

ORIGINAL ARTICLE

Contact and aeroallergens in adulthood atopic dermatitis

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Abstract

Background Atopic dermatitis (AD) is a clinically well-defined, chronic-intermittant, genetically predisposed skin disease. The increasing number of adult cases observed in the last years has turned the attention to ascertaining factors eliciting skin symptoms. Studies have revealed numerous environmental components (e.g. contact and aeroallergens) that may play an important role in sustaining the symptoms.

The aim of the study was to search for contact allergens and aeroallergens triggering the skin disease in adult AD patients.

Methods Patients over 18 years from our Atopy Outpatient Department were included in the study. Diagnosis of AD was based on the clinical criteria of Hanifin and Rajka. The distribution of skin symptoms was characteristic for adult AD: hands, shoulders, neck, flexures, face and eyelids. The extremities and the trunk were less involved. The potentially provoking contact and aeroallergens were examined in symptom and drug-free period with atopy patch and epicutaneous tests (APT, ET), which were supplemented by *in vitro* allergy and Prick tests. The relevance of sensitization was evaluated by the comparison of *in vivo* and *in vitro* test results, medical history and skin symptoms.

Results A total number of 34 cases of adult AD (23 women and 11 men) were studied. Four of them were classified into the intrinsic group (IG; 12%), and 30 were classified into the extrinsic group (EG; 88%). The incidence of contact sensitization to environmental allergens was remarkable: 13 of the EG, 1 of the IG (14 of 34, 41%). In the IG, a late thiomersal positivity was detected without clinical relevance. In the EG, epicutaneous standard series late positivity was seen in 13 patients, in four of them with multiple sensitivity. The allergens causing positivity were nickel (6 of 13), thiomersal (3 of 13), mercury-amidochlorate (3 of 13), mercury-chloride (2 of 13), iodine chlorhydrxyquin (1 of 13), lanalcolumn (1 of 13) and fragrance mix (1 of 13). Among the detected allergens, the following were relevant: lanalcolumn (1 of 13: cosmetics), fragrance mix (1 of 13: cosmetics), nickel (1 of 13: metal objects), thiomersal (1 of 13: eyedrops).

No immediate response was seen with APT. Relevant late positivity was shown with APT test in one patient in the IG (1 of 4) to *Dermatophagoides pteronyssinus*. We observed late positivity in 18 patients in the EG (18 of 30). Among the detected allergens, the following were clinically relevant: *D. pteronyssinus* and/or *Dermatophagoides farinae* (15 of 18), cat epithel (4 of 18), timothy pollen (1 of 18) and dog epithel (1 of 18).

Furthermore, we examined the relevance of APT, specific immunoglobulin E (IgE) tests and Prick tests. We observed multiplex positivity by specific IgE tests, APT and Prick tests in 14 patients in EG. Sensitization to *D. pteronyssinus* and/or *D. farinae* (11 of 14) cat epithel (4 of 14), dog epithel (1 of 14) and timothy pollen (1 of 14) proved to be clinically relevant with the atopic skin symptoms and medical history.

Conclusion The proportion of contact sensitization to environmental allergens in the 34 adult atopic patients was remarkable (14 of 34, 41%). Out of the verified contact allergens, nickel, fragrance mix, thiomersal and lanalcolum proved to be relevant. House dust mite and cat epithel proved to be the most common relevant aeroallergens. *D. pteronyssinus* and *D. farinae* sensibilization was high, particularly in patients with severe skin symptoms on the face, eyelids and hands. Pollens should be considered in patients with seasonal relapse of AD. Sensitization to animal epithel was usually indicated by the flare-up of skin symptoms upon contact with animals. The relevance of the eliciting effects of sensitization could easily be supported in most cases by the medical history and the distribution of skin symptoms. In some adult AD patients with long-lasting AD, the relevance of triggering factors is hard to determine.

Background

Atopic dermatitis (AD) is a clinically well-defined, inflammatory, chronic-intermittant, genetically predisposed, itching skin disease elicited by various factors.^{1,2} The latest nomenclature (AD/eczema syndrome) suggests that the name covers a number of subtypes. Intrinsic AD (IAD) is differentiated from the much more common extrinsic type (EAD) by total serum immunoglobulin E (IgE) within the normal range, by the lack of specific IgE positivities and by the fact that no immediate skin reaction to environmental allergens or respiratory involvement can be observed in these patients.^{3–5} Although the clinical symptoms and the T-cell repertoire within the lesional skin of IAD and EAD seem to be similar, the inflammatory microenvironment and the patients immuno-phenotypical characteristics is different in the two subgroups.^{6–10} The allergological management and treatment of the intrinsic and extrinsic groups require different approaches; the probability of the development of an 'atopic march' is much lower in the intrinsic group. The prevalence of IAD is low among adult patients.^{3,5}

