Clinical Outcomes of Switching from Original Omalizumab to an Intended Copy Biosimilar in Chronic Urticaria: A Case Series Highlighting Global Regulatory Discrepancies

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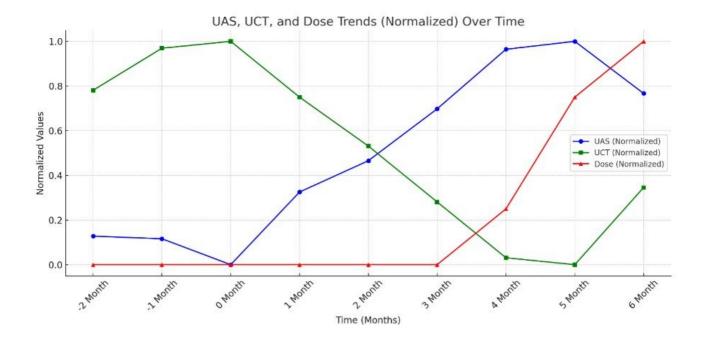
Introduction & Objectives: Omalizumab, a monoclonal anti-IgE antibody, is a recommended treatment for chronic spontaneous urticaria (CSU) unresponsive to antihistamines. While rigorously tested biosimilars of omalizumab have been approved in some regions, In India an "intended-copy biosimilar" (ICB) was introduced in 2020, with approval based on structural similarity rather than clinical trials. This study presents a real-world case series comparing the efficacy and safety of this ICB omalizumab with the original biologic in CSU management.

Materials & Methods: We retrospectively reviewed 9 CSU patients (mean age 37.11 ± 13.24 years) who had been transitioned from original omalizumab to an ICB due to unavailability of the original biologic. Disease control was assessed using Urticaria Activity Score (UAS) and Urticaria Control Test (UCT) scores before and after the switch.

Results: Prior to switching, patients demonstrated well-controlled disease with low mean UAS (3.77 \pm 2.73 and 3.66 \pm 2.39 at two and one month prior, respectively) and high mean UCT scores (14.55 \pm 1.23 and 15.22 \pm 0.66). Following the transition to ICB omalizumab, disease control progressively deteriorated, with mean UAS increasing to 12.11 \pm 6.62 and mean UCT decreasing to 11.77 \pm 3.19 by month 5. Dose escalations were required in several patients to regain partial disease control. Despite increased doses, disease control with ICB omalizumab was not equivalent to that achieved with the original biologic. **

Conclusion: This case series suggests potential differences in efficacy between ICB omalizumab and the original biologic in treating CSU. While ICBs offer cost advantages, their use raises concerns about efficacy and the need for increased dosing. The findings highlight global discrepancies in biosimilar approval processes and the importance of rigorous clinical testing for all biosimilar products. We suggest there is a need for a standardized nomenclature to differentiate between various types of biosimilar products.

Figure 1_ Graphical representation of UAS, UCT, and Average Dose per patient of the drug and their relation (Data normalized)



An unusually severe case of shiitake mushroom dermatitis with features of drug reaction with eosinophilia and systemic symptoms

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Introduction & Objectives: Shiitake mushroom dermatitis is a well-documented phenomenon in the literature seen after consuming raw or undercooked shiitake mushrooms (Lentinus edodes). It is a toxic dermal reaction characterised by widespread pruritic flagellate erythema within 24 to 72 hours after shiitake mushroom consumption. However, shiitake dermatitis with systemic features of drug reaction with eosinophilia and systemic symptoms (DRESS) are rare. We report a case of severe shiitake mushroom dermatitis with atypical systemic features meeting DRESS criteria. A 51-year-old man presented with acute unilateral periorbital oedema and pruritic flagellate erythema with no obvious drug precipitants. He was initially managed as allergic contact dermatitis in the emergency department. Further inquiry revealed a history of raw shiitake mushroom ingestion 48 h before the onset of symptoms, which led to a working diagnosis of shiitake mushroom dermatitis. Rheumatological and other drug causes of flagellate erythema and periorbital oedema were excluded from the patient's history, clinical and laboratory findings.

Materials & Methods: -

Results: Skin biopsies of the patient's flagellate erythema showed mixed spongiotic and interface inflammatory reactions with a perivascular lymphocytic infiltrate and marked eosinophilia supportive of shiitake mushroom dermatitis. Thrice daily topical corticosteroids of methylprednisolone 0.1% fatty ointment and betamethasone dipropionate 0.05% ointment to his face and body under wet wraps were commenced with good symptomatic relief. The patient initially presented with apyrexia and mild eosinophilia but then developed pyrexia, hypereosinophilia, neutrophilia and transaminitis, with widespread morbilliform eruption with dorsal oedema of his hands. His unilateral periorbital oedema also progressed to bilateral periorbital oedema without visual compromise. Based on the above investigations, the patient was suspected of having probable DRESS, with a RegiSCAR score of 5. The patient required an escalation in therapy to oral prednisolone to achieve clinical and biochemical resolution of his symptoms.

Conclusion: We report an unusually severe case of shiitake mushroom dermatitis complicated by systemic features compatible with DRESS. Our case highlights that shiitake mushroom dermatitis may not always be a benign, self-limiting disease, and underscores the importance of prompt recognition and management of shiitake dermatitis, which may progress to DRESS and necessitate prolonged oral and topical corticosteroid therapy.

Single-Cell Transcriptomic Analysis Reveals Immune Dysregulation and Epidermal Dysfunction in Primary Cutaneous Amyloidosis

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Introduction & Objectives: Primary cutaneous amyloidosis (PCA) is a chronic pruritic skin disorder characterized by localized deposition of amyloid proteins in the skin without systemic involvement. Although chronic friction, genetic predisposition, and environmental factors have been implicated, the underlying pathogenesis remains poorly understood. This study aims to characterize the immune and epidermal cellular landscape of lichen PCA lesions, with a particular focus on keratinocyte dysfunction and immune dysregulation.

Materials & Methods: Single-cell RNA sequencing (scRNA-seq) was conducted on skin samples from three patients with PCA and three healthy controls (HCs) to identify major cell populations and assess differential gene expression and cellular phenotypes.

Results: scRNA-seq analysis revealed nine major cell types in PCA lesions. Keratinocytes exhibited upregulation of apoptosis-related pathways and pro-inflammatory genes, along with altered differentiation trajectories, including terminal differentiation arrest in specific subpopulations. Enhanced IL-13 signaling was associated with keratinocyte dysfunction, while increased IL-4 and IL-31 expression contributed to a pro-inflammatory milieu. Furthermore, two previously uncharacterized macrophage subsets—KRT1+ macrophages and IGFBP7+ macrophages—displayed reduced phagocytic function, impairing amyloid fibril clearance and promoting their accumulation in the skin.

Conclusion: This study identifies IL-13-driven keratinocyte dysfunction and impaired macrophage-mediated clearance as central mechanisms in PCA pathogenesis. These insights advance our understanding of PCA and may guide the development of targeted therapies focused on modulating IL-13 signaling and restoring immune homeostasis in affected skin.

A review of potential pathomechanisms of dupilumab-associated ocular surface disease

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Introduction & Objectives:

Dupilumab-associated ocular surface disease (DAOSD) affects up to one-third of patients receiving dupilumab for atopic dermatitis (AD), with real-world data indicating a discontinuation rate of approximately 5%. Notably, this adverse effect is rarely observed in patients treated with dupilumab for non-AD conditions. This suggests a unique interaction between AD and the development of DAOSD.

This narrative review aims to synthesise current evidence on the pathomechanisms and predictive biomarkers of DAOSD.

Materials & Methods:

A systematic search was conducted using terms related to "dupilumab" and "ocular surface disease" (e.g. dry eye, conjunctivitis, eye inflammation) across Medline (Ovid), Pubmed and Embase. Original articles, which explored clinical predictors or pathogenesis of DAOSD were included.

Results:

Emerging evidence suggests that DAOSD is driven by multifactorial and interrelated pathways. Patients with AD, unlike those with asthma, eosinophilic oesophagitis, or chronic rhinosinusitis with nasal polyposis, are at higher risk—likely due to a predisposition for pre-existing ocular surface disease (OSD), which compromises epithelial barrier function. This may permit increased penetration of serum dupilumab into ocular tissues, where it can exert direct local effects.

Blockade of IL-4 and IL-13 reduces the stimulus for goblet cell hyperplasia and mucin secretion, resulting in decreased mucin production on the ocular surface, which could cause both irritative dry eye symptoms and affect the microbiome. When an altered microbiome is combined with dupilumab's known ability to unmask a TH1 inflammatory, it seems plausible that this can promote a persistent cycle of Th1 and Th17-driven inflammation.

Conclusion:

This review outlines potential mechanisms underlying DAOSD, particularly in the context of AD. Our findings support the hypothesis that DAOSD arises from the complex interplay of impaired barrier function, mucin deficiency, microbiome disruption, and immune dysregulation. Further research is needed to elucidate these pathways and inform targeted strategies for prevention and management.

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Intertriginous and Symmetrical Flexural Exanthema: A Case Induced by a Combination of Paracetamol, Codeine, and Caffeine

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Introduction & Objectives Baboon syndrome is a rare cutaneous reaction often associated with delayed-type (Type IV) hypersensitivity, mediated by T lymphocytes. The term "Baboon syndrome" refers to the characteristic symmetrical erythematous involvement of the buttocks and inguinal folds, resembling the natural pigmentation seen in baboons. This condition is most frequently triggered by medications such as β -lactam antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs), or certain anesthetics. The present case is linked to the intake of an analgesic combining paracetamol, codeine, and caffeine.

Materials & Methods This study presents a single clinical case of a drug-induced cutaneous eruption consistent with Baboon syndrome. Data were collected through direct clinical observation, patient interview, and review of medical records. The diagnostic workup included a comprehensive physical examination and laboratory testing to rule out systemic involvement, infection, or alternative dermatological diagnoses. A skin biopsy was not performed due to the acute onset of symptoms, the typical clinical presentation, and the favorable response to symptomatic treatment. The diagnosis was based on the temporal association between drug intake and rash onset, the symmetrical distribution of lesions, and the exclusion of other potential causes. The resolution of symptoms following discontinuation of the suspected medication further supported the diagnosis.

Case Presentation A 31-year-old woman with no significant medical history presented to the emergency department with a skin rash that appeared one day after taking two capsules of a medication containing 400 mg paracetamol, 20 mg codeine, and 62.5 mg caffeine for headache relief. She reported a similar episode three months earlier after taking the same medication, with skin lesions appearing four days post-intake and resolving spontaneously within two weeks, without medical consultation. On admission, the patient was alert, hemodynamically and respiratorily stable, afebrile, and exhibited no systemic symptoms. Dermatological examination revealed a bilateral and symmetrical pruritic erythematous-papular eruption predominantly involving the popliteal fossae and perimammary areas. A V-shaped erythema was observed in the inquinal region, with extension to the inner thighs and lower back. In some areas, the lesions had coalesced into large purpuric plaques. There was no mucosal involvement, and Nikolsky's sign was negative. The total affected body surface area was estimated at 16%. No lymphadenopathy was detected, and the remainder of the physical examination was unremarkable. Laboratory investigations, including markers of systemic inflammation and infectious screening, were within normal limits. The suspected medication was immediately discontinued. Treatment with oral antihistamines and topical corticosteroids led to complete resolution of the lesions within one week. The diagnosis of Baboon syndrome was established based on clinical history, symptom chronology, and exclusion of other possible etiologies.

