Skin Deep: Insights into Atopic Dermatitis

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Abstract:
Atopic dermatitis (AD) is a substantial clinical challenge due to its chronic nature and profound impact on patient’s quality of life. This review offers a thorough examination of AD, covering its historical background, clinical presentation, etiology, and epidemiological patterns. By delving into the intricate histopathological aspects, it elucidates the underlying pathophysiological mechanisms driving AD. Additionally, it assesses the effectiveness of phototherapy and diverse treatment options in addressing this multifaceted condition. By consolidating existing knowledge, this review aims to deepen our understanding and guide future strategies for managing AD effectively.

Keywords: Atopic Dermatitis, Eczema, Allergic Dermatitis, Skin Inflammation, Dermatological Disorders, Dermatology, Treatment.

Introduction:
Atopic dermatitis most frequently occurs in infants, typically manifesting between 2 to 6 months old, and may resolve by early adulthood. The fundamental concept of AD involves an immune response malfunction leading to excessive inflammatory cells in the skin, resulting in various symptoms such as swelling and itchy, reddened skin¹. Individuals predisposed to dry skin are more susceptible to water loss, irritation, and rash development due to alterations in their skin barrier. While it can significantly improve or even resolve completely in some children as they age, it generally persists as a long-term chronic medical condition.²
Pathogenesis response of atopic dermatitis for allergies, itch is the most factors that affect the skin during inflammation it’s a most common factor for AD, and at the same time it’s difficult to manage the Compliant topic of atopic dermatitis patient. Rather than itching it provides the inflammation and due to the itching, it produced scratches on the skin.

All types of Eczema cause irritation and redness which are common symptoms but AD is the most severe and chronic. Other forms of eczema include:

- Contact dermatitis
- Stasis dermatitis
- Nummular dermatitis
- Neurodermatitis
- Seborrhoea dermatitis
- Dyshidrotic dermatitis
- Contact dermatitis:

Contact dermatitis occurs when the skin comes into direct contact with chemicals or metal ions, resulting in toxic effects without inducing a T cell response (contact irritants) or by eliciting a delayed hypersensitivity reaction (contact allergens).

- **Stasis dermatitis**: Stasis dermatitis is a skin condition that typically affects the hands and legs, triggered by repeated exposure to irritant substances. It develops as a result of poor blood flow and venous insufficiency, caused by fluid accumulation due to venous hypertension, valve destruction, or obstruction.

- **Seborrhoeic dermatitis**: Seborrhoeic dermatitis is a common skin condition that affects the scalp, oily areas of the face, sides of the nose, and chest. It is not contagious and may resolve without treatment.

- **Nummular dermatitis**: Nummular dermatitis also known as discoid eczema, is characterized by clusters of round plaques typically found on the lower legs and back of the hands, but it can also affect the scalp, face, and trunk. It is caused by xerosis (dryness) and dehydration, as well as staphylococcal aureus infection.

- **Neurodermatitis**: Neurodermatitis is also known as Lichen Simplex Chronicus, can be triggered by factors such as tight clothing, insect bites, nerve injuries, or dry skin.

**Signs and symptoms:**
The signs and symptoms of atopic dermatitis (eczema) can manifest anywhere on the body and vary greatly from person to person. They may include darkened skin with cracks and intense itching (pruritus), with the rash appearing differently depending on skin tone.

**Symptoms can encompass:**
- Crusting and oozing
- Thickened skin
- Darkening of the skin around the eyes
- Bleeding or ear discharge
- Small pus-filled bumps and yellow crusts

Atopic dermatitis often begins around age 5 and can persist into adolescence and adulthood, with symptoms able to onset at any age.
In infants, eczema may present as widespread or confined to the face, scalp, and extensor regions of the arms and legs, characterized by erythema, papules, vesicles, excoriations, oozing, and crusting. The diaper area may also be affected due to excessive moisture from itching, leading to sleep disturbances and fussiness.