The incidence of contact sensibilization among AD patients is concordant with the data observed in the non-atopic population. Haptens may provoke allergic reactions by penetrating the damaged epidermal barrier.^{11,12} The defective epidermal barrier and the continuous contact with various therapeutic and skin care products promotes the development of sensitization. Nickel, latex, fragrance mix and balsam of Peru have been found to be the most frequent sensitizers in adult atopics.^{13,14} The IgE-mediated contact reaction elicited by aeroallergens is an important pathogenetic factor in AD.² The skin symptoms of AD may be flared up by aeroallergen exposition: house dust mite, pollen, animal epithel. Skin symptoms of atopy can be seen in such cases first of all on the face, neck, hands and, depending on the season, on body parts not covered with

clothes. Atopy patch test (APT) is an important diagnostic tool in patients with an air-exposed AD distribution pattern and is helpful for determining the clinical relevance of aeroallergens.^{2,15}

Numerous reports have been published about the childhood AD; however, the AD persisting also in adulthood, and the AD developing *de novo* in adulthood, got into the focus of interest only within the last years. Studies investigating the possibility of primary and secondary prevention of adult AD have revealed numerous factors playing a role in triggering and sustaining the disease.^{11,16–22}

Here, we studied AD patients older than 18 years for aero and contact allergens flaring up the skin symptoms and compared our results with the current data in the literature.

Materials and methods

Thirty-four AD patients over 18 years of age from the Atopic Outpatient Department of the university have been studied. Diagnosis of AD was based on the criteria of Hanifin and Rajka.¹ All the patients were symptom-free at time of testing. They did not take any antihistamine, and they applied only indifferent topical treatment 1 week before the tests and at the time of testing. We used for epicutan standard series *Brial-Allergen D-Greven Hungarian Panel*, Prick test *Alk Abello Spain* (Table 1) and Atopy Patch Test *Stallergenes France* (Table 3). Assessments of the Prick tests were done at 20 and 40 min. By epicutaneous and APT assessment were done first at 20 and 40 min and then we followed the skin reactions on the test sites until day 7 (days 1–7). Among *in vitro* tests, total IgE (ELISA) and specific IgE panel (CLA-MAST; Table 2) tests were performed. The results of the *in vivo* and *in vitro* tests and data of the medical history and clinical symptoms of the patients were related.

Table 1 ALK Abello Prick Test

1. <i>Dermatophagoides pteronissinus</i> (Dp.)	Mite
2. <i>Dermatophagoides farinae</i> (Df.)	Mite
3. <i>Felis domesticus</i> (Fd.)	Cat
4. <i>Canis familiaris</i> (Cf.)	Dog
5. <i>Cupressus sempervirens</i> (Cs.)	Cypress
6. <i>Phleum pratense</i> (Pp.)	Timothy
7. <i>Artemisia vulgaris</i> (Av.)	Mugwort
8. <i>Plantago lanceolata</i> (Pl.)	Plantain
9. <i>Betula pubescens</i> (Bp.)	Birch
10. Pollens V. (<i>Dactylis glomerata</i> , <i>Lolium perenne</i> , <i>Phleum perenne</i> , <i>Phleum pratense</i> , <i>Poa pratensis</i> ; 5G)	
11. Negative control	
12. Positive control (histamine 10 mg/mL)	

Results

Age and sex distribution

A total number of 34 cases of AD cases (23 women and 11 men) were examined for the study. The youngest patient was 18; the the oldest was 64 at the time of testing. The average age was 28 years.

Intrinsic group

There were three female patients and one male patient (12% of the total patient number) without rhinitis, conjunctivitis, or asthma bronchiale in the personal history. Their total serum IgE level was in the normal