Conclusion Baboon syndrome is a rare but benign drug-induced cutaneous eruption. Early recognition and prompt discontinuation of the offending drug are essential for rapid symptom resolution. Confirming the diagnosis is important to prevent recurrence upon future exposure to the same or cross-reactive medications.

RANK and RANK-L in dermatology: a comprehensive review

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Introduction & Objectives:

The receptor activator of NF-kB (RANK) and its ligand (RANK-L) are key regulators initially recognized for their role in bone metabolism but have been implicated in various epithelial and immune functions. Beyond its role in skeletal biology, RANK-L has been identified as a mediator in skin immunity and tumorigenesis. We aimed to study its role in dermatology in a comprehensive systematic review.

Materials & Methods:

A literature search was performed in Scopus, Web of Science, PubMed and Cochrane using keywords related to RANKL and dermatology related conditions. English-language articles on RANK-RANK-L signaling in skin immunity, inflammation, wound healing, and tumorigenesis were included. Non-dermatological studies were excluded. Relevant articles were selected based on title, abstract, and full-text review.

Results:

RANK-RANK-L signaling axis regulates dendritic cell functions, such as enhancement of T-cell activation, the release of pro-inflammatory cytokines, and the prolongation of cell survival. RANK-L, expressed on inflamed keratinocytes, activates epidermal Langerhans cells (LCs), and modulates peripheral CD4+CD25+ regulatory T cells (Treg) and peripheral tolerance. Additionally, RANK-L transcription is upregulated during the hair follicle growth phase. In pathological contexts, RANK-RANK-L signaling has been implicated in skin carcinogenesis, including melanoma, extramammary Paget's disease (EMPD) and cutaneous angiosarcoma. Therapeutic blockade strategies have shown to improve both survival and progression in melanoma and EMPD. In inflammatory skin diseases, there is a significant increase in RANK-L level in psoriasis compared to cutaneous lupus erythematosus (CLE), suggesting a role in disease pathogenesis. There are also experiments highlighting RANK-L's role in wound healing. In infectious skin diseases, RANK-L modulates macrophages during Leishmania infection. RANK-L signaling induces antiviral CD8+ T cell responses in herpes simplex virus type 1 (HSV-1) infection and candidiasis.

Conclusion:

RANK-RANKL signaling is considered as regulator of skin immunity, tumorigenesis, inflammation, and infection. Experimental and clinical studies are required to further elucidate the key points in the exact role of RANK or RANK-L in dermatology disorders.

Environmental Pollutant-Induced Skin Barrier Dysfunction and Allergic Sensitization: A Narrative Review

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Introduction and Objectives

Allergic skin diseases such as atopic dermatitis and urticaria are becoming more prevalent, which has led to increasing interest in environmental factors related to skin barrier failure. Toxin entry is blocked, as is immune response, via the outermost epidermal layer. When breached, this shield allows for the entry of allergens and first contact with the immune system, thus contributing to the "outside-in" hypothesis. This article examines the effects of environmental pollution on the skin barrier and allergic skin disease.

Materials and Methods

A comprehensive search was performed in PubMed, Web of Science, Scopus, and Google Scholar for articles published in English until April 2024. Inclusion criteria were peer-reviewed studies addressing the effect of environmental pollutants on skin barrier function, epidemiological associations with atopic skin diseases, and clinical or mechanistic information. Of the 40 papers found, 26 were relevant according to methodological and thematic criteria. Data such as types of pollutants, exposure, biological mechanisms, immunological responses, and clinical outcomes were extracted. Results were qualitatively analyzed.

Results

Fine particulate matter (PM2.5, PM10) and per- and polyfluoroalkyl substances (PFAS) were consistently associated with barrier impairment. These mediators of pollution negatively impacted skin barrier proteins (filaggrin, loricrin, involucrin) and tight junction proteins (claudin-1, occludin, ZO-1), and produced oxidative stress via activation of the aryl hydrocarbon receptor. Th2-biased immune responses and inflammation followed. A multicenter study of 41,447 children demonstrated that the risk of eczema increased by 1.28 times due to PM2.5 exposure. Similarly, prenatal PFAS exposure was associated with a 1.72-fold higher risk of offspring eczema. Microplastics entered the skin and destroyed the integrity of follicles, while PFAS interfered with the function of epidermal lipids.

Conclusion

Environmental pollutants impair skin barrier function and facilitate allergic skin disease. Nevertheless, significant gaps regarding pollutant-specific thresholds, host factors affecting individual susceptibility, and interventions that restore the skin barrier remain to be addressed. Prospective longitudinal studies are needed to guide public health implementations and drive clinical insights in preventing pollution-induced skin disease.

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Beyond the Sting: Delayed Cutaneous Reactions to Jellyfish Envenomation

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Introduction & Objectives:

Jellyfish stings (*Rhizostoma pulmo*) are a common marine hazard, often resulting in immediate skin reactions such as pain, erythema, and urticaria. However, delayed hypersensitivity reactions are less frequently reported. We present a case series of three distinct delayed cutaneous responses following jellyfish stings in the Mediterranean Sea.

Observation:

Three patients, including a 6-year-old girl and two 24-year-old women, developed delayed cutaneous reactions following stings from Rhizostoma pulmo jellyfish. The latency period ranged from 36 hours to four weeks after exposure. One patient developed acute localized exanthematous pustulosis, characterized by sterile pustules on erythematous, edematous skin localized periorally, without vesicles, itching, or other lesions. No systemic involvement was observed, and the lesions completely resolved within four days with the use of topical corticosteroids. Another patient exhibited facial edema and eczematous lesions mimicking angioedema, leading to a diagnosis of allergic contact dermatitis. The absence of systemic symptoms and a history of allergen exposure resulted in a diagnosis of allergic contact dermatitis secondary to the sting. Symptoms resolved within a week following a short course of dexamethasone sodium phosphate injections at a dose of 4 mg/day for three days. The third case presented as a lichen planus-like eruption on the wrist and hand. A biopsy confirmed the diagnosis of lichen planus, suggesting a delayed immune response to jellyfish venom components. The lesions improved with topical corticosteroids. In total, all symptoms were resolved completely within variable timeframes, with no recurrence.

Results:

Jellyfish envenomation is a well-recognized cause of immediate skin reactions, but delayed cutaneous manifestations remain poorly understood. The immune response to jellyfish venoms likely involves both innate and adaptive mechanisms. Nematocyst toxins contain proteins, peptides, and other bioactive molecules that can induce allergic and inflammatory responses. The resolution of symptoms with topical corticosteroids, along with the delayed onset, further supports an immune-mediated inflammatory response. Jellyfish venom components may act as persistent antigenic stimuli, triggering chronic immune activation. The role of nematocyst toxins in triggering immune-mediated skin conditions is increasingly recognized, highlighting the need for clinicians to consider marine envenomation as a potential cause of atypical dermatoses.

Conclusion:

These cases illustrate the diverse spectrum of delayed cutaneous reactions to jellyfish stings, as their presentation can mimic other dermatologic conditions. Early recognition and appropriate management can prevent unnecessary interventions and promote the resolution of symptoms.

A Case Report of MHC Class I Deficiency with Necrotizing Granulomatous Dermatitis and Fungal Infections

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Introduction & Objectives:

Primary immunodeficiency diseases (PID) are a group of diseases characterized by chronic and/or recurrent bacterial, fungal, protozoal and viral infections that develop as a result of primary or congenital immune deficiency disorders. The etiological distribution of primary immunodeficiencies is as follows: humoral immunodeficiencies 50-60%, T-cell immunodeficiencies 10-15%, combined immunodeficiencies 15-30%, immunodeficiencies due to phagocytic system disorders 10-15%, and immunodeficiencies due to complement system disorders 1-3%. MHC class I deficiency is an extremely rare autosomal recessive primary immunodeficiency (PID) that thus far has been reported in only a few cases worldwide. It represents a heterogeneous group of disorders that collectively share a decreased surface expression of HLA class I molecules.

The objective of this study is to present a rare case of MHC class I deficiency in a 36-year-old female patient, who experienced dermal manifestations and severe fungal infections. We aim to underscore the importance of early diagnosis, genetic counseling, and comprehensive management in patients with rare primary immunodeficiencies.

Materials & Methods:

36-year-old female patient presented to our clinic with a known diagnosis of MHC Class I deficiency under follow-up. The patient had a history of recurrent infections and had been receiving intravenous immunoglobulin (IVIg) therapy monthly for the past 5-6 years. Dermatological examination of the patient revealed erythematous nodules and plaques on the face, and occasionally ulcerated lesions with discharge. To investigate the extent of infection, a CT scan of the paranasal sinuses was performed, revealing findings suggestive of pansinusitis with implications for fungal infection, nasal septum perforation, and significant findings on brain MRI, including lacunar infarcts and cerebral/cerebellar atrophy and fungal infection. A skin biopsy was performed to further investigate the dermatological lesions. Histological examination indicated necrotizing granulomatous dermatitis. When the patient's history was evaluated together with histomorphological findings by the pathologist, a granulomatous dermatitis with an infectious cause was suspected in the case. Therefore, it was recommended to investigate clinically and microbiologically in terms of infectious pathologies with granulomas such as protozoans, bacteria, fungi, and parasites.

Results:

The imaging studies corroborated the clinical suspicion of fungal infections alongside the detected sinusitis. The skin biopsy elucidated a granulomatous reaction with necrotizing features categorized typically in infectious processes, leading us to consider infectious causes seriously. In this case with MHC class 1 deficiency, monthly IVIg therapy and fungal infection treatment were continued to be applied together.

Conclusion:

This case exemplifies the complex interplay between immunodeficiency and infectious pathology, particularly in the context of MHC Class I deficiency. Timely recognition and evaluation of PID are crucial for effective

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management and prevention of associated complications. Finally, maintaining a high index of suspicion for atypical infections in patients with known immunodeficiencies can lead to improved outcomes through early intervention and treatment adjustments.

Diagnostic pitfalls and clinical mimics of subacute cutaneous lupus erythematosus

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Introduction & Objectives: Subacute cutaneous lupus erythematosus (SCLE) diagnosis is made based on distinctive clinical features, laboratory studies, histology, and antibody serology. However, overlapping clinical features in the absence of additional diagnostic tests can make clinical diagnosis difficult. Through this retrospective analysis, we aimed to** examine the frequency of SCLE misdiagnosis, to explore differential diagnoses and potential factors that may contribute to diagnostic accuracy.

Materials & Methods: This study included 102 patients hospitalized at a tertiary-level hospital in a five-year period (October 2018 – October 2023), carrying the diagnosis of SCLE. Upon exclusion of prevalent (N=8) and unconfirmed cases (N=7), fifty incident histopathologically confirmed cases of SCLE were identified, while 37 of the patients received an alternative final diagnosis. Referral and final diagnosis, as well as clinical and demographic data were obtained from medical records.

