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Objectives: To investigate whether and by what means tourists travelling to holiday destinations in the tropics and subtropics seek to prepare their skin for the planned sun exposure, to examine their sun protective behavior, and to assess their sunburn rate during the vacation.

Methods: Between February and April 2013, we conducted structured face-to-face interviews among passengers waiting in the departure or the baggage claim area at the Airport Basel-Mulhouse (Switzerland/France). Passengers of at least age 18 with Caucasian skin whose holiday destination was the Caribbean (Cancun, Punta Cana), the Canary Islands (Fuerteventura, Gran Canaria, Teneriffa) or North Africa (Marrakech, Hurghada, Sharm el-Sheikh) were eligible for interviews.

Results: We completed 533 interviews with departing and 324 interviews with homecoming tourists. Of the departing tourists, 10.1% visited a solarium within the 4 weeks preceding the vacation, 72.2% of them with the intent of preparing their skin for the anticipated sun exposure and thereby preventing sunburn. Furthermore, 7.8% sought to prepare the skin by taking dietary supplements such as carotenoids (however, 59.5% started the supplementation less than 9 weeks before departure and were thus unlikely to benefit from any extra protection). Almost all (97.4%) departing tourists had sunscreen in their luggage. The majority used sunscreen with a medium to very high sun protection factor (SPF 15-20: 8.3%; SPF 25-30: 46.2%; SPF \geq 40: 41.2%). Yet, 21.0% of sunscreen users stated to reduce the SPF on average by half after some days of sun exposure. Other sun protective items in the tourists' luggage included sunglasses (93.8%), sunhat (63.6%), and clothes with integrated UV protection (4.1%).

Of the homecoming tourists, 79.0% nearly always applied sunscreen on sunny days, whereas only 34.0% and 38.9% usually wore a sunhat and stayed in the shade around noon, respectively. Of concern, 44.4% affirmed to have suffered from sunburn during their vacation (nearly every third sunburn was described as painful). Male gender, younger age, not wearing a sunhat and only sometimes using sunscreen were associated with increased odds of sunburn.

Conclusion: The observed sunburn rate was alarmingly high. Future skin cancer prevention programs should reveal common misconceptions in terms of preparing the skin for the sun and emphasize the avoidance of sunburns, the correct use of sunscreen as well as the importance of covering up and seeking shade.

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In vivo differentiated Th9 cells are enriched in skin-homing and skin-resident T cells

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In this study, we sought to investigate the antigen-specificity and cytokine profile of human tissue-homing and tissue-resident memory T helper cells. Human skin-homing (CLA+) and gut-homing (α 4 β 7+) memory T helper cells isolated from PBMCs were stimulated with a broad panel of viral, bacterial, and fungal pathogens and proliferation and cytokine production was measured. Additionally, tissue-resident T cells from skin and gut were isolated and analyzed for their cytokine profile.

In accordance with current concepts of tissue-specific imprinting of homing receptors in naive T cells in the course of infection, pathogen-specific T cells in PBMCs showed homing potential to the predominant site of infection of the respective pathogen. Intriguingly, cytokine analysis revealed that IL-9 was exclusively produced by CLA+ T cells stimulated with *Candida albicans* but not by α 4 β 7 or CLA-/ α 4 β 7- T cells. No other pathogens elicited significant production of IL-9 in any subpopulation of T cells. Further investigation of the cytokine profile of skin-homing T helper cells showed that TGF- β induces the expression of IL-9 but not IL-4, IL-17, or interferon- γ in CLA+ but not CLA-memory T cells. These IL-9 producing cells also lack the regulatory T cell maker FoxP3, thus showing the phenotype of bona fide Th9 cells. To assess whether the skin-homing Th9 cells found in the peripheral blood are indeed present in the skin, we analyzed the cytokine profile of tissue-resident T cells isolated from healthy skin and gut using the explant culture technique. In accordance with our previous findings, skin-resident T cells contained a distinct population of Th9 cells whereas gut-resident T cells did not.

These results indicate that human Th9 cells distinctly home to and reside in the skin and that they may show distinct antigenic specificity to the cutaneous pathogen *C. albicans*. Thus, our data establish a link between tissue-specific imprinting of homing potential and pathogen-specific imprinting of cytokine profiles during the course of T helper differentiation.

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Possible involvement of Ambroxol as trigger of an erythema exsudativum multiforme majus/Stevens-Johnson Syndrome overlap

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Objective: To characterize the blister cells isolated from an erythema exsudativum multiforme majus/Stevens-Johnson Syndrome (EEMM/SJS) overlap and to investigate its cause.