In childhood, the rash is commonly found on the inner knees and elbows, extending to the neck, hands, buttocks, and legs. Thickened skin knots may develop, accompanied by persistent itching. In adults, atopic dermatitis affects 2 to 3% of individuals, often presenting with less pronounced rashes but with symptoms such as exceptionally dry and easily irritated skin, hand rashes, and eye issues. Long-term AD can lead to thickened and leathery skin patches, darker or lighter than surrounding skin, perpetually itchy and potentially contributing to feelings of sadness and anxiety due to discomfort and sleep disturbances. In Ad they are divided into the three stage in mild, moderate and severe kind of eczema that shown in the given Fig. 2.

Causes:
The causes of atopic dermatitis (eczema) are multifactorial and involve various interrelated factors:

- **Genetics:** There is a strong genetic predisposition to atopic dermatitis, with family history playing a significant role. Specific genetic variations affect the skin’s barrier function, immune response, and susceptibility to allergies and inflammation.16,21

- **Immune Dysfunction:** Individuals with atopic dermatitis often exhibit altered immune responses, leading to inflammation and skin irritation. This immune dysregulation can result in a cycle of itching, scratching, and skin damage.

- **Skin Barrier Dysfunction:** Compromised skin barrier function allows moisture loss and allergen penetration, contributing to dryness, itching, and sensitivity. Genetic mutations affecting skin barrier maintenance are implicated in this dysfunction.25

- **Environmental Triggers:** Various environmental factors, such as irritants and allergens, can exacerbate atopic dermatitis symptoms. These include harsh soaps, detergents, fragrances, pollen, dust mites, and fluctuations in humidity and temperature.
• **Allergic Reactions:** Allergic reactions to foods, airborne allergens, or contact allergens can trigger or worsen atopic dermatitis symptoms in some individuals, although atopic dermatitis itself is not solely caused by allergies.\(^{11}\)

• **Microbiome Imbalance:** Disruptions in the skin microbiome composition can influence the development and severity of atopic dermatitis.

• **Stress and Emotional Factors:** Emotional stress and psychological factors can impact symptom severity by increasing inflammation and discomfort.

• **Hormonal Changes:** Hormonal fluctuations, particularly in women during pregnancy or menstruation, can affect the severity of atopic dermatitis symptoms.

It’s crucial to acknowledge that atopic dermatitis is indeed a complex condition, and its development involves various factors unique to each individual. Managing atopic dermatitis typically requires a comprehensive approach, including trigger avoidance, proper skincare practices, medication usage as prescribed by healthcare professionals (such as topical corticosteroids or immunomodulators), and lifestyle adjustments to minimize flare-ups and discomfort. If experiencing symptoms of atopic dermatitis, seeking guidance from a healthcare provider for accurate diagnosis and management is advisable.\(^{11}\)

Atopic dermatitis involves extremely dry skin due to its reduced moisture retention capacity, leading to heightened sensitivity to certain stimuli, increased itching, and discomfort. While the exact cause of atopic dermatitis remains unknown, it likely encompasses multiple contributing factors. Current understanding suggests that atopic dermatitis primarily involves immune system dysregulation, with cytokines playing a central role. Specific cytokines, particularly IL-4, IL-13 (associated with the Th2 pathway), and IL-22 (associated with the Th22 axis), contribute to inflammation and barrier abnormalities, resulting in the clinical manifestations of eczema.

Immune-mediated and hereditary defects in the skin barrier are strongly associated with atopic dermatitis. This barrier breakdown leads to increased skin permeability and a loss of antibacterial properties. A key hereditary defect implicated in this process is the decreased expression of filaggrin, a protein encoded by the FLG gene located on chromosome 1. Filaggrin is crucial for binding keratin fibres in epidermal cells. Its deficiency is linked to conditions like ichthyosis vulgaris and is associated with persistent, severe, and early-onset atopic dermatitis. The absence of filaggrin leads to coenocyte deformation, flattening surface skin cells, disrupting the organization of extracellular lipids. This results in a decrease in natural moisturizing factors and an increase in skin pH, promoting serine protease activity.\(^{20}\) Serine proteases break down proteins that maintain epidermal cell cohesion and lipid-processing enzymes. Additionally, serine proteases generate active cytokines like IL-1a and IL-1 beta, further supporting skin inflammation.\(^{7}\)

