

Atopic Dermatitis in Adults

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Atopic dermatitis (AD) is a chronically relapsing eczematous disease, more common in infants and children than in adults and very rare after midlife. The diagnosis of AD is not always easy in adults, especially when the extension of lesions is limited and their distribution atypical. The aim of this study was to investigate epidemiologic and clinical features of adult AD. The medical files of 332 consecutive AD patients were reviewed to ascertain family and personal history of atopy, age at onset, morphology and localization sites of AD lesions, serum total immunoglobulin E levels, skin prick-test and patch-test results. The present study has show that the disease is more frequent in females and during the third decade of life, starts after the 18th year in slightly fewer than half the patients (47.6%), is prevalently localized in the limb flexures, eyelids, and perioral region, but also in the forehead, cheeks, and anterolateral region of the neck, where it is mainly mild to moderate. AD is of the intrinsic type in 30.4% of cases. Positive patch-test reactions to chemical allergens have been observed in 23.8% of patients. These are very important, because they may influence the occupational choices and the development of hand dermatitis.

ATOPIC DERMATITIS (AD) is a common chronically relapsing inflammatory skin disease characterized by itching eczematous lesions that are symmetrically distributed in peculiar sites and are associated with xerosis and often with atopic habitus.¹ Atopy is a personal or familial tendency to produce immunoglobulin E (IgE) antibodies in response to low doses of allergens (usually proteins) and to develop typical symptoms such as asthma, rhinoconjunctivitis, and eczema or dermatitis.²

In 1983, Wüthrich proposed to divide patients with the clinical phenotype of AD into two subtypes: “intrinsic” (or “nonallergic”) AD and “extrinsic” (or “classic” or “allergic”) AD.³ Intrinsic AD (IAD) is characterized by an absence of association with other atopic diseases, negative prick-test results for common inhalant and food allergens, normal total serum IgE level, and a lack of allergen-specific serum IgE antibodies to common aeroallergens and food allergens. Conversely, extrinsic AD (EAD) is associated with allergy to aeroallergens or food allergens.

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DOI 10.2310/6620.2011.10042

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AD can occur at any age, but it is more common in infants and children. The lesions arise in the first year of life in the majority (at least 60%) of cases and before 5 years of age in another 30% of cases.⁴ The disease appears after age 20 in only 2% of patients,⁵ and it is rare after midlife.⁶ However, the frequency of AD in adults is much higher because the skin lesions do not improve with time in 30 to 60% of infants or young children.^{7,8} The incidence of AD has been increasing over the past three to four decades, especially in the higher social classes and in countries with greater economic development.⁹ It is estimated that 10 to 15% of the children living in industrialized regions¹⁰ and 2 to 10% of adults¹¹ are affected by AD.

The diagnosis of AD is generally clinical, but diagnosis is not always easy with adults, particularly when the extension of lesions is limited, when the lesions' distribution is atypical, when the minor cutaneous atopy signs are not present, and when atopic mucous manifestations are not associated. In many cases, the most commonly employed diagnostic criteria (such as those of Hanifin and Rajka¹² and those of the UK Working Party¹³) cannot be satisfactory, especially when AD starts when the patient is more than 18 years of age.

The aim of this prospective study was to investigate epidemiologic and clinical features of adult AD.

Materials and Methods

From January 2004 to December 2007, 332 consecutive AD subjects older than 18 years (145 males [43.7%; mean age,

29.9 yr] and 187 females [56.3%; mean age, 30.9 yr]) were investigated in our outpatient section after written informed consent was obtained. In all enrolled subjects, AD was diagnosed according to the criteria of Hanifin and Rajka.¹²

The clinical data (family history of AD, family or personal history of rhinoconjunctivitis or bronchial asthma or both, age at onset of cutaneous lesions, and morphology and localization of dermatitis in the 3 years before our clinical examination) and the results of investigations (serum total IgE, skin-prick tests, and patch tests) were collected in a record for statistical analysis. The chi-square test and Fisher exact test were used to analyze the results, and *p* values of less than .05 were regarded as significant.

