Original paper

The role of *Staphylococcus aureus* in atopic dermatitis: microbiological and immunological implications

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Abstract

Introduction: Atopic dermatitis (AD) is an inflammatory disease characterised by chronic and recurrent course. Its predominant symptom is skin pruritus. Therefore, many AD patients have recurrent skin infections and are susceptible to the colonisation of apparently healthy skin and nasal vestibule by *Staphylococcus aureus* (*S. aureus*). Some *S. aureus* strains are capable of producing exotoxins.

Aim: To assess the relation between the total IgE (tIgE) and asIgE targeted against SEA (SEA-sIgE) and SEB (SEB-sIgE), as indicators of the severity of the course of AD, and the presence of S. aureus on apparently healthy skin, in skin lesions and in the nasal vestibule.

Material and methods: The research was performed in a population of 134 AD patients (61 men and 73 women) aged 2–86 years. Three smears were collected for microbiological investigations: from the nasal vestibule, from the skin where lesions appeared at the moment of investigations and from the skin which was free from the eczema. On collection the material was cultured on solid and broth mediums. After incubation each medium was thoroughly analysed for the presence of *S. aureus*.

Results: There was a statistically significant correlation between healthy skin colonisation by *S. aureus* and increased SEA-sIgE. The same correlation was proved between healthy skin colonisation by *S. aureus* and increased SEB-sIgE. There was a statistically significant correlation between colonisation of the nasal vestibule by *S. aureus* and the SEA-sIgE and SEB-sIgE serum concentration.

Conclusions: It seems that the colonisation of the lesioned skin, healthy skin and the anterior nares by *S. aureus* is related with higher tIgE serum concentration, which translates to more severe course of the disease. Significantly increased SEA-IgE and SEB-IgE concentrations were observed in the patients whose tIgE serum concentration was statistically higher.

Key words: atopic dermatitis, *Staphylococcus aureus*.

Introduction

Atopic dermatitis (AD) is an inflammatory disease characterised by chronic and recurrent course. Its predominant symptom is skin pruritus [1]. It is often related with the positive family history of atopy [2]. Disrupted epidermal barrier mechanisms seem to play a significant role in the AD pathogenesis [3].

During the course of an acute phase of AD we can observe imbalance between Th1 and Th2 cells, the latter being more numerous [4]. In consequence, there is an intensified humoral response and reduced cellular immunity, which leads to higher susceptibility to infections [2, 5]. Therefore, many AD patients have recurrent skin infections and are susceptible to the colonisation of apparently healthy skin and nasal vestibule by *Staphylococcus aureus* (*S. aureus*) [6, 7]. The pathogen is commonly thought to exacerbate the dermatological condition [8].

Some *S. aureus* strains are capable of producing exotoxins, such as staphylococcal enterotoxins A (SEA),

B (SEB), C (SEC), D (SED) and the toxic shock syndrome toxin (TSST-1) [9].

These infectious agents may function as superantigens (SAgs), causing non-specific stimulation of T lymphocytes (polyclonal T lymphocyte activation). They may also act as classic allergens, inducing response with allergen-specific IgE (asIgE) [10].

Increased production of IgE antibodies proves the advantage of humoral factors in AD. However, the serum concentration of this immunoglobulin is normal in about 20% of patients. IgE synthesis depends on a wide range of endogenic factors, such as cytokines and superficial particles, environmental factors (allergens, parasites, drugs) and genetic predispositions [11].

There are increasingly frequent opinions that IgE is produced not only in response to airborne and food allergens, but it is also induced by autoimmune allergens [12]. This phenomenon applies to 23–91% of AD patients [13].

Aim

The aim of the study was to assess the relation between the total IgE (tIgE) and asIgE targeted against SEA (SEA-sIgE) and SEB (SEB-sIgE), as indicators of the severity of the course of AD, and the presence of *S. aureus* on apparently healthy skin, in skin lesions and in the nasal vestibule.

