Обзор / Review

Principles of treatment of contact allergic dermatitis: features associated with children and adolescents

REV — обзорная статья

https://doi.org/10.53529/2500-1175-2025-2-29-37

Date of receipt: 09.01.2024
Date of acceptance: 23.05.2025
Date of publication: 17.06.2025

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Abstract

Introduction. Contact allergic dermatitis (CAD) is known to be one of the most prevalent allergic diseases of skin, so its research is of a high interest. Besides clarification of modern approaches to the treatment of contact allergic dermatitis is undoubtedly of current interest. The increase in the growth of contact allergic dermatitis in children explains the relevance of solving the problem of treating the disease in this age group.

Purpose of the lecture. The purpose of this lecture is to review modern approaches to the treatment of contact allergic dermatitis taking into account current clinical guidelines with an emphasis on childhood.

Materials and Methods. This lecture presents consideration of modern principles of treatment of contact allergic dermatitis taking into account the specific features of pediatric practice. A non-systematic literature review was conducted. Pharmacological mechanisms of main medications used are discussed. Focus is based on rational skin therapy. Besides information is given about topical glucocorticosteroids and principles in choosing of concrete group and formulation of them. Also characteristics of topical calcineurin inhibitors are given, and their role in treatment of contact allergic dermatitis is explained. In addition, mechanism of the "vicious circle" during secondary infection and treatment tactics are described.

Results. Increased prevalence of contact allergic dermatitis in children depends primarily on household contact with chemicals and metals, as well as on the use of topical medications. This should be taken into account in prescription of elimination regime. Choice of the class and the formulation of topical corticosteroids should be made differentially taking into account the age, structural features of the child's skin, its sensitivity in different areas and the stage of the inflammatory process. Based on indications topical calcineurin inhibitors might be used in treatment of contact allergic dermatitis especially in pediatric practice. They are characterized by the absence of those side effects which are common during use of topical corticosteroids. Secondary infection which is quite often observed in CAD in childhood requires timely administration of antiseptics and combined topical medications containing corticosteroids, antibiotics and antifungal components.

Conclusion. Contact allergic dermatitis has good prognosis in case of implementation of elimination measures, adherence to treatment algorithm in accordance with clinical guidelines and age-based characteristics.

Keywords: contact dermatitis, contact allergic dermatitis, topical glucocorticosteroids, topical calcineurin inhibitors

Conflict of interests:
Author declares no conflict of interests.

For citation: Vasileva A.A. Principles of treatment of contact allergic dermatitis: features associated with children and adolescents. *Allergology and Immunology in Pediatrics*. 2025; 23 (2): 29–37. https://doi.org/10.53529/2500-1175-2025-2-29-37

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Принципы терапии аллергического контактного дерматита: особенности у детей и подростков

https://doi.org/10.53529/2500-1175-2025-2-29-37

УДК 616.5-001.1-08-053.2/.053.6
Дата поступления: 09.01.2024
Дата принятия: 23.05.2025
Дата публикации: 17.06.2025

