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Immunodermatology: at a Glance

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ABSTRACT

Background: Immunodermatology is a medical specialty specializing in detecting and treating skin conditions induced by a compromised immune system response. Each cellular element of the skin undergoes a unique developmental process and serves a specific function within the skin. Many disorders affecting epithelial organs, including the skin, mucous membranes, digestive tract, and respiratory tracts, require immunodermatological testing for diagnosis and treatment. Immunodermatology, a field at the intersection of dermatology and immunology, continues to evolve, with new research being published annually. **Review:** There are numerous dermatological conditions related to immunodermatology. Advances in immunology and dermatology have enhanced our understanding of the skin as an active immune organ. Immunodermatology encompasses a wide range of diseases involving both innate and adaptive immunity. Despite growing research, many aspects remain under investigation. **Conclusion:** The skin's immunological function could be viewed as a complex and multifaceted interplay between signal processing and defense reactions. Immunodermatology continues to expand with ongoing innovations in diagnostics and therapeutics, highlighting its importance in future clinical and research developments.

Keywords: Immunodermatology, innate immunity, adaptive immunity, diagnostic test.

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BACKGROUND

Immunodermatology is a medical specialty that focuses on the diagnosis and treatment of skin problems induced by an inadequate immune response. Immunodermatological testing is critical for detecting and treating a wide variety of illnesses that affect epithelial organs, including the skin, mucous membranes, digestive tracts, and respiratory tracts. The main line of defense that opposes external infections is the role of the skin and mucosal epithelium, preventing pathogens from passing past physical, chemical, and microbiological constraints to the epithelium and tissues.[1,2] Interleukins, key immune mediators involved in cell differentiation, migration, and immune regulation, play a central role in the complex interplay among diverse skin cells like keratinocytes, melanocytes, and Langerhans cells, each with distinct origins and functions.[3] Immunodermatology is a developing discipline of dermatology and immunology, with new studies loaded every year. This review is aimed to elucidate the basics of immunodermatology, diagnostic methods in immunodermatology, and selected diseases and conditions associated with immunodermatology.

REVIEW

In recent years, immunodermatology has evolved rapidly due to advances in molecular biology, genomics, and immunotherapy. Techniques such as single-cell RNA sequencing and spatial transcriptomics have unveiled new insights into skin immune cell interactions in both healthy and diseased states.[4] The role of Th17 cells, IL-23, and tissue-resident memory T cells has been extensively

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documented in chronic inflammatory conditions.[5–7] These discoveries have not only deepened the mechanistic understanding of immunodermatologic diseases but also guided the development of targeted biologic therapies.[8]

Building upon these early discoveries, the recognition of immune-related mechanisms in various dermatological conditions marked a pivotal moment in dermatological research. The concept of the skin immune system (SIS) has been refined to include a highly organized structure of resident and recruited immune cells, collectively referred to as skin-associated lymphoid tissue (SALT).[9,10] These include Langerhans cells, dermal dendritic cells, tissue-resident memory T cells, innate lymphoid cells, and mast cells, which interact dynamically with keratinocytes and structural components of the skin to maintain immune surveillance and respond to external insults.[8,11]

Recent advances have emphasized the unique immunological topography of skin, shaped by its stratified epithelium, adnexal structures, and distinct metabolic and microbial niches. These specialized microenvironments orchestrate both innate and adaptive immune responses, enabling rapid defense through antimicrobial peptides, dendritic cell activation, and pattern recognition receptors, while also supporting antigen-specific memory via tissue-resident T cells, B cells, and regulatory immune networks.[12] This coordinated immune architecture ensures that the skin functions not only as a barrier but also as an active immunological organ capable of immediate and memory-driven responses.[9]

The body's main line of defense against microbes is innate immunity, which acts to reduce infection in the hours after pathogen contact. The skin's innate immune system provides a rapid, non-specific first line of defense.[12] This system is primarily composed of physical barriers (e.g., the stratum corneum), soluble mediators such as antimicrobial peptides (AMPs), and innate immune cells including keratinocytes, Langerhans cells, dermal dendritic cells, mast cells, and innate lymphoid cells (ILCs). Keratinocytes play a central role, not only by forming a structural barrier but also by producing cytokines, chemokines, and AMPs such as cathelicidins and β-defensins in response to microbial invasion or injury.[13,14] Keratinocytes act as immune sentinels by expressing pattern recognition receptors (PRRs), such as Toll-like receptors (TLRs) and NOD-like receptors (NLRs), that detect microbial components and endogenous danger signals.[9,13–15] Upon activation, these cells release proinflammatory cytokines (e.g., IL-1β, IL-6, TNF-α), chemokines, and antimicrobial peptides like cathelicidin and β-defensins, which limit pathogen invasion and modulate immune recruitment.[15,16]

