

2 The History of Atopic Eczema/Dermatitis

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2.1 Introduction

The clinical delineation as well as the nosology of the disease currently designated as atopic dermatitis or atopic eczema has been far from straightforward. Psoriasis, another common inflammatory skin disorder, had an opposite fate. Psoriasis derives from the Greek ψωρα, to have the itch, an old name for scabies. Psoriasis could have been considered initially as an absurd name for the disease it designates, as psoriasis and scabies do not look alike. But it is indeed a great name, because the word easily gained universal recognition, and nobody would propose to change its name now in the third millennium. As noted more than 80 years ago by Sabouraud, “*psoriasis a l’avantage inestimable de ne plus rien signifier que ce qu’il désigne* (psoriasis has the invaluable advantage of meaning no more than what it designates)” [1]. One could add “no more and no less.” Interestingly, the controversy over terminology has not yet abated for atopic eczema (e.g., [2, 3]), reflecting the different views of the clinicians and investigators in the field, who would be pleased to add meaning from their own field of interest in relabeling the disease. A recurrent wish in the history of eczema has been to expunge the word “eczema” from the medical literature (e.g., Hyde, “the passing of eczema” [4–6]), because of how difficult it is to define, and of the confusion generated in this area of dermatological knowledge. Interestingly, significant advances in the clinical delineation of the entity we today refer to as atopic eczema were probably achieved when our ancestor dermatologists had the opportunity to visit each other in their clinics or when they could examine patients together at international meetings. Jadassohn says that during his stay in Paris in 1896 he was able to establish connections between clinical subtypes (e.g., lichen Vidal, neurodermatitis,

prurigo diathésique, prurigo Besnier), which he could subsequently separate clearly from the rest of the eczema group [7]. Such pragmatic approaches were invaluable when the nomenclature confused everybody. Another striking example was reported in 1912 by Sir Malcolm Morris, president of the Dermatology Section at the Royal Society of Medicine: “At the International Medical Congress in London in 1881, Mr. Morrart Baker exhibited three cases which were identified by Kaposi and the younger Hebra and Unna as types of the prurigo of Hebra, and this recognition is a landmark in the history of prurigo in this country” [8].

2.2 Precursors of Atopic Eczema

One of the problems in identifying precursor entities is that the Willanist approach, which has dominated dermatology for the last two centuries, has put the emphasis on objective elementary lesions such as vesicles (herpes, eczema), papules (strophulus, lichen, prurigo), etc., and did not include the major subjective symptom, pruritus, which has been rightly considered since Besnier as “*le premier symptôme et le symptôme premier* (the first and primary symptom)” [9] of what we now call atopic eczema/dermatitis. One of the explanations of the confused state of the nomenclature is that atopic eczema resisted Willanism because of its protean clinical presentation, which physically is more recognizable using pattern rather than elementary lesion analysis [10]. However, the literature, case reports, drawings, paintings, photographs, and moulages together bring us back to the origins and allow us to propose retrospective diagnoses.

Although one can find descriptions compatible with a chronic pruritic condition, which could be atopic

eczema in Hippocrates's texts, the first allusion to the atopic syndrome was given by the historian Suetonius [11]. Emperor Augustus is said to have suffered from itchy dry patches of the skin and also from seasonal respiratory disorders.

The first dermatological book, *De morbis cutaneis*, was written in 1572 by an Italian physician, Girolamo Mercurialis [12]. Mercurialis still considered diseases in the antiquated way and classified skin disorders according to their primary location into two categories, i.e., head and scalp, and others. Among head disorders, *achores* designates an oozing pruritic condition that occurs in suckling infants and may be linked to the mother's milk. In this traditional conception of diseases, oozing was perceived as a salutary excretion of viciated humors and had to be respected.

