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# 1 Severe Atopic Dermatitis and its Difficult Clinical Management

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## 5 Abstract

6 Introduction: This paper will cover new updates on atopic dermatitis as a chronic and  
7 inflammatory condition that affects people of all ages but is most common in children. Its  
8 etiology involves genetic, immunological, and environmental factors, with risk factors such as  
9 maternal exposure during pregnancy, irritants, climate change, pollution, and more.  
10 Methodology: The current study is a literature review, the database of which was taken from  
11 the SciELO (Scientific Electronic Library Online) and PubMed platforms. Results: Atopic  
12 dermatitis is a chronic and relapsing disease that affects individuals of all ages, but especially  
13 children. It is an inflammatory condition that has a multifactorial etiology involving genetic,  
14 immunological, and environmental factors that damage the continuity of the epidermis. The  
15 incidence can vary according to geographical region as well as ethnicity. It is generally more  
16 common in developed countries, with around 15

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18 *Index terms—*

## 19 1 Introduction

20 his paper will cover new updates on atopic dermatitis as a chronic and inflammatory condition that affects people  
21 of all ages but is most common in children. Its etiology involves genetic, immunological, and environmental  
22 factors, with risk factors such as maternal exposure during pregnancy, irritants, climate change, pollution, and  
23 more. Genetics plays an important role, and recent studies have identified links with specific chromosomes.  
24 The diagnosis is clinical and based on symptoms such as itching and skin lesions characterized by areas of  
25 lichenification, papules, and nodules. Differential diagnosis includes other skin conditions and is often associated  
26 with other atopic diseases. The treatment of atopic dermatitis varies according to its severity. Moisturizers  
27 play a key role, and phototherapy, which uses UV radiation, is an effective option. Topical therapy with  
28 corticosteroids and calcineurin inhibitors is necessary. In more severe and resistant cases, systemic therapies,  
29 such as immunosuppressants and immunobiologicals, can be considered. Advances in research and treatment have  
30 improved the quality of life of patients with atopic dermatitis, and the approach is multidisciplinary, involving  
31 different health professionals. It is essential to understand the treatment options available and adapt them to  
32 the needs of each patient.

## 33 2 II.

## 34 3 Methodology

35 The current study is a literature review, the database of which was taken from the SciELO (Scientific Electronic  
36 Library Online) and PubMed platforms. The research was carried out in October 2023, meeting the inclusion  
37 criteria of articles from 2017 to 2023 in Portuguese and English, online texts and full texts, theses, master's  
38 dissertations, book chapters, monographs, and literature in magazines and scientific journals. Health descriptors  
39 (DeCS) were used to better evaluate the texts: "atopic dermatitis", "treatment," and "skin diseases".

## 40 4 III.

## 41 5 Results

42 Atopic dermatitis is a chronic and relapsing disease that affects individuals of all ages, but especially children. It is  
43 an inflammatory condition that has a multifactorial etiology involving genetic, immunological, and environmental  
44 factors that damage the continuity of the epidermis. incidence can vary according to geographical region as well  
45 as ethnicity. It is generally more common in developed countries, with around 15% to 20% of children and  
46 1 to 3% of adults being affected, and its growth can be explained by urbanization and pollution added to  
47 the context, which are significant risk factors for this condition. [1] Among the risk factors, there are those  
48 related to the environment and those related to the individual. As environmental factors, it is possible to list  
49 maternal exposure during pregnancy: irritants and agents that cause itching, climate change, humidity, radiation,  
50 pollutants, exposure to smoke, very concentrated water, diet, among other factors. Genetics has been gaining  
51 more and more strength in the cause of AD. Recent studies have found that atopic dermatitis is related to  
52 chromosome 3p and also to segments 3q14, 13q14, 15q14, and 17q21. In addition, other studies have described  
53 the immunological theory that it is explained T by the Th2 response, which involves the activation of interleukins  
54 and their receptors as well as the activation of some skin barrier genes, such as the LAMA3, TEM 79, FLG2, and  
55 LELP1 genes. Atopic dermatitis develops due to a dysfunction in the barrier, an immune alteration that leads  
56 to an inflammatory response, or a combination of the two. [1] The diagnosis of atopic dermatitis can be made  
57 by the skin's immune system.

