

Characterization of *Staphylococcus aureus* cutaneous infections in a pediatric dermatology tertiary health care outpatient facility

Alex G. Ortega-Loayza, MD,^a Stephanie A. Diamantis, MD,^b Peter Gilligan, PhD,^c and Dean S. Morrell, MD^b
 Richmond, Virginia, and Chapel Hill, North Carolina

Background: Epidemiology and patterns of antibiotic resistance for *Staphylococcus aureus* are changing in the United States.

Objective: We sought to determine the epidemiology and antibiotic susceptibility profiles in *S aureus* cutaneous infections in a pediatric dermatology tertiary health care facility in North Carolina.

Methods: We conducted a prospective observational study involving pediatric patients (n = 93, age < 18 years) with signs of skin and soft tissue infections seen at a pediatric dermatology clinic between 2005 and 2007.

Results: We analyzed 141 cultures from 93 pediatric dermatology patients. *S aureus* was recovered from 97 cultures, of which 32% were methicillin-resistant *S aureus* (MRSA). In the pediatric dermatology clinic, children with atopic dermatitis accounted for 66% of the cultures; however, the presence of atopy did not represent a risk factor to acquire MRSA infection ($P = .190$; odds ratio = 1.643 [95% confidence interval: 0.672-4.014]). In all, 97 cultures were tested for antibiotic susceptibility and demonstrated the following resistance patterns: penicillin (86%), erythromycin (46%), methicillin (32%), clindamycin (22%), gentamicin (3%), vancomycin (0%), and trimethoprim-sulfamethoxazole (0%). Of the pediatric dermatology outpatient MRSA infections, the resistance patterns were as follows: erythromycin (71%), clindamycin (16%), gentamicin (2%), and trimethoprim-sulfamethoxazole (0%).

Limitations: This study addressed a select population of children in North Carolina and may not generalize to different clinical settings or regions.

Conclusion: Cutaneous *S aureus* infections in an outpatient pediatric dermatology tertiary health care facility demonstrated less resistance than previously reported from inpatient and emergency department settings. In our population, clindamycin and tetracyclines are still effective antibiotic choices in the majority of MRSA infections. Local prevalence and susceptibility of community-acquired MRSA as well as individual risk factors should be considered for diagnosis and treatment. (J Am Acad Dermatol 10.1016/j.jaad.2009.07.030.)

Key words: atopic dermatitis; methicillin resistance; pediatric; *Staphylococcus aureus*.

From the Department of Internal Medicine, Virginia Commonwealth University^a; and Departments of Dermatology^b and Pathology and Laboratory Medicine,^c University of North Carolina.

Funding sources: None.

Conflicts of interest: None declared.

Accepted for publication July 13, 2009.

Reprints not available from the authors.

Correspondence to: Dean S. Morrell, MD, Department of Dermatology, University of North Carolina, Chapel Hill, 3100 Thurston-Bowles Bldg, CB #7287, Chapel Hill, NC 27599. E-mail: morrell@med.unc.edu.

Published online February 20, 2010.

0190-9622/\$36.00

© 2009 by the American Academy of Dermatology, Inc.

doi:10.1016/j.jaad.2009.07.030

S *taphylococcus aureus* is a pathogen well known for causing skin and soft tissue infections (SSTIs) including furuncles, carbuncles, cellulitis, and skin abscesses.¹ Methicillin-resistant *S aureus* (MRSA) was first reported in the 1960s in the United Kingdom² and was primarily a nosocomial pathogen confined to hospitals and long-term care facilities.^{2,3} Traditionally, risk factors for nosocomial (or hospital-acquired [HA]) MRSA infection have included recent hospitalization, surgery, dialysis, residence in a long-term care facility, permanent indwelling catheter, or percutaneous medical device.⁴⁻⁶ In the late 1980s, MRSA began to present in healthy children without the traditional health

care—associated risk factors; however, many of these children had underlying chronic medical conditions requiring frequent health care contact and were classified as having community-onset MRSA.⁷⁻⁹ Then, in the early 1990s, several investigators reported cases of community-acquired (CA) MRSA infections among children without any predisposing risk factors or underlying medical problems.^{6,10-25} These reports of CA-MRSA challenged the accepted fact that MRSA is a pathogen confined to the hospital environment.²⁶ Many of the CA-MRSA isolates were associated with crowded living conditions, involvement in competitive contact sports, substance abuse, or child care attendance.^{5,13,18,27-29} Moreover, Hussain et al³⁰ noted a reservoir of asymptomatic MRSA colonization in healthy children who lacked traditional risk factors. In recent years, CA-MRSA has emerged as an important pathogen in the community setting, and its incidence is on the rise nationwide.^{31,32}

