

Atopic Dermatitis in Adults: A Diagnostic Challenge

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■ Abstract

Atopic dermatitis (AD) has a prevalence of 1%-3% in adults. Adult-onset AD has only been defined recently, and lack of familiarity with this condition and confusion regarding the appropriate terminology persist. AD may first appear in childhood or de novo in adults and is characterized by pronounced clinical heterogeneity. The disease often deviates from the classic pattern of flexural dermatitis, and there are forms of presentation that are specific to adults, such as head-and-neck dermatitis, chronic eczema of the hands, multiple areas of lichenification, or prurigo lesions. Although diagnosis is clinical, adult-onset AD frequently does not fit the traditional diagnostic criteria for the disease, which were developed for children. Thus, AD is often a diagnosis of exclusion, especially in de novo cases. Additional diagnostic tests, such as the patch test, prick test, skin biopsy, or blood test, are usually necessary to rule out other diseases or other types of eczema appearing concomitantly with AD. This article presents an update of the different forms of clinical presentation for AD in adults along with a proposed diagnostic approach, as new treatments will appear in the near future and many patients will not be able to benefit from them unless they are properly diagnosed.

Key words: Atopic dermatitis. Adult. Diagnosis. Patch testing. Prick testing.

■ Resumen

La dermatitis atópica (DA) en el adulto tiene una prevalencia del 1-3%. Es una entidad de reciente acuñamiento, que no todo el mundo conoce y sobre la que existe una gran confusión terminológica. Puede iniciarse en la infancia o presentarse de "novo" en el adulto. Presenta una gran heterogeneidad clínica y con frecuencia no sigue el patrón clásico de dermatitis flexural. Además, existen formas de presentación más propias de adulto como son la dermatitis de la cabeza y el cuello, eczema crónico de manos, áreas de liquenificación múltiple o lesiones de prurigo. Aunque su diagnóstico es clínico, muchas veces la DA del adulto no cumple los criterios diagnósticos "clásicos" de DA, pues están pensados para niños. Por eso, suele ser un diagnóstico de exclusión, sobre todo los casos de "novo". Suele precisar de la realización de pruebas diagnósticas para descartar otras enfermedades distintas u otro tipo de eczema sobreañadido a la DA. Las pruebas diagnósticas que pueden resultar útiles para ello son: pruebas epicutáneas, prick test, biopsia cutánea y una analítica sanguínea. Realizamos una actualización de las distintas formas de presentación clínica de la DA del adulto y establecemos unas pautas para llegar a su diagnóstico, pues en un futuro inmediato, con la aparición de nuevos tratamientos, muchos de estos pacientes no podrán beneficiarse de los mismos por no estar adecuadamente diagnosticados.

Palabras clave: Dermatitis atópica. Adulto. Diagnóstico. Pruebas epicutáneas. Prick test.

1. Introduction

Atopic dermatitis (AD), or atopic eczema, is a common, chronic inflammatory disease. Onset is usually in early childhood. The disease progresses with a chronic recurrent course before disappearing some time before puberty. However, it may persist into adulthood or present *de novo* during that period [1-3]. Bannister and Freeman [4] recently introduced the term *adult-onset atopic dermatitis*. This concept has received little attention in the literature compared with AD in children, despite the considerable impact of severe AD on adult patients, probably owing to a lack of acceptance or a lack of familiarity with the disease [5].

Diagnosis of AD is based on clinical criteria and is relatively straightforward in children presenting with chronic eczema and in adults whose AD has persisted since childhood [6-13]. AD is difficult to diagnose when it appears during adolescence or later and when the forms of presentation differ from those most commonly seen in children. There is a tendency to believe that the clinical presentation is similar in children and adults, and AD is suspected for primarily flexural or symmetrical eczema. However, some forms of AD are more specific to adults, including head-and-neck dermatitis, hand eczema, multiple areas of lichenification, or prurigo lesions [14]. In these situations, adult-onset AD is a diagnosis of exclusion and usually leads to additional tests to rule out other diseases, which may be less common than AD.

