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The Immune Response to *S. aureus* in Atopic Dermatitis

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The skin of patients with atopic dermatitis is heavily colonized with *S. aureus*, and their immune response to *S. aureus* shows some particular features: (1) A selective hyporesponsiveness to purified *S. aureus* cell walls in delayed type hypersensitivity skin reactions. (2) The presence of IgE to cell walls and soluble antigens of *S. aureus* in patients with high serum IgE levels. (3) Elevated cell wall IgE do not correlate with positive immediate skin reactions to whole *S. aureus* and their cell walls. (4) Regional lymphadenopathy but not impetiginization is associated with high total IgE and *S. aureus* cell wall IgE. We suggest that these changes in the immune response to *S. aureus* are releated to the chronic *S. aureus* colonization of the skin. *Key words: Atopic dermatitis; S. aureus; Skin testing; IgE.*

The skin of patients with atopic dermatitis (AD) is heavily colonized witih *S. aureus* (1, 3). The reaction of the immune system of these patients to the chronic *S. aureus* colonization is unknown. Here we present the results of some parameters of the immune response to *S. aureus*. Their *S. aureus* skin colonization were also quantitatively analyzed (Hauser et al., in press).

MATERIALS AND METHODS

Patients and controls. 21 patients were studied (13 females, 8 males, mean age 26.1 years). 19 patients fulfilled 4, 3 patients 3 of the main features defined by Hanifin & Rajka (2). The patients met a mean of 10.6 minor features. 6 patients had regional lymphadenopathy and 14 at least one impetiginized skin lesion, 22 healthy individuals (13 females, 9 males, mean age 30.1 years) served as controls.

Skin tests. 15 patients and 20 controls were i.c. tested with 0.1 ml suspension of *S. aureus* (strain H, heat inactivated 10 μg/ml dry weight) and purified *S. aureus* cell walls (PCW, strain H, 10 μg/ml dry weight) suspended in Krebs-Ringer phosphate buffer pH 7.4. Immediate and delayed type hypersensitivity skin reactions (ISR, DHR) were read at 15–30 min and 48 h after injection respectively.

Total and S. aureus IgE. Patient-sera were tested for total IgE (PRIST, Phadebas). IgE to PCW was determined using a radioimmunoassay described by Schopfer et al. (6). The results are expressed as % binding to PCW of added counts of 125I antihuman IgE (Pharmacia) after incubation of the test serum. IgE to soluble protoplast antigens of *S. aureus* (SAP) was detected by an immunoblot method. SAP were separated by polyacrylamide gel electrophoresis and transferred to nitrocellulose. Nitrocellulose strips were incubated with the test serum and then with 125I antihuman IgE (Pharmacia). The strips were washed and exposed for 4 days on X-ray film. Bound 125I antihuman IgE was detected as discrete bands.

RESULTS AND DISCUSSION

As can be seen from Table I, AD patients showed less frequently positive DHR to PCW and whole *S. aureus* than our control population ($p<0.05$, $0.1>p>0.05$). However, patients reacted more often to tetanus toxoid than to *S. aureus* and their cell walls ($p<0.05$) rendering a general hyporesponsiveness of the skin for delayed skin reactions unlikely. This finding suggests that AD patients show a selective hyporesponsiveness to *S. aureus*

