133 Atopic Dermatitis

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Definition

Atopic dermatitis or infantile eczema is a skin inflammation characterized by intense pruritus and scratching, which result in skin damage. The skin lesions manifest in the form of papulation, excoriation, oozing, crusting, and secondary infection. The severity and intensity of symptoms vary from one patient to another. The hallmark of atopic dermatitis (AD) is itching. The skin changes that follow are due to traumatization of the skin by persistent scratching. The symptoms are made worse by increased heat, perspiration, excessive dryness, irritation, psychological tension, and secondary infections.

Epidemiology

Although AD is a common allergic disease of infancy and childhood, its exact incidence is not known. But the incidence seems to be increasing. There are no racial or geographical differences and girls may be slightly more affected. It may affect 5–20% of children, but some studies estimate the incidence to be between 1% and 4%, depending on the population studied and the methodology of the study. The higher figures are in urban population. Most infants develop AD below the age of 1 in 60% of cases and by the age of 5 in another 30%. It is unusual for an infant below 2 months of age to develop AD. The occurrence of AD is much higher in families with a history of allergy. About 75% of infants and children with AD either have another allergy or have a strong family history of atopy.

Pathogenesis and Genetics

The pathogenesis of AD is more complex than it was previously thought. This includes impaired epidermal barrier function, immune disorders in which T-cells, Langerhans cells, and immune effector cells induce inflammatory response to various environmental factors such as irritants, infections, chemicals, and allergens. The integrity of the epidermis is important for a healthy skin. This integrity is kept by the interaction of keratinocytes and a variety of proteins such as Filaggrin, enzymes, and lipids. Disruption of this barrier allows foreign antigen to penetrate and come in contact with immune cells and release proinflammatory agents that lead to the clinical and pathological manifestations of AD. Atopic skin keratinocytes are defective in binding water, which is important for a healthy epidermal barrier. This dryness leads to pruritus with scratching, skin trauma, and inflammation. Several genetic factors involved in the epidermal permeability barrier defect have been described. These include Filaggrin mutation that leads to icthyosin (R 501X and 2282dL4), and defective Spink5 that leads to cleavage of intercellular attachments, and hence, the corneocyte cohesion, which weakens the skin barrier function. The defects open the way for foreign antigens to enter through the epidermis and interact with immune cells, leading to sensitization and inflammation. AD is a genetic disease based on twin studies and family history. The trait is more often inherited through a maternal gene rather than a paternal one. Many patients have Filaggrin mutations.

Clinical Manifestations

Clinical features of atopic dermatitis depend on the severity and chronicity of inflammation. The most prominent feature of atopic dermatitis is itching. The skin is usually dry or erythematous with some degree of lichenification, or oozing, crusting, and acutely inflamed, depending on the stage of inflammation. Skin manifestations go through different stages, depending on the chronicity of symptoms and the age of the patient. Classification of atopic dermatitis in relation to age is divided into three groups:

1. Infantile – from 2 months to 2 years
2. Childhood – from 2 to 10 years
3. Adolescent – from 11 to 20 years

In infants, the early feature is dry erythema on the cheeks, which may become oozy with crust formation and secondary infection. The eczema may spread to involve the forehead, scalp, and postauricular areas. It may also

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involve the extensor surfaces of the upper and lower extremities and may become generalized. The baby is usually irritable and scratches the skin constantly. The baby may look unhappy due to severe itching, which may interfere with feeding and sleep. This stage has a tendency to improve as infants grow older. Once an infant starts crawling, the skin's dryness increases and the papules tend to become larger, confluent, and crusty. In older children, the skin lesions have a tendency to involve the flexural areas, with the antecubital and popliteal fossae and the back of the neck being the preferred areas. Skin infection may complicate the picture further and leads to confusion in diagnosis. In chronic severe eczema, the skin of the eyelids becomes thickened and forms transverse lines known as Dennie–Morgan lines.

Complications

Complications of atopic dermatitis in both infants and children include

1. Secondary infections with *Staphylococcus aureus*, herpes simplex, herpes zoster (eczema herpeticum), and molluscum contagiosum. Herpes simplex may become disseminated, causing serious consequences.
2. Subcapsular cataract occurs in about 16%.
3. Keratoconus and ulceration of the cornea.
4. In cases of severe generalized eczema, psychological complications may lead to withdrawal of the child from social activities.

Differential Diagnosis

Seborrheic dermatitis is easy to differentiate; it usually starts as cradle cap with thick, greasy, yellowish scales. It begins before the age of 2 months and causes minimal or no itching. In comparison, atopic dermatitis starts after the age of 2 months with intense itching. Classic seborrheic dermatitis follows the hairline with slight erythema, while atopic dermatitis is inflamed mostly at the center, and when scales are present, they are usually dry. In addition, the smell of seborrheic dermatitis (mouse-like) is characteristic.