Key to the innate immune response is the recognition of conserved microbial components, known as pathogen-associated molecular patterns (PAMPs), and host-derived danger signals (DAMPs) via PRRs such as TLRs and NLRs.[17] Activation of these receptors leads to downstream signaling cascades, culminating in the secretion of proinflammatory cytokines (e.g., IL-1β, TNF-α) and chemokines that recruit neutrophils, monocytes, and other immune effectors.

Additional innate players, including mast cells, ILCs, natural killer (NK) cells, and macrophages, contribute to inflammation, tissue repair, and microbial defense, often interacting with the skin's commensal microbiota to maintain homeostasis or trigger inflammation.[12,18] Mast cells and ILCs, particularly ILC2s and ILC3s, are increasingly recognized for their roles in cutaneous immune homeostasis and disease. Mast cells respond rapidly to stimuli by releasing histamine, proteases, and cytokines, contributing to both host defense and hypersensitivity reactions. ILCs mirror the function of T-helper cells and modulate epithelial barrier function and tissue repair.[18,19] Importantly, innate immune cells within a highly interactive network, engaging in continuous crosstalk with adaptive immune components and the resident microbiota. These interactions are critical for initiating appropriate inflammatory responses, facilitating pathogen clearance, and directing the nature and magnitude of downstream adaptive immunity in a context-dependent manner.[20]

The adaptive immune system of the skin comprises antigen-specific responses mediated by T and B lymphocytes.[12,21] Upon antigen recognition and activation by antigen-presenting cells (APCs) such as Langerhans cells and dermal dendritic cells, naïve T cells differentiate into effector subsets (e.g., Th1, Th2, Th17, Treg), while B cells may produce antibodies or function as antigen-presenting cells.[7,22] This system provides immunological memory and precision, allowing tailored responses to pathogens, allergens, or autoantigens. Resident Langerhans cells and dermal dendritic cells further survey the environment and initiate adaptive responses by presenting antigens to T cells.[9,15]

A hallmark of cutaneous adaptive immunity is the presence of tissue-resident memory T cells (TRM), especially CD8+ TRM in the epidermis and CD4+

TRM in the dermis. These cells persist long-term after infection or inflammation and can rapidly initiate secondary responses upon antigen re-exposure.[23,24] Additionally, regulatory T cells (Tregs) are enriched in the skin, particularly around hair follicles, where they modulate immune responses, prevent autoimmunity, and support tissue repair. The balance between effector T cells and Tregs is critical for maintaining skin immune homeostasis.[25]

Although less abundant than T cells, B cells contribute to skin immunity through local antibody production and antigen presentation.[26] Recent studies suggest the presence of inducible skin-associated lymphoid tissue (iSALT) during inflammation, where B cell activity may be enhanced. Furthermore, autoimmune skin diseases such as pemphigus vulgaris and bullous pemphigoid highlight the pathological roles of autoreactive antibodies. The dynamic interplay between skin-resident B cells, antibodies, and local cytokine environments continues to be an emerging area in immunodermatology research.[27]

Extending from the fundamental mechanisms of antigen recognition, a comprehensive understanding of the immune system not only underpins the pathogenesis of immunodermatological diseases but also informs various diagnostic approaches. Procedures such as drug provocation testing, skin patch testing, skin prick testing, and the autologous serum skin test are essential tools used to evaluate hypersensitivity reactions, identify allergens, and explore autoimmune involvement in chronic skin disorders.[28–30]

Drug provocation testing (DPT), also known as controlled drug challenge, remains the gold standard for diagnosing non-immediate and immediate hypersensitivity reactions when clinical history and in vitro or skin testing yield inconclusive results.[21,28,31] It involves the supervised administration of a suspected drug in gradually increasing doses to reproduce a hypersensitivity reaction under controlled settings. The test is particularly valuable for evaluating adverse cutaneous drug reactions, including delayed-type hypersensitivity, urticaria, and fixed drug eruptions and also requires specialized medical facilities and trained staff.[12,32]