Results: Of 87 patients included in the final analysis, in 50 (57.5%) the final diagnosis of SCLE was established. SCLE was clinically recognized in 8/32 (25%) cases before our center, and in 30/50 (60%) cases during outpatient examinations at our clinic. Cutaneous lupus erythematosus was suspected in 20/32 (62.5%) cases before our center and in 45/50 (90%) at our clinic. Most common referral misdiagnoses of SCLE were chronic cutaneous lupus erythematosus – CCLE (N=5), unspecified cutaneous lupus erythematosus (N=7), unspecified dermatitis (N=4), and pityriasis rosea (N=2). On the other hand, at our clinic SCLE was most-commonly mistaken for CCLE (N=11). Other than the more common discoid appearance of lesions (55.0% vs. 26.7%, p=0.043), no other significant differences were found between the misdiagnosed and clinically recognized SCLE patients. In 37/87 (42.5%) cases the referral diagnosis of SCLE was ultimately refuted, in favor of CCLE (N=9), psoriasis (N=5), erythema annulare centrifugum (N=3), photodermatitis (N=3), contact allergic dermatitis (N=2) and acute syndrome of apoptotic pan-epidermolysis (N=2), among other diagnoses.

Conclusion: Subacute cutaneous lupus erythematosus was often clinically misdiagnosed before hospital admission – it was unrecognized in 75% of cases prior to referral to our center, while over 40% of cases referred as SCLE received a different final diagnosis. The most common alternative diagnosis in both circumstances was CCLE. Our findings suggest that a combination of clinical, histopathological, and immunological findings is necessary to establish an adequate diagnosis of SCLE, given the broad spectrum of differential diagnoses.

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The Impact of Methylene Blue Mediated Photodynamic Therapy on Cellular Immune Function in Patients with Multiple Common Warts

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Introduction & Objectives:

Common warts, caused by human papillomavirus (HPV), are a prevalent dermatological condition often managed with ablative therapies. Many therapeutic modalities are available. Methylene blue mediated photodynamic therapy (MB-PDT) is emerging as a non-invasive treatment option. However, its impact on the local and systemic cellular immune responses in patients with multiple common warts remains largely unexplored.

This study aimed to investigate the effect of MB-PDT on the cellular immune function in patients with multiple common warts by evaluating changes in the specific cytokine profiles.

Materials & Methods:

This prospective randomized controlled trial was carried out on thirty patients with multiple clinically and dermoscopically confirmed common warts. Patients received MB-PDT according to a standardized protocol. Peripheral blood samples were collected at baseline, one month and six months post-treatment. Serum levels of cytokines TNF- α and, IL-2, were measured using ELISA. Clinical response to MB-PDT was assessed at one and six months after treatment.

Results:

Our preliminary results indicate that MB-PDT treatment led to a significant decrease in the serum level of IL 2 and TNF- α at 1- and 6-months post-treatment (p < 0.05). Correlation analysis revealed a potential association between changes in serum cytokines level and clinical response to MB-PDT.

Conclusion:

This study provides novel insights into the immunomodulatory effects of MB-PDT in patients with multiple common warts. The observed changes in cellular immune function, in the form of alterations in cytokine profiles, suggest that MB-PDT may not only exert a direct cytotoxic effect on wart tissue but also influence the local and potentially systemic immune response against HPV. Further investigation with a larger cohort and longer follow-up is warranted to fully elucidate the long-term immunological consequences and optimize the clinical application of MB-PDT for common warts.

Characterization of the dermal immune response after UV-B provocation

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Introduction & Objectives:

The ultraviolet-B (UV-B) model is a skin inflammation model that has been broadly used in inflammatory pain studies. Although there are some studies investigating the inflammatory response of the skin to UV-B, the indepth characterization of the immune response in healthy volunteers is lacking. The aim of this study was to characterize the dermal immune response of healthy volunteers following a UV-B skin challenge and to evaluate test-retest variability of the UV-B response for later integration into phase 1 proof-of-mechanism studies with novel immunomodulatory agents.

Materials & Methods:

In this clinical study, the skin on the upper back of 10 healthy participants was irradiated with two times the minimal erythema dose of UV-B on two different study days, two weeks apart. The inflammatory response was evaluated using non-invasive imaging techniques to measure skin erythema and perfusion. Skin biopsies were taken 3 hours, 6 hours, and 24 hours post-challenge in the first period, and 24 hours post-challenge in the second period. Biopsies were subjected to RNA sequencing and examined for interferon-stimulated genes (ISG) expression.

Results:

UV-B increased erythema which peaked 6 hours post-UV-B and remained elevated for 24 hours post-UV-B. UV-B increased perfusion from 3 hours post-UV-B and peaked at 24 hours post-UV-B. The level of induction was consistent between participants and between the two periods. RNA sequencing data of the skin biopsies revealed ISG induction at 24 hours post-UV-B in both periods.

Conclusion:

This study demonstrated the feasibility of using UV-B provocation in healthy volunteers for proof-of-mechanism clinical studies with novel immunomodulatory agents.

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Acute Urticaria in Lyme Disease: A Case Report and Diagnostic Challenge

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Introduction & Objectives:

Lyme disease is a systemic bacterial infection caused by *Borrelia burgdorferi* and transmitted through the bite of an Ixodes tick. Common cutaneous manifestations include erythema migrans, borrelial lymphocytoma, and acrodermatitis chronica atrophicans. However, in rare cases, the disease may initially present as acute urticaria, which significantly complicates diagnosis—especially in the absence of typical epidemiological indicators. We present a clinical case in which urticarial rash was the only symptom that led to the early identification of Lyme borreliosis

Materials & Methods:

A 38-year-old woman presented with sudden-onset, localized urticarial lesions on the posterior aspect of the right thigh. The lesions recurred every two days, each time in a different location, with no other areas affected. She had independently undergone initial Lyme serologic screening, which was negative. She denied any tick bites or recent exposure to wooded areas. The patient was prescribed rupatadine 10 mg daily and advised to repeat serological testing via immunoblot after four weeks. The rash resolved within two days of starting antihistamine therapy. However, three weeks after stopping rupatadine, the urticarial lesions reappeared with greater intensity. Immunoblot testing at that time revealed positive IgM antibodies against p31 and p17 *Borrelia* proteins.

Results:

In this case, acute urticaria was the sole cutaneous manifestation of early Lyme disease. Following confirmation of the diagnosis, a standard course of doxycycline was initiated, resulting in complete remission with no further recurrence.

Conclusion:

This case illustrates that acute urticaria can, in rare circumstances, be the only dermatologic sign of early Lyme borreliosis, even in the absence of classic symptoms or clear exposure history. Timely repeat serologic testing allowed for diagnostic confirmation and the initiation of effective treatment. Our experience highlights the importance of maintaining a broad differential diagnosis in patients with atypical or treatment-resistant urticaria, and considering Lyme disease as a potential underlying cause.

The Multifaceted Clinical Presentations of Carmine Allergy

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Introduction & Objectives:

We present 2 cases with variable presentations of carmine allergy.

Materials & Methods:

Case 1 is an atopic 40-year-old lady who presented with anaphylaxis 30 minutes after breakfast consisting of croissant, fruits, and red velvet cake. She was treated for anaphylaxis in the emergency department (ED). On another occasion, she developed hives, lip swelling, and abdominal discomfort after chicken salad and negroni. She also had hives and abdominal discomfort after consuming butter and red velvet cookies. She self-medicated with oral antihistamines both episodes. She has tolerated other baked foods in between and after these incidences. She has eaten charcuterie without any issues. She uses lipstick of pink and red shades but never developed any reaction. Carmine dye immunoglobulin E (IgE) was positive (0.94 kUL). Skin prick test (SPT) was positive to red velvet mix containing carmine. After diagnosis carmine allergy, she had another reaction after she unknowingly ate beef patty containing carmine. Symptoms resolved with antihistamines. Case 2 is a healthy 28year-old lady who developed rashes, eye swelling, throat tightness and dypsnoea shortly after drinking strawberry milk. She was treated with intramuscular promethazine, oral prednisolone and antihistamines at the ED. She often drinks strawberry milk of a different brand. E120 was present in the brand she reacted to. She eats Taiwanese sausage and red velvet cake with no issues. Her cosmetic use includes eyeliner, blush, and lipstick. She had three episodes of eye swelling with no clear triggers that resolved with antihistamines. Her carmine dye IgE was low (0.18 kU/L). SPT was negative to both brands of strawberry milk, regardless of carmine content but positive to commercial carmine reagent. She was diagnosed with carmine allergy.

Results:

Cochineal dye is a natural red colour extracted from dried female cochineal insects. Carminic acid in cochineal dye is further processed to produce carmine. Immediate type hypersensitivity reactions including anaphylaxis following ingestion of foods containing carmine have been reported, from red-coloured bakes (red velvet cake and macarons), red-coloured drinks (strawberry milk, yogurt, campari) to processed meat (artificial crab meat, sausage, charcuterie and even salmon meat). The suspected allergen protein is 38kDa in size. Awareness on allergic reactions from carmine or cochineal extract came about in the 2000s. Most cases involve females, who are more susceptible due to cutaneous sensitization through cosmetics containing carmine. Some reported local cutaneous symptoms from cosmetics containing carmine.

Takeo et al. proposed a diagnostic chart for patients with suspected carmine allergy. In a Polish study, skin prick test was more specific, while specific IgE to cochineal extract/carmine was more sensitive, although they had a low cut-off of 0.01 kU/L. Both our cases were proven with positive skin tests to carmine and did not proceed to oral provocation tests due to risk of anaphylaxis. Carmine allergy is potentially missed without proper history taking. Physicians should recognise carmine as a possible hidden food allergen, often masquerading as idiopathic anaphylaxis or other food allergies.

Conclusion:

Carmine allergy is under-recognised and under-reported. We would like to highlight carmine as a potential hidden food allergen.

Briquilimab Potently Inhibits Stem Cell Factor (SCF)/c-Kit Signaling and Induces Mast Cell Apoptosis

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Introduction & Objectives:

The activation and survival of mast cells (MCs) rely on SCF/c-Kit signaling. We hypothesized that briquilimab, a humanized aglycosylated monoclonal antibody (mAb) that binds to the SCF ligand binding domain of c-Kit, would effectively inhibit SCF/c-Kit signaling, leading to MC apoptosis.

Materials & Methods:

Briquilimab's effects on MC survival/apoptosis signaling were evaluated in primary human MCs (CD34-Fc epsilon RI+c-Kit+) differentiated from mobilized peripheral CD34+ cells. Briquilimab was compared to a tool compound mAb that inhibits c-Kit dimerization (JSP084) and the small molecule multityrosine kinase inhibitor, imatinib.

