# Atopic Dermatitis (Eczema) — Symptoms and Treatment

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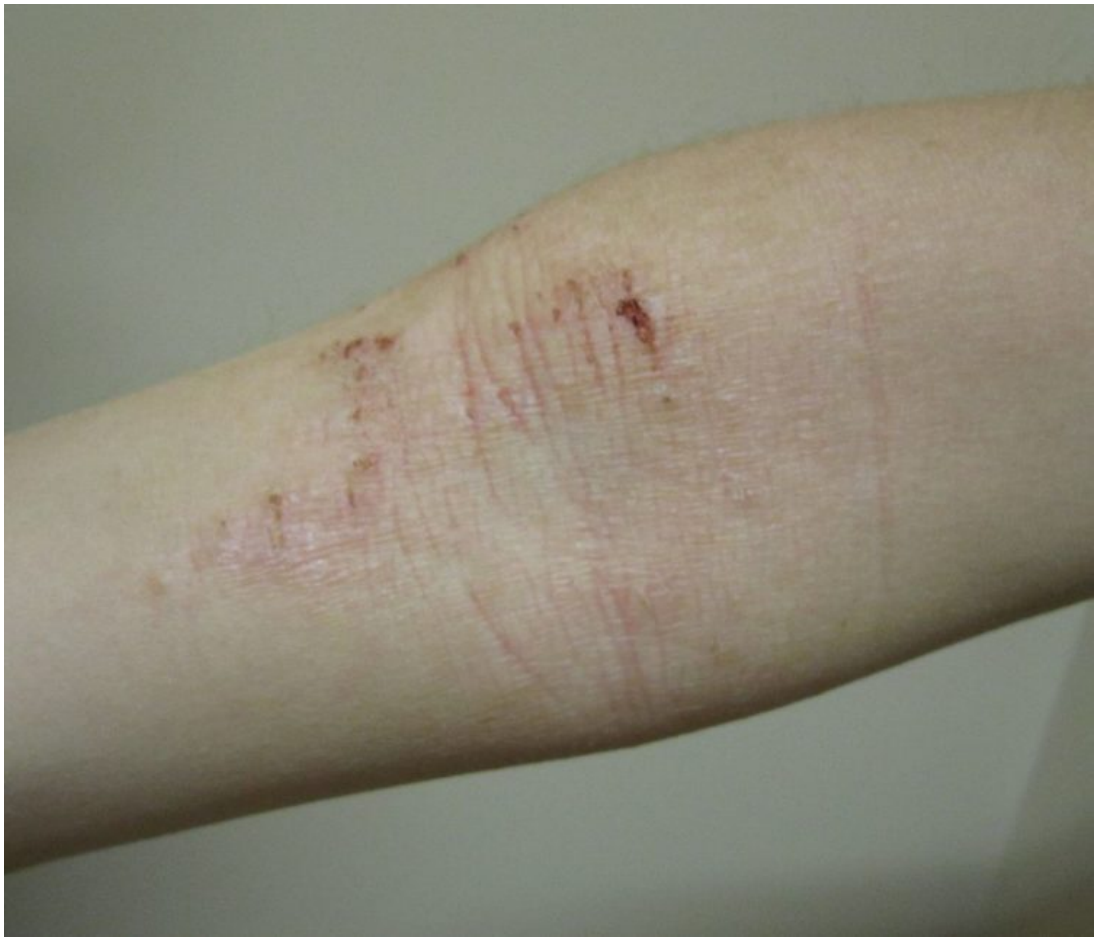
**Atopic dermatitis is a common, chronic dermatological disorder of unknown origin characterized by intense itching and eczematous lesions. In this chapter, after an introduction to general terminology for skin lesions, epidemiology, clinical features, diagnosis and management of atopic dermatitis are briefly discussed. As the diagnosis is purely clinical, differentiation from alternative diagnoses is also important. Emollients, topical corticosteroids, and trigger avoidance constitute the mainstay of management.**



