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The Georg Rajka Symposia, which focus on all aspects of atopic dermatitis (AD), have previously been held in Norway, Denmark, Germany, France, USA, and Japan. In January 2012 the 7th Georg Rajka International Symposium was held in Tanzania, emphasizing that AD is a truly global skin problem. The setting for the symposium, at the Regional Dermatology Training Centre (RDTC) in Moshi, Tanzania, could not be surpassed. Moshi is located close to the cradle of the origin of mankind approximately 2–3 million years ago. Participants experienced wonderful views of Mount Kilimanjaro (Fig. 1), the beautiful African landscape and its vegetation, including coffee plantations, the vivid life in Moshi city, the friendliness of the Tanzanians, and had the opportunity to go on safaris, including observing the migration of up to 2 million wildebeests and zebras on the Serengeti Plain, where lions can be seen following their "food supply".

How was it possible to concentrate on AD in this delightful setting? Well, 101 participants did, including young students and doctors from several African countries, Europe, South Korea, and USA. There was a good mixture of participants, from the "masters of AD" to students who just wanted to learn more about AD. Georg Rajka was not able to participate in person, but he conveyed his greetings and good wishes for a successful meeting, and thanked the organizers for their substantial effort. He was particularly pleased that the meeting was being held in Africa, highlighting that AD is a global skin health problem.

RDTC has its own almost 20-year history. Henning Grossmann and Constantin Orfanos have been encouraged to publish how a brilliant idea, to promote skin health, can be realized. Much discussion took place, some of it heated, but the results are certainly impressive: 216 community dermatologists from 15 African countries, specialists in skin health, have completed a 2-year training course in dermato-venereology including leprosy and returned to their home countries to continue their work. It has been a long and difficult journey to get to this point, but today even young medical doctors can be trained in dermato-venereology at RDTC. Thus, RDTC is an important part of the medical educational system, not only in Tanzania, but in a significant part of East and Central Africa.

Fig. 1. Mount Kilimanjaro viewed from the congress in Moshi.

Fig. 2. Doctor Peter Schmid-Grendelmeier wearing a polo shirt designed for the meeting.

In order to run RDTC funding is badly needed. At the beginning it was very difficult to access sufficient funds. The expense of training a student for a 2-year period is now approximately 7,000 USD per year. Al Kopf, Terrence Ryan, Roderick Hay and others have put a great deal of energy into the issue of funding. Henning Grossmann, John Masenga, young dermatologists, and the local staff have put much energy into development of the centre. A significant change was put into effect at the World Congress of Dermatology (WCD) in Paris in 2002, when our French colleagues gave one-third of the surplus back to the International League of Dermatological Societies. This has now become a rule: 50% of the surplus of a WCD must go to improve global skin health, including venereology. At the meeting in Moshi, Professor Kyu Han Kim (Fig. 3) a member of the organizing committee of the 22nd WCD in Seoul in May

2011 was warmly applauded by the participants when he informed the meeting that the Korean Dermatology Association will contribute approximately 1.5 million USD. We hereby extend our congratulations and thanks to the KDA for their very significant support for global skin health.

John Masenga, Moshi, Tanzania, director of the RDTC, related the history of RDTC since its opening in 1997 and informed us that, in addition to 216 educated community dermato-venereologists, there are now 11 specialists from 5 African countries trained in a 4-year training programme, and a further 13 residents currently enrolled to become dermato-venereologists.

Roderick Hay, London, UK, president of the International Foundation of Dermatology (IDF; www.ilds.org), gave a short introduction highlighting that skin symptoms are among the top 5 diseases in primary practise and that 53% of skin diseases are skin infections/infestations.

Claire Filler, UK, described podoconiosis, which is a severe lymphoedema of the foot and lower leg seen in persons who walk bare-foot on red soil. The soil, stemming from volcanic ash, contains tiny particles of silica that enter through small fissures in the skin, leading to blockage of the lymph drainage system. There seems to be a genetic predisposition for the disease. Cleaning of the skin, compression and wearing shoes could alleviate many symptoms. The best help and advice for patients is given by persons who themselves have had podoconiosis. More information can be found at: www.messyfoot.uk.com.

