5th GEORG RAJKA
INTERNATIONAL SYMPOSIUM ON ATOPIC DERMATITIS, KYOTO
MAY 11-13, 2008

PROGRAM

FORWARD

Dear AD friends and colleagues of all over the world.

Welcome to Kyoto, one of the oldest and most beautiful city in Japan.

It is my great pleasure to host 5th International Symposium on Atopic Dermatitis under the honorary presidency of Georg Rajka and Kazuya Yamamoto. This time, emeritus professors of Shigeo Ofuji (Kyoto University) and Masami Uehara (Shiga Medical School) also play the part of presidency, since it is hardly possible for us to entertain the progress of AD study in Japan without superior contribution of these distinguished physician scientists to the clinical and basic research of atopic dermatitis.

The 5th Rajka symposium should be memorable because the meeting is held for the first time in an Asian country. The tradition of Rajka symposium is to encourage collaboration through better interaction among individuals with a various background including dermatologists, pediatricians, immunologists, allergologists, just to name a few. I hope that the international collaboration will be more reinforced than ever through this symposium.

Please discuss and debate to elucidate the nature of this enigmatic disease.

Enjoy your stay in Kyoto!

Masahiro Takigawa
Chair of the Symposium

5th Georg Rajka International Symposium on Atopic Dermatitis

ISAD2008/Organization

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Shigeo Ofuji (Kyoto, Japan)
Kazuya Yamamoto (Tokyo, Japan)
Masami Uehara (Shiga, Japan)

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ISAD 2008 / Program

LEGEND
Keynote Lectures: KL
Invited Communications: IC
Oral Communications: OC
Posters: P

May 11, Sunday

OPENING/WELCOME **13:00/13:15**
Chairs: G. Rajka, S. Ofuji, K. Yamamoto & M. Uehara

Welcome
M. Takigawa

SESSION 1 **Definition, Incidence, Prevalence, and Epidemiology of Atopic Dermatitis** **13:15/15:10**
Chairs: C-F. Wahlgren (Sweden), J. Ring (Germany), K. Tamaki (Japan)

1. KL: Atopic dermatitis: One or several diseases? 13:15/13:35
   T. Bieber, Germany

2. IC: Diagnostic criteria for atopic dermatitis: a systematic review 13:35/13:50
   E.E.A. Brenninkmeijer, M.E. Schram, M.M.G. Leeflang, J.D. Bos, P. I. Spuls, The Netherlands

3. IC: Controversies in atopic dermatitis 13:50/14:05
   P. I. Spuls, E. Brenninkmeijer, J. H. S. Smitt, J. D. Bos, The Netherlands

4. OC: Atopy, minimal inflammation, autoimmunity –Uncommon assotiation of diseases, or false atopic and autoimmune regulation? 14:05/14:15
   E. Szakos, E. Solyom, Hungary

5. IC: Lessons about eczema from the International Study of Asthma and Allergies in Childhood (ISAAC) Phase Two 14:15/14:30
   C. Flohr, UK

6. IC: Atopic Eczema in subSaharan Africa 14:30/14:45
   P. Schmid-Grendelmeier, Switzerland

7. IC: Incidence of childhood atopic dermatitis in Japan 14:45/15:00
   H. Uchi, M. Furue, Japan

8. OC:Cumulative prevalence of atopic eczema in Slovakia 15:00/15:10
   I. Chromej, Z. Frlickova, I. Chribikova, D. Zaborska, S. Malisova, Slovak Republic

P-1. Atopic dermatitis, dry skin and serum IgE in children in a community in Japan
   T. Wakamori, N. Katoh, S. Hirano, S. Kishimoto, K. Ozasa, Japan

P-2. The statistical findings of atopic dermatitis at the southern part of Tama district in Tokyo
   N. Higashi, T. Nakata, R. Kano, H. Koganei, K. Ueno, M. Ohta, M. Ozawa, S. Kawasaki, Japan

P-3. Prognostic factors of adult patients with atopic dermatitis
   N. Katoh, S. Hirano, S. Kishimoto, Japan

P-4. Cardiovascular risk factors and psychiatric comorbidity in patients with atopic eczema. A population-based case-control study
   J. Schmitt, U. Maywald, N. M. Schmitt , M. Meurer, W. Kirch, Germany

OPENING ADDRESS: Professor Georg Rajka **15:45/16:00**

SESSION 2 **Clinical Features of Atopic Dermatitis** **16:00/17:00**
Chairs: G. Girolomoni (Italy), A. P. Oranje (The Netherlands), Y. Tokura (Japan)

9. KL: Characteristics of atopic eczema in adults 16:00/16:20
   J. Ring, Germany

10. OC: Low basal serum cortisol in patients with severe atopic dermatitis: potent topical corticosteroids wrongfully accused 16:20/16:30
C A.F.M. Bruijnzeel-Koomen, I M Haeck, L T Mik, E G W M Lentjes, E. Buskens, D. Hijnen, K. Guikers, M. S. de Bruin-Weller, The Netherlands

11. OC: Low bone mineral density in adult patients with atopic dermatitis: topical corticosteroids wrongfully accused 16:30/16:40
I. M. Haeck, L. T. Mik, E. G. W. M. Lentjes, H. J. J. Verhaar, N. A.T. Hamdy, C. A. F. M. Bruijnzeel-Koomen, M. S. de Bruin-Weller, The Netherlands

12. OC: Increased platelet activation markers in patients with atopic dermatitis 16:40/16:50
R. Tamagawa-Mineoka, N. Katoh, E. Ueda, K. Masuda, S. Kishimoto, Japan

13. OC: A possible role of prolactin for exacerbation of atopic dermatitis 16:50/17:00
H. Sugiura, S. Sugiura, T. Uenishi, H. Ebise, T. Kimura, M. Tazuke, Y. Miyahira, Y. Sugiura, I. Kato, M. Fujimiya, B.Bai, M. Uehara, H. Sato, Japan

P-5. Clinical differences between atopic and atopiform dermatitis
E. E. A Brenninkmeijer, P. I. Spuls, R. Lindeboom, J. H. S. Smitt, J. D. Bos, The Netherlands

P-6. A case of atopic dermatitis with infective endocarditis
K. Maruo, S. Fukushima, M. Kidoh, E. Kudo, H. Ihn, Japan

SESSION 3 **Genetics of Atopy and Atopic Dermatitis, and Animal Models** **17:00/18:30**
Chairs: K. Cooper (USA), A. D. Irvine (Ireland), I. Katayama (Japan),

14. KL: Filaggrin mutations in atopic dermatitis 17:00/17:20
A. D. Irvine, Ireland

15. OC: Raman spectroscopy in atopic dermatitis 17:20/17:30
P. J. Caspers, G. J. Puppels, P. M. J. H. Kemperman, H. B. Thio, The Netherlands

16. IC: Prevalent and rare filaggrin mutations in Japanese patients with atopic dermatitis 17:30/17:45
T. Nomura, M. Akiyama, W. H. I. McLean, H. Shimizu, Japan & UK

17. KL: Animal model of atopic dermatitis 17:45/18:05
H. Mizutani, Japan

18. IC: Use of animal model in developing therapeutic agent for atopic dermatitis 18:05/18:20
K. H. Kim, J. Y. Kim, Korea

19. OC: Defective barrier function in an experimental model of Atopic Dermatitis in high IgE Producing Beagles 18:20/18:30
R. Marsella, D. Samuelson, K. Doerr, K. Hightower, L. Harrington, USA

P-7. Evaluation of FITC-induced atopic dermatitis-like disease in NC/Nga mice using CAST-grid, a computer aided morphometric system
M. Hvid, H.K. Jensen, B. Deleuran, K. Kemp, C. Andersson, M. Deleuran, C. Vestergaard, Denmark

P-8. Reduction of IgE production by oral administration of silk-peptide in NC/Nga mice
Y. Ikegawa, S. Sato, S. Takenaka, Y. Garbeen, T. Nishide, F. Furukawa, Japan

WELCOME COCKTAIL **18:45/21:00**

May 12, Monday

SESSION 4 **Skin Barrier Pathology in Atopic Dermatitis** **8:00/9:15**
Chairs: K. Thestrup-Pedersen (Denmark), J. I. Harper (UK), T. Shiohara (Japan)

20. KL: Genetics of atopic eczema 8:00/8:20
S. Weidinger, Germany

21. IC: Defects of the skin barrier and how this influences the pathophysiology of atopic dermatitis 8:20/8:35
J. I. Harper, UK

22. IC: Psychological stress and skin barrier function 8:35/8:50
E. H. Choi, Korea

23. OC: Skin barrier function and expression of antimicrobial peptides in atopic dermatitis after treatment with pimecrolimus or betamethasone cream 8:50/9:00
J. M. Jensen, M. Witt, S. Pfeiffer, R. Gläser, R. Fölster-Holst, E. Proksch, Germany

24. IC: Regulatory effects of IgE on innate immune responses 9:00/9:15
T. Shiohara, Y. Mizukawa, Japan

P-9. Therapeutic implications of the differential effects of topical corticosteroids and calcineurin inhibitors on the skin barrier
M.J. Cork, J. Varghese, A. Sultan, R. Guy, M. Lane, T. AlEnezi, J. Hadgraft, S.J. Ward, UK,

P-10. Pathogenesis and unique ultrastructural characteristics of ichthyosis prematurity syndrome (IPS)
D.Khnykin, I.Hausser, J.Rønnevig, F.-E. Johansen, F. Jahnsen, Norway

SESSION 5 **Immunology of Atopy and Atopic Dermatitis** **9:15/10:15**
Chairs: T. Luger (Germany), T. Bieber (Germany), Y. Miyachi (Japan)

25. KL: Atopic dermatitis and chemokine 9:15/9:35
K. Tamaki, Japan

26. IC: The role of CD8+ T cells in the initiation of the atopic dermatitis lesions 9:35/9:50
A. Hennino, France

27. OC: Differential gene expression in CD4+Tcells from atopic dermatitis patients is due to selective expression in the skin homing T cells 9:50/10:00
D. J. Hijnen, E. H. Nijhuis, L. Koenderman, C. A. F. M. Bruijnzeel-Koomen, M. S. de Bruin-Weller, E. F. Knol , The Netherlands

28. IC: Langerhans cells and prostaglandins: contribution to the etiology and pathogenesis of atopic dermatitis and related disorders 10:00/10:15
K. Kabashima, Y. Tokura, Japan

P-11. Genotype and functional study of TLR-2 and TLR-4 in a French atopic dermatitis cohort
F. Boralevi, C Ged, T Hubiche, H. Martin, H. Verneuil, A. Taieb, C. Dadrinche, France

P-12. CD4+CD25high Tcells and FoxP3positive Tcells are decreased in atopic dermatitis patients after cyclosporinA treatment
D. Hijnen, M.S. de Bruijn-Weller, C.A.F.M. Bruijnzeel-Koomen, M. Laaper-Ertmann, I. Haeck, A.A. van Kraats, E.H. Nijhuis, E.F. Knol, The Netherlands

P-13. Interleukin-13 and interferon-gamma producing skin resident CD8 T cells: a vicious circle of barrier disruption of the skin in atopic dermatitis
D.J. Hijnen, C. A. Bruijnzeel-Koomen, I. M. Haeck, E. F. Knol, T. S. Kupper, R. A. Clark, USA & The Netherlands

P-14. 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
R.L.Orfali, M. N. Sato, R. Takaoka, A. J. S. Duarte, E. A. Rivitti, V. Aoki, Brazil

P-15. The expression of MCP-1, IL-6 and IL-8 in human cell lines induced by house dust mite, *Dermatophagoides pteronissinus*
J-S. Lee, I. S. Kim, K–B. Suhr, J-H. Kim, D. H. Kim, H. J. Choi, C-Y. Yun, Korea

SESSION 6 **Role of Allergens and Food Allergy in Atopic Dermatitis** **10:45/12:30**
Chairs: C. Thijs (The Netherlands), Z. Ikezawa (Japan), K. H. Kim (Korea)

29. KL:Role of food allergy in infants and children with eczema 10:45/11:05
K. Beyer, Germany

30. IC: Breastfeeding and atopic dermatitis, new insights beyond the controversy 11:05/11:20
C. Thijs, The Netherlands

31. IC: Skin tests in atopic dermatitis 11:20/11:30
K. Matsunaga, Japan

32. IC: LEDGF/DFS70, a major autoantigen of atopic dermatitis, is a component of keratohyalin granules 11:30/11:40
K. Sugiura, Japan

33. IC: Identification of allergens in wheat allergy 11:40/11:50
E. Morita, JAPAN

34. KL: Treatment of childhood recalcitrant atopic dermatitis 11:50/12:10
A. P. Oranje, The Netherlands

35. OC: Role of foods in irregular aggravation of skin lesions in children with atopic dermatitis 12:10/12:20
T. Uenishi, H. Sugiura, T. Tanaka, M. Uehara, Japan

36. OC: Infants with atopic dermatitis - a 10-year follow-up study 12:20/12:30
O-M. Kekki, T. Aaltonen, A. Koskinen, H. Kautiainen, K. Turjanmaa, Finland

P-16. Identification and characterization of a novel allergen, Pen ch 33, from *Penicillium chrysogenum* and its role in atopic dermatitis
C-Y. Chu, C-H. Chan, J-G. Chuang, L-P. Chow, Taiwan

P-17. House dust mite allergen: One of possible factors inducing TSLP expression
M. H. Oh, S. H. Oh, J. H. Lee, K. H. Lee, Korea

P-18. Sensitization to turnip rape: a comparison between Finnish and French children with atopic dermatitis
S. Poikonen, F. RancÈ, T.J. Puumalainen, G. Le Manach, H. Kautiainen, T.Palosuo, T. Reunala, K. Turjanmaa, Finland

P-19. Clinical improvement and laboratory changes in 23 adolescent patients with atopic dermatitis undergoing subcutaneous specific immunotherapy with house dust mite allergens
K-B. Suhr, Y-S. Kim, J-S. Yoon, J-S. Lee, C-Y. Yun, Y-J. Seo, Korea

LUNCH SEMINAR **12:45/13:45**

Chair: Y. Tokura (Japan)

Psychopharmacology and dermatology: the behavioural toxicity of antihistamines
Ian Hindmarch, UK

This seminar is sponsored by sanofi aventis.

SESSION 7 **Microbial Superinfections in Atopic Dermatitis** **14:00/15:00**
Chairs: K. H. Lee (Korea), K. Iwatsuki (Japan), M. Takigawa (Japan)

37. KL:Atopic Dermatitis and Infections 14:00/14:20
A. Kapp, T. Werfel, Germany.

38. IC:Microbial factors in the aggrevation of atopic eczema 14:20/14:35
M. Mempel, Germany

39. IC: Staphylococcal virulence factors and atopic dermatitis 14:35/14:50
K. Iwatsuki, Japan

40. OC:Atopic dermatitis is closely related with non-bullous impetigo caused by group A streptococcus (GAS) 14:50/15:00
M. Kurata, K. Hayakawa, T. Shiohara, Japan

P-20. Contamination of emollient creams and ointments with staphylococcus aureus - in children with atopic dermatitis
J. Carr, M. Akram, A. Sultan, L. Hunter, M. Moustafa, A. Messenger, P. Fenton, M. J Cork, UK

P-21. Staphylococcus aureus suppression with sodium hypochlorite baths and intranasal mupirocin decreases atopic dermatitis clinical severity
B. Tlougan, J. Huang, S. Patel, K. Bauer, M. Abrams, S. Ortiz, D. West, A. Rademaker, A.S. Paller, USA

P-22. Distribution of SEA, SEB and TSST-1 produced by *Staphylococcus aureus* in the lesional skin of atopic dermatitis patients using immunohistochemical analysis
S. M. Kim, H. W. Lee, J. M. Kim, H. Y. Kim, B. S. Kim, D. W. Kim, Korea

P-23. The biological investigation on the distribution of *Malassezia* yeasts on atopic dermaitits patients
J. H. Ko, B. H. Oh, S. M. Kim, Y. C. Song, S. H. Lim, Y. W. Lee, Y. B. Choe, K. J. Ahn, Korea

SESSION 8 **Itching and Neurological Regulation of Inflammation** **15:00/16:30**
Chairs: A. Giannetti (Italy), M. Schmelz (Germany), M. Furue (Japan)

41. KL: Neuroinflammation and therapeutic potential of neuromediation in pruritus and inflammation 15:00/15:20
T. A. Luger, Germany

42. IC: Neuroimmunology of atopic dermatitis 15:20/15:35
U. Raap, A. Kapp, Germany

43. IC: Neurophysiology of itching 15:35/15:50
M. Schmelz, Germany

44. IC: Bradykinin is a potent pruritogen in atopic dermatitis: A switch from pain to itch 15:50/16:00
A. Ikoma, Japan

45. IC: Mechanism of itch in atopic dermatitis–Involvement of epidermal opioid systems– 16:00/16:10
M. Tominaga, K. Takamori, Japan

46. OC: Inhibiting epidermal nerve elongation is not sufficient for controlling itch/scratching in hapten-induced Th2-type chronic dermatitis 16:10/16:20
M. Kido, S. Takeuchi, S. Hayashida, M. Furue, Japan

47. OC: Dermal fibroblasts in atopic dermatitis skin lesion synthesize ARTEMIN reactive with peripheral nerve 16:20/16:30
H. Murota, S. Kitaba, M. Terao, M. Tani, S. Sano, I. Katayama, Japan

P-24. Altered expression of brain opioid receptors in atopic dermatitis model mice exposed to psychological stress
H. Amano, I. Negishi, A. Hiroshi, O. Ishikawa, Japan

SESSION 9 **Psychosomatic Aspects, Stress, and Quality of Life** **17:00/18:00**
Chairs: A. Kapp (Germany), U. Gieler (Germany), H. Hashizume (Japan)

48. KL: Psychosomatic approach to atopic dermatitis – Stress, behaviour and psychotherapy 17:00/17:20
U. Gieler, Germany

49. OC: Recalled burden of everyday life. 10 –year follow up-study of atopic and food allergic children 17:20/17:30
T. Aaltonen, O-M. Kekki, H. Kautiainen, A. Koskinen, K. Turjanmaa, Finland.

50. OC: Depression and atopic dermatitis 17:30/17:40
Y. Kataoka, Japan

51. OC: Functional analysis of the habitual scratching of patients with atopic dermatitis and behavioral intervention 17:40/17:50
Y Ohya, N Kojima, I Nomura, M Narita,T Fukuie, K Nakatani, N Gocho, T Oishi, K Satsuka, K Horimukai, K Yoshida, Japan

52. OC: EMDR, a more developed method, for controlling habitual scratching from traumatic memories of AD patients 17:50/18:00
E. Ueda, S. Kugo, N. Katoh, S. Kishimoto, Japan

P-25. Negative body image impairs the quality of life of japanese adult patients suffering from atopic dermatitis
Y. Higaki, I. Watanabe, Tomoko Masaki, T. Kamo, M. Kawashima, T. Satoh, S. Saitoh, M. A. Gupta, Japan & Canada

EVENING SEMINAR **18:10/19:10**

Chair: S. Shimada (Japan)

Regulatory T cells in autoimmune, inflammatory, and allergic diseases
Masahiro Ono, Japan

This seminar is sponsored by NOVARTIS.

SOCIAL GATHERING at SAKURA **19:30/21:30**

May 13, Tuesday

SESSION 10 — **Evidence-based Treatment** — **8:00/9:00**
Chairs: H. C. Williams (UK), A. S. Paller (USA), M. Kawashima (Japan)

53. KL: Treatment of Childhood Atopic Dermatitis — 8:00/8:20
A.S. Paller, USA

54. IC: Clinical trials of atopic dermatitis: problems and solutions — 8:20/8:40
H. Williams, UK

55. OC:Pet exposure and risk of eczema: a systematic review — 8:40/8:50
S. M. Langan, C. Flohr, H. C. Williams, UK

56. OC: A survey of skin care practices in infants prior to atopic dermatitis development — 8:50/9:00
M. E. Rendell, B. M. Simpson, T. M. Berry, S. Baig-Lewis, E. L. Simpson, USA

P-26. Kampo as a complementary therapy for patients with recalcitrant atopic dermatitis: Double-blind, randomized placebo-controlled study
H. Kobayashi, M. Ishii, S. Takeuchi, Y. Tanaka, T. Shintani, A. Yamatodani, T. Kusunoki, M. Furue, Japan

SESSION 11. — **New Frontiers in Therapy** — **9:00/10:30**
Chairs: C. Pincelli (Italy), A. Taïeb (France), S. Shimada (Japan)

57. KL: Pharmacogenetics and atopic dermatitis — 9:00/9:20
C. Pincelli, Italy

58. IC: A therapeutic effect of STAT6 decoy oligodeoxynucleotides ointment in atopic dermatitis — 9:20/9:30
K. Igawa, T. Satoh, H. Yokozeki, Japan

59. IC: Development of NF-kappa B decoy ointment and clinical trial for atopic dermatisis — 9:30/9:40
K. Tamai, Y. Kaneda, R. Morishita, I. Katayama, Japan

60. IC: An update on topical calcineurin inhibitors — 9:40/10:00
C. Paul, France

61. OC: Efficacy and safety of pimecrolimus cream 1% in 1088 infants with atopic dermatitis:
results of the three year double-blind, vehicle controlled phase of the study of the atopic march — 10:00/10:10
J. M. Hanifin, M. Boguniewicz, L. Eichenfield, A. S. Paller, L. C. Schneider, J. M. Spergel, M. L. Figliomeni, T. Hultsch, J. Nyirady, R. K. Zeldin

62. OC: A pilot study of a petrolatum-based emollient for the primary prevention of atopic dermatitis — 10:10/10:20
T. M. Berry, S. Baig-Lewis, S. J. Tofte, E. L. Simpson, USA

63. OC: IFN-γ-induced specific oral tolerance induction (IGI SOTI) for food allergy
(Seoul Allergy Protocol, SAP) in atopic dermatitis — 10:20/10:30
G. Noh, D. J. Lee, H. J. Chung, Korea

P-27. First experience with enteric-coated mycophenolate sodium (Myfortic®) in severe recalcitrant adult atopic dermatitis: an open label study
S. G. A. van Velsen, I. M. Haeck (presentor), C. A. F. M. Bruijnzeel-Koomen, M. S. de Bruin-Weller, The Netherlands

P-28. Effect of anti-helminthic treatment on exercise-induced bronchospasm, allergen skin sensitisation, and immunological responses: A randomised, double blind, placebo-controlled trial in Vietnam
C. Flohr, L. N. Tuyen, S. Lewis, R. J. Quinnell, T. T. Minh, J. Campbell, C. Simmons, G. Telford, A. Brown, T. T. Hien, J. Farrar, D. I. Pritchard, J. Britton, H. C. Williams, UK & Vietnam

P-29. Management of atopic dermatitis patient
J. Lipozenčić, A. Basta-Juzbašić, B. Marinović, Croatia

P-30. Keishibukuryogan decreases the disease activity and the level of serum Th2 type chemokines and MIF in atopic dermatitis
T. Makino, M. Furuichi, H. Watanabe, T. Yamakoshi, M. Shimizu, Y. Yoshihisa, T. Shimizu, Japan

P-31. Effect of full spectrum light for the treatment of atopic dermatitis
H. I. Lee, Y. K. Rho, B. J. Kim, M. N. Kim, Korea

P-32. Are biologics safe in the treatment of atopic dermatitis? A review with a focus on immediate hypersensitivity reactions
M. S. Bremmer, S. Baig-Lewis, S. F. Bremmer, E. Simpson, USA

P-33. Skin protease inhibitors: a new treatment for atopic dermatitis
S. Danby, M. Moustafa, A.L. MacGowan, S.J. Ward, M.J. Cork, UK

SESSION 12 **Information and Education of Patients: Worldwide Experiences in Quality of Care** **11:00/12:10**
Chairs : C Paul (France), J. F. Stalder (France), H. Nakagawa (Japan)

64. KL: Confronting patient's and doctor's perspectives in the management of atopic dermatitis 11:00/11:20
A. Taïeb, France

65. IC: Structured educational program for atopic dermatitis children and caregivers 11:20/11:35
D. Staab & the German Atopic Dermatitis Intervention Study Group, Germany

66. IC: Therapeutic education in atopic dermatitis : worldwide experiences 11:35/11:50
JF Stalder*, A Ball*, U Gieler, M Deleuran, D Marcoux, T Werfel, T Diepgen, S Lewis-Jones, C Gelmetti, A Torrello, C Chiaverini, JP Lacour, L Misery, S Barbarot*, France

67. OC: Psychometric properties of outcome measurements for atopic eczema. A systematic review and survey involving experts and consumers 11:50/12:00
J. Schmitt, S. Langan, H.C. Williams, on behalf of the European Dermato-Epidemiology Network, UK

68. OC: Developing an association for patients with atopic dermatitis 12:00/12:10
R. Takaoka, V. Aoki, Brazil

P-34. Oriented Patient Education Network (OPEN project): a tool for therapeutic patient education.
J.F. Stalder*, A. Ball*, U. Gieler, M. Deleuran, D. Marcoux, T. Werfel, T. Diepgen, S. Lewis-Jones, C. Gelmetti, A. Torrello, C. Chiaverini, J.P. Lacour, L. Misery, S. Barbarot*, * France

CLOSE OF MEETING

ISAD2008/Abstracts

SESSION 1
Definition, Incidence, Prevalence, and Epidemiology of Atopic Dermatitis

1. KL: ATOPIC DERMATITIS: ONE OR SEVERAL DISEASES?

T. Bieber
Dept. of Dermatology and Allergy, University of Bonn, Germany

Atopic dermatitis (AD) is a chronic inflammatory skin disease which has been divided in at least 2 different forms: atopic (IgE-associated; extrinsic) and non atopic (non-IgE-associated; intrinsic) dermatitis. AD develops on a complex genetic background, the so-called atopic diathesis. Genetic epidemiological studies based on so-called linkage analysis with full genome scan strategies as well as association studies and case control studies have unraveled several chromosomal loci with putative candidate genes encoding for immunologic relevant pathways. More recently, a mutation in the gene encoding for Filaggrin (FLG) has been reported to be highly associated with certain forms of AD with early onset in about 30% of the European population but not in Japanese Ad patients. FLG mutations are linked to the well known dysfunction of the epidermal barrier in AD. Thus, AD may emerge on the background of at least 2 sets of genes: one related to structural proteins involved in the epidermal barrier function and one related to immunological mechanisms involved in increased IgE synthesis.
AD is in most (70%) but not all the patients characterized by the presence of elevated total serum IgE levels. However, a subgroup of atopic patients (30%) exhibits normal IgE levels and mechanisms contributing to the so-called extrinsic/IgE-mediated and the intrinsic/non-IgE-mediated forms have been the matter of intensive research work in the last years. We have now increasing evidence for the putative role of autoimmune phenomenons in the complex pathophysiology of AD. A new picture emerges in which the natural history of AD seems to be divided in 3 phases: (i) an initial non-atopic form (eczema) occurring in the early infancy. This is then followed in 60 to 80% of the cases by (ii) a sensitization to food and/or environmental allergens with the development of the IgE-associated (true AD). In this form, it is speculated that antigen presenting cells expressing the high affinity receptor for IgE (FcεRI) play a major role in the control of the inflammation. Consequently, these AD patients will have benefit from prevention measurements. Finally, most probably due to molecular mimicry, an IgE sensitization to self-proteins is observed in a high proportion of children and adults with AD. This concept should have a profound impact on the future management of the disease.

