



Published in final edited form as:

Pediatr Dermatol. 2014 ; 31(3): 305–308. doi:10.1111/pde.12195.

Antibiotic Sensitivity and Resistance Patterns in Pediatric Staphylococcal Scalded Skin Syndrome

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Abstract

Historical resistance patterns often guide empiric antibiotic choices in staphylococcal scalded skin syndrome (SSSS), but little is known about the difference in susceptibility between SSSS and other childhood staphylococcal infections. A retrospective chart review of culture-confirmed cases of SSSS seen in the inpatient dermatology consultation service at the Children's Hospital of Philadelphia between 2005 and 2011 was performed. Most cases of SSSS at our institution are due to oxacillin-susceptible *Staphylococcus aureus*, and approximately half of the cases are due to clindamycin-resistant strains. Clindamycin and a penicillinase-resistant penicillin are suggested as empiric treatment for SSSS until culture susceptibility data are available to guide therapy.

Staphylococcal scalded skin syndrome (SSSS) is a pediatric emergency characterized by painful desquamation around orifices and in flexural skin due to exfoliative toxins produced by epidermolytic *Staphylococcus aureus*. SSSS most often affects newborns and children younger than 5 years of age and has an approximate 5% mortality because of complications of sepsis, superinfection, and electrolyte imbalances (1).

Penicillinase-resistant penicillins (e.g., oxacillin), first- and second-generation cephalosporins, and clindamycin are recommended therapies (1). Antibiotic resistance is a growing concern, with reports of cases caused by methicillin-resistant *S. aureus* (MRSA) (2–8) (Table 1). Historical resistance patterns in an area often guide empiric antibiotic choices, although little is known about whether antibiotic resistance differs in SSSS from that in other childhood staphylococcal infections. The goal of this study was to determine antibiotic resistance patterns and associated risk factors to guide empiric therapy for SSSS.

METHODS

After institutional review board approval, a retrospective chart review of inpatient dermatology consultations at the Children's Hospital of Philadelphia from 2005 to 2011 was

performed. Inclusion criteria were clinical documentation of SSSS diagnosis and growth of *S. aureus* from skin culture. Statistical analyses were performed using STATA/IC 11.0 software (StatCorp, LP, College Station, TX). Fisher exact tests were used for categorical variables and Wilcoxon–Mann–Whitney tests were used for non-parametric continuous variables. The Wilcoxon signed-rank one-sample median test was used to compare resistance to historical hospital antibiotic resistance data. Oxacillin discs were used in susceptibility testing, an equivalent method for determining methicillin resistance. Cases from the literature were obtained by searching the English-language literature in PubMed using the keywords “staphylococcal scalded skin” and “susceptibility,” “resistance,” “methicillin,” “methicillin resistance” or “clindamycin.” Reports with skin culture-confirmed *S. aureus* were included.

RESULTS

Twenty-one patients with culture-confirmed SSSS were identified (10 boys, 11 girls, ages 0.5–68 months, median 18 months, interquartile range 3–36 months). Eight children were started on clindamycin monotherapy, nine on clindamycin and another agent, one on cefazolin and vancomycin, and three on three or more antimicrobials.

Three children (14%) grew oxacillin-resistant *S. aureus* and 10 (48%) grew clindamycin-resistant *S. aureus*. One child had oxacillin-resistant and clindamycin-resistant cultures at separate sites (scalp and perioral) and was discharged home on both agents and lost to follow-up. Three children with clindamycin-resistant cultures were discharged home on clindamycin monotherapy. The remaining 17 children were discharged on microbial agents to which their cultures were susceptible.

The rate of oxacillin susceptibility was significantly higher than hospital cultures (86% SSSS vs 52% hospital median; $p < 0.001$), whereas clindamycin susceptibility was significantly lower than in hospital cultures (52% SSSS vs 82% hospital median; $p < 0.001$), suggesting lower rates of methicillin resistance and higher rates of clindamycin resistance in SSSS than in other staphylococcal infections (Table 2).

Clindamycin resistance was seen in younger children (median age 2.8 months clindamycin resistance versus 31 months clindamycin susceptible; $p = 0.03$). There was no significant difference in the median age of those with oxacillin resistance or sensitivity ($p = 0.31$). There was no significant variation in resistance pattern for oxacillin or clindamycin based on sex, history of atopic dermatitis, or length of hospital stay (Table 3).

DISCUSSION

Eight-six percent of SSSS cases at the Children’s Hospital of Philadelphia are due to oxacillin-susceptible *S. aureus*, and clindamycin resistance is seen in 52% of cases and may disproportionately affect younger children. Our data add to the case reports and series originating from the United Kingdom, Japan, France, China, and Taiwan that document patterns of antibiotic susceptibility and resistance in SSSS (2–7). A Taiwanese retrospective study reported that only 31% of SSSS and staphylococcal toxic shock syndrome cases were due to oxacillin-susceptible *S. aureus*, while 37% were due to clindamycin-susceptible *S.*

aureus (6). A recent retrospective study from China found lower rates of clindamycin susceptibility (~14%), but all SSSS isolates were oxacillin susceptible (9). These findings suggest that regional differences are important factors to consider. Our data represent the first report of susceptibility patterns in the United States.

