

***Staphylococcus aureus* Antibiotic Susceptibilities in Infections in an Outpatient Dermatology Office on O'ahu**

Kimberly R. Theos DO, MS; Kory M. Johnson BA; and Douglas W. Johnson MD

Abstract

Staphylococcus aureus is a pathogen that causes skin and soft tissue infections (SSTIs) in dermatology patients. There is an increasing rate of methicillin-resistant *S aureus* (MRSA) reported in the dermatology literature since 1987. This report profiles the antibiotic susceptibilities of methicillin-sensitive *S aureus* (MSSA) and MRSA in an outpatient office in Hawai'i. This is a retrospective study done by chart review from 2012 to 2014. Demographics, anatomical site of infection, clinical diagnoses and antimicrobial susceptibility patterns were analyzed and compared. Of the 66 samples, 57% were males and 43% were females. *S aureus* was more commonly found in impetigo, folliculitis, furuncles and secondarily infected psoriasis and more commonly located on the extremities. MSSA accounted for 73% (48) of the cases and MRSA accounted for 27% (18) of the cases. The antibiotics most effective against all *S aureus* cultures for outpatients were linezolid (100%), trimethoprim sulfamethoxazole (95%) and tetracyclines (94%). Linezolid (100%), trimethoprim sulfamethoxazole (100%) were most effective against MRSA isolates. Our *S aureus* and MRSA antimicrobial susceptibility results are similar to the local Hawai'i outpatient antibiogram collected from a large private laboratory in Hawai'i in 2014 and the current Infectious Disease Society of America guidelines. This study may be helpful in guiding empiric treatment of SSTIs suspected to be caused by *S aureus*.

Keywords

Staphylococcus aureus, methicillin-sensitive *S aureus*, methicillin-resistant *S aureus*, antimicrobial susceptibility, dermatology, outpatient, Hawai'i

Abbreviations

CDC = Centers for Disease Control and Prevention

DLS = Diagnostic Laboratory Services, Inc

IDSA = Infectious Disease Society of America

MRSA = methicillin-resistant *S aureus*

MSSA = methicillin-sensitive *S aureus*

OD QMC = Outpatient Dermatology Office from Queen's Medical Center

SSTIs = skin and soft tissue infections

Introduction

Staphylococcus aureus is a common pathogen implicated in a variety of skin and soft tissue infections (SSTIs) seen in the dermatology setting. The most common SSTIs seen are impetigo, cutaneous abscess, cellulitis, furuncle, carbuncle, folliculitis, secondary infections in psoriasis and various secondarily infected dermatoses. Infections can be caused by methicillin-sensitive *S aureus* (MSSA) and methicillin-resistant *S aureus* (MRSA). MRSA can be further classified as community associated (CA-MRSA) or health care associated (HA-MRSA). CA-MRSA and HA-MRSA are genetically, epidemiologically and phenotypically different. The Centers for Disease Control and Prevention (CDC) distinguishes the two strains as follows:

CA-MRSA infection is classified as community associated if it develops in an individual without a history of MRSA isolation

or if a positive culture is obtained in the outpatient setting or within 48 hours of hospitalization.¹

HA-MRSA infection is identified when MRSA is isolated from a patient within 48 hours of hospitalization with risk factors for resistant infection including; dialysis, previous colonization, surgery during the past year; a permanent medical device or catheter; or hospital, hospice or nursing home admission.¹

Prior to the 1990s, MRSA was uncommon outside of the health care environment.² Over the past 15 years, there has been a worldwide epidemic of CA-MRSA SSTIs.² A comprehensive literature review and clinical update published in 2017 showed that during the 2000s there have been increasing rates of CA-MRSA widely reported in the United States and Canada.³ The same review reported increasing rates of CA-MRSA while HA-MRSA is generally declining.³

MRSA was first isolated from dermatology outpatients in 1987.⁴ From 1988 to 1996 the rates of MRSA in two dermatology clinics in Texas from all patients rose from 1.5% to 11.9%.⁵ More recently, there have been several other reports of MRSA in the outpatient dermatology setting with higher rates ranging from 21%-35.7%.⁶⁻⁹ In one of the larger retrospective cases series done in the dermatology setting, the rate of MRSA significantly increased by 17% during 2008-2010 from the previous 3 years reviewed.⁸