Material and methods

The research was performed as a routine diagnostic procedure in a population of 134 consecutive AD patients (61 men and 73 women) aged 2–86 years. Our group of 134 patients included 51 children and adolescents up to 18 years, and 83 adults (78 patients up to 60 years and only 5 patients over 60 years). The recruitment of patients followed the AD diagnostic criteria developed by Hanifin and Rajka [14]. Three smears were collected for microbiological investigations: from the nasal vestibule, from the skin where lesions appeared at the moment of investigations and from the skin which was free from the eczema. No healthy skin smears were collected from some patients as they suffered from erythroderma. Other patients, who have been consulted at the dermatological outpatient clinic for a follow-up examination, had no inflammatory lesions after remission of the disease. Patients with a history of a systemic or local antibiotic therapy in the last 4 weeks were eliminated from the study group. Only patients who had received the last dose at least 2 weeks earlier were qualified for the research. No smear was collected from the anterior nares of the patients suffering from upper respiratory tract infections because the research results might have been falsified by the possible predominance of another aetiological factor of the infection. Smears were collected from three places: the nasal vestibule and/or apparently healthy skin and/

or diseased skin to sterile swabs which had been moistened with sterile saline for better adsorption of microorganisms from the surface of the mucosa and/or skin. On collection the material was cultured on solid and broth mediums provided by bioMerieux and Argenta. Culture was carried out on the Columbia agar with 5% sheep blood and Chapman's medium. After incubation each medium was thoroughly analysed for the presence of *S. aureus*. The strains were identified and their sensitivity to antibiotics was assessed by means of the Vitek 2 system (bioMerieux).

Apart from that, about 10 ml of venous blood was collected from each patient. The serum samples were stored at a temperature of –75°C until analysis. The tIgE and asIgE were measured by means of the fluoro-immuno-enzymatic method, according to the manufacturer's instructions (UniCAP, Phadia). The asIgE values greater than 0.7 kU/l (i.e. class 2) were regarded as a considerably higher level of antibodies. The Mann-Whitney test was used for comparison of the tIgE serum concentration, SEA-sIgE and SEB-sIgE as well as the frequency of *S. aureus* incidence on apparently healthy skin, in skin lesions and in the anterior nares.

Fisher's exact test was used to examine the relation between the incidence of *S. aureus* on apparently healthy skin and in skin lesions and the high tIgE serum concentration according to the age norm.

Results

The mean tIgE in the patients with *S. aureus* on apparently healthy skin was 2,695 ±2,249.1 kU/l. When the culturing from apparently healthy skin gave negative results, the mean tIgE was 1,428 ±1,830.8 kU/l.

The mean tIgE in the patients with *S. aureus* in skin lesions was 2,460 ±2,190.7 kU/l. In the group of patients without *S. aureus* in skin lesions, the mean tIgE was 939 ±1,229.4 kU/l.

In the group of patients carrying *S. aureus* in the nasal vestibule, the mean tIgE was 2,483 ±2,159.1 kU/l. In the patients who did not carry *S. aureus*, the mean tIgE was 927 ±1,542.8 kU/l.

The statistical analysis of the results of tIgE measurements in the patients' serum showed that there was a statistically significant relation between the presence of *S. aureus* in different locations and the tIgE level (Table 1).

As far as SEA is concerned, in the patients with *S. aureus* in skin lesions, the mean SEA-sIgE was 1.65 ±3.742 kU/l. In those without *S. aureus* in that location, the mean SEA-sIgE was 1.69 ±5.318 kU/l (Table 2).

In the patients with positive *S. aureus* cultures on apparently healthy skin, the mean SEA-sIgE was 2.55 ±4.909 kU/l. In those with negative cultures, the mean SEA-sIgE was 0.604 ±0.914 kU/l (Table 2).

If the patients carried *S. aureus* in their nasal vestibule, the mean SEA-sIgE was 2.14 ±4.397 kU/l. The mean

SEA-sIgE in the patients without *S. aureus* in their anterior nares was 1.362 ±3.802 kU/l (Table 3).

As far as SEB is concerned, the mean serum SEB-sIgE values amounted to 1.13 ±1.804 kU/l in the patients with *S. aureus* in skin lesions. If *S. aureus* was not found, the SEB-sIgE value was 0.417 kU/l.

