LASOTA, Nina, DEMIDOWICZ, Gabriela, TRĄBKA, Natalia, LASEK, Patryk, SMERDZYŃSKI, Maciej, ŁACH, Katarzyna, ŚCIURKA, Kinga, KOWALCZYK, Klaudia, PANUCIAK, Kinga and KOZICKA, Karolina. Atopic dermatitis - itchy problem of children and adults. Journal of Education, Health and Sport. 2024;59:54-72. eISSN 2391-8306.
https://dx.doi.org/10.12775/JEHS.2024.59.004
https://apcz.umk.pl/JEHS/article/view/48165
https://zenodo.org/records/10654945

The journal has had 40 points in Minister of Science and Higher Education of Poland parametric evaluation. Annex to the announcement of the Minister of Education and Science of 05.01.2024 No. 32318. Has a Journal's Unique Identifier: 201159. Scientific disciplines assigned: Physical culture sciences (Field of medical and health sciences); Health Sciences (Field of medical and health sciences).
Punkty Ministerialne 40 punktów. Załącznik do komunikatu Ministra Nauki i Szkolnictwa Wyższego z dnia 05.01.2024 Lp. 32318. Posiada Unikatowy Identyfikator Czasopisma: 201159. Przypisane dyscypliny naukowe: Nauki o kulturze fizycznej (Dziedzina nauk medycznych i nauk o zdrowiu); Nauki o zdrowiu (Dziedzina nauk medycznych i nauk o zdrowiu).© The Authors 2024;
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The authors declare that there is no conflict of interests regarding the publication of this paper.
Received: 17.01.2023. Revised: 08.02.2024. Accepted: 12.02.2024. Published: 13.02.2024.

Atopic dermatitis - itchy problem of children and adults

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Abstract

Atopic dermatitis is a chronic inflammatory disease with recurrent exacerbations, persistent itching, erythema, dry skin due to damage to the epidermal barrier, and staphylococcal infections. The causative factors are mutations in the gene encoding filaggrin, dysregulation of the immune system, changes in the skin microbiome and lipids in the stratum corneum and deficiency of antimicrobial peptides AMPs. The disease mainly affects children, causing a significant deterioration in the quality of life, and its first symptoms occur in approximately 90% before the age of 5. Lesions most often appear on the bends of elbows and knees, on the face and neck, but may also affect the skin of the entire body (erythroderma). The location of the eruptions depends on age. Atopic dermatitis is the result of complex genetic, epigenetic, environmental and immunological interactions with a coexisting epidermal barrier defect. The disease is diagnosed based on the Hanifin and Rajka criteria. Treatment of atopic dermatitis is symptomatic and selected individually. They include the elimination of provoking factors, care of the epidermal barrier, and anti-inflammatory and anti-pruritic therapy.

Key words: atopic dermatitis; skin itching; emollients; glucocorticosteroids; Hanifin and Rajka criteria.

Aim of the study: discussion of the causes of atopic dermatitis, clinical picture, local and general treatment methods.

Materials and methods: The review was based on the analysis of materials collected in the "Pubmed" database, books and other scientific articles.

Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases affecting both children and adults. It is accompanied by intense itching and dryness of the skin, as well as inflammatory skin lesions with an eczema-like morphology, which contribute to a significant deterioration of the patient's quality of life. It is a genetically determined disease (the most important is a defect in the filaggrin protein, which causes dysfunction of the epidermal barrier and causes dry skin), exacerbated by environmental factors. In 50% of cases, atopic dermatitis is diagnosed already in the first year of life, but its onset may also occur only in adulthood [1,2]. The disease diagnosed in childhood persists in adulthood in approximately 20% of patients. The clinical picture and severity of the disease vary greatly, so the diagnosis of AD is not always obvious, especially in adults. The diagnosis of atopic dermatitis is based on the clinical picture of the disease and the interview.

Epidemiology

It is estimated that 5-9% of children and 0.9-1.4% of adults in Poland suffer from atopic dermatitis. The first symptoms appear in 45% of children by the age of 6 months. In 40-80% of children, the disease disappears by the age of 5 [1,23].

Etipathogenesis

The disease develops under the influence of genetic, environmental, immunological factors and a defect in the epidermal barrier.