The biology and clinical picture of CA-MRSA appears to differ from that of HA-MRSA.^{1,9,27,32-38} Antibiotic resistance to methicillin and other semisynthetic penicillins is conferred to *S aureus* by the *mecA* gene that is located on a mobile genetic element known as a staphylococcal cassette chromosome (staphylococcal cassette chromosome *mec*). *Mec A* encodes for penicillin binding protein 2a, which decreases the organism's affinity for beta-lactam antibiotics.¹⁰ HA-MRSA strains contain staphylococcal cassette chromosome *mec I* and *II*, which are larger and have the capacity for multidrug resistance. However, CA-MRSA strains contain staphylococcal cassette chromosome *mec IV*, which is much smaller and does not confer multidrug resistance.^{2,10,34} In fact, most of the CA-MRSA strains are susceptible to non-beta-lactam antibiotics such as trimethoprim-sulfamethoxazole (TMP-SMX) and clindamycin. CA-MRSA strains also tend to carry virulence factors such as Panton-Valentine leukocidin, which have been associated with SSTIs.¹⁰

Although primary treatment of SSTIs continues to be incision and drainage, the emergence of MRSA as a community pathogen has complicated the choice

of initial empiric antibiotic therapy.³⁵ Regional antimicrobial susceptibility patterns and type of clinical infection should guide initial antibiotic choices.³⁹ As the epidemiology of SSTIs is continually evolving, we wanted to characterize the epidemiology and antibiotic susceptibility profiles of staphylococcal isolates from pediatric SSTIs in an outpatient tertiary health care facility in North Carolina.

CAPSULE SUMMARY

- Cutaneous *Staphylococcus aureus* infections in an outpatient pediatric dermatology tertiary health care facility demonstrated less resistance than previously reported from inpatient and emergency department settings.
- Clindamycin is an effective antibiotic choice in 84% of methicillin-resistant *S aureus* infections in the pediatric outpatient population in North Carolina.
- Tetracyclines are an effective antibiotic choice in 94% of age-appropriate methicillin-resistant *S aureus* infections in the pediatric outpatient population in North Carolina.
- Local prevalence and susceptibility of community-acquired methicillin-resistant *S aureus* as well as individual risk factors should be considered for diagnosis and treatment.

METHODS

A prospective observational study was conducted between January 2005 and December 2007. All pediatric patients (n=93, age < 18 years) with signs of skin infection (pustule, crust, or abscess formation) seen at a pediatric dermatology clinic between 2005 and 2007 were included. Microbiological culture from each lesion was obtained using a sterile tolyethylene terephthalate-tipped swab during the visit and transported to the laboratory in Stuart transport medium using a TransPorter device (HealthLink, Jacksonville, FL). Specimens were plated on chocolate, colistin-nalidixic 5% sheep blood

and MacConkey agars, incubated at 35 °C, and examined daily for 3 days. Colonies typical of *S aureus* were identified using standard methods. Cefoxitin disk diffusion screening was used to detect methicillin resistance. Susceptibility to other antimicrobials was performed by disk diffusion or in the case of vancomycin by E-test using minimum inhibitory concentration of greater than 2 µg/mL to indicate reduced susceptibility to vancomycin. All isolates were tested by the disk approximation technique for inducible clindamycin resistance (D-test). Isolates that were D-test positive were considered to be clindamycin resistant. Susceptibilities of the outpatient pediatric dermatology patients were compared with our institution's total outpatient antibiograms for the same period of time.

Univariate (frequencies and percentages for qualitative variables and media, measures of central tendency and dispersion for quantitative variables) and bivariate (χ^2) analyses were performed. If the variables were statistically significant, they were then tested in a multinomial regression model

Abbreviations used:

CA:	community-acquired
ED:	emergency department
HA:	hospital-acquired
MRSA:	methicillin-resistant <i>Staphylococcus aureus</i>
MSSA:	methicillin-sensitive <i>Staphylococcus aureus</i>
SSTI:	skin and soft tissue infection
TMP-SMX:	trimethoprim-sulfamethoxazole

(multivariate analysis) calculating the odds ratio and confidence intervals. All the analyses were made using software (SPSS, Version 16.0 for Windows, SPSS Inc, Chicago, IL) with a significance level of $\alpha = 0.05$.

RESULTS

We analyzed 141 cultures from 93 patients. A total of 71 patients had *S aureus* isolates. In all, 31 patients had multiple cultures (obtained at different office visits). Thirteen (42%) of the 31 children with multiple cultures showed consistent isolates (9 with methicillin-sensitive *S aureus* [MSSA]; 4 with MRSA). Four of the 31 children with multiple cultures switched isolates from MSSA to MRSA or vice versa. Demographic breakdown of the patients is presented in Table I.

