ARTICLE

Role of *Staphylococcus aureus* Nasal Colonization in Atopic Dermatitis in Infants

The Generation R Study

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Objective: To study the association between *Staphylococcus aureus* nasal colonization and atopic dermatitis (AD) in infancy.

Design: Population-based prospective cohort study of pregnant women and their children.

Setting: This project was embedded in the Generation R Study.

Participants: A total of 1079 postnatal Dutch infants/children participated in the focus cohort.

Main Exposures: Nasal swabs for *S aureus* cultivation were taken at ages 1.5, 6, and 14 months.

Main Outcome Measure: Questionnaires that pertain to AD and confounders (birth weight, gestational age, sex, and parental eczema) were completed prenatally and postnatally. The outcome was AD in the first and second years of life.

Results: A first positive culture for *S aureus* at age 6 months was associated with AD prevalence in the first and second years of life (adjusted odds ratio [aOR], 2.13; 95% confidence interval [CI], 1.17-3.87; and aOR, 2.88; 95% CI, 1.60-5.19, respectively) and also with severity (aOR, 3.27; 95% CI, 1.30-8.03). Moreover, frequent colonization in the first year of life (≥2 times) held a 4.29-fold (95% CI, 1.03- to 17.88-fold) risk of moderate to severe AD in the second year of life.

Conclusion: Colonization with *S aureus* at age 6 months and frequent colonization in the first year of life are associated with AD and its severity in young children.

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STAPHYLOCOCCUS AUREUS IS A commensal organism in humans and the cause of a wide range of infections. Besides its role in several invasive diseases, it plays an important role in cutaneous diseases, including atopic dermatitis (AD),[1-3] an inflammatory skin disease that usually presents itself in the first years of life.[4,5] As reported in many studies, *S aureus* is the most important pathogen associated with AD. Skin colonization with *S aureus* is known to be related to AD disease severity.[6]

A significant fraction of the healthy population is colonized with *S aureus* on epithelial surfaces, of which the anterior nares are the most frequent carriage sites.[1,7,8] Longitudinal studies[9-12] distinguish three carriage patterns in healthy adults: noncarriers, intermittent carriers, and persistent carriers. Persistent carriers have a well-documented higher risk of *S aureus* infection, but those carriers barely exist among the infant population.[13-16] The anterior nares may serve as an important endogenous reservoir for involvement in AD, reaching a colonization prevalence of 39% to 82% in adult patients with AD.[17,18] *Staphylococcus aureus* might play a role in the chronicity and severity of AD through its release of superantigenic exotoxins.[19] Specifically, colonization with superantigen-producing *S aureus* is associated with increased severity of AD. *Staphylococcus aureus* enterotoxins A through E and toxic shock syndrome toxin 1, which act as superantigens, have been shown to trigger AD occurrence and severity.[20,21] *Staphylococcus aureus* enterotoxins[22] increase inflammation in AD and provoke the generation of enterotoxin-specific IgE, which correlates with the severity of the disease.[19,23,24]

Longitudinal data on nasal colonization with *S aureus* in infancy were recently described.[16] In addition, we aim to assess the risk of AD after nasal colonization with *S aureus* in healthy infants in the first year of life.

METHODS

STUDY DESIGN AND POPULATION

This project was embedded in the Generation R Study, a population-based prospective cohort study

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Table 1. Population Descriptive[a]

	Total Cohort (N=1079)	Atopic Dermatitis: First Year of Life: No (n=706)	Atopic Dermatitis: First Year of Life: Yes (n=259)	Atopic Dermatitis: Second Year of Life: No (n=685)	Atopic Dermatitis: Second Year of Life: Yes (n=273)
Birth weight, mean (SD), g	3509 (538)	3506 (546)	3537 (505)	3523 (532)	3507 (554)
Gestational age, median (95% range), wk	40.3 (37.1-42.1)	40.3 (37.1-42.1)	40.4 (37.1-42.1)	40.3 (37.1-42.1)	40.3 (36.7-42.1)
Sex, No. (%)					
Female (reference)	521 (48.3)	350 (50.4)	125 (51.7)	332 (48.5)	133 (48.7)
Male	558 (51.7)	356 (49.6)	134 (48.3)	353 (51.5)	140 (51.3)
Eczema symptoms of the mother, No. (%)					
No (reference)	897 (96.6)	595 (97.5)	210 (93.8)	573 (97.1)	221 (95.7)
Yes	32 (3.4)	15 (2.5)	14 (6.2)	17 (2.9)	10 (4.3)
Eczema symptoms of the father, No. (%)					
No (reference)	848 (95.6)	562 (96.2)	203 (92.7)	552 (96.7)	211 (91.7)
Yes	39 (4.4)	22 (3.8)	16 (7.3)	19 (3.3)	19 (8.3)