Serum total IgE level was determined with radio-immunoassay. Levels greater than 100 IU/mL were considered abnormal. Skin-prick tests were carried out on the volar surface of the forearm according to the criteria established by the Società Italiana di Allergologia e Immunologia Clinica (SIAIC).¹⁴ A series of 20 allergen extracts (inhalants, pollens, and foods), histamine dihydrochloride (10 mg/mL) as positive control, and saline as negative control (Lofarma, Milan, Italy) were used. Patch testing was carried out on each patient's back with the Società Italiana di Dermatologia Allergologica Professionale e Ambientale Vsidapa standard series (FIRMA, Florence, Italy) according to criteria established by the Gruppo Italiano Ricerca Dermatiti da Contatto e Ambientali (GIRDCA).¹⁵ Van der Bend Square Chambers (van der Bend B.V., Brielle, the Netherlands) were used, and only strong positive reactions (++ and +++) were considered.

Oral corticosteroids, antihistamines, and ultraviolet therapy were discontinued at least 3 weeks before the skin tests. No topical corticosteroids or immunosuppressive agents were used at the time of testing.

On the basis of clinical data, results of skin tests, and total serum IgE, the patients were separated into two groups (IAD and EAD patients) according to the criteria proposed by Wüthrich.³ The results were evaluated in their entirety but also by comparing the two groups.

The Eczema Area and Severity Index (EASI) was used for scoring the severity of dermatitis.¹⁶ The EASI is a composite index that includes an assessment of the percentage of area involved in each of the four body regions (head and neck, upper limbs, trunk, and lower limbs) and an assessment of four clinical signs (erythema, infiltration or papulation, excoriation, and lichenification). The sum of these scores gives the EASI

total, which could range from 0 to 72 (the maximum score).

In this study, the severity of AD was graded as mild (EASI score < 8), moderate (EASI score of 8–15), or severe (EASI score > 15).^{17,18}

The study was approved by the local ethics committee (Comitato Etico Aziende Sanitarie Umbria, Perugia, Italy).

Results

AD was mild in 88 patients (26.5%), moderate in 62 patients (18.7%), and severe in 182 patients (54.8%). Of these 332 AD patients, 167 (50.3%), 94 (28.3%), 47 (14.2%), 16 (4.8%), and 8 (2.4%) were aged 18 to 27 years, 28 to 37 years, 38 to 47 years, 48 to 57 years, and more than 57 years, respectively.

The distribution of age at the onset of AD is shown in Table 1. The eczematous lesions appeared after age 18 for 158 patients (47.6%), without statistically significant difference in regard to sex (47.1% for females vs 48.3% for males). In only a quarter of cases (25.9% [28.9% in males, 23.5% in females]) did the lesions appear during the first 3 years of life.

A positive family history of atopic diseases (AD or mucosal atopy) was found in the first-degree relatives of 122 subjects (36.7%). Seventy-six of these were females (40.6% of 187 females), and 46 males (31.7% of 145 males), but the sex-related difference was not statistically significant. Also, the age of AD onset was not influenced by family atopy because the skin lesions appeared in the first 18 years of life in 64 of 174 subjects (36.8%) and after the eighteenth year of life in 58 of 156 subjects (36.7%).

Personal mucosal atopy (rhinoconjunctivitis, asthma, or both) occurred in 192 AD subjects (57.8%), without significant statistical difference between males (94 of 145 [64.8%]) and females (98 of 187 [52.4%]) or between AD onset before (93 of 174 [53.4%]) and after (99 of 158 [62.6%]) the eighteenth year of life.

