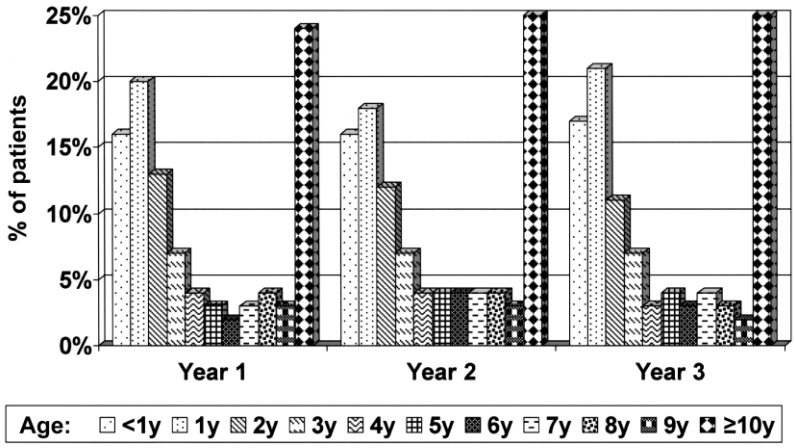

Figure 4. The annual age distribution of children as a percentage of the total number of patients with community-acquired *Staphylococcus aureus* infection at Texas Children's Hospital over 3 consecutive years, from 1 August 2001 through 31 July 2004. y, years.

the difference was not significantly different ($P = .18$). The sites of the invasive infections are shown in table 3. Musculoskeletal and pulmonary infections were the most common invasive infections caused by CA-MRSA isolates, whereas osteomyelitis, septic arthritis, bacteremia, and lymphadenitis were the most common types of invasive CA-MSSA infection. Over the 3 years of the study, 4 children with invasive infections died as a result of *S. aureus* infection; 3 of these children were infected with CA-MRSA isolates, and 1 was infected with CA-MSSA. The ages of these children were 1.5, 3.8, 13.4, and 14.1 years.

Antibiotic susceptibilities. The rates of clindamycin or erythromycin resistance for CA-MRSA and CA-MSSA isolates during the 3 years of the study are shown in table 4. Clindamycin resistance increased significantly among both CA-MRSA isolates ($P = .003$) and CA-MSSA isolates ($P = .00003$) over the 3 years, although resistance remained at low levels (percentage range of CA-MRSA isolates with resistance, 2%–6%). Each year, ~95% of CA-MRSA isolates were resistant to erythromycin, compared with 44%–50% of CA-MSSA isolates. The distribution of clindamycin susceptibilities for all 3 years is shown in figure 5. The number of CA-MRSA isolates with inducible MLS_B resistance increased each year. Inducible MLS_B resistance was found in 27 (44%) of the 62 clindamycin-resistant CA-MSSA isolates, compared with 6 (4.5%) of 132 clindamycin-resistant CA-MRSA isolates ($P < .000001$). Virtually all community-acquired *S. aureus* isolates were susceptible to trimethoprim-sulfamethoxazole each study year.

DISCUSSION

CA-MRSA infections are increasing in the United States and many other areas around the world. Infections caused by these organisms have been observed in many different patient populations, including children, neonates [13], prisoners [14], military personnel [15], athletes [16], HIV-infected individuals [17], and patients with eczema [17], among others. The vast majority of CA-MRSA infections are skin and soft-tissue infections.

In February 2000, one-third of community-acquired *S. aureus* isolates recovered from children at TCH were already found to be MRSA; by November 2000, that proportion had increased to one-half [5]. In September 2000, the TCH medical staff received a letter indicating that the majority of *S. aureus* isolates obtained from children with community infections seen at TCH were MRSA. Obtainment of specimens for culture from all abscesses and skin lesions, when possible, as well as from other sites, was highly encouraged, and management strate-

Table 2. Racial/ethnic distribution of children with community-acquired *Staphylococcus aureus* infections at Texas Children's Hospital from 1 August 2001 through 31 July 2004.

Isolate, patient race/ethnicity	No. of infected children			
	Study year 1	Study year 2	Study year 3	Total, no. (%)
MRSA				
Asian	13	11	10	34 (1.3)
African American	248	370	427	1045 (39.3)
White	135	225	321	681 (25.6)
Hispanic	144	272	372	788 (29.6)
Other	11	35	40	86 (3.2)
Unknown	0	2	23	25 (0.9)
MSSA				
Asian	14	10	9	33 (3.6)
African American	73	79	97	249 (27.1)
White	59	94	106	259 (28.2)
Hispanic	71	115	116	302 (32.9)
Other	3	31	26	60 (6.5)
Unknown	0	1	15	16 (1.7)

NOTE. $P < .000001$ for distribution between methicillin-susceptible *S. aureus* (MSSA) and methicillin-resistant *S. aureus* (MRSA) isolates.