Results:

Briquilimab bound to c-Kit with higher affinity than JSP084 and blocked SCF ligand-binding to c-Kit. Briquilimab was more potent than JSP084 at inhibiting IgE/Fc epsilon RI-mediated MC degranulation, c-Kit receptor internalization, and pan-phosphorylation of c-Kit. Specifically, phosphorylation of Tyr721, which plays an important role in promoting MC survival, was inhibited by briquilimab more potently than JSP084. Interestingly, low (~1 nM) concentrations of JSP084 showed c-Kit agonism with an increase of Tyr721 phosphorylation, whereas briquilimab remained inhibitory. Briquilimab also effectively inhibited phosphorylation of FOXO3a, a target transcription factor of SCF/c-Kit/PI-3** kinase/Akt signaling and resulted in an increase of pro-apoptotic Bim protein. Consistent with briquilimab's effects on inducing pro-apoptotic signaling, briquilimab increased MC Caspase-3/7 activity in a more potent, rapid, and transient manner compared to JSP084, leading to MC apoptosis. Both briquilimab and JSP084 were significantly more potent than imatinib at inhibiting SCF/c-Kit signaling and inducing MC apoptosis.

Conclusion:

Briquilimab's potent inhibition of SCF/c-Kit signaling and rapid induction of MC apoptosis** may provide a promising treatment option for MC-mediated diseases.

Skin disorders in Common Variable Immunodeficiency

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Introduction & Objectives:

Common variable immunodeficiency (CVID) is the most frequent inborn error of immunity (IEI). CVID comprises a group of heterogeneous disorders defined by low serum immunoglobulin levels, impaired antibody response to infections and vaccines, and increased susceptibility to infections. Skin disorders are a common clinical feature in IEI and may be among the presenting manifestations. Identifying skin manifestations linked to CVID may help early diagnosis of the IEI and timely identification of autoimmune comorbidities during follow-up.

Objective: Identify the most frequent skin disorders in patients with common variable immunodeficiency.

Materials & Methods:

We performed a cross-sectional study, in which we identified cases of common variable immunodeficiency (CVID) by searching the medical records of the immunology department from April 2024 to April 2025. The diagnosis of CVID was made based on the Pan American Group for Immune Deficiency criteria. To be included they needed to have a complete medical record with age at the diagnosis, physical evaluation, and treatment. Clinical and demographic information was then retrieved from medical records.

Results: We included** 40 patients with a mean age of 36 years (SD \pm 17.4). The most frequent comorbidity was hypothyroidism (n:3, 7.5%). Skin disorders were present in 35% (14) of the cases. The most common skin manifestations were skin infections (n:4, 7.5%) including oral candidiasis, herpes labialis, molluscum contagiosum and recurrent pyogenic infections followed by dermatitis-like-lesions (n:3, 7.5%) including atopic dermatitis, dyshidrotic eczema, and seborrheic dermatitis. The most frequent autoimmune skin disease was vitiligo (n: 2, 5%) followed by pyoderma (n:1, 2.5%) and SLE (n:1, 2.5%). Infrequent manifestations in single cases included lipodermatosclerosis, rosacea, oral aphthae and xerosis.

Conclusion: In our study of 40 patients with CVID, the most frequent dermatological manifestations were infectious diseases, dermatitis-like-lesions and autoimmune hypopigmentation disorders.



Briquilimab, an Anti-c-Kit Antibody, Induces Durable Depletion of Mast Cells (MCs) Across Multiple Tissues in Mice Expressing Chimeric Human/Mouse CD117 (c-Kit)

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Introduction & Objectives:

Briquilimab, a humanized anti-c-Kit antibody, inhibits MC development, function, and survival by blocking SCF binding to c-Kit. We evaluated depletion and repopulation kinetics of tissue-resident MCs in human/mouse (h/m) CD117 mice treated with briquilimab.

Materials & Methods:

25 mg/kg briquilimab was intravenously administered once into male h/mCD117 mice, which express chimeric human extracellular/mouse intracellular c-Kit in lieu of wild-type mouse c-Kit. Pharmacokinetics, blood counts, bone marrow (BM) hematopoietic stem cells (HSCs, LineagecKit+Sca+CD150+Flt3-) and MC progenitors (MCPs, LineagecKit+ScaLy6cFcepsilon-RI-alphaBeta-7-integrin+CD27-), and tissue-resident MCs (by toluidine blue) were evaluated at various time points (up to 29 weeks) following briguilimab treatment.

Results:

Briquilimab serum concentrations were below detection limit by 3-4 weeks posttreatment. Blood hemoglobin and leukocytes and BM HSC/MCP frequency were decreased at 2 weeks, returning to baseline by 3-4 weeks post-briquilimab. Significant reductions of MCs (>80%) were observed at 2-4 weeks post-briquilimab across multiple tissues, including skin, lung, tongue, and stomach. Early evidence of MC repopulation was observed in the tongue starting at 8 weeks, skin starting at 14 weeks, and stomach starting at 29 weeks post-briquilimab, whereas lung MCs remained significantly reduced at 29 weeks. At 29 weeks post-briquilimab, skin and tongue MCs had returned to baseline levels.

Conclusion:

Although HSCs/MCPs return to baseline in BM by 4 weeks post-briquilimab in this model, repopulation of tissue-resident MCs to baseline appears to take significantly longer, and the rate of MC repopulation may vary by tissue. These data suggest that briquilimab can induce durable MC depletion across multiple tissues, and offer insights into potential dosing intervals for MC-mediated diseases.

Analysis of serum biomarkers in patients with chronic spontaneous urticaria - a prospective study

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Introduction & Objectives: Chronic spontaneous urticaria (CSU) is an inflammatory skin disease of a not known cause, characterized by hives, itching and possible associated angioedema, and impaired quality of life (QoL), lasting for at least six weeks and. The aim of this study was to determine CSU serum biomarkers and to compare them with QoL in CSU patients.

Materials & Methods: Our study included 41 patients with CSU, 32 women and 9 men (78%:22%). In most patients (44%), CSU lasted between 3 and 6 months. We analyzed serum biomarkers associated with CSU (IL-6, CBC, ESR, CRP, TSH, T3, T4, anti-TPO, anti-TG, D-dimers, and vitamin D), and compared them with CSU activity as measured by the Urticaria Activity Score (once-daily UAS and UAS7), CSU control as measured by the Urticaria Control Test (UCT), and patients' QoL as measured by the Dermatology Life Quality Index (DLQI) and Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL). These parameters were reevaluated after three months of standard treatment.

Results: Most patients had moderate CSU (39%) and reported a low impact of CSU on DLQI (42%), although 90% had uncontrolled disease. A total of 43% experienced a moderate CSU impact on daily life, while only 5 patients had a severe CSU form. Basopenia significantly correlated with daily CSU severity (once-daily UAS, p=0.017), while ESR values were a significant predictor of weekly CSU activity (UAS7,p=0.038). Elevated serum IL-6 was more frequently observed in patients with moderate to severely impaired DLQI. Serum T4 levels correlated with CSU duration, while T3 correlated with reduced DLQI. The most significant correlation was observed between their impaired QoL and disease-specific QoL in CSU patients (a linear positive correlation, r=0,838, p<0,001). After three months of standard CSU treatment, only CRP levels showed a statistically significant negative correlation with disease control (as measured by the UCT questionnaire).

Conclusion: Basopenia was a significant predictor of daily disease severity, while ESR values were significant predictors of weekly disease activity. Standard CSU treatment was associated with decreased disease activity, improved disease control, and enhanced patient quality of life.

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Allergic Contact Dermatitis in Psoriasis: A Case Report.

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Introduction & Objectives:

The interplay between allergic contact dermatitis (ACD) and psoriasis remains a subject of clinical debate. We present a case of a patient with psoriasis who developed ACD secondary to shoe components, highlighting the diagnostic challenges in differentiating between these entities when they coexist.

Observation:

A 71-year-old woman with a history of hypertension presented with chronic, pruritic plaques on the dorsal aspect of both feet. Clinical examination revealed well-demarcated, erythematosquamous plaques characteristic of psoriasis on the dorsal surfaces of the feet, hands, and elbows. Notably, the lesions on the dorsa of the feet and hands had an eczematous morphology with weeping and crusting, raising the suspicion of secondary ACD. Given the patient's report of pruritus and regular use of tanned leather shoes, patch testing was performed using the standard European baseline series. Measurements were taken at 48 and 72 hours according to the recommendations of the International Contact Dermatitis Research Group (ICDRG). Results showed positive reactions to potassium dichromate (+++), a leather tanning agent, and mercaptomix (++) and mercaptobenzothiazole (+), rubber accelerators found in footwear. Following avoidance of the implicated allergens, the patient experienced marked improvement of the lesions on the dorsa of the feet, with almost complete resolution of the hand lesions.

Discussion:

The relationship between psoriasis and ACD is complex. Studies suggest that

patients with psoriasis may be at increased risk for developing ACD, possibly due to impaired epidermal barrier function and frequent use of topical corticosteroids, which may act as sensitizers. Common contact allergens reported in sensitized psoriatic patients include nickel sulfate, formaldehyde, corticosteroid mixtures, and potassium dichromate, which is consistent with our patient's findings. ACD may further disrupt the epidermal barrier in psoriasis, complicating disease management and potentially leading to treatment resistance. In our patient's case, the diagnostic challenge is to differentiate between: (1) eczematized psoriasis resulting from chronic topical corticosteroid use or sensitization to shoe components; and (2) ACD superimposed on psoriasis, the latter possibly induced by Koebner's phenomenon at the site of eczematous inflammation.

Conclusion:

We emphasize the importance of patch testing in psoriasis patients with treatment-resistant lesions or clinical suspicion of contact allergy.



"Allergic Contact Dermatitis Induced by MIT Presenting as Angioedema: A Case Report"

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Introduction & Objectives:

Methylisothiazolinone (MIT) is widely used as a preservative in personal care products, household items, and paints. In recent years, it has been increasingly recognized as a potent contact sensitizer, leading to strict regulatory measures to limit its use. This case report describes an unusual presentation of allergic contact dermatitis (ACD) mimicking angioedema, triggered by exposure to an anti-stain spray containing MIT.

Observation:

A 31-year-old woman with no prior medical history was referred for persistent

eyelid edema lasting 15 days. Clinical examination revealed bilateral erythematous and pruritic eyelid edema, accompanied by eczematous patches on the lateral neck. Notably, there was no labial edema or respiratory involvement.

The diagnosis of ACD was suspected due to the presence of pruritus, the prolonged clinical course, and the association with distant eczematous lesions.

Patch testing with the European baseline series was performed after the

resolution of eczema lesions. Readings at 48 and 72 hours, in accordance with

ICDRG recommendations, showed a strong positive reaction to methylchloroisothiazolinone and MIT (++/++).

A detailed analysis of the patient's anti-stain spray confirmed the presence of MIT, supporting the clinical relevance of the patch test findings.

Discussion:

ACD due to MIT can present with a wide spectrum of clinical manifestations. In this case, the patient exhibited eyelid angioedema; however, the pruritic nature, erythema, and desquamation suggested an underlying ACD rather than true angioedema.

Similar cases have been reported in the literature, likely attributable to the volatile nature of MIT. Despite stringent European regulations limiting MIT exposure in cosmetics, vigilance remains essential due to the continued use of this preservative in various consumer products.