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Аннотация

Актуальность. Аллергический контактный дерматит является одним из наиболее распространенных аллергических заболеваний кожи, в связи с чем высок научно-практический интерес к данной патологии. Увеличение роста аллергического контактного дерматита у детей и подростков объясняет актуальность решения проблемы лечения заболевания в этой возрастной группе.
Цель лекции. Целью данной лекции является рассмотрение современного подхода к лечению аллергического контактного дерматита с учетом актуальных клинических рекомендаций с акцентом на детский возраст.
Материалы и методы. Настоящая лекция представляет собой изложение современных принципов терапии аллергического контактного дерматита с учетом особенностей в детской практике. Проведен несистематический обзор литературы. Обсуждаются механизмы, лежащие в основе действия основных групп лекарственных препаратов. Уделяется внимание рациональной наружной терапии кожного воспалительного процесса. Рассматриваются топические глюкокортикостероиды и принципы выбора как конкретной группы данных препаратов, так и их лекарственной формы. Дается характеристика и объясняется место топических ингибиторов кальциневрина в терапии аллергического контактного дерматита. Описывается механизм «порочного круга» при вторичном инфицировании и рассматривается тактика лечения.
Результаты. Рост распространенности аллергического контактного дерматита у детей зависит прежде всего от бытового контакта с продуктами химической промышленности и металлами, а также от использования наружных лекарственных препаратов. Это следует учитывать при обеспечении элиминационных мероприятий. Выбор класса топических ГКС и формы препаратов следует осуществлять дифференцированно с учетом возраста, особенностей строения кожи ребенка, ее чувствительности на разных участках и стадии воспалительного процесса. В лечении АКД, особенно в детской практике, с учетом показаний могут быть использованы топические ингибиторы кальциневрина, не имеющие побочных эффектов, присущих ТГКС. Вторичное инфицирование, часто наблюдаемое при АКД у детей, требует своевременного назначения антисептиков и комбинированных топических препаратов, содержащих ГКС, антибиотики и антимикотики.
Заключение. Аллергический контактный дерматит имеет благоприятный прогноз при грамотно осуществляемых элиминационных мероприятиях, при соблюдении алгоритма лечения в соответствии с клиническими рекомендациями и с учетом возрастных особенностей.

Ключевые слова: контактный дерматит, аллергический контактный дерматит, топические глюкокортикостероиды, топические ингибиторы кальциневрина

Конфликт интересов:
Автор заявляет об отсутствии конфликта интересов.

Для цитирования: Васильева А.А. Принципы терапии аллергического контактного дерматита: особенности у детей и подростков. *Аллергология и иммунология в педиатрии*. 2025; 23 (2): 29–37. https://doi.org/10.53529/2500-1175-2025-2-29-37

INTRODUCTION

Contact dermatitis is a fairly common inflammatory skin disease that occurs when the skin is directly exposed to various external factors and may have an acute or chronic course. There is known simple irritant contact dermatitis and allergic contact dermatitis (ACD). While simple irritant contact dermatitis has no immune mechanism, ACD is an allergic skin disease, the pathogenesis of which is based on a delayed-type hypersensitivity reaction (DTH)[1]. The most frequently mentioned contact allergens are: metals chromium, cobalt and nickel, rubber and rubber products, some medicines, disinfectants, formaldehyde, resins and a number of other substances [1, 2].

There is a rather high (about 16.5%) prevalence of ACD in children of different ages [3]. This is due, in particular, to the widespread use of chemical industry

[1] Clinical guidelines. Contact dermatitis. [internet]. 2024.

products in the home: detergents, cleaning agents, as well as contact with dyes used in the manufacture of children's clothing and toys. In children of the first year of life, ACD is mainly associated with the use of children's cosmetics and laundry detergents [4]. A high prevalence of ACD to nickel is noted in all age groups (about 10%). This may be due to contact with toys, stationery, hairpins, etc., and may be due to exposure to nickel. In adolescence, nickel-associated ACD is often associated with wearing metal jewelry made of nickel alloys, piercing products, contact with hardware, etc. Allergic contact dermatitis to various cosmetics is also more often observed in adolescents [5, 6]. Regardless of age, the cause of ACD in children may be contact with rubber products and medicines.

Clinical signs of ACD appear 10-14 days or more after the initial contact with the allergen. In the case of repeated contact with the allergen (hapten), 12-48 hours must elapse before symptoms appear. In situations of repeated skin exposure to neomycin sulfate, nickel, paraphenylenediamine and thixocortol pivalate, late delayed manifestations of ACD may occur, i.e. in this case several days later. The clinical symptoms of acute ACD are hyperemia, edema, and sometimes papules and vesicles at the site of contact with the allergen. In some cases, short-term, unexpressed areas of mottling may form (eczematized ACD). In chronic ACD there is stagnant erythema, infiltration, lichenification, and in exacerbation there is eczematization with mottling [7].

In some cases, systemic allergic contact dermatitis is observed, with localized or generalized cutaneous inflammation resulting from systemic re-exposure to the allergen. This variant of dermatitis has been described in sensitization to certain drugs, nickel, rosin, Peruvian balsam, parabens, cinnamon aldehyde, spices (cloves, cinnamon, nutmeg, cayenne pepper). The skin process may form both in places of previous localization of ACD and on previously unaffected areas and accompanied by general symptoms (headache, weakness, arthralgia, nausea, vomiting, diarrhea) [8].