[a]Data were missing for mother's eczema symptoms (n=150), father's eczema symptoms (n=192), atopic dermatitis between ages 6 and 12 months (n=114), and atopic dermatitis in the second year of life (n=121).

of pregnant women and their infants/children. Detailed assessments were conducted with 1232 pregnant Dutch women and their infants/children. Three infants died perinatally. The remaining mothers gave birth to 1244 infants, of whom 138 were excluded because consent was withdrawn after birth. Twins (n=27) were excluded because they are related, which leaves 1079 infants in the group of postnatal participants. All the children were born between February 1, 2003, and August 1, 2005.[25,26] The medical ethics committee of the Erasmus Medical Center approved the study. Written informed consent was obtained from all the participants.[26]

The infants/children visited the Generation R Study center at age 1.5 months (n=884), 6 months (n=882), and 14 months (n=863). At each visit, nasal samples for *S aureus* isolation were collected: 627 infants had a swab taken at age 1.5 months, 832 at age 6 months, and 757 children at age 14 months. A total of 758 infants/children attended all the visits; 443 provided 3 swabs to use for longitudinal analysis. The number of infants with a swab at age 1.5 months is considerably lower than at the other visits owing to a later start of swab sampling as part of the visit to the research center. None of the infants/children had used antibiotic drugs in the preceding 48 hours.

S AUREUS ISOLATION

Research nurses obtained a nasal swab for *S aureus* isolation at each visit. Nasal samples were taken by the use of a swab that was rubbed through the nostrils. The methods of sampling had been described in more detail previously.[16] Colonization with *S aureus* was analyzed at 1.5, 6, and 14 months of age. In addition, we assessed the importance of the first positive culture result. To assess the importance of frequent *S aureus* colonization in the first year of life on the development of AD, 3 groups of infants were created: never positive, positive once, and positive twice or more.

EXPOSURES AND COVARIATES

Information about date of birth, birth weight, and sex was obtained from midwives and from hospital registries. Gestational age was based on pregnancy dating by means of early ultrasound. Information on parental history of eczema was obtained via prenatal questionnaires.

ATOPIC DERMATITIS

Information that pertains to AD was obtained by the use of an age-adapted version of the validated questionnaire of the International Study of Asthma and Allergies in Childhood at ages 12 and 24 months.[27,28] Parents were asked questions that pertain to previous episodes of eczema, AD treatment, and episodes of itchy rash. These categories were combined to define a dichotomous outcome: presence or absence of AD in the first and the second years of life. The severity score was based on questions that pertain to the level of suffering. Questions related to continuous or intermittent rash, rash clearance, and whether infants were kept awake because of the itchy rash. This resulted in 3 groups: no AD, mild AD (episode of rash without additional symptoms), and moderate to severe AD (episode of rash with additional symptoms).

DATA ANALYSES

We compared the 443 infants with all 3 swabs available with the total cohort of 1079 infants available for postnatal analysis. To study the association between colonization and AD in the first and the second years of life, we performed univariate and multivariate binary logistic regression, adjusted for important confounders such as sex, gestational age, birth weight, and parental history of eczema. To study the association between colonization and severity of AD in the second year of life, we conducted multinomial logistic regression analyses, univariate and multivariate. Infants with missing data for the outcome variable were excluded from the analyses (11.2% of 1079 infants); missing data for the confounders were analyzed in the model as a separate category and, thus, were accounted for in the analyses. Measures of association are presented by crude odds ratios (ORs) and adjusted ORs (aORs) with 95% confidence intervals (CIs). Statistical analyses were performed by the use of a commercially available software program (SPSS version 11.0 for Windows; SPSS Inc, Chicago, Illinois).

RESULTS

Table 1 provides characteristics of infant/child participants and their parents. Of the 1079 participants, 48.3% were girls (n=521), mean (SD) birth weight was 3509 (538) g, and median gestational age was 40.3 weeks (95% range, 37.1-42.1 weeks). Eczema symptoms occurred in 3.4% of the mothers (n=32) and in 4.4% of the fathers (n=39). In the period of 6 to 12 months of age, 259 of 1079 participants (24.0%) experienced AD symptoms.

