

Abstract N°: 644**Real-life Utility of Basophil Activation Test in the Diagnosis of Immediate Hypersensitivity Drug Reactions**

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Introduction & Objectives: The basophil activation test (BAT) is a flow cytometry laboratory technique that assesses the level of activation indicators expressed on the basophils' surface. We conducted a real-life study in a prospective cohort of patients with reported drug hypersensitivity reactions to determine the true relevance of the Basophil Activation Test (BAT) as a diagnostic tool for the assessment of immediate hypersensitivity reactions to medicines.

Materials & Methods: We prospectively assessed individuals who had a clinical suspicion of immediate hypersensitivity reactions to drugs over a two-year period. The allergological evaluation was carried out in accordance with the guidance of the EAACI. In all patients, BAT was performed using the activation markers CD63.

Results: In total 13 patients with 54 reported immediate drug hypersensitivity reactions to medications were included in this study. In total, there were 92.3% (12/13) females and 7.70 (1/13) males. The mean age of the patients was 47.31 ± SD 19.94 years. There were 35.2% (19/54) antibiotics tested, followed by 24.1% (13/54) corticosteroids, 14.8% (8/54) iodinated contrast medium, and 5.6% (3/54) NSAIDs. 69.2% (4/13) of the patients yielded a positive BAT, whereas 30.8% (4/13) had a negative BAT result. The sensitivity of BAT 5% CD63+ basophils was 69.2% (9/13) and specificity was 100% for drug allergies.

Conclusion: The sensitivity of BAT for drug allergies is limited, but it can nevertheless be very helpful before contemplating provocation testing in cases of life-threatening drug allergies where patients cannot be re-challenged or in cases of medications for which no other tests are available or their results are ambiguous.



Abstract N°: 695**Preventative effects of Siegesbeckia herbal extract against PM10 in xerosis mouse model**Nam Gyoung Ha^{*1}, MI Hee Kwack², Gi Ung Ha¹, Seon Hwa Lee¹, Dae-Lyong Ha¹, Weon Ju Lee¹¹Kyungpook National University Hospital, Dermatology, Daegu, Korea, Rep. of South, ²Kyungpook National University School of Medicine, Immunology, Daegu, Korea, Rep. of South**Introduction & Objectives:**

Particulate matter (PM) can cause oxidative stress, inflammation, and skin aging. We investigated the effect of Siegesbeckia herbal extract (SHE) against PM10 in xerosis mouse model.

Materials & Methods:

Acetone was applied on the dorsal skin of the 7 week-old nude mice for 5 min. Tape stripping was also performed on the dorsal skin of the 7 week-old nude mice. After then, vehicle, PM10 100 μ /ml, PM10 100 μ + 100 μ of SHE 10 μ /ml, or 100 μ of SHE 10 μ /ml was applied the mice for 1 week. Skin hydration was measured. Real-time PCR and enzyme-linked immunosorbent assay (ELISA) for inflammatory cytokines, and immunofluorescence staining for keratinocyte differentiation markers were performed.

Results:

PM10 decreased skin hydration and SHE increased skin hydration in the mice. PM10 upregulates the expression of inflammatory cytokines, including IL1 β , IL4, IL6, IL8, and TNF- α in the mice and SHE inhibited the upregulation of inflammatory cytokines. ELISA showed the same result with real time PCR. PM10 downregulates the expression of keratinocyte differentiation markers, including loricrin, involucrin, and filaggrin, in keratinocytes of the mice and SHE prevented the downregulation of the keratinocyte differentiation markers.

Conclusion:

PM10 can aggravate xerosis mouse model in skin hydration, inflammatory cytokine, and keratinocyte differentiation markers. In addition, SHE can modulate changes in the xerosis mouse model by PM10.



Abstract N°: 1048**Tattoo reactions in a Melanoma patient treated with BRAF and MEK inhibitors**

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Introduction & Objectives: Reactions to tattooing are very frequent manifestations that can be classified as: acute inflammatory reactions, allergic reactions from hypersensitivity, granulomatous and pseudolymphoma type reactions. Most granulomatous reactions are observed in patients with sarcoidosis and, more rarely, are drug-induced.

Materials & Methods: We present the case of a 40 years old patient with Dabrafenib and Trametinib therapy from July 2022 for melanoma IIIID BRAFV600E-mutated that comes to our attention for the appearance of erythema, edema and flaking associated with itchy symptoms only in tattoos with black pigment saving colored ones. The patient reports that the reactions had appeared more pronounced in more recent tattoos than in older ones.

Results: Patch tests with the SIDAPA (Società Italiana di Dermatologia Allergologica Professionale e Ambientale) baseline series (Euromedical, Calolziocorte, Italy) were performed. Patch tests were applied on the back and left in occlusion for 2 days with AI Test (Euromedical) on Scanpor Tape (Norgesplaster, Vennesla, Norway). Readings performed at day D2, D4 and D7 showed negative reaction. The skin biopsy reveals "moderate lymph-histiocytic inflammatory infiltration (CD3+, CD68+ and CD163+) at which an abundant proportion of blackish exogenous pigment is found". High potency topical corticosteroid is prescribed and complete resolution of lesions is observed in two weeks without the need to discontinue systemic therapy with Dabrafenib and Trametinib.

Conclusion: Drug-induced tattoo reactions are rare events and, indeed, only four cases similar to ours are present in the literature: three of these describe frankly granulomatous findings at biopsy, the other only mild lymphocytic infiltration similar to that found in our experience. In our case, unlike the others, the suspension of systemic treatment was not necessary to obtain the resolution of skin manifestations.



Abstract N°: 1762**Allergic contact dermatitis: knowledge, attitudes, and management in general practice**

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Introduction & Objectives:

Allergic contact eczema (ACE) is the 2nd most common cause of eczema. It is a very common inflammatory skin condition. The aim of our study is to evaluate the knowledge of general practitioners (GPs) regarding the management of ACE.

Materials & Methods:

This is a descriptive cross-sectional study conducted in May 2022 through a 18-question form, containing information about the physicians and their knowledge about the management of ACE.

Results:

A total of 96 general practitioners responded to the questionnaire, of whom 52% were between 25 and 35 years old and 30% between 35 and 45 years old with a female-to-male ratio of 1.8. Almost half of them worked in the private sector with a practice duration of more than 5 years for 84% and 94% managed ACE. ACE represented between 20 and 40% of all consultations in 79% of cases and the hands were the most frequently affected area. Difficulty in making a positive diagnosis was encountered in 56% of cases and the reasons for referring patients to a dermatologist are diverse: chronicity (50%), resistant forms (84%), occurrence of complications (41%) and sometimes even immediately (10%). Moreover, 57% found difficulties in differentiating between acute and chronic forms. Regarding the diagnosis, 38% responded that it relied on history and clinical examination (CE), 16% on histology, 22% on skin tests (ST) only and only 24% combined history, CE and ST. In addition, 89% of them thought that these STs are always positive in ACE. Only one-third knew the most frequently encountered allergens. Symptomatic treatment of ACE relied on topical corticosteroids (TCS) in 42% of cases, TCS combined with antihistamines in 26%, systemic corticosteroids in 23% and antihistamines alone in 9%. Avoidance of the allergen was systematic in all responses. Finally, only 36% of the physicians considered that occupational eczema would justify a work stoppage.

Conclusion:

This study highlights the difficulties encountered by GPs in the management of ACE. It is a frequent reason for consultation in general medicine. This benign dermatosis represents a public health problem due to its increasing prevalence, chronic and refractory forms, and the difficulty in identifying the allergen. Diagnosis relies mainly on interrogation and CE, which will guide the realization of STs. However, these STs are not always positive. Some atypical forms, including chronic eczema, could mislead the physician. Symptomatic treatment relies on DCs, avoidance of the allergen, which is a prerequisite for healing since there is no possibility of desensitization, and prevention, which represents a crucial step. It is thus important to inform patients. Eczemas of occupational origin may even justify a work stoppage and require professional reclassification. Continuous training of GPs in dermatology, particularly in the management of ACE, would allow for better management of this disease.

Abstract N°: 2006**Autophagy ..the secret behind vitiligo**Hanan Rabeeh Nada*¹¹Cairo, Dermatology, Cairo, Egypt**Introduction & Objectives:**

Autophagy is a lysosomal degradative process that is essential for the cell viability, homeostasis, and maintenance. The objective of this work was assessment of the level of microtubule-associated protein 1 light chain 3 (LC3)-I, LC3-II, and beclin 1 as indicators of autophagy and superoxide dismutase (SOD) and malondialdehyde (MDA) as indicators of oxidative stress in patients with vitiligo.

Materials & Methods:

This comparative case-control study was conducted on 20 patients with nonsegmental vitiligo as well as 20 controls. LC3-I, LC3-II, and beclin 1 tissue expressions were detected by western blot analysis, whereas MDA and SOD were measured by the colorimetry method in the tissue homogenate.

Results:

The LC3-I, LC3-II, beclin 1, and SOD levels were significantly lower in lesional skin than nonlesional skin of patients as well as both lesional and nonlesional skin of patients than controls ($P < 0.001$)

Conclusion:

Downregulated autophagy as evident by downregulated levels of autophagic markers together with dysregulated oxidative stress species could play a role in the pathogenesis of vitiligo, and optimizing autophagy could open a new era in vitiligo treatment



Abstract N°: 2065**The role of microRNAs in the regulation of the generation and maintenance of skin resident memory T cells**

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Introduction & Objectives: Contact allergy to at least one allergen is common in the European population with a prevalence of 27%. It can develop into allergic contact dermatitis (ACD), which is an inflammatory skin condition characterized as a delayed-type hypersensitivity reaction manifesting as skin rash and it is known that allergen-specific epidermal tissue resident (TRM) cells are important in the development of ACD. It is known that miRNAs can regulate various components of our immune system, including TRM cells. However, the precise mechanism of how they regulate the generation and maintenance of different T cell subsets in the skin is not known. This project aimed to identify miRNAs that are important for the generation and maintenance of TRM cells in a mouse model of ACD.