The primary indication for DPT is to confirm or exclude drug hypersensitivity when other diagnostic methods, such as skin tests or in vitro assays, are negative or inconclusive. DPT is particularly indicated in cases of suspected non-severe cutaneous adverse drug reactions, such as maculopapular eruptions, fixed drug eruptions, and mild urticaria or angioedema, especially when accurate identification of the offending drug is essential for future treatment decisions.[28,33] It is also used to assess tolerance to alternative drugs within the same class or to verify drug tolerance following desensitization protocols. In some cases, DPT can aid in identifying cross-reactivity patterns, particularly with beta-lactam antibiotics, NSAIDs, or local anesthetics.[32,34]

Prior to DPT, careful patient selection and risk stratification are essential. The test is contraindicated in patients with a history of severe life-threatening reactions such as Stevens-Johnson Syndrome, toxic epidermal necrolysis, drug reaction with eosinophilia and systemic symptoms (DRESS), or anaphylaxis.[28,35] Comprehensive assessment, including a detailed clinical history, prior skin tests (e.g., patch or prick testing), and laboratory evaluation, helps identify candidates in whom DPT can be safely conducted. Protocols may vary depending on the suspected drug, type of hypersensitivity, and clinical setting, but most involve incremental dosing with close monitoring of systemic and cutaneous responses.[36–38]

However, DPT not only serves as a diagnostic tool but also guides therapeutic decisions by confirming or excluding drug allergies, thereby reducing unnecessary drug avoidance and facilitating safe pharmacologic management.[39] In dermatologic practice, it is particularly useful for confirming causality in cases of drug-induced exanthems, phototoxic reactions, and delayed hypersensitivity to topical or systemic agents. Proper interpretation of DPT results requires correlation with clinical context and other immunologic tests, underscoring the importance of multidisciplinary expertise in managing complex immunodermatologic cases.[32,40]

Given the complexity of immune-mediated skin reactions, selecting the appropriate diagnostic modality is critical to accurate evaluation and management.[35] While DPT is instrumental in assessing immediate and some delayed drug hypersensitivities, other methods are more suitable for investigating chronic eczematous conditions and contact allergens. In this context, patch testing emerges as the gold standard for diagnosing type IV hypersensitivity reactions, particularly allergic contact dermatitis.[41,42]

Patch testing is a standardized diagnostic method primarily used to identify type IV (delayed-type) hypersensitivity reactions, particularly in patients with suspected allergic contact dermatitis (ACD). It involves the topical application of allergens under occlusion to intact skin, typically on the back, to assess the patient's response after 48 to 96 hours. The goal is

to reproduce and interpret localized inflammatory reactions that mirror the clinical manifestations seen in contact allergy[21,41,43].

Patch testing is most useful in evaluating chronic eczema, hand dermatitis, facial dermatitis, and occupational skin disorders.[44,45] A positive patch test indicates sensitization but does not always imply clinical relevance; hence, results must be interpreted in the context of the patient's exposure and history. False positives and irritant reactions can occur, emphasizing the importance of trained dermatological evaluation and consistent application protocols.[41,46]

Despite its value, patch testing has limitations. Patch test cannot detect immediate-type hypersensitivity (e.g., urticaria or anaphylaxis), and not all allergens are available in a suitable testable form. Additionally, some reactions may be missed due to inadequate skin penetration or late-onset responses.[41,47] While there are no apparent contraindications to patch testing, pregnant women should avoid it. Despite the fact that the substance is absorbed in trace amounts and does no damage to the baby, pregnancy-related immune changes influence the reaction to patch testing.[48] Advances such as atopy patch testing, photo-patch testing, and the use of molecular allergens are expanding the utility of this diagnostic method in both clinical and research settings.[49,50]

To address the limitations of patch testing in detecting immediate hypersensitivity reactions, the skin prick test (SPT) serves as a complementary diagnostic modality. Particularly suited for identifying IgE-mediated responses, SPT is widely utilized in immunodermatologic practice to evaluate conditions such as urticaria, anaphylaxis, and allergic contact dermatitis with suspected type I hypersensitivity components.[21,51] SPT plays a central role in evaluating cutaneous manifestations of allergic diseases such as atopic dermatitis, urticaria, and angioedema, particularly when these are triggered by aeroallergens, food, or drugs. The test involves the percutaneous introduction of standardized allergen extracts into the skin, typically the volar forearm or upper back, followed by observation of a wheal-and-flare reaction within 15–20 minutes. A positive response suggests sensitization and supports a clinical diagnosis of IgE-mediated allergy.[52,53]

