Summary

Atopic dermatitis in children: Clinical features, pathophysiology and treatment


Introduction

- Atopic dermatitis (AD) is a chronic, relapsing, highly pruritic dermatitis. It generally develops during childhood, with a characteristic age-dependent distribution.
- AD is common, affecting 10%-20% of children.
- AD is associated with elevated levels of total IgE and IgE level correlates with disease severity.
- Although allergen-specific IgE levels may be elevated, clinical allergy is not necessarily present.
- Associated comorbidities can significantly impair quality of life. They include infections (e.g., *Staphylococcus aureus* superinfection and eczema herpeticum), chronic pruritus and sleep disturbance.
- Associated conditions include poor school performance, poor self-esteem and family dysfunction.

Clinical features

- In 90% of patients, AD begins in the first 5 years of life.
- It is characterised by a chronic, relapsing, pruritic dermatitis; xerosis is common in children.
- Table 1 lists the 5 major diagnostic criteria, which are often accompanied by minor features.
- Acute lesions are pruritic papules with erythema, excoriations and serous exudate.
- Chronic lesions are characterised by areas of lichenification and fibrotic nodules, often accompanied by acute lesions.
- Common triggers for flares include heat, seating, anxiety, frustration and infections.
- Food allergy may play a role in some patients, especially younger children.

<table>
<thead>
<tr>
<th>Table 1. Diagnostic criteria for AD</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Major criteria</strong></td>
</tr>
<tr>
<td>1. Pruritus</td>
</tr>
<tr>
<td>2. Characteristic morphology and distribution: Facial and extensor involvement in infants and children; flexural involvement with lichenification in adults</td>
</tr>
<tr>
<td>3. Chronic or chronic, relapsing course</td>
</tr>
<tr>
<td>4. Personal or family history of atopy, including asthma, allergic rhinitis, atopic dermatitis</td>
</tr>
<tr>
<td>5. Onset before 2 years of age</td>
</tr>
</tbody>
</table>

Infectious complications
1. **S. aureus**
More than 90% of AD patients are colonised by *S. aureus* on the skin and nares. Intra-familial transmission may occur, causing recolonization after a course of antibiotics. Clinical signs indicating treatment with topical or systemic antibiotics include honey-coloured crusting, pustules and folliculitis. Patients with severe AD, even in the absence of these signs may benefit from treatment with antibiotics.

2. **Viral infections**
   i. Eczema herpeticum (EH): results from dissemination of the Herpes simplex virus (HSV-1 or HSV-2) in patients with AD, commonly with the first exposure. Risk factors for EH include early-onset and severe AD, marked elevations in total IgE, elevated allergen-specific IgE levels, peripheral eosinophilia, and the presence of filaggrin mutations. Lesions may be complicated by secondary infection with *S. aureus*. Fever, malaise and lymphadenopathy are common. Severe disease, including keratoconjunctivitis and multi-organ involvement, which may be fatal requires rapid diagnosis and treatment with anti-viral medication.
   ii. Eczema coxsackium: disseminated coxsackie A6 viral infection.
   iii. Eczema vaccinatum: smallpox vaccination or contact with persons vaccinated for smallpox can result in fatal dissemination of the virus.
   iv. Mulluscum contagiosum.

**Differential diagnosis**
- Contact dermatitis
- Seborrheic dermatitis
- Drug reactions
- Infantile psoriasis
- Scabies
- Nutritional deficiencies – zinc/biotin
- Acrodermatitis enteropathica
- Netherton syndrome
- Ichthyosis vulgaris
- Peeling skin disorder, type B
- Severe dermatitis, multiple allergies and metabolic wasting (SAM) syndrome
- Primary immunodeficiency diseases & Omenn syndrome
- Lymphocytic-variant Hypereosinophilic syndrome (HES)
- Cutaneous T cell lymphoma

Clinical features that may indicate investigation for an alternative diagnosis include:
- Severe and extensive skin involvement, especially if beginning at or near birth
- Recurrent or severe infections, especially recurrent abscesses, lymphadenitis, pneumonia
- Late onset, after age 20 years
- Absence of concomitant allergic disease
- Persistent blood eosinophilia (absolute eosinophil count >1000 cells/μL)
- Diffuse eczematous rashes after age 5
- Unusual distribution

**Pathophysiology**
AD is associated with both disruption of the epithelial barrier of the skin and allergic inflammation of the skin in a person with a genetic predisposition to atopy. AD may be the initial step in the ‘atopic march’.

