

## The Itch-Scratch Cycle: Quality of Life Assessment and Management of Atopic Eczema in Children

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### Abstract

Atopic Eczema in children is a common condition with increasing prevalence. Its impact on the quality of life of the affected child and its family is often underestimated. This review summarizes recent research on the impact on the quality of life of atopic eczema in children and the available quality of life assessment tools as well as management principles according to recently updated care guidelines. Healthcare providers should be familiar with the presentation, basic assessment and management of atopic eczema in children and adopt a holistic approach to the condition.

**Keywords:** Dermatitis; Atopic/Diagnosis; Dermatitis; Atopic/Immunology; Dermatitis; topic/Therapy; Quality of life; Severity of illness index

### Introduction

Atopic Eczema (AE) affects more than 10% of the pediatric population worldwide [1,2]. It is the most common chronic inflammatory skin condition in children. In the United States, it is estimated that approximately 10-20% of children are affected and there is evidence that the incidence is increasing [3]. AE carries significant, often underestimated, morbidities and costs. More than half of affected children suffer from sleep disturbances, while more than 25% report problems with sports, school or holidays [4]. A study in Australia found that caring for a child with AE has a greater impact on a family's quality of life than caring for a child with diabetes [5]. A recent Cochrane review focused on the psychological and educational tools available for AE in children [6]. In this setting, all healthcare providers as well as students and staff working with families should be familiar with the presentation, pathogenesis and management of AE in children. They should also be able to measure the impact on quality of life and the response to treatment by validated, repeatable assessment tools.

### Presentation: The Itch-Scratch Cycle

To assess the impact on quality of life, a study in Australia included 48 randomly selected children with atopic eczema and compared their family impact score to 46 children with insulin-dependent diabetes [4]. Higher financial costs, sleep disturbances, interruptions to employment and the time-consuming daily skin treatments contributed to AE's greater impact on quality of life. In addition, the researchers postulated other contributing factors, including parental feelings of guilt, effects of sleep deprivation on parents and children, behavioral problems, sibling rivalry, as well as effects of eczema on the child's psychological development, childhood self-esteem, and socialization skills [4]. Parents spent an average of two to three hours

each day in treating the eczema and reported being particularly concerned about the amount of time the child spent scratching.

Although the presentation of AE varies with age, dry skin and itchiness tend to remain constant features. In infancy, atopic eczema is characterized by vesicular, weeping lesions, particularly on the face and usually sparing the diaper area. In childhood, erythema and dryness tend to affect flexural surfaces [7]. The itching sensation pervades AE throughout all ages and at all body sites. Pruritus can result from internal and external factors. Environmental triggers include nylon clothing, dust, pets, sweating and shampoos, to name only a few [8].

Environmental triggers can induce pruritus by binding IgE, leading to histamine release and the stimulation of nociceptors. This produces inflammation and the characteristic pruritus. As the child reacts to the pruritus by scratching, it exacerbates the genetically and immunologically conditioned skin barrier defect. Cytokine-amplified expression of neural growth factors leads to increased sensitization of nociceptors in the epidermis and epidermodermal junction [9]. Scratching, thus, invites increased exposure to irritants and increased stimulation of the nociceptors. It effectively sets up a vicious circle of inflammation, increased itching and more scratching, which results in more inflammation and further break-down of epithelial integrity. As the inflammation continues, healing cannot occur and the fired-up immune system receives additional fuel from new environmental irritants.

### Genetics

The pruritus associated with AE is produced by multi-level interactions of genes, immunological pathways and environmental agents. The impairment in the skin's natural barrier function is thought to originate at the level of the genome. More than eighty genes have been associated with AE [10]. The most consistently replicated evidence points at the gene encoding filaggrin, a skin matrix protein promoting keratin aggregation. Deficiencies in other key molecules, such as ceramides, also play a key role. A defect in the epithelial barrier

favors allergen absorption which can lead to leucocyte sensitization and the surge in immunoglobulin and cytokines associated with subsequent exposure to the allergen [11]. In 2009, a French research group convincingly showed that the inflammation of AE can be the product of uncontrolled protease activity and that such inflammation can occur independently of environmental influences and independently of the adaptive immune system [12].