58 The diagnosis of atopic dermatitis is clinical, with pruritus being an obligatory symptom. In addition, the signs  
59 and symptoms must be associated with the patient's personal history. The skin lesions are usually characterized  
60 by areas of lichenification, papules, and nodules, as well as nummular eczema. Other manifestations include  
61 inflammation of the dry lips, infranasal erosion, intra-auricular tears, retroauricular intertrigo, eczema on the  
62 fingers, nipple, and pityriasis alba. The presence of erythema varies according to race, with blacks showing  
63 gray and Caucasians red. [1,2] The differential diagnosis includes other skin diseases, such as infections (e.g.,  
64 scabies), other forms of eczema (allergic contact dermatitis, irritant-toxic eczema, seborrheic eczema), and, in  
65 babies, seborrheic dermatitis. Patients often have associated diseases, including other atopic conditions (asthma,  
66 allergic rhinoconjunctivitis), rarely vernal keratoconjunctivitis, giant papillary conjunctivitis, superficial punctate  
67 keratitis, atopic keratoconjunctivitis, or otitis externa and media. Food allergies are demonstrable in 30% of  
68 children with severe atopic dermatitis, and immediate type 1 hypersensitivity to cow's milk, chicken eggs, peanuts,  
69 soy, and nuts is common. If atopic dermatitis is suspected, potential psychosomatic, allergic, or environmental  
70 triggers should be identified. The importance of these triggers varies greatly between individuals, and their  
71 prevention is a component of the personalized treatment plan. The role of dietary factors is often overestimated,  
72 particularly in childhood; instead, acute and chronic skin irritations and cold temperatures should always be  
73 considered as potential triggers of skin barrier dysfunction. Infections and vaccines can also aggravate atopic  
74 dermatitis, but children and adults with atopic dermatitis should be vaccinated. [2] To help with diagnosis,  
75 allergy testing can be useful. The presence of sensitivity to a certain type of food does not imply the need for  
76 abstinence or treatment; only clinically relevant food allergies of the immediate type or very marked reactions of  
77 the late type are an indication for targeted elimination of the allergen. In cases of doubt, provocative tests should  
78 be carried out under appropriate medical supervision. In cases of persistent atopic dermatitis and hypersensitivity  
79 to house dust mite allergens, hypoallergenic mattress covers and frequent washing of pillows and comforters are  
80 recommended. What to do in cases of sensitization to pet allergens must be decided individually. Patch testing  
81 with contact allergens is recommended for the additional demonstration of allergic contact dermatitis, which is  
82 difficult to distinguish from concomitant atopic dermatitis on clinical grounds alone. [3,4,5] In the case of allergic  
83 contact dermatitis, it is also possible to test for the presence of allergic contact dermatitis.

84 In addition to allergic tests, we can analyze eosinophilia. The presence of eosinophilia and elevated serum IgE  
85 levels is common in patients with atopic dermatitis (AD), but they are not specific to the condition. Eosinophilia  
86 is related to the severity of the disease and the deposition of extracellular proteins in the skin. Elevated serum  
87 IgE levels have limited diagnostic value, as high values can suggest allergic sensitization, but normal values do not  
88 rule out allergy. Patients with mutations in the filaggrin gene tend to have higher levels of serum IgE. However,  
89 IgE dosage is not useful as a biomarker for assessing AD exacerbations, and IgE depletion does not reduce AD  
90 symptoms. High levels of IgE in umbilical cord blood may indicate a risk of developing AD at 6 months of age  
91 [4].

