



Organizer:

Professor Laurent Misery, University of Brest, France

Organization Committee:

Claire Abasq

Nicholas Boulais

Nicolas Lebonvallet

Christelle Le Gall-Ianotto

Laurent Misery

Anne-Marie Roguedas-Contios

Contact Address:

Itch 2011/MCI, 24 Rue Chauchat, 75009 Paris

Tel : +33 1 53 85 82 61; Fax : +33 1 53 85 82 83

Website: <http://www.itchbrest.com>

E-mail: registration@itchbrest.com

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IFSI Board Members:

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SUNDAY, SEPTEMBER 4, 2011

- 15:00 **Registration**
- 17:00–19:00 **IFSI Board of Directors**
- 20:00 **Welcome Reception**, on a boat (with a grant of Maruho)

MONDAY, SEPTEMBER 5, 2011

- 07:30–09:00 **SIG Meeting: Itch Questionnaires**
Chairs: *Elke Weisshaar and Gil Yosipovitch*
- 09:00–09:30 **Opening of the Congress**
Chairs: *Sonja Ständer and Laurent Misery*
- 09:30–11:00 **Psychological and Epidemiological Aspects (IP01–04)**
Chairs: *Jacek Szepietowski and Kenji Takamori*
- 09:30–09:45 Itch in adolescents, *Jon Anders Halvorsen*
- 09:45–10:00 Mental induction of itch, *Jörg Kupfer*
- 10:00–10:15 Stress and itch in chronic skin diseases, *Andrea Evers*
- 10:15–10:30 Neural correlates of delusional infestation, *Markus Kölle*
- 10:30–11:00 **Free communications (FC01–02)**
Influence of negative and positive emotions on the sensitivity to itch and pain, *Antoinette van Laarhoven, Annika Walker, Oliver Wilder-Smith, Sabine Kroeze, Piet van Riel, Peter van de Kerkhof, Floris Kraaimaat, Andrea Evers*
Impact of the 2011 Great East Japan Earthquake on patients with skin diseases – an experience from participating in a dermatological support group that went to the disaster stricken areas, *Toshiya Ebata*
- 11:00–11:30 **Coffee Break and Poster Session**
- 11:30–12:30 **Clinical and Pathophysiological Aspects (1) (IP05–08)**
Chairs: *Alan Fleischer and Toshiya Ebata*
- 11:30–11:45 Drug-induced pruritus, *Jacek Szepietowski*
- 11:45–12:00 Aquagenic pruritus in polycythemia vera, *Christelle Le Gall*
- 12:00–12:15 Pruritus in cutaneous T-cell lymphomas, *Nicolas Meyer*
- 12:15–12:30 Pruritus and amyloidosis, *Akio Tanaka*
- 12:30–14:00 **Lunch and Poster Session**
- 14:00–15:30 **Clinical and Pathophysiological Aspects (2) (IP09–10)**
Chairs: *Ethan Lerner and Masutaka Furue*
- 14:00–14:15 Pruritus in human AD-mechanisms and managements of intractable itch, *Kenji Takamori*
- 14:15–14:30 Pruritus in canine atopic dermatitis, *Thierry Olivry*
- 14:30–15:30 **Free communications (FC03–06)**
Topically applied semaphorin 3A ointment inhibits scratching behaviors and improves skin inflammation in NC/Nga mice with atopic dermatitis. *Osamu Negi, Mitsutoshi Tominaga, Kenichi Taneda, Atsuko Kamo, Suhandy Tenggara, Kenji Takamori*

- Gender specific differences in itch processing – a functional MRI study. *Astrid Stumpf, Markus Burgmer, Gudrun Schneider, Gereon Heuft, Martin Schmelz, Ngoc Quan Phan, Sonja Ständer, Bettina Pfeleiderer*
- Artemin expression in pruritic skin diseases: Histopathological analysis. *Megumi Nishioka, Hiroyuki Murota, Ichiro Katayama*
- Evaluation of the relationship between stress, pruritus and quality of life in lichen planus. *Adam Reich, Kalina Welz-Kubiak*