The researchers used the pathogenic mutation of Netherton syndrome at SPINK5, which encodes the protease inhibitor 'Lymphoepithelial KAZAL-type-related Inhibitor' (LEKTI), to create a mouse model which showed activation of the proinflammatory and pro-allergic pathway in utero, i.e. prior to the exposure of epithelial cells to the environment. LEKTI is a marker of epithelial differentiation and lack of LEKTI causes stratum corneum detachment due to protease hyperactivity [13]. Thus, deficiency of LETKI, like deficiency of filaggrin, leads to a skin barrier defect promoting allergen absorption. While filaggrin mutations are clearly linked to AE, a recent British cohort study did not show an association between filaggrin mutations and the severity of AE [14].

## Management of Atopic Eczema in Children

Updated guidelines on the management of atopic dermatitis have been recently published by the American Academy of Dermatology [15]. One key to the therapeutic management of AE is the breaking of the itch-scratch cycle [16]. This involves avoiding triggers in the environment, restoring the skin barrier function, and modulating the immune response with medication, either locally or systemically. Experienced practitioners generally adopt a holistic approach that focuses on individual presentation and the impact on the quality of life of the individual (and family). Patient/Family education is important not only to eliminate environmental influences but also to ensure compliance with treatment. Concerns over the side effects of corticosteroids often lead to unnecessary suffering. Simple measures, such as avoiding over-heating or the use of mild soaps can be helpful.

Trigger factors, including diet, pets and nylon clothing, should be avoided but only as a temporary therapeutic trial. Special diets can be expensive and represent an additional, often unnecessary burden to the patient and the patient's family. They are indicated only in severe eczema or in cases of failure to thrive. It is also important to educate carers how to recognize the features of flares and the signs of superimposed infection. Discussions in clinics can be supplemented by written information and practical demonstrations of how to apply to topical treatments.

Emollients form the foundation of AE management and should be used even when there are no visible lesions. Hydration through bathing and soap substitutes are also important at the baseline. Topical corticosteroids constitute the next step. Their potency and the duration of treatment are tailored according to severity. Certain sites, such as the face, the axillae and groins are particularly sensitive and require special care. In some circumstances, topical calcineurin inhibitors are alternatives to steroids. In addition, tacrolimus has been shown to offer significant benefits as maintenance therapy on previously affected skin [17]. Bandages can be useful adjuncts to topical treatments and help prevent excoriations through itching and superinfections. The ultimate step involves the use of systemic agents and phototherapy, which usually require specialist supervision.

Infections, including viral, bacterial and fungal, can significantly complicate AE. While bacterial colonization, either directly or through

superantigens, can contribute to skin inflammation and disease severity, effective treatment is controversial. A 2008 Cochrane review failed to find clear evidence of benefit for antimicrobial interventions [18]. Moreover, overzealous prophylactic treatment can also lead to the emergence or spread of resistant strains. On the other hand, bleach baths have been shown to decrease the incidence or severity of secondary bacterial infection [19].

There is also a confusing array of complementary therapies for AE. Oenothera oil (evening primrose) was once a popular alternative for steroid-phobic parents but the majority of current evidence suggests that it offers limited or no benefit [20,21]. Similarly, probiotics administered during pregnancy and/or early infancy have been said to reduce the incidence and severity of AE [22] but other evidence, including a randomized control trial, failed to confirm this [23]. Other complementary modalities include traditional Chinese medicine and herb-based medications, including St. John's Wort, chamomile extract and avocado oil [24]. An important caveat with these medications is the possible adulteration with steroids.

