

REVIEW ARTICLE

Atopic dermatitis in older patients: particular points

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Abstract

We review the particular characteristics of atopic dermatitis (AD) in adult life, and compare findings with those of AD in childhood. AD affects 1–3% of adults world-wide, and can present as adult-onset AD, or as infantile/childhood AD that persists, or recurs after many years. Eczema in adults usually exists for years, compromising quality of life, sex life and occupational choices. The flexural areas, shoulders, head-and-neck, and hands are typically affected. In elderly adults, eczematous erythroderma is common. The intrinsic (non-IgE-allergic) eczema subtype affects 5–15% of cases. Classical food allergy has a low importance, although non-IgE-mediated and pseudoallergic reactions can cause eczema. Sensitivity to aeroallergens, especially dust mite, is demonstrated in the majority of adult AD patients, including elderly adults, by immunoglobulin E-mediated tests and/or atopy patch tests. Occupational allergic and irritant contact dermatitis is increased. In adults, as in children, *Staphylococcus aureus* colonization is very high, whereas adult skin is more heavily colonized with *Malassezia* yeasts. Immediate and delayed sensitization to *Malassezia sympodialis* is specific for intrinsic and extrinsic AD, occurring especially in head-and-neck eczema. Concerning therapy, older patients are prone to certain adverse drug effects. In conclusion, differences exist between childhood and adult disease. As we should be seeing more adults with AD in the future, there is a need for more clinical and immunological studies in older patients.

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Keywords

adult, allergy, atopic dermatitis, eczema, intrinsic, sensitization

Conflict of interest

None declared.

Introduction

Atopic dermatitis (AD) is a common, pruritic, eczematous, inflammatory skin disease, with a chronic and relapsing course that can affect only the skin, or be a manifestation of a systemic disorder that also includes allergic rhinitis, asthma and food allergy.¹ It is a disease mostly of childhood, but also of adult life. This article focuses on particular characteristics of adult AD, including those adults with AD since childhood and those with adult-onset AD, and on differences that exist between disease in young patients and older patients, according to recent, relevant articles.

Epidemiology

The world-wide prevalence of AD has increased two- to threefold over the past 30 years.¹ Relatively few epidemiological studies deal with adults (>18 years old) with AD. Studies from the previous decade found that the prevalence in adults aged above 20 years

old, was approximately 2%, while the 1-year period prevalence in adults over the age of 40 years was 0.2%.² Recently, the prevalence of AD in adults was assessed to range from 1% to 3%.³ The lifetime prevalence of AD is considerably lower in the elderly, compared with younger adults, although elderly patients with AD are increasing in industrialized countries.^{4,5} Adults with a longer duration of school education appear to have a higher disease risk, but no differences in social class over time were noted.^{4,6} Considering the sex ratio, there appears to be a female predominance, although in elderly adults (>65 years old), a male dominance is reported.^{7–10}

The classical course of childhood eczema shows improvement by adolescence.^{1,2} In a UK study, 74% of the children were clear from symptoms after the age of 16 years.¹¹ However, a 24-year follow-up study in Swedish children, found that 62% of previous inpatients and 40% of outpatients still had dermatitis.⁷ In elderly adults with AD, various patterns of eczema were seen during a lifetime and recurrence of eczema after many years was common.^{5,10}

Adult-onset AD is not rare, especially in the third decade of life.¹² A study from a tertiary skin centre in Singapore, found that 13.6% of AD patients had onset after the age of 21 years.¹³ Among 2604 patients attending a contact dermatitis clinic in Australia, 9% suffered from adult-onset AD.⁸ The prevalence of AD in Nigeria was 8.5%, and 24.5% of patients had onset after age 21 years.¹⁴

Finally, the majority of adults (59%) still reported eczema after 25–38 years.⁹ The few follow-up studies performed in adults with AD show that eczema severity decreases over the years.^{9,15,16} Head-and-neck eczema was a prognostic factor for disease persistence in Swedish adults, whereas Japanese investigators found that high values of serum total immunoglobulin E (IgE) and a long duration of eczema were poor prognostic factors, predicting persisting eczema after 10 years in adults.^{9,15,16} The increased prevalence of AD in children and the observation that AD in most adults continues for many years, suggests it is very likely we will be seeing more older patients with AD in the future.^{9,15}

Quality of life

Quality of life is compromised in adults with AD, both related to disease severity and to emotional components.^{17–20} Among adult skin disease outpatients, evaluated using the Dermatology Life Quality Index, AD patients were the worse scoring group.¹⁸ Severe AD, may be considered equal to angina pectoris, chronic anxiety, rheumatoid arthritis, multiple sclerosis or regional oesophageal cancer.¹⁹ AD affects quality of life in adults by increasing psychological stress and patients suffer from fatigue, perceived helplessness, anxiety and depression.²⁰