Materials & Methods: In this study, a contact hypersensitivity mouse model was used where the mice were sensitized on the ears with the 1-Fluoro-2,4-dinitrobenzene (DNFB) or olive oil:acetone (OOA) and challenged on the ears with DNFB or OOA after a minimum of 21 days. The response was analyzed at different time points. We analyzed the mRNA and miRNA expression levels in the epidermis and sorted TRM cells.

Results: As expected the challenge with DNFB led to an increase in ear thickness and in the number of TRM cells in the epidermis compared with the control group. We identified several miRNAs differentially expressed upon challenge with DNFB (Let7a, miR-18a, miR-150, and miR-31) in the epidermis. Additionally, we were able to detect decreased miR-31 and IL34 expression in the sorted TRM cells in the DNFB group compared with the control group. It has been previously shown that IL-34 contributes to the development and maintenance of specific immune cells in a tissue-specific manner. Interestingly, the only miRNA to target IL-34 is miR-31. The stimulation of activated CD8 T cells with IL-34 led to the decreased proliferation of the CD8 T cells and differential expression of CD25 on the cells.

Conclusion: Our results demonstrate that there are miRNA expression changes in response to contact allergens in the contact hypersensitivity mouse model and miRNAs could contribute to the maintenance and regulation of TRM cells. More precisely we show that miR-31 and IL34 are downregulated in TRM cells in response to DNFB and therefore might play a role in the pathogenesis of ACD by regulating the viability and activity of immune cells.

Abstract N°: 2199**Association between nickel hypersensitivity and device syndrome after patent foramen ovale closure in female patients: preliminary results of a randomized - controlled trial**

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Introduction & Objectives:

Percutaneous patent foramen ovale (PFO) closure has been performed widely as secondary prevention in patients with cryptogenic stroke. Two devices are approved by Food and Drugs Administration (FDA) and are used commonly; Amplatzer® PFO occluder and Gore Helex® septal occluder. Both devices' frame is constructed by nitinol, an alloy of nickel and titanium. While it is known that nickel remains the most frequent cause of hypersensitivity reaction globally, data regarding nickel hypersensitivity secondary to PFO closure are sparing. Our randomized - controlled trial investigates whether individuals with known nickel hypersensitivity experience more adverse events after device implantation and compare the adverse events between two devices. Objective of this analysis is to explore whether female patients with known nickel hypersensitivity undergoing PFO closure presents more adverse events.

Materials & Methods:

Consecutive patients undergoing PFO closure were enrolled in our trial and were randomized to receive either Amplatzer® or Gore® device, with parallel assignment and randomization 1:1. Nickel skin patch tests were performed both prior and 90 days after the procedure. During three-months follow-up, clinical manifestations and transthoracic echocardiographic findings are evaluated and associated with patch skin tests.

Results:

A total of 20 female patients with completed follow-up are included in the present analysis. Their mean age was 38.3 years old. Clinical symptoms associated with device syndrome (palpitations, dyspnea, rash, chest pain) were met in 9 patients. A total of 13 patients were diagnosed with nickel hypersensitivity. The presence of symptoms differs significantly among the patients with positive and negative nickel skin patch results ($p=0.042$). Moreover, we did not find any interaction comparing the two devices.

Conclusion:

Our preliminary analysis of female patients showed that positive nickel skin patch test is related with more symptoms associated with device syndrome. Completion of our study is mandatory for exacting more consistent conclusions.

Abstract N°: 2474**Evaluating the efficacy of a neurosensine-enriched dermocosmetic in patients with sensitive skin and/or allergies: A one-month observational study**

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Introduction & Objectives: Sensitive skin and allergies are influenced by various factors, including demographic characteristics, environmental triggers, and living conditions. Specific dermocosmetic products (DC) are designed to alleviate symptoms associated with these conditions. In this study, our objectives are to describe the baseline profile of patients with sensitive or intolerant skin and allergies (demography, main triggers, living environment, type of allergy) and assess the efficacy of a DC after one month of use, based on clinical evaluations by dermatologists and self-assessments by patients.

Materials & Methods: This observational study was conducted in dermatologist offices of 6 countries with a total of 2,018 patients with sensitive skin and/or allergy. Patients were assessed at baseline and after one month of using a DC containing shea butter and glycerine moisturizer ingredients in combination with neurosensine, sphingobioma, neurofense ingredients that target the signs of skin sensitivity and support the skins barrier function.

Results: The study included 79.8% female, with a mean age of 37.6 (range 3-89) and 57.0% having phototype I/II. The majority of participants (77.8%) resided in a city. Among the participants, 68.8% had cutaneous allergies, 24.5% had respiratory allergies, 18.2% had eye allergies, and 11.7% had a food allergy. After using the DC for one month, there were noticeable improvements in all parameters, as assessed by both dermatologists and patients. Participants reported a reduction in skin itching, irritation, burning sensations, and discomfort after exposure to various environmental factors.

Conclusion: This study demonstrates the effectiveness of the DC in alleviating symptoms associated with sensitive skin and allergies. The findings provide valuable insights into the baseline profile of patients with these conditions and highlight the potential benefits of using DC to improve skin health and overall quality of life.** C1 - Internal use

C1 - Internal use



Abstract N°: 2877**Drug-Induced Erythromelalgia: A Case Report**Mouhsine Zineb¹, Fatim Zahra El Fatoiki^{1, 1}, Hali Fouzia¹, Ahlam Miftah², Fouad Haddad³, Soumia Chiheb¹¹UCH Ibn Rochd , Department of Dermatology and Venereology, , casablanca,²Faculty of Medicine and Pharmacy, Laboratory of Pharmacology, casablanca, ³UCH Ibn Rochd , Gastrologic department, casablanca**Introduction:**

Erythromelalgia is a rare paroxysmal acrosyndrome that most often affects the lower limbs bilaterally and symmetrically. It is caused by a combination of neurological and vascular disorders and can be triggered by a variety of factors. We report an unusually rapid onset of erythromelalgia following the initiation of treatment with metronidazole, ciprofloxacin, and infliximab.

Case report:

A 38-year-old patient, with no history of smoking or alcoholism, was followed up for ileo-coecal Crohn's disease after initially receiving corticosteroid therapy and azathioprine. Due to therapeutic inefficiency, a first course of infliximab was administered. Due to the appearance of a deep peri-uterine collection, the patient underwent surgical drainage and was administered antibiotics: metronidazole, ciprofloxacin, amoxicillin-clavulanic acid, and enoxaparin. After 4 weeks, the patient developed insomniac pain with burning, tingling, and paresthesias in both feet, associated with erythema and marked and persistent edema. These symptoms were relieved by elevating the limbs and immersing them in cold water.

The dermatological examination revealed edema in both legs that extended to the bucket, accompanied by a hot and painful erythema in both feet without any other associated signs. The neurological examination revealed spontaneous hyperalgesia and palpation with sharp Achilles reflexes without any motor deficits or amyotrophy. The blood count and plasma protein electrophoresis were normal on a biological level, and the immunological test was negative. The electroneuromyogram showed a predominantly sensitive polyneuropathy.

The diagnosis of induced erythromelalgia was made due to the negativity of the etiological examination, the chronology, and the history of multiple drug intakes. The imputability study revealed a score of I5B4 for infliximab, ciprofloxacin, and metronidazole, an I2B2 score for amoxicillin-clavulanic acid, and an I2B1 score for enoxaparin. In addition to discontinuing the incriminated drugs, the patient was treated symptomatically with acetylsalicylic acid, level II analgesics, amitriptyline, and pregabalin, leading to almost complete resolution of the cutaneous and neurological signs.

Discussion:

Erythromelalgia is characterized by the triad of erythema, increased local warmth, and paroxysmal pain. The triggering or exacerbation of the crisis by warmth or physical activity, as well as its amelioration by immersion of the limb in cold water, is pathognomonic of this pathology. It can be primary or secondary to various etiologies, such as hematological disorders, neoplasia, and metabolic diseases. Drugs have also been implicated in its occurrence, mainly iodinated contrast agents, calcium channel blockers, and bromocriptine, but no case reports have previously implicated ciprofloxacin, metronidazole, or infliximab as being responsible for erythromelalgia. Peripheral neuropathy induced by the prolonged administration of these drugs has been described but remains rare, in contrast to flushing, which is a frequent side effect of infliximab in particular.

The pathogenic mechanism is common, with a double component: neurological, which consists of a primary dysfunction of the small nerve fibers; and vascular, which is characterized by an alteration of the microcirculation and hypoxia.

Treatment usually consists of discontinuation of the offending drug and symptomatic therapy.

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Abstract N°: 2878**The scent of grape fruit methane (thiocineol) induced a specific intracellular calcium increase in human keratinocytes**

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Introduction & Objectives:

Sensory irritation can be induced when keratinocytes and/or peripheral free nerve endings directly sense odorants or fragrances via G-protein coupled olfactory receptors or TRP channels. This stimulation can trigger a neuro-inflammatory response in keratinocytes, which can ultimately lead to a typical toxic-irritant acute-chronic contact dermatitis. The objective of this study was to screen 27 frequently used fragrances for their potential to induce a transient change in calcium level in the cultured human keratinocytes. It also further explored the potential signalling pathway of thiocineol, a grape fruit methane, selected for its unique and robust calcium fluxes in human keratinocytes.