Conclusion:

ACD to MIT is polymorphic and may manifest as pruritic eyelid angioedema. This clinical presentation should prompt clinicians to consider ACD as a differential diagnosis, warranting patch testing to identify the causative allergen and implement appropriate avoidance strategies.

"Prevalence and Clinical Relevance of Contact Sensitization in Patients with Lichen Planus: Analysis of a 69-Patient Cohort"

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Introduction & Objectives:

Few studies reported the association between contact sensitization and lichen planus (LP). Through this study we aimed to evaluate the prevalence of contact sensitization in patients with cutaneous and/or mucosal lichen, to identify the main responsible allergens and to assess the impact of avoiding the relevant allergens.

Materials & Methods:

It was a longitudinal study conducted in the Dermatology Department of Monastir. The study period was from January 2024 to November 2024. Patients with histologically confirmed LP were collected. All patients were tested with the European Baseline Series (BSE). Patients with dental materials were tested also with the Dental Series (DS). Two readings were performed at H48 and H72. Eviction of pertinent positive allergens was indicated.

Results:

We collected 69 cases of Lichen. The majority (81,2%) (n=59) had skin involvement. Six patients (8,6%) had an isolated involvement of the oral mucosa and 4 patients (5,8%) had involvement of the genital mucosa. The patch tests were positive in 43 patients (62.3%). These tests were considered relevant in 41 cases (59,4%). Twenty patients (29%) were sensitized to one allergen and 23 (33,3%) had polysensitization. Twenty-Five patients had positive reactions to at least one of the metals: Nickel in 30.4% of cases, Chromium in 13% and Cobalt in 10,1%. Positive reactions to perfumes were noted in 9 patients (13%). The responsible allergens were: Peru Balsam (11,5%), Fragrance Mix I (5,8%), Fragrance Mix II and Lyral, each found in 1.4% of cases. These tests were relevant in 10.1% for Peru Balsam, 4,3% for Fragrance Mix I and 1,4% for both Fragrance Mix II and Lyral. Seven patients (10,1%) had positive reactions to benzisothiazolinone (BIT). These tests were relevant in 4 cases (5,8%). Lastly, 3 patients (4,3%) had positive reactions to Textile Dye Mix which were relevant in two cases. For the 18 (26,1%) patients tested with the Dental Series, 12 (17,4%) had at least one positive test. Ten allergens were responsible for these reactions. The most frequent allergen was palladium, found in 5 cases (7,2%), followed by Mercury and Nickel, each found in 4 cases (5,8%). An eviction was recommended for 42 patients in our series. It was carried out in 24 cases (57,1%). A physical examination was carried out 3 months after eviction and we noticed a complete improvement in 4 cases (16%), partial improvement in 18 cases (72%) and no improvement in 3 cases (12%).

Conclusion:

Many recent studies report the association between oral LP and sensitization to metals from dental materials. Only few studies discuss the association between contact sensitization and cutaneous LP. Based on the positivity and the relevance of the results of the epicutaneous tests in our study, we emphasize the role of metals and fragrances in the onset or aggravation of lichen planus.

Further larger studies could establish the relevance of this association and the impact of the eviction.

17 SEPTEMBER - 20 SEPTEMBER 2025 POWERED BY M-ANAGE.COM

Localized urticaria arising in well healed pemphigus vulgaris scars : recall phenomenon?

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Introduction & Objectives:

Unlike Koebner's phenomenon, recall phenomenon is rarely seen and is a much less known entity in dermatology. Its pathogenesis remains obscure. It is thought to be due to pathological anatomical changes in the previously traumatized area. Through this case of urticaria triggered by Rituximab, confined to the sites of old, completely healed lesions of pemphigus vulgaris, we will explore potential mechanisms underlying site-specific hypersensitivity reactions in the context of immune reactivation and highlight the need of clinical awareness of atypical cutaneous adverse effects associated with Rituximab, particularly in patients with a history of autoimmune blistering disorders. To our knowledge, no similar case has been previously reported.

Materials & Methods:

We report the case of a patient with a history of pemphigus vulgaris in clinical remission who developed localized urticarial lesions confined to sites of previously healed disease right after receiving rituximab infusion. Clinical evaluation included detailed dermatological examination and photographic documentation. Investigations were performed to rule out other systemic or allergic causes. The temporal relationship to Rituximab administration, lesion distribution, and clinical history were analyzed to assess drug causality.

Results:

60-year-old female, treated with corticosteroid therapy for severe pemphigus vulgaris with complete healing of the lesions. At the very first minutes of her first Rituximab infusion, urticarial plaques had arisen exactly at the same sites as the old scarring hyperpigmented lesions of her pemphigus, with no involvement of healthy skin. The rash completely resolved after stopping the infusion and administering antihistamines, with no recurrence.

Conclusion:

Classically, recall dermatitis refers to chemotherapy-induced reactivation of skin lesions caused by radiotherapy months or even years earlier. This concept has now been extended to include factors such as trauma, burns, ultraviolet light, insect bites and surgical incisions. In our case, the involvement of mast cells and their accumulation at the site of trauma would be the most likely mechanism, given the higher numbers of these cells and their greater degranulation in scar tissue. This theory is supported by the unique property of mast cells to release preformed cytokines, leading to the rapid onset of urticarial lesions after induction. The persistence of memory TCD8 cells in the epidermis, as observed in fixed drug eruption, may also be involved. On the other hand, some pharmacological agents can induce a chemical interaction with genetically sensitized epidermal cells, as is the case with Rituximab in our patient. These results indicate that some immunological alterations induced locally by previous trauma, even years before, can make the skin site more susceptible by creating an allergic response mediated by memory T cells, leading to mast cell activation. Some authors have reported that in scar tissue, fibrosis alters immune surveillance, particularly by lymphocytes, leading to abnormal antigen presentation and thus susceptibility to various inflammatory processes. Another proposed theory is the excessive activation of proinflammatory cytokines through aberrant wound healing. These abnormal anatomic conditions undoubtedly must have taken some considerable part in the induction of urticaria in our patient and cannot be excluded as

possibilities.

Nodular Cutaneous Lymphoid Hyperplasia Treated with Low Dose Methotrexate and Intralesional Triamcinolone Injections: Case Report

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Introduction & Objectives:

Cutaneous lymphoid hyperplasia (CLH) refers to a group of reactive, lymphocyte-rich infiltrates that clinically and/or histologically resemble cutaneous lymphomas. It is typically triggered by chronic and persistent antigenic stimulation, which leads to the proliferation of T and/or B cells and the development of cutaneous lymphoid hyperplasia. Although various potential causes have been identified—such as infections, medications, and insect bites—the majority of cases remain idiopathic. Newly proposed classification divides CLH into 4 major groups: (1) Nodular CLH, (2) CLH as simulators of mycosis fungoides (pseudo-MF) and of other CTCLs, (3) Other CLH and (4) Intravascular CLH. Nodular CLH is considered the most common and classical form. It typically presents as a solitary, bluish to erythematous nodule, most often located on the face, chest, or upper extremities. The combination of patient's history, clinical signs, histologic findings and possible adjunct laboratory tests is needed to ensure correct diagnosis. Treatment options include topical or intralesional corticosteroids, cryotherapy, laser therapy, and surgical excision. Methotrexate has also been reported as an effective therapeutic agent, particularly when used in combination with other treatment modalities. We present a case report of Nodular CLH on the face which was treated with both intralesional triamcinolone and oral methotrexate for 5 months with complete resolution of the nodule. **

Materials & Methods:

A 25-year-old Filipino male presented with a one-year history of a solitary, occasionally pruritic, erythematous plaque on the left malar area. He was previously diagnosed with nodulocystic acne but noted no improvement despite treatment with benzoyl peroxide gel, tretinoin 0.05% cream, and multiple intralesional corticosteroid injections. On physical examination, a solitary, erythematous nodule, approximately 1 cm in diameter was observed on the left medial lower cheek. No palpable lymph nodes were noted. The patient denied any associated systemic symptoms and the rest of the examination was unremarkable.

Results:

A 4mm skin punch biopsy was done which revealed a nodular dermal lymphohisticocytic infiltrate without significant epidermal involvement. The infiltrate consists of small to medium-sized lymphocytes with germinal centers. Immunohistochemistry highlights the infiltrate to be composed of mixed T-cells (CD3) and B-cells (CD20). He was subsequently treated with weekly low dose methotrexate (7.5 mgs/week) for five months, in combination with monthly intralesional triamcinolone injections (10 mgs/ml), which resulted in complete resolution of the nodule. No recurrence was observed after 2 years of follow up.

Conclusion:

Cutaneous lymphoid hyperplasia (CLH) is a rare, benign disorder marked by reactive, lymphocyte-rich infiltrates that can closely resemble cutaneous lymphomas both clinically and histologically. Due to its uncommon presentation, CLH should be included in the differential diagnosis of persistent erythematous nodules, particularly those located on the face, chest, or upper extremities and unresponsive to conventional therapies. Furthermore,

dermatologists may consider low dose methotrexate combined with intralesional triamcinolone injections as a potential therapeutic option in refractory cases of CLH.

Expression Characterization of YKL-40 in Murine Model of Atopic Dermatitis and the Impact of Its Silencing on Immune Inflammatory Responses

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease with significant psychosocial and economic burdens. Despite advances targeting IL-4Rα/JAK-STAT pathways, refractory cases persist. YKL-40, a novel inflammatory marker linked to Th2 immunity, is elevated in AD and correlates with disease severity and key cytokines (IL-4, IL-13, TARC). STAT3/NF-κB/NLRP3 pathways are critical in AD pathogenesis, regulating inflammation and inflammasome activation. We hypothesized that YKL-40 drives AD via Th2 responses and STAT3/NF-κB/NLRP3 signaling, and silencing it could alleviate inflammation.

Materials & Methods:

C57BL/6 mice were divided into control, AD model (DNCB-induced), and intervention groups (dexamethasone, shNC lentivirus, shYKL-40 lentivirus). Skin and serum samples were analyzed on day 30. HE staining assessed histopathology; ELISA measured YKL-40/IgE; RT-qPCR/Western blot/immunohistochemistry evaluated YKL-40 and signaling molecules (STAT3, NF-κB, NLRP3). Spleen index, cytokine mRNA (IL-4, IL-5, IL-13, IFN-γ, IL-1β), and CD4/IL-4 immunofluorescence were analyzed.

Results:

- \1. AD mice showed epidermal hyperplasia, immune cell infiltration, and elevated serum YKL-40/IgE (R^2 =0.8126, P<0.001).
- \2. YKL-40 expression increased in AD skin (mRNA: P<0.01; protein: P<0.001).
- $\$ 3. shYKL-40 silencing reduced skin inflammation, spleen index (P<0.001), serum YKL-40 (P<0.001), and IgE (P<0.01).
- \4. Silencing suppressed Th2/Th1 cytokines (IL-4, IL-5, IL-13, IFN- γ , IL-1 β ;*P*<0.05-0.0001) and CD4/IL-4 expression (*P*<0.05-0.001).
- \5. STAT3/NF-κB/NLRP3 pathway activation (p-STAT3/STAT3, p-p65/p65, p-IκB/IκB, NLRP3) was reduced post-silencing (*P*<0.05-0.001).