We believe that it is important to carry out an update of the different forms of clinical presentation and establish guidelines for the diagnosis of AD in adults, since in the near future, some patients will be unable to benefit from new treatments for AD unless they are properly diagnosed.

2. Definition

According to the guidelines of the American Academy of Dermatology (AAD), AD is a chronic, pruritic, inflammatory skin disease that occurs most frequently in children but that can also affect adults. The course of the disease is relapsing, and it is frequently associated with elevated levels of serum immunoglobulin E (IgE), individual or family history of type I allergies, allergic rhinitis, and asthma [11]. Diagnosis of AD is based on clinical findings and personal and family medical history. If in doubt, diagnostic criteria or additional tests can be applied. According to the European Task Force on Atopic Dermatitis (ETFAD)/European Academy of Dermatology and Venerology (EADV) Eczema Task Force position paper, the diagnostic power of an experienced clinician is superior to all available diagnostic criteria, although standardized criteria are needed for epidemiological research and for clinical trials [12].

Several sets of criteria for diagnosing AD have been proposed [6-13]. The most widely used are those developed by Hanifin and Rajka [6], namely, pruritus, typical morphology and pattern of eczema, relapsing course, and personal or family medical history. These are complemented by 21 minor criteria, some of which are very imprecise [6]. Cases fulfilling at least 3 major and 3 minor criteria are considered AD. The UK Working Party criteria attempted to simplify the diagnostic process by stating that itchy skin changes had to have been

diagnosed during the previous year and patients had to present 3 or more of the following: onset prior to 2 years of age, history of involvement of skin folds, generalized dry skin, presence of other atopic diseases, and visible flexural eczema [7-9]. Onset in early childhood and a flexural pattern of eczema complicate the diagnosis of AD in adults. The new AAD guidelines no longer consider early onset to be an essential feature, while the Japanese guidelines do not consider the age of onset at all [10]. Moreover, both sets of guidelines distinguish between the typical patterns of eczema lesions according to age group, with the flexural pattern being more typical in children [10]. Likewise, the Japanese guidelines no longer require the existence of a personal or family history of atopy or IgE reactivity in order to reach a definitive diagnosis [10-11].

This latest consideration represents a significant advance, given the tendency to assume that AD must be associated with other atopic diseases or elevated levels of IgE. Studies show that at least 5%-15% of atopic patients do not present with high total IgE (this is known as intrinsic AD) [15]. More recent diagnostic criteria—specific to adolescents and adults—have been proposed from China and include only 3 items, thus making them quite practical. The criteria are symmetrical eczema for more than 6 months (mandatory) plus personal or family (up to 3 generations) history of atopic disease and/or elevated serum levels of total IgE and/or allergen-specific IgE and/or eosinophilia. These guidelines do not consider pruritus owing to its lack of specificity to AD and its prevalence in a number of dermatological conditions. Similarly, they do not mention xerosis owing to the subjectivity of the term [13].

Another point to consider is the considerable confusion surrounding the terms used to classify eczema. Most authors agree that exogenous eczema (or contact dermatitis) should be separated from endogenous eczema. The so-called endogenous eczemas include seborrheic dermatitis in infants and in adults, AD, discoid or nummular eczema, xerotic eczema, stasis dermatitis, endogenous eczema of the hands and feet (pompholyx or dyshidrotic eczema), and other unclassified or nonspecific types of endogenous eczema [16]. Most endogenous eczemas, including the nonspecific kinds, could be considered clinical forms of atopic dermatitis. In fact, the authors who coined the term *unclassified endogenous eczema* argued that a large proportion of those affected by it could have late-onset AD, despite having no personal or family history of atopy (a third of the patients in their study had elevated levels of IgE) [16]. In their definition of AD, the European Task Force rightly states that in the past, terms such as neurodermatitis, neurodermatitis, endogenous eczema, and constitutional eczema were all used to describe AD [12]. However, we believe that seborrheic dermatitis in adults and stasis dermatitis, which are traditionally considered endogenous eczemas, are different from AD and should be classified as such.

