

Forum for Nordic Dermato-Venereology

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32nd Nordic Congress of Dermato-Venereology

18–20 August 2013 in Tampere, Finland



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Programme and Abstracts

WELCOME TO TAMPERE

Welcome to the 32nd Nordic Congress of Dermato-Venereology to be held in Tampere Hall, Tampere, Finland on 18–20 August 2013.

Nordic dermatologists have a tradition of close collaboration, sharing experience and also, enjoying a good time together – since 1910, the founding of the Nordic Dermatology Association. We have met every few years in various charming Scandinavian university cities and will now join for the 32nd time, on August 18-20, 2013 in Tampere Hall. Tampere is a lively and innovative university city, located between two beautiful lakes in Southern Finland.

During three days we will hear the plenary talks of several international leading dermatologists, on topics ranging from the latest knowledge in common skin diseases to novel approaches in targeting severe inherited skin diseases. There will be three parallel sessions every day, covering dermato-venereology from contact dermatitis through sexually transmitted diseases to skin tumors. We wish to offer up-to-date information and inspiration as well for private as academic dermatologists. One important goal of our meeting is to facilitate networking between young dermatologist, who will meet in their own special forum. Also, the valuable contribution of our sponsors and exhibitors is acknowledged.

On behalf of the Finnish Dermatological Society and the Finnish Local Organizing Committee I wish you all warmly welcome. The organizers hope that you will enjoy every aspect of the congress in Tampere!

Annamari Ranki, Congress President

PROGRAMME

Sunday 18 August

Keynote lecture

Howard Maibach	Clinical Challenges in Percutaneous Absorption
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Monday 19 August

Plenary lectures

Jonathan Barker	Psoriasis: from genetic discovery to clinical utility
Jouni Uitto	Personalized Medicine for Heritable Skin Diseases

Psoriasis and comorbidities

Chairs: Jonathan Barker & Tarja Mäлкönen

Jonathan Barker	Epidemiology and pathogenesis of metabolic syndrome and its consequences in psoriasis
Tarja Mäлкönen	The effect of psoriasis treatment on the cardiovascular risk
David Hägg, M Eriksson, A Sundström, M Schmitt-Egenolf	The higher proportion of men with psoriasis treated with biologics may be explained by more severe disease in men

Young dermatologists' forum

Chair: Sampsa Kauppi

Sampsa Kauppi	Update on dermatological side effects of novel targeted cancer therapies
Noora Neittaanmäki-Perttu	Photodynamic therapy: conventional vs. natural daylight-mediated treatment: an economical view
Sampsa Kauppi, Noora Neittaanmäki-Perttu	Brief history the Young dermatologists Finland

Drug and food allergy

Chairs: Mika Mäkelä & Klaus E Andersen

Mika Mäkelä	Oral immunotherapy of severe food allergy
Antti Lauerma	Drug allergy - from mechanisms to diagnosis
Carl Kyrklund, H Hyry, K Alanko	Allergic contact dermatitis from transdermal buprenorphine

Contact dermatitis

Chairs: Heidi Sösted & Kristiina Aalto-Korte

Kristiina Aalto-Korte	Contact allergy to epoxy compounds
Heidi Sösted	Contact dermatitis to hair dye ingredients
Jussi Liippo	Lichen allergy - sensitisation and contact dermatitis from nature and cosmetics
KF Mose, KE Andersen & LP Christensen	Heterogenous distribution of methacrylate allergens throughout petrolatum in commercially available patch test preparations
F Andersen, KH Andersen, KF Mose & KE Andersen	Elicitation study on oak moss absolute

Photodermatology

Chairs: Erna Snellman & Leena Koulou

Amra Osmancevic	An update on vitamin D
Tapio Rantanen	Update on Skin Photoprotection
Riikka Pastila	Sunbeds: What's in there?

Cutaneous lymphomas

Chairs: Robert Gniadecki & Annamari Ranki

Robert Gniadecki	How to diagnose and manage common cutaneous T-cell lymphomas?
Panagiota Mantaka	What is special about special subtypes of mycosis fungoides?
Liisa Väkevää	Difficult-to-diagnose cutaneous lymphomas
Annamari Ranki	The spectrum of B-cell lymphomas
Robert Gniadecki & Annamari Ranki	Nordic lymphoma registries and future Nordic collaboration

Genodermatoses

Chairs: Jouni Uitto & Anders Vahlquist

Anders Vahlquist	Congenital Ichthyosis and other Disorder of Cornification - An Update
Sirkku Peltonen	What is New in Neurofibromatosis 1
Jouni Uitto	Differential Diagnosis of Cutaneous Elastin Disorders - Cutis Laxa vs. PXE
Barbara Gasior-Chrzan	Cowden's syndrome (multiple hamartoma)

STD Genital dermatology

Chairs: Harald Moi & Eija Hiltunen-Back

Anne Olaus Olsen	Anal dysplasia and cancer
Eija Hiltunen-Back	Ulcer vulvae acutum Lipschütz
Harald Moi	IUSTI Guidelines on gonorrhea treatment
Erika Wikström, H-M Surcel, M Merikukka, P Namujju, H Öhman, K Tasanen, A Tiitinen, J Paavonen & M Lehtinen	Overtime chlamydia trachomatis serotype distributions in fertile-aged Finnish females

Acne & Rosacea

Chairs: Frank Powell & Gregor BE Jemec

Frank Powell	Demodex mites cause rosacea
Gregor B.E. Jemec	Do sebaceous glands protect against hidradentis
Riitta Palatsi, HL Kelhala, S Lehtimäki, N Fyhrquist, J Väyrynen, M Kallioinen, M Kubin, K Tasanen, H Alenius, A Lauerma	Expression of IL-23/IL-17A pathway in early inflamed acne lesions

Atopic dermatitis

Chairs: Enikö Sonkoly & Sakari Reitamo

Sakari Reitamo	Modulation of atopic dermatitis by effective long-term treatment
Sol-Britt Lonne-Rahm	Psychological aspects of atopic dermatitis
Maria Bradley	Filaggrin and atopic dermatitis
Enikö Sonkoly	MicroRNAs – novel therapeutical targets in atopic dermatitis?
Ville Kiiski, A Remitz, S Reitamo, J Mandelin & O Kari	Long-term safety of topical pimecrolimus and topical tacrolimus in atopic blepharitis

Pediatric dermatology

Chairs: Sirkku Peltonen and Leena Ackermann

Katariina Hannula-Jouppi	Netherton syndrome
Nicolas Kluger, A Bouissou, L Tauzin, J Puechberty & O Dereure	Congenital linear streaks of the face and neck and microphthalmia in an infant girl
Katariina Hannula-Jouppi	Acrodermatitis enteropathica

Lupus

Chairs: Filippa Nyberg & Jaana Panelius

Riitta Luosujärvi	Videocapillaroscopy as a new tool in examination of connective tissue diseases
Filippa Nyberg	Epidemiology and treatment lines of cutaneous lupus
Jaana Panelius	Serodiagnosis and immunopathogenesis of cutaneous lupus

Tuesday 20 August

Plenary lectures

Leena Brückner-Tuderman	Skin fragility: Novel approaches with exome sequencing and disease proteomics
Gunnar Nilsson	Mast cell and skin

Bullous diseases

Chairs: Leena Brückner-Tuderman & Kaisa Tasanen-Määttä

Anna-Kaisa Försti, J Jokelainen, M Timonen, K Tasanen	Increasing incidence of bullous pemphigoid in Finland
Laura Huilaja	Gestational pemphigoid
Lauri Tolkki, J Höök-Nikanne	A severe and treatment resistant case of pemphigoid gestationis
Kaisa Hervonen	Dermatitis herpetiformis

Teaching dermatology

Chairs: Outi Kortekangas-Savolainen & Anita Remitz

Outi Kortekangas-Savolainen & Anita Remitz	How can we improve dermatologic teaching?
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Pigmented lesions & Melanoma

Chairs: Olle Larkö & Olli Saksela

Olle Larkö	New imaging techniques in the diagnosis of melanoma
Carin Sandberg	Mobile teledermoscopy for fast-track management of skin cancer
Olli Saksela	Risk of new melanomas in multinevus patients
Olga Tatti, P Pekkonen, T Holopainen, P Maliniemi, J Lohi, V Rantanen, S Hautaniemi, A Ranki, K Alitalo, P Ojala, J Keski-Oja, K Lehti	MT3-MMP controls a proteolytic switch between blood vascular and lymphatic invasion of melanoma cells

Non-melanoma skin cancer & Actinic keratosis

Chairs: Lasse R Braathen & Sari Koskenmies

Lasse R. Braathen	Introduction
Sari Koskenmies	Etiology and treatment options for non-melanoma skin cancer & actinic keratosis
Lasse R. Braathen	The field cancerisation concept and its implication for the choice of treatment
Stine Wiegell	Daylight-Photodynamic Therapy (D-PDT); the painless option
Ann-Marie Wennberg	Pain management of conventional PDT
Lasse R. Braathen & Sari Koskenmies	Selected cases. Problem based learning with discussion
Antti P Kaukinen, IT Harvima	Mast cells and regulatory T cells are increased in basal cell carcinoma
Mehdi Farschian, L Nissinen, E Siljamäki, A Kivisaari, P Riihilä, R Ala-Aho, M Kallajoki, M Toriseva, R Grénman, J Peltonen, T Pihlajaniemi, R Heljasvaara & V-M Kähäri	EPHB2 receptor modulates gene expression signatures involved in migration and invasion of cutaneous SCC cells

Vasculitis

Chairs: Tom Pettersson & Annikki Vaalasti

Tom Pettersson	The immunology of vasculitis
Annikki Vaalasti	Cutaneous vasculitic ulcers
Jaakko Antonen	Pharmacotherapy of vasculitis

Cutaneous microbiome and infections

Chairs: Harri Alenius & Antti Lauerma

Harri Alenius	Skin microbiome – what do we know?
Antti Lauerma	Interaction of microbial infections and immunity
Bardur Sigurðsson & R Baran	The prevalence of onychomycosis – a review of the literature

Mast cells in dermatology

Chairs: Gunnar Nilsson & Ilkka Harvima

Klas Nordlind	Stress, nerves and mast cells in psoriasis
Leena Ackerman	Mastocytosis
Ilkka Harvima	Mast cells as targets for novel therapy
Tiina Lipitsä, A Naukkarinen, IT Harvima	Mast cell chymase can degrade the immunoreactants C3, fibrin and fibrinogen in cutaneous vasculitis
Salla Haimakainen, A Kaukinen, M-M Suttle, J Pelkonen, IT Harvima	Variation of CD40 ligand in mast cells of psoriatic skin, solar keratosis and epithelial carcinomas

Common and uncommon dermatoses on dark skin

Chairs: Nicolas Kluger & Ken Malanin

Ken Malanin	General features of dark skin
Kari Saarinen	Challenging clinical cases on dark skin
Nicolas Kluger	The management of hyperpigmented and hypopigmented disorders in dark skin

Wound repair

Chairs: Veli-Matti Kähäri & Baldur Baldursson

Veli-Matti Kähäri	Cellular events in wound repair
Baldur Baldursson	Development and application of biomaterials in wound care
Astrid H Lossius, TK Bergersen, M Lorentzen & J Austad	Contact allergy in patients with chronic leg ulcers
Kirsi Isoherranen, L Norvio, L Jeskanen	Teriparatide-induced calciphylaxis successfully treated with sodium thiosulphate

Health economics and dermatology

Olle Larkö

Nordic perspective in dermatology

ABSTRACTS for oral presentation

OCCUPATIONAL CONTACT ALLERGY TO EPOXY COMPOUNDS

Aalto-Korte K.