Table 2 Spec. IgE panel

Code no.	English	Latin
f1	Egg white	
f2	Milk	
f3	Codfish	<i>Gadus morrhua</i>
fl3	Peanut	<i>Arachis hypogaeae</i>
fl4	Soybean	<i>Glycine max</i>
f20	Almond	<i>Prunus amygdalus</i>
f85	Celery	<i>Apium graveolens</i>
f256	Tomato	<i>Lycopersicon esculentum</i>
f4	Wheat	<i>Triticum vulgare</i>
f8,f7,f9	Cereal II (corn, oat, rice)	<i>Zea mays</i> , <i>Avena sativa</i> , <i>Oriza sativa</i>
f33,f208,Rf306	Orange citrus mix	<i>Citrus sinensis</i> , <i>Citrus</i> sp.
k82	Latex	Latex
m3	<i>Aspergillus</i>	<i>Aspergillus</i>
m5	<i>Candida</i>	<i>Candida</i>
m1	Penicillium	Penicillium
t14,t12	Poplar mix (cotton wood, willow/asper)	<i>Populus/Salix</i>
t2,t3,t4	3 trees mix (black alder, white birch, american hazelnut)	<i>Alnus glutinosa</i> , <i>Betula alba</i> , <i>Corylus americana</i>
t9,Rt210,t15	3 trees mix (olive, privet, ash)	<i>Olea</i> , <i>Ligustrum</i> , <i>Fraxius</i>
t7	Oak mix	<i>Quercus</i>
g2	Bermuda grass	<i>Cynodon dactylon</i>
g3,g6,g5,g8	4 grass mix (orchard grass, timothy, perennial rye, kentucky blue)	<i>Dactylis glomerata</i> , <i>Phleum pratense</i> , <i>Lolium perenne</i> , <i>Poa</i>
g12	Cultivated rye	<i>Secale cereale</i>
w10,w11,w17	Chenopod mix II (russian thistle, lamb's quarter, burning brush)	<i>Chenopodium</i> spp., <i>Salsola kali</i> , <i>Chenopodium album</i> , <i>Kochia</i>
w9	English plantain	<i>Plantago lanceolata</i>
w1,w3	Ragweed mix (short ragweed, giant ragweed)	<i>Ambrosia</i> sp.
w6	Mugwort	<i>Artemisia vulgaris</i>
g202	Corn pollen	<i>Zea mays</i> pollen
g15	Wheat pollen	<i>Triticum vulgare</i> pollen
e4	Cow	<i>Bos</i> sp.
e1	Cat	<i>Felis silvestris</i>
e5	Dog	<i>Canis familiaris</i>
e3	Horse	<i>Equus caballus</i>
i6	Cockroach mix	<i>Periplaneta</i>
me85,me86,e70	Feather mix (chicken, duck, goose)	<i>Gallus domesticus</i> , <i>Anas domestica</i> , <i>Anser anser</i> f. <i>domestica</i>
d1	Mite: <i>D. pteronyssinus</i>	<i>Dermatophagoides pter.</i>
d2	Mite: <i>D. farinae</i>	<i>Dermatophagoides far.</i>

Table 3 STALLERGENES – APT

1. <i>Dermatophagoides pteronissinus</i> (Dp.)	Mite
2. <i>Dermatophagoides farinae</i> (Df.)	Mite
3. Felis (F)	Cat
4. Canis (C.)	Dog
5. Dactylis (Dac.)	Orchard grass
6. Phleum (Phle.)	Timothy
7. Artemisia (A.)	Mugwort
8. Phlantaginaceae (Phl)	Plantain
9. Betula (B.)	Birch
10. 5 Grass mix (Dactylis, Lolium, Anthoxanthum, Poa, Phleum; 5GX)	
11. negative controll (petrolatum)	
12. positive controll (0.5% Na-dodecylsulphate ad aqua destill.)	

range (below 100 U/mL). They did not have any serum specific IgE positivity, and their Prick testing remained negative. We classified them into the intrinsic group. Their skin symptoms were localized on the hands, neck, flexures and the face, and on the eyelids as well. The symptoms of AD appeared in women at the ages of 15, 18 and 26 and in the male one at the age of 5.

No immediate reactions were seen with APT in the intrinsic group. We observed late APT positivity in one out of the four patients to *Dermatophagoides pteronyssinus* and to orchard grass. We considered the possibility of former sensitization as to be clinically relevant, while the patient had severe skin symptoms on the face and on the eyelids. In another patient, a late thiomersal positivity was detected without any confirmed clinical relevance (Table 4).

Extrinsic group

Thirty AD patients (P1–P30) – 10 men and 20 women – were selected in the extrinsic group (88% of the total patient number). Their average age was 8 years at the onset of skin disease. Their symptoms distributed on the face, eyelids, over the flexures and hands. The extremities (arms, legs) and the trunk had milder symptoms. 20 patients had rhinitis and/or asthma bronchiale in the medical history. Total

serum IgE was evaluated in 23 patients. In the seven AD patients with normal serum IgE levels, specific IgE reactivity and rhinitis and/or asthma bronchiale was observed.