S aureus typically causes cutaneous abscesses involving the lower extremities but can involve the upper extremities, abdominal wall and face.⁸ CA-MRSA skin lesions commonly present as an erythematous abscess or furuncle with or without surrounding cellulitis.¹⁰ Purulent cellulitis is more likely to be caused by CA-MRSA.³ Predominant sites of infections caused by HA-MRSA involve the respiratory tract, urinary tract, bloodstream and postsurgical sites.³

Before the emergence of MRSA, antibiotic selection was less challenging, as cephalosporins were an appropriate choice for most presumed *S aureus* infections. One way MRSA differs from MSSA is its resistance to penicillin, which is termed methicillin or oxacillin resistant.³ Susceptibility to clindamycin, trimethoprim sulfamethoxazole and tetracyclines are usually retained in CA-MRSA.³ In contrast, HA-MRSA is highly resistant to most oral antibiotics. Most hospitals now utilize a monthly-updated antibiogram that lists all of the culture results for the community in an effort to guide empiric treatment for both outpatient and inpatient infections. This is a helpful resource for clinics although cultures are routinely used to guide therapy in SSTIs given changing antimicrobial resistance patterns.

Given these findings, it is imperative that dermatologists

and other health care practitioners are aware of the current antimicrobial susceptibility profile to effectively treat patients with *S aureus* infections. To our knowledge there are no current studies reporting rates of *S aureus* antibiotic susceptibilities in the Hawai'i dermatology clinic setting. The purpose of this study is to investigate the antibiotic susceptibility profiles of *S aureus* isolates in Hawai'i from a dermatology office to better guide empiric antibiotic therapy in the outpatient setting in Hawai'i.

Methods

This was a retrospective observational study analyzing *S aureus* isolates collected from patients seen at the dermatology clinic located on the campus of Queen's Medical Center in Honolulu, Hawai'i. The Queen's Medical Center Research and Institutional Review Committee (RA-2018-035) approved this study. Chart review was done to identify patients with positive *S aureus* cultures. The first *S aureus* positive culture was identified on March 29, 2012 and the last one recorded was October 7, 2014. Antibiotic susceptibility reports for the cultures were retrieved from the established laboratory account for this clinic called Diagnostic Laboratory Services, Inc (DLS) located on the campus of Queen's Medical Center in Honolulu, Hawai'i. DLS is a large private laboratory that serves all of Hawai'i, Guam and Saipan and provides local antibiograms. Antibiotic susceptibility testing was done using the DLS protocol using the Vitek 2 system and for MRSA using the agglutination with penicillin binding protein. Clindamycin resistant testing is also done with the Vitek 2 system or the D-zone test using the Kirby Bauer method. Per the DLS protocol, the Kirby Bauer disk diffusion test is a secondary test used if the organism does not grow. Demographic data collected for this study included patient age, gender, anatomical site of infection and clinical diagnosis by chart review. MRSA susceptibility patterns from our outpatient dermatology clinic were compared with the DLS outpatient antibiogram for Hawai'i in 2014¹¹ and Hawai'i outpatient data collected from the State of Hawai'i Antimicrobial Resistance Project (SHARP) during 2000-2002.¹² The SHARP study collected data from two large private clinical laboratories that serve over 85% of the population of Hawai'i.

Results

We analyzed 66 *S aureus* cultures from 63 patients. One patient had four cultures obtained at different office visits. There were 36 males and 27 females (Figure 1). Age distributions of all *S aureus* cultures are represented in Figure 2. Thirteen percent of cultures were obtained from children age 17 and under, and 87% were obtained from adults 18 years and older.

Of the 66 *S aureus* samples, 73% (48) were MSSA and 27% (18) were MRSA. There were only three MRSA cultures in the pediatric age group and the remaining 15 were in the adult age group.

Antibiotic susceptibilities were available in all 66 cases. Susceptibility patterns for all *S aureus* (MSSA and MRSA) cultures are represented in Table 1. The antibiotic susceptibility patterns