Finnish Institute of Occupational Health (FIOH)

Epoxy compounds are among the most important causes of occupational allergic contact dermatitis. They are widely used in construction work and many types of industries. Typical products include e.g. 2-component paints and glues, floor coatings, and seaming and waterproofing materials in tile setting. Epoxy pipe relining is a rapidly increasing trade with an extensive risk of skin exposure to epoxy chemicals. In Germany, an increasing prevalence of contact allergy to epoxy compounds has been observed in the building trade, especially in workers with an employment of shorter than 2 years. Sensitization often leads to severe symptoms and inability to work further in epoxy using trades.

Epoxy products usually have at least 2 components, resin and hardener. At FIOH, the most commonly positive epoxy hardeners since 2001 have been m-xylylenediamine, 2,4,6-tris-dimethylaminomethylphenol (tris-DMP) and isophoronediamine. According to the national Product Register of Chemicals in Finland tris-DMP is the most commonly declared hardener in epoxy products.

The most commonly used epoxy resin is diglycidyl ether of bisphenol A (DGEBA). There are other epoxy resins e.g. diglycidyl ether of bisphenol F (DGEBF). DGEBF epoxy resins are widely used as such in applications requiring chemical resistance and also together with DGEBA epoxy resins. According to animal tests and clinical experiences DGEBF and DGEBA cross react. At FIOH an in-house test substance of DGEBF was included in the baseline series in 1999–2011. Among 1972 patients screened 66 (3.3%) had positive reactions to DGEBF and 96 (4.9%) to DGEBA. Concomitant reactions to DGEBF and DGEBA were common. Independent DGEBF allergies were seen in 5 patients and independent DGEBA allergies in 35 patients. Specific exposure to DGEBF was found in 26 patients. Nevertheless, we did not regard the screening with DGEBF very useful.

There is a great need for prevention of contact allergy to epoxy compounds.

ALLERGIC CONTACT DERMATITIS FROM TRANSDERMAL BUPRENORPHINE

Alanko K., Hyry H., Kyrklund C.

Skin and Allergy Hospital, Helsinki University Central Hospital, Finland

Introduction. Buprenorphine is a opioid analgesic widely used to treat moderate to severe pain. We report three cases of allergic contact dermatitis to a transdermal delivery system (TDS) containing buprenorphine verified by a positive patch test reaction.

Patient 1 had been applying transdermal buprenorphine (TDB) with good pain control. During the treatment the skin under the patch turned red. The patient was patch tested with of the parts of the TDS containing buprenorphine and fentanyl as well as the surrounding adhesive part. The test was strongly positive for the buprenorphine TDS but negative for the other tested substances.

Patient 2 suffered from chronic pain in her right lower limb. Treatment included oral as well as transdermal buprenorphine. After reporting severe skin irritation on the site of the TDB, she was tested with the part of TDS containing buprenorphine and the surrounding adhesive part. The test was strongly positive for the buprenorphine TDS. All other tested substances were negative. The patient was using oral buprenorphine without signs of systemic contact dermatitis.

Patient 3 was given TDB for Complex Regional Pain Syndrome. The skin under the TDB became irritated. The patient was tested with the part of TDS containing buprenorphine and the surrounding adhesive part.

Patch tests with fentanyl, tramadol and oxycodone and codeine were performed. The test was strongly positive for buprenorphine. All other tested substances were negative.

Conclusion. A delayed type IV allergic reaction to buprenorphine was verified by a positive patch test in all three cases. Only 8 cases of patch test-proven allergic contact dermatitis from buprenorphine have previously been described. Allergy to buprenorphine might be more common than previously suspected.

One patient was given both transdermal and oral buprenorphine, but only developed skin symptoms from TDB, indicating that systemic contact dermatitis from buprenorphine does not always develop in skin contact-sensitised patients.

Two of our patients were tested for contact allergy to fentanyl, both negative. Patients developing a contact dermatitis with TDB probably tolerate transdermal fentanyl.

COMPLEMENT FACTOR H – A NOVEL BIOMARKER FOR PROGRESSION OF CUTANEOUS SQUAMOUS CELL CARCINOMA

Ala-aho R.^{1,2}, Grénman R.⁴, Kallajoki M.³, Kähäri V.-M.^{1,2}, Meri S.⁵, Nissinen L.^{1,2}, Peltonen J.⁶, Peltonen S.¹, Riihilä P.^{1,2}

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The incidence of cutaneous squamous cell carcinoma (cSCC) and its precancerous forms is increasing globally. Inflammation is a typical feature of cutaneous SCC. We have studied the expression of complement system inhibitors in cSCC. Expression profiling of cSCC cell lines ($n=8$) and normal human epidermal keratinocytes ($n=5$) with Affymetrix and quantitative RT-PCR. This data revealed upregulation of complement factor H (CFH) and factor H like protein-1 (FHL-1) in cSCC cell lines. The expression of CFH and FHL-1 mRNAs was also significantly higher in cSCC tumors ($n=6$) than in normal skin ($n=11$) ($p=0.001$). Analysis of CFH and FHL-1 expression in vivo in invasive cSCCs ($n=65$), in situ cSCCs ($n=38$) and premalignant lesions (actinic keratoses, $n=37$) by immunohistochemistry showed that they were specifically expressed by tumor cells in cSCCs ($p=0.035$) and the staining intensity was stronger in cSCCs than in in situ cSCCs and actinic keratoses. The expression of CFH by cSCC cells was upregulated by IFN- γ and the basal CFH and FHL-1 expression was dependent on ERK1/2 and p38 signaling. Knock-down of CFH and FHL-1 expression inhibited proliferation and migration of cSCC cells and inhibited basal ERK1/2 activation. These results provide evidence for a role of CFH and FHL-1 in cSCC progression and identify them as novel progression markers and potential diagnostic and therapeutic targets in skin SCCs.

A CASE OF MEMBRANOUS LIPODYSTROPHY OBSERVED IN A PATIENT WITH ASYMPTOMATIC YELLOWISH MACULAR RASH WITH REPEATED PATHOLOGICAL FRACTURES IN SWEDEN

Al-Bayatti A.¹, Fureman H.², Jacobsson B.⁴, Rozell B.³

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Membranous lipodystrophy is characterized by the presence of microcysts lined by amorphous, eosinophilic material in arabesque appearance. We have a case of 39-year-old woman who has a progressive asymptomatic yellowish macular rash on the trunk, arms and thighs since 8 years. She had repeated pathological fractures of left arm 2004 and 2009, in addition to left tibia and head of femur 2011. Histopathology examina-

tion of a biopsied yellowish skin lesion showed membranous lipodystrophy. We wish to report a case of membranous lipodystrophy in patient with asymptomatic yellowish macular rash and repeated pathological fracture.

MT3-MMP CONTROLS A PROTEOLYTIC SWITCH BETWEEN BLOOD VASCULAR AND LYMPHATIC INVASION OF MELANOMA CELLS

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Lymphatic invasion of tumor cells correlates with poor melanoma prognosis, but the molecular determinants of lymphatic and blood vascular invasion have remained poorly understood. We find here that membrane-type-3 matrix metalloproteinase (MT3-MMP), over-expressed in nodular-type melanoma and melanoma lymph node metastases, functions as a molecular switch of vascular invasion. Silencing of MT3-MMP in metastatic WM852 melanoma cells resulted in a shift from lymphatic to hematogenic intravasation in conjunction with increased tumor growth, collagen degradation, and accumulation of the cell-surface collagenase, MT1-MMP. In culture, the MT3-MMP-depleted cells lost cohesive growth phenotype and acquired an MT1-MMP-dependent collagen invasive phenotype with single cell motility. In human melanoma tumors, cohesive morphology was associated with low MT1-MMP and/or high MT3-MMP expression. Further, prominent lymphatic invasion was observed in the highly MT3-MMP expressing human melanoma tumor, whereas no lymphatic vessel invasion occurred in the tumor with low MT3-MMP expression. Therefore, by supporting cohesive cell growth and by reducing MT1-MMP-dependent collagen degradation and cell invasion, MT3-MMP can impair blood vascular invasion and steer melanoma cells into more permissive lymphatic dissemination.

ELICITATION STUDY ON OAK MOSS ABSOLUTE

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Introduction. To determine the elicitation frequency of contact allergy of a new quality of oakmoss absolute (NOM, with

lowered atranol and chloroatranol content) and compare it to the "classic" quality of oakmoss absolute (COM) at the maximum level allowed by the International Fragrance Association Standard (0.1% in hydroalcohols) using repeated open application testing (ROAT) and a patch test serial dilution test at the end of the study

Methods. Thirty volunteers with and thirty volunteers without known sensitization to oak moss underwent repeated open application tests with dilutions of classic and new oak moss, furthermore they were patch tested with a dilution series of oak moss formulations.

Preliminary results. The study was finalized on May 5th 2013, thus data analysis is not yet finalized. Preliminary analysis of the ROAT-data shows that 21/30 sensitized individuals developed contact dermatitis to COM. Only 5 of these developed contact dermatitis to NOM. Mean no of days to development of dermatitis was 13 days for NOM and 7 days for COM. Data analysis has not started yet for

Conclusion. Final data and conclusions will be presented at the meeting. Preliminary data suggest that the new formulation of oak moss causes significantly less elicitation of dermatitis than the classic formulation in volunteers known to be sensitized. Neither formulation elicited contact dermatitis in control persons.

HETEROGENOUS DISTRIBUTION OF METHACRYLATE ALLERGENS THROUGHOUT PETROLATUM IN COMMERCIALY AVAILABLE PATCH TEST PREPARATIONS

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Introduction. In previous studies, it has been shown that there is a lack of stability of methacrylate allergens, when stored in patch test chambers and in test syringes. The primary concern of this study was to investigate whether there is also a heterogenous distribution of methyl methacrylate (MMA) and 2-hydroxyethyl methacrylate (2-HEMA) in commercially available patch test preparations.

Methods. A total of 12 fresh patch test syringes were obtained from three patch test suppliers in Europe. The content of each syringe was divided into 5 segments of equal size. Four consecutive petrolatum samples from the initial part of each segment were analyzed quantitatively by means of high-performance liquid chromatography (HPLC).

Results. A decreased concentration of MMA was observed in the initial segment in all 6 patch test preparations, whereas

4 of 6 patch test preparations of 2-HEMA were in accordance with the stated concentrations. The concentration of MMA increased markedly from the top segment close to the tip of the syringe to the bottom segment adjacent to the piston in 4 syringes. In contrast, syringes with 2-HEMA maintained a constant concentration throughout the test preparation, apart from 2 syringes. Overall, 6 of 12 patch test syringes showed a large variation in allergen distribution throughout petrolatum.

Conclusion. The distribution of methacrylates in petrolatum may be heterogenous – even in fresh commercially available patch test syringes. This should be taken into consideration together with other sources of variation in diagnostic patch testing.

EPHB2 RECEPTOR MODULATES GENE EXPRESSION SIGNATURES INVOLVED IN MIGRATION AND INVASION OF CUTANEOUS SCC CELLS

Ala-aho R.¹, Farshchian M.¹, Grénman R.³, Heljasvaara R.⁵, Kallajoki M.², Kivisaari A.¹, Kähäri V.-M.¹, Nissinen L.¹, Peltonen J.⁴, Pihlajaniemi T.⁵, Riihilä P.¹, Siljamäki E.¹, Toriseva M.¹

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Introduction. Cutaneous SCC (cSCC) is the second most common cutaneous malignancy in white population. We have studied the role of Eph receptor tyrosine kinases in cSCC.

Methods. Cutaneous SCC cell lines and tumors were obtained with consent from Turku University Hospital. Gene expression analysis was performed with oligonucleotide-based microarray, SOLiD™ whole transcriptome analysis, and real-time PCR. Western blot (WB) was used to study protein levels. Immunohistochemistry of human tissue microarrays and chemically induced mouse cSCC were performed using specific antibody against EphB2. Proliferation, migration and invasion assays were performed following EphB2 knock-down.