In epicutaneous standard series, late positivity was seen in 13 patients, in four of them with multiple sensitivity. The allergens causing positivity were nickel (6x), thiomersal (3x), mercury-amidochlorate (3x), mercury-chloride (2x), iodine chlorhydrdoxyquin (1x), lanalcolumn (1x) and fragrance mix (1x). According to the patients' observations, in four of them, materials containing the detected allergens aggravated the skin symptoms: lanalcolumn (facial symptoms: externae, cosmetics – P6), fragrance mix (hand involvement: cosmetics – P14), nickel (hand: metal objects, costume ornaments – P18), thiomersal (eyelids: eyedrops – P4).

No immediate reactions were seen with APT in the extrinsic group. Late positivity was observed in 18 patients. We observed *D. pteronyssinus* and/or *Dermatophagoides farinae* positivity in 15 patients; 11 of them had symptoms on the face and/or the eyelids, and 9 of them on the hands. All patients with severe eyelid symptoms were positive to house dust mite by APT tests.

Four patients were positive to cat epithel and reported the exacerbation of the hand symptoms upon contact with cats (P2, P16, P23, P25). In one case, with a timothy pollen sensitivity, the patient's AD skin symptoms worsened noticeable in the pollen season (P7). One dog epithel-positive patient regularly observed the flare-up of hand and face eczema on contact with a dog (P23).

Further aeroallergens inducing late APT positivity were orchard grass (3x), plantain (2x), mugwort (3x), timothy (1x) birch (1x) and dog epithel (1x). The clinical relevance is in these cases questionable since the patients were unable to report a clear correlation between allergen exposition and aggravation of skin symptoms (Table 5).

Relevance of specific IgE, APT and Prick tests in the extrinsic group

We observed multiplex positivity by APT, specific IgE tests and Prick tests in 14 patients with extrinsic AD (P2, P5, P7, P8, P11, P13, P15, P16, P18, P20, P23, P25, P27, P28).

Table 4 IG

No. of patient/gender	Total IgE level U/ml	Specific IgE	Routine patch test	APT	Prick test	Skin symptoms localisation	Data in the medical history
1/female	normal	negative	negative	negative	negative	Ear, hands	None
2/female	normal	negative	negative	Df.D2-7+++ Dac.D3-7+++	negative	Face, eyelids, neck, hands, occiput	Severe hand symptoms on face, eyelids, neck
3/female	normal	negative	Thiomersal D3-7+++	negative	negative	Flexural	None
4/male	normal	negative	negative	negative	negative	Hands	None

Table 5 EG

No. of patient/gender	Total se. IgE (U/ml)	Specific se. IgE	Routine patch test	APT	Prick test	Skin symptoms localization	Data in the medical history
1/female	780	e1:4, e5:4, d2:1, w6:2, 4gmix:1, e3:1, e4:1, g12:2, g202:3	Negative	Negative	Fd., Cf., Pp., Av., Bp., 5G	Hands, flexures, mamilla	Skin symptoms worsening due to contact with cat or dog asthma bronchiale, rhinitis
2/female	292	w6:1, e1:4, e5:4, d1:4, d2:4	Mercury amidochlor D2++, D3-7+++	Dp.D2-7+++, Df.D2-7++, F.D3-7++, DacD2-7+++	Dp., Df., Fd., Cf., Cs., Pp., Av.	Eyelids, hands, flexures, arms	Perennial rhinitis, asthma bronchiale, hand skin sympt. worsening due to contact with cat
		g2:1, 4gmix:4, g12:4, w9:1, w1+w3:4 g202:1, g15:4, e4:1, e3:1	Mercury chlorid D2++, D3-7+++	Phle.D2-7++, Phl.D2-7++, B.D3-7+++	Pl., 5G		
3/female	115	4gmix:3, g202:1, e5:2, e1:4, w1+w3:1, g12:1	Iodine chlorhydroxyquin D2-7+++	Negative	Fd., Cf., Pp., 5G	Hands, flexural	Rhinitis
4/male	110	e1:3	Thiomersal D2-7++	Dp.D3-7++	Fd.	Eyelids, flexures	Pet keeper (cat), eyelids sympt. worsening due to contact with eyedrops
5/female	120	4gmix:1, d1:1, d2:1	Negative	Dp.D2-7++, Df.D2-7+++ Dac.D2-7++, A.D3-7++	Av., Pp., 5G	Eyelids, hands	
6/male	743	e1:4, e5:4	Lanalcolumn D4-7++, Nickelsulfat D5-7++	Negative	Fd, Cf.	Face, flexures	Skin symptoms worsening due to contact with dog and with cosmetics
7/female	206	g15:2, g202:1, e5:2, e1:4, w1+w3:1, g12:3	Negative	Phle.D2-7++	Fd., Cf., Pp., 5G	Hands, flexures	Skin symptomsworsening in pollen season, rhinitis in Spring months
8/male	893	d2:1, w6:4, g202:1, e5:4, e3:3, e1:4, e4:1, w1+w3:1, f2:1	Negative	Df.D3-7+++ Dp.D3-7+++ A.D3-7++, Phl.D3-7++	Df., Dp., Av., Pl., Fd., Cs., Bp.	Face, hands, flexures	Asthma bronchiale
9/female	331	g15:4, g2:4, d2:1, t7:1, g202:4, w9:1, e1:1, w1+w3:1, e4:1, g12:4	Negative	Negative	Pp., Av., Pl., 5G	Flexures	Rhinitis in spring months
10/male	> 2000	d1:1, d2:2, fl:4, f20:1, t7:1, g2:1, 4gmix:4, g12:4	Negative	Negative	Df., Dp., Pp., Pl., 5G	Face	Skin symptoms worsening in pollen season, and due to dust and contact with cat
		w9:2, w1+w3:4, w6:2, g202:4, g15:4					
11/male	568	w6:4, e1:4, e5:4, e3:4, i6:4, feathermix:3, d1:3, d2:3, fl:4, g12:1, w9:1, w1+w3:4, g202:4, g15:4	Negative	A.D3-7++	Av., Df., Dp., Fd., Cf., Cs., Pp., 5G	Shoulders, flexures, arms	Rhinitis in August, asthma bronchiale
12/female	693	f2:1, 4gmix:4, g12:4, g202:4, g15:2, d1:1, d2:1	Negative	Negative	Df., Dp., Pp., 5G	Face, flexures, neck, hands	