In all cultures, MSSA was noted in 66 (46.8%) and MRSA was noted in 31 (22%). Of positive *S aureus* cultures, MRSA accounted for 32% of all *S aureus* isolates. Other isolates are shown in Table II. Within our institution's total outpatient *S aureus* isolates, 54% were MRSA. Antibiotic susceptibilities were determined in 97 of 141 cultures; negative cultures and cultures with isolates other than MSSA and MRSA were not included in our analysis. Resistance patterns are presented in Table III. Resistance patterns of our institution's total *S aureus* outpatient isolates are presented in Table IV. During the study period, tetracycline sensitivities were not routinely performed on younger pediatric patients. Of those tested, 94% of MRSA strains ($n = 31$) were susceptible to doxycycline, whereas all MSSA strains ($n=38$) were susceptible.

Among the pediatric dermatology cultures, 89 (63.1%) of 141 cultures were obtained from the extremities, 18 (12.8%) on the scalp, 11 (7.8%) on the face, 5 (3.5%) on the neck, 4 (2.8%) on the buttocks, 3 (2.1%) on the abdomen, and 3 (2.1%) in other locations. Only 5 cultures were sent to the microbiology laboratory with the clinical diagnosis of an abscess; all were positive for MSSA. Only 1 of the 5 patients with clinical abscess carried a diagnosis of atopic dermatitis. Seasonal distribution was winter

(15.6%), spring (17%), summer (30.5%), and fall (36.9%).

Atopic dermatitis did not appear to be an independent risk factor for the development of MRSA infection, and patients with atopic dermatitis did not demonstrate a significantly different resistance pattern to methicillin ($P = .190$; odds ratio = 1.643 [95% confidence interval: 0.672-4.014]). In addition, there was no difference between atopic and nonatopic patients regarding antibiotic susceptibilities. Of the patients with atopic dermatitis, 71% of skin cultures grew *S aureus*.

A culture from the scalp represented an independent risk factor for MRSA infection ($P = .005$; odds ratio = 7.097 [95% confidence interval: 1.835-27.442]). No significant variation in clindamycin resistance was noted between different years or different seasons. No cases of MRSA were accompanied by bacteremia or admission to the hospital (data not shown).

DISCUSSION

Epidemiology of MRSA in pediatric patients

Multiple studies characterizing the prevalence of MRSA have been conducted during the past several years as CA-MRSA has become more commonplace in emergency departments (EDs), inpatient facilities, and outpatient facilities throughout the United States. However, few studies address the prevalence of MRSA in outpatient tertiary care subspecialty clinics such as ours. Moreover, patterns of antibiotic susceptibility tend to differ between settings and geographic locations.

Inpatient departments and ED

Most studies examining the epidemiology of CA-MRSA have been conducted from tertiary care inpatient facilities and EDs. In these settings, multiple studies have confirmed the increase in prevalence of MRSA and the variability in susceptibility profiles of the organism in different geographic areas.

In a retrospective review, investigators in Chicago, IL, found an increased prevalence of CA-MRSA from the period of 1988 to 1990 to the period of 1993 to 1995 in children with no predisposing risk factors.¹⁵ Studies of children in South Texas and New England also showed an increased number of CA-MRSA isolates in children with no predisposing risk factors.¹⁰⁻¹² Kaplan et al³² conducted a prospective study out of a Texas pediatric hospital from 2001 to 2004 and found the percentage of CA-MRSA increased from 71.5% to 76.4% (95.6% were from SSTIs), and the rate of clindamycin resistance also increased. In a hospital in Baltimore, MD, 45% of pediatric cutaneous *S aureus* infections were caused

Table I. Demographics of our population

	N (%)	M (%)	F (%)	Age <5 y (%)	Atopic component (%)
Caucasian	47 (51.6)	24 (51.1)	23 (48.9)	20 (42.6)	24 (51.1)
AA	31 (33.3)	15 (48.4)	16 (51.6)	22 (71)	27 (87.1)
Other*	15 (16.1)	8 (53.3)	7 (46.6)	8 (53.3)	10 (66.6)
Total	93	47	46	50	61

AA, African American; F, female; M, male.

*Includes Latino, Asian, and Native American.

by MRSA and 84% of those were CA. Of those CA-MRSA strains, 98% were susceptible to TMP-SMX and 94% were susceptible to clindamycin.³¹ Within our total inpatient (non-intensive care department) *S aureus* isolates, 56% were MRSA with 97% sensitive to TMP-SMX. Johnson et al⁴⁰ also noted an increase in CA-MRSA infections in a rural tertiary care children's hospital in Kentucky from 2004 to 2005. In this population, 90% of CA *S aureus* infections were SSTIs, and greater than 95% were susceptible to TMP-SMX.