Results. Specific upregulation of EphB2 was noted in cSCC cell lines ($n=8$) and tumors ($n=6$) compared with normal keratinocytes ($n=5$) and healthy skin ($n=7$) using Affymetrix-based profiling, SOLiD™ analysis, quantitative RT-PCR, WB and immunofluorescence staining. Immunohistochemistry revealed tumor cell-specific overexpression of EphB2 in cSCC in situ ($n=56$) and cSCC ($n=68$) compared with actinic keratoses ($n=69$) and normal skin ($n=12$) ($p<0.001$). Moreover, upregulation of EphB2 expression was noted in DMBA-TPA-induced mouse cSCCs ($n=19$) compared with normal skin ($n=13$) ($p<0.001$). EphB2 knockdown showed inhibition of proliferation, migration and invasion of cSCC

cells. Microarray analysis identified 2460 differentially expressed genes ($p < 0.05$) in cSCC cell lines ($n = 3$) following EphB2 knockdown. Gene expression profile after EphB2 knockdown was subjected to Ingenuity Pathway Analysis (FC (log2) > 0.75 and $p < 0.05$). Over 11% of downregulated genes belonged to peptidases classification. Invasion of tumor cells (z-score = -2.099 , $p < 0.001$) and migration of tumor cells (z-score = -2.358 , $p < 0.001$) were among the top biofunctions significantly decreased after EphB2 knockdown.

Conclusion. These findings provide evidence for the role of EphB2 in progression of cSCC and particularly in invasion and migration of SCC cells, suggesting it as a therapeutic target in these invasive and metastatic tumors.

CONTACT ALLERGY IN PATIENTS WITH CHRONIC LEG ULCERS

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Introduction. Patients with chronic leg ulcers are exposed to different ointments and wound dressings over years. A defect skin barrier and potential sensitizers under occlusive bandaging could predispose to contact allergy, which may contribute to prolonged wound healing. We wanted to explore whether the "Leg ulcer series" (LUS), a special patch test of 27 substances relevant to wound treatment, gives additional information to the European standard series (ESS).

Methods. Patients with chronic leg ulcers (duration > 6 weeks) and eczema visiting our leg ulcer clinic were included. All patients ($n = 97$) were patch tested with LUS following standard guidelines. 52 of the patients were also tested with ESS and 5 additional substances: Intracite gel, Brulidine, Hydrocortisone and Cain mix 3 and 5.

Results. Of the 97 patients included, 36 were men and 61 women; median age was 78 years, range 34–99. The duration of ulcer varied from 6 weeks to 40 years (mean 3.82 years, SD 6.82). 31 of the 97 patients tested with LUS (32%) had positive reactions, the most common allergens being Benzalkonium chloride, Wood tar mix and Fusidine. 27 of the 52 patients tested with ESS (52%) had positive reactions, the most common substances being Peru Balsam, Perfume mix and Colophony. We found no association between a positive test result and duration of ulcer > 1 year (OR 0.77, 95% CI 0.34–1.74, $p = 0.54$), nor any correlation between number of positive reactions and duration of ulcer ($r = -0.05$, $p = 0.64$).

Conclusion. Contact allergy is frequent in patients with chronic leg ulcers and eczema, and these patients should be patch tested routinely. LUS gives relevant additional information and should be included in the standard test repertoire, as test results may guide further wound treatment.

OPTICAL COHERENCE TOMOGRAPHY OF NMSC UNDERGOING IMIQUIMOD THERAPY

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Introduction. To investigate the potential of optical coherence tomography for non-invasive monitoring of BCC and AK during treatment with imiquimod.

Methods. 16 patients with biopsy-verified BCC- and AK- lesions were OCT-scanned before, during and after treatment with imiquimod. The lesions were identified with OCT using specific parameters suggested in the literature. At the end of treatment biopsies were taken from any remaining lesions clinically identified or using OCT.

Results. BCCs were identified with OCT in 5/8 cases. In the remaining 3 cases the OCT-image deviated from normal skin, but we could not identify classical BCC-structures according to suggested OCT-criteria. Only in one case we could monitor BCC-structures during a complete treatment due to the reduced quality of images during active treatment. All BCCs had been eliminated when the treatment had ended. However clinically we observed new structures in the skin that were ambiguous and open to misinterpretation. OCT was able to invalidate the clinical suspicion of BCC, and this was histologically confirmed. OCT could identify all AKs at all visits but the image quality was impaired during active treatment. A significant decrease of the thickness was observed after one week of treatment ($p = 0.04$). 4 weeks after end of treatment imiquimod had eradicated 2/8 AKs, and a significant decrease in thickness was observed ($p = 0.02$). In 7/8 cases the eradication was seen both in the OCT-images as clinically.

Conclusion. OCT could identify superficial BCC and AK before a treatment with imiquimod. Furthermore, OCT could identify or exclude BCC or AK lesions after an ended treatment in most cases. Poor image quality particularly due to the treatment made the monitoring during treatment difficult. In some cases imiquimod left benign but clinically misleading and cosmetically unfavourable structures in the skin.

NAIL PSORIASIS AND PSORIATIC ARTHRITIS

Baran R.², Löve T.J.³, Sigurgeirsson B.¹

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Lately nail psoriasis has gained interest in rheumatology and dermatology. It is a common disorder, which causes pain and restrictions in daily activities in half of those affected and cosmetic problems in almost all. The nail dystrophy in patients with psoriasis can be an indicator of on-going involvement of the

distal phalanx and individuals with psoriasis are at an increased risk for developing arthritis in their lifetime. Psoriatic arthritis usually arises in patients with a history or with co-existing skin lesions. In about 70% of cases the onset of skin lesions precedes that of arthritis whereas the arthritis precedes the skin disease in only about 15% of cases; and the two occur simultaneously in the other 15%. We propose a new classification system of nail changes in patients with skin psoriasis and psoriatic arthritis.

- Psoriatic Arthritis without Skin and Nail Involvement
- Patients with Psoriatic Skin Disease and a Normal Nails
- Patients with Psoriatic Skin Disease and Clinical Nail Disease
- Early Nail Psoriatic Arthritis (Early Joint Manifestations in Psoriasis)
- Late Nail Psoriatic Arthritis

The diagnosis of psoriatic arthritis is challenging and the dermatologist is uniquely placed to identify it at a stage when progressive damage can be minimized. We believe that this classification system is a useful tool for the dermatologist, increases the awareness of psoriatic arthritis and aids with treatment decisions.

THE PREVALENCE OF ONYCHOMYCOSIS – A REVIEW OF THE LITERATURE

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Onychomycosis is the most frequent nail disease and accounts for up to 50% of all nail diseases. Assessment of the prevalence of fungal nail disease is important to determine the size of the therapeutic problem and to better understand the etiology and changes over time. The true prevalence of onychomycosis is far from resolved and cited prevalence figures in the literature are highly variable. When Medline was searched for studies on onychomycosis published during the year of 2012 we were able to locate 21 study who cited the prevalence of onychomycosis. Most studies cited an upper and lower prevalence number. The mean prevalence cited in all studies was 11.4. The average prevalence lower limit cited was 5.0 (median: 2; range: 2–16.6). The mean upper limit was 17.7 (median: 15.3; range: 3–40). This data clearly demonstrates that authors of scientific papers on onychomycosis cite a wide range of prevalence figures when citing the prevalence of onychomycosis. The literature was searched for studies that have examined the prevalence of onychomycosis. Eleven population-based studies have been published in the literature. Based on these studies it is likely that the true prevalence of onychomycosis in the general population in Europe and the US is between 2 and 8%, although considerable geographical variations are likely to exist. These results and results from hospital-based studies will be presented.

PSORIASIS ASSOCIATED IgA NEPHROPATHY UNDER INFlixIMAB THERAPY

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Introduction. The prevalence of renal disease in psoriasis is unknown and a true causative link is still debated. However, some glomerulopathies, including IgA nephropathy, have been reported more frequently in psoriatic patients. We report here an additional case that occurred under infliximab therapy.

Case Report. A 56 year-old Caucasian male had a past history of severe psoriasis and peripheral arthritis since his teen age. His previous treatments included: gold therapy, methotrexate and etanercept. Primary failure of etanercept prompted to initiate infliximab in august 2009. Under treatment, he disclosed microscopic hematuria and proteinuria (from 1g to 2,5 g/24h). Renal function was mildly impaired (creatinemia 100 µmol/L, GFR 73 ml/min). Infliximab was withdrawn after 8 infusions. A renal biopsy presented findings for a severe IgA nephropathy. Angiotensin converting enzyme inhibitor and salt free diet were initiated. Because of a cutaneous and rheumatic relapse, ustekinumab was started in July 2010. After a year of treatment (6 injections, 45 mg), cutaneous and joint manifestations have improved while proteinuria dropped up to 0,3 g/24h and GFR is at 57 ml/min.

Discussion. IgA nephropathy is the most common form of glomerulonephritis in patients with psoriasis and hematuria. Even though it is usually benign, IgA nephropathy may lead to renal failure prompting surveillance and sometimes treatment. In case of secondary nephropathy, the renal disease usually subside when the primary disease has been controlled. In our case, infliximab had no effect on proteinuria while ustekinumab seemed to improve proteinuria by controlling psoriasis.

Conclusion. Despite being rare, anomalies on urinalysis such as albuminuria and/or hematuria should raise concern on a potential glomerular dysfunction in these patients. Biologics seem to have an impact indirectly on the nephropathy through the control of psoriasis related inflammation.

CONGENITAL LINEAR STREAKS OF THE FACE AND NECK AND MICROPTALMIA IN AN INFANT GIRL

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Introduction. We report here a case of Microphthalmia with Linear Skin defects (MLS) syndrome/MIDAS (Microphthalmia, Dermal Aplasia and Sclerocornea) syndrome in an infant.

Patient. A newborn girl presented with markedly depressed, well-demarcated, red-pink streaks involving the right side of the face, the neck and the ipsilateral hand following Blaschko's lines and small-sized or aplastic fingernails on the involved hand. Ophthalmologic evaluation revealed right microphthalmia, aniridia and sclerocornea. Transfontanellar, lung, heart and abdominal imaging were unremarkable. MLS/MIDAS syndrome was considered. Both the infant and her mother (who was free of any lesion) carried a 11,5 Mb terminal deletion of the short arm of one of the X chromosomes including the HCCS gene with a 46 X, del(X)(p22.2) karyotype characteristic of this condition. At the age of 4 months, tachycardia and limited signs of heart failure developed with multiple ectopic atrial tachycardia, efficiently controlled by amiodarone. The right eye malformation was surgically managed with an ocular prosthesis and a favourable outcome.

Discussion. MLS/MIDAS syndrome is a rare X-linked dominant neurocutaneous disease with in utero male lethality presenting with congenital linear atrophic streaks affecting face and neck and ocular abnormalities. Additional manifestations include developmental delay, short stature, heart, central nervous system and genitourinary tract abnormalities. The HCCS gene on the Xp22.2 region encoding the mitochondrial holo-cytochrome c-type synthase, involved in the mitochondrial respiratory chain and in apoptosis pathways, is a candidate gene. Cases in males are exceptional. Intrafamilial variability has been previously emphasized. The mother carrying the same genetic abnormality may be totally asymptomatic. The specific pattern of cutaneous lesions with streaks following Blaschko's lines might be related to post-zygotic genomic mosaicism with tissue specific X-inactivation.

Conclusion. The dermatologist is at the front line for initial diagnosis and subsequent management that usually implies a multidisciplinary approach along with genetic counselling.

