

A Long View: Conceptions of Atopic Dermatitis Through the Ages

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Atopical dermatitis (AD) has likely been with us since the very beginning, in some form or another. Although the specific disease entity called atopic dermatitis was only first described in the 20th century, there are many descriptions that may represent AD and its myriad subtypes before it was fully defined. Atopic dermatitis affects nearly 20 percent of children in developed countries, and the prevalence has been rising.^{1,2} Many patients and parents express concerns that this disease is something new and foreign, possibly triggered by elements of modern life. While such hypotheses could be true and may help explain the rising incidence, there is a certain comfort in knowing that our forebears contested with similar skin problems. By reviewing the disease from a historical perspective, we may be able to gain an enhanced understanding of the disease and its subtypes moving forward.

ANCIENT HISTORY

The Ebers Papyrus, one of the earliest known medical documents, was written by the Ancient Egyptians around 1500 BC. Included in its dermatology section are remedies to “still” itching of the skin, including such concoctions as onion and bean-based topical poultices and injections of fresh milk and sea-salt.^{3,4} Around 400 BC, Hippocrates offered a causal explanation for skin disease, describing it as a cutaneous rectification of internal humoral imbalances.⁵ Some centuries later, the Roman physician Celsus described the condition “scabies,” which was characterized by a “certain degree of hardness of the skin with pustules, some humid and some dry” and Roman poet Suetonius described what appears to be the atopic syndrome in Emperor Augustus.^{6,7} The Persians contributed their medical knowledge as well, and Avicenna (980-1037 AD) wrote an influential text called Canon of Medicine that contained multiple conditions and treatments consistent with our modern-day understanding of AD and dry skin.^{8,9}

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PRE-MODERN ERA

The early pre-modern era was marked by several accounts of an infantile skin condition characterized by pruritus and oozing, particularly on the face and head. The first documented dermatology text, written by Italian physician Mercurialis in 1572, and later works by English surgeon Daniel Turner and French dermatologist Alibert (who called the disorder *tinea muequese*), contain various descriptions of this infantile dermatosis, which may represent an early precursor of AD, though it clearly has features of seborrheic dermatitis as well.^{10,11} These pre-modern era physicians maintained their belief in the Hippocratic theory, believing that cutaneous problems were manifestations of essential excretory processes occurring as a result of humoral imbalance.^{12,13} Daniel Turner even explained that curing itch would pose danger to the patient by driving excrements back into the blood and nervous fluid.¹¹

The early 1800s brought great changes within the field of dermatology. Willan and Bateman, English physicians, introduced a new system for skin diseases that categorized them based on the primary lesion.^{10,14} They also coined the term ‘eczema’, categorized as a vesicular disorder, for the first time. Willan and Bateman’s ‘eczema’ does not appear to be an early description of AD, but rather a set of skin conditions caused by the sun and external irritants.¹⁴ Their works do describe disorders that more closely resemble

AD, however, for example strophulus confertus and lichen agrius, both papular disorders, and porrigo larvalis, a pustular disorder similar to tinea muquese.^{15,16}

The conception of eczema developed over the course of the 19th century, with unique contributions from various individuals. Rayer, in 1835, was the first to explain the disorder's chronic nature.¹⁰ Although Rayer's notion of a relapsing and remitting skin disorder did not differentiate between chronic eczema in children and other types of chronic lesions, it nonetheless enhanced our understanding of the persistent character of the disease.^{14,17} In 1865, Erasmus Wilson described infantile eczema in detail, modeling the disease after tinea muquese and porrigo larvalis, but also mentioning its possible continuation into adulthood.¹⁸ In 1860, Viennese dermatologist von Hebra introduced a distinctive clinical entity characterized by urticaria in infancy, followed by pruritic papules most severely affecting the extensor surfaces.¹⁰ Skin became thickened, rough, and excoriated.¹⁹ While sharing some features with AD and often considered its precursor, the infantile urticaria and extensor distribution of Hebra's prurigo are somewhat inconsistent with modern-day AD.¹⁶ In 1892, revered French physician Besnier laid the foundation for our modern-day AD with a novel disorder characterized not by the existence of a specific primary lesion, but rather its chief symptom—pruritus. Besnier even linked the disorder to asthma and hay fever.^{10,14}

