

Prevalence and treatment of *Staphylococcus aureus* colonization in patients with mycosis fungoides and Sézary syndrome

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Summary

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Key words

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Conflicts of interest

None declared.

Background Mycosis fungoides (MF) and Sézary syndrome (SS), variants of cutaneous T-cell lymphoma, may arise from antigen-driven clonal expansion and accumulation of helper-memory T cells. Superantigens from *Staphylococcus aureus* can stimulate T cells.

Objectives (i) To determine the prevalence of *S. aureus* carriage in nares and skin in patients with MF/SS compared with historical rates in other conditions. (ii) To determine whether eradication of *S. aureus* carriage is associated with clinical improvement.

Methods Skin and nares cultures were performed prospectively. Patients with positive nares and skin cultures were treated with oral antibiotics and intranasal mupirocin 2% and samples were taken for reculturing at 3 days, 4 weeks and 8 weeks. An exact binomial test was used to compare the carriage rates among different groups.

Results Among 106 patients with MF/SS, 67 (63%) had skin colonization and 57 (54%) had nasal colonization. *Staphylococcus aureus* was isolated from 44 patients, 33 (31%) each from skin and nares. Colonization was highest in erythrodermic SS (48%), similar to atopic dermatitis (64%), and lowest in MF without erythroderma (26%), psoriasis (21%), and the general population (10%). Oral and topical antibiotics eradicated *S. aureus* colonization in nares in 28 of 33 (85%) patients and in MF skin lesions in 30 of 33 (91%) patients at 4–8 weeks, with rapid clinical improvement seen in 58% of *S. aureus*-colonized patients.

Conclusions Staphylococcal carriage in nares and skin lesions of patients with MF is similar to that in atopic dermatitis. Eradication of staphylococci from the skin is possible with treatment and was associated with clinical improvement.

Mycosis fungoides (MF), the most common form of cutaneous T-cell lymphoma (CTCL), is defined by the presence of neoplastic (atypical) CD4⁺ CD45RO⁺ (helper/memory) T lymphocytes in the epidermis.¹ Sézary syndrome (SS) is defined by generalized erythroderma, and blood involvement: an absolute Sézary cell count of 1000 cells μL^{-1} , demonstration of phenotypic abnormalities, or a T-cell clone by molecular or cytogenetic methods.² MF has a peak incidence in the sixth and seventh decades of life.³ Although MF often presents with limited pleomorphic skin lesions, 50% of patients with early-stage disease have circulating atypical T-cell clones detected.⁴ Patients with clonal T-cell receptor gene rearrangements in different lesions or sites are more likely to progress than are patients with oligoclonal or polyclonal T-cell prolifer-

ation.⁵ Spectratyping has shown profound depletion of the T-cell repertoire in most patients with advanced disease and half of the patients with early-stage disease, suggesting chronic antigen stimulation.⁶

Staphylococci of the Micrococcaceae family are nonspore-forming Gram-positive bacteria with a tendency to form clusters. Staphylococci colonize human skin, especially the anterior nares, axilla, and the intertriginous inguinal and perineal areas, where MF lesions first appear.⁷ Healthy adults have skin carriage rates of pathogenic *Staphylococcus aureus* ranging from 11% to 32%, while colonization by coagulase-negative staphylococci (CNS) – strains of *S. epidermidis*, *S. saprophyticus* and *S. haemolyticus* – is nearly universal.^{8,9} In a study of hospital personnel who had 760 cultures made, 86% carried CNS in

the nares, 25% carried *S. aureus*, 4.9% carried methicillin-resistant *S. aureus* (MRSA), and 43% carried methicillin-resistant CNS.¹⁰

Staphylococcus aureus infections occur in all age groups and are transmitted mainly by person-to-person contact, from skin lesions or asymptomatic nasal carriers. Opportunistic *S. aureus* infections are frequent in patients with defects in the integument, i.e. eczema or pediculosis.¹¹ High rates of *S. aureus* carriage are reported in patients with atopic dermatitis, psoriasis, dialysis and human immunodeficiency virus infection^{7,8,12–24} (Table 1) but the rate of *S. aureus* colonization in patients with CTCL (MF/SS) is unknown.