Similar descriptions can be found under various denominations in the major textbooks of the proto-dermatological era; for example, Daniel Turner in 1714 mentions crusts and scabies (*pruritus*) in children; François Boissier de Sauvages describes *tinea lactea* (milky tinea) in 1763; Jean-Louis Alibert (1768–1837), the founder of French dermatology and first physician in the Hôpital Saint-Louis, gives precise descriptions of pruritic oozing eruptions in infants, under the headings *teigne muqueuse* and *achor muqueux*, the ancient word already used, among others, by Mercurialis. *Teigne muqueuse*, or mucous tinea, designates an oozing condition, and was opposed to milky tinea, a dry (scaly), benign, more frequent condition, that we now refer to as infantile seborrheic dermatitis. Consequently, as noted in Chap. 6, an itchy oozing cephalic dermatitis of infants has been clearly delineated since the beginnings of the dermatological literature.

The clinical revolution proposed by Plenck, developed by Willan and Bateman and followed by the majority of dermatologists after them, mainly consisted in an entirely new way of looking at skin diseases. Willan and Bateman [13] described skin diseases according to the primary lesion. The chapter on papular conditions includes strophulus in infants and lichen and prurigo in children and adults. Eczema is a vesicular condition, and most cases clearly refer to external causes such as sunburn or toxic chemicals. Porrigo is a pustular condition of the scalp and one of the forms of porrigo, *porrigo larvalis* (meaning like a mask) is very similar to the old milky crust and to our modern atopic eczema/dermatitis (Fig. 2.1).



Fig. 2.1. *Porrigo larvalis willani*. This picture of a severe infantile form of porrigo (a Latin word, synonym for tinea), one of the pustular diseases in Willan-Bateman's works, is considered by many authors as a precursor of the disease now referred to as atopic eczema/dermatitis. *Larvalis* means "ghost-like mask". Interestingly, vesicular eczema and papular prurigo in these authors are more distant to AE. (Thomas Bateman. Delineations of cutaneous diseases. London, 1817. Plate XXXVII.)

After Willan and Bateman, Pierre Rayer is to be credited with the distinction between acute and chronic eczema [14] and with precise descriptions of small children with a chronic eczema of the head and other parts of the body.

Erasmus Wilson [15] gave a detailed account of infantile eczema, a frequent and severe skin disease, and recognized that in this condition many elementary lesions, not only vesicles, could be found. Here, Wilson made a very important point, since Willanist authors clearly found it difficult to describe a disease that could not be ascribed to one and only one elementary lesion. In isolating infantile eczema, Wilson successfully escaped the Willanist classification and doctrine.

Indeed, the clinical aspects of child, adolescent, and adult phases are more difficult to trace back, but the categories “lichen” and “prurigo” as well as “eczema” from the old authors encompass clinical precursors of modern atopic eczema. The archives of the Museum of the Hôpital Saint Louis, Paris, show the successive reassessments of diagnoses given to the moulages and the relationships between those categories.

A turning point in the mid-nineteenth century was the isolation by Hebra, first chair of Dermatology in Vienna, of a “constitutional prurigo” [16], which attracted much attention and caused his followers many worries. Hebra described a chronic, recurrent skin disorder characterized by intensely pruritic papules and nodules on the trunk and limbs (Fig. 2.2). It usually began during infancy in the form of an urticarial rash followed by millet-sized or slightly larger pruritic papules that eventually became covered by a blood-colored crust. Itching was constant and extensor surfaces were mostly affected. Inguinal and axillary lymphadenopathy was constant. The disease had no known cause and was very difficult to treat. His successor and son-in-law Kaposi faithfully reproduced Hebra’s description in his popular textbook [17]. Due to this dogmatic description, the disease remained controversial and was considered to be extremely rare in other European countries and the United States. The mostly extensor distribution of Hebra’s prurigo made it difficult to fit chronic flexural eczema into the modern view of atopic eczema, but Hebra’s name was progressively synonymous of the severest and most recalcitrant forms of chronic eczema/prurigo in children and adults (prurigo ferox) (Fig. 2.3). This description and the discomfort it has generated in successive generations of dermatologists until the 1930s tells us how much the old masters and especially Hebra were revered. In 1912, the first three questions raised after a parliamentary style presentation of debate concerning the prurigos [8] derived directly from Hebra’s original flawed description (for the relation with urticaria and its distribution pattern): (1) Should Hebra’s name be dropped out of the nomenclature of prurigo? (2) Should the term “prurigo” be limited to affections presenting the papule described by Hebra and the subsequent lichenification? (3) Does prurigo begin as an urticaria? Hebra’s prurigo description was sharply criticized but still formed the clinical and conceptual framework of a “prurigo disease.”