THE FIELD CANCERISATION CONCEPT AND ITS IMPLICATION FOR THE CHOICE OF TREATMENT

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The term field cancerisation was introduced in 1953 based on a review of tumors of the lip, oral cavity and pharynx. It was concluded that the majority of the tumors had multicentric

origin and multifocal growth, and that they were probably caused by a regional carcinogenic activity of some kind. In skin an analogous situation is found. The major skin carcinogenic source is the UVB in sunlight, and sun-damaged skin is a frequent finding in the elderly population today. In these sun-damaged areas, usually of the bald scalp, the ears, decollete and the dorsum of hands and underarms, multiple and recurring non-melanoma skin cancer (NMSC) may develop. These patients then suffer from field cancerisation, and they need treatment of these larger areas, thus restricting the treatment options to therapies that allow to treat larger areas without too much discomfort and with a good cosmetic outcome.

EXPERIMENTALLY INDUCED PSORIATIC LESION ASSOCIATES WITH TRANSIENT DECREASE IN IL-33 IMMUNOSTAINING IN EPIDERMIS

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Introduction. The early cellular mechanisms that lead to psoriasis after mild damage in the epidermis are poorly known. Interleukin-33 (IL-33) is a novel alarmin of the immune system that is released upon cell injury. Therefore, the purpose was to clarify the possible role of IL-33 after mild damage of epidermis in psoriatic skin.

Methods. The Köbner reaction was induced in uninvolved psoriatic skin of 18 patients using the tape-stripping technique, and thereafter a sequence of biopsies was collected for immunohistochemical analysis of IL-33 at 0d, 2h, 1d, 3d and 7d. Eight patients developed the Köbner reaction as judged later after 2–3 weeks. The release of IL-33 immunoreactivity from damaged keratinocytes was also analyzed in cell culture after freeze-thawing of monolayer keratinocytes by using ELISA, Western blotting and confocal microscopy.

Results. When compared to the Köbner-negative group ($n=10$), the thickness of epidermis was slightly decreased in the Köbner-positive group. Furthermore, IL-33 staining first decreased in keratinocyte nuclei in 2h-1d-3d biopsies, but then increased again in those of 7d biopsies in the Köbner-positive group, but not in the negative group. Cultured keratinocytes expressed IL-33 immunoreactivity showing either nuclear or cytoplasmic staining pattern, and a 32-kDa full-length IL-33 could be detected in the necrotic cell supernatant (NCS) after freeze-thawing. Interestingly, the NCS of keratinocytes stimulated cultured cord blood-derived mast cells to release IL-6 and IL-8 immunoreactivities.

Conclusion. The rapid decrease in epidermal thickness and IL-33 staining associates with Köbner-positivity but not with

–negativity. Experiments with damaged cultured keratinocytes suggest that this decrease is due to IL-33 release. Epidermal damage and IL-33 may be one of the first factors that trigger psoriatic inflammation.

FOLLICULOTROPIC MYCOSIS FUNGOIDES: A SEPARATE ENTITY WITHIN CUTANEOUS T-CELL LYMPHOMAS?

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Folliculotropic mycosis fungoides is a variant of mycosis fungoides with clinical similarities but distinct histopathological and, in some cases, clinical features. **METHODS:** We describe here the clinical presentation, pathology findings and treatment outcome in 22 Norwegian patients. All patients were diagnosed and followed-up between 1997 and 2013 at Oslo University Hospital. **RESULTS:** A wide spectrum of skin lesions, both typical as well as atypical for mycosis fungoides such as leonine facies, acneiform lesions, psoriasiform plaques, prurigo-like, purulent ulcerations and cystic milia-like lesions were seen. Histological examination showed characteristic infiltration of hair follicles with neoplastic T-cells and partial destruction of the former. A CD4+ immunophenotype of the neoplastic T cells with loss of one or more T-cell markers was demonstrated. Generally, patients were given more aggressive therapeutic regimens according to stage than patients with conventional mycosis fungoides, and showed a trend towards more rapid progression. **CONCLUSION:** This case series confirms the distinct clinical and histological as well as prognostic features of folliculotropic mycosis fungoides. It is still unclear whether folliculotropic MF is genetically different compared to conventional mycosis fungoides and whether it constitutes a separate cutaneous lymphoma type.

TOPICAL NON-PEPTIDE RECEPTOR ANTAGONISTS; APREPITANT AND TELCAGEPANT IN CONTACT DERMATITIS. AN EXPERIMENTAL STUDY AND REVIEW OF LITERATURE

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Introduction. Contact dermatitis can be modulated by such neurotransmitters of sensory nerve fibers as substance P (SP) and calcitonin gene-related peptide (CGRP). The first generation receptor antagonists were peptides with large molecules and had to be injected intracutaneously. The purpose of this study was to examine the topical effects of non-peptide antagonists

to substance P (aprepitant) and CGRP (telcagepant), respectively, on delayed and immediate inflammatory reactions in the skin and on associated pruritus.

Methods. A lipophilic formulation of aprepitant 5% and a hydrophilic formulation of telcagepant 1% were developed. Their effect on the skin barrier was measured in terms of transepidermal water loss (TEWL). Patch tests in patients allergic to nickel and prick test reactions to histamine were used as models for delayed and immediate contact dermatitis, respectively.

Results. None of the pre-treatments increased TEWL, suggesting there to be no impairment of the skin barrier. Histamine prick tests induced a flare with a mean area of 662±275 mm² and a weal with a mean volume of 49±11 mm³. These reactions were not affected significantly by any of the pre-treatments. Pre-treatment with aprepitant and its vehicle alone resulted in a potentiation of the infiltration of nickel reactions compared with test-reactions obtained after no pre-treatment (1147±423 mm³ and 1427±566 mm³ vs 683±202 mm³) ($p=0.03$). It can be explained by an improved penetrance of nickel by the vehicle. Telcagepant induced vasoconstriction in the skin but did not change the infiltration of nickel reactions.

Conclusion. The data suggest that the topical application of non-peptide antagonists penetrate the skin but do not inhibit contact dermatitis or pruritus.

THE HIGHER PROPORTION OF MEN WITH PSORIASIS TREATED WITH BIOLOGICS MAY BE EXPLAINED BY MORE SEVERE DISEASE IN MEN

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Introduction. The sex ratio of the prevalence of psoriasis is balanced. In recent years several reports have documented that men receive more systemic or UV treatment than women, and different hypotheses were made. In PsoReg, the national registry for systemic treatment of psoriasis in Sweden, we have, like other European registries, observed a predominance of men (59%), especially of men treated with biologics (63%). The objective of this study was to analyse if women are discriminated by not having the same access to the high-priced biologics.

Patients and Methods. Population based cohort study using data from a nationwide quality register of psoriasis patients; 2294 patients with moderate to severe psoriasis receiving systemic treatment from a specialist in dermatology were included. Main outcome measures: Time to initiation of biologic treat-

ment. A multiple Cox proportional hazard's regression was performed, with time to initiating a biologic treatment as the outcome in order to assess the independent role of the patient's sex in initiating such therapy. The psoriasis severity was defined as a time-varying variable.

Results. Men had more severe psoriasis than women according to the Psoriasis Activity and Severity Index (PASI), regardless of age at enrolment, and throughout the study period. The analysis in the multiple Cox regression show that age, psoriasis severity and psoriasis arthropathy were relevant factors for initiating biologic therapy, whereas sex is not.

Conclusion. Although as many women as men are believed to suffer from psoriasis, men seem to be more severely affected by psoriasis. The asymmetry in allocation of biologic therapy thereby probably reflects the differing disease activity between the sexes, and is not a discrimination of women per se.

INCREASING INCIDENCE OF BULLOUS PEMPHIGOID IN FINLAND

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Introduction. The aim of this study was to investigate the incidence of bullous pemphigoid (BP) in Northern Finland, and whether the incidence has changed over time.

Patients and Methods. This was a retrospective database study of all BP cases diagnosed in the Oulu University Hospital, Finland between 1985 and 2009. One hundred seventy-two BP patients, living in the Northern Ostrobothnia Hospital District (NOHD), were diagnosed. One hundred fifty-four were included to the final analysis according to the diagnostic criteria: clinical features characteristic of BP and positive direct immunofluorescence in the skin biopsy. If the direct immunofluorescence was negative, positive BP180 ELISA in serological assays was required. The age-standardized incidences of BP were calculated by the direct standardization method, using the NOHD-population and the general European population as a reference. Incidence rate ratios (IRR) were estimated by the Poisson regression model. To derive adjusted IRRs, age and sex was used as potential confounding factors.

Results. The crude incidence of BP was 17/1 000 000 person-years (95% CI 15 to 20) between 1985–2009. Using the general European population as a reference the age-standardized incidence was 14/1 000 000 person-years (95% CI 12 to 17). The incidence of BP increased 1.8 –fold (IRR 1.8; 95% CI 1.3 to 2.6, $p < 0.001$) in 2005–2009 compared with the mean incidence level of BP between 1985 and 2004, but after the adjustment for age and sex the increase was 1.4 –fold (IRR 1.4; 95% CI 1.0 to 2.0, $p = 0.045$). The incidence

of BP increased with age in both genders and was highest among elderly men.

Conclusion. This is the first study with immunohistologically verified BP diagnoses that reports the increase in the incidence of BP in age and sex adjusted population.

COWDEN'S SYNDROME (MULTIPLE HAMARTOMA)

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Cowden syndrome is inherited disease in autosomal dominant pattern. The gene Cowden syndrome is located on chromosome 10q22-q23 and is known as PTEN. A 64-year-old man is presented. He had multiple mucocutaneous facial papules (trichilemmomas), oral mucosal papillomatosis and acral and palmoplantar keratoses; adenoma of thyroid; multiple polyposis of gastrointestinal tract. The mental retardation have been specified. The treatment with electrosurgery was partially beneficent.

PHOTODYNAMIC THERAPY: CONVENTIONAL VS. NATURAL DAYLIGHT-MEDIATED TREATMENT: AN ECONOMICAL VIEW

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Introduction. Natural daylight photodynamic therapy (NDL-PDT) effectively treats actinic keratoses (AK) visible to the eye, as well as the subclinical field cancerization area. The NDL-PDT is assumed to be less time consuming, and thus more cost-effective than conventional artificial red LED-light mediated PDT (LED-PDT). In this study we compared the time consumption of the nurse and the patient and the efficacy in order to evaluate the cost-efficacy of these two treatment methods in a randomized study conducted in Finland.

Patients and Methods. Forty-two patients were randomized to two groups to receive either the LED- or NDL-PDT using methylaminolevulinate (MAL) as a sensitizer. Altogether 126 gr I-III AKs were treated, gr I lesions once and gr II-III lesions twice. The clinical outcome ratio, where special attention was put on three defined lesions in each volunteer, was done at 6 months. Time consumption of the nurse and patients was registered. During and after the treatment the patients assessed the grade of pain using a visual analog scale (VAS).

Results. The LED-PDT cured 88,9 % of lesions, and the NDL-PDT 68,3% ($p = 0.015$). The gr I lesions, treated only once, showed no statistical difference in clearance (the LED-PDT 86,3%, $n = 51$ and the NDL-PDT 73,3%, $n = 45$ respectively,

$p=0.100$). A statistically significant difference was detected between clearance of thicker (gr I-II) lesions which were treated twice (100% clearance, $n=12$ vs. 53,3% clearance, $n=15$, $p=0.014$). The difference in time consumption was statistically significant (287 min LED-PDT vs. 223 min in NDL-PDT, $p=0.010$ for patients), and (74 min for LED-PDT vs. 47 min for NDL-PDT, $p<0.001$ for nurses) with NDL-PDT being less time-consuming. Pain as a function of time, during and after NDL-PDT, was significantly ($p<0.001$) lower than pain experienced in the LED-PDT group.

Conclusion. The NDL-PDT was less time-consuming and painful, and thus more convenient for the patient. The NDL-PDT also consumed less nurses time, which might lead to expense savings for the clinic. For the thicker (gr II-III) lesions treated twice, the clearance-rate of the NDL-PDT was lower than for the LED-PDT. Thus, in the Northern latitudes the NDL-PDT might not be the first choice of treatment. Further research is warranted to show if the efficacy can be increased by restricting the illumination time-window for the NDL-PDT to mid-summer only.