2. IC: DIAGNOSTIC CRITERIA FOR ATOPIC DERMATITIS: A SYSTEMATIC REVIEW

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Background Atopic dermatitis (AD) has a wide spectrum of dermatological manifestations. Despite various validated sets of diagnostic criteria that were developed over the last decades, there is still disagreement about its definition. Nevertheless, clinical studies require valid diagnostic criteria for reliable and reproducible results.
Objective To summarize the evidence concerning the validity of diagnostic criteria for AD.
Methods Systematic literature searches were performed in Medline, Embase and Cochrane databases to identify relevant studies concerning diagnostic criteria and validation studies. To assess the methodological quality The Quality Assessment of Diagnostic Accuracy tool (QUADAS) was used. Results of validation studies were presented in a Receiver Operating Characteristic (ROC) plot.
Results Twenty articles, published between 1994 and 2007, were included in this systematic review (SR). Of these articles that met the inclusion criteria, 27 validation studies were identified. Two validation studies of the Hanifin and Rajka diagnostic criteria showed a sensitivity and specificity ranging from 87.9% to 96.0% and from 77.6% to 93.8%, respectively. Nineteen validation studies were identified of the U.K. diagnostic criteria with a sensitivity and specificity ranging from 10% to 100% and 89.3% to 99.1%, respectively. The Schultz-Larsen criteria were validated in three validation studies with a sensitivity from 88% to 94.4% and specificity from 77.6% to 95.9%. The Diepgen, Kang en Tian and ISAAC criteria were only once validated. For the Millennium criteria, Danish Allergy Research Centre (DARC) criteria, Lillehammer criteria and Japanese Dermatology Association criteria, no validation studies were found. Applying the QUADAS tool, validation studies investigated showed differing methodological strength.
Conclusion Ten sets of diagnostic criteria for AD were found. For these criteria lists, 27 validation studies could be included in this systematic review. Most of the validation studies were performed concerning the U.K. diagnostic criteria. Other sets of criteria should be more validated following the quality criteria. Besides improvement of methodological design for validation studies, uniform use of well-validated and applicable diagnostic criteria is needed to improve future (intervention) studies and to compare study results.

3. IC: CONTROVERSIES IN ATOPIC DERMATITIS

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International consensus about the genetics, pathogenesis, epidemiology, diagnosis and therapy of atopic dermatitis (AD) is far from sufficient. This may be related to the fact that it is such a common disease in which many different medical disciplines are involved.
In genetics, the human genome organization (HUGO) seems to have not yet officially accepted the ATOD terminology for susceptibility genes.
In pathogenesis, there is the controversy between what might be called the corneocentric and immunocentric hypotheses of the disease. In the corneocentric approach, development of IgE-mediated allergies is thought to be secondary to the epidermal barrier defect, allowing penetration of allergens into the skin with subsequent sensitization. In the immunocentric approach, development of IgE-mediated allergies is thought to be defining the disease.
In epidemiology, there are different explanations for the increase in the incidence and prevalence of AD in many countries over the past 20 years. The most important is the 'hygiene hypothesis', but other theories also exist, including the diagnostic hypothesis (assuming more awareness of the entity), the introduction of glucocorticoids around 1950 (supposed to have increased the phenomenon of tachyphylaxis), the 'old mother' proposition, and the humidity theory.
A major source of confusion, with implications for studies into the genetics, pathogenesis, epidemiology and therapy of AD is in the lack of consensus about the definition. There are many different sets of criteria, including those of Hanifin and Rajka, the U.K. diagnostic criteria, the Schultz-Larsen criteria, the Diepgen, Kang & Tian and ISAAC criteria. And there are the Millennium criteria, Danish Allergy Research Centre (DARC) criteria, Lillehammer criteria and Japanese Dermatology Association criteria.
Although formulation of hypotheses is essential for progress in the understanding of AD, the lack of consensus in its definition is also hampering that advancement.

4. OC: ATOPY, MINIMAL INFLAMMATION, AUTOIMMUNITY –UNCOMMON ASSOTIATION OF DISEASES, OR FALSE ATOPIC AND AUTOIMMUNE REGULATION?

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Background: Different atopic diseases can occure consecutively, or in the same time. Autoimmune and minimal inflammation usually involve paralell many organ. Some papers presented the occurrence of IgE or other isotype of autoantibodies in atopic dermatitis. Autoimmune endocrine, sceletal, inflammatory bowel and/or skin diseases are rare in atopic patients. Authors analized data of atopic patients suffering from nonatopic, noninfetious inflammatory diseases also. Materials: history of 17 patients, carried out at Pediatric Health Centre in Miskolc, Hungary were examined retrospectively. Results: 10 woman and 7 man were in that group with atopic and autoimmune diseases. Excluding a case of girl with alopecia areata initially, atopic inflammation was the 1st manifestation of patients. 10 of 17 had sceletal, 9/17 thyroid, 7/17 gastrointestinal inflammation. Various autoantibodies were increased. Disfunction of involved thyroid glands appeared after years. Discussion: Thymic-derived CD4+CD25+Foxp3+ natural T-regulatory cells play an important role in maintaining self-tolerance and preventing autoimmunity. Transcription factor Foxp3 is expressed in regulatory T cells. It is required for their development. Genepolymorfisms, involving in immunoregulation lead to inflammatory diseases. Follow up patients in team help prevent and/or managing complications.

5. IC: LESSONS ABOUT ECZEMA FROM THE INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD (ISAAC) PHASE TWO

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The International Study of Asthma and Allergies in Childhood (ISAAC) is the biggest epidemiological allergy study ever conducted. The second phase of ISAAC recruited 28,591 schoolchildren age 8-12 years from 28 study centres in both developed and developing nations to evaluate the prevalence and risk factors of allergic disease. Children were examined for flexural eczema and also had skin prick testing performed for environmental allergens. In addition, a questionnaire tool was used to determine eczema prevalence. Since the same methodology was used across all study centres, direct comparisons between populations are possible.
We used the ISAAC Phase Two data set to determine and to compare the strength of the association between allergen skin sensitization and eczema both in developing and industrialized countries and found that this association was generally weak and more variable than previously suggested. Furthermore, the strength of this association was positively linked to gross national income. This suggests that allergen skin sensitization is possibly an epiphenomenon of disease activity rather than a uniform cause of flexural eczema.
Since the second phase of ISAAC employed both questionnaires and a standardized and validated protocol for physical examination to detect flexural eczema, we also used this opportunity to examine how reliable prevalence estimates based on questionnaire measurement were at the population and the individual level compared to estimates derived from physical examination. Overall, the ISAAC eczema questionnaire tool performed adequately for prevalence estimates at population level, but for individual level risk factor analyses skin examination is the better and more reliable outcome measure.

6. IC: ATOPIC ECZEMA IN SUBSAHARAN AFRICA

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Abstract not available

7. IC: INCIDENCE OF CHILDHOOD ATOPIC DERMATITIS IN JAPAN

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Recent nation-wide study on atopic dermatitis (AD) in Japan based on regular health check-ups by dermatologists elucidated the prevalence of AD in childhood. On the other hand, there has been no nation-wide study on the incidence of AD in childhood. We have annually examined children 5 years of age or younger in nursery schools in Ishigaki Island, Okinawa, Japan. Ishigaki Island with a population of 45,000 lies in a subtropical region and is far away from Japan's mainland. Prevalence of AD among children in Ishigaki Island is lower than that in Japan's mainland. During a 3-year follow-up study, more than 70% of children with AD experienced spontaneous regression, while 5.5% of children without AD developed AD. Since symptoms are known to become apparent during the first 5 years of life in most AD patients, it would be important to determine the incidence, prevalence and risk factors of AD in childhood.

8. OC: CUMULATIVE PREVALENCE OF ATOPIC ECZEMA IN SLOVAKIA

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In the past decades, there has been increasing effort to quantify atopic eczema in more precise epidemiological terms. The occurrence of the disease follows geographical, economical, genetic and temporal clues. Phenotype expression of atopic eczema is a result of complex interaction of endogenous and environmental factors that are still poorly defined or unknown. ISAAC (International study of asthma and allergies in childhood) is the global initiative aiming at collecting baseline measures and providing a framework to study occurrence, severity, course and etiological factors of eczema and other related disorders. Slovakia is an East-European country that has been going through tremendous political, social and economical changes that might have impact on the prevalence of atopic diseases. However, the epidemiology of atopic eczema has not been a subject of systematic study until now.
The primary objective of our study was to estimate the cumulative prevalence of atopic eczema in school children of 6-7 years of age within a specified geographical area.
During January-February 2008, one-page questionnaire in a pre-paid return envelope was distributed among all 6-7-year old school-children in two districts. Questions were modified and extended version of ISAAC core questionnaire. School authorities and teachers reinforced the issue of early filling-in by parents and return of questionnaires.
Questionnaires were distributed to 986 children and 763 (77%) were answered and duly returned by the parents. Proportions of positive answers to particular questions were calculated using the total number of distributed questionnaires as a denominator. Then, the lower limit of occurrence was estimated as following: 5,6% of children were told by a physician to have atopic eczema, 4,7% had any eczema in predilection areas and 3,3% had any eczema outside predilection sites.
Atopic eczema is higly probable to occur in 10,3% of Slovak children up to the age of 7 years. This is about a double of the prevalence estimated by Bobak et al. (1995) in a neighbouring Czech region more than a decade ago. Prevalence of all cases of eczema (13,6%) is very similar to that recently reported in Slovakia by Dunlop et al. (2006) in 1-year old infants (15,6%).
Ongoing study is supported by Vega research grant 1/4248/07.

P-1. ATOPIC DERMATITIS, DRY SKIN AND SERUM IGE IN CHILDREN IN A COMMUNITY IN JAPAN

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Background: No studies have examined changes in prevalence, serum IgE and the natural history of atopic dermatitis in a community as a long-term prospective investigation.
Methods: We performed skin examinations, a questionnaire answered by parents and measured serum total IgE, house dust mite- and Japanese cedar pollen-specific IgE levels in primary school children and junior high school students in a Japanese community once a year over a period of 9 years.
Results: The median prevalence of atopic dermatitis in all students (395 in 2004 to 586 in 1996) was 7.6% (6.1%-10.4%). The prevalence and the area of skin eruptions of atopic dermatitis decreased with growth. The serum total and house dust mite-specific IgE level was high in atopic dermatitis patients, and significant differences were noted in the serum total and house dust mite-specific IgE levels at lower grades between children with and without later remission of skin eruptions. The IgE levels increase in the order of healthy skin < dry skin < atopic dermatitis. In children with dry skin alone without atopic disorders such as atopic dermatitis, asthma, urticaria, allergic rhinitis and conjunctivitis, levels of total IgE, house dust mite- and Japanese cedar pollen-specific IgE were significantly higher in subjects than in subjects

with healthy skin.
Conclusion: Based on these findings, infantile IgE level serves as a prognostic index, and sensitization to inhalant allergens may be established easily in individuals with clinical dry skin, even when atopic dermatitis is not present, and this may lead to the development of atopic disorders.

P-2. THE STATISTICAL FINDINGS OF ATOPIC DERMATITIS AT THE SOUTHERN PART OF TAMA DISTRICT IN TOKYO

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[Aim] The roles of familial factor in the development of atopic dermatitis (AD) are not clearly established. This study examined the relation between familial factor (birth month, sibling number, parental history of AD) and AD at the southern part of Tama district in Tokyo. [Methods] Two hundred forty seven AD families were surveyed. Two hundred fifty two patients, age 9 months to 45 years with mild to severe AD (Group A: male 120, female 132) and total 387 AD patients who were patients in Group A and AD patients in their family combined (Group B: male 185, female 204) were examined. [Results] Patients mean age was 18.4 years in Group A, 23.8 years in Group B. The patients with AD of the autumn birth were more abounding than that of the summer birth (Group B). There was no parental allergy in 24% of patients with AD. Thirty four percent patients with AD had the AD parents. The incident in which the parent was AD was 29.3% in AD of only one child, 30% in AD of two children, 13.2% in AD of three children and 40% in AD of more than four children. The female patients with AD were 3.5 times as likely as male patients with AD in only one child. The proportion in which the first-born child was a female patient with AD were 1.3 times as likely as the proportion in witch first-born child was a male patients in two children (p=0.0165). The ratio in which the first-born child is AD (33.8%) and the ratio in which the second-born child is AD (33.1%) and the ratio in which both the first-born child and the second-born child are AD (33.1%) were equal in two children. The proportion in which the second-born child was a female patient with AD were 1.5 times as likely as the proportion in which the second-born child was a male patients with AD in three children. However there was no statistical significant difference. [Conclusion] The results from this study suggest that there were many variations between familial factor and development of AD. It was proven beyond a doubt that parental allergic disease thickly related the development of AD due to many previous reports, however there was no parental allergy in quarter patients with AD. Thus further investigations are needed to interpret the familial and environmental factor in the pathogenesis of AD.

P-3. PROGNOSTIC FACTORS OF ADULT PATIENTS WITH ATOPIC DERMATITIS

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The increased prevalence of atopic dermatitis (AD) in adults in recent decades suggests that dermatologists may be expected to estimate the prognosis of the adult patients with AD when they visit as new patients. We therefore evaluated the change in the extent of involvement and analyzed the factors contribute to the prognosis of adult AD. A retrospective chart review was performed for 65 adults patients (median age 25 years at first visit) with AD who had been followed monthly for over 10 years. The median area of the involvement at first visit was 19 %. The area of the eruptions and peripheral eosinophil counts decreased significantly in the fifth and tenth years with standard treatment. The values of IgE were also reduced after ten years. Patients with high values of serum total IgE, peripheral eosinophil count, and duration of AD had wide areas of eruptions 10 years after the first visit. Total IgE had the highest correlation with area of involvement after 10 years. Although the prognosis of adult atopic dermatitis is not poor, patients with high IgE values are expected to have ongoing eczema with wide distribution after ten years of follow-up.

P-4. CARDIOVASCULAR RISK FACTORS AND PSYCHIATRIC COMORBIDITY IN PATIENTS WITH ATOPIC ECZEMA. A POPULATION-BASED CASE-CONTROL STUDY

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Valid and generalizable data on the overall morbidity of patients with atopic eczema is limited. In order to determine the association between atopic eczema and major cardiovascular risk factors as well as psychiatric disorders we performed a case-control study utilizing the population-based administrative outpatient health-care and prescription databases of Saxony, Germany. Case patients (n=6296) were defined as subjects who were diagnosed with atopic eczema and received anti-inflammatory topical treatment. For each case patient a single individually-matched control with the same age and sex, but without atopic eczema was randomly selected. Odds ratios (OR) were calculated based on the observed prevalences of major psychiatric disorders (depression, schizophrenia, personality disorders) and cardiovascular risk factors (obesity, hypertension, hyperlipidemia, atherosclerosis) among cases and controls. Significantly higher proportions of patients with atopic eczema had concurrent depression (OR 1.85; 95% confidence interval [95%CI] 1.44 to 2.40), schizophrenia (OR 2.26; 95%CI 1.29 to 4.11), and personality disorders (OR 1.85; 95%CI 1.19 to 2.92). Patients with atopic eczema were at significantly increased risk of being obese (OR 1.24; 95%CI 1.07 to 1.44), whereas the prevalences of other cardiovascular risk factors (hypertension [OR 1.03; 95%CI 0.89 to 1.20]; hyperlipidemia [OR 1.18; 95%CI 0.90 to 1.57], atherosclerosis [OR 1.08; 95%CI 0.78 to 1.50]) were similar among patients with atopic eczema and controls. This study strongly

suggests an increased risk of depression and other major psychiatric disorders in patients with atopic eczema. Although there might be a weak association between atopic eczema and obesity, our study indicates that atopic eczema is not associated with cardiovascular risk factors on the population level.

SESSION 2
Clinical Features of Atopic Dermatitis

9. KL: CHARACTERISTICS OF ATOPIC ECZEMA IN ADULTS

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Abstract not available

10. OC: LOW BASAL SERUM CORTISOL IN PATIENTS WITH SEVERE ATOPIC DERMATITIS: POTENT TOPICAL CORTICOSTEROIDS WRONGFULLY ACCUSED

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Background: Topical corticosteroids are extensively used to treat atopic dermatitis (AD). Temporary reversible suppression of hypothalamic-pituitary-adrenal (HPA) function has been shown but sound evidence of permanent disturbance of adrenal gland function is lacking. Objectives: The aim is to relate basal cortisol levels to: prior use of topical corticosteroids, disease activity and investigate the effect of topical steroid treatment during hospitalization. Methods: Two groups of AD patients were evaluated: 25 inpatients with severe AD (group 1) and 28 outpatients with severe, but stabalized AD (group 2). During hospitalisation patients were treated with potent topical corticosteroids (250-300 grams per week). In group 1 morning basal serum cortisol levels were measured at admission and discharge; in group 2 once. Use of topical corticosteroids 3 months prior to the cortisol measurement was recorded and disease activity was monitored using the Six Area Six Sign Atopic Dermatitis (SASSAD) score and serum thymus and activation-regulated chemokine (TARC) levels. Results: On admission, basal cortisol levels in group 1 were significantly ($p<0.001$) decreased in 80% of the patients. In group 2 the basal cortisol level was normal in all but 3 patients. Group 1 had on admission had a significantly lower cortisol level than group 2 ($p<0.001$). Disease activity in group 1 on admission was significantly higher than in group 2 ($p<0.001$). There was no difference in use of topical corticosteroids in the 3 months before cortisol measurement. In group 1, at discharge from hospital, basal cortisol levels increased significantly ($p<0.0001$) and disease activity (TARC and SASSAD) decreased significantly ($p<0.001$). Ongoing investigation reveals that this finding is consistent in a larger group of patients. Conclusions: Disease activity, rather than the use of topical corticosteroids are responsible for the low basal cortisol values in patients with severe AD.

11. OC: LOW BONE MINERAL DENSITY IN ADULT PATIENTS WITH ATOPIC DERMATITIS: TOPICAL CORTICOSTEROIDS WRONGFULLY ACCUSED

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Background: Atopic dermatitis (AD) is a chronic inflammatory skin disease commonly treated with topical corticosteroids. Fear of local and systemic side effects influence therapy compliance while evidence that topical corticosteroids induce systemic side effects such as osteoporosis have not yet been adequately addressed. Objective: The aim of this study was to assess bone mineral density (BMD) using Dual-Energy X-ray Absorptiometry (DXA) in patients with moderate to severe AD in relation to use of topical corticosteroids. Methods: 125 patients with AD (64 men and 61 women, 17 to 82 years), were recruited from the Department of Dermatology of the University Medical Center Utrecht. The use of corticosteroids was evaluated using pharmacy records. BMD was measured using DXA (Hologic QDR X-Ray Bone Densitometer) analysing the lumbar spine and both hips and a blood sample was taken for the measurement of serum biochemical parameters of disease and bone metabolism. Results: In 41 of the 125 patients (32.8%; group B) a lowered BMD was found (Z-score = -1) in minimally one of the three sites measured by DXA. In this group, in 4 of the 41 patients (3.2%) osteoporosis was diagnosed (Z-score = -2.5). 84 patients (67.2%; group A) had a normal BMD in all three sites. Comparing group A and group B, there was no significant difference in the amount of topical corticosteroids used (modified amount) in the 2 years prior to DXA. There was a significant difference between the sexes: 28 males (43.8%) vs 13 females (21%) had

a lowered BMD. Serum biochemical parameters of disease and bone metabolism were normal and did not differ between the groups. Conclusions: In this study, about 30% of the AD patients have a lowered BMD, but this is not related to the amount of topical corticosteroids used in the past. Future research is necessary to reveal if a decreased BMD in AD is a consequence of chronic inflammation.

12. OC: INCREASED PLATELET ACTIVATION MARKERS IN PATIENTS WITH ATOPIC DERMATITIS

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In addition to their role in hemostasis and thrombosis, platelets are important for assisting and modulating inflammatory reactions. Activated platelets play a role in the pathomechanism of inflammatory diseases such as asthma and inflammatory bowel disease. In patients with atopic dermatitis (AD), scratching due to severe itch often results in excoriation and subsequent platelet aggregation at the inflamed lesion, but little is known about platelet activation in patients with AD. The aim of this study was to investigate the plasma levels of platelet-derived microparticles (PDMP), soluble P-selectin (sP-selectin), β-thromboglobulin (β-TG) and platelet factor 4 (PF4) as platelet activation markers in patients with AD, and to determine the relationships between these markers and disease severity. Plasma levels of PDMP, sP-selectin, β-TG and PF4 were measured by enzyme-linked immunoassay in 16 healthy controls and 34 patients with AD. The relationships between these markers and disease severity based on the SCORAD index, blood eosinophilia, serum IgE and serum lactate dehydrogenase were investigated in the patients. Plasma levels of PDMP, sP-selectin, β-TG and PF4 were significantly higher in patients with AD compared with healthy controls, and plasma levels of PDMP and sP-selectin correlated with the SCORAD index in the patients. Our results show that blood platelets are activated in patients with AD, suggesting that activated platelets may play a role in the pathomechanism of AD. The correlation of the PDMP and sP-selectin levels with the SCORAD index suggests that plasma PDMP and sP-selectin may be markers of disease severity in AD.

13. OC: A POSSIBLE ROLE OF PROLACTIN FOR EXACERBATION OF ATOPIC DERMATITIS

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(Background) Facial erythema often appears in infant, adolescent, or pregnant patients with atopic dermatitis (AD), but the cause of the facial erythema has not fully clarified. (Objectives) We examined a possible role of prolactin for exacerbation skin lesions of AD, especially facial erythema. (Methods) Blood prolactin levels of 6 pregnant women with AD and breast milk prolactin levels of 22 mothers whose infants have AD were measured. Expression of prolactin, prolactin receptor, signal transduction and activation of transcription (STAT) 5a, and suppressors of cytokine signaling (SOCS) 3 were immunohistologically examined in 40 skin lesions of patients with AD (33 from trunk and 7 from face). We also examined skin of 8 normal controls. (Results) The blood prolactin levels were 90-197ng/ml, milk prolactin levels were 0.5-31ng/ml. Both blood and breast milk prolactin levels were almost within normal ranges. Strong positive staining of prolactin, prolactin receptor, STAT5a, and SOCS3 were seen in eccrine glands and eccrine ducts in skin lesions of patients with AD and skin of normal controls. However, expression of nuclear staining of prolactin and STAT5a were increased in keratinocytes of the skin lesions, especially in the keratinocytes near pilocebaceous area of atopic red face. Although prolactin receptor showed ubiquitous expressions in keratinocytes and eccrine organs in the AD skin lesions as well as normal controls, strong expressions of the prolactin receptors were seen in most keratinocytes in upper area of keratotic cell layer of skin lesions of AD. (Conclusion) A prolactin-STAT5a axis might be involved in a pathway for exacerbation of AD, especially for aggravation by sweats and for facial lesions of AD.

