Annual Meeting 2014 of the Swedish Society of Dermatology and Venereology

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The Annual Meeting of the Swedish Society of Dermatology och Venereology (SSDV) was held in Göteborg 13–16 May, 2014. Below are summaries of some of the lectures as well as some photos from the meeting. This annual meeting was well attended by 216 participants and sponsors altogether.

Introduction

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Dermato-Venereology is currently undergoing big changes, partly by rapid increases in common diseases like skin cancer, and partly by new treatment possibilities. One of the items covered during the conference was contact allergy. Recent research data has focused on oxidation products as contact allergens. They seem to be responsible for much of what we earlier thought was non-allergic responses in the skin. A special session dealt with contact allergy during the meeting. The meeting was inaugurated by the President, Professor Jan Faergemann and the Director of the Sahlgrenska University Hospital, Barbro Fridén.

A major part of our daily practice deals with skin cancer. Several sessions dealt with this item from new diagnostic tools to discussions regarding new therapies and their place in clinical practice. Giuseppe Argenziano, Reggio Emilia, informed us with an update on dermoscopy (see below). Thomas Rustemeyer, Amsterdam, informed us about the latest in skin immunology and systemic contact allergy (see below).

Venereology is another important part of our discipline. A symposium dealt with HPV and vaccines. Gonorrhoea is exhibiting new resistance problems and a special section discussed this important problem.

Phototherapy of skin diseases has been used for many years for psoriasis, atopic dermatitis and other conditions. New approaches were discussed during the meeting resulting in consensus how to handle patients. One symposium reported on new PhD theses in dermato-venereology. We are happy for the ones writing a PhD thesis but believe that more dermatologists should have this education.

Tropical dermatology is becoming more important due to travelling and immigration. One section was devoted to atopic dermatitis. The incidence of this chronic disease has risen rapidly in recent years. Filaggrin, microbiology and the role of vitamin D were discussed. Vitamin D was also discussed concerning its role in melanoma. Registry studies are easily carried out in Sweden. A special section dealt with the ethical aspects of this, as new EU roles will probably come.

At the end of the meeting there was a traditional What's new symposium where news regarding the whole area of dermato-venereology was presented.

Professor Jan Faergemann, President for the SSDV's Annual Meeting opened the meeting and informed about the interesting lectures to come.

Update on Dermoscopy

Giuseppe Argenziano, PhD, Associate Professor
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Most melanomas are easy to be diagnosed clinically and dermoscopically. The question remains open concerning the correct strategies to detect those melanomas that look morphologically inconspicuous from a clinical and/or dermoscopic point of view. In our estimation, when morphology is not enough to recognize melanoma, one has to use specific management strategies. Herein we summarize the following 7 simple and practical rules that outline the need for a more general approach integrating clinical information with dermoscopic examination: 1) Look basically at all lesions; 2) Undress high-risk patients; 3) Use the 10 second rule in single lesions; 4) Compare and monitor multiple moles; 5) Excise doubtful nodular lesions; 6) Combine clinical and dermoscopic criteria; and 7) Combine clinical and histopathologic criteria.

Some questions were raised after the interesting lecture by Giuseppe Argenziano.

Immunology of Contact Allergy – An Update

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Contact allergy has been one of the classical examples of acquired T-cell-mediated immunity since the discovery of lymphocyte-mediated reactions. Hence, crucial steps in the immunological cascade of contact allergy have been unraveled since then. Research focusing on physico-chemical properties of contact allergies has discovered specific properties of contact allergens. These little molecules share binding capacities with (endogeneous) peptides which are required to become fully immune-competent. Along with this line of research, allergen-driven activation of distinct types of antigen-presenting cells in epidermal and dermal tissues has been investigated. Recently, the generation of unspecific "danger-signals" by the irritant capacities of contact allergens has dawn special attention. In 2011, it has been discovered that contact allergens can bind to and activate Toll-like-receptors (TLRs) and, thereby, activate the pro-inflammatory cascade that is mediated by inflammasomes. This activation of innate immune reactions contributes to the allergenic properties of contact allergens and the activation capacities for T cells. Whereas in mice CD8+ T cells are the principal effector cell types, they seem to be less