TWENTIETH CENTURY AND BEYOND

The 1900's brought dramatic changes in the nomenclature and diagnosis of AD. The terms 'allergy' and 'atopy' were first introduced by Von Pirquet, and Coca and Cooke, respectively.^{20,21} Atopy was described as a hypersensitivity to allergens, exhibiting as asthma and hay fever. Soon after, in 1933, the term 'atopic dermatitis' was coined by Wise and Sulzberger, who described the disorder as a diffuse, pruritic condition in individuals with a family history of atopy and flexural distribution, among other characteristics.^{22,23} Although the term highlighted the link between AD and atopy, Sulzberger mentioned that a diagnosis of AD was possible even without these other atopic manifestations.¹⁴ The first widely-used diagnostic criteria for AD were developed by Hanifin and Ranjka in 1980, in which at least three of four major criteria (pruritus, flexural surface in adults/extensor in infants, chronic dermatitis, personal/family history of cutaneous/respiratory atopy) were required for diagnosis.²⁴ In 1994, Williams et al. modified this and called it the UK Working Party criteria.²⁵

Some of the first scientific studies involving AD explored the role of allergy. Blackfan, in 1916, followed by Talbot, and

Wise and Sulzberger, found that AD patients had greater hypersensitivity to allergens during cutaneous testing, compared to healthy patients.²⁶⁻²⁸ Restriction of the respective foods and allergens from their diet and environment was found to help their disease. Subsequent experiments have continued to investigate the allergy and AD, including various studies in the 1960s involving IgE antibodies.²⁹⁻³² The remainder of the 20th century and new millennium have brought much expansion to the realm of AD, and research now reaches beyond simple studies on allergy to intricate interactions between the skin barrier, genetic susceptibility, immunologic response, and more.

TREATMENT OF AD

The treatment of AD has changed dramatically through the centuries, reflecting the prevailing etiopathogenesis of the time. Hippocrates' humoralist theory dominated well into the 1800s, causing most people to be hesitant in treating AD, for fear that doing so would interrupt the body's attempt at restoring balance.^{10,12,13} Some treatments were actually meant to increase salutary oozing, such as wrapping the body with rubber, while some accelerated toxic eliminations, including bloodletting.¹³ Von Hebra was one of few early physicians who actually identified the importance of treating the skin in AD, suggesting topical therapies to alleviate symptoms.¹⁹

Starting in the late 19th century, the Hippocratic humoralist theory for disease began to fade. Thinking that AD might be related to infantile milk consumption, some physicians proposed modifications to or replacements for milk.^{13,20} Others advocated dietary restrictions based on positive reactions during cutaneous allergen testing, and this became popularized in the 20th century when allergy-based research studies were taking place.^{14,22} In 1952, the effectiveness of Compound F, or hydrocortisone, was first reported by Sulzberger and Witten, and the successive development of various topical steroids revolutionized AD management.³³ More recently, other skin-based treatments such as topical calcineurin inhibitors and phototherapy, as well as systemic therapies, have added to our compendium of treatments for AD.

CONCLUSION

As we continue into the 21st century, we have undoubtedly entered a time of rapid and exciting change in the understanding and treatment of AD. With deeper knowledge of the skin barrier and the immune system than ever before, the discussion has moved into new, undiscovered territories such as cutaneous (and intestinal) microbiota, the nervous system in the perception of itch, and totally new therapeutic approaches to AD. By looking back at its complex and meandering historical roots, we are forced

to remain humble and keep our minds open as we work towards mastering this troubling disease. ■

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