Fig. 3. Professor Kyu Han Kim (*left*), a member of the organizing committee of the 22st World Congress of Dermatology (WCD), May 2011, Seoul, and Dr Henning Grossmann (*right*).

Alain Taiëb, Bordeaux, France, reported that approximately 25% of AD patients reach adulthood with their disease (>18 years), a fact also shown by Herd et al. (Br J Dermatol 1996; 135: 18). Thus, quite a significant number continues to have AD into adulthood. He mentioned the filaggrin studies (Irvine A et al, NEJM 2011; 315: 365) and their influence on disease expression. The hyperlinearity and dryness of the skin on the palms is known as a "hand-shake-sign", i.e. one can diagnose a filaggrin mutation from a handshake.

Gail Todd, Cape Town, South Africa, and *Arjan Hogewoming*, Kigali, Rwanda, discussed the epidemiology of AD in Africa. Some studies 15–20 years ago observed that there was no AD among nearly 1,000 school-children, but AD now appears to be an increasing problem. A study of 5–8-year-old school-children in different countries revealed prevalences of AD among school-children in Gabon, Ghana and Rwanda of 2.5–4.5%, 1.2–1.8% and 0.7–0.9%, respectively. Twenty-five percent of the children had tinea capitis. The children were examined by 2 Dutch dermatologists. In Tanzania AD has been observed among 5.2% of children, and in Nigeria among up to 23% of children. At RDTC approximately one-third of skin diseases are AD. *Gail Todd* reported that the most important risk factor for AD was a family history of the disease, as in Europe, and that food allergy was slightly associated with AD, but that parasites in the stools were not, as was confirmed by other studies. Worms can protect against type I allergy, but for eczema the results vary. In HIV patients the prevalence of eczema is low. Likewise, malaria appears to confer a protective effect for atopic eczema. In one of the coffee-break discussions *John Masenga* mentioned that atopic eczema seems not to be present in albino subjects, but no proper study of this has been conducted. Finally, *Gail Todd* noted that, in African patients, the extensor sides of the extremities are more commonly affected than the flexural sides.

Alain Irvine, Dublin, Ireland, gave a brilliant overview of filaggrin and the strong association of loss-of-function mutations with both AD (30–50% in heterozygous and approximately 90% in homozygous persons) and ichthyosis vulgaris. Eczema, asthma and eczema herpeticum are clinically more severe and persistent in people who have filaggrin (FLG) mutations. It has been shown among 6,971 children of up to 11 years of age that eczema is more persistent among those with FLG mutations (Henderson J et al., JACI 2008; 121: 872), and the copy number of the gene influences disease severity. Brown et al. (JACI 2011; 127: 661) have observed that FLG mutations are associated with a 5.4 × increase in peanut allergy. Another observation is that the presence of an FLG mutation and a cat in the house increases the risk of eczema, as do FLG mutations and older siblings (Cramer C et al., JACI 2010: 125: 1254). *Alain Irvine* does not think that further FLG mutations will be discovered.

Bilcha Kasshundra, Ethiopia, presented data on 107 Ethiopian patients with AD (children and young adults) and observed that there were no FLG mutations, except for a new mutation not previously reported (Winge et al., Br J Dermatol 2011; 165: 1074). Although a minor study, it illustrates that genes and AD are a complex area, again underlined by a recent study (Paternoster L, et al., Nature Genetics, 2011, e-pub) that 3 loci on the epidermal differentiation complex and cytokine gene cluster are strongly associated with AD.

Regina Fölster-Holst, Kiel, Germany, talked about the deficient skin barrier in AD patients and described a new non-invasive technique, whereby the lipid structures of the outer layer of the epithelium could be shown (www.lipbarvis.com). Studies in infants and children are pending. FLG mutations are clearly associated with increased transepidermal water loss (TEWL) as measured using Raman spectroscopy. Th2 cytokines will diminish FLG expression in epithelial tissue.

