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CONTACT ALLERGENS AS ENVIRONMENTAL FACTORS IN PATIENTS WITH ATOPIC DERMATITIS

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ABSTRACT
Purpose: The objective of this pilot study is to examine in atopic dermatitis (AD) patients possible contact allergens, using Patch test, to evaluate the levels of total IgE in them, to determine the familial and personal history of atopy and thus to determine the subtype- "extrinsic" or "intrinsic" AD. *Methods*: Patch testing with European Baseline Series was used in 15 AD patients. The serum levels of IgE are evaluated, using immunochemical automated analyzer on the base of chemiluminescence. The diagnose "atopic dermatitis" was set by the diagnostic criteria of Hanifin and Rajka. *Results:* Seven (46.67 %) of the patients had positive reactions to some of the tested allergens. Four patients did not have any positive reactions but higher IgE. These 11 patients (73.33 %) are classified as "extrinsic" AD. The most frequent contact allergen is Ni. Four patients (26.67 %) are determined as "intrinsic" AD. *Conclusions:* Our pilot study shows near in the half of the AD patients reactions to some of the tested allergens, which supposed the role of the environment and the contact allergens as triggers in the exacerbation of AD. We consider that the AD specifying into "extrinsic" and "intrinsic" subtype could help for the right course of treatment, diet and suspect allergens avoidance.

Key words: Atopic dermatitis, Patch test, contact allergens, environment

BACKGROUND

Atopic dermatitis (AD) is a chronically relapsing, highly pruritic, inflammatory skin disease, which affects between 10-20% of the child population and 1-3% of the adults. Important hallmarks of AD are a barrier dysfunction, causing xerosis cutis and IgE-mediated sensitization to food and environment stimuli. The clinical manifestation of the disease varies with age. The mechanisms of AD pathogenesis remain unclear. A lot of studies show the interaction between environmental, genetic and immunological factors in the development and progression of the disease. (1)

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Atopic dermatitis often is the first step in the atopic march, including also allergic rhinitis, conjunctivitis and asthma. It is known that AD is associated with atopy, which is defined as a genetic predisposition of the immune system to produce excessive quantity IgE antibodies in answer to minimal environment stimuli. It was found out that AD starts earlier in patients with personal and family history of atopy and these patients have severer clinical symptoms. (2)

In the last years, according to the patophysiology AD is divided into two subtypes: "extrinsic", IgE- mediated form and "intrinsic", non- IgE- mediated form. However, in both forms, dry skin due to barrier dysfunction is an important characteristic and in most cases the absence of IgE-sensitization is only a transient factor (3). "Extrinsic" AD is observed in 80% of the AD patients, has early onset, severe course and is characterized with high serum levels of total and allergen-specific

IgE towards some food and air-allergens; positive prick-test and/or concomitant allergic rhinoconjunctivitis or asthma. Tokura in his review from 2010, noticed that total serum IgE are significant associated with allergen specific IgE, that is why the total serum IgE could be used as a clinical parameter for differentiation between „extrinsic" and "intrinsic" AD. (4)

„Intrinsic" AD has onset after 20 years old, affects about 20% of the AD patients; the serum levels of total and allergen-specific IgE are in range. There is no sensitivity to air or food allergens and no atopic diathesis. Also it is known that the normal range of IgE does not discount high allergen-specific IgE antibodies. Authors interpret the immunologic differences in the both forms "extrinsic" and "intrinsic" AD as two subtypes of one disease with similar clinical phenotype. (5)

Many studies attach importance to the contact- and aero-allergens, which could aggravate the skin symptoms in the course of AD. According to most investigations carried out among adult AD patients, the most common contact allergens are: Ni, Cr, Co, Latex, Peruvian balsam and Fragrance mix. It is considered that the sensibility to metals can be accepted in case when the lesions covered mainly the hands, while in case they are covered the head and neck, especially in women, it is better to consider sensibility to perfumes. The sensitiveness aggravates the AD, but the atopy determines susceptibility to the sensitiveness. (6)

The hypothesis, that environment factors aggravate AD symptoms direct attention to identifying them through different methods, which aggravate the course of the disease. In order to realize that in the practice often - "Patch test", "Prick test" and "Atopy Patch test" are applied.

