

Report

Skin colonization of *Staphylococcus aureus* in atopic dermatitis patients seen at the National Skin Centre, Singapore

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Abstract

Objective This prospective study sought to determine the bacterial colonization rates on eczematous and non-eczematous skin and nasal mucosa of patients with atopic dermatitis attending a tertiary dermatologic referral clinic in Singapore. The colonization rates were evaluated according to age, sex, race, and severity of dermatitis compared with controls. The results may help to determine whether antibiotics should be considered in the treatment of atopic dermatitis.

Patients Patients, of any age, presenting with atopic dermatitis at the subsidized clinic of the National Skin Centre, Singapore, between 23 August 1996 and 14 September 1996, were included in the study.

Results Thirty-three patients with atopic dermatitis were seen at the outpatient clinic during the study period. *Staphylococcus aureus* was isolated in 69.7% of the eczematous lesions and in 42.4% of non-eczematous skin of patients with atopic dermatitis. *S. aureus* was isolated in 53% of patients with mild dermatitis, and in 100% with moderate and severe dermatitis. The nasal carriage rate of *S. aureus* was higher in atopic dermatitis patients (51.5%) than in non-atopics (35%) (not significant). *S. aureus* was isolated in 42% of non-eczematous skin in atopics compared with only 5% in the control group ($p = 0.003$). In patients with atopic dermatitis, all *S. aureus* isolated was sensitive to cloxacillin, cephalixin, clindamycin, and co-trimoxazole; 92% was sensitive to erythromycin, but only 13% was sensitive to penicillin and ampicillin. In the control group, all *S. aureus* isolated was sensitive to cloxacillin, cephalixin, erythromycin, clindamycin, and co-trimoxazole, but only 13% was sensitive to penicillin and ampicillin, and 87% to tetracycline.

Conclusions This study confirmed that the skin of patients with atopic dermatitis was more frequently colonized with *S. aureus* than that of non-atopics. The more severe the dermatitis, the higher the rate of colonization. *S. aureus* is also more often present in non-eczematous skin of atopics than of non-atopics. There is also a higher percentage of *S. aureus* nasal carriage in patients with atopic dermatitis than in non-atopics. Hence antibiotics may have a role in the treatment of atopic dermatitis. Because 87% of *S. aureus* is resistant to penicillin and ampicillin, antibiotics such as cloxacillin and cephalixin should be used to eradicate *S. aureus* in the skin of atopic dermatitis individuals.

Atopic dermatitis is a skin condition characterized by dryness, erythema, and extreme pruritus.¹ Bacterial infections are more frequently observed in patients with atopic dermatitis than in non-atopic individuals. These infections may have a role in the exacerbation of atopic dermatitis.² *Staphylococcus aureus* has been found to be the predominant skin organism in atopic individuals.³ Few studies have been performed on the skin colonization and role of *S. aureus* in patients with atopic dermatitis in the tropics. We have investigated the prevalence and role of *S. aureus* skin colon-

ization in patients with atopic dermatitis, and the relation between *S. aureus* skin colonization and clinical disease severity in patients at the National Skin Centre, Singapore. We discuss the role of antibiotics in the treatment of atopic dermatitis.

Materials and methods

Patients who presented with atopic dermatitis at the outpatient clinic of the National Skin Centre, Singapore, between 23

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August 1996 and 14 September 1996, were included in the study. Twenty patients without atopic dermatitis, age and sex matched, were recruited at the same time to act as controls. They included patients with benign skin tumors, vitiligo alopecia (various causes), and viral warts (excluding those with bacterial skin infections). All patients had received no oral or topical antibiotic therapy for 1 week prior to the study.

The following definitions were used. *Atopic dermatitis* was defined as a skin condition with three or more of the following criteria: (i) pruritus; (ii) typical morphology and distribution of flexural lichenification or linearity in adults, or facial and extensor involvement in infants and children; (iii) chronic or chronically relapsing dermatitis; (iv) personal or family history of atopy (bronchial asthma, atopic dermatitis, and allergic rhinitis). *Controls* included those without atopic dermatitis, including patients with benign skin tumors, vitiligo, alopecia, and viral warts. *Active eczematous lesions* refer to skin lesions which are erythematous, oozing, with vesiculation, crusting, excoriations, and erosions. *Non-eczematous normal looking skin* refers to uninvolved skin lesions with no erythema, vesicles, oozing, crusting, erosions, or excoriations. The *severity of dermatitis* was classified as (i) 'mild' when there was less than 25% total body skin involvement, (ii) 'moderate' when there was 25%–50% involvement, and (iii) 'severe' when there was more than 50% involvement.