The causes of eczema (atopic dermatitis) encompass a combination of factors including immune system activation, genetics, microbiome, environmental triggers, and stress. In atopic dermatitis, there’s often an imbalance in the immune system, marked by an abundance of Th2 cells and associated cytokines, which contribute to the breakdown of the skin’s barrier function. This imbalance allows for the penetration of irritants and allergens, leading to water loss and potential entry of substances like soap, solvents, and pollens. Furthermore, inadequate levels of certain proteins in the skin can compromise its health, while interactions between dermal T- cells and antigens prompt Langerhans cells to exacerbate the Th2 response, worsening the barrier deficit.\(^{18}\) Additionally, reductions in essential components like the fatty acid ceramide and filaggrin, along with decreased antimicrobial peptides, further disrupt the skin’s integrity,
promoting the proliferation of harmful bacteria and increasing susceptibility to infections that are harder to treat.

The unique distribution of active lesions of AD is thought to be caused by several organisms and even other reasons are:

Environment: Environmental triggers like food additives, fragrances, and allergens such as grass or dust mites can irritate the skin, while low humidity and sweating can worsen symptoms like dryness and itching in eczema.

Stress: Stress can increase cortisol levels, leading to greasy skin and potentially triggering eczema flare-ups, making skin recovery more challenging.

**Epidemiology:**

Epidemiology, a method for identifying factors leading to disease, indicates that in industrialized nations, atopic dermatitis affects approximately 1/150 individuals over their lifetime. However, between 1950 and 2000, its prevalence increased. Notably, India’s prevalence, as per the International Study of Asthma and Allergy in Childhood (ISAAC), is lower than global rates at ages 6-7 (2.7%) and 13-14 (3.6%), suggesting a fluctuating global epidemic of allergic diseases. Estimates show AD lifetime prevalence ranges from 10%-30% in children to 2%-10% in adults, with a 2-3 times growth over the last three decades in industrialized nations, as highlighted by ISAAC.23

**Natural history:**

Atopic dermatitis, initially described as an inflammatory skin disease by Fred Wise and Marion Sulzberger in 1933, has a lifetime prevalence of approximately 20%.12 In India, around one in five infants experiences infantile AD by 5.2 months, and childhood AD affects them until about 3.47 years old.

Adult-onset atopic dermatitis, replacing hand eczema as the primary manifestation in adulthood, poses career concerns for about 50% of individuals with AD, with up to 95% experiencing onset before age 5. Early-onset AD is associated with sensitivity to various allergens in 52–75% of cases.

Children with moderate to severe AD have a 50% chance of developing asthma and a 75% chance of experiencing fever. Late-onset AD is linked to lower sensitivity rates.

**Diagnosis:**

Diagnosing atopic dermatitis can be challenging as its skin lesions resemble those of other types of eczema, like contact dermatitis, characterized by redness, swelling, vesicles, and crusting. Diagnosis relies on patient characteristics and eczema distribution.

Various scoring methods, such as the Eczema Area and Severity Index (EASI), aid in assessing AD severity. While primarily used in clinical studies, these scales can also benefit routine practice. The diagnostic criteria proposed by Hanifin and Rajka in 1980 remain widely utilized in establishing atopic dermatitis diagnosis.14

**Histopathology:**

Histopathological features common to various types of dermatitis, including allergic contact dermatitis, do not significantly impact the diagnosis of atopic dermatitis (AD). However, immunostaining can detect by-products like eosinophil major basic protein, eosinophil cationic protein, and eosinophil-derived neurotoxin, indicating increased eosinophil presence in the dermis of chronic AD lesions.10
Persistent eczema typically exhibits sparse lymphocytic infiltrates, thickened stratum spinosum (acanthosis), and a thicker stratum corneum (hyperkeratosis). These histological findings aid in understanding the chronic nature and pathological changes associated with atopic dermatitis.\(^1\)\(^7\)