In a study of staphylococcal line sepsis in hospitalized patients, identical strains were cultured from both blood and nares,¹⁰ suggesting that nasal colonization is clinically significant. We previously reported 11 of 12 patients with erythrodermic MF or SS with indwelling catheters inserted for extracorporeal photopheresis who developed staphylococcal sepsis and whose skin improved quickly on intravenous

antibiotics.²⁵ Staphylococcal sepsis and colonization of skin were associated with disease progression including clinical exacerbation of erythroderma and pruritus, increased white blood cell counts and absolute CD4+ cell counts, and high lactate dehydrogenase. Intravenous antibiotics are often followed by rapid clinical improvement in days, and decreased absolute CD4+ cell counts. In a second prospective study of 42 patients with erythrodermic MF/SS, 32 (76%) had positive staphylococcal cultures from either the skin or blood, including 16 (50%) with *S. aureus*. Skin lesions in six patients were colonized by a toxic shock syndrome toxin 1 (TSST-1) strain and their blood had expected TSST-1-driven V β 2 clone expansion.²⁶ These observations led to the hypothesis that staphylococcal superantigens and/or enterotoxins may serve as persistent antigens or superantigens in erythrodermic MF/SS.²⁶ Although *S. aureus* infections and sepsis frequently occur in patients with CTCL,²⁷ the prevalence of *S. aureus* carriage in skin and nares by stage of MF and the success of eradication have not been previously determined.

Colonization of <i>Staphylococcus aureus</i>	n	Carrier rate (%)	Reference (first author and year)
General population		11–32	Kloos (1994) ⁷
Anterior nares		20, 10–45	Kolmos (1999) ¹²
Cutaneous lesions or axilla		< 10	Nobel (1969) ¹³
Vaginal carriage		10	Waldvogel (2000) ¹⁴
Children	374	44.3	Smith (1966) ¹⁵
Newborns		6–24	Fekety (1958) ¹⁶
Physicians, nurses, hospital ward attendants		50–90	Waldvogel (2000) ¹⁴
Atopic dermatitis	28		Nobel (1969) ¹³
Anterior nares		79	
Cutaneous lesions or axilla		64	
Psoriasis	33		Klein (1997) ¹⁷
Anterior nares		33	
Cutaneous lesions or axilla		21	
Cirrhosis liver		56	Chapout (1999) ¹⁸
Diabetes mellitus type 1	71	46	Berman (1987) ¹⁹
Diabetes mellitus type 2	188	27	Boyko (1989) ²⁰
Dialysis			
Haemodialysis	454	51	Berman (1987) ¹⁹
Continuous ambulatory peritoneal dialysis	605	43	Davies (1989) ²¹
Chronic renal failure	38	21	Goldblum (1978) ²²
Human immunodeficiency virus	33, 231		Nobel (1969) ¹³
Anterior nares		27, 49	Nobel (1969) ¹³
Cutaneous lesions or axilla		3, NA	Nobel (1969) ¹³
Drug addicts			
Intravenous drug users	288	55	Tuazan (1974) ⁸
Intravenous drug users with infective endocarditis		10–27	Bayer (2000) ²³
Nonintravenous drug users	603	25	Tuazan (1974) ⁸
Perennial allergic rhinitis	65	44	Shiomori (2000) ²⁴
Cutaneous T-cell lymphoma	106		Present study
Anterior nares	33	31	
Cutaneous lesions (excluding axilla)	33	31	

Table 1 Prevalence of *Staphylococcus aureus* colonization in skin diseases and normal controls

Materials and methods

Study design

To determine the rate of staphylococcal carriage in nares and skin among patients with MF/SS, we enrolled all patients aged 18 years or older with newly diagnosed MF, regardless of stage, presenting to the M.D. Anderson Cancer Center CTCL clinic between June 1997 and December 1999. Patients were excluded for immunodeficiency, nasal rhinitis or polyps or steroid use, history of eczema or psoriasis, current antibiotic or investigational drug use, or pregnancy. Patients were required to sign informed consent approved by the institutional review board. Patients were staged for degree of skin, blood and lymph node involvement by the TNM staging system. Extent of clinical disease was calculated by percentage of body surface area (BSA) involved with MF at baseline, 4 weeks and 8 weeks post-treatment. Cultures from intranasal sites were obtained by placing a cotton bud swab in the anterior nares, applying gentle pressure, and rotating the swab. The most erythematous cutaneous lesion from each patient was also cultured. Culture and sensitivity results were interpreted by the microbiology laboratory staff blinded to the patient's status.

