PC01

False beliefs about food allergies in Asian children with atopic eczema

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Common food or inhalant allergens are considered complex causative factors that can affect the clinical course of atopic eczema (AE). Especially in Asian cultures, many people tend to consider food an important aggravating cause of AE, especially meats such as pork and chicken.

To assess the associations between the results of MAST-CLA and actual clinical aspects caused by specific allergens that patients thought worsen AE conditions, we retrospectively reviewed medical records.

A total of nine-hundred and seventy-three patients with AE under twenty years old, who were evaluated by MAST-CLA between March 2004 and February 2012 at the AE Clinic of Seoul National University Hospital, were reviewed through the electronic medical record system. All the patients or their parents had answered questions about which food or inhalant allergens worsened clinical symptoms of AE or caused cutaneous manifestations of allergic hypersensitivity.

Comparing the results of MAST-CLA to subjective causative allergens, the most common symptom-inducing allergens were wheat, milk, pork, chicken, and beef. Interestingly, specific IgE levels associated with pork and chicken were actually low at 7.6% and 1.1%, respectively as a result of MAST-CLA testing. In addition, among the patients whose subjective clinical course of AE was aggravated related to pork, only 12.3% (n=31) of patients showed positive MAST results (more than class level 2 was defined as ‘positive’) to pork-specific IgE, whereas no significant clinical relevance was found in most of them (87.7%, n=221). This tendency was also observed in the results for chicken-specific IgE. Only 2.7% of patients who thought chicken was a significant aggravating factor of AE revealed a positive result in the chicken-specific IgE test, whereas 97.3% showed a negative result for the MAST-CLA test.

In Asian culture, with the influence of oriental herbal medicine, many people believe that certain kinds of ‘red meat’, particularly ‘pork’ or ‘chicken’, can cause allergic reactions. Clinicians and patients should consider that commonly believed food allergens, especially pork and chicken, actually do not trigger symptomatic aggravation of AE. Moreover, in Asian cultures, patient education to correct false beliefs about food allergies is needed.

References
1. Shin JW, Jin SP, Lee JH, Cho S. Analysis of MAST-CLA Results as a Diagnostic Tool in Allergic Skin Diseases. Annals of dermatology 2010; 22(1): 35-40.
2. Ramesh S. Food allergy overview in children. Clinical reviews in allergy & immunology 2008; 34(2): 217-30.

PC02

Molecular Analysis of Malassezia Microflora on the Skin of the Patients with Atopic Dermatitis

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The yeasts of the genus Malassezia are members of the normal flora on human skin and they are found in 75~80% of healthy adults. Since its association with various skin disorders have been known, there have been a growing number of reports that have implicated Malassezia yeast in atopic dermatitis. The aim of the present study is to isolate the various Malassezia species from atopic dermatitis patients by using 26S rDNA (ribosomal Deoxyribonucleic acid) PCR-RFLP and to investigate the relationship between a positive Malassezia culture and the severity of atopic dermatitis.

Cultures for Malassezia yeasts were taken from the scalp, cheek, chest, arm and thigh of 60 patients with atopic dermatitis. We used a rapid and accurate molecular biological method 26S rDNA PCR-RFLP, and this method can overcome the limits of the morphological and biochemical methods.

Positive Malassezia growth was noted on 51.7% of the patients with atopic dermatitis by 26S rDNA PCR-RFLP analysis. The overall dominant species was M. sympodialis (16.3%). M. restricta was the most common species on the scalp (30.0%) and cheek (16.7%). M. sympodialis (28.3%) was the most common species on the chest. The positive culture rate was the highest for the 11~20 age group (59.0%) and the scalp showed the highest rate at 66.7%. There was no significant relationship between the Malassezia species and SCORing for Atopic Dermatitis (SCORAD).

The fact that the cultured species was different for the atopic dermatitis lesion skin from that of the normal skin may be due to the disrupted skin barrier function and sensitization of the organism induced by scratching in the atopic dermatitis lesion-skin. But there was no relationship between the Malassezia type and the severity score. The severity score is thought to depend not on the type, but also on the quantity of the yeast.

References

Aspres N, Anderson C. Malassezia yeasts in the pathogenesis of atopic dermatitis. Australas J Dermatol 2004;45:199-207.

PC03 - Withdrawn

PC04

Quantitative assessment of sweat in atopic dermatitis: a pilot study

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Sweat is known to regulate skin homeostasis via thermoregulation, protection against infection, and humidity retention. On the one hand, sweat is also considered as a major aggravating factor of atopic dermatitis. Then, how should we manage sweating in patients with atopic dermatitis? To resolve the different interpretations of sweat, we should evaluate the differences in quality of sweat between atopic dermatitis and healthy subjects.

Sweat derived from atopic dermatitis and healthy subjects was assessed in protein-concentration and pH-measurement. Study subjects were chosen from inpatient with atopic dermatitis and healthy applicants. Sweat was corrected by method previously established by Yokozeki, et al.

Sweat-volume was small in atopic dermatitis subjects. Protein-concentration in all sweat derived from subjects with atopic dermatitis was increased compared to that with healthy subjects. PH-measurement results in sweat of atopic dermatitis was comparable to that of healthy subjects.

We found that the higher protein concentration of sweat might be an one of the characteristic of atopic dermatitis. PH of sweat had a little association with symptom of atopic dermatitis. Relation of concentrated sweat on pathogenesis of atopic dermatitis should be evaluated in a future.

PC05

Effect of Di(2-ethylhexyl) Phthalate on skin health of Seoul citizen having environmental disease

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Phthalate is plastic softner and important environmental endocrine hormone. Atopic dermatitis has many environmental issue in this pathogemsis. Our previous epidemiological study revealed that Potential nonmonotonous association between di(2-ethylhexyl) phthalate (DEHP) exposure and atopic dermatitis in Korean children. We want to study the direct effect of diethylhexylphtalate(DEHP), the diethylbutylphtalate (DBP), the diisonylphtalate (DINP) on keratinocyte to figure out the relationship with atopic dermatitis.

We treated the phthalates on keratinocyte in various concentration (0-100uM) and time (6-48hr) to see the expression of the TSLP (Thymic stromal lymphopoietin) which has been considered as the most important cytokines in AD and the antimicrobial peptide. We also check the effect of phthalates on skin barrier function using acute animal barrier recovery model .

The increased expression of TSLP on 24hr after the treatment of DBP 1uM as 2.8 times DHEP100uM as 2.8 times and DINP 0.1uM as 1.7 times was examined in our study. The phthalates also affected on the decreased expression of AMPs(human beta defensin 3 and cathelicidin . We can also see the negative effect on the skin barrier recovery function after acute skin barrier disruption on hairless mouse by the phthalates.

We postulated the possibility of the negative effect of phthalate on the pathogesis atopic dermatitis. The environmental cause can be the direct issue to atopic dermatitis

References

1. Andrade AJ, Grande SW, Talsness CE, Grote K, Chahoud I. A dose-response study following in utero and lactational exposure to di-(2-ethylhexyl)-phthalate (DEHP): nonmonotonic dose-response and low dose effects on rat brain aromatase activity. Toxicology 2006;227(3):185–92.

2. Soumelis V, *et al*. Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP. Nat Immunol 2002;3:673–-680.

PC06

Reduced stratum corneum lipid chain length relates to an impaired skin barrier function in atopic dermatitis patients

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An important feature of atopic dermatitis (AD) is a decreased skin barrier function. This barrier function is primarily located in the stratum corneum (SC) comprised of corneocytes and lipids (ceramides, free fatty acids (FFAs), and cholesterol). The composition and organization of these lipids are crucial for a proper skin barrier function, but the importance of the chain length distribution of the ceramides and FFAs for the impaired skin barrier in AD is not known. Therefore, the aim of this study is to elucidate the lipid chain length distribution in non-lesional and lesional skin of AD patients and relate this with the skin barrier function.

We performed a clinical study in which the SC lipids and their importance for the skin barrier function was examined in AD patients and compared with control subjects. The lipid composition was examined with mass spectrometry. In particular the carbon chain length of the ceramides and FFAs was investigated in relation to the density of the SC lipid organization (examined by infrared spectroscopy) and the transepidermal water loss (TEWL), a marker for the permeability barrier.

A reduction was observed in the FFA and ceramide chain lengths for both non-lesional and lesional SC of AD patients compared to control skin. In lesional skin the reduction in chain length was more pronounced than in non-lesional skin1. This reduction in lipid chain length correlated excellent with a less dense lipid organization and a reduced skin barrier function. Besides, we examined the effect of mutations in the filaggrin gene on the lipids properties, a major predisposition factor for development of AD2. However, no association was observed between lipid properties and filaggrin mutations.

The current study provides insights into the role of the SC lipid chain length and shows that the lipids play a role in the impaired skin barrier of AD patients. These results may provide opportunities for studies on skin barrier repair by topical treatments and shows evidence that normalisation of the lipid synthesis may enhance normalisation of the skin barrier function.

References

1. van Smeden J, Janssens M, Bouwstra JA *et al*. Exp Dermatol. 2014: 23:45-52.

2. Palmer C N, Irvine A D, Terron-Kwiatkowski A *et al*. Nat Genet 2006: 38: 441–446.

PC07

Eczema ≠ eczema: The transcriptional heterogeneity of eczema

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It is an unresolved riddle why within the heterogeneous group of eczemas some entities are self-limited while others are chronic and relapse. In this pilot study, we compared the molecular signature of allergic contact dermatitis (ACD) to nickel (n=10), nummular or dishydrotic eczema (nAE, n=8), and atopic eczema (AE, n=6) by performing whole genome expression analysis of lesional as compared to autologous non-involved skin. We found the transcriptional variability in the ACD group to be smaller compared to the one in chronic eczemas (nAE and AE), which was reflected by the fact that 172 genes were exclusively regulated in ACD but not in chronic eczemas, and only 28 genes were exclusively regulated in chronic eczemas. 33 genes were regulated in common, among them many epithelial antimicrobial peptides. Interestingly, a mutual antagonistic picture was observed regarding genes of the epidermal differentiation: while genes of the LCE3 family were strongly up-regulated in nAE and AE, they were unchanged in ACD as compared to autologous non-involved skin. Inversely, LCE1 and LCE2 genes were down-regulated exclusively in ACD. Regarding the immune system, a similar pattern was observed in all eczema forms, with a general trend of stronger regulation in ACD. Notably, ACD reactions to nickel were accompanied by activation of the inflammasome, extracellular matrix and cell-cell adhesion molecules/cytotoxicity. In summary, the epithelial signature seems to discriminate self-limited from chronic eczema forms. Based on this study, further investigations with larger cohorts seem promising.

PC08

Contact sensitization in patients with and without atopic dermatitis

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Both atopic dermatitis and contact sensitization are common conditions, however, a definite understanding of the relationship between contact sensitization and atopic dermatitis has not been reached.

In this descriptive study we investigated the differences between positive patch tests in patients with and without atopic dermatitis in a patch test cohort and explored the influence of disease severity.

Patch test results, atopic dermatitis diagnosis, and demographic variables were taken from a database, including all patients patched tested at Bispebjerg and Roskilde Hospitals from January 2009 to January 2013. Severe atopic dermatitis was defined as systemic therapy or hospitalization due to atopic dermatitis.

The study included 2,221 patients; 293 patients with atopic dermatitis and 1,928 without. 41.0% of patients with and 46.2% of patients without atopic dermatitis had at least one positive patch test (p=0.092). More patients with severe atopic dermatitis had multiple positive patch test reactions compared with non-severe atopic dermatitis patients (19.4% vs. 10.0%, p=0.046).

Overall, we found similar frequencies of positive patch tests in patients with and without atopic dermatitis. A higher frequency of multiple sensitizations was, however, found in patients with severe atopic dermatitis.

PC09

Chronic actinic dermatitis in a ethnically diverse UK referral population: a 5 year retrospective study

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Chronic actinic dermatitis (CAD) is a photosensitive dermatitis most commonly affecting elderly Caucasian men with a history of atopic dermatitis. Patch and photopatch testing is positive in 75% of these patients (1). It is well recognised that CAD can occur in all races but the prevalence and age-distribution of CAD within the multi-ethnic UK population is unknown.

We studied the prevalence of CAD in all patients undergoing diagnostic phototesting for ultraviolet radiation (UVR) sensitivity at a single tertiary referral centre over a 5 year period (Jan 2007-Dec 2011). A total of 778 patients were referred with suspected photosensitivity. The age-range was 1 year – 91 years. The male to female ratio was 1:1.4 and the ratio of white-skinned patients (skin types I-IV) to patients with constitutively pigmented skin (V&VI) was 2:1. A diagnosis of CAD was made on the basis of the patient's 24h phototesting results and clinical history

Patients with CAD had a history of atopic dermatitis that became worse with sunlight exposure and all showed abnormal sensitivity to ultraviolet radiation, 24h after diagnostic phototesting. 99 out of 778 patients (13%) had CAD with exquisite photosensitivity, requiring only seconds of UVR exposure to produce dermatitis. In these patients, the prevalence of CAD increased with age ($p< 0.01$). 8 patients presented with CAD between the ages between the ages of 10-19yrs, increasing steadily across each decade to 20 patients at 70-79yrs. There were equal numbers of males and females and surprisingly, twice as many patients with pigmented skin (V&VI) than white skin (I-IV). 82 out of 99 patients were patch tested and 60% of these were positive to one or more contact allergens.

When the skin-types were analysed separately: In white skin-types I-IV (n=35), CAD was commonest in elderly men aged 70-79 (n=11). At all other ages the number of patients with CAD was ≤ 5. In pigmented skin-types V&VI (n=66), a high incidence of CAD was also seen in elderly men (n=8), but also in young women aged 20-29y (n=10) and 30-39y (n=9). There was no difference in the incidence of contact allergies in the different skin types.

CAD is more common in patients with pigmented skin than white skin, frequently affects females and occurs at a younger age and across a wider age distribution than previously reported.

References

1. Dawe et al. The natural history of chronic actinic dermatitis Arch Dermatol 2000; 136: 1215-1220

2. Russell et al., The photosensitivity dermatitis and actinic reticuloid syndrome (chronic actinic dermatitis) occurring in seven young atopic dermatitis patients. Br J Dermatol 1998; 138: 496-501

PC10

Food allergy and eczema: what is the link? A systematic review

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The interplay between food allergy (FA) and eczema remains highly controversial and poorly understood in the paediatric setting. We reviewed the evidence for an association between the two, as well as looking for insights into the nature of this link, namely the impact of FA on the severity and natural history of eczema.

Medline and Embase were systematically searched from inception to the end of December 2013 for studies investigating any link between FA and eczema, producing 2043 hits in total. We selected studies in which at least a proportion of subjects had eczema and an overlapping proportion of subjects had FA, as evidenced by skin prick testing (SPT), specific IgE (sIgE), or food challenges. A total of 65 studies were identified, of which 15 were population-based studies, 8 were high-risk birth cohort studies in which parents were selected for atopy, and the rest were studies comprising patients with either established eczema or preceding food allergy. A quality score was assigned to each paper, but methodological differences and study heterogeneity precluded formal meta-analysis.

The relative prevalence between FA and eczema was investigated in all articles. In the nine population-based studies of highest quality, the likelihood of positive SPT to common foods was up to six times higher in eczema sufferers vs. healthy controls (OR=6.18, 95% CI 2.94-12.98), whilst the likelihood of egg-specific SPT sensitization was up to nine times higher (OR=9.53, 95% CI 2.40-37.82). The largest study in an unselected population showed a 27% rate of positive SPT to common foods amongst infants with eczema. 23 studies additionally addressed the question of whether FA impacts on eczema severity, with most data providing evidence of a more severe eczema phenotype in patients with FA. Three studies supported the hypothesis that FA is associated with increased eczema chronicity, suggesting that FA also impacts on the natural history of eczema. Despite the fact that several papers presented data relating to the sequence of allergic and atopic progression, including measurements of cord blood IgE, it remains unclear whether there is a predominant temporal pattern in which either FA or eczema typically precedes the other.

This systematic review confirms a strong overall association between FA and eczema. There is also evidence to suggest that FA is associated with a more severe and persistent eczema phenotype. However, further prospective studies utilizing standardised methodology and outcomes are required to advance our understanding of this field.

PM01

Atopic Dirty Neck or Acquired Atopic Hyperpigmentation? – An epidemiological and clinical study from the National Skin Centre Singapore

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"Atopic Dirty Neck" (ADN) is a poorly understood and peculiar form of acquired hyperpigmentation seen in atopic dermatitis (AD) patients. The aim of this study was to determine the epidemiology, clinical features and pathological findings of ADN in AD patients seen at the National Skin Centre, Singapore.

We performed a cross-sectional study of all cases of ADN seen over a 5 month period. All consecutive AD patients with a clinical diagnosis of ADN seen at the Paediatric Dermatology and Adult Eczema Clinics at our centre were invited to participate. All subjects underwent clinical examination, photography and completed standardized questionnaires on their condition and quality of life. In addition, 4 patients underwent biopsies of lesional and non-lesional skin for clinicopathological correlation.

Out of 544 AD patients examined, 78 (14.3%) had ADN. It was most prevalent in male patients in their 3nd decade (35.6%). There was a male:female ratio of 7:1. The onset of the pigmentation was most commonly reported between 13 and 20 years old. It was uncommon in children < 12 years. There was no racial predilection among the different ethnic groups represented, namely Chinese, Malay and Indian races. The majority of cases had moderate to severe AD with a mean objective SCORAD of 38.5±12.7. In 29.6% of subjects, there was also axillae and/or flexural involvement of the pigmentation. Key histopathological features were increased epidermal melanin, increased dermal melanophages, thickened basement membrane and a dense superficial perivascular infiltrate. Patients were emotionally most disturbed by the appearance of the 'dirty neck' (81.9%), and felt frustrated (70.8%), embarrassed (68.1%) and unattractive (59.7%) because of the appearance.

ADN has a high prevalence amongst Asians with AD, in particular, in adolescent males with underlying moderate to severe eczema. Clinicopathological correlation suggests that the pathogenesis is complex and results from both frictional melanosis and post-inflammatory hyperpigmentation. The rippled appearance and the onset in adolescence is likely due to accentuation of the juxtaclavicular beaded lines. Optimal control of eczema may improve and potentially prevent the development of ADN. This study also reveals that physicians must

consider the psychosocial impact of the pigmentation. We propose the name “acquired atopic hyperpigmentation” as a less stigmatizing name, which also underscores our finding that the acquired pigmentation is not limited to the neck in about 1/3 of the cases.

References

1. Colver GB, Mortimer PS, Millard PR, Dawber RPR, Ryan TJ. The 'dirty neck'--a reticulate pigmentation in atopics. Clin Exp Dermatol 1987; 12(1):1-4

2. Manabe T, Inagaki Y, Nakagawa S, Miyoshi K, Ueki H. Ripple pigmentation of the neck in atopic dermatitis. Am J Dermatopathol 1987; 9(4):301-307.

PM02

Thymic stromal lymphopoietin downregulates filaggrin expression by STAT3 and ERK phosphorylation in keratinocytes

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Atopic dermatitis (AD) is a chronic inflammatory skin disease that is characterized by a defective skin barrier and Th2 immune response. Most patients with AD show reduced expression of filaggrin, which plays an important role to maintain intact skin barrier function. Recent studies have reported that inflammatory cytokines downregulate filaggrin expression. Meanwhile, thymic stromal lymphopoietin (TSLP), which skews the immune reaction in Th2 direction, is a critical cytokine in development of allergic diseases including AD. The aim of this study was to investigate whether TSLP can modulate filaggrin expression in keratinocytes.

In this study, we demonstrated the presence of a TSLP receptor in keratinocytes for the first time. We also found that filaggrin expression was significantly reduced by TSLP in human keratinocytes and this process was mediated by STAT3- and/or ERK1/2-dependent signaling pathways.

This study is the first demonstration of the presence of a TSLP receptor in keratinocytes and discloses that TSLP may downregulate filaggrin synthesis in human keratinocytes. The result suggests that while skewing the immune response in a Th2 direction, TSLP also contributes to barrier dysfunction. In addition, we demonstrated that the downexpression of filaggrin by TSLP is mediated by STAT3- and/or ERK-dependent pathways.

These results suggest that TSLP and the related downstream molecules might be a target to ameliorate the disrupted barrier in patients with AD.

References

1.Allakhverdi Z, Comeau MR, Jessup HK *et al*. (2007) Thymic stromal lymphopoietin is released by human epithelial cells in response to microbes, trauma, or inflammation and potently activates mast cells. J Exp Med 204:253-8

2.Barker JN, Palmer CN, Zhao Y, *et al*. (2007) Null mutations in the filaggrin gene (FLG) determine major susceptibility to early-onset atopic dermatitis that persists into adulthood. J Invest Dermatol 127:564-7

PM03

Correlation between Results of the Multiple Allergosorbent Test-Chemiluminescent Assay (MAST-CLA) and Clinical Severity of Atopic dermatitis

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Atopic dermatitis is a chronic, relapsing, inflammatory skin disease related to other atopic symptoms like allergic rhinitis, allergic conjunctivitis, and asthma. Hereditary factors and exogenous factors are important in the development of clinical signs of the disease. Atopic dermatitis is representative allergic skin diseses that can be mediated by IgE. Many tests to detect specific IgE antibody including RAST, FAST, MAST-CLA(The multiple allergosorbent test-chemiluminescent assay) are used. MAST-CLA is a assay for serum allergen-specific IgE, and allows up to 35 allergens to be tested simultaneously. The study about the relationship between the result of MAST-CLA and the clinical severity of atopic dermatitis is not copious in the Korean literature. The purpose of this study was to determine whether there was a correlation between abnormal immunologic findings on the MAST-CLA and clinical severity of disease in atopic dermatitis patients

Our study was designed by analyzing patients with atopic dermatitis via medical records and photos and the MAST-CLA(MAST immunosystem, Inc., California, USA) with a total IgE and 35 allergen-specific IgE in 433 patients. The Eczema Area and Severity Index(EASI) scores of the patients and the result of MAST-CLA were analyzed.

Among the subjects(mean age=9.4 years), 79.9% of patients showed elevated serum total IgE levels more than class level 2 and 53.2% revealed at least more than one allergen-specific IgE by MAST-CLA. The main positive allergens were D. farinae(43.0%), D. pteronyssinus(38.1%), Housedust(25.4%), Dog(15.0%), Milk(12.2%), Egg White(12.2%). A positive correlation was obtained between total IgE levels and the number of positive allergen-specific IgEs in MAST-CLA. The relationship between the clinical severity of atopic dermatitis(EASI scores) and total IgE levels and the number of allergen-specific IgEs showed statistical significance. The 0～2 year-old group and 13～18 year-old group showed higher positive rate of food allergens, the positive rate of aeroallergens were 3～6 year-old group 47.0%, 7～12 year-old group 56.3%, 13～18 year-old group 75.0%, over 18 year-old group 59.4%.