Table 1 IgE antibodies' serum levels according to the age

"Patch test" is an epicutaneus test for in vivo visualization of IV type allergic reaction and this is meant to reproduce „in miniature" eczematous reaction by applying different allergens under occlusion over intact skin. (7) „Patch test" is a standard for diagnostics of allergic dermatitis. The application of the Standard allergen series also can be used for screening in patients with atopic component, having the symptoms of the "atopic march". In the last ten years for studying the environmental factors, it is included also for AD (8). According to a lot of scientists, carrying out of "Patch testing" is with a high diagnostic value for AD. (9)

MATERIALS AND METHODS

Fifteen patients with atopic dermatitis between the age of 11 and 80 have been studied, including ten (66.67 %) women and 5 (33.33 %) men. Informed consent has been given by all participants. The diagnosis of "atopic dermatitis" was set by the diagnostic criteria of Hanifin and Rajka. All the patients were symptom-free during the study. They have not taken any antihistamines and have not been under immunosupressive therapy during the patch testing. Peripheral blood was obtained and determined the total serum levels of IgE, using immunochemical automated analyzer on the base of chemiluminiscence with referent levels specific for the different age (table 1). For epicutaneus testing we used the European standard series – IQ Ultra **(Table 2)**. It concerned 28 allergens. We have checked the results on the 48th hour (2nd day), 72nd hour (3rd day) and on the 7th day also. The information for the personal and family history of atopy was according to the anamnesis data and medical documentation.

Table 1. *IgE antibodies' serum levels according to the age*

Newborn children: < 1.5 IU/ml
Till 1 year: < 15 IU/ml
From 1 to 5 years: < 60 IU/ml
From 6 to 9 years: < 90 IU/ml
From 10 to 15 years: < 200 IU/ml
Adults: < 100 IU/ml

Table 2. *Eropean Standart Basic Series*

№	Allergen	Concentration	Vechiculum
1	Kalium bichromas	0.5	Vaselinum album
2	4- phenylendiamininum	1.0	Vaselinum album
3	Thiuram mix	1.0	Vaselinum album
4	Neomycinum sulfas	20.0	Vaselinum album
5	Cobaltum chloridum	1.0	Vaselinum album
6	Benzocainum	5.0	Vaselinum album
7	Nickelum (II) sulfas	5.0	Vaselinum album
8	Clioquinol (Vioform)	5.0	Vaselinum album
9	Colophonium	20.0	Vaselinum album
10	Paraben mix	16.0	Vaselinum album
11	N-isopropyl-N-pheny l-4-phenylendiaminum	0.1	Vaselinum album
12	Lanolin alcohol	30.0	Vaselinum album
13	Mercapto mix	2.0	Vaselinum album
14	Epoxy resin	1.0	Vaselinum album
15	Balsamun peruvianum	25.0	Vaselinum album
16	4-tert-Butylphenol formaldehydum	1.0	Vaselinum album
17	2-Mercaptobenzo thiazolum	2.0	Vaselinum album
18	Formaldehydum	1.0	Aqua destillata
19	Parfum mix	8.0	Vaselinum album
20	Sesquiterpenum mix	0.1	Vaselinum album
21	Quaternium 15	1.0	Vaselinum album
22	Primin	0.01	Vaselinum album
23	Cl+Me-isothiazolinonum	0.01	Aqua destillata
24	Budesonidum	0.1	Vaselinum album
25	Tixocortol-21-pivalatum	0.1	Vaselinum album
26	Methyldibromoglutaronitril um	0.5	Vaselinum album
27	Fragrance mix II	14.0	Vaselinum album
28	Lyral	5.0	Vaselinum album

RESULTS

- In 7 (46.67 %) of our AD patients we have observed positive reaction **(Fig. 1)** to the following allergens: NI (5 patients) **(Pic. 1)**, NI and Co (1 patient), K_2Cr_2O7 (1 patient);

  - only in 2 of them we determined high serum levels of total IgE antibodies;

- in 8 (53.33 %) AD patients we have not observed sensibility to any of the examined allergens, but:

  - in 4 of them the serum levels of the total IgE were higher, out of range;

- altogether in 5 of the AD tested patients (with positive reaction or high total IgE) we found out family or/and personal positive anamnesis of atopy, so:

1. These 11 patients (73.33 %)- with positive Patch test and higher IgE, we diagnosed as "extrinsic" AD.

- In the rest 4 (26.67%) of the tested AD, we did not observed:

  - sensibility to any of the examined allergens,
  - higher levels of total serum IgE,
  - positive family or/and personal anamnesis for atopy, so:

