The Long-Term Course of Atopic Dermatitis

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KEYWORDS

• Atopic dermatitis • Eczema • Atopic eczema • Epidemiology • Natural history • Clinical course

KEY POINTS

- Atopic dermatitis (AD) is a chronic, relapsing condition, meaning that the intensity of symptoms usually fluctuates over time.
- Changes in skin physiology may be evident from birth, suggesting that AD may be a lifelong condition marked by intermittent symptoms/disease activity.
- Because AD is episodic, AD incidence, prevalence, persistence, remission, flare, and long-term control require careful definition.
- Improved measurement of the frequency and duration of active disease periods can help to elucidate more about the clinical course AD and the role of treatment in long-term outcomes.

INTRODUCTION

Atopic dermatitis (AD) (also known as atopic eczema or eczema) is by definition a chronic condition. The original diagnostic criteria proposed by Hanifin and Rajka and the most recent guidelines issued by the American Academy of Dermatology both include a "chronic or relapsing" history as an essential feature.[1,2] Little is written, however, about the clinical course of AD.[3] This could be because many patients with AD present with symptoms early in life, and hence most research has focused on pediatric disease. Although there are relatively few publications about adult disease, recent population-based estimates of AD prevalence among US children and adults were similar.[4–6] These data suggest either AD begins in childhood and persists through adulthood, childhood AD remits for some and begins in adulthood for others, or some combination thereof. A number of practical and methodological challenges to studying a chronic episodic condition have limited the description of the long-term course of AD. In the following sections, we review the available data and discuss the implications for clinical care and future research.

WHY IS THE LONG-TERM COURSE OF ATOPIC DERMATITIS IMPORTANT TO STUDY?

Data about the long-term course of AD are necessary for informing clinicians and patients about prognosis and guiding treatment decisions at an individual level and for planning at the health systems level. Traditionally, AD was considered a pediatric condition and families were told most children "outgrow" AD by adolescence. Such imprecise information is insufficient for patients

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who desire detailed prognostic data. Moreover, it is insufficient for understanding the impact of potentially disease-modifying interventions, a topic of particular salience in the current era of systemic drug development.

WHEN DOES ATOPIC DERMATITIS BEGIN?

The symptoms of AD may begin at any age, although many sources suggest that most incident AD occurs in early childhood. Estimates may be affected by study designs that focus only on pediatric or clinic populations or by the diagnostic criteria used. For example, a recent review in the *Lancet* states "in roughly 60% of cases, the disease manifests during the first year of life," citing a prospective study that follows patients until age 7 and a retrospective cohort of clinic patients.[7–9] Studies including only children may underestimate the average age of disease onset because they would not capture adult-onset cases. Similarly, clinic-based samples are likely biased toward patients with more persistent or severe disease that begins earlier in life, and may not be not be representative of the general AD population. Additionally, some commonly used diagnostic criteria, including the Hanifin and Rajka criteria[2] and the UK Working Party criteria,[10] include onset in childhood as a minor criterion. Studies using these criteria may estimate lower rates of adult disease compared with studies that do not select patients based on age of onset. Data that are less likely to be susceptible to selection bias suggest that AD may commonly begin in adulthood. For example, a population-based survey in the United States found that 54% of those with AD reported disease onset after age 18.[11] More data are needed to understand disease incidence over the life span and whether adult-onset disease is different from disease that begins in childhood.

DOES ATOPIC DERMATITIS PERMANENTLY RESOLVE, AND IF SO, WHEN?

Existing data are unable to answer this question. An older review found that 50% to 70% of individuals with AD improved over 10 years of follow-up, although the definition of clearance varied by study and ranged from 11% to 92%.[3] Population-based birth cohort studies with multiple assessments of individuals over 2 decades found that rates of "short-term" or "apparent" clearance decreased when accounting for subsequent recurrences using estimates of annual period prevalence repeated every 3 to 7 years.[12–15] More frequent measurement of disease activity every 6 months in a US cohort of children and young adults with AD who had prior treatment with a topical calcineurin inhibitor (and therefore may be more likely to have persistent disease) suggests that although some patients seem to improve with age, most continue to have active disease at multiple time points.[16] Longitudinal studies that follow individuals throughout adulthood are needed to better understand the periodicity of disease activity and patterns over the life course.

IS ATOPIC DERMATITIS A LIFELONG CONDITION?

Genetic and physiologic data support the idea of AD as a lifelong condition. It is well established that AD runs in families, and in the past decade genetic discoveries have implicated multiple genes involved in the development and maintenance of the skin barrier and immune function.[17,18] Patients with AD often have xerosis that predates their diagnosis. In fact, "a history of generally dry skin from birth" was found to be one of the most predictive characteristics and hence was included among the minimum set of discriminators in the UK Working Party diagnostic criteria.[10] Although the evidence is mixed,[19] some studies have shown that physiologic differences, such as transepidermal water loss (TEWL), may precede the clinical manifestations of AD and are detectable as early as day 2 after birth.[20,21] Moreover, experimental evidence from 2 randomized trials suggest that maintenance of the skin barrier with emoillients during the neonatal period may delay or prevent the development of clinical signs of AD.[22,23]

These data suggest that individuals with AD have an elevated probability of developing clinical symptoms throughout life, as illustrated in **Fig. 1**. Even normal-appearing skin in patients with AD has evidence of differences in skin barrier function, dendritic cell population, and cytokine profiles, supporting the concept of subclinical disease.[24] The factors influencing the transition to clinically

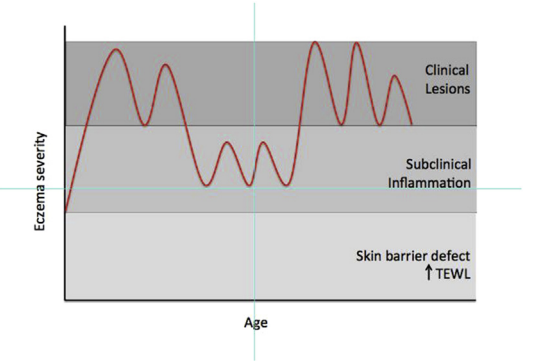

Fig. 1. Hypothetical example illustrating the long-term course of AD.

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