Thomas Rustemeyer together with the moderator for the present session Lina Hagvall.

important in man. Here, allergen specific T cells are mainly CD4+ cells. Recent studies have described further subtypes with distinct homing properties (cells expressing CLA, CCR10 receptors) and secretion patterns of inflammatory or regulatory mediators. Among them are Th1, Th2, Th17 and Th22. Based on these findings different clinical pictures of contact allergy can now be better understood. Contact allergic reactions can show very different clinical pictures. Not only the classical eczematous reactions, but also non-classical presentations as lichenoid and granulomatous reactions have been diagnosed as contact allergic. Future research will provide new insights in immunoregulation of inflammatory cascades and development of tolerogenic reactions. This might contribute to improved prevention and therapy strategies of contact allergy.

Tropical Dermatology

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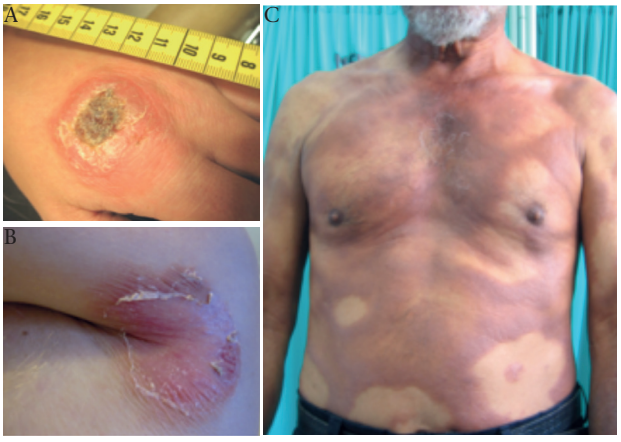
Skin diseases are a significant problem all over the world. Dematologists are consulted more and more often for imported dermatological diseases because of the increasing travel to and from tropical countries. Dermatologic problems are the third most common cause of morbidity in returning travellers. The increasing global refugee situation is also emphazising the importance of a clinical knowledge in the care for patients from other parts of the world.



A) Cutaneous leishmaniasis. B) Blister beetle dermatitis. C) Borderline tuberculoid leprosy. *(Photo: L Dotevall)*

Skin diseases may be caused by a large variety of reasons; insect bites, local or disseminated infections, tumours or be signs of other systemic diseases or syndromes. The lecture on tropical dermatology at SSVD had the aim to give an overview of the typical dermatological symptoms and epidemiology for some common and uncommon tropical skin conditions.

Filaggrin – a multifunctional protein

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Mutations in the filaggrin gene (*FLG*) are common in patients with atopic dermatitis (AD) but also very common in the general population. In Northern Europe 10% of the population have *FLG*-mutations regardless of having AD or not. Why is that? Has it been an evolutionary advantage of having a *FLG*-mutation, leading to a mild skin barrier defect?

The *FLG* gene is encoding the filaggrin protein and the degrading factors are aminoacids including histidine. They act as a "natural moisturing factor" and lowers skin pH. This is of importance when it comes to developing AD. *Another* degrading product from filaggrin is that trans-urocanic acid (UCA) reduce UVB uptake in the skin and act as a "sunscreen". Having *FLG*-mutations leads to less production of trans-UCA and therefore an increased UVB uptake. It has been shown that individuals with *FLG*-mutations have 10% higher 25-hydroxy vitamin D concentrations in serum (1). This might be an explanation for an evolutionary natural selection of individuals with *FLG*-mutations among people migrating to Northern Europe where UVB has been needed for preventing richitis. It is not only mutations within the filaggrin gene that increase the risk of developing AD. *FLG* also demonstrates intragenic copy number variations, which alleles are encoding 10, 11 or 12 filaggrin monomers that affect the amount of filaggrin protein in the epidermis. Brown et al. (2) have shown that, regardless of *FLG*-mutations, having short alleles are an independent risk factor for developing AD.