SPECIFICS OF ELIMINATION MEASURES

Elimination measures to exclude or reduce contact with causative allergens are important in the management of patients with allergic diseases. Recommendations for elimination of the causative allergen play a crucial role in the management of patients with ACD. It is often not possible to achieve complete elimination in ACD because a large number of commonly used household and industrial products may contain substances that cause the disease. Therefore, when recommending elimination of contact allergens to the patient or the child's parents, it is important to outline the range of possible uses of these substances, which can be very extensive, making it difficult to achieve complete elimination.

When providing recommendations for patients, it should be considered that continued exposure to nonspecific skin triggers exacerbates the course of ACD and reduces the effectiveness of therapeutic interventions.

PHARMACOTHERAPY

Pharmacotherapy of ACD should be prescribed regarding the severity, stage of the inflammatory process and its prevalence, the patient's age, as well as the presence of comorbidities. In the external therapy of ACD, topical glucocorticosteroids (TGCS) remain the “gold standard” of anti-inflammatory external therapy [1]. Currently, they have no alternative in terms of both speed and severity of anti-inflammatory action [9]. In the course of therapy with TGCS, it is necessary to follow the instructions for the use of the drugs, including the frequency of their application to the skin, duration of use and age restrictions. TGCS classifications take into account the strength of their anti-inflammatory effect. The international classification implies division of all TGCS according to this criterion into 7 classes [8].

One of the main factors determining the efficacy of topical glucocorticosteroids is the rate of absorption of the drugs by different skin layers. There are two known ways of TGCS penetration into the skin: it can occur directly transepidermally (the main way) or through hair follicles, sweat or sebaceous glands. A number of factors determine the degree of skin permeability for TGCS: properties of the active components of the drug and its base, the place of application of the drug, skin condition, etc. The patient's age is

Table 1. **Topical corticosteroids which are used in treatment of allergic contact dermatitis in accordance with clinical guidelines and instruction to medication (author's table)**
Таблица 1. **Топические ГКС, рекомендованные к применению при АКД в соответствии с Клиническими рекомендациями и инструкциями по применению (таблица автора)**

International non-proprietary name	Activity group	Age
Clobetasol propionate 0,05 %, cream	Class 1 (very strong)	From 1 year
Betamethasone dipropionate 0,05 %, ointment, cream	Class 1 (very strong)	From 1 year
Mometasone furoate 0,1 %, ointment	Class 2 (strong)	From 2 years
Betamethasone valerate 0,1 %, ointment	Class 2 (strong)	From 6 months
Fluticasone propionate 0,005 %, ointment	Class 2 (strong))	From 10 years
Mometasone furoate 0,1 %, cream	Class 4 (moderate strength)	From 2 years
Methylprednisolone aceponate 0,1 %, cream, ointment, oily ointment, lotion	Class 4 (moderate strength)	From 4 months
Betamethasone valerate 0,1 %, cream	Class 5 (moderate strength)	From 6 months
Hydrocortisone butyrate 0,1 %, cream, ointment, emulsion	Class 5 (moderate strength)	From 6 months
Fluticasone propionate 0,05 %, cream	Class 5 (moderate strength)	From 10 years
Hydrocortisone acetate 1 % ointment	Class 7 (weak)	From 2 years

important, which is associated with the peculiarities of skin structure in children, affecting the absorption of the drug. The skin of the face, neck, folds (as well as other large folds) and groin area is characterized by high sensitivity to the action of TGCS [10, 11]. If inflammation in ACD is localized in these areas, the use of TGCS with a lower degree of activity is recommended [12, 13].