Contact dermatitis is rather uncommon in infants and children. The common causes are earrings, wristwatches, and metal buttons in trousers. The site of dermatitis correlates with the size and site of the causative metal.

Primary immunodeficiency syndromes include *Wiskott–Aldrich syndrome*, which is characterized by eczema, immunodeficiency, thrombocytopenia, and bleeding early in infancy. It is X-linked, and there is usually a history of similar cases in the family. *Severe combined immunodeficiency (SCID)* is very easy to differentiate from atopic dermatitis. The history of severe infections with low virulence and uncommon organisms makes the diagnosis easy. The dermatitis in SCID is due to graft-versus-host disease, and pruritus is unusual. *Hyper-IgE syndrome* (Job syndrome) is very easily confused with atopic dermatitis. In hyper-IgE syndrome, the level of serum IgE is extremely high, and the infant has a history of deep-seated infections, including sinusitis and skin and pulmonary abscesses. The distribution of the eczematoid eruption in hyper-IgE syndrome is different from that of severe atopic dermatitis. The first involves the entire skin from head to toe, and patients have coarse facial features. The color of the eczema ranges from coppery red to violaceous red, with distribution mostly on the extensor surfaces. ➤ *Table 133.1* summarizes the most important differential points between atopic dermatitis and other conditions.

Diagnosis

History and physical examination are usually enough to make the diagnosis of atopic dermatitis. The minimal criteria to establish the diagnosis should include the followings: chronic or recurrent dermatitis with itching, characteristic distribution in relation to age, and white dermographism. The history should include detailed questioning regarding the age of onset, severity of symptoms, and manifestations of other allergic diseases, both in the patient and relatives. Evolution of the skin eruption, the presence of pruritus, and the effect of seasonal variations are pertinent questions in history taking. Triggers such as foods, clothes, drugs, and changes in weather should be inquired into. If food is suspected to be a trigger for the patient's symptoms, confirmation by oral challenge and appropriate tests, performed by a physician experienced in the field of allergy, should be sought. Frequency of bathing and showers are important to know, because of their drying effect on the skin. By physical examination, the patient may have a classic appearance and distribution of atopic dermatitis; in addition, other stigmata of allergy may be present.

Diagnostic procedures include skin prick test. Allergens should include inhalants and common foods consumed by the patient. All positive tests should be confirmed by elimination and oral challenge. Other diagnostic tests include complete blood count, serum IgE level, and culture from surfaces of the infected skin. If the child has extensive skin involvement, skin testing may not be possible. In this case,

Table 133.1
Differential diagnosis of atopic dermatitis

	AD	Seborrhea	Contact dermatitis	WAS	SCID/GVHD	HIE
Itching	+ + + +	+	+ + +	+ + +	0	+ + +
Age of onset	Early (>2 months)	<2 months	Late	V. early	<2 months	V. early
Bleaching	+	0	+	+ + +	0	+
Distribution	Typical	Typical	Localized and characteristic	0	0	Generalized
Deep infection	0	0	0	Yes	Yes	Yes
Crusts	With infection	Greasy	With infection	With infection	No	Abscesses
Serum IgE	↑↑↑	N	N	↑↑↑	↓	↑↑↑↑
Sex	Any	Any	Any	Male	Any	Any
Platelets	Normal	Normal	Normal	V. low	Normal	High
Allergens	Food and others	None	Metals and others	None	None	Food
Prognosis	Good; development of other allergies	Excellent	Excellent	Guarded unless transplanted	Guarded unless transplanted	Poor
Inheritance	±Atophy	0	0	X-linked	X-linked or autosomal recessive	Autosomal recessive

AD, atopic dermatitis; *WAS,* Wiskott–Aldrich syndrome; *SCID*, severe combined immunodeficiency; *GUHD,* graft-versus-host disease; *HIE*, hyper IgE

a radio allergo sorbent tes (RAST) for the common foods and inhalants allergens is an alternative diagnostic tool. Although the majority of infants and children with atopic dermatitis react to foods, the results should not be taken as cause and effect unless confirmed by elimination and challenge.

Management

Patients with atopic dermatitis live in a vicious cycle of scratching and skin inflammation, which aggravate each other. Therefore, the management of atopic dermatitis should attack two points in this vicious cycle: (1) stopping the itching and (2) healing the inflamed skin.