P-5. CLINICAL DIFFERENCES BETWEEN ATOPIC AND ATOPIFORM DERMATITIS

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Background: Atopic dermatitis (AD) has been divided into the “extrinsic type” and the “intrinsic type”, in which the “intrinsic type” is characterized by the absence of allergen-specific IgE. Still, there is no consensus whether this “intrinsic type” of AD, which we denominate as atopiform dermatitis (AFD), is a distinct entity. Although several studies exist about the prevalence of AFD, there is lack of knowledge and understanding about the different and specific characteristics of AFD

Objective: A case-control study was performed to describe the characteristics of AFD and to evaluate the clinical differences between AFD and AD.
Methods: Patients with the clinical diagnosis of AD were selected. Based on the outcomes of a skin prick test (SPT) and/or a Phadiatop blood test a case and a control group were generated. Cases consisted of patients with negative outcomes of both SPT and Phadiatop test. Controls were tested positive for one or both tests. All patients were evalu-

ated for medical history, quality of life, severity of disease and for the clinical features of the Hanifin and Rajka, U.K. Working Party's and the Millennium criteria. To identify diagnostic features that were associated with AFD, odds ratios (OR) and 95% confidence intervals (CI) were calculated.
Results: Nine percent of patients with a clinical diagnosis of AD had a confirmed diagnosis of AFD (34 out of 403). Personal atopic history was significantly less present in patients with AFD compared to the control group (asthma and conjunctivitis p<0.01 and hay fever and allergic rhinitis p<0.001). AFD patients had less frequent a family history of atopy (p<0.001, OR=0.02). Influence of emotional or environmental factors was significantly less reported in AFD patients than in AD patients (p<0.01, OR=0.32). Observationally, a positive Dennie-Morgan sign was significantly more present in the AFD patients than in AD patients (p<0.05, OR=2.76). Several features were negatively associated with AFD: recurrent conjunctivitis (p< 0.01, OR=0.17), pityriasis alba (p<0.01, OR=0.30), palmar hyperlineairity (p<0.01, OR=0.16) and keratosis pilaris (p<0.05, OR=0.27) were less present in AFD patients compared to AD patients.
Conclusion: Indications were found to consider AFD as a distinct entity distinct from AD with several specific characteristics. Recognition of AFD is inevitable in order to diagnose, inform and treat patients appropriately. With a distinction between AFD and AD, patients groups are better defined and more homogenous.

P-6. A CASE OF ATOPIC DERMATITIS WITH INFECTIVE ENDOCARDITIS

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Background: Recently, we can find some case reports of severe atopic dermatitis with infective endocarditis, even though those patients had no history of heart diseases.
Case Report: A 34-year-old man with a history of severe atopic dermatitis from infancy was admitted to the local hospital with complaints of high fever and diarrhea. The high fever was resistant against antibiotic therapy, and because of the exacerbation of atopic dermatitis, this patient was referred to our hospital. Because this patient had an Osler's nodule on his left 1st toe, we performed an echocardiogram on this patient. An echocardiogram showed vegetation on the mitral valve. Blood culture test demonstrated MRSA, and this patient was diagnosed as having infective endocarditis. The patient was effectively treated with vancomycin (2g/day) and gentamycin (60mg/day) without operation. Colonization of *Staphylococcus aureus* is most commonly observed in skin lesions of atopic dermatitis, and its incidence is significantly higher in patients with atopic dermatitis than in healthy individuals. As this patient had MRSA in skin lesions, the presence of atopic dermatitis may be closely related to the occurrence of infective endocarditis.
Conclusion: We suggest that it is very important to perform an echocardiogram for severe atopic dermatitis with high fever.

SESSION 3
Genetics of Atopy and Atopic Dermatitis, and Animal Models

14. KL: FILAGGRIN MUTATIONS IN ATOPIC DERMATITIS

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Filaggrin is a key barrier protein that is abundant in the stratum corneum and has a role in compaction of keratin filaments, thus contributing to barrier formation. Filaggrin has an additional role in regulating stratum corneum hydration. In 2006 loss-of-function mutations in filaggrin (*FLG*) were first shown to be strongly associated with eczema. These findings have now been replicated in numerous studies involving many thousands of patients in European, Chinese and Japanese populations. In some series *FLG* mutations are found in approximately 50% of individuals with eczema. The genetic architecture of *FLG* related eczema risk is complex with up to 6 recurrent mutations in the European population and several other family specific mutations. In the Irish and British populations two mutations (R501X and 2282del4) are the most significant. Overall in European populations, around 10% of the population carries a *FLG* mutation. Within eczema, *FLG* mutations appear to confer an additional risk of associated asthma and development of specific allergies and elevated IgE. This lecture will review basic filaggrin biology and the genetic studies of *FLG* in eczema to date.

15. OC: RAMAN SPECTROSCOPY IN ATOPIC DERMATITIS

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Common loss-of-function genetic variants of filaggrin are a major predisposing factor for atopic dermatitis. Filaggrin is an essential protein for the integrity of the stratum corneum barrier. It plays a role in the aggregation of keratin filaments into bundles and it supplies the free amino acids that act as a "natural moisturizing factor" in the stratum corneum. An impaired filaggrin production may therefore affect the skin barrier in more than one way. Growing evidence now supports the hypothesis that patients with AD have an inherited skin barrier defect. In this view, reduced filaggrin causes a compromised barrier and increased exposure to allergens, followed by allergic sensitization and finally development of AD. A rapid and easy-to-use non-invasive method to indicate a filaggrin defect would open possibilities for therapy, aiming at

the prevention of allergic sensitization and onset of the atopic march. This is especially true for infants since most of the children with AD develop the disease within their first year.
Raman spectroscopy is a rapid, non-invasive method to obtain detailed molecular information of tissues. Today, it is already successfully used to measure the content and spatial distribution of the filaggrin-derrived components within the stratum corneum *in vivo*[1]. In a recent study we have detected significantly reduced levels of NMF in the stratum corneum of carriers of a filaggrin mutation as compared to non-carriers[2] using *in vivo* confocal Raman spectroscopy.
We conclude that perspectives of Raman spectroscopy as an easy, rapid, non-invasive tool to screen infants for predisposing factors for AD, enabling targeted preventive action against this widespread disease.

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16. IC: PREVALENT AND RARE FILAGGRIN MUTATIONS IN JAPANESE PATIENTS WITH ATOPIC DERMATITIS

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Atopic dermatitis (AD) has increased in frequency in recent decades and now affects 15-20% of the population in the developed countries. Recently mutations in the gene encoding filaggrin (*FLG*) have been shown to be major predisposing factors for AD. In early 2007, we identified two Oriental specific *FLG* mutations in Japanese families with IV and reported that the mutations were also significant predisposing factors for AD in Japan. However, the frequency of *FLG* mutations observed in our Japanese AD cohort (5.6%), was much lower than that seen in Europeans (up to 48%). We studied further ten Japanese families with IV and identified four additional nonsense mutations in *FLG*. In addition to the six *FLG* mutations we have identified so far, R501X, that is the most common *FLG* mutation in Europe, was also reported to be carried by only one Japanese family with IV. In total, there are at least seven *FLG* variants in the Japanese population, including five that are prevalent. Here we show that about 25% of patients in our Japanese AD case series carry one or more of these seven *FLG* mutations and these variants are also carried by 4% of general Japanese control individuals. There is significant statistical association between the seven *FLG* mutations and AD (χ^2 $P=1.75\times10^{-6}$; heterozygous odds ratio 6.8, 95% CI 2.5-18.5). These data emphasize that skin barrier impairment due to reduced filaggrin expression plays an important role in the pathogenesis in AD and sheds further light on the genetic architecture of atopy in Japan.

17. KL: ANIMAL MODEL OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a common, chronic inflammatory disease and impairs patient's quality of life because of itching and poor appearance. It is a social needs to develop safe and effective therapy for AD. To clarify pathogenesis of AD and establish therapeutic strategy, basic research is required using animal models. There is some limitation in application of experimental data obtained by animal models because of species differentiation. However, animal models supply substantial information to investigators. Especially new approach to AD therapy is not available without animal models.
Animal models of AD are approximately categorized into three groups; spontaneous AD models, induced AD models by exogenous stimuli, and gene manipulated AD models. Canine and other important spontaneous animal models are reported. However, mouse models have advantages in their short life cycle and clear genetic background and easy gene manipulation. Then, mouse models conducted recent progress in immunology of AD.
Here we review recently reported mouse AD models focusing immune systems, skin barrier, itching and potent AD therapies.

18. IC: USE OF ANIMAL MODEL IN DEVELOPING THERAPEUTIC AGENT FOR ATOPIC DERMATITIS

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Animal models of atopic dermatitis (AD), generally mice, have been developed. The mice can be categorized into 3 groups; 1) mouse models with spontaneous manifestations of AD-like skin lesions. Representative model for this group is NC/Nga mouse. Even the mouse in this group needs additional haptens to induce dermatitis effectively. 2) genetically engineered mouse such as transgenic or knockout mouse. 3) hapten-induced mouse model. Different strains of mice such as BALB/c mouse and C57BL/6 mouse have been used.
Each model has its own advantages and disadvantages. In the spontaneous mouse models, the incidence for developing AD-like lesions is too low and reproducibility is poor. Genetically engineered models have limited usefulness especially in studying pathogenesis of AD and also limited availability. In hapten-induced models, various types of inflammation can be induced by changing haptens or mouse strains,. The basic problem with these animal models is whether these can really reflect human AD. Skin lesions with underlying inflammation look quite similar irrespective of different mouse models. Practically the only indicator that the induced skin lesions can reflect human AD is that the skin lesions show Th2 phenotype.

Until now NC/Nga mouse is the best characterized animal model of AD. However, we do not have standardized method to develop AD-like lesions consistently in NC/Nga mice. Based on our experience with NC/Nga mice, haptens, especially TNCB, must be used weekly to have consistency and reproducibility in making AD-like skin lesions.

19. OC: DEFECTIVE BARRIER FUNCTION IN AN EXPERIMENTAL MODEL OF ATOPIC DERMATITIS IN HIGH IGE PRODUCING BEAGLES

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An experimental model of Atopic Dermatitis has been identified in a colony of high IgE Beagles. These dogs are epicutaneously sensitized to house dust mites (HDM, Dermatophagoides farinae) and develop clinical lesions that are compatible with the human counterpart clinically, histologically, and immunologically after environmental exposure to the allergen. Preliminary studies had also shown that these dogs have increased Transepidermal Water Loss and decreased filaggrin expression compared to normal controls. These changes are further aggravated by allergen exposure, are particularly evident in young individuals, and in body areas typically predisposed to eczema.
The purpose of this study was to investigate the electron microscopy (TEM) of the upper layers of the epidermis before and after allergen challenge. For this purpose, the atopic dogs and normal controls were environmentally challenged with HDM three days in a row. Clinical signs were scored and skin biopsies were taken before and after allergen exposure. Ultrastructurally, TEM of the upper layers of the epidermis revealed that atopic dogs have abnormalities in lamellar bodies secretion and extracellular lamellar bilayer structure when compared to controls, even before allergen exposure. Allergen challenge further precipitated these changes in atopic individuals leading to a consistent widening of the intercellular spaces, release of lamellar bodies and disorganized lipid lamellae. Lamellar lipid delamination was common as well as widening of lipid lamellae (cisternae). It is concluded that these dogs reproduce many of the features of the human disease, including abnormalities of the barrier function, and can be used as experimental model for it.

P-7. Evaluation of FITC-induced atopic dermatitis-like disease in NC/Nga mice using CAST-grid, a computer aided morphometric system

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BACKGROUND: The NC/Nga mouse spontaneously develops eczematous atopic dermatitis (AD)-like skin lesions when maintained under conventional conditions but not under specific pathogen-free (SPF) conditions. Hence, there is a need for an AD model in mice housed under SPF-conditions, as this is mandatory for research animals in many countries.
OBJECTIVE: We evaluated the use of the hapten FITC as an inducer of AD-like disease in NC/Nga mice maintained under SPF-conditions.
METHODS: Using a CAST-grid (computer assisted stereological toolbox) as a stereological method, the mice were sensitized to FITC, and the histological efficiency of disease induction with regard to inflammation, CD4+ and CD8+ lymphocytes in addition to mast cells, was evaluated.
RESULTS: FITC does indeed induce AD-like lesions in the NC/Nga mice when considering the histological appearance of the mice, however, when evaluating the immunological response in the affected areas of the mice with regard to the CD4/CD8 ratio, we found that the immune response in the NC/Nga mice does not resemble AD–skin lesions in humans.
CONCLUSION: These results stress the importance of an assessment of not only the histological, but also the immunological appearance of the skin when evaluating AD-like disease in mice as a model for AD in humans.

P-8. Reduction of IgE production by oral administration of silk-peptide in NC/Nga mice

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Objective The incidence of atopic dermatitis has recently increased in industrialized countries. To develop a new food material to improve atopic dermatitis, we investigated effect of partially hydrolyzed silk-protein (silk-peptide) on immunoglobulin E (IgE) production in NC/Nga mice as a model of atopic dermatitis.
Materials and Methods The silk-peptide (100 mg/day) was administrated to NC/Nga mice by orally for 8 weeks, and amount of IgE in serum and clinical scores of NC/Nga mice were measured once a week during the experimental period. To illustrate the mechanism, we examined, in vitro, the effect of silk-peptide on IgE and cytokine production in spleen cells from OVA-immunized BALB/c mice. Amounts of IgE and cytokines were measured by Enzyme-Linked Immunosorbent Assay (ELISA).
Results The clinical scores on the NC/Nga mice fed the silk-peptide by orally were improved compared to those of control group and serum IgE concentration in the silk-peptide fed group clearly decreased. In vitro, the levels of INF-gamma (Th1 type cytokine) secreted from the spleen cells treated with the silk-peptide were higher than those in the control. The levels of IL-4 (Th2 type cytokine) from the treated spleen cells appeared to be lower than those in the control.
Conclusion The silk-peptide we prepared has an ability to

improve the atopic dermatitis in NC/Nga mice. The inhibition of IgE secretion would be mediated by induction of Th1 cells increase. Further studies to reveal its mechanism of the anti-allergic action are in progress.

SESSION 4
Skin Barrier Pathology in Atopic Dermatitis

20. KL: GENETICS OF ATOPIC ECZEMA

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Abstract not available

21. IC: DEFECTS OF THE SKIN BARRIER AND HOW THIS INFLUENCES THE PATHOPHYSIOLOGY OF ATOPIC DERMATITIS

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Abstract not available

22. IC: PSYCHOLOGICAL STRESS AND SKIN BARRIER FUNCTION

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Skin diseases such as atopic dermatitis and psoriasis are adversely affected by psychological stress (PS), but the pathophysiologic link between PS and disease expression remains unclear. By some series of recent studies, PS decreases epidermal proliferation and differentiation, impairs permeability barrier homeostasis, decreases stratum corneum (SC) integrity and increases the severity of group A *Streptococcal pyogenes* cutaneous infection in mice. PS also increases the production of endogenous glucocorticoids (GC), and both systemic and topical GC cause adverse effects on epidermal structure and function similar to those observed with PS. By the mechanisms that PS impairs the functions of SC, permeability barrier and antimicrobial defense, PS decreases epidermal cell proliferation, impaires epidermal differentiation, decreases the density and size of corneodesmosomes (CD), and decreases an expression of epidermal antimicrobial peptide (AMP) such as cathelicidin and mouse beta defensin 3. Barrier dysfunction is resulted from decreased production and secretion of lamellar bodies (LB), which in turn, could be attributed to a decrease of epidermal lipid synthesis. Topical physiologic lipids mixture composed of equimolar cholesterol, ceramides and free fatty acids, normalized barrier homeostasis, SC integrity and AMP level in PS mice. Therefore, PS inhibition of epidermal lipid synthesis results in decreased LB production and secretion, as well as decreased CD and AMP delivery to LB, which are compromising permeability barrier homeostasis, SC integrity and antimicrobial defense.

Two interventions such as RU-486 and antalarmin were used to confirm the hypothesis that increased endogenous GC in PS mediates its adverse cutaneous effects. RU-486, a GC receptor antagonist, inhibits GC action, and antalarmin, a corticotropin releasing hormone (CRH) receptor antagonist, prevents increased GC production in the face of PS. Inhibition of either GC action or production prevents the PS-induced decline in epidermal cell proliferation and differentiation, impairment in permeability barrier homeostasis, decrease in SC integrity and decrease of AMP expression. Thus, many of the adverse effects of PS on the structure and function of epidermal permeability and antimicrobial barrier can be attributed to increased endogenous GC. Conversely, approaches that either reduce GC production or action might benefit skin diseases provoked or exacerbated by PS.

Physiologic lipid replacement, PS reduction such as aroma therapy and meditation, and GC receptor antagonists could also be beneficial in PS induced, barrier associated dermatoses, such as atopic dermatitis and psoriasis, and cutaneous infection.

23. OC: SKIN BARRIER FUNCTION AND EXPRESSION OF ANTIMICROBIAL PEPTIDES IN ATOPIC DERMATITIS AFTER TREATMENT WITH PIMECROLIMUS OR BETAMETHASONE CREAM

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Atopic dermatitis is characterized by a compromised skin barrier, which facilitates the invasion of allergens, followed by immunological reactions and aggravation of the disease. Mutations in the filaggrin gene contribute to disturbed epidermal differentiation and barrier function and lead to reduced stratum corneum hydration and dry skin. Here we investigated whether treatments with pimecrolimus (PIM) or betamethasone valerate (BMV) improve skin barrier, epidermal differentiation, and antimicrobial peptide expression in AD. In a randomized, double blinded, intra-individual (left-right arm) comparison study, 15 patients with mild to moderate AD were treated on one upper limb with PIM cream 1% and on the other with 0.1 % BMV cream twice daily for three weeks. Significant reduction in clinical symptoms, lesion size,

and pruritus was already seen after the first week of treatment in both groups. Transepidermal water loss a functional marker of the inside-outside barrier improved in both groups. However, stratum corneum lipid layers and lamellar body extrusion assessed by electron microscopy showed normalization of stratum corneum barrier morphology after treatment with PIM but not with BMV. Enhanced epidermal proliferation in AD, was reduced 49% by PIM compared to 74% reduction by BMV. The pronounced effect of BMV may be considered a suppression exceeding the normal level thus contributing to the known skin atrophy. Consistent with the clinical improvement of AD after 3 weeks treatment, both interventions induced the differentiation markers involucrin, loricrin, and filaggrin and reduced the expression of antimicrobial peptides, hBD-2, hBD-3, psoriasin, RNase-7, and LL-37. The reduction of antimicrobial peptides was more pronounced with BMV than with PIM – suggesting better protection from bacterial colonization after PIM treatment. In summary, both PIM and BMV improved AD in regard to clinical symptoms and the expression of filaggrin, involucrin, and loricrin. The side-effects of epidermal thinning became apparent already after three weeks of treatment with BMV but not with PIM. Restoration of the skin barrier in AD was more complete with PIM than with BMV.

24. IC: REGULATORY EFFECTS OF IGE ON INNATE IMMUNE RESPONSES

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IgE is considered to have an important role in the pathogenesis of atopic dermatitis (AD) and in further accelerating its severity. The role of scratching has also been regarded as being deleterious to the host. Thus, a dogma has been established that emphasizes deleterious effects of IgE and scratching on skin inflammation while ignoring the alternative possibility that they may have a potentially beneficial and protective role. In this regard, we found that initial hapten exposure to either the footpad or the ear protected from scratching can evoke Toll-like receptor (TLR) 2-depedent rapid swelling responses showing a time course similar to immediate-type hypersensitivity (ITH) mediated by IgE/FcεRI-dependent mast-cell degranulation, although this response was previously regarded as being due to irritative effects of epicutaneously applied hapten. This innate-type ITH-like response is mediated by neuromedin U (NMU), the neuropeptide released from keratinocytes upon hapten exposure. Surprisingly, this response can paradoxically be inhibited by IgE in a hapten-independent manner, while hapten-specific IgE is essential for FcεRI-dependent ITH detected at the site subject to scratching, such as the ear. The inhibitory effect of IgE on TLR2-dependent mast cell activation is confirmed in mast cell knock-in mice reconstituted with cultured bone marrow-derived mast cells from either wild type (WT), $TLR2^{-/-}$ or $NMU^{-/-}$ mice. Thus, although IgE may have originally evolved to regulate innate immune responses, it would become deleterious to the host only when innate immune responses occur more extensively and repeatedly than originally designed and thereby require the simultaneous delivery of both IgE and scratching. AD could then be the consequence of the combined protective effects of IgE and scratching that may individually serve to prevent collateral tissue damage to the host's tissue from excessive innate immune responses.

P-9. THERAPEUTIC IMPLICATIONS OF THE DIFFERENTIAL EFFECTS OF TOPICAL CORTICOSTEROIDS AND CALCINEURIN INHIBITORS ON THE SKIN BARRIER

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Topical corticosteroids (TCS) can be very effective in the short-term treatment of flares of atopic eczema, but prolonged use can induce thinning of the stratum corneum thereby allowing enhanced penetration of allergens and consequent exacerbation of atopic eczema. This effect is particularly important in sensitive skin sites, such as the face and intertriginous areas, where the skin is already very thin and has a much lower skin barrier reserve against penetration of allergens and irritants. The purpose of this study was to compare the effect of TCS with that of the calcineurin inhibitor pimecrolimus and with no treatment, on the integrity of the skin barrier in volunteers (with or without a history of atopic eczema), assessed using the tape stripping and transepidermal water loss (TEWL) assay.
One fingertip unit of betamethasone valerate, either 0.1% or 0.025%, or hydrocortisone 1%, was applied, BID, to the right forearm for 14, 30 or 45 days respectively. A similar area was treated on the left forearm with pimecrolimus cream and a third area was left untreated.
A considerably greater TEWL was observed after removing 16, 18 and 20 tape strips following treatment with the potent TCS and the moderately potent TCS, than with either pimecrolimus or no treatment. An increased TEWL, following tape stripping, was also seen after six weeks treatment with hydrocortisone acetate 1%, especially if the volunteer had a previous history of atopic eczema.
We have demonstrated, using in situ zymography and RT-PCR, that topical corticosteroids induce increased protease expression in the skin. Patients with atopic eczema have a genetic predisposition to enhanced protease activity and this explains why prolonged use of even a mild potency TCS caused damage to the skin barrier, particularly in cases where there is a previous history of atopic eczema.

P-10. PATHOGENESIS AND UNIQUE ULTRASTRUCTURAL CHARACTERISTICS OF ICHTHYOSIS PREMATURITY SYNDROME (IPS)

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IPS is a rare form of autosomal recessive congenital ichthyosis. Key features are premature delivery (30-32 weeks) and thick caseous desquamating epidermis and respiratory symptoms at the time of birth. A striking finding in IPS is an extremely high number eosinophils and high serum-IgE levels that strongly suggest involvement of IPS gene in the development of atopic disorders. Recently, the IPS gene locus has been mapped to chromosome 9q34.11, which includes 4 candidate genes, but most of these genes have not been functionally characterized and no mutation have been identified so far.
Ultrastructurally IPS is characterized by aggregations of membrane-like curved structures in the upper epidermal cells and within horny scales. Nature of these intracellular structures is not yet clear, but apparently formation of these structures in upper epidermal layers will lead to impaired barrier function of the skin. In ongoing project we want to characterize the molecular and cellular mechanisms of pathogenesis in IPS, including barrier dysfunction of the skin and regulation of eosinophil and IgE production in IPS patients. It could be speculated that the skin barrier function is responsible for the increased production of eosinophils and IgE in IPS patients, due to increased exposure of allergens to the immune system. However, the levels of blood eosinophils at birth in IPS patients are extremely high (>50%). This shows that there is reduced regulation of eosinophil production also in utero (before the body is in contact with external allergens), indicating that the protein encoded by IPS gene may have a more direct effect on eosinophil production. Based on these findings we put forward two hypotheses: 1) The IPS gene is involved in the barrier function of the skin, and the increased levels of IgE and eosinophils are secondary to the epithelial barrier defect; 2) the IPS gene is expressed in lymphoid, as well as in epithelial tissues and directly involved in the regulation of eosinophil and IgE production.