SPT is valued for its simplicity, safety, and rapid results, making it a first-line test in allergy work-ups. It has high sensitivity and specificity when performed with standardized extracts and interpreted in correlation with clinical history.[54] In dermatology, this is especially relevant when investigating atopic dermatitis flares related to environmental allergens or identifying triggers in chronic spontaneous urticaria or food allergy-associated dermatoses. The test can also be used to evaluate potential cross-reactivity in patients with polysensitization or coexisting atopic conditions.[55,56]

However, SPT is not without limitations. False positives may occur due to dermographism or improper technique, while false negatives can result from antihistamine use, chronic skin conditions, or insufficient allergen potency.[54] Therefore, a careful clinical correlation and, if necessary, additional serologic or provocation tests are recommended for a definitive diagnosis. SPT is generally contraindicated in patients with severe dermatographism, extensive eczema, or a history of anaphylaxis to the tested allergen.[57,58]

While SPT is effective for identifying IgE-mediated allergies, it is often insufficient in evaluating chronic spontaneous urticaria (CSU), especially when an autoimmune mechanism is suspected. In such cases, the autologous serum skin test (ASST) has emerged as a valuable in vivo diagnostic tool for detecting functional autoantibodies or other serum factors capable of inducing mast cell degranulation.[59,60]

ASST involves the intradermal injection of the patient's own serum to detect circulating factors, most notably autoantibodies against FcεRI or IgE, that can induce mast cell degranulation and histamine release.[59,61] ASST has demonstrated a sensitivity of approximately 70% and a specificity of 80%, making it a useful screening method for identifying autoimmune urticaria A positive wheal-and-flare response suggests autoreactivity and may support a diagnosis of autoimmune urticaria. Clinically, a positive ASST has been associated with more severe disease manifestations, including higher urticaria activity scores and an increased risk of angioedema. Conversely, a negative ASST result may predict a better prognosis, with some studies suggesting a higher likelihood of disease remission within two years . These associations underscore the potential role of ASST in guiding management decisions and prognostication in CSU patients.[61,62]

While ASST is widely utilized due to its simplicity and low cost, challenges remain regarding its specificity and standardization, warranting cautious interpretation alongside clinical correlation and other immunologic assessments. The test lacks standardization, and its interpretation can be subjective, leading to variability in results.[59,62,63]

These limitation in diagnostic tools highlight the need for a broader understanding of immune-mediated skin conditions. One of the most frequently encountered is allergic contact dermatitis (ACD), which arises from immune reactions to typically harmless environmental substances. ACD is a prevalent immunologically mediated skin disorder characterized by an eczematous reaction following exposure to specific environmental allergens. It represents a classic example of a delayed-type (Type IV) hypersensitivity reaction, wherein sensitized individuals develop cutaneous inflammation upon re-exposure to allergens such as nickel, fragrances, preservatives, and certain topical medications. ACD is more common in women than in men and is the most common type of occupational skin disease. ACD is an eczematous skin reaction to chemicals at non-toxic doses that involves immune cell sensitization and often develops upon repeated exposure to the agent. In contrast, the same drug has no effect on people who are not sensitized.[1,64]

The pathogenesis of ACD involves two distinct phases, sensitization and elicitation. During the sensitization phase, allergens penetrate the stratum corneum and are captured by epidermal Langerhans cells, which process and present them to naïve T cells in regional lymph nodes, leading to the development of memory T cells.[65] Upon subsequent exposure, these memory T cells recognize the allergen and initiate an inflammatory cascade, resulting in the clinical manifestations of ACD. While traditionally associated with a Th1-dominant response, recent studies suggest that certain allergens, such as nickel, may also elicit Th2-mediated pathways, indicating a more complex immunological interplay.[35,48,66]

Clinically, ACD presents as pruritic, erythematous, and vesicular lesions localized to the site of contact with the offending allergen. Diagnosis primarily relies on a thorough patient history and physical examination.[30,67] However, patch testing remains the gold standard for identifying specific contact allergens. This diagnostic procedure involves the application of standardized allergen panels to the skin under occlusion, typically on the back, with readings taken at 48 and 72 hours to assess for delayed hypersensitivity reactions.[44,66,68]