## General Terminology for Skin Lesions

- **Macule:** A non-palpable lesion < 1 cm
- **Patch:** A non-palpable lesion > 1 cm
- **Papule:** An elevated lesion > 1 cm in diameter
- **Plaque:** A flat-topped elevated lesion > 1 cm in diameter

- **Nodule:** A rounded elevated lesion > 1 cm in diameter
- **Tumor:** An elevated lesion > 2 cm in diameter
- **Vesicle:** A blister filled with clear fluid, having < 1 cm diameter
- **Pustule:** A blister filled with pus, having < 1 cm diameter
- **Bulla:** A vesicle filled with fluid, having > 1 cm diameter
- **Erosion:** Lesion due to partial-thickness loss of the epidermis
- **Ulcer:** Lesion due to full-thickness loss of the epidermis

# Definition of Atopic Dermatitis

Atopic dermatitis can be considered a disease of **altered skin barrier** integrity due to **immune dysregulation**. Atopic dermatitis is a chronic relapsing inflammatory skin disease that often precedes asthma and other allergic disorders. The main features of the skin condition are intense **pruritus** and **eczematous skin lesions**.

# Epidemiology of Atopic Dermatitis

The lifetime prevalence of atopic dermatitis in school-aged children in the United States has been reported to be up to 17 %. There is a considerable variable range of prevalence of atopic dermatitis based on the studied population (8.7—18 %) suggesting that environmental and genetic factors contribute significantly to the disease.

A family history of atopic dermatitis or other allergic conditions put the child at an increased risk of developing the disorder. Moreover, the previous history of atopy in the patient is an important risk factor for atopic dermatitis.

# Etiology of Atopic Dermatitis

Atopic dermatitis is a multifactorial disease with clinical presentation determined by complex interactions between different etiological factors described below.

## Genetic factors

Among multiple possible candidate loci, important susceptibility loci associated with atopic dermatitis include those on **1q21**, **3p24-22**, **3q21** and **17q25**. As epidermal barrier dysfunction plays an important role in the pathogenesis of atopic dermatitis, mutations of **filaggrin gene** in the epidermal differential complex (1q21) are associated with early-onset, persistence into adulthood and worse prognosis.

**Antigen presentation, cell-mediated and humoral immune response** pathway genes such as the monocyte differentiation antigen, GATA-binding protein 3, interleukin-4 and 18 genes, nucleotide-binding oligomerization domain 1, and Toll-like receptor 2 were linked to atopic dermatitis.

## Hereditary factors

As genes related to IgE responsiveness (11q13) are more frequently inherited from the maternal side than from the paternal side, the risk of development of atopic dermatitis is higher in children having an atopic mother than having an atopic father.

## Prenatal factors

Sensitization to foods and aeroallergens can occur during intrauterine life, although its exact role is not clear. **Elevated cord blood IgE** levels increase the risk of development of subsequent atopy.

## Environmental factors

"**Hygiene hypothesis**" partly explains the higher prevalence of atopic dermatitis in "clean" Westernized countries. Clean environment and delayed exposure to microbes and allergens are thought to shift immune responses towards atopy; early life exposure to microbes may help the maturation of the immune system and plays a preventive role. The role of indoor air pollutants such as **cigarette smoke** and **nitric oxide** has also been suggested.

## Immune dysregulation

**The Th2 response** is usually a normal immune response in the fetus. During the postnatal period, the maturity of the immune system is associated with the dominance of Th1 response and increased production of interferon (IFN)-γ. However, in atopic individuals, a typical immune response is characterized by Th2 responses, increased interleukin (IL-4, IL-5, and IL-13) and decreased **IFN-γ**. Serum total IgE is elevated in ~ 80 % of the patients with atopic dermatitis.

# Pathology and Pathophysiology of Atopic Dermatitis

With increased understanding of the pathophysiology of atopic dermatitis, **leaky epithelial barrier** as a result of structural abnormalities in the epidermis and chronic immune dysregulation play an important role in the pathogenesis of atopic dermatitis. An **epithelial barrier disruption** increases the susceptibility to environmental irritants and allergens. Increased **transepidermal water loss (TEWL)** and abnormal **ceramide** synthesis are important factors causing dryness of the skin.