3. Epidemiology

The prevalence of AD has increased worldwide over the past 30 years [3,4], to the extent that it is now one of the most common chronic diseases, affecting about a fifth of the population in developed countries. Prevalence in children is estimated at 15% to 30%, while in adults estimates range from

0.3% to 14.3% [13,15,17], with most authors agreeing that it stands between 1% and 3% [18]. While considerably lower in the elderly (>65 years), the percentage of cases in this age group is increasing in industrialized countries [15].

Although AD can appear at any time during an individual's life, about 60% of cases are thought to present during the first year [17], and 60%-74% of cases in children resolve before the age of 16, with the rest persisting into adulthood [15]. However, this supposed rate of clearance is probably around 53% owing to relapses over the course of adolescence and early adulthood. It is worth noting that a fair percentage of people with childhood AD experience recurrence when they enter the workforce. Most cases take the form of hand eczema, but some are more extensive [19]. In a recent study carried out in China, investigators reported that 77.5% of patients presented with AD after age 12 and suggested that late-onset AD is quite common [13]. Between 9% and 47% of cases of AD also appear *de novo* in adults (≥ 18 years), although the most widely accepted proportion is 9%-24.5% [2,5,15]. Among adults who develop AD, peak incidence occurs at age 20-40 years [20], although the disease does not completely subside after that. If we count all the patients whose AD persists after childhood, those who experience a relapse, and those who first present with AD as adults, the proportion of adult patients with AD rises to 45% [21]. With regard to sex, AD in adults occurs predominantly in women, although this trend is reversed in individuals aged over 65, when more men are diagnosed [15].

Intrinsic AD, defined by low levels of serum IgE and the absence of specific sensitization to aeroallergens or foods, has traditionally been considered an infrequent subtype in adults. However, current studies report values ranging from 5.4% to 45% [26]. This pronounced variability in the estimated prevalence in adults is mainly due to differences in diagnostic criteria. It is important to note that all of the published population-based studies acknowledge the risk of recall bias in these patients, who may not remember childhood episodes of eczema. We have observed this phenomenon first-hand, with many patients providing relevant information on their history of dermatitis only at follow-up, not during the initial visit. Likewise, there are patients with chronic generalized eczema who, during initial consultations, do not remember having had rhinitis or allergic conjunctivitis but who later provide these data, thus facilitating classification of their case as adult AD. Although many questions on the natural history of late-onset AD remain unanswered, some experts maintain that most (80%) will eventually improve [15]. One possible explanation for this, apart from the course of the disease, is early treatment and hygiene measures for prevention.

4. Clinical Presentation of AD in Adults

4.1 Clinical Patterns

AD in adults is characterized by marked clinical heterogeneity, with numerous clinical profiles that do not always coincide with those observed in children. The course of AD is generally intermittent, with phases of latency and exacerbation. Clinical features may differ depending on the

patient's age and on whether the disease is acute or chronic. Hello et al [14] distinguish 3 broad clinical patterns:

1. Chronic, persistent form
2. Relapsing course
3. Adult-onset AD

The chronic, persistent form of adult AD includes patients who have had AD since childhood. About 20%-30% of childhood cases persist into adulthood, and these constitute the best-recognized group of patients with adult AD. Many patients have severe disease that is very difficult to manage. They usually have diffuse, symmetrical, and flexural dermatitis, primarily with eczema of the face, but also with uneven involvement of the trunk and limbs. Involvement of the hands is variable and largely depends on the patient's occupation. In some patients, we observe clinical presentations that indicate chronicity, such as dirty neck and vitiligo-like and highly lichenified lesions in the flexural areas [22-24]. The association with alopecia areata is, in our experience, an indicator of severe disease.

The relapsing form occurs in about 12.2% of patients with childhood AD, whose disease apparently resolves before or during adolescence and then recurs in adulthood. We believe that cases in this subgroup are more frequent than has been reported. People who had AD as children commonly develop chronic hand eczema when they enter the workforce, leave their parents' home, or assume household burdens (domestic work or childcare). Many of these patients are diagnosed with chronic hand eczema due to contact irritants rather than due to atopy; this is because it is practically impossible to distinguish between the two clinically. Although not all people with contact hand eczema have AD, people with AD are prone to hand eczema when they have 'wet' jobs that require handling irritating substances. Thus, it is of great interest to scale up occupational education and prevention measures in this group [25]. Additionally, Williams et al [27] have described cases of occupational contact dermatitis that interact with atopy to cause endogenous-like eczema, even in people who have been asymptomatic since childhood [12,15]. This scenario is probably not rare, as we have seen patients with acute episodes of AD brought on by working conditions (eg, heat, dust, and other contaminants) whose disease subsided completely after changing job responsibilities.