Total IgE levels and the number of allergen-specific IgE could be a good predictor for each other. And both of them could be used to predict the clinical severity of atopic dermatitis

References

1. Hanifin JM, Rajka RG. Diagnostic features of atopic dermatitis. Acta Derm Venereol 1980;92:44-47

2. Hanifin JM, Thurston M, Omoto M, Cherill R, Tofte SJ, Graeber M. The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. Exp Dermatol 2001;10:11-18

PM04

Higher frequencies of antigen-specific CD1a-restricted T-cells in patients with Atopic Dermatitis

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T cells recognising lipids in the context of CD1 molecules have been described, with increasing evidence that these cells play an important role during infection, inflammation and malignancy[1] but their role in atopic dermatitis (AD) remains undefined.

CD1a is highly expressed by Langerhans cells of the epidermis and these cells are enriched in atopic eczema skin. It has recently been shown that CD1a-restricted T cells circulate at far

higher frequencies than previously considered, and can infiltrate human skin and produce Interferon-gamma (INFγ) and Interleukin-22 (IL-22).[2]

T-cells were isolated from fresh peripheral blood mononuclear cells (PBMCs) of 10 control and 10 AD patients by CD3+ MACs bead separation giving a T-cell purity of 97-99%.
T-cells were then rested for a period of 3-4 days in Interleukin-2 (IL-2) containing T-cell medium, before CD1a-reactivity was analysed by IFNγ ELISpot with K562 cells transfected with empty vector (K562-EV), K562s transfected with CD1a (K562-CD1a), and K562-EV and K562-CD1a pulsed for 24 hours with atopic allergens of interest (House Dust Mite, Cat and Grass).

Antigen-specific CD1a-restricted T-cells were found to be present in the blood of healthy controls and AD patients on ex-vivo analysis, and were present in significantly higher frequencies in the blood in AD patients compared to healthy donors ($p<0.01$).
The ex-vivo allergen-specific CD1a-restricted T-cell response could be reduced by anti-CD1a antibody, demonstrating CD1a specificity, and antigen-specific CD1a-restricted T-cells were also found to respond to CD1a+ monocyte-derived dendritic cells on ex-vivo analysis.
T-cells isolated from skin suction blister cells from a patient with AD also responded in a CD1a-restricted manner to K562-CD1a and CD1A+ monocyte-derived dendritic cells.

Antigen-specific CD1a-restricted T-cells specific to a number of atopic allergens of interest (House Dust Mite, Cat and Grass) were found to be present in significantly higher frequencies in AD patients compared to healthy donors on ex-vivo analysis, suggesting that they may play a role in clinical atopic disease. We are currently characterising the antigenic determinants of this CD1a-restricted response.

References

1 Silk JD, Salio M, Brown J, Jones EY, Cerundolo V. Structural and functional aspects of lipid binding by CD1 molecules. Annu Rev Cell Dev Biol 2008; 24:369-95.

2 de Jong a, Pena-Cruz V, Cheng TY, Clark RA, Van Rhijn I, Moody DB. CD1a-autoreactive T cells are a normal component of the human alpha beta T cell repertoire. Nat Immunol 2010; 11(12):1102-9.

PM05

Membrane vesicles from Staphylococcus aureus are detected in eczematous atopic dermatitis skin and induce inflammatory cytokines in Raw 264.7 macrophages

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Recently, it has been reported that S.aureus-derived membrane vesicles (MVs) induce atopic dermatitis-like inflammation through up-regulation of IL-4, IL-5, IFN-γ, and IL-17 in mouse skin. In the present study, we demonstrated that MVs of S.aureus were found in eczematous lesional skin of atopic dermatitis by immunohistochemistry (IH). Furthermore, IL-6, TNF-α, and nitric oxide (NO) productions were increased in S.aureus-derived MV-treated Raw 264.7 macrophages. Our data showed that S.aureus was cultured from eczematoid atopic skin lesions. Consistent with these findings, increased expression of protein A, which is a component of MVs, was clearly observed in the stratum corneum and epidermal layers by immunohistochemical staining. In contrast, the other AD patient, who has been suffering from AD for several years, showed dry skin with itching without evidence of S.aureus infection. We did not find any increased expression of protein A by immunohistochemical staining from this AD patient's lesional skin. Next, to examine the effects of MVs on the secretion of inflammatory cytokines, including TNF-α and IL-6 in RAW264.7 cells. RAW264.7 cells were activated with LPS (0.5 μg/ml) or with various concentration of MVs (0.005, 0.01, 0.05, 0.1, 0.5, and 1 μg/ml) for 24 h. RAW264.7 cells treated with various concentrations of MVs significantly induced production of TNF-α and IL-6 in a dose-dependent manner. Furthermore, to elucidate what signaling pathways were related to inflammatory mediators by MVs in RAW264.7 macrophage cells, modifications of the phosphorylation of MAPKs, such as p38 MAPK, ERK and JNK in LPS- or MVs-treated RAW264.7 macrophage cells were investigated. Taken together, *S.aureus*-derived MVs are located in the epidermis, especially inside the cytoplasm of keratinocytes, of eczematous AD skin lesions, and trigger inflammatory responses in AD through MAPKs-mediated up-regulation of inflammatory cytokines. Our study evidently shows that *S.aureus* plays an important role as an aggravating factor in AD pathogenesis.

It was still largely unknown which mechanisms are involved in S.aureus-derived membrane vesicles (MVs) inducing atopic dermatitis-like inflammation in tissues.

We examined the localization of MVs from S.aureus in eczematous lesional skin and studied the effect of MVs-induced inflammatory cytokine expressions in Raw 264.7 cells.

We demonstrated that MVs of *S.aureus* were found in eczematous lesional skin of atopic dermatitis by immunohistochemistry (IH). S.aureus-derived MVs are located in the epidermis, especially inside the cytoplasm of keratinocytes, of eczematous AD skin lesions, and trigger inflammatory responses in AD through MAPKs-mediated up-regulation of inflammatory cytokines.

Our study indicates that Mvs from *S.aureus* will play an important role as an aggravating factor in AD pathogenesis.

References

1. Lebon A, Labout JA, Verbrugh HA, Jaddoe VW, Hofman A, van Wamel WJ, van Belkum A, Moll HA. Role of Staphylococcus aureus nasal colonization in atopic dermatitis in infants: the Generation R Study. Arch Pediatr Adolesc Med 2009;163:745-9.

2. Huang JT, Abrams M, Tlougan B, Rademaker A, Paller AS. Treatment of Staphylococcus aureus colonization in atopic dermatitis decreases disease severity. Pediatrics 2009;123:e808-14.

3. Cho JW, Cho SY, Lee KS. Roles of SEA-expressing Staphylococcus aureus, isolated from an atopic dermatitis patient, on expressions of human beta-defensin-2 and inflammatory cytokines in HaCaT cells. Int J Mol Med 2009; 23:331-5.

4. Schlievert PM, Case LC, Strandberg KL, Abrams BB, Leung DY. Superantigen profile of Staphylococcus aureus isolates from patients with steroid-resistant atopic dermatitis. Clin Infect Dis 2008;46:1562-7.

5. Hong SW, Kim MR, Lee EY, Kim JH, Kim YS, Jeon SG, Yang JM, Lee BJ, Pyun BY, Gho YS *et al*. Extracellular vesicles derived from Staphylococcus aureus induce atopic dermatitis-like skin inflammation. Allergy 2011;66:351-9.

6. Wai SN, Lindmark B, Soderblom T, Takade A, Westermark M, Oscarsson J, Jass J, Richter-Dahlfors A, Mizunoe Y, Uhlin BE. Vesicle-mediated export and assembly of pore-forming oligomers of the enterobacterial ClyA cytotoxin. Cell 2003;115:25-35.

7. Gehrmann U, Qazi KR, Johansson C, Hultenby K, Karlsson M, Lundeberg L, Gabrielsson S, Scheynius A. Nanovesicles from Malassezia sympodialis and host exosomes induce cytokine responses-novel mechanisms for host-microbe interactions in atopic eczema. PLoS One 2011;6:e21480.

PM06

Surface protein marker of the induced regulatory T cells in NC/Nga mice

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CD25+ CD4+ regulatory T cells (Tregs) are known as a key modulator of immune self-tolerance and also have been found in atopic dermatitis (AD) patients. Since it has been rarely known that the different functional role between naturally occurring Tregs (nTregs) in thymus and induced Tregs (iTregs), and their surface marker proteins, we designed the experiments to separate two different subpopulations of Tregs, nTregs from thymus of healthy control mice and iTregs from spleen from the AD model mice.

We initially observed AD-like skin lesions in NC/Nga mice sensitizing D. farinae ointments for six weeks and we measured their significant increases of serum IgE level and enhanced IL-4 production from Th2 subsets. CD4+ CD25+ Treg cells were separated from those AD-like mice and healthy control mice using MACS®, with high separation purity confirmed by flow cytometry analysis. Membrane proteins were extracted from CD4+ CD25+ Tregs and labeled with TMT reagents for 1DLC-MS/MS analysis.

As a result of TMT-labeling method, we obtained 533 protein, 63 membrane proteins and 16 plasma membrane proteins identification list, including H-2 class II histocompatibility antigen, receptor-type tyrosine-protein phosphatase C and leukocyte surface antigen CD47, based on database research.

Considering the increased ratios of selected proteins in iTreg cell population and their functional roles that have been elucidated from many research groups, we believed that CD47 might be a key marker protein or functional regulator of iTregs. We confirmed the expression of CD47 was enhanced in iTregs compared to nTregs by Western blot analysis. Now that expression pattern of FOXP3 and CD47 in vitro iTregs seems to be negatively correlated, we assumed CD47 might be a prospective marker protein which acts as a counter marker protein of FOXP3.

References

1.Van VQ, Darwiche J, Raymond M, Lesage S, Bouguermouh S, Rubio M, *et al*. Cutting edge: CD47 controls the in vivo proliferation and homeostasis of peripheral CD4+ CD25+ Foxp3+ regulatory T cells that express CD103. J Immunol 2008;181:5204-8.

2.Ohkura N, Kitagawa Y, Sakaguchi S. Development and Maintenance of Regulatory T cells. Immunity 2013;38:414-23.

PM07

The house dust mite allergen Der p1 induces production of thymic stromal lymphopoietin in HaCaT cells via proteinase-activated receptor 2

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There is accumulating evidence that the epithelial cell–derived cytokine thymic stromal lymphopoietin (TSLP) may initiate asthma or atopic dermatitis through a dendritic cell–mediated T helper (Th)2 response. The aim of this study was twofold: (1) to investigate whether house dust mite allergen Der p1 could induce production of TSLP in a human keratinocyte cell line HaCaT and (2) to demonstrate that Der p1 directly activates proteinase-activated receptor 2 (PAR-2) in HaCaT cells and induces expression of TSLP.

Cultured HaCaT cells were treated with house dust mite allergen rDer p1 (0.1ug/ml, 1ug/ml and 10ug/ml) and PAR-2 specific agonist SLGIKV (500uM). The presence of TSLP in culture supernatant was determined by ELISA. Expression of TSLP mRNA was examined by real-time PCR. The intracellular calcium concentration of HaCaT cells was studied under the treatment with rDer p1 (10ug/ml) and SLGIKV (500uM) by confocal laser scanning microscope, which reflected activation of protease-activated receptor-2. The inhibition effect of PAR-2 specific antagonist VKGILS (500uM) on rDer p1 induced intracellular calcium influx in HaCaT cells was also evaluated.

TSLP protein in supernatant of rDer p1 groups (1ug/ml, 155.5±5.9pg/ml; 10ug/ml, 228.8±28.7pg/ml)were significantly higher than that of negative control (54.3±13.9 pg/ml, $P<0.0001$) and the levels of TSLP elevated with increase of concentration of rDer p1. PAR-2 agonist SLGIKV (166.2±8.8 pg/ml) also induced significantly elevated expression of TSLP in HaCaT cells compared with negative control (54.3±13.9 pg/ml, $P<0.0001$). TSLP mRNA expression in both rDer p1 group (10ug/ml) and SLGIKV group reached peak value at 8 hours after stimulation (3.28±0.27 relative fold and 2.15±0.26 relative fold, respectively). Intracellular calcium influx indicated by fluorescence elevated in both rDer p1 group (10ug/ml) and SLGIKV group. rDer p1(10ug/ml) induced intracellular calcium influx decreased 50% when HaCaT cells were pre-treated with PAR-2 specific antagonist VKGILS.

House dust mite allergen rDer p1 induces expression of pro-Th2 cytokine TSLP in human HaCaT cells by partially binding and activation of PAR-2 receptors.

References

1. Soumelis V, Reche PA, Kanzler H, *et al*. Human epithelial cells trigger dendritic cell mediated allergic inflammation by producing TSLP. Nat Immunol, 2002, 3(7):673-680.

2. Kato T, Takai T, Fujimura T, Matsuoka H, Ogawa T, Murayama K, Ishii A, Ikeda S, Okumura K, Ogawa H. Mite serine protease activates protease-activated receptor-2 and induces cytokine release in human keratinocytes. Allergy, 2009, 64(9):1366-1374.

PM08

CXCR4 activated invariant natural killer T cells trigger an innate allergic immune response in atopic dermatitis

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Atopic dermatitis (AD) is a highly pruritic, chronic relapsing inflammatory skin disease. Although invariant natural killer T (iNKT) cells have been shown to play a critical role in the pathogenesis of asthma, the role of iNKT cells in atopic dermatitis (AD) has not been well evaluated.

Therefore, to understand the role of iNKT cells CXCR4 in atopic dermatitis (AD) in the view of innate immunity, we investigated whether iNKT cells, T cells CXCR4, and SDF1 alpha in patients with AD were increased. Also, we aimed to explore the cells' effects on healthy control T cells activated by thymic stromal lymphopoietin (TSLP), which is highly expressed in keratinocytes of AD along with CXCR4, SDF1 alpha, CD8 and CD4 on iNKT. Immunohistochemistry was used to evaluate iNKT cells and CXCR4, SDF1 alpha expression in AD and HC skin with concurrent evaluation of healthy controls (HCs) iNKT cells' expression of CXCR4.Transwell migration assay using SDF1 alpha was performed to understand how healthy control T cells or iNKT cells modulate cell migration and TSLP's direct effect on healthy control T cells.

Immunohistofluorescence analysis of iNKT and CXCR4 was expressed in AD skin. CXCR4 or SDF1- alpha was increased in lesional skin but not in the sera of patients with AD compared with HC. Moreover, iNKT cells decreased CXCR4 mRNA. The SDF1a induced migration of healthy controls (HCs) iNKT cells and healthy controls (HCs) T cells.

Validation of protein expression level for SDF1a in HC T cells treated with TSLP directly activated healthy control T cells to secrete SDF1-a and CD3.

Increased CXCR4 and SDF1 alpha activated by AD iNKT skin but decreased CXCR4 by AD iNKT cells. Increased healthy controls (HCs) T cells activated by TSLP, especially in patients with severe AD, might play an essential role in the innate allergic immune response in AD.

References

1.Wu WH, Park CO, Oh SH, Kim HJ, Kwon YS, Bae BG, Noh JY, Lee KH , *et al*. Thymic stromal lymphopoietin-activated invariant natural killer T cells trigger an innate allergic immune response in atopic dermatitis. J Allergy Clin Immunol. 2010 Aug;126(2):290-9, 299.e1-4.

2. Wang H, Zeng X, Fan Z, Lim B, *et al*. RhoH plays distinct roles in T-cell migrations induced by different doses of SDF1 alpha. Cell Signal. 2010 Jul;22(7):1022-32.

PM09

Expression of regulatory molecules in eczematous dermatitis, psoriasis and normal skin

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Eczematous dermatitis (ECZ) and psoriasis (PSO) are two of the most common chronic inflammatory skin diseases. Both are primarily immune-mediated diseases and each represents prototypical Th2 and Th1 disease, respectively. There are many reports about comparing the characteristics of cytokines, chemokines and immune cells between eczematous dermatitis and psoriasis. However, there are only few studies comparing the expression of regulatory molecules between two diseases. Therefore, we set our study to compare the expression of galectin-1, 3, 9

Therefore, we set our study to compare the expression of galectin-1, 3, 9 (Gal-1, 3, 9) and programmed death ligand-1, 2 (PD-L1, 2) in eczematous dermatitis, psoriasis and normal skin (NL).

Paraffin sections were stained with above mentioned antibodies. Gal-1 was not expressed in epidermis of ECZ, PSO and NL. In dermis, Gal-1 was expressed in all three groups, however, Gal-1 positive cells were scattered in NL, but significantly greater numbers of dermal cells

expressed Gal-1 in NL and PSO. Gal-3 was heavily expressed in normal epidermis. The epidermis of PSO also showed diffuse expression of Gal-3, but intensity was much lower than NL. Gal-3 was partially expressed in epidermis of ECZ, but intensity was lowest compared to PSO and NL. In dermis, Gal-3 positive cells were scattered in PSO and NL, but barely detectable in ECZ. Gal-9 showed diffuse and dense expression in epidermis of NL, but in EZ and PSO, it was merely detectable. There were no cells expressing Gal-9 in dermis in all three groups. In normal skin, PD-L1 was diffusely expressed in epidermis and focally expressed in a few cells of dermis. Staining results of PD-L1 in PSO showed similar results with NL, but intensity was much lower in PSO. In ECZ, PD-L1 was only focally expressed in both epidermis and dermis with less intensity. PD-L2 was expressed in epidermis of NL and PSO with low intensity and dermal cells were barely detectable in both groups. In ECZ, PD-L2 was not detected in both epidermis and dermis.

With regard to regulatory molecule expression, EZ, PSO and NL showed different patterns. Differentially expressed Gal-1, 3, 9 and PD-L1, 2 could explain chronicity each disease and differences between EZ and PSO. However, our results are only preliminary. Therefore, further in vitro, in vivo and functional studies are needed to reveal the clinical relevance of our findings.

References

1.Kimata H. Enhancement of IgE production in B cells by neutrophils via galectin-3 in IgE-associated atopic eczema/dermatitis syndrome. Int Arch Allergy Immunol.128(2):168-70.

2.Igawa K. *et al*. Regulatory mechanisms of galectin-9 and eotaxin-3 synthesis in epidermal keratinocytes : possible involvement of galectin-9 in dermal eosinophilia of Th1-polarized skin inflammation. Allergy.61(12):1385-91.

PM10

Correlation between pyrrolidone carboxylic acid levels and caspase-14 expression in corneocytes and the severity of clinical symptoms or lesional inflammation in atopic dermatitis

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Dry skin in AD mainly results from barrier impairment due to deficiency of ceramide and natural moisturizing factors including pyrrolidone carboxylic acid (PCA). We quantitated PCA, caspase-14, and cytokines in corneocytes of AD patients to analyze their correlations with disease severity, genetics, barrier function, and skin inflammation.

A total of 73 persons were enrolled: 21 patients with mild AD, 21 with moderate-to-severe AD, 13 with X-linked ichthyosis (XLI) as a negative control for filaggrin gene (*FLG*) mutation, and 18 healthy controls.

Only 3 out of 42 AD patients had a pK4022X FLG mutation. The amount of PCA in corneocytes decreased in the lesional skin of the AD patients, and even in the non-lesional skin of moderate-to-severe AD, but not in healthy control nor in XLI patients. Moreover, it decreased as skin barrier functions were decreased. We also found that the amount of caspase-14 significantly decreased in lesional skin. However, XLI patients showed an expression level of caspase-14 similar to that of the healthy control patients. Moreover, like PCA quantity, it significantly decreased even in the non-lesional skin of the moderate-to-severe AD. The correlation between PCA quantity and caspase-14 level in lesional skin followed a proportionate relation. These results suggest that decreased expression of caspase-14 in corneocytes results in a defect of filaggrin monomer degradation, leadings to decreased quantities of PCA.

Collectively, the quantities of PCA and caspase-14 in the corneocytes of the lesional skin of AD did reflect the severity of AD and correlate with the degree of lesional inflammation.

References

1.Kezic S, Kammeyer A, Calkoen F, *et al*. Natural moisturizing factor components in the stratum corneum as biomarkers of filaggrin genotype: evaluation of minimally invasive methods. Br J Dermatol. 2009:161:1098-1104.

2.Hoste E, Kemperman P, Devos M, *et al*. Caspase-14 is required for filaggrin degradation to natural moisturizing factors in the skin. J Invest Dermatol. 2011:131:2233-2241.

PM11

Activation of local cortisol by 11β-HSD1 in keratinocytes is important in supressing local inflammation

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Glucocorticoids (GCs) are one of the most effective anti-inflammatory drugs to treat acute and chronic inflammatory diseases. Cortisol is the endogenous GC that is released in

response to various stressors. Over the last decade, extraadrenal cortisol production in various tissues is reported. Skin is also known to synthesize cortisol though de novo pathway and through activating enzyme. 11β-hydroxysteroid dehydrogenase 1 (11β-HSD1) is the enzyme that catalyzes the conversion of hormonally inactive cortisone into active cortisol in cells. We recently reported that 11β-HSD1 is also expressed in keratinocytes and regulating inflammation and proliferation of keratinocytes (1, 2). Association of 11β-HSD1 in skin aging and skin tumors are also reported. In addition to these findings, we recently found that the expression of 11β-HSD1 is decreased in lesional skin of atopic dermatitis.

In this study, to know the function of 11β-HSD1 during inflammation in vivo, we created keratinocyte-specific-11β-HSD1 knockout mice (11β-HSD1 KO mice) and analysed the response to various inflammatory stimuli such as UVB irradiation and hapten application. UVB irradiation increased the expression of 11 β-HSD1 in mouse skin and in keratinocytes in culture. The expression of 11β-HSD1 was also increased by various pro-inflammatory cytokines and haptens in keratinocytes. Inflammatory response to UVB irradiation (1000 mJ/cm2) were more severe in 11β-HSD1 KO mice compared with wild type mice shown by increased CXCL-1 and IL-6 production. The number of infiltrating neutrophils in the skin was also increased in 11β-HSD1 KO mice. In addition, response to UVB irradiation were also accelerated in keratinocytes in culture derived from 11β-HSD1 KO mice compared with keratinoyctes derived from wild type mice.

The expression of 11β-HSD1 in keratinocytes was increased by various inflammatory stimuli. On the other hand, the expression of 11β-HSD1 was decreased in atopic dermatitis skin. Local cortisol activation in keratinocytes by 11β-HSD1 might suppress skin inflammation as keratinocyte-specific 11β-HSD1 KO mice showed enhanced inflammatory response. Taken together, 11β-HSD1 is important in regulating the local inflammation, and decreased 11β-HSD1 in keratinocytes might be modulating inflammation in atopic dermatitis.

References

1. Terao M, Murota H, Kimura A, Kato A, Ishikawa A, Igawa K, Miyoshi E, Katayama I. 11β-Hydroxysteroid dehydrogenase-1 is a novel regulator of skin homeostasis and a candidate target for promoting tissue repair. PLoS One. 2011;6(9):e25039

2. Itoi S, Terao M, Murota H, Katayama I. 11β-Hydroxysteroid dehydrogenase 1 contributes to the pro-inflammatory response of keratinocytes. Biochem Biophys Res Commun. 2013 Oct 18;440(2):265-70

PM12

Stimulation by parabens up-regulate TSLP expression in human normal keratinocytes and affect negatively on skin barrier function on murine model.