In 94.5% of cases, the involved skin was more or less reddened, lichenified, and covered with whitish

Table 1. Age at Onset of Atopic Dermatitis in 332 Adult Patients

Age at Onset (yr)	AD Patients (N = 332)	Males (n = 145)	Females (n = 187)
0–3	86 (25.9%)	42 (29.0%)	44 (23.5%)
4–10	47 (14.2%)	20 (13.8%)	27 (14.4%)
11–18	41 (12.3%)	13 (9.0%)	28 (15.0%)
> 18	158 (47.6%)	70 (48.3%)	88 (47.1%)

AD = atopic dermatitis.

pityriasiform scales, hemorrhagic and sometimes honey-colored crusts, linear scratch marks, and fissures. The skin lesions were distributed symmetrically. The hair was dry and lusterless when the lesions were localized on the scalp (6.1%), but a pronounced loss was observed only in four cases (1.2%). Asteatosis of clinically healthy skin and pruritus were nearly constant (91.9%) and were very severe in a third of cases. Nummular (15 patients), seborrheic dermatitis-like (7 patients), and prurigo-like (5 patients) patterns were the most prevalent morphologic types of dermatitis.

The body-site distribution of lesions in the 3 years before our clinical examination is reported in Table 2. Upper limbs (62.6%) were the main sites of involvement; in this area, the lesions were most commonly located on the antecubital flexures (32.8%) and hands (15.7%). The other sites were the face (44.9%) (particularly the eyelids, perioral region, forehead, and cheeks), lower limbs (36.1%) (above all, the popliteal flexures), neck (22.0%) (mainly the anterolateral surface), and trunk (20.8%). In regard to sex, the forehead and cheeks of females and the thighs, legs, and feet of males were significantly more often

involved ($p < .05$). Dermatitis was localized in the nipple area only in two females, and the elbows were grayish, asteatotic, and keratotic in five patients.

Serum total IgE levels were elevated in 205 (61.7%) patients, without statistically significant differences in regard to sex (males: 92 of 145 [63.4%]; females: 113 of 187 [60.4%]) or the age of AD onset (before the eighteenth year: 111 of 174 [63.8%]; after the eighteenth year: 94 of 158 [59.5%]). IgE levels greater than 300 IU/mL were observed in 88 (26.5%) patients (43 males and 45 females).

One or more positive prick-test reactions to aeroallergens and food allergens were seen in 227 subjects (68.4%). These reactions were significantly more common in males (111 [76.5%]) than in females (116 [62.0%]) ($p < .01$). Inhalants (178 [92 males and 86 females]) and pollens (175 [87 males and 88 females]) were more frequently involved than foods (37 [18 males and 19 females]) (Table 3).

Of the 79 patients (23.8%) who had positive patch-test results, 25/145 (17.2%) were males and 54/187 (28.9%) were females. Twenty-three patients had multiple sensitivity. Statistical analysis showed a significant correlation to female sex ($p < .05$). The most common causes of positive reactions were nickel sulfate (39 patients [49.4%]), cobalt chloride (10 [12.7%]), fragrance mix (9 [11.4%]), and potassium dichromate (8 [10.1%]). The relevance of

Table 2. Localization Sites of Adult Atopic Dermatitis in the 3 Years before Clinical Examination

Localization Sites	AD Patients (N = 332)	Males (n = 145)	Females (n = 187)
Face	149 (44.9%)	55 (37.9%)	94 (50.3%)
Forehead	65 (19.6%)	20 (13.8%)	45 (24.1%)
Eyelids	75 (22.6%)	29 (20.0%)	46 (24.6%)
Retroauricular folds	28 (8.4%)	13 (9.0%)	15 (8.0%)
Cheeks	60 (18.1%)	17 (11.7%)	43 (23.0%)
Perioral region	71 (21.4%)	21 (14.5%)	50 (26.7%)
Neck	73 (22.0%)	33 (22.8%)	40 (21.4%)
Anterolateral surface	58 (17.5%)	26 (17.9%)	32 (17.1%)
Posterior surface	22 (6.6%)	8 (5.5%)	14 (7.5%)
Upper limbs	208 (62.6%)	89 (61.4%)	119 (63.6%)
Arms	26 (7.8%)	12 (8.3%)	14 (7.5%)
Antecubital flexures	109 (32.8%)	48 (33.1%)	61 (32.6%)
Forearms	40 (12.0%)	19 (13.1%)	21 (11.2%)
Hands	52 (15.7%)	28 (19.3%)	24 (12.8%)
Trunk	69 (20.8%)	32 (22.1%)	37 (19.8%)
Anterior trunk	48 (14.5%)	24 (16.5%)	24 (12.8%)
Posterior trunk	27 (8.1%)	12 (8.3%)	15 (8.0%)
Lower limbs	120 (36.1%)	62 (42.8%)	58 (31.0%)
Thighs	32 (9.6%)	20 (13.8%)	12 (6.4%)
Popliteal flexures	64 (19.3%)	27 (18.6%)	37 (19.8%)
Legs	35 (10.5%)	22 (15.2%)	13 (7.0%)
Feet	24 (7.2%)	16 (11.0%)	8 (4.3%)

AD = atopic dermatitis.