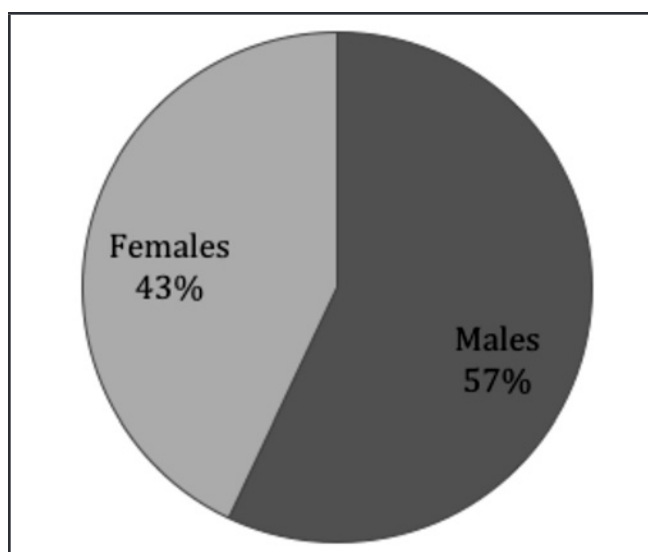


Figure 1. *S aureus* Cultures by Patient Sex.

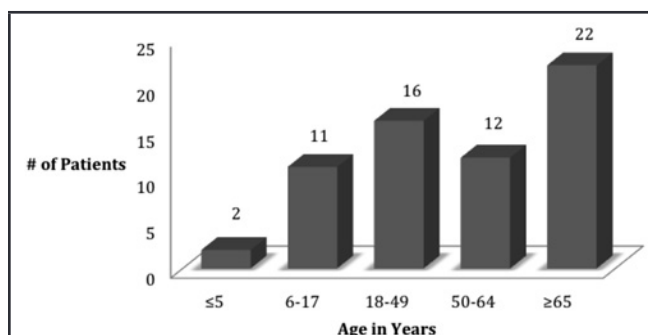


Figure 1. *S aureus* Cultures by Patient Age Groups.

Table 1. Antibiotic Susceptibility Profile of All *S aureus* Isolates (MSSA and MRSA) Collected from OD QMC.

Antibiotic	Percentage (n)
Erythromycin	65 (43)
Oxacillin	73 (48)
Cefazolin	73 (48)
Ciprofloxacin	83 (55)
Moxifloxacin	85 (56)
Clindamycin	86 (57)
Tetracycline	94 (62)
Trimethoprim sulfamethoxazole	95 (63)
Vancomycin	100 (66)
Linezolid	100 (66)
Nitrofurantoin	100 (66)
Rifampin	100 (66)
Gentamicin	100 (66)

n = number

OD QMC = Outpatient Dermatology Office at Queen's Medical Center, Honolulu, HI

are as follows: erythromycin (65%), oxacillin (73%), cefazolin (73%), ciprofloxacin (83%), moxifloxacin (85%), clindamycin (86%), tetracycline (94%), trimethoprim sulfamethoxazole (TMP-SMX) (95%), vancomycin (100%), Linezolid (100%), nitrofurantoin (100%), rifampin (100%) and gentamicin (100%).

The susceptibility profiles in Table 1 show that the most effective antibiotics for all *S aureus* (MSSA and MRSA) SSTIs is linezolid followed by trimethoprim sulfamethoxazole and tetracyclines. Of the total *S aureus* isolates tested from our clinic, clindamycin had a susceptibility of 86%.

MRSA susceptibility profile for the 18 cases is demonstrated in Table 2. The antibiotic susceptibility patterns are as follows: erythromycin (22%), ciprofloxacin (56%), moxifloxacin (61%), clindamycin (78%), tetracycline (78%), trimethoprim sulfamethoxazole (TMP-SMX) (100%), vancomycin (100%), linezolid (100%), nitrofurantoin (100%), rifampin (100%) and gentamicin (100%).

Linezolid and trimethoprim are 100% susceptible against MRSA and could be used as first-line treatment (Table 2). The susceptibility of MRSA to clindamycin and tetracycline's was less at 78% each supporting its potential use as a therapeutic second-line agent. Although all *S aureus* and MRSA cultures were susceptible to vancomycin and gentamicin, their use is mainly for inpatients and not discussed here. Refer to the discussion section regarding the current antibiotic recommendations per IDSA guidelines.

Clinical diagnoses were determined by a board certified dermatologist and were available for only 54 of our patients by chart review. Twelve of the 66 *S aureus* cultures had no confirmed diagnoses and were not included. The term "infected" has been used for some of the clinical diagnoses since these were secondarily infected and therefore warranted a culture. Impetigo represented 13% of the *S aureus* infections.