SESSION 5
Immunology of Atopy and Atopic Dermatitis

25. KL: ATOPIC DERMATITIS AND CHEMOKINE

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Atopic Dermatitis(AD) is a chronic inflammatory skin disease that is characterized by pruritic eczematous lesions and is associated with elevated serum IgE levels, specific IgE environmental allergens such as house dust mites, and tissue and peripheral blood eosinophilia. AD is characterized by the predominant infiltration of Th_2-cells, the increased secretion of Th_2-cytokines such as IL-4 and IL-5 in the acute phase of lesional skin. Chemokines are small secreted molecules that regulate leukocyte trafficking via their corresponding seven-transmembrane-spanning, G-protein coupled receptors. In this talk I will focus on the role of Th_2 chemokine CCL17 and CCL27, and their corresponding receptor CCR4 in AD. Furthermore I will also talk about cutaneous T cell attracting chemokine (CTACK)/CCL27 and its receptor CCR10.

26. IC: THE ROLE OF CD8+ T CELLS IN THE INITIATION OF THE ATOPIC DERMATITIS LESIONS

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Abstract not available

27. OC: DIFFERENTIAL GENE EXPRESSION IN CD4+TCELLS FROM ATOPIC DERMATITIS PATIENTS IS DUE TO SELECTIVE EXPRESSION IN THE SKIN HOMING T CELLS

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CD4+ Tcells play an important role in the pathogenesis of atopic dermatitis (AD), both systemically as well as in affected tissues. Recently, we have demonstrated two groups of differentially expressed genes in freshly isolated CD4+Tcells of AD patients compared to healthy controls (HC). One group of genes, related to skin homing of Tcells (CCR10, CCR4, CRTH2 and FUCT-VII), displayed increased expression. Another group of genes, related to apoptosis/proliferation (NR4A2, TNFAIP3, JUNB, C-JUN and GADD45A), displayed decreased expression. Remarkably, no genes directly related to Th2 or Th1 were found to be differentially expressed. Aim: To establish if the skin homing population of CD4+Tcells is the population with decreased expression of apoptosis-related genes.
Methods: CD4+Tcells of 8 AD patients and 5 HC were isolated by MACS (CD14- and CD4+). Subsequently, cutane-

ous lymphocyte-associated antigen (CLA)-expressing Tcells were purified by flow cytometry. Gene expression in the CLA+ and CLA- population was determined by quantitative RT-PCR. Results: Expression of the group of skin homing genes was comparable in CLA+CD4+T cells of AD patients and HC. However, the expression of the apoptosis/proliferation-related genes was significantly lower in the CLA+ population of the AD patients compared to HC, but was comparable in both CLA- populations.
Discussion: AD patients are characterized by increased numbers of CLA+CD4+T cells that directly affects the expression of skin homing genes in the total CD4+ population. However, these CLA+CD4+Tcells are qualitatively different from healthy controls by the decreased expression of apoptosis-related genes.

28. IC: LANGERHANS CELLS AND PROSTAGLANDINS: CONTRIBUTION TO THE ETIOLOGY AND PATHOGENESIS OF ATOPIC DERMATITIS AND RELATED DISORDERS

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Antigen-specific skin immune responses, such as contact dermatitis and atopic dermatitis, are initiated by antigen uptake and migration of cutaneous dendritic cells, such as Langerhans cells and dermal dendritic cells. These cutaneous dendritic cell functions are thought to be modulated by a wide variety of mediators, however, precise mechanism remains unknown. Prostanoids, including prostaglandin (PG)E2, PGD2, PGI2, PGF2 and thromboxane (TX)A2, are one of lipid mediators to play pathophysiological roles in the body. They exert their functions acting at its specific G protein coupled receptors EP, DP, IP, FP, and TP, respectively. EP has 4 subsets, EP1, EP2, EP3, and EP4.
PGE2, PGD2, and TXA2 are known to be induced in the skin and regional lymph nodes upon foreign antigen exposure. On the other hand, EP2, 3, 4, DP are expressed on cuteneous dendritic cells, suggesting that prostanoids play some roles on antigen exposure to the skin. In the skin prostanoids have biphasic roles. Maturation and migration of cutaneous dendritic cells are enhanced by EP4, but suppressed by EP3 and DP receptor. These results suggest that prostanoids have multiple roles in the cutaneous immune responses in a context dependent manner.

P-11. GENOTYPE AND FUNCTIONAL STUDY OF TLR-2 AND TLR-4 IN A FRENCH ATOPIC DERMATITIS COHORT

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Introduction: The primary impairment of the epidermal barrier demonstrated in atopic dermatitis (AD) may facilitate Staphylococcus aureus (SA) exotoxin penetration through the skin. We have previously shown that SA enterotoxin B (SEB) can induce monocyte-derived dendritic cells activation through toll like receptor (TLR) 2 and TLR4 signalling (Mandron et al., JACI 2006). Our objectives were (1) to study TLR2 and TLR4 as atopic dermatitis susceptibility genes in France, and (2) to compare SEA and SEB-induced cytokine responses in monocytes isolated from $TLR2^{R/Q}$ and $TLR4^{D/G}$ variants in AD and controls. Methods: 145 patients with AD, were enrolled in the TLR2 and TLR4 polymorphism study. The mean SCORAD index was 25. An ethnically matched control group of 52 phenotypically anonymous healthy adult blood donors served as control. Patients and controls were subsequently grouped into $TLR2^{wt}$-$TLR4^{wt}$, $TLR2^{R/Q}$-$TLR4^{wt}$, $TLR2^{wt}$-$TLR4^{D/G}$ and $TLR2^{R/Q}$-$TLR4^{D/G}$ groups. CD14+ monocytes were isolated, cultured during 24 hours and stimulated with 10 ng ml^{-1} of highly purified SEA, SEB and LPS. IL-1β, IL-5, IL-6, IL-8, IL-10, TNFα and IP-10 (CXCL10) were measured in the supernatant. Results: The allelic frequencies of the TLR2 D753G and TLR4 D299G polymorphisms were respectively 0.02 and 0.066 in the AD group, and respectively 0.043 and 0.049 in the controls. SEB or SEA stimulation increased significantly TNF-α, IP-10 and IL-6 production but had no significant effect on IL-8 production by monocytes from AD and controls. LPS enhanced the production of IP-10 in controls, but not in AD patients. SEB-induced TNF-α production decreased significantly in $TLR2^{R/Q}$ variants, whereas SEB-induced IP-10 production increased in both $TLR2^{R/Q}$ and $TLR4^{D/G}$ variants. SEB- and LPS-induced TNF-α secretion, together with LPS-induced IP-10 secretion decreased significantly in $TLR4^{D/G}$ variants in controls but not in AD patients. An unexpected higher level of IP-10 upon LPS stimulation was observed in $TLR4^{D/G}$ AD compared to $TLR4^{wt}$ AD.
Discussion: Previous studies have shown an association for both $TLR2^{R/Q}$ and $TLR4^{D/G}$ variants with sepsis and asthma, but have led to conflicting results in AD. In our French population, the $TLR2^{R/Q}$ polymorphism was rarely found, and no significant association was shown with AD. It has been shown that monocytes from AD are functionally defective in their capacity to produce the proinflammatory TNF-α cytokine after TLR2 stimulation (Hasannejad et al., 2007). This is in accordance with our results obtained upon SEB stimulation as a putative TLR2 ligand. Interestingly, we found that the monocyte functional defect in AD also affects the production of IP-10, a chemokine which may play an important role by attracting activated TH1 cells. Our results suggest that in AD patients, TLR4 signalling could have a deleterious effect on IP-10 secretion mediated by TLR2 activation. It has been recently demonstrated that TLR2 was involved in sensing of SEB on dendritic cells before its delivery into the cytosol for interaction with the nucleotide-binding oligomerization domain (NOD) 1. How TLR2-mediated NOD1 and TLR4 signalling could be connected and regulated in AD patients is an opened question. Our study further sustain the notion that a better knowledge on interaction of SEB with TLR2 and TLR4 could provide new clues on how SA toxins may drive innate as well as adaptive defense against bacterial damages associated with atopic dermatitis.

P-12. CD4+CD25 HIGH TCELLS AND FOXP3 POSITIVE TCELLS ARE DECREASED IN ATOPIC DERMATITIS PATIENTS AFTER CYCLOSPORINA TREATMENT

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Cyclosporin A (CsA) is increasingly used in the treatment of severe atopic dermatitis (AD). Although highly efficacious and relatively safe, recent reports have shown that in vitro and in animal models CsA induces suppression of naturally occurring CD4+CD25+ T regulatory cells (Tregs). The objective of this study was to investigate the in vivo effects of CsA treatment on peripheral blood T cell subsets in AD patients. In addition, the effects on the expression level of genes related to Tcell survival and regulatory Tcells, previously found differentially expressed in AD patients, were investigated.
Methods: Eleven patients with severe AD were included. PBMCs were isolated at timepoints 0, 3 and 6 weeks after CsA treatment and the following subsets were analyzed by FACS: CD3+, CD4+, CD8+, CD45RO+, CD45RA+, CD4+CLA+, CD4+CCR4+, CD4+CD25+, CD4+CD25high. In addition, at similar timepoints CD4+ Tcells were isolated by MACS beads and the expression levels of FoxP3 and several apoptosis and migration-related genes, were investigated by quantitative-PCR.
Results: All patients showed rapid improvement of disease activity after treatment with CsA. Interestingly, the percentages of CD4+CD25high Tregs, and FOXP3+CD4+ Tcells were significantly increased compared to healthy controls, but decreased after 3 and 6 weeks of treatment. No significant changes in the percentages of CD3+, CD4+, CD8+, CD45RO+, CD45RA+, CD4+CD25+, CD4+CCR4+, and CD4+CLA+ populations were found. In addition, FOXP3, CCR4 and GADD45A mRNA expression levels in CD4+ Tcells significantly decreased.
Conclusion: The current study is the first to show that CsA treatment in vivo significantly decreases the percentage of CD4+CD25high Tcells and reduces FOXP3 and GADD45A expression in CD4+ Tcells from patients with AD.

P-13. INTERLEUKIN-13 AND INTERFERON-GAMMA PRODUCING SKIN RESIDENT CD8 T CELLS: A VICIOUS CIRCLE OF BARRIER DISRUPTION OF THE SKIN IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is an inflammatory skin disease characterized by barrier dysfunction of the skin and infiltration of activated T cells. We have isolated the T cells from skin lesions of AD via short-term explant cultures and compared them to cells isolated from normal skin. AD skin lesions contain an expanded population of CD8 T cells compared to normal skin (mean 20% vs. 4%). Strikingly, 41% of CD8 T cells produced interferon-gamma (IFNg) and 42% produced interleukin-13 (IL-13); these populations were mutually exclusive. In fact, we found production of IL-13 by up to 60% of the total T cells (CD4 and CD8) infiltrating AD lesions. The vast majority of AD CD8 T cells expressed CD49a, similar to recent findings in psoriasis and suggesting epidermal targeting. Both IFNg and IL-13 have profound but distinct proinflammatory effects in tissue. However, we found co-expression of Tc1 and Tc2 subsets in atopic dermatitis skin. Previous work has shown that IFNg production by T cells renders keratinocytes more susceptible to Fas/FasL-induced apoptosis and may contribute to barrier dysfunction. IL-13 produced by T cells plays a pivotal role in the induction of epithelial apoptosis in ulcerative colitis and induces MMP-9 and chemokine production by keratinocytes. We hypothesize that skin infiltrating IL-13 and IFNg producing CD8 T cells play a central role in maintaining the disruption of the epidermal barrier, through induction of keratinocyte apoptosis and by facilitating inflammatory cell influx. Epidermal injury renders the skin susceptible to external stimuli resulting in a vicious circle of barrier disruption and inflammation that may be pivotal in both the initial induction as well as the switch to chronicity in AD skin lesions. Our work suggests that agents targeting the activity of CD8 T cells in AD may improve both the inflammatory and barrier disruption aspects of the disease.

P-14. 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

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Introduction: Atopic dermatitis (AD) is a chronic, inflammatory disease with a high prevalence and complex etiopathogenesis. *Staphylococcus aureus* is present in 80 -100% of AD patients, and secretes exotoxins that might relate to its pathogenesis. Methods: Thirty-eight AD adults and 33 controls were evaluated for proliferation response of peripheral blood mononuclear cells (PBMC) to staphylococcal enterotoxins A and B (SEA and SEB) and for interleukin (IL)-18 secretion. PBMC were stimulated with SEA and SEB, phytohemaglutinin (PHA), pokeweed (PWM), tetanus toxoid (TT) and *Candida albicans* (CMA). IL-18 secretion was measured by ELISA in the culture supernatants and in sera of AD patients and controls. Results: A significant inhibition of PBMC proliferative response to SEA, PHA, TT and CMA of AD patients was detected (P = 0.05). Moreover, an increased level of IL-18 was detected both in serum samples and culture supernatants from AD patients (P = 0.05). Conclusions: A decreased PBMC proliferation response to distinct antigens and mitogens (SEA, PHA, TT and CMA) in adults with AD suggest a compromised immune profile. On the other

hand, augmented IL-18 secretion may enhance the immune dysfunction observed in AD, leading to constant skin inflammation.

P-15. THE EXPRESSION OF MCP-1, IL-6 AND IL-8 IN HUMAN CELL LINES INDUCED BY HOUSE DUST MITE, *DERMATOPHAGOIDES PTERONISSINUS*

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The house dust mite (*Dermatophagoides pteronissinus*) has been known as one of pathogenic factors in allergic diseases. Pro-inflammatory cytokines such as monocyte chemotactic protein 1 (MCP-1/CCL2), IL-6, and IL-8 (CXCL8) play pivotal roles in mediating the infiltration of various cells into the skin of atopic dermatitis and psoriasis. In the present study, we investigated the effect of *D. pteronissinus* extract (DpE) on expression of MCP-1/IL-6/IL-8 mRNA and protein, and the signal transduction in the human monocytic THP-1 and human eosinophilic EoL-1 cells. The mRNA and protein expression of MCP-1, IL-6, and IL-8 were measured by performing RT-PCR and ELISA. The mRNA and protein expression of MCP-1, IL-6 and IL-8 were elevated by DpE in a time and dose-dependent manner in THP-1 and EoL-1 cells. In addition, the concentration of MCP-1, IL-6 and IL-8 increased in serum of patients suffering from atopic dermatitis, compared with the cytokine concentration in normal serum. Taken together, these results indicate that DpE can trigger allergic response through the increased expression of pro-inflammatory cytokines and the cytokine measurement after DpE treatment may be used as a helpful screening system for the treatment of atopic dermatitis and other allergic diseases.

SESSION 6
Role of Allergens and Food Allergy in Atopic Dermatitis

29. KL: ROLE OF FOOD ALLERGY IN INFANTS AND CHILDREN WITH ECZEMA

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Eczema is a common disease in infancy and childhood. Often eczema and food allergy occur in the same patient. It had been shown in a birth cohort study that the prevalence of IgE-mediated food allergy increased with an increase in the severity of eczema. The relative risk of an infant with eczema having IgE-mediated food allergy was 5.9 for the most severely affected group.
Both, typical immediate types of allergic reactions as well as late phase reactions with worsening of the skin are observed in patients suffering from eczema. Clinical studies have revealed that more than 50% of affected children with eczema that can be exacerbated by certain foods will react with a worsening of skin eczema either alone or in addition to immediate symptoms. The most common food allergens in infancy and childhood are cow's milk, hen's egg, peanuts, tree nuts, wheat, soy, fish and shellfish. In older children pollen-associated food allergies might become important.
Food can be a relevant trigger factor of eczema. However, unnecessary diets which are not based on a proper diagnosis may lead to malnutrition and additional psychological stress on patients suffering from eczema. A thorough diagnostic procedure including the patient's history, measurement of sensitization and its clinical relevance is of great importance. In the majority of case oral food challenges are necessary to prove the diagnosis.
Infants and children with eczema often show improvement of their skin condition over time. In parallel, the development of tolerance is common in cow's milk and hen's egg allergy. Sensitization to peanuts is also common in infants and children with eczema. In contrast to cow's milk and hen's egg allergy, many of these patients retain their allergic reactions to peanuts until adulthood. Especially, the later development of asthma in these patients put them at risk for severe anaphylactic reactions.

30. IC: BREASTFEEDING AND ATOPIC DERMATITIS, NEW INSIGHTS BEYOND THE CONTROVERSY

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Research on breastfeeding and atopic diseases is plagued by a long history of inconsistent findings between epidemiological studies. Most studies found a protective effect of breastfeeding and delayed introductions of solids, but many other studies have found contradictory results, and some suggest that the protection may depend on maternal atopic constitution. Recent studies on breast milk immune factors, fatty acids composition, and the role of gut microbiota of the child have offered clues to the understanding of these inconsistencies. Crucial for causal inferences from epidemiological observational studies is their longitudinal design, with separation in time between cause and effect. This is illustrated by recent findings from the KOALA Birth Cohort Study, the Netherlands, and other birth cohort studies. Investigation of the composition of breast milk has elucidated the role of breast milk immune factors in (like TGF-beta and soluble CD14), and fatty acids (as determined by maternal diet during pregnancy and lactation). In addition, the type of infant feeding determines the early development of gut microbiota in the first months of life, a critical period in immune development. We found that colonisation with Escherichia coli was associated with an increased risk of subsequent develop-

ment of atopic eczema, whereas Clostridium difficile was associated with an increased risk of both atopic eczema and atopic sensitisation (specific IgE against food allergens). Finally, detailed analysis of the age of introduction of cow's milk products and solids revealed that, contrary to expectation, a delayed introduction was associated with a higher risk of development of atopic eczema and sensitisation, when the duration of breastfeeding was taken into account.
Based on these studies we conclude that, first, the protective effect of breastfeeding on the development of atopic eczema is closely linked with protection against allergic sensitisation to food allergens; second, that the protective effect is dependent on maternal intake of omega-3 long chain polyunsaturated fatty acids (and possibly enhanced by transvaccenic acid and conjugated linoleic acid from ruminant (dairy) origin, while deteriorated by industrially hardened transfatty acids); third, that immune effects of breast milk are (at least partially) mediated by its influence on gut microbiota and oral tolerance induction; and finally, that oral tolerance to cow's milk and other potential allergens is possibly enhanced by introduction of these foods at a time when the infant is still (partially) breastfed. Implications for prevention of atopic disorders pertain to: maternal diet during pregnancy and lactation; duration and exclusivity of breastfeeding and timing of introduction of other foods; composition of artificial infant formula; transmission of maternal gut bacteria to the infant; and targeted oral tolerance induction.

Publications from the KOALA Birth Cohort Study:
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&cmd=Search&itool=pubmed_Abstract&term=Thijs-CT%20%5bau%5d%20OR%20Thijs-c%20%5bau%5d%20NOT%20Thijs-CM%20%5bau%5d%20AND%20(KOALA%20OR%20Penders)%20

31. IC: ALLERGEN TESTS IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a multifactor-determined inflammatory skin disorder, in which intrinsic or genetic, and extrinsic or environmental factors are related. Among the extrinsic factors, allergens such as inhalant and food allergens may cause eczema from IgE-mediated reactions. Contact dermatitis and contact urticaria often trigger, exacerbate and even prolong the conditions of AD. Current therapy of AD is directed to suppress the inflammatory infiltrate and reduce these triggering factors. Therefore allergen tests are important to treat and care the AD patients.
The following tests are available and useful in order to identify these allergens.
1. IgE-mediated reactions
Atopy patch test (APT) is an epicutaneous patch test with allergens known to elicit IgE-mediated reactions, and the evaluation of eczematous skin lesions after 24h to 72 h, was developed as a diagnostic tool for characterizing patients with aeroallergen-triggered AD.
Skin prick test (SPT) is a standard and useful in vivo skin test to detect specific IgE antibodies against the suspected allergens.
Specific IgE (sIgE: CAP-FEIA) is an in vitro test for specific IgEs against various allergens.
For food allergens, provocation tests should be carried out to reveal clinical relevance of the allergens that trigger or exacerbate AD.
Positive APT reactions are associated with allergen-specific T-cell responses[1]. The APT specificity exceeds the specificity of the classic tests of IgE-mediated hypersensitivity, SPT and sIgE. However, sensitivity of APT was lower than the classic tests.
2. Cell-mediated reactions
Patch test is an epicutaneous test to identify contact allergens. Topical medicaments sometimes elicit contact dermatitis and exacerbate and prolong AD.
Repeated open application test or use test are useful to reveal contact allergens in AD.
Reference
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P.J.Frosch , T.MennÈ , J.-P.Lepoittevin Ed., Contact Dermatitis, Springer-Verlag Berlin Heidelberg, 2006, pp391-399.

32. IC: LEDGF/DFS70, A MAJOR AUTOANTIGEN OF ATOPIC DERMATITIS, IS A COMPONENT OF KERATOHYALIN GRANULES

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LEDGF/DFS70 is a transcriptional cofactor, survival factor, and a receptor of the HIV-1 integrase. It is also a major autoantigen in patients with atopic dermatitis (AD), because autoantibodies to this protein are found in approximately 30% of AD patients. To better understand the role of autoantibodies and autoantigens in the pathogenesis of AD, we examined the distribution of LEDGF/DFS70 in the epidermis of normal human skin by light and electron microscopic immunocytochemistry. Increased amounts of LEDGF/DFS70 were located in the nuclei of cells in the basal layer, while the cytoplasm of cells in the granular layer stained for LEDGF/DFS70 by light microscopy. Using immunoelectron microscopy, we observed the accumulation of LEDGF/DFS70 in keratohyalin granules (KG) in the cytoplasm of cells in the granular layer. In addition, Bip/GRP78, a master chaperone of the endoplasmic reticulum stress response, co-localized with LEDGF/DFS70 in the KG. These results suggest that LEDGF/DFS70 is predominantly located in the nucleus of the basal epidermal cells and translocates into the cytoplasm during differentiation. Once in the cytoplasm, LEDGF/DFS70 accumulates in the KG in the granular layer.

33. IC: IDENTIFICATION OF ALLERGENS IN WHEAT ALLERGY

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Wheat has been recognized as one of the most important allergens in the patients with food allergy. In Japan wheat ranks as the third most frequent food allergen and especially the first in the patients with food-dependent exercise induced anaphylaxis (FDEIA). The pathogenic mechanisms include IgE-mediated allergy and probably cell-mediated in atopic dermatitis. In the IgE-mediated wheat allergy clinical manifestations are symptoms on the skin, the gastrointestinal tract and the respiratory tract. Wheat allergens for the respiratory symptoms are typically water-soluble proteins and those for FDEIA are water-insoluble proteins. FDEIA is mostly observed in adults and exhibited severe allergic reactions such as shock or hypotension. A challenge test consisting of ingestion of the assumed food followed by intense physical exercise is the only reliable method to determine the causative food and to diagnose the disease. However, the challenge test is not always safe. So an in vitro diagnostic method is necessary for patients with FDEIA. Several gliadins and glutenins have been reported as major allergens in wheat-dependent exercise-induced anaphylaxis (WDEIA). We revealed that omega-5 gliadin and high molecular weight-glutenin subunit is major allergens in WDEIA. A simultaneous detection of specific IgE to epitope sequences of both omega-5 gliadin and high molecular weight glutenin subunit is found to be a reliable method for diagnosis of WDEIA. On the other hand, immunoreactive gliadins appeared in the sera of patients during the challenge test with both wheat-exercise and wheat-aspirin challenges in parallel with allergic symptoms. These findings suggest that exercise and aspirin facilitate allergen absorption from the gastrointestinal tract.