Management of ACD centers on the identification and avoidance of the causative allergen. Topical corticosteroids are the first-line treatment to reduce inflammation and alleviate symptoms. In more severe or widespread cases, systemic corticosteroids may be warranted. Additionally, patient education on allergen avoidance and the use of barrier protection strategies are crucial components of long-term management.[68,69]

Recent advances in immunodermatology have introduced novel diagnostic approaches that complement traditional patch testing in ACD.[48] Molecular allergen characterization now enables the identification of specific haptens and their T-cell epitopes, allowing for more precise and personalized allergen profiling. Transcriptomic and proteomic analyses of lesional skin and peripheral blood have revealed distinct cytokine signatures, such as IL-17 and IFN-γ, that help differentiate ACD from other eczematous dermatoses. In vitro assays like the lymphocyte transformation test (LTT) and ELISpot offer non-invasive methods to detect allergen-specific T-cell reactivity, providing diagnostic alternatives when patch testing is inconclusive or contraindicated.[70] Additionally, non-invasive imaging modalities such as reflectance confocal microscopy (RCM) and optical coherence tomography (OCT) are being explored to visualize epidermal and dermal changes in real time. These innovations mark a significant step toward precision diagnostics in ACD, although broader clinical validation and accessibility remain ongoing challenges.[66,68,71]

While ACD results from external allergen exposure, other chronic inflammatory skin diseases involve more complex underlying mechanisms. Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder characterized by a complex interplay of genetic, immunologic, and environmental factors.[1,72] A hallmark of AD is skin barrier dysfunction, often attributed to mutations in the filaggrin (FLG) gene, which encodes a protein essential for epidermal barrier integrity. Loss-of-function mutations in FLG compromise the skin's barrier, leading to increased trans-epidermal water loss and heightened susceptibility to environmental allergens and irritants. This barrier impairment facilitates colonization by pathogens such as Staphylococcus aureus, which is detected in over 90% of AD lesions and exacerbates inflammation through the release of superantigens and toxins. Immunologically, AD is predominantly driven by a Th2-skewed response, with elevated levels of interleukins IL-4 and IL-13 promoting IgE production and eosinophil activation.[55,73–75]

The exact cause of AD is unknown, but it is believed to result from a combination of genetic, environmental, and immune system factors. A key feature of AD is a compromised skin barrier, which allows moisture to escape and irritants or allergens to enter more easily. This can lead to inflammation and

the characteristic symptoms of AD. Three major factors contribute to the development of atopic dermatitis, a weakened epidermal constraint, immunological abnormalities, and an altered skin microbiota.[64] Clinically, patients often present with pruritic, eczematous lesions and may exhibit elevated serum IgE levels and peripheral eosinophilia, correlating with disease severity.[19,74,76]

The diagnosis of AD, also known as atopic eczema, is primarily clinical, based on characteristic features such as chronic or relapsing eczematous lesions, pruritus, and a personal or family history of atopy. Physical examination often reveals flexural distribution in older children and adults, and facial or extensor involvement in infants. While no single laboratory test confirms the diagnosis, adjunctive tests may support clinical findings. Elevated serum IgE levels and peripheral eosinophilia are frequently observed in patients with moderate-to-severe AD and may indicate a more allergic or extrinsic phenotype, although their presence is neither specific nor required for diagnosis. Importantly, recent guidelines emphasize that elevated IgE should not be used in isolation to define disease severity or guide treatment, as intrinsic (non-IgE mediated) variants of AD also exist. Patch testing may be warranted in adults with atypical or treatment-resistant presentations to evaluate for concomitant allergic contact dermatitis. Advances in diagnostic precision now also consider emerging biomarkers and disease endotyping, which may inform treatment decisions and predict therapeutic response, particularly in the era of biologic and targeted therapies.[73,74,77]