**Phototherapy:**
Phototherapy can be a beneficial treatment option for patients with widespread atopic dermatitis (AD) or those who do not respond well to topical medications alone. It can be used in conjunction with topical corticosteroids (TCSs) to manage AD symptoms effectively. Phototherapy, including exposure to natural sunlight or specific UV-light spectrums like UVB (280–320 nm), narrowband UVB (311–313 nm), UVA (320–400 nm), medium and high-dose UVA1 (340–400 nm), PUVA, and balneal-PUVA, has shown promising results in reducing pruritus and improving AD symptoms within the first two weeks of treatment.\(^8\)\(^,\)\(^13\)

**Risk factor:**
Genetics, particularly mutations in the filaggrin gene, and environmental factors play significant roles in atopic dermatitis risk, with family history being a substantial risk factor.
The two primary risk factors for atopic dermatitis (AD) are genetics and the environment. Genetic factors play a significant role in AD, with several genes, including those related to epidermal structure and immune function, being implicated in its development\(^18\). Mutations in the filaggrin gene are particularly strong genetic risk factors for AD, affecting a substantial portion of AD patients. Environmental factors also contribute to AD risk, although fewer definitive factors have been identified. Lifestyle choices and certain environmental exposures may play a role in increasing the prevalence of AD, but the exact mechanisms are still being studied.\(^15\)

**Treatment:**
The treatment of atopic dermatitis aims to manage the chronic nature of the condition since it is incurable. Treatment goals include reducing the frequency, duration, and severity of disease flares, as well as preventing future flare-ups\(^6\)\(^,\)\(^8\). Emollient creams or ointments are often recommended as the primary treatment to help maintain skin hydration and prevent flare-ups. Additionally, various other treatments such as topical corticosteroids, moisturizers, antihistamines, and immunomodulators may be prescribed depending on the severity of symptoms and individual patient needs.\(^13\)\(^,\)\(^22\)

**OTC treatment:**
Over-the-counter treatments for atopic dermatitis include antihistamines to alleviate itching, some of which contain sedative ingredients for sleep aid, such as Cetirizine, Chlorpheniramine, Doxylamine, and Fexofenadine. Pain relievers like Tylenol or ibuprofen can help manage discomfort and inflammation.\(^24\) Topical corticosteroids, like hydrocortisone, are available in various formulations (gel, cream, lotion, ointment) to relieve inflammation and itching. It’s essential to follow dosage instructions to prevent side effects.\(^8\)

**Prevention:**
Preventing eczema flare-ups can be aided by establishing a basic skincare routine:
- Moisturize the skin at least twice daily using creams, ointments, or lotions, opting for products that
are gentle and non-irritating. Petroleum jelly can be particularly helpful for preventing atopic dermatitis.

- Take short, warm showers or baths, avoiding hot water.
- Use mild, non-soap cleansers without dyes, alcohols, or fragrances, especially for young children.
- Avoid harsh scrubbing while washing clothes.
- Gently pat the skin dry with a soft towel after bathing and apply moisturizer while the skin is still damp.
- Maintain consistent humidity and temperature levels to avoid rapid fluctuations.
- Minimize exposure to known allergens and irritants.
- Avoid touching or scratching irritated skin.
- Use over-the-counter antihistamines for intense itching as needed.  

Management:

ABCDE management strategy for atopic itch is summarized. Then a corresponding management strategy is: Avoid allergen/irritant for trigger; Barrier repair for impaired skin barrier; Control inflammation for flaring allergic skin inflammation; Decrease itch for intractable itchy desire leading to scratch; Educate patients for improved understanding and cooperation on the patient.

Fig 3. Management of atopic dermatitis in ABCDE manner

Conclusion:
Atopic dermatitis (eczema) presented a complex and challenging disorder for both patients and physicians, recent advances in understanding both genetic and environmental factors in eczema pathogenesis have provided valuable initiative into the disease. Overall, this combined understanding of genetic and environmental influences offers promising avenues for developing more effective treatments and preventive strategies for eczema.

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