Table 3. Positive Prick-Test Reactions to Aeroallergens and Foods in 332 Adult Atopic Dermatitis Patients

Allergen	Positive Reactions		
	Total	Males	Females
Gramineae mix	115	56	59
<i>Dermatophagoides pteronyssinus</i>	94	42	52
<i>Dermatophagoides farinae</i>	84	35	49
<i>Olea europaea</i>	52	27	25
<i>Cupressus sempervirens</i>	48	21	27
Plantaginaceae mix	41	25	16
<i>Parietaria</i> mix	36	20	10
<i>Corylus avellana</i>	31	19	12
Compositae mix	27	13	14
Betulaceae mix	23	13	10
Animal dandruff	18	11	7
<i>Ambrosiae</i> mix	14	9	5
Tomato	5	3	2
Fish mix	4	3	1
Apple	4	—	4
Hazelnut	4	1	3
Kiwi	4	3	1
Cow's milk	3	2	1
Chicken egg white	3	2	1

positive reactions remained unexplained for 6 of 10 patients sensitized to cobalt chloride (all sensitized to nickel sulfate) and for 2 of 8 patients sensitized to potassium dichromate.

On the basis of the results, EAD was diagnosed in 231 subjects (69.6%) (115 males and 116 females; mean age, 31.6 yr), and IAD was diagnosed in 101 subjects (30.4%) (30 males and 71 females; mean age, 27.1 yr). There were no significant differences between the two AD subgroups in the frequency of the age at lesion onset (Table 4) and the localization site (Table 5), whereas familial atopy was significantly more frequent for EAD subjects (89 [38.5%]) than for IAD subjects (33 [32.7%]), especially for those whose lesions appeared after age 18 (EAD group: 38 of 114 [33.3%]; IAD group: 3 of 44 [6.8%]; $p < .01$). Positive patch-test reactions were observed in 51 (22.1%) EAD patients and 28 (27.7%) IAD patients, without qualitative differences (Table 6).

Discussion

Numerous original articles, reports, and reviews have been published about AD in infants and children. However, the epidemiologic and clinical aspects and the factors that play a role in triggering and sustaining the AD persisting in adulthood or the AD developing de novo in adults have been less investigated. There are only a few studies on AD in adults, and these are based on hospital patient records^{19–23} or questionnaires.²⁴

Our study has confirmed no significant preponderance of females among adult AD patients.^{17,18,20} This is in contrast to other investigators' results,^{21,24} but the discrepancy could be due to the different selection of patients (Italian Navy Hospital patients) in one instance²¹ and the different investigative method (questionnaires) in another.²⁴ The higher prevalence in females than in males seems to be typical for adult AD because it was not found for AD in infants and children.²⁵

Table 4. Age at Onset of Lesions in 231 Adult Patients with Extrinsic Atopic Dermatitis and 101 Patients with Intrinsic Atopic Dermatitis

<i>Age at Onset (yr)</i>	<i>EAD Patients (n = 231)</i>	<i>IAD Patients (n = 101)</i>
0–3	60 (26.0%)	26 (25.7%)
4–10	32 (13.9%)	15 (14.9%)
11–18	25 (10.8%)	16 (15.8%)
> 18	114 (49.3%)	44 (43.6%)

EAD = extrinsic atopic dermatitis; IAD = intrinsic atopic dermatitis.