References

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2. Brown SJ, Kroboth K, Sandilands A, et al. Intragenic copy number variation within filaggrin contributes to the risk of atopic dermatitis with a dose-dependent effect. J Invest Dermatol 2012; 132: 98–104.

Atopic Dermatitis, Microorganisms and Vitamin D

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Atopic dermatitis (AD) is a chronic, pruritic, relapsing inflammatory skin disease predisposing to bacterial and viral infections (e.g. *Staphylococcus aureus* and Herpes simplex virus) due to a complex interplay of epidermal barrier dysfunction and dysregulated immune response. Vitamin D is a pluripotent steroid hormone. In addition to its role in calcium homeostasis and bone metabolism, vitamin D has an immunomodulatory effect and a potential antimicrobial activity.

Recently there have been several reports that vitamin D plays a role in the pathogenesis of many diseases including AD though the results from the studies regarding the potential association of AD and vitamin D have been controversial.

The aim of this presentation was to elucidate the possible mechanisms by which vitamin D can positively affect different parts of the immune system, thus contributing to the reduction of the susceptibility in colonization and infection by different microorganisms in AD individuals and subsequently leading to an amelioration of the severity and symptoms of AD.

One of these mechanisms is vitamin D-induced production of antimicrobial peptides (AMPs) These peptides are important for the skin's innate antimicrobial defence. It is shown that in AD skin there is both reduced expression and production of AMPs. A well studied AMP in the skin is cathelicidin (LL-37). In infected or injured tissue, activation of Toll-like receptor 2 (TLR2) results in expression of enzyme CYP27B, causing conversion of 25-hydroxyvitamin D to the active 1,25 dihydroxyvitamin D and subsequent induction of cathelicidin. Vitamin D supplementation could induce increase in cathelicidin expression in AD skin.

A Th2 shift in immune response in AD patients benefits antigen presenting cells, overreaction against microorganisms and even more immunoglobulin E (IgE) sensitization to microbial antigens which may cause a more severe disease. The modulating effect that vitamin D has in the balance between Th1/Th2 cytokine response leading to reduced IgE production by B-lymphocytes is another possible mechanism.

Mohs surgery in Sweden

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Mohs micrographic surgery (MMS) is the treatment of choice for recurrent and aggressive basal cell carcinomas (i.e. morphoeic, infiltrative, micronodular and basosquamous histopathological subtypes) located around the eyes, nose, lips and ears. The technique allows for complete examination of all tissue margins intraoperatively ensuring a minimized risk of recurrence and avoiding unnecessary removal of healthy tissue in areas where large margins can compromise both the functional and cosmetic outcome.

At Sahlgrenska University Hospital in Gothenburg, Sweden we have over 30 years of experience with MMS and have shown that the 5-year recurrence rates are as low as 3.3% for the above-mentioned indications. In comparison, excisions of primary and recurrent morphoeic basal cell carcinomas with a 5-mm margin render incomplete removal in approximately 20% and 40% of the cases, respectively.

Despite these enormous differences, MMS is underused in most parts of Sweden and the rest of Scandinavia since the technique is currently only available in Gothenburg, Lund and Stockholm in Sweden; in Oslo, Norway and in Copenhagen, Denmark. In total, only 350 patients are treated with MMS in Scandinavia every year when approximately 6 times as many patients would clearly benefit from it.

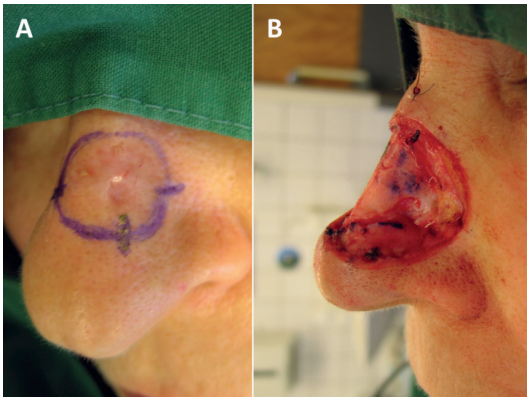

Fig. 1. A) Presurgical clinical demarcation of an aggressive basal cell carcinoma on the dorsum of the nose. B) The surgical defect after 4 stages of Mohs micrographic surgery with complete clearance of the tumour.