Carsten Flohr, London, UK, studied a large cohort of Vietnamese children. Intestinal worms reduce type I allergies to environmental allergens by 30%. Treatment of the worms led to an increase in type I allergies. These results have been confirmed in studies from Brazil. *Carsten Flohr* mentioned research by Mpairwe et al. (Pediatr Allergy Immunol 2011; 22: 303), who showed that pregnant women treated with praziquantel had children, who, at 1 year of age, had a 2.5× increase in eczema, and those treated with albendazole had children with a 1.8× increase in eczema at 1 year, thus indicating that worm infestation during intrauterine growth may reduce eczema expression. However, one cannot exclude that the drugs may themselves alter eczema expression. A Danish Trichuris study on hay fever showed no protective effect.

Thomas Werfel, Hannover, Germany, stated that one-third of patients with AD had type I allergy towards *Staphylococcus aureus* and fibronectin-binding proteins. The alpha-toxins of *S. aureus* induce IL17, IL22 and IL31 in keratinocytes (Niebuhr et al. JACI 2010; 126: 1176). His group have observed that 10–15% of patients with AD have a mutation in the TLR2 receptor, leading to reduced innate immunity. Reductions in beta-defensin have been observed in acute lesions (patch tests), whereas the chronic phase of eczema has a more normal beta-defensin level. Recently, they have observed type I allergy towards alpha-NAC, a protein occurring in normal skin, indicating that allergy is linked to autoimmunity.

Amy Paller, Chicago, USA, confirmed the high prevalence of *S. aureus* on AD skin. In San Diego multiple-resistant *S. aureus* (MRSA) bacteria now occur in 14% of patients (Matiz et al., Pediatr Derm 2011; 28: 6), whereas in Toronto they observed only 1% MRSA on AD skin. Fifty-three percent of the steroids used by the patients are found to be contaminated with bacteria. Patients should therefore keep their emollients, steroids and topical calcineurin inhibitors in the refrigerator and not touch the creams with their fingers, but use disposable applicators. Vitamin D augments antimicrobial peptides in the epidermis (Li, JID 2009; 129: 498). Studies have shown that a twice weekly bath in hypochlorite water diminishes eczema activity (Huang, Pediatrics 2009; 123: 808).

Andreas Wollenberg, Munich, Germany, discussed hyper IgE syndrome (Job's syndrome), in which mutations have been observed in *STAT3* and *DOCX8* genes. Patients with *Candida albicans* nail infections are likely to have STAT3 mutations.

Roger Launer, Davos, Switzerland, described the PASTURE study, which found that mothers with a child having eczema living on farms had a 23.3% history of "atopy", compared with 34.6% among mothers who do not live on farms. However, the author did not record whether the age of the mothers on farms at the birth of their first child was the same as for non-farm mothers. Overall, AD was not significantly different between farm-children and non-farm children. For those children whose mothers were actively working on a farm, and who were exposed to more animals, less early-life eczema was present, although not among children with late-onset AD.

Martin Glatz, Zürich, Switzerland, observed that type I allergy towards *Malassezia furfur* increased with the age of the AD patient.

Joanne Chalmers, Nottingham, UK, presented an excellent Cochrane Review confirming breastfeeding and its protective effect towards eczema development, including studies on hydrolysed milk, and omega 3/6 fatty acids. There were no publications confirming cow's milk avoidance as a protective measure against atopic eczema.

Mübeccel Akdis, Davos, Switzerland, discussed the importance of histamine receptor 2. Histamine and AD has been a focus of intense studies for decades, but the fact that antihistamine drugs are not clinically helpful in AD brings their importance into question. However, this author is convinced that perhaps 10–20% of patients with AD urticarial reactions participate in the clinical picture, especially via type I allergy, hence it is advisable to try antihistamines in severe cases, at least for a period of time. *Mübeccel Akdis* mentioned that in HR2 –/– mice, Th1 and Th2 activity is increased.