The depth of TGCS penetration into the skin depends on the form of the drug, which is selected regarding the stage of inflammation. Thus, in acute inflammation characterized by edema, vesicles, maceration and maceration, high skin permeability is observed. In this situation, there is the choice of products in the form of lotion, aerosol, cream and lipocrem depending on the specific skin manifestation. This is due to the fact that the lowest permeability is observed in drug solutions and lotion. If the drug is in the form of cream, its skin penetration will be greater than that of solution but less than that of ointment. Maximum dermal absorption of topical GCS is possible when using preparations in the form of ointment. Therefore, when choosing the form of TGCS in chronic dermatitis manifested by dry skin and lichenization, when there is difficult accessibility for penetration of topical GCS, it is advisable to choose ointment forms of preparations (ointment, oily ointment) for application to the skin. The ointment base of the preparation also contributes to moisturizing the stratum corneum of the epidermis, which, in turn, increases skin permeability [10]. The high fat content in the base of the preparation can provide an additional occlusion effect [14]. When choosing the form of topical GCS, the localization of the inflammatory process is also taken into account, which affects the penetration of the drug due to the peculiarities of the skin structure in different areas. In case of inflammation in the scalp, face and folds, preference should be given to aerosols, lotions, gels and creams that do not contain a fatty base [10].

Age-specific skin characteristics in children, among other criteria, are considered in the instructions for the drugs when determining the age barriers for prescribing specific TGCS, their dosage forms and mode of use[1] (Table 1).

Methylprednisolone aceponate 0.1% in the form of cream, ointment, emulsion can be used from 4 months of age.

Etamethasone valerate 0.1% (cream, ointment) is approved for use in children from 6 months of age, and betamethasone dipropionate 0.05% in the form of cream for the treatment of ACD - from the age of 1 year. Betamethasone dipropionate 0.05% in the form of a spray and mometasone furoate (cream, ointment 0.1%) can be used in children over 2 years of age.

Cream for external use clobetasol propionate 0.05%, according to the instructions, is allowed for use in children over 1 year of age.

Hydrocortisone butyrate 0.1% (ointment, cream, lipocrem, emulsion) is allowed for use from 6 months of age. According to the instructions, hydrocortisone acetate 1% in the form of ointment can be used from the age of 2 years.

[1] Clinical guideline. Contact dermatitis. [internet]. 2021.

Fluticasone propionate 0.05% cream is contraindicated for use in children under 10 years of age.

Safety of TGCS when administered in children is one of the key factors in selection of a particular drug and its dosage form.

Should be borne in mind that for the use of TGCS in children from the activity group "very strong": clobetasol propionate 0.05% (cream), betamethasone dipropionate 0.05% (ointment, cream, spray) - there should be strict indications. Great caution is required when prescribing the above drugs during the growth period in children. In the Clinical Guidelines for Contact Dermatitis there is an indication to avoid the use of clobetasol propionate 0.05 % in children, authorized according to the instructions for use from 1 year of age.

Regarding the nature and localization of the skin process in dermatitis, the child's age in the acute period of dermatitis, it is preferable to use TGCS of medium or strong activity. These groups of drugs effectively control the symptoms of inflammation, quickly restore the barrier function of the skin and thereby reduce the systemic absorption of drugs. It is indicated that short courses (3 days) of strong drugs are comparable in efficacy and safety to long courses (7 days) of weak TGCS. The duration of a continuous course of TGCS in children should be, on the one hand, sufficient to achieve the effect and at the same time, in order to ensure safety, minimized as much as the clinical situation allows. It is emphasized that in children the continuous course of this group of drugs should not exceed 2 weeks, and a gradual reduction in the frequency of their application to the skin is recommended if there is a significant reduction in inflammatory symptoms [14].

The group of topical calcineurin inhibitors (tacrolimus and pimecrolimus) used in the treatment of contact dermatitis deserves special attention.

These drugs may be the drugs of choice when inflammation is localized in the face, especially in children. Prolonged use of TGCS in the face can lead to a number of complications: skin atrophy, development of steroidal rosacea. The use of corticosteroids in the periorbital region may cause an increase in intraocular pressure. In such situations, replacement of TGCS with calcineurin inhibitors is justified. The use of tacrolimus and pimecrolimus in the treatment of contact dermatitis is indicated in the presence of contact hypersensitivity to TGCS [15, 16].