Materials & Methods:

27 odorant compounds, commonly used in cosmetics and consumer products, were evaluated. Calcium imaging technique analyses the real time $[Ca^{2+}]_i$ changes in response to transient exposures to external stimuli. Thiocineol concentrations of 50 μ M, 100 μ M, 250 μ M, 500 μ M, 1 mM, 2 mM, and 5 mM were tested (Fig. 2a). It was further tested in foreskin fibroblasts, HEK293FT (embryonic kidney cells), and peripheral neurons (Fig. 2b). Keratinocytes were stimulated with thiocineol in the calcium free interstitial solution. An array of inhibitors were applied to gain more insights into the possible pathway of thiocineol-induced $[Ca^{2+}]_i$ (Fig. 2a).

Results:

Initial calcium imaging revealed that out of the 27 commonly used odorants, six induced a strong and reproducible intracellular calcium response (Fig. 1a). Thiocineol was shown to induce intracellular calcium influxes in keratinocytes (Fig. 1c). A repeated application of 1 mM thiocineol revealed a consistent and application-dependent response (Fig. 1c). It was further found that thiocineol increased $[Ca^{2+}]_i$ in keratinocytes and fibroblasts while there was little or no effect in renal and neuronal cells. When keratinocytes were stimulated in a calcium free interstitial solution the calcium signals were reduced or abolished.

During testing of inhibitors, it was seen that suramin, an inhibitor of G-protein signalling, blocked the calcium fluxes while ruthenium red, a broad spectrum TRP blocker, reduced $[Ca^{2+}]_i$ in keratinocytes. U73122, an inhibitor of phospholipase C (downstream of $G\alpha_q$ subunit) and to a lesser extent with MDL-12, an inhibitor of adenylyl cyclase (downstream of $G\alpha_s$ subunit) diminished the $[Ca^{2+}]_i$ influxes evoked by thiocineol. Pre-treatment with dantrolene, a ryanodine receptor inhibitor (downstream of $G\alpha_s$ signalling), significantly reduced the calcium response.

Conclusion:

The majority of the odorant compounds did not induce any significant calcium signal. However, it was observed and described here for the first time that the grapefruit methane, thiocineol, can induce strong calcium signals in

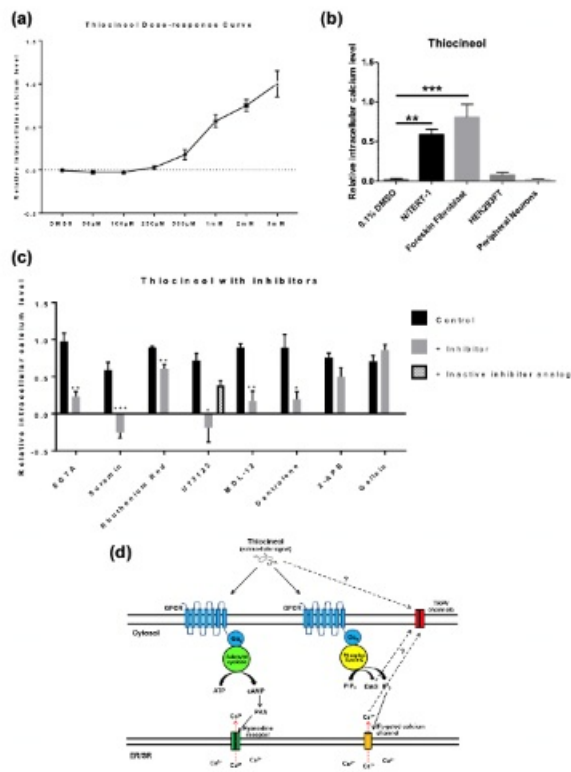


Figure 2. Effect of inhibitors on thiocineol-induced calcium signals, dose-response curve of thiocineol, thiocineol effect in different cell types and possible signalling pathway activated by thiocineol

(a) Relative calcium responses provoked by different concentrations of thiocineol (50 μM, 100 μM, 250 μM, 500 μM, 1 mM, 2 mM, 5 mM)..

(b) Comparison of calcium signals induced by 1 mM thiocineol in N/TERT-1, Foreskin fibroblast, HEK293FT, Peripheral neurons

(c) Comparison of calcium responses in control and inhibitor-treated N/TERT-1 cells; Control: 1 mM thiocineol (n>3), EGTA: 1 mM EGTA (n=3), Suramin: 1mM suramin (n=3), 10 μM ruthenium red (n>3), U73122: 10 μM U73122 (n>3), MDL-12: 125 μM MDL-12 (n>3), Inactive inhibitor analogue of U73122: 10 μM U73343 (n>3), Dantrolene: 60 μM Dantrolene (n=3), 2-APB: 80 μM 2-APB (n=3), Gallein: 30 μM gallein (n=3).

(d) Possible calcium signalling pathways induced by thiocineol in keratinocytes based on the sites of action by classical signalling pathway inhibitors



Abstract N°: 2924**Eczema over nuchal nevus simplex, Meyerson phenomenon? 4 cases**Aïcha Salhi¹, Odile Enjolras², Michel Wassef², Assya Djeridane¹, Abdelhamid Aitbenamar³¹Heliport de l'hôpital militaire, Djasr Kasentina, Algeria, ²Lariboisière Hospital AP-HP, Paris, France, ³Clinique RAHMOUNI Djilali (ex Les Orangers), El Mouradia, Algeria

Introduction & Objectives: Meyerson phenomenon (MP) is characterized by an eczematous halo around a pre-existing skin lesion. This phenomenon has frequently been described around melanocytic lesions or non-melanocytic skin neoplasms (lentigo, keloid dermatofibroma...). Only few cases related to vascular lesions have been reported in the literature, the first one published in 1996 concerned 3 infants with MP overlying capillary malformations CM of the occipital region and the nape of the neck. Cases with MP are usually treated with steroid ointment. In case of recurrence, pulsed dye laser PDL allows complete healing by removing the vascular mark. Pathogenesis of MP is not clear. It is generally more common in atopics. However the interaction between CD4 T lymphocytes and ICAM-1 may play an important role. It may be precipitated by atopy or vascular laser treatment of the capillary malformation CM. We report here the cases of 4 infants presenting MP overlying a "salmon patch: nevus simplex" on the nape of their neck.

Observation: Case1 A 7 month-old girl had since birth a salmon patch on the back of the neck. This lesion was complicated by an eczematous eruption as she was 6 month-old. The vascular lesion was covered by a congestive erythema with oozing vesicles, yellowish crusts and white scales. The infant was turning her head to rub her neck against her clothes while moaning with confirmed pruritus. The lesion considered as MP was treated with desonide ointment during one week with good result but it relapsed. The same treatment was repeated with a permanent cure. Case2 An 8-month-old girl had a congenital salmon patch on the nape of her neck covered for a few days with eczema. A single course of topical steroids was enough to cure eruption. Case 3 A 4 month-old girl had a congenital naevus flammeus on the occipital scalp and a salmon patch on the nape of the neck since birth. A congestive scaly eruption covered the salmon patch with severe itching and spared the naevus flammeus. Steroid ointments were used with transient resolution. During 2 years several flares necessitated topical steroid courses because PDL was not available. The MP ceased as she was 17 month-old. Case 4 A 9 month-old boy had a congenital salmon patch on the back of his neck. He developed atopic dermatitis since he was 4 month-old. He had vesicles and scales on his salmon patch each time he presented an atopic dermatitis flare. Steroid ointment was used on all lesions at each flare and complete improvement was finally achieved.

Discussion: Meyerson phenomenon or "halo-eczema" developing over vascular anomalies is rare. MP needs to be differentiated from halo nevus, cause in this last the naevus disappear when the halo resolves. Pathogenesis of MP is not clear; however the interaction between CD4 T lymphocytes and ICAM-1 may play an important role. Pigmentary disturbance in halo nevus, in contrast, is mediated through CD8 cells.

Conclusion: A better understanding of MP's pathogenesis could even shed light on the differences between nevus simplex and nevus flammeus or PWS which are however both capillary malformations.



Abstract N°: 3103

Bimekizumab improves key patient-reported symptoms of axial spondyloarthritis including spinal pain and fatigue: results from two phase 3 studies

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Introduction & Objectives:

Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A. BKZ improved signs and symptoms and reduced disease activity up to Week (Wk) 24 in patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA) and radiographic axSpA (r-axSpA; i.e., ankylosing spondylitis)¹ in the phase 3 studies BE MOBILE 1 (NCT03928704) and BE MOBILE 2 (NCT03928743), respectively; all primary and ranked secondary endpoints at Wk 16 were met, including change from baseline (CfB) in nocturnal spinal pain.² Here, we evaluate the impact of BKZ in pts with nr-axSpA and r-axSpA on major contributors to disease burden (e.g., spinal pain, stiffness and fatigue)³ to Wk 24 in both studies.

Materials & Methods:

BE MOBILE 1 and 2 were conducted in parallel and had similar designs, with a 16-wk double-blind period followed by a 36-wk maintenance period. Pts were randomised to BKZ 160 mg Q4W or placebo (PBO); all pts received BKZ 160 mg Q4W from Wk 16 onward.² We report proportion of pts achieving selected thresholds at Wk 16 for low pain (total and nocturnal spinal pain score: $\leq 0/1/2/3/4$) and improvement in fatigue (Functional Assessment of Chronic Illness Therapy [FACIT]-Fatigue score: ≥ 4 -point increase from baseline [BL]) using non-responder imputation. Mean CfB to Wk 24 in total spinal pain, nocturnal spinal pain, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) morning stiffness (mean of BASDAI questions 5 and 6) and FACIT-Fatigue scores are reported using multiple imputation.

Results:

254 pts with nr-axSpA (BKZ: 128; PBO: 126) and 332 with r-axSpA (BKZ: 221; PBO: 111) were randomised; 94.5% and 94.3% completed to Wk 24, respectively. Across both studies, mean BL scores for all reported outcomes indicated high symptom severity (**Figure 1, 2**).