General Management

Excessive dryness, perspiration, and overheating should be avoided as much as possible. Rough fabrics in clothing should be avoided and soft fabrics made of cotton or silk should replace them. Nails should always be kept trimmed to minimize trauma to the skin from scratching.

To bathe or not to bathe? It is a known fact that frequent bathing with soap and water increases skin dryness and, hence, pruritus and scratching of the skin. The traditional teaching to the patient is not to bathe or at least to minimize bathing and showers to once a week. From a practical point of view, it is extremely difficult for the patient and family to accept this recommendation due to hygienic reasons. Therefore, the recommendations in this regard should take into account the social habits and living conditions of the patient and the family. The parents should follow their usual practice of bathing their child as long as they apply moisturizing creams and lotions immediately after the bath or shower. Soap that has a high content of fat is preferred, and it is also preferable not to use scented or perfumed soap. The parents should be encouraged to use creams and lotions of their choice as liberally and as often as they desire.

Antipruritic Medications

Any of the following antihistamines can be used to relieve itching. cyproheptadine (Periactin) in a dose of 2 mg every

6–8 h, or hydroxyzine 5 mg every 6 h, can be used in infants younger than 6 months. The dose can be increased to 10 mg every 6 h in older children. The latter drug is tolerated very well, and the dose can be increased by 6 mg every 5–7 days. Because itching is worse at night, it is advisable to double the dosage at bedtime. If hydroxyzine is not enough to relieve the symptoms, diphenhydramine (Benadryl) in a dose of 0.5–1 mg/kg (maximum 25 mg) every 6 h can be added. The treatment with antihistamines should be given on a continuous basis rather than intermittently. Relieving the itch will help the skin to heal faster, and therefore the need for anti-inflammatory drugs will decrease.

Control of Infection

If there is evidence of skin infection, antibiotics that are active against *S. aureus* should be used. Topical antibiotics should be completely avoided in patients with dermatitis. Patients with a history of frequent skin infections may benefit from prophylaxis with long-term antibiotics active against *S. aureus.* Erythromycin is an alternative drug when the patient is allergic to penicillins.

Dietary Manipulation

Dietary restriction should be reserved for those infants who have definite evidence of allergy to food. If there is evidence of coexistence of respiratory allergy, such as allergic rhinoconjunctivitis and/or bronchial asthma, and the allergen cannot be avoided, immunotherapy guided by history and skin tests may be added to the treatment.

Local Treatment

In the acute weeping phase, topical application of a wet dressing should be used at least four times a day on the oozing areas. Burow's solution is aluminum acetate 1:40 and can be prepared by dissolving Domeboro in 500 mL of tap water. A clean gauze is then soaked in the solution and applied to the oozing area. Once the skin becomes relatively dry and less inflamed, with no oozing, corticosteroid creams can be applied once to twice a day. In cases where the skin is thick and lichenified with no signs of infection, corticosteroid ointment can be applied but avoid skin folds and facial areas. Extremely thick eczematous areas on the extremities need an occlusive dressing with steroid ointment. In very severe cases, systemic, short-acting corticosteroid administration may become necessary for the control of inflammation. Ultraviolet light (PUVA) or cyclosporin A may be used in extremely resistant generalized dermatitis.

In some patients with atopic dermatitis, hypopigmented or discolored areas appear after healing and may be of concern to them. In these cases, reassurance is all that is needed, because the skin color will go back to normal in due time. Topical potent fluorinated corticosteroids should never be applied to facial areas, especially around the eyes. The preferred corticosteroid is 0.5–1% hydrocortisone cream applied twice to three times a day for facial dermatitis. Topical calcineurin inhibitors such as tacrolimus and pimecrolimus applied twice daily have been introduced recently. In very severe cases, oral cyclosporine A may be used with caution.

Prognosis and Prevention

Although prognosis depends on the severity and extent of skin involvement, at least 50% of infants with atopic dermatitis become asymptomatic as they grow older. If there is a positive family history of allergy, atopic dermatitis in early infancy is an indication that other forms of allergy will follow. This knowledge is useful to the treating physician and the family in planning treatment and prophylaxis. Approximately 70% of infants and children who start with atopic dermatitis and have a positive family history of atopy end up with bronchial asthma and allergic rhinitis. If the cord blood IgE level of an infant is greater than 1 U/mL along with a positive family history, the chances of development of atopic dermatitis and other allergies in that infant are extremely high. Mothers of such infants should be advised to breast-feed their babies and to be cautious in introducing solid foods or cow's milk formula into their infant's diet before the age of 6 months. Mothers should also avoid potentially allergenic foods such as milk, eggs, peanuts, and fish in their diet while nursing their infants.

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