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Some ingredients of dermatological formulations result in skin irritation and allergy. In particular, preservatives have been reported extensively as a cause of allergic contact dermatitis. The study focused on parabens which have been used extensively as antimicrobial preservatives in foods, drugs and cosmetics. Thymic stromal lymphopoietin (TSLP) is an IL-7 related cytokine, produced by epithelial cells, that has been linked to atopic dermatitis and asthma. TSLP expression is up-regulated in the lesions of allergic patients. Here we want to the direct effect of TSLP expression when stimulated by parabens in human normal keratinocytes.

Methyl paraben(MP), propyl paraben(PP) and butyl paraben(BP) of various parabens are used widely. The study investigated the effects exposure to MP, PP and BP on keratinocytes in vitro. Normal human keratinocytes was cultured in the medium containing MP, PP and BP. The following changes were analysed: proliferating ability, TSLP mRNA expressions and the relationship with Nf-kappa B mechanism. We also the check the effect of parabens on skin barrier recovery.

MP, PP and BP decreased the proliferating ability of keratinocytes especially PP and BP affect at low concentration rather than MP. And PP and BP increase the expressions of TSLP mRNA in keratinocytes but MP doesn't. Interestingly effect of PP and BP that increased the expressions of TSLP mRNA confirmed in allowed concentration for use in cosmetics products by Ministry of Food and Drug Safety.This effect has been oartically mediated by the NF-kappa B mechanism. We can also see the negative effect on the skin barrier recovery function after acute skin barrier disruption on hairless mouse by the parabens

These results suggest that parabens which have been used in cosmetics might influence the atopic dermatitis through decreased the proliferating ability and increased the expressions of TSLP mRNA of keratinocytes and barrier function, This study can induce critical and scientific concerns about the usage of parabens on any cosmetics for atopic dermatitis patients.

References
1.Leung DYM and Bieber T. Atopic dermatitis. Lancet 361 151-160. (2003)
2.Steven F Zieglar and David Artis., Sensing the outside world: TSLP regul;ates barrier immunity. Nat Immunol. 11(4) : 289-293(2010)
3.Steven F Zieglar., The role of thymic stromal lymphopoietin(TSLP) in allergic disorders. Current Opinion in Immunology. 22:795-799 (2010)
4.Heather M. Harville, Richard Voorman and Jeffery J. Prusakiewicz. Comparison of Paraben Stability in Human and Rat Skin. Drug Metabolism Letters, 1, 17-21. (2007)
5.Ishiwatari, T. Suzuki, T. Hitomi, T. Yoshino, S. Matusukuma, T, Tsuji. Effects of methyl parabens on skin keratinocytes. Jounal of APPLIED TOXICOLOGY, 27 : 1-9, S, (2007)

PM13

Biopsychosocial factors associated with Prurigo Nodularis in Endogenous Eczema

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Prurigo nodularis is a dermatological manifestation secondary to chronic scratching or picking on focal areas of the skin. Its pathogenesis remains poorly understood, and limited data has indicated its association with psychological factors.

Aim: To determine the biological, psychological and social factors associated with the occurrence of prurigo nodularis in patients with underlying endogenous eczema.

A case-control questionnaire –based study on patients with endogenous eczema, with and without prurigo nodules, was performed. The Impact of Skin Disease on Daily Life questionnaire was used to assess dimensions of physical functioning, including extent and severity of skin disease, itch, pain, fatigue and scratching, as well as dimensions of psychological and social functioning, including mood, illness cognition, disease-related impact, stigmatization and social support.

Thirty-six cases and 47 controls were recruited. Patients with endogenous eczema and prurigo nodules indicated a higher itch score on the visual analog scale over the previous 4 weeks compared to those without prurigo nodules ($p=0.0292$). There were no significant differences between the 2 groups in the scores reflecting the other parameters of physical, psychological and social functioning.

In patients with endogenous eczema, those with prurigo nodules experience a greater itch intensity compared to those without prurigo nodules. There were no other physical,

psychological and social factors that were found to be associated with the occurrence of prurigo nodules in endogenous eczema.

References:

1.G. Schneider, J. Hockmann, S. Stander, T.A. Luger, G. Heuft. Psychological factors in prurigo nodularis in comparison with psoriasis vulgaris: results of a case–control study G. Schneider *et al* British Journal of Dermatology 2006. 154, pp61–66

2.A. Iking, S. Grundmann, E. Chatzigeorgakidis, N.Q. Phan, D. Klein, S. Stander. Prurigo as a symptom of atopic and non-atopic diseases: aetiological survey in a consecutive cohort of 108 patients. J Eur Acad Dermatol Venereol. 2013;27:550–557.

PM14

Interleukin 33 may deteriorate skin barrier function in atopic dermatitis

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A paradigm shift within the field of atopic dermatitis (AD) is directing focus on the defective skin barrier as an early mediator of disease. Recent data supports an impaired stratum corneum as a primary event, leading to increased penetration of allergens and inflammation. IL-33, a newly described cytokine in the IL-1 family has been of major interest in the pathogenesis of AD. IL-33 is often described as an "alarmin" and shows resemblance to other damage-associated molecular pattern (DAMP) molecules like IL-1α and high mobility group box 1 (HMGB1) protein. It is constitutively expressed in keratinocytes, has no secretory apparatus but is released when cells are presented to allergens, biomechanical stress or apoptosis – all key elements in the pathogenic pathway of AD. IL-33 works as a dual function protein possessing proinflammatory capacity as a cytokine and significant transcriptional repressor properties as an intracellular nuclear factor.

We have investigated the impact of IL-33 on transcription and translation of the skin barrier proteins filaggrin, involucrin and loricrin.

Primary keratinocytes from healthy donors (n=5) cultured with supplemented $CaCl_2$ (1.3 mM) were stimulated for 24 or 96 hours with different concentrations of IL-33 (2, 20 and 100 ng/mL) using IL-25 (10 and 100 ng/mL) as positive control and vehicles as negative control. RT-qPCR was used as primary method of analysis.

IL-33 (100 ng/mL) stimulation for 96 hours significantly downregulates the expression of both the filaggrin and involucrin gene. The involucrin gene shows a dose-dependent

downregulation when stimulated for 96 hours with IL-33. IL-25 (100 ng/mL) significantly downregulates the filaggrin gene but upregulates the loricrin gene. No significant regulation of the filaggrin, the involucrin or the loricrin gene was observed when keratinocytes were stimulated with IL-33 for 24 hours.
We hypothesize that IL-33 may play a significant role in skin inflammation and hence could be a contributor to a functional aggravation of skin barrier dysfunction in atopic dermatitis.

PM15

IL-17A as an inducer for Th2 immune responses in murine atopic dermatitis models

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Atopic dermatitis (AD) is generally regarded as a Th2-mediated inflammatory skin disease. Although the number of interleukin (IL)-17A-producing cells is increased in the peripheral blood and in acute skin lesion of AD patients (ref 1), the role of IL-17A in the pathogenesis of AD remains unclear. To clarify this issue**,** we used murine AD models in IL-17A-deficient condition. In a repeated hapten application-induced AD model, the skin inflammation, IL-4 production in the draining lymph nodes, and hapten-specific IgG1 and IgE induction were suppressed in IL-17A-deficient mice. $V\gamma4^+$ γδ T cells in the skin draining lymph nodes and $V\gamma5^-$ dermal γδ T cells in the skin were the major source of IL-17A. Consistently, in flaky tail (*Flg*$^{ft/ft}$ *ma/ma*) mice, spontaneous development of AD-like dermatitis and IgE induction were attenuated by IL-17A deficiency. Moreover, Th2 differentiation from naïve T cells was promoted *in vitro* by the addition of IL-17A. Taken together, our results suggest that IL-17A mediate Th2-type immune responses and that IL-17A signal may be a therapeutic target of AD (ref 2).

Ref 1. Koga C, Kabashima K, Shiraishi N, Kobayashi M, Tokura Y. Possible pathogenic role of Th17 cells for atopic dermatitis. J Invest Dermatol. 2008 Nov;128(11):2625-30.
Ref 2. Nakajima S. *et al*. IL-17A as an inducer for Th2 immune responses in murine atopic dermatitis models. J Invest Dermatol. (in press)

PM16

House dust mite allergen induces atopic dermatitis via toll-like receptor 1 and 6 triggering of keratinocytes

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Among environmental factors, house dust mite (HDM) allergens are important for the development of atopic dermatitis (AD) as well as asthma and rhinitis. In airway allergy, activation of innate immunity by HDM allergens plays an important role in disease pathogenesis. However, information regarding the activation of innate immunity by HDM in the skin is limited. We investigated whether HDM allergens activate the innate immunity in epidermal keratinocytes and a murine model with AD-like lesions.

Firstly, the mRNA levels of pattern recognition receptors (PRRs), antimicrobial peptides (AMPs) and epidermal immunologic/physical barrier elements were assayed using real-time RCR and were compared between control and HDM group both *in vitro* and *in vivo*. Then, the association between the activated PRRs and secretion of certain immunologic cytokines were examined using HaCaT cells stimulated with HDM. The importance of specific PRRs was studied by knocking down their expression through transfection of HaCaT cells with siRNAs.

In HaCaT cell stimulated with HDM, the mRNA levels of PRRs (TLR1/6/9 and NOD2) were significantly increased in the HDM group compared to the control group. The secretion of AMPs such as β-defensin2, S100A9 and dermcidin also increased. A significant increase of mRNA levels of immunologic barrier components such as IL-25 and IL-33 and physical barrier proteins including claudin-1 and claudin-23 were detected. In addition, the changes with similar tendency was shown in a murine model with AD-like lesions. Both *in vitro* and *in vivo*, HDM activated TLR1/6/9, NOD2 and release of the innate proallergic cytokines, IL-25 and IL-33. The inhibition of TLR6 on HaCaT cells abolished HDM induced release of IL-25 and IL-33. Moreover, TLR6 triggering on HaCaT cells caused production of IL-25 and IL-33. The suppression of TLR1 inhibited the release of IL-33 from HaCaT cells. TLR9 and NOD2 had no effects on the release of IL-25 and 33.

In this study, we found HDM induced activation of TLR1 and TLR6 may cause the polarization towards a Th2 immune response through the release of IL-25 and IL-33. These findings provide the evidence that HDM allergens may promote AD development and aggravation through activation of innate immune system.

References

1. Kuo IH *et al*. The cutaneous innate immune response in patients with atopic dermatitis. J Allergy Clin Immunol 2013;131:266-78.

2. Dai X *et al*. Mite allergen is a danger signal for the skin via activation of inflammasome in keratinocytes. J Allergy Clin Immunol 2011;127:806-14.

PM17

Protease effect of prolactin-induced protein for human stratum corneum

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Major diagnostic criteria for atopic dermatitis include chronically relapsing dermatitis at the predilection sites such as the antecubital flexures or popliteal fossae and in the neck region. These sites correspond to regions of the body that tend to accumulate sweat. Exocrine fluids, such as saliva and sweat are clinically known to provoke or exacerbate atopic skin lesions. However, the underlying mechanism for this aggravation has not been established. Prolactin-induced protein (PIP) is abundant in exocrine fluids and displays aspartic protease activity. We aimed to determine the effect of PIP as a protease on normal skin structure.

Using an adhesive-tape stripping technique, we applied hPIP(29-63) peptide three times a day for two days on the corneocytes of the face from control subjects and infants and children with eczema, and then analyzed with light microscopy.

We repeatedly applied PIP peptide comprising the aspartic peptidase activity (hPIP(29-63)) onto the surface of a three dimensional (3D) human skin model three times a day for five consecutive days and then analyzed any changes to the stratum corneum and epidermis using light microscopy and scanning electron microscopy.

Corneocytes treated with hPIP peptide(29-63) were morphologically deteriorated even in normal individuals and more markedly in patients with infantile eczema or child AD patients. The peptide hPIP (29-63) appeared to digest the stratum corneum and had a proliferating effect on epidermal keratinocytes within the 3D human skin model.

Our results suggest that aspartic peptidase of PIP found in sweat or saliva deteriorates corneocytes as a *de novo* manner and potentially leads directly to provoke proliferation of epidermal keratinocytes without external antigenic factors.

PM18

Histamine H4 receptor stimulation modulates the differentiation process and down-regulates chemokine release in human monocyte derived macrophages

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Histamine is an important mediator of biological functions and present in high amounts in inflammatory skin lesions of atopic dermatitis. Such skin lesions evoke a migration of monocyte precursor cells, in part via histamine induced chemotaxis, into the inflamed tissue whereby they differentiate into macrophages. Macrophages play a crucial role in the concept of cytokine and chemokine networking in atopic dermatitis. The expression and function of the histamine receptors, especially the histamine H4 receptor (H4R), has already been determined on monocytes and various subtypes of antigen presenting cells and T cells in our previous studies. However, the effects of histamine on the two major subtypes of human macrophages (M1 resp. M2 macrophages) have not been studied in detail yet.

Therefore, our aim was to assess a functional role of the histamine receptors, with focus on the histamine H4 receptor, on these professional phagocytes.

Here we could show that polarized M1 and M2 macrophages express the H1R, the H2R and the H4R but not the H3R on mRNA level. On M2 macrophages we observed an up-regulation of the H1R and H4R upon activation with IL-4. Interestingly we could show that the phenotype of M1 and M2 macrophages was significantly altered when H4R ligands were added continuously to the media during the period of differentiation. A significant up-regulation of the macrophage marker CD68 and a down-regulation of CD163 were detected by flow cytometry in response to treatment with the H4R agonist.

Furthermore, fully differentiated macrophages were stimulated and the cell free supernatants were analyzed by ELISA. When stimulated with IFN-γ and LPS in the presence of histamine or a H4R agonist, M1 macrophages produced substantially lower amounts of the chemokines CCL4, CXCL9 and of interferon-γ induced protein 10 (IP-10, CXCL10).

In conclusion, we could show that the H4R is functionally expressed on activated macrophages. The down-regulation of CCL4, CXCL9 and IP-10 will lead to decreased migration of immune cells (particularly Th1 lymphocytes) to the site of inflammation and

might have implications for the treatment of allergic skin diseases since H4R agonists may attenuate the inflammatory response.

PM19

Non-invasive assessment of the lipid structure and water holding properties of the stratum corneum *in vivo* by ATR-FTIR using a fibre optic probe in patients with atopic dermatitis and healthy controls

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A skin barrier defect arising as a result of a combination of genetic and environmental factors is a primary event in the development of atopic dermatitis (AD). Attenuated Total Reflectance (ATR)-Fourier Transform Infrared (FTIR) spectroscopy has been used to quantify the defect in stratum corneum (SC) lipid structure exhibited by AD patients, and associated this with reduced barrier function.[1] FTIR has also shown promise for the assessment of water content, and natural moisturising factor (NMF) levels, in the surface of the SC of healthy volunteers.[2]

The aim of this study was to assess these properties throughout the SC in AD patients and healthy controls, with and without xerosis induced by intensive washing, by combining tape-stripping with FTIR spectroscopy using a novel flexible fibre optic system.

The skin of five patients with AD was assessed on each forearm (volar side) using biophysical techniques in conjunction with tape-stripping. For comparison 9 volunteers with no history of skin disease were assessed: untreated on one forearm and following intensive washing for 7 days on the other (site randomised).

Intensive washing accurately modelled the biophysical properties (elevated TEWL and decreased hydration) of AD skin. In healthy skin lateral lipid packing was predominantly orthorhombic in the deeper layers of the SC, becoming more hexagonal towards the surface. AD skin, but not intensively washed skin displayed a striking shift in lateral chain packing and conformation from orthorhombic to hexagonal. This shift correlated with skin barrier function (r=0.6373). Throughout the SC, water content was significantly reduced in AD skin compared to controls (29% on average). Intensive washing reduced water content in the superficial layers of the SC, while levels were similar in the deeper layers. Quantification of water content by FTIR was directly correlated with capacitance measurements (r =0.6322),

and demonstrated greater specificity. Compared to controls, both AD skin and washed skin displayed reduced NMF (26% and 9% decrease in carboxylate group respectively). FTIR determined NMF levels correlated with PCA quantification by HPLC (r =0.5620), the amount of water held in the SC (r =0.8086) and lipid structure (r =0.7915).
FTIR using a fibre probe is a validated and convenient method for assessing both the lipid structure and water holding properties of the SC, with clinical application for the multimodal characterisation of the skin barrier in patients from birth at any body site.

References

1.Janssens M, van Smeden J, Gooris GS *et al*. Increase in short-chain ceramides correlates with an altered lipid organization and decreased barrier function in atopic eczema patients. Journal of lipid research 2012; 53: 2755-66.
2. Brancaleon L, Bamberg MP, Sakamaki T *et al*. Attenuated total reflection-Fourier transform infrared spectroscopy as a possible method to investigate biophysical parameters of stratum corneum *in vivo*. J Invest Dermatol 2001; 116: 380-6.

PM20

Evaluation of polyfunctional T cells to staphylococcal enterotoxins A and B in adults with atopic dermatitis

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The aim of this study was to evaluate the diversity in T cell functional against staphylococcal enterotoxins A and B, including mono and polyfunctional subsets, in adults with atopic dermatitis (AD).
We selected 9 males and 6 females diagnosed as AD, aged between 20 and 59 years (mean age 32.06), and 10 healthy controls (HC - 3 males and 8 females), aged between 25 and 41 years (mean age 29.7). Peripheral blood mononuclear cells (PBMC) were stimulated with staphylococcal enterotoxins A (SEA) and B (SEB). Intracellular IL-17a, IL-22, IFN-γ, MIP-1b and TNF in TCD4+ cells were assessed by flow cytometry (LSRFortessa, BD Biosciences) and analysis was performed utilizing FlowJo 9.7.2 software.
We showed a reduced secretion of IFN-γ, IL-17a, IL-22, and TNF by CD4+ T cells in AD patients, when compared to HC in a monofunctional response to SEA and to SEB. T cell polyfunctional analysis induced by SEA and SEB was performed; a Boolean gating analysis

showed, among all possible combinations, a preserved CD4+ T cell secreting simultaneously five cytokines (IL-17a, IL-22, IFN-γ, MIP-1b and TNF). Decreased percentage of one subset secreting four cytokines and three subsets for triple secreting cytokines to SEA were observed in AD group compared to HC, involving TNF, IL-17a, IL-22, and IFN-γ, secretions in these conditions. Conversely, we observed in the profile of CD4+ T cells responsiveness to SEB, a decreased response of subsets secreting triple cytokines in AD group, when compared to HC.

In monofunctional and polyfunctional CD4+ T cells evaluation, SEA and SEB similarly induce suppressed cytokines response. However, when we analyze a complete functionality panel of five positive cytokines (IL-17a, IL-22, IFN-γ, MIP-1b and TNF), CD4+ T cells in AD show a preserved function. Our findings reinforce the suppressed response to Staphylococcus aureus in AD patients among differentiated subsets of CD4+T cells simultaneously secreting mono or multiple cytokines.

References:

1.Orfali RL, Sato MN, Takaoka R, Azor MH, Rivitti EA, Hanifin JM, *et al*. Atopic dermatitis in adults: evaluation of peripheral blood mononuclear cells proliferation response to Staphylococcus aureus enterotoxins A and B and analysis of interleukin-18 secretion. Exp Dermatol. 2009;18(7):628-33.

2.Leung DY. New insights into atopic dermatitis: role of skin barrier and immune dysregulation. Allergol Int. 2013;62(2):151-61.

PM21

Uncovering risk factor-dependent mechanisms for development of atopic dermatitis using a systems biology approach

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Extensive clinical research has identified several risk factors for development of atopic dermatitis (AD), characterized by the loss of epidermal homeostasis, which appears as defective barrier function and exacerbated inflammation. Examples include high pH and low expression of filaggrin, LEKTI, and anti-microbial peptides (AMPs).

The pathogenic effects of the risk factors are often convoluted, and occur through their complex interferences with diverse biochemical processes that control epidermal homeostasis. For example, reduced filaggrin expression and elevated protease activity by

high pH or low LEKTI levels impair barrier formation, and the abundance of AMPs and protease activity affect the speed of resolving inflammation. While a complex interplay and regulated coordination between these biochemical processes is necessary for healthy epidermal function, it can cause epidermal-wide disruptions by propagation and synergistic effects of risk-factor-induced disturbances.

We constructed the first mathematical model of AD[1], to uncover how different risk factors lead to development of AD. The model mathematically describes the biochemical processes, based on information from clinical and experimental studies, and different risk factors are described by different parameter values. The computer simulation of models corresponding to patients with different risk factors allowed us to evaluate the impacts of individual risk factors and their combinations on epidermal homeostasis. This unravelled risk factor-dependent mechanisms leading to AD.

Model simulations showed that low filaggrin expression leads to recurrent flares of inflammation due to continuous protease activation, and that high pH condition results in persistent barrier damage. We also predicted synergistic effects caused by co-occurring risk factors.

The *in-silico* experiments agree with experimental data and reproduced the clinical features of AD. The model could exhibit recurrent inflammation, which is clinically known but difficult to observe in experiments. We are currently extending our mathematical model to reproduce aberrant expression patterns of terminal differentiation markers that characterize the late stages of AD.

Computer simulations of our mathematical model enabled the quantitative evaluation of the relative contributions of individual and combined risk factors to the pathogenic process. We uncovered risk factor-specific mechanisms leading to the development of AD. Mathematical models provided a framework to integrate scattered experimental and clinical data and allowed us to analyse complex biochemical interactions. Our new approach contributes to the prevention and treatment of AD. Further collaborative research on this complex disease is encouraged[2].

References

1. Domínguez-Hüttinger, E., Ono, M., Barahona, M., & Tanaka, R. J. (2013). Risk factor-dependent dynamics of atopic dermatitis: modelling multi-scale regulation of epithelium homeostasis. Interface Focus, 3(February), 20120090. doi:http://dx.doi.org/10.1098/rsfs.2012.0090

2. Tanaka, R. J., & Ono, M. (2013). Skin Disease Modeling from a Mathematical Perspective, 133(6), 1472–1478. doi:10.1038/jid.2013.69

PM22

Eosinophilia in patients with atopic dermatitis is associated with increased expression of CCR3 and decreased expression of CD23 and CD62L

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Eosinophils, multifunctional polymorphonuclear leukocytes, are implicated in the pathogenesis of numerous inflammatory allergic processes, including atopic dermatitis. The aim of this study was to evaluate the activation markers expression on eosinophils from peripheral blood of atopic dermatitis (AD) adults.

This work enrolled 26 AD patients (14 males and 12 females, aged between 21 and 61 years) and 25 healthy controls (8 men and 13 females, aged between 22 and 58 years), from the University of Sao Paulo Medical School - Brazil. The utilized severity score was EASI (Eczema Area and Severity Index), and patients were graded as mild (24%), moderate (38%) and severe (38%). Eosinophils (lineage cocktail 1- CCR3+) from peripheral blood were analyzed for CCR3, CD38,CD69, CD23 and CD62L by flow cytometry (LSRFortessa, BD Biosciences) and analysis was performed using FlowJo 7.5.6 software.