Adult-onset AD is difficult to detect, and diagnosis often comes only after ruling out other diseases, especially allergic contact dermatitis. A biopsy is often necessary to confirm the case as eczema. An estimated 18.5% of all cases of AD first appear in adulthood [14], usually in individuals aged 20 to 40 years but also in elderly patients, where clinicians rarely suspect AD. Moreover, this form includes clinical presentations that are rare in children (eg, nummular eczema, prurigo, and head-and-neck dermatitis), probably owing to the differing environmental exposures between these 2 age groups [5].

4.2 "Typical" Forms of Clinical Presentations in Adults

The characteristic presentation of AD in adults is generally inflammatory eczema with areas of lichenification (lichenified/exudative eczematous pattern). Although this form is predominantly flexural, only about 10% of the cases are

Table 1. Clinical Forms of Presentation of AD in Adults

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- Lichenified/exudative flexural dermatitis, almost always associated with head-and-neck eczema and/or hand eczema
 - Head-and-neck eczema
 - Seborrheic dermatitis-like dermatitis
 - Portrait dermatitis
 - Hand eczema
 - Chronic hand eczema
 - Dry fingertip eczema
 - Dyshidrotic eczema of the hands
 - Generalized eczema
 - Inflammatory pattern
 - Lichenoid pattern
 - Prurigo
 - Localized: neck, shoulders, and upper limbs
 - Generalized
 - Nummular eczema
 - Erythroderma
 - Psoriasiform dermatitis. Syndrome overlap
 - Multiple lesions of chronic lichen simplex
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purely flexural. Other areas are also involved, especially the face (48%) and hands (46%), followed by the extensor surfaces of the limbs (33%) and trunk (30%) [1,28]. Approximately 10% of patients do not present a flexural pattern at all. It is important to highlight that it is not possible to differentiate extrinsic and intrinsic AD based only on the clinical presentation of the lesions [15].

For instructive purposes, we can distinguish various clinical forms (see below), although these forms commonly appear together [10] (Table 1).

Head-and-neck eczema

The involvement of the face and neck, whether accompanied or not by lesions in the antecubital and popliteal fossa, is probably the most characteristic form of adult AD, and it is also known as head-and-neck dermatitis (Figure 1). On the face, both the eyelid and the lips tend to be involved. Chronic atopic cheilitis is also common in young women [14,15]. In the most chronic cases, hyperpigmented and lichenified areas are visible on the neck; this phenomenon is known as ‘dirty neck’ due to its unclean appearance (Figure 2). Not infrequently, it resembles airborne eczema, with involvement of the thorax, axillas, back and upper limbs, and, to a lesser extent, the lower limbs. In these cases, clinicians should look for hypersensitivity to environmental allergens that might be aggravating AD (Figure 3).

Another pattern, observed above all in adolescents, is the “portrait” type (Figure 4), wherein the head-and-neck eczema extends to seborrheic areas of the trunk (upper chest and back). At times, its morphology is similar to that of folliculitis, and it is distributed like a sculptural bust. In these cases, some authors have pointed to *Pityrosporum ovale* as the trigger [14].



Figure 1. Head-and-neck dermatitis. Typical distribution of atopic dermatitis in adults.



Figure 2. Dirty neck, a clinical indicator of chronicity.

Hand eczema

The association between AD and hand eczema is well documented. Authors estimate that somewhere between a third and half of all patients with hand eczema have atopy, while the hands are involved in 60%-70% of people diagnosed with



Figure 3. Airborne dermatitis. It is advisable to explore the potential role of airborne allergens in triggering the flare-up or in contributing to the persistence of the disease.