A greater proportion of both nr-axSpA and r-axSpA pts treated with BKZ vs PBO achieved lower total and nocturnal spinal pain scores at Wk 16 (**Figure 3**). Pts treated with BKZ also achieved reductions from BL in mean total spinal pain, nocturnal spinal pain and BASDAI morning stiffness scores to Wk 24, with separation from PBO

observed at the first post-BL assessment (Wk 1; **Figure 1**). Responses at Wk 24 for pts who switched from PBO to BKZ at Wk 16 approached those seen in BKZ-randomised pts.

Similarly, at Wk 16, a higher proportion of pts achieved ≥ 4 -point improvement in FACIT-Fatigue score with BKZ vs PBO (nr-axSpA: 70.3% vs 45.2%; r-axSpA: 66.1% vs 49.5%). Improvement in FACIT-Fatigue scores to Wk 24 were also observed across nr-axSpA and r-axSpA pts treated with BKZ, with separation from PBO at first post-BL assessment (Wk 4; **Figure 2**). Among pts who switched from PBO to BKZ at Wk 16, responses at Wk 24 approached those seen in BKZ-randomised pts.

Conclusion:

Treatment with BKZ resulted in rapid and clinically relevant improvements in spinal pain, morning stiffness and fatigue in pts with active axSpA regardless of radiographic classification (nr-axSpA and r-axSpA), with separation from PBO at first post-BL assessment. These findings emphasise the benefit of BKZ for clinical symptoms which are important to pts and have significant impact on their daily lives.

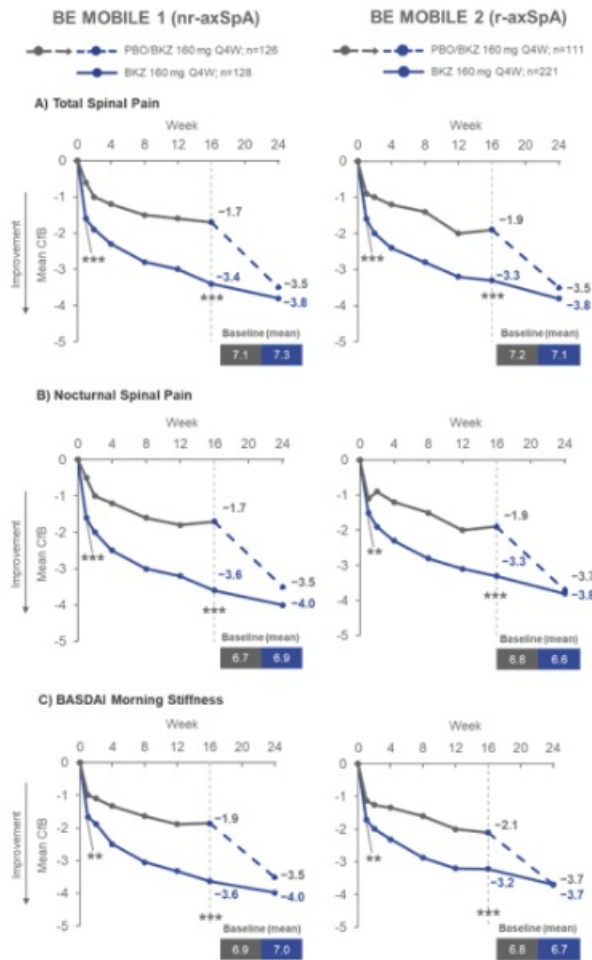
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Funding

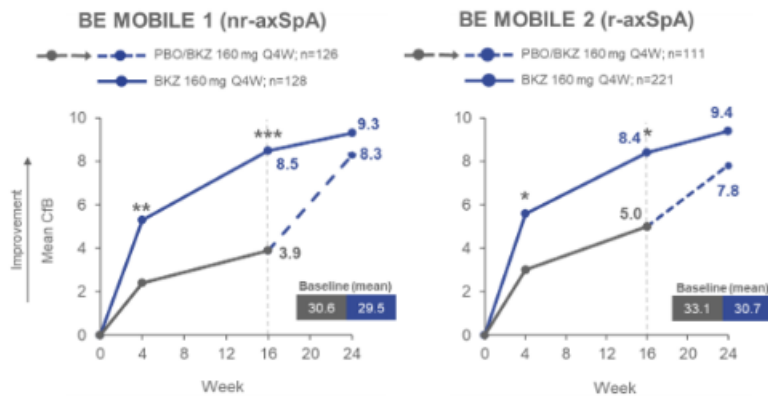
These studies were funded by UCB Pharma. Medical writing support was provided by Costello Medical.

Figure 1. Mean change from baseline in (A) total spinal pain, (B) nocturnal spinal pain and (C) BASDAI morning stiffness scores to Week 24



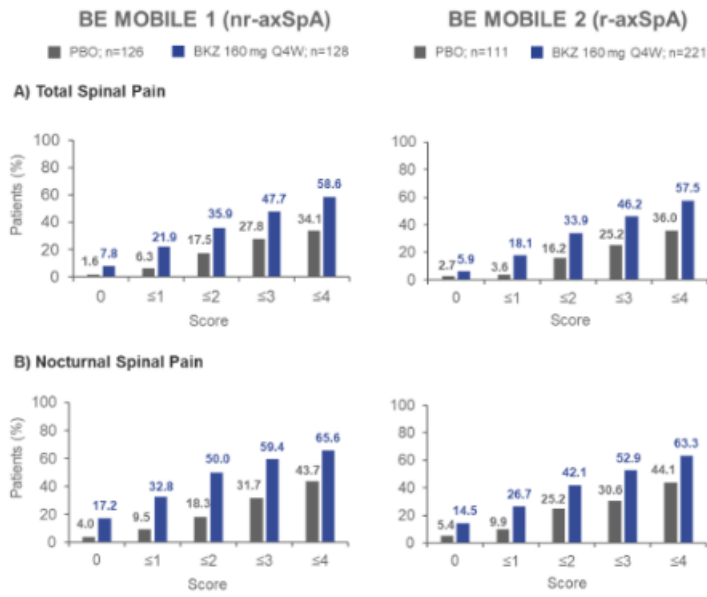
Randomised set. Multiple imputation. Spinal pain scores range from 0–10 with lower scores reflecting better health status. BASDAI morning stiffness score assessed as mean of BASDAI questions 5 and 6; scores range from 0–10 with lower scores reflecting better health status. Nominal p values were calculated at Week 1 and Week 16 for total spinal pain, and at Week 2 for nocturnal spinal pain; these did not control for multiplicity. p values calculated at Week 16 for nocturnal spinal pain were part of a hierarchical gatekeeping strategy and used reference-based multiple imputation. ** $p \leq 0.01$; *** $p \leq 0.001$. p values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indication of statistical significance. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CFB: change from baseline; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Figure 2. Mean change from baseline in FACIT-Fatigue score to Week 24



Randomised set. Multiple imputation. FACIT-Fatigue score ranges from 0–52 with higher scores reflecting better health status. Nominal p values were calculated at Week 4 and Week 16, and do not control for multiplicity. * $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$. p values without any multiplicity adjustment are indicated as nominal p values and should not be used as an indication of statistical significance. BKZ: bimekizumab; CFB: change from baseline; FACIT: Functional Assessment of Chronic Illness Therapy; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.

Figure 3. Achievement of (A) total and (B) nocturnal spinal pain scores below varying thresholds at Week 16



Randomised set. Non-responder imputation. Spinal pain scores range from 0–10 with lower scores reflecting better health status. BKZ: bimekizumab; nr-axSpA: non-radiographic axial spondyloarthritis; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis.



Abstract N°: 3511**Comparison of skin suction blistering with and without heating in a local LPS challenge model in healthy volunteers**

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Introduction & Objectives:

Suction blisters induced by negative pressure on the skin can be used to study the local immune response and skin restoration. Studies have reported a positive effect of skin heating on blister induction time and volume. However, the effect of heat on endpoints like cytokine release and cellular responses measured in blister exudate is unknown. Intradermal administration of LPS in healthy adults results in an acute, localized, and transient inflammatory reaction that can be used as a *in vivo* inflammatory model. The aim of this study was to investigate the effect of heat on blister formation and inflammatory response in an intradermal LPS challenge model in healthy volunteers.

Materials & Methods:

Twelve healthy volunteers were included in this study. Each participant received 2 intradermal LPS injections on the volar forearms. Suction blisters were induced on these areas 6 hours later. In addition, two other blisters were formed on unchallenged skin. LPS injections were randomized over the proximal and distal forearms. The orifice plate was heated for blisters formed on the right arm, and not heated at the left arm for all participants. A clinical score was used to evaluate LPS-induced erythema. Tolerability of the added heat was evaluated using the NRS pain. Blister fluid was harvested for evaluation of cytokines by MSD and cellular response by flow cytometry.

Results:

LPS-induced erythema was similar prior to the start of blister formation for the heated and non-heated blisters. The number of total cells in blister exudate was significantly higher in the blisters after intradermal LPS compared to the blisters made on untreated skin ($P < 0.0001$). Overall, skin heating did not impact immune cell attraction, except for NK cells (significantly higher number of cells upon heating) ($P = 0.0083$). Blister exudate volume was significantly higher in the blisters upon heating ($P = 0.0117$). Heating resulted in significantly lower concentrations of IL-8 ($P = 0.0001$) and IL-10 ($P = 0.0056$) upon LPS challenge. Heat reduced blister formation time (LPS: 67 ± 14 minutes and non-LPS blisters: 81 ± 16 minutes for heated skin, versus LPS: 98 ± 28 minutes and non-LPS blisters: 119 ± 24 minutes for non-heated skin). Skin heating, combined with blister formation, was well tolerated.