Patients with AD had a higher frequency of CCR3+ eosinophils, which was related to disease severity. Frequency of CD62L (L-selectin) and CD23 (low affinity IgE receptor) expression in eosinophils were reduced in patients with AD, compared to healthy controls. CD69, an early activation marker, was increased, while CD38, a late activation marker, was not altered in AD individuals.

Eosinophilia is a hallmark in atopic dermatitis. Eosinophils in AD patients are characterized by enhanced CCR3 expression, with acute activated profile and reduced expression of CD23 and CD62L. Our findings suggest that activated eosinophils in AD exhibit a potential augmented migration, in response to tissular chemokine production.

References:

1. Rosenberg HF, Dyer KD, Foster PS. Eosinophils: changing perspectives in health and disease. Nat Rev Immunol. v.13 n.1,p.9-22. 2013.

2. Leung DY. New insights into atopic dermatitis: role of skin barrier and immune dysregulation. Allergol Int. v.62,n.2,p.151-61. 2013.

PM23

Eczema remains active in a majority of children in the PEER cohort with age

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Our aim was to examine the longitudinal course of eczema disease activity among children and teens in a prospective observational cohort.

We analyzed self-reported disease control every six months among a cohort of 2,010 patients in the Pediatric Eczema Elective Registry with mild to moderate eczema and at least 6 years of follow-up. We calculated the average level of reported disease control across the population by age, and tested for linear trends over time. We then examined individual disease trajectories using ordered logistic regression and calculated the proportion of individuals who achieved a period of remission (defined as complete disease control and no use of prescription medications for eczema).

Seventy-six percent of patients reported disease onset by age 2, and the mean age at cohort entry was 6.7 years (standard deviation 3.9). The mean duration of follow-up was 7.4 years (standard deviation 0.9). The average level of disease control across the population remained fairly constant among respondents of different ages. Older children reported a slightly higher proportion of visits with complete control (0.4% increase in odds of complete control over each 6-month period; $p<0.0001$) and a slightly lower proportion of visits with poor control (0.1% decrease, $p<0.0001$), but there were no significant differences in the proportion of respondents reporting good and limited control with increasing age.

Ordered logistic regression that accounted for repeated measures among patients showed a 2% increase in the odds of better disease control with each 6-month period ($p=0.001$). This association became insignificant when we excluded the baseline visit. Only 52% of the population ever reported a 6-month period of complete control, and 683 or 34% achieved at least one period of remission. Among these patients, 331 or 48% subsequently reported disease activity or medication use, suggesting that a minority of children outgrew their disease during the period of observation.

The average level of disease control was not associated with age at enrolment, providing some reassurance that the persistent nature of eczema in this population was not due to selection of older children with more recalcitrant disease.
These data contribute to sparse literature on the temporal nature of eczema disease activity among older children and teens. The average level of disease control across the population remained fairly constant and the majority of subjects did not appear to outgrow their eczema.

PP01

A protocol for a randomised controlled trial to determine whether application of emollient from birth can prevent eczema in high risk children (BEEP Trial).

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There is a growing interest in skin barrier enhancement using emollients as a means of preventing skin disease. The aim of the BEEP trial is to determine whether advising parents to apply emollient to their child for the first year of life in addition to standard skin care advice can prevent eczema developing compared to standard skin care advice only. The trial will also show whether the intervention can delay the onset, or reduce the severity of eczema and prevent associated conditions such as asthma.
The BEEP trial will take place in the UK, starting mid 2014. It will be a pragmatic, parallel group, multicentre, assessor-blind, randomised controlled primary prevention trial testing the effectiveness of full body daily application of emollient for the first year of life. Parents in both groups will receive general advice on best practice skin care. A total of 1282 term infants at high risk of developing eczema (parent or full sibling with asthma, eczema or allergic rhinitis) will be enrolled. Parents will be approached and consented during pregnancy or immediately after giving birth, and will commence the study as soon as possible after the

baby is born. The primary outcome will be assessed at 2 years of age by research nurses blinded to group allocation. Parents will complete questionnaires at 3, 6, 12 and 18 months, and thereafter annually until the child's 5th birthday.

The primary outcome will be the difference between the two groups in the proportion of infants who have developed eczema over the last year measured at 2 years of age (defined as meeting the UK working party refinement of Hanifin and Rajka criteria). Since parents are unblinded, this objective, assessor-blinded measure was chosen to minimise information bias. Secondary outcomes will include parental report of eczema, the proportion of infants with visible eczema at 2 years, time to onset of eczema, severity of eczema measured by EASI and POEM, rate of skin infections and accidental slippages due to application of skin products, parental reported wheezing, quality of life, and cost effectiveness. A stratified subgroup analysis will look at the effect of mutations in the gene encoding filaggrin. Long term outcomes will determine whether any effect is sustained into later childhood (up to 5 years of age). This trial will provide clear and straightforward guidance for health professionals about whether they should be recommending emollients for the prevention of eczema in infants at high risk.

PP02

Complementary and alternative medicines and childhood eczema: A US population-based study

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The prevalence of complementary and alternative medicine (CAM) use in US children with eczema is unknown. Further, it is unknown whether CAM use in the US is associated with higher eczema prevalence.

We analyzed data from the 2007 National Health Interview Survey that included a nationally representative sample of 9,417 children ages 0–17 years to determine the rates of CAM in children with eczema and determine whether CAM use for other disease is associated with eczema prevalence.

Overall, 46.9% (95% confidence interval: 45.6–48.2%) of children in the US used ≥1 CAM, with 0.99% (0.28–1.71%) using CAM specifically to treat their eczema, including herbal

therapy (0.46%), vitamins (0.33%), Ayurveda (0.28%), naturopathy (0.24%), homeopathy (0.20%) and traditional healing (0.12%). Several CAM used for other purposes were associated with increased eczema prevalence, including herbal therapy (survey logistic regression; adjusted odds ratio [95% CI]: 2.07 [1.40–3.06]), vitamins (1.45 [1.21–1.74]), homeopathic therapy (2.94 [1.43–6.00]), movement techniques (3.66 [1.62–8.30]) and diet (2.24 [1.10–4.58]), particularly vegan diet (2.53 [1.17–5.51]).
Multiple CAM are commonly used for the treatment of eczema in US children. However, some CAM may actually be harmful to the skin and be associated with higher eczema prevalence in the US.

PP03

Use of an emollient to control skin microbiome dysbiosis associated with atopic dermatitis

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Historically, skin microbiome has been studied using culture-based methods giving a biased view of easy to grow fungi and bacteria such as Staphylococus or Malassezia. Recent advances in DNA Sequencing technology have allowed a comprehensive picture of the bacterial community by providing both identification and relative abundances of all present species. This extraordinary scientific breakthrough paves the way to understand how bacterial communities interacts with the host immune system in specific skin disorders such as atopic dermatitis.

Skin microbiome is diversified across individuals. In an attempt to characterize the skin microbiome specifically associated with the clinical symptoms occurring in AD patients, we designed a study on 50 patients with AD (mean SCORAD 33 ± 6 at the inclusion) before and after a 3 month treatment period with an emollient. Skin swabs from lesional skin and from the proximal unaffected skin were sampled to extract, amplify and sequence the 16S rRNA bacterial gene to analyze the composition of bacterial communities.

We found that microbial community structures were dramatically different in AD patients compared to that of healthy subjects for a given zone. In AD patients, microbial diversity was decreased in unaffected skin areas and even more in lesional areas. In AD patients, we confirmed, as published, the greater proportion of *Staphylococcus* in affected areas. Besides,

we demonstrated that the skin commensal S. *epidermidis* specie was also overrepresented in lesional areas together with *S. haemoliticus*, newly characterized *Staphylococcus* specie in AD. The treatment with an emollient significantly reduced the level of all *Staphylococcus* species correlating with the improvement of the disease severity without any antibacterial therapy. The other main bacteria genera *Propionibacterium, Streptococcus, Alycyclobacillus* and *Corynebacterium* were more similar after treatment than before treatment confirming the capacity of the emollient to promote bacterial diversity associated with clinical benefits. Finally, the analysis by genus pointed out a new bacterium that has never been described before in this pathology.

We demonstrated that the comparison of affected and unaffected adjacent skin from the same atopic patient provides deeper insight onto the characterization of bacterial communities involved in the skin dysbiosis. These data support the importance of emollient in the management of atopic dermatitis and pave the way to new antimicrobial and promicrobial therapeutics for a wide array of skin diseases including AD and/or other chronic dermatosis.

PP04

The impact of atopic dermatitis on children and their families

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Background: Atopic dermatitis (AD) is a disorder affecting the quality of life (QOL) of children and their families. The author conducts counseling sessions for these children and their parents on the second Saturday of every month.

To assess the impact of AD on the QOL children and their families.

Using questionnaire instruments described by Lewis-Jones and Finlay, 4324 children with atopic dermatitis detected at an urban children's hospital (The CHILDS Trust Hospital, Chennai, India) were assessed along with their parents. The assessment was also done on normal siblings of the affected children.

There was noticed substantial negative impact on the QOL of the affected children, their parents, and siblings. The commonest among the affected children was the physical demand of scratching, among their parents was the financial burden towards treatment, and among their siblings was the social deficit of answering queries at school.

This study emphasizes the need for counseling and the utmost kindness and empathy to be shown to patients and their family members

References

1. Lewis-Jones MS, Finlay AY, Dykes PJ. Measurement of the impact of atopic dermatitis on infant's and their families lives. British Journal of Dermatology 1999; 141 (Suppl 55): 105-106.

PP05

Papular Urticaria - An early marker of Atopic March

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Background: Papular urticaria is a common and often annoying disorder manifested by chronic or recurrent papules caused by a hypersensitivity reaction to the bites of mosquitoes, fleas, bedbugs, and other insects.

To study the association of papular urticaria and atopy and its relevance with serum Ig E levels and 'absolute eosinophil count'

Five hundred consecutive children with papular urticaria were included in the study. History of atopy and features of cutaneous atopic disease complex was noted down. Serum Ig E and absolute eosinophil count was recommended in all patients.

Of included children, 70% had history of atopy, of which 24% had personal history of atopy and 46% had family history of atopy. Only ninety patients returned with Serum Ig E and absolute eosinophil count (AEC) results and all had elevated serum Ig E and AEC levels.

The history of atopy (both personal and family) should be viewed seriously in all papular urticaria children. This study reflects the atopic tendency in all papular urticaria patients and its early recognition and treatment will prevent the so called 'atopic march' in the child.

References

1.Neaville WA, Tisler C, Bhattacharya A; et al. Developmental cytokine response profiles and the clinical and immunologic expression of atopy during the first year of life. J Allergy Clin Immunol. 2003; 112(4):740-746.

2.Howard R, Frieden IJ. Papular urticaria in children. Pediatric Dermatol. May-Jun 1996; 13(3):246- 249.

PP06

Development of Korean Dermatological Association (KDA)-Questionnaire for Atopic Dermatitis

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Various diagnostic tools for atopic dermatitis (AD) have been proposed for both hospital- and community-settings. Hanifin and Rajka's criteria are regarded as a standard for AD diagnosis in hospital-setting, not for community-setting. The full-questionnaire-based ISSAC criteria have been world-widely used for epidemiological study, but there is a big discrepancy between ISSAC and clinical examination in AD prevalence. The U.K. Working Party's criteria have been validated world-widely in dermatological fields, showing a wide variation in validation results. This study was aimed to develop full-questionnaire-based diagnostic criteria for AD in community-setting.

We prepared questions by modifying Hanifin & Rajka's criteria and KDA's diagnostic criteria for AD (Choi *et al*, 2012). We classified questions into 3 subgroups: 1) major criteria, 2) localized eczemas of minor criteria, and 3) environmental factors of minor criteria. At first, we selected candidate questions with high sensitivity from the 3 subgroups by surveying in both hospital-based and community-based settings. Next, we performed 2nd-round study to validate our new questionnaire consisting of 2 major and 9 minor criteria in community-based setting.

Mandatory major criteria were 2 questions of 'recurrent attack of pruritic skin eruptions during last one year' and 'typical distribution of eczema'. Minor criteria were consisted of 9 questions of atopy history (1), localized eczemas (6), and environmental factors (2). Noticeably, 'atopy history' was included into minor criteria instead of major criteria due to its low specificity. 'Generalized skin dryness' and 'itch by sweating' were included into 2 environmental factors by their high sensitivities. '2 major + 2 minor or more' satisfied AD criteria among tested variable combinations of 2 mandatory major and 9 minor criteria. Next, validation of questionnaire was performed in community-based setting of elementary and preschool children, covering 4-12 years of ages. A cross-sectional survey on 1,395 children from elementary schools and 376 children from preschools revealed very satisfactory results

with high sensitivity (over 80%) and positive predictive value (over 74%), judging from dermatologists' clinical examination as a gold standard.

We propose new questionnaire-based diagnostic criteria for childhood AD, which show satisfactory outcomes in epidemiological surveys on childhood AD.

Reference

Choi WJ, Ko JY, Kim JW, *et al*. Prevalence and risk factors for atopic dermatitis: a cross-sectional study of 6,453 Korean preschool children. Acta Derm Venereol 2012, 92, 467-471.

PP07

The SCIN (Skin Care Intervention in Nurses) Trial. A cross-sectional feasibility study in Wales (Stage 1).

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To inform the implementation of a large-scale cluster randomised controlled trial in England.

The main objectives of the feasibility study are:

1. To assess better the numbers of eligible participants that can be expected in the main study and the response rates that are likely to be obtained
2. To test the main study protocol and instruments, including the photographic method of assessing the presence and severity of dermatitis (1,2)
3. To test the study intervention, a behavioural change programme (BCP)
4. To assess the baseline prevalence of hand dermatitis to refine power calculations for the main study
5. To test the feasibility of recruitment of participants through the occupational health (OH) service.

Key Steps of Research Procedure:

1. All student nurses who are due to start their first clinical placement, and who had a history of atopic disease or hand dermatitis and all intensive care unit (ICU) nurses at the study site will be identified by the lead OH clinician and Head of ICU respectively and invited to participate.
2. Participants will complete a baseline questionnaire and have their hands photographed and swabbed.
3. The student nurses will be offered the BCP and will be provided with a personal supplies of emollient

4. Optimal equipment for hand cleansing and drying will be placed on ICU along with dispensers of moisturising cream. ICU staff will be offered the BCP.
5. Two weeks after the BCP is offered, participants will be asked to complete a second questionnaire exploring their beliefs regarding dermatitis prevention behaviours and their views on the BCP.
6. The dermatologists will review any problems associated with the photographic method for assessing the severity of dermatitis.
7. A purposive sample of participants and the lead OH clinician will be interviewed to seek qualitative feedback on experiences and application of research tools and processes.

The main purpose of this presentation is to provide an overview of the SCIN trial feasibility study. It is likely that the SCIN research team will be able to provide delegates with a draft summary of key findings.

We anticipate the findings from this study will enhance our knowledge and understanding of research approaches that can be adopted by researchers to investigate hand dermatitis and dermatitis-prevention in healthcare settings.

References

1. Coenradds, P., Van Der Walle, H., Thestrup-Pedersen, k., Ruzicka, T., Dreno, B., De La Loge, C., Viala, M., Querner, S., Brown, T and Zultak, M (2005). Construction and validation of a photographic guide for assessing severity of chronic hand dermatitis. The British journal of dermatology, 152(2), pp. 296-301.

PP08

Dust Mite Avoidance for the Primary Prevention of Atopic Dermatitis: A Systematic Review and Meta-Analysis

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House dust mite (HDM) sensitization plays a controversial role in the development of atopic dermatitis (AD) leading some to recommend avoidance strategies to prevent AD onset. There are no systematic reviews to date addressing the impact of HDM avoidance in the primary prevention of AD. We aimed to evaluate whether HDM avoidance strategies reduce the risk of developing AD in high risk infants compared to randomized controls.

We performed a systematic review (PROSPERO# CRD42012003352) of randomized, controlled trials of high risk infants treated with a HDM avoidance intervention. Studies were obtained by searching MEDLINE, PubMed, Scopus, The Cochrane Library, and The Global

Resource of Eczema Trials databases. Additional studies were identified through hand search. Search terms included atopic dermatitis, eczema, atopy, dust, mite, pyroglyphidae, dermatophagoides, blomia, euroglyphus, randomized and controlled. Data were extracted independently by two reviewers using predefined criteria including measures of quality. Summary analysis was based on a random effects model. Seven randomized controlled trials met our inclusion criteria (total n=3040). Studies were largely unblinded but otherwise of reasonable quality. Dust mite avoidance provided no benefit in the prevention of AD (relative risk (RR)=1.00, 95% Confidence Interval (CI)=0.86 to 1.17, I^2=31%). A subgroup analysis of patients randomized to a multifaceted allergen avoidance approach also failed to demonstrate a statistically significant benefit (n=1600, RR=0.95, 95% CI=0.79 to 1.15, I^2=0%).

Dust mite avoidance strategies alone or in combination with additional allergen avoidance modalities do not decrease the risk of developing AD and should not be recommended for this purpose. The utility of HDM for the treatment of AD or for the prevention and treatment of asthma or seasonal rhinoconjunctivitis are outside the scope of this review.

PT01

Food hypersensitivity of adult atopic dermatitis in Korea

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It is known that atopic dermatitis (AD) is associated with food or environmental allergens and increased levels of serum IgE 1. However, the role of hypersensitivity to food antigens in adult patients has remained controversial 2. The aim of this study was to evaluate the relationship of food hypersensitivity and AD in 126 Korean adult subjects.

Patients with AD were assessed for a previous history of food hypersensitivity that aggravated the symptoms of AD. Blood samples were taken from the patients to measure food allergen specific IgE. Based on history and lab results, open oral food challenge tests were performed.

Of 126 subjects, thirty three (26.2%) claimed to have experienced previous food hypersensitivity. Both pork and wheat (n=5) took the lead, followed by beef (n=4) and crustaceans (n=3). Twenty (15.9%) had elevated levels of food specific IgE; with beef (n=7),

pork (n=6), milk and wheat (n=5) being the most common. However, when the open oral food challenge tests were conducted in 48 subjects with self-reported food hypersensitivity or elevated food specific IgE, only one showed positive reactions. This subject had a previous history of pork consumption exacerbating AD.

Though some subjects claimed to have a history of AD aggravation related to food intake, when an actual open oral food challenge test was conducted, corresponding results were rare in adults. Our study result shows only 0.79% positive reactions for adults. We could conclude that adults are less sensitive than children regarding the relationship between AD and food hypersensitivity.

References

1.Werfel T, Kapp A. Environmental and other major provocation factors in atopic dermatitis. Allergy 1998; 53: 731-9.

2.Worm M, Forschner K, Lee HH, Roehr CC, Edenharter G, Niggemann B, Zuberbier T. Frequency of atopic dermatitis and relevance of food allergy in adults in Germany. Acta Derm Venereol 2006; 86: 119-22.

PT02

Beneficial Effect on Dry Skin by Using Neutral Soap

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Xerosis is a medical term for dry skin or a skin condition with reduced hydration to below 10 % on the skin stratum corneum water contents, and one of major feature of atopic dermatitis[1]. Clinically, patients with xerosis may present rough skin with red spots and cracks and may experience pruritus. The aim of this study was to find out the beneficial effect on xerosis and the influence on skin barrier impairment after using the neutral soap.

A randomized, comparative clinical trial for effectiveness and recovery of skin barrier function of neutral pH bar soap (Dove®) compared with control bar soap (Ivory®) on the 60 patients with xerosis. The patients were analyzed by PGA (physician's global assessment of clinical response), clinical grading scores for visible dryness and tactile roughness

evaluations (5-point scale), transepidermal water loss (TEWL), and self-examination of itching (10cm VAS)
PGA was improved by 2 weeks of using neutral soap (Dove; 45.8%, Ivory; 29.2%). Visible dryness (5-point scale) was improved in both study groups. TEWL seemed more decreased in neutral soap group than in control group (Dove; 0.99±0.7, Ivory; 1.6±2.4), although statistically insignificant. Itch was decreased in both groups.
The experimental group's PGA score has improved compared to that of the control group. Additionally, skin dryness evaluation through visual observation and tactile sensation generally improved. Based on these results, the neutral pH of the mild soap and the DEFI technology are predicted to improve skin barrier function in xerosis patients.
References 1. Warner RR & Lilly NA. Correlation of water content with ultrastructure in the stratum corneum. In:Elsner P, Berardesca E & Maibach HI eds. Bioengineering of the skin: Water & the stratum corneum CRC press Inc. 3-12, 1994

PT03

Validation of a new multidimensional scale to evaluate itch in children from 6 to 14 years : Leuven itch scale childrens version (LIS-C) and parents version (LIS-P).

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As itch is a subjective finding, it is difficult to measure it, especially in children. A few years ago we developed the Leuven Itch Scale (LIS), which assesses seven aspects of itch: occurrence, severity, sensory perception, distress , location, consequences and treatment and provided evidence for its validity (1) . The measure has been developed for use in adults and is not suitable for children under the age of 14 years.
Aims

- to adapt the LIS questionnaire for child- and parent-report for children 6-14 years old
- to investigate the validity of the scale to measure itch
- to investigate parent-child agreement in the reporting of itch

1 Child- (LIS-C) and parent- (LIS-P)report versions were constructed by simplifying and adapting questions used in the original LIS. Pilot-testing in a small group of children with atopic dermatitis (AD) and their parents (n=14) was performed in order to evaluate the comprehensibility of the questions. When necessary questions were adapted.

2 The final questionnaires were administered to 48 children with AD and their parents.

a) Children who attended the out patient clinic and parents filled out the questionnaires independently.

b) For each patient, the severity of AD was measured by the same physician using the SCORAD

c) Spearman Rank correlations (ρ) were calculated for all comparisons.

- The children and parent versions of the scale had a good validity for content and internal structure. Floor and ceiling effects were not detected , what confirms that this scale can measure a range of clinical differences .
- Physician's ratings of the extent and severity of AD are significantly correlated with parent-reports of itch (ρ's ranging from .49 to .56, all $p<.0001$) but largely unrelated to child-reports of itch (ρ's ranging from .21 to .35, all $p>.01$).
- There is a moderate agreement between child- and parent-reports of frequency of itch ($\rho=.47$), severity of itch ($\rho=.41$) and distress accompanying itch ($\rho=.51$).

LIS-C and LIS-P are valid scales, to measure itch in children. The moderate correlation with the physicians scoring of severity of AD does not argue against the validity, as there is no linear relationship between itch and the severity of skin lesions. The finding that physician's ratings of AD severity have a higher correlation with LIS-P scores than with LIS-C scores was unexpected. A possible explanation is that ratings by parents are more strongly influenced by the objective clinical signs they perceive, whereas the ratings by children reflect their subjective feelings. This could also explain the moderate agreement between LIS-C and LIS-P.

References

1.Haest C, Casaer MP, Daems A, *et al*. .Measurement of itching: validation of the Leuven Itch Scale.