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Table 2. Association Between *Staphylococcus aureus* Colonization and Atopic Dermatitis in Infancy/Childhood[a]

	Atopic Dermatitis, No. (%)					
	First Year of Life			Second Year of Life		
	No (n=706)	Yes (n=259)	aOR (95% CI)[b]	No (n=685)	Yes (n=273)	aOR (95% CI)[b]
S aureus at age 1.5 mo						
No	198 (47.5)	63 (42.6)	1 [Reference]	204 (48.0)	61 (42.7)	1 [Reference]
Yes	219 (52.5)	85 (57.4)	1.23 (0.83-1.81)	221 (52.0)	82 (57.3)	1.29 (0.87-1.90)
S aureus at age 6 mo						
No	452 (81.4)	151 (72.2)	1 [Reference]	448 (81.9)	151 (70.9)	1 [Reference]
Yes	103 (18.6)	58 (27.8)	1.67 (1.15-2.44)[c]	99 (18.1)	62 (29.1)	1.86 (1.28-2.69)[c]
S aureus at age 14 mo						
No	439 (85.1)	166 (85.1)	NA	438 (85.7)	161 (83.0)	1 [Reference]
Yes	77 (14.9)	29 (14.9)	NA	73 (14.3)	33 (17.0)	1.20 (0.76-1.89)
First positive culture result						
Never	112 (25.9)	30 (18.8)	1 [Reference]	118 (27.3)	30 (18.4)	1 [Reference]
Age 1.5 mo	182 (42.0)	77 (48.1)	1.59 (0.98-2.59)	221 (51.0)	82 (50.3)	1.36 (0.83-2.23)
Age 6 mo	60 (13.9)	33 (20.6)	2.13 (1.17-3.87)[c]	54 (12.5)	38 (25.3)	2.88 (1.60-5.19)[c]
Age 14 mo	79 (18.2)	20 (12.5)	NA	40 (9.2)	13 (8)	1.60 (0.88-2.91)
S aureus frequency[d]						
Never	112 (37.2)	30 (26.1)	NA	163 (42.9)	41 (32.5)	1 [Reference]
Once	132 (43.9)	55 (47.8)	NA	172 (45.3)	61 (48.4)	1.18 (0.69-2.01)
≥2 Times	57 (18.9)	30 (26.1)	NA	45 (11.8)	24 (19.0)	2.03 (1.10-3.74)[c]

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; NA, not applicable (because the determinant should occur before the outcome).
[a] Of the total group (N=1079), 627 participants had a swab at age 1.5 months, 832 at 6 months, and 757 at 14 months.
[b] Adjusted for sex, birth weight, gestational age, and the eczema history of the parents.
[c] $P<.05$.
[d] Only 443 participants with 3 swabs available were analyzed.

A total of 273 of 1079 infants (25.3%) participants experienced AD in the second year of life (Table 1).

Table 2 shows the multivariate analyses. Colonization with *S aureus* at 6 months was associated with AD in the first and the second years of life (aOR, 1.67; 95% CI, 1.15-2.44; and aOR, 1.86; 95% CI, 1.28-2.69, respectively). Participants with their first positive swab result at age 6 months (a negative swab result at 1.5 months) had an even greater increased risk of AD symptoms in the first (aOR, 2.13; 95% CI, 1.17-3.87) and second (aOR, 2.88; 95% CI, 1.60-5.19) years of life. Participants with a higher frequency of colonization in the first year of life (≥2) had an increased risk of AD in the second year of life (OR, 2.00; 95% CI, 1.10-3.63), and this effect remained significantly associated after adjustment for confounders (aOR, 2.03; 95% CI, 1.10-3.74).

Of the 273 children with AD in the second year of life, 55 (20.1%) had moderate to severe AD and 218 had a mild phenotype (79.9%) (**Table 3**). Colonization with *S aureus* was also correlated with severity of AD. Infants colonized at age 6 months had an increased risk of mild and moderate to severe AD in the second year of life. However, a higher risk was found for those with moderate to severe AD (aOR, 3.27; 95% CI, 1.30-8.03) compared with mild AD (aOR, 1.57; 95% CI, 1.04-2.37). Frequent *S aureus* colonization in the first year of life (≥2 times) was associated with moderate to severe AD symptoms (aOR, 4.29; 95% CI, 1.03-17.88) but not with mild AD (aOR, 1.71; 95% CI, 0.89-3.31) in the second year of life.