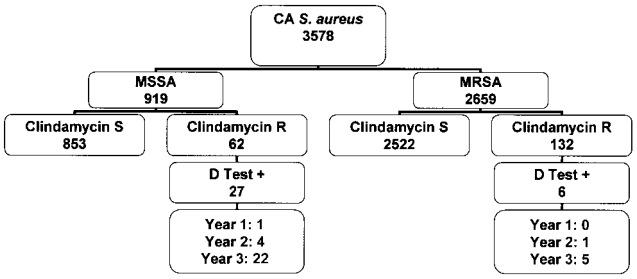

Figure 5. Breakdown of clindamycin susceptibility among 3578 community-acquired (CA) *Staphylococcus aureus* isolates, subdivided by methicillin susceptibility, at Texas Children's Hospital from 1 August 2001 through 31 July 2004. Numerical values are no. of isolates. $P = .00003$ for the distribution of *D* test–positive (+) isolates (i.e., those with inducible clindamycin resistance) among methicillin-susceptible *S. aureus* isolates (MSSA) and methicillin-resistant *S. aureus* isolates (MRSA). S, susceptible; R, resistant.

gies with antibiotics were suggested. Prospective surveillance of community-acquired *S. aureus* infections at TCH was initiated on 1 August 2001. Over the next 3 years, we observed increasing numbers of *S. aureus* infections yearly for both MSSA and MRSA isolates. In addition, an increasing number of children have been admitted to the hospital each year because of skin and soft-tissue infections. Because the letter encouraging medical staff to obtain specimens for culture was mailed almost 1 year before this current surveillance started, and because the number of admissions related to *S. aureus* infections have increased dramatically, we do not believe the increasing numbers of *S. aureus* infections during the 3 years of this report can be explained simply by the more frequent or aggressive performance of culture for skin and soft-tissue infections.

The 7-valent pneumococcal conjugate vaccine (PCV7) was licensed in 2000, and by mid-2000 it was routinely administered to infants, starting at age 2 months. PCV7 vaccination is associated with a decrease in the nasal colonization of the 7 serotypes contained in the vaccine. Two groups have observed that children who either were not colonized in the anterior nose with pneumococci or were colonized with nonvaccine-serotype pneumococci were more likely to be cocolonized with *S. aureus* than were children whose anterior nares were colonized with pneumococci of the serotypes in the conjugate vaccine [18, 19]. The authors of those studies suggested that *S. aureus* and PCV7 vaccine-serotype pneumococci compete for colonization sites in the anterior nares. Furthermore, an increased incidence of *S. aureus*–related acute otitis media was noted among children >12 months of age who received PCV7 followed by 23-valent pneumococcal polysaccharide vaccine, compared to the incidence among children who received control vaccine [20].

Is there a relationship between the increasing numbers of community-acquired *S. aureus* infections we have observed in the children at TCH and the widespread use of PCV7? If there is an association, it is reasonable to suggest that since PCV7 is administered predominantly to children <24 months of age, this age group should account for an increasing proportion of all the infections caused by *S. aureus.* During the 3 years of the study, the age distribution of the infections did not change substantially. The proportion of cases occurring in children aged <12 months or in those aged 13–24 months was virtually identical for each of the 3 years. Thus, our data would not support the idea that the use of PCV7 is associated with the increasing numbers of *S. aureus* infections we encountered.

Several different molecular-typing schemes have been developed for *S. aureus* and have been useful in the analysis of the epidemiology of the CA-MRSA isolates. Using PFGE fingerprints for a national database of MRSA isolates, McDougal et al. [8] described 8 lineages, designated "pulsed-field type," clusters USA100 through USA800. The developed nomenclature was confirmed with 2 other molecular-typing methods, multilocus sequence typing and staphylococcal protein A gene (*spa*) typing, and strains were further characterized by their staphylococcal chromosomal cassette (SCC) *mec* type. Seven of the pulsed-field type lineages included both MRSA and MSSA isolates. Two community-acquired *S. aureus* lineages of importance were described. Within the USA400 cluster (sequence

Table 3. Sites and types of infection with community-acquired *Staphylococcus aureus* in children at Texas Children's Hospital from 1 August 2001 through 31 July 2004.