Concerning the degree of handicap in relation to the choice of education and occupation, 38% of AD patients had abstained from a specific education, or job, due to AD, and even mild-to-moderate disease causes handicap, as seen from increased sick leaves and early retirement pensions.²¹ Finally, a decrease in sexual desire due to AD was noted in 57.5% of the patients, while 36.5% of partners reported that eczema had an impact on their sex life.²²

Disease subtypes and clinical features

Two subtypes of AD are distinguished, the extrinsic (IgE-allergic) type and the intrinsic (non-IgE-allergic) type, both with the same clinical features. A recent, well-carried out investigation in 259 adult patients found that only 5.4% fulfilled the criteria of intrinsic AD.²³ Other studies classified 85–88% of adult patients in the extrinsic subtype.^{12,24} Among 16 elderly adults with AD, 12.5% had the intrinsic subtype.¹⁰ These findings support that intrinsic eczema is an uncommon entity in adults with AD and it raises the need for further investigation.²³

Many major and minor criteria exist as guidelines for arriving at a diagnosis of AD, but little is known about the validity of these criteria in adult AD.^{15,25} Pruritus is severe in active disease and it is present in all phases and ages of AD. Dry skin is another

characteristic seen across all ages and is typically made worst by irritation. The diagnosis of AD in adults requires the exclusion of allergic contact dermatitis, seborrhoeic dermatitis, psoriasis, scabies and cutaneous lymphoma.

The characteristic distribution in adults (>18 years old) is inflammatory eczema with lichenification, affecting the flexural and extensor areas, hands, shoulders, neck, face and eyelids.^{8,9,15,24} The head-and-neck distribution is more common in adults than in children, often occurring without any history of childhood eczema (Figs 1–2).¹⁵ The prevalence of hand dermatitis is more common in atopics, especially women, and occupational irritants and domestic work favour its development.⁷ Nummular lesions are a common non-typical morphological variant in adult AD.¹²

Characteristics of AD in the elderly subjects remain unclear and all relevant articles are from Japan.^{5,10,26} The term senile type AD was first used to refer to ages above 50 years old, but is not widely used.²⁶ AD in the elderly subjects (>65 years old), showed a man : woman ratio of 3 : 1.¹⁰ Clinical features appear to resemble the adult phase, except that lichenifications in the elbow and knee folds are uncommon.^{5,10} Important clinical manifestations were eczematous erythroderma (62.5%) and unclassified chronic eczema (31.3%).¹⁰ Differences between AD in childhood and in adults are given in (Table 1).



Figure 1 Typical lesions of adult atopic dermatitis on the arm.



Figure 2 Typical lesions of adult atopic dermatitis on the neck.

Table 1 Epidemiological and clinical differences between atopic dermatitis in early and older life [references shown in italics]

Parameter	Childhood	Adult
Prevalence, %	1–20 [25]	0.2–3 [2,3]
Social class	Important [1]	Not important [6]
Sex dominance	Slight female [1]	Female [8,15]/Elderly: male [10]
Clinical features	Age related [25]	Flexural sites, head-neck, hands [15,24]/Elderly: erythroderma, less flexural fold lichenification [5,10]
Allergic subtype, %	44 [69]	85–95 [12,23]/Elderly: 87.5 [10]

Pathogenesis

Genetic factors

Genetic factors are a strong risk factor for AD. In European adults, null mutations in the epidermal barrier protein filaggrin gene, resident on the epidermal differentiation complex (1q21), were a predisposing factor for persisting eczema of early-onset, and the allergic subtype.^{27,28} Japanese investigators found that polymorphism in the promoter of the interferon gamma receptor 1 gene are a genetic risk factor for the development of cataract in AD.²⁹

Skin barrier dysfunction

The hallmark of AD is epidermal barrier dysfunction, documented by increased transepidermal water loss, and leading to increased skin penetration of allergens, microorganisms and irritants.²⁵ Mutations in the filaggrin protein gene and reduction in stratum corneum lipids (ceramides) are important factors for barrier dysfunction.^{27,28,30,31} Normal-appearing aged skin is deficient in ceramide, as compared with that of the younger, healthy controls.³⁰ Thus, decreased stratum corneum lipids, especially ceramides,

appear to be a major aetiological factor for atopic dry skin and aged skin.³⁰

Immune dysregulation

The acute inflammatory phase of AD is dominated by activation of T helper type 2 (Th2) cells and induction of IgE production, whereas Th1 cell cytokine responses of delayed hypersensitivity are more dominant in the chronic phase.²⁵ Skin proteins released by scratching, foods, environmental airborne allergens and products of infectious pathogens can induce allergen-specific IgE (sIgE) antibodies in AD patients.^{25,31} In addition, delayed eczematous reactions after the topical application of atopic allergens [atopy patch test (APT)] and contact allergens are seen.²⁴ Hypersensitivity responses in adults, as compared with children with AD, are shown in (Table 2).