Fig. 2.2. Hebra’s prurigo. This severe form of prurigo predominated on the extensor surfaces of the lower limbs. (Ferdinand Hebra, 1865: *Atlas der Hautkrankheiten. Bilder (Images) von Dr Anton Elfinger und Carl Heitzmann*. Wien. Book 5, plate 7)

Another major milestone in this premodern period of atopic eczema was the prominent role of the French school in delineating and characterizing a group of diseases featuring chronic relapsing lichenified lesions (Vidal, Jacquet, Brocq, Besnier). Besnier, the leader of the Saint Louis school, is now the best known for his first contribution named “*Première note et observations préliminaires pour servir d’introduction à l’étude des prurigos diathésiques (dermites multiformes prurigineuses chroniques exacerbantes et paroxystiques du type du prurigo de Hebra)*” (First report and preliminary observations ... on diathetic prurigo [itchy multiforme chronic exacerbating paroxystic dermatitis of Hebra’s prurigo type])” presented at the Société Française de Dermatologie et de Syphiligraphie in 1892 [9], and his major article “*Eczéma*” in *La Pratique Dermatologique*, published in 1900 [18] (Fig. 2.4).

Fig. 2.3. Hebra's prurigo in a French dermatology clinic. French dermatologists only rarely observed typical Hebra's prurigo. Less severe forms, with flexural involvement, were designated as "Hebra's prurigo, French type." Dr. Sézary, photograph Maire, 1934. From the Musée photographique de l'Hôpital Saint Louis, Paris



Besnier's major points were the following:

1. Pruritus is the major symptom (in contrast with the papule being the primary lesion in Hebra's prurigo) of an itchy diathesis.
2. Accompanying lesions are not specific.
3. Internal manifestations can occur, namely emphysema, asthma, hay fever, and also an association with "neurasthenia."
4. A hereditary predisposition in some organs may occur.
5. The disease is not restricted (as repeated since Hebra's description of a prototypical poor, Central European Jew) to lower social classes.

In describing a skin disease with both lichenified (papular) and eczematous (vesicular) lesions, and in emphasizing the preeminence of a pruriginous diathesis, Besnier successfully escaped the dominant Willanist nosology, as Wilson had done previously for infantile eczema. So Besnier paved the way toward the modern delineation of atopic eczema/dermatitis. Although this description is clearly an anticipation of modern atopic dermatitis, it lacks the link with infantile ecze-

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Fig. 2.4. The wax moulage collection of the Hôpital Saint Louis contains more than 4,500 works of art. Only one of them was diagnosed by Besnier himself as Besnier's prurigo. Earlier diagnosis by Du Castel had been chronic pruritus and/or generalized lichen planus. Moulage 2175, general collection, Musée de l'Hôpital Saint Louis, Paris

ma. It is worth mentioning here that a few years earlier, Hutchinson had mentioned the link between infantile eczema and Hebra's prurigo [19].

The contribution of Besnier is best put in the context of the Saint Louis school as detailed by Brocq in his numerous and copious papers on the subject [20, 21]. Brocq is himself, together with his co-worker Jacquet, the originator of the concept of lichenification, which formed a link between eczema and prurigo. He stated in 1896, "*Si l'on fait table rase de la théorie de la lichénification, sur laquelle repose la conception du lichen simplex chronique (Vidal), comment arrivera-t-on à comprendre les éruptions de l'eczéma lichénifié, du prurigo de Hebra, des prurigos diathésiques de M.E. Besnier?* (If one disregards the theory of lichenification on which lies the conception of lichen simplex chronicus [Vidal], how would it be possible to understand the skin symptoms of lichenified eczemas, Hebra's prurigo, Mr. Besnier's diathetic prurigos?)" Brocq's graphic representation (Fig. 2.5) features a continuum between Hebra's prurigo and eczema, Besnier's prurigo being situated between the two. This contribution is now largely forgotten, but the cli-

nical and pathological steps needed to theorize lichenification and thus to properly reclassify the old "lichen" group after the isolation of lichen (ruber) planus by Erasmus Wilson in 1869 was a highly necessary and not an easy task, as shown by Brocq's contemporaries' reactions to this theory.