Susceptibility %	OD QMC 2012-2014 n = 18	DLS Outpatient Data for Hawaii in 2014 n = 1641	Hawai'i Outpatient Data 2000- 2002* n = 5135
Erythromycin	22	17.5	52
Ciprofloxacin	56	NR	NR
Moxifloxacin	61	71	NR
Tetracycline	78	95	84
Clindamycin	78	74	69
Trimethoprim Sulfamethoxazole	100	92	96
Vancomycin	100	100	100
Linezolid	100	100	NR
Nitrofurantoin	100	100	NR
Rifampin	100	100	97
Gentamicin	100	NR	NR

NR = Not Reported. n = number. OD QMC = Outpatient Dermatology Office at Queen's Medical Center. DLS = Diagnostic Laboratory Services. *SHARP study during 2000-2002.

Folliculitis, furuncles and secondarily infected psoriasis each represented 7% of the cases. Abscesses and secondarily infected nummular eczema each represented 6% of the cases. Infected ulcers, cellulitis, paronychia, infected actinic keratosis, infected cutaneous horn, infected trauma site, infected squamous cell carcinoma, infected lichen simplex chronicus and conjunctivitis each represented less than 4% as shown in Table 3.

MRSA was implicated in 22% of secondary infections in psoriasis, 17% of folliculitis, 11% of furuncles, 11% of unknown diagnoses and 6% each for infected ulcers, cellulitis, abscesses with cellulitis, impetigo, infected cutaneous horn and secondary infections in atopic dermatitis and dermatitis (Table 3).

Table 3. Clinical Diagnoses of *S aureus* infections from OD QMC, (N=54).

	Percentage (n)	MRSA % (n)*
Impetigo	13 (7)	6 (1)
Post-surgical	11 (6)	0
Atopic dermatitis	11 (6)	6 (1)
Dermatitis	11 (6)	6 (1)
Folliculitis	7 (4)	17 (3)
Furuncle	7 (4)	11 (2)
Psoriasis	7 (4)	22 (4)
Abscess	6 (3)	6 (1)
Nummular eczema	6 (3)	0
Cellulitis	4 (2)	6 (1)
Ulcer	4 (2)	6 (1)
Actinic keratosis	2 (1)	0
Paronychia	2 (1)	0
Cutaneous horn	2 (1)	6 (1)
Trauma	2 (1)	0
Conjunctivitis	2 (1)	0
Lichen simplex chronicus	2 (1)	0
Squamous cell carcinoma	2 (1)	0

n = number. *2 MRSA cultures with unknown diagnoses.
OD QMC= Outpatient Dermatology Office at Queen's Medical Center.

Table 4. Distribution of culture sites from OD QMC, a total of 65 samples.

	Percentage (n)
Extremities	49 (32)
Face	17 (11)
Head and Scalp	12 (8)
Back	5 (3)
Abdomen	3 (2)
Axilla	3 (2)
Other	11 (7)

n = number. OD QMC = Outpatient Dermatology Office at Queen's Medical Center.

Comparisons of the anatomical distribution of culture sites were available in 65 of the cases (Table 4). Among the cultures 32 (49%) were obtained from the extremities, 11 (17%) from the face, 8 (12%) from the scalp and 7 (11%) from a site not listed (other). Back, axilla and abdomen collectively accounted for less than 11% of the culture sites.

Discussion

S aureus causes a variety of uncomplicated and complicated SSTIs that are frequently encountered in the practices of dermatologists. Uncomplicated *S aureus* SSTIs include impetigo and abscesses. Impetigo can be treated with topical antibiotics.^{2,13} Uncomplicated cutaneous abscesses can be treated with incision and drainage alone based on several randomized control trials comparing incision and drainage with or without antibiotic therapy.^{2,13} Per IDSA guidelines, antibiotic therapy is recommended for abscesses associated with severe or extensive disease, rapid progression in the presence of associated cellulitis, signs and symptoms of systemic illness, associated comorbidities or immunosuppression, extreme age, abscess in an area difficult to drain, associated septic phlebitis, and lack of response to incision and drainage alone.¹³ Pretreatment bacterial cultures are crucial to confirm exact pathogen but do not deliver a useful result in time for the initiation of therapy. Therefore, empiric antibiotic treatment should be guided by antimicrobial resistance patterns in the community and then tailored to its antibiotic susceptibility testing results.