92 Atopic dermatitis varies in its presentation, from mild to severe forms that require intensive treatment. To  
93 standardize treatment and follow-up, a score called SCORAD has been developed, which takes into account the  
94 extent of the disease, the severity of the lesions, and subjective symptoms such as itching. The resulting score  
95 classifies AD as mild, moderate, or severe. SCORAD can be calculated quickly and even has apps to make it  
96 easier to use. Another score, the EASI, excludes subjective symptoms, allowing for a more objective assessment  
97 of lesions in different areas of the body. Both the SCORAD and the EASI are considered the best instruments  
98 for assessing the clinical signs of AD, while other instruments have not been recommended due to inadequate  
99 measurement properties. [4,5] The EASI is also considered the best instrument for assessing the clinical signs of  
100 AD.

101 Severe atopic dermatitis is characterized by extensive, generalized, red rashes with some degree of inflammation

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102 that may have crusts, exudates, and areas of lichenification associated with intense pruritus that interfere with  
103 quality of life. In this type of AD, skin infections are more frequent. [4,6] The treatment of atopic dermatitis is  
104 not recommended.

105 Treatment for severe atopic dermatitis is complex, as it often does not respond to conventional therapy.  
106 Considering the chronicity of AD and the different levels of severity, the goals of AD treatment are to reduce  
107 the extent and severity of lesions; reduce pruritus and improve sleep quality; maintain normal daily activities;  
108 improve quality of life; maximize disease-free periods; prevent infectious complications; and avoid or minimize  
109 adverse treatment events.

110 Improving the skin barrier in atopic dermatitis involves the regular use of moisturizers, which help restore  
111 moisture to the skin and reduce dryness, itching, and inflammation. Clinical studies have shown that the use of  
112 moisturizers improves the severity of the disease and reduces the need for topical anti-inflammatory medications.  
113 The recommended amount varies with age.

114 Moisturizers for atopic dermatitis contain emollients, occlusive substances, and humectants to maintain  
115 hydration, reduce water evaporation, and increase hydration of the stratum corneum. It's important to choose  
116 a moisturizer with few ingredients, without fragrances or sensitizers, to avoid allergic reactions. The choice of  
117 texture (lotion, cream, or baume) can vary according to preference and climate. It is recommended to apply  
118 the moisturizer two or three times a day, especially after bathing and on areas with or without lesions. Daily  
119 baths with warm water and physiological pH soaps or bath oils are recommended to avoid drying out the skin.  
120 New moisturizers contain ingredients such as cannabinoids, bioactive lipids, and modulators of the microbiome  
121 to provide additional benefits to the skin, such as regulating lipid production, reducing itching, and modulating  
122 the skin's microbiota. [2,5,6] Phototherapy is a modality used to treat skin lesions.

123 Phototherapy is a treatment modality for various inflammatory and immune-mediated diseases that uses  
124 ultraviolet (UV) wave spectra to irradiate the patient's skin. In atopic dermatitis (AD), two effective modalities  
125 are UVA-1 and narrowband UVB (UVB-FE), the latter being safer. Phototherapy acts by suppressing the skin's  
126 immune system, reducing the response of lymphocytes involved in AD, improving the skin barrier, and reducing  
127 *Staphylococcus aureus* infections. [3,5,6] It is recommended as an adjuvant treatment for atopic dermatitis.

128 It is recommended as an adjuvant treatment in cases where topical treatments fail before systemic immunosup-  
129 pressive medications. Efficacy varies between patients, but RUVB-FE has shown benefits in improving eczema  
130 and reducing pruritus in clinical studies. The safety and efficacy of phototherapy with RUVB-FE have been  
131 proven in patients aged three and over, with remission rates of more than 50% in one year of treatment, especially  
132 in children with higher phototypes. However, equipment availability and costs can be limitations to accessing  
133 this treatment, and exposure to phototherapy can raise concerns about the risk of skin cancer, especially in  
134 pediatric patients. Although it is an effective option, phototherapy faces challenges related to cost, accessibility  
135 to equipment, and possible exposure to skin cancer, especially in children, limiting its use in some regions.  
136 New technologies and more affordable devices could improve the availability of phototherapy in the future. [5]  
137 Topical therapy is necessary for all patients, regardless of the severity of AD. This includes the use of topical  
138 corticosteroids and topical calcineurin inhibitors as a base treatment. New topical therapies, such as topical  
139 phosphodiesterase-4 inhibitors and topical Janus kinase inhibitors, are also emerging, although they are not yet  
140 available in Brazil [5,6,7].

