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CLINICAL MANIFESTATIONS, DIAGNOSIS AND MANAGEMENT DRUG ERUPTION IN CHILDREN.



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Abstract. Drug eruptions represent an important group of cutaneous adverse drug reactions in pediatric patients and constitute a significant challenge in clinical practice. These reactions develop as a consequence of exposure to medications and may range from mild, self-limiting skin manifestations to severe and potentially life-threatening systemic conditions. The increasing use of antibiotics, nonsteroidal anti-inflammatory drugs, anticonvulsants, and other pharmaceutical agents in pediatric healthcare emphasizes the importance of understanding drug-induced skin reactions. The present article aims to analyze the clinical manifestations, etiological factors, diagnostic approaches, and management strategies associated with drug eruptions in children.

Key words: Drug eruption, children, pediatric dermatology, adverse drug reactions, drug hypersensitivity, maculopapular rash, urticaria, Stevens–Johnson syndrome, toxic epidermal necrolysis, diagnosis, treatment.

1. Introduction. Drug eruptions are among the most clinically relevant adverse effects of pharmacological treatment in children. They are characterized by changes in the skin and, in some cases, mucous membranes following exposure to a medication. These reactions may occur through immunological or non-immunological mechanisms and demonstrate considerable variation in clinical presentation, severity, and duration.

The increasing availability and utilization of pharmaceutical products have improved the treatment of childhood diseases. However, the widespread administration of medications has also increased the importance of identifying and managing adverse drug reactions. Antibiotics, antipyretics, analgesics, anticonvulsants, and other therapeutic agents are commonly prescribed in pediatric practice and may contribute to the development of cutaneous reactions in susceptible individuals.

Children represent a particularly important population because their physiological and immunological characteristics differ from those of adults. Developmental changes in drug metabolism, immune-system function, body composition, and elimination processes may influence the clinical expression of adverse drug reactions. Furthermore, the recognition of drug eruptions in children is complicated by the high prevalence of infectious diseases that may independently produce similar dermatological manifestations. Therefore, accurate diagnosis is necessary not only for the

management of the immediate dermatological condition but also for the optimization of future pharmacological treatment.

2. Literary review. Drug-induced cutaneous reactions have been investigated extensively in dermatology, pediatrics, clinical pharmacology, and allergology. Contemporary research emphasizes their heterogeneous nature and the need to distinguish uncomplicated dermatological manifestations from severe systemic hypersensitivity reactions. Nguyen, Gabel, and Yu (2020), in their review entitled *Pediatric Drug Eruptions*, examined the clinical characteristics and management of common drug-associated dermatological conditions in children. The authors highlighted the importance of distinguishing drug eruptions from infectious exanthems and other pediatric skin disorders. Their work demonstrates that clinical presentation alone may be insufficient to establish a definitive diagnosis, particularly when multiple medications have been administered [1].

Del Pozzo-Magaña and Liy-Wong (2024), in *Drugs and the Skin: A Concise Review of Cutaneous Adverse Drug Reactions*, discussed the classification, pathophysiological mechanisms, and clinical assessment of drug-induced skin reactions. Their analysis emphasizes the broad spectrum of cutaneous adverse reactions and the importance of evaluating clinical morphology, medication history, and systemic manifestations [2].

Neustädter and colleagues (2024) investigated the problem of incorrect beta-lactam antibiotic allergy labeling in children. Their consensus paper indicates that many delayed skin eruptions occurring during antibiotic treatment are associated with underlying infections rather than genuine drug hypersensitivity. The authors support carefully selected diagnostic approaches that allow unnecessary allergy labels to be removed when clinically justified [4].

Recent investigations have also focused on severe cutaneous adverse reactions. Kuyucu and colleagues (2025) published a European Academy of Allergy and Clinical Immunology (EAACI) position paper concerning the diagnosis and management of DRESS syndrome in children. The document describes the complex immunopathogenesis of DRESS, including drug-specific immune activation, genetic susceptibility, and possible viral reactivation. It also emphasizes comprehensive clinical evaluation and systematic assessment of organ involvement [5].

3. Materials and metods. The present study was designed as a narrative literature review aimed at summarizing contemporary scientific evidence concerning drug eruptions in pediatric patients. The methodological approach involved descriptive analysis, comparative evaluation, clinical classification, and qualitative synthesis of published research findings.

Scientific publications and clinical recommendations addressing pediatric adverse drug reactions were considered, with particular attention to literature published between 2020 and 2025, supplemented by relevant established clinical guidance. The literature was identified through a targeted review of scientific resources, including PubMed-indexed publications, international allergy and dermatology literature, and publicly available clinical guidance from recognized medical organizations.

4. Results and discussion. The reviewed literature indicates that drug eruptions in children are associated with several groups of pharmaceutical agents. Antibiotics are frequently implicated because they are widely prescribed for bacterial infections in pediatric practice. Beta-lactam antibiotics, including penicillins and cephalosporins, are commonly suspected in children who develop skin rashes during treatment. However, not every eruption associated with antibiotic administration represents a genuine allergic reaction.

In many cases, the underlying viral infection contributes to the appearance of the rash. Consequently, establishing a causal relationship between a medication and a cutaneous reaction requires careful evaluation of the clinical context. Nonsteroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, constitute another important category of medications associated with urticaria, angioedema, and other hypersensitivity manifestations. Anticonvulsant medications, including

carbamazepine, lamotrigine, and phenytoin, may be associated with delayed hypersensitivity reactions and, in susceptible patients, severe cutaneous adverse reactions. Individual susceptibility is influenced by genetic predisposition, immune-system characteristics, previous exposure to medications, concurrent infections, and the administration of multiple pharmaceutical agents. The literature therefore supports a multifactorial understanding of pediatric drug eruptions rather than a purely medication-dependent explanation. Drug eruptions demonstrate considerable clinical diversity. Their manifestations range from localized skin changes to extensive mucocutaneous involvement accompanied by systemic complications.