The efficacy of intranasal mupirocin plus oral antibiotics in eliminating *S. aureus* nasal carriage was studied prospectively. Patients with a positive nasal culture at baseline were instructed to treat their nares with topical nasal mupirocin twice daily for five consecutive days and then weekly. Patients with positive skin cultures also received oral antibiotics (dicloxacillin 250 mg four times daily, or cefalexin 1 g daily for penicillin-allergic patients) for 4 weeks. Cultures of nares and skin were repeated at 72 h, 4 weeks and 8 weeks post-treatment.

Statistical analysis

An exact binomial test was used to compare the rate of *S. aureus* carriage in lesions and nares of patients with MF/SS with that of the general population and patients with atopic dermatitis and psoriasis.

Results

Carriage rate of *Staphylococcus aureus* in skin and nares in patients with mycosis fungoides/Sézary syndrome by stage

One hundred and six patients newly or recently diagnosed with biopsy-confirmed MF or SS had samples cultured from nares and skin. The demographics and colonization results are summarized in Table 2. Sixty-nine patients had samples taken on their first visit, and 37 on the first return visit. Positive cultures for any strain of *Staphylococcus* were present in 63 patients, and 44 (42%) had a positive culture for *S. aureus* from either skin (31%) or nares (31%). *Staphylococcus aureus* was present in both skin and nares in 22 patients (21%) (Table 2). Six

Table 2 Demographics and colonization rate of patients with mycosis fungoides/Sézary syndrome (n = 106)

Age (years), median (range)	59 (22–59)
Sex, M/F (n)	62/44
Visit, first/return (n)	69/37
Culture positive for any <i>Staphylococcus</i> strain, n (%)	
Skin	63 (59)
Nares	57 (54)
Culture positive for <i>Staphylococcus aureus</i> , n (%)	
Skin	33 (31)
Nares	33 (31)
Either	44 (42)
Both	22 (21)

Table 3 *Staphylococcus aureus* colonization by stage of mycosis fungoides/Sézary syndrome (SS)

Stage	No. patients (n = 106)	<i>Staphylococcus aureus</i>	
		Skin, n (%)	Nares, n (%)
IA	39	6 (15)	8 (21)
IB, IIA	24	7 (29)	8 (33)
IIB	13	7 (54)	6 (46)
III	13	3 (23)	3 (23)
IVA	12	8 (67)	7 (58)
IVB	5	2 (40)	1 (20)
All patients	44	33 (75)	33 (75)
EE/SS ^a	25	12 (48)	10 (40)

^aEE/SS indicates a subset of patients with > 80% erythroderma (EE = exfoliative erythroderma).

patients had MRSA. Two of the six had MRSA in both skin and nares. MRSA was cultured from one patient with stage IA MF and four patients with erythrodermic MF. Rare pathogens, cultured from nares or skin of nine patients, included beta-haemolytic *Streptococcus*, Gram-negative rods, *Propionibacterium acnes*, coccobacilli, *Enterococcus*, *Escherichia coli*, *Pseudomonas*, *Serratia marcescens* and *Pantoea agglomerans*.

Staphylococcus aureus colonization rates were identical between patients with newly diagnosed (41%) and previously diagnosed MF/SS (41%). The colonization rate by TNM staging is shown in Table 3. Twelve of 25 (48%) patients with erythrodermic SS were colonized with *S. aureus* in skin compared with six of 39 (15%) patients with stage IA MF. The highest colonization rate (54%) was seen in seven of 13 stage IIB patients.

Eradication of *Staphylococcus aureus* carriage in nares and skin of patients with mycosis fungoides/Sézary syndrome

Table 4 lists 44 patients with MF/SS who were colonized with *S. aureus* in skin or nares, with their response to treatment.

Table 4 Response to antibiotic treatment in 44 patients colonized with *Staphylococcus aureus*