2.3 Toward a Modern Definition

At the turn of the twentieth century, a precursor picture of modern atopic eczema was clearly emerging, but the scientific approach was still hampered by the overabundant descriptions of the eczema/prurigo group. "Over-refinement in interpretation of details and failure to grasp essentials have been responsible for this confusion" [22]. The distinction between eczema, which, except for Hebra's school, largely meant dermatitis due to internal causation, and true dermatitis (which meant external causation, especially contact or occupational dermatitis, the so-called dermatitis venenata), clearly separated in late nineteenth century dermatology textbooks, tended to disappear progressively, because of pathophysiologic considerations, especially the better understood contact allergy phenomena following the pioneering work of Jadassohn in Bern. Similarly, semiological subtleties that opposed disparate clinical entities, especially papular dermatoses (including prurigos) and vesicular ones (eczema group), were replaced by unifying concepts such as the lichenification theory of Brocq and that of neurodermatitis, which places neurogenic (or angioneurotic) processes at the center of the stage and also groups difficult-to-classify diseases such as vitiligo and urticaria in some textbooks [23–25]. Thus, the old and loosely defined concept of diathesis, rejuvenated within the pruriginous diathesis of Besnier, came under scientific scrutiny, with its various facets that we are still investigating, i.e., allergic (Table 2.1), neurogenic, biochemical, nutritional, and infectious. "*Der Begriff der Idiosyncrasie ist seither (1900) der Gegenstand eingehendster Erörterungen gewesen* (The concept of idiosyncrasy has since then (1900) been the subject of an in-depth debate)" [26].

The move from purely clinical grounds toward biologic medicine characterizes this period and underlies this scientific questioning. In this respect, the proceedings of the 1900 (Paris) and 1930 (Copenhagen) International Congresses of Dermatology, at which plenary

Table 2.1. Historical lexicon (from [10])

Descriptive variants of eczema in clinical precursors of atopic eczema

Eczema rubrum: excoriated acute eczema, mostly situated on extensor aspects of limbs (also named eczema madidans, meaning shiny, humid)

Eczema rimosum: eczema fissuratum, palmoplantar eczema

Some synonyms

Papular urticaria: strophulus simplex intertinctus (Willan-Bateman), lichen urticatus, lichen simplex aigu (Vidal), prurigo simplex (Brocq), strophulus pruriginosus (Hardy), acne urticata, prurigo infantilis (Hutchinson) first grade of lichen agrius (prurigo of Hebra)

Prurigo of Hebra: Lichen agrius (Willan-Bateman), Lichen polymorphe ferox (Vidal)

Lichenification: lichen simplex chronicus (Vidal), *Lichénification circonscrite*, *lichen circumscriptus*, *névrodermite circonscrite* (Jacquet), *prurit avec lichénification* (Brocq)

Severity grading of prurigo: Ferox (Vidal-Brocq) > gravis (Hebra) > mitis (Kaposi)

Prurigo hiemalis (Duhring): itchy xerosis in wintertime, common in North America

Prurigo lymphadénique (Dubreuilh): nonspecific itchy skin manifestations of Hodgkin's lymphoma

Acute papular eczema (German school) = lichenoid eczema (Hebra) = miliaria rubra (?)

