3rd Scandinavian Conference on Epidermolysis Bullosa for Healthcare Professionals, Helsinki, 24–25 April 2008

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Sirkku Peltonen from the Department of Dermatology at the University of Turku, attended the 3rd Scandinavian Conference on Epidermolysis Bullosa in Helsinki, Finland. She here gives a summary of the meeting.

The 3rd Scandinavian Conference on Epidermolysis Bullosa (EB) for Healthcare Professionals was organized by the EB patient organization DEBRA Finland and Finnish Central Organisation for Skin Patients (Iholiitto ry), with the help of the Genodermatosis Section of the Finnish Dermatological Society (SILY) (Fig. 1). The meeting was held in the Marina Congress Center in the heart of Helsinki. On the first day there were approximately 80 participants, both doctors and lay group representatives from the Nordic countries, and on the second day approximately 50 Finnish dermatologists joined the congress in order to update their knowledge on the newest scientific and clinical progress of blistering skin diseases.

Fig. 1. The Organizing Committee of the 3rd Scandinavian Conference on Epidermolysis Bullosa for Healthcare Professionals. From left: Sirkku Peltonen, Hannele Heikkilä, Ulpu Saarialho-Kere, Marja-Leena Tuomi, Outi Ritvola, Kaisa Tasanen and Risto Heikkinen. In addition, Mikko Blomqvist from DEBRA Finland and Heikki Vaisto from Finnish Central Organisation for Skin Patients participated in the organization of the meeting. (Photography: Mervi Viteli-Hietanen from the Finnish Central Organisation for Skin Patients).

First, the audience learned how the nomenclature of EB has changed. Different types of EB have traditionally been named after the doctors who described the features of the disease, such as Köbner, Herlitz and Hallopeau. A consensus meeting was held in Vienna in 2007, at which EB was renamed, based on the level of blistering, inheritance and severity. *Docent Kaisa Tasanen* from Oulu, Finland, introduced the audience to the new names, which are published in, Fine et al., J Am Acad Dermatol 2008; 58: 931–950. The diagnosis of EB should be based on immunofluorescence mapping. Because of many candidate genes, mutational analysis should not be considered as a first-line diagnostic test for EB. Electron microscopy is likely to play a decreasing role in the future, especially as there are only a few recommended reference laboratories worldwide.

Professor Jouni Uitto (Fig. 2) from Thomas Jefferson University, Philadelphia, USA, reviewed the work done on EB in his laboratory over the past 20 years. During this time, there has been enormous progress in understanding of the molecular background of blistering skin diseases. Ten different genes are known to cause EB (this excludes Kindler syndrome). A total of 783 distinct mutations have been found in genes causing EB in Uitto's department in Thomas Jefferson University. The exact molecular diagnosis has profound consequences for the prognosis of the disease and for genetic counselling. Pre-natal diagnosis has provided the correct genotype/phenotype prediction in 185 cases, which is 100% of cases. The next challenge after diagnostics is treatment. Luckily, animal models recapitulate features of EB and can be used for clinical testing of various approaches. Questions such as gene replacement versus repair of the defective gene, *ex vivo* versus *in vivo* approach, and the selection of the gene delivery system (viral versus physical/chemical) have to be answered using animal models before testing the methods in humans. Most recently, emphasis seems to be shifting to cell- and protein-based systems. The cell-based systems utilize the capacity of bone marrow stem cells to differentiate into several somatic lineages. The challenge in this approach is to identify cell types producing collagen VII, and then to correct the collagen VII gene in stem cells.

Professor Leena Bruckner-Tuderman from Freiburg, Germany (Fig. 2) summarized the approaches of her laboratory towards understanding the pathogenic process of mitten deformity seen in dystrophic EB. Collagen VII knockout mice have been

Fig. 2. Jouni Uitto from Philadelphia, USA, and Leena Bruckner-Tuderman from Freiburg, Germany, in discussion with doctor Sirpa Asko-Seljavaara (middle), who is a plastic surgeon and a member of the Finnish Parliament. She was invited to give the official opening and welcoming speech to the congress participants. (Photography: Mervi Viteli-Hietanen from the Finnish Central Organisation for Skin Patients).

a valuable model in understanding the development of mitten deformity, which is an active transforming growth factor (TGF)-beta mediated fibrotic process. There are also increased numbers of myofibroblasts, which mediate contractile fibrosis. Even as little as 10% of the normal collagen VII level in the skin confers a better prognosis than knockout. Injection of normal fibroblasts into dermis increased the amount of type VII collagen. Apparently the cross-talk between fibroblasts and keratinocytes is needed in production of anchoring fibrils, and restoring the basement membrane.

Leena Bruckner-Tuderman also updated our knowledge on Kindler syndrome. The main clinical features include skin fragility and photosensitivity. In early childhood patients seem to have EB. Later in life they develop pigment anomalies, poikiloderma, gingival fragility, fibrosis and early wrinkling of the skin. Their risk of skin cancer is also elevated. The epidermis shows a variable level of cleavage leading to blistering. Kindler syndrome is caused by a loss of function mutation in a new actin cytoskeleton linking protein kindlin-1. The mutation leads to reduced lysyl oxidase activity and abnormal Wnt signalling. The phosphorylated kindlin-1 protein is in the junction of integrin and epidermal growth factor receptor pathway. These have an impact on dermal homeostasis and affect keratinocyte adhesion, migration, polarization and proliferation.

