

Progress in Dermatology Symposium, Uppsala, Sweden: An Overview

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Acta Dermato-Venereologica arranged an international symposium entitled Progress in Dermatology, in Uppsala, Sweden on 3 October 2008 in connection with the Uppsala University Hospital's 300 year anniversary.

Some of the members of the Advisory Board of *Acta Dermato-Venereologica* were invited speakers at this symposium. A short extract of their lectures is provided below:

Tilo Biederman, Tübingen, Germany: *The Impact of Innate Immunity in Atopic Dermatitis*

Tilo Biederman presented an update on how innate immunity and atopic dermatitis are linked. Innate immunity is the important front-line of the immune system and normally acts more rapidly than adaptive immunity. Importantly, recently discovered filaggrin mutation in atopic dermatitis patients, which leads to altered barrier function of the skin, facilitates microbial colonization or infection. Moreover, barrier dysfunction predisposes individuals to develop Th2 immune responses that inhibit innate immune functions, further reducing anti-microbial defence mechanisms. Consequently, the early defect in innate immunity causes chronic stimulation of both innate and adaptive immunity, leading to persistent skin inflammation. Thus, modulating the innate immune system in atopic dermatitis patients can help to treat atopic dermatitis or even stabilize atopic skin and prevent inflammation. This could be done by stimulating the innate immune system with non-pathogenic bacteria that are tolerated by the skin. In fact, this approach is under investigation, and studies using cream containing the non-pathogenic bacteria *Vitreoscilla filiformis* are underway. The mainstay of therapy for atopic dermatitis

should thus be stabilization of the skin barrier and immune homeostasis.

Gil Yosipovitch, Salem, USA: *Itch? More than Scratching the Surface*

Knowledge of the specific itch-transmitting nerve fibres and their activation is increasing. Sensory nerve fibres extend to the epidermis, even as high as to the stratum granulosum. Damage to the nerve fibres in the epidermis and dermal epidermal junction is one possible explanation for chronic pruritus. The itch signal is transmitted to the central nervous system by two types of C nerve fibres: histamine-sensitive and non-histamine-sensitive. In addition, keratinocytes function as itch receptors, since keratinocytes have many receptors for various neuromediators involved in itch, such as nerve growth factors, opioids and substance P. Itch has a powerful effect on attention; it cannot be ignored. In a recent large survey of atopic eczema patients, scratch was reported as highly pleasurable and correlated with itch intensity. However, it has not always been recognized that itch and pain occur simultaneously. In this survey 59% of those with atopic eczema reported their itch to be associated with pain. In treatment, reduction of itch intensity is a prime goal, and this should be done by inhibiting itch transmission both peripherally and centrally. The effects of itching and scratching on the central nervous system can be visualized using positron emission tomography and functional magnetic



Fig. 1. Tilo Biedermann, Tübingen, Germany.



Fig. 2. Gil Yosipovitch, Salem, USA.



Fig. 3. Irene Leigh, Dundee, UK.



Fig. 4. Jouni Uitto, Philadelphia, USA.

resonance imaging. Drugs that reduce central sensitization of chronic itch in the brain include anti-depressants from the serotonin and norepinephrine reuptake inhibitor (SNRI) group, such as mirtazapine, and neuroleptics such as gabapentin and pregabalin. Combination therapy includes mirtazapine and gabapentin. New compounds that may be effective for treatment of itching are becoming available. For example, opioid kappa agonists are being developed. Butorphanol is an analgesic inhaler that is used for acute pain. It has kappa opioid agonist and mu antagonistic effects and is used for severe cases of chronic itch.

Irene Leigh, Dundee, UK: *Skin Cancer and Human Papilloma Viruses*

Ninety percent of non-melanoma skin cancers contain human papilloma viruses (HPVs). Immunosuppressed patients are susceptible to extensive wart infection. Initially the warts are classical, but become atypical, especially in sun-exposed areas. The number of keratotic skin lesions is strongly associated with cancer risk and other risk factors. Eventually, in renal transplant patients the squamous cell carcinoma (SCC) risk is increased 100-fold, and cancers occur 15 years earlier than expected. Carcinomas develop quickly, and often resemble keratoacanthomas. Clinically the lesions may not appear to be as aggressive as by microscopy, but the prognosis of metastatic carcinoma is poor. Based on multiplex polymerase chain reaction studies, it can be concluded that, in renal transplant patients, 75% of SCCs are HPV-DNA positive, with mixed HPV genotypes, while in immune-competent patients only 32% of SCCs are HPV-positive. Thus, the role of HPV in immunosuppressed patients is even more pronounced than in immunocompetent persons.

Jouni Uitto, Philadelphia, USA: *Progress in Heritable Skin Diseases*

Research on heritable bullous skin diseases has come a long way; from cloning of genes, finding mutations and developing

diagnostics, to the present hottest topic, gene therapy. The gene therapy methods being studied include several alternative approaches: gene replacement/gene repair, in vivo/ex vivo, cell therapy/protein therapy. Current work in the Uitto laboratory includes protein therapy for junctional epidermolysis bullosa and cell therapy in the form of bone marrow transplantation. The diagnostics have also become more sensitive to enable pre-implantation diagnosis and prenatal diagnosis from foetal cells or free foetal DNA as early as 5 weeks of gestation.

Jonathan Rees, Edinburgh, UK: *Dermatology's 21st Century Problem: How to Attach Semantics to Images*

The central problem of diagnosis in dermatology is how to attach semantics to images. Text searching is easy, but how do we index images and make matches automatically. Human visual processing is complex, but some results from the field of computer vision suggest that diagnosis of lesions may be managed automatically in the near future. Jonathan Rees described attempts to utilize three-dimensional image-capture systems and early work leading up to the development of a content-based image retrieval system (CBIR).



Fig. 5. Jonathan Rees, Edinburgh, UK.