## Patient-Assessed Severity Measures

A holistic approach requires careful assessment of the impact on the child's (and its family's) quality of life. The relationship between severity and the impact on the quality of life is neither direct nor linear. A child with severe but relatively non-pruritic lesions may lead a near-normal lifestyle, while another with deceptively mild lesions may deprive the whole family of sleep. Methods of measuring quality of life range from general health measures, such as the Sickness Impact Profile and General Health Questionnaire, over dermatology-specific measures, such as the dermatology life quality index (DLQI) [25] to disease-specific measures, such as the validated [26] Patient Oriented Eczema Measure (POEM) [27,28].

There is no generally-accepted gold standard for quality of life assessment and often researchers use their own, individually developed tools. However, assessment tools can be validated across different settings, such as those with a high disease burden versus those with a lower disease burden. This achieves a degree of objectivity for comparing the impact on quality of life and for tailoring treatment appropriately. Validated assessment tools are useful not only for purposes of research but also in following individual patients over time.

The children's DLQI is a ten-item cartoon-supported questionnaire that aims particularly at the child's perception of how AE affects the child's life. Questions cover the effect on sleep, school work, athletic activities, clothing, friendships, social life and holidays. In comparison, the POEM is a seven-item questionnaire that allows the child's carers to record the frequency of symptom occurrence, including pruritus, bleeding, xerosis, desquamation and sleep disturbance. More recently, an Infant's Dermatitis Quality of Life index (IDQoL) and Dermatitis Family Impact questionnaire (DFI) were designed to study the quality of life in children with AE in a multicenter investigation [25]. While dermatology teams have traditionally relied on their perception of how a skin condition affects their patients' life, such questionnaires provide a tool for measuring disease severity in terms of the patient's perspective.

Additionally, locally adapted questionnaires can help elucidate baseline information. Such questionnaires allow the patient's family or carers to expressly note their views on triggering factors, their concerns about treatments already tried and their expectations form

the consultation. Some questionnaires may even help as checklists during busy clinics ensuring that important triggering factors, such as pets, are not forgotten in the history and that the impact on the patient's sleep, school and social life is adequately explored. When properly filed in a patient's health record, the questionnaires can also constitute an easy reference source for future appointments.

## Outlook

Novel treatments are continuously trialled but more evidence-based management strategies are urgently needed. Progress in basic science research will lead to new treatment targets for AE. As the immunological pathways are elucidated, the efficacy, dosing and duration of treatment with biologicals must be systematically investigated [25]. Analogously, as the defects in the skin barrier dysfunction are better understood, barrier repairing agents containing molecules deficient in AE, such as ceramides and certain fatty acids, may be increasingly employed. One multi-centre, randomized trial compared a physiological-lipid based formulation to a mid-potency steroid and found its efficacy comparable [25].

Another approach may be desensitization to known triggers by allergen-specific immunotherapy, a strategy already successfully employed in asthma and allergic rhinitis [25]. Anti-histamines have been notoriously ineffective in targeting the recalcitrant pruritus associated with AE. Novel approaches to breaking the itch-scratch cycle may involve targeting itch-receptors directly or introducing antibodies to cytokines found responsible for promoting the inflammation-itch pathway.

However, in addition to researching new treatments, established management regimes must be optimized. Recent studies suggest that the use topical calcineurin inhibitors during quiescent periods may improve skin barrier function [25]. Whatever therapeutic approach is used, it must be tailored to the individual circumstances of the affected child and its family. Patient-assessed severity measures are increasingly used in clinical practice and should form part of the management routine. Although more challenging in the pediatric population, these assessments are particularly important as the child's quality of life, the family's quality of life, the child's psychosocial development and perhaps even the child's confidence in the medical profession are implicated.

## Conclusion

AE in children is a common condition with increasing prevalence. All healthcare provider need to be familiar with its presentation and significant impact on individual and family quality of life. Treatment needs to be individualized but guidelines for the management of AE are available, together with objective tools for assessment of the impact on quality of life. Thus, a holistic approach, involving assessment and management, is crucial.

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