For atopic dermatitis patients, two swabs using sterile cotton-tipped swab sticks rolled over the skin surface twice were taken for culture and sensitivity studies; one swab was taken from the eczematous lesion and the other from non-eczematous (normal looking) skin. One swab was taken from the forearm of normal looking skin of control patients. Swabs were also taken from the right anterior nares of all the patients. A nurse was assigned to take the swabs from the sites chosen by the authors.

Skin swabs for bacterial culture were sent to the Department of Pathology of the Singapore General Hospital for processing. At the microbiology laboratory, cultures were prepared on blood and eosin methylene blue agar plates and in Robertson's cooked meat broth, which were incubated overnight at 35 °C. Standard techniques were used for the isolation and identification of recognized bacterial pathogens. Antibiotic susceptibility tests were performed by the agar diffusion method according to the *National Committee for Clinical Laboratory Standards* (1990 NCCLS Document M2-A4, volume 10, number 7).

The culture and sensitivity results of each subject were collated, and the prevalence of positive cultures was compared, according to age, sex, race, and severity of dermatitis, with the controls. Statistical analysis was performed using the chi square test and the Fisher's exact test. A *p* value of less than 0.05 was considered to be statistically significant.

Results

Thirty-three patients with atopic dermatitis were included in the study. Table 1 shows the demographic data of the patients. Their mean age was 12.7 years (range, 3 months to 32 years). There were 19 males (57.6%) and 14 females (42.4%), with a 1.3 : 1 male to female ratio. Of these, 26 (78.8%) were Chinese. Twenty age- and sex-matched controls with a mean age of 13.7 years were recruited.

Table 2 shows the *S. aureus* skin colonization rate according to the severity of dermatitis and age group. Of the 33 patients with atopic dermatitis, 17 (52%) had mild dermatitis, 13 (39%) had moderate dermatitis, and three (9%) had severe dermatitis. Nine (53%) patients with mild dermatitis had *S. aureus* colonization in the skin, whereas all patients with moderate and severe dermatitis had *S. aureus* colonization on eczematous skin (*p* = 0.01). There was no significant difference in the *S. aureus* colonization rates between the different racial groups. All patients with moderate and severe dermatitis had positive cultures for *S. aureus* regardless of racial group (Table 3).

Staphylococcus aureus colonization on non-eczematous atopic skin and controls

Forty-six per cent of non-eczematous skin of patients with atopic dermatitis had positive cultures for *S. aureus*, whereas only one (5%) patient in the control group had a positive culture. A positive nasal culture for *S. aureus* was also higher (18/33 = 54%) in atopic patients than in the controls (35%) (not significant) (Table 4). Fifty-three (53.5%) positive cultures for *S. aureus* were obtained from the skin/nasal mucosae of patients with atopic dermatitis, whereas only eight (20%) positive cultures were obtained from the skin/nasal mucosae of the control group.

Antimicrobial sensitivity of *Staphylococcus aureus* in atopic dermatitis patients and controls

Antimicrobial sensitivity testing to penicillin, cloxacillin, ampicillin, cephalixin, erythromycin, clindamycin, and co-trimoxazole was performed on all the cultured *S. aureus* strains. Tetracycline sensitivity was tested only in 33 of the positive cultures from the atopic group and six from the controls. The results show that *S. aureus* was very sensitive to cloxacillin, cephalixin, clindamycin, and co-trimoxazole; however, 92.5% (49/53) of the *S. aureus* isolated from the atopic group was sensitive to erythromycin and 72.7% (24/53) was sensitive to tetracycline. Only 13% of *S. aureus* was sensitive to penicillin and ampicillin in atopics and controls (Table 5). There was no statistical difference in the sensitivity of *S. aureus* to the various antibiotics tested between the atopics and controls.