Table 5 (Continued)

No. of patient/gender	Total se. IgE (U/ml)	Specific se. IgE	Routine patch test	APT	Prick test	Skin symptoms localization	Data in the medical history
13/female	80	d1:4, d2:4, e1:1	Thiomersal D2-7++	Df.D2-7++, Dp.D2-7++	Df., Dp., Fd., Cf., Av., 5G	Face, hands, flexures	Rhinitis in spring months
14/female	78	e5:4	Nickelsulfat D2-7+++, Fragrance mixD2-7+++	Dac.D4-7+++	Fd., Cf., 5G	Hands, flexures, arms	Skin symptoms worsening due to contact with dog, dust, cosmetics
15/female	37	d2:1	Negative	Df. D4-7++	Dp., Df., Fd., Pp., 5G	Face, neck, flexural	Skin symptoms worsening due to contact with cat, dog, rhinitis in Jun–July
16/male	11	g15:2, g2:1, w6:1, 4gmix:4, g202:1, t7:2, g12:3	Thiomersal D4-7++	Dp.D4-7++, F.D4-7++	Fd., Pp., Bp., 5G	Hands, flexures	
17/female	73	negative	Negative	Df.D4-7++	Negative	Face, eyelids, flexures	Rhinitis in spring months
18/female	> 1000	d1:4, d2:4, w6:4, g202:3, g15:4, e4:1, e1:4, e5:3	Nickelsulfat D2-7+++	Df.D3-7++, Dp.D3-7+++	Df., Dp., Fd., Cf., Pp., Av., Bp., 5G	Face, neck, hands, arms	Skin symptoms worsening due to contact with metals, dust. Asthma bronchiale
19/male	323	feathermix:1, f20:1, t7:4, g2:2, 4gmix:4, w9:2, g12:4, w1+w3:4 fl4:2, t7:2, g2:1, 4gmix:2, g12:1, w9:2, w1+w3:2, w6:1, g202:2, g15:3, e4:2, e1:2, e5:2, i6:2, d2:2	Mercury amidochlor. D1+, D2-7+++ Mercury chlorid D2-7+++	Negative	Fd., Cf., Pp., Av., Bp., Pl., 5G	Hands	Pet keeper (dog), rhinitis
20/female	249	e1:4, w1+w3:2	Nickelsulfat D4-7+++	Df.D4-7+++	Df., Fd., Cf., Pp., 5G	Face, neck, trunk, flexures	Pet keeper (cat)
21/female	9	d2:3	Negative	Negative	Negative	Hands, arms, trunk	Pet keeper (dog), rhinitis Pet keeper (dog,cat), skin sympt. worsening due to contact with cat, dog, rhinitis, asthma bronchiale
22/female	147	w1+w3:2, w6:3, g202:1	Negative	Negative	Df., Pp., Av., Bp., 5G	Flexures, arms, legs	
23/male	1000	e1:4, e5:4, d1:4, d2:4	Nickelsulfat D3-7+++	Dp.D2-7+++, Df.D2-7++, F.D2-7++, C.D2-7++	Df., Dp., Fd., Pp., Bp., 5G	Face, eyelids, hands, trunk, flexures	
24/female	120	negative	Nickelsulfat D3-7+++	Negative	Negative	Trunk	Skin symptoms worsening due to contact with dog, cat (pet keeper) and dust, rhinitis, asthma bronchiale
25/female	> 1000	e1:3, d1:3, d2:3, g12:3, g202:2, g15:1, e5:2	Negative	F. D3-7++, Dp.D3-7++, Df. D4-7++	Dp. Df., Fd., Cf., Pp., Av., Pl., 5G	Hand, arms, legs, trunk	
26/female	281	w1+w3:2, w6:3	Negative	Df.D4-7++, Phle.D4-7++	Df., Fd., Av., Pl.	Hands, flexural, trunk	Rhinitis May–Sept.
27/female	over 1000	d1:3	Negative	Dp.D4-7++, Df.D3-7++	Negative	Face, hands, flexures, arms	Rhinitis in April
28/male	3	d1:3, d2:2, e5:2, 4gmix:2	Negative	Dp.D2-7+++, Df.D2-7++, C.D2-7++	Df., Dp., Pp., Pl.	Trunk	Rhinitis, asthma bronchiale
29/male	119	d1:2, d2:2	Negative	Negative	Df., Dp., Fd.	Flexures	Perennial rhinitis
30/female	126	w6:2, w1+w3:3	Mercury amidochlor D3-7+++	Negative	Df., Dp., Av., Pp., 5G	Face	Rhinitis

