



The history of atopic dermatitis



Owen N. Kramer, BS^a, Mark A. Strom, BS^b, Barry Ladizinski, MD^c, Peter A. Lio, MD^{b,*}

^aUniversity of Illinois at Chicago College of Medicine, Chicago, IL

^bDepartment of Dermatology, Northwestern University Feinberg School of Medicine, Chicago, IL

^cDivision of Dermatology, Stroger Hospital of Cook County, Chicago, IL

Abstract Fred Wise (1881–1950) and Marion Sulzberger (1895–1983) are often credited with introducing the term *atopic dermatitis* to dermatology in 1933. This definition was based on *atopy*, a term first created by Arthur Coca (1875–1959) and Robert Cooke (1880–1960) in 1923, when they recognized an association between allergic rhinitis and asthma. Despite its recent introduction into our medical lexicon, historical precursors of atopic dermatitis date back to at least as early as 69–140 CE. In this contribution, we highlight both the prominent individuals credited with shaping the disorder into our current interpretation and the suspected historical precursors of this disease and reported treatments.

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Ancient era until beginning of the modern era

Although even earlier descriptions of itchy skin conditions exist,¹ the earliest account of what may have been atopic dermatitis (AD) dates back to the times of Roman historian Suetonius (69–140 CE).² As seen in translations of his prominent book, *The Twelve Caesars*, Suetonius described in detail a cutaneous affliction of Emperor Augustus, noting “a number of hard, dry patches suggesting ringworm, caused by an itching of his skin” as well as “seasonal disorders,” noticing that he experienced in the early spring “a tightness of the diaphragm; and when the sirocco blew, catarrh.”³ Centuries later, in 543 CE, Aëtius of Amida (502–575) was the first person recorded to have used the word *eczema*. Aetius used the term to represent “boiling out,” referring to the idea of an “inward heat, which drives off the humours of the body from its surface like the seething of a boiling fluid.”⁴ This antiquated medical

theory regarding “body humors” was an important basis of diseases and treatments in ancient times, with some physicians following its doctrine up until the 20th century. Although it is difficult to know for certain what skin condition Aëtius was indicating when he spoke of eczema, it has been suggested that he was likely referring to furuncles.^{5,6}

In 1572, the first dermatologic text was written by Girolamo Mercuriale (1530–1606), an Italian physician, who described “achores,” a pruritic oozing condition seen in suckling infants.⁷ Similar representations of AD were later described by other physicians, including the English surgeon Daniel Turner (1667–1740), who described crusts and pruritus in children in 1714,⁸ and the French physician and botanist François Boissier de Sauvages de Lacroix (1706–1767), who in 1763 described a dry and scaly condition that became known as “tinea lactea.” Soon after, in 1806, Jean-Louis Alibert (1768–1837), founder of French dermatology, described a disorder known as “*teigne muqueuse*” (mucous tinea), which represented a pruritic, oozing condition in infants.⁷ Of note, some of these presentations, particularly “tinea lactea,” may in fact refer to infantile seborrheic dermatitis rather than AD⁷; however, the presence of pruritus in several of these diseases may suggest AD as the underlying diagnosis.¹

* Corresponding author: Peter Lio, Medical Dermatology Associates of Chicago, 363 W. Erie Street, Suite 350, Chicago, IL 60654.

E-mail address: p-li@northwestern.edu (P.A. Lio).

The 19th century

The 19th century represents the period when dermatology came of age. English physicians Robert Willan (1757-1812) and Thomas Bateman (1778-1821) developed an innovative classification scheme that would group dermatologic diseases according to their primary skin lesion,⁵ though the scheme was criticized by some at the time for its lack of distinction of etiology and pathophysiology.⁹ Willan and Bateman also further developed the term *eczema* to represent “an eruption of minute vesicles, noncontagious, crowded together; and which from the absorption of fluid they contain form into thin flakes or crusts. This eruption is generally the effect of irritation, whether internally or externally applied”⁶; moreover, although it was known that eczema manifested itself through numerous vesicles, a difference between acute and chronic eczema was lacking.