Pallin et al⁴¹ analyzed data from a representative sample of US ED visits from 1993 to 2005 and found the number of ED visits for SSTIs increased during that time period paralleling the emergence of CA-MRSA. These authors noted a nearly 3-fold increase in the annual number of ED visits for SSTIs. In addition, antibiotics with activity against CA-MRSA were prescribed with greater frequency. A study from two pediatric EDs in distinct geographic areas also showed an increase in the prevalence of CA-MRSA in pediatric patients presenting with SSTIs. Hasty et al³³ noted 22% of bacterial cultures were positive for CA-MRSA, and 80% of those cultures were obtained from abscesses. Analysis of pediatric patients without frequent health care contact presenting to an ED in Chicago, IL, found 26.4% of children were colonized with *S aureus* and 8.3% of those were MRSA.¹³

Outpatient

In the outpatient setting as well, CA-MRSA prevalence is on the rise, further complicating diagnosis, treatment, and prevention of SSTIs. In an adult outpatient dermatology clinic, 53% of *S aureus* cultures were MRSA. In this population, CA-MRSA occurred more frequently in men and most often in the lower extremities.⁵ An outpatient pediatric dermatology clinic reported a series of 8 case reports of CA-MRSA, all of which were SSTIs, and 3 were patients with atopic dermatitis.⁴² Pediatric patients may also be reservoirs of asymptomatic colonization for MRSA. One pediatric outpatient facility in Chicago, IL, noted 24.4% of children were colonized

with *S aureus* with 2.5% of those isolates MRSA.³⁰ In 2004, MRSA accounted for 23.8% of SSTIs in US pediatric outpatients in contrast to Canada and Germany (<2%), France (4%), and Italy (6.9%).⁴³ In our pediatric dermatology clinic, 22% of all cultures (and 32% of *S aureus* cultures) were positive for MRSA compared with 54% of all outpatient *S aureus* cultures at our institution.

Demographic characteristics

Fridkin et al⁴ examined the incidence of CA-MRSA in 3 distinct communities (Baltimore, MD; Atlanta, GA; and Minneapolis, Minnesota) and noted significantly higher incidence of CA-MRSA in children younger than 2 years and among African Americans in Atlanta, GA. In a pediatric health care facility in Minneapolis, MN, CA-MRSA infections were more likely than HA-MRSA infections to be from a SSTI (80% compared with 59%) and to be from an ethnic minority group (82% vs 55%).⁴⁴ In our pediatric dermatology outpatient population, MRSA was higher in female patients and in African American children, but not statistically significant in comparison with other sex/race groups. The majority of our MRSA cultures were obtained from extremities (18/31, 58%) and scalp (9/31, 29%), with scalp location being a significant risk factor for MRSA.

MRSA in children with atopic dermatitis

Children with atopic dermatitis are deficient in antimicrobial peptides such as human beta-defensin-3 and cathelicidins, which render them more susceptible to infections with organisms such as *S aureus*.⁴⁵ Therefore, one might reasonably conclude the incidence of MRSA infections is increased in those children with atopic dermatitis; few studies address this specific issue. Gong et al⁴⁶ examined children with atopic dermatitis in China and found an increased colonization rate with *S aureus* in these patients that correlated directly with eczema severity. Investigators in a South Korean clinic noted a 75.4% incidence rate of *S aureus* colonization in children with atopic dermatitis with 18.3% CA-MRSA.⁴⁷ In another study, 22%

Table II. Microbiology of skin infections caused by *Staphylococcus aureus* and other bacteria

	Cultures (n = 141)	Percentage
MSSA	66	46.8
MRSA	31	22
Gram-negative rods	3	2.1
<i>Enterococcus</i> species	1	0.7
Coagulase-negative <i>Staphylococcus</i>	13	9.2
<i>Streptococcus</i> species	5	3.5
Diphtheroids	2	1.4
Mix flora	5	3.5
Skin flora	15	10.6

MSSA, Methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*.

Table III. Patterns of resistance in pediatric dermatology patients infected by *Staphylococcus aureus*

	MSSA (n = 66)	MRSA (n = 31)	Total (n = 97)
Penicillin	52 (78.8%)	31 (100%)	83 (85.6%)
Methicillin	0 (0%)	31 (100%)	31 (32%)
Erythromycin	23 (34.8%)	22 (70.5%)	45 (46.4%)
Clindamycin	16 (24.2%)	5 (16.1%)	21 (22%)
Gentamicin	1 (1.5%)	1 (1.5%)	2 (2.1%)
Vancomycin	0 (0%)	0 (0%)	0 (0%)
TMP-SMX	0 (0%)	0 (0%)	0 (0%)

MRSA, Methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; TMP-SMX, trimethoprim-sulfamethoxazole.

of the children with moderate to severe atopic dermatitis had nares colonized with *S aureus*, suggesting this area may be an important reservoir.⁴⁸ In a retrospective study in children with atopic dermatitis, the prevalence of MRSA increased in children older than 5 years.⁴⁹ In our study, 23 (74%) of 31 MRSA cultures were obtained from children who had an atopic component; however, we did not find a statistical difference between atopy and MRSA versus non-MRSA infection ($P = .190$). Because very few of our cultures were from clinically diagnosed abscesses, it is possible that the incidence of MRSA in our patients with atopic dermatitis is actually higher, and they sought medical care elsewhere (ie, local ED) for emergent management.