If *S. aureus* was found on apparently healthy skin, the SEB-sIgE values amounted to 2.15 ±3.849 kU/l. If *S. au-*

Table 1. The mean tIgE in the atopic dermatitis patients' serum, allowing for the presence of *S. aureus* in different locations, and the results of statistical analysis

tIgE [kU/l]	*Staphylococcus* found	*Staphylococcus* not found	Statistical significance
Skin lesions:	*n* = 64	*n* = 15	*p* = 0.0316*
Mean tIgE ± SD	2,460 ±2,190.7	939 ±1,229.4	
Median	2,103	479	
Min.–max.	2.63–5,001	10.3–3857	
Healthy skin:	*n* = 48	*n* = 31	*p* = 0.0272*
Mean tIgE ± SD	2,695 ±2,249.1	1,428 ±1,830.8	
Median	2829	848	
Min.–max.	2.63–5,001	12.1–5,001	
Anterior nares:	*n* = 67	*n* = 12	*p* = 0.0216*
Mean tIgE ± SD	2,483 ±2,159.1	927 ±1,542.8	
Median	2,263.0	191.0	
Min.–max.	2.63–5,001	10.3–5,001	

Mann-Whitney test.

Table 2. The tIgE results exceeding the age norm, with reference to the presence of *S. aureus* in different locations, and the results of statistical analysis

Skin lesions	tIgE greater than normal – age norm interpretation		Statistical significance
	S. aureus found	*S. aureus* not found	
	56/64 (83.6%)	11/15 (73.3%)	*p* = 0.2269**
Healthy skin	42/48 (87.5%)	25/31 (80.7%)	*p* = 0.5238**
Anterior nares	58/67 (86.6%)	8/12 (66.7%)	*p* = 0.1031*

*Mann-Whitney test, **Fisher's exact test.*

Table 3. The mean SEA-sIgE in the atopic dermatitis patients' serum, allowing for the presence of *S. aureus* in different locations, and the results of statistical analysis

SEA-sIgE [kU/l]	*S. aureus* found	*S. aureus* not found	Statistical significance
Skin lesions:	*n* = 65	*n* = 15	*p* = 0.2071*
Mean SEA-sIgE ± SD	1.65 ±3.742	1.69 ±5.318	
Median	0.5	0.34	
Min.–max.	0.004–27.6	0.04–20.9	
Healthy skin:	*n* = 49	*n* = 31	*p* = 0.0103*
Mean SEA-sIgE ± SD	2.55 ±4.909	0.604 ±0.914	
Median	0.74	0.34	
Min.–max.	0.004–27.6	0.004–3.89	
Anterior nares:	*n* = 69	*n* = 12	*p* = 0.0271*
Mean SEA-sIgE ± SD	2.14 ±4.397	1.36 ±3.802	
Median	0.5	0.34	
Min.–max.	0.004–27.6	0.004–13.4	

Mann-Whitney test.

Table 4. The mean SEB-sIgE in the atopic dermatitis patients' serum, allowing for the presence of *S. aureus* in different locations, and the results of statistical analysis

SEB-sIgE [kU/l]	*S. aureus* found	*S. aureus* not found	Statistical significance
Skin lesions:	*n* = 65	*n* = 15	*p* = 0.0731*
Mean SEB-sIgE ± SD	1.13 ±1.804	0.417 ±0.598	
Median	0.35	0.28	
Min.–max.	0.0–12.4	0.02–2.45	
Healthy skin:	*n* = 49	*n* = 31	*p* = 0.0044*
Mean SEB-sIgE ± SD	2.15 ±3.849	0.404 ±0.428	
Median	0.79	0.34	
Min.–max.	0.0–21.3	0.002–1.85	
Anterior nares:	*n* = 69	*n* = 12	*p* = 0.0323*
Mean SEB-sIgE ± SD	1.84 ±3.426	5.54 ±18.348	
Median	0.39	0.31	
Min.–max.	0.0–21.3	0.01–63.8	

Mann-Whitney test.

Table 5. The number of patients with positive IgE antibodies specific to SEA and/or SEB

Antibodies	SEA-sIgE (%)	SEB-sIgE (%)	SEA-sIgE or SEB-sIgE (%)	SEA-sIgE and SEB-sIgE (%)	tIgE (%)
Patients	44/134 (32.8)	44/134 (32.8)	55/134 (41)	33/134 (24.6)	107/134 (79.8)

Table 6. A comparison of data of four patients with the highest SEA-sIgE and SEB-sIgE levels

Parameter	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Female	Male	Male	Female
Age	25	39	28	6
Total IgE [kU/l]	3857	> 5000	> 5000	> 5000
SEA-sIgE [kU/l]	20.9 (class 4)	27.6 (class 4)	4.48 (class 3)	13.4 (class 3)
SEB-sIgE [kU/l]	2.45 (class 2)	2.27 (class 2)	21.3 (class 4)	63.8 (class 5)
SA on AS	No	Yes	Not achieved done	Not achieved done
SA on UAS	Not achieved done	Yes	Yes	Not achieved done
SA in AN	Not achieved done	Yes	Yes	No

SA – Staphylococcus aureus, AS – affected skin, UAS – unaffected skin, AN – anterior nares.

reus was not found in that location, the mean SEB-sIgE was 0.404 ±0.428 kU/l.