Methods: The cutaneous eruption was classified according to consensus definitions and histological analysis. Blister cells were analyzed for their expression of lineage and activation markers and cytotoxic

molecules using flow cytometry. T cell reactivity for potentially causative drugs was assessed by lymphocyte transformation tests (LTT).

Results: The healthy 58 year-old woman suffered from mild respiratory tract infection and therefore started treatment with the secretolytic drug Ambroxol. One week later, she presented with large palmar and plantar blisters, painful mucosal erosions, and flat atypical target lesions and maculae on the trunc, thus showing the clinical picture of an EEMM/SJS overlap. This diagnosis was supported by histology.

Analysis of blister cells showed that they mainly consisted of CD8+ and CD4+ T cells and a minor population of NK cells. Both the CD8+ T cells and the NK cells were highly activated and expressed Fas ligand and the cytotoxic molecule granulysin. In addition, both T cells and NK cells were positive for the chemokine receptor CCR4.

Surprisingly, the LTT performed on PBMCs in the acute phase was positive for Ambroxol (SI=2.9) whereas a LTT from a healthy but exposed individual did not show unspecific proliferation. Laboratory tests for common infectious causes of EEMM were negative.

Conclusions: The highly activated CD8+ T cells and NK cells expressing FasL and granulysin in blister fluids of EEMM/SJS further support a key role of immune cell-mediated cytotoxicity in blistering skin reactions. The upregulation of the skin-homing receptor CCR4 on NK cells from blister fluids indicates that cutaneous recruitment of NK cells may contribute to widespread keratinocyte death in these reactions. Finally, the positive LTT for Ambroxol together with the medical history, negative test for common infectious causes and histology (eosinophils) indicates that drug hypersensitivity to Ambroxol may have contributed to the EEMM/SJS in this patient. Further investigations of cutaneous adverse drug reactions to Ambroxol are thus warranted.

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Treatment of Severe Cold Contact Urticaria with Omalizumab – Case Reports

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We report 2 patients with cold urticaria with different response to treatment with omalizumab (Xolair®). Cold contact urticaria (CCU) is a common subtype of physical urticaria. It is characterized by the development of wheal and/or angioedema within minutes after cold contact. Clinical manifestation of CCU can range from mild, localized whealing to life-threatening anaphylactic shock reactions. Omalizumab has been described to be useful in cases of chronic urticaria (chronic spontaneous urticaria) and may be an interesting option for treatment of CCU. We describe one patient with significant and long-lasting improvement of symptoms after 300mg Omalizumab every 4 weeks for 3 months and one without any improvement after anti-immu-

noglobulin E therapy.

In our case reports, we want to highlight that there is still a small group of patients without benefit from omalizumab treatment. It is necessary to identify this minor subgroup of patients where omalizumab does not represent an effective treatment possibility. We also review the literature and compare with other cases of CCU treated with Omalizumab.

References

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A patient with metastatic melanoma under combination therapy with a selective BRAF and MEK inhibitor

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We report the case of a 75-year-old man who suffered from metastatic melanoma on his scalp, pT4b pN3 M1b. The patient received several excisions with a latissimus dorsi flap and a neck dissection of lymph nodes from level V. Two months later the PET-scan showed local progression of the tumor. Genetic testing confirmed a BRAF V600E mutation. We decided to include him into the GSK Combi-V trial (MEK116513) that investigated the combined therapy with dabrafenib, a selective BRAF inhibitor, and trametinib, a selective MEK inhibitor. In the first week of therapy the patient responded well and showed clinical regression of the metastases. Nevertheless, one week later the metastases started to progress rapidly. CT scan confirmed the tumor spreading. As the response to immunotherapy is delayed we decided to treat the patient with chemotherapy. The patient declined any systemic therapy but wished only palliative care.

Targeted therapy with a BRAF kinase inhibitor in melanoma patients with a BRAF V600 mutation is known to develop resistance. To prevent this resistance a phase I and II trial of combined treatment with dabrafenib and trametinib compared to monotherapy with dabrafenib has been conducted (funded by GlaxoSmithKlein). Flaherty et al. [1] showed that progression free survival was significantly improved with the combined therapy (9.4 months versus 5.8 months). Also the rate of complete or partial response was significantly higher in the combination group (76% versus 54%). Furthermore the combination of dabrafenib and trametinib showed less adverse events than the monotherapy with dabrafenib.

References

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