House dust mite elicited positive responses with all the three methods in 8 cases (P2, P8, P13, P15, P18, P23, P25, P28); seven of them had severe skin symptoms on the face, eyelids and the neck; five of eight patients had hand symptoms as well. In two cases, APT and special IgE (P5, P27), and in one case (P20) APT and Prick tests, were jointly positive to house dust mite. These patients had also AD symptoms on the face, eyelid, hand and neck.

Cat epithel was positive with all three tests in three patients (P2, P23, P25). In one further case, it was positive with APT and Prick tests jointly (P16). The skin symptoms of this four affected patients worsened upon contact with cats.

We observed positivity to timothy pollen in one subject with both APT and Prick tests; the symptoms of the patient worsened in pollen season (P7).

One patient was positive to dog epithel by APT and special IgE jointly, and the symptoms flared up after this patient caressed the animal (P23).

Furthermore, we detected with all three tests or with APT and Prick test and/or IgE tests positivity to some pollens: mugwort (3 cases), platan (2 cases), timothy (1 case), and to dog epithel (1 case). Their relevance, however, couldn't be confirmed by clinical symptoms, data of the medical history and patients' observations (Table 5).

Discussion

Previously, AD patients were thought to be less susceptible to contact allergic reactions. The low sensitization rate was explained by Th2 dominance, by enhanced interleukin-4 (IL-4) and IgE production, and decreased interferon- γ (IFN γ) level. Atopic skin tends to have false-positive, irritative responses even in a symptom-free condition: the ratio of irritative reactions is increased in chronic AD.^{11,23–25}

It is known today that the prevalence of contact sensitivity among AD patients is concordant with data in the normal population. While genetic susceptibility is essential in AD, the external environmental effects are important in both forms of eczemas. Immunological processes are characteristic by both, although with different mechanisms.^{11,13,19,25,26}

Allergic contact dermatitis (ACD) is an acquired skin disease, which develops via small chemical haptens at the site of contact in previously sensitized patients. Active skin diseases leading to the damage of the skin barrier, such as AD predispose individuals to ACD.^{11,19,25,26} ACD is a classical type IV immune response. The process is initiated by haptens of low molecular weight binding to the epidermal carrier molecules. The immune system becomes sensitized to the hapten, and the re-exposition to the identical substance induces the inflammation and the clinical symptoms characteristic of allergic contact

dermatitis. In the pathogenesis of ACD, a decisive but not exclusive role is attributed to the IL-2 and IFN γ producing Th1 cells. AD is also an immune-mediated disease. Earlier, an exclusive importance of the Th2 subpopulation has been attributed to the pathogenesis. Today, more and more data support the role of the Th1 population in the process.^{11,27–30} While some possible common contact points of the two pathomechanisms remain to be further discovered, the clinical evidence already proved the coexistence of the two diseases.