An additional analysis was performed to assess whether infants with AD in the first year of life have an increased risk of colonization as a result. We did not find a significant association between AD in the first year of life and *S aureus* colonization at age 14 months.

Because we selected 443 of 1079 infants for a part of the analyses, selection bias may have occurred. Overall, looking at the differences between the selected 443 infants with 3 swabs available and the total cohort of 1079 infants, the selected infants had fewer missing data from the questionnaires. The infants without 3 swabs available were more likely to have filled out the questionnaire incompletely or not at all.

Of the 443 selected participants, 26.0% had AD in the first year of life and 23.3% in the second year of life. We missed data that pertain to AD symptoms for 6.1% and 4.3% in this selected group. Of the remaining participants in the total cohort (n=636), 22.6% and 26.7% experienced AD in the first and second years of life, respectively, and data were missing for 13.7% and 16.0% in the first and second years of life, respectively. The eczema history of the mother was similar in the group of 443 participants as from the total cohort (82.8% and 83.3%, respectively). Missing data were fairly equal in these groups (15.1% vs 13.1%), contrary to the eczema history of the fathers, which was missing more often in the total cohort vs the selected group (21.7% vs 12.2%).

COMMENT

Bacterial colonization is considered to be an important factor in the pathogenesis of AD.[29] We found a clear association, after adjustment for important confounders, between the prevalence of *S aureus* nasal colonization at

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Table 3. *Staphylococcus aureus* Colonization and Atopic Dermatitis Severity in the Second Year of Life

	Atopic Dermatitis in the Second Year of Life			
	Mild (n=218)		Moderate to Severe (n=55)	
	OR	aOR[a]	OR	aOR[a]
S aureus at age 1.5 mo				
No	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.09 (0.73-1.65)	1.15 (0.75-1.75)	2.37 (0.97-5.80)	2.24 (0.90-5.57)
S aureus at age 6 mo				
No	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.57 (1.05-2.35)[b]	1.57 (1.04-2.37)[b]	3.39 (1.77-6.49)[b]	3.27 (1.30-8.03)[b]
S aureus at age 14 mo				
No	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Yes	1.43 (0.89-2.28)	1.39 (0.87-2.24)	0.51 (0.15-1.72)	0.50 (0.15-1.68)
S aureus[c]				
Never	1 [Reference)	1 [Reference]	1 [Reference]	1 [Reference]
Once	1.06 (0.61-1.86)	1.07 (0.61-1.89)	2.19 (0.57-8.42)	2.11 (0.54-8.25)
≥2 Times	1.70 (0.90-3.22)	1.71 (0.89-3.31)	4.67 (1.17-18.70)[b]	4.29 (1.03-17.88)[b]

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; OR, odds ratio.
[a] Adjusted for sex, birth weight, gestational age, and the eczema history of the parents.
[b] $P < .05$.
[c] Only 443 participants with 3 swabs available were analyzed.

6 months of age and the occurrence of AD in the first and second years of life in a healthy cohort. Moreover, frequent nasal colonization with *S aureus* in the first year of life held an increased risk of AD in the second year of life; this risk was especially increased in moderate to severe AD. This finding is in line with previous studies that show a relationship between *S aureus* and AD in several ways. Semic-Jusufagic et al[24] showed, in a similar cohort study, a positive association between specific IgE staphylococcal enterotoxin mix and AD in children. Other studies[21,30] reported increased levels of antistaphylococcal IgE and staphylococcal toxins A to E in the serum of patients with AD. No other studies, to our knowledge, have reported on nasal colonization of *S aureus* as a risk factor that precedes AD in infants.

Colonization at age 6 months may be a critical event in the development of the immune system of infants. Barely any immunoglobulins from the mother are left at this age, and the immune system of the infant is still developing. It, therefore, is important to take this moment in the first year of life into account during the study of bacterial colonization and the development of AD in childhood.