Mechanisms that may be involved in the pathophysiology of AD include the following:
1. Genetic factors: the genetic contribution to AD is estimated at 80%.
2. Barrier defects in the skin: mutations in genes critical to normal barrier function of the skin (prevention of water loss and defence against penetration of irritants, immunogens and pathogens), include those in filaggrin (FLG), desmoglein-1 (DSG1), corneodesmosin (CDSN) and serine protease inhibitor Kazaltype 5 (SPINK5).

3. Defects in the immune pathway may be necessary in addition to skin barrier defects and other pathologies in AD. Some of these may include hyper-IgE syndromes, helper T cell-mediated inflammation, impairment in CD4+T cells, and increased expression of interleukin-31 (IL-31) and other proteins responsible for pruritus and hyperalgesia.

Clinical management

1. General principles
   - The aims of treatment are to improve quality of life, prevent infectious complications and minimise potential side effects of treatment.
   - Optimal control of all symptoms is best achieved through hydration, restoration of the skin barrier (emollients) and control of skin inflammation (topical immunosuppressants).
   - Because AD is characterised by unpredictable flares, a comprehensive home treatment plan is necessary, including steps to manage an acute flare.
   - Patient education should include clinical features and associations of the disorder, natural history, review of potential triggers for flares, discussion of medications and potential side effects, and provision of an individualised treatment plan.
   - Multidisciplinary treatment teams may be helpful in moderate to severe cases.

2. Hydration and use of occlusive topical moisturisers
   - Treatment guidelines recommend regular skin hydration with soaking baths and use of occlusive topical ointments and creams for optimal control, which reduces requirement for topical and systemic immunosuppressants. The most important aspects of treatment are daily soaking baths of 15 minutes in lukewarm plain water, with immediate application of occlusive ointments (soak-and-seal), and application of occlusive treatments through the day. In severe flares, baths may be increased to two or three times daily; showers are less effective.
   - Emollients should be applied to dry skin immediately after the soaking bath, since they impede water loss from the skin, restore skin integrity, reduce pruritus and reduce requirements for corticosteroids. Although ointments are more effective than creams, a cream may be better tolerated during hot, humid days and during school, thereby improving compliance. Patients should be given both a cream and an ointment and educated on the benefits of each. Lotions are not effective in AD.

3. Topical corticosteroids
   - Topical corticosteroids are the most effective treatment to reduce inflammation. They also reduce pruritus and *S. aureus* colonisation of the skin.
   - They may be used on an as needed basis to control flares or, in more severe cases, for maintenance treatment.
   - In children, the corticosteroid with the lowest potency required to manage inflammation should be used. A comprehensive treatment plan should contain instruction of step-wise adjustment in topical corticosteroid potency appropriate to flare severity and the area of the body involved. Once the flare is controlled, the potency should be stepped down to prevent rebound exacerbations.
   - Lower potency corticosteroid should be used for areas of the body with thinner skin, including the face, eyelids, genitalia and intertriginous areas, and for all areas of skin of infants and toddlers.
Topical corticosteroids should be applied before application of emollient, which should only be applied to unaffected areas of the skin. Application of the emollient over the corticosteroid application dilutes the corticosteroid and unnecessarily spreads it to unaffected areas of skin.

- In patients with AD, systemic corticosteroids should not be used, even in severe disease.
- In addition to the potential for adverse effects, when discontinued they cause a rebound inflammatory response often with more severe flare.
- Wet wraps consisting of application of dilute topical corticosteroid and emollients after a soaking bath, followed by a layer of wet dressing or cloths then dry cloths, can be used in patients with moderate-severe disease and without an adequate response to standard skin care. However, they can result in maceration of the skin, folliculitis and enhanced absorption of topical corticosteroids and should only be used under close medical supervision.

4. **Topical calcineurin inhibitors**
Calcineurin inhibitors do not cause skin atrophy and may be useful in controlling AD involving the face and eyelids, and also for maintenance treatment where long-term anti-inflammatory treatment is required.

5. **Antimicrobial treatment**
- Antimicrobial treatment should be guided by antimicrobial sensitivity testing.
- Dilute bleach baths (twice weekly) in addition to application of mupirocin twice daily for 5 days (repeated monthly over a period of 3 months) may be considered in children with moderate-severe AD, evidence of secondary *S. aureus* infection and who have required more than one course of systemic antibiotics for *S. aureus* infection.
- Mupirocin may be applied to excoriated skin to prevent infection.
- Where familial transmission is suspected, mupirocin may also be used to treat other family members who may be carriers.

6. **Antihistamines are ineffective in the management of AD and do not reduce pruritus**

**Conclusion**
AD results from a defective skin barrier and immune dysregulation. An effective management strategy must target both and include a comprehensive treatment plan for maintenance therapy and management of acute flare ups. Patient education is essential.