Conclusion:

This study confirms findings from previous intradermal LPS challenge studies in healthy volunteers. Skin heating had a positive effect on blister induction time and volume, and limited impact on immune cell attraction and cytokine release. We conclude that skin heating can be implemented in blister induction, but for certain endpoints this may have impact which should be considered.



Abstract N°: 3643

Lupus miliaris disseminates faciei or localised acute Graft-versus-Host Disease ? A diagnostic dilemma occurring after hematopoietic stem cell transplantation

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Introduction & Objectives:

Hematopoietic stem cell transplantation (HSCT) continues to be the mainstay of treatment for many hematological diseases. There can be significant complications, however, and often these complications are manifested in the skin as an eruption. We present an interesting case of Lupus miliaris disseminates faciei (LMDF) occurring after allogenic stem cell transplantation. To our knowledge, our patient is the second report of LMDF occurring after HSCT.

Results:

A 36-year-old woman underwent autologous Stem Cell Transplant (SCT) for Acute Myeloid Leukemia (AML). Although the leukemia was initially treated with intensive induction polychemotherapy, remission was not achieved. Thus, the patient received three cycles of cytarabine and subsequently underwent SCT and prophylaxis for GVHD was performed with cyclosporine. Two months after discontinuation of cyclosporine , she presented to our dermatological department complaining of non-pruritic, papular eruptions on the face. The patient denied any fever, cough, dyspnea, lymphadenopathy, scleral or conjunctival pain or erythema, visual disturbances, or arthralgias. She denied any history of tuberculosis or any other cutaneous and/or systemic complaints.

Physical examination revealed numerous small, reddish brown papules ranging in size from 1mm to 3 mm, located around the mouth and nose, with symmetric distribution, no facial erythema with telangiectasias and flushing was observed. Dermoscopy of lesions showed structureless yellow-red areas and white areas suggestive of early scarring in a linear pattern, along with short linear and branching vessels arranged radially.

Laboratory results showed: A normal blood cell count, metabolic panel were normal. Venereal Disease Research Laboratory (VDRL) and HIV tests were negative. Calcium and angiotensin-converting enzyme levels were normal. A tuberculin skin test was negative, anti-nuclear antibody screen was also normal. A chest radiograph showed no abnormalities. Pulmonary function tests were unremarkable.

The first anatomopathological examination pointed to tuberculous lupus. She was diagnosed with skin tuberculosis at another hospital.

Histopathological analysis of skin specimens was repeated several times in order to exclude other granulomatous dermatosis. The second skin biopsy specimen revealed findings of acute graft-versus-host reaction. The patient was treated with prednisone, but the cutaneous process persisted.

The last skin biopsy revealed an epithelioid cell granuloma with central necrosis and surrounding lymphocytic infiltrate with multinucleate giant cells. PAS stain was negative for fungi and the acid-fast stain was negative for mycobacteria.

A diagnosis of LMDF was made depending on the above clinical and histological features.

Topical tacrolimus was then introduced, achieving significant improvement in 2 months, resulting in rapid flattening of the papular lesions leaving depressed, atrophic, varioliform scars.

Conclusion:

This is a rare case of LMDF occurring after HSCT, which showed rapid improvement with topical tacrolimus. We speculate this represents an unusual form of localised cutaneous graft-versus-host disease.

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Abstract N°: 3662

Allergy in total knee replacement surgery: Is it a real problem? - A case report

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Introduction & Objectives: Metal allergy or sensitivity after knee implantation is rare but possible. Most reactions to knee replacements are hypersensitive reactions and referred to as delayed-type hypersensitivity. It occurs due to the natural corrosion of metals over time that ultimately trigger the inflammatory immune response. When [immune system](#) overreacts or launches a defensive assault on the artificial joint and surrounding tissues, beginning local inflammation. Metal hypersensitivities typically present as contact dermatitis and can appear from 4 week to 2 years after the initial surgery, even without any history of reaction before.

Materials & Methods: A 40-year-old male presented with skin rash, and itching under his right knee that had started 4 days ago. He underwent total knee arthroplasty (TKA) 6 months ago due to trauma. On skin examination revealed erythematous maculopapular, edematous, bullous and scaly plaque lesions around his knee. The right knee was obviously swollen. During hospitalization, skin rash was disseminated over his face, trunk and extremities. He hadn't any significant medical history of allergy and he had no medication.

His white blood cell count and neutrophil differentiation were normal, but eosinophil differentiation was increased. Furthermore, C-reactive protein and erythrocyte sedimentation rate were mildly elevated. Knee aspiration revealed no evidence of bacterial infection. Radiographs demonstrated appropriate position and fixation of the cemented implants. After exclusion of other diagnosis and taking a short period of topical and systemic steroids, his skin lesions improved.

Results: Any metal that comes into contact with body tissues will corrode to some degree. This corrosion causes the formation of metal ions that ultimately trigger the inflammatory immune response. Clinical presentation of metal hypersensitivity is unspecific and symptoms are common to other complications. It is a very rare condition and is usually a diagnosis of exclusion. [Joint aspiration](#) can be used to obtain and evaluate the composition of immune cells in the knee fluid sample. The most common symptoms are joint effusion, swelling, stiffness, persistent pain at rest and decreased range of motion; less frequently, it is characterized by eczematous dermatitis, which can be local or generalized, extended to the neck, buttock and extremities. Rarely, a general complication may occur, such as rhinitis, itching or asthma, hair loss and alopecia. No generally accepted and reliable tests are available for the clinical diagnosis of metal hypersensitivity.

Good results have been reported after short-term therapy including topical and systemic steroids in treatment of cutaneous dermatitis. If the symptoms do not resolve, surgery with a hypoallergenic implant should be considered.

Conclusion: Metal hypersensitivity is a rare condition. Routine allergy testing prior to TKA is not recommended, unless a clear history of reactions has been reported. In cases of positive history and positive tests, a hypersensitivity-friendly implant should be considered. However, there is still a lack of evidence regarding correlation between metal hypersensitivity and implant-related complications. As a matter of fact, after TKA, one-stage revision surgery for metal or bone cement hypersensitivity should be considered only after ruling out most common causes of TKA failure and even after a short-term therapy aiming to solve cutaneous dermatitis and pain.

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Abstract N°: 4256

Terbinafine resistance in two cases of tinea faciei

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¹Mater Hospital, Dublin, Ireland

Terbinafine resistance in two cases of tinea faciei

L Victory, P Lenane

Introduction:

We report two separate cases of tinea faciei in young women both demonstrating resistance to terbinafine.

The dermatophytes *T. rubrum*, *T. interdigitale* and *T. mentagrophytes*, are the main aetiological agents of dermatophytosis of skin and nails in humans. [1] The acquired resistance of dermatophyte fungi to antifungal medication (both topical and oral) is on the rise globally. Terbinafine therapy is usually effective in eradicating infections by inhibiting their squalene epoxidase (SQLE) enzyme, but increasing numbers of clinically resistant cases and mutations in the SQLE gene have been documented recently. Sensitivity testing is becoming standardised and more widely available in some countries.

A 31 year old lady was referred to the dermatology outpatients with a two month history of a pruritic well demarcated erythematous rash on her chin. The patient received oral flucloxacillin and topical fucibet prescribed by the general practitioner, for presumed impetigo. There was no improvement noted from this treatment.

This lady has a background medical history significant for relapsing remitting multiple sclerosis diagnosed in 2019. In terms of medications she is on dimethyl fumarate for management of her MS.

She was reviewed in the dermatology clinic and the differential diagnosis was tinea faciei.

A Potassium hydroxide (KOH) direct microscopy confirmed the presence of trichophyton rubrum confirming the diagnosis of tinea faciei. She was commenced on oral terbinafine 250mg once daily by mouth for two weeks. There was some slow improvement in the rash while on oral terbinafine. It was noted in clinic that the rash was slow to improve on oral terbinafine and this was felt to be due to either terbinafine resistance or this lady's treatment for her multiple sclerosis. The terbinafine was continued for three months in total.

Following three months of oral treatment, this patient had an ongoing rash on her chin and we opted to switch to oral itraconazole 200mg once daily for four weeks duration. Following treatment with oral itraconazole the rash has fully cleared from her chin.

A 15 year old lady presented to a paediatric emergency department with a six month history of an extensive annular rash covering her face, neck, chest and arms. The general practitioner had previously prescribed topical daktacort, oral terbinafine (one week), topical fucibet and topical elocon without response.

A 4mm punch biopsy was performed due to an unclear diagnosis. The histology reported mild hyperkeratosis, spongiosis with occasional necrotic keratinocytes and evidence of fungal hyphae.

Skin scrapings confirmed trichophyton rubrum. This lady was commenced on oral terbinafine 250mg once daily for four weeks. Unfortunately there was very little response to oral terbinafine and she then required oral itraconazole for one month.

Conclusion:

These two cases demonstrate terbinafine resistance and emphasize the importance in sensitivity testing before prescribing antifungals. This new clinical entity is thought to be a consequence of the irrational use of over-the-counter corticosteroid–antifungal combinations, resulting in the emergence of terbinafine resistant isolates. #

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Abstract N°: 4474**Clinical significance of neutrophil extracellular traps (NETs)-associated markers in systemic lupus erythematosus (SLE)**Branka Bonaci-Nikolic^{*1, 1}, Ivica Jeremic², Aleksandra Nikolic³, Miloš Nikolić⁴

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Introduction & Objectives:

Neutrophil extracellular traps (NETs) are the main source of autoantigens in systemic lupus erythematosus (SLE). We investigated the clinical importance of NETs-associated markers in SLE.