In the immune system, **naïve Th0 cells** differentiate into Th2 cells, which affect interactions between **dendritic antigen-presenting cells** and **$CD4^+$ helper T-lymphocytes**. The role of allergy is best explained by mixed IgE/T-cell-mediated mechanisms; both food allergens and inhalant allergens are known to exacerbate the disease.

Colonization of the skin by **Staphylococcus aureus** and **M. furfur** is increased and superantigens from staphylococci cause exacerbation of atopic dermatitis. Different neuropeptides, mainly substance P and **calcitonin gene-related peptide (CGRP)**, play an important role in various clinical features of atopic dermatitis. **Sweating** and **psychological stress** is also known to cause aggravation of symptoms.

# Clinical Features of Atopic Dermatitis

Intense pruritus is a cardinal symptom. Skin lesions may be in the form of **macular erythema**, **papular** or **papulovesicular lesions,** or **eczematous lesions** with crusting. **Lichenification** and **excoriation** may be present; secondary infections are also

common.

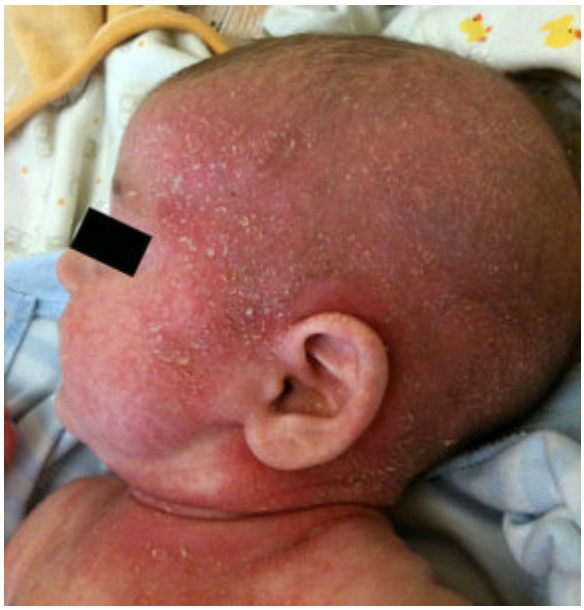


Image: “Inflamed atopic dermatitis on the head of a 2-months-old child,” by Gzzz. License: CC BY-SA 4.0

Clinical presentation of typical atopic dermatitis varies according to age. In infancy, the face is most commonly involved, sparing the **napkin area**.

The extensor aspects of the knees are involved later during infancy, especially after the child begins to crawl. Most commonly involved sites after the age of 18—24 months include the flexures of the elbows and knees, and the sides of the neck, wrists, and ankles. Involvement of the hands and flexures is also most common during late childhood and adulthood; coarse pitting and ridging may be seen in the nails.

The nipples may be involved in adolescent and young women. Vermilion of the lips and adjacent skin also may be involved. Adults also may demonstrate photosensitivity.

In addition to atopic lesions, generalized dryness of the skin is very common in atopic dermatitis**; ichthyosis vulgaris**, **keratosis pilaris**, **pityriasis alba**, hyper linear palms, **perifollicular accentuation**, **prurigo,** and abnormal cutaneous vascular responses may also be present.

Other atopic disorders such as **allergic rhinitis**, **asthma**, and food allergies are present in 30—50 % of the patients with atopic dermatitis. **Infantile seborrheic dermatitis** may precede the onset of atopic dermatitis in many infants. The incidence of irritant contact dermatitis, **lip-lick cheilitis**, drug sensitivity, and **alopecia areata** is significantly greater in atopic dermatitis.

Being a chronic relapsing condition, behavioral disturbances and emotional distress are common in children with atopic dermatitis; growth delay can occur in children with severe disease. Secondary bacterial (streptococci and staphylococci) and viral infections (herpes simplex virus, possibly viral warts and **molluscum contagiosum**) can complicate atopic dermatitis.