	No. of cases of infection	
Site or type of infection	MRSA	MSSA
Abscess		
Epidural	3	1
Lung	2	0
Paraspinal	1	1
Renal	1	0
Sacral	1	0
Bacteremia	4	7
Empyema	9	2
Endocarditis	0	2
Lymphadenitis	7	16
Meningitis	0	1
Myositis	8	7
Osteomyelitis	54	28
Peritonitis	1	0
Pneumonia	14	2
Septic arthritis	9	10
Septicemia	3	0
Total	117	76

NOTE. MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus.*

Table 4. Antibiotic susceptibilities of community-acquired *Staphylococcus aureus* isolates recovered from children at Texas Children's Hospital from 1 August 2001 through 31 July 2004.

Isolate, antibiotic, and susceptibility	No. (%) of isolates		
	Study year 1	Study year 2	Study year 3
MRSA			
Clindamycin[a]			
Not susceptible	13 (2)	51 (6)	72 (6)
Susceptible	538	864	1120
Erythromycin[c]			
Not susceptible	521 (95)	883 (97)	1121 (94)
Susceptible	30	32	71
MSSA			
Clindamycin[b]			
Not susceptible	4 (3)	21 (6)	40 (11)
Susceptible	216	309	328
Erythromycin[c]			
Not susceptible	96 (44)	164 (50)	179 (49)
Susceptible	124	166	189

NOTE. MRSA, methicillin-resistant *S. aureus*; MSSA, methicillin-susceptible *S. aureus*.

[a] Values in parentheses are the percentage resistant to clindamycin yearly. $P = .003$, by χ^2 test for trend.

[b] Values in parentheses are the percentage resistant to clindamycin yearly. $P = .00003$, by χ^2 test for trend.

[c] Values in parentheses are the percentage resistant to erythromycin yearly.

type [ST] 1) is MW2, a CA-MRSA strain that caused rapidly fatal infections in children from Minnesota [8, 21]. Furthermore, CA-MRSA isolates associated with severe disease in Chicago were indistinguishable from MW2 [7]. USA300 (ST8) is the other community-acquired *S. aureus* lineage found widely throughout the United States [8, 22]. It is predominant in Houston and other regions in Texas, and it is also associated with severe disease, occasionally with fatal outcome [23].

In a previous study, we noted that in the early part of 2000, ~50% of the CA-MRSA isolates from TCH were USA300 [24]. Since 2003, >90% of the pediatric CA-MRSA isolates analyzed at TCH were USA300/ST8 and characteristically carried the *pvl* gene (encoding the cytotoxin Panton-Valentine leukocidin [PVL]) and the determinant for SCC *mec* type IV resistance [24]. Thus, in a short period of time, USA300 established itself as the predominant *S. aureus* clone causing infections among children who were cared for at TCH. A similar phenomenon of a dominant MRSA clone emerging in a community over a relatively short period of time has been observed by others [25, 26]. It is not known why USA300 is so capable of rapidly spreading in a community or why it causes infections seemingly more readily than do other *S. aureus* clones. The suggested role of PVL in enhancing the organism's ability to spread rapidly or to increase severity of invasive infections is under investigation [27]. Nevertheless, as in our first study [5], a greater percentage of CA-MSSA isolates (8.2%) than CA-MRSA isolates (4.4%) was recovered from patients with invasive infections. The reason for this difference remains unknown but may be related to differences in the presence of certain virulence genes [24].

Osteomyelitis and septic arthritis are among the most common invasive infections caused by CA-MRSA isolates. The strains with the *pvl* gene have been associated with more complications of osteomyelitis than have isolates without the gene—for example, deep venous thrombophlebitis, which has been rarely reported in children with *S. aureus* osteomyelitis, or the development of chronic osteomyelitis [11, 28]. CA-MRSA is now the most common organism isolated from children at TCH with pneumonia and empyema [29]. Myositis and pyomyositis caused by *S. aureus* have also been encountered more frequently since 2000; this may be related, in part, to the greater use and sensitivity of MRI in detecting these infections [30, 31]. However, it is possible that CA-MRSA and CA-MSSA strains that carry the *pvl* gene can invade and infect muscle tissue more readily than can *pvl*-negative strains. Extensive infections of the epidural space overlying the spinal cord and life-threatening infections caused by CA-MRSA isolates are now encountered with a greater frequency than was noted for such infections caused by CA-MSSA isolates at TCH in the years preceding this surveillance study or in large published series of children [23, 32].