2.Burns. 2011;37:939-50.

PT04

Change in antimicrobial susceptibility of skin-colonizing Staphylococcus aureus in Korean patients with atopic dermatitis during ten-year period

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Staphyococcus aureus (*S. aureus*) has an important role as an aggravating factor in atopic dermatitis (AD) patients and *S. aureus* colonization show a strong correlation with clinical severity of AD. Recently, antibiotic resistance is increasing worldwide in the treatment of *S. aureus*, and especially methicillin resistant *S. aureus* (MRSA). We investigated to assess change of antimicrobial susceptibility of *S. aureus* in AD and investigate the difference regarding patients' age and disease duration.

AD patients were enrolled for the study at the times of their first visits to Pusan National University Hospital from September 2003 to August 2005 (group A) and from August 2010 to March 2012 (group B). We investigated the frequency of S. aureus colonization in skin lesion and anterior nares, and the change of antimicrobial susceptibility according to time period, age, and disease duration.

Of 295 AD cases, *S. aureus* were cultured from 215 (72.88%) in skin lesion and 153 (51.86%) in anterior nares. MRSA was isolated on 3.12% of skin lesion and 7.02% of anterior nares in group A, whereas 10.38% of skin lesion and 17.39% of anterior nares in group B. Regardless of age and disease duration, relatively low susceptibility (66.98 % in skin lesion and 60.87% in anterior nares) was shown against fusidic acid in recent years. Susceptibility to erythromycin was significantly higher in group B than group A.

There was no significant change of antimicrobial susceptibility of *S. aureus* except erythromycin during 10 years against our concern. However, relatively high MRSA isolation rate and fusidic acid resistance rate in recent AD outpatients suggest that community could be the source of antibiotic resistance *S. aureus* and give dermatologists a message of careful use of antibiotics.

References

1. Aly R, Maibach HI, Shinefield HR. Microbial flora of atopic dermatitis. Arch Dermatol 1977;113:780–782.

2. David TJ, Cambridge GC. Bacterial infection and atopic eczema. Arch Dis Child 1986;61:20–23.

PT05

Where have the children gone: Is infected childhood eczema still a primary care problem?

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Staphylococcus aureus is commonly found on eczematous skin. However, currently there is little evidence as to whether antibiotic treatment benefits children presenting in primary care with suspected infected atopic dermatitis (AD). Furthermore, there is limited evidence for the use of oral versus topical antibiotics. A Cochrane systematic review published in 20081, included 21 studies and 1018 participants, failed to find convincing evidence of benefit from antimicrobial interventions for people with clinically uninfected and clinically infected AD. The authors concluded that, "Further large studies with long-term outcomes and clearly defined participants are urgently required"[1]

CREAM is a double-blind, randomised controlled trial currently recruiting from general practices and dermatology units. Participating clinicians identify children with suspected infected eczema. If they are eligible, and their parent or guardian agrees, the child is randomised to receive one of three treatments: Oral antibiotic and placebo cream; oral placebo and antibiotic cream; or oral placebo and placebo cream. Participating children are followed-up over 12 months. A research nurse visits each child during the first 4 weeks and uses POEM, EASI, and other established questionnaires to assess the severity of eczema; quality of life for child and family; and healthcare consultations. Skin, nasal and oral swabs are taken. The child's parent / guardian is asked to complete a diary during the first 4 weeks to record symptom severity and use of medication. At 3 and 12 months, the parent / guardian repeats the questionnaires and swabs.

The study is aiming to recruit a total of 516 children over 12 months. However, 6 months into recruitment, has only recruited 58 participants.

Procurement of the Investigational Medicinal Product (IMP), contractual and regulatory issues, and problems with a computerised prompt system aimed to improve recruitment, have all resulted in delays in getting sites set-up and started. However, the main problem seems to be a lack of children presenting with suspected infected eczema.

Feedback from GPs suggest that these children seem to be consulting less frequently, possibly because those with more severe eczema are being referred to secondary care and

then being seen in community-based / nurse-led dermatology clinics for subsequent flares in their eczema.

Our poster will present updated recruitment figures and a more comprehensive analysis of the recruitment problems, as well as the results of interventions aimed at improving recruitment, such as expanding to include community-based or nurse-led dermatology clinics.

References

Birnie AJ, Bath-Hextall FJ, Ravenscroft JC, Williams HC. Interventions to reduce Staphylococcus aureus in the management of atopic eczema. Cochrane database of systematic reviews (Online) 2008(3):CD003871.

PT06

Patch testing in patients with recalcitrant atopic dermatitis

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Atopic dermatitis is a chronic eczematous skin disease. Most patients with atopic dermatitis are responsive to conventional treatment, such as topical steroids; however, some patients are refractory to the treatment. The influence of contact sensitivities on the course of patients with recalcitrant atopic dermatitis is not known. Therefore, we evaluated the positivity of patch testing in patients with recalcitrant atopic dermatitis.

We evaluated 24 patients with atopic dermatitis who had failed conventional therapy. Patch testing was performed in these patients with the Japanese standard series, metal series, topical medicaments, and cosmetics. The results were assessed after 48 and 72 hours according to the recommendations of the International Contact Dermatitis Research Group.

Positive patch testing with the allergens mentioned above was found in 7 patients. The results showed that 1 patient tested positive to topical steroids, 1 patient to topical antibiotics, 2 patients to cosmetics, 1 patient to perfume, 1 patient to p-phenylenediamine, 3 patients to thimerosal, 1 patient to Balsam of Peru, 1 patient to chromium, and 1 patient to mercury. Avoidance of topical medicaments, cosmetics, and hair dye improved skin symptoms in 5 patients. The relationship between the dermatitis and contact allergens was not clear in the remaining 2 patients showing positive patch testing.

This study shows that contact allergens, such as topical medicaments, cosmetics, and hair dye, can induce delayed-type hypersensitivity reactions and may be critical factors causing

eczematous lesions in patients with recalcitrant atopic dermatitis. Patch testing is useful in determining factors that contribute to the worsening of atopic dermatitis in patients.

PT07

Effect of Emollients Containing Vegetable-derived Lactobacillus in the Treatment of Atopic Dermatitis Symptoms : Split-Body Clinical Trial

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Atopic dermatitis (AD) patients suffer from xerosis. Proper skin care, including the use of emollients, may help improve xerosis and minimize disease exacerbation. Lactobacillus sakei probio 65, isolated from the Korean vegetable-based product kimchi, can decrease IL-4 and Ig-E levels and inhibit Staphylococcus aureus. Moreover, it has reportedly shown positive dermatological effects in both animal and clinical studies.

To compare the effects of an emollient that contains Lactobacillus (treated) with a normal emollient (control) on AD.

This double-blind, randomized, split-body clinical trial involved 28 patients with AD. The patients applied the Lactobacillus-containing emollient on one side of their body and the control emollient on the other side twice daily for 4 weeks. Trans-epidermal water loss (TEWL) and skin capacitance were evaluated and investigator global assessment (IGA) and the visual analogue scale (VAS) were administered on weeks 0, 1, 2, and 4.

The treated sides had significantly lower TEWL and VAS values and significantly higher skin capacitance values over time than the control sides.

Topical application of Lactobacillus-containing emollients may improve the skin permeability of patients with AD.

References

1. Woo SI, Kim JY, Lee YJ, Kim NS, Hahn YS. Effect of Lactobacillus sakei supplementation in children with atopic eczema–dermatitis syndrome. Ann Allergy Asthma Immunol. 2010;104:343-348

2. Joo SS, Won SS, Nam SY, Kim YB, Lee YC, Park SY, Park HY, Hwang KW ,Lee DI. Therapeutic Advantages of Medicinal Herbs fermented with Lactobacillus Plantarum. in Topical Application and its Activities on Atopic Dermatitis. Phytother Res. 2009;23: 913-919.

PT08

Inappropriate amount of topical tacrolimus is applied in Korean patients with eczema

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To investigate the frequency of application and amount of topical tacrolimus used during the treatment of eczema in Korean patients

A total of 165 eczema patients were included in this study. The number of application per day during the first and second week was inquired. The amount of tacrolimus ointment used for 2 weeks was also assessed. The standard amount of used tacrolimus was calculated by the finger tip unit (FTU, 1 FTU = 0.5 g for 2% of body surface area).

After 2 weeks of treatment, mean number of application was 24.3 times ± 7.6, whereas, the instructed number of application was 28 times. In the number of application, 120 (72.7%) and 102 (61.8%) of patients followed the prescription at the first and second week, respectively. On the contrary, mean amount of application per 2% of body surface area was 0.56 g ± 0.60. Only 37 (22.4%) patients applied between 80% and 120% of standard amount.

Korean patients with eczema tend to apply topical tacrolimus less frequently and moreover in fewer amounts. Therapeutic education and clear instructions regarding not only the frequency but also the amount of application are needed to improve therapeutic outcome during topical treatments.

References

1.Devaux S, Castela A, Archier E, Gallini A, Joly P, Misery L, *et al*. Adherence to topical treatment in psoriasis: a systematic literature review, J Eur Acad Dermatol Venereol 2012; 26:61-67

2.Storm A, Benfeldt E, Andersen SE, Serup J. A prospective study of patient adherence to topical treatments: 95% of patients underdose, J Am Acad Dermatol 2008;59:975-980

PT09

Successful Treatment of Lichen Spinulosus in Atopic Dermatitis Patient with Topical Tacrolimus

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Lichen spinulosus is an uncommon idiopathic cutaneous eruption characterized by follicular keratotic spiny papules that are grouped in large patches. There has been few reports of lichen spinulosus with atopic dermatitis.

A 9-year-old boy presented to our clinic with an asymptomatic skin eruption on chin that appeared suddenly few month ago when his atopic dermatitis flared up. Skin biopsy specimens demonstrated a keratotic plug in the follicular infundibulum, mild epidermal papillomatosis and spongiosis. First, we applied a topical tretinoin but he suffered from stinging sensation, dryness and aggravation of atopic dermatitis on applied part. Therefore, we elected to use topical tacrolimus daily to treat atopic dermatitis lesions.

Both atopic dermatitis and lichen spinulosus lesions improved after 2 weeks of treatment. After 4 weeks, the lesions had cleared almost completely.

So we report that lichen spinulosus is associated with atopic dermatitis and tacrolimus is effective in treating not only atopic dermatitis but also lichen spinulosus.

References

1. Breithaupt AD, Alio A, Friedlander SF. A comparative trial comparing the efficacy of tacrolimus 0.1% ointment with Aquaphor ointment for the treatment of keratosis pilaris. Pediatr Dermatol. 2011 Jul-Aug;28(4):459-60.

2. Boyd AS. Lichen spinulosus: case report and overview. Cutis. 1989 Jun;43(6):557-60.

PT10

Effect of Topical Application of Quercetin on Atopic Dermatitis in NC/Nga Mice

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Atopic dermatitis (AD) is the most common and relapsing allergic disease of the skin. It is characterized by pruritic and eczematous skin lesions. AD is caused by the complex interaction of genetic and environmental factors that result in immune system dysregulation. Type 2 helper T (Th2) cells show the increased production of IL-4, which stimulates plasma cells to increase IgE production as well as promotes further Th2 cell development in AD. Recent studies have revealed IL-4, IFN-γ produced by Th1 cells is also observed at both mRNA and protein levels in the lesions of AD patients. These reports suggest that both Th1

and Th2 subsets contribute to the pathogenesis of AD. Up to the present, AD has been regarded as an intractable dermatologic disorder, those treatment modalities mainly include corticosteroid, anti-histamines and immune suppressants. Due to the side effects developed during the therapy and the recurrence after cessation of the therapy, these treatments had limited value as therapeutic agents. It is imperative that alternative and compensatory agents be developed promptly to treat this condition. Recently, phytochemical therapeutics has been tried as potential therapeutic agents for AD. Quercetin-3-O-α-L-rhamnopyranosyl-2''-gallate (QRG) is one of the flavonol glycoside galloylate isolated from the leaf of Acer ginnala Maxim and is known to exert several anti-oxidative and anti-inflammatory activites. According to the previous study, QRG inhibited proinflammatory cytokine expression through modulation of the activation of NF-kB in human cell adn downregulated eosinophil and IL-5 production in murine model of asthma. In addtion, it also showed that inhibitory effect of QRG and tannic acid on angiogenesis and TARC expression in NC/Nga mice. In the present study, we investigated the anti-inflammatory and anti-immunological effects of QRG and AD in NC/Nga mice.

References

1. Schultz Larsen F. The epidemiology of atopic dermatitis. Monogr Allergy. 1993;31:9-28.
2. Thepen T, Langeveld-Wildschut EG, Bihari IC, van Wichen DF, van Reijsen FC, Mudde GC, *et al*. Biphasic response against aeroallergen in atopic dermatitis showing a switch from an initial TH2 response to a TH1 response in situ: an immunocytochemical study. J Allergy Clin Immunol. 1996;97(3):828-37.
3. Chen L, Martinez O, Overbergh L, Mathieu C, Prabhakar BS, Chan LS. Early up-regulation of Th2 cytokines and late surge of Th1 cytokines in an atopic dermatitis model. Clin Exp Immunol. 2004;138(3):375-87.
4. Grewe M, Bruijnzeel-Koomen CA, Schopf E, Thepen T, Langeveld-Wildschut AG, Ruzicka T, *et al*. A role for Th1 and Th2 cells in the immunopathogenesis of atopic dermatitis. Immunol Today. 1998;19(8):359-61.
5. Spergel JM, Mizoguchi E, Oettgen H, Bhan AK, Geha RS. Roles of TH1 and TH2 cytokines in a murine model of allergic dermatitis. J Clin Invest. 1999;103(8):1103-11.
6. Moharram FA, Marzouk MS, Ibrahim MT, Mabry TJ. Antioxidant galloylated flavonol glycosides from Calliandra haematocephala. Nat Prod Res. 2006;20(10):927-34.
7. Noh SU, Cho EA, Kim HO, Park YM. Epigallocatechin-3-gallate improves Dermatophagoides pteronissinus extract-induced atopic dermatitis-like skin lesions in

NC/Nga mice by suppressing macrophage migration inhibitory factor. Int Immunopharmacol. 2008;8(9):1172-82.

PT11

Measurement properties of measures of health-related quality of life (HrQoL) measurement instruments for atopic eczema: protocol for a systematic review

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The Harmonising Outcome Measures in Eczema (HOME) initiative defined clinical signs, symptoms, specific quality of life and long-term control of flares as the core outcome domains to be applied in all future atopic eczema trials. It is unclear which measurement instruments are appropriate to assess health-related quality of life (HrQoL) in atopic eczema. Therefore, we outline a plan of research to systematically assess measurement properties of HrQoL measurement instruments specific for atopic eczema.

A systematic literature review of the measurement properties of dermatology specific and atopic eczema specific HrQoL measures will be performed. A study will be included if (a)there is a full text paper, (b)the paper is published in English, (c)the measurement instrument is self-reported (d)it concerns the development and/or validation of the measurement properties of a dermatology-specific or eczema-specific HrQoL measurement instrument and (e)it is carried out in a population of atopic eczema patients. Articles that report on a measurement instrument as an outcome in a clinical trial without any explicit validation are not considered eligible. A systematic literature search will be performed in PubMed and in EMBASE. The highly sensitive search filter for finding studies on measurement properties as suggested by the COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) group (www.cosmin.nl) will be used to identify articles. The systematic electronic search will be supplemented by handsearching of reference lists of included studies and those who inaugurated an instrument will be contacted to identify further studies. Relevant data from all included articles will be summarized in evidence-tables. Both assessment of study eligibility and data abstraction will be performed independently by two reviewers.

The COSMIN checklist (2) will be used to evaluate the methodological quality of included studies. An overall quality score is obtained for each measurement property separately. Next, predefined criteria will be used to rate the quality of each measure. These criteria are in accordance with the OMERACT filter which has been adopted by the HOME initiative. If several studies exist for one measure, findings will be synthesized by combining them, based on number and methodological quality of the studies and consistency of results. For each instrument identified in the review, a standardized recommendation for usage or required future validation work will be made depending on the scale quality and on the methodological quality of included studies.

References

1.Schmitt J, Spuls P, Boers M, Thomas K, Chalmers J, Roekevisch E, *et al*. Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. Allergy. 2012;67(9):1111-7

2.Mokkink LB, Terwee CB, Knol DL, Stratford PW, Alonso J, Patrick DL, *et al*. The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: a clarification of its content. BMC Med Res Methodol. 2010;10:22.

PT12

The impact of psychological stress on adolescent case with atopic dermatitis: questionnaire-based retrospective assessment

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Recently, the number of adolescent and adult case with atopic dermatitis is becoming increasingly common. However, underlying reason for this phenomenon remains obscure. To address this issue, we should explore the aggravating cause of this age-group with atopic dermatitis. Of particular interest was how stress contributes to the disease-aggravation.

First-year students at Osaka University were asked about allergic diseases using postal interview sheets. Personal and family histories of doctor-diagnosed allergic diseases, the UK diagnostic criteria for atopic eczema, clinical courses, aggravating factors, presence or absence of stress, type of stress, and personal coping ability against stress (Brief COPE) were included in the questionnaires.

The mean age of the first-year students (n=3,037) was 18.3±0.46 years (male:2066, female 971). The prevalence ratio of adolescent atopic dermatitis diagnosed by the UK criteria was about 10.2%. Multivariate logistic analysis revealed that psychological stress significantly raised the risk of protracted atopic dermatitis. The adolescent cases with atopic dermatitis feel their skin symptoms, external application of drugs, anxiety about disease, and hospital visit to be stress. Regarding the measurement of coping ability, adolescent cases tended to be capable in ability of contiguity and acceptance to stress.

Stress was major aggravating factor of adolescent case with atopic dermatitis. We should make an effort at stress reduction.

References

Kijima A, Murota H, *et al*. Prevalence and impact of past history of food allergy in atopic dermatitis. Allergol Int. 2013;62:105-12.

PT13

A 25-Year Overview Of The Atopic Dermatitis Outpatient Clinic- University Of Sao Paulo Medical School, Brazil.

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We performed an epidemiological profile of AD patients from our outpatient clinic, from the University of Sao Paulo, Brazil, in the last 25 years. Few data on patients with atopic dermatitis have been reported in Brazil.

Our analysis included 2,440 individuals diagnosed as AD (according to Hannifin and Rajka´s criteria). Gender distribution revealed: 1,272 females (52%) and 1,168 males (48%), as seen in the literature. Concerning ethnics, 71% of these individuals referred themselves as white (1,721), 20% as mulatto (493), 7% as African-Brazilians (169), 2% as Asians (37), one as Indian (native Brazilian), and 1% (19) did not mention their ethnicity. Age of first appointment varied from 3 months to 87 years old (median age=12). At first appointment, 342 patients were above 18 years old (14%). The number of recorded appointments varied from 1 to 91 (mean of 8/patient). In the last 10 years, 396 (30%) of 1,353 patients seen in our clinic were above 18yo. Among this group, we selected 89 adults (55 females and 34 males)

who agreed to participate in the study. Analyzed parameters included: severity index (SCORAD), IgE serum levels, eosinophil blood levels and the association of AD with other atopic diseases as asthma and rhinitis.

Our results showed: mean SCORAD of 41.94 (range: from 2 to 100.2); IgE serum levels from 92 to 89,800 UI/ml (mean 18,512 UI/ml) and eosinophil blood count from 0.1% to 32.6% (mean 9.6%). When considering association of AD with other atopic manifestations, we found nine patients (10%) with exclusive skin involvement, 18 (20%) with associated rhinitis, 19 (22%) with asthma, and 42 (48%) with history of both asthma and rhinitis. We found positive correlation between IgE serum levels and eosinophilia with disease severity (SCORAD), but no relation between IgE and respiratory disease. It is relevant to point out that our AD clinic belongs to a tertiary hospital, to where patients are referred from either primary or secondary care, justifying high SCORAD, high levels of circulating IgE and eosinophilia.

AD is a chronic disease that usually initiates in early childhood. It may be long-lasting, and reach adulthood, usually in association with respiratory atopic disease. The correct and early diagnosis of AD, education measures and possible prevention actions could be tools to improve disease severity and its long course.

References:

1.Orfali RL, Shimizu MM, Takaoka R, Zaniboni MC, Ishizaki AS, Costa AA, et al. Atopic dermatitis in adults: clinical and epidemiological considerations. Rev Assoc Med Bras. 2013;59(3):270-5.

2.Williams HC, Grindlay DJ. What's new in atopic eczema? An analysis of systematic reviews published in 2007 and 2008. Part 1. Definitions, causes and consequences of eczema. Clin Exp Dermatol. 2010;35(1):12-5.

PT14

How to measure clinical signs of atopic dermatitis? A systematic review and recommendation

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Currently there is a lack of standardization of outcome measures in atopic dermatitis (AD)-trials which hampers evidence-based communication. The international Harmonizing Outcome Measures for Eczema (HOME)-initiative defined clinical signs, symptoms, quality of life and long term control as core outcome domains for AD trials (1; 2).

We conducted a systematic review on measurement properties of measure instruments for clinical signs of AD, aiming to provide evidence-based recommendations for the measurement of clinical signs in AD-trials. Validation studies on instruments measuring clinical signs of AD were graded regarding their validity, reliability, sensitivity to change/responsiveness, and interpretability. Overall scale quality was assessed based on predefined criteria.

Out of sixteen instruments identified to assess the clinical signs of AD, the Eczema Area and Severity Index (EASI) and the Severity Scoring of Atopic Dermatitis Index (SCORAD) are the best validated instruments. The EASI has adequate validity, responsiveness, internal consistency, and intra-observer reliability, intermediate inter-observer reliability but unclear interpretability and feasibility. The SCORAD has adequate validity, responsiveness, inter-observer reliability, interpretability and unclear intra-observer reliability.

EASI and SCORAD are the best instruments to assess clinical signs of AD. The other 14 instruments
identified and critically appraised are (currently) not recommended due to unclear or inadequate measurement properties.

References

1.Schmitt J, Langan S, Stamm T, Williams HC. Core outcome domains for controlled trials and clinical
recordkeeping in eczema: international multiperspective delphi consensus process. J Invest Dermatol 2011; 131(3):623-30.

2.Schmitt J, Spuls P, Boers M, Thomas K, Chalmers J, Roekevisch E *et al*. Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. Allergy 2012; 67(9):1111-7.

PT15

Creating new solutions for the patient with atopic dermatitis

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Atopic dermatitis (AD) is a chronic skin disease with a complex pathogenesis, increasing prevalence and difficult management. On a recent survey conducted on the Internet by the Brazilian Atopic Dermatitis Association, nearly 80% of patients suffering with AD showed dissatisfaction with their treatment. The common perception is that doctors do not know how to manage the disease. Patients complain that doctors do not show a clear knowledge of the disease and fail to provide any emotional support. Consequently patients report seeing many doctors to treat their condition. There is a strong need to create new solutions for the patient with AD.

Design thinking is a creative innovation methodology originally used by designers to enhance the look and functionality of products. More recently, this process has also been used to tackle complex social and healthcare problems. Consequently, we have started to use design thinking principles (empathy, collaboration and experimentation) to improve the treatment of patients with AD.