Professor Anders Vahlquist from Uppsala gave a talk entitled: Diagnostics and care of EB in Sweden. He related some interesting epidemiological observations. Junctional EB is much more common in Sweden and Norway than in Finland or Denmark. This is based on a founder mutation in Lam B3 (p.R635X), which occurs in northern Sweden. To reach a diagnosis a rapid genetic test to detect this mutation is performed in all children born with a clinical picture of junctional EB. Recessive forms of EB are increasing in number in Sweden. This is probably due to immigration from the Middle-East. Among the immigrants, consanguineous marriage is common. Thus, half of the children with recessive EB nowadays have a foreign background, and the demand for prenatal diagnosis and carrier analysis is increasing.

In EB simplex increased foot blistering due to sweating is a problem. There is a promising clinical trial to reduce sweat-induced foot blistering associated with EB simplex using botulinum toxin treatment.

Medical geneticist Sirpa Kivirikko from Helsinki summarized the epidemiology of EB in Finland. In contrast to Sweden, the incidence if recessive dystrophic EB is very low. The Finnish Central Organisation for Skin Patients estimates that there are about 200 patients with EB in Finland. Approximately two children with severe EB are born each year.

The Great Ormond Street Hospital in London, UK, has a long expertise in treating EB patients. The audience of the meeting, both doctors and patients, were given a lot of basic data, new information and practical tips on very important issues such as dressings and nutrition. If one needs an expert opinion on dressings for various EB blisters, *Jackie Denyer* is the person to consult. She is closely following product development of dressings and related articles. For example, silver garments without seams can be worn as undergarments, pyjamas and socks to prevent blistering by clothing. *Leslie Haynes* and *Neil Shah* have years of experience on the nutrition and gastroenterological problems faced by EB patients.

The spectrum of hereditary bullous diseases other than EB was introduced by *Professor John McGrath* from London, UK. These include, for example, Naegeli-Franchetti-Jadassohn ectodermal dysplasia, which is caused by keratin-14 mutations. The clinical picture includes nail onycholysis, plantar keratoderma and the patients have no fingerprints. Desmosomes are important for cell adhesion, keratinocyte maturation and the heart. This becomes evident from the clinical features of desmosomal genodermatoses, which show blistering, palmoplantar keratodermas and cardiomypathies. In addition, nail deformities and sparse, woolly hair are characteristics of diseases caused by mutations in genes for desmosomal components.

Classification of ichthyoses may be in transition from clinical image-based towards molecular defect-oriented approach. *Christina Has* from Freiburg, Germany, introduced the novel data on the molecular background known on ichthyoses at

present. At least one outcome of the mutation analyses is that very different clinical features may be caused by mutations in the same gene. On the other hand, mutations in different genes, especially those of peroxidated lipid pathway can cause similar phenotypes, based on the function of the proteins.

When the next referral for EB arrives, a useful website to look at might be: www.netzwerk-eb.de. And for more up-to date information on ichthyoses look at the NIRK (the Network for Ichthyoses and Related Keratinization Disorders) website: www.netzwerk-ichthyose.de

The lectures were excellent and enjoyable. In addition, meeting EB patients outside of the doctor's office, listening to their experience of doctors, healthcare and life in general was very enlightening (Fig. 3). Joint meetings of doctors and patient organizations might also be very useful in several other disease groups. Representatives of DEBRA and Iholiitto are thanked for organizing of the meeting in a very professional and pleasant manner.

Fig. 3. Panel discussion was held on the topic: Focus on everyday life with EB. The panel: Jesper Bønning, Liina Härkönen, Ruth Bernssen Bø and Jussi Lindevall exposed the audience to several touching experience, opinions and questions, which inspired the delegates to participate in discussion. (Photography: Mervi Viteli-Hietanen from the Finnish Central Organisation for Skin Patients).

Paediatric Dermatology Meeting in Gothenburg, Sweden, 25–26 April, 2008

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This meeting was organized by SSDV Foundation for International Dermato-Venereology. Gunnar Nyman is the treasurer in Foundation for International Dermato-Venereology and one of 20 participants at the meeting.

A symposium was held in Gothenburg on 25–26 April 2008 for 20 dermatologists with an interest in paediatric dermatology (2 participants from each of Estonia, Latvia, Lithuania, Ukraine and 12 from Sweden). The purpose of the meeting was to learn more about paediatric dermatology, but above all to initiate and/or enhance contacts and, it is hoped, future co-operation in this field among our countries. The number of participants was intentionally small enough to allow everyone to get to know each other. The meeting was held at Ågrenska Foundation, south of Gothenburg. This former children's hospital is now a centre for teaching and supporting children with rare diseases and their families, located in a beautiful setting beside the sea.

After an introduction to the Ågrenska Foundation, one colleague from each country presented their situation in our speciality, with the focus on paediatric dermatology, its possibilities and problems. After lectures covering vascular malformations, neonatal lupus erythematosus (LE), Gianotti-Crosti syndrome, Henoch-Scönlein purpura, bullous impetigo and staphylococcal scalded skin syndrome (SSSS) there were case presentations by our guests.

There was also ample time for informal discussions, both during the breaks, at the welcome dinner the day before, and the next day during a visit to the outpatient clinic at Östra Hospital, where *Dr Ann Broberg*, who was responsible for