The clindamycin resistance rate among CA-MRSA isolates varies across the United States. Clindamycin resistance rates for both CA-MRSA and CA-MSSA isolates increased significantly over the 3 years of surveillance, although the rates were much lower than those reported in other areas [33]. We have also noted that the inducible MLS_B resistance phenotype accounts for a small but growing proportion of community-acquired *S. aureus* isolates with clindamycin resistance. Inducible MLS_B resistance has been significantly more common among CA-MSSA isolates than among CA-MRSA isolates at TCH. If clindamycin resistance rates continue to increase in our area, clindamycin will be less useful for empiric treatment for suspected *S. aureus* invasive infections, and alternative antibiotics, such as linezolid, will be used more commonly [34]. The antibiotic-susceptibility patterns of community-acquired *S. aureus* isolates are critical to monitor, but it is unclear how this can be accomplished at a local, state, or national level. The Centers for Disease Control and Prevention and other agencies are discussing how this type of information can be made available to primary health care providers so that the most appropriate antibiotics can be selected for empiric treatment of the wide variety of infections caused by *S. aureus*.

CA-MRSA infections are now encountered in many communities in the United States as well as throughout the world. At TCH, the percentage of community-acquired *S. aureus* isolates that are methicillin resistant has increased yearly and is now >75%. Furthermore, the absolute number of CA-MRSA

infections has increased >2-fold, and the number of CA-MSSA infections has almost doubled over the 3-year period of surveillance. A single clone of CA-MRSA has become dominant and is responsible for an increasing number of cases of invasive infection. Physicians caring for children throughout the United States and the world are likely to face the same problem with CA-MRSA that we have described in this report, as the USA300 or other CA-MRSA clones are introduced into their communities.

Acknowledgments

Financial support. This study was funded in part by a grant from Pfizer.

Potential conflicts of interest. S.L.K. has received a grant from Pfizer to study *S. aureus* infections in children. All other authors: no conflicts.