Figure 5. Dyshidrotic eczema of the hands. There is debate as to whether this condition is a clinical form of atopic dermatitis.



Figure 6. Chronic hand eczema. It is very difficult to distinguish the irritant contact and atopic variants based on clinical characteristics.



Figure 4. Folliculitis-like morphology; typical pattern in adolescents.

AD [25,29-31]. Thus, the presence of chronic hand eczema in adults should always raise the suspicion of adult AD.

The clinical presentation of atopic chronic hand eczema is not always the same. We can distinguish at least 3 morphological clinical forms: acute relapsing dyshidrotic eczema (pompholyx), a chronic form of irritant contact dermatitis, and chronic dry fingertip dermatitis.

Some authors consider dyshidrotic eczema to be a distinctly different form of hand eczema that does not occur in the context of AD. It consists of recurrent flare-ups of blistering on the palm of the hand and/or the sides of the fingers (Figure 5). Sometimes the volar side of the fingers and periungual skin are affected, and there may also be involvement of the palmar

surface. These flare-ups may occur at intervals every few weeks or months, or they may be so frequent as to give rise to chronic hand eczema.

The chronic form of irritant contact dermatitis may present either as dry chronic eczema with fissures or as fingertip dermatitis combining dyshidrotic lesions during the acute periods. It may affect any area of the hand, although most cases entail dermatitis on the dorsal and volar surface of the wrists and on the dorsum of the hands and fingers [32]. Involvement of the flexor side of the wrist is not always present, although it is still quite characteristic [29] (Figure 6). In our opinion, this form is clinically indistinguishable from irritant contact eczema and is usually a combination of this condition and AD [30]. If we consider that chronic hand eczema may be the first or only manifestation of AD, it is logical that diagnosing AD in such patients (with no other criteria of atopy) is so difficult [33]. It is highly likely that we are underdiagnosing AD in these cases. Quite often, patients report brief episodes of itching, redness, and edema following contact with food. In these cases, we should consider the existence of protein contact dermatitis, especially in patients who handle food.

Atopic hand eczema may present elsewhere, for example, the fingertips (pulpite sèche), where it is also very difficult to differentiate from chronic irritant contact eczema. Likewise,

the anatomical snuffbox may show lichenified lesions with unclear borders. Nummular, pruritic lesions may also develop on the dorsum of the hands [29]. In short, hand eczema may occur on any part of the hand.



Figure 7. Generalized eczema with an inflammatory pattern.



Figure 8. Alopecia areata, an indicator of severe disease when accompanied by atopic dermatitis.

Generalized eczema

Severe AD is usually diffuse, mainly affecting the face, neck, hands, and flexures, although all regions of the body can be affected to some degree. We can distinguish between 2 clinical patterns—inflammatory versus lichenoid—which help us to make therapeutic decisions. Patients presenting with the inflammatory pattern are “red” in appearance (Figure 7). The skin shows diffuse erythema, with predominantly acute, exudative, and crusted eczematous lesions, which are sometimes accompanied by profuse scaling. This pattern is frequently associated with signs of superinfection and looks very severe. Its maximum expression would be as erythroderma. The appearance of areas of alopecia areata alongside the findings described indicates a high level of severity (Figure 8). We support treating these patients with a short course of oral corticosteroids, antibiotics, and ciclosporin. We avoid phototherapy, which patients with generalized eczema do not tend to tolerate.

The other pattern is characterized by lichenification, excoriations, crusts, and xerosis (Figure 9). It gives the impression of chronicity, and its maximum expression would be lichenoid erythroderma. The most severe cases present



Figure 9. Generalized eczema with lichenoid pattern, combining lichenification, xerosis, excoriations, and crusts.