2. These patients we diagnosed as "intrinsic" AD. **(Table. 3**); **(Fig. 2)**

Patient	Patch test's results	Total serum IgE levels	Family/personal anamnesis for atopy
P 1/f, 18 years old	NI - (+)	IgE - in range	negative
P 2/f, 11 years old	NI - (+++)	IgE - in range	negative
P 3/f, 27 years old	NI - (+), Co - (+)	IgE - 189.8 IU/ml	positive
P 4/f, 49 years old	K2Cr2O7 – (+)	IgE - in range	negative
P 5/f, 44 years old	NI - (++)	IgE - in range	positive
P 6/f, 12 years old	NI - (++)	IgE - in range	negative
P 7/m, 80 years old	(-) p-я	IgE - in range	negative
P 8/m, 50 years old	(-) p-я	IgE - in range	negative
P 9/m, 28 years old	(-) p-я	IgE - 2292 IU/ml	negative
P 10/f, 20 years old	(-) p-я	IgE - 125.3 IU/ml	negative
P 11/m, 23 years old	(-) p-я	IgE - in range	negative
P 12/m, 22 years old	(-) p-я	IgE - 153.1 IU/ml	positive
P 13/f, 24 years old	(-) p-я	IgE - 164.2 IU/ml	positive
P 14/f, 58 years old	(-) p-я	IgE - in range	negative
P 15/f, 37 years old	NI - (++)	IgE - 5066 IU/ml	positive

Table 3. *Distribution of the patients according to the results: patch testing, total serum levels of IgE, family or/and personal anamnesis for atopy.*

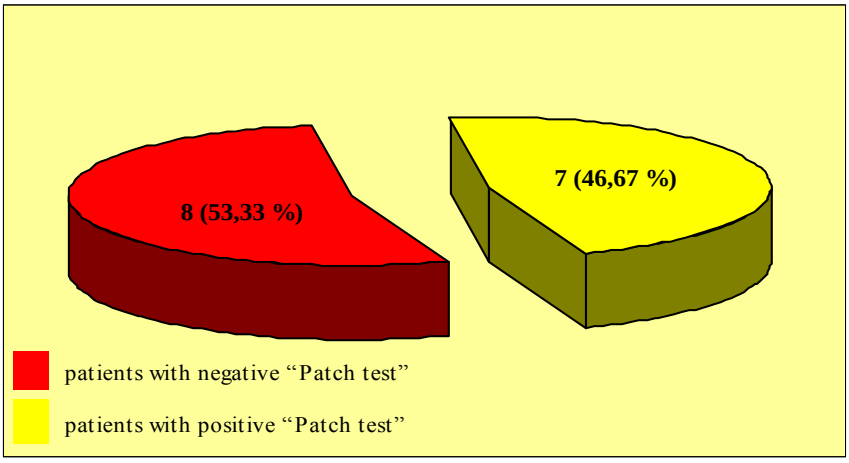
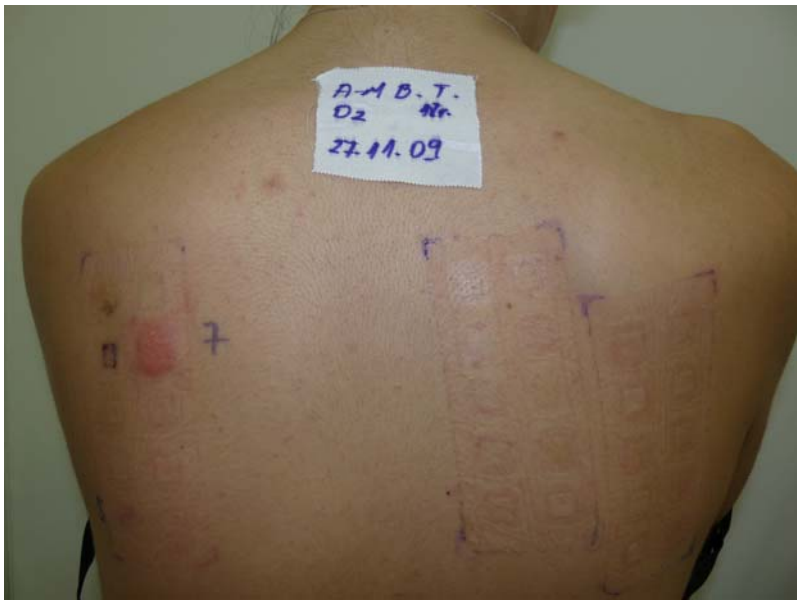


Fig. 1. Distribution of AD patients with positive and negative "Patch test"



Pic 1. A-M.B.T. 18y., 2nd day

+++ Ni (position 7)