Environmental factors provoking atopic eczema in predisposed people: food allergens, airborne allergens (house dust mites, pollen from trees, grasses, weeds, animal epidermis and hair, fungi, Staphylococcus aureus proteins, non-protein allergens - haptens), cosmetics, water, chlorine, wool , sweat, climatic factors: humidity, temperature, stress.

Factors that influence the epidermal barrier defect include: disorders of lipid composition and protein expression (mainly filaggrin [FLG]), inhibition of the function of antibacterial peptides (AMP-antimicrobial peptide) and serine protease inhibitors, as well as excessive activity of serine proteases and excessive serine proteases [3,4].

Additional factors influencing the occurrence of atopic dermatitis include exposure to allergens:

- digestive

- airborne (house dust mites, pollen from trees, grasses, weeds, animal epidermis and hair)

- mushrooms

- Staphylococcus aureus proteins

- non-protein allergens – haptens

So far, two groups of genes responsible for atopic dermatitis have been identified:

1) Genes encoding structural and functional proteins of the epidermis (filaggrin gene), genes encoding intercellular junction proteins, a gene encoding a serine protease inhibitor, and the mast cell chymase gene.

2) Genes encoding proteins that play a role in immune regulation (innate or adaptive). The STAT6 and FOX3 transcription factor genes are responsible for regulating the differentiation of lymphocytes towards Th2, which leads to increased activity of interleukins (IL) 4, 13, 18, 31 and their receptors, as well as genes encoding subunits with high affinity for IgE [1-3] .

In the course of atopic dermatitis, a four-fold increase in transepidermal water loss (TEWL) is observed. A damaged skin barrier also allows transepidermal penetration of microorganisms and allergens and may result in inflammation. It has been proven that type 2 Th helper cells and other T cells contribute to the pathogenesis of atopic dermatitis. In the acute and chronic phases, a Th2 response was observed, which led to an increase in the activity of IL4, IL5, IL13 and IL31 [2,3].

Genetic inheritance plays a fundamental role in the predisposition to atopic dermatitis. Research results confirm that a mutation in the filaggrin gene increases the risk of atopic dermatitis four times, and the presence of two mutations increases it by 80 times. The presence of mutations in the filaggrin gene is associated with severe atopic dermatitis, increased IgE levels and an increased frequency of asthma co-occurrence. This gene encoding the protein filaggrin is considered the best genetic marker of atopic dermatitis. The consequence of FLG deficiency is a deficiency of the natural moisturizing factor (NMF) and,

consequently, reduced hydration of the stratum corneum, increased TEWL value, skin pH and allergen penetration [4,5].

It has been noticed that women are more likely to suffer from atopic dermatitis during adolescence and adulthood. This may be due to the fact that female sex hormones, including estradiol, increase inflammation mediated by Th2 lymphocytes [3,4]. In in vivo studies, an allergic reaction was observed after subcutaneous injection of estradiol in mice. Subsequent studies have shown a direct effect of estradiol on mast cell degranulation, while tamoxifen (a selective estrogen inhibitor) inhibits the degranulation of rat mast cells in response to the administration of histamine and other allergens. The study was conducted in the middle of the ovulatory cycle, when the concentrations of estradiol and luteinizing hormone were the highest. Unlike estrogens, the male steroid hormone dehydroepiandrosterone (DHEA) has an inhibitory effect on the development of atopy. Studies in mouse models have documented a reduction in inflammation and Th2 response under the influence of DHEA. The results of in vitro studies clearly show that human peripheral blood mononuclear cells treated with DHEA produce a significantly lower amount of IL4, which is a key mediator in the synthesis of IgE. It has also been shown that men suffering from atopic dermatitis have lower serum DHEA concentrations compared to the control group [4].

Mast cell chymase (MCC - mast cell chymase belongs to the group of serine proteases secreted by skin mast cells and has a significant relationship with the development of atopic dermatitis in adults. MCC plays a key role in the immune system by regulating the concentration of cytokines in the serum, especially IL4. In A study on animal models showed an increase in IgE secretion in vitro after the addition of MCC, while the addition of an MCC inhibitor to a mouse model of atopic dermatitis significantly reduced scratching. The 1930/A polymorphism of the MCC gene is correlated with the occurrence of atopic dermatitis in adults, but is not associated with allergic rhinitis and asthma. Other studies have documented significant lower IgE concentrations in the serum of AD patients with the 1903/A polymorphism. This suggests that MCC may play a role in atopic dermatitis in adults [4].