Design thinking is a human-centered approach that, when applied to healthcare, involves listening closely to patients' needs and problems. These problems may include common, but not always acknowledged complaints brought on by the disease, such as compulsive itching, prejudice, depression and cost of medication. Through a series of established steps, new solutions to improve the quality of care can be created. These solutions can include creation of support groups for patients and families, more collaboration among healthcare professionals and more scientific events dedicated to AD. Design thinking allows effective solutions to appear from patients themselves rather than being imposed by the healthcare professional. It also involves working in collaboration with a multidisciplinary team that includes patients and their families, doctors, psychologists, nurses, social workers and others.

Contrary to the belief that medication alone can treat and solve all problems, design thinking shows that in order to be effective, the management of AD must constitute a much broader approach, encompassing emotional, social, cultural and financial factors.

References

1.Brown T, Change by Design: How Design Thinking Transforms Organizations and Inspires Innovation, HarperCollins (2009)

2.Brown T, Wyatt J, Design Thinking for Social Innovation, Stanford Social Innovation Review, 8:1 (2010)

PT16

BATHE – Bath Additives in the Treatment of Childhood Eczema

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Emollients form the mainstay of treatment for childhood eczema. There are three methods of application: leave-on emollients (emollients applied to the skin and left to soak in); soap substitutes (emollients used instead of soap); and bath emollients or additives (oil and/or emulsifiers dispersed in the bath).

A systematic review has revealed no convincing evidence for the use of bath emollients in the treatment of eczema (1), yet they are widely prescribed at a cost of over £16m per year to the UK National Health Service (1) and represent 38% of the total costs of eczema treatments prescribed to preschool children in the UK (2). There is widespread clinical consensus on the need for leave-on emollients and soap substitutes, but less certainty regarding the benefits of bath emollients.

BATHE is a pragmatic randomised controlled trial based in UK general practice starting in late 2014. We plan to recruit 423 children aged 1 to 12 years who have a diagnosis of atopic eczema in their GP record. We will recruit through GP mail-out and opportunistic recruitment. We will randomise participants to 2 groups: (1) standard eczema care without bath emollients; (2) regular bath emollients prescribed by the GP in addition to standard eczema care.

Our primary outcome measure is well-controlled weeks assessed by administering POEM (Patient-Oriented Eczema Measure) questionnaires weekly for 16 weeks. Secondary outcomes include: number of eczema exacerbations resulting in a primary healthcare consultation over 1 year; eczema severity over 1 year assessed by monthly POEM scores; disease-specific quality of life, measured by DFI (Dermatitis Family Impact); generic quality of life as measured by the Child Health Utility 9D (CHU 9D) and the Health Utility Index II (HUI2); type (strength) and quantity of topical steroid/calcineurin inhibitors prescribed, measured by GP record review at 12 months.

This trial should answer the question about the clinical and cost-effectiveness of including bath emollients in the standard management of atopic eczema in children.

References

1.Drug & Therapeutics Bulletin Bath emollients for atopic eczema: why use them? Drug & Therapeutics Bulletin 2007; 45:73-5

2.Emerson RM, Williams HC, Allen BR. What is the cost of atopic dermatitis in preschool children? British Journal of Dermatology 2001; 144(3):514-22

PT17

Choice Of Moisturiser in Eczema Treatment (COMET): feasibility study protocol

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Eczema is the most common inflammatory skin disease of childhood. It can have a significant impact on the quality of the affected child's life and that of their family. Moisturisers (emollients) are the mainstay of treatment but despite their importance, there is a weak evidence to guide which should be used first or even how often. More information on emollient effectiveness emerged as one of the top four priorities (shared by patients/carers and clinicians) in a recent prioritisation exercise of treatments for eczema (Batchelor *et al* 2013)

COMET is an NIHR Research for Patient Benefit funded study to determine the feasibility of a large trial to answer the research question "What is the most clinically and cost effective primary emollient to prescribe for infants with eczema?" A feasibility study is necessary because there are a number of key uncertainties, including: optimal means of patient recruitment; the choice of interventions; and the feasibility of long-term patient-reported data collection.

We aim to recruit 160 children aged between 1 month and 3 years of age with eczema via their general practice. Participants will be randomised to one of four commonly used treatments (Aveeno®, Diprobase®, Doublebase® or Hydromol®) which represent the different classes of emollient (lotion, cream, gel and ointment respectively), and followed-up for 3 months. During this time, carers will be asked to complete daily diaries about their child's symptoms, use of emollients and other treatment for eczema; and a researcher (blinded to the treatment) will independently assess the severity of eczema at monthly

intervals. As part of the study, an iOS/Android "app" will be developed and the completeness of participant data collected by this route compared with conventional paper diaries.

In addition to establishing the feasibility of the definitive study, we will undertake important methodological work to establish the minimal clinically important differences (MCID) of a biophysical (corneometry) and an objective clinical (EASI) measure of eczema severity. Establishing the MCID thresholds (and hence what proportion of patients can be considered "responders") will aid the interpretation of previous studies of emollients and inform future trials of eczema treatments.

References

Batchelor JM, *et al*. "The Eczema Priority Setting Partnership: a collaboration between patients, carers, clinicians and researchers to identify and prioritize important research questions for the treatment of eczema." British Journal of Dermatology 2013 168(3): 577-582.

PT18

What is the ideal proactive therapy for atopic dermatitis?

22 cases of severe atopic dermatitis who finally achieve disease-free by accurate proactive therapy combined with monitoring of serum biomarker, thymus and activation-regulated chemokine (TARC) levels

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Recently proactive therapy with topical corticosteroid (TCS) or topical calcineurin inhibitor shows good evidence for preventing flares and long-term control of atopic dermatitis. This strategy depends on the fact of existence of subclinical inflammation or skin-barrier defect of normal-looking atopic dermatitis skin. However no one knows precise way of ideal proactive therapy at this time. What is the treatment goal? How long intermittent application should be continued? What strategy is the best way? And so on.

In Japan, serum TARC level has been commercially measured under health insurance support since 2008 as a highly sensitive biomarker of atopic dermatitis. We can speculate the intensity of subclinical Th2-type inflammation by this biomarker.

Severe Atopic dermatitis patients who have been treated by our topical “tight control” strategy were reviewed. “Tight control” strategy consists of three steps. Firstly all skin and serum TARC level is normalized by intensive TCS treatment within 1 month. Secondly almost same topical treatment is continued maintaining normal serum TARC level for 1 to 2 months. Thirdly frequency of TCS application was gradually reduced with monitoring serum TARC level below 600 pg/ml. The patients who have achieved ideal treatment goal that is disease-free with only emollient in two years were retrospectively investigated

22 cases who finally reached to ideal goal were observed. Despite of their initial severe skin lesions, normal skin appearance treated by emollient with only minimal anti-inflammatory drugs has been maintained for more than 6 months. Their initial abnormally high serum TARC level (1124～62610 pg/ml) were rapidly normalized and maintained below 600pg/ml by our “tight control” topical treatment.

More accurate proactive therapy with monitoring of subclinical inflammation by serum TARC level has a possibility for better outcome.

References

1. Kataoka Y TARC as a clinical biomarker in atopic dermatitis: J Dermatol, in press

2. Kakinuma T, Tamaki K. TARC in atopic dermatitis: Serum TARC level is closely related with disease activity. J Allergy Clin Immunol 2001；107：535-41.

PT19

Change of mothers’ anxiety about corticosteroids after parental education on atopic eczema

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The anxiety of using corticosteroids leads poor adherence of patients. Providing accurate information in patient education is considered to relieve the anxiety about corticosteroids. Parents of children with atopic eczema not only have the anxiety of using topical corticosteroid to their children but also have the anxiety about their children’s future. The aim of this study was to evaluate these anxieties before and after parental education.

Between September 2011 and August 2012, we asked mothers with eczema children to answer the same questionnaires before and after the physical examination and one-hour

education session at the first visit to allergist clinic of National Center for Child Health and Development. At the next visit within 2 months, they answered the questionnaire again. We evaluated the anxiety of using topical corticosteroid to their children (DIRECT anxiety) and about their children's future (FUTURE anxiety) with visual analogue scales (0 to 100), and eczema severity with Patient-Oriented Eczema Measure (POEM) on the questionnaire. Participants were 277 mothers and the mean age of their children was 4.6 years. The scores of DIRECT and FUTURE anxiety were decreased after education from 54.8 ± 29.5 (mean ± SD) and 62.8 ± 34.0 to 27.6 ± 25.0 and 38.5 ± 30.7, respectively ($P<0.01$, $P<0.01$). The improvement was remained on the score of 26.7 ± 27.2 and 30.0 ± 28.3 at the next visit. POEM improved from 10.2 ±7.5 to 2.9 ±3.7 at the next visit. The overall decreases of DIRECT and FUTURE anxiety scores were 36.7 and 31.3 points in POEM-improved parents, otherwise those were 17.7 and 15.9 points in POEM-unimproved parents ($P<0.01$, $P<0.01$). Parents' anxiety about corticosteroids was relieved immediate after their educated. The failure of acute eczema treatment was associated with reduction of the education effect.

References

Charman CR *et al.* Arch Dermatol. 2004 Dec;140(12):1513-9.

PT20

Histamine-free diet in adult patients with atopic dermatitis

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In adult patients with atopic dermatitis (AD), causal relationship between food and disease exacerbation is relatively weak compared to childhood patients.[1] However, there are many patients who report food-related aggravation of their skin symptoms, and some of them may have histamine intolerance.[1] There have been a few studies which presented higher basal plasma histamine concentrations in patients with AD than in healthy controls.[2] The aim of this study was to evaluate the role of ingested histamine in adult AD and to investigate the effect of histamine-free diet in adult patients with AD.

Adult patients with AD (18 years old or more) and healthy controls were enrolled. Foods with high amounts of histamine were prohibited to all patients for 4 weeks. No diet restriction was done to the healthy controls. Eczema area and severity index (EASI) and degree of pruritus

using visual analogue scale (VAS) were evaluated. Plasma histamine levels and DAO activity were determined and compared with those of the control group.
Seventeen adult patients were recruited and among them, 12 completed the 4 weeks of histamine-free diet. The basal plasma histamine levels in patients and healthy volunteers showed no significant difference. The basal DAO activity was significantly higher in patients compared to that of the healthy controls. There was no significant difference in plasma histamine level after the histamine free-diet. Also, DAO activity did not change after the histamine-free diet. Likewise, EASI and VAS score was similar before and after the diet. Ingested histamine might be unrelated with AD severity and histamine-free diet is unhelpful for adult patients with AD.

1. Chang DS, Seo SJ, Hong CK. Patch test and specific IgE level with food antigens in atopic dermatitis patients. Korean J Dermatol 2002;40:1028-1034
2. Maintz L, Novak N. Histamine and histamine intolerance. Am J Clin Nutr 2007;85:1185–1196.

PT21

Topical tacrolimus for atopic dermatitis: a systematic review.

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Atopic dermatitis is a chronic inflammatory skin condition that affects both children and adults, and has an important impact on the quality of life. Topical corticosteroids are the first-line therapy, however, they can be associated with significant adverse effects when used chronically. Topical tacrolimus might be an alternative to this problem, hence this review, which aims to establish more accurate guidelines for its use, as well as to further assess its safety.

We searched randomized controlled clinical studies analyzing patients with moderate to severe atopic dermatitis (both pediatrics and adults) using topical tacrolimus at any dose, course duration, and follow-up time compared to other active treatments on the following databases up to July 2013: the Cochrane Skin Group Specialized Register, CENTRAL, MEDLINE, EMBASE and LILACS. A separate search for adverse effects of topical tacrolimus in non-RCTs was undertaken on MEDLINE and EMBASE on 30 July 2013.
A total of 24 papers reporting 21 studies were included in this review (5981 participants). We analyzed as primary outcomes: physician's assessment and participant's self assessment of global response of improvement; occurrence and severity of adverse effects. As secondary outcomes: affected body surface area (BSA); eczema area and severity index (EASI); quality of life.
Tacrolimus 0.1% showed a superior efficacy than other treatments, except for moderate-to-potent corticosteroids, where no significant difference was found in most of the analyses. Tacrolimus 0.03% was superior to mild topical corticosteroids and pimecrolimus and inferior to tacrolimus 0.1% and also had no significant difference when compared to moderate-to-potent corticosteroids. The variability of drug doses, outcomes and follow-up periods made it difficult to carry out a meta-analysis, but subgroup analysis was done.
Burning and pruritus were more frequent in the calcineurin inhibitors users and no significant difference was found in the occurrence of skin infection. Symptoms were mild and transient. Serious adverse events were rare and were considered not to be related to treatment in most instances. No cases of lymphoma were noted on the trials. Safety analysis was also done on non-RCT, observational and retrospective studies, as narrative analyses.
Tacrolimus ointment is safe and effective for moderate to severe AD in children and adults. To date there is no evidence to support FDA´s warning on topical tacrolimus risk of malignancies.
References
1. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration. Available from www.cochrane-handbook.org, 2011
2. Koo, J. Y.; Fleischer, A. B. Jr.; Abramovits, W.; Pariser, D. M.; McCall, C. O.; Horn, T. D.; Gottlieb, A. B.; Jaracz, E., and Rico, M. J.. Tacrolimus ointment is safe and effective in the treatment of atopic dermatitis: results in 8000 patients..Journal of the American Academy of Dermatology2005;53(2 (Suppl 2)):S195-205.

PT22

What should General Practice Trainees learn about childhood atopic dermatitis? A modified Delphi study exploring the views of healthcare professionals and parents of children with atopic dermatitis.

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Increasing evidence indicates that effective atopic dermatitis (AD) control not only improves quality of life but may also prevent the atopic march.[1] The Royal College of General Practitioners' (RCGP) curriculum does not currently provide any specific learning outcomes on AD management although the importance of better knowledge on the part of both healthcare professionals (HCPs) and patients is recognised, with recent NICE guidelines stating that "a lack of education about therapy leads to poor adherence and consequently to treatment failure." [2] We aimed to gain consensus on learning outcomes to inform curriculum development for doctors training in the management of AD.

A modified Delphi method was used. Questionnaires were distributed to gather the views of a range of HCPs, including general practitioners (GPs), dermatologists and dermatological nurses, as well as parents of children with AD attending the dermatology clinic. Questionnaires contained a number of items under the broad categories of knowledge, management, practical skills and attitudes relating to AD, with every participant asked to accept, reject or question the inclusion of each item in the curriculum and provide comments. Additional questions on psychosocial aspects of AD were also included in the questionnaire completed by parents.

91 questionnaires were distributed to 61 HCPs and 30 parents; 81(89%) were returned. All HCPs and parents agreed that learning should focus on the common clinical features, complications and management of AD. There was agreement on the need to appreciate the psychosocial impact of AD with parents particularly highlighting the importance of trainee awareness of disruption to social and physical activities. Areas of divergence included knowledge of alternative therapies (68% of parents supported these in contrast to 0.1% of HCPs). Parents also felt GPs should better understand how to identify, manage and refer severe AD and recognised the opportunities associated with the role of the specialist eczema nurse. GPs did not feel it was important to address steroid phobia, in contrast to both

dermatologists and parents, a divergence which may partly reflect the fact that the parents' children with AD were attending the specialist clinic.

In addition to identifying important areas which should be included as learning outcomes on AD management in the RCGP curriculum, this study also highlights the importance of patients and their parents as a valuable resource in the development of medical education.

References

1.Bieber T. Atopic dermatitis. N Engl J Med 2008; 358(14):1483-94.

2.National Institute for Health and Clinical Excellence. Atopic eczema in children: management of atopic eczema in children from birth up to the age of 12 years. London:NICE, 2007. www.nice.org.uk/CG057.

PT23

Successful long-term control of severe refractory atopic dermatitis by accurate proactive therapy combined with monitoring of serum biomarker, thymus and activation-regulated chemokine (TARC) levels

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Topical corticosteroid (TCS) and topical calcineurin inhibitor is the main way of anti-inflammatory treatment in atopic dermatitis. Nevertheless the precise strategy of TCS treatment has not been established but it has depended on each physician's art. Recently proactive therapy shows good evidence for preventing flares and long-term control. However more definite way is needed because there are some cases that fail to achieve initial remission or relapse during maintenance period especially in severe refractory group. In Japan, serum TARC level has been commercially measured under health insurance support since 2008 as a highly sensitive biomarker of atopic dermatitis (AD). After years of experience, we realized TARC is an extremely useful clinical biomarker to achieve successful treatment outcome of AD.

329 severe refractory AD adults who have participated in our 2-week admission program combined with remission induction by intensive TCS and simultaneous education by medical team were retrospectively observed. The strategy of this program is rapid normalization and maintaining normal serum TARC levels using appropriate TCS. Quality of life (atopic dermatitis Quality of life Japan; ADQOL-J), Investigator Global Assessment (IGA) score,

serum TARC level, necessitated TCS amount were measured at initial, 2-week later, 3-month later, 6- month later were measured.

279 patients were followed for more than 6 months after the admission program. Mean ADQOL-J score at each observing point were 63.6, 25.4, 25.6, and 25.4, respectively. Mean serum TARC level were 10846, 701, 1224, and 984pg/ml respectively. At the time of 6th month, the ratio of patients whose IGA score was ≦1, 2, 3 with less than twice weekly TCS were 54.2%, 27.7%, 3.9% respectively. In respect of long-term maintenance of serum TARC level lower than 700 pg/ml for 6 months, patients whose serum TARC level succeeded to drop less than 700 pg/ml after initial 2-week intensive treatment were significantly more favorable than patients who failed it (55% vs 19.2%, $p<0.001$).

Accurate proactive therapy with monitoring serum TARC level is a promising way of long-term control even for severe refractory AD patients. Rapid normalization and maintaining normal serum TARC levels using appropriate topical treatment is a reasonable strategy for alleviating inflammation without up-regulating cytokine expression. Dermatologists will be able to make great progress in treating AD by adopting biomarkers such as serum TARC levels for accurately assessing non-visible subclinical disorders.

References

1. Yoko KATAOKA. TARC as a clinical biomarker in atopic dermatitis: J Dermatol, in press

2. Kakinuma T, Tamaki K. TARC in atopic dermatitis: Serum TARC level is closely related with disease activity. J Allergy Clin Immunol 2001: 107; 535-41.

PT24

How useful is escalation of treatment as a measure of disease flare in eczema trials? A validation study

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It has been agreed by international consensus that long-term control of flares should be included as a core outcome domain in future eczema trials (1). However, it is unclear how this should be defined and measured (2).

Data from two completed eczema studies (Study A: n=336; Study B: n=60) were used to evaluate the use of 'escalation of treatment' as a measure of eczema flares. Data were

collected using daily diaries (Study A: paper; Study B: electronic). Data were analysed separately for the two studies in order to explore the consistency of findings across the two datasets. Flares defined by escalation of treatment was assessed for feasibility (is it feasible and acceptable for use in a variety of settings); truth (is the flare definition measuring something meaningful); and discrimination (can the scale detect real differences in eczema control reliably)?

Daily data collection was resource intensive for researchers and time consuming for participants. Nevertheless, the amount of missing data was generally low (94% of all possible daily data points were completed at 4 months for Study A and 60% for Study B). The lower completion rate for Study B is probably due to the use of electronic diaries that prohibited the entry of data after midnight each day.

Overall there was a good level of agreement between 'bother' scores (measured on a scale from 0 to 10) and escalation of treatment: ROC curve 0.70 (95% CI 0.69, 0.71) for Study A and 0.73 (95% CI 0.71, 0.74) for Study B.

For both datasets, participants whose bother score worsened relative to the previous day were twice as likely to escalate treatment if they experienced a one-point increase in bother, or four times as likely to escalate treatment if the bother score increased by two points or more, compared to those whose bother score was the same or worse ($p<0.0001$).

In comparison with validated eczema severity scales, there was a significant relationship between severity scores and the number of days when escalation of treatment was required in the preceding week. For POEM and SASSAD, both scales rose by about half a point for each unit increase in the number of days with a flare.

Capturing long-term control in long-term studies remains a challenge and is potentially burdensome for patients and researchers. Nevertheless, our experience from two large-scale, prospective studies would suggest that escalation of treatment may be a useful way of capturing eczema flares.

References

1.Schmitt, J.; Spuls, P.; Boers, M.; Thomas, K.; Chalmers, J.; Roekevisch, E. et al Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. Allergy 2012; 67 (9): 1111-1117

2.Langan S, Thomas KS, Williams HC What is meant by a "flare" in atopic dermatitis? Archives of Dermatology 2006; 142: 1190-1196.

PT25

Exploring expectation bias in trials of non-pharmacological interventions for eczema.

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Non-pharmacological interventions for eczema are popular amongst patients. Such interventions can be difficult to blind, with the result that trials are often open-label or at best, observer-blind. This presents difficulties for the interpretation of trial findings and challenges for researchers.

We report on the experiences from two trials of non-pharmacological interventions for eczema (SWET - water softeners; CLOTHES - silk clothing), with a view to highlighting i) the impact of expectation bias on trial outcomes; ii) potential challenges faced when disseminating trials with high expectation bias; and iii) reflections on methods that might be used to minimise bias in future trials.

Participants in the control group for both trials are offered the opportunity to use the trial interventions at the end of the study period. For SWET (which is now completed) this was successful in boosting recruitment, reducing contamination of the intervention, and minimising loss to follow-up for the control group. However, it t is possible that in taking this approach the potential for expectation bias is increased, as it implies that the intervention is likely to be beneficial.

The SWET trial showed clear evidence of expectation bias in favour of water softeners. There was no evidence of a treatment effect in any of the objective outcome measures, whereas for subjective outcomes a significant difference was seen. It is likely that expectation bias accounted for up to 20% of the treatment response. Disseminating these results to patients and clinicians was challenging as interpretation of the findings was contingent on an understanding of the importance of objective outcomes in unblinded trials

There are several ways in which expectation bias can be minimised including using an objective primary outcome (e.g. EASI or objSCORAD), and ensuring that opportunities for unblinding are minimised. Investigator training should emphasise the need to demonstrate equipoise over the value of the active intervention whilst enrolling participants and how to communicate the importance of the trial design effectively. Participants should be helped to understand that they are making a valuable contribution to the trial, regardless of their allocated intervention; If the study includes children, special effort should be made to ensure that both the parents and children have this understanding.

Expectation bias is often a problem for the design, conduct and interpretation of eczema trials in which blinding of participants is not possible. By addressing such issues at the design stage, researchers can reduce the impact of this bias to some degree.

PT26

Azathioprine treatment of severe atopic dermatitis in a university department

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A subset of patients with severe atopic dermatitis remains recalcitrant to recommended topical agents, and consequently, requires systemic immunomodulatory drugs to obtain sustained control of symptoms.

We present data on adherence and safety of azathioprine used in a five-year consecutive cohort of adult patients with atopic dermatitis from a university department. Data were retrieved through retrospective review of patient records.