If the patients carried *S. aureus* in their nasal vestibule, SEB-sIgE was 1.84 ±3.426 kU/l. SEB-sIgE in the patients without *S. aureus* in their anterior nares was 5.54 ± 18.348 kU/l (Table 4).

There was a statistically significant correlation between healthy skin colonisation by *S. aureus* and increased SEA-sIgE. The same correlation was proved between healthy skin colonisation by *S. aureus* and increased SEB-sIgE. There was a statistically significant correlation between colonisation of the nasal vestibule by *S. aureus* and the SEA-sIgE and SEB-sIgE serum concentration. There was no statistically significant correlation

between the colonisation of skin lesions by *S. aureus* and the SEA-sIgE value. The correlation between the colonisation of skin lesions by *S. aureus* and the SEB-sIgE serum concentration was within the significance limit.

The skin colonisation of *S. aureus* was very similar in both children (45%) and adults (49%). Nasal carriage also occurred at a very similar level – children 47% and adults 53%. The difference occurred only in the colonisation of the healthy skin (children 27% and adults 41%).

In total, 55 out of 134 patients (41%) had positive SEA-sIgE or SEB-sIgE results. 44 out of 134 patients (32.8%) had positive SEA-sIgE results. The same number of patients, i.e. 44 out of 134 (32.8%) had positive SEB-sIgE results. In 107 out of 134 patients (79.8%) the tIgE

was higher than the age norm. In 33 out of 134 patients (24.6%), both the SEA-sIgE and SEB-sIgE were significantly higher (Table 5).

In the population of AD patients, the highest SEA-sIgE values were noted in classes 4 and 3. As far as SEB-sIgE is concerned, the highest values were noted in classes 5 and 4. The group with the highest values consisted of four patients: two men and two women aged 6, 25, 28 and 39 years. All of them had higher tIgE levels than the age norm (3 patients > 5000 kU/l, 1 patient – 3857 kU/l). The patients were hospitalised at the local Clinic of Dermatology and they had erythroderma diagnosed (Table 6).

Discussion

Abeck and Mempel *et al.* stress a big contrast between the incidence of skin colonisation by *S. aureus* in healthy patients (2–25%) and the incidence of the bacteria in AD patients, which ranges from 76% on apparently healthy skin to as much as 100% in oozing lesions [15].

30–60% of *S. aureus* strains isolated from AD patients are capable of producing exotoxins, which are superantigens [7, 9, 16, 17].

The study by Langer *et al.* confirmed the presence of *S. aureus* strains capable of synthesising exotoxins with SAg characteristics in 65% of AD patients. The clinical picture of AD was more severe in this group of patients. The researchers also proved that epidermal application of SEB caused skin inflammation [18].

Strange *et al.* were the first researchers to prove that SAgs caused erythema and inflammatory infiltration both in AD patients' apparently healthy skin and in healthy patients' skin [19].

SAgs are thought to be capable of stimulating cytokine production in T lymphocytes and macrophages [20], which results in a more intense manifestation of SAgs-mediated diseases [21].

However, many researchers question the role of SAgs in AD. Jappe *et al.* stress the fact that only about 50% of isolated *S. aureus* strains are capable of producing SAgs. On the other hand, SAgs-producing strains can be found in healthy people [22].

In the study by Zollner *et al.*, 57% of *S. aureus* strains isolated from AD patients produced exotoxins with SAg properties. In the control group of healthy patients, this value amounted to 33%. The researchers observed that the presence of *S. aureus* strains, which were capable of producing SAgs, was related with more acute AD and a higher SCORAD (SCORing Atopic Dermatitis) score. The course of the disease was not related with the SEA-sIgE and SEB-sIgE values. What is more, the colonisation by SAgs-producing *S. aureus* strains was related with considerably lower tIgE values, according to the theory that a high SAg concentration inhibited IgE production [9].