Cezmi Akdis, Davos, Switzerland, introduced the "keep away, wash away, suppress" concept on "allergic barriers" (eczema and asthma). He reported that, among approximately 200,000 genes, 2,000 are upregulated in atopic skin. Interferon-gamma upregulates 9 genes in keratinocytes. The skin inflammation leads to

apoptosis in keratinocytes, leading to histological spongiosis in the epidermis, and 99% of the inflammation is of antigen non-specific T cells. Tight junctions between keratinocytes can be opened by IL35 secreting T cells so cells can pass into the epidermis. However, other studies have shown that the epidermis contains 1:20 to 1:50 times less T cells than the dermis.

Melanie Miyanii DeSouza, Nairobi, Kenya, gave an excellent lecture on the health service in Kenya, where the 35 million inhabitants are served by approximately 6,000 medical doctors, and where 1 dermatologist serves approximately 1.5 million people. In contrast there are approximately 200,000 traditional healers, who supply 80% of health services. The size of the country and its infrastructure, with difficulties such as flooding of roads, is not advantageous for accessing health services. Pharmacists play a part in provision of healthcare, and often sell medication based on their beliefs.

Peter Elsner, Jena, Germany, gave a detailed presentation on a clinically significant topic: textiles and AD. Fabric softeners used for cotton do not induce increased skin irritation. The addition of silver to the fibres reduces the numbers of *S. aureus* on the skin, and, in patients with mild eczema, slightly improves eczema (Gauger 2006). However, this textile (SeaCell) is quite expensive.

Sibylle Schliemann, Jena, Germany, discussed sensitive skin syndrome (subjective, sensitivity to cosmetics, ultraviolet light, heat, cold, wind, but with no visible signs) being more common in women than men and more common among patients with AD, rosacea and persons with previous dermatoses. The application of 5% lactic acid to the nasolabial fold can distinguish a "stinger" from a "non-stinger". It is speculated that neurogenic inflammation via C-fibres plays a part, as increased cortical cerebral activity is observed in persons with sensitive skin. No clinical manifestations are associated with sensitive skin syndrome.

Ulf Darsow, Munich, Germany, discussed itch and variations, such as tickling and burning, also involved in itch. He mentioned www.itchforum.net as a website for further information on itch, together with several articles (Weishaar E et al., Acta Derm Venereol 2011, Oct, e-pub). The visual analogue scale (VAS) carries a high variability and does not quite parallel with SCORAD (Scoring Atopic Dermatitis), being scored significantly higher when analysing AD patients. Buddenkotte et al. (Allergy 2010; 65: 805) have discussed the many mediators of itch, where IL31, especially, seems to be a major player. Brain-derived neural factor (BDNF) and substance P are also associated. IL31 serum levels correlate with SCORAD (Raap U et al. JACI 2008; 122: 421). It seems that atopic itch is worse than urticarial itch.

Elopy Sibanda, Harare, Zimbabwe, discussed allergy and HIV. Persons with type I allergies in Zimbabwe have house dust mite as the most common allergy (more than 52%), followed by allergy to *Cynodon dactylon* (38%). The house dust mite allergens in Zimbabwe are Derp2 and p7, especially, and not Derp1 as in Europe. He mentioned 87 HIV+ patients, where allergic symptoms were present in 67. Twenty-four percent had allergic rhinitis, 18% had asthma, 15% had eczema and 16% had urticaria. Allergies observed were towards Der pI, peanut and *Cladosporium*. Eczema may be present if the CD4+ count is above 350/µl, otherwise eczema is not observed in CD4+ lymphopenic patients.

Kim Thomas, Nottingham, UK, presented the SWET study, which revealed some interesting results. "Hard water" is associated (statistically) with an increased prevalence of atopic eczema. The content of calcium in hard water is above 200 mg $CaCO_3$ per litre of water. They selected 310 children aged 6 months to 16 years with a SASSAD (six area, six sign atopic dermatitis) above 10, installed a "soft water machine", in which sodium chloride is exchanged with calcium in order to bring the calcium concentration below 20 mg/l. Saliva was sampled, and one-third of the children had an FLG mutation. A control group of children was included and SASSAD scoring was performed. There was no clinical improvement with the soft-water intervention when looking at SASSAD. However, when following the POEM score (Patient Oriented Eczema Measuring), eczema improved significantly ($p<0.001$) as did "well-controlled weeks" ($p<0.04$) and eczema family impact ($p<0.05$). There was no interference in the therapy given, i.e. the parents/children were allowed to follow their own therapy and no instructions were given by the dermatologists involved. It must also be explained that, during the 12-week intervention period, SASSAD was only reduced on average from 25 to 20, meaning that the eczema was not well-controlled. Thus, any "intervention" improves eczema as observed in other studies, but the study clearly shows that treatment strategies were not optimal. Better instruction in topical therapy is thus of utmost importance, rather than water softening.