Antibiotic susceptibility and resistance patterns

Although incision and drainage is the primary treatment for uncomplicated skin and soft tissue abscesses, patients who do not improve or those

Table IV. Patterns of resistance of our institution's outpatient *Staphylococcus aureus* isolates

	MSSA	MRSA	Total
Penicillin	80%	100%	81%
Methicillin	0%	100%	54%
Erythromycin	37%	93%	67%
Clindamycin	24%	34%	29%
Gentamicin	1%	3%	2%
Vancomycin	0%	0%	0%
TMP-SMX	3%	2%	2%

MRSA, Methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-sensitive *Staphylococcus aureus*; TMP-SMX, trimethoprim-sulfamethoxazole.

who have large lesions (>5 cm), systemic symptoms, or an immunocompromised state should receive appropriate antibiotic therapy.^{4,28,50} As CA-MRSA becomes more commonplace in outpatient settings, clinicians need to be aware of antibiotic resistance patterns in their community.

Although CA-MRSA is genetically distinct from multidrug-resistant health care-associated MRSA, it is not yet known whether the antibiotic susceptibilities of CA-MRSA are relatively universal and stable.⁵¹ It is clear that CA-MRSA has an antibiogram that is quite distinct from HA-MRSA. Clindamycin susceptibility is much more frequent in CA-MRSA, and these organisms are universally susceptible to TMP-SMX. Resistance is variable to erythromycin with most studies showing macrolide resistance of greater than 80%. The CA-MRSA organism also tends to be highly sensitive to doxycycline as well. Resistance to penicillins is presumed to be independent of the development of macrolide resistance.⁵² Nosocomial strains of MRSA tend to be uniformly resistant to macrolides and clindamycin, making vancomycin the drug of choice.^{53,54} However, multiple studies of children around the country presenting in different clinical settings have shown CA-MRSA to have different resistance patterns (Table V). In our population, 29% and 84% of MRSA strains were susceptible to erythromycin and clindamycin, respectively. Of cultures tested for tetracycline susceptibility ($n = 69$), the majority (94% of MRSA and 100% of MSSA) were susceptible to doxycycline, similar to the institution's antibiogram for all patients regardless of patient location. In addition, all strains of MRSA at our center were susceptible to TMP-SMX. Within our institution, MRSA sensitivity is similar for inpatients and outpatients, except for clindamycin (inpatient 44%; outpatient 66%).

Clindamycin can be a good alternative for treating CA-MRSA, but inducible clindamycin resistance is an emerging problem in areas with significant

Table V. Antibiotic susceptibilities for methicillin-resistant *Staphylococcus aureus* in different geographic areas

Study	Location	Group	Setting	Susceptibilities, %				
				Clindamycin	Gentamicin	Erythromycin	Tetracycline	TMP-SMX
Fridkin et al ⁴ (2005)	Atlanta, GA;	Children and adults	Inpatient/outpatient	87	97	11	89	97
	Baltimore, MD;			85	93	12	61	83
	Minneapolis, Minnesota			88	93	47	91	99
Herold et al ¹⁵ (1998)	Chicago, IL	Children	Inpatient	76	96	32	ND	100
Dietrich et al ¹⁰ (2004)	Providence, RI	Children	Inpatient/outpatient	74	100	48	67	100
Fergie and Purcell ¹² (2001)	Texas	Children	Inpatient/outpatient	92	ND	22	54	98
Naimi et al ³⁸ (2003)	Minneapolis, MN	Children and adults	Inpatient/outpatient	83	94	44	93	95
Hussain et al ⁶ (2000)	Chicago, IL	Children	Inpatient	70	90	60	ND	90
Campbell et al ⁵⁵ (2003)	Kentucky	Children	Inpatient/outpatient	67	ND	22	ND	97
Kaplan et al ³² (2005)	Texas	Children	Inpatient/outpatient	95	ND	3	ND	
Hasty et al ³³ (2007)	South East	Children	ED	98	98	2	ND	100
	Southern California			96	100	0	74	100
Johnson et al ⁴⁰ (2007)	Kentucky	Children	Inpatient/outpatient	98	100	0	98	96
Chen et al ³¹ (2006)	Baltimore, MD	Children	Inpatient/outpatient/ED	91	ND	4	69	96
Groom et al ¹⁷ (2001)	Rural Midwest	Children and adults	Inpatient/outpatient	98	98	72	100	100
Current study (2008)	North Carolina	Children	Outpatient	84	98	29	ND	100

ED, Emergency department; ND, not determined; TMP-SMX, trimethoprim-sulfamethoxazole.

erythromycin resistance. Erythromycin resistance methylase genes A and C encode for a protein that induces a conformational change in ribosomal RNA preventing clindamycin binding. The D-zone test is a marker for inducible clindamycin resistance.^{2,50} It has been proposed that clinicians can use erythromycin resistance as a marker for inducible clindamycin resistance.^{2,10,31} Among our institution's culture, this approach is not accurate as only 6% of CA-MRSA demonstrated inducible clindamycin resistance. Clinicians should depend on standard operating laboratory procedure of inducible resistance by D-testing, a well-established test in the clinical microbiology laboratory.