Patient	Stage	New/Est	Sex	Race	Ab	BL, S/N	72 h, S/N	4 weeks, S/N	8 weeks, S/N	BR	DR (weeks)	Therapy received
1	IA	New	F	W	D	+/-	+/-	-/-	-/-	PR	36	TAC
2	IA	New	F	W	D	+/-	-/-	-/-	-/-	PR	48	Cl
3	IA	New	F	W	N	-/+	-/-	-/-	-/-	PR	52	CP
4	IA	New	M	W	D	+/+	-/-	-/-	-/-	CR	20	NM
5	IA	New	M	W	D	-/+	-/-	-/-	-/-	CR	8	NM
6	IA	New	M	W	A	+/+	-/-	-/-	-/-	PR	36	TAC
7	IA	New	M	W	N	-/+	-/-	-/-	-/-	PR	48	CP
8	IA	New	M	H	D	+/+	+/+	+/+	+/+	SD	0	CM
9	IB	New	M	W	N	-/+	ND	ND	ND	ND	0	TAC
10	IB	New	F	W	D	+/+	-/+	-/-	-/-	PR	20	NM
11	IB	New	F	W	D	+/+	-/-	+/+	-/-	CR	72	TAC/hydrocortisone
12	IB	New	F	W	Cl	+/+	-/-	-/-	-/-	CR	48	NM
13	IB	New	M	W	Cl	+/+	-/-	-/-	-/-	PR	32	ECP
14	IIA	New	M	W	Cl	+/+	-/+	-/-	-/-	PR	48	IFN, isotretinoin
15	IIB	New	M	W	D	+/+	-/-	-/-	-/-	CR	24	None
16	IIB	New	M	B	N	-/+	+/+	+/-	+/+	SD	20	NM
17	IIB	New	F	B	D	+/+	+/-	+/-	-/-	CR	16	DAB-IL2
18	IIB	New	M	W	D	+/-	-/+	-/-	-/-	SD	0	CM
19	IIB	New	M	W	D	+/+	+/+	-/-	-/-	SD	0	IFN
20	IIB	New	F	W	Cl	+/-	+/-	-/-	-/-	SD	0	ECP
21 ^a	III	New	F	W	D	-/+	-/-	-/-	-/-	SD	0	CM
22 ^a	III	New	F	W	Naf	+/+	-/-	-/-	-/-	PR	8	ECP, TAC
23 ^a	IVA	New	M	H	Cl	+/-	+/-	+/-	+/-	SD	0	ECP
24 ^a	III/IVA	New	M	H	C	+/+	-/-	-/-	-/-	CR	48	Bexarotene
25 ^a	III/IVB	New	F	W	C	-/+	-/-	-/-	-/-	PR	8	ECP
26 ^a	IVA/III	New	M	B	D	-/+	-/+	-/-	-/-	CR	8	None
27 ^a	IVA/III	New	F	W	D	+/-	-/-	-/-	-/-	PR	8	Bexarotene
28	IVB	New	M	W	D	+/-	-/-	-/-	-/-	SD	0	None
29 ^a	IVB/III	New	M	H	D	+/-	+/-	-/-	-/-	PR	48	PUVA, IFN, isotretinoin
30	IA	Est	M	W	N	+/-	-/-	-/-	-/-	CR	48	PUVA
31	IA	Est	M	W	D	-/+	-/-	-/-	-/-	CR	40	TAC
32	IA	Est	M	W	N	-/+	ND	ND	ND	ND	0	NM, CP, TAC
33	IB	Est	M	W	D	+/+	+/-	-/-	-/-	PR	48	Topical steroids
34	IB	Est	M	W	D	-/+	-/-	-/-	-/-	CR	8	None
35	IIA	Est	M	W	C	+/-	-/-	-/-	-/-	PR	72	Bexarotene
36	IIB	Est	F	W	D	+/+	-/-	-/-	+/-	SD	0	BCX
37	IIB	Est	F	B	D	+/+	-/-	-/-	-/-	PR	8	CHOP/Flud
38 ^a	III	Est	M	B	Cl	+/-	+/-	+/-	+/-	SD	0	TAC
39 ^a	III	Est	M	W	D	+/+	-/-	-/-	-/-	SD	0	NM
40 ^a	III/IVA	Est	M	W	C	+/+	+/+	+/+	-/-	SD	0	CHOP/Flud
41	IVA	Est	M	W	N	+/+	+/+	-/-	-/-	SD	0	NM
42	IVA	Est	F	B	D	+/+	+/+	+/+	-/-	PD	0	IFN, isotretinoin
43	IVA	Est	F	B	D	+/+	+/+	+/+	-/+	SD	0	Bexarotene
44 ^a	IVA/III	Est	M	B	D	+/+	+/+	-/-	-/-	SD	0	Isotretinoin/IFN

Est, established (previously diagnosed); F, female; M, male; W, white; H, Hispanic; B, black; Ab, antibiotic; D, dicloxacillin; N, none; A, ampicillin; Cl, clindamycin; Naf, nafcillin; C, cefalexin; BL, baseline; S/N, skin/nose; ND, not determined; BR, best response; PR, partial response; CR, complete response; SD, stable disease; PD, progressive disease; DR, duration of response; TAC, triamcinolone; CP, clobetasol propionate; NM, nitrogen mustard; CM, combined modality; ECP, extracorporeal photopheresis; IFN, interferon; PUVA, psoralen + ultraviolet A; CHOP, cyclophosphamide, doxorubicin, vincristine and prednisone; Flud, fludarabine. ^aErythrodermic.