Our research proved that the presence of *S. aureus* in different locations was related with higher tIgE in the AD patients' serum.

IgE production in response to bacterial SAgs is secondary to the activation of B lymphocytes, which depends on the presence and activation of T lymphocytes. High SAg concentrations inhibit IgE production. It is probably caused by IFN-γ and/or IFN-α, which is produced in response to high bacterial SAg concentrations. Zollner *et al.* surprisingly observed that the tIgE in AD patients colonised by SAg-producing *S. aureus* strains was lower than in the patients with *S. aureus* strains incapable of SAg production. Thus, the local high SAg concentration reduces IgE production. IFN-γ induction is characteristic of chronic lesions in the course of AD [9].

Yagi *et al.* presented the detectability of SAg-producing *S. aureus* strains in different locations on AD patients' skin. They found 40.7% on apparently healthy skin, 61.7% in non-oozing eczemas, described as excessive dryness, and as much as 75.3% in oozing lesions [23].

In view of the observations made by Zollner *et al.* and Yagi *et al.*, we can suppose that the presence of an SAg-producing *S. aureus* strain on lesioned skin (this is, where it grows dynamically), especially in oozing lesions, will inhibit IgE synthesis and in consequence, SEA/SEB-asIgE. On the contrary, on apparently healthy skin, where the count of SAg-producing *S. aureus* strains is low, the production of IgE as well as SEA/SEB-asIgE is high. This might explain our observations.

Apart from that, we observed that the colonisation of healthy skin by *S. aureus* caused an increase in SEA-sIgE and SEB-sIgE. We also observed a significant increase in the SEA-sIgE and SEB-sIgE serum concentration if *S. aureus* strains were found in the nasal vestibule. We did not observe any statistically significant relation between the colonisation of lesioned skin by *S. aureus* and the SEA-sIgE value. As far as SEB-sIgE is concerned, the relation was within the significance limit.

There are numerous reports which show that the SEA-sIgE and SEB-sIgE serum concentration is high both in AD children and adults [24–28].

Leung *et al.* found SEA-sIgE, SEB-sIgE and TSST-sIgE in 57% of AD patients [24]. Tada *et al.* noted that in 80% of AD patients, the SEA-sIgE or SEB-sIgE values exceeded 0.35 kU/l [25]. According to Bunikowski *et al.*, the SEA-sIgE or SEB-sIgE serum concentration was greater than 0.7 kU/l in 34% of AD children [26].

Lin *et al.* proved an increase in the SEA-sIgE or SEB-sIgE serum concentration in most AD children (88%) (respectively, they regarded values exceeding 0.16 kU/l and 0.7 kU/l to be positive) – SEA-sIgE was found in 70% of the children and SEB-sIgE was also found in 70% of this age group. Increased SEA-sIgE or SEB-sIgE values were very rarely observed in a group of children with dermatoses other than AD, although they were colonised by *S. aureus* strains producing exotoxins with SAg charac-

teristics [27]. Our research proved positive SEA-sIgE and SEB-sIgE values in AD patients (32.8% and 32.8%, respectively). There were positive SEA-sIgE or SEB-sIgE values in 41% of the patients. There were increased both SEA-sIgE and SEB-sIgE values in 24.6% of the AD patients. The researchers suggest that SEA-sIgE and SEB-sIgE may be characteristic of AD. They indicate that *S. aureus* induces asIgE-mediated immune response by causing an exotoxin with SAg characteristics to penetrate into the skin [27]. Like Bunikowski *et al*., they confirm the relation between the SEA-sIgE and SEB-sIgE serum concentration and the intensity of skin lesions [26]. However, Tada *et al*. did not note this relation [25].