The psychological problems among parents and patients were discussed by several presenters. A detailed description of the options for psychological interventions was given by *Uwe Gieler*, Giessen, Germany. He acknowledged that there were difficulties in inviting parents for psychodermatological guidance. However, in Germany there are approximately 250 centres with 2,000 trainees in psychological interventions (Weishaar et al., Acta Derm-Venereol 2008; 88: 234, the GADIS study). Stress in Nc/NgA mice leads to an increase in nerve growth factor, substance P and TEWL. In humans BDNF and keratinocyte growth factor + receptor N1 are increased. More information is available from www.psychodermatology.com.

Phyllis Spuls, Amsterdam, The Netherlands, examined the outcome parameters used in the many studies on treatment efficacy in AD. They observed 56 different outcome measures, but found SCORAD, POEMS and EASI (Eczema Area and Severity Index) to be the "standards". Jochen Schmitt et al. (JID 2011; 131: 623) have published a paper on this subject. Further information is available from: www.homeforeczema.org.

Help for patients in Switzerland is impressive, as a major organization has been established (www.aha.ch). *Katrin Brunner*, Zürich, Switzerland, a marketing director, presented the organization, which has an annual budget of approximately 2 million CHF with 18 employees. This should be held against the fact that 10% of the population have eczema, 10% asthma and 15% allergic rhinitis; thus a significant proportion of the Swiss population is affected by "allergy". She also alluded to new scoring systems, whereby patients can submit daily/weekly subjective scoring via their iPhones (or similar android devices) to computer systems, which then analyse the results. This is an option for future clinical trials.

Alain Taïëb, Bordeaux, France, reviewed new treatment options in AD, but concluded that there were no biologicals with a convincing beneficial effect. MAFT mice in sterile conditions could develop hyper IgE, which was linked to increases in IL6, IL17 and IL23. However, impaired IL17 has been observed in an autosomal dominant form of hyper IgE syndrome (Milner et al. Nature 2008; 452: 773) involving STAT3 mutations. Thymic stromal lymphopoietin knock-out mouse cannot establish skin inflammation. He commented briefly on systemic therapy of AD with methotrexate and azathioprine. Cyclosporin A (CsA) is the most efficacious drug, but he reported that it carries more side-effects.

Mandy Schramm, Amsterdam, The Netherlands, presented a study on 20 patients treated with 10–22.5 mg methotrexate per week for 12 weeks, compared with 22 patients treated with azathioprine at a starting dosage of 1.5 mg/kg/day increased to 2.5 mg/kg/day. Methotrexate led to a 39% reduction in SCORAD, but 4 of 20 patients had to receive prednisone rescue and discontinue methotrexate. Azathioprine led to a 42% reduction in SCORAD and 2/22 needed prednisone rescue. There was some difficulty in understanding, for the 12-week follow-up period, which group showed a slight clinical improvement, patients without treatment or those on topical therapy.

Helen Nankervis, Nottingham, UK, described whether randomized controlled trial studies on AD followed the rules, e.g. were they registered before the first patient was included. Only 5 of 109 studies fulfilled all criteria, to the major annoyance of Hywel C. Williams, who will participate in the next International Atopic Dermatitis Symposium 2014 in Nottingham (www.nottingham.ac.uk/dermatology).