In *A Theoretical and Practical Treatise on the Diseases of the Skin*, Pierre-François Olive Rayer (1793-1867), a French physician, wrote extensively about eczema, recognizing three varieties that were also described by Willan, including eczema simplex, eczema rubrum, and eczema impetiginodes.¹⁰ Rayer also recognized the concept of eczema as a relapsing and remitting, chronic condition, noting that he had “seen the disease get well and recur twelve or fourteen times within the space of a few months”¹¹; however, it is important to recognize that during much of history, there was a lack of distinction between contact dermatitis and atopic dermatitis and, as alluded to, it appears that the term *eczema* was often used during this period to refer to the conditions that occurred when one was exposed to sun, mercury, toxic chemicals, and irritants.⁵ As such, Rayer may have grouped together several different pruritus skin conditions. Still, he made a perceptive distinction in his book, stating that eczema was not to be confused with other vesicular eruptions, such as those “artificially produced by the sun’s rays.”¹¹

Another prominent figure in the history of AD was Sir Erasmus Wilson (1809-1884), who was noted to be the “greatest dermatologist of his time.”¹² As with Rayer, Wilson also commented on the distinction between acute and chronic eczema, stating, “If I were asked how I should distinguish between an acute and a chronic eczema, I should say that the acute stage was denoted by erythematous congestion and moist excoriation, and the chronic stage by infiltration and desquamation, the infiltration giving rise to thickening and induration.”¹³ Wilson labeled the chronic stage of eczema as psoriasis and pityriasis, and thus it is unclear if he was referring to chronic eczema as a separate disease process from acute eczema.¹⁴ Wilson commonly remarked on eczema in his many lectures presented at the Royal College of Surgeons of England in 1871. It was during this time that Wilson proposed many interesting theories about the clinical course, comorbid conditions, and treatment of eczema. For example, Wilson suggested that eczema’s various lesions (eg, vesicles and scales) might be attributed to the duration of the disease, among other factors. Additionally, as seen in the past, Wilson commented on the association of the cutaneous lesions with that of respiratory

symptoms, stating that bronchitis and catarrh are essentially eczemas of the mucous membranes.¹⁵ Wilson is also acknowledged for his detailed accounts of infantile eczema, recognizing that, in addition to adult eczema, vesicles as well as other primary lesions (eg, papules) may be present.

Ferdinand Ritter von Hebra (1816-1880) later described a disorder now considered to be most similar to our current understanding of AD. Von Hebra was an accomplished physician and is credited for being the founder of the Vienna School, which was considered the “first and most important school of dermatology within the German speaking area of Europe.”^{16,17} In 1860, von Hebra provided a report of a disorder very similar to AD that came to be known as von Hebra prurigo. Von Hebra prurigo was described as a chronic disorder in infants and young children that was thought to present initially with urticaria and eventually manifest with pruritic papules on the trunk and limbs.⁷ There are several case reports of von Hebra prurigo documented in the literature that describe this presentation in detail,¹⁸⁻²⁰ one of which in particular described in detail the severity and persistence of pruritus in a 7-year-old child, noting that “the child tore his skin in efforts to mitigate his suffering” and “at times sleep [for the child] was impossible,” and that the condition was “worse in [the] winter, [and] better in [the] summer.”¹⁸ A biopsy specimen of von Hebra prurigo was also described as having “swollen” retes and “hyperplasia of all the cutaneous structures, especially papillae, which were infiltrated with cellular elements.”

Ernest Besnier (1831-1909), a French dermatologist, is perhaps most renowned for coining the word *biopsy* and educating the masses on its use in securing a diagnosis¹⁶; however, he is similarly recognized for proposing a disorder that many physicians come to recognize today as a precursor to infantile eczema, which he called “prurigo diathésique.”²¹ Besnier is acclaimed for highlighting that individuals who developed diathetic prurigo had an inherited predisposition.²¹ In addition to this predisposition, common associations with Besnier’s diathetic prurigo included a “sensitivity” to food²² and “respiratory symptoms” that developed over time.²¹ Amazingly, many centuries after Suetonius (c69–after 122 CE) first described what appeared to be an atopic association in Emperor Augustus (27 BCE–14 CE), Besnier’s diathetic prurigo theory appeared to be a significant advancement in the investigation of atopy and eczema.