34. KL: TREATMENT OF CHILDHOOD RECALCITRANT ATOPIC DERMATITIS

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Atopic dermatitis is a multifactorial determined inflammatory skin disorder, that is common in children and in which genetic factors play a dominant role [1]. Exacerbations and remissions characterise the course of atopic dermatitis. Different factors play a role. One of these is food allergy, particularly in young children. Inhalation allergy and contact allergy are other factors. Current therapy of AD is directed to suppress the inflammation and reduce triggering factors. Goals of current standard therapy are improvement of the skin-barrier, blocking of receptors and reduction of the inflammatory infiltrate. Advanced treatment of severe AD in children includes:

- General and preventive aspects
- An individualised therapeutic regimen and use of emollients
- Local application of corticosteroids
- Local application of topical immune modulators
- Wet wrap techniques using diluted corticosteroids
- Local or systemic antibiotics
- Systemic treatment in recalcitrant disease (cyclosporin, azathioprine)
- Dietary elimination and oral probiotics
- Other and experimental therapies

To evaluate effects of therapy, it is important to score the severity of AD. Different scoring-systems are available, of which the SCORAD-index, objective SCORAD and EASI are the best validated systems [2,3]. Because the SCORAD is time-consuming, for routine use we derived a simpler scoring-system from this and called it TIS: three-items severity score, involving the representive erythema, oedema and excoriations [4,5]. Each item can be graded on a scale of 0-3. Maximal TIS-score is 9. In a validation retrospective study we determined the TIS-score of 152 children. The TIS-score is a good assesment method for routine use [5,6]. Daily bathing (maximum time of 5 minutes), application of emollients and use of soap substitutes are recommended. A recent publication favours for adults and older children longterm bathing for 20 minutes at evening followed by application of creams [7]. Daycare oriented care with education for the parents and the children and support of them will improve the care of children and parents. In erythrodermic or severe refractory AD, different variations of wet wrap techniques can be used [8,9]. The wet wrap technique is a kind of occlusive treatment. The resorption of the topical corticosteroid is increased to 10% under occlusion, while hydration of the skin leads to a 4- to 5- fold increase in absorption. Although rapid improvement of atopic dermatitis occurred, adrenal pituitary suppression limited long-term use [10]. Betamethasone and even hydrocortisone acetate 1% application resulted in HPA-axis suppression. Fluticasone propionate 0.05% is a corticosteroid with an improved benefit- risk ratio. Therefore it looks more suitable for the wet wrap technique for long-term treatment. This therapy with a potent diluted corticosteroid cream with minor systemic side-effects is an interesting and promising option in children, but also in adults. The WWT is usually more effective than treatment with the topical immunomodulators (TIM).

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35. OC: ROLE OF FOODS IN IRREGULAR AGGRAVATION OF SKIN LESIONS IN CHILDREN WITH ATOPIC DERMATITIS

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Background: Foods as a trigger of atopic dermatitis have long been the subject of debate. We previously reported that foods played an important role in unpredictable, irregular aggravation of skin lesions in adult patients with the disease. In the present study, we selected children with atopic dermatitis who showed irregular aggravation of skin lesions and tried to see whether foods could provoke the irregular worsening of dermatitis in children with the disease.
Methods: The study population consisted of 69 children with atopic dermatitis who showed unpredictable, irregular aggravation of skin lesions. They ranged in age from 3 to 15 years. They were asked to keep a diary of foods and skin conditions for 2 months. We then chose food items which were eaten, not every day, but on the day or the preceding day of the irregular exacerbation. Elimination and open challenge tests with suspected foods were performed. Challenge-positive foods were determined by evaluating comparable before-after challenge photographs. When possible, specific IgE antibodies to the offending foods were measured by the radioallergosorbent test (RAST). We then observed the skin conditions for 3 months during which patients were prohibited from eating the offending foods.
Results: Challenge-positive foods were confirmed in 52 (75%) of the 69 patients examined. Predominant offending foods were chocolate, cheese and yogurt. Specific IgE values to offending foods were mostly negative. Exclusion of the offending foods brought about a progressive improvement of the disease.
Conclusion: Foods play an important role in irregular aggravation of skin lesions in children with atopic dermatitis.

36. OC: INFANTS WITH ATOPIC DERMATITIS - A 10-YEAR FOLLOW-UP STUDY

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Objectives Food allergy has been regarded as the main reason of atopic dermatitis (AD) in infants under 1 year of age. The aim of this study was to clarify weather strict individual elimination diets aiming to total clearance of atopic dermatitis in infants ("zero tolerance") had a favorably effect on future atopic manifestations.
Patients and methods Altogether 201 children participated in the study (girls=74, boys=127). Originally they were, at age of under 12 months, referred to Tampere University Hospital during years 1996-97 because of AD. Majority of them had multiple food allergies and wide elimination diets were needed. They were re-examined (during years 2006-7) with large skin prick- and atopy patch-test panels, present atopic diseases were examined and severity of atopic dermatitis was scaled by SCORAD. Growing of children was measured.
Results Based on open food challenge tests, allergies to basic foods (milk, egg, soy, fish, wheat, barley, rye, oats) still existed in 33% of children. Altogether 29% suffered from asthma and 70% had seasonal pollen allergy-related symptoms. Almost a quarter (24%) of children were scored under 1 point of SCORAD-value and majority (87%) had their SCORAD-value under 20. Sex and age matched mean height levels did not deviate from that of general age group.
Conclusion Striving for "zero tolerance" of AD by means of tailored elimination diets does not seem to stop the atopic march in infants and small children with food allergies, but only a few of them suffer from severe AD at the age of 10-11 years. Growth of these children is not unfavorably affected by elimination diets, either.

P-16. IDENTIFICATION AND CHARACTERIZATION OF A NOVEL ALLERGEN, PEN CH 33, FROM *PENICILLIUM CHRYSOGENUM* AND ITS ROLE IN ATOPIC DERMATITIS

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Fungi grow almost everywhere and various fungal species have been demonstrated to elicit allergic symptoms and to sensitize patients, including atopic dermatitis (AD). Many reports have defined that *Penicillium chrysogenum* (*P. chrysogenum*), one of the most frequently isolated indoor molds, as an aeroallergen, but the relationship between exposure to aeroallergens and occurrence of AD was rarely studied. In the present study, we used the proteomic approach combined with immunoblotting using serum samples form AD patients to comprehensively analyze the IgE-reactive components secreted from *P. chrysogenum.* Sera from 20 penicillium-sensitized atopic patients were first analyzed their IgE binding to the secreted extract of *P. chrysogenum* by immunoblotting. Of the prominent bands, allergens with molecular masses around 16 kDa were detected by 95 % (19 of 20) of these sera. Allergens with molecular masses of 33, 46, 52, 68, and 97 kDa were recognized at a high frequency of 55–85 %, whereas the recognition rate for those with molecular masses of 26, 28, and 38 kDa was lower (~34-45 %). Among 11 IgE-reactive spots, we identified five known allergens and one novel allergen. Based on the internal sequences derived from nanoLC-MS/MS and N-terminal sequencing, we

accomplished the structural characterization of the novel protein—Pen ch 33. We found that over 85% (36/42) AD patients were positive for IgE binding to Pen ch 33. Furthermore, we characterized the allergenicity *in vitro* and *in vivo,* and IgE-binding cross reactivity of Pen ch 33 by various functional analyses. Pen ch 33 possesses high prevalence of IgE-reactivity and evokes allergic symptoms after intradermal skin tests among AD patients. Besides, Pen ch 33 shows IgE cross reactivity with its homologue from *A. fumigatus*, suggesting that the novel protein is a potential common allergen.

P-17. HOUSE DUST MITE ALLERGEN: ONE OF POSSIBLE FACTORS INDUCING TSLP EXPRESSION

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Human thymic stromal lymphopoietin (TSLP) is a novel IL-7-like cytokine produced by human epithelial, stromal, and mast cells. TSLP-activated human dendritic cells induce the generation of CD4+ Th cells with a pro-allergic phenotype and also induce the differentiation of CD8+T cells into IL-5 and IL-13 producing cytolytic effector cells. It has been reported that TSLP is highly expressed in the lesional keratinocytes of atopic dermatitis but not in the non-lesional keratinocytes of atopic dermatitis or other types of disease with skin inflammation. However, what kind of factors can induce TSLP expression remains unclear.
House dust mites (HDMs) represent significant indoor allergen sources for patients with atopic dermatitis. To verify whether the HDMs can affect expression of TSLP or not, we performed a RT-PCR to detect TSLP expression from cultured keratinocytes which was treated by dust mite allergen. And we undertook immunohistochemistry to detect TSLP in normal tissue which was co-cultured with dust mite allergen. We found only HDMs cannot induce TSLP mRNA expression, but HDMs mixed with dendritic cells can induce TSLP mRNA expression from cultured keratinocytes. On the immunohistochemistry, we also found tissue co-cultured with dust mite allergen showed TSLP expression in epidermis, comparing to untreated tissue.
It is possible to speculate that HDMs may be one of important factor which induce TSLP expression in skin, resulting in atopic dermatitis-like environment.

P-18. SENSITIZATION TO TURNIP RAPE: A COMPARISON BETWEEN FINNISH AND FRENCH CHILDREN WITH ATOPIC DERMATITIS

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Background: Finnish children with atopic dermatitis (AD) are frequently sensitized to turnip rape and oilseed rape, suggesting that these plants are new potential food allergens. We examined whether French children are also reactive to these oilseed plants and whether mustard could be the cross-reacting allergen.
Methods: Fourteen Finnish and 14 French children (mean ages 3.8 and 4.7 years) with AD and positive skin prick test (SPT) to turnip rape were challenged with turnip rape and mustard. IgE antibodies were measured by ImmunoCAP and ELISA, and cross-reactivity was examined by ELISA inhibition. Twenty-eight age- and sex-matched children with AD and negative SPT to turnip rape and oilseed rape served as controls.
Results: Labial or oral challenge to turnip rape was positive in 14 (100%) Finnish and five (36%) French children. Mustard challenge was positive in five (36%) Finnish and five (36%) French children. IgE antibodies to oilseed rape and mustard were frequent in the Finnish and French children (71% - 100%), but uncommon (4%) in the controls. IgE levels to purified 2S albumins were elevated in most Finnish and French children. IgE inhibition experiments showed similar cross-wise inhibition patterns.
Conclusions: French children with atopic dermatitis are also reactive to turnip rape and show IgE antibodies to turnip rape, oilseed rape and mustard similarly to the Finnish children. 2S albumin allergens in the seeds of these plants are highly cross-reactive and therefore, they all could be important sensitizers in children with atopic dermatitis.

P-19. CLINICAL IMPROVEMENT AND LABORATORY CHANGES IN 23 ADOLESCENT PATIENTS WITH ATOPIC DERMATITIS UNDERGOING SUBCUTANEOUS SPECIFIC IMMUNOTHERAPY WITH HOUSE DUST MITE ALLERGENS

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Background: Sensitization to inhalant allergens such as house dust mite (HDM) allergens is the most common in adolescent and adult patients suffering from atopic dermatitis patients (AD). Specific immunotherapy (SIT) against HDM might represent an attractive therapeutic option for the long-term treatment of these patients. However, studies on the effecitiveness of HDM SIT in patients with AD have provides controversial clinical results. Furthermore data on the immunological changes induced by SIT in AD patients are rare.
Methods: Twenty-three adolescent or adults with a chronic course of atopic dermatitis, SCORAD ‡40 and allergic sensitization to house dust mites [specific IgE to Dermatophagoides pteronyssinus and Dermatophagoides farinae in RAST >15 IU/ml] were included in the study. Subcutaneous SIT with a house dust mite preparation (Der p/Der f, ALAVAC®, Allergy Therapeutics Inc.) applying induction and maintenance doses in weekly intervals for 1 year. Simultaneously the patients were treated with systemic anti-

histamines and topical steroids. The main outcome measures addressed the change of the SCORAD, the wheal size in skin prick test with Der p and Der f, and the immunological data such as TARC, MCP-1, IFN-r, IL-4, IL-5, IL-6, IL-8, IL-10, IgG_1, IgG_4 to Der p and Der f after 3, 6, 9 and 12 months of SIT in comparison with the value at baseline.
Results: The SCORAD declined in 80 percent of AD, and then the use of topical corticosteroids and systemic antihistamines was significantly reduced. Twenty percent of AD was temporarily worsened within 4 weeks after SIT. Therefore they increased antihistamine and topical medicaments, then tolerated. In most of AD the wheal sizes of Der p and Der f were reduced after 3 months of SIT. In immunological study, the level of IL-8 remarkably increased in the sera of the patients during SIT. Der p/Der f IgG1 and IgG4 also were increased by SIT. But the level of the tolerogenic cytokines IL-10 and TGF-beta slightly changed.
Conclusions: Allergen-SIT for 1 year with a house dust mite preparation is able to improve the eczema in patients with atopic dermatitis who are sensitized to house dust mite allergens and reduces the need for topical corticosteroids. But the laboratory changes of the tolerogenic cytokines were not consistent with the previous reports. Furtherly we need to evaluate precise mechanism of tolerance induction during SIT.

LUNCH SEMINAR

PSYCHOPHARMACOLOGY AND DERMATOLOGY: THE BEHAVIOURAL TOXICITY OF ANTIHISTAMINES

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One of the mainstays of pharmacological treatment regimens in dermatology is the antihistamine group of drugs. Histamine is an important neurotransmitter playing an essential role both in the regulation of circadian rhythms and in the maintenance of daytime wakefulness and histamine-1 receptors (H1Rs) are widely distributed throughout the brain. It necessarily follows that any drug which is capable of passing through the blood-brain barrier and of 'antagonising' the H1Rs will necessarily cause disruption of circadian rhythms and loss of arousal and awareness-in direct proportion to the extent of the drug's penetration of the brain.
Antihistaminic action in the brain precipitates a widespread psychopharmacological impairment of daytime cognitive function and leads directly to safety critical deficits in a patient's ability to perform the activities of everyday living in the home, at work and on the road. Furthermore, centrally impairing antihistamines do not only endanger patient's who are operating machinery or driving cars etc. but they also compromise intellectual functions which will diminish scholastic abilities.
The objective impairment of performance, cognitive function and intellectual abilities caused by antihistaminic agents is an intrinsic feature of the psychopharmacological properties of the drug and must not be confused with the subjective complaints of tiredness, daytime sedation etc which many dermatology patients make.
Patients' subjective reports of the psychopharmacological activity of a drug result from an amalgam of personal feelings and perceptions. It is absolutely impossible to determine the extent to which a patient's judgements are due to the actions of the drug per se, or to the influence of idiosyncratic assessments of other factors. The severity (physical discomfort) of the condition and its impact on quality of life, employment, social interactions, sleep, learning ability, relationship with the physician etc. will all influence patient ratings.
In short; patients' subjective ratings of the perceived sedative properties of drugs are of no scientific value simply because neither patient nor physician knows how to separate the true drug effects from the countless other feelings contributing to the overall rating.
The extent of the penetration of the CNS following the use of different antihistamines can be definitively demonstrated from PET scans. However, the extent of the impairment of cognitive function can only be measured by direct testing of cognitive abilities- via valid psychometrics.
The impairment of cognitive function, as measured on objective psychometric tests, has been shown to correlate with: a raised risk of accident; a reduced quality of life; lower scholastic competence; lower treatment compliance and poor therapeutic response.
A review of the extent of impairment of cognition caused by antihistamines, will be presented and reveal substantial differences between individual medications in the extent of their intrinsic behavioural toxicity.
From a psychopharmacological standpoint, there exists only one possible class division: between those antihistamines which impair cognition, learning and the safe performance of the tasks of everyday living (includes the majority of currently available treatments) and; those (currently only fexofenadine) for which there is no objective evidence of any impairment, even when used at supra-clinical recommended doses.

This seminar is sponsored by sanofi aventis.

SESSION 7
Microbial Superinfections in Atopic Dermatitis

37. KL: ATOPIC DERMATITIS AND INFECTIONS

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Atopic dermatitis (AD) is complicated by the frequent concurrent skin colonization with *Staphylococcus aureus (S. aureus),* by a lack of cutaneous defence to herpes simplex virus and by a frequent colonoziation of the skin with the

yeast malassezia sympodialis. This is associated with defects the innate cutaneous immune response: Keratinocytes stimulated with TH-2 cytokines are incapable to up-regulate the production of antimicrobial peptides (HBD-2, HBD-3, LL-27) and it has been shown that the lack of these peptides may account for the susceptibility of AD patients to bacterial and viral infections in the skin compartment. In addition, a single nucleotide polymorphism (SNP) for TLR-2 (TLR-2 R753Q in the intracellular portion of the receptor) has been described which is associated with *S. aureus* infections. Heterozygous AD-patients with the mutant TLR-2 R753Q allele exhibit a unique phenotype characterized by severe eczema and high IgE levels. Since cell wall constituents of staphylococcal aureus are known to directly interact with TLR2 and both T-cells and monocytes with the R753Q SNP show different functional responses to TLR ligands this polymorphism may both be involved in the susceptibility of AD patients to staphylococcal infections of the skin and a higher inflammatory response to *S. aureus* in colonized skin.
Many, but not all, *S. aureus* strains carry the capacity to produce exotoxins with superantigenic properties able to activate T cells in an unspecific manner. In this context local application of superantigens triggers recruitment and activation of T cells in and to the dermis. More recently, staphylococcal superantigens have been shown to inhibit the suppressive function of regulatory T cells of AD patients and to induce the pruritic cytokine IL-31 in TH-2 lymphocytes. Furthermore, a number of patients suffering from severe AD respond to staphyloccocal exotoxins with a specific immune response which is associated with detectable specific T-cell responses and specific IgE levels in the circulation. Since AD improves also in patients colonized with non-toxigenic *S. aureus* strains upon antimicrobial treatment other *S. aureus* derived factors must be involved in the pathogenesis of AD. One of them is α-toxin, a pore forming cytotoxin. A wide range of human cells, among them keratinocytes and lymphocytes, are lysed by α-toxin with greatly varying susceptibility. Sublytic concentrations of α-toxin have paradox stimulating effects on human T cells which respond very efficiently with proliferation and IFN-γ secretion to α-toxin.

38. IC: MICROBIAL FACTORS IN THE AGGREVATION OF ATOPIC ECZEMA

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The isolation of *Staphylococcus (S.) aureus* from the skin of atopic eczema (AE) patients is one of the most characteristic findings seen in this particuliar disease with colonization rates of about 90 % of the investigated patients. In line, almost every patient with AE also shows at least transiently colonization with yeast such as *Malassezia spp*. The discussion on the importance of microbial factors on the pathogenesis of eczema and the therapeutical implications began more than 100 years ago. Since then, our knowledge for both, the staphylococcal virulence factors and the implications for the human host defense system have dramatically increased and today the colonization of *S. aureus* on the eczematous skin and the immunological reaction to yeasts- as to *S. aureus*-components is considered as one of the most important triggering factors for the initiation and perpetuation of the typical skin inflamation. The interaction between microbes and the eczematous skin comprises particular adhesion structures, the production of toxins and imunostimulatory products, and the induction of specific IgE. The chronicity of the disease also renders therapeutic attempts often unsuccessful and requires good knowledge of the particular interaction microbes-inflamed skin.

39. IC: STAPHYLOCOCCAL VIRULENCE FACTORS AND ATOPIC DERMATITIS

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The virulence factors produced by *S. aureus* have a wide array of biological properties, including disruption of the epithelial barrier, inhibition of opsonization, interference with neutrophil chemotaxis, cytolysis of neutrophils, and inactivation of antimicrobial peptides. These virulence factors not only induce infectious diseases such as impetigo and cellulitis but also aggravate atopic dermatitis. Teichoic acid manifests immunomudulatory effects via Th2 cytokine production. Furthermore, *S. aureus* expresses exotoxins with biological properties of superantigens that induce T-cell activation with subsequent anergy and immunosuppression. Staphylococcal enterotoxins A (SEA) and B (SEB) stimulate expression of ICAM-1 and HLA-DR in normal human keratinocytes, and more than half of patients with atopic dermatitis have specific IgE antibodies to SEA and/or SEB in their serum. Epicutaneous sensitization with SEB elicites a local, cutaneous inflammatory response with infiltration of eosinophils and mononuclear cells, and Th2 immune responses with increased IgE synthesis. Patients with atopic dermatitis have significantly increased numbers of regulatory T (Treg) cells with normal immunosuppressive activity. However, after superantigen stimulation, Treg cells lose their immunosuppressive activity. These data suggest a novel mechanism by which superantigens could augment T-cell activation in patients with atopic dermatitis. Therapeutic procedures to selectively eradicate pathogenic *S. aureus*, with simultaneous protection of *S. epidermidis*, have been made possible by application of a low-pH cream and a gluco-oligosaccharide that inhibits the attachment of *S. aureus* cells on the epithelial surfaces.

40. OC: ATOPIC DERMATITIS IS CLOSELY RELATED WITH NON-BULLOUS IMPETIGO CAUSED BY GROUP A STREPTOCOCCUS (GAS)

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It is well known that the skin of patients with atopic dermatitis is susceptible to infection by gram-positive bacteria. How-

ever, the relationship between atopic dermatitis and GAS infection has remains to be fully understood. We identified 103 patients with cutaneous GAS infection in our department for a period of 5 years between 2002-2006. The information, including clinical diagnosis, disease severity, and coexisting diseases, especially atopic dermatitis, was obtained from the medical records. Non-bullous impetigo is the most prevalent diagnosis accounting for 32 % (31/97), followed by tinea pedis with secondary infection(18%, 17/97), and cellulites(11%, 11/97). Frequency of coexisting atopic dermatitis is 77%(24 patients) in non-bullous impetigo, compared with 9% in cellulites, 0% in tinea pedis with secondary infection, and 8 % in other miscellaneous diseases. Severity of atopic dermatitis at the time when the patients suffered from cutaneous GAS infection was assessed according to the criteria of Rajka and Langeland, being classified into 3 grades from mild to severe. Severity of non-bullous impetigo was assessed according to the body temperature and the affecfed area. Patients with fever more than 38.0ºC and/or impetigo lesions on more than 20% (by rule of nine) of their body area were classified as severe. Patients who did not meet these criteria were classified to be mild-moderate. Six of 10 patients with severe atopic dermatitis had severe non-bullous impetigo, while only four of 13 patients with mild and moderate atopic dermatitis suffered from severe non-bullous impetigo, suggesting a correlation between disease severity of atopic dermatitis and non-bullous impetigo. Taken together, our observation indicates that atopic dermatitis is closely related to non-bullous impetigo among cutaneous GAS infections. Treatment of atopic dermatitis may lead to preventing patients from suffering severe non-bullous impetigo.

P-20. CONTAMINATION OF EMOLLIENT CREAMS AND OINTMENTS WITH STAPHYLOCOCCUS AUREUS - IN CHILDREN WITH ATOPIC DERMATITIS

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Staphylococcus aureus is a major environment trigger in atopic dermatitis. Unpreserved cosmetic lotions have been identified as a cause of cutaneous infections and even septicaemia. In our clinic, we identified a 2-year-old child, with atopic eczema, who developed multiple abscesses and septicaemia that recurred repeatedly despite intravenous antibiotics and surgical drainage. When the child was admitted, we found that his parents were treating him with an emollient, which they had purchased over the counter, outside the UK. Culture of this emollient revealed > 10^7 staphylococcus aureus per gram. Removal of this contaminated emollient resulted in rapid resolution of the child's infected lesions.
This led us to conduct an audit of bacterial contamination of prescribed, licensed, emollient creams and ointments that had been used to treat children with atopic eczema, who were attending our clinic. Seventy-three containers of ointments & creams were collected. Swabs were taken from the rims, nozzles and contents of the containers. 53% of the containers were infected, 25% with staphylococcus aureus, 11% with gram negative bacteria and 17% with normal skin flora. Both unpreserved ointments, such as 50/50 white soft paraffin/liquid paraffin (WSP/LP), and preserved creams, were found to be infected.
We teach parents of children with AD, that ointments should be decanted with a clean spoon into a separate container for application and that hands should not be put directly into the main container and have ask them not to keep pots of 50/50 WSP/LP for more than one week. Keeping emollients in the fridge would also decrease the chance of rapid bacterial growth.
Infection of children with atopic dermatitis from their own emollients should be considered as a possible cause of recurrent infective exacerbations.

P-21. STAPHYLOCOCCUS AUREUS SUPPRESSION WITH SODIUM HYPOCHLORITE BATHS AND INTRANASAL MUPIROCIN DECREASES ATOPIC DERMATITIS CLINICAL SEVERITY

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Staphylococcus aureus (*S. aureus*) infection is both a complication of atopic dermatitis (AD) and a trigger of exacerbations. A randomized investigator-blinded placebo-controlled study of children and adolescents (6 months to 17 years) with moderate to severe AD and secondary bacterial infection was performed to determine the incidence of methicillin-resistant *S. aureus* (MRSA) colonization and whether suppression of *S. aureus* growth with sodium hypochlorite (bleach) baths and intranasal mupirocin improved eczema severity (EASI score; primary objective). Subjects with superinfected AD were treated with oral cephalexin for 14 days and either concurrent intermittent intranasal mupirocin ointment (Centany®) and at least twice weekly sodium hypochlorite baths (1/4 cup of 0.125% solution in $^1/_2$ bathtub) [treatment group] or intranasal petrolatum ointment and water [placebo group] for 3 months. Thirty-one subjects were enrolled and 21 subjects completed the study. Subjects in the treatment group showed greater median reduction from baseline ($\pm$SD) in EASI scores at both the 1 month visit (-5.8 $\pm$ 10.3) and the final 3 month visit (-12.9 $\pm$ 12.9) when compared to the placebo group at 1 month (-1.4 $\pm$ 5.9) (p=0.047) and final (-1.4 $\pm$ 5.7) (p=0.0023) visits, respectively. Likewise, median percent change to 3 months in EASI was significant (p<0.0009) with a decrease in eczema severity of -40.6% $\pm$ 32.2 in the treatment group (versus -12.3% $\pm$ 21.7 in the placebo group). At baseline, 2/27 subjects who grew *S. aureus* from affected skin and 1/25 from the nares showed MRSA, considerably less than the percentage of MRSA among *S. aureus* in skin/wound cultures in the general population at Children's Memorial Hospital (10%). These data suggest that chronic use of dilute bleach baths and intermittent application of intranasal mupirocin ointment decrease the clinical severity of AD.