Table 1 Demographic data of 33 atopic dermatitis patients included in the study

Age group (years)	Sex		Race			Total
	Male patients	Female patients	Chinese	Malay	Indian	
<10	6 (46%)	7 (54%)	9 (69%)	4 (31%)	0	13
10–19	6 (54%)	5 (46%)	9 (82%)	1 (9%)	1 (9%)	11
>19	7 (78%)	2 (22%)	8 (89%)	1 (11%)	0	9
Total	19 (58%)	14 (42%)	26 (79%)	6 (18%)	1 (3%)	33

Table 2 Skin *Staphylococcus aureus* colonization rates in 33 atopic dermatitis patients according to age group and severity of dermatitis

Age group (years)	Severity/% positive culture						Total	+ ve culture
	Mild	+ ve culture	Moderate	+ ve culture	Severe	+ ve culture		
<10	8 (62%)	5 (63%)	5 (38%)	5 (100%)	—	—	13	10 (77%)
10–19	5 (45%)	5 (100%)	5 (45%)	5 (100%)	1 (10%)	1 (100%)	11	11 (100%)
>19	4 (44%)	3 (75%)	3 (33%)	3 (100%)	2 (22%)	2 (100%)	9	8 (89%)
Total	17 (52%)	13 (76%)	13 (39%)	13 (100%)	3 (9%)	3 (100%)	33	29 (89%)

There was no statistical difference in the prevalence of *S. aureus* skin colonization between the different age groups and severity of dermatitis.

Table 3 *S. aureus* colonization on eczematous skin of atopics according to severity and race

Race	Severity/% positive culture						Total	+ ve culture
	Mild	+ ve culture	Moderate	+ ve culture	Severe	+ ve culture		
Chinese	13 (50%)	9 (69%)	10 (38%)	10 (100%)	3 (22%)	3 (100%)	26	22 (85%)
Malay	4 (67%)	4 (100%)	2 (33%)	2 (100%)	—	—	6	6 (100%)
Indian	—	—	1 (100%)	1 (100%)	—	—	1	1 (100%)
Total	17 (52%)	13 (76%)	13 (39%)	13 (100%)	3 (9%)	3 (100%)	33	29 (88%)

There was no statistical difference in the severity of dermatitis and *S. aureus* colonization rates between the different races.

Table 4 *S. aureus* colonization rates on eczematous and non-eczematous skin of atopic dermatitis patients and controls

Age (years)	Eczematous skin	Non-eczematous skin		Nasal carriage	
	Atopics	Atopics	Controls	Atopics	Controls
<10	9/13 (69%)	5/13 (38%)	1	6/13 (46%)	2
10–19	8/11 (73%)	5/11 (45%)	0	6/11 (55%)	3
>19	6/9 (67%)	4/9 (44%)	0	6/9 (67%)	2
Total	23/33 (70%)	14/33 (42%)	1/20 (5%)	18/33 (55%)	7/20 (35%)

The *S. aureus* colonization rate was significantly higher in eczematous skin than in non-eczematous skin of atopic dermatitis patients (chi square = 3.9, $p = 0.04$).

Table 5 Antimicrobial sensitivity of *S. aureus* on skin of atopics and controls

Antibiotics	Sensitive	
	Atopics (n = 53)	Controls (n = 8)
Penicillin	7 (13%)	1 (13%)
Ampicillin	7 (13%)	1 (13%)
Cloxacillin	53 (100%)	8 (100%)
Cephalexin	53 (100%)	8 (100%)
Clindamycin	53 (100%)	8 (100%)
Co-trimoxazole	53 (100%)	8 (100%)
Erythromycin	49 (92%)	8 (100%)
Tetracycline	24 (73%)	5 (83%)

There was no statistically significant difference in antibiotic sensitivity between atopics and controls.

Discussion

Atopic dermatitis is a genetically determined skin disorder profoundly influenced by external/environmental factors.⁴ The pathogenesis of atopic dermatitis is still unknown. Atopic dermatitis is frequently associated with elevated immunoglobulin E (IgE) levels. The disease usually arises during early infancy, childhood, or adolescence. Diagnosis is based on a combination of clinical and historic parameters, such as morphologic skin lesions, chronic relapsing course, pruritus (which is a hallmark), and a personal and/or family history of atopy.⁵