Topical calcineurin inhibitors belong to the class of ascomycin macrolactams with anti-inflammatory and immunosuppressive action. The drugs have high affinity for the skin, local immunotropic activity and high selectivity of anti-inflammatory action. Unlike corticosteroids, they do not affect the structure of the skin and, therefore, can not cause its atrophy. Topical calcineurin inhibitors are able to inhibit proliferation and activation of CD4+ T-lymphocyte-helper cells. In addition, they influence on nerve fibers, affecting the functioning of ion channels associated with the release of neuropeptides and substance P. The action of substance P is associated with a transient burning sensation after application of the drugs. These preparations are also characterized by short-term stimulation of excessive release of inflammatory factors with their subsequent depletion. These mechanisms explain the subsequent antipruritic effect of the preparations [15, 16, 17].

Having a more selective mechanism of action than TGCS, topical calcineurin inhibitors do not cause side effects inherent to TGCS. At the same time, their clinical efficacy has been described, in particular in the treatment of ACD [8, 15].

It should be noted that pimecrolimus (1% cream for external use) is contraindicated for use in children under 3 months of age. Tacrolimus (0.03% ointment) is approved for use in children from the age of 2 years, and in the form of 0.1% ointment it is contraindicated for use in children under 16 years of age.

The question of systemic glucocorticosteroids is raised in severe, widespread and systemic allergic contact dermatitis, when external therapy alone is ineffective. Dermatitis is considered widespread when more than 20% of the skin is affected. In these cases, systemic short-acting oral or parenteral GCS are administered depending on the severity of the skin process and body weight of the child: in the dose of prednisolone from 0.5 to 1 mg / kg (maximum 60 mg per day). Equivalent doses of other glucocorticosteroids may be used[1]. The course is 3-5-7 days. [6, 8]. The algorithm of systemic GCS withdrawal is carried out in each specific case in accordance with generally accepted rules depending on the course duration and drug dose.

[1] Allergology and Clinical immunology (Edition: clinical guidelines) / edited by R. M. Khaitova, N. I. Ilyina... C. 18.

In both simple contact dermatitis and ACD, excoriations and fissures are often observed in the inflamed area and secondary infection must be prevented or eliminated. These situations occur most often in pediatric ACD. The use of antiseptics, disinfectants and methylene blue can be considered for this purpose. For external application, a solution of fucorcin can be used. On the skin area treated in this way, after the liquid dries, you can use preparations in the form of ointments. Fucorcin is contraindicated in women during pregnancy, as well as during breastfeeding. The use of 1% aqueous solution of methylene blue is allowed during pregnancy and breastfeeding. The drug is authorized for use in children from the moment of birth[1].

In contact dermatitis (simple and allergic) against the background of itching, as a rule, excoriations are observed, which leads to the violation of skin integrity with the subsequent accession of secondary infection. In this case, the predominant bacteria are Staphylococcus aureus and group A hemolytic streptococci [18]. With secondary infection of simple irritant and ACD in the clinical picture there is an increase in erythema and the appearance of pustules. Precipitation boundaries are clear. Pronounced fine-platelet desquamation, as well as crusts of honey-yellow colour may appear in the inflammation area [19].

The formation of a "vicious circle" in case of secondary infection in skin diseases is of interest. Interleukins 31 and 33 (IL-31 and IL-33) are involved in the mechanism of skin itching and inflammation. In turn, skin scratching stimulates additional release of IL-33 from keratinocytes, which is also responsible for suppressing the production of protective skin proteins and, as a consequence, for disruption of the mechanical skin barrier [20]. The situation is aggravated in case of secondary skin infection. Infectious agents can induce IL-31 production by monocytes and macrophages, which leads to increased itching and skin damage due to scratching. This causes increased inflammation and bacterial colonization of the skin [21].

Considering the issues of secondary infection in dermatitis, it is necessary to separately touch on infections of fungal etiology. Patients with various skin diseases are at risk for the occurrence of mycoses. Mycotic infection in dermatitis for a long time remains undetected, often considered as a manifestation of the underlying disease, supports the skin inflammatory process, aggravating the course of the disease. Patients with various skin diseases are at risk of mycosis occurrence [21, 22].