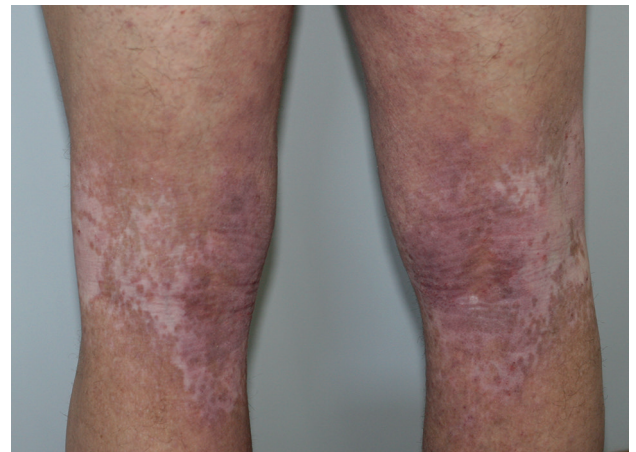


Figure 10. Vitiligo-like lesions in areas of chronic lichenification.

with dirty neck and achromic lesions (eg, vitiligo) in the most lichenified flexural areas (Figure 10). We usually try phototherapy in combination with slow-acting drugs that have few adverse effects and that can therefore be taken over longer periods of time. Examples of these would be methotrexate, azathioprine, and mycophenolate mofetil.

Nummular eczema

Nummular eczema is very common, at least in Chinese and Indian adults with AD (about 17%) [5,13]. The lesions are round, inflamed sores that are located most often on the lower limbs (Figure 11). They tend to be quite refractory to treatment [14]. This morphological variant is not specific to AD, as it also occurs in people with allergic contact eczema due to fragrances or preservatives contained in hygiene products.

Erythroderma

The differential diagnosis of erythroderma should always include the possibility of severe AD. Over 90% of the skin surface is red, dry, and lichenified (Figure 12). Intense pruritus is accompanied by general discomfort, asthenia,

shivering, and signs of dehydration. Peripheral “dermopathic” adenopathies can be observed. Erythroderma is frequent in the elderly [14,15].

Nodular prurigo

Welfer et al [34] point to prurigo as a clinical form that is characteristic in adults. In a Chinese series, 30% of adults with AD presented with this variant [13]. It usually appears at 40-50 years of age and consists of highly pruriginous papules and lumps, generally on the shoulder girdle and arms [34] (Figure 13). The lumps may appear somewhat artificial and give the impression that they were provoked intentionally. Generalized pruriginous lesions are not uncommon and generally require a biopsy to exclude other serious diseases, including cutaneous lymphomas (Figure 14) [1,12]. However, we believe that clinicians should consider AD for any patient presenting with chronic pruriginous lesions.

Lichen simplex

Lichen simplex or lichenification is common in adult AD. Indeed, the concomitant or sequential presence of 2 or more



Figure 11. Nummular eczema. This manifestation should be considered a clinical form of atopic dermatitis after exclusion of allergic contact dermatitis via patch testing.



Figure 13. Prurigo of the neck, shoulders, and upper limbs. Typical in adults; may appear self-inflicted.



Figure 12. Erythroderma. Biopsy is essential to rule out other diseases, especially cutaneous lymphomas.



Figure 14. Elderly patient with generalized prurigo lesions. Biopsy is always advisable to rule out lymphoma.



Figure 15. Psoriasiform dermatitis. Syndrome overlap with eczematous lesions in flexural areas and small psoriasiform plaques of diffuse distribution.

plaques of lichen simplex in a single patient should alert clinicians to the possibility of AD.

Psoriasiform dermatitis

Some patients present with diffuse, psoriasiform cutaneous lesions on the trunk and limbs, with involvement of the flexures. It is difficult to determine whether these lesions are eczema, eczematized psoriasis, or both. At times, the progress and presence of psoriatic lesions in typical areas such as the elbows, knees, nails, or scalp enable us to reach a diagnosis. The association between the 2 conditions has been described as psoriasis-eczema overlap or eczematous psoriasis. Typically, people with psoriasis-eczema overlap have both flexural eczema and psoriatic lesions, and although no thick plaques are present, patients experience more intense itching than in isolated psoriasis [35] (Figure 15).

Miscellaneous

Other typical sites of adult AD include the nipples, and in women, the labia [1]. Lesions at these locations are very distressing and have a considerable impact on quality of life and sexual health.



Figure 16. Photoaggravated dermatitis. This condition occurs in a small percentage of patients, and clinical management is difficult.