Management strategies focus on restoring the skin barrier and modulating the immune response. Regular use of moisturizers, particularly those containing ceramides and other physiological lipids, is fundamental in repairing barrier function and reducing flare-ups. Foundational care includes consistent use of emollients containing ceramides, urea, or colloidal oatmeal, which support barrier repair, reduce transepidermal water loss, and decrease the need for pharmacologic agents. Topical anti-inflammatory treatments, primarily corticosteroids and calcineurin inhibitors (such as tacrolimus and pimecrolimus), remain first-line therapies for acute flares and maintenance in sensitive areas. Non-steroidal topical agents like crisaborole, a PDE-4 inhibitor, provide alternatives for mild-to-moderate AD, especially in pediatric populations. In moderate-to-severe cases unresponsive to topicals, systemic treatments are considered. Dupilumab, a monoclonal antibody targeting the IL-4 receptor α subunit, has revolutionized AD treatment by interrupting IL-4 and IL-13 signaling and significantly reducing disease severity and pruritus, with a favorable safety profile. Emerging biologics such as tralokinumab (anti–IL-13) and lebrikizumab, along with Janus kinase (JAK) inhibitors like upadacitinib and abrocitinib, offer new options by modulating broader immune pathways involved in AD pathogenesis.[74,78] Adjunctive therapies include phototherapy (narrowband UVB), or natural compounds particularly for patients with widespread or recalcitrant disease, and antimicrobial strategies to address Staphylococcus aureus colonization, such as bleach baths and intranasal mupirocin. Education on trigger avoidance, appropriate skincare routines, and treatment adherence is crucial, as is psychological support, given the chronic burden of disease and its impact on quality of life. The future of AD management is increasingly driven by precision medicine approaches, with ongoing research into endotyping and biomarker-guided therapies to optimize outcomes.[19,72,79,80]

Following the discussion of atopic dermatitis, it is important to distinguish it from other pruritic skin disorders such as chronic urticaria, which presents with distinct clinical and immunopathological features. In contrast to AD, which is characterized by persistent eczema and barrier dysfunction, chronic urticaria involves transient wheals or hives and is often associated with underlying autoimmune or idiopathic immune activation. Urticaria, more often referred to as hives, is a condition in which pruritic, erythematous papules or plaques with superficial skin edema occur on a periodic basis. Acute urticaria is distinguished from chronic urticaria by the duration of the symptoms. Acute urticaria, defined as hives lasting less than six weeks, affects approximately 15%–23% of the population, though cases are likely underreported due to the disease's brief duration.[81–83]

Urticaria and/or angioedema that occurs frequently are symptoms of chronic urticaria. Chronic spontaneous urticaria (CSU) and chronic inducible urticaria (CIndU) are the two categories into which the current definitions and classifications divide chronic urticaria based on its development and chronological course. A spontaneous incidence of wheals and/or angioedema lasting six weeks or longer is referred to be CSU. These terms are interchangeable with "chronic urticaria" and "chronic idiopathic urticaria." The term "CIndU" refers to the occurrence of wheals that are caused by physical factors (such as touch or intense pressure) and last for a total of six weeks or

longer. It's the same as "physical urticaria." According to coding records in health systems across the globe, the point prevalence of chronic urticaria varies from 0.1 to less than 1%. The majority of patients are above 20, and females are impacted at least twice as frequently as males. The prevalence ranges from less than 1% to nearly 5% in youngsters.[82,84]

At least 2 possible causes of CSU, 2 autoimmune endotypes, are recognized with different types of autoantibodies that have been associated with the activation of skin mast cells. Type I autoimmune endotype of CSU (type I aiCSU) also called autoallergic CSU which is characterized by aberrant production of IgE antibodies. In contrast to classical type I hypersensitivity and allergy, which involve exogenous allergens, type I aiCSU is characterized by IgE antibodies directed to self-antigens (also called autoallergens). Similarly, type IIb hypersensitivity is characterized by an antibody-dependent process in which specific IgG antibodies bind to autoantigens to create pathogenic states. Therefore, patients with CSU who harbor IgG autoantibodies have been classified into the autoimmune type IIb endotype, different to type IIa that involves cytolytic destruction of targeted cells. An overlap between the 2 endotypes has been recently reported.[63,85] Numerous CSU patients claim that their illness has gotten worse in reaction to triggers like stress, infections, certain meals, or taking nonsteroidal anti-inflammatory medicines.[86] A recent study indicates that the mast cell-specific Mas-related G protein-coupled X2 receptor (MRGPRX2) plays a critical role. Stress-related neuropeptides, defensins, pseudoallergens, and other medicines can all activate this.[64,83]