Ethical Aspects of Register-based Research

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This presentation aimed at updating the audience on laws and regulations with focus on research ethics in register-based research. Relevant parts from the Ethical Review Act, the Personal Data Act and the Public Access to Information and Secrecy Act were reviewed.

One central issue in register-based research is how to handle the demand for informed consent when sensitive personal data are used. If personal data from a large number of persons are handled, the research is in the interest of society and the risk of violating the integrity of persons is low, the Regional Ethical Review Board can accept that research is conducted without informed consent.

A prerequisite for informed consent is that the research person is well informed about the scope of the research. The Swedish LifeGene Project was stopped because the objectives of the project were too unclear and so the informed consent was judged invalid. To enable the project to proceed, a new act with lower demands on specified objectives was issued. This act is valid until Dec 31, 2015. Meanwhile, new regulations for register-based research are investigated and a new proposal is expected by June 30, 2014.

Photodynamic Therapy – An Update

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The incidence of skin cancer is increasing rapidly in Sweden. Some recent developments will be discussed below.

Daylight photodynamic therapy (PDT) has been introduced in Denmark recently. The cause for this development is the, sometimes severe, pain connected with the treatment. As the power density of light activating protoporphyrin IX generated from deltaaaminolevulinic acid (ALA) is less than in common treatment lamps, patients experience less pain than with conventional treatment. Long-term results seem promising. However, as the therapy involves staying outdoors during several hours, it is not possible to use during a substantial part of the year. Using ordinary indoor equipment with possibilities to regulate power density will possibly be equally efficient.

Ablative fractional laser resurfacing has been introduced by Dr Merete Haedersdal in Copenhagen. A laser is used to drill small "holes" in the skin, whereby ALA can penetrate more easily. This leads to a better penetration of ALA or its methylester making it possible to treat thicker lesions. Today, PDT is limited by the poor penetration of ALA.

Organ transplant patients run a 100-fold increase in the risk of contracting skin cancer. PDT has been shown to be an effective way of dealing with this.

Malignant Melanoma and Vitamin D

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Vitamin D produced in the skin after exposure to UVB (290-315 nm) is a potent molecule important for cell growth, cell proliferation, cell differentiation and cell apoptosis. Vitamin D acts through vitamin D receptors (VDRs), which are expressed in almost all cell types including cancer cells. VDRs are expressed in keratinocytes, melanocytes and melanoma cells indicating the potential role of vitamin D in pathogenesis and progression of skin cancer. Vitamin D can reduce and prevent keratinocytic carcinoma via inhibition of the hedgehog signaling pathway and upregulation of nucleotide excision repair enzymes.

The incidence of cutaneous malignant melanoma (MM) is constantly increasing, which might be due to frequent intermittent and excessive sun exposure. UVB, but also UVA, have carcinogenic effects on skin cells through different mechanisms involving direct and indirect DNA damages (cyclobutane pyrimidine dimers, 6-4 photoproducts and reactive oxygen spaces), which activates oncogenes, inactivates tumour suppressor genes and induces skin carcinogenesis. Modern life style implies increasing exposure to UVA which might be more dangerous than UVB exposure. Moreover UVA can destroy

The group of Photodermatology: *From left*: Amra Osmancevic, Desiree Wiegleb-Edström, Meirav Holmdahl, Birgitta Stymne and Lena Hagströmmer.

already produced vitamin D and UVA ant-mutagenic responses are not as effective as those induced by UVB (thickening of the skin and induction of p53 and p16). Although sun-related hypothesis cannot be directly connected to extra-cutaneous types of MM, the potential role of vitamin D insufficiency due to strict sun avoiding behaviour has been discussed. Some epidemiological studies show that higher levels of vitamin D are correlated with reduced melanoma risk and improved survival.