We identified 59 immunosuppressant-naïve patients with severe atopic dermatitis in whom systemic immunomodulatory treatment was initiated. Of these, 43 (73%) begun treatment with azathioprine; 16 men (mean age 35.8 years) and 27 women (mean age 34.2 years). Duration of treatment ranged between 9 days and 53 months. After one and two years, 51% and 29%, respectively, of the patients were still treated with azathioprine. The most common causes of discontinuation of treatment were lack of effect (32%) and gastrointestinal side effects (22%). The strongest predictor of adherence to treatment was female sex: hazard ratio (risk of treatment failure in men compared with women) = 1.24 (0.52-2.96), p=0.621. Also, age (p=0.926), blood eosinophil count (p=0.912), TPMT enzyme activity (p=0.454), gender of the prescribing physician (p=0.500), and number of physicians consulted before initiation of treatment (p=0.455) did not significantly predict adherence to treatment.

The median adherence time to azathioprine in patients with severe atopic dermatitis is approximately one year. One third of patients discontinue due to lack of effect of azathioprine. Larger studies are needed to further clarify the causes for sustained adherence to azathioprine in patients with atopic dermatitis.

PT27

A systematic review of topical steroid withdrawal ("steroid addiction") in patients with atopic dermatitis

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The National Eczema Association has received an increasing number of patient inquiries regarding "steroid addiction syndrome", coinciding with the growing presence of internet sites and blogs dedicated to this topic. While many of the known side effects of topical corticosteroids (TCS) are addressed in treatment guidelines, "steroid addiction" or "withdrawal" are not explicitly discussed. We aimed to assess the current state of the evidence regarding topical corticosteroid withdrawal.

We conducted a systematic review of topical corticosteroid withdrawal (PROSPERO:CRD42013005370). Our objective was to address the following questions: 1. What are the clinical features of steroid withdrawal? 2. What are the risk factors? 3.What are the treatment options for this condition? We searched Ovid Medline, Pubmed, and The Cochrane Library from January 1946 to January 2014, using search terms relating to topical corticosteroid withdrawal, addiction, abuse, tolerance, rebound, dependence, rosacea, red skin, red face, red scrotum, tachyphylaxis and status cosmeticus. Titles and abstracts were screened by two reviewers. References of key papers were hand searched to find additional articles. The remaining papers were studied by two reviewers for relevance. Patients to be considered to be TCS withdrawal all had skin effects after discontinuation of TCS and in areas of TCS use.

Our initial search yielded 282 results. After screening, 66 articles remained. Review of the references of key articles added 69 citations. The 135 full-text articles were then evaluated using inclusion/exclusion criteria.

Preliminary results reveal studies of steroid withdrawal are limited to case reports and case series. Steroid withdrawal does appear to be a distinct clinical adverse effect of TCS therapy. Steroid withdrawal occurred primarily on head, neck and genital area due to the inappropriate continuous use of potent TCS. The condition was characterized by either an erythematous or papulopustular reactions within 24-72 hours of TCS discontinuation. The location, rapid onset, prominent burning symptoms, and severity of the eruption distinguishes it from simple recurrent or persistent eczema.

Steroid withdrawal is likely a distinct clinical adverse effect of TCS misuse distinct from other known adverse effects such as atrophy, perioral dermatitis, and telangiectasia. The next steps in our project include reviewing remaining non-English papers, classification of the different clinical withdrawal subtypes and elucidation of risk factors for corticosteroid withdrawal.

References

1. Eichenfield LF1, Tom WL1, Chamlin SL2, Feldman SR3, Hanifin JM4, Simpson EL4, Berger TG5, Bergman JN6, Cohen DE7, Cooper KD8, Cordoro KM5, Davis DM9, Krol A4, Margolis DJ10, Paller AS11, Schwarzenberger K12, Silverman RA13, Williams HC14, Elmets CA15, Block J16, Harrod CG17, Smith Begolka W18, Sidbury R19. Guidelines of care for the management of atopic dermatitis: Section 1. Diagnosis and assessment of atopic dermatitis. J Am Acad Dermatol. 2014 Feb;70(2):338-51.

2. Schünemann H, Hill S, Guyatt G, Akl EA, Ahmed F. The GRADE approach and Bradford Hill's criteria for causation. J Epidemiol Community Health. 2011 May;65(5):392–395. PMID: 20947872

PT28

Economic biopsy: Why and how should we undertake economic research into eczema?

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Eczema is common, costly and has a similar impact on health-related quality of life as other common childhood conditions such as asthma and diabetes.

It is expected that clinical care will be informed by clinical evidence of effectiveness of interventions to treat or prevent eczema and numerous resources now exist to facilitate access to this evidence, including the Global Resource of Eczema Trials (GREAT) database (http://www.greatdatabase.org.uk/,Nankervis, *et al* 2011), maps of systematic reviews of eczema (http://www.nottingham.ac.uk/scs/documents/documentsdivisions/documentsdermatology/methodologicalresources/mapsofsystematicreviewsonatopiceczema.pdf), and Cochrane reviews (http://www.thecochranelibrary.com/details/browseReviews/576991/Atopic-dermatitiseczema.html?page=2).

However, there is a dearth of economic evidence to inform health care funding decisions in the area of eczema. To illustrate this, a search of the GREAT database (which includes over

600 trials, Nankervis *et al*, 2011) using the search terms ‘cost*’ or ‘econ*’was undertaken which retrieved just 3 systematic reviews and 18 trials. Of these only the 3 systematic reviews and 4 of the trials actually measured costs or undertook an economic evaluation directly (3 of these trials only measured medication or direct treatment costs). It is not enough, within a resource limited health system, to show that an intervention or service is effective. Evidence of cost effectiveness is also important to demonstrate value and to aid prioritisation.

This presentation will address three questions:

1) Why is it important to undertake economic research into eczema?
2) What economic research methods are available for use in eczema?
3) What challenges exist in undertaking economic research into eczema?

The purpose of the presentation is to increase awareness of the importance and methods available for economic research into eczema to strengthen the evidence base supporting eczema care. It will assume no prior knowledge of economic research methods.

The presentation will review the published economic evidence available for eczema. It will also illustrate the economic methods, and challenges to their use, as they have or are being applied in two UK NIHR funded trials of eczema treatments (Softened Water in Eczema Trial (SWET)(Thomas 2011) and Silk therapeutic clothing for the long term management of eczema in children trial (CLOTHES)).

References

1.Nankervis H, Maplethorpe A, Williams HC. Mapping randomized controlled trials of treatments for eczema--the GREAT database (the Global Resource of EczemA Trials: a collection of key data on randomized controlled trials of treatments for eczema from 2000 to 2010). BMC Dermatol. 2011 May 18;11:10. doi: 10.1186/1471-5945-11-10.

2.Thomas K, Koller K, Dean T, O'Leary C, Sach T, Frost A, Pallett I, Crook A, Meredith S, Nunn A, Burrows N, Pollock I, Graham-Brown R, O'Toole E, Potter D, Williams H. A multicentre randomised controlled trial and economic evaluation of ion-exchange water softeners for the treatment of eczema in children: the Softened Water Eczema Trial (SWET). Health Technol Assess. 2011 Feb;15(8):1-156.

PT29

First experience with extended release tacrolimus (Advagraf®) in the treatment of adult patients with severe recalcitrant atopic dermatitis

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There is an increasing number of patients with severe recalcitrant atopic dermatitis (AD) and non-responsiveness and/or side effects to commonly used immunosuppressive drugs (eg. cyclosporin A (CsA), azathioprine, mycophenolic acid, methotrexate). As extended release tacrolimus (Advagraf®) is closely related to CsA (both calcineurin inhibitors) but exerts a more favourable safety profile due to association with a stable blood level, especially on blood pressure and renal function, this may be an alternative treatment. The advantage of Advagraf® compared to other second line treatment options might be the fast clinical response and the once daily dosing only, which may increase the adherence to therapy.

Nine patients with severe recalcitrant AD were treated with Advagraf® for 6 months. All patients discontinued several other oral immunosuppressive drugs due to non-responsiveness and/or side effects. Advagraf® was started with 0.2 – 0.3 mg/kg (body weight) and adjusted during treatment based on the clinical response, the occurrence of side effects and serum tacrolimus levels. Disease activity was monitored using the Six Area, Six Sign Atopic Dermatitis (SASSAD) severity score and measurement of the level of serum thymus and activation-regulated cytokine (sTARC). Safety laboratory parameters and serum tacrolimus levels were evaluated.

Nine patients were treated (mean age 42.5 years (SD 16.4)) with Advagraf®. The dose ranged from 7 to 15 mg/day. Serum tacrolimus levels showed a wide variation (10.6 μg/L (SD 6.3)) two weeks after starting.

Mean SASSAD (SD) scores decreased from 31 (9.8) to 15 (7.2) (p=0.02) and mean sTARC levels (SD) from 3088 (1460) pg/mL to 1245 (921) pg/mL (p=0.02) after two weeks of Advagraf® treatment. Two out of nine patients had to discontinue Advagraf® within six months due to gastro-intestinal symptoms and serum creatinine level increase, respectively. After six months of treatment disease activity remained stable in seven patients (mean SASSAD score 10 (4.9) (p=0.02); mean sTARC 1987 (2260) pg/mL (p=0.09).

Advagraf® treatment can be considered in patients with severe recalcitrant atopic dermatitis, in which treatment options are very limited. However, side effects leading to discontinuation of treatment did occur in our study. Dosing of Advagraf® must be adapted in each individual

patient, using serum tacrolimus levels and therapy response. More research is needed to investigate whether Advagraf® is a better treatment option than CsA in the management of patients with severe recalcitrant AD.

PT30

Kidney function during long-term treatment with Cyclosporin A in patients with severe atopic dermatitis

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Cyclosporin A (CsA) is an effective drug in the treatment of patients with severe atopic dermatitis (AD) not responding to topical treatment and/or UV light. A limitation of CsA use is the risk on serum creatinine increase. However, kidney function data related to treatment duration and reversibility after discontinuation are lacking. The objective of this study was to investigate the course of serum creatinine levels during long-term CsA treatment and after discontinuation of treatment in patients with severe AD treated in daily practice.

The medical records of all patients with severe AD treated with CsA between November 1994 and March 2013 at the Department of Dermatology of the University Medical Center Utrecht were analysed with respect to serum creatinine levels during and after CsA treatment. The following data were recorded a) serum creatinine level at baseline, b) serum creatinine at 3 weeks of CsA treatment (high dose: 5 mg/kg), c) mean serum creatinine level during maintenance phase (intermediate dose: 3-3.5 mg/kg), and if available d) first serum creatinine level after discontinuation (at least 2 weeks) of CsA treatment and e) the most recent serum creatinine level after cessation of CsA.

176 episodes of CsA treatment were identified with a median duration of 280 days (interquartile range: 203-568). Mean of serum creatinine levels increased 6.5% compared to baseline during high dose CsA (5 mg/kg) and 5.3% compared to baseline during intermediate dose (1-3 mg/kg).

Serum creatinine levels increased >30% in 27 (15.3%) patients, resulting in dose adjustment. Patients showing >30% increase were significant older compared to patients with <30% increase (42.4 vs. 34.9 years; p=0.006). Follow-up data showed decrease towards baseline levels in all patients.

CsA treatment results in an initial increase of serum creatinine levels, which than remain stable at intermediate dosage, and return towards baseline after discontinuation. Our data suggest a limited risk in the majority of patients treated with CsA. Higher age is a risk factor for serum creatinine of >30% compared to baseline. Upon prompt cessation in patients with >30% increase, creatinine returns towards pre-CsA levels. Therefore, prolonged CsA treatment of AD with frequent creatinine monitoring appears safe.

PT31

Validity assessment of measures for sweating to patient with atopic dermatitis: in point of both promoting sweating activities and rinsing sweat off.

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Sweat has been thought to implicate in exacerbating atopic dermatitis in diverse ways. Recent reports suggest that impaired sudomotor function contributes to the pathogenesis of atopic dermatitis. Decreased sweat volume might impair moisturization, protection against infections, and thermoregulatory ability. These results raised us to think that both promoting sweating activities and rinsing sweat off might be effective for symptom reduction.

Adult cases with atopic dermatitis, who consulted our patient clinics of Osaka university hospital and Shimane university hospital, were enrolled to this study. Study was performed during summer season (June to September). Subjects were educated about both good and bad aspects of sweat, and were encouraged to have daily sweating activities such as exercise and bathing. Subjects were also instructed to rinse sweat off after sweating. Efficacy of this instruction was evaluated with disease severity (EASI), work place productivity (WPAI), patient's satisfaction level, and impression of sweating activities at before and 1-month after intervention.

After 1 month of initiation of this study, EASI score was significantly improved. Although almost all subjects had unfavorable impression against sweating activities, about half of them become to have favorable impression after sweating activities. As for measures to rinse sweat off, showering, rinsing lesional skin with tap water, and wet wipes had made the contributions to symptom amelioration. Impairment of work place productivity was on a declining trend during the sweating-intervention.

Education about measures against sweating to patient with atopic dermatitis might be conducive to symptom amelioration.

PT32

The Global Resource of EczemA Trials (GREAT) database

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Identifying relevant randomised controlled trials (RCTs) published on eczema treatment is a difficult and time consuming task. Much time is wasted by researchers and guideline writers duplicating similar searches for the same information. This UK National Institute for Health Research funded project aims to identify, organise and abstract data for all trials of eczema treatment in order to reduce duplication of effort and speed up future eczema research.

The Global Resource of EczemA Trials (GREAT) database is an online, freely accessible database of information on RCTs of treatments for eczema relevant to researchers. The included RCTs must have a comparator, be randomised, be conducted in people with established eczema and include at least one efficacy outcome. The database contains details of trial interventions, treatment schedule and dose; inclusion and exclusion criteria; withdrawals; outcomes and methods of measurement; main reported results; adverse events; quality of reporting, author's conclusions and the trial report citation. The user can browse the database for trials of interest through lists of treatment categories and treatments, or the database can be comprehensively searched using keywords within particular fields or across the entire database.

The new database contains entries for over 500 RCTs and 59 systematic reviews covering 12 main treatment categories. Trials in any language are included. The RCTs cover: topical treatments such as topical corticosteroids (169), topical calcinuerin inhibitors (74) and emollients (31); systemic treatments such as azathioprine, ciclosporin, prednisolone and immunotherapy (56); non-pharmacological interventions such as specialised clothing and education (76); dietary interventions such as gamma-linoleic acid supplements and probiotics (88); antimicrobials such as mupirocin (32); antihistamines such as cetirizine (68); and complementary therapies such as Chinese Herbal Medicine (26). The database has already been used to demonstrate a widespread problem of selective reporting outcome bias.[1]

The free of charge database can be accessed at www.greatdatabase.org.uk, and will be updated on an ongoing basis. The GREAT database will facilitate future research on eczema treatments by reducing the time taken to identify eczema RCTs of interest.

References

1. Nankervis H, Baibergenova A, Williams HC, Thomas KS. Prospective registration and outcome-reporting bias in randomized controlled trials of eczema treatments: a systematic review. J Invest Dermatol. 2012;132(12):2727-34.

PT33

Effectiveness of an educational-communicative intervention on caregivers whose children have Atopic Dermatitis at QUITO, ECUADOR.

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The Atopic Dermatitis prevalence at our center has risen, where the poor eczema knowledge from the caregivers difficult its treatment. The average 15 minutes medical consultation is insufficient to explain the course of the disease and its management.

Four educational workshops were conducted aimed at caregivers of children under 19 years with Atopic Dermatitis. Each session lasted three hours. Parents were trained in basic pathophysiology of atopy, self-care measures, detection of infectious lesions, well use of home remedies, management of topical corticosteroids and warning signs, throughout significant adults learning techniques and educational materials designed for this purpose. To assess the study effectiveness the data was collected by a qualitative and quantitative view. Qualitative: through self-filling sheets about what their problems were and their use of home remedies. Also by audio recordings during the workshops and drawings made by patients one week after their parents attended the session. Quantitative: they took a practical assessment with a doll that simulated lesions of atopy versus infectious and were asked to answer a survey called PASECI modified (*Parental Self-Efficacy with Eccema Care Index*), before and one week after the workshop.

Total sample size was 50 caregivers from 26 patients, with 12 participants per workshop Mothers were the primary caregiver (46%) from the 76% women participants. Qualitative Results: 121 problems were identified, leaded by itching (13.22%), patient´s mood disorders (9.92%) and lots of physicians (7.44%). 73% of caregivers had used hot talc, chamomile water or oil. 31% had used alcohol or hydrogen peroxide to solve their children´s eczemas. The most talked topic by caregivers was emotionally suffering, seen as a family crisis. Also appeal to bad experiences with other doctors and the lack of information they received. All drawings showed application of appropriate self-care measures. Quantitative results: the

study showed high statistical significance (p = 0.000). All survey questions results improved after workshops. The overall result before the workshop was a score of 258.08/400 and a week later was 331.44/400.The average doll practical assessment was 18.8/20.
This study exposes a poor communication between physicians and caregivers. An educational intervention improves parents knowledge and management of the disease, change certain behaviors, and improves self-efficacy. Therefore, caregivers are key elements in Atopic Dermatitis treatment.

References

1.Mitchell, A. E., & Fraser, J. A. (2011). Parents ' self-efficacy , outcome expectations , and self-reported task performance when managing atopic dermatitis in children : Instrument reliability and validity. International Journal of Nursing Studies, 48(2), 215–226. doi:10.1016/j.ijnurstu.2010.06.008

2. Wenninger, K., Kehrt, R., Ruden, U. Von, Lehmann, C., Binder, C., Wahn, U., & Staab, D. (2000). Structured parent education in the management of childhood atopic dermatitis : The Berlin model. Patient Education and Counseling, 40, 253–261

PT34

Stratification of the EASI score using an anchor-based method – an interpretability study

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Why did we do this study: Clinical signs are a core outcome domain for atopic dermatitis (AD) trials. A recent systematic review[1] found the EASI and SCORAD to be the best instruments available to measure clinical signs of AD. Specifically the EASI was found to be valid and internally consistent, carry adequate intraobserver reliability, intermediate interobserver reliability and adequate responsiveness. The main disadvantage of the EASI is that data on interpretability is lacking (definition of ranges of the EASI that represent mild to severe clinical signs of AD). Lack of floor or ceiling effect and acceptability (ease of use) have not been reported as well. We aimed to measure these qualities of the EASI score.

We performed an open, retrospective study of pediatric and adult patients with AD recruited from tertiary care. The EASI was used to measure AD clinical signs against a physician-assessed anchor relating to disease severity – the Investigator Static Global Assessment (ISGA), based on the design of a previous study[2]. Acceptability was assessed by timing the EASI scoring process for a subset of patients.

In our preliminary results a total of 116 AD patients were included in the study: 86 adults≥16 years and 30 children; 64 females and 52 males; median age 29 years, range 7 months – 73 years. The mean EASI score was 16.2 (range 0–66, SD 15.8). The mean ISGA score was 3 (range 0–5, SD 1).

Interpretability: The mean, mode, and median of the ISGA scores for each EASI score were used to construct possible EASI bandings. The proposed banding for EASI scores are: 0 (clear / almost clear); 1-6 (mild); 7-21 (moderate); 22-50 (severe); 51-72 (very severe). Kappa coefficient 0.87.

Acceptability: The EASI was timed for 29 of the patients with an average of 6.1 minutes (range 2-20 minutes, SD 4.6 minutes).

Floor or ceiling effects: Under 15% of the respondents achieved the highest or lowest possible scores.

The suggested banding of the EASI score into clinically meaningful strata promotes its use as an outcome measure in future AD trials. The EASI has also shown adequate acceptability and lack of floor or ceiling effects. A follow up trial with added subjects will enhance the precision of the banding at the higher EASI scores, which were not fully represented in our study.

1. Schmitt J, Langan S, Deckert S, Svensson A, von Kobyletzki L, Thomas K, Spuls P, on the behalf of the Harmonising Outcome Measures for Atopic Dermatitis (HOME) Initiative. Assessment of clinical signs of atopic dermatitis: A systematic review and recommendation. J Allergy Clin Immunol. 2013 Sep 11; PMID: 24035157

2. Charman C, Venn A, Ravenscroft J, Williams H. Translating Patient-Oriented Eczema Measure (POEM) scores into clinical practice by suggesting severity strata derived using anchor-based methods. Br J Dermatol. 2013;

PT35

House dust mite reduction and avoidance measures for treating eczema: A Cochrane Review

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Eczema is a worldwide problem affecting 5% to 20% of children and around 2 per cent of adults with substantial economic costs. House dust mite reduction and avoidance measures, if effective, could be a simple, accessible and beneficial option for many.

We searched The Cochrane Skin Group Specialised Register, CENTRAL (2013, Issue 1), MEDLINE, EMBASE and two other databases up to 22 January 2013, and ongoing trials databases on 31 January 2013.

Two authors independently checked the titles and abstracts to identify randomised controlled trials (RCTs) of any house dust mite reduction and avoidance measures for the treatment of eczema. People of any age, diagnosed by a clinician using the Hanifin and Rajka (Hanifin 1980) or UK diagnostic criteria (Williams 1994) were included. Primary outcomes were clinician assessed global eczema severity using a named scale or modification and participant/caregiver assessed eczema related quality of life, using a named instrument.

Seven RCTs were included with 324 participants aged 2-65 years, four of which were of complex interventions. Study quality was generally poor. Eczema severity was measured with named scales in three; SCORing Atopic Dermatitis (SCORAD) in two small, short term studies, one of which failed to show significant benefit and the other not conducting an appropriate between group analysis. One study found a modest, statistically significant benefit with a bedding system, benzyltannate spray and vacuuming, with mean Six Area Six Sign Atopic Dermatitis (SASSAD) score difference compared to control of 4.2 (95%Cl 1.7-6.7), p = 0.008. One study measured quality of life but used a generic self-assessment (SF36). Another study recorded participant assessed skin status, finding no significant difference when using allergen impermeable encasings and acaricide spray, and no difference in topical corticosteroid use (p = 0.624). Four trials assessed changes in participant house dust mite sensitivity using different methods: three finding no significant differences and one, significant reduction in serum HDM IgE, IgG and total IgE with vacuuming and/or natamycin spray.

These few, small, low quality trials do not provide enough evidence to recommend any of the house dust mite reduction and avoidance measures tested. Any modest responses reported were in 'atopic' eczema, so wider use may be of limited benefit. These are achievable interventions however, therefore large, high quality, long term trials of single measures are worth pursuing in order to resolve current uncertainties once and for all.

References
1.Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. Acta Derm Venereol Suppl (Stockh) 1980; 92:44-7.
2.Williams HC, Burney PG, Pembroke AC, Hay RJ. The U.K. Working Party's Diagnostic Criteria for Atopic Dermatitis. III. Independent hospital validation. Br J Dermatol 1994; 131:406-16.

PT36

Experiences of carers managing childhood eczema and their views on its treatment: qualitative study

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The main cause of treatment failure for atopic eczema in children is thought to be non-concordance with the use of prescribed treatments (1). A first step in addressing adherence is to understand carers' current beliefs around childhood eczema and what they understand about its diagnosis, prognosis and treatment.