Vitamin D3 also plays an important role in the functioning of the epidermal barrier and the immune response. The results of many studies also indicate that vitamin D3 supplementation has a positive effect on the skin condition of patients suffering from atopic dermatitis. The vitamin has a beneficial effect on the microbiome, which in turn affects the immune system and reduces skin inflammation [6].

The role of psychological stress in the course and severity of atopic dermatitis is also known. Research results confirm that increased stress contributes to the exacerbation of changes in adults and children [4]. There is a correlation between stress, the nervous system and the skin. Acute and chronic stress increases the release of neuromodulators that contribute to inflammation [7]. During acute stress, the secretion of corticotropic hormone increases, followed by glucocorticoids, which promote the Th2 response and inhibit the Th1 response. Patients suffering from AD also have a greater predisposition to depression [8-10].

The influence of diet on the course of atopic dermatitis is well known. Some patients have indications for the use of elimination diets, which allow for satisfactory clinical improvement. The use of stimulants is also a key aspect influencing the course of the disease. Alcohol consumption has been proven to be a factor that exacerbates the disease. A study on animal models showed an increase in the concentration of IL6, IL10 and IL18 cytokines after alcohol consumption. They are responsible for the severity of itching and inflammation [11]. Smoking in early adolescence or childhood exposure to tobacco smoke significantly increases the incidence of atopic dermatitis in adulthood [12].

Living in large urban agglomerations often involves exposure to a large number of irritating environmental factors. Nitrogen dioxide is the main component of air pollution, which contributes to damage to the epidermal barrier and causes increased water loss in patients [4,13]. A positive correlation has been demonstrated between exposure to nitrogen dioxide and the occurrence of atopic dermatitis [4,14]. Moreover, exposure to diesel exhaust fumes increases the production of IgE93, which confirms that it is an environmental factor increasing the risk of developing atopic dermatitis [4,15].

Clinical picture

The basic clinical symptoms of atopic dermatitis are eczematous lesions, the location and clinical picture of which depend on age, and skin itching.

In infants, exudative-inflammatory foci are mainly found on the face and scalp.

In childhood, lesions occur around the joints of the wrists, hands and neck and have the features of eczema with symptoms of lichenification.

In adolescents and adults, eczema with lichenification occurs mainly with periodic exacerbations, and the lesions - in addition to the joint areas, face and hands - usually affect the upper parts of the trunk. Eczema lesions, of varying severity, may also affect all locations.

Special places

The description of the characteristic features of infantile and childhood atopic dermatitis applies to all patients. However, not everyone, but many, experience additional changes characteristic of the disease: discoloration/shading of the skin around the eyes, Dennie-Morgan symptom, Hertoghe's symptom, inflammation of the labial area and perioral area, torn earlobe, nipple eczema, atopic cradle cap, symptom of painted nails, enlarged lymph nodes, hyperlinearity of hands and feet.

Diagnosis criteria

Atopic dermatitis is diagnosed based on the presence of the Hanifin and Rajka criteria. These include interview data, clinical symptoms and laboratory test results. Diagnosis requires the presence of 3 out of 4 major features and 3 out of 23 minor features.

Hanifin and Rajka criteria

Features greater

1. Itching

2. Chronic and recurrent course

3. Typical location of skin lesions (face in childhood, joint area in adults)

4. Personal and/or family history of atopic disease (atopic asthma, allergic rhinitis)

Features smaller

1. Dry skin

2. Eczema of the hands and/or feet

3. Onset by age 5

4. White dermographism

5. Lower eyelid fold (Dennie-Morgana)

6. Itching after sweating

7. Food intolerance

8. Increased IgE concentration

9. Cervical fold

10. Exacerbation after stress

11. Wool intolerance

12. Positive results of skin prick tests (most often food allergens in children, airborne allergens in adults.

13. Susceptibility to bacterial and/or viral skin infections

14. Cheilitis

15. Bruising around the eyes

16. Keratosis pilaris and/or ichthyosis

17. Recurrent conjunctivitis

18. Pityriasis alba

19. Nipple eczema

20. Cataract

21. Keratoconus

22. Accentuation of hair follicles

23. Facial erythema

SCORAD scale

In the SCORAD (scoring atopic dermatitis) scale, the severity of atopic dermatitis (AD) is assessed on the basis of objective symptoms - the extent of lesions (A) and their severity (B) and subjective symptoms (itching and sleep disturbances) experienced by the patient over the

last 72 days. h (C). The severity of changes is calculated using the SCORAD formula: A/5 + 7B/2 + C.