Conclusion:

YKL-40 is upregulated in AD and correlates with IgE. Silencing YKL-40 attenuates skin inflammation, Th2/Th1 responses, and STAT3/NF-KB/NLRP3 signaling, highlighting its role as a therapeutic target. This study provides mechanistic insights into YKL-40-driven AD pathogenesis and supports further exploration of YKL-40 inhibitors for clinical translation

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Latex Allergy in Spina Bifida- The Indian Paradox?

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Introduction & Objectives:

Latex allergy is a concern in children with Spina Bifida (SB) and global studies report a higher prevalence of latex sensitivity in SB patients, but data from India is limited. This study aims to evaluate the prevalence of latex allergy in Indian children with SB to determine if global assumptions hold true in this population.

Objective: To evaluate the prevalence of latex allergy in children with SB attending a tertiary care center in Southern India.

Materials & Methods:

This cross-sectional study included 78 SB patients (mean age:5.88years) comprising both open and closed cases. Patients were referred from neurosurgery to dermatology for assessment. Latex sensitivity and allergy were evaluated using patient history of atopy, skin prick tests, serum IgE levels, and ImmunoCap RASTs. Statistical analysis was performed.

Results:

Of the 78 patients, 6.4% had a personal history of atopy and 34.6% had a family history. Elevated IgE levels were found in 28%. Latex allergy was negative in 97.4% of cases via prick tests and 85.9% via RAST. Only 2.5% tested positive for latex allergy via the prick test, and none via RAST. No significant associations were found between latex allergy, type of SB(open vs. closed), or the number of surgeries. A significant correlation was observed between IgE levels and the age at first surgery(Spearman's rho = 0.456, p < 0.001), though not with the number of surgeries.

Conclusion:

The study found a low prevalence (2.5%) of latex allergy in Indian children with SB, challenging global assumptions of higher rates. This suggests that genetic, environmental, or regional factors may influence the prevalence. Routine testing for latex allergy may not be necessary unless additional risk factors are present. Further research is required to understand these disparities and modify preventive strategies accordingly.

From Remedy to Rash: Pustular Allergic Contact Dermatitis Caused by a Propolis-enriched Honey

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Introduction & Objectives:

Pustular allergic contact dermatitis (PACD) is an uncommon variant of contact dermatitis characterized by sterile pustules, often mimicking infectious or autoimmune blistering disorders. Propolis, also known as bee glue, is an adhesive resin that honeybees produce by mixing saliva and beeswax with the exudate they collect from plants. Historically, it has been used for wounds, psoriasis, atopic dermatitis, aphthous ulcers, warts and herpes. We report a case of PACD of topical application of propolis-enriched honey.

Materials & Methods:

NA

Results:

A 21-year-old male presented with a three-day history of acute pruritic eruption on the dorsal aspects of both hands. He reported no personal or family history of skin disorders, atopy, or regular medication use. The eruption developed three days after applying propolis-enriched honey to treat xerosis. Physical examination revealed multiple erythematous papules with numerous small non-follicular pustules overlying symmetrical erythematous-yellowish plaques on the dorsal hands. Microbiological cultures of pustular contents were sterile, showing no pathogenic growth. Histopathological examination of a skin biopsy demonstrated spongiform sterile pustules containing neutrophils, epidermal spongiosis with eosinophilic exocytosis, and a perivascular lymphohistiocytic dermal infiltrate with eosinophils. Special stains for infectious organisms were negative, and no follicular involvement was observed. Patch testing performed according to International Contact Dermatitis Research Group guidelines, using both the European Baseline Series and Cosmetic Series, revealed positive reactivity to propolis. These findings confirmed the diagnosis of PACD secondary to topical propolis-enriched honey application. Cessation of the offending agent and initiation of topical corticosteroid therapy resulted in significant clinical improvement within ten days.

Conclusion:

This case demonstrates a rare presentation of PACD induced by topical propolis-enriched honey, highlighting the diagnostic challenges created by its clinical resemblance to infectious or autoimmune pustular disorders. The combination of characteristic clinical findings, histopathological features, and sterile cultures confirmed the diagnosis of PACD while effectively excluding infectious etiologies and other sterile pustular conditions such as acute localized exanthematous pustulosis (ALEP) and pustular psoriasis. Patch testing positivity to propolis identified the causative allergen, consistent with previous reports establishing propolis as a known contact sensitizer. The rapid clinical resolution following allergen avoidance and topical corticosteroid therapy reinforces both the inflammatory nature of PACD and the critical importance of early allergen recognition.

While propolis enjoys widespread use in traditional medicine, it contains potent sensitizing compounds that can

provoke atypical cutaneous reactions including PACD.

In conclusion, this case underscores the necessity of clinicopathological correlation for pustular eruptions, the role of patch testing in identifying fewer common triggers, and the potential for nature products like honey to induce severe cutaneous hypersensitivity. Increased awareness of PACD's features among clinicians can prevent misdiagnosis and unnecessary systemic therapies.

Transcriptomic analysis of allergic patch test reactions in non-atopic patients: a comparative study across multiple allergens

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Introduction & Objectives:

Immune mechanisms underlying elicitation in allergic contact dermatitis (ACD) have yet to be fully elucidated. Previous studies have shown a double-faceted nature of ACD with both common biomarkers among different allergens and allergen-specific imprinting, albeit with discordance in terms of relevant pathways involved. Several factors, including co-existing atopic dermatitis, may influence immune reactions. We aim to characterize molecular signatures and their immune mechanisms of different relevant allergens (nickel, 2-hydroxyethylmethacrylate [2-HEMA], methylisothiazolinone [MIT], formaldehyde) in strong and extreme positive (2/3+) patch test reactions of patients without atopic dermatitis.

Materials & Methods:

A transcriptomic analysis of 40 skin biopsies of ACD reactions (11 nickel, 10 MIT, 10 2-HEMA, 9 formaldehyde) and 19 controls (petrolatum-occluded skin) was performed using RNA sequencing. Differentially-expressed genes (DEG) were assessed and enriched functional pathways were obtained with an over-representation analysis for allergens.

Results:

ACD molecular profiling revealed a strong, common imprinting of DEG among allergens versus controls (n=814), with further partially-shared DEG among allergens (n=664) and allergen-specific DEG (n=430). The most relevant shared pathways were associated with immune adaptive and innate responses. All allergens exhibited mixed effector immune responses, mainly type 1 and 3 immunity, and, to a lesser extent, type 2 immunity. Furthermore, partially-shared and unique DEG were associated with further inflammatory pathways, particularly for nickel and 2-HEMA.

Conclusion:

This study confirms shared ACD imprinting among different allergens and shared pathways' predominant role in ACD elicitation in patients without atopic dermatitis, alongside allergen-specific immune processes and mixed effector responses (type 1, 3 and 2).

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When the immune system takes over in the operating theatre: Management of testing in suspected allergic reactions during surgical procedures

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Introduction & Objectives: Allergic reactions during surgical procedures under general anaesthesia are rare but potentially life-threatening complications in perioperative care. Proper diagnosis of these reactions is essential for safe planning of future anaesthetic procedures. Various medications administered before or during the procedure may be responsible. The standard approach for allergy testing in suspected drug-induced perioperative reactions includes in vitro testing followed by in vivo skin prick test (SPT), intradermal test (IDT), and provocation testing.

Materials & Methods: We present two clinical cases involving patients who experienced grade III anaphylactic reactions according to the Ring and Messmer classification at the induction of anaesthesia. The first case involves a 65-year-old female patient who developed an anaphylactic reaction following administration of propofol, sufentanil, rocuronium and cefuroxime. The second case involves a 35-year-old female patient with an anaphylactic reaction after administration of propofol, sufentanil and atracurium at the beginning of the surgical procedure.

Results: In the first case report, basophil degranulation testing was initially performed for all suspected drugs and returned negative results. Subsequently, SPT identified a positive reaction to cefuroxime within 5 minutes. Due to negative results in SPT for the remaining drugs, IDT were conducted for sufentanil, propofol and rocuronium, all of which were negative. This was followed by drug provocation testing, which also yielded negative results. In the second case report, alternative medications were tested as substitutes for the suspected allergens. SPT and IDT were conducted for etomidate, followed by a provocation test, with no allergic reaction confirmed. The second drug was morphine, which triggered generalised pruritus, facial erythema and hypotension within 10 minutes after the SPT. The testing was immediately terminated and anti-allergic therapy was initiated, leading to patient stabilisation.

Conclusion: The most commonly implicated drugs in perioperative allergic reactions are neuromuscular blocking agents and antibiotics, but reactions may also be caused by opioids, NSAIDs, general anaesthetics, contrast agents, disinfectants, or latex. In our cases, allergies to cefuroxime and morphine were confirmed. Despite the structural similarity between natural opioids like morphine and synthetic opioids such as sufentanil, the risk of cross - reactivity is considered low. Nevertheless, further testing with sufentanil is recommended in future evaluations. Both cases involved female patients, a group known to have increased susceptibility to drug-induced allergic reactions during anaesthesia. The standard diagnostic pathway for suspected anaesthetic drug allergies includes in vitro testing, followed by SPT, IDT and drug provocation testing. However, this approach is hindered by the lack of standardisation — for many drugs, validated concentrations for skin testing are still unavailable. Moreover, commercially prepared testing kits are not widely accessible, increasing the risk of irritant reactions or false - negative results. Given the potential risks involved, provocation testing must be performed in the presence

of an anaesthesiologist, with continuous patient monitoring.

Vulvar eczema with striking edema: a case to remember

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Introduction & Objectives:

Allergic contact eczema of the vulva is often secondary to hygiene products or medicinal topicals such as antifungals or topical steroids. The objective of this report is to raise awareness of povidone-iodine as a potential allergen in vulvar eczema, demonstrated through an extreme clinical case.

Materials & Methods:

An 18-year-old female patient was admitted to the gynecological intensive care unit for acute pyelonephrotis complicated by bilateral infectious pleuro-pneumonia during an ongoing pregnancy of 33 weeks 6 days of gestation. She was treated with triaxon 2g/day, gentamycin 160 mg/day and ciprofloxacin 400 mg/day. The onset symptoms dates back to third day of hospitalization, marked by vulvar pruritus occuring 48 hours after placement of a urinary catheter with disinfection using Povidone-iodine. The condition worsened following the second application of povidone-iodine, leading to pruritic vulvar edema.

Results:

Clinical examination revealed a conscious, hemodynamically stable, and afebrile patient. Examination of the vulva showed significant pruritic and painful edema of the labia minora, with the presence of a few vesicles. Given this presentation, allergic contact eczema was suspected and confirmed by positive patch testing. The patient was treated with topical beclomethasone for five days, with a favorable outcome. Povidone-iodine avoidance was recommended.

Conclusion:

Povidone-iodine contact dermatitis is a common allergic reaction. When localized to the vulva, it primarily manifests as edema, erythema, and vesiculation, sometimes extending beyond the vulvar margins.