Ide *et al*. reported that in a group of AD children increased SEA-sIgE and SEB-sIgE serum concentration amounted to 33.6%. Positive SEA-sIgE results amounted to 17.9%, whereas positive SEB-sIgE results amounted to 29.3% (values exceeding 0.7 U/ml, i.e. class 2, were considered positive). The greatest number of increased values was found in a group of schoolchildren, whereas the smallest number was noted in infants. The tIgE serum concentration was significantly higher in the group of children with positive SEA-sIgE or SEB-sIgE values. Interestingly, the researchers concluded that the percentage of positive SEA-sIgE or SEB-sIgE values in the patients whose clinical condition deteriorated in the summer months was higher than in patients whose clinical condition exacerbated in the winter. This phenomenon may have been related with better conditions for the growth of *S. aureus*, higher temperatures and air humidity in the summer. *S. aureus* was isolated in all the patients with positive SEA-sIgE or SEB-sIgE values. There was no difference between the incidence of the MRSA strain in the AD patients with positive or negative SEA-sIgE or SEB-sIgE values. Apart from that, the researchers confirmed the fact that significantly higher values corresponded with acute AD. It seems that the percentage of positive SEB-asIgE was higher than the percentage of positive SEA-asIgE. SEB is related with a local infection, whereas SEA is usually found in the toxic shock syndrome [28]. Our patients with the highest SEA-sIgE and SEB-sIgE values were characterised by more severe AD. Exacerbations required hospitalisation. The adult patients were aged 25-39 years and there was a 6-year-old girl.

Langer *et al*. obtained 44% of positive SEA-sIgE values and 47% of positive SEB-sIgE values (values exceeding 0.35 U/ml were interpreted as positive). The SEA-sIgE values ranged from 0.44 to 21.40 kU/l (4.07 ±5.84 kU/l, mean ± SD), whereas the SEB-sIgE values ranged from 0.38 to 89.60 kU/l (9.20 ±22.63 kU/l, mean ± SD). The researchers conducted patch tests, using different concentrations of SEA and SEB extracts in AD patients and healthy subjects. They observed dose-dependent SEA and SEB reactions. They suggested that the reaction to patch tests resulted from the superantigen characteristics of SEA and SEB. Langer *et al*. proved that stimula-

tion through SEA and SEB application caused a higher percentage of positive reactions to patch tests in comparison with the application of a single agent. In view of this fact, the colonisation by *S. aureus*, which is capable of SAgs production, may intensify the skin reaction to common allergens among AD patients [18].

Reefer *et al*. noted that the tIgE value was increased in 42% of AD patients. Apart from that, the researchers observed higher SEA-sIgE and SEB-sIgE concentrations (corresponding to values > 0.75 IU/ml) only in the patients whose tIgE serum concentration exceeded 800 IU/ml [29]. Our observations revealed higher tIgE than the age norm in 79.8% of the AD patients. 67 out of 134 patients (50%) exceeded the tIgE of 1,000 kU/l. Reefer *et al*. observed positive asIgE values in reaction to both toxins in 82% of the patients whose tIgE was greater than 2,000 kU/l. There was no asIgE in reaction to any bacterial products (a wide range of bacterial and fungi products were investigated) in patients with low tIgE (≤ 35 IU/ml). Reefer *et al*. proved that asIgE targeted against microbial allergens was very often found in AD patients with increased tIgE [29]. In our study, among the AD patients with SEA-sIgE values of class 2 or higher, there were 43 out of 44 (97.7%) patients with tIgE greater than 1,000 kU/l (there was only one patient whose SEA-sIgE value was in class 3 and tIgE amounted to 379 kU/l). Similarly, the SEB-sIgE value in 44 patients was categorised at least as class 2. They included 40 patients (90.9%) with tIgE > 1,000 IU/ml (4 patients with SEB-sIgE in class 2, the tIgE values were: 121 kU/l, 54.5 kU/l, 514 kU/l and 379 kU/l). There was one patient with the tIgE value of 379 IU/ml, SEA-sIgE in class 3, and SEB-sIgE in class 2.

Bunikowski *et al*. proved that in AD children with positive SEA-sIgE/SEB-sIgE results there were more episodes of *S. aureus* superinfection than in children with negative results [26].

Conclusions

It seems that the colonisation of the lesioned skin, healthy skin and the anterior nares by *S. aureus* is related with higher tIgE serum concentration, which translates to more severe course of the disease. It seems that the colonisation of the healthy skin and the nasal vestibule by *S. aureus* (not lesioned skin, though) is related with a higher asIgE concentration with reference to both staphylococcal enterotoxins. However, the phenomenon needs further research in larger groups of AD patients. Significantly increased SEA-IgE and SEB-IgE concentrations were observed in the patients whose tIgE serum concentration was statistically higher.

Conflict of interest

The authors declare no conflict of interest.

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