To determine whether eradication of *S. aureus* was possible, sequential cultures were taken at 3–7 days, 4 weeks and 8 weeks. We also assessed the patients' clinical response to treatment using the BSA assessment (Fig. 1). Twenty-five patients colonized in skin and nares received nasal mupirocin

2% and oral dicloxacillin 250 mg four times daily for 1 month. One patient with SS was treated with intravenous nafcillin; one patient took oral ampicillin 1 g daily. Three penicillin-sensitive patients received oral cefalexin 1 g daily for 4–8 weeks, and six received oral clindamycin 300 mg twice daily.

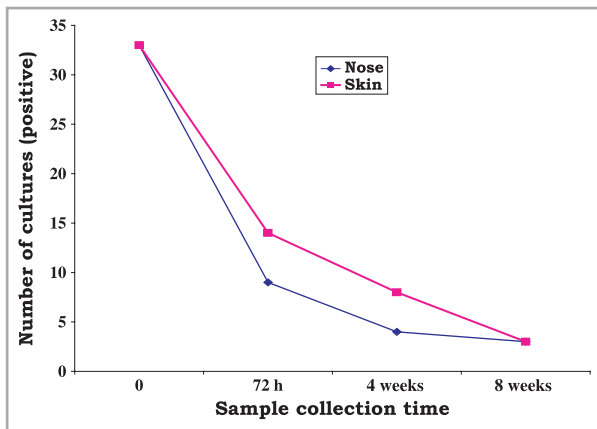


Fig 1. Effect of antibiotic treatment on number of *Staphylococcus aureus*-positive cultures. Plot of positive *S. aureus* cultures in nares and skin of patients with cutaneous T-cell lymphoma at baseline, and at 72 h, 4 weeks and 8 weeks after antibiotic therapy.

Thirty-three patients were colonized with *S. aureus* in skin: 21 were new patients and 12 were seen on their second visit. Repeat skin cultures were negative at 4–8 weeks in 30 of 33 (91%) patients. Post-treatment nares cultures were negative in 18 of 21 (86%) new patients, nares cultures remained positive in two patients, and one patient was lost to follow-up. Fifteen previously diagnosed patients had positive *S. aureus* isolates from nares or skin and nine (60%) were positive at both sites. Ten of 12 patients had negative post-treatment cultures from nares, one was not cleared, and one patient was lost to follow-up. The overall intent-to-treat success rate of clearance of nasal colonization was 28 of 33 (85%) at 8 weeks (Fig. 1). Side-effects attributed to mupirocin in three patients were runny nose, nasal stuffiness and headaches.

Skin response to anti-*Staphylococcus aureus* therapy

When antibiotics were administered alone or with mid-potency topical triamcinolone cream, clinical improvement in redness and extent of skin involvement was observed as early as 4–8 weeks in patients with all stages of MF/SS (Fig. 2, Table 4). Clinical response was defined as > 50% improvement from baseline in the percentage BSA involvement with patches, plaques or tumours. Complete clinical response (CR) required 100% clearing of skin with no residual involvement. Among 44 patients colonized in nares or skin with *S. aureus* at baseline, 25 (57%) achieved at least partial response (PR) at 4–8 weeks after oral antibiotics and mupirocin (Table 4, Fig. 2). Twelve of the 25 were also using concomitant topical mid-potency steroid cream and 13 were not. Failure to eradicate *S. aureus* was observed in only three patients who had persistently positive cultures, and their lesions failed to improve on oral antibiotic therapy.