Although the understanding of dermatologic diseases significantly improved over the late 19th and early 20th centuries, it was clear that the etiology of eczema and AD was not understood. In 1890, Paul Gerson Unna (1850-1929), well known for his development of the Unna boot, boldly asserted that the etiology of eczema was due to “the inoculation of a germ.”²³ His beliefs are relayed through Louis Duhring (1854-1913), who stated that Unna believed “this germ is doubtless of vegetable nature, and increase and proliferates in the epidermic structures only, requiring probably a condition of the skin suitable for its reception and development.” Unna ultimately defined eczema as “a chronic parasitic catarrh of the skin, with desquamation, itching, and the disposition to

respond to irritation by exudation, and well-marked inflammation.” With this assertion in mind, Unna believed that local treatment should “always have in view the destruction of every single germ in the depths of the epidermis.”²³ It is striking perhaps that only now, nearly 125 years later, do we have truly compelling evidence about the role of *Staphylococcus aureus* in AD,^{24,25} possibly giving some credence to this theory.

The 20th century

It was essential in the 20th century that researchers and clinicians consolidate as well as refine the historical illnesses previously described to develop a more concrete depiction of atopic dermatitis. This could not be accomplished without the development of concepts such as “allergy” by Clemens von Pirquet (1874-1929) in 1906 and “atopy” by Arthur Coca (1875-1959) and Robert Cooke in 1923. When first coined, allergy (*allergie*) represented “altered reactivity,” whereas atopy was derived from the Greek word *atopia*, meaning “without place.”^{7,26} These term proposals were pivotal points in history that would direct efforts toward advancing our understanding of allergic phenomena including atopic dermatitis. Soon after, in 1933, Fred Wise and Marion Sulzberger proposed the term *atopic dermatitis*. This concept encompassed a disease that was heralded by infantile eczema, localized to areas such as the face and flexural folds, and occurred in an individual with a family history of atopic disorders.²⁷ Importantly, Sulzberger and Wise used this term to both isolate AD from a heterogeneous mixture of pruritic skin disorders and to distinguish the etiology from a psychologic and neurologic origin established by the term *neurodermatitis*.²⁸ Coca and Sulzberger later added this term to the group of genetically predisposed allergic conditions such as hay fever and asthma.²⁶ Coca continued to develop the idea of allergic processes and proposed a previously suggested notion of individuals having “adverse reactions to foods.” This preoccupation would consume Coca as he became fixated with symptoms he experienced in response to ingesting various substances. Reportedly, his breadth of “food allergies” resulted in a significant change in his diet and cooking habits such as using a “personal supply of sugar that was refined through 9 successive dialyses or hydrolyzed lactose.” He even went as far as to only read newspapers that were preheated in an oven and refrained from eating foods made with aluminum pots or on a gas stove.²⁶ Though Sulzberger also initially believed that food allergens played a role in the pathogenesis of AD, after conducting exposure and elimination experiments, he later concluded that additional determinants played a role in the pathogenesis.²⁸

Our understanding of allergic processes and AD continued to progress, and in 1967 Gunnar Johansson (1911-1998) and Hans Bennich discovered immunoglobulin E (IgE),²⁹ with subsequent determination of an association of serum levels with allergic asthma.³⁰ This discovery and relationship would soon extend to AD; for example, in 1978 Bruno Wüthrich

published a paper reporting that patients with AD had on average higher serum IgE levels compared with controls, a relationship that had also been noted in several former studies. Wüthrich firmly believed that IgE was more than an associated finding and that it played an important role in the generation of observed cutaneous changes in atopic dermatitis; however, the relevance of this finding in the pathogenesis of AD remains, even to this day, incompletely understood. Still, this finding eventually spawned a plethora of studies including recent investigations into the utility of serum IgE as a biomarker for predicting outcomes³¹ as well as studies evaluating the efficacy of anti-IgE treatments (eg, omalizumab).³² This finding was considered quite noteworthy and was included as a minor feature in the first diagnostic criteria for AD.

In 1980, Jon Hanifin and Georg Rajka proposed the first widely used set of diagnostic criteria for AD.³³ The criteria included four major features (pruritus, characteristic morphology and distribution, chronicity of lesions, and personal or family history of atopy) as well as a plethora of minor features such as early age of onset, xerosis, hyperlinear palms, elevated IgE, and Dennie-Morgan folds (infraorbital lines). Diagnosis required three or more major features as well as three or more minor features. Hanifin and Rajka also recognized several synonyms for AD such as atopic eczema, Besnier prurigo, and infantile eczema. Criteria for AD would be revisited over the following years on several occasions. One noteworthy instance occurred in 1997 when Williams et al proposed the UK diagnostic criteria that established the six “most useful” diagnostic criteria for AD.³⁴ The criteria were similar to those described by Hanifin and Rajka; however, they were simplified to include history of pruritic skin changes, personal history of asthma, history of xerosis, visible flexural dermatitis, history of flexural dermatitis, and onset before age 2 years. Williams et al suggested that the addition of other criteria was likely to have an adverse effect without improving discernment of the disorder by the clinician.