P-22. DISTRIBUTION OF SEA, SEB AND TSST-1 PRODUCED BY *STAPHYLOCOCCUS AUREUS* IN THE LESIONAL SKIN OF ATOPIC DERMATITIS PATIENTS USING IMMUNOHISTOCHEMICAL ANALYSIS

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Skin colonization of *Staphylococcus (S.) aureus* is often related with atopic dermatitis (AD), and various exotoxins of *S. aureus* have been implicated in the etiology of AD. Recently, we had demonstrated that the most of *S. aureus* strains (97.2%) colonized in the skin of AD patients carried genes encoding staphylococcal enterotoxin A (SEA) and/or toxic shock syndrome toxin-1 (TSST-1). This result led us to assume that SEA and/or TSST-1 play an important role in the development of AD. Here, we investigated the distribution of SEA, SEB and TSST-1 in the lesional skin of adolescent and adult patients with AD using immunohistochemical analysis as well as the correlation between AD severity and exotoxins (SEA, SEB and TSST-1) expression. In immunohistochemical analysis, SEA and TSST-1 were abundantly detected in the lesional skin of all AD patients with a higher level of SEA than that of TSST-1, whereas SEB was just a little detected. Double immunohistochemical staining with SEA and *S. aureus* protein A (SPA), a surface molecule of *S. aureus,* showed co-localization of SEA and *S. aureus* itself. Histopathologically, the lesional skin of AD patients showed the infiltration of inflammatory cells in the dermis and superficial colonization of *S. aureus* in the epidermis. In conclusion, although there was no definite correlation between AD severity and exotoxins (SEA and TSST-1) expression, SEA and TSST-1 might play a role partly in some patients with AD.

P-23. THE BIOLOGICAL INVESTIGATION ON THE DISTRIBUTION OF *MALASSEZIA* YEASTS ON ATOPIC DERMAITITS PATIENTS

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Malassezia yeasts, since first reported in 1889, are known to be implicated in various diseases, including pityriasis versicolor, seborrheic dermatitis and *Malassezia* folliculitis. Recently, there have been a growing number of reports which show the implication of *Malassezia* yeasts in atopic dermatitis, acne vulgaris. To investigate the relationship of *Malassezia* yeasts with other diseases, many researches on the distribution of *Malassezia* yeasts are conducted. But, in our country, the research on the distribution differences of *Malassezia* yeasts and quantitative feature of that in the normal or abnormal skin is not sufficient.
So, in this study, to overcome the limit of the pre-existing classical methods and more precise identification *Malassezia* yeasts, we use the novel molecular biological technique, 26S rDNA PCR-RFLP. We distribute the yeasts from atopic dermatitis patients to achieve the fundamental databases proving the relationship of *Malassezia* yeasts with diseases. And we also identify the yeasts from atopic dermatitis patients, then, onthis basis, we analyse the differences of body areas, age groups with the normal control groups.

SESSION 8
Itching and Neurological Regulation of Inflammation

41. KL: NEUROINFLAMMATION AND THERAPEUTIC POTENTIAL OF NEUROMEDIATION IN PRURITUS AND INFLAMMATION

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There is ample evidence for a close crosstalk between the cutaneous nerve system and the immune system for the regulation of inflammation and pruritus. Components of neurogenic inflammation include neuropeptides such as substance P (SP), calcineurin gene related peptide (CGRP) vasointestinal peptides (VIP) and others. Accordingly SP belonging to the tacchinine family significantly was found to contribute to itch, vasodilatation, and inflammation. Increased amounts of SP are expressed in pruritic skin lesions and genetic deletion of SP specific neurokinin 1 receptor (NK1R) in mice protects these animals from the inflammatory response to allergens. Finally treatment of pruritic skin diseases with an NK1R antagonist resulted in a significant amelioration of itch. Recently receptors expressed on epidermal cells and nerves such as protease activated receptor (PAR2) and transient receptor potential vanilloid 1 (TRPV1) significantly were found to contribute to neurogenic inflammation. Accordingly, activation via PAR2 results in the release of proinflammatory neuropeptides such as SP and to induce pruritus and an inflammatory response. Moreover, TRPV1 (vanilloid receptor) a member of the recently detected TRP super family was found to be expressed on dermal nerve fibers, keratinocytes and mast cells. Targeting TRPV1 with capsaicin or calcineurin inhibitors appears to be a promising approach for the treatment of pruritus. Interleukin 31 (IL-31) is a recently described cytokine which is released by CD 45 RO+/CLA+ T-cells upon stimulation with staphylococcal superantigens. IL-31 was found to be upregulated in pruritic skin lesions and the IL-31 receptor is expressed in dorsal root ganglia as well as keratinocytes. Thus targeting IL31 as well as other neuromediators may provide a novel strategy for the development of anti-inflammatory and antipruritic drugs.

42. IC: NEUROIMMUNOLOGY OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a chronically relapsing inflammatory skin disease characterized by eczematous skin lesions and intense pruritus. The contribution of key effector cells of the immune system including eosinophil granulocytes, chemokines, defective skin barrier function, genetic predisposition, and environmental triggers has been well characterized in AD. In addition, recent studies have revealed a major role for neuroimmune interaction mechanisms in AD. In this regard, pruritus which presents one of the key features of AD is often resistant to H1 antihistamine treatment. Therefore, other mediators than histamine including neuropeptides, neurotransmitters, and neurotrophins have been suggested for a contribution in AD.
Neuropeptides and neuropeptide-positive nerve fibres are prominently increased in AD lesions. The density of nerve fibres is increased while peripheral nerve endings are in an active state of excitation. Neurotrophins, which have been particularly described for their functional role on nerve cells, are increased in the peripheral blood and AD skin. Neurotrophins and neuropeptides can modulate the functional activity of eosinophils and sensory nerves in AD. Further, eosinophils are capable of neurotrophin as well as neuropeptide production, pointing to bidirectional interaction mechanisms between sensory nerves and eosinophils in AD.
We have therefore developed the concept of a neuroimmune network between target effector cells and sensory nerves that link pathogenic events to dysfunctions of the cutaneous immune and peripheral nervous system in AD.
Understanding the pathomechanisms of AD neuroimmunology not only improves our understanding but may also improve our current and future therapeutic strategies for AD.

43. IC: NEUROPHYSIOLOGY OF ITCHING

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Itch is an aversive sensation distinct from pain and provoking opposing reflex patterns. The discovery of histamine-sensitive itch-selective neurons in the periphery and in the spinal cord has suggested a specific neuronal system underlying the itch sensation. The idea of two separate neuronal systems for pain and itch is in accordance with the antagonistic interaction: scratch-induced pain can abolish and analgesic opioids can generate itch.
Recent data show astonishingly similar mediators and mechanisms of neuronal sensitization in the periphery and the central nervous system in itch and pain: such as proteinase-activated receptors (PAR-2), nerve growth factor (NGF) and endothelin on the peripheral level and identical patterns of sensitization on spinal level. As similar mediators and mechanism are involved in both itch and pain, it is obvious that therapeutic approaches might also be similar in some cases. Most recently, the idea of a specific neuronal system for itch has been challenged by results on the histamine-independent pruritogen cowhage: neurons responding to cowhage could not be differentiated from classic nociceptors. The implications of these findings on the basic theory of itch might appear purely theoretic, however, for the discovery of therapeutic targets the nature of the involved neurons and the mechanisms by which they elicit pruritus is of crucial importance in particular for histamine-independent itch.

44. IC: BRADYKININ IS A POTENT PRURITOGEN IN ATOPIC DERMATITIS: A SWITCH FROM PAIN TO ITCH

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Background: Our previous studies have revealed that mechanical, thermal and electrical stimuli evoke itch in eczematous skin of patients with atopic dermatitis, while pain in their non-eczematous skin and in healthy volunteers. This suggests that eczematous skin is sensitized to itch.
Objective: To investigate the influence of itch sensitization on the role of inflammatory mediators. Procedures: Histamine, serotonin and bradykinin were applied by iontophoresis to eczematous and visually non-eczematous skin of fourteen patients with atopic dermatitis, and normal skin of fifteen healthy volunteers. Application of each substance was done in the same skin area before and three hours after administration of placebo or antihistamine (olopatadine hydrochloride: h1-blocker). Intensities of itch and pain sensation and areas of flare and wheal were measured.
Results: Histamine-induced flare was larger in healthy volunteers than in eczema and non-eczema of patients. There was otherwise no significant difference in pain, flare and wheal. On the other hand, all the substances induced significantly more intense itch in eczema than in non-eczematous skin of patients. Even bradykinin, which is well known as a representative of pain mediators, induced intense itch in eczema. Although histamine-induced reactions were suppressed almost completely by antihistamines, bradykinin- and serotonin-induced reactions were not, suggesting that bradykinin and serotonin induce itch in eczema independently of histamine.Conclusion: These results implicate that eczematous skin of patients with atopic dermatitis is sensitized to itch and that non-pruritic inflammatory mediators such as bradykinin can therefore turn into potent pruritogens.

45. IC: MECHANISM OF ITCH IN ATOPIC DERMATITIS–INVOLVEMENT OF EPIDERMAL OPIOID SYSTEMS–

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The mu-opioid (beta-endorphin/mu-opioid receptor) and kappa-opioid (dynorphin A/kappa-opioid receptor) systems play pivotal roles in the modulation of pruritus in the central nervous system. The mu-opioid system has also been identified in human epidermis, raising the possibility that the system induces the peripheral itch. However, the precise distribution of the kappa-opioid system has not yet been clarified in human epidermis. To address this issue, RT-PCR and immunohistochemical analyses were performed on cultured keratinocytes and normal skins from humans. The analyses revealed that epidermal keratinocytes express kappa-opioid receptor and its ligands, dynorphin A (1-17) and (1-8). Moreover, expression for mu- and kappa-opioid systems was examined immunohistochemically in skin biopsies from healthy volunteers and patients with atopic dermatitis (AD) before and after PUVA therapy. Our expression analyses showed that only the kappa-opioid system, not the mu-opioid system, was downregulated in the epidermis of AD patients. The downregulation of the mu-opioid system and the restoration of the kappa-opioid system by PUVA therapy were observed in the AD patients, concomitant with a decrease of VAS scores. These results suggest epidermal opioid systems are associated with the modulation of pruritus in AD.

46. OC: INHIBITING EPIDERMAL NERVE ELONGATION IS NOT SUFFICIENT FOR CONTROLLING ITCH/SCRATCHING IN HAPTEN-INDUCED TH2-TYPE CHRONIC DERMATITIS

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Controlling itch/scratching is important for the treatment for atopic dermatitis (AD). However, it is known that simple use of antihistamines is not sufficient for controlling itch in AD, suggesting involvement of factors other than histamine in the pathogenesis. Altered nerve fiber structure, specifically sensory nerve elongation within lesional epidermis, is in the spotlight as a cause of such persistent itch. CX-659S (CX), a MAPK/ERK kinase (MEK) 1/2 inhibitor, is a newly-developed anti-inflammatory agent and some of MEK 1/2 inhibitors are known to inhibit neurite growth in vitro. Therefore, we hypothesized that such agents might attenuate itch/scratching behavior via inhibiting epidermal nerve elongation in chronic dermatitis. To test this idea, we developed a mouse model of Th2-type chronic dermatitis using repetitive hapten painting with or without topical application of various anti-inflammatory agents such as MEK1/2 inhibitors (CX), immunosuppressants (FK506: FK) or corticosteroids (Betamethasone Valerate: BV). FK significantly inhibited both epidermal nerve elongation and skin inflammation and could also inhibit scratching behavior in this model. CX strongly inhibited epidermal nerve elongation and BV showed strong anti-inflammatory effects, but neither agent inhibited scratching behavior of mice. We next hypothesized that combination of strong anti-inflammatory effects and inhibiting epidermal nerve elongation might be necessary for controlling scratching behavior. To test this idea, we examined the effects of CX + BV mixture in this model. However, CX + BV mixture did not inhibit scratching behavior of mice, although the mixture showed strong inhibition of both epidermal nerve elongation and skin inflammation. Overall, these findings suggest that inhibiting epidermal nerve elongation may not be sufficient for controlling itch/scratching in hapten-induced Th2-type chronic dermatitis.

47. OC: DERMAL FIBROBLASTS IN ATOPIC DERMATITIS SKIN LESION SYNTHESIZE ARTEMIN REACTIVE WITH PERIPHERAL NERVE

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Itch is the major symptom of atopic dermatitis (AD), and impairs quality of life in these patients. In the recent reviews, not only histamine but also other pruritogens are involved in the mechanisms of itch and aggravate atopic dermatitis. Substance P (SP) has demonstrated various functions such as chemical mediator in the case of immunoresponse, and neurotransmitter in subjective symptoms like pain and itch. Although dermal fibroblasts may be candidate SP-responsive cells, little is known about the effect of SP. We have investigated the expression profiling of genes that are induced by substance P-treatment in normal human dermal fibroblast (NHDF) using macro-gene array. Based on this study, we focused on de novo artemin (ARTN), which is a member of the glial cell line-derived neurotrophic factor related family, gene transcription in NHDF after SP-stimulation. Besides SP-treated NHDF, RT-PCR revealed the basal level of ARTN mRNA expression in the normal human epidermal keratinocyte and Hacat cell. SP-treated NHDF-derived conditioned medium induced a proliferative response in a neuroblastoma cell line, and this phenomenon was suppressed by neutralization of ARTN. Furthermore, we verified that dermis of AD skin lesions exhibit intense immunoreactivity for ARTN, while psoriasis and healthy controls are less intense. In situ hybridization assay also revealed that expression of ARTN mRNA in dermal fibroblast was observed in AD skin lesion, but not in healthy control. Colabeling with artemin and its potent receptor GFRα3 showed massive sprouting of GFRα3-positive peripheral nerve fibers in ARTN accumulated dermal areas. SP-treated dermal fibroblast-derived artemin can be assumed to contribute to peripheral nerve sprouting. Our findings indicate
novel functional aspects of SP, and may lead to a better understanding of novel mechanisms of altered skin innervation in atopic dermatitis.

P-24. ALTERED EXPRESSION OF BRAIN OPIOID RECEPTORS IN ATOPIC DERMATITIS MODEL MICE EXPOSED TO PSYCHOLOGICAL STRESS

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【Objectives】 Atopic dermatitis is a common pruritic inflammatory skin disease. It has been well recognized that environmental factors such as mites and dusts exacerbate atopic dermatitis, and psychological stress also induces itch that leads to the exacerbation of atopic dermatitis.
Recently, we have demonstrated that psychological stress by itself can induce scratching behaviour and trigger atopic dermatitis-like skin lesions in atopic dermatitis model mice, NC/Nga. Additionally, we have shown that pretreatment with corticotropin-releasing factor (CRF) inhibits scratching behaviour. In this study, to explore the mechanism how psychological stress can induce itch and also how CRF inhibits scratching behaviour, we investigated the expression level of opioid receptors (μ and κ) mRNA in brain as well as other parameters. 【Results】 Under SPF condition, psychological stress elicited atopic dermatitis-like skin lesions along with the increased level of serum IgE in NC/Nga mice. Both μ-opioid receptor antagonist and CRF suppressed scratching behaviour. Psychological stress decreased the mRNA expression of μ and κ -opioid receptors in brain, and pretreatment with CRF restored the mRNA levels of μ and κ -opioid receptors to those of non-treated control mice. 【Conclusion】 Our data indicate that CRF may suppress stress-induced scratching behaviour via through the restoration of decreased expression of μ and κ-opioid receptors in brain.

SESSION 9
Psychosomatic Aspects, Stress, and Quality of Life

48. KL: PSYCHOSOMATIC APPROACH TO ATOPIC DERMATITIS – STRESS, BEHAVIOUR AND PSYCHOTHERAPY

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Psychological factors seem to be important in atopic dermatitis as significant modulators of the disease. Stress increases atopic dermatitis symptoms depending on the severity of stress. It is widely accepted, that stress can induce or exacerbate atopic dermatitis. The physiological mechanisms, that mediate this negative influence of stress to atopic dermatitis, are not clearly understood.
Newer studies try to point out the close connection between epidermal nerve fibers and brain, together with new developments in brain research and studies with neuropeptides in skin diseases which are mainly involved with epidermal nerve fibers (Undem et al 2000).
Neuroimmunological, psychoendocrinological studies and examination of integrity and function of skin barrier under stress. Different neuropeptides and neurotrophines seem to play an important role in stress-induced neurogenic inflammation and connection of nervous and immune system. Mast cells play a key-role in the development of inflammatory reaction to stress. Skin barrier is altered by stress by means of increased cortisol level. Thereby lamellar body secretion is decreased and epidermal expression of antimicrobial peptides (β-defensin and cathelicidin) is downregulated.
In the past years it becomes more and more evident, that atopy-relevant effector cells, such as mast cells and Langerhans cells form a close anatomical relationship with nerve fibers staining positive for a number of neuroactive substances, for instance substance P, vasoactive intestinal polypeptide (VIP) peptide or Nerve Growth Factor (NGF) (Gieler et al 2002). Regarding this close anatomical relationship of nerve terminals and effector cells in atopic eczema, it seems possible that stress-induced stimulation of nerve fibers induces secretion of neuroactive substances. There are a growing number of studies indicating that atopic eczema patients show disturbances in neuroimmunological pathways so that some authors stated that 'psychological stress may be conceptualized as a social pollutant that, when 'breathed' into the body, may disrupt biological systems related to inflammation through mechanisms potentially overlapping with those altered by physical pollutants and toxicants' (Wright et al 2005). Functional changes in the hypothalamus-pituitary-adrenal cortex-axis are under discussion.
The influence of serious events in life and of stressors of various degrees on the immune system is known (Kodama et al 1999). The autonomic nervous system acts as the connector between feelings and subsequent somatic response.
Psychotherapy seems, with regard to that psychoimmunological pathway, a possible adjunctive treatment possibility for atopic dermatitis patients. Relaxation programs, behavioural and psychodynamic psychotherapy were studied in some rare studies in atopic dermatitis patients. Moreover, an education program for atopic dermatitis patients is in the meantime established for a better coping with the disease. Educational programmes aim to empower patients and/or carers in solving the problems arising from chronic diseases, and meta-analysis of results has highlighted the need to develop standardized methodologies so that any improvements in disease self-management can be more accurately assessed. Although several educational interventions have been developed for adult AD patients, the literature on educational programmes for children and their parents is sparse. The German Atopic Intervention Study (GADIS) was set up to develop standardized interventions for AD self-management, and to address their effects.
It can be concluded that these educational programmes for the parental management of AD in children, and self-management of adolescents, improve disease control and should be integrated into routine care.

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49. OC: RECALLED BURDEN OF EVERYDAY LIFE. 10 –YEAR FOLLOW UP-STUDY OF ATOPIC AND FOOD ALLERGIC CHILDREN

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Objectives: The focus is to describe the multidimensionality of the experienced burden of the families of children with atopic dermatitis (AD) and food allergy. Another aim is to ascertain out how the recalled experience of everyday life is connected to the severity of the symptoms of the children, when they were less than 12 months old.
Methods: The data was collected by using the illness specific Quality of Life Questionnaire constructed by the researchers. 201 families completed the questionnaire at the 10-year follow up. The children had first attended the clinic when they were less than 12 months old. Baseline grading at AD was classified retrospectively: Mild, moderate and severe clinical status.
Results: A factor analysis was conducted for the variables concerning the burden caused by the child´s atopy. A three-factor solution gave the best interpretable result. The most prominent factor reflected the sleepless nights and anxiety (*awake* factor). Other two factors were the *accuracy* (when preparing the food) and the *arduousness* of everyday life in general. The only statistically significant relationship ($p < 0.001$) was found between the baseline AD grading and the *awake* factor.
Conclusion: It is possible to argue that the experienced burden is a multidimensional phenomenon even at the level of everyday practicalities. The study shows a strong relationship between the number of sleepless nights and amount of anxiety and the severity of the disease. No doubt, the connection is a familiar phenomenon in clinical practises and even scientifically, but it may still be an under-explored issue.

50. OC: DEPRESSION AND ATOPIC DERMATITIS

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Suffering from chronic disease is a risk factor for depression. Atopic dermatitis patients are supposed to have risk of depression. On the other hand, in our clinical experiences exacerbations of atopic dermatitis were sometimes seen followed by onset of depression. To clarify the relationship of dermatitis activity and depressive status, atopic dermatitis patients in our hospital were retrospectively reviewed.
The subject was defined that atopic dermatitis patients over 15 years old who were followed by the author. The diagnosis of depression was based on DSM-Ⅳ. There were 29 patients who were complicated with depression among 1000 patients of adult type atopic dermatitis. 22 patients were supposed to fall into depression after some life events, 7 patients were considered to fall into it in the course of longstanding uncontrolled severe atopic dermatitis. In the former group skin symptoms of 19 patients were aggravated with the onset of depression, 1 patient improved, and 2 patients unchanged. On the contrary after getting improvement of depressive status of 26 patients who were able to be followed, skin symptoms of 19 were improved, 2 aggravated, 3 unchanged.
These results show that complication of depression is an aggravating factor of atopic dermatitis. Depression is known as a systemic disorder not only of mood but also of endocrine and autonomic nervous system. Several mechanisms are presumed to induce the aggravation of atopic dermatitis in depressive status. Once the dermatitis aggravated, depressive patient more suffers falling into the vicious circle of dermatitis and depressive disorder. Dermatologists should be aware of depression as a complication and also an aggravating factor of atopic dermatitis.

51. OC: FUNCTIONAL ANALYSIS OF THE HABITUAL SCRATCHING OF PATIENTS WITH ATOPIC DERMATITIS AND BEHAVIORAL INTERVENTION

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To stop itch-scratch vicious cycle is very important for the treatment of atopic dermatitis, but physical restriction such as restraint bandage application is not preferable especially for children, from developmental points of view.
The aim of this study is to verify the effectiveness of our behavioral intervention based on the functional analysis for the patients and/or their parents.
We experienced 19 in-patients (from 4 months old to 16 years old) with habitual scratching in our department from April 2007 to March 2008. Although their skin conditions were fairly improved after admission because of application of topical steroids, their scratching behavior persisted and they failed to maintain remission by intermittent application of topical steroids. Functional analysis revealed that most of their scratch-

ing behaviors were reinforced by the operant conditioning. Behavioral therapy teams were organized by a psychologist, nurses and doctors. After starting behavioral intervention, most of the patients stopped habitual scratching in a few weeks and got normal skin without eczema. They could maintain their remission by intermittent application of topical steroids and/or tacrolimus even after discharge.
In an elder case, habitual scratching was shaped not only by the operant conditioning but also by the respondent conditioning with their emotional distress. Relaxation training and desensitization therapy was carried out for the respondent conditioning and he overcame his scratching.
To overcome intractable itch-scratch cycle caused by habitual scratching, behavioral therapy we have developed would be the most appropriate approach to be applied for patients with atopic dermatitis including children.

52. OC: EMDR, A MORE DEVELOPED METHOD, FOR CONTROLLING HABITUAL SCRATCHING FROM TRAUMATIC MEMORIES OF AD PATIENTS

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For improving atopic eczema, it is always necessary to reduce habitual scratching of refractory atopic dermatitis (AD) patients. To date, some psychological approaches, such as a cognition behavioral therapy or a habit reversal, have been applied for AD patients in addition to guidelined medical treatment, and any given effect of those therapies have been reported. However, it is also true that, for some patients, these approaches are not enough yet in present, in terms of bio-psycho-social medicine.
Then we propose that we should provide a substantial effective treatment for such patients who have traumatic stress in the background. In the case of those patients, EMDR (Eye Movement Desensitization and Reprocessing) that is recently used for treatment of PTSD (post traumatic stress disorder), is thought to be directly effective for these serious AD patients.
Here we report a case of a 20-year-old man who presented chronic AD with habitual scratching, and had difficulty in recovering by standard medical treatment using topical corticosteroids. By applying EMDR for the traumatic memory, he came to recognize the positive cognition, " I am OK just the way I am.", and his amount of scratching related to stress was clearly reduced and the SCORAD improved 64.2 to 24.0. The score of SDS, STAI-I, II, psychosomatic scale for AD and skindex29 were changed from 75 to 35, 72 to 32, 75 to 33, 44 to 26, 62.9 to 19.0.
These results suggest that EMDR is useful and very effective for controlling the habitual scratching from stress of traumatic memory on refractory AD patients.