Atopic dermatitis is often accompanied by different ocular abnormalities such as conjunctival irritation, **keratoconjunctivitis**, **keratoconus**, **Trantas dots** (limbal deposits of eosinophils), bilateral subcapsular cataracts, spontaneous retinal detachment, etc. **Dennie-Morgan fold**, a skin fold under the lower eyelids, is commonly present,

though it can be present in non-atopic children also. **Hertoghe's sign** (thinning or absence of a lateral portion of the eyebrows) may be present.

Other conditions more commonly present in patients with atopic dermatitis are cartilaginous pseudocyst of the external auricle, **olecranon bursitis**, and **pretibial bursitis**. The overall risk of cancers is reduced in patients with atopic dermatitis as compared to the general population.

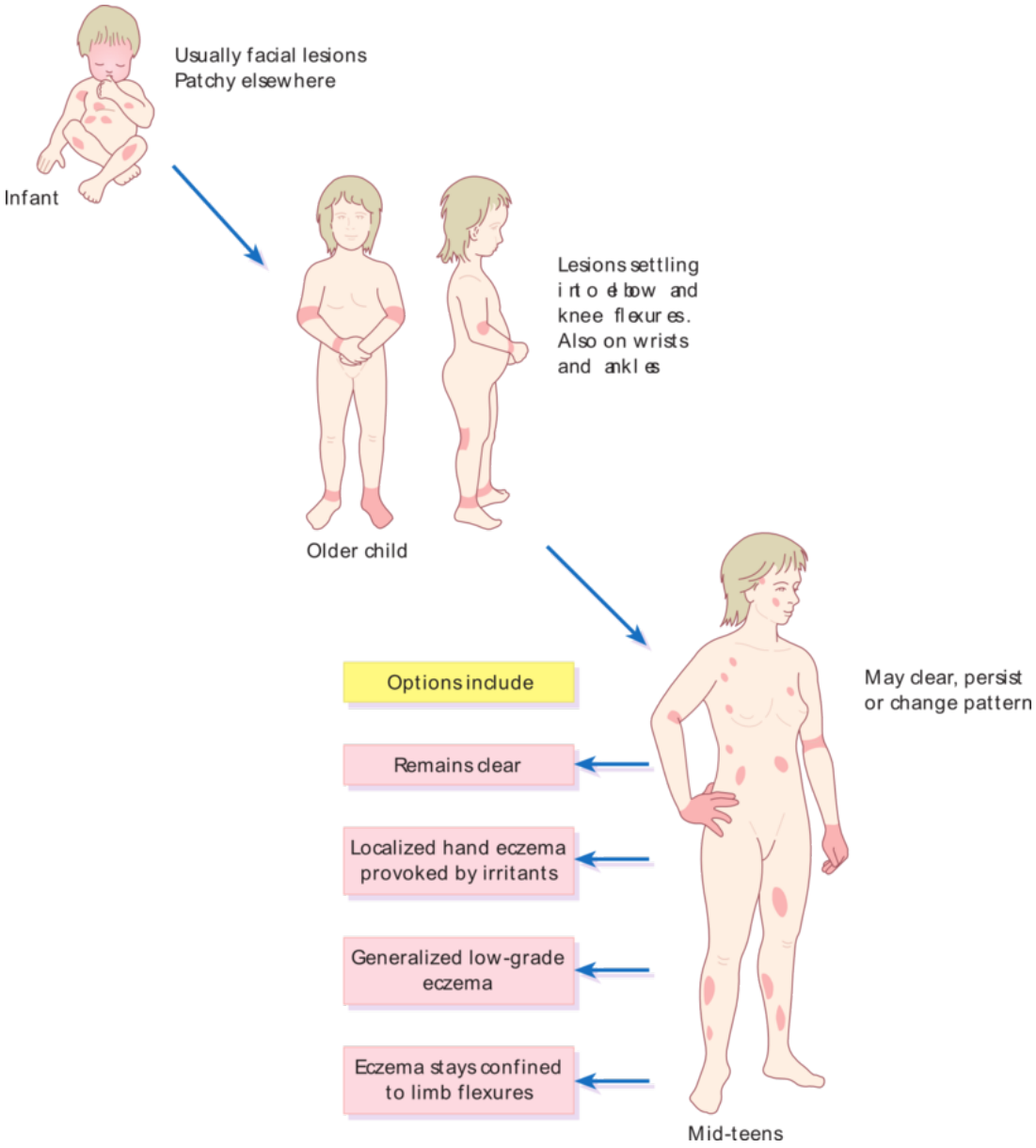



Image: "The pattern of atopic eczema varies with age," by Madhero88. License: CC BY-SA 3.0