Finally, AD skin is characterized by defective cutaneous immune responses to microorganisms.³¹ The production of antimicrobial peptides is decreased in AD skin.³¹ As vitamin D is involved in this defence pathway, low vitamin D levels in older adults might increase susceptibility to infections.³²

Table 2 Sensitization to allergens in atopic dermatitis patients [reference number is shown in italics]

Positive reactions	Children	Adults
Autoantibodies		
IgE to skin protein, %	80 (infants) [31]	25 [31]
Foods		
Food-sIgE, or prick test, %	37 (infants)-18 [69]	24–66 [35]/Elderly: 62.5 [10]
APT to wheat, celery, egg white, %	15, 12, 11 [36]	8, 8, 11 [36]
OFC, %	46–60 [37]	Low, but unclear [38]
OFC without food-specific IgE, %	10–25 [37]	59 [37]
OFC to pollen-related foods, % of birch-sensitive patients	33 [37]	46 [39]
Aeroallergens		
Aeroallergen-sIgE, or prick test, %	18 (infants)-67 [69]	65 [44], 80–83 [35]/Elderly: 86 [10]
Dust mite-sIgE, or prick test, %	20–60 [70], 81 [41]	59 [44], 45–83 [35], 98 [41]/Elderly: 86 [10]
APT to dust mite, %	30–50 [70], 44–64 [71]	44 [44], 45 [43], 56 [46]
Microorganisms		
<i>Staphylococcus aureus</i> superantigen-sIgE, %	34 [49]	57 [49]
<i>Malassezia</i> sIgE, or prick test, %	17 [72], 12.5 [41]	29 [15], 51 [53], 46–53 [52], 65 [41]
APT to <i>Malassezia</i> , %		24 [46], 38 [53], 49 [52]
Contact allergens		
Standard patch test, %	43 [73]	40 [24,56]

APT, atopy patch test; OFC, oral food challenge; sIgE, specific IgE.

Triggers of AD

Psychological stress

Complex psycho-neuro-immunological interactions are involved in eczema.³³ Stress alters skin barrier function, T-cell immune responses and antimicrobial immunity, and it induces pruritus, leading to further skin damage from scratching.³³ AD patients suffer from stress-related exacerbations and stress is one of the most important trigger factor of eczema.³ Psychological stress-reduction interventions improve skin manifestations and patient well-being.³³

Foods and airborne allergens

Food and airborne allergens (aeroallergens) can play a role as trigger factors in adults with AD. Sensitization is typically demonstrated in adult AD, including elderly adults, particularly in moderate–severe disease.^{10,34–36} With regard to clinical relevance, the APT was recently found to have a higher specificity, based on history, as compared with allergen-sIgE, or skin prick tests, in children and adults with AD.³⁶

Classical food allergy has small clinical importance in adults with AD, in contrast to children.^{37,38} However, foods can play a ‘non-classical role’ in eczema. Foods cross-reacting to birch pollen can trigger AD, after oral challenge, in birch-sensitized adults with a negative food history.³⁹ Most children with AD that react to foods have positive skin prick tests or sIgE, whereas this may not be true for adults.³⁷ Finally, certain foods (alcohol, food additives) may cause exacerbations of eczema through non-immune mechanisms and clinical improvement was found in 63% of adult patients after 6 weeks on a low pseudoallergen diet.⁴⁰

Total IgE and aeroallergen-sIgE levels are the highest in AD, compared with other atopic diseases, and no decrease is seen with ageing.^{34,41} Adults with, moderate–severe, refractory AD have positive skin prick tests to multiple aeroallergens.³⁵ The dominant IgE antibody in adult AD is dust mite, irrespective of total serum IgE levels.⁴² Among elderly patients, 86% had aeroallergen sIgE, mostly against dust mite, followed by pollens.¹⁰ Among 115 adult patients, 54% demonstrated one or more positive APT to aeroallergens, compared to 6% of healthy controls.⁴³ Based on APT studies in adult AD, dust mite is the most common and clinically relevant allergen, while positivity is the highest in head-and-neck eczema (56%) and the intrinsic subtype (67%).^{24,43–46}

Skin microorganisms

Atopic dermatitis predisposes to skin infections, microbial skin colonization and sensitization to skin microorganisms.^{47,48} Microorganisms may be a trigger factor for eczematous reactions in sensitized AD patients. *Staphylococcus aureus* colonization is high in adults (86%) and is associated with eczema severity.⁴⁷ sIgE against *S. aureus* toxins with superantigen properties is detected in over half of adult patients and correlates

with eczema severity.^{48,49} The highest prevalence (92%) of IgE antibodies against *S. aureus* enterotoxins was seen in adult patients with total IgE levels >2000 IU/mL.⁴² *Staphylococcus aureus* α -toxin promotes immune responses that contribute to chronic eczema and 34% of adult patients had α -toxin-producing strains isolated from the skin.⁵⁰