For patients with suspected CSU, the diagnostic and prognostic workup must include a thorough medical history, physical examination, basic tests (such as differential blood count, C-reactive protein (CRP), and/or erythrocyte sedimentation rate (ESR), as well as evaluation of disease activity, impact on quality of life, and disease control. A physical examination and a comprehensive evaluation of the patient's medical history are necessary to diagnose chronic urticaria. A thorough history should be taken, covering the following topics: the onset time of symptoms; the length of time that a particular wheal occurs; the size, shape, color, and distribution of wheals; the characteristics of the wheals; and personal and family history.[62,84,87] Treatment for chronic urticaria aims to relieve symptoms and improve the patient's quality of life. The first line of treatment involves second-generation antihistamines, with the dosage adjustable up to four times the standard dose. However, if symptoms remain intolerable after 2–4 weeks, omalizumab can be added. If symptoms persist after 6 months, cyclosporine should be considered.[86]

In addition to chronic urticaria, other immune-mediated skin conditions such as cutaneous adverse drug reactions (CADR) represent a significant diagnostic and therapeutic challenge due to their variable clinical manifestations and complex immunopathogenesis. Both minor erythematous skin lesions and considerably more severe reactions, such Lyell's syndrome, are included in this section. A diverse range of clinical patterns without particular characteristics indicating drug causation are included in this diverse field. Finding the causal factor is quite important.[40,88] The majority of systemic medications have the potential to cause challenging cutaneous responses. Contrast media and some drug classes, including allopurinol, antibiotics, anticonvulsants, antineoplastic medications, and nonsteroidal anti-inflammatory medicines, are recognized to be frequent offenders. Antibiotics and anti-epileptics develop toxidermia problems in 1% to 5% of treatments.

Immunological mechanisms are frequently involved in CADR. In these situations, skin symptoms may manifest alone or in conjunction with symptoms that impact many other organs. Anaphylaxis, acute generalized exanthematous pustulosis (AGEP), drug-induced hypersensitivity syndrome (DIHS), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) are among the disorders classified under the category of severe cutaneous adverse drug reactions (ADRs). Urticaria and anaphylaxis are two of these symptoms that are usually brought on by IgE-mediated type I hypersensitivity reactions. On the other hand, severe cutaneous adverse drug reactions (ADRs) other than anaphylaxis and exanthematous eruptions are delayed reactions involving type IV hypersensitivity reactions mediated by T cells. T cell-mediated reactions as the underlying immunological mechanism are further supported by the identification of drug-reactive T cells and their correlation with human leukocyte antigen (HLA) in delayed adverse drug reactions.[89,90]

The first and most crucial step in managing CDRs is to stop the offending drug as soon as possible. Modifying the dosage or discontinuing the offending agent is the most crucial step in treating an ADR. The symptomatic treatment later depends on the clinical manifestation that occurred.[36,91]

If urticaria occurred, treat with antihistamines such as diphenhydramine, cetirizine, levocetirizine, and

loratadine. Topical corticosteroids and oral antihistamines are effective for treating exanthematous drug eruptions. Symtompatic treatment of pruritus and skin inflammation of AGEP can be managed with topical corticosteroids. SJS and TEN are severe ADRs and should be managed in a tertiary care facility that can treat burns patients. In addition to stopping the offending agent, management should focus on supportive care and preventing short- and long-term complications. The patient will need wound care, fluid management, pain control, and management of other complications such as sepsis. Besides supportive care, pharmacotherapy with cyclosporin or etanercept might be beneficial in cases of severe skin involvement. Anaphylaxis constitutes a medical emergency. The offending agent should be immediately stopped, and IM epinephrine should be administered promptly.[91,92]

CONCLUSION

The skin represents the body's first line of defense, functioning as an integrated physical, chemical, and microbiological barrier that protects underlying tissues from environmental insults and microbial invasion. Each component of the skin's immune architecture contributes uniquely to host defense, forming a sophisticated network that mediates both innate and adaptive immune responses. This immunological complexity reflects a dynamic interplay between cellular signaling, pathogen recognition, and tissue homeostasis. Immunodermatology represents a rapidly evolving field at the interface of dermatology and immunology, offering critical insights into the mechanisms underlying a wide spectrum of immune-mediated skin disorders. As immunodermatologic research continues to progress, this review highlights current concepts in immunodermatology and underscores the need for continued research to address the growing prevalence and complexity of immune-mediated dermatoses. Future advances in immunophenotyping, genomics, and therapeutic development are expected to refine diagnostic accuracy and optimize management approaches, ultimately improving patient outcomes in clinical dermatology.

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