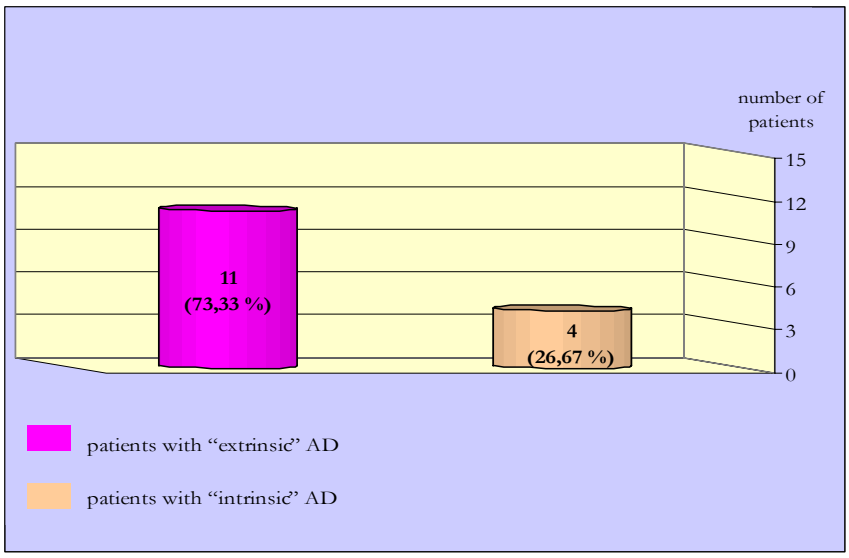


Fig. 2. Distribution of the patients according to the subtype AD: "extrinsic" AD or "intrinsic" AD

DISCUSSION

According to our pilot study 73 % of the tested AD patients, it is concern "extrinsic" subtype AD, which is comparable with the literature data. (10)

The presence of normal total IgE serum levels in 5 of our patients with "extrinsic" AD, does not exclude the presence of allergen sensitivity to other allergens. It means that it is necessary to implement the additional tests: "Atopy patch test" and "Prick test" also.

Atopic dermatitis is found often and takes severer course in patients with personal or family history of atopy (11). The anamnesis for atopy in our patients is associated with high levels of total IgE and/or positive Patch test in the "extrinsic" AD patients, but without significant difference.

The most common allergen according to us is Ni (40 %), as it was observed in most of the studies also. We have found also manifestation of more than one allergen - NI (+), Co (+) in our case. Recently a lot of studies show multiple sensibility to more allergens in one patient (12), but in our case we have determined only one AD patient, which could be explicable with the small group of patients at this stage of the study.

A number of studies determined various environment factors (contact-, aero- or food-allergens), which sustain the skin symptoms in AD and make the exacerbations frequent. Pónyai and al. examined 34 AD patients: 23 women and 11 men in the age over 18 years old, separated them into two groups – "extrinsic" and "intrinsic" AD. Thirty of the patients tally the „extrinsic" AD criteria and 4 belong to the "intrinsic" AD group. The authors regard that haptens can provoke allergic reactions through penetration via the destroyed epidermal barrier. The defect barrier and also the continuing contact with skin therapeutically and supporting products, provoke also skin sensibility. From the taken Patch test with the most common allergens, the mainly irritators in the patients with „extrinsic" AD are: nickel (6), thiomersal (3), mercury-amidochlorat (3), mercury-chloride (2), fragrance mix (1) (13). Some scientists consider metal sensitivity if symptoms affect more hands, and fragrance sensitization predominantly in women, when the affected area is the neck (14). We did not found any relation between the spread of the lesions and the results from the patch testing, but we render this also to the less number of patients in our pilot study.

The large frequency of positive reaction to contact allergens (46.67 % of our tested patients), shows the influence of the environment factors in the running of the atopic dermatitis. With the progressive of the age and chronification of the disease increase the frequency of influence of the contact allergens. Atopic individuals may have false-positive, irritative reactions even in a symptom-free condition and the ratio of the irritative reactions increases in chronic AD (15), as it is in our case.

CONCLUSIONS

The world industrialization changes the course of the allergy diseases and especially the skin conditions.

In our pilot study nearly half of the AD patients showed reactions to some of the tested allergens, which supposed the role of the environment and the contact allergens as triggers in the exacerbation of the disease.

Determining the type of AD and knowing the allergen sensitizing as environmental factors will help the patients to have the right course of treatment, diet and suspect allergens avoidance.

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