VARIATION IN EXPRESSION OF CD40 LIGAND IN MAST CELLS OF PSORIATIC SKIN, SOLAR KERATOSIS AND EPITHELIAL CARCINOMAS

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Introduction. Mast cells are important in many biological functions, including tumorigenesis. However molecular mechanisms of mast cell function in malignant changes are poorly known. For unknown reason up to 70% of solid tumors, in particular epithelial carcinomas, express CD40. Because mast cells can express CD40 ligand (CD40L), we compared the expression of CD40L in mast cells of healthy, inflamed and malignant skin.

Methods. Expression of CD40L in tryptase-positive mast cells was investigated in lesional and non-lesional skin samples from patients with psoriasis ($n=10$), solar keratosis (SK) ($n=7$), basal cell carcinoma (BCC) ($n=10$) and squamous cell carcinoma (SCC) ($n=10$). To this end, cryosections prepared from skin biopsies (4 mm) were processed for the sequential double-staining method where tryptase was first identified enzyme histochemically followed by photomicrographing, then CD40L immunohistochemically and finally re-photomicrographing.

Results. In the non-lesional skin of SCC and psoriasis, the total number of tryptase-positive mast cells was higher than in the non-lesional skin of SK and BCC. In all disease states studied, the percentage of mast cells expressing CD40L was

higher in lesional skin biopsies ($49\pm27\%$ for psoriasis, $53\pm19\%$ for SK, $29\pm16\%$ for BCC, and $28\pm12\%$ for SCC) compared to non-lesional skin samples ($25\pm26\%$ for psoriasis, $37\pm22\%$ for SK, $14\pm13\%$ for BCC, and $18\pm6\%$ for SCC) ($p<0.003$). Interestingly, however, in the lesional and non-lesional skin of BCC and SCC the percentage of CD40L-positive mast cells was lower when compared to lesional and non-lesional skin of psoriasis and SK.

Conclusion. Even though CD40L is upregulated in lesional skin mast cells in all diseases studied, the expression level appears to be lower in epithelial carcinomas. This can imply to a possible reduced antitumoral response by mast cells.

MAST CELL CHYMASE CAN DEGRADE THE IMMUNOREACTANTS C3, FIBRIN AND FIBRINOGEN OF CUTANEOUS VASCULITIS

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Introduction. Mast cells are typically located around blood vessels and are activated during cutaneous vasculitis. Consequently, the cells release potent serine proteinases, including chymase, that can effectively degrade a variety of matrix proteins. Because the immunoreactants of vasculitis (immunoglobulins, fibrin and C3 products) precipitate to vessel walls, the purpose was to clarify whether chymase can degrade these proteins and clear the lesion from them.

Methods. Cryosections from skin vasculitis lesions were treated with 5 µg/ml rh-chymase or diluent control for 24h followed by routine immunofluorescence (IF) analysis (IgM, IgA, IgG, fibrinogen and C3c). In addition, the degradative effect of rh-chymase on purified human IgG, C3, fibrin and fibrinogen was studied biochemically by using electrophoresis (SDS-PAGE) and different functional assays.

Results. Rh-chymase treatment of cryosections from up to 10 skin specimens revealed that the IF-staining of C3c disappears almost completely, but no apparent changes were observed in fibrinogen or any immunoglobulin stainings. In SDS-PAGE analysis after 2h-incubation of up to 10 µg/ml rh-chymase with proteins, the enzyme degraded C3 and fibrinogen; both α - and β -chains of C3 and especially the α -chain of fibrinogen. No degradation of IgG was observed. Rh-chymase treatment of fibrinogen for 2h resulted in increased thrombin-induced clotting time. In addition, crosslinked fibrin gel prepared from pure fibrinogen or plasma was solubilized by 10 µg/ml rh-chymase.

Conclusion. Chymase released from activated mast cells can degrade the immunoreactants C3, fibrin and fibrinogen of vasculitis and possibly clear the lesion from them. Moreover, chymase may be a previously un-recognized antithrombotic enzyme.

CHYMASE IS PARTIALLY INACTIVATED IN ATOPIC DERMATITIS BUT LOW CHYMASE CONCENTRATION IS STIMULATORY TO PERIPHERAL BLOOD IMMUNE CELLS

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Introduction. Mast cell (MC) chymase has a candidate gene for atopic dermatitis (AD) and can participate in the pathogenesis of the disease. Therefore, the purpose of this study was to investigate the expression and function of MC chymase in AD.

Methods. The expression of MC chymase protein and chymase activity were assessed in the cryosections of lesional and non-lesional skin of 17 patients with moderate-to-severe AD using immunohistochemistry and enzyme histochemistry. Additionally, the effect of rh-chymase on the proliferation of T cells and peripheral blood mononuclear cells (PBMCs) was investigated in cell cultures using 3H-thymidine incorporation.

Results. The number of MCs with chymase protein was greater in lesional dermis than in nonlesional dermis ($p=0.035$) but chymase enzyme activity was reduced in lesional dermis ($p<0.001$) indicating partial inactivation. Interestingly, low concentrations of rh-chymase (10–100 ng/ml) stimulated the proliferation of T cells and PBMCs from atopic patients whereas higher concentrations (100–1000 ng/ml) switched the stimulation to inhibition.

Conclusion. The results suggest that chymase can actively stimulate inflammatory cells in AD even though is partially inactivated, and therefore it can serve a suitable target for drug development in AD.

MAST CELLS AND REGULATORY T CELLS ARE INCREASED IN BASAL CELL CARCINOMA

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Introduction. The immune cells and immunosuppression in the peritumoral matrix of basal cell carcinoma (BCC) can participate in the development of BCC. Recently, experimental results have been presented that the interaction between mast cells (MCs) and regulatory T cells (RegTs) can lead to tolerance or immunosuppression. Therefore, the presence of MCs, RegTs and their morphological contacts was studied in BCC.

Methods. Punch biopsies were taken from the lesional and healthy-looking skin of 17 patients with BCC. Subsequently, the biopsies were processed for 5- μ m-thick cryosections. Mast cell tryptase was stained enzyme histochemically and the marker of RegTs, FoxP3, immunohistochemically. These staining methods were further used in the double-staining

method. The cells and morphological contacts (the percentage of tryptase-positive MCs with at least one contact with FoxP3-positive RegTs) were counted in a peritumoral dermal area of 2 mm (width) x 0.6 mm (depth) using a Leica microscope equipped with an ocular grid.

Results. The number of both FoxP3-positive RegTs and tryptase-positive MCs were higher in the BCC lesion ($p<0.0001$) when compared with the healthy-looking skin. Morphological contacts between FoxP3-positive RegTs and tryptase-positive MCs were significantly ($p<0.0001$) increased in the BCC lesion as well when compared with those in the healthy-looking skin (from $1,0\pm1,0/\text{mm}^2$ to $25,6\pm21,7/\text{mm}^2$).

Conclusion. These findings suggest that the interaction between MCs and RegTs can lead to an immunosuppressive state in the peritumoral tissue of BCC resulting in a condition that favors BCC growth

ULCUS VULVAE ACUTUM LIPSCHÜTZ

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Lipschütz ulcer is an underdiagnosed disorder that presents as an acute painful necrotic vulvar ulcers in young prepubertal or pubertal girls without any history of sexual contact. Austrian colleague Lipschütz reported already in 1913 a series of young virginal girls with fever, genital ulceration and lymphadenomegaly. However the natural history, etiology and effective treatment are still incompletely understood. Nowadays Lipschütz ulcer refers to an ulceration of vulva of nonvenereal origin and is also known as acute genital ulcer (AGU). The onset is preceded by an acute systemic illness. Fever, lymphadenopathy, malaise or influenza-like symptoms may be present. Primary Epstein-Barr virus (EBV) infection is the most frequently reported etiology, but other infectious agents like cytomegalovirus (CMV), mycoplasma pneumoniae and influenza A virus are probably implicated. The diagnosis is established clinically and often made retrospectively by exclusion after ruling out STIs, trauma, autoimmune causes, drug reactions and local manifestations of systemic illness. Laboratory evaluation commonly include bacterial culture, herpes simplex virus (HSV) culture or PCR, a complete blood count and serologic testing or PCR for EBV. The histologic findings are nonspecific; superficial edema and dilated capillaries with neutrophilic infiltration and ulceration. The management of ACU is mainly supportive and consists of symptomatic treatment. Often oral and topical antibiotic and corticosteroid therapy are used. Lesions heal spontaneously in a few weeks with no sequelae. There are reports that some patients have at least one recurrence. It is important to keep AGU in mind as a differential diagnosis of vulval ulceration to avoid misdiagnoses and unnecessary invasive investigations.

A SEVERE AND TREATMENT RESISTANT CASE OF PEMPHIGOID GESTATIONIS

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Introduction. Pemphigoid gestationis is a rare polymorphic inflammatory bullous dermatosis of pregnancy and the postpartum period. The eruption normally clears within 6 months postpartum. The purpose of this abstract is to present a case of exceptionally treatment resistant and severe pemphigoid gestationis requiring high doses of prednisolone and additional immunosuppressing drugs.

Patient. 27-year-old otherwise healthy woman who presented with intensely pruritic rash starting in the third trimester of pregnancy. In the beginning the rash was considered to be polymorphic eruption of pregnancy (the patient refused skin biopsy) and thus treated with UVB and low dose prednisolone. However because of only partial response a skin biopsy was obtained and pemphigoid gestationis was diagnosed. BP180 antibodies were present in exceptionally high levels (> 150 U/ml). Skin symptoms worsened after delivery and thus prednisolone was started with a dose of 0.5 mg/kg daily. Cyclosporin A 3g/kg daily was added to treatment only 3 days later. At first remission was obtained.

Results. When tapering the prednisolone dosage the disease activated and persisted. Eight months later the disease was still active and as the patient ceased lactation, methotrexate was added to treatment with a dose of 20 mg weekly. This finally led to remission and BP180 antibodies started to decline. Cycloporine A was ceased and Prednisolone lowered to 10 mg daily. Even now, 14 months postpartum the disease requires immunosuppressive therapy with methotrexate and tends to relapse if medication is tapered. A hydatid mole and choriocarcinoma have been excluded.

Conclusion. Regardless of its self-limiting tendency pemphigoid gestationis can also be severe and resistant to a number of treatments.

TERIPARATIDE-INDUCED CALCIPHYLAXIS SUCCESSFULLY TREATED WITH SODIUM THIOSULPHATE

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Introduction. Calciphylaxis is a cutaneous ischemic small vessel vasculopathy typically seen in patients with chronic kidney disease (1). Sodium thiosulfate has been reported to be an effective treatment in calciphylaxis associated with chronic

kidney disease (1, 2). However, calciphylaxis has also been observed in nonuremic patients and there are few reports describing effective treatments in this patient group.

Case Report. Our patient is a 68 years old woman with a previous history of asthma, high blood pressure, osteoporosis and rheumatoid arthritis. She had normal renal function. She developed several painful ulcers in both legs with no response with traditional wound treatments. Skin biopsy revealed calciphylaxis as the etiology of the ulcers. Teriparatide, which she had received for the treatment of osteoporosis, was thought to be the causative agent. After diagnosis, sodium thiosulfate was started as a dose of 25 g/100 ml intravenously 3 times a week. This treatment resulted in prompt relief of pain and the ulcers began to diminish in size and depth. The patient received sodium thiosulfate for 4 months, and it was discontinued before complete healing of the ulcers due to her wish.

Conclusion. Sodium thiosulfate was an effective treatment of calciphylaxis in our patient with teriparatide-induced calciphylaxis and normal renal function.