We found that the severity of AD was associated with *S aureus* nasal colonization. Infants who test positive at age 6 months have not only an increased risk of AD but also a significant increased risk of moderate to severe AD compared with noncarriers. Moreover, a more than 4-fold risk was found in this cohort for participants with at least 2 instances of *S aureus* colonization in the first year of life. This result is additional to data pertaining to severity presented by other researchers.[24] Several studies[24,31,32] describe an association between colonization and a higher eczema severity score.

This study provides data that pertain to nasal colonization of *S aureus* that precedes AD adjusted for several confounders, which support a direct link between colonization and AD in one of the largest birth cohorts to be studied. In our study, 443 was the smallest number of infants with all 3 swabs available: this number is large compared with the numbers from other studies of its kind. A larger sample was studied for the individual swab results. Selection bias may have occurred by the choice to analyze 443 infants of the total cohort of 1079. These 443 infants were selected based on their attendance at the research center and willingness to provide a nasal swab. One can speculate whether these are children with fewer or more physical problems. Either the parents may be more willing to participate when their child is ill or medical care is sought in different ways when the child is too ill to participate, with the implication that study participation in that instance is not wanted by the parents. However, because we do not see great differences in AD prevalence between the selected 443 participants and the total cohort, selection by AD is not likely to have happened. It could be the case for other illnesses and infections, and selection bias by socioeconomic status may have occurred.

In addition to the analyses of bacterial colonization that precede episodes of AD, we also analyzed bacterial colonization after an episode of AD in the first year of life, which showed no significance. This result allows us to draw conclusions that pertain to AD after bacterial colonization with *S aureus* rather than the other way around.

Symptoms of AD were not confirmed by any of the physicians in this study. However, the questionnaire used was validated and age adapted.[27,28] Information bias owing to knowledge of the main determinant is unlikely to have occurred because the parents, who filled out the questionnaire that pertains to AD and confounders, were not notified of the colonization status of their infants.

We did not study methicillin-resistant *S aureus* (MRSA) colonization in this study. Not only was this phenomenon outside the scope of this study, but the prevalence of MRSA in the Netherlands is among the lowest in the world.[33] To study MRSA in a Dutch population cohort would not be very important. Nasal colonization and colonization of the affected skin in patients with AD are strongly associ-

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ated, which may explain a pathophysiologic role for *S aureus* nasal colonization and AD.[34] One can speculate about a systemic release of enterotoxin-specific IgE against superantigens of *S aureus* that could lead to AD.

These results are in line with, and in addition to, literature that suggests a potentially pathophysiologic role for *S aureus* in AD.[24,29] Further studies are required to clarify the exact pathophysiologic role of *S aureus* colonization in relation to AD.

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Correction

Incorrect Data: In the Original Article entitled "Role of *Staphylococcus aureus* Nasal Colonization in Atopic Dermatitis in Infants: The Generation R Study" (2009;163[8]:745-749), incorrect data appear in **Table 2** and **Table 3**, footnotes *a* and *d* in Table 2, footnote *d* in Table 3, and the text. The corrected tables appear here. In addition, the text referring to Table 2 and Table 3 on page 746 should read as follows: "At each visit, nasal samples for *S aureus* isolation were collected: 622 infants had a swab taken at age 1.5 months, 774 at age 6 months, and 706 children at age 14 months. A total of 758 infants/children attended all the visits; 353 provided 3 swabs to use for longitudinal analysis." The text referring to Table 2 and Table 3 on page 747 should read as follows: "Because we selected 353 of 1079 infants for a part of the analyses, selection bias may have occurred. Selected infants had fewer missing data from the questionnaires."

"Of the 353 selected participants, 26.0% had AD in the first year of life and 23.3% in the second year. We missed data that pertain to AD symptoms for 6.1% and 4.3%, respectively. Of the remaining participants in the total cohort (n=636), 22.6% and 26.7% experienced AD in the first and second years of life, respectively, and data were missing for 13.7% and 16.0%, respectively. The eczema history of the mother was similar to the total cohort." The text referring to Table 2 and Table 3 on page 748 should read as follows: "In our study, 353 was the smallest number of infants with all 3 swabs available. A larger sample was studied for the individual swab results. These 353 infants were selected based on their attendance at the research center and willingness to provide a nasal swab. One can speculate whether these are children with fewer or more physical problems. Either the parents may be more willing to participate when their child is ill or medical care is sought in different ways when the child is too ill to participate, with the implication that study participation in that instance is not wanted by the parents. However, because we do not see great differences in AD prevalence between the selected 353 participants and the total cohort, selection by AD is not likely to have happened."