Although most people with AD see improvement after exposure to sunlight, a small proportion, mostly adults, experience photoaggravated dermatitis (Figure 16). Therapeutic management of these cases is much more challenging.

5. Diagnosis

The diagnosis of AD is usually based on clinical features and associated signs, as well as on morphology and the pattern of skin lesions [36]. While we always consider the possibility of AD in children with eczema, the first diagnostic suspicion in adults is contact eczema. Liu et al [13] reported that over 90% of Chinese dermatologists would respond to symmetrical flexural dermatitis with a diagnosis of contact eczema instead of AD. Furthermore, it is likely that clinicians worldwide share this inclination owing to poor familiarity or resistance to the idea of adult-onset AD [5].

According to ETFAD/EADV [12], the experience of clinicians is more important than the availability of diagnostic criteria; however, epidemiological research and clinical trials highlight the need for standardized criteria. Therefore, upon clinical suspicion of adult AD, health professionals should consider the clinical criteria discussed above (see “Definition”), take a thorough personal and family medical history, and determine levels of total serum IgE. It is important to keep in mind that the presence or positivity of these aspects only supports—rather than confirms—the diagnosis. At the same time, according to the AAD guidelines, AD is a diagnosis of exclusion and can only be determined after ruling out all of the other diseases included in the differential diagnosis (Table 2) [12]. Adult AD is more straightforward in people who had AD or have had AD since childhood.

A recent review established a consensus on when and how to perform patch testing in patients with AD [37]. In adult-onset disease, performance of patch tests should always be based on clinical findings. If the results are negative, AD becomes more likely. If the results are positive, we should determine whether they are relevant, and if so, eliminate or avoid the source of the allergen. If the disease persists, even if less severely, despite avoidance of the allergen, we should once again consider adult AD. Patch testing is also very useful in patients with chronic AD whose condition does not improve despite adequate treatment, as there is often additional allergic contact dermatitis

Table 2. Differential Diagnosis of Atopic Dermatitis in Adults

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- Contact dermatitis (both allergic and irritant)
 - Cutaneous T-cell lymphoma (mycosis fungoides, Sézary syndrome)
 - Atypical psoriasis
 - Eczema-like cutaneous drug eruption (especially in polymedicated elderly patients)
 - Seborrheic dermatitis
 - Factitious dermatitis
 - Dermatophytosis
 - Scabies
 - Dermatitis herpetiformis
 - Ichthyosis
 - Actinic prurigo
 - Erythroderma due to other causes
-

at play [34]. Indeed, AD constitutes a key risk factor for allergic contact sensitization, with about 40% of adults with AD testing positive for at least 1 allergen in a standard patch test series [1]. Ingredients in hygiene products (preservatives, fragrances, and emulsifiers) and topical treatments may all act as contact allergens [12,15,34]. Practitioners should also remember to perform late readings to rule out allergy to corticosteroids. In some patients with severe AD, we can never perform patch testing because there are always lesions on their back or arms or because they are taking oral immunosuppressants. In these cases, we advise carrying out the patch tests when possible, even when conditions are not optimal, and interpreting the

results with due caution, as the chances of an irritant patch reaction increase. In patients taking immunosuppressants, we should undertake late readings to avoid false negatives.

The diagnostic value of the prick test is more controversial. While it is true that many patients with AD are sensitized to airborne allergens and/or food allergens, the role these allergens play in the development or exacerbation of AD is not clear, and the presence of sensitization alone is not sufficient to recommend allergen avoidance or therapy. It would seem sensible to request a prick test for airborne allergens in patients presenting with an airborne pattern of eczema on the face (with involvement of the eyelids), neck (with involvement of the retroauricular area), and exposed areas of upper limbs and flexures (especially the axillas and antecubital fossa). Caution is warranted when interpreting results. Avoidance measures may be implemented for positive airborne allergens (especially dust mites), even without knowing whether they act as allergens or irritants (pseudoallergens). However, these measures do not always change the course of the disease. Immunotherapy has produced heterogeneous results. Prick tests could be ordered for foods in adults with generalized AD. However, although food allergies are infrequent in adults, certain foods, such as carrots, hazelnuts, and celery, which generate cross-reactions with airborne allergens, can trigger flare-ups in people sensitized to pollen. However, only half of adult patients sensitized to 1 or more foods see any improvement upon eliminating it from their diet. In patients with chronic hand eczema who present itching and edema when handling food, we should consider performing a prick-prick test to rule out probable protein contact dermatitis, as this is more frequent in the atopic population. Pending the approval of standardized test materials, the atopy patch test (for airborne allergens or foods) is not yet a part of routine diagnostic recommendations [1,12,34,38].