Kristian Thestrup-Pedersen, Aarhus, Denmark, considered the contours of AD, given the many pieces of its puzzle that are presently available. He pointed to epidemiological studies indicating that, even before disease expression, some aspects concerning the eczematous child are different (increased gestational age, increased birth weight, less eczema in infants later developing type I diabetes mellitus), and also observations made when eczema is present (increased thymic index, a doubling of lymphocytes in the peripheral immune system, significant fluctuations in CD8+ T blood lymphocytes TREC levels and possible indications of immature T lymphocytes among skin-homing T cells when looked at in IL2- and IL4-driven T cell lines from skin biopsies. There are results showing IgE allergy to normal proteins in human skin and observations of increased ANA in patients with atopic eczema. This links allergy with auto-immunity and we should not neglect to speculate whether AD is a cell-mediated autoimmune disease early in life, in which immature T cells home to ectodermal tissue (skin) and in which the inflammation is not initially antigen-driven by external allergens, but rather by an internal correction of an unbalanced immune system. This, in many ways, leads to augmentation of IgE and thus an ability to establish type I allergies to own or environmental allergens. He considers ectodermal tissue to carry the genetic defect (FLG and other gene defects), creating a background for skin inflammation to be present. There appear to be no observations that contradict such a hypothesis.

Henning Grossmann, Moshi, Tanzania, (Fig. 4), described the system of traditional healthcare providers (THCP) and the African clinical picture of eczema. He considered 6 subgroups: the folliculocentric picture (keratosis pilaris), nummular eczema, lichen planus-like, extensor patterns, post-inflammatory hypopigmentations (pityriasis alba) and generalized xerosis.

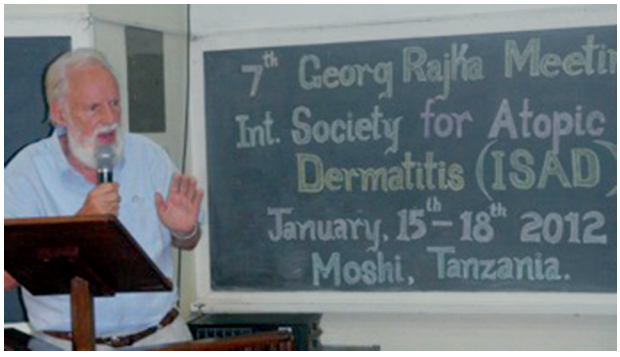

Fig. 4. Dr Henning Grossmann presenting his lecture.

It is very difficult to see erythema and white dermographism in dark skin.

Among THCP there are 4 groups: herbalists, herbalists with a ritual, ritualists with herbals, and spiritualists. Skin diseases are among the most common conditions, and there is a great lack of medical doctors; THCP are present in rural areas at a ratio of 1:100 population, and, in urban areas, at 1:400 population. Approximately 20% of THCP are herbalists. THCP are accepted and highly respected by the local population. From the medical point of view the fact that they recommend emollients is beneficial. Western-style medicine in Africa is not affordable and not sustainable; the costs of treatment for HIV, tuberculosis (TB) and malaria are simply too high. He recommended that the medical community work with a positive attitude with THCP.

Peter Schmid-Grendelmeier, Zürich, Switzerland, touched upon the DoiT learning dermatology website (www.swisdom.org), which is very elaborate and helpful for studying dermatology in detail. He also mentioned the EASIdig, a system whereby non-dermatologists can learn to evaluate AD activity (Tremp et al., Dermatology 2011; 223: 68).

John Masenga, RDTC, Moshi, Tanzania, presented a session of clinical pictures of dermatology at RDTC. This was enormously impressive, with clinical pictures one rarely sees elsewhere, although it also demonstrated how improvements in dermatological care are badly needed among African patients.

Finally, *Johannes Ring*, Munic, Germany, suggested forming not only the International Symposium for Atopic Dermatitis, but the International Society for Atopic Dermatitis. He thanked the organizers and participants for a wonderful meeting.

Left: Two women with albinism at the Regional Dermatology Training Centre (RDTC) meeting. *Middle:* Handicraft made by patients with albinism. *Right:* Two new wards, donated by the Barbara A. Stiefel Foundation, for inpatients with dermatological diseases, which include a burns unit.