IDSA's recommended empiric oral antibiotic therapy for CA-MRSA in outpatients with SSTI include clindamycin, trimethoprim sulfamethoxazole, linezolid or a tetracycline (doxycycline or minocycline).¹³ Based on our data, the best empiric outpatient antibiotics for presumed *S aureus* SSTIs are linezolid, trimethoprim sulfamethoxazole or tetracyclines. Clindamycin could be used as an alternative agent if there were contraindications to the first line agents. Our data supports IDSA's guidelines for empiric treatment of CA-MRSA in outpatients with SSTIs. It is important to mention that the recommended oral antibiotic therapy for outpatients with non-purulent cellulitis is generally a beta-lactam oral antibiotic directed against beta-hemolytic streptococci.¹³ The specific management of SSTIs caused by MSSA versus MRSA is beyond the scope of this article. Our goal is to help guide empiric antibiotic therapy within our community of Hawai'i and therefore includes combined antimicrobial susceptibilities for all *S aureus* cultures. The purpose of analyzing MRSA susceptibilities alone was to show efficacy of antibiotics given the increasing rates of CA-MRSA.

More than half of the *S aureus* cultures were in males and from patients older than 18 years of age (Figures 1 and 2). The most common culture site was from the extremities; followed by the face and scalp. A similar distribution pattern was observed in another review done by Dimantis in 2011¹⁴ and consistent with data from a comprehensive review.²

Of the 66 samples analyzed in our study, 73% were MSSA and 27% were MRSA. Similar rates of MRSA were observed in two other studies. One study was conducted from a private pediatric

dermatology office from 2005-2007 and showed a MRSA rate of 27.3%.⁷ The other study was done in six US dermatology centers from five states in 2010-2012 and revealed a MRSA rate of 29.7%.⁹ However, these differ from two other published outpatient dermatology case reviews that reported their rate of MRSA at 21% in 2007 and 35.7% in 2005-2011, each from a private dermatology office in the US.^{6,8} It is evident that MRSA rates have increased over time in dermatology patients since the first study in 1988 that showed a MRSA rate of 1.5% and then rose to 11.9% by 1996.⁵ In a large epidemiologic study done in Hawai'i from 2000-2002, the prevalence of MRSA from 5,135 outpatient cultures was 22%,¹² lower than our reported rate but consistent with the rising rates of MRSA overtime. It is difficult to draw conclusions given the small number of studies analyzing *S aureus* infections in the dermatology setting and the variation in CA-MRSA prevalence based on geographic in the United States.

When comparing our data locally, our MRSA susceptibility data is similar to the Hawai'i DLS outpatient antibiogram from 2014 shown in Table 2. MRSA was 100% susceptible to linezolid, 95% to tetracycline, 92% to trimethoprim sulfamethoxazole, and 74% to clindamycin. The efficacy of trimethoprim sulfamethoxazole against MRSA in the outpatient setting appears to have lessened in Hawai'i since 2000-2002. There also appears to be more resistance to tetracycline and less resistance to clindamycin over the years when comparing our data to Hawai'i.

A similar retrospective study was performed from 2005 to 2011 in a dermatology clinic at the University of Miami.⁸ Of the 387 isolates in that study, 64.3% were MSSA and 35.7% were MRSA. The antibiotic susceptibility data from 2011 were chosen for comparison purposes due to closer temporal correlation. MSSA data are as follow: linezolid (100%), vancomycin (100%), trimethoprim-sulfamethoxazole (100%), gentamicin (100%), tetracyclines (90%), levofloxacin (95%), clindamycin (90%) and erythromycin (65%). Similar findings were observed when comparing these data with our data and showed that linezolid, trimethoprim-sulfamethoxazole and tetracyclines are most effective against *S aureus* for outpatients. The Miami MRSA susceptibility data showed linezolid (100% susceptibility), vancomycin (100%), trimethoprim-sulfamethoxazole (90%), gentamicin (100%), tetracyclines (90%), levofloxacin (40%), clindamycin (70%) and erythromycin (30%). A similar trend was observed when comparing their MRSA data to ours. However, all *S aureus* and MRSA in our study had slightly higher susceptibility to trimethoprim-sulfamethoxazole at 95% and 100%, respectively. Data support the use of these particular outpatient antibiotics in the dermatology clinics. Our clindamycin data showed more resistance for all *S aureus* and MRSA at 86% and 78%, respectively. This demonstrates that certain geographical locations have differing susceptibilities patterns and again supports the use of local antibiograms.