Therapy

Early remedies and treatments

When reviewing the history of treatments for AD it is important to remember that the prevailing thought of “humors” guided medical therapy for the majority of history, and thus treating eczema in patients was an unpopular and purportedly unwise decision.³⁵ In fact, the oozing often present in eczema was thought to be essential to the healing process.³⁵ Surprisingly, even into the late 19th century, physicians continued to perpetuate this theory, including Jean-Louis Alibert, who defended the oozing eczema, calling it “salutary”³⁶; moreover, the prevailing belief was that treating the cutaneous manifestations of eczema would lead to increased risk of acquiring internal disease. Ernest Gaucher (1854-1918) is particularly notable for preserving this theory, describing dangers of

clearing eczema in children during the first International Congress of Dermatology in 1889.³⁷ Examples of these reported dangers included gout, rheumatoid arthritis, dysentery, and severe pulmonary and cerebral complication.³⁸ Gaucher even stated that he had once seen a child who was cured of eczema and as a result subsequently developed “pulmonary congestion” and quickly died³⁸; nonetheless, even though some physicians such as Gaucher instilled fear in those who sought to alleviate or cure eczema in their patients, it did not halt them in their pursuit.

In the 19th century, Wilson suggested an array of treatments for infantile eczema, one of which included covering the eruption with benzoated zinc ointment in combination with spirits of wine. He also emphasized the use of proper nutrition and supplementation with Fowler solution, a tonic containing potassium arsenite, touted to be helpful for many disorders.³⁹ Wilson commented on the use of benzoated zinc ointment, stating that it “removes the scales, heals chaps and fissures, and relieves in some degree the itching, but does nothing towards the dispersion of the thickening and induration of the tissues—that is, towards the cure of the disease.”¹³ In addition to treatments for eczema, there were many reported treatments for other suspected precursors to AD, such as von Hebra prurigo. In 1879, Henry Boenning described a case of von Hebra prurigo that was refractory to many treatments such as “animal oils, iron, iodine, regulation of diet, exercise, etc.”¹⁸ For this refractory case he decided to use sulfur ointment with carbolic acid, applied twice daily over thickened skin and papules, and preceded by a hot bath; 2 weeks after initiation of treatment, “the papules had almost entirely disappeared.”¹⁸

As medical theory changed, so did the perceptions of diseases and their subsequent treatments. It was not until the late 19th or early 20th century that the basis of medicine fully departed from the once heavily favored desire to maintain equilibrium of the body’s “humors.” Austrian dermatologist von Hebra and his student and son-in-law, Moritz Kaposi (1837–1902), strongly opposed the approach of prolonging the exudation or oozing in eczema. On the contrary, von Hebra stated in 1846 that his strongest desire in all of his studies was to cure chronic diseases of the skin.⁴⁰ Von Hebra and Kaposi suggested the use of topical treatments as the backbone of eczema therapy, including tar and sulfur; moreover, von Hebra appears to have suggested some of the good skin care that we still encourage to this day, such as using “not-too-warm-bathing” and emollients.⁴⁰ Von Hebra also mentions a treatment involving the ancient remedy of “*althæa decoctum*,” a decoction made from the plant sometimes called “marsh mallow” (*Althaea officinalis*), for treating childhood eczema, although it is unclear if this is in the form of oral or topical use.⁴⁰

Conclusions

The history of AD is vast, with a variety of individuals contributing a range of precursors eventually leading to our

modern-day conception. Although AD extends to ancient times, most of the evolution of AD has occurred in recent centuries. The 20th century was particularly prolific and included the introduction of atopy and allergy, the birth of the term *atopic dermatitis*, the discovery of IgE, and the proposal of the first diagnostic criteria for AD. Lastly, because our understanding of AD has accelerated in the last century, we are amidst an exciting opportunity in history to uncover the remaining intricacies of AD.

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