141 Topical corticosteroids have a mechanism of action that includes anti-inflammatory, anti-proliferative, and  
142 immunosuppressive effects. They are the first treatment option for acute attacks of AD, as long as they are  
143 applied correctly, in the appropriate potency for each area, and in the necessary quantity. The potency of the  
144 corticosteroid should be adapted to the severity of the lesion and the region treated, avoiding potent corticosteroids  
145 in thin-skinned areas, such as the face, and giving preference to medium-and low-potency corticosteroids in  
146 children. [6,7] The use of corticosteroids in children is also recommended.

147 Various approaches can be used for systemic treatment. In cases of recurrent skin infections, especially  
148 with *S. aureus*, topical antibiotics can be used. Systemic antibiotics, such as first-generation cephalosporins,  
149 may be indicated for extensive surfaces. Immunosuppressants, such as systemic corticosteroids, cyclosporine A  
150 (CsA), methotrexate (MTX), azathioprine (AZA), and mycophenolate mofetil (MFM), are reserved for severe  
151 and refractory cases. The use of systemic corticosteroids should be extremely cautious due to their side effects.  
152 Cyclosporine A (CsA) is recommended as a first-line treatment for severe cases of AD in adults, children,  
153 and adolescents. Methotrexate (MTX) is an accessible and low-cost alternative, especially for severe cases.  
154 Azathioprine (AZA) is considered a second-line option when cyclosporine is not effective or is contraindicated.  
155 Mycophenolate mofetil (MFM) is a third-line therapy used in severe cases, although there is less evidence of  
156 efficacy on a large scale. [6] Immunobiology represents a class of drugs that are accessible and affordable,  
157 especially for severe cases.

158 Immunobiology represents a class of pharmacological agents used to treat inflammatory and allergic diseases.  
159 They are designed to target mediators of allergic inflammation, such as cytokines, and have played an important  
160 role in the treatment of immunemediated diseases. Currently, these drugs are used to modulate the immune  
161 response, including blocking IgE and various cytokines, such as IL-4, IL-13, IL-22, IL-32, IL-17, and IL-23, which  
162 play a key role in the pathogenesis of diseases such as atopic dermatitis. Immunobiologicals are considered safe  
163 and can be prescribed on the basis of clinical assessment without the need for extensive laboratory tests, making

164 them a valuable option for patients with moderate to severe atopic dermatitis who do not respond adequately to  
165 other treatments. [7] The use of immunobiologicals in the treatment of atopic dermatitis is also important.

166 Learning about atopic dermatitis and how to treat it properly is important for making sure the patient has a  
167 good quality of life. In the worst cases, treating the condition can be more difficult and require the work of many  
168 professionals and areas of the patient's life. Studies on new technologies and approaches are increasingly being  
169 invested in research, and each year the treatment becomes more effective and evolves for individuals. [1,3] IV.

### 170 **6 Conclusion**

171 In summary, atopic dermatitis is a complex, multifactorial condition that affects individuals of all ages. A clinical  
172 diagnosis is essential, and treatment varies according to severity. Recent advances, such as systemic therapies and  
173 immunobiologicals, offer new hope for patients with severe forms of the disease. The multidisciplinary approach  
174 and constant research contribute to improving the quality of life of those affected, highlighting the importance  
175 of personalized treatment that adapts to individual needs.

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