The predisposition to allergic dermatitis in this area can be explained by the structural and morphological characteristics of the vulvar epithelium, along with its biophysical properties. Specific factors such as hydration level, occlusion, and friction forces influence tissue permeability and susceptibility to irritants and contact allergens.

The main drugs responsible for allergic contact dermatitis include antibiotics, antifungals, anesthetics, and antiseptics, with povidone-iodine being one of the most common culprits, as seen in our patient.

Currently, the diagnosis of allergic contact dermatitis is based on medical history, clinical presentation, and positive patch tests. Treatment relies on short-term topical corticosteroids with an appropriate potency and formulation, depending on the lesion's location and extent. Avoidance of the offending allergen is essential for resolution and prevention of recurrence.

beneath the rash: histamine intolerance and skin disorders - what do we know so far?

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Introduction & Objectives:

Histamine plays an important role in inflammatory and immunological processes as well as being a neurotransmitter. It is mainly metabolized by diamine oxidase (DAO) extracellularly and histamine-N-methyltransferase (HNMT) in the intracellular space. Appropriate functioning of these 2 enzymes is a key in preventing the accumulation of histamine.

Histamine intolerance is a non-allergic reaction (non-IgE mediated) caused by a dysregulation of its degradation system. It is a multifactorial condition which can be caused by genetic polymorphism of both DAO and HNMT, DAO and HNMT deficiency whether acquired or reversible, dysbacteriosis, drugs including some anti-histamines (Cimetidine and dihydralazine). Histamine accumulation causes gastro-intestinal and extraintestinal symptoms including the skin.

Materials & Methods:

A targeted literature review was undertaken to understand the relationship between HIT and dermatological conditions namely atopic eczema and chronic spontaneous urticaria.

Results:

Significant reduction in DAO level with P<0.001 was demonstrated in 2 studies in patients with atopic eczema compared to healthy individuals. Slight reduction in DAO levels in patients with chronic idiopathic urticaria was also reported. Two main interventions were examined; low histamine diet and DAO oral supplementation.

Low histamine diet for a period of 3 to 4 weeks showed improvement in 4 out of 5 studies identified in patients with chronic spontaneous urticaria as below:

study1: partial to complete remission with histamine levels falling after 3 weeks (P<0.05)

study2: 46% of patients demonstrated improvement with reduction in UAS7 (P < 0.0001)

study3: significant reduction in UAS4 in all patients (P = 0.004)

study4: improvement of both USS and UAS (P=0.010 and P=0.006 respectively)

For patients with atopic eczema, trial of low histamine diet showed a reduction of SCORAD in all patients with p<0.001 and positive response to diet in one third of patients with p=0.002 in a case control study.

Regarding diamine oxidase supplementation, a randomized double-blind placebo-controlled study demonstrated UAS7 improvement (p=0.041) in patients with chronic spontaneous urticaria and reduction of daily antihistamines use (p=0.049)

Conclusion:

Current evidence is highly suggestive of element of histamine intolerance in patients with atopic dermatitis and chronic idiopathic urticaria. Low histamine diet and diamine oxidase supplementation demonstrated a degree of efficacy in symptoms control of these conditions.

It is highly advisable to check for histamine intolerance in patients presenting with atopic dermatitis and chronic idiopathic urticaria as HIT presents with unspecific symptoms and tends to be easily missed and underdiagnosed.

A low TFM soap bar containing plant-derived polysacchrides improves skin defense via Anti-Microbial Peptides boost and leads to pathogen protection.

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Introduction & Objectives:

The skin functions as both a physical barrier, protecting against environmental stressors and dehydration, and as an immunological barrier, utilizing antimicrobial peptides (AMPs) to combat pathogens. Compromise of these barriers increases infection and inflammation risks, driving demand for sustainable formulations that enhance structural and immune barrier defenses. Current preclinical models often inadequately assess how topically applied products modulate skin barriers and antimicrobial activity. This study employs ex vivo human skin explants to evaluate sustainable, low Total Fatty Matter (TFM) soap bars formulated with plant polysaccharides, which aim to synergize sustainability benefits (reduced TFM) with barrier reinforcement and anti-microbial peptide (AMP)-driven pathogen defense.

Materials & Methods:

Skin explants were cultured using standard protocols [Park GH et al. 2015]. Explants were treated with soap using a wash protocol that was used in human volunteer studies [Mathapathi MS. et.al]. Skin AMP and barrier biomarkers were measured using standard qPCR and ELISA protocols.

Results:

Our data using skin explants indicated that skin cleansing with sustainable polysaccharide containing soap bars with boosted skin anti-microbial peptides (AMPs) like cathelicidin (LL37), RNase-7, and β -Defensin. Using quantitative biomarker analysis, we found that treatment with sustainable soap bars upregulate barrier-related biomarkers (Filaggrin, PNPLA1) which again can lead to the boost of epidermal integrity. When challenged with *S.aureus* soap treated explants exhibited significant pathogen reductions: where AMP-enhancing formulations reduced bacterial colonization (evidenced by CFU/cm² assays). Overall, treatment of skin explants with low TFM sustainable soap bars formulated with plant polysaccharides , neutralized pathogens, and modulated anti-microbial peptides, while preserving and boosting skin barrier integrity.

Conclusion:

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Using skin ex-vivo models we demonstrate that cleansing with low TFM sustainable soap bars with plant polysaccharides, leads to the enhancement of skin barrier properties and immune barrier strength. For testing skin cleansers and their impact of skin barrier properties, such ex-vivo models help bridge the gap between in vitro studies and human clinical trials.

Analysis of allergenic compounds in a selection of 300 commercial moisturizing products

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Introduction & Objectives:

The market for moisturizers products is extensive. These products can be a source of contact allergens and play a major role in the development of allergic contact dermatitis (ACD) particularly in patients with atopic dermatitis (AD). The aim of this study is to determine the frequency of the main allergens in a sample of moisturizers available in a north African country.

Materials & Methods:

We conducted a descriptive survey between January and March 2023, visiting supermarkets, health and beauty stores and pharmacies in a north African country. The lists of ingredients of 300 moisturizer products were collected. Allergenic ingredients were identified based on the International Nomenclature of Cosmetic Ingredients (INCI) and cross-referenced with known allergens.

Results:

A total of 300 moisturizers marketed by 87 laboratories were identified. One hundred fifty-three products came from supermarkets (51%), while 147 products (49%) came from pharmacies and parapharmacies. The majority of products (72,7%) were imported from Europe. 83% were leave-on products, while 17% were rinse-off products. The average number of allergens per product in our series was 1,73. Only 10% of the products were labeled "allergen-free." Local-made products and those purchased in large retail stores contained significantly more allergens. Fragrances were the most common allergens (84,7%). Only 15,3% of the products contained neither explicit fragrances nor essential oils or plant extracts. Only a quarter of products labeled as "fragrance-free" were actually free of fragrances. Isothiazolinones were found in 7% (n=21) of the products, mainly in leave-on products and in local-made moisturizers. Formaldehyde and formaldehyde releasers were present in 10.3%. They were more commonly found in supermarkets and in leave-on products. Parabens were found in 10.7%. Two of these products contained a hidden paraben under the name Hydroxybenzoate. Most of these products were sold in large retail stores. Nearly a third of these products were intended for sensitive skin. Propylene glycol was present in 28%. A quarter of the products containing propylene glycol were labeled as hypoallergenic. Phenoxyethanol was found in 37.7%. Products containing phenoxyethanol were more frequently sold in large retail stores.

Conclusion:

Moisturizers play a crucial role in managing skin conditions like AD. However, they can also trigger ACD due to certain allergenic ingredients. Fragrances and preservatives are the leading causes of cosmetic allergies. 90% of the moisturizing cosmetic products in our sample contained at least one allergen. Fragrances, phenoxyethanol, and propylene glycol were the top three allergens in our series. A study by Hamann et al. found that 89% of 187 pediatric skincare products labeled "hypoallergenic" or "dermatologist-tested" contained at least one contact allergen. The persistence of isothiazolinones in leave-on moisturizing cosmetics in our country, despite their formal ban in Europe since 2017, is problematic. The implementation of legislation in non-European countries to prohibit isothiazolinones in leave-on cosmetic products would contribute to addressing this issue. Fragrance allergy is a frequent cause of ACD in patients with AD. The dermatologist's role is particularly challenging,

especially since labels like "fragrance-free" and "hypoallergenic" have proven to be unreliable in practice, as our study clearly demonstrated.

Unexpected Anaphylaxis After Cystoscopy: The Hidden Risk of Ortho-Phthalaldehyde

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Introduction & Objectives:

Perioperative anaphylaxis is an uncommon but potentially life-threatening reaction. Ortho-phthalaldehyde (OPA), a high-level disinfectant increasingly used in medical device reprocessing, has been identified as a rare cause of anaphylaxis. Here, we report a case of OPA-induced anaphylaxis following cystoscopy.

Materials & Methods:

A 66-year-old woman was referred to our adult clinical immunology and allergic diseases outpatient clinic following an anaphylactic reaction during a routine cystoscopy. She had undergone multiple cystoscopic procedures for bladder polyps since 2016. Approximately 15 minutes after the most recent procedure was completed, she developed symptoms consistent with grade four anaphylaxis, including nausea, vomiting, generalised urticaria, lip angioedema, peripheral numbness, chills, transient speech difficulty, and hypotension (blood pressure: 80/30 mmHg). Prompt initiation of anaphylaxis treatment led to complete resolution of symptoms, with no evidence of a prolonged or biphasic reaction.

Results:

An allergy workup was conducted four weeks after the index reaction to identify the causative agent. Procedural documentation confirmed the use of latex gloves, povidone-iodine, and a lubricating gel containing 2% lidocaine hydrochloride and 0.05% chlorhexidine dihydrochloride. No systemic medications were administered periprocedurally. After informed consent was obtained, skin testing was performed using latex, povidone-iodine, the lubricating gel in its original form, lidocaine, and chlorhexidine, all of which yielded negative results. Subcutaneous provocation testing with lidocaine at recommended incremental dilutions was also negative. Serum-specific IgE to latex was within normal limits.

Further investigation focused on a disinfectant solution containing 0.55% OPA, which was routinely used for sterilising cystoscopy equipment at the hospital. A skin prick test with OPA was performed: the positive control produced a 5×5 mm wheal, while 0.55% OPA yielded an 8×8 mm wheal with central grey-black discolouration and a surrounding flare measuring 45×45 mm at 15 minutes. The same test was negative in two healthy, non-atopic control subjects. Based on the clinical history, temporal association with exposure, and positive skin test results, OPA was identified as the likely trigger of the anaphylactic reaction. A subsequent cystoscopy using OPA-free cystoscope was uneventful, with no recurrence of allergic symptoms.

Conclusion:

Ortho-phthalaldehyde is a high-level chemical disinfectant commonly used to reprocess medical devices. Although anaphylaxis associated with OPA exposure has been reported in various settings, including cystoscopy, laryngoscopy, and colonoscopy, the majority of documented cases have emerged from the urological literature. OPA is a low-molecular-weight compound (molecular weight ~134 Da). Demonstrating the involvement of specific IgE in hypersensitivity reactions induced by low-molecular-weight agents is often challenging. Nonetheless, in the present case, skin testing yielded a positive result, suggesting the presence of OPA-specific IgE

and supporting the diagnosis of an IgE-mediated mechanism.