Materials & Methods:

We compared NETs-associated markers in SLE patients (n = 111) with healthy controls (n = 50). In 35 de novo SLE patients, we studied correlation between NETs-associated markers [DNase I concentration, myeloperoxidase (MPO) activity, anti-MPO antibodies, cell-free DNA (cfDNA), NETolytic activity] with serological parameters [anti-dsDNA antibodies, C3, C4 and B-cell activating factor (BAFF) levels] and disease activity determined by modified SLE Disease Activity Index (M-SLEDAI-2K).

Results:

In comparison with healthy controls, SLE patients had higher cfDNA, MPO activity, anti-MPO antibodies ($p < 0.001$), BAFF and DNase I concentration ($p < 0.01$). Contrary, NETolytic activity was lower in SLE patients ($p < 0.05$), despite higher concentration of DNase I. MPO activity and cfDNA levels showed correlation with DNase I concentration ($p < 0.001$, $p < 0.01$, respectively). BAFF levels correlated with cfDNA, DNase I concentration and MPO activity ($p < 0.05$). Anti-dsDNA antibodies showed correlation with MPO activity ($p < 0.01$), cfDNA and BAFF levels ($p < 0.001$). Anti-dsDNA and C3 levels were independent predictors of M-SLEDAI-2K in multivariate analysis ($p < 0.01$).

Conclusions:

We demonstrated that sera of SLE patients have decreased NETolytic activity, leading to increased levels of various NETs-associated markers, which correlate with anti-dsDNA antibodies in de novo SLE. We showed that BAFF participates in a complex relationship between NETosis and anti-dsDNA antibodies production. These findings have important implications for a better understanding of SLE pathogenesis and development of therapy that inhibits persistence of NETs and disease progression.

Abstract N°: 4605**Vascularite urticarienne: environ 7 cas**

Ikram Meghoufel¹, Tareq Bahlaq¹, Mekki Sahar¹, Haoui Hanane¹, Serradj Amina¹

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Introduction & Objectives:

Urticarial vasculitis represents 5 to 10% of chronic urticaria[1]. Predominantly in adult women[2]; A distinction is made: Hypocomplementemic urticarial vasculitis or McDuffie vasculitis and normo-complementemic urticarial vasculitis[3].

Materials & Methods:

We report the cases of 7 patients who were followed for urticarial vasculitis (UVA) at the dermatology department of the EHU of Oran over a period of 2 years (from January 1, 2020 to November 30, 2021). The diagnosis of urticarial vasculitis was made in front of the association of clinical, anatomopathological and immunological arguments.

For each patient, epidemiological data, clinical and paraclinical characteristics of UVA at the time of diagnosis, associated systemic diseases, therapeutic modalities and evolution of the condition were collected.

Results:

The 7 patients were female, the average age was 40.42 years with extremes ranging from 22 to 73 years, 2 patients (28.57%) had a personal history of idiopathic thrombotic purpura and depression (14.28% each).

The average duration of symptoms before diagnosis was 2 years with extremes ranging from one month to 8 years. The major clinical sign was urticarial plaques in all our patients, followed by sequellar lesions in 5 patients (71.42%), whereas purpuric lesions were present in only 2 patients (28.57%).

The average skin surface area (SSA) affected was 25.71% with extremes ranging from 18% to 50% of SSA. The dominant functional sign was pruritus which was present in all patients (100%), only one patient had pain and burning (14.28%). Angioedema was noted in 2 patients (28.57%) (Figure 01). For immunological tests: antinuclear factors were positive in only 1 patient (14.28%). For immunological tests: antinuclear factors were positive in only 1 patient (14.28%) with a speckled appearance; the complement C3 level was normal in all patients; C4 was decreased in 3 patients (42.85%); the C1q level was measured in only 3 patients, of which it was low in one (33.33%). The skin biopsy showed signs of perivascular infiltrate in favor of UV in all patients, one patient had arthralgia (14.28%). The impact on quality of life was very important in 2 patients (28.57%) and moderate in 3 cases (42.85%) (figure 2).

Antihistamines were prescribed in 6 patients (85.71%), Opocalcium® in 2 patients (28.57%), oral corticosteroids in 1 case (14.28%), Dapsone® in 1 case and dermocorticoids in 3 cases (42.85%).

The evolution under treatment was favorable in 4 patients (57.14%) and not satisfactory in the rest.

Conclusion:

This study describes the characteristics of patients with urticarial vasculitis showing the spectrum of clinical, immunological manifestations and therapeutic management as well as the impact on the quality of life of

patients.

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Abstract N°: 4628**Flow-mediated skin fluorescence as a potential tool in the measurement of endothelial dysfunction in patients with primary and secondary Raynaud's phenomenon.**

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Flow-mediated skin fluorescence as a potential tool in the measurement of endothelial dysfunction in patients with primary and secondary Raynaud's phenomenon.**Introduction & Objectives:**

Mixed connective tissue disease and systemic sclerosis are characterized by dysfunction of microcirculation, which can be observed in capillaroscopic examination. Flow-mediated skin fluorescence (FMSF) is a non-invasive method used to assess the endothelial dysfunction based on NADH fluorescence measurement during ischemia and reactive hyperemia. Previous studies showed the utility of FMSF in the measurement of endothelial dysfunction in patients with: chronic heart failure, diabetes, chronic obstructive pulmonary disease and systemic lupus. This is the first study in which FMSF was used to assess endothelial dysfunction in patients with Raynaud's phenomenon.

The aim of our study was to assess endothelial dysfunction with FMSF in patients with primary, secondary Raynaud's and healthy controls. Another aim of the study was to compare FMSF results in patients with normal, non-specific and scleroderma-like pattern in capillaroscopy.

Materials & Methods:

Patients included to the study were men and women over 18 years of age, patients of Departments of Dermatology, Rheumatology and Immunology, University Hospital in Krakow, Poland. We included 106 individuals: 51 with secondary Raynaud's (e.g., patients with systemic sclerosis, mixed connective tissue disease, systemic lupus), 26 with primary Raynaud's and 29 controls. Exclusion criteria were: the presence of clinically evident atherosclerosis, diabetes, pregnancy and active cancer.

Results:

Patients with primary, secondary Raynaud's and healthy controls differed significantly in assessed FMSF parameters: HRindex% (p = 0.013), RHR% (p = 0.011), PSD1 (p < 0.0001), FM (p < 0.0001), PSD2 (p = 0.0014), FM(R) (p = 0.0015), endo(R)% (p = 0.024), neuro(R)% (p = 0.0022), myo(R)% (p = 0.0012), HS (p < 0.0001), log(HS) (p < 0.0001), ENDO (p = 0.0002), NEURO (p = 0.0004), MYO (p < 0.0001), MYO(R) (p < 0.0001). There were significant changes in FMSF parameters between normal capillaroscopy, non-specific and scleroderma-like patterns: HRindex% (p = 0.0001), HRmax% (p = 0.0002), RHR% (p = 0.0005), PSD1 (p = 0.0008), FM (p = 0.0026), endo(R)% (p = 0.017), myo(R)% (p = 0.026), HS (p = 0.018), log(HS) (p = 0.017), ENDO (p = 0.018), NEURO (p = 0.006), MYO (p = 0.001), MYO(R) (p = 0.018).

Conclusion:

Flow-mediated skin fluorescence is a promising tool in the assessment of endothelial dysfunction in patients with

connective tissue diseases. Patients with systemic disease and prominent scleroderma-like pattern in capillaroscopy were characterized by the most severe endothelial dysfunction measured with FMSF.

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Abstract N°: 5191**Understanding the allergenicity of birch pollen: influencing environmental factors and associated health effects**

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Introduction & Objectives:

Challenging environmental conditions, such as the increasing effects of climate change, can affect the plant allergenicity, modify pollen characteristics and influence the occurrence and intensity of allergic respiratory diseases. This study aims to investigate the correlation between pollen data from birch trees grown under different climatic conditions and the molecular composition of the pollen, as well as the skin prick test (SPT) responses in allergic patients. Understanding the underlying processes may help in the prediction and management of allergic diseases, especially in the context of climate change.

Materials & Methods:

Birch pollen samples were collected from 2019 to 2022 at different locations in Europe. Information on abiotic factors (air temperature, relative humidity, global solar radiation, air pollution) and biotic factors (tree growth parameters, cherry leaf roll virus infection) was collected. Standardised pollen extracts were prepared, and correlations were made between environmental and tree-specific data, allergenicity-related parameters (total protein content, Bet v 1 content, lipid mediators, lipopolysaccharide (LPS), serotonin, histamine) and skin prick test (SPT) results (wheal-size). Three settings were studied: genetically identical birch trees in international phenological gardens (ROI-1), individuals of different tree clones in a seed plantation (ROI-2), and trees along an altitudinal gradient with different genetic backgrounds and climatic conditions (ROI-3).

Results:

In general, pollen allergenicity was influenced by the genetic background of the trees, with year-to-year variation having an even greater effect. Of the measured pollen-intrinsic parameters, Bet v 1 and total protein content were the strongest predictors of the severity of the SPT result. In ROI-1 and ROI-2, wheal size was more strongly correlated with the total protein content than with Bet v 1. Significant negative correlations were observed between the variables stem circumference and Bet v 1 or wheal size. In addition, wheal size showed a significant negative correlation with the altitude of the tree location. Finally, we observed a significant positive correlation between the Bet v 1 content and the mean temperature of the previous 3 months before flowering onset.

Conclusion:

Our results suggest that the allergenic potential of birch pollen varies annually and is influenced by both, the

genetic background of the tree and the prevailing climatic factors. While Bet v 1 is the major birch allergen, allergenicity of birch pollen may depend on different compounds in the pollen matrix, such as histamine and LPS. Birch trees at higher altitudes or in cooler regions produce less allergenic pollen, suggesting that trees in warmer climates tend to increase allergenicity due to environmental stress. In the context of climate change, this may imply that adverse health effects for atopic individuals.