References

1. Herold BC, Immergluck LC, Maranan MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. JAMA **1998**; 279:593–8.
2. Naimi TS, LeDell KH, Boxrud DJ, et al. Epidemiology and clonality of community-acquired methicillin-resistant *Staphylococcus aureus* in Minnesota, 1996–1998. Clin Infect Dis **2001**; 33:990–6.
3. Purcell K, Fergie JE. Exponential increase in community-acquired methicillin-resistant *Staphylococcus aureus* infections in South Texas children. Pediatr Infect Dis J **2002**; 21:988–9.
4. Vandenesch F, Naimi T, Enright MC, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* carrying Panton-Valentine leukocidin genes: worldwide emergence. Emerg Infect Dis **2003**; 9:978–84.
5. Sattler CA, Mason EO Jr, Kaplan SL. Prospective comparison of risk factors and demographic and clinical characteristics of community-acquired, methicillin-resistant versus methicillin-susceptible *Staphylococcus aureus* infection in children. Pediatr Infect Dis J **2002**; 21:910–7.
6. Centers for Disease Control and Prevention. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*—Minnesota and North Dakota, 1997–1999. JAMA **1999**; 282:1123–5.
7. Mongkolrattanothai K, Boyle S, Kahana MD, Daum RS. Severe *Staphylococcus aureus* infections caused by clonally related community-acquired methicillin-susceptible and methicillin-resistant isolates. Clin Infect Dis **2003**; 37:1050–8.
8. McDougal LK, Steward CD, Killgore GE, Chaitram JM, McAllister SK, Tenover FC. Pulsed-field gel electrophoresis typing of oxacillin-resistant *Staphylococcus aureus* isolates from the United States: establishing a national database. J Clin Microbiol **2003**; 41:5113–20.
9. Buckingham SC, McDougal LK, Cathey LD, et al. Emergence of community-associated methicillin-resistant *Staphylococcus aureus* at a Memphis, Tennessee Children's Hospital. Pediatr Infect Dis J **2004**; 23: 619–24.
10. Martinez-Aguilar G, Hammerman WA, Mason EO Jr, Kaplan SL. Clindamycin treatment of invasive infections caused by community-acquired, methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* in children. Pediatr Infect Dis J **2003**; 22:593–8.
11. Martinez-Aguilar G, Avalos-Mishaan A, Hulten K, et al. Community-acquired, methicillin-resistant and methicillin-susceptible *Staphylococcus aureus* musculoskeletal infections in children. Pediatr Infect Dis J **2004**; 23:701–6.
12. NCCLS. Performance standards for antimicrobial disk susceptibility tests: approved standard, 8th edition. Wayne, PA: NCCLS, **2004**.
13. Healy CM, Hulten KG, Palazzi DL, Campbell JR, Baker CJ. Emergence of new strains of methicillin-resistant *Staphylococcus aureus* in a neonatal intensive care unit. Clin Infect Dis **2004**; 39:1460–6.
14. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections in correctional facilities—Georgia, California, and Texas, 2001–2003. MMWR Morb Mortal Wkly Rep **2003**; 52:992–6.
15. Baum SE, Morris JT, Dooley DP, Watson R. Methicillin-resistant *Staphylococcus aureus* in an adult military beneficiary population lacking risk factors: susceptibility to orally available agents. Mil Med **2003**; 168:126–30.
16. Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants—Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000–2003. MMWR Morb Mortal Wkly Rep **2003**; 52:793–5.
17. Iyeer S, Jones DH. Community-acquired methicillin-resistant *Staphylococcus aureus* skin infection: a retrospective analysis of clinical presentation and treatment of a local outbreak. J Am Acad Dermatol **2004**; 50:854–8.
18. Bogaert D, Belkum A, Sluijter M, et al. Colonisation by *Streptococcus pneumoniae* and *Staphylococcus aureus* in healthy children. Lancet **2004**; 363:1871–2.
19. Regev-Yochay G, Dagan R, Raz M, et al. Association between carriage of *Streptococcus pneumoniae* and *Staphylococcus aureus* in children. JAMA **2004**; 292:716–20.
20. Veenhoven R, Bogaert D, Uiterwaal C, et al. Effect of pneumococcal conjugate followed by polysaccharide pneumococcal vaccine on recurrent acute otitis media: a randomized study. Lancet **2003**; 361:2189–95.
21. Baba T, Takeuchi F, Kuroda M, et al. Genome and virulence determinants of high virulence community-acquired MRSA. Lancet **2002**; 359:1819–27.
22. Feil EJ, Cooper JE, Grundmann H, et al. How clonal is *Staphylococcus aureus?* J Bacteriol **2003**; 185:3307–16.
23. Gonzalez BE, Martinez-Aguilar G, Hulten KG, et al. Severe staphylococcal sepsis in adolescents in the era of community-acquired methicillin-resistant *Staphylococcus aureus.* Pediatrics **2005**; 115:642–8.
24. Mishaan AMA, Mason EO Jr, Martinez-Aguilar G, et al. Emergence of a predominant clone of community *Staphylococcus aureus* among children in Houston, Texas. Pediatr Infect Dis J **2005**; 24:201–6.
25. Dufour P, Gillet Y, Bes M, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in France: emergence of a single clone that produces Panton-Valentine leukocidin. Clin Infect Dis **2002**; 35:819–24.
26. Diep BA, Sensabaugh, Somboona NS, et al. Widespread skin and soft-tissue infections due to two methicillin-resistant *Staphylococcus aureus* strains harboring the genes for Panton-Valentine leukocidin. J Clin Microbiol **2004**; 42:2080–4.
27. Gillet Y, Issartel B, Vanhems P, et al. Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotizing pneumonia in young immunocompetent patients. Lancet **2002**; 359:753–9.
28. Gorenstein A, Gross E, Houri S, Gewirts G, Katz S. The pivotal role of deep vein thrombophlebitis in the development of acute disseminated staphylococcal disease in children. Pediatrics **2000**; 106:e87. Available at: http://www.pediatrics.org/cgi/content/full/106/6/e87. Accessed on 3 May 2005.
29. Schultz KD, Fan LF, Pinsky J, et al. The changing face of pleural empyemas in children: epidemiology and management. Pediatrics **2004**; 113:1735–40.
30. Gubbay AJ, Isaacs D. Pyomyositis in children. Pediatr Infect Dis J **2000**; 19:1009–13.
31. Beissert M, Schultz G, Chittka B, Darge K. Ultrasound and MRI features of pyomyositis in children. Eur Radiol **2003**; 13:1050–5.
32. Auletta JJ, John CC. Spinal epidural abscesses in children: a 15-year experience and review of the literature. Clin Infect Dis **2001**; 32:9–16.
33. Frank AL, Marcinak JF, Mangat PD, et al. Clindamycin treatment of methicillin-resistant *Staphylococcus aureus* infections in children. Pediatr Infect Dis J **2002**; 21:530–4.
34. Kaplan SL, Deville JG, Yogev R, et al. Linezolid versus vancomycin for treatment of resistant gram-positive infections in children. Pediatr Infect Dis J **2003**; 22:677–86.