Itchy bubo of Hebra: lymph node enlargement in chronic prurigo

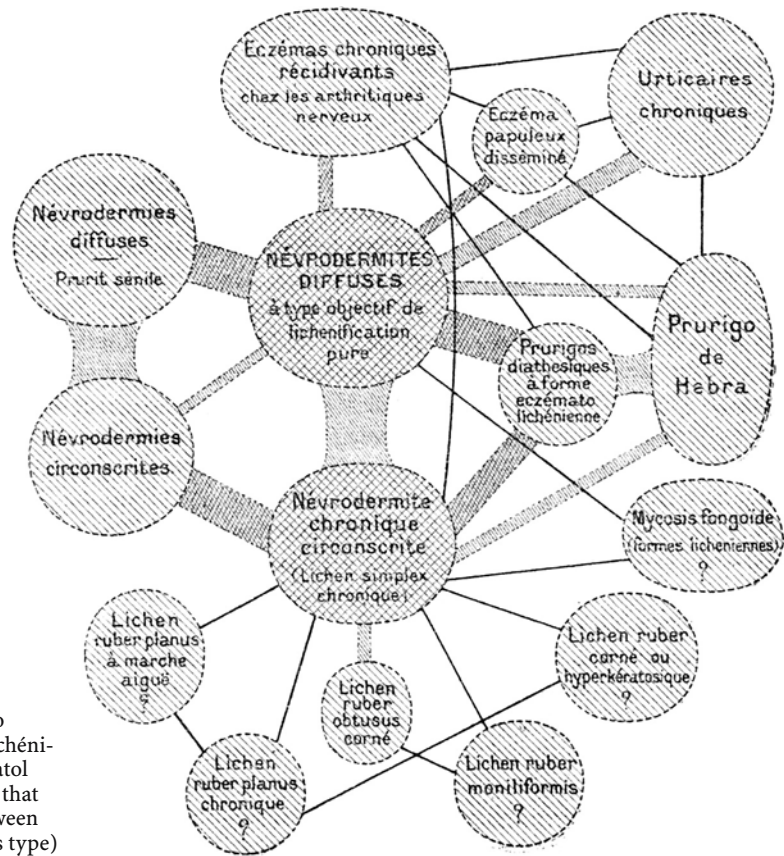


Fig. 2.5. The nebula of eczema according to Brocq (Nouvelles notes cliniques sur les lichénifications et les névrodermes, *Ann Dermatol Syph* 1896, 3ème série, T VII, p 925). Note that Besnier's diathetic prurigo is situated between neurodermatitis and true prurigo (Hebra's type)

Table 2.2. 1900–1935: the great mix of allergy with eczema (from [10])

1902: Portier and Richet discovered anaphylaxis in dogs injected with nonlethal doses of actinotoxin (the contrary of phylaxis; the net effect is to decrease immunity).
1903: Arthus described eponymous phenomenon, local adverse effect of sequential injections of rabbits with horse serum.
1906: Meltzer noted similarities between anaphylaxis and asthma and Wolff-Eisner suggested that hayfever is caused by hypersensitivity to pollen proteins.
1906–1911: Von Pirquet described serum sickness and tuberculin test and, based on work on reactions to vaccines in humans, defined allergy, which means altered reactivity whatever the causation.
1912: Schloss described allergy to egg in a child with urticaria.
1909: Smith described positive skin tests in a patient allergic to buckwheat.
1916: Blackfan described cutaneous testing with food proteins in a series of eczema patients (mostly infants), passive transfer experiments fail to show anaphylaxis in recipient guinea pigs; further testing in America by Talbot in Boston.
1921: Prausnitz and Küstner demonstrated the passive transfer of allergy by serum (fish allergy of K transmitted to P).
1923: Coca and Cooke proposed the name atopy (meaning strange disease in ancient Greek) to designate a type of heritable hypersensitivity to common environmental allergens noted in asthma and hay fever.
1925: Coca and Grove proposed calling “atopic reagins” the substances responsible for the passive transfer of allergy.
1929: Bloch and Prieto described dermal and epicutaneous positive testing to hen's egg in an 8-months-old baby with eczema, plus positive passive transfer in normal human recipients.
1933: Wise and Sulzberger, discussing recent work on eczema (Rost and Ormsby papers), proposed a name and clinicobiological criteria for atopic dermatitis.
1935: Hill and Sulzberger described the natural history and clinical symptoms of atopic dermatitis from infancy to adulthood.