Although AD is first of all considered to be a childhood disease, the number of symptomatic cases in adulthood is remarkable, and AD may even start first in adulthood ('adult onset AD'). Numerous studies discussed the occurrence of childhood AD and its prognostic factors. The adult form, however, started to attract attention only recently.^{13,31,32} These studies already attribute a significant role to the contact and aeroallergens that may flare up atopic skin symptoms. According to previous observations, nickel, chrome, cobalt, latex, fragrance mix and balsam of Peru are the most common contact allergens among adult atopics.^{11,14,18,19,23,26,31,33} We should consider metal sensitivity if symptoms affect the hands, whereas in case of symptoms on the head and neck, we should consider fragrance sensitization – especially in women. One can observe a high number of clinically irrelevant sensitization in the adult onset group. Thiomersal is the most common clinically not relevant allergen. Considering that topical steroids are one of the basics of the treatment, the possibility of steroid allergy also emerges in therapy resistant cases. This is a two-way process: sensitization exacerbates the symptoms of AD, but atopy itself also predisposes to the development of sensitivity.^{13,14,19,31,34}

Of Hungarian authors, Cserhalmi *et al.*²³ reported the results of their epicutaneous tests with allergens in atopic patients. Their investigations confirm the eliciting role of environmental contact factors with the leading of nickel. The high incidence of lanalcolum sensitization reported in their study is explained by iatrogeny. Other contact allergens provoking positive responses were cobalt, paraben, wood-tar, cathon, thiomersal, chrome, TMTD and mercury-amidochloratum. The ratio of sensitization was higher in AD patients with other atopic diseases, such as rhinitis, conjunctivitis and bronchial asthma.

The IgE-mediated contact reaction elicited by aeroallergens is an important pathogenetic factor in AD.² The skin symptoms of AD may be triggered and enhanced by aeroallergen exposition (house dust mite, pollen, animal epithel). If an adult atopic patient has symptoms on air-exposed surfaces (face, décolletage, lower arm, hands), the eliciting role of aeroallergens is likely, especially if the patient is less symptomatic or is symptom-free on skin surfaces covered with clothes. Anamnestically, it is important

that skin symptoms improve in high mountains (1500 m above sea level) and on the sea coast; whereas they deteriorate in pollen season, at dusty workplaces and among animals. The avoidance of aeroallergens is usually very difficult for patients.³⁵

A subgroup of atopic patients responds with positive skin reactions after putting environmental aeroallergens on the skin. APT (an epicutaneous test with allergens eliciting IgE-mediated reactions) may be regarded as a kind of 'provocation test' in these patients. Epicutaneous application of aeroallergens by APT on unaffected atopic skin elicits eczematoid reactions in 30–50% of patients with AD. Based on the comparison of the obtained results, the anamnesis, the clinical picture and other tests (Prick test, specific IgE, total IgE), one can determine the relevance of an allergen's capacity to elicit eczematous skin symptoms.^{2,13,15,35,36}

The central role of the IL-4, IL-5, IL-13 producing Th2 cells is known in the pathomechanism of AD. In patients with AD, IL-4 and IL-5 producing cells of Th0/Th2 type are dominant in acute skin symptoms. The immediate APT reaction is characterized by increased IL-4 production and Th2 infiltration for 24 h. In chronic skin lesions, however, the majority of lymphocytes have a Th1 cytokine profile and produce IFN γ . The development of a late APT reaction is preceded by a switch from the original Th0/Th2 cytokine profile to Th1. The process is accompanied by increasing IFN γ production.^{2,12,15,27,36,37}

One of the most frequently studied aeroallergens is house dust mite. Sensitization to house dust mite should definitely be considered in case of medium and severe symptoms on skin parts not covered with clothes (face, eyelids, neck and the hands). The symptoms may improve after the elimination of mites in many patients.^{12,38–40} In Central Europe, *D. pteronyssinus* and *D. farinae* are the most important pathogens. Their allergens derive from their excrement (Derp1 and Derf1: water soluble and heat unstable glycoproteins) and from the body of the mite (Derp2 and Derf2: water soluble and heat stable glycoproteins). A person with normal skin leaves 0.5–1 g of epithelium in the bed a week, which provides food enough for thousands of mites for months. There is a close correlation between medium and severe skin symptoms and the mite concentration measured in the bed mattress and on the floor of the bedroom. In these cases, the successful elimination of mites results the improvement of skin symptoms.^{18,20,41,42} Based on APT performed by Holm et al. in Sweden with 81 adult AD patients, sensitization to house dust mite was 56%.³⁹