Given the results of this study, we have continued the practice of starting cephalexin in non-penicillin allergic patients with signs of cutaneous infection. Penicillin-allergic patients are initially treated with oral clindamycin or doxycycline (depending on age). When cultures and sensitivities are available, antibiotics are adjusted if resistance to the

first antibiotic is present and signs of infection persist.

CONCLUSION

CA-MRSA has become an increasingly common pathogen in outpatient pediatric tertiary care facilities. Outpatient pediatric dermatology cultures demonstrate relatively low MRSA incidence compared with national reports and among our institution's outpatient isolates. Clindamycin, tetracyclines, and TMP-SMX continue to be effective antibiotic agents within our population. Regional resistance patterns have implications in management and treatment.

REFERENCES

1. McCaig LF, McDonalds LC, Mandal S, Jernigan DB. *Staphylococcus aureus*—associated skin and soft tissue infections in ambulatory care. *Emerg Infect Dis* 2006;12:1715-23.
2. Le J, Lieberman JM. Management of community-associated methicillin-resistant *Staphylococcus aureus* infections in children. *Pharmacotherapy* 2006;26:1758-70.

3. Jarvis WR, Thornsberry C, Boyce J, Hughes JM. Methicillin-resistant *Staphylococcus* at children's hospitals in the United States. *Pediatr Infect Dis* 1985;4:651-5.
4. Fridkin SK, Hageman JC, Morrison M, Sanza LT, Corno-Sabetti K, Jernigan JA, et al. Methicillin-resistant *Staphylococcus aureus* disease in three communities. *N Engl J Med* 2005;352:1436-44.
5. Cohen PR, Kurzrock R. Community-acquired methicillin-resistant *Staphylococcus aureus* skin infection: an emerging clinical problem. *J Am Acad Dermatol* 2004;50:277-80.
6. Hussain F, Boyle-Vavra S, Bethel CD, Daum R. Current trends in community-acquired methicillin-resistant *Staphylococcus aureus* at a tertiary care pediatric facility. *Pediatr Infect Dis J* 2000;19:1163-6.
7. Boxerbaum B, Jacobs MR, Cechner RL. Prevalence and significance of methicillin-resistant *Staphylococcus aureus* in patients with cystic fibrosis. *Pediatr Pulmonol* 1988;4:159-63.
8. Hulten KG, Kaplan SL, Gonzales BE, Hammerman WA, Lamberth LB, Versalovic J, et al. Three-year surveillance of community onset health care-associated *Staphylococcus aureus* infections in children. *Pediatr Infect Dis* 2006;25:349-53.
9. Zaoutis TE, Toltzis P, Chu J, Abrams T, Dul M, Kim J, et al. Clinical and molecular epidemiology of community-acquired methicillin-resistant *Staphylococcus aureus* infections among children with risk factors for health-associated infection 2001-2003. *Pediatr Infect Dis J* 2006;25:343-8.
10. Dietrich DW, Auld DB, Mermel LA. Community-acquired methicillin-resistant *Staphylococcus* in southern New England children. *Pediatrics* 2004;113:347-52.
11. Sattler CA, Mason EO Jr, Kaplan SL. Prospective comparison of risk factors and demographic and clinical characteristics of community-acquired, methicillin-susceptible *Staphylococcus aureus* infection in children. *Pediatr Infect Dis J* 2002;21:910-6.
12. Fergie JE, Purcell K. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in South Texas children. *Pediatr Infect Dis J* 2001;20:860-3.
13. Suggs AH, Maranan MC, Boyle-Vavra S, Daum R. Methicillin-resistant and borderline methicillin-resistant asymptomatic *Staphylococcus aureus* colonization in children without identifiable risk factors. *Pediatr Infect Dis J* 1999;18:410-4.
14. Frank A, Marcinak JF, Mangat PD, Schreckenberger PC. Community acquired and clindamycin-susceptible methicillin-resistant *Staphylococcus aureus* in children. *Pediatr Infect Dis J* 1999;18:993-1000.
15. Herold BC, Immergluck LC, Maranan MC, Lauderdale DS, Gaskin RE, Boyle-Vavra S, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in children with no identified predisposing risk. *JAMA* 1998;279:593-8.
16. Buckingham SC, McDougal LK, Cathey LD, Comeaux K, Craig AS, Fridkin SK, 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.