## Diagnosis of Atopic Dermatitis

Diagnosis of atopic dermatitis is mainly clinical. **UK refinement of Hanifin and Rajka's diagnostic criteria for the diagnosis of atopic dermatitis** include the presence of an itchy skin condition, **plus at least three of the following:**

- Onset < 2 years of age;
- History of involvement of skin crease (including cheeks in children < 10 years);
- History of generalized dry skin;

- Personal history of other atopic diseases (or history of any atopic disease in a first degree relative in children < 4 years of age);
- Visible flexural dermatitis (or dermatitis of the cheeks/forehead and the outer limbs in children < 4 years of age).

As per the **American Academy of Dermatology 2014 guidelines**, pruritus and eczema are essential features, while the early age of onset, atopy, and xerosis are important features for the diagnosis of atopic dermatitis.

There is no specific investigation to diagnose or to rule out atopic dermatitis, but the following abnormalities support the diagnosis:

- **Elevated serum total IgE** (seen in 80 % of the patients);
- **Positive skin prick tests** to food and/or inhalant allergen/s;
- **Elevated serum specific IgE** to food and/or inhalant allergen/s;
- **Positive patch tests** to contact allergens.

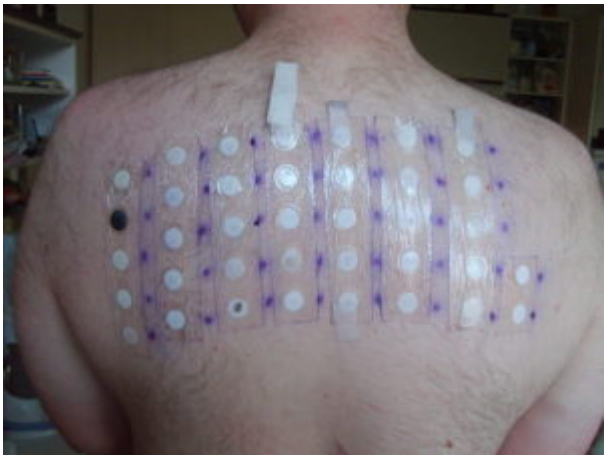


Image: "Patch test," by Jan Polák. License: CC BY-SA 3.0

Some authorities recommend atopy patch tests for foods and aeroallergens, while skin application food test (SAFT) may have a role in the management of IgE-mediated contact urticaria syndrome in children with atopic dermatitis.

Bacteriological and virological investigations may be required to diagnose secondary infections, especially when there is deterioration of the disease.

## Differential Diagnoses of Atopic Dermatitis

- Scabies;
- **Seborrheic dermatitis;**
- Immunodeficiencies;
- Metabolic/genetic disorders (**phenylketonuria**, **agammaglobulinemia**, anhidrotic ectodermal defect, celiac disease, **Netherton's syndrome**, **Wiskott-Aldrich syndrome**);
- Contact dermatitis;
- Hyper-IgE syndrome (involvement of scalp, axillae, and groins; cold abscesses and pulmonary involvement);
- Hypereosinophilic syndrome (cardiac involvement, involvement of other viscera)
- **Pachydermatous eosinophilic dermatitis** (hypertrophic genital lesions, peripheral blood eosinophilia, eosinophil-rich lymphohistiocytic cutaneous

infiltrate);
- **Ichthyoses;**
- Cutaneous T-cell lymphoma;
- **Psoriasis;**
- Erythroderma due to other causes;
- Photosensitivity dermatoses.