Considering current knowledge on biological effects of the sun on vitamin D synthesis, skin carcinogenesis, cell damage repair mechanisms and health in general, short and sensible sun exposure between 11–12 a.m. might be most beneficial.

What's New?

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Here are some reflections on recently published papers:

– A French national study collecting all cases of inflammatory bowel disease concludes that isotretinoin use for severe acne is not associated with an increased risk for ulcerative colitis but there is a lower risk for Crohn's disease.

– An Italian study found that supervised diet and regular exercise for 5 months in a group of patients with moderate–severe psoriasis and BMI > 25 resulted in a significant reduction of PASI and weight compared to control subjects – we are not surprised but I think we should do better to encourage our patients to follow this example!

– The new Il-17 blocking monoclonals seem to achieve PASI 75 in more than 75–80% and PASI 90 in more than half of the patients after 12 weeks – will we go for PASI 90 in the near future?

– An oral (small molecule) Janus-kinase inhibitor is approved in the US for severe therapy-resistant rheumatoid arthritis and is now in phase-3 clinical studies for psoriasis with a clinical efficacy after 12 weeks similar to etanercept 50 mg twice weekly.

– At last, a monoclonal against IL-4 and IL-13, dupilumab, has been produced and examined in patients with moderate–severe adult atopic dermatitis and insufficient response to standard topical therapies. EASI, SCORAD and pruritus scores were significantly lower than in placebo-treated patients.

– Some patients with generalized pustular psoriasis have a mutation in the gene for IL-36 receptor antagonist resulting in more of the proinflammatory IL-1 cytokine family. Treatment with an IL-1 receptor antagonist, e.g. anakinra, has proven effective.

– An anti-IgE monoclonal, omalizumab, produces fast and effective relief of symptoms in significantly more patients with chronic spontaneous urticaria resistant to 4-fold increase of standard doses of non-sedating antihistamines than non-treated control subjects.

Annual General Meeting of SSDV

Agneta Andersson, SSDV Registry

In the midst of all this highly scientific information, SSDV also held its Annual General Meeting.

Education: Oliver Seifert (responsible for Education within SSDV) reported on the development of the various educational topics that have been on the agenda during the year.

Change of meeting name: A suggestion has been raised to change the name of the present meeting in the future. Everybody was in favour of this change and it was decided that the name of the meeting should be SSDV's Spring Meeting instead of SSDV's Annual Meeting (to avoid mix-up with the Annual General Meeting). New bylaws were therefore discussed to reflect this change and were thereafter unanimously accepted by the audience.

A new website: A new website (www.ssdv.se) has been created during the year and a lot of new features have been implemented. Christian Steczkó-Nilsson (responsible for the website in collaboration with Agneta Andersson) briefly informed about the already existing news, but also about some forthcoming details. It is the hope that this website should be a common meeting place for the SSDV members.

New members: Since last meeting (May 2013), 31 new membership applications have been received and these new members were heartily welcomed. The Board of SSDV expressed that they were very happy for the inflow of new members.

Thank you: The present President (Tore Särnhult) now terminates his 2-year period as the leader of SSDV and at the end of the meeting he handed over the gavel to John Paoli for the next 2 years.

A protocol with full information about this meeting is available at the website www.ssdv.se (under Document; after log-in by members only).

Agneta Andersson, who had worked with parts of the arrangements of this meeting, together with one of the participants, Ylva Enström.

Part of the Board of SSDV (2013– 2014). L*eft photo*: Oscar Zaar (Resident's Representative), Kari Nielsen (Treasurer), Virginia Zazo (General Secretary), John Paoli (Vice President) and Tore Särnhult (President). *Right photo*: Oliver Seifert (Recidency Programme Coordinator), Christian Steczko-Nilsson (Congress Secretary/Website Coordinator), Peter Gisslén (Private Practice Representative), Per-Anders Mjörnberg (Venereology Representative).