sessions were devoted to eczema, show that the impetus stimulating clinical research in this field was driven by biology. Bacteriology predominated in 1900 with the discussion of the “parasitic” theory of eczema formulated by Unna 10 years earlier [27] and leading to investigations using cultures and inoculations. The first three decades of the twentieth century were characterized by the overwhelming success of allergic theories in medicine, and Darier could state in 1930, after summarizing briefly the history of eczema: “*Les dermatologistes se rangent en deux clans : les nosologistes qui ont cherché une maladie-eczéma et qui ont compris que la clé du problème est dans une prédisposition spéciale ; et les morphologistes qui ne voient qu’un syndrome-eczéma, lequel n’est qu’une réaction de la peau provoquée par les causes les plus diverses. Il appartenait à l’ère actuelle de serrer le problème de plus près en rattachant la prédisposition aux phénomènes biologiques généraux* (Dermatologists can be separated into two groups: nosologists who looked for an eczema-disease and who have understood that the key of the problem is in a peculiar predisposition; and morphologists who only envision an eczema-syndrome, which is no more than a cutaneous reaction provoked by the most varied causes. Our era had to grasp the problem more closely and to correlate predisposition to general biologic phenomena)”. He goes further later stating that “*l’expression eczéma allergique est un pléonasm* (the name allergic eczema is a pleonasm)” [25].

Jadassohn was clearly more prudent at the same congress. His basic position was the need to define clinical subsets more clearly before investigating pathogenesis. Making early clinical remarks concerning *faits de passage* between circumscribed neurodermatitis (lichen Vidal chronicus) and more disseminated cases with similar lichenified features, he discussed the urgent need to clarify the nomenclature in this particular subset of patients. The extreme confusion generated by the variety of diagnoses given to similar patients was stigmatized: “*Nirgends wohl variieren die Diagnosen der einzelnen Kliniken so sehr wie auf diesem Gebiet – ganz abgesehen von den Differenzen in der Nomenklatur*. (Nowhere have diagnoses in various university clinics varied so much as in this field – not to mention differences in nomenclature.)” The opposite views held by Darier and Jadassohn (which correspond more generally to the global-vitalist vs analytic-deterministic conceptions of medicine) were resolved, however, because of a common interest in newer diathetic conceptions developed by Czerny [28] and

Rost [29], which were based on epidemiologic and biologic considerations and were quite advanced intermediates on the path of the not yet formulated concept of atopic eczema. Classifications relying only on clinical grounds could thus be helped by the association with constitutional traits, and more specifically with the association with asthma. Jadassohn [26] specifically established a link between (a) this constitutional trait and the *Exsudativer Status*, defined by Rost, which also included white dermatographism and the biological marker of hypereosinophilia, and (b) the role of the environment, namely antigens defined in the work of Storm van Leeuwen who had already proposed allergen-free rooms for treating such patients.

The role of the American schools of pediatrics and dermatology was quite important during this period, from the detailed clinical studies of White and Bulkley to the pioneering work of Blackfan [30] and Talbot [31] in food allergy. The presence of reagins in the skin, as demonstrated by the positivity of skin tests to dietary allergens, and in the blood, as demonstrated by Prausnitz-Küstner passive transfer experiments, could be considered as the biological markers of infantile eczema, and in their landmark footnote [32] Wise and Sulzberger indeed included them in the criteria for atopic dermatitis. It must be stressed that the very authors who described the positivity of skin tests to dietary allergens, mainly hen’s egg, in infantile eczema, also insisted on the fact that these allergens could not be implicated as causative factors.

The link between Europe and the United States was indeed made by an American-born dermatologist, Marion Baldur Sulzberger, who, after training with Jadassohn and Bloch in Germany and Switzerland, returned to the US to make his seminal contributions unifying the pediatric and adult fields, coining with Wise the name “atopic dermatitis,” which later made possible the use of an efficient topical therapy.