LONG-TERM SAFETY OF TOPICAL PIMECROLIMUS AND TOPICAL TACROLIMUS IN ATOPIC BLEPHAROCONJUNCTIVITIS

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Introduction. Topical corticosteroids are widely used for atopic blepharoconjunctivitis (ABC) but long-term use causes adverse effects like cataract, intraocular pressure (IOP) elevation and skin atrophy. Topical pimecrolimus and tacrolimus are more recent treatment options and there are only a few studies of the use of them in ABC. The objectives were to evaluate their long-term safety and tolerability on the eyelid skin and to evaluate and compare their efficacy in ABC.

Patients and Methods. A chart review of ABC patients treated at the Helsinki Skin and Allergy Hospital in 2001–2011 was performed. Main outcomes and measures were: IOP changes, ocular adverse effects, malignancies, discontinuation rates, and changes in severity of blepharitis and conjunctivitis symptoms.

Results. The number of eligible patients was 330 of which 33 patients used pimecrolimus cream and 297 tacrolimus ointment. The mean follow-up times were 1.5 years for tolerability and efficacy, and 5.8 years for malignancies. No adverse effects on vision, cornea or lens or malignancies were observed. Discontinuation rates due to intolerance/insufficient efficacy were 33%/23% with pimecrolimus and 9.1%/1.6% with tacrolimus. Number of patients with elevated IOP decreased 75–80% and the mean IOP 0.5–0.6 mmHg, in both groups. For blepharitis/conjunctivitis components of ABC, treatment re-

sponse rates were 79%/55% with pimecrolimus and 90%/80% with tacrolimus. Compared to pimecrolimus, tacrolimus showed better efficacy with odds ratios 2.37 (CI 0.90–6.22) for blepharitis and 2.34 (CI 1.02–5.40) for conjunctivitis.

Conclusion. Topical pimecrolimus and tacrolimus are safe treatment options showing better long-term safety profiles than topical corticosteroids. Tacrolimus seems better tolerated and more effective than pimecrolimus, has a favorable effect on conjunctivitis symptoms, and does not increase IOP. Hence, tacrolimus ointment is a possible first-line treatment option in long-term management of ABC.

THE EFFECT OF REHABILITATION IN SUNNY CLIMATE ON SKIN PATIENTS' SYMPTOMS, QUALITY OF LIFE, UV-RADIATION DOSE AND VITAMIN D STATUS

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Introduction. In Finland patients with atopic dermatitis (AD), psoriasis or psoriatic arthritis can apply for a 2-week rehabilitation arranged in Puerto Rico, Gran Canaria. These courses provide with education, peer support, physical exercise, supervised sunbathing and balneotherapy. We studied the effects of the courses on participants' life quality, UV-radiation dose, serum 25(OH)D concentration and skin and joint symptoms.

Patients and Methods. Altogether 228 subjects in 10 courses were asked to fill self-administered questionnaires (DLQI, RAND-36, PO SCORAD, SAPASI, HAQ, BASFI, BASDAI) before, after and 3 months after the course. Thirty subjects used UV-dosimeters and provided us with serum samples before, after and 3 months after the course for 25(OH)D analyses.

Results. We have analyzed the 1st course including 13 AD, 22 psoriasis and 16 psoriatic arthritis patients. The mean DLQIs at 3 measure points were 7.2, 1.9 ($p < 0.05$) and 3.9 ($p < 0.05$) in the AD group and 6.1, 1.8 ($p < 0.05$) and 5.2 ($p > 0.05$) in the psoriasis group. The mean PO SCORADs were 30.6, 11.1 and 20.6 and mean SAPASIs 7.0, 1.9 and 3.2. The decreases were statistically significant. The RAND-36s indicate significant improvement in several sub-scales in both groups after the course, but not after 3 months. The joint symptom scales HAQ, BASFI and BASDAI improved significantly during the course, but not after 3 months.

Conclusion. Two-week rehabilitation in sunny climate improves AD patients' skin symptoms and life quality for at least 3 months. Skin symptoms in psoriasis improve significantly for 3 months but joint symptoms seem to relapse, which might be the reason for lesser life quality improvement. The remaining questionnaires and 25(OH)Ds will be analyzed shortly for more evidence.

10-YEAR FOLLOW-UP STUDY OF 160 CHILDREN WITH ATOPIC DERMATITIS AND WHEAT ALLERGY

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Introduction. Food allergy plays a pathogenic role in children with atopic dermatitis (AD). Wheat is among the six most common foods causing allergy in children and wheat allergy (WA) is affecting 0.4%–1% of them.

Methods. Altogether 160 infants <1 year of age with recalcitrant AD had WA diagnosed with open food challenges, skin prick test (SPT), specific IgE (sIgE) and atopy patch test (APT). Based on diagnosing method children were divided into three groups: groups 1 and 2 (immediate or delayed challenge reaction to wheat), and group 3 (positive SPT/APT/sIgE, positive elimination response and home challenge to wheat). In addition to wheat, also rye, barley and oat were eliminated from the child's diet in order to diminish AD symptoms to minimum. In subgroups of children also rye and oat were challenged. The development of wheat tolerance was followed by oral challenges. Height and weight were measured and ISO-BMI (an extension of Body Mass Index) was calculated at follow-up.

Results. At 10-year follow-up 12 (7.5%) children had ongoing WA, 10 of them avoiding also rye and barley. Children in group 3 recovered fastest from WA, median wheat elimination time being 2.0 years. In groups 1 and 2 respective values were 3.0 years. Altogether 10/12 WA children had a positive SPT reaction to gliadin. ISO-BMI was within normal range in all three WA groups, height below -2SD was discovered in 7(4%) patients.

Conclusion. The early diagnosis of WA and the fastness of undertaking the elimination diet associates with the rapidity of outgrowing from WA. Despite extensive elimination diets at baseline no marked underweight was observed in study patients. WA associates with allergy to rye, barley and oat. Positive SPT to gliadin predicts a long lasting WA.

MELANOMA ON TATTOOS: TWO FINNISH CASES

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Introduction. The potential carcinogenic effects of tattoos and tattoo inks remain unclear. We report 2 cases of melanoma occurring on tattoos in Finnish patients.

Case Reports. Patient 1. In June 2006, a 61-year-old male presented with an inflammatory ulcerated tumoral plaque of the right thigh overlying an old tattoo. A superficial, extensive, heterogenous and asymmetric pigmented lesion underlying and in the vicinity of the tumor had evolved during the past 5 years. Physical examination and full body CT scan were normal. Excision of the lesion disclosed a nodular melanoma (Breslow thickness 15 mm, Clark level IV). Sentinel lymph node exploration was negative. No relapse had occurred before 2009, after which no information was available.

Patient 2. In May 2012, a 32-year-old male presented with a 1.3 cm brown, polychromatic, asymmetric lesion on the upper back with a large black tattoo performed a couple of years earlier. A one millimeter mole pre-existed before the tattooing and gradually changed during the following years. Physical examination was otherwise normal. Pathology of the surgically removed mole confirmed the diagnosis of a nonulcerated superficially spreading type melanoma (Breslow thickness 0.4 mm, Clark level II). The patient has been symptom-free for 6 months.

Discussion. To date, approximately 50 cases of skin cancers have been reported on tattoos, including 15 melanomas. It is unknown whether the pathogenesis of a melanoma on a tattoo is any different from a melanoma on plain skin. Several studies have stressed the presence of potential carcinogenic or pro-carcinogenic products in tattoo inks. However, the prevalence of tattoos and melanoma increase in the population. Most of the reported melanomas developed on dark tattoos. Therefore, if tattoos have a role in melanoma growth, it may be in masking the clinical malignant modifications and delaying the diagnosis, rather than in having a true and direct carcinogenic effect.

Conclusion. The association between melanoma and tattooing remains fortuitous thus far. Tattoos can delay the clinical diagnosis of a melanoma.

HYPERPIGMENTATION OF THE FOREHEAD AFTER BAPTISM: A PHOTOTOXIC REACTION DUE TO CHRISM

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Introduction. Chrism is a consecrated oil used in Christian churches in the administration of certain sacraments and ecclesiastical functions. During baptism and confirmation, it is applied on the forehead. To date, only one case of phototoxic reaction has been published. We report here a second case.

Case Report. An otherwise healthy 20 month-old boy presented with a chronic hyperpigmentation of the forehead evolving for a year. The mother noted the pigmentation the same day he was baptized one year ago, outside of the church without any preceding rash, after the priest applied the oil. The family spent the whole day outside in the sun. Pigmentation waxed and waned the whole year. Anamnesis, location on the ointment area, application of a perfumed oil and possible photosensitivity prompted to diagnose a "dermatite en breloque" related to Chrism. No treatment was given and the pigmentation finally faded.

Discussion. Chrism is made of olive oil and scented with a sweet perfume. It is consecrated by the bishop at the Mass of the Chrism during the Holy Thursday. The oil is then used during the whole year for various sacraments. Fischer reported a case of "cross" on the forehead of a baby related to bergamotte and lime in the oil. In our case, the perfume was most likely responsible for the reaction but we could not trace back its composition. The frequency of such reaction is not known. It could be underestimated in case of discrete lesions or the diagnosis made by the parents and the pigmentation fades with time.

Conclusion. Chrism may be responsible for a pigmented contact photodermatitis. The anointed should maybe wash out the oil after sacrament to avoid such pigmentation in case of immediate sun exposure afterwards.

BENCHMARKING UNDERGRADUATE DERMATOVENEREOLOGICAL EDUCATION IN FINLAND

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Introduction. A benchmarking of undergraduate dermatovenereological education in Finland was performed in 2010.

Methods. A survey was sent to clinical instructors in all five medical faculties.

Results. No nationwide core analysis of the teaching content has been performed, albeit the topics and the total number of teaching hours were quite similar in all five faculties. Teaching methods differed somewhat. The results were presented in the first national meeting of clinical instructors in Dermatove-

nerology in 2010 and will be presented again in the Nordic Congress on Dermato-Venereology.

Conclusion. The first meeting resulted in ongoing networking of clinical instructors: since 2010 the clinical instructors have had an annual meeting as a satellite of the meeting of The Finnish Dermatovenereological Society.

NEW IMAGING TECHNIQUES IN THE DIAGNOSIS OF MELANOMA

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The incidence of malignant melanoma is increasing rapidly in the Nordic countries. Also, mortality is high. A dermatologist is better at diagnosing melanoma than doctors from other disciplines. However, even dermatologists miss a substantial fraction of possible melanomas. Hence, new imaging devices must be developed to facilitate diagnosis. In the session, examples of new techniques such as digital dermatoscopy, siascopy etc will be discussed.

OVERTIME CHLAMYDIA TRACHOMATIS SEROTYPE DISTRIBUTIONS IN FERTILE-AGED FINNISH FEMALES

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Introduction. While the occurrence of *Chlamydia trachomatis* has been high in the affluent countries for several decades little is known about the ecology of *C. trachomatis* serotypes. We studied the distribution of *C. trachomatis* serotypes in Finnish women from the 1980's to the 2000's.

Methods. 1,169 healthy subjects testing positive for *C. trachomatis*-specific IgG antibodies were available from a large subcohort of 11067 15–29-years old women belonging to the Finnish Maternity Cohort of the National Institute for Health & Welfare. They represented *C. trachomatis* seropositives in the 1980's ($n=358$), 1990's ($n=480$) and 2000's ($n=331$). *C. trachomatis* serotype-specific IgG antibodies were measured by the microimmunofluorescence method.

Results. *C. trachomatis* serotype distributions were almost similar in the 1980's and 2000's serotypes G, E and J being the most prevalent. In the 1990's these serotypes were partially outcompeted by serotype D, overall and especially in the 23 to

28 year-old women. In the 1990's also the relative proportions of women positive for >2 serotypes were the highest.