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Abstract N°: 5397**Development and validation of measurement instruments for the recording of patient-defined Benefit Assessment in Therapy of Bronchial Asthma and Allergic Rhinoconjunctivitis**Slatina Christov¹, Marina Otten¹, Matthias Augustin¹¹UKE, Institute for Health Services Research in Dermatology and Nursing (IVDP), Hamburg**Introduction & Objectives:**

Asthma bronchiale (AB) and Allergic Rhinoconjunctivitis (AR) are both chronic diseases which have an enormous impact on the health-related quality of life (HRQoL). Conventionally, the patient benefits of a certain therapy are measured by deriving information from HRQoL instruments. With the Patient Benefit Index for Asthma bronchiale (PBI-AB) and the Patient Benefit Index for Allergic Rhinitis (PBI-AR), standardized tools for AB and AR were developed and validated. To assess commonalities of the PBI-AB and the PBI-AR specific for the assessment of benefit in the treatment of both diseases.

Materials & Methods:

Review of the PBI-AB and PBI-AR.

Results:

The patients achieved a mean PBI of 2.3 ± 1.1 (Median: 2.3, $n = 100$) and ranged from 0 to 4. The PBI was slightly higher for men (2.5 ± 1.0) than for women (2.1 ± 1.1).

Applying a threshold of PBI 1, $n = 86$ patients (87.8%) attained relevant benefit from current treatment.

Distribution of the PBI-AB. The patients achieved an index value of 2.1 ± 1.1 at home. At the second time point, there was a slight increase with an index value of 2.2 ± 1.2 . Thus, a relevant patient-defined benefit of the therapy was found at both time points. One question of this study was whether the patient-defined benefit depends on sociodemographic and clinical parameters.

Conclusion:

The Patient Benefit Index are both valid and feasible practical instruments for recording patient benefit. The achieved mean of both PBI versions were over the value of 2.1 ± 1.1 .



Abstract N°: 5418**Grading of patients with indolent systemic mastocytosis (GRAMMY).**

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Introduction & Objectives: This study aimed to investigate the heterogeneity within the group of patients with indolent systemic mastocytosis (ISM), which is the most common subtype of systemic mastocytosis (SM) and generally has a favorable prognosis. Recently, smoldering SM (SSM) has been recognized as a distinct subtype of SM due to the higher risk of disease progression. Although the clinical significance of the World Health Organization (WHO) classification, which categorizes non-advanced mastocytosis into cutaneous mastocytosis (CM), ISM, and SSM, is widely acknowledged, there is limited research on the variability within the ISM subgroup. Therefore, the objective of this study was to identify subtypes among ISM patients based on specific clinical and laboratory parameters.

Materials & Methods: Medical records of 270 patients who gain *KIT* D816 mutation as detected in either peripheral blood (PB) or bone marrow (BM) were analyzed. Clinical and laboratory parameters, including WHO-criteria for SM, were further investigated. Among the patients who met the WHO-criteria for ISM, a total of 86 individuals were included. A hierarchical cluster analysis was performed using a machine learning-based *gower* algorithm applied to 29 numerical and categorical variables.

Results: Most of ISM patients were females (n=60, 69.8%) with mean age of 53 years (min-max: 18-84) and median disease duration of 13 years (IQR: 8-20). Anaphylaxis (29/63, 46.0%), mastocytosis in the skin (MIS; 67/77, 87.0%), osteopenia and/or osteoporosis (53/75, 70.7%), osteosclerosis (3/75, 4.0%), spontaneous fractures (7/43, 16.3%), high serum basal tryptase levels (sBT, ≥ 20 ng/ml; 66/84, 78.6%), hepato- and/or splenomegaly (14/68, 20.6%), presence of dense MC infiltrates in BM (77/86, 89.5%), CD25 expression in BM (88/101, 74.6%) and signs of dysmyelopoiesis (16/85, 18.8%) were present in some of patients. The median *KIT* D816V allele burden in PB was 0.80% (IQR: 0.25-2.55) and median sBT was found to be 34.8 ng/ml (IQR: 21.0-76.0). Within the group of ISM patients we identified distinct clusters different in age, *KIT* D816V allele burden, sBT level, total IgE, lactate dehydrogenase (LDH), alkaline phosphatase (AP) and absolute neutrophil counts (ANC). Further analysis is needed to identify the predictive value of these parameters for disease progression.

Conclusion: Our data show various subtypes of patients within ISM group with distinct clinical and laboratory characteristics. Identifying ISM subtypes could provide valuable insights into the disease and help predict patients at risk of progression.



Abstract N°: 5461**Patch Test On Steven Johnson Syndrome Patient With Human Immunodeficiency Virus**Aris Cahyono¹, Muhammad Irawanto¹¹Sebelas Maret University, Dermatology and Venereology, Surakarta, Indonesia

Introduction & Objectives: Human immunodeficiency virus (HIV) is a contagious disease of an immune system that has developed over the years into one of the most refined human beings. Highly active antiretroviral therapy has significantly reduced HIV morbidity and mortality. The prevalence of drug hypersensitivity in HIV patients occurs about 100 times more often than in the global population.

Materials & Methods: A 36-year-old male with a history of maculopapular eruption and Steven Johnson's syndrome supported by aluvia[®], tenofovir, lamifudine, evafirenz, nevirapine, lamifudine-zidovudine, paracetamol, clindamycin, folic acid, cotrimoxazole, ibuprofen and amoxicillin. The drug patch test was performed 6 weeks after the patient was free of skin lesions and did not use corticosteroids and antihistamines. The drug patch test sites were performed with 1%, 5%, 10%, and 20% concentrations of antiretroviral (ARV) in the petrolatum and others drugs 10% concentrations in the petrolatum. Chamber is opened after 48 hours and ready to reading, and we are reading again at 72 hours and 96 hours after the application.

Results: The results are (+) in lamivudine, nevirapine and cotrimoxazole.

Conclusion: The drug patch test can be proven. Nevirapine is a non-nucleoside reverse transcriptase inhibitor that has the most common side effects of cutaneous adverse drug reaction (CADR). Lamivudine is an ARV that has very minimal toxicity, although in this case proved positive. Cotrimoxazole is reported to have caused more than 50% of ADR when administered simultaneously with antiretroviral drugs so the use of this drug requires special surveillance to predict the occurrence of CADR. Negative drug patch test in other drugs will not allow for negative results that may result from low concentrations and patch testing procedures that performed.



Abstract N°: 5516**Prospective Cohort Study: Hexyl-2,5-diaminobenzoate is a Hypoallergenic Alternative for Patients with Allergic Contact Dermatitis to Para-Phenylenediamine**

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³University of Minnesota Medical School, Minneapolis, United States,⁴University of Minnesota, Department of Dermatology, Minneapolis, Minnesota, United States, ⁵University of Minnesota, Fairview Compounding Pharmacy, Minneapolis, United States, ⁶Skin Research Institute of Singapore (SRIS), Singapore, Singapore,⁷ASTAR Skin Research Labs, Singapore, Singapore, ⁸Medical University of South Carolina, Department of Drug Discovery, College of Pharmacy, Charleston, United States

Introduction & Objectives:

Hair dyes, such as p-phenylenediamine (PPD), are a frequent cause of potentially severe allergic contact dermatitis and are the most used active ingredients in permanent hair dyes. Sensitization to PPD can impact quality of life due to physical, medical, financial, and social burdens. Our group previously described the synthesis, safety profile, and hair dye properties of novel hair dye alternatives: hexyl-2,5-diaminobenzoate (PPD6) and hexyl 2-amino-5-((4-aminophenyl)amino)benzoate (PPD7). In this next stage of dye development, a small clinical trial was performed for PPD6 and PPD7. The objective was to test the allergenicity of PPD6 and PPD7 with patch tests in individuals with a previously proven contact allergy to PPD.

Materials & Methods:

A prospective cohort study at the University of Minnesota conducted patch testing to PPD6 and PPD7. Inclusion criteria consisted of a current or previously relevant positive patch test reaction to PPD or PTD, and age 18 to 90 years old. Exclusion criteria included use of oral immunosuppressive, anti-inflammatory, and/or chemotherapy medications within one month of study visit; use of systemic steroids within 4 weeks of study visit; immunocompromised state; liver disease; human immunodeficiency virus; use of illicit drugs within the past 6 months; and pregnancy. PPD6 and PPD7 were applied on the upper arms of participants in patch test chambers (Chemotechnique IQ Ultimate) on day one and removed on day 2 with readings and photodocumentation at Day 2 and Day 4. Other data collected included demographics (age, sex, race, ethnicity), medication history (past month), atopy (allergic rhinitis, atopic dermatitis, nasal polyposis, asthma, peripheral eosinophilia, eosinophilic esophagitis), history of reactions to hair dye (date, location), and patch test history.

Results:

A total of 8 subjects were included from October 2021 to May 2022 at the University of Minnesota. All subjects were female (8/8), while most subjects were Caucasian (7/8), over 40 years of age (6/8), and endorsed a history of atopy (6/8). None of the subjects (0/8) reacted to PPD6 in the 1% or higher 2% concentration, while the majority (6/8) of the subjects reacted to PPD7 (1% and 2%) and/or to the commercially available PTD 1% (3/8) and ME-PPD 1% (6/8).** Subjects #3-6 had slightly reduced reaction strength to ME-PPD and PPD7 compared to PPD, and subjects #7-8 had no cross-reactions to ME-PPD and PPD7.