Table 2. Association Between *Staphylococcus aureus* Colonization and Atopic Dermatitis in Infancy/Childhood[a]

	Atopic Dermatitis, No. (%)					
	First Year of Life			Second Year of Life		
	No (n=706)	Yes (n=259)	aOR (95% CI)[b]	No (n=685)	Yes (n=273)	aOR (95% CI)[b]
S aureus at age 1.5 mo						
No	195 (47.2)	63 (42.6)	1 [Reference]	201 (47.6)	61 (43.3)	1 [Reference]
Yes	218 (52.8)	84 (57.4)	1.21 (0.82-1.78)	221 (52.4)	80 (56.7)	1.24 (0.83-1.83)
S aureus at age 6 mo						
No	417 (81.8)	140 (71.4)	1 [Reference]	413 (81.9)	142 (71.0)	1 [Reference]
Yes	93 (18.2)	56 (28.6)	1.77 (1.20-2.61)[c]	91 (18.1)	58 (29.0)	1.84 (1.25-2.70)[c]
S aureus at age 14 mo						
No	413 (85.3)	154 (84.6)	NA	406 (85.8)	151 (82.5)	1 [Reference]
Yes	71 (14.7)	28 (15.4)	NA	67 (14.2)	32 (17.5)	1.23 (0.77-1.97)
First positive culture result						
Never (reference)	87 (22.4)	23 (15.2)	1 [Reference]	90 (23.0)	25 (16.4)	1 [Reference]
Age 1.5 mo	212 (54.5)	84 (55.6)	1.46 (0.86-2.47)[c]	216 (55.2)	79 (52.0)	1.30 (0.77-2.20)
Age 6 mo	54 (13.9)	31 (20.5)	2.25 (1.17-4.30)[c]	50 (12.8)	34 (22.4)	2.59 (1.34-4.91)[c]
Age 14 mo	36 (9.3)	13 (8.6)	NA	35 (9.0)	14 (9.2)	1.39 (0.64-3.02)
S aureus frequency[d]						
Never	87 (37.0)	23 (24.2)	NA	90 (35.6)	25 (29.4)	1 [Reference]
Once	102 (43.4)	44 (46.3)	NA	115 (45.5)	32 (37.6)	1.02 (0.56-1.87)
≥2 times	46 (19.6)	28 (29.5)	NA	48 (19.0)	28 (32.9)	2.0 (1.04-3.98)[c]

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; NA, not applicable.
[a] Of the total group (n=1079), 622 participants had a swab at age 1.5 months, 774 at 6 months, and 706 at 14 months.
[b] Adjusted for sex, birth weight, gestational age, and the eczema history of the parents.
[c] $P<.05$.
[d] Only 353 participants with 3 swabs available were analyzed.

Table 3. *Staphylococcus aureus* Colonization and Atopic Dermatitis Severity in the Second Year of Life

	Atopic Dermatitis in the Second Year of Life			
	Mild (n=218)		Moderate to Severe (n=55)	
	OR	aOR[a]	OR	aOR[a]
S aureus at age 1.5 mo	1.04 (0.69-1.58)[b]	1.10 (0.72-1.67)[b]	2.34 (0.96-5.72)[b]	2.21 (0.89-5.48)[b]
S aureus at age 6 mo	1.56 (1.03-2.38)[b,c]	1.55 (1.01-2.37)[b,c]	3.36 (1.72-6.53)[b,c]	3.30 (1.68-6.47)[b,c]
S aureus at age 14 mo	1.52 (0.94-2.45)	1.45 (0.89-2.37)	0.52 (0.16-1.74)	0.50 (0.15-1.70)
S aureus[c]				
Never	1 [Reference]	1 [Reference]	1 [Reference]	1 [Reference]
Once	0.93 (0.49-1.74)	0.94 (0.49-1.80)	1.57 (0.38-6.43)	1.57 (0.37-6.69)
≥2	1.79 (0.90-3.58)	1.69 (0.81-3.49)	4.38 (1.08-17.69)[d]	4.50 (1.04-19.43)[d]

Abbreviations: aOR, adjusted odds ratio; OR, odds ratio.
[a] Adjusted for sex, birth weight, gestational age, and the eczema history of the parents.
[b] No infection is the Reference group.
[c] $P<.05$.
[d] Only 353 participants with 3 swabs available were analyzed.

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