Clindamycin is a bacteriostatic agent that is favored in the setting of cutaneous staphylococcal infection because of excellent skin penetration. Clindamycin also inhibits bacterial toxin production, making it a preferred agent for toxin-mediated diseases like SSSS. Given the frequency of clindamycin resistance in our population, we caution against empiric clindamycin monotherapy in the setting of SSSS and suggest that it be used along with a penicillinase-resistant penicillin.

Limitations of the study include restriction to dermatology consultation cases, which may select for more severe cases with confounding factors affecting resistance patterns, exclusion of cases without culture data, and limitation to a single institution. The historical microbiology data were not specifically skin culture data, although blood and sterile tissues (including amniotic, joint, pleural, pericardial, cerebrospinal, ventricular, and synovial fluid) were excluded in all years except 2005, when the only data available were for all *S. aureus* isolates. No antibiogram data were available in 2007, although our study included only one case from 2007. Antibiogram and resistance patterns did not significantly vary in the years examined. We did not examine toxin production by the isolated organisms. Although most SSSS cases are attributed to exfoliative toxin A–producing toxins, there are reports of SSSS due to nonexfoliative toxin-producing strains (4), and there may be correlations between antibiotic susceptibility and toxin production that warrant further investigation.

This retrospective study suggests that oxacillin-susceptible and often clindamycin-resistant strains of *S. aureus* predominantly cause SSSS, which may have a susceptibility profile different from that of other forms of childhood staphylococcal infections. This is important when selecting empiric therapy for a disease with potential morbidity and mortality. Based on these data, we suggest that penicillinase-resistant penicillins be used along with clindamycin for empiric SSSS therapy until culture sensitivities are available to guide therapy. Further study with larger cohorts of patients from multiple regions and follow-up data are needed to validate these findings.

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TABLE 1

Reports of Susceptibility in SSSS

Author	Year	Study design	Location	Study details	Susceptibility
Murono et al (10)	1988	Retrospective	Japan	Molecular epidemiologic analysis of 74 strains of <i>S. aureus</i> from pediatric patients with SSSS from 1974 to 1984	100% oxacillin susceptible
Richardson et al (2)	1990	Case report	United Kingdom	Outbreak of MRSA in a nursery with 1 baby, out of 12 affected, developing SSSS	Penicillinase-negative MRSA (full susceptibilities not reported)
Yokota et al (3)	1996	Case report	Japan	One 6-month-old with SSSS	MRSA (full susceptibilities not reported)
Acland et al (4)	1999	Case report	United Kingdom	One 69-year-old man with SSSS attributed to MRSA	MRSA (full susceptibilities not reported)
Yamaguchi et al (5)	2002	Retrospective	Japan	Molecular epidemiologic analysis of 88 <i>S. aureus</i> isolates from outpatients with bullous impetigo	95% oxacillin susceptible; only 4 isolates were highly resistant to oxacillin, although 35 showed borderline to moderate resistance
Chi et al (6)	2006	Retrospective	Taiwan	16 cases of SSSS and staphylococcal toxic shock syndrome	31% oxacillin susceptible, 37% clindamycin susceptible
Neylon et al (11)	2010	Case series	Ireland	5 cases of neonatal SSSS	100% oxacillin susceptible
Shi et al (8)	2011	Case report	Japan	16-day-old neonate with SSSS	MRSA (full susceptibilities not reported)
Lamand et al (7)	2012	Retrospective	France	349 cases of SSSS, bullous impetigo and generalized exfoliative syndrome	One case of MRSA (in a post-varicella generalized exfoliative syndrome)
Li et al (9)	2013	Retrospective	China	8 cases of neonatal SSSS	100% oxacillin susceptible, 14% clindamycin susceptible

MRSA, methicillin-resistant *Staphylococcal aureus*.

TABLE 2

Comparison of Antibiotic Susceptibility Rates in SSSS to Historic Controls

Year	Oxacillin susceptibility, %	Clindamycin susceptibility, %
Historical rates 2005–2011, median (range)	52 (47–56)	82 (74–91)
SSSS rate 2005–2011	86*	52*

* p value for one-sample median test <0.001.

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TABLE 3

Comparison of Risk Factors According to Antibiotic Resistance

Risk factor	Overall (N = 21)	Oxacillin resistant, n = 3	Oxacillin susceptible, n = 18	p	Clindamycin resistant, n = 10	Clindamycin susceptible, n = 11	p
Age, months, median (IQR)	18 (3–36)	32 (15–61)	15 (3–36)	0.31	3 (1–31)	31 (15–61)	0.03
Male, %	10 (48)	1 (33)	9 (50)	0.54	5 (50)	5 (46)	0.59
History of atopic dermatitis, %	5 (24)	1 (33)	4 (22)	0.58	3 (30)	2 (18)	0.45
Length of hospital stay, days, median (IQR)	3 (2–4)	2 (2–5)	3 (2–4)	0.60	3 (3–4)	3 (2–4)	0.38

IQR, interquartile range.

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