2.4 Historical Landmarks in the Modern History of Atopic Eczema

The acceptance of the concept of a continuum between infantile eczema (Fig. 2.6) and chronic later phases (neurodermatitis in children and diathetic prurigo in adults) was not yet clearly widely accepted until the mid of the XXth century in the French textbooks [33,

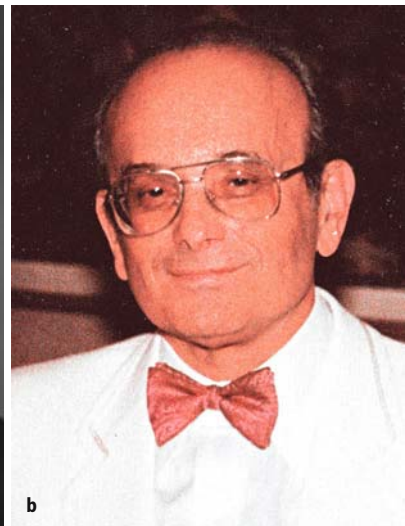
34]. The concept of atopic dermatitis was considered as an Americanism that did not bring much new understanding to the disease. The name “constitutional eczema” was preferred by Robert Degos who had a profound influence on French dermatology in the second half of the twentieth century, whereas “neurodermatitis” was most popular among German-speaking dermatologists during the same period, “atopic eczema” being mostly adopted by British dermatologists. The major importance given to allergy in the first decades of the twentieth century somewhat abated during the post-Second World War period, probably because of the minor influence of diet management and absence of an effect of desensitization procedures in children and adults with atopic eczema, in contrast with the clear improvement provided by topical steroids introduced by Sulzberger in 1952. The β -adrenergic blockade theory proposed by Szentivanyi [35] shed new light on a possible unifying molecular/cellular diathesis and was still *en vogue* until the 1980s. However, the discovery of the IgE molecule identified to be the allergy reagent by the Ishizakas [36] and the high IgE serum levels detected in patients with atopic dermatitis by Juhlin and his Swedish colleagues [37] have shifted, especially since the 1980s, more attention on the IgE-mediated phenomena, with a special emphasis on food allergy in children [38] and the role of IgE receptors on skin mast cells and later on Langerhans cells [39] and eosinophils, suggesting a tentative unifying mechanism linking early and late immune responses. The most

recent period has also been characterized by more emphasis on definitions based on reliable and validated criteria (Hanifin and Rajka, 1980 [40]; Fig. 2.7; Wil-



Fig. 2.6. This picture from the Photographic Museum of L’Hôpital Saint Louis dates back to 1901 and is one of the earliest “live” representations of infantile eczema. For technical reasons, there is no wax moulage of infantile eczema

Fig. 2.7. Jon Hanifin (a) and Georg Rajka (b), pioneers of a modern conception of atopic dermatitis. Their paper “Diagnostic features of atopic dermatitis. *Acta Derm Venereol* 1980 (Suppl 92): 44–47” is one of the most frequently cited of the dermatological literature. Rajka’s portrait is from the supplement 114 (1985) of *Acta Derm Venereol*, published on his 60th birthday



liams et al. 1994 [41]), as well as on genetic [42, 43] and epidemiologic [44] studies, which have tried to balance the inherited and environmental influences and to sort out the factors implicated in the increasing prevalence of the disorder. Meanwhile, scoring systems have been proposed to measure outcomes in clinical trials with the beginning of evidence-based medicine in this field (e.g. SCORAD and the precursor scoring systems) [45]. The rediscovery of the importance of the skin in a common skin disease is probably not the least paradoxical of recent years, with the emerging concept of a failure of the skin barrier systems involving both immune and nonimmune factors.