The effective protection against house dust mite means dust control, regular vacuum cleaning (with HEPA screener), decreasing room temperature (below 20 °C) and humidity (below 50%) and avoidance of fitted carpets. It is useful

to choose mattresses and pillows stuffed with materials that do not provide living space for mites and to cover them with 'encasing' materials. It is required for the so-called 'encasing' materials to let through humidity and vapour and not to be permeable for even very tiny (1–5 μ m) particles.^{12,13,18,38,39}

Sensitization to animal epithel is typical in veterinary surgeons, animal carers, laboratory workers and also in pet keepers. According to the investigations of Sustaival,²² dog and cat epithel sensitizations are the most common among Californian veterinarians. If the sensitivity is clinically relevant, it is necessary to avoid the particular animal. The Feld1 allergen of cats, however, is present in the living space for a longer time even after the animal has left; therefore, in such cases, one should not expect immediate improvement.^{17,18,20,22,43} It is definitely hard to avoid aeroallergens of animal origin if the patient at relatives', friends', at the workplace or kindergarten gets into contact with animals or a person, who, carrying the allergen on their own clothes counts as 'contact person'.

Of aeroallergens, airborne pollens are the most problematic for patients to avoid. In fortunate cases, the difficulties limit to a particular time of year. If pollens flare up skin symptoms in an AD patient, it is advised to avoid open air programmes in that period and to spend the summer holidays in pollen-free places (sea coast, high mountains). Patients carry the pollens on themselves (on their skin, hair); thus, thorough personal hygiene is particularly important in the exposed period (e.g. daily hairwash). Drying the clothes in open air should be avoided, and it is also advisable to vacuum clean as often as possible. It is difficult to judge the eliciting role of pollens since the wind may carry the tiny particles to long distances from the plant.¹⁸

The increasing number of adult AD cases observed in the past years has turned the attention to ascertaining factors eliciting skin symptoms. Studies have revealed numerous environmental factors that may play a role in sustaining the symptoms. Of these, great importance is attached to contact and aeroallergens. We included in our study 34 subjects over 18 years of the patients at our Atopy Outpatient Department. Four of them were classified in the intrinsic, and 30 in the extrinsic group. We observed sensitization to one or more contact environmental allergens in 14 of the patients. The detected allergens were nickel, thiomersal, mercury-amidochlorate, mercury chloride, iodine chlorhydroxyquin, lanalcolum and fragrance mix. The following allergens were relevant in four cases according to the patients' observations: thiomersal (eye drops – eyelid involvement), lanalcolum (facial symptoms – cosmetics), fragrance mix (hands – cosmetics) and nickel (hands – metal objects).

No immediate response was seen with APT. Relevant late positivity was shown with APT in the intrinsic group

in one patient to *D. pteronissinus*. A late positivity with APT was found in 18 of 30 extrinsic AD patients. *D. pteronissinus* and/or *D. farinae* (15 of 18), cat epithel (4 of 18), dog epithel (1 of 18) and timothy (1 of 18) were clinically relevant allergens. Other allergens showing late APT positivity without clinical relevance were dog epithel and some pollens (mugwort, plantain, orchard grass, timothy and birch).

We examined the relevance of APT, specific IgE tests and Prick tests. We observed multiplex positivity by APT, specific IgE tests and Prick tests in 14 patients with extrinsic AD. Sensitization to *D. pteronissinus* and/or *D. farinae* (11 of 14), cat epithel (4 of 14), dog epithel (1 of 14) and timothy (1 of 14) proved to be clinically relevant with the atopic skin symptoms.

Conclusions

The proportion of contact sensitization to environmental allergens in the 34 adult atopic patients was remarkable (14 of 34, 41%). Out of the verified contact allergens, nickel, fragrance mix, thiomersal and lanalcolum proved to be relevant. In our study, house dust mite and cat epithel proved to be the most common relevant aeroallergens. *D. pteronissinus* and *D. farinae* sensibilization was high, particularly in patients with severe skin symptoms on the face, eyelids and hands. Pollens should be considered in patients with seasonal relapse of AD. Sensitization to animal epithel (cat, dog) was usually indicated by the flare-up of skin symptoms upon contact with animals. The relevance of the eliciting effects of sensitization could easily be supported in most cases by the medical history and the distribution of skin symptoms. In some adult AD patients with long-lasting AD, the relevance of triggering factors is hard to determine.

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