Conclusion. The temporary *C. trachomatis* serotype replacement among females parallels changes in the sexually active population in the 1990's in Finland.

PSYCHOLOGICAL ASPECTS OF ATOPIC DERMATITIS

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The mood is important for the wellbeing. Several questionnaire surveys of patients indicate that atopic dermatitis may have a negative effect on quality of life and that skin disease can affect the quality of life as much as severe heart disease, asthma or diabetes. Patients with atopic eczema describe themselves as less attractive, some are disgusted by themselves and feel shame and guilt. Some people find it difficult to accept a disease that is chronic and they have to live with the rest of their lives. It becomes a vicious cycle, where the negative thoughts exacerbate feelings of skin symptoms. Patients with atopic dermatitis may have high levels of anxiety, difficulty managing anger and they have a more severe eczema during stressful periods which has been shown in two pilot studies. Cognitive psychology, is an evidence-based form of psychotherapy, can be useful in stress-related eczema to help the patient to live a better life in which the patient schooled in awareness how he/she takes responsibility for his/her chronic disease.

NAIL FOLD VIDEOCAPILLAROSCOPY - A NEW TOOL IN EXAMINATION OF CONNECTIVE TISSUE DISEASES: LINK TO CLINICAL PATHOLOGICAL ISSUES IN DIFFERENT AUTOIMMUNE DISEASES

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Nail fold videocapillaroscopy is a fundamental imaging technique used in the clinical examination of patients with different autoimmune diseases. There is a widespread and growing interest in nail fold videocapillaroscopy. It has evident diagnostic and prognostic power especially in systemic sclerosis (SSc), but also in other systemic connective tissue diseases. Nail fold videocapillaroscopy is based on light microscopy, usually using 200 x magnification lens. Capillaries are visualized through the skin. It is a safe, without any risk for radiation, easy to repeat and cost saving tool. The Italian physician Giovanni Rasori in the XVIII century first noted the close relationship of conjunctivae inflammation and capillary loops. However, Maurice Raynaud in 1862, presented this

phenomenon named by him as Raynaud's phenomenon. Raynaud's phenomenon is very usual in population, occurring in 15–20% of young females. However, Raynaud's phenomenon is usually the first clinical sign of micro vascular deviation seen in patients of early autoimmune rheumatic diseases. When occurring in patients at 40 years or more of older, it needs careful examination and nail fold videocapillaroscopy offers a good tool to distinguish the primary Raynaud's phenomenon from secondary one. Imaging of micro vascular anatomy and function of vessels during Raynaud's phenomenon was first performed by magnifying glass usually having a magnification capacity of 20. In 1939 Otfried Muller published first colour capillaroscopy images painted micro vessel loops by him using a simple capillaroscopy technique. Since 1980 a growing interest of nail fold videocapillaroscopy with new equipment's has improved the visual image and raised the importance of nail fold videocapillaroscopy in a new level of the value of it in the clinical practice. During this lecture we are taking a closer look into the nail fold videocapillaroscopy technique, which is the base of classifying the findings and some examples of its findings in different systemic rheumatic diseases at the time of the diagnosis of the diseases as well as at the follow up of the response of the treatment.

Conclusion. Microcirculation seems to have a fundamental role in basic of many different rheumatic diseases as well as some other systemic diseases like diabetes mellitus. However the specific role of the endothelium in different diseases may vary according the disease. Any pathological disturbances in the endothelial of the vascular system may result in a chronic disease with impair organ function. Nail fold videocapillaroscopy gives us a delicate tool to see and measure changes in endothelium early as well as follow the micro vascular functions during the treatment and in some situation also predict the prognosis.

TACHYKININ EXPRESSION IN ATOPIC DERMATITIS AND RELATION TO ANXIETY TRAITS AND DEPRESSION

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Atopic dermatitis (AD) is an often severely itching, chronic, inflammatory skin disorder. AD may worsen due to stress and anxiety. Different neuromediators, such as tachykinins, have been suggested to influence the level of inflammation as well as being involved in stress and anxiety. The expression of substance P, neurokinin A (NKA) and the neurokinin (NK)-1 receptor (R) was studied in the skin, as well as possible corre-

lations to clinical and psychodemographic parameters, of 28 AD patients. The extent of the disease was assessed (SCORAD), as well as the degree of subjective pruritus (visual analogue scale). The level of chronic stress was determined (salivary cortisol test), in addition to anxiety traits (Swedish Universities Scales of Personality), and depression (Montgomery-Åsberg Depression Rating Scale-Self assessment). Skin biopsies were stained using a biotinylated-streptavidine method. There was an increase of substance P and NKA positive nerve fibres and also of NKA+ cells, in lesional compared to non-lesional skin, while no differences for NK1-R+ cells. There was a correlation between NK1-R+ cells, and acanthosis and inflammation, in lesional skin. There was also a correlation between NK1-R+ cells in lesional and non-lesional skin, and depression score. NK1-R+ cells correlated to cortisol ratio in non-lesional skin. NKA+ cells correlated to acanthosis in non-lesional skin. We also found a correlation between NKA+ fibres in lesional skin and cortisol ratio. Tachykinins are likely to have a role in the inflamed skin of AD. In addition, there is a correlation between NK1-R+ cells and depression score and chronic stress, which suggest that tachykinin signaling pathways are of interest in stress worsened AD.

IUSTI GUIDELINES ON GONORRHOEA TREATMENT

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In 2008, the World Health Organization (WHO) estimated 106 million cases of gonorrhoea among adults globally, a similar global incidence to genital chlamydial infections. In Europe, gonorrhoea is the second most common bacterial sexually transmitted infection (STI), i.e., after chlamydial infections. There is considerable geographic variation in its distribution and infection reported three times more frequently in men than women, which probably reflects the significantly higher proportion of symptomatic men and the burden of infection in men who have sex with men (MSM). In the Nordic countries, gonorrhoea is mainly a disease among MSM and heterosexual men having had sex in high-endemic countries. In MSM, a high proportion of gonorrhoea will be found in anus and pharynx, often asymptomatic. Culture should always be used for diagnostic in order to facilitate susceptibility testing. However, NAAT has a higher sensitivity, especially in samples from anus and pharynx, and culture may be used as a supplement if positive in NAAT. *Neisseria gonorrhoeae* has shown a remarkable capacity to develop resistance to multiple classes of antibiotics including penicillins, tetracyclines, macrolides and fluoroquinolones. After a steady rise in minimum inhibitory concentrations (MICs) in recent years, resistance and even clinical failures to extended-spectrum cephalosporins

(ceftriaxone and cefixime) have now been confirmed. In this emergent situation including the fear that gonorrhoea may become untreatable, the WHO has published the 'Global Action Plan to Control the Spread and Impact of Antimicrobial Resistance in *Neisseria gonorrhoeae*'. European Centre for Disease Prevention and Control (ECDC) has also prepared a response plan for the European Union. Ceftriaxone and cefixime have a strong evidence-base for efficacy in the treatment of gonorrhoea and have been the principal recommended treatments. As a consequence combination antimicrobial therapy is now recommended. According to limited data, combination antimicrobial therapy with third generation cephalosporins and azithromycin seems to show synergy in-vitro and in-vivo. The recommended first line treatment according to recent European IUSTI-guidelines is 500 mg ceftriaxone i.m. and 2 gram azithromycin p.o. as direct observed therapy. If treatment after susceptibility testing, according to the test results

STRESS, NERVES AND MAST CELLS IN PSORIASIS

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Psoriasis may worsen due to psychological stress. Psychological stress induces an activation of the hypothalamic-pituitary-adrenal (HPA) axis with an activation of stress hormones, neurotrophins, neuropeptides, such as substance P, calcitonin gene-related peptide (CGRP) and vasoactive intestinal polypeptide (VIP), and of the sympathetic nervous system with release of monoamines, such as norepinephrine. There is a close association between sensory nerves and mast cells in psoriasis, the number of these nerves and mast cells also being increased in involved psoriatic skin. Mast cells may produce and have receptors for different neuromediators, such as substance P and other tachykinins. Mast cells may upon nerve stimulation release cytokines, such as IL-6 and TNF-alpha, and neuropeptides, such as VIP, which may have impact on Th17 maturation, mast cells also being able to secrete IL-17 on their own. Sensory nerves expressing substance P and CGRP may be essential in interacting with mast cells in psoriasis, and these neuropeptides and mast cells may have a role also during psychic stress. In addition, pruritus perception may be associated with stress in psoriasis and tachykinin receptor bearing immune cells have been shown to correlate with such pruritus. Interestingly, we might also consider the brain, during stress, as an important area for interaction between mast cells and T cells, such as Th17 cells, which cells may pass the blood brain barrier and affect skin inflammation. There is a complex interaction between psychological stress, sensory nerves and mast cells in psoriasis.

ANAL DYSPLASIA AND CANCER

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Anal dysplasia (anal intraepithelial neoplasia) is a precancerous condition induced by human papillomavirus (HPV), which may progress to invasive cancer. The natural history of the disease is not fully understood but appears to be similar to the development of invasive cancer from pre-malignant disease in the uterine cervix. The worldwide incidence of anal cancer in the general population although low, has increased over the past three decades. The increase has been alarmingly high among HIV positive men who have sex with men. Immunocompromised individuals and those previously treated for HPV related premalignant disease also represent high-risk groups for the development of anal dysplasia and cancer. It is however noteworthy that the majority of cases of anal and perianal cancer continuously are diagnosed in heterosexual and otherwise healthy men and women. There are numbers of challenges to be addressed as long as there is no consensus about the optimal management of HPV induced anal intraepithelial neoplasia. Screening algorithms and follow-up routines are in demand. A wide range of treatment modalities, including topical and ablative therapy, is available. However, randomised controlled trials (RCT) assessing evidence based effective intervention or therapy are lacking. In the Nordic countries, multi centre studies may be the best way to contribute to more knowledge about predictors of disease progression and elucidating appropriate management of the disease. The positive effect of prophylactic HPV vaccination on a population basis will not be seen for many years. In the meantime, the diagnosis of HPV related precancerous lesions in unvaccinated "high risk" individuals, may be missed or delayed. Therefore, optimal regimes for screening, intervention and follow-up of anal dysplasia in high-risk groups, is a priority.

AN UPDATE ON VITAMIN D

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Vitamin D is a hot topic in medical research and the knowledge about its vital role in health and disease is constantly increasing. Vitamin D is an essential steroid for calcium homeostasis and skeletal health, for regulation of cellular growth, cell proliferation and cell differentiation. Vitamin D regulates the immune system, controls cancer cell growth and plays a role in the regulation of blood pressure. Therefore, vitamin D insufficiency may cause many chronic diseases that affect both children and adults. Vitamin D3, or cholecalciferol, is

produced in the skin by ultraviolet radiation (290–315 nm) of 7-dehydrocholesterol and is then hydroxylated in the liver into 25-hydroxyvitamin D [25(OH)D], which is the major circulating metabolite. The optimal level of serum 25-hydroxyvitamin D is 30–100 ng/mL (or 75–250 nmol/L). The cut-off level for serum 25(OH)D, which is taken as a diagnostic value for vitamin D insufficiency, has varied over the years. The concentration of circulating 25(OH)D3 shows seasonal variation at higher latitudes due to the lack of sun exposure during the winter which may induce D-vitamin insufficiency. An individual variation in vitamin D concentrations due to genetics and non-linear response between vitamin D intake and 25(OH)D concentrations have also been observed. There is no sufficient evidence to recommend screening individuals who are not at risk for deficiency. Only individuals at high risk for vitamin D inadequacy as older adults (>70 years), individuals with limited sun exposure, people with dark skin, people with fat malabsorption and obese persons should be considered for 25(OH)D testing. Sun exposure is the major source of vitamin D for humans although many dermatologists believe that it is inappropriate to recommend intentional exposure to natural or artificial UV to achieve adequate vitamin D level. Balancing photoprotection is important to prevent photodamage but a short sun exposure at the midday is commonly sufficient to achieve optimal vitamin D status.