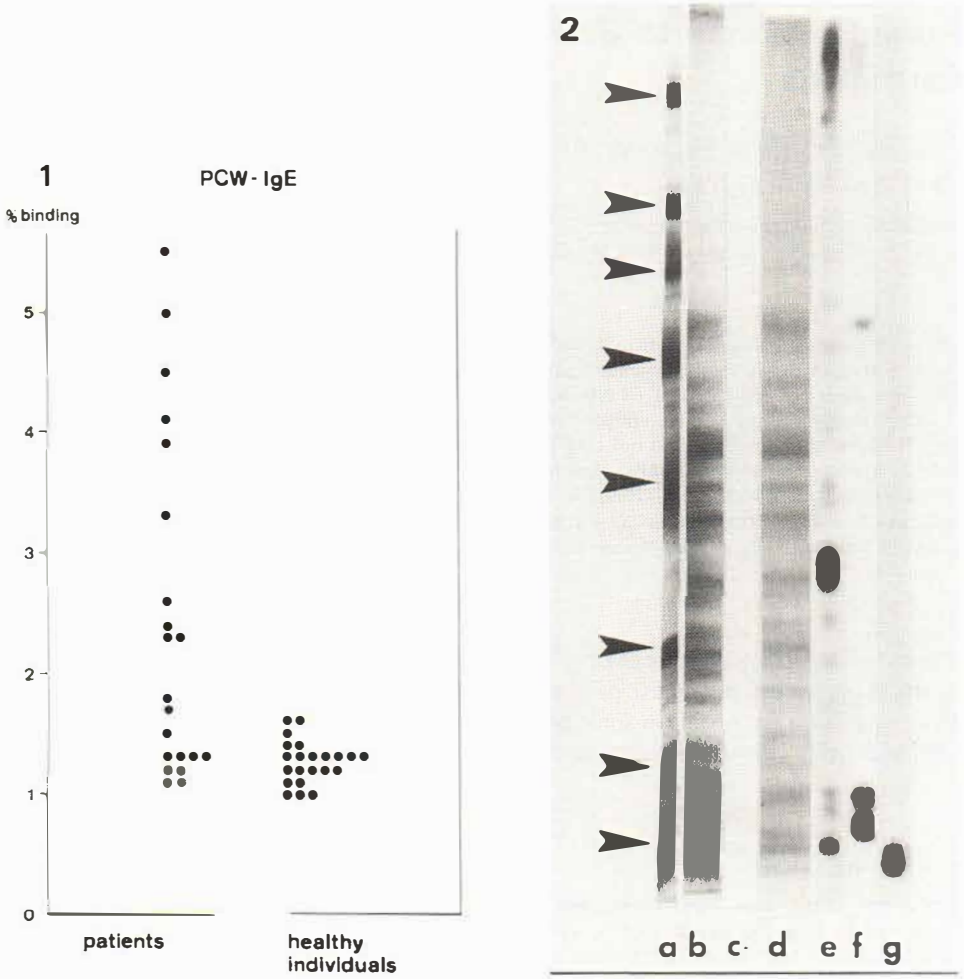

Fig. 1. IgE to PCW. Values from 21 patients with AD and 22 healthy individuals. 57% of the patients had elevated PCW-IgE, i.e. >1.6% binding (mean + 2 SD of the control group).

Fig. 2. Immunoblot for IgE to SPA. Arrowheads = molecular weight standards (from top to bottom: 220, 116, 92, 66, 45, 31, 21, 14 kilo Dalton). a = molecular weight standards, b = electrophoresis gel before transblot, c = electrophoresis gel after transblot, d = transblot, e = *S. aureus* Hyper-IgE syndrome, f = AD patient, g = AD patient, a–d = amido black stain, e–g = autoradiography.

DHR whereas they seem to be able to respond to an occasionally encountered microbial antigen. The hyporesponsiveness may be linked to the chronic *S. aureus* skin colonization.

Fig. 1 shows values for PCW IgE in patients and controls. The 2 groups differ significantly ($p<0.001$). Compared to the controls 57% of the patients show elevated PCW IgE, i.e. >1.6% binding (mean +2 SD of the controls). Increased IgE to PCW, although higher levels, have been found in the sera of patients with the Hyper-IgE-syndrome (6) as has high IgE to whole *S. aureus* (5).

Positive ISR were not found to be more frequent in the patients, nor in the subgroup with increased serum PCW IgE levels (Table II). Again, the presence of large amounts of

Table I. *Delayed type hypersensitivity skin reactions in healthy individuals and AD patients to whole S. aureus, PCW and tetanus toxoid*

Patients	
(A) Tetanus toxoid	7/15[a]
(B) S. aureus, i.c.	1/15
(C) PCW, i.c.	0/15
Healthy individuals	
(D) S. aureus, i.c.	7/20
(E) PCW, i.c.	6/20

[a] Positive skin tests/individuals tested. Positive skin test: >2 mm infiltration with erythema. A vs. B, A vs. C $p<0.05$, B vs. D $0.01>p>0.05$, C vs. E $p<0.05$.

Table II. *Serum PCW-IgE and immediate skin reactions in healthy individuals and AD patients*

	Normal[b] PCW–IgE	Increased[b] PCW–IgE
Patients		
S. aureus, i.c.	1/7[a]	1/8
PCW, i.c.	2/7	0/8
Healthy individuals		
S. aureus, i.c.	6/20	0/0
PCW, i.c.	5/20	0/0

[a] Positive skin tests/individuals tested. Positive skin test: >5 mm urticarial reaction.
[b] Normal PCW-IgE correspond to <1.6% binding, increased PCW-IgE to >1.6% binding. See also Fig. 1.

S. aureus on the skin may be responsible for this observation. Exhaustion of local specific IgE may play a role.

10 out of 21 patients showed IgE to SPA. Examples, including a patient with Hyper-IgE-syndrome are shown in Fig. 2.

Comparing clinical and serological data of patients the following associations were found: High total IgE (>20000 U/ml) correlated with elevated PCW IgE and positive SPA IgE (both $p<0.025$). In addition, palpable regional lymphadenopathy was associated with high total IgE and increased PCW IgE (both $p<0.025$). In contrast, impetiginization was not associated with any of the data. The presence of *S. aureus* IgE in patients with AD suggests a relation to the chronic skin colonization by *S. aureus*. Furthermore, the association of high total IgE, increased PCW IgE and positive SPA IgE including the positive association with regional lymphadenopathy migh represent features of a common underlying immunopathologic process. This process might be evoked by the skin colonization.

In addition, on basis of an altered immune reactivity, scratching and subsequent increased diffusion of bacterial products and fragments into the skin may significantly contribute to the genesis of the cutaneous pathology of AD. This speculation fits with the observation that antibacterial therapy ameliorates the skin lesions in AD (4).

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REFERENCES

1. Aly R, Maibach HI, Shinfield HR. Microbial flora of atopic dermatitis. Arch Dermatol 1977; 113: 780.
2. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol (Stockholm) 1980; Suppl 92: 44.
3. Leyden JJ, Marples RR, Kligman AM. Staphylococcus aureus in the lesions of atopic dermatitis. Br J Dermatol 1974; 90: 525.

4. Leyden JJ, Kligman AM. The case for steroid-antibiotic combinations. Br J Dermatol 1977; 96: 179.
5. Schopfer K, Baerlocher K, Price P, Kech U, Quie PG, Douglas SG. Staphylococcal IgE antibodies, hyperimmunoglobulinemia E and Staphylococcus aureus infection. N Engl J Med 1979; 300: 835.
6. Schopfer K, Douglas SD, Wilkinson BJ. Immunoglobulin E antibodies against Staphylococcus aureus cell walls in the sera of patients with hyperimmunoglobulinemia E and recurrent staphylococcal infection. Infect Immun 1980; 27: 563.

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