To assess the skin surface affected by lesions (A), the so-called rule nine, and the result is divided by 5.

Intensity of changes (B):

- erythema
- swelling/lumps
- exudative lesions and crusts
- erosions
- lichenization (i.e. thickening of the epidermis, increased furrowing and patching of the skin)
- dry skin (in areas not affected by lesions) is assessed on a scale of 0–3.

The severity of subjective symptoms reported by the patient (C - pruritus and sleep disturbances) is assessed using a visual analog scale ranging from 1 to 10 (in the case of children <7 years of age, this is done by the parent).

Based on the SCORAD scale, there are 3 degrees of severity of AD:

- light form (<25 points)
- moderate form (25–50 points)
- severe form (>50 points) [23].

A patient can receive a maximum of 103 points and a minimum of 0. A result of 0 means that the examined person does not currently have atopic lesions or any other symptoms of the disease.

A variant of the SCORAD scale is oSCORAD (objective SCORAD), which eliminates the assessment of subjective symptoms by the patient. The maximum score on this scale is 83 points, but in the most severe cases, an additional 10 points can be added for changes that disfigure or limit the patient's functioning.

Based on the oSCORAD scale, there are 3 degrees of severity of AD:

- mild form (<15 points)

- moderate form (15-40 points)
- severe form (>40 points).