Due to a decrease in cell-mediated immunity and malfunctioning chemotaxis, bacterial or viral infections are common in atopic dermatitis.⁶ The density of *S. aureus* skin colonization is increased in atopic dermatitis patients, which may account for the frequent staphylococcal skin infections.⁷ Leyden *et al.*³ isolated *S. aureus* from chronic lichenified plaques in 91% of 50 atopic dermatitis patients and from exudative lesions in 100% of 20 further atopic dermatitis patients. Aly *et al.*⁷ isolated *S. aureus* in 93% of eczematous skin, 76% of non-eczematous skin and in 79% of the anterior nares of patients with atopic dermatitis, compared with an isolation rate of less than 5% from normal individuals. In our study, *S. aureus* was isolated in 69.7% of eczematous skin and 42% of non-eczematous skin of patients with atopic dermatitis, but in only 5% of the 20 controls. This difference was statistically significant. The rate of *S. aureus* nasal carriage in atopic dermatitis patients of 51.5% was higher than that in the controls (35%), although the difference was not statistically significant. The lower rate of nasal carriage compared with other studies may be due to the lower proportion of patients with severe dermatitis, because it is associated with the severity of dermatitis. Our findings support previous results that *S. aureus* colonization is increased on eczematous and

non-eczematous skin and in the anterior nares of patients with atopic dermatitis compared with normal individuals.⁸

The close association between the severity of dermatitis and the skin colonization of *S. aureus*⁶ was confirmed in our study. No difference was noted in the skin colonization rates of *S. aureus* between the different racial and age groups. The role of staphylococcal enterotoxins (superantigens) in skin inflammation is well established.^{9,10} These superantigens are believed to play a role in eczema in atopic dermatitis. Elimination of *S. aureus* may help to eliminate these superantigens and to alleviate the severity of atopic dermatitis.

The high prevalence of skin colonization of *S. aureus* in atopic dermatitis patients, and the higher rates in patients with severe dermatitis, may support the use of antimicrobials in the treatment of patients with severe dermatitis and of topical and/or systemic antimicrobials during the initial therapy of all atopic dermatitis to eradicate all *S. aureus* infection for the control of dermatitis. Systemic antibiotics are preferred over topical antibiotics to reduce the risk of sensitization.

The antimicrobials of choice for treating patients with atopic dermatitis should include only the penicillinase-resistant anti-staphylococcal antimicrobials as our findings indicated that 87% of *S. aureus* isolated was penicillin and ampicillin resistant. Our results showed that all *S. aureus* isolated was sensitive to cloxacillin, cephalexin, clindamycin, and co-trimoxazole. Of significance was the increasing resistance of *S. aureus* to erythromycin (8%). All strains of *S. aureus* were sensitive to co-trimoxazole, a relatively cheap antibiotic compared with the new generation of penicillins and cephalosporin. The disadvantage of co-trimoxazole is the higher incidence of adverse drug reactions, but it is a suitable anti-staphylococcal antibiotic for adults.

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Koch on staining bacteria

Koch was able to avoid all these difficulties in a brilliant manner. His new procedure consisted of 'drying the bacterial suspension in a very thin layer on the cover glass in order to fix the bacteria in one plane, of treating this smear with stains and washing, in order to return the bacteria to their natural form and to make them clearly visible, so that the preparation thus obtained could be mounted in preserving fluids and finally be photographed for obtaining accurate pictures'. Koch accomplished the drying by taking a small drop of the fluid under investigation—putrefying blood, tooth scrapings, or putrefying infusions—on a scalpel and spreading it with a circular motion in the thinnest possible layer, so that the bacteria, blood corpuscles, etc., were not piled up but were separated from each other by larger or smaller spaces. To his surprise he saw that the bacteria adhered to the glass like stiff bodies surrounded by a mucous membrane and dried without appreciably changing their shape either in length or width. The only changes occurring which he could observe consisted in the flattening of spherical, lobate, or branched zoological masses and in the conversion of spiral bodies into wavy lines. On the addition, however, of a drop of potassium acetate solution (1 part to 2 parts distilled water), the mucous sheath of the bacteria could be made to swell up again so that the zoogloea and the spirals resumed their natural form. He showed by means of experiments in returning the dried preparations to water or glycerin that the smear could be quickly loosened and floated off the glass. By immersing the cover glass in absolute alcohol or even better 0.5% chromic acid, the smear could be made almost impossible to remove; but the bacteria, whose mucous sheathes could no longer swell up, could not resume their natural shape. The only practical means, which also served as a splendid preservative, was the solution of potassium acetate. The smallest forms became thereby so pale that it seemed necessary to make them more distinct by means of dyes.

From Conn HJ. *The History of Staining*. Genera, New York: Biotech, 1948.

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