In case of ACD complicated by microbial infection, timely use of combined topical medicines containing GCS in combination with an antibiotic (gentamicin, fusidic acid, neomycin, etc.) or GCS in combination with an antibiotic and antimycotic component (natamycin, clotrimazole, etc.) is indicated [8].

The following combinations of topical GCS and antibiotic are available: betamethasone + gentamicin; hydrocortisone + oxytetracycline, or hydrocortisone + chloramphenicol, or hydrocortisone + fusidic acid; betamethasone + fusidic acid. In contrast, the drugs containing topical GCS, antibiotic and antimycotic in their composition include: combination of betamethasone with gentamicin and clotrimazole or combination of hydrocortisone with neomycin and natamycin. When using combined agents containing TGCS, antibiotic and antimycotic, high concentrations of active substances in the focus of lesions in the skin area are provided. In this case, it is reasonable to recommend short courses of combined topical glucocorticosteroids (usually lasting 1 week).

Systemic antibiotics are indicated if there is no response to topical combination therapy and in cases of widespread bacterial infection on the skin[2].

The question of the advisability of using systemic antihistamines in ACD is often raised. There are no convincing data demonstrating the efficacy of H1-histamine receptor blockers in the treatment of ACD [8]. There are recommendations for their use to reduce pruritus. Clinical guidelines indicate the expediency of parenteral administration of systemic antihistamines, belonging to the first generation, in case of severe pruritus. In case of indications for the use of systemic antihistamines in children, preference should be given to oral non-sedative antihistamines of II generation as safer drugs[3].

Systemic blockers of H1-histamine receptors can be used to reduce the intensity of itching, but only as part of the complex therapy of allergic contact dermatitis.

[1] Clinical guideline. Contact dermatitis. [internet]. 2021.
[2] Allergology and Clinical immunology (Edition: clinical guidelines) / edited by R. M. Khaitova, N. I. Ilyina ... C. 18.
[3] Clinical guideline. Contact dermatitis. [internet]. 2021.

H1-histamine receptor blockers in forms for topical application (gels, creams, etc.) are not recommended for the treatment of ACD.

CONCLUSION

If elimination can be achieved, allergic contact dermatitis most often has a favorable prognosis. Thus, in case of timely elimination of contact with the identified causative allergen, clinical symptoms completely regress in 1-3 weeks [23]. Otherwise, the disease acquires a chronic course, in which, even after the elimination of the causative factor, the pathologic skin process may continue for a long time and require therapy in accordance with the peculiarities of the clinical picture in each case. However, chronic ACD in children is observed very rarely, as it is mainly associated with occupational factors, and it is not always possible to exclude contact with them. The modern approach to the therapy of ACD provides, first of all, the prescription of topical GCS. The choice of a specific drug and its dosage form is determined by the nature and stage of the inflammatory process. The key factor in the choice of topical GCS in pediatric practice is their safety. Topical calcineurin inhibitors, inferior in strength of anti-inflammatory effect to TGCS, but free of their side effects, can be used when indicated. Since in ACD there is often secondary infection, the use of antiseptics remains relevant, including for prophylactic purposes. In cases of ACD complicated by microbial infection, it is recommended to prescribe combined topical medications containing GCS in combination with antibiotic or antibiotic and antimycotic regarding frequent acceding fungal infection. As for the use of GCS in ACD, they are prescribed in severe, widespread and systemic allergic contact dermatitis.

ACD treatment algorithm is based on modern clinical guidelines, regarding individual approach to compel therapy of this common allergic skin disease.

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FINANCING SOURCE

Author declares that no funding was received for this study.

ИСТОЧНИК ФИНАНСИРОВАНИЯ

Автор заявляет об отсутствии спонсорской поддержки при проведении исследования.

AUTHOR'S CONTRIBUTION TO THE WORK

Alla A. Vasileva — data collection and analysis , writing the manuscript.

ВКЛАД АВТОРА В РАБОТУ

Васильева А. А. — сбор материала, анализ полученных данных, написание статьи.