Conclusion:

The results from in vitro/in chemico tests and these patch tests on PPD sensitized patients indicate that PPD6 offers a safe alternative for patients with sensitizations to PPD, which is not the case for the commonly used alternatives PTD, ME-PPD, and also our compound PPD7. It is hypothesized that the potential reduction in skin sensitization by PPD6, compared to PPD7 and PPD, is due to the presence of moderate electron withdrawing groups at the ortho position of PPD. This would decrease electron density and prevent protein binding to the electrophilic (or electron-poor) benzene ring.** Since the meta position would then be unavailable for nucleophilic substitution due to the presence of the amino group, there would be less binding of nucleophilic skin proteins on the benzene ring of PPD6. PPD6 thus may be a hypoallergenic alternative for permanent dark hair dye in patients with contact allergy to PPD, and may also prevent future contact allergy to PPD. However, further studies are needed using PPD6 as hair dye in PPD allergic individuals.

Figures:

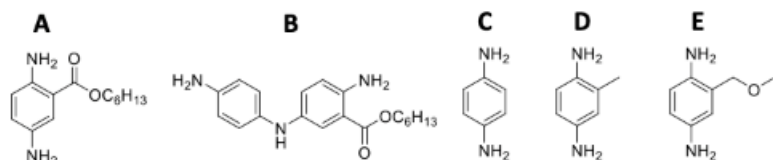


Fig. 1. Molecular structure of PPD6 and PPD7. Molecular structure of (A) PPD6, (B) PPD7, (C) PPD, (D) PTD, and (E) ME-PPD. ME-PPD, 2-methoxymethyl p-phenylenediamine; PPD, p-phenylenediamine; PTD, p-toluenediamine; PPD 6, Hexyl-2,5-diaminobenzoate; PPD 7, hexyl 2-amino-5-((4-aminophenyl)amino)benzoate.

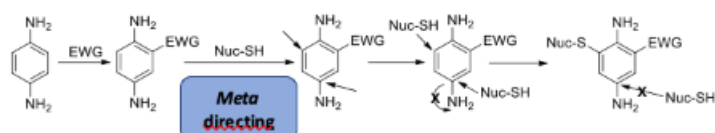


Fig. 2 Plausible protein binding mechanism of ortho electron withdrawing group (EWG) substituted monomeric derivative PPD6; (EWG: COOC6H13).

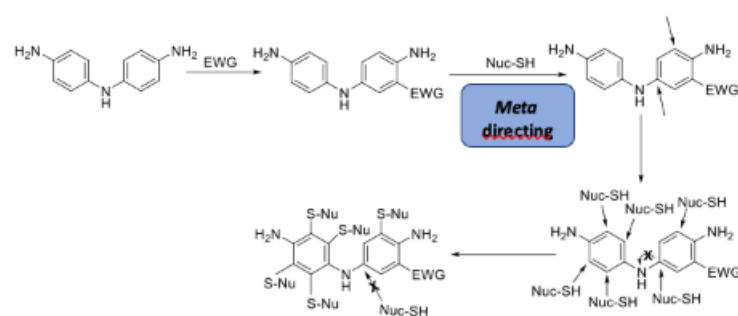


Fig. 3 Plausible protein binding mechanism of ortho electron withdrawing group (EWG) substituted dimeric derivative PPD7; (EWG: COOC6H13).

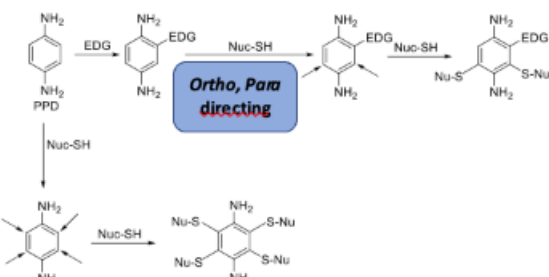


Fig. 4 Plausible protein binding mechanism of hair dyes PPD and ortho electron donating group (EDG) substituted derivatives PTD; (EDG: CH3), ME-PPD; (EDG: CH2OCH3).

Subject	Allergen (reaction strength)
1	Fragrance mix I (++) , fragrance mix II (++) , citral (++) , 3-aminophenol (++) , p-aminophenol (++)
2	4-aminobenzene (++) , disperse orange 3 (++) , glycerol thioglycolate (++) , p-aminophenol (+) , fragrance mix I (+/-) , amidoamine (+/-) , linalool (+/-) , methylisothiazolinone (+/-) , personal hair dye product (+)
3	Benzoyl peroxide (++) , bacitracin (++)
4	p-aminophenol (++)
5	Nickel (++) , fragrance mix II (+) , p-aminophenol (+) ,
6	No additional sensitizations
7	Methylisothiazolinone (++) , Methylchloroisothiazolinone (+) , two personal hair dye products (++)
8	Dimethylaminopropylamine (++) , butylhydroxytoluene (+)

Table 1. Past patch test reactions excluding PPD and PTD. Past patch test reactions of the included subjects, excluding reactions to PPD and PTD.

Subject	PPD 1%	PTD 1%	ME-PPD 1%	PPD6 1%	PPD6 2%	PPD7 1%	PPD7 2%	Petrolatum 100%
1	+++	++	+++	-	-	+++	+++	-
2	++*	++	++	-	-	++	++	-
3	++*	+ / ++	++	-	-	+ / ++	+ / ++	-
4	+++	-	+ / ++	-	-	+	+	-
5	+++	-	+	-	-	+ / ++	+ / ++	-
6	+	-	+ / -	-	-	+ / -	+ / -	-
7	+++*	-	-	-	-	-	-	-
8	++*	-	-	-	-	-	-	-

Table 2. Patch test reactions to PPD compounds. Vehicle for all allergens was petrolatum.



Abstract N°: 6277**A case of Urticaria Pigmentosa in an 18-month-old Filipino Male**Tanya Rae Cuatriz^{*1}, Wilsie Salas-Walinsundin¹¹East Avenue Medical Center, Dermatology, Quezon City, Philippines**Introduction & Objectives:**

Mastocytosis comprises a group of disorders characterized by an abnormal increase in mast cells in various organs, including the skin. Urticaria pigmentosa is the most prevalent form of cutaneous mastocytosis and can be associated with systemic manifestations. The objective of this case study is to highlight the importance of dermatologists in recognizing and diagnosing this rare disease in children.

Materials & Methods:

We present the case of an 18-month-old boy diagnosed with Urticaria pigmentosa. The patient exhibited multiple generalized hyperpigmented macules, papules, and plaques that appeared at 6 months of age. Additionally, the patient displayed a positive Darier's sign and experienced intermittent episodes of vomiting and diarrhea. Initial laboratory results were within normal limits.

Results:

A skin biopsy was performed, confirming the diagnosis of urticaria pigmentosa. CD117 and Giemsa stains were consistent with the diagnosis. The management approach included the administration of antihistamines, topical corticosteroids, and emollients. These interventions resulted in the flattening and fading of hyperpigmented lesions and improvement of symptoms.

Conclusion:

This case emphasizes the essential role of dermatologists in recognizing and diagnosing mastocytosis, particularly in pediatric patients. Although cutaneous manifestations of this heterogeneous mast cell disorder are generally benign, systemic involvement can occur. Therefore, it is crucial to conduct a comprehensive evaluation, including a detailed medical history, thorough physical examination, and review of symptoms, to initiate a comprehensive diagnostic workup. Timely diagnosis, early intervention, and appropriate referrals are paramount in reducing the associated morbidity and mortality of this condition.



Abstract N°: 6403**Foxy eyes but with a price : what to expect from microblading of the eyebrows**Zineb Fajri¹, Hanane Baybay¹, Sarah Elloudi¹, Zakia Douhi¹, Meryem Soughi¹, Fatima Ezzahra Mernissi¹¹CHU Hassan II, dermatology venereology, fes , Morocco**Introduction & Objectives:**

Permanent eyebrow makeup is a kind of cosmetic tattooing that has become very popular in the last decade , not only for aesthetic purposes but also in dermatological cases such as total alopecia, hypothyroidism or chemotherapy-induced madarosis. Although it is considered to be a safe procedure, it can nevertheless cause adverse skin reactions at the tattoo site, including infections, allergic reactions and even sarcoid reactions. These reactions can lead to a reduction in the quality of life. We report four cases of adverse reactions following microblading of the eyebrows.

Materials & Methods:

We report four cases of diverse side effects of microblading of the eyebrows. Patients were examined by dermoscopy . The diagnosis was confirmed by histology for two patients.

Results:

Observations 1 and 2 :

The first and second patients were a 34 and 40-year-old women presenting erythematous lesions on the eyebrows. The gap between the last placement of the cosmetic tattoo and the onset of the symptomatology was 1 year for the first and 2 years for the second. Dermatological examination revealed multiple confluent erythematous papules in a linear pattern, they are located in eyebrows at the site of microbleeding. Dermoscopic examination revealed a yellow-orange appearance to the vitreous pressure and irregularly scattered colored areas between the gray-brown areas of the tattoo. Anatomopathological examination revealed a sarcoidosis-like granulomas for both patients . The biological and radiological examinations came back without anomaly for the first patient, for the second patient, the thoracic scanner objectified a pulmonary attack compatible with a sarcoidosis. The first patient, who had localized eyebrow involvement, received intralesional corticosteroids on the eyebrows, and the second patient, who had pulmonary involvement, received intralesional injections on the eyebrow and synthetic antimalarials, and oral corticosteroids, with good progression for both.

Observation 3 and 4:

The third and fourth patients were a 38 and 46 year-old women consulting for erythematous, oozing, pruritic lesions after microblading of the eyebrows, reporting having had similar reactions following tattooing. The dermatological examination revealed the presence of edematous erythematous plaques surmounted by vesicles with crumbling contours located on both eyebrows. The diagnosis of contact eczema was retained and the patients were put on a low class topical corticosteroids for 10 days with good improvement.

Conclusion:

The side effects of microblading remain diverse ranging from contact dermatitis to granulomatous reactions . Hence, an early diagnosis and an adapted management allows to avoid the inflammatory and granulomatous reactions that can have serious consequences.

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