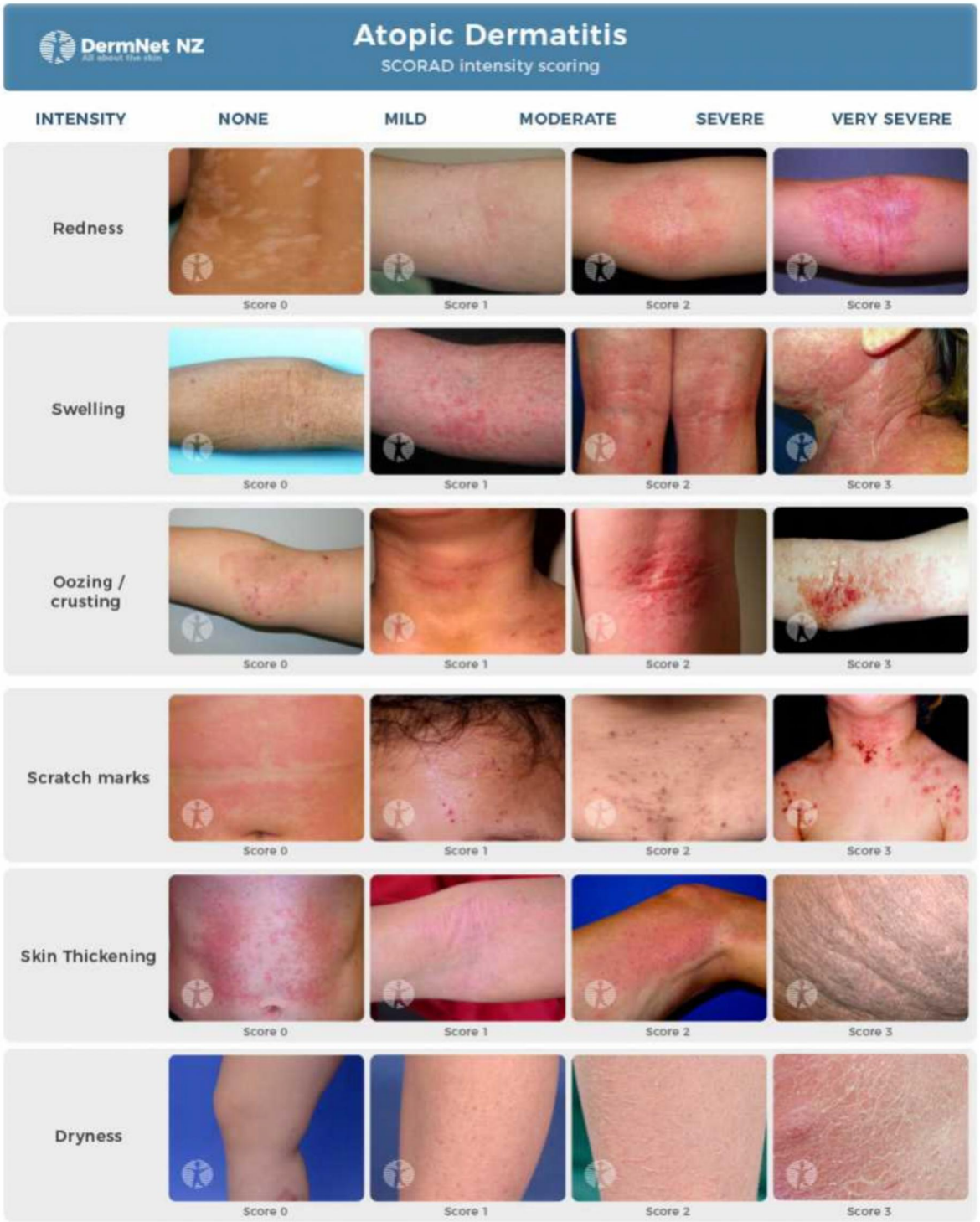

Table 1. Source https://dermnetnz.org/topics/scorad

Additional tests

Determination of total IgE concentration.

Assessment of sensitization to protein, food and air allergens in patients with treatment-resistant atopic dermatitis.

Histological examination, especially in the case of erythroderma in the course of atopic dermatitis.

Alternatively, a bacteriological swab from the nose/skin.

Differentiation

Other forms of eczema not meeting the Hanifin and Rajka criteria.

Scabies.

Dermatitis herpetiformis.

Seborrheic dermatitis of infancy.

Contact dermatitis.

Mycosis of smooth skin.

Pityriasis redx.

Cutaneous lymphoma (may develop in patients with severe forms of atopic dermatitis; histological examination of skin lesions is decisive) [23].

Treatment - general recommendations

All patients need skin care, which in mild cases may be the only and sufficient form of treatment. It involves quick baths ≤ 5 minutes, at a temperature of 27-30°C and the use of emollients. Baths increase the hydration of the stratum corneum and remove allergens and irritating compounds from the skin surface. Within 3-5 minutes after bathing, emollients are applied to slightly damp skin - neutral biological compounds that maintain proper hydration and elasticity of the skin.

Emollients

They contain occlusive substances (Vaseline, paraffin, mineral oils) that reduce transepidermal water loss (TEWL), water-binding humectants (e.g. urea, sorbitol, glycerol, lactic acid) and lipids that seal the epidermal barrier (ceramides, cholesterol, polyunsaturated fatty acids) [19]. Emollients reduce the clinical symptoms of atopic dermatitis in children and adults and prevent recurrence of lesions after external pharmacological treatment. Modern emollients are sometimes enriched with additional active substances with anti-inflammatory properties. It is recommended to use emollients 2-3 times a day, in an amount of at least 200 g per week in small children and 500 g per week in adults [22,24].

The drugs of choice in the treatment of skin inflammation are externally applied glucocorticosteroids. If improvement is achieved, glucocorticosteroid preparations with a higher anti-inflammatory effect should be replaced with those with a weaker effect [25].

Calcineurin inhibitors (0.1% and 0.03% tacrolimus and 1% pimecrolimus) are administered twice a day. After the active lesions disappear, it is recommended to continue using tacrolimus twice a day on a chronic basis. After the active changes have subsided, it is recommended to continue using tacrolimus twice a week on a chronic basis - this is the so-called proactive therapy aimed at treating subclinical changes and preventing relapses [22,27].

Cyclosporine is currently the drug of first choice in patients with atopic dermatitis requiring general treatment. In adults, 2.5 to 5 mg/kg body weight is used. The duration of treatment is determined individually, but in most cases it does not exceed 2 years. Use in cycles lasting an average of 12 weeks may be considered [28].

Dupilumab (IL4 and 13 inhibitor) is a biological drug that can be used in moderate to severe form of AD. Currently, the drug is used as a second-line drug after the first failure of general therapy. The drug is administered in the following schedule: 600 mg in two injections of 300 mg each, followed by 300 mg s.c. every 2 weeks [29].