Maculopapular eruption, also referred to as morbilliform or exanthematous drug eruption, is a common form of delayed cutaneous drug reaction. It is characterized by erythematous macules and papules that frequently begin on the trunk and subsequently spread to the extremities. The eruption may be symmetrical and accompanied by pruritus. Symptoms often develop several days after medication exposure, although the timing varies according to previous sensitization and individual patient characteristics. Most uncomplicated cases resolve following withdrawal of the responsible medication, provided that no severe or progressive features are present.

Urticaria is characterized by transient, raised, pruritic wheals resulting from the release of inflammatory mediators, including histamine. Drug-associated urticaria may occur as part of an immediate hypersensitivity reaction. Nevertheless, acute urticaria in children frequently develops in association with infections, and the presence of wheals during medication use does not independently establish drug allergy. When urticaria is accompanied by respiratory compromise, circulatory symptoms, or other manifestations of anaphylaxis, emergency medical treatment is necessary.

Fixed drug eruption is distinguished by the recurrence of well-defined erythematous or violaceous lesions at the same anatomical sites following repeated exposure to the responsible medication. Lesions may be localized or, less commonly, widespread. After resolution, they frequently leave residual hyperpigmentation. Recognition of the recurrent anatomical pattern is important for establishing a suspected diagnosis.

Serum sickness-like reactions may present with skin eruptions, fever, and joint symptoms following exposure to certain medications. These reactions should be distinguished from classical immune-complex-mediated serum sickness because their underlying mechanisms and laboratory findings may differ.

SJS and TEN are severe mucocutaneous reactions characterized by extensive keratinocyte injury and epidermal detachment. Patients may initially develop fever, malaise, and painful skin lesions, followed by mucosal inflammation, blistering, and epidermal separation. These conditions represent medical emergencies requiring immediate withdrawal of suspected causative medications and specialized hospital care.

DRESS syndrome is a potentially severe delayed hypersensitivity reaction involving the skin and internal organs. Clinical manifestations may include widespread rash, fever, facial edema, lymphadenopathy, hematological abnormalities, and hepatic or renal involvement. Unlike uncomplicated exanthematous reactions, DRESS may continue to evolve even after the suspected medication has been discontinued. The 2025 EAACI position paper emphasizes the necessity of assessing organ involvement and providing individualized management and appropriate follow-up [5].

Accurate diagnosis requires a comprehensive assessment of the patient's clinical history, medication exposure, rash morphology, and associated symptoms.

The chronological relationship between drug administration and the onset of symptoms is particularly important. Clinical assessment should document the name of each medication, treatment indication, administered dose, route of administration, duration of exposure, and previous history of similar reactions.

Physical examination should focus on the distribution and morphology of the eruption, mucosal involvement, fever, lymphadenopathy, facial edema, and possible systemic manifestations. Laboratory investigations may be required when severe drug hypersensitivity is suspected. Depending on the clinical presentation, investigations may include a complete blood count, liver-function tests, renal-function tests, and other targeted examinations. Skin biopsy may provide additional diagnostic information in selected atypical or severe cases, although histopathological findings must be interpreted alongside the clinical presentation.

Allergy testing should be selected according to the suspected reaction mechanism and clinical risk. Skin testing and drug provocation procedures have specific indications and limitations.

For appropriately selected children with a low-risk history of suspected beta-lactam allergy, a supervised oral drug challenge may be considered by qualified specialists. Such procedures should not be performed in cases with a history suggesting severe cutaneous adverse reactions unless an expert service determines a different appropriate investigative strategy. Differential diagnosis is essential because viral exanthems, bacterial infections, inflammatory dermatological disorders, and other systemic diseases can mimic drug-induced skin reactions. The findings of the reviewed literature reinforce the principle that temporal association alone is not sufficient to establish drug causality.

The management of pediatric drug eruptions depends on the severity, clinical phenotype, suspected mechanism, and overall condition of the child. The initial clinical priority is to identify a potentially responsible medication and determine whether the reaction includes features of systemic involvement. When a drug reaction is suspected, clinicians should assess the need to discontinue the suspected medication and select an appropriate therapeutic alternative.

The present literature review demonstrates that antibiotics, nonsteroidal anti-inflammatory drugs, and anticonvulsants are among the pharmaceutical agents frequently associated with suspected pediatric drug eruptions. However, the presence of a skin rash during medication administration does not necessarily confirm drug hypersensitivity, since infectious diseases and other dermatological conditions may produce similar manifestations.

Early diagnosis depends on the comprehensive evaluation of medication history, clinical morphology, reaction timing, and possible systemic involvement. Particular attention should be paid to recognizing warning signs of severe cutaneous adverse reactions, including Stevens–Johnson syndrome, toxic epidermal necrolysis, and DRESS syndrome. The management of drug eruptions should be individualized according to clinical severity and patient characteristics. Appropriate discontinuation of the suspected causative medication, supportive treatment, specialist consultation, and careful follow-up are essential for reducing complications and improving patient outcomes. Furthermore, rational prescribing practices, accurate medical documentation, and parental education play important roles in preventing recurrent reactions. Evidence-based assessment of suspected drug allergies can also prevent unnecessary restrictions on future therapeutic options.n In conclusion, improving awareness of pediatric drug eruptions among healthcare professionals and promoting standardized diagnostic and management approaches are essential for strengthening medication safety in children. Future research should focus on age-specific risk factors, improved diagnostic techniques, and the development of individualized therapeutic strategies for pediatric patients.

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