17. Groom AV, Wolsey DH, Naimi TS, Smith K, Johnson S, Boxrud D, et al. Community-acquired methicillin-resistant *Staphylococcus aureus* in a rural American Indian community. *JAMA* 2001;286:1201-5.
18. Shahin R, Johnson IL, Jamieson F, McGeer A, Tolkin J, Ford-Jones EL. Methicillin-resistant *Staphylococcus aureus* carriage in a child care center following a case of disease: Toronto child care center study group. *Arch Pediatr Adolesc Med* 1999;153:864-868.
19. Centers for Disease Control and Prevention. Four pediatric deaths from community-acquired methicillin-resistant *Staphylococcus aureus*: Minnesota and North Dakota, 1997-1999. *MMWR Morb Mortal Wkly Rep* 1999;48:707-10.
20. Gorak EJ, Yamada SM, Brown JD. Community-acquired methicillin-resistant *Staphylococcus aureus* in hospitalized adults and children without known risk factors. *Clin Infect Dis* 1999;19:797-800.
21. Frank AL, Marcinak JF, Mangat PD, Schreckenberger PC. Increase in community-acquired methicillin-resistant *Staphylococcus aureus* in children. *Clin Infect Dis* 1999;29:935-6.
22. Rathore MH, Kline MW. Community-acquired methicillin-resistant *Staphylococcus aureus* infections in children. *Pediatr Infect Dis J* 1989;8:645-7.
23. Moreno F, Crisp C, Jorgenson JH, Patterson JE. Methicillin-resistant *Staphylococcus aureus* as a community organism. *Clin Infect Dis* 1995;21:1308-12.
24. Naimi TS, Ledell KH, Boxrud DJ, Groom AV, Steward CD, Johnson SK, et al. Epidemiology and clonality of community-acquired methicillin-resistant *Staphylococcus aureus* in Minnesota, 1996-1998. *Clin Infect Dis* 2001;33:990-6.
25. Feder HM Jr. Methicillin-resistant *Staphylococcus aureus* infections in 2 pediatric outpatients. *Arch Fam Med* 2000;9:560-2.
26. Centers for Disease Control. Community-acquired methicillin-resistant *Staphylococcus aureus* infections—Michigan. *MMWR Morb Mortal Wkly Rep* 1981;130:185-7.
27. Eady EA, Cove JH. Staphylococcal resistance revisited: community-acquired methicillin-resistant *Staphylococcus aureus*—an emerging problem for the management of skin and soft tissues infections. *Curr Opin Infect Dis* 2003;16:103-24.
28. Elston DM. Community-acquired methicillin-resistant *Staphylococcus aureus*. *J Am Acad Dermatol* 2007;56:1-16.
29. Adcock PM, Pastor P, Medley F, Patterson JE, Murphy TV. Methicillin-resistant *Staphylococcus aureus* in two child care centers. *Infect Dis* 1998;178:577-80.
30. Hussain F, Boyle-Vavra S, Daum RS, Borchardt SM, Boxrud DJ, Etienne J. Community-acquired methicillin-resistant *Staphylococcus aureus* colonization in healthy children attending an outpatient pediatric clinic. *Pediatr Infect Dis J* 2001;20:763-7.
31. Chen AE, Goldstein M, Carroll K, Song X, Perl TM, Siberry GK. Evolving epidemiology of pediatric *Staphylococcus aureus* cutaneous infections in a Baltimore hospital. *Pediatr Emerg Care* 2006;22:717-23.
32. Kaplan SL, Hulten SG, Gonzales BE, Hammerman WA, Lamberth L, Versalovic J, et al. Three-year surveillance of community-acquired *Staphylococcus aureus* infections in children. *Clin Infect Dis* 2005;40:1785-91.
33. Hasty MB, Klasner A, Kness S, Denmark TK, Ellis D, Herman MI, et al. Cutaneous community-associated methicillin-resistant *Staphylococcus aureus* among all skin and soft-tissue infections in two geographically distant pediatric emergency departments. *Acad Emerg Med* 2007;14:35-40.
34. Buescher SE. Community-acquired methicillin-resistant *Staphylococcus aureus* in pediatrics. *Curr Opin Pediatr* 2005;17:67-70.
35. Chen CJ, Huang YC, Chiu CH, Su LH, Lin TY. Clinical features and genotyping analysis of community-acquired methicillin-resistant *Staphylococcus aureus* infections in Taiwanese children. *Pediatr Infect Dis J* 2005;24:40-5.
36. Marcinak JF, Frank AL. Treatment of community-acquired methicillin-resistant *Staphylococcus aureus* in children. *Curr Opin Infect Dis* 2003;16:265-9.
37. Moran GJ, Krishnadasan A, Gorwitz RJ, Fosheim GE, McDougal LK, Carey RB, et al. Methicillin-resistant *S aureus* infections among patients in the emergency department. *N Engl J Med* 2006;355:666-74.
38. Naimi TS, LeDell KH, Como-Sabetti KM, Borchardt SM, Boxrud DJ, Etienne J, et al. Comparison of community- and health