## Therapy of Atopic Dermatitis

The mainstay of management of atopic dermatitis includes emollients, topical corticosteroids, control of the itching, reduction of triggers and education of the parents.

Bathing followed by an immediate, generous application of emollients/moisturizers helps to maintain hydration of the skin, reduces episodes of inflammation and improves the efficacy of topical corticosteroids. Soaps and foaming detergents should be avoided. Ointments are preferred for chronic lichenified lesions, while lotions or creams are preferred for exudative lesions.

Topical corticosteroids suppress inflammation, and their selection depends upon the severity of dermatitis, the site of lesions and the age of the patient. Topical corticosteroids with less potency (e.g., hydrocortisone 1 %) are used in children < 1 year of age and over the eyelids, face, axillae, groins, and the inner thighs.

An exacerbation of dermatitis is initially treated for 3—7 days by a topical corticosteroid with potency (medium potency — e.g., **triamcinolone acetonide** ointment 0.1 % or desonide 0.05 %; high potency, e.g., clobetasol ointment 0.05 %) that is adequate to control inflammation, followed by reduction in steroid potency or infrequency of application.

Local side effects of topical corticosteroids include **telangiectasis** and **striae**; systemic side effects are possible but rare if topical corticosteroids with appropriate potency are used in appropriate frequency for an appropriate duration. The fingertip unit can be used to educate parents about the number of topical corticosteroids.

Itching is the most difficult symptom to treat, and $H_1$-antagonists are used to control itching. Sedating **antihistamines** (hydroxyzine, diphenhydramine or promethazine) are more effective than non-sedating second-generation antihistamines. A bed-time dose may be helpful to reduce nocturnal itching. Side effects like drowsiness, lack of concentration, paradoxical excitation in children, etc. are common with sedating antihistamines.

**Oral antibiotics** (flucloxacillin or erythromycin) are indicated in suspected staphylococcal skin infection and in patients with recurrent flares of atopic dermatitis due to staphylococcal infections. Systemic antiviral agents are indicated in patients with herpes simplex infection.

Once a flare of atopic dermatitis is controlled, measures to maintain control include continuous and liberal use of emollients, trigger avoidance, optimum use of topical corticosteroids and/or calcineurin inhibitors and parental education.

Trigger avoidance is very important to reduce the frequency of exacerbations and thus to reduce medication requirements. Skin irritants such as soaps, detergents, woolen clothes, etc. and activities causing excessive perspiration should be avoided; cotton clothing is usually more comfortable. Stress reduction should be emphasized when appropriate.

Dietary modifications for food allergies and environmental measures for inhalant allergies are helpful only when one or more allergen/s are known and identified to aggravate atopic dermatitis in the particular patient. Allergen-specific immunotherapy may benefit selected patients, but its exact role is yet to be clear.

Second-line options for severe or unresponsive disease include intensification of topical corticosteroids by increasing their potency or frequency, wet-wrap technique, **topical calcineurin inhibitors**, phototherapy (Ultraviolet B – UVB, UV-A, narrow-band UVB, psoralen plus UVA – PUVA), oral corticosteroids, immunomodulators (low-dose cyclosporin, azathioprine, methotrexate, mycophenolate mofetil, etc), bleach baths, etc.

Topical **calcineurin inhibitors** (tacrolimus 0.03 % ointment and pimecrolimus 1 % cream for children aged > 2 years; tacrolimus 0.1 % ointment for patients aged > 16 years) are effective anti-inflammatory agents that are very effective against pruritus; burning and warmth at the site of application are important side effects. Crisaborole is a topical phosphodiesterase-4 inhibitor which is used in mild-to-moderate atopic dermatitis as a non-steroidal agent.

## Progression and Prognosis of Atopic Dermatitis

Usually, atopic dermatitis tends to improve with age and in ~ 50 % of the patients, remission is seen by age of 13 years. Risk factors associated with persistence of the disease into adult life include early onset of the disease, severe atopic dermatitis, family history of atopic dermatitis, the presence of allergic rhinitis and asthma, and increased specific IgE to foods and inhalant allergens at 2 years of age.

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