Furthermore, antibiotic therapies should also be guided by their side effective profile, cost and availability. Linezolid is FDA approved for treatment of MRSA SSTIs but is limited

by hematologic toxicity, peripheral and optic neuropathy and lactic acidosis.¹³ Trimethoprim sulfamethoxazole is not FDA approved for staphylococcal infections, however 95-100% of CA-MRSA strains are susceptible in vitro and is a good option for outpatient treatment of SSTIs.¹² Trimethoprim sulfamethoxazole has not been evaluated for the treatment of CA-MRSA in children and it should be used with caution in the elderly taking renin-angiotensin inhibitor and those with chronic kidney disease due to the risk of hyperkalemia.¹³ Doxycycline is FDA approved for *S aureus* SSTIs and not specifically for MRSA and more invasive infections given limited data.¹³ Clindamycin is FDA approved for the treatment of serious infections due to *S aureus* but not MRSA infections; however, it is widely used for SSTIs. Clindamycin use is limited by diarrhea and in up to 20% of patients *Clostridium difficile* associated diarrhea can occur.¹³ Of note, the actual risks and perceived risks can vary between medical specialties. For example, there is strong concern about the risk of toxic epidermal necrolysis with sulfa drugs such as trimethoprim sulfamethoxazole among dermatologists.

One major concern with the use of clindamycin in CA-MRSA infections is the possibility of inducible resistance to clindamycin seen in erythromycin resistant/clindamycin susceptible strain.¹³ This type of resistance is not readily detected by standard in vitro testing methods unless measures that induce clindamycin resistance are included.¹⁵ A disk induction testing call the “D-zone test” can be used to test inducible clindamycin resistance.¹⁵ In our study, we had 14 (21%) of *S aureus* isolates that exhibited the erythromycin resistant/clindamycin susceptible phenotype.

Our data shows that rifampin was 100% effective against *S aureus* MRSA; however, it is not recommended as monotherapy against *S aureus* or MRSA due to rapid development of resistance.¹³ Nitrofurantoin also demonstrated 100% efficacy against *S aureus* in vitro in our study; however, it is used primarily for urinary tract infections. Pregnant patients should confer with their physicians, as their recommendations are different.

The clinical manifestations seen were generally associated with purulence or abscesses, which is typical for *S aureus* infections.² The most common clinical diagnoses were impetigo, folliculitis, furuncles, abscesses and secondary infections in atopic dermatitis, dermatitis and psoriasis (Table 3). We also observed *S aureus* implicated in post-surgical infections. This is consistent with *S aureus* as the causative pathogen for post-surgical SSTIs.³ MRSA infections were more commonly cultured from folliculitis, furuncles and secondary infections seen in psoriasis (Table 3). Since this was a retrospective study done by chart review, it is inferred that these particular diagnoses were infected and warranted a culture. Knowledge of the anatomic locations and morphology of *S aureus* infections is of relevance to guide clinicians in accurate diagnosis and appropriate treatment.

Limitations

There are limitations to our study. This study addressed a select population of dermatology patients in Hawai‘i and may not be generalizable to different clinical settings or regions. Since this was a retrospective study recommending empiric antibiotic treatment, we did not include specific antibiotics used in each case and their clinical outcomes. A future study in the same setting analyzing directed antibiotic therapy and their outcomes would be of relevance. One variable that may have affected the results is that some patients could have been colonized with *S aureus* rather than infected. This study should be repeated to compare rates of *S aureus* and observe if our data is the same or changing.

Conclusion

Most uncomplicated SSTIs can be treated with topical agents and local incision and drainage. All complicated SSTIs concerning for *S aureus* should be treated with empiric antibiotics guided by local antibiotic susceptibility patterns. SSTIs should have cultures obtained to determine the exact pathogen to guide therapy. Our study shows the best empiric treatment for presumed *S aureus* infections in Hawai‘i outpatients is with linezolid, trimethoprim sulfamethoxazole or tetracycline. Clindamycin could be used as a second line therapy but there are risks of inducible resistance. Certain side effects and limitations are important to consider when choosing antibiotic therapy. This study may be helpful in guiding empiric treatment of SSTIs suspected to be caused by *S aureus*.

Conflict of Interest

None of the authors identify any conflicts of interest.

Authors' Affiliation:

- John A. Burns School of Medicine, University of Hawai‘i, Honolulu, HI

Correspondence To:

Kimberly R. Theos DO; University of Hawai‘i Residency Programs, 1356 Lusitana St. Suite 507, Honolulu HI 96813; Email: theos@hawaii.edu

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