Dendritic cell homeostasis in the skin depends on ILCs-derived IL-13

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Introduction & Objectives:

The maintenance of skin homeostasis relies on barrier integrity and effective immune surveillance. Innate lymphoid cells (ILCs) are innate immune cells, which reside in barrier tissues such as gut, lung, and skin in steady-state. ILC2s produce type 2 cytokines interleukin (IL)-13 and IL-5, which has been implicated in tissue repair and modulation of eosinophils function. However, the specific role of ILC-derived IL-13 in shaping skin immune cell networks remains poorly understood. Furthermore, published evidence suggests that skin ILCs may exhibit transcriptional and functional overlap between ILC2 and ILC3 subsets. Our study aims to investigate whether ILC2s-derived IL-13 contributes to the maintenance of skin dendritic cell (DC). In addition, we aim to dissect whether skin ILC heterogeneity and plasticity influence immune regulation in steady-state.

Materials & Methods:

Nmur1iCre-eGFPeId2fl/fl, RORgtiCreId2fl/fl and IL13iCre-eYFPRosa26LSL-RFP mice were maintained and bred in a SPF facility. Male mice aged 8 -14 weeks were used for all experiments. Single-cells suspensions were incubated on ice with anti-CD16/32 antibody and a panel of fluorescent-conjugated antibodies. A public scRNA-seq dataset (GSE120787) of mouse skin ILCs was re-analyzed. ILCs were isolated from epidermis, dermis and subcutis. Datasets from skin layers were batch-corrected by using Harmony.

Results:

ScRNA-seq data revealed that ILCs showed distinct transcriptomic profiles from different layers. Subcutaneous ILC2s shared a common transcriptional signature with ILC2s in other barrier organs, expressed phenotypical markers ST2 and KLRG1 and enriched for type 2 cytokines IL-13, IL-5. Dermis and epidermis ILCs showed more diversity expressed ILC2-associated genes *Il13, Il5* and ILC3 key transcription factor retinoic acid receptor-related orphan receptor (ROR)γt, indicating the presence of heterogeneous ILC populations. Consistent with *Il13* gene expression, IL-13 fate-labeling analysis validated that IL-13 production by ILC2 and other ILC subsets. Given that IL-13 was required for CD11blo skin DC2 development, we tested whether these cells were altered in the absence of ILC2 using ILC2-deficient mice. Despite a deficiency of ILC2s, the frequency of CD11blo DC2s was unaffected in ILC2-deficient mice. Similarly, in *Nmur1iCre-eGFP Il4/13fl/fl* mice, CD11blo DC2s were comparable to those in littermate controls. Given the observed heterogeneity of skin ILCs, which displayed both ILC2 and ILC3 signatures, we proposed that IL-13 derived from non-ILC2 subsets might compensate for the absence of ILC2s. To test this, we generated mice deficient in both ILC2s and ILC3s. Consistent with the finding that CD11blo DC2s required IL-13, this subset was significantly decreased in mice lacking both ILC2 and ILC3 but not in ILC3-deficient mice and littermate controls.

Conclusion:

Here we describe skin-resident ILC-derived IL-13 plays a critical role in maintaining the homeostasis of CD11blo DC2s in steady-state. While ILC2s are the major source of IL-13, their absence alone has no effect on CD11blo DC2s. Instead, the combined deficiency of both ILC2 and ILC3 populations results in a significant reduction of

CD11blo DC2s, highlighting the functional redundancy and plasticity within the skin ILC compartment. These findings reveal the broader role of ILC-derived IL-13 in regulating dendritic cell networks and maintaining immune homeostasis in the skin.

Generalized bullous fixed pigmented erythema mimicking toxic epidermal necrolysis: About two-cases

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Introduction:

Fixed pigmented erythema (FPE) is a cutaneous adverse drug reaction characterized by recurrent skin lesions that reappear at identical sites upon re-exposure to the causative agent. The generalized bullous form is rare and may clinically mimic toxic epidermal necrolysis (TEN). This resemblance can lead to inappropriate management, highlighting the importance of accurate diagnosis.

We report two cases of generalized bullous FPE initially suspected to be Lyell syndrome, where clinical evolution and histopathological findings enabled correct diagnosis and appropriate therapeutic management.

Case 1: A 58-year-old woman with no significant medical history developed a generalized pruritic bullous eruption 24 hours after taking etoricoxib. On examination, she was hemodynamically and respiratorily stable, with erythematous macules on the trunk and limbs, extensive post-bullous erosions, a positive Nikolsky sign, with a "wet sheet" appearance on the back, and fissured cheilitis. Laboratory tests were unremarkable. Skin biopsy revealed minimal epidermal necrosis with perivascular lymphocytic infiltration. Drug causality assessment implicated etoricoxib. The patient improved with dual antihistamine therapy and local wound care.

Case 2:

A 51-year-old man, with a history of schizophrenia treated with levomepromazine and diazepam for 10 years, presented with generalized erosions that developed within 24 hours after taking omeprazole. On admission, the patient was conscious, hemodynamically and respiratorily stable, and exhibited large post-bullous erosions on the back, buttocks, and thighs, along with hyperpigmented macules on the trunk and a positive Nikolsky sign, but no oral or conjunctival mucosal involvement. Laboratory tests were unremarkable, and the biopsy supported a diagnosis of FPE. The pharmacological investigation implicated omeprazole as the cause. The patient's condition improved favorably with antihistamines and topical ointment dressings.

Conclusion

Generalized bullous FPE although rare, poses a major diagnostic challenge due to its clinical similarity to TEN. The distinctive feature of these cases lies in the absence of severe systemic involvement despite extensive skin lesions, along with a misleading positive Nikolsky sign, and favorable progression with simple antihistamine treatment eliminating the need for aggressive therapy or intensive care measures typically reserved for Lyell syndrome. These cases highlight the importance of histology and pharmacological investigation to avoid inappropriate management but performing a skin patch test that was not possible in these cases remains the key to diagnosis. The drugs most frequently implicated in FPE include nonsteroidal anti-inflammatory drugs (such as etoricoxib), antibiotics (sulfonamides, tetracyclines), anticonvulsants, and, more rarely, proton pump inhibitors (omeprazole). This warrants heightened vigilance when prescribing these medications, especially in cases of recurrent lesions at the same sites.

Overview of dermatologic symptoms in idiopathic mast cell activation syndrome - case series

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Introduction & Objectives:

First proposed as a distinct idiopathic disorder in 2010, mast cell activation syndrome (MCAS) is finding increasing use as a diagnosis for signs and symptoms involving the dermis, gastrointestinal tract, and cardiovascular system. The definition of MCAS is based on three types of criteria that all have to be met for diagnosis to be established: episodic, objective signs and symptoms consistent with mast cell activation involving at least two organ systems (skin, upper or lower respiratory systems, gastrointestinal or cardiovascular); laboratory markers of MC activation (event-related serum tryptase level elevated above 120% of the individual's serum baseline + 2 ng/mL) and clinical response to drugs that counteract MC mediators or prevent their release. We present clinical and paraclinical characteristics of a cohort of patients with primary MCAS evaluated between January 2022 and December 2024.

Materials & Methods:

The objective of this study was to describe the clinical and paraclinical characteristics of a cohort of patients with primary MCAS. The following data were collected: demographic, mast cell activation-related symptoms, history of anaphylactic shock and bone fracture, general osteoporosis risk factors, and time between first clinical symptoms and MCAS diagnosis. Laboratory values included level of mast cell tryptase in blood, level of bone marrow tryptase, presence of mast cells by immunohistochemical analysis on bone marrow biopsyskin biopsy, molecular, immunophenotypic analysis of bone marrow mast cells. The diagnosis of MCAS was established in 12 patients: three (25%) male and 9 (75%) female with a median age of 42 years at diagnosis time. The median time from first symptoms to diagnosis was 48 months.

Results:

Eleven patients (91%) had skin manifestations: 5 (45%) angioedema, 6 (54%) chronic urticaria, 8 (72%) pruritus and 8 (72%) flushing. Five patients (41%) had a history of idiopathic anaphylactic shock. Ten patients (83%) presented with gastrointestinal symptoms (diarrhea, vomiting, and/or abdominal pain) and one (8%) with pollakiuria.

The median basal serum tryptase level was 5.7 μ g/L, No patient had increased mast cells inbone marrow biopsy and for three patients (25 %) the number of mast cells identified in skin was >20/field (x 40). Bone densitometry was abnormal for only one patient (8%) with osteopenia.

Conclusion:

In conclusion MCAS is characterized by a high frequency of skin manifestations and diagnosis is delayed by a mean of four years. The frequency of idiopathic anaphylactic shock (41%) seems more important than in those of systemic mastocytosis. The median basal serum tryptase levels are within normal limits even in patients experiencing serious mast cell activation-related symptoms showing the limited utility of these parameters to establish MCAS diagnosis.

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Contact dermatitis secondary to the application of Euphorbia helioscopia, commonly known as "euphorbe réveille-matin."

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Introduction

The spurges (Euphorbia helioscopia L) are toxic plants that naturally grow in the mid-European regions. The most toxic part is the milky sap (latex), which can induce severe contact dermatitis and conjunctivitis if it comes into contact with the skin or eyes. We report a case of a patient presenting with a case of contact dermatitis associated with secondary conjunctivitis following the local application of Euphorbia helioscopia. There are few documented cases of contact dermatitis in the literature attributed to the plants of Euphorbia helioscopia L.

Case report:

The patient is a 57-year-old woman with no notable medical history, particularly no history of atopy or plant use. She presented with alopecic lesions on the eyebrows and preauricular temporal regions, having directly applied Euphorbia helioscopia through friction to treat the alopecic lesions, with no history of oral ingestion. Eight hours later, she noticed the sudden appearance of a poorly defined erythematous and edematous plaque with intense pruritus. The plaque was covered with crust and exhibited oozing at the site of plant application, accompanied by swelling of the upper eyelids and ocular burning. The condition showed improvement following a ten-day prescription of dermocorticoids, along with the application of a protective and reparative barrier cream, corticosteroid eye drops, and healing eye drops. The toxic agent was avoided during the course of treatment.

Discussion:

Contact dermatitis includes irritant and allergic forms, with irritant dermatitis caused by a local innate immune response to the offending agent, as seen in our patient. In contrast, allergic dermatitis involves a delayed hypersensitivity reaction mediated by sensitized T lymphocytes. In this case, the causative agent was *Euphorbia helioscopia*, a toxic plant traditionally used for scalp treatments. Its milky sap contains irritant compounds, notably 12-deoxyphorbol, responsible for severe skin irritation and other systemic symptoms upon skin, eye, or oral exposure.

Conclusion:

this case emphasizes the need to raise awareness among the general population and healthcare professionals regarding the toxicity of Euphorbiaceae, particularly Euphorbia helioscopia. This plant has the potential to cause severe skin irritation and conjunctivitis upon contact with the skin or eyes, as evidenced in our patient.