P-25. NEGATIVE BODY IMAGE IMPAIRS THE QUALITY OF LIFE OF JAPANESE ADULT PATIENTS SUFFERING FROM ATOPIC DERMATITIS

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Atopic dermatitis, with severe itching lingering on with persistence, affects patients' quality of life. The disease also affects the patients' physical appearance which may directly impair their body image. In what respect, this negative body image influences other factors like impairing patients' life quality, was the purpose of this study.
To identify the psychological aspects including body image which may influence importantly the quality of life in Japanese patients, a cross-sectional questionnaire study was carried out using a battery of instruments: the Japanese version of Skindex-16, General Health Questionnaire 30(GHQ30), Liebowitz Social Anxiety Scale(LSAS), CES-D scale and Cutaneous Body Image Scale(CBIS).
As a result, 69 patients (mean age 30.1 years, 71% female) completed the questionnaires. The mean scores of Skindex-16 were Symptom:46±24; Emotions:66±25; Functioning:29±25, suggesting that the disease's impact on the emotional side of quality of life was considerable. The mean score of CBIS was 3.2±1.8 and was significantly lower than that of the general population. The scores of "Emotions" were significantly correlated with those of GHQ(γ=0.298), CES-D(γ=0.298), LSAS(performance/anxiety γ=0.388), and CBIS(γ=–0.447). A stepwise multiple regression analysis revealed that CBIS(β=–0.360) and LSAS performance/anxiety (β=0.325) stand in a very close relationship with "Emotions"(adjusted R^2=0.278,p=0.000).
These findings suggest that the negative body image plays an important role in impairing the quality of life in patients with atopic dermatitis. To improve their quality of life, an adequate approach for the betterment of their body image should be considered.

EVENING SEMINAR

REGULATORY T CELLS IN AUTOIMMUNE, INFLAMMATORY, AND ALLERGIC DISEASES

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Accumulating evidence indicates that abnormalities of naturally arising CD4+ regulatory T cells (Tregs) contribute to the pathogenesis of various autoimmune, inflammatory, and allergic diseases. In this seminar, I will introduce recent key findings in basic and clinical studies to understand what kinds of disease occur in Treg abnormalities, and how Tregs control these diseases at system, cellular and molecular levels. First, genetic deficiency of Tregs causes autoimmune and allergic IPEX (immunodysregulation, polyendocrinopathy, enteropathy, X-linked) syndrome as seen in mutations of the *FOXP3* (forkhead box P3) gene, the master control gene of Tregs. Second, recent findings by us and others suggest that abnormalities of Tregs significantly contribute to the pathogenesis of common autoimmune diseases. Here I present a model whereby the degree of abnormalities of Tregs determines the severity of diseases and the organ involvement of inflammatory processes in each genetic background.
Finally, I will talk about the molecular mechanisms of FOXP3 in Treg function. Recently, we reported that FOXP3 controlled Treg function via interacting with Runx1 (runt-related transcription factor 1)/AML1. In this seminar, I will show that Treg-specific inhibition of the Runx complex results in dysfunction of Tregs, and thereby leads to the development of autoimmune diseases. Moreover, global analysis of Runx-target genes in Tregs gives clues for further studies on the pathogenesis of inflammatory diseases. Clarification of molecular mechanisms of Tregs would give new insights into immunoregulatory genes and uncover the hidden associations between autoimmune, inflammatory, and allergic diseases in humans.

This seminar is sponsored by NOVARTIS.

SESSION 10
Evidence-based Treatment

53. KL: TREATMENT OF CHILDHOOD ATOPIC DERMATITIS

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Topical steroids remain the mainstay of therapy for pediatric atopic dermatitis (AD), with novel forms of delivery and increased cosmetic acceptability leading to increased patient compliance. The popularity of topical calcineurin inhibitors has waned with the introduction of the Black Box warning in the U.S., but studies to date have not shown evidence of a relation to cancer. in children or adults. Alternative topical agents have focused on repairing the "barrier defects" in skin and in decreasing the risk of bacterial infection. Recurrently infected patients often respond to systemic antibiotics, both with respect to infection and the severity of the dermatitis. While the benefit of adding topical antibiotics to topical anti-inflammatory medications is controversial, increasing evidence suggests the value of dilute sodium hypochlorite (bleach) baths and intranasal application of mupirocin in decreasing the recurrence of infections and improving the AD itself. This non-antibiotic approach may be particularly valuable given the increasing predominance of MRSA as a medical problem. Topically applied antimicrobial peptides may suppress both *S. aureus* and viral infections (herpes, molluscum), and may be available in the near future to compensate for the cytokine-induced deficit in antimicrobial peptide expression in patients with AD. Recent studies have also shown that poor compliance is a significant problem and that educational programs improve outcome. More severely affected individuals may require systemic anti-inflammatory agents, particularly azathioprine or cyclosporine. Mycophenylate mofetil and methotrexate may be associated with fewer side effects, and efalizumab is showing promise among the biologics.

54. IC: CLINICAL TRIALS OF ATOPIC DERMATITIS: PROBLEMS AND SOLUTIONS

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I shall provide an overview of common pitfalls and problems encountered in reporting of randomised controlled trials (RCTs) of atopic dermatitis, along with possible solutions. The talk is informed by an the analysis of almost 300 RCTs published in a large systematic review published in 2000[1], plus regular updates of systematic reviews of published trials of atopic dermatitis that have appeared since in the in the Skin Disorders Library annual evidence updates[2]. Common problems include: design games such as choosing an inappropriate comparator, using a clinically meaningless outcome, using too many different outcomes or failing to include long term outcomes such as disease remission rates in what is a chronic disease for most patients. Analysis games includes failing to use the correct statistical test, failing to compare outcomes between groups, and failing to include all those randomised in the final analysis. Write-up games include incorrect interpretation of a "negative" result, overenthusiastic interpretation of post hoc subgroup analysis and various ways of trying to "save face" in inconclusive studies with mechanistic smoke screens. Reporting games include failure to publish "negative" studies, delayed publication of negative studies and duplicate publication of positive studies. The so-

lutions are relatively straightforward and include (i) all trials in atopic dermatitis should be registered in the public domain (ii) the scientific community need to get together to agree on a minimum list of preferred common outcomes as has been done in rheumatoid arthritis[3] and (iii) all trials should be reported fully using the CONSORT statement. We still have a long way to go.

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55. OC: PET EXPOSURE AND RISK OF ECZEMA: A SYSTEMATIC REVIEW

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We sought to systematically search, summarize and critically appraise the literature to examine whether early pet exposure is associated with an increased risk of eczema.
We searched Medline (1950 to March 1st 2008) supplemented by citation lists in retrieved articles and direct contact with researchers. No language restrictions were imposed. Cohort studies that were sufficiently similar were pooled in a meta-analysis. Meta-analysis was not possible for cross-sectional studies owing to large differences in methods and populations.
Evidence from longitudinal studies showed that previous exposure to dogs (pooled odds ratio (OR) =0.66, 95% confidence interval (CI) 0.53-0.83), or 'any furry pet' (pooled OR=0.80, 95% CI 0.75-0.85) is associated with a lower risk of eczema. Past exposure to cats (pooled OR =0.92, 95% CI 0.73-1.15) showed no association with eczema. However, in the only cohort study that adjusted for avoidance behaviour, this "protective effect" disappeared (for cats OR=0.80, 95% CI 0.33-1.97). Stratified analysis by family history in three birth cohort studies showed dog exposure might be protective in patients with atopic families in two studies and associated with a borderline increase in risk in the other study. For cats, one study showed reduced risk in atopic families only; the other studies showed no effect. Eight cross-sectional studies evaluated past pet exposure; a protective effect was seen in three studies for any pet, dog or cat; no study demonstrated an increased risk.
There was no clear evidence that early pet exposure is associated with increased risks of subsequent eczema. We found some evidence of a possible protective effect of early pet exposure (especially dogs), but this might be explained by avoidance behaviour in high risk families.

56. OC: A SURVEY OF SKIN CARE PRACTICES IN INFANTS PRIOR TO ATOPIC DERMATITIS DEVELOPMENT

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BACKGROUND
Genetic studies of filaggrin have revealed that a genetically-determined defective skin barrier may initiate atopic dermatitis (AD). Water, soap, and some lotions are thought to be detrimental to the skin barrier and may worsen the skin barrier function in infants predisposed to the development of AD. Our hypothesis is that certain skin care practices during infancy may modify the development of AD in high-risk individuals. The objective of this study was to identify the most common skin care practices used during the first 6 months of life in children who later developed AD.
METHODS
A cross-sectional survey of the parents of 81 children with a history AD was performed. Information regarding bathing, cleansing, and moisturization was gathered for the period of time between birth and AD development. Information was gathered for only children who were under the age of six to improve parental recall.
RESULTS
The average age of onset for AD was 7.3 +/- 10.1 months. Approximately half (50.6%) of parents noted skin xerosis in their infant and 24.7% noted signs of ichthyosis on the pretibial skin. The average number of baths per week was 4.1+/-2.2. Moisturizers were used on 75.3% of infants beginning at an average age of 2.9 months. The most common type of moisturizer used was a lotion from a pump dispenser, used in 64.2% of those who used moisturizers. In this small sample, no associations were seen between the number of baths per week, or the type of lotion used, and the age of onset of AD.
CONCLUSIONS
These data reveal that the skin of a large majority of infants at-risk for the development of AD becomes exposed to frequent bathing and watery lotions at an early age. Lotions are generally not recommended for children with established AD as they are thought to worsen the skin barrier due to their high water content. Our findings highlight the need for further research on the potential effects that certain skin care practices may have on the infant skin barrier and on AD development in high-risk infants.

P-26. KAMPO AS A COMPLEMENTARY THERAPY FOR PATIENTS WITH RECALCITRANT ATOPIC DERMATITIS: DOUBLE-BLIND, RANDOMIZED PLACEBO-CONTROLLED STUDY

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Although many patients with atopic dermatitis (AD) are successfully treated with standardized therapy, there exist recalcitrant cases showing aggravation during the treatment over years. For such cases, we have utilized traditional herbal (Kampo) medicine as a complementary therapy. In Kampo, prescriptions are chosen according to the patients' conditions based on traditional Japanese medicine in relation to ancient Chinese concepts (essential Qi-, yin-yang- or five phase theory etc). Hochuekkito is a Kampo medicine that has been shown to be effective for patients with Kikyo (Qi-deficiency; delicate, easily fatigable, or hypersensitive) constitution. Previous reports have suggested that Hochuekkito is effective for a certain subgroup of patients with AD. In this multicentre, double-blind, randomized, placebo-controlled study, 91 Kikyo patients with AD were enrolled. All patients continued their ordinary treatments (topical steroids, topical tacrolimus, emollients or oral antihistamines) before and after their protocol entry. Hochuekkito or placebo was orally administered twice daily for 24 weeks. The skin severity scores, total equivalent amount (TEA) of topical agents used for AD treatment, prominent efficacy rate and aggravated rate were monitored and evaluated. Seventy-seven out of 91 enrolled patients completed the 24-week treatment course. The TEA of topical agents was significantly ($P<0.05$) lower in the Hochuekkito group than that of placebo group, although the overall skin severity scores were not statistically different. The aggravation rate was significantly ($P<0.05$) lower in the Hochuekkito group (3%; 1 of 37) than that of placebo group (18%; 7 of 39). Only mild adverse events such as nausea and diarrhea were noted in both groups without statistical difference. This placebo-controlled study demonstrates that Hochuekkito is a useful adjunct to conventional treatments for Kikyo patients with AD (Evid-based Complement Alternat Med 2008; doi: 10.1093/ecam/nen003).

SESSION 11
New Frontiers in Therapy

57. KL: PHARMACOGENETICS AND ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a complex genetic disorder influenced by environmental factors. The mode of inheritance and genes involved are not clear.
Traditional therapeutic strategies for AD include moisturizers, topical and systemic steroids, and immunosuppressive agents. In everyday practice, we observe AD patients with different response to topical treatment. For example, tacrolimus ointment is very efficacious in the treatment of AD, while there are patients who fail to respond. Moreover, an important alert has been released recently on the possible carcinogenicity of this drug.
Inter-individual variation in drug response is a major problem in medicine and no biomarkers are available to predict which group of patients responds positively, which patients are non-responders and who experiences adverse reactions for the same medication and dose. An understanding of the variability in efficacy and toxicity of the same dose of therapies would allow safer and more efficient treatments.
Pharmacogenetics and pharmacogenomics are relative new disciplines that should be able to provide the data for a better approach to therapy. Although often used interchangeably, pharmacogenetics implies the study of DNA variation in relation to differential drug response, while pharmacogenomics studies the mRNA and protein expression patterns in relation to differential drug response and it relates mostly to drug development. Whatever the name, these disciplines lead to the concept of personalized medicine which is a major challenge for the future.
Progress was recently made in searching the disease-susceptibility genes of AD via both the linkage studies and candidate gene approaches. Many genome wide linkage studies mapped a number of putative susceptibility regions on chromosomes 1q21 (ATOD2), 3q21 (ATOD1), 5q31-q33 (ATOD6), 13q12-q14 (ATOD5), 17q25 (ATOD4), 20p (ATOD3). Candidate region linkage studies identify other susceptibility loci on 5q23–33, 11q13, and 13q12–14. At least 28 candidate genes have to date been verified in association studies, but only association with genes of interleukin (IL)-4, IL-13, IL-4RA, mast cell chymase, and serine protease inhibitor, kazal-type 5 have been replicated in more than two different studies. More halpotype tests and family-based association studies may help to shed more light for the candidate gene approach. The effect of environmental trigger may also have to be considered to elucidate the real face of the disease.
The more we know about the genetic background of different groups of patients, the easier will be to carry out pharmacogenetics studies. At the moment, there are few examples of pharmacogenetics applied to dermatology. For instance, following immunosuppressive therapy, a subset of 41 genes was identified with significantly altered expression levels in patients who responded to therapy. These genes may serve both as novel target of therapy and predictive markers of clinical efficacy. As far as drug development is concerned, the use of pharmacogenomics in clinical trials will help to identify a patient subpopulation, based on genetic markers, who are more likely to respond to the drug and have less chances to suffer adverse reactions.

58. IC: A THERAPEUTIC EFFECT OF STAT6 DECOY OLIGODEOXYNUCLEOTIDES OINTMENT IN ATOPIC DERMATITIS

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Signal transducers and activators of transcription 6 (STAT6) play a crucial role in the transactivation of IL-4 and IL-13, which are involved in the pathogenesis of atopic dermatitis (AD). We have reported that the topical application of STAT6 decoy oligodeoxynucleotides (ODNs) inhibited skin inflammation of several mouse models of AD. In this study, we evaluated the clinical effect of topical STAT6 decoy ODNs ointment in human AD patients.
With the approval of local ethical committee of our university, informed consent was obtained from adult AD patients who were enrolled in this study (n=10, age: 32.5±5.8) . The ointment containing 2% STAT6 decoy ODNs was applied to lesions (erythema on the face or the trunk) twice daily. Clinical effect was evaluated at 2 and 4 weeks. Skin conditions were evaluated by the clinical score using Eczema Area and Severity Index (EASI) and photography. A visual analogue scale (VAS) was examined for the evaluation of pruritus. Eosinophil counts in peripheral blood and serum IgE levels were also examined.
One patient dropped out at the third week. In eight cases, clinical scores of the lesion were improved at the fourth week (mean: 40% of first clinical score). Moreover, in these cases, remarkable improvement of VAS was observed (mean: 30% of first VAS score). Neither eosinophil counts nor serum IgE levels were improved.
In conclusion, topical STAT6 ODNs ointment has a therapeutic potential as a novel treatment for AD.

59. IC: DEVELOPMENT OF NF-KAPPA B DECOY OINTMENT AND CLINICAL TRIAL FOR ATOPIC DERMATISIS

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NF-kappa B is a nuclear protein which regulates various inflammatory-relating genes such as TNF-α, IL (interleukin)-1β, IL-6, IL-8 receptor, MHC (major histocompatiblity complex) class I, MHC class II, CD80, CD86, ICAM-1 (intercellular adhesion molecule-1), VCAM-1 (vascular cell adhesion molecule-1), COX-2, collagenase I, so on. Activation of NF-kappa B has been shown to be involved in the pathogenesis of inflammatory diseases including rheumatoid arthritis, inflammatory bowel diseases and atopic dermatitis (AD).
In 1997, Morishita et al reported that ìNF-kappa B decoy DNAî, a double stranded deoxy-oligo DNA harbouring NF-kappa B-binding sequences, can competitively interfere binding of NF-kappa B to the promoter regions of the NF-kappa B-activating genes, resulting in inactivation of those genes in vitro and in vivo. Furthermore, administration of the NF-kappa B decoy DNA could ameliorate pathogenic inflammatory condition of myocardial infarction in rat model.
With those background described above, we have been trying to develop NF-kappa B decoy ointment to treat patients suffering from AD. We first evaluated an effect of the ointment containing 1.6% of NF-kappa B decoy DNA on the dermatitis of NC/Nga mouse, which naturally develops dermatitis associated with mast cell infiltration and serum IgE elevation under conventional circumstances as shown in AD patients. In the experiment, topical application of the ointment to NC/Nga mice clearly demonstrated prevention and amelioration of the dermatitis, suggesting effectiveness of NF-kappa B decoy DNA ointment on AD treatment. We then proceeded to clinical trials of 2.0 % NF-kappa B decoy DNA ointment to treat patients with AD. Since we had predicted a difficulty of topical administration due to a large molecular weight of the DNA, we evaluated therapeutic effect of the decoy DNA particularly on the lesions of the face, which is well known to have a lower barrier function as compared to the other regions of the body. Patients with severe facial AD involvements clearly showed almost complete remission in 3 weeks after the decoy applications. Relatively milder facial AD also revealed less but significant improvement in 4 weeks. In contrast, AD lesions on the trunk and the extremities did not show significant difference between the decoy DNA and white petrolatum for their outcomes, suggesting lower efficiency of the decoy DNA penetration in those regions. No side effect was observed locally and systemically in the 10 patients involved in the study.
In conclusion, we believe that NF-kappa B decoy DNA ointment is a unique and effective option to treat AD, especially for their severe facial involvements.

60. IC: AN UPDATE ON TOPICAL CALCINEURIN INHIBITORS

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Topical calcineurin inhibitors (TCI) have been used for more than 10 years to treat atopic dermatitis. In most countries, they have been positioned as second-line agents for patients unresponsive or intolerant to topical corticosteroids. TCI have received a lot of attention in the media following the 2006 decision from Health Authorities in US and EU to insert a safety warning regarding the possible risk of malignancies associated with their use. The concern came mainly from animal studies with high doses of calcineurin inhibitors which showed that massive exposure to these compounds was associated with the development of lymphoma. The Health Authorities decision was precipitated by spontaneous reports of malignancies in patients treated with TCI and by the high level of use (and also off-label use) of TCI in the population. High usage was obviously encouraged by vigorous marketing efforts from the companies promoting the drugs. Following this decision which was amplified by a media campaign, a massive reduction in the prescription and in the use of TCI was observed between 2006 and 2007. Two years after these events there is very little data to support these concerns. Systemic exposure after topical use of TCI was shown to be minimal in numerous pharmacokinetic studies. No sign of systemic immunosuppression and no reduction of response to vaccination has been demonstrated. Results of clinical and

epidemiological studies demonstrate that the risk of lymphoma and skin malignancies in patients treated with topical calcineurin inhibitors is not increased versus the risk in patients not treated or in patients treated with topical corticosteroids. Education of patients is important to promote optimal use of these agents.

61. OC: EFFICACY AND SAFETY OF PIMECROLIMUS CREAM 1% IN 1088 INFANTS WITH ATOPIC DERMATITIS: RESULTS OF THE THREE YEAR DOUBLE-BLIND, VEHICLE CONTROLLED PHASE OF THE STUDY OF THE ATOPIC MARCH

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BACKGROUND: An explanation for the "atopic march" is epicutanous sensitization through skin of patients with atopic dermatitis (AD) leading to an increase in development of allergic rhinitis and asthma. The double blind phase of this ongoing 6-year study investigated whether long term management of AD with pimecrolimus cream 1% (PIM) provided better control of AD over 3 years than a corticosteroid (CS)-based regimen. The ongoing, open label phase will assess whether commencement of PIM soon after diagnosis of AD reduces the incidence of asthma at 6 years of age compared with delaying intervention by 3 years.

METHODS: In the 3 year, double blind phase, infants 3-18 months of age with AD for 3 months or less at enrollment, at least mild AD (based on Investigator Global Assessment [IGA]), and a family history of atopy were randomized 1:1 to receive intermittent, need-based treatment with PIM or vehicle cream. Rescue medications were moderately potent-to-potent topical corticosteroids (CS). The three year analysis assesses the effect of PIM compared to a CS-based regimen on AD control based on proportion of disease free days reported on an electronic diary, change from baseline in IGA, AD Body Surface Area (BSA, 0-100%), and Eczema Area and Severity Index (EASI, 0-72). Safety was assessed based on physical exam, interviews with the primary caregiver, and review of diary data.

RESULTS: Will be presented.

62. OC: A PILOT STUDY OF A PETROLATUM-BASED EMOLLIENT FOR THE PRIMARY PREVENTION OF ATOPIC DERMATITIS

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BACKGROUND
Previous atopic dermatitis (AD) prevention studies have focused on maternal or infant allergen avoidance. Decades of research have yielded no consistently-effective approaches. Recent genetic studies of filaggrin reveal AD may largely be caused by a primary skin barrier defect. There have been no published studies evaluating skin barrier protection for the primary prevention of AD. Our hypothesis is that correction of the early skin barrier defect in AD with emollients may delay the onset, or prevent the development, of AD. The objective of this study was to evaluate the feasibility and safety of emollient use in high-risk infants as a potential AD prevention strategy.
METHODS
Fifteen out of a planned twenty mother-baby pairs have been recruited so far in a 2 year study. The baby must have been part of a high-risk family with at least one parent or sibling having a history of AD and one family member with either allergic rhinitis or asthma. A bland petrolatum-based emollient was started within 1 week of birth and applied once daily to all body surfaces except the diaper area at least once daily. Skin exams and measurements of skin barrier function were performed at 1, 6, and 12 months.
RESULTS
There have been no adverse events thus far in the trial and compliance has been excellent with an average of 5.6 applications per week at Month 1, and 7 times per week at Month 6. The average length of follow-up to date has been 387 days. Transepidermal water loss and skin hydration have been equivalent to that expected of normal skin. One of fifteen infants has been diagnosed with AD, and one infant has been diagnosed as possible AD. At 2 years, approximately half of these high-risk infants would be expected to develop AD.
CONCLUSIONS_Skin barrier protection using an emollient early in life appears to be a feasible and safe approach to AD prevention. Preliminary results suggest a protective effect, however controlled studies are needed.

63. OC: IFN-γ-INDUCED SPECIFIC ORAL TOLERANCE INDUCTION (IGI SOTI) FOR FOOD ALLERGY (SEOUL ALLERGY PROTOCOL, SAP) IN ATOPIC DERMATITIS

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Food allergy play important roles in atopic dermatitis and the only therapeutic approach for food allergy has been known as the avoidance of causative foods. Specific oral tolerance induction (SOTI) for food allergy has been tried with limited successes during last decases. Tolerance induction for milk allergy was successfully tried by IGI SOTI with Seoul Allergy Protocol (SAP) in previous report. In this study, IFN-γ-induced specific oral tolerance induction (IGI SOTI) with Seoul allergy protocol (SAP) was successfully performed for the allergy to the expanded kinds of food.

Among 4000 atopic dermatitis patients, 250 cases were selected and received IGI SOTI with Seoul allergy protocol (SAP) for 7 years from 2001 Jan. 1 to 2008 Feb. 29 in this study. For the diagnosis of food allergy, oral challenge test were tried. Diet elimination was preceded and the improvement of atopic dermatitis was verified before challenge test. A total of 250 cases who showed food allergy to seven foods (Milk , 100 cases; egg 50 cases; soybean, 20 cases; wheat, 20 cases; beef, 20 cases; chicken, 20 cases; pork, 20 cases) were tried by IGI SOTI with SA Protocol (SAP). SA Protocol was consisted of 7-day course. IFN-γ was injected subcutaneously to patients with the dose of 50Ïg for over or equal to 30 kg, or equivalent dose. Foods were ingested within 10 minutes after IFN-γ injection. The quantity of food was increased like 1/4, 1/4, 1/2, 1/2, 1, 1, and 1.5 portion of food along the days. Skin prick test, allergy patch test, the measurement of total IgE and specific IgE, and complete blood count with differential count were performed before and after IGI SOTI.