- care-associated methicillin-resistant *Staphylococcus aureus* infection. JAMA 2003;290:2976-84.
39. Swanson DS. Methicillin-resistant *Staphylococcus aureus* infections in children. Mo Med 2006;103:77-80.
 40. Johnson PN, Rapp RP, Nelson CT, Buttler JS, Overman S, Kuhn RJ. Characterization of community-acquired *Staphylococcus aureus* infection in children. Ann Pharmacother 2007;41:1361-7.
 41. Pallin DJ, Egan DJ, Pelletier AJ, Espinola JA, Hooper DC, Carmago CA. Increased US emergency department visits for skin and soft tissue infections, and changes in antibiotic choices, during the emergence of community-acquired methicillin-resistant *Staphylococcus aureus*. Ann Emerg Med 2008;51:291-8.
 42. Groner A, Laing-Grayman D, Silverberg NB. Outpatient pediatric community-acquired methicillin-resistant *Staphylococcus aureus*: a polymorphous clinical disease. Cutis 2008;81:115-22.
 43. Jones ME, Karlowsky JA, Draghi DC, Thornsberry C, Sahm DF, Bradley JS. Rates of antimicrobial resistance among common bacterial pathogens causing respiratory, blood, urine, and skin and soft tissue infections in pediatric patients. Eur J Clin Microbiol Infect Dis 2004;23:445-55.
 44. Jungk J, Como-Sabetti K, Stinchfield P, Ackerman P, Harriman K. Epidemiology of methicillin-resistant *Staphylococcus aureus* at a pediatric healthcare system, 1991-2003. Pediatr Infect Dis J 2007;26:339-44.
 45. Kisich KO, Carspecken CW, Fieve S, Boguniewicz M, Leung DY. Defective killing of *Staphylococcus aureus* in atopic dermatitis is associated with reduced mobilization of human beta-defensin-3. J Allergy Clin Immunol 2008;122:62-8.
 46. Gong JQ, Lin L, Lin T, Hao F, Zeng FQ, Bi ZG, et al. Skin colonization by *Staphylococcus aureus* in patients with eczema and atopic dermatitis and relevant combined topical therapy: a double-blind multicenter randomized controlled trial. Br J Dermatol 2006;155:680-7.
 47. Chung HJ, Jeon HS, Sung H, Kim MN, Hong SJ. Epidemiological characteristics of methicillin-resistant *Staphylococcus aureus* isolates from children with eczematous atopic dermatitis lesions. J Clin Microbiol 2008;46:991-5.
 48. Hon KLE, Lam MCA, Leung TF, Kam WYC, Li MCA, Ip M, et al. Clinical features associated with nasal *Staphylococcus aureus* colonization in Chinese children with moderate-to-severe atopic dermatitis. Ann Acad Med Singapore 2005;34:602-5.
 49. Arkwright PD, Daniel TO, Sanyal D, David T, Patel L. Age-related prevalence and antibiotic resistance of pathogenic staphylococci and streptococci in children with infected atopic dermatitis at a single-specialty center. Arch Dermatol 2002;138:939-41.
 50. Kil EH, Heymann WR, Weinberg JM. Methicillin-resistant *Staphylococcus aureus*: an update for the dermatologist, part 3, clinical management. Cutis 2008;81:327-35.
 51. Chambers HF. The changing epidemiology of *Staphylococcus aureus*? Emerg Infect Dis 2001;7:178-82.
 52. Smith SM, Mangia A, Eng RHK, Ruggeri P, Cytryn A, Tecson-Tumang F. Clindamycin for colonization and infection by methicillin-resistant *Staphylococcus aureus*. Infection 1988;16:95-7.
 53. Shimiori T, Miyamoto H, Makishima K. Significance of airborne transmission of methicillin-resistant *Staphylococcus aureus* in an otolaryngology-head neck surgery unit. Arch Otolaryngol Head Neck Surg 2001;127:644-8.
 54. Kil EH, Heymann WR, Weinberg JM. Methicillin-resistant *Staphylococcus aureus*: an update for the dermatologist, part 4, additional therapeutic considerations. Cutis 2008;81:343-7.
 55. Campbell AL, Bryant KA, Stover B, Marshall GS. Epidemiology of methicillin-resistant *Staphylococcus aureus* at a children's hospital. Infect Control Hosp Epidemiol 2003;24:427-30.