Table 3. Diagnostic Procedures in Atopic Dermatitis (AD)

Clinical History	<ul style="list-style-type: none"> – Chronic eczema – Personal and family history of atopy
Physical Examination	<ul style="list-style-type: none"> – Morphology and/or typical distribution of eczema in adults – Prurigo lesions – Multiple areas of lichenification
Patch Test	<ul style="list-style-type: none"> – De novo AD – Chronic AD/hand eczema refractory to treatment – Atypical/changing distribution of dermatitis – Pattern suggestive of allergic contact dermatitis – Before starting immunosuppressant therapy (if possible)
Prick Test	<ul style="list-style-type: none"> – History of immediate allergic reaction or development of dermatitis after allergen exposure – Chronic AD with airborne pattern – Generalized AD in patient with sensitization to pollen – Consider prick-prick test in chronic hand eczema if history is suggestive of protein contact dermatitis
Skin Biopsy	<ul style="list-style-type: none"> – Chronic AD, refractory to treatment – Morphological variant of prurigo – Erythroderma – Rule out other diseases, eg, psoriasis, cutaneous drug eruption, dermatitis herpetiformis (direct immunofluorescence), lymphoma (immunohistochemistry)
Blood Testing	<ul style="list-style-type: none"> – Total IgE, eosinophilia – Lactate dehydrogenase, antitransglutaminase antibodies

It is not necessary to perform a skin biopsy to reach a diagnosis for AD. Although biopsy can prove useful in corroborating the diagnosis of eczema, it does not help to differentiate between types, as all eczemas share the same histological pattern, namely, spongiotic dermatitis, with predominance of spongiosis in the acute phase and of hyperkeratosis in the chronic phase. The presence of eosinophils does not signal any particular type of eczema. On the other hand, skin biopsy is very useful in cases of chronic eczema that do not evolve satisfactorily, as it helps to rule out other conditions such as cutaneous lymphoma (this may require multiple biopsies), dermatitis herpetiformis, drug eruptions (especially in polymedicated and elderly patients), and psoriasis [34].

Despite advancing knowledge in genetics and in the etiological-pathogenic mechanisms of AD, there is currently no tissue or blood biomarker that enables a definitive diagnosis of AD. The most useful indications are probably an increase in total IgE and hypereosinophilia, although these are in no way specific to this disease.

The scientific community has not reached any consensus on the optimal diagnostic workup for adults with suspected AD. In Table 3, we present our proposal in this regard.

6. Conclusions

The incidence of AD is increasing steadily, especially in industrialized countries. The diagnostic criteria for this disease are basically clinical, and diagnosis is relatively easy in children with eczema. However, we often fail to consider the possibility of AD in adults unless they have had the disease since childhood. Moreover, in adults, the clinical and morphological characteristics of AD differ from those seen in children. The most frequent clinical presentations are flexural dermatitis with involvement of the face and neck and chronic hand eczema. The clinical variant of nodular prurigo is not uncommon.

Diagnosis is often a challenge owing to the absence of specific or adapted criteria for AD in the adult population. Thus, it is a diagnosis of exclusion that we can only reach after performing patch testing to rule out allergic contact dermatitis and/or cutaneous biopsy to rule out other diseases (eg, cutaneous lymphoma, dermatitis herpetiformis).

AD has a considerable impact on patients' and their families' quality of life, with important economic and social implications. It is most probably underdiagnosed, although it is essential that specialists are able to recognize it when deciding on the appropriate course of treatment.

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Conflicts of Interest

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