All patients were obtained tolerance for allergy to the all expanded kinds of food in this study by IGI SOTI with SA protocol. The significant conversion of reaction to allergy patch test was observed by IGI SOTI with SA protocol. There was no other remarkable change in laboratory findings with the insignificant laboratory changes like decreased eosinophil %, increased total IgE after IGI SOTI with SA protocol. No one has shown recurrence for several months to over 7 year.

Conclusively, the tolerance for allergy was completely induced regardless of kinds of food without recurrence for 7 years by the new advanced and curative therapy, IFN-γ-induced specific oral tolerance induction (IGI SOTI) with Seoul Allergy Protocol (SAP) in this report. The immunologic essence for allergy and the exact immunologic mechanisms for tolerance induction should be clarified. And this therapy maybe cast a important clue for the fundamental solution for allergy.

P-27. FIRST EXPERIENCE WITH ENTERIC-COATED MYCOPHENOLATE SODIUM (MYFORTIC®) IN SEVERE RECALCITRANT ADULT ATOPIC DERMATITIS: AN OPEN LABEL STUDY

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Background: Severe atopic dermatitis (AD) can be succesfully treated with oral immunosuppressives such as cyclosporin (CsA), azathioprine (Imuran) or systemic corticosteroids. However, some patients develop adverse effects or are unresponsive to these first-choice oral immunosuppressive drugs.

Objective: To evaluate whether enteric-coated mycophenolate sodium (EC-MPS) is an effective treatment in patients with severe, recalcitrant AD. Patients/Methods: Ten patients with severe, recalcitrant AD were treated with EC-MPS 720 mg twice daily for six months. All patients had to discontinue other oral immunosuppressives (CsA) due to adverse effects (n=8) or non-responsiveness (n=2). Disease activity was monitored using the Severity Scoring of Atopic Dermatitis (SCORAD) score and the Leicester Sign Score (LSS). Additionally, the level of serum thymus and activation-regulated cytokine (TARC) was measured. During treatment, laboratory examination was performed to monitor possible adverse events. Serum total immunoglobulin E (IgE) was followed during treatment. Use of topical corticosteroids was recorded before and during treatment. Results: During treatment with EC-MPS the mean SCORAD (p=0.04), LSS severity (p=0.01), LSS extent (p=0.01) and serum TARC (p=0.03) decreased significantly after 2 months and was consistent during the six month treatment period. Additionally serum total IgE decreased during treatment (p=0.05). There was no difference in use of topical corticosteroids in the six months prior to treatment compared to the six month treatment period. None of the patients discontinued the use of EC-MPS and only mild adverse effects were seen. Conclusions: In this study EC-MPS in a dose of 720 mg twice daily for 6 months has proven to be an effective and well tolerated therapy for severe, recalcitrant AD patients.

P-28. EFFECT OF ANTI-HELMINTHIC TREATMENT ON EXERCISE-INDUCED BRONCHOSPASM, ALLERGEN SKIN SENSITISATION, AND IMMUNOLOGICAL RESPONSES: A RANDOMISED, DOUBLE BLIND, PLACEBO-CONTROLLED TRIAL IN VIETNAM

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Background: Observational studies suggest that infection with geohelminths protects against clinical allergy and allergen skin sensitisation, and that such effects are mediated by geohelminth-induced cytokine responses. We conducted an intervention study to test this hypothesis.

Methods: We randomly allocated 1566 Vietnamese schoolchildren aged 6 to 17 to receive either anti-helminthic therapy or placebo at 0, 3, 6 and 9 months, and compared presence of flexural eczema on physical examination, change in exercise induced bronchoconstriction, allergen skin sensitisation to house dust mite (Dermatophagoides pteronyssinus and farinae) and cockroach (Periplaneta americana), and questionnaire-reported wheeze and rhinitis between 0 and 12 months.

Results: 1487 children (95% of those randomised) completed the study. The commonest helminth infections were hookworm (65%) and Ascaris lumbricoides (7%). There was no effect of therapy on occurrence of flexural eczema (adjusted OR=1.17, 0.39-3.49, p=0.8), exercise-induced bronchoconstriction (within-participant mean % fall in peak flow from baseline after anti-helminthic treatment 2.25 (SD 7.3) vs placebo 2.19 (SD 7.8, p=0.9), or on the prevalence of questionnaire-reported wheeze (adjusted OR=1.16, 95% CI 0.35-3.82, p=0.8) and rhinitis (adjusted OR=1.39, 0.89-2.15, p=0.1). However, anti-helminthic therapy was associated with a significant increase in allergen skin sensitisation in the treatment group (adjusted OR=1.31, 1.02-1.67, p=0.03). Post-hoc analysis suggests that this effect was particularly strong for children infected with Ascaris lumbricoides at baseline (adjusted OR=4.90, 1.48-16.19, p=0.009), most of whom were also infected with hookworm. Allergen skin sensitisation was inversely related to hookworm specific IL-10 at baseline (adjusted OR per pg/mL=0.82, 0.68-0.99, p=0.04), but neither IL-10 nor any of the other immunological markers changed

significantly after anti-helminthic therapy compared to placebo.
Conclusions: This study suggests that regular anti-helminthic treatment over a 12 months period in children from a helminth endemic area increases the risk of allergen skin sensitisation, but not of clinical allergy such as eczema. While parasite-induced IL-10 may play a role in helminth-induced immuno-modulation of allergen skin sensitisation, additional immunological mechanisms are likely to be involved.

P-29. MANAGEMENT OF ATOPIC DERMATITIS PATIENT

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Summary of the objectives. Management of atopic dermatitis (AD) is clinical challenge .Optimal skin care and hydration, identification and avoidance of specific and non-specific trigger factors is needed. The goal was to point out therapeutic agents for use according to disease severity. According clinical diagnosis after Hanifin and Rajka and SCORAD index we used in our 50 patients (aged 2-30) basic therapy for solely dry skin, low-to-mid potency topical corticosteroids (TCs) and/or topical calcineurin inhibitors (TCIs) for mid to moderate AD, mid-high potency (TCS/TCIs for moderate-severe AD, and systemic therapy.
Results. In 45 out of 50 patients was beneficial therapeutic respond. In five cases a wet layer of cotton dressing in combination with antiseptics or TCs has been used for cases of exacerbated AD skin lesions. For Staphylococcal secondary infection we ordered cephalosporins for 7 to 10 days in six patients. Cetirizin and loratadin were ordered in 36 patients. Cyclosporine A or phototherapy was used in 10 patients each for recalcitrant severe AD. A combination of different topical agents was used, too.
Conclusion. Although there has been an enormous progress in our understanding of the molecular biology of AD, it seems that management currently focuses on avoidance of triggers, use of skin hydration and reduction of skin inflammation. There are no disease-modifying drugs.

P-30. KEISHIBUKURYOGAN DECREASES THE DISEASE ACTIVITY AND THE LEVEL OF SERUM TH2 TYPE CHEMOKINES AND MIF IN ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a chronic inflammatory skin disorder and is characterized by the predominant infiltration of Th2-type cells in the acute phase of skin lesions. Thymus and activation-regulated chemokine (TARC/CCL17), cutaneous T cell attracting chemokine (CTACK/CCL27) and macrophage derived chemokine (MDC/CCL22) were identified as a selective chemoattractant for Th2 type cells. The serum levels of these Th2 type chemokines were significantly increased in patients with AD and are correlated with the severity. Furthermore, the serum level of macrophage migration inhibitory factor (MIF), which is one of the immunoregulatory cytokines involved in T cell activation, was also elevated during the active stage of AD. Keishibukuryogan (KBG) is a Kampo formula composed of five kind of crude drugs, Cinnamomicorte, Moutan cortex, Paeoniae radix, Persicae semen and Hoelen. KBG has been administrated to patients with blood stagnation in Japan. This study investigated the effect of KBG on disease activity and Th2 type chemokines and MIF production in AD patients. Thirty three patients with AD were administered 7.5 g of KBG for 4 to 6 weeks in addition to their prescribed medications. The clinical severity of AD was assessed using the SCORing Atopic Dermatitis (SCORAD) index. For the assessment of itch, a visual analogue scale (VAS) score was used. The serum levels of TARC, CTACK, MDC and MIF were measured with enzyme-linked immunosorbent assay (ELISA). The SCORAD index and VAS score were decreased by the administration of KBG. The serum level of TARC, CTACK, MDC and MIF in the AD patients was higher than that of normal controls. These elevated serum levels were decreased by administration of KBG. These results suggest that KBG may improve AD by the inhibitory effect on Th2 type chemokine production and the anti-inflammatory activity.

P-31. EFFECT OF FULL SPECTRUM LIGHT FOR THE TREATMENT OF ATOPIC DERMATITIS

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Background : Recently, atopic dermatitis is supposed to be associated with many cytokines of Type 1 Helper T Cell (Th1) and Type 2 Helper T Cell (Th2). For the treatment of AD, phototherapy, cyclosporine, immunosuppressants have replaced steroid because steroid has many side effects. Among many methods of phototherapy, Full Spectrum Light (FSL) therapy device is a special instrument generates wavelength spectrum similar to sunlight.
Objectives : The aim of this study is to evaluate the effectiveness of FSL on the treatment of atopic dermatitis.
Methods : The subjects of this research were four patients with atopic dermatitis who have suffered it for a long period of time despite systemic steroid and antihistamine therapies. For six weeks, their lesions were irradiated using FSL for 20 minutes twice per week. For assessing the change of severity of AD, photographs and blood tests including eosinophil count, serum IgE and cytokines were taken every two weeks. In addition, erythema and melanin index were measured by using mexameter MX18(Courage & Khazaka Electronic, Cologne, Germany).
Results : Improvement was observed clinically on the acute lesion of the all patients. Serum cytokines revealed decline of IL-4, IL-13 and increment of IL-12, FANTES. Erythema index was decreased while melanin index was increased af-

ter FSL treatment.
Conclusion : The results of this research demonstrated that FSL device can be effective and generally well-tolerable method for the treatment of atopic dermatitis.

P-32. ARE BIOLOGICS SAFE IN THE TREATMENT OF ATOPIC DERMATITIS? A REVIEW WITH A FOCUS ON IMMEDIATE HYPERSENSITIVITY REACTIONS

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BACKGROUND
Although there are now several approved biologics for the treatment of psoriasis, there are no biologics currently approved for the treatment of atopic dermatitis (AD). One possible reason for this discrepancy may be a concern of developing protein-based therapies for a patient population with elevated IgE levels and the perceived greater likelihood for developing type 1 hypersensitivity reactions to proteins.
The objective of this study was to review the literature regarding the use of biologic therapies in AD to estimate the risk of adverse reactions to biologic therapies with an emphasis on type 1 immediate hypersensitivity events including urticaria, angioedema, and anaphylaxis. We also focused on adverse drug reactions that may be unique in nature or frequency in this patient population.
METHODS
We reviewed the English literature using Pubmed for studies that used biologic agents in the treatment of patients with AD. All study designs were included in our analyses including randomized controlled studies, case series, and case reports.
RESULTS
A total of 17 published studies and 2 follow-up studies were identified comprising 254 patients with AD exposed to biologics. No Type 1 hypersensitivity events were identified attributable to biologic use. The only adverse event that may be unique to patients with AD is a higher than expected incidence of thrombocytopenia with the use of efalizumab which occurred in 2 of 13 patients.
CONCLUSIONS
The use of biologics in AD appears safe and, to date, there does not appear to be a higher incidence of type I hypersensitivity reactions. There do not appear to be any side effects unique to this patient population except a possible higher incidence of thrombocytopenia with efalizumab therapy.

P-33. SKIN PROTEASE INHIBITORS: A NEW TREATMENT FOR ATOPIC DERMATITIS

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Breakdown of the skin barrier is a key event in the development of atopic dermatitis (AD). Changes in at least four groups of genes in children with AD lead to enhanced protease activity within the epidermis, resulting in skin barrier breakdown. Inhibition of this protease activity could provide a valuable treatment opportunity for AD. A series of experiments was designed to evaluate the activity of three Skin Protease Inhibitors *in vitro* and *in vivo*.
Skin Protease Inhibitors were tested initially *in* vitro using a chromogenic substrate for the serine protease α-chymotrypsin. The effect of these inhibitors on protease activity within skin tissue sections was subsequently determined using *in situ* zymography (Hachem JP, *et al* JID 2003, Aug:121(2):345-53). Finally, novel, pre-clinical formulations containing the Skin Protease Inhibitors were tested for their ability to reduce steroid-induced protease activity *in vivo* in volunteers using *in situ* zymography.
The novel skin protease inhibitors YC1015, YC1016, YC1017, at 20mM, resulted in significant reduction of α-chymotrypsin *in vitro* by 32, 57, and 26 %, respectively (values provided are means). At a concentration of 40mM, YC1018 resulted in a 62 % reduction (5-fold) of α-chymotrypsin activity. Further to this, combinations of YC1015 and YC1018 significantly inhibited casein-specific protease activity found in the epidermis at concentrations down to 1mM for skin tissue sourced from three independent volunteers. Treatment of the forearms twice a day with a potent topical corticosteroid (TCS) induced protease expression within the epidermis. This increase in protease activity was reduced when formulations containing YC1015 and YC1018 were applied after the TCS treatment. The Skin Protease Inhibitors, in combination with an optimal emollient formulation, could provide a new approach to restoring the defective skin barrier in atopic dermatitis.

SESSION 12
Information and Education of Patients: Worldwide Experiences in Quality of Care

64. KL: CONFRONTING PATIENT'S AND DOCTOR'S PERSPECTIVES IN THE MANAGEMENT OF ATOPIC DERMATITIS

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During the last twenty years, I have been actively involved in the direct care of both children and adults with atopic derma-

titis, including clinical trials and personal research. « Du temps perdu á la recherche » as a distinguished british professor put it inspired by Proust, I have gained the impression that my interaction with patients benefited from this kind of mixed practice, because I could probably tell better the areas of uncertainty vs important facts which have begun to be considered with more attention recently in the pathophysiologic puzzle of the disease (1). There is a feeling which is not yet evidence-based that the more AD turns out to be a true skin disease, the more dermatologists can help. I have also extensively read about this disorder and its management when writing a book about the history of the disease (2). Our current perspectives and those of our patients still mirror closely those of the beginnings of scientific dermatology, at the end of the XIXth century. The quality of life, or something similar because the name did not exist, was clearly depicted by Hebra in his textbook « Lorsqu'on envisage le cours de la vie d'une personne affectée de cette maladie, combien dans son enfance son habitude constante de se gratter l'a fait gronder par ses maîtres, (…) combien, plus tard, elle est raillée par ses compagnes (…) combien (…) il lui est difficile de se créer un intérieur ou de se marier, - on ne sera pas surpris qu'une personne tourmentée d'une maniére aussi terrible prenne la vie en dégoût … » (3). Although clearly recognized by doctors, the sufferings of the patients are frequently forgotten in the heat of the scientific discussion, as highlighter by a discussant at the 1900 world congress : « N'oublions pas qu'en clinique l'intérêt du malade doit prévaloir…tâchons de trouver un moyen efficace pour combattre les démangeaisons de l'eczéma. Ce point mériterait peut être d'être étudié au prochain congrés ».

This talk will discuss three points frequently raised when we talk about their disease with our patients namely causality in eczema ; compliance ; clinical benefit of an intervention.

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65. IC: STRUCTURED EDUCATIONAL PROGRAM FOR ATOPIC DERMATITIS CHILDREN AND CAREGIVERS

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Background: Atopic dermatitis (AD) in childhood is a common disease with prevalence rates as high as 20 %. Its early onset in infancy and its chronic relapsing course put a special burden on families. Supporting parents in dealing with the management of AD presents a challenge for physicians. Lack of information, overstrain, helplessness and lack of confidence in medical treatment lead to suboptimal management and increasing use of health care resources. Our project was set up to develop a structured education program for parents, schoolchildren and adolescents to improve the self management of AD and to assess its effects.
Methods: 7 German hospitals participated in this multicentre randomised controlled trial. The participants of three age groups were evaluated separately: parents of children aged 3 mo to 7 years (n=274 in the intervention group and n=244 in the control group)), children from 8 – 12 years and their parents (n= 102 and 83) and adolescents form 13 – 18 years (n=70 and 50). The intervention consists of 6 group sessions, two hours each, over a period of 6 weeks. The control group was offered the opportunity to participate in the program one year later. The outcomes were changes in severity of eczema (SCORAD), subjective severity, and quality of life of the parents assessed over 12 months.
Results: Significant improvements in severity of eczema and subjective severity compared to the controls were seen in all age groups. Parents of children younger than 8 y experienced significantly better improvement of their QoL in all the domains, parents of the older children in 3 of the five domains.
Conclusion: Age related educational programs for the control of atopic dermatitis are effective in the long term management of the disease.

66. IC:THERAPEUTIC EDUCATION IN ATOPIC DERMATITIS : WORLDWIDE EXPERIENCES

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Patient education is an increasingly essential element in the care of chronically ill people. Atopic dermatitis affects the patient's quality of life and forces them to take an active role in their local treatment. Several projects, independent from each other, have been developed worldwide in the field of therapeutic education.
Confronted with Atopic patients' generally low therapeutic adhesion and the potential of patient education in dealing with this problem, we carried out an international inventory of the present situation.

Method:
In order to identify the international situation we sent a complete questionnaire to experts working in different countries, in European hospital environments. The questionnaire was composed of 25 open questions dealing with both individual structures and global patient education policy in each country.

Results:
12 experts were contacted and 11 accepted to reply to the questionnaire representing 11 hospital centres in 7 different countries.
A *collective approach* had been developed in the all the centres except in the UK. An individual approach was mentioned in some centres for out-patients (UK, France) and for in-patients (Germany). In the individual approach, doctors, nurses or both conducted the interviews and follow-ups were done by the nurses (France). In the UK, the patient education programmes were mostly performed by nurses.
The *profile of patients* who came to the atopic schools was moderate to severe according to the SCORAD (40 on average) and always corresponded to a treatment failure.
The majority of the *workshops were organised* according to age and the training courses were conducted by dermatologists (France, Germany, Denmark, Italy, Spain), nurses (UK) or psychologists. In some centres in Germany, paediatricians, nutritionists or psychosomatic trainers were

involved in the patient or parent's training.
The *number of patients* integrating the education programme depended on the experience and the history of each centre: 50 patients/year in the newer schools in France but up to 200/centre in Germany. Each workshop was composed of 5 to 10 patients or parents.
Different *educational support tools* were used in the different atopic schools (representative dolls, Teddy bears, educational packs specific to each team, images, handouts, dvds…) but each trainer was free to choose the tool he preferred and the tools were chosen according to the content of the course. Power-point was rarely used (only Denmark and Italy).
The *patient's progress* was mainly evaluated using an objective score (SCORAD index, quality of life scores) and the acquired competencies were evaluated by questionnaires (Germany), even though these competencies are rarely evaluated today, for lack of adapted tools. Finally, a global satisfaction evaluation was carried out after each workshop by either the patient or the parent.
The relationship between the atopic school and the private practitioners was variable and globally poor. Private dermatologists participated in some atopic schools but only those who had both a private and hospital practice. Contacts with other patient education teams were often cited particularly those working with asthma or food allergy (France, Germany).
In the majority of cases a specific staff training existed. But in some countries (Spain or Italy) there was no specific organisation dedicated to training in patient education.

The creation of atopic schools depended on the initiative of motivated dermatologists involved in the field of atopic eczema. At the beginning, grants from private companies were obtained but the medical and nurses teams were mostly paid by the hospital (Canada, Denmark).
Patient associations and support groups played a minimal role in the atopic schools even if there was some close contact with some groups willing to cooperate with medical staff.
At a national level there was some discrepancy in the functioning of the atopic schools between Europe and Canada. The oldest experiences had been developed in Germany with the GADIS project where the atopic schools were popular. In the other countries the experts stated that patient education was at the early stages of development.

Therapeutic education programs are not equally developed in the different countries.
We can conclude, therefore, that there is a considerable need to promote education programs in Dermatology in order to respect the WHO's recommendations (*) in this field.
The OPEN project promotes patient education in chronic skin disease and attempts to offer support to existing and emerging teams in setting up educational structures by associating recommendations, reference documents and clinical research.

* Continuing Education Programmes for Health Care Providers in the Field of Prevention of Chronic Diseases. http://www.euro.who.int/document/e63674.pdf

67. OC: PSYCHOMETRIC PROPERTIES OF OUTCOME MEASUREMENTS FOR ATOPIC ECZEMA. A SYSTEMATIC REVIEW AND SURVEY INVOLVING EXPERTS AND CONSUMERS

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Valid and reliable outcome assessment is one of the most fundamental prerequisites for evidence-based practice. Despite its high prevalence, morbidity, and economic impact the comparative validity and reliability, sensitivity to change and ease of use of outcome measurements for assessing atopic eczema severity is unclear. We performed a systematic review and survey of clinical experts and patients to assess the psychometric properties of named outcome measurements for atopic eczema. Based on pre-specified criteria we aimed to provide evidence-based recommendations on which outcomes to use in clinical research and for clinical monitoring.
Twenty published outcome measurements were identified. There is evidence of adequate construct validity for three measurements (Severity Scoring of Atopic Dermatitis index (SCORAD), Eczema Area and Severity Index (EASI), Three Item Severity Score), adequate internal consistency of one scale (Patient-Oriented Eczema Measure (POEM)), adequate inter-observer reliability of five measurements (Basic Clinical Scoring System, Nottingham Eczema Severity Score, Objective Severity Assessment of Atopic Dermatitis, Six Area, Six Sign Atopic Dermatitis severity score, SCORAD), adequate test-retest reliability of one scale (POEM), and adequate sensitivity to change of three measurements (EASI, SCORAD, Investigators¥ Global Atopic Dermatitis Assessment). Most outcome measurements have adequate content validity as assessed by patients and experts.
There are too many published outcome measures for atopic eczema. Most have not been tested properly or perform adequately when tested, and their continued use hampers scientific communication. Only SCORAD, EASI, and POEM have been tested sufficiently and performed adequately enough to be recommended for future studies and clinical practice.

68. OC: DEVELOPING AN ASSOCIATION FOR PATIENTS WITH ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a chronic, pruritic and inflammatory skin disease with an increasing prevalence in the last decades. This complex condition, with its multifaceted etiopathogenesis, affects not only the patient, but also the entire family, often leading to a disruption of family routine and worsening of patient's quality of life. Usually, a better understanding and improvement of this skin condition is not entirely achieved in one single medical consultation, justifying the need for complementary assistance.
The creation of an association for patients and families affected by AD, may improve the health and quality of life of those individuals through support, education and research. A multidisciplinary team, including physicians and other health care professionals (e.g. psychologists, nurses and social

workers), patients and volunteers, is essential for the success of an association. Moreover, education about the disease is provided by the distribution of booklets, video presentations and lectures.
Support groups are the essence of an AD association since they provide an intense exchange among patients and families that share similar challenges and experiences. Support group usually breaks isolation and improves adherence to treatment.
The AD association can also provide support for health professionals, by organizing scientific meetings and offering specialized medical information.
In summary, an atopic dermatitis association should work as a task force, where every member is crucial to reach the final goal: the patient´s well-being.

P-34. ORIENTED PATIENT EDUCATION NETWORK (OPEN PROJECT): A TOOL FOR THERAPEUTIC PATIENT EDUCATION.
http://web.mac.com/dermatodelouest/OPEN/accu.html

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One of the main causes of treatment failure in atopic dermatitis is the weak adhesion to the prescribed treatment, in particular concerning local treatments and the use of corticoids. Patient education is one of the most adapted responses to this problem.

In order to respect the WHO recommendations and because of the lack of a coherent and structured policy for dermatology, we have developed a network called «OPEN Dermatology » (Oriented Patient Education Network). This network will function through a web site whose principal objectives are to:

- Identify worldwide experiences in the field of patient education.
- Offer support to existing and emerging teams in setting up education structures by associating recommendations, reference documents, and clinical research.
- Ensure the promotion of patient education applied to chronic skin disease.
- Promote patient education by associating the patients and the care-givers.

Different headings were created for therapeutic patient education in general, and for the WHO recommendations.
A large survey was carried out of the main experts who had developed atopic schools in their respective countries. The results were presented in the form of transcribed and audio interviews. The educational material developed around a self asessment tool is presented. This is to be used in the creation of a self assessment score called the PO-SCORAD (patient oriented scorad index). Educational guidelines for the patient are included in the site in the form of a film. This film offers the experts the possibility to train the doctors and the patients in why and how to use the self asessment score.
Other tools which are used by the different teams are presented in their original version but certain documents have been translated into English. In the future this site will include clinical research projects in the field of patient education and will be accessible to a large public.

Conclusion :
This project was launched with help of the Pierre-Fabre foundation. OPEN Dermatology is a network project that promotes and communicates patient education in dermatology, particularly for atopic dermatitis but also for other forms of chronic dermatitis (psoriasis, acne…). The site is a platform for communicating experience in this field and pooling resources.

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