2.5 The History of Atopic Eczema Treatments

Many authors, including Alibert, who was very sensitive to the patients' feelings, and Hebra, gave precise accounts of the sufferings of chronic eczematous patients and of the burden of the disease at a time when no effective treatment could be proposed. Various etiopathogenic views on the disease affected the type of therapy proposed. The extrinsic view defended by Hebra's disciples influenced many cumbersome and messy external therapies (but probably the most effective at that time), the digestive and subsequent food allergy theories were implemented to starve many patients without obvious clinical benefit, and systemic treatments focusing on the internal diathesis were not devoid of danger (e.g., arsenic, mercury, strychnine). Interestingly, opposite principles have been defended with equal enthusiasm, such as dairy diet vs avoidance of dairy products, immunosuppression vs immunostimulation [10].

However, one of the most striking facts in history, still rampant in current practice, is the fundamental question: to treat or not to treat eczema? The humoral medicine still vivid in Alibert's *Précis* stigmatized as imprudent the doctor who aimed at reducing oozing too quickly in acute eczema. At the end of the nineteenth century, Gaucher was a strong advocate of the alternating or metastatic theory, due to the accumulation of toxic substances in internal organs "*il est souvent dangereux de guérir l'eczéma* (it is often hazardous to cure eczema)" [46]. The fear of rapid death in infants with eczema admitted to hospital wards was indeed still well entrenched until 30 years ago. Data

from the Bordeaux Children's Hospital pediatric dermatology ward, opened in 1919, show clearly that infants admitted for benign skin conditions such as infantile seborrheic dermatitis, atopic eczema, or scabies continued to die, probably because of superinfection until the 1950s and the massive introduction of antibiotics [47].

However, these views were already challenged long ago by skeptics who recognized that eczema could not be healed rapidly (Fournier, Malcolm Morris). Among them, early proponents of the diathesis theory were eager to treat early in order to correct constitutional factors (Bazin), and either blood letting or laxatives, as well as dangerous systemic drugs were still favored interventions in the nineteenth century. Another means invented by Colson and applied by Hardy in Paris was to facilitate skin exudation (*saignée séreuse*) using rubber wraps [48], a technique also used by Hebra in Vienna. This method was still in use until the Second World War. More classically, Lassar's paste and various tar preparations were in use before the introduction of topical steroids following the principles of the Vienna school, giving preeminence to external treatments. The role of water has also been a long-lasting historical debate, a total avoidance of water and soaps being advocated by leaders such as Sabouraud, who prescribed just cleansing skin with oil.

Cortisone was used systemically in infants and children with atopic eczema in the early 1950s [49]. The dramatic improvement of the disease did not last long, however, and the problem of maintenance treatment was rapidly identified as troublesome because of potential serious side effects on the child's growth and development. The introduction of topical compounds (compound F) pioneered by Sulzberger was a real revolution [50], without the systemic side effects of oral cortisone, but side effects were described and evaluated more lately in the 1970s, mostly in other skin disorders. However, both physicians and lay people have been influenced negatively by this reassessment of topical steroid therapy and (dermo)corticophobia has become progressively endemic throughout the world.

2.6 What History Tells Us Today

The ups and downs of the microbial, immune, digestive, and neurogenic theories of atopic eczema must be

kept in mind when investigating the field today. For example, the questions that were debated a century ago on the parasitic etiology of eczema at the Paris International Congress still make sense today, and some early experiments with bacterial culture supernatants on volunteers [51, 52] have been replicated without reference to those sources in the era of modern immunology and superantigens [53, 54]. The precursors in this field were indeed more investigative than we usually think today and a lot of good work was done in the pre-Medline era.

The disease still resists a unifying view, but historical considerations and the hesitations of our ancestors in this field are probably relevant in current clinical, pathophysiologic, and therapeutic issues. Let us raise a few questions in which historical insight is valuable:

1. Is infantile eczema the same disorder as that found at later stages?
2. Is there one or several diseases or pathophysiologic processes behind what we call atopic eczema?
3. How allergic is atopic eczema?
4. Are the lessons learned from topical steroids applicable to topical immunomodulators such as tacrolimus and pimecrolimus?

The historical roots of these questions would need several pages of development. Chapter 6 on infantile eczema addresses some of these questions.

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