Table 5. Localization Sites of Lesions in Extrinsic and Intrinsic Atopic Dermatitis in the 3 Years before Clinical Examination

<i>Localization Sites</i>	<i>EAD Patients (n = 231)</i>	<i>IAD Patients (n = 101)</i>
Face	106 (45.9%)	43 (42.6%)
Forehead	47 (20.3%)	18 (17.8%)
Eyelids	53 (22.9%)	22 (21.8%)
Retroauricular folds	18 (7.8%)	10 (9.9%)
Cheeks	44 (19.0%)	16 (15.8%)
Perioral region	49 (21.2%)	22 (21.8%)
Neck	50 (21.6%)	23 (22.8%)
Anterolateral surface	44 (19.0%)	14 (13.9%)
Posterior surface	11 (4.8%)	11 (10.9%)
Upper limbs	147 (63.6%)	61 (60.4%)
Arms	18 (7.8%)	8 (7.9%)
Antecubital flexures	73 (31.6%)	36 (35.6%)
Forearms	27 (11.7%)	13 (12.9%)
Hands	39 (16.9%)	13 (12.9%)
Trunk	45 (19.5%)	24 (23.8%)
Anterior trunk	33 (14.3%)	15 (14.8%)
Posterior trunk	20 (8.7%)	7 (6.9%)
Lower limbs	80 (34.6%)	40 (39.6%)
Thighs	24 (10.4%)	8 (7.9%)
Popliteal flexures	45 (19.5%)	19 (18.8%)
Legs	24 (10.4%)	11 (10.9%)
Feet	18 (7.8%)	6 (5.9%)

EAD = extrinsic atopic dermatitis; IAD = intrinsic atopic dermatitis.

Our results also show large differences in adult AD prevalence among age groups. The mean age of our patients was 30.4 years, without significant relationship to sex. The disease was progressively less frequent in successive decades and very rare in patients older than 57 years. The same age-related trend was reported by Ozkaya²² among 63 patients with AD that began after the age of 18 years and by Saeki and colleagues²³ among Japanese government officials or their family members

Table 6. Most Frequently Positive Patch-Test Reactions in Atopic Dermatitis Patients Sensitized to Contact Allergens

<i>Contact Allergen</i>	<i>AD Patients (N = 79)</i>	<i>EAD Patients (n = 51)</i>	<i>IAD Patients (n = 28)</i>
Nickel sulfate	39 (49.4%)	25 (49.0%)	14 (50.0%)
Cobalt chloride	10 (12.7%)	7 (13.7%)	3 (10.7%)
Fragrance mix	9 (11.4%)	4 (7.8%)	5 (17.9%)
Potassium dichromate	8 (10.1%)	5 (9.8%)	3 (10.7%)
PTBFR	7 (8.9%)	5 (9.8%)	2 (7.1%)
Balsam of Peru	6 (7.6%)	4 (7.8%)	2 (7.1%)

AD = atopic dermatitis; EAD = extrinsic AD; IAD = intrinsic AD; PTBFR = *p*-tert-butylphenol formaldehyde resin.

visiting the Health Service Center for an annual health checkup.

Adult AD has a broad range for age at onset, but this study suggests that AD is a childhood disease that extends into adult life in only half (52.4%) of cases. Therefore, the early age of onset (infancy and childhood) is a less important diagnostic criterion for adults than for those in other periods of life.

As with AD in children, AD in adults is based primarily on historical and clinical data, but IgE levels and the results of skin-prick tests with environmental allergens may be useful. However, the association with rhinoconjunctivitis and asthma (57.8%), elevated serum total IgE levels (61.7%), and one or more positive results of skin-prick tests with aeroallergens (59.6%) seems to be more prevalent than is a positive history for atopic diseases in first-degree relatives (36.7%) and sensitivity to food allergens (11.4%). The results were not statistically correlated with the sex of patients or the age at AD onset.

The diagnostic value of family history is less important in adult AD than in childhood-onset AD, for which prevalence varies between 58% and 68%.²⁴ This could be due to the lesser reliability of anamnestic data at this time.