Tralokinumab (an IL-13 inhibitor) is also a biologic recommended for the treatment of moderate to severe atopic dermatitis in adult patients who require systemic therapy. The recommended dose of tralokinumab for adults is an initial dose of 600 mg (four 150 mg injections) followed by 300 mg (two 150 mg injections) administered subcutaneously every two weeks. Administration of this dose every 4 weeks may be considered [23].

Upadcaytinib is a selective JAK-1 inhibitor approved for the treatment of moderate to severe AD in people who are candidates for systemic therapy. The recommended dose is 15 mg or 30 mg orally once daily, depending on the severity of the skin lesions [30].

Abrocitinib is also a selective JAK1 inhibitor with a similar therapeutic indication. The recommended starting dose is 200 mg once daily. In patients ≥65 years of age, the recommended starting dose is 100 mg once daily. During treatment, the dose may be decreased or increased depending on tolerability and effectiveness. The maximum daily dose is 200 mg [23,31].

Baricitinib is a JAK1 and JAK2 inhibitor with a similar therapeutic indication as the other JAK inhibitors mentioned. The recommended dose is 4 mg once daily and 2 mg as maintenance therapy. A dose of 2 mg once daily is recommended for patients 75 years of age and older [32].

A JAK inhibitor is also available for the treatment of local dermatitis. Ruxolitinib (a JAK1 and JAK2 inhibitor) 1.5% cream can be used in mild to moderate atopic dermatitis. The medicine is applied twice a day to an area of no more than 20%. The patient should not use more than 60g/week or 100g/2 weeks. Chronic, uninterrupted use is not recommended.

Another new drug for topical use is 2% crisaborole (crisaborole), a phosphodiesterase 4 (PDE-4) inhibitor. This medicine is usually used for approximately 3 months [23].

The general use of glucocorticosteroids in AD should be limited to short-term use in cases of severe disease exacerbation.

Antipruritic agents can be used with first- and second-generation antihistamines, the effectiveness of which is sometimes very limited. Therefore, in some patients it is necessary to use neuroleptics to reduce itching.

UVB311 or UVA1 phototherapy may be a good solution for some patients with moderate atopic dermatitis. PUVA can be used, but many experts consider it inappropriate to use PUVA in diseases for which other effective treatments exist. The limitation of phototherapy is its low availability. Rare side effects include: erythema and tenderness after radiotherapy, pruritus, sunburn and skin damage, skin cancer, melanoma, lentigines, photosensitivity reactions (mainly polymorphic light eruptions), folliculitis, photoonycholysis, HSV reactivation, facial hirsutism and cataract [26].

Methotrexate and azathioprine are sometimes used in the treatment of atopic dermatitis, but their effectiveness is very limited in many cases.

Staphylococcus aureus predominates in the skin bacterial flora of patients with atopic dermatitis [21]. Any exacerbation of atopic dermatitis symptoms may be related to a skin infection or the presence of Staphylococcus aureus in the anterior nares. Bacterial eradication reduces severe skin lesions. The use of antiseptic baths with the addition of sodium hypochlorite reduces the number of bacteria, may reduce itching and improve the clinical condition of the skin [22].

Preventive actions also include the elimination of potential irritating and allergenic factors in professional and non-professional settings.

Conclusions

In most cases, atopic dermatitis begins in the first year of life, but the disease can also develop in adulthood. Atopic dermatitis manifests itself in varying severity and clinical picture, which is why its diagnosis is not always obvious. The long-term, recurrent course of the disease accompanied by intense itching and skin lesions, which constitute a significant cosmetic defect and limit basic life functions, is the cause of mental disorders - anxiety disorders and psychoses. Therefore, cooperation with a psychologist or psychiatrist is important.

Disclosure

The authors declare that they have no financial or non-financial conflicts of interest that could influence the interpretation of the study results or the content of this manuscript. This work was carried out independently, without external funding or support.

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Obtaining financing: Not applicable

All authors have read and agreed with the published version of the manuscript.

Financing statement

The authors declare that there are no conflicts of interest or financial disclosures associated with this scientific work

Institutional Review Board Statement

Not applicable

Statement of informed consent

Our work did not involve direct research on humans or obtaining their consent to participate in the study

Data Availability Statement

As a review, our work does not contain new data or analyses. Therefore, there are no specific data sets or data availability for reporting. The information and findings presented in this review are based on previously published research, which can be accessed through the appropriate sources cited in the reference section.

Declaration of conflict of interest

The authors declare that there are no significant conflicts of interest related to this research work.

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