We carried out a qualitative study to explore parents' and carers' views of childhood eczema and its treatment. Parents or carers of children aged five or less who had consulted with eczema were invited to participate by general practices in the South of England. We interviewed 31 parents of children with eczema. Interviews followed a semi-structured interview guide and were audio-recorded and transcribed. Analysis was carried out thematically and iteratively using a constant comparative approach. QSR NVivo 9 facilitated coding and organisation of data.

Many parents expressed frustration with both medical care and prescribed treatments. They felt their child's suffering was not 'taken seriously' and experienced messages about a 'trial and error' prescribing approach and assurance that their child would 'grow out of it' as a further 'fobbing off', or dismissal. Many carers were ambivalent about eczema treatments, mainly topical corticosteroids but also the long-term use of emollients. Most families raised the topic that they believed dietary exclusions could be a cure for eczema, and were disappointed that health care professionals were not more interested in this. Families varied in the extent to which they felt able to manage eczema and the length of time taken to gain

control. In some instances this was linked to not understanding advice or receiving conflicting advice from different health care providers.

Other qualitative studies have explored the impact of eczema on families but there has been less exploration of families' accounts of barriers and facilitators to the use of treatments. We found that many parents were frustrated with their perception of the treatment plan suggested by their health care providers. Poor concordance with treatments seems unsurprising in this context. Acknowledging the impact of the condition, greater attention to how key messages are delivered and addressing carers' treatment beliefs are likely to improve engagement with effective self care.

References

1.NICE guidelines

PT37

Supporting self-care for families of children with eczema: pilot RCT of web-based intervention with health care professional support

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Childhood eczema causes significant distress to children and their families through sleep disturbance and itch. The main cause of treatment failure is non-use of prescribed treatments due to carers not understanding treatments, child refusal or therapy being too time-consuming (1).

We set out to develop a web-based intervention to support families of children with eczema. We wished to design a trial to test this intervention so carried out a pilot trial to test study procedures and to explore whether support from a health care professional (HCP) is necessary to engage participants with the intervention.

We developed a web-based intervention using LifeGuide software and following the PRECEDE-PROCEED model (2). Our target behaviour was regular emollient and we identified multiple behaviour change techniques to attempt to influence this. In order to test the intervention, carers of children with eczema were invited through primary care mail-out and randomised to three groups: (i) website only; (ii) website plus HCP support; (iii) usual care. Patient Oriented Eczema Measure (POEM) scores were measured online by carer report

at baseline and 12 weeks. Qualitative interviews were carried out with 26 participants to explore their experiences of participating in the study.

143 carers were recruited through 31 general practices. We found a decrease of 2 or more in follow-up compared with baseline POEM score in 23/42 (55%) of participants in the website only group, 16/49 (33%) of the usual care group and 18/47 (38%) in the website plus HCP group. There were no consistent differences in website use between 'website only' or 'website plus HCP' groups.

Qualitative interviews with participants suggested that HCP support was valued highly only by a minority, generally those who were less confident in eczema management or less confident using the internet.

Our pilot trial demonstrated the potential for greater improvements in POEM scores in both website intervention groups. A full scale trial is needed to quantify the effectiveness and cost-effectiveness of this intervention to determine whether it should be widely promoted to families of children with newly-diagnosed eczema.

In this study population, HCP support was not strongly valued by participants and did not lead to better outcomes or website use than the web-based intervention alone.

References

1.Beattie PE, Lewis-Jones MS. Parental knowledge of topical therapies in the treatment of childhood atopic dermatitis. Clinical and Experimental Dermatology 2003; 28:249-553

2.Green LW, Kreuter MW. Health Promotion Planning: An Educational and Ecological Approach. Mountain View, CA: Mayfield; 1999

PT38

A Novel New Sodium Hypochlorite Formulated Wash as an Adjunctive Approach to the Management of Pediatric Subjects with Moderate to Severe Atopic Dermatitis Colonized with Staphylococcus aureus

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Children with atopic dermatitis (AD) are usually colonized by *Staphylococcus aureus* (*S. aureus*) and bacterial overgrowth is thought to contribute to disease exacerbations.[1] Dilute sodium hypochlorite (bleach) baths have been shown to decrease AD severity[2], but are not practical for individuals who prefer showers. This trial evaluated the AD improvement in

infection-prone moderate-to-severe *S. aureus* colonized subjects who cleansed with a sodium hypochlorite (0.006%)-formulated wash once daily.

Subjects were recruited from pediatric outpatient dermatology clinics in two large U.S. urban centers. Cutaneous *S. aureus* colonization was first confirmed by positive bacterial culture of affected skin. Assessments occurred at 3 office visits over a 6-week period (2012-2013) and included Eczema Area and Severity Index (EASI), Investigator Global Assessment (IGA), Body Surface Areas (BSA), Pruritus Visual Analog Scale (VAS), Children's Dermatology Life Quality Index (CDLQI) and Family Dermatology Life Quality Index (FDLQI) to assess response in this open-label intervention.

The cohort included 40 subjects (62.5% male and with mean age of 8.5±9.0 yrs). Mean change from baseline in IGA at 2 and 6 wks was 0.9±0.9 (22.8% improved; P<.00001) and 1.2±1.1 (33.8% improved; P<.00001), respectively. Mean change in EASI score was 4.8±6.9 at 2 wks (34.3% improved; P<.0001) and 6.2±8.1 at 6 wks (43.8% improved; P<.0001). Mean change in BSA was 6.5±12.5 at 2 wks (23.8% improved; P<0.01) and 10.4+15.2 at 6 weeks (35.0% improved; P<.001). Mean change in VAS was 2.4±2.9 (31.2% improved; P<.00001) at 2 wks and 2.7±3.2 (36.8% improved; P<.00001) at 6 wks. Mean change in CDLQI score was 4.8+5.1 (40.7% improved; P<.00001) at 2 wks and 5.0±5.7 (32.4% improved; P<.00001) at 6 wks. Mean change in FDLQI score was 2.6±4.3 (13.3% improved; P<.001) at 2 wks and 5.3±5.4 (43.1% improved; P<.00001) at 6 wks.

Use of the sodium hypochlorite-formulated wash led to significant decreases in mean IGA, EASI, BSA, Pruritus VAS, CDLQI and FDLQI scores at 2 and 6 wks of use, and thus represents a simple alternative to bleach baths.

References

1.Balma-Mena *et al*. Int J Dermatol. Colonization with community-acquired methicillin-resistant Staphylococcus aureus in children with atopic dermatitis: a cross-sectional study. Int J Dermatol. 2011 Jun; 50(6): 682-8.

2.Huang JT, Abrams M, Tlougan B, Rademaker A, Paller A. Treatment of Staphylococcus aureus Colonization in Atopic Dermatitis Decreases Disease Severity. Pediatrics. 2009; 123(5): e808-14.

PT39

Depth-dependent resistance profiles characterise function and structure of stratum corneum

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We want to study which aspects of the stratum corneum (SC) structure and function are disturbed in atopic dermatitis (AD) patients.

The most appropriate treatment for atopic dermatitis (AD) depends on how the skin is damaged. Unfortunately, this is currently hard to diagnose, as conventional measurements for the level of skin damage, such as transepidermal water loss (TEWL), cannot discriminate between different types of skin damage. A novel quantitative way to characterise the function and structure of SC is needed.

We have proposed a method to calculate how resistance against loss of water varies along the depth of the SC. This calculation requires TEWL measurements, data from in-vivo measurement of water concentration along the depth of SC (for example by confocal Raman spectroscopy), and a simple mathematical model we developed to represent how water propagates through the SC. We further defined quantitative indices of the resistance profiles to characterise both functional and structural properties of the SC.

The calculated resistance profile characterises differences in SC function and structure for different skin sites and age groups, using experimental Raman and TEWL data1. This suggests that the calculated resistance profiles can uniquely characterise the barrier status of the SC, and thus will be applicable to deduce AD patient-specific SC barrier damage. Furthermore, the resistance profiles effectively predict and reproduce the effects of various skin treatments. In silico experiments of water application to the skin show how different resistance profiles from various skin sites lead to different water absorption and desorption dynamics. We also demonstrated that the resistance profiles can quantitatively evaluate the effects of application of oil on the SC barrier.

Resistant profiles are useful for studying AD patient-specific function and structure of the SC. It can be used to determine possible causes requiring different treatment, and allows the testing of treatment to restore a correctly functioning permeability barrier and hydration of AD skin. By comparing differences between healthy SC and SC of AD patients, we can see how AD affects the function and structure of the SC, how the SC barrier is inflicted in AD

and we can propose appropriate treatment to restore the SC to a competent permeability barrier and increase hydration.

References:

1.Nikolovski J, Stamatas GN, Kollias N, Wiegand BC. (2008). Barrier function and water-holding and transport properties of infant stratum corneum are different from adult and continue to develop through the first year of life. J Invest Dermatol. 128(7):1728-36. doi: 10.1038/sj.jid.5701239

PT40

Which factors predict remission of infant atopic dermatitis? A systematic review

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About half of all infants with atopic dermatitis (AD) are free of signs and symptoms at age 6 years. Parents of infants with AD are very interested in the chance for complete remission. Knowledge about factors associated with remission of AD is also important for identifying risk groups and to subsequently develop individualized models of care for infants with AD. We aimed to investigate predictors for remission of infant AD until school age.

A systematic review of clinical and epidemiological studies investigating the impact of filaggrin loss-of-function mutations, sex, pet exposure, topical anti-inflammatory treatment of infant AD, severity of infant AD and atopic sensitization during infancy on complete remission until age 6-7 years was performed. Systematic electronic searches (Cochrane Library, Medline; search date: 05Sept. 2013) were performed. Studies identified for full-text review were assessed with qualitative data analysis (Newcastle Ottawa Scale, NOS). For quantitative analyses, the primary measure of association was the odds ratio (OR), a random-effect meta-analysis of qualitatively homogenious studies was planned.

3315 abstracts were identified, 1637 randomized controlled trials (RCTs) and 1678 observational studies. Eighteen articles, seventeen reporting on cohort studies and one RCT were identified for full-text review. Finally only two cohort studies met the inclusion criteria (1, 2). Study quality was good according to the NOS.

Pet exposure during early infancy tended to decrease the chance of remission until school age, but the association was not statistically significant (adjusted OR 2.33; 95% confidence interval 0.85-6.38). Ballardini et al. (2) reported that parental allergy and sex did not influence remission of AD but did not show specific results. Illi et al. (1) investigated the impact of severity of infant AD on the course of disease; however, specific results concerning the effect of severity of infant AD on complete or partial remission at age 6-7 years were not provided. None of the studies explored the impact of filaggrin loss-of-function mutations, topical anti-inflammatory treatments of AD or atopic sensitisation in infancy on the likelihood of remission of infant onset AD until age 6-7 years, although data on some of these factors was obtained.

In conclusion, pet keeping in the home in early childhood may decrease the chance of remission of AD until school age. Parental allergy and sex did not predict remission of infant onset AD until age 6-7 years. For individualised patient information and disease modifying therapies clearly studies are needed which focus on remission of AD.

References

1.Illi S, von Mutius E, Lau S, Nickel R, Gruber C, Niggemann B, et al. The natural course of atopic dermatitis from birth to age 7 years and the association with asthma. J Allergy Clin Immunol. 2004; 113(5): 925-31.

2.Ballardini N, Kull I, Lind T, Hallner E, Almqvist C, Ostblom E, et al. Development and comorbidity of eczemaAD, asthma and rhinitis to age 12: data from the BAMSE birth cohort. Allergy. 2012; 67(4): 537-44.

PT41

Measurement properties of symptoms measurement instruments for atopic eczema: protocol for a systematic review

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The Harmonising Outcome Measures in Eczema (HOME) initiative defined clinical signs, symptoms, quality of life and long-term control of flares as core outcome domains to be applied in future atopic eczema (AE) trials. To date, it is unclear which outcome

measurement instruments are appropriate to assess symptoms in AE. In a former systematic review we extracted the symptom outcome measurement instruments used in AE trials using the GREAT database. 76% of randomized controlled trials in AE of the last 12 years reported symptoms, 42% using SCORAD. Now we present the protocol for a systematic review of the measurement properties of symptom measurement instruments.

What are we going to do?

A systematic literature review of the measurement properties of symptom outcome measurement instruments used for AE will be performed. A study will be included if it is a full text paper, concerns the development ("development paper") and/or evaluation of the measurement properties ("validation paper") of a symptom measurement instrument (including composite instruments) used for AE. The measurement instrument must be self-reported. Articles that report an eligible measurement instrument, e.g. as an outcome in a clinical trial without any explicit validation are not considered eligible. A systematic literature search will be performed in PubMed and EMBASE. The highly sensitive PubMed search filter for finding studies on measurement properties as suggested by COSMIN will be used to identify relevant articles. Systematic electronic search will be supplemented by handsearching of reference lists of studies included. Authors who inaugurated an instrument will be contacted for further evidence. Relevant data from all included articles will be summarized in evidence-tables. The selection and data extraction will be done independently by two reviewers.

The COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN) checklist will be used to evaluate the methodological quality of included studies (www.cosmin.nl). An overall quality score is obtained for each measurement property separately. Next, predefined criteria will be used to rate the quality of each measure. These criteria are in accordance with the OMERACT filter which has been adopted by the HOME initiative. If several studies exist for one measurement instrument, findings will be synthesized by combining them, based on number and methodological quality of the studies and consistency of results. For each instrument identified in the review, a standardized recommendation for usage or required future validation work will be made depending on the scale quality and on the methodological quality of included studies.

References

1. Schmitt J, Spuls P, Boers M, Thomas K, Chalmers J, Roekevisch E, Schram M, Allsopp R, Aoki V, Apfelbacher C, Bruijnzeel-Koomen C, Bruin-Weller M, Charman C, Cohen A, Dohil M, Flohr C, Furue M, Gieler U, Hooft L, Humphreys R, Ishii HA, Katayama I,

Kouwenhoven W, Langan S, Lewis-Jones S, Merhand S, Murota H, Murrell DF, Nankervis H, Ohya Y, Oranje A, Otsuka H, Paul C, Rosenbluth Y, Saeki H, Schuttelaar ML, Stalder JF, Svensson A, Takaoka R, Wahlgren CF, Weidinger S, Wollenburg A, Williams H. Towards global consensus on outcome measures for atopic eczema research: results of the HOME II meeting. Allergy 2012 Sep;67(9):1111-7. doi: 10.1111/j.1398-9995.2012.02874.x.

PT42

Clinically meaningful evaluation of flare prevention data – a graphic approach

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Impaired innate immunity, distorted adaptive immunity and skin barrier dysfunction contribute to the development of atopic dermatitis skin lesions. From a patient's view, the disease is running in flares.

In AD patients, subclinical inflammation has been described in skin areas without visible disease. Proactive therapy is a novel treatment concept based on long term, low dose, intermittent application of anti-inflammatory, topical medication to frequently relapsing body regions and must by combined with daily use of emollients. Most trial reports show Kaplan-Meier diagrams for verum and placebo group. Extractable parameters of trial data from flare prevention studies should allow comparison of published and future trial results.

Potentially useful parameters include the median time to first flare, the number of flares during study time, the ratio of median time to first flare between verum and placebo group, the percentage of patients profiting from treatment at a fixed time point or the percentage of patients having flared at end of study. Trial duration and disease severity of the study population may heavily influence some of these parameters.

The specific positive and negative aspects of each outcome parameter must be kept in mind if trial data is compared. The percentage of patients having flared at end of study is especially vulnerable to this bias, as it is not controlled by any data derived from the control group. The ratio of median time to first flare between verum and placebo group is clinically meaningful, but may not be accessible in trials with short duration or mildly affected patients. The percentage of patients profiting from treatment at a fixed time point is a pragmatic parameter for comparing trials of different duration.

The choice of the parameters used in comparing proactive trials in atopic dermatitis is an essential feature of a meta-analysis, as it greatly influences the results, and its selection should be justified.

PT43

A Cochrane systematic review of specific allergen immunotherapy for the treatment of atopic eczema

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Specific allergen immunotherapy (SIT) is a treatment which may improve disease severity in people with atopic eczema (AE). We performed a Cochrane systematic review and meta-analysis1 to assess the efficacy and safety of SIT for reducing symptoms in people with AE. We searched six databases up to January 2014 including MEDLINE and EMBASE, and ongoing trial databases. We also searched abstracts from recent European and North American allergy meetings, and the references of identified review articles. There were no language or publication status restrictions. We included randomised controlled trials (RCTs) of SIT using standardised allergen extracts compared to placebo or standard treatment in children and adults with a proven allergy to food or inhalant allergens; administered via subcutaneous, sublingual, oral, and intradermal routes. Primary outcomes included the proportion of participants with good or excellent improvement in a participant or parent reported global assessment of disease severity at the end of treatment.

We identified nine RCTs including a total of 490 participants. The trials had some risk of bias with five trials noting high rates of loss to follow up. Patient/parent assessment of global disease activity was reported in three trials, two of which where meta-analysis was possible and showed a risk ratio [RR] 1.37 (95% CI 0.34 to 5.53) for disease improvement with SIT. Patient/parent assessment of symptom severity was reported in three trials, of which only1 open-label trial showed a significant and clinically meaningful difference in eczema symptoms at the end of treatment in favour of SIT – mean symptom score 37.3 (95% CI 32.4

to 42.1) after active treatment; 80.8 (95% CI 75.8 to 85.7) after placebo treatment (P<0.001). SIT was not associated with increased systemic adverse reactions compared with control treatment (4 trials, RR 0.82, 95% CI 0.34 to 2.00). We were unable to identify a patient group or mode of treatment with different efficacy or safety, although these analyses were generally inconclusive due to limited data.

Although there were positive findings in some trials, there was no clear evidence of benefit for SIT compared with placebo or standard treatment for AE. There were no significant adverse effects attributable to SIT. Further high quality RCTs using modern allergen formulations, with a proven track record in other allergic conditions, and patient-reported primary outcome measures are needed.

References

1. Higgins JPT, Green S (editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

PT44

Healthcare utilization and expenditures in adult eczema: A US population based study

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Little is known about the public health burden of adult eczema in the US. The goal of this study was to determine the out-of-pocket costs, healthcare access and utilization in adult eczema in the US.

We used the 2010 National Health Interview Survey from a nationally representative sample of 27,157 adults age 18–85 years.

Adults with eczema and eczema with asthma and/or hay fever (EAH) had $1,497 and $1,800 per person-year compared with $1,298 in those without eczema. Adults with eczema and EAH were significantly more likely to have ≥6 lost workdays (survey multinomial logistic regression; adjusted odds ratio [95% confidence interval] for eczema: 1.48 [1.19–1.84]; EAH: 1.78 [1.34–2.36]) and 3-5 (eczema: 1.49 [1.21–1.83]; EAH: 2.06 [1.53–2.76]) and ≥6 days (eczema: 1.72 [1.41–2.08]; EAH: 3.69 [2.91–4.69]) days in bed compared with no eczema. Adults with eczema and/or EAH had significantly increased odds of doctor visits, urgent care or emergency department visits, homecare visits and hospitalizations. Adults with eczema

and EAH were more likely to report being unable to afford prescription medications (aOR [95% CI] for eczema: 1.49 [1.24–1.80]; EAH: 2.50 [1.98–3.14]) and having delayed care (eczema: 1.45 [1.22–1.71]; EAH: 2.07 [1.63–2.62]) and not being able to get care (eczema: 1.34 [1.11–1.62]; EAH: 2.24 [1.70–2.94]) because of worry about the related costs. Latent class analysis was performed and identified 4 distinct classes of healthcare utilization in adult eczema.

This study provides US population-based estimates of the public health burden of eczema in adults. The results suggest substantial out-of-pocket costs, indirect costs from lost work and sick days and increased healthcare utilization.

PT45

Childhood eczema is associated with injury requiring medical attention

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Children with eczema have multiple risk factors for accidental injuries, including sleep impairment and sedating anti-histamine usage.

We used the 2007-2008 National Survey of Children's Health to determine the prevalence of injuries requiring medical attention from a nationally representative sample of 27,556 children age 0-5 years.

Children with eczema compared to those without eczema had a higher 1-year prevalence of injury requiring medical attention compared with those that had no eczema (12.9% vs. 10.0%; Rao-Scott chi square test, P<0.0001). Children with eczema had higher odds of sustaining injuries requiring medical attention even after controlling age, sex, household income, family structure, and highest level of parental education in multivariate logistic regression models (adjusted odds ratio [95% confidence interval] = 1.65 [1.08–3.26]). In particular, eczema was associated with higher odds of injury in the home (2.69 [1.26–5.77]), but not at child care (1.44 [0.45–4.62]) or other place (0.28 [0.13–0.63]). In contrast, children with diabetes, another chronic disease of childhood, did not have higher odds of sustaining injuries (0.88 [0.17–4.43]).

The results of this study suggest that children with eczema have higher rates of accidental injuries. Further, this association appears to be specific to eczema and perhaps other atopic

disorders, but not merely related to chronic disease in general. Future studies are needed to better understand the reasons behind and develop interventions to prevent injuries in eczema.

PT46

Sleep disturbances in adults with eczema are associated with poor overall health

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Eczema is associated with intense pruritus that can negatively impact upon sleep. However, little is known about the burden of sleep disturbance in adult eczema.

We used the 2012 National Health Interview Survey, a nationally representative sample of 34,613 adults age 18-85 years, to determine the prevalence of sleep disturbance in eczema and its impact on overall health.

Adults with eczema had significantly higher rates of prolonged fatigue (32.8% vs. 14.1%), daytime sleepiness (26.0% vs. 11.7%) and insomnia (34.4% vs. 18.2%) than those without eczema (Rao-Scott chi square, $P<0.0001$). These associations remained significant in multivariate models controlling for history of other atopic disorders and socio-demographics. There was a significant interaction between eczema and sleep disturbance as predictors of overall health status. Adults with eczema and sleep disturbance had poorer overall health and more symptoms of psychological comorbidity than those with either eczema or sleep disturbance.

These data suggest that sleep disturbance weighs heavily on adults with eczema. Future studies are warranted to better characterize sleep disturbances in eczema and develop strategies for treatment and prevention.

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Topical calcineurin inhibitors and cancer in children. A register study

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FDA and EMEA health agencies have labeled topical calcineurin inhibitors (TCI) with a black box warning due to a theoretical risk of inducing skin cancer and lymphoma. The compounds were marketed in Denmark in 2002 for the use in atopic dermatitis (AD).

In the time period 2004 to 2011 we looked at the period prevalence of cancer among children (0 to 18 years inclusive) who were prescribed TCIs, children who were prescribed topical steroids (TS), but not TCIs, and 20% of the background population (BGP) and compared data with the Danish Cancer Registry.

The study analysis will be complete within the next month and the ISAD Organising Committee have agreed this submission is valid.

We found no difference between the incidence of malignancies between AD patients treated with TCI and AD patients treated with TS, but both groups show an increased period prevalence of lymphoma/haematological malignancies. Since there are no restrictions on TS for the use in AD one could argue that there should be no restrictions on TCI's either.