Malassezia yeast colonization is higher in adults, as compared with children with AD.⁵¹ The prevalence of sIgE antibodies to the species *Malassezia furfur* is also much greater in adult patients.⁴¹ IgE antibodies against *Malassezia* species were found mostly among adult patients with elevated total IgE levels.⁴² Sensitization to *Malassezia sympodialis* is specific for intrinsic and extrinsic AD, and adults with ongoing eczema and head-and-neck eczema are prone to sensitization.^{15,46,52,53} Among 132 adult patients, 51% showed a positive skin test and 38% a positive APT to *M. sympodialis*, as compared to 55% and 41% with head-and-neck eczema.⁵³ Adults with intrinsic eczema show both positive IgE-mediated (36–50%) and APT (38%) reactions to *M. sympodialis*.⁵²

Contact allergens and irritants

The relationship between atopy and contact allergy remains unclear. AD is a risk factor for allergic contact sensitization, according to a recent Scandinavian adult population study.⁵⁴ Contact allergy increases with age in atopics.⁵⁵ At least one positive patch test to standard series was found in approximately 40% of AD patients aged 15 years or more.^{24,56} Nickel, constituents of cosmetics and topical treatments are relevant contact allergens.^{24,25}

Atopic dermatitis is aggravated by irritants. Excessive washing, soaps and detergents can induce flares of AD in daily life.²⁵ AD is the most common cause of occupational dermatitis and doubles the risk of developing irritant dermatitis, particularly in occupations involving wet work.⁵⁷ In atopic adults, occupational contact dermatitis can precipitate generalized eczema with an AD pattern.⁵⁸ Eczema can persist even after removal from a high-risk occupation.^{57,58} Thus, pre-employment counselling of adolescents and adults with atopic eczema is important.^{57,58}

Treatment

Regardless of age, the successful approach to the management of AD requires a combination of interventions and treatments. The goals of treatment are to identify, eliminate and prevent, specific and non-specific trigger factors, while preventing skin damage and improving barrier function.

Topical treatment

Emollients should be applied on involved and non-involved skin, and continued long after other treatments have been stopped.²⁵ There may be a role for therapeutic baths in salt-rich water that improve skin barrier function.⁵⁹ To decrease the bacterial and fungal load, topical antiseptics, topical antifungals and topical

antibiotics can be applied.²⁵ However, *S. aureus* strains resistant to topical antibiotics have emerged.^{47,48}

The use of topical steroids for acute flares, together with maintenance topical calcineurin inhibitors, is recommended.²⁵ Topical tacrolimus is more effective than pimecrolimus in adults with moderate-to-severe AD, but both agents have a similar safety profile and can be applied on areas with sensitive, thin skin (face, eyelids).^{60,61} In adults with AD, tacrolimus ointment was effective and well tolerated, for up to 2 and 4 years.^{62,63} Adults with refractory AD greatly benefit from 7 days of wet-wrap dressings with diluted steroids.⁶⁴

Systemic treatment

Sedating antihistamines can reduce itch during relapses, but they affect driving skills, and should not be combined with alcohol, or certain antidepressants.²⁵ For acute flare-ups, short courses of oral steroids (20–40 mg prednisolone) can be useful.²⁵ Older patients should be closely monitored for increased blood glucose, increased blood pressure and ocular side-effects. Daily supplementation with probiotic-rich yogurt benefited adults with moderate AD, in a small, placebo-controlled, study.⁶⁵

For widespread bacterial skin infections, erythromycin, clarithromycin, semisynthetic penicillins or cephalosporins, used for 7–10 days, are effective, but recolonization occurs soon after treatment.^{25,48} *Staphylococcus aureus* is universally resistant to penicillin in adults.⁴⁷ In adults with IgE hypersensitivity to skin yeasts and positive cultures, oral ketoconazole improved eczema, but long-term studies are lacking.⁶⁶

Phototherapy is a well-established second-line treatment for adult and adolescent patients with AD, and UVB in combination with UVA is most effective.²⁵ In severe AD, cyclosporin A is effective, and effectiveness has been shown to be similar in adults and children, although tolerability was better in children.⁶⁷ It should be used in limited patients because of serious side-effects, and serum creatinine and blood pressure must be closely monitored.⁶⁷ Interferon γ and infliximab have been tried in severe AD, but there are too few, well-carried out, studies to justify their use in adults.⁶⁷ Finally, a recent, placebo-controlled study in adults with AD sensitized to dust mite, demonstrated improvement in severity scoring, after 4 months of specific immunotherapy with dust mite, especially in patients with severe AD.⁶⁸

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