The median duration of response of MF skin lesions in the 25 responders was 36 weeks (range 8–72). Ten of 25 patients (shown in Fig. 2) had 100% reduction in BSA, i.e. complete

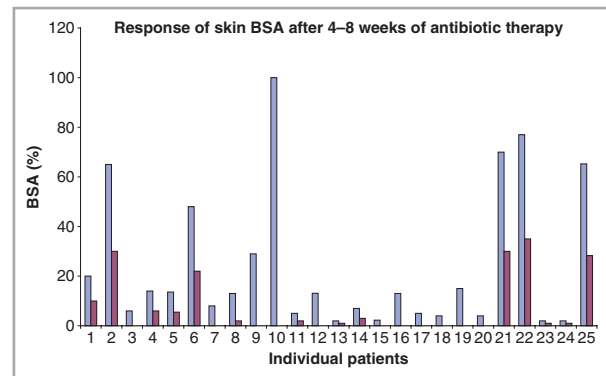


Fig 2. Clinical response of 25 patients with cutaneous T-cell lymphoma to 4–8 weeks of antibiotic therapy. The percentage of body surface area (BSA) involvement in each of 25 responding patients is plotted as two shaded bars representing baseline (blue) vs. post-treatment extent (purple).

skin responses, and three of the 10 received only oral antibiotics without topical therapy. Of the 19 of 44 patients with *S. aureus* who did not achieve a PR or CR, 16 (36%) had stable disease, one (2%) had progressive disease, and two were lost to follow-up. In the group of 33 patients with *S. aureus* colonization limited to the skin at baseline, 19 significantly improved (overall response rate of 58%). We did not observe any cases of resistance arising to oral dicloxacillin during this study.

Figure 2 shows the clinical response as measured by change in BSA in responding patients. Among 25 patients who had > 50% erythroderma at baseline, 12 were colonized with *S. aureus*. Six of the 12 (50%) had dramatic reductions in their BSA with antibiotic treatment (Fig. 2). Two achieved complete skin responses at 4–8 weeks. None progressed and two additional patients cleared completely by 48 weeks on chronic antibiotics and oral bexarotene. Figure 3 shows a patient with erythrodermic SS with fissures colonized with MRSA whose skin improved following vancomycin. Five of six colonized stage IA patients cleared their skin lesions with oral antibiotic therapy – two with CR and three with PR. Seven of 13 (54%) stage IIB patients were colonized with *S. aureus* (Table 3). Three (43%) responded to antibiotics including two with CR, one of whom received no other therapy.

Comparison of *Staphylococcus aureus* skin carriage in mycosis fungoides/Sézary syndrome, atopic dermatitis and psoriasis

Pubmed and Mdconsult searches from 1963 to present were used to obtain the historical carriage rates in different groups of T-cell-mediated skin diseases (Table 1). The exact binomial test was used to compare the rate of colonization by *S. aureus* in patients with MF with that of axillary skin in the general population, as well as lesions from patients with atopic dermatitis and psoriasis. The *S. aureus* skin colonization rate of 31% for all patients with MF/SS was significantly higher than



Fig 3. Patient with erythrodermic Sézary syndrome with fissures colonized with methicillin-resistant *Staphylococcus aureus* (MRSA) that improved following vancomycin. Hands (a, b) with MRSA colonization and (c, d) after clearing with antibiotics.

the 10% reported in the general population ($P < 0.0001$) and lower than the rate of 21% for psoriasis lesions (Table 5). Patients with erythrodermic SS had a significantly higher carriage rate (48%) than the general population (10%), MF patients without erythroderma (26%) ($P < 0.0001$) and

patients with stage IA MF (15%). The highest colonization rate of *S. aureus* (64%) was reported in patients with atopic dermatitis and was not significantly different from the 48% in patients with erythrodermic SS ($P = 0.15$).

Discussion

This is the first study to determine the colonization rate of *S. aureus* in patients with MF/SS and to address whether eradication of *S. aureus* is possible and is associated with clinical improvement. The patients were enrolled and cultures made prospectively, but historical controls were used for comparison. This trial was not randomized with regard to therapy effects. An overall skin carriage rate of 31% for *S. aureus* among the entire group of all patients with MF/SS was significantly higher than the 10% colonization rate reported for the general population ($P < 0.0001$) and lower than the 64% rate reported for patients with atopic dermatitis ($P < 0.0001$). Patients with erythrodermic SS had a higher *S. aureus* colonization rate (48%) than patients with nonerythrodermic MF (26%) and this rate was not statistically significant from the

Table 5 Comparison of *Staphylococcus aureus* skin carriage rates among patient groups