SUNBEDS –WHAT’S IN THERE?

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The skin cancer incidence has increased substantially over the past decades and the role of ultraviolet (UV) radiation in the etiology of skin cancer is well established. Epidemiological data suggest elevated incidences of both melanoma and non-melanoma skin cancer associated with indoor tanning. During a cosmetic indoor tanning session, people expose themselves to a large quantity of UV radiation – especially to UVA radiation. A major problem with UVA wavelengths is that UVA provides a tan, but does not offer the protection from the subsequent UV exposure and against the erythema formation. In 2009, the International Agency for Research on Cancer (IARC) classified artificial UV tanning devices as carcinogenic to humans. IARC based their opinion on the definitive meta-analysis of large number of studies that evaluated the association between sunbed exposure and skin cancers (IARC, 2007). This meta-analysis revealed a 75% increased risk of melanoma for individuals that had had their first indoor tanning exposure under the age of 35. An earlier Scandinavian prospective cohort study had already shown very strong evidence for a causal relationship between sun bed use and malignant melanoma among females in the 20–29 year age group who used a sun

bed more than once a month (Veierod et al. 2003). These results supported the previous notion that adolescence and early adulthood appear to be the most sensitive age periods for UVR exposure, either from natural or artificial sources. In addition, frequent indoor tanning has recently been linked with addictive qualities, suggesting that tanning behavior exhibits signs of dependence (Nolan&Feldman 2009). Taken all these findings together, it is not surprising that many Nordic countries have forbidden, or are in process to forbid, the sunbed use from the minors.

THE ASSOCIATION BETWEEN ENDOPLASMIC RETICULUM STRESS GENES AND PSORIASIS VULGARIS

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Plaque Psoriasis is a frequent, chronically relapsing, immune-mediated systemic disease with characteristic skin changes. The role of cytokines in its development is well known and has been studied for decades. The endoplasmic reticulum (ER) is a central organelle of each eukaryotic cell as the place of lipid synthesis, protein folding and protein maturation. The ER is the major signal transducing organelle that senses and responds to changes of the homeostasis. Conditions interfering with the function of ER are collectively called ER stress. ER stress is induced by accumulation of unfolded protein aggregates (unfolded protein response, UPR) or by excessive protein traffic (ER overload response, EOR). ER stress is involved in different human pathologies, including chronic inflammations. The aim of our study was to explore if the SNPs in ER stress related genes are associated with higher risk for psoriasis vulgaris. We studied 29 SNPs in the following ER stress genes: ATF6 (chr1), HSPA5 (chr9), HSP90B1 (chr12), ERN1 (chr17), XBP1 (chr22). The study group was composed of 566 psoriasis vulgaris patients and 308 healthy control individuals. Single marker analysis resulted in significant associations with two SNPs in the ERN1 (Endoplasmic Reticulum to Nucleus Signaling) gene (rs2172679, p=0.065; rs9916168, p=0.0002) and with one SNP in the HSP90B1 (Heat Shock Protein 90kDa Beta (Grp94), Member 1) gene (rs17034977, p=0.023). ERN1 is a transmembrane receptor of ER and detects unfolded or misfolded protein loads in the ER lumen. HSP90B1 act as molecular chaperone (they fulfill crucial roles in intracellular transport, the maintenance of proteins in an inactive form and the prevention of protein degradation) being associated with protein folding and activating ER stress signaling path-

ways. Our study is the first attempt to find genetic associations between the ER stress genes and psoriasis and we were able to find preliminary evidence, that they could be involved in the pathogenesis of this inflammatory disease.

THE SPECTRUM OF B-CELL LYMPHOMAS

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Primary cutaneous lymphomas show a growing incidence but the underlying mechanisms remain largely unknown. Primary cutaneous B-cell lymphomas (CBCL) represent 20-25% of all primary cutaneous lymphomas. Their classification is based on the ontogenic stage of the malignant B cells. Thus, the three main groups of CBCL are: primary cutaneous follicle center lymphoma (PCFCL), primary cutaneous marginal zone B-cell lymphoma (PCMZL) and primary cutaneous diffuse large B-cell lymphoma (PCLBCL, PCLBCL-LT). Skin biopsy with immunohistology with B-cell markers is decisive in the classification. Strong expression of Bcl-2, Bcl-6, and CD10 should raise suspicion of a systemic follicular lymphoma with secondary skin involvement. CD5 and cyclin D1 immuno-stainings are used to differentiate PCMZL from the rare cutaneous manifestations of mantle cell lymphoma (CD5+, cyclin D1+). PCFCL typically presents as solitary or grouped tumors on the head or on the trunk, extracutaneous dissemination is rare but cutaneous relapses are frequent. The 5-year survival is 95%, irrespective of relapses. Bcl-6+ is typically positive. Solitary/localized lesions are treated with local radiotherapy, excision or with intralesional rituximab injections, three times a week in 4 week cycles. Even relapses responded well to rituximab treatment. Systemic rituximab (for 4-8 weeks) is used for multiple/widespread lesions. PCFCL localized in the legs needs aggressive therapy. PCMZL mostly involves the trunk and upper extremities as solitary or multiple papules, plaques, or nodules. The disease course is indolent but often persistent. Long-term immune stimulation, like infections with Hepatitis C, H pylori, *Borrelia burgdorferi* can be involved in the development of MZL. Bcl2 + marker is positive. Solitary/localized lesions can be just followed up or treated with local radiotherapy, excision or with intralesional rituximab injections. PCLBCL-LT has the worst prognosis with 5-year survival of 50% despite systemic chemotherapy. It presents as solitary or multiple tumors mainly on the leg(s). Relapses and extracutaneous dissemination are common. Typically, the cells are Bcl-2+, MUM-1+, FOXP1+. EORTC and ISCL have published consensus recommendations for the management of cutaneous B-cell lymphomas (Senff et al., Blood 2008).

MODULATION OF ATOPIC DERMATITIS BY EFFECTIVE LONG-TERM TREATMENT

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Long-term maintenance treatment with topical corticosteroids or topical calcineurin inhibitors (TCIs) has shown better effectiveness compared to standard flare treatment. The study duration with topical corticosteroids has not exceeded 6 months, whereas with TCIs controlled studies for up to one year are available. In long-term studies with topical tacrolimus ointment, we have seen good disease control for up to 10 years with effects on itching, partial reversal of skin atrophy, and the reduction in the need to use tacrolimus ointment and emollients. Biomarkers of Th2 polarity are predictive of staphylococcal colonization of the skin. Effective treatment resulted in elimination of staphylococci, improvement of nasal and respiratory symptoms, a significant decrease in total immunoglobulin E (IgE) levels and a shift in the inflammation towards Th1 polarity. No long-term adverse events have been recorded. Patient adherence to treatment was found to be an important factor for a modulation of atopic dermatitis towards health.

MICRORNAs ARE ASSOCIATED WITH THE PATHOGENESIS OF VITILIGO

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Introduction. miRNAs are associated with many diseases (e.g. psoriasis) but they have not been studied in relation to vitiligo so far. The aim of this study was to evaluate the potential role of inflammation-related miRNAs in the pathogenesis of vitiligo.

Patients And Methods. We determined the relative expression of miRNAs connected to immunomodulation (miR-10a, miR-99b, miR-125a, miR-125b, miR-146a, miR-511) and melanogenesis (miR-145) in the lesional and non-lesional skin of vitiligo and psoriasis patients and in the skin of healthy volunteers using quantitative real-time polymerase chain reaction.

Results. The expression of miR-125b was increased and the expression of miR-145 was decreased in the lesional skin from vitiligo patients when compared with the skin from healthy individuals ($p < 0,05$ and $p < 0,05$, respectively). The expres-

sion of miR-99b was elevated both in the lesional ($p<0,001$) and non-lesional ($p<0,01$) skin from vitiligo patients. Both, in the lesional and non-lesional skin from psoriasis patients, the expression of miR-99b ($p<0,01$ and $p<0,01$, respectively), miR-125b ($p<0,05$ and $p<0,05$, respectively) and miR-511 ($p<0,001$ and $p<0,01$, respectively) were increased when compared with the control skin. miR-146a, previously associated with psoriasis, was highly expressed in the lesional psoriatic skin of our study as well ($p<0,001$).

Conclusion. The results of the study show that miRNAs may be involved in the vitiligo-associated changes in the skin. Increased expression of miRNAs related to inflammation (miR-99b, miR-125b) in both vitiligo and psoriatic skin indicate that certain inflammatory processes are similar in the pathogenesis of these diseases. Decreased expression of miR-145 in vitiligo skin when compared with other groups, indicates that miR-145 might have a role in the destruction of melanocytes. The increased level of miR-146a and miR-511 only in the psoriatic skin implies the possibility that these miRNA-s are specific for psoriasis.

CONTACT DERMATITIS TO HAIR DYE INGREDIENTS

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Background: p-Phenylenediamine (PPD) is the primary patch test screening agent for hair dye contact allergy, while 100 different hair dye chemicals are allowed.

Objectives: To examine if PPD is an optimal screening agent for diagnosing hair dye allergy or if other clinically important sensitizers exist.

Patients/methods: 2939 consecutive patients in 12 dermatology clinics were patch tested with 5 hair dyes available from patch test suppliers. Further, 22 frequently used hair dye ingredients not available from patch test suppliers were tested in subgroups of about 500 patients each.

Results: A positive reaction to PPD was found in 4.5% of patients, 2.8% reacted to toluene-2,5-diamine (PTD), 1.8% to p-aminophenol, 1% to m-aminophenol, 0.1% to resorcinol; all together 5.3% ($n=156$). Dying hair was the most frequently reported cause of the allergy (55.4 %); so-called 'temporary henna' tattoos were the cause in 8.5% of the cases. p-Methyl-

aminophenol, gave reaction in 20 patients (2.2%), 3 of them with clinical relevance and no co-reaction to the above 5 well known hair dyes.

Conclusion: Hair dyes are the prime cause of PPD allergy. PPD identifies the majority of positive reactions to PTD, p-aminophenol and m-aminophenol, but not all, which justifies additional test with hair dye ingredients from the used product.

OPTICAL COHERENCE TOMOGRAPHY IMAGING OF NON-MELANOMA SKIN CANCER UNDERGOING PHOTODYNAMIC THERAPY REVEALS SUBCLINICAL RESIDUAL LESIONS

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Introduction. We investigated optical coherence tomography (OCT) morphology in in-vivo non-melanoma skin cancer (NMSC) during the photodynamic therapy (PDT) treatment process and studied the use of OCT in evaluating the treatment response.

Methods. OCT is a non-invasive imaging technology based on infrared light interferometry. It provides real-time, 5–8 micrometer resolution images of skin to a depth of around 2 mm. A total of 18 biopsy-proven basal cell carcinoma (BCC) lesions and actinic keratoses (AK) were monitored by OCT during two sessions of PDT treatment. At 3-months follow-up the patients were assessed both by OCT and clinically.

Results. The diagnostic OCT features of BCC and AK have previously been studied. All investigated lesions were identified by OCT and displayed at least one OCT characteristic before PDT treatment. At 3 months follow-up, recurrence was suspected clinically in 5/18 cases, with OCT in 7/18 cases. OCT correctly identified all of the residual lesions also found by the clinical examinations. In both cases where recurrence was only found in OCT, this was subsequently confirmed by histology.

Conclusion. At 3-months follow-up OCT identified 29% more recurrences than clinical examination alone. Early detection of residual tumor tissue after PDT allows for earlier re-treatment. It is suggested that OCT can detect subclinical residual NMSC and AK after PDT treatment and the use of OCT as a supplement to clinical follow-up examination could potentially influence patient management after PDT treatment.

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