Atopic Dermatitis – A Disease to "Hit Early and Hit Hard"

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Louise Lönndahl participated in the 32nd Nordic Congress of Dermato-Venereology. Read her summary below of one of the sessions.

During this year's Nordic Congress of Dermato-Venereology several interesting symposia on various subjects were held in Tampere, Finland. The subject closest to my own research area was the symposium about atopic dermatitis (AD). *Dr Sakari Reitamo*, from Finland, that so kindly hosted the congress this year, started off by pointing at the importance of effectively treating the disease early after onset. He and his collegues had been able to show that treating the eczema in early childhood affects the further development of atopic manifestations later in life. Also, maintenance treatment, in this case a topical steroid twice a week, was shown to dramatically decrease flare-ups. This could probably be due to the lower provocation from the external environment through a more intact skin barrier. Another good choice for local treatment is tacrolimus, which has been shown to be a relatively safe treatment. The speaker finished his talk by using a citation from an earlier published study "Hit early and hit hard". This I think we, as clinicians, should bare in mind when we meet young patients with AD.

The next speaker, *Dr Sol-Britt Lonne-Rahm*, Stockholm, gave us a presentation of the psychological aspects of AD. She emphasised that this group of patients and their families have a reduced quality of life and that we have a high responsibility in helping these patients also in this matter. The patients may also have higher anxiety levels and in many patients there is a pattern of worsening during stress. Dr Lonne-Rahm suggested psychotherapy as a useful tool in treatment of AD.

The session then went deeper into the pathogenesis of the disease and first in line was *Dr Maria Bradley*, Stockholm, who presented how the skin barrier and *filaggrin* gene is thought to play a role in the development of AD. Filaggrin is a shortening of "filament-associated protein" which is found in the epidermis, were it has functions involved in water retention. There are over 40 different mutations in this gene and they are common in the population. In Asian and European populations the mutations are associated with development of AD. Also healthy people have mutations, 7.5% compared to 21% in patients with AD. It has been discussed why the mutations are so common, and in line with the evolutionary theory there is probably some kind of evolutionary benefit. One could speculate that a higher penetrance of antigen through the skin could result in some low-dose vaccine for certain pathogens. Also, it has been shown that patients with mutations in the *filaggrin* gene had a 10% higher level of vitamin D in serum.

The level of epidermal filaggrin could vary depending on mutations but also upon how many repetitions there are on one allele and the expression may also be up- or down- regulated. So independent of the reason to why we have low levels of filaggrin, Dr Bradley believes that in the future there might be a possibility to treat AD with filaggrin replacement. Also one could speculate whether filaggrin may somehow be used as natural sunscreen and protect from skin cancer. Thus, Dr Bradley also underscored at AD as a complex disease and that the skin barrier defect only is part of the whole picture.

Following this interesting presentation, *Dr Enikö Sonkoly*, Stockholm, continued with a cutting-edge presentation about the novel treatments of AD and micro-RNA (miRNA) as potential targets for the future. Micro-RNAs are short, non-coding RNAs that regulate expression of other genes. Dr Sonkoly has shown that when screening AD patients one could see that several miRNAs are differently expressed in these patients. For example, miR-155 is overexpressed in AD. This miR-155 is required for adaptive immuneresponses, both T-cell and B-cell responses. Trigger factors seem to increase miR-155. One of the target genes is now known, being CTLA-4, which signals T-cell proliferation. Dr Sonkoly suggested that miRNAs will be targets for novel therapies in the future and that some are already tested in animal models with good result. One of the difficulties in finding new miRNAs for the future is to figure out their target genes. Most of the new biological drugs, directed to IL-4, IL-5, TNF-α, IgE and CD20 do not seem to have the effect one could have hoped for. Probably IL-17 is a potential target as well. The interesting thing with miRNAs is that they have not only one but many target proteins, probably related in function. This makes one believe that treatment focused on miRNAs is a more logical and effective way to go.

The session was then terminated by *Dr Ville Kiiski*, Helsinki, presenting his results of treating blepharoconjunctivitis in

patients with AD. Blepharoconjunctivitis is the most common ocular complication of AD. There is a need for long-term treatment. Earlier, topical steroids were commonly used and this was combined with side effects such as intraocular pressure elevation, skin atrophy, etc. Therefore, Dr Kiiski and his group have evaluated the safety and efficacy of treatment with pimecrolimus and tacrolimus in long-term use. There was in this study no reports of malignancies, no raised intraocular pressure. There were, however, some cases of herpes simplex virus (HSV) outbreaks, most of them at the beginning of treatment. The results showed a higher effect and better compliance in the group receiving tacrolimus. Also, one should consider HSV prophylaxis to patients with previous HSV episode.

In summary, the session covered both clinical and preclinical research and treatment from the very start of AD in childhood to the very latest biological treatments for patients with long-term and severe symptoms. We are all aware of the complexity of this skin disease and we see the need for more research and novel treatments in the future.