Skin carriage rate	General population 10%	Atopic dermatitis 64%	Psoriasis 21%
All MF/SS 31%	$P < 0.0001$	$P < 0.0001$	$P = 0.018$
EE/SS ^a 48%	$P < 0.0001$	$P = 0.15$	$P = 0.005$
MF 26%	$P < 0.0001$	$P < 0.0001$	$P = 0.34$

MF, mycosis fungoides; SS, Sézary syndrome. ^aEE/SS indicates a subset of patients with > 80% erythroderma (EE = exfoliative erythroderma). P-values indicate pairwise comparisons between subsets of cutaneous T-cell lymphoma and three conditions with reported skin carriage rates.

colonization rate in patients with atopic dermatitis (64%; $P = 0.15$). We have confirmed our previous observations that erythrodermic patients are frequently colonized with *S. aureus*^{25,26} and that *S. aureus* can be a clinically significant factor.²⁷ *Staphylococcus aureus* colonization and erythroderma appear to accompany diseases with a Th2 profile leading to eosinophilia and pruritus: Leung et al.²⁸ have shown that patients with atopic dermatitis have high levels of anti-IgE to skin staphylococcal exotoxins, thought to cause pruritus.

In a double-blind multicentre randomized trial examining *S. aureus* colonization and treatment in eczema and atopic dermatitis, bacteria were cultured from 74.8% of eczema lesions (79.8% were *S. aureus*) and from 34.5% of normal skin samples (80.5% were *S. aureus*).²⁹ *Staphylococcus aureus* carriage was associated with worse grading of disease. A superior therapeutic effect was observed in atopic patients on topical mupirocin and hydrocortisone butyrate compared with antibiotic vehicle plus topical steroid ($P = 0.05$). Although our study was not randomized, we eradicated *S. aureus* carriage with a combination of mupirocin and oral antibiotics. Twenty-five (57%) of colonized patients had significant improvements in their skin following eradication of staphylococci including 12 with concomitant topical steroids. There were 10 patients with CR and three had only antibiotic therapy. Six patients with early-stage MF were colonized: four cleared completely, and one cleared partially on antibiotics, suggesting a pathogenic role in some patients with early-stage MF/SS.

The anterior nares are a reservoir for *S. aureus* colonization leading to increased risk of sepsis after surgery or haemodialysis (Table 1).³⁰ Mupirocin is effective against MRSA and *S. aureus* when applied intranasally for 5–7 days, and eliminated carriage in hospital personnel for at least 3 months.^{31–34} Nasal cultures remained negative in 52% at 6 months and 47% at 12 months.³¹ We found *S. aureus* nares colonization in 31% of new or returning patients with MF, suggesting that it was not acquired in the clinic. Eradication of *S. aureus* in 85% of positive carriers and 91% of those with skin colonization was achieved.

Staphylococcus aureus is accepted as a dangerous pathogen in patients with CTCL,²⁷ but its role in causing T-cell expansion is not well accepted. We reported *S. aureus* line sepsis in 11 of 12 patients with MF/SS using indwelling Hickman catheters for photopheresis,²⁵ and found that TSST-1 strains of *S. aureus* were present in SS patients with the expected V β 2 clonal T-cell expansion.²⁶ Tokura et al.³⁵ first demonstrated that Sézary cells respond to superantigenic staphylococcal enterotoxin in a manner restricted by their V β usage. Superantigens in colonizing skin flora could provide chronic antigen persistence driving MF, as hypothesized by Tan et al. in 1974.³⁶

Because the severity of MF/SS is graded by the extent and degree of skin erythema,³⁷ clinicians need to be aware of the contribution of *S. aureus* colonization. Clearance of *S. aureus* colonization with antibiotics can be associated with partial and complete skin responses and reduced pruritus. There is also a beneficial effect of making skin pH acidic for reducing *S. aureus* carriage.³⁵ In our study 58% of all patients with MF/SS

experienced improvement in their skin lesions when treated with nasal mupirocin in combination with oral antibiotics at the 4- to 8-week time point. Flares of erythroderma were also observed in conjunction with recolonization of the skin with *S. aureus* or MRSA.

As the most common cause of death in patients with MF/SS is from infection,²⁷ especially from the use of indwelling catheters, attention to the colonization state of patients with CTCL is recommended. Mortality in patients with CTCL is high from sepsis and SS patients with sepsis often do not manifest fever. Identification and treatment of *S. aureus* would be expected to prevent unnecessary deaths, reduce morbidity, and ultimately prolong overall survival.

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