The role of food allergens as an aggravating factor is less important in adults, although pollen-associated food allergens have been suggested as playing a role in up to 15% of severely affected patients with AD.²⁶ Moreover, sensitivity to classic food allergens such as milk and eggs has been shown only rarely (7.4%) and often is not clinically relevant.²⁷

The diagnosis of adult AD is mostly clinical and is based on the typical morphology and distribution of lesions. The picture is similar to that in later childhood, with lichenification, especially of the antecubital flexures, eyelids, perioral region, and popliteal flexures. However, involvement of the forehead, cheeks, and anterolateral region of the neck is very common in adults,^{24,28} whereas the frequency of hand involvement is variable (50.0% according to Sandström Falk and Faergemann²⁸ and 12.8% in our study). When the hands are affected, the differential diagnosis between AD and irritant contact dermatitis may be difficult. Diagnosis is enabled by (1) the lichenified and minimally phlogistic aspect of the lesions, (2) the lesions' sharp margins and symmetrical distribution, (3) the prevalent localization on the backs of the hands and fingers (especially the knuckles) and on the volar side of the wrists, (4) severe pruritus, (5) a chronic course with temporary remissions in summer, (6) an association with atopic mucous manifestations, (7) a positive family history of atopy, and (8) increased serum IgE levels.

Adult AD may sometimes have atypical morphologic aspects such as nummular, follicular, prurigo-like, and seborrheic dermatitis.^{22,29} Neck pigmentation (also called ripple pigmentation, dirty neck, or poikiloderma-like skin changes) has also been reported.^{30,31} However, xerosis of uninvolved skin and itching are constant and are most severe in the winter months.

The role of contact allergy in AD patients is often underestimated. Our study showed a high prevalence of positive patch-test reactions (23.8%), which were significantly more common in females than in males ($p < .05$), as we reported previously.^{32,33} The most common sensitizers were metals (nickel sulfate, cobalt chloride, and potassium dichromate) and fragrance, but their clinical relevance was not always evident. However, the identification of contact allergens is very important because it may influence the clinical course of AD, the patient's occupational choices, and the development of hand dermatitis among those who work in certain occupations (such as hairdressers, cleaners, metalworkers, mechanics, and nurses). The data support the importance of patch testing and preventive strategies for AD patients when occupational choices are made, especially when these choices implicate exposure to sensitizing compounds.

The positive patch-test reactions were not related to the two subtypes of AD (IAD and EAD). In our series, the prevalence of adult IAD (30.4%) was slightly higher than the mean values (20%) reported by others in children or in groups of patients of various ages who are affected by AD.^{34–36}

As with infants and children,³⁷ IAD in adults does not differ from EAD with regard to age at onset and to the features and distribution of lesions, whereas it is significantly more common in females (70.3% for IAD vs 50.2% for EAD) than in males and in the youngest adults (mean age, 27.1 yr for IAD patients vs 31.6 yr for EAD). It is possible that some IAD patients could develop respiratory allergies or allergic conjunctivitis in the future. The prevalence of atopic diseases in relatives was significantly higher among EAD subjects than among IAD subjects.

Conclusion

Adult-onset AD is an important subtype of AD, especially in young adults. As with children and adolescents, diagnosis is generally clinical because there are no specific laboratory markers. The clinical diagnosis includes features such as pruritus, a chronic or chronically relapsing course, typical morphology and distribution of lesions, personal or family history of asthma, and allergic

rhinoconjunctivitis. Nevertheless, AD can sometimes have a different morphology (ie, a nummular, prurigo-like, or seborrheic dermatitis-like morphology) and can occur with normal levels of total and allergen-specific serum immunoglobulin E in about a third of cases. Adult AD is mainly mild to moderate, but it is severe in 15.7% of our patients. In such cases, or when the lesions are localized on the hands, the social and economic implications are very important.

Finally, it has been reported that aeroallergens likely play an eliciting role when the lesions are localized on air-exposed surfaces, especially if the patient is symptom free on clothes-covered areas and if skin symptoms deteriorate during pollen season, or when the patient works in dusty workplaces or among animals.³⁸ However, our data on the localization sites of adult AD (see Table 5) are not in agreement because there was no more facial involvement in the IAD than there was in the EAD.

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