- 15:30–16:00 **Coffee Break and Poster Session**
- 16:00–17:30 **Clinical and Pathophysiological Aspects (3) (IP11–12)**
Chairs: *Sonja Ständer and Gil Yosipovitch*
- 16:00–16:15 Role of proteases, proteinase-activated receptors and peptidases in skin inflammation and skin barrier function, *Martin Steinhoff*
- 16:15–16:45 **Free communications (FC07–08)**
Differential processing of cowhage and histamine itch in health and disease. Insights into brain processing of chronic pruritus revealed by arterial spin labeling fMRI, *Alexandru D.P. Papoiu, Robert Coghill, Robert Kraft, Gil Yosipovitch*
Expression profiles of thermo-Trp channels in chronic pruritus, *Heike Benecke, Julia Wördehoff, Tobias Lotts, Martin Marziniak, Thomas A. Luger, Hanns Hatt, Sonja Ständer*
- 16:45–17:00 Pruritus from the sea, *Laurent Misery*
- 17:00–17:15 **Presentation of the Acta Dermo-Venereologica**, *Anders Vahlquist*
- 17:15–18:00 **General Assembly of IFSI**
- 18:00–18:30 **Board of Directors of IFSI**
- 19:00 **Gala Evening, Awards and Visit of Oceanopolis**

TUESDAY, SEPTEMBER 6, 2011

- 09:00–10:30 **Biological and physiological aspects (1) (IP13–16)**
Chairs: *Earl Carstens and Satoshi Takeuchi*
- 09:00–09:15 Neurotrophins and itch, *Martin Schmelz*
- 09:15–09:30 The mechanism by which cathepsin S triggers PAR2 activation, *Ethan Lerner*
- 09:30–09:45 Inhibitory neurons of the dorsal horn play a crucial role in dampening itch, *Sarah Ross*
- 09:45–10:00 Mrgprs are itch receptors, *Xinzhong Dong*
- 10:00–10:30 **Free communications (FC09–10)**
A role of matrix metalloproteinase-8 in dermal nerve growth: Implications for possible application to pruritus involving skin nerve from *in vitro* models, *Mitsutoshi Tominaga, Suhandy Tenggara, Atsuko Kamo, Kenji Takamori*
Functional differentiation between histamine and cowhage itch in humans, *Roman Rukwied, Benjamin Weinkauff, Martin Dusch, Jasper van der Ham, Justus Benrath, Matthias Ringkamp, Martin Schmelz*

10:30–11:00 **Coffee Break and Poster Session**11:00–12:30 **Biological and Physiological Aspects (2) (IP17–20)**Chairs: *Sonja Ständer and Kenji Takamori*11:00–11:15 VGLUT2+ neurons and itch, *Klas Kullander*11:15–11:30 Role of spinal neurotransmitter receptors in itch, *Ferda Cevikbas*11:30–11:45 Animal models of itch sensitization, *Earl Carstens*11:45–12:00 Itch sensitization in humans: Inflammatory and non-inflammatory mechanisms, *Akihiko Ikoma*12:00–12:30 **Free communications (FC11–12)**Punctate chemical stimulation with histamine and capsaicin activates a subset of polymodal nociceptors in monkey, *Matthias Ringkamp, Jasenka Borzan, Kaitlin Schaefer, Timothy Hartke, Richard Meyer*Warming enhances serotonin-evoked itch via TRPV4, *Tasuku Akiyama, Margaret Ivanov, Masaki Nagamine, Mirela Carstens, Akihiko Ikoma, Ferda Cevikbas, Jon Levine, Martin Steinhoff, Earl Carstens*12:30–14:00 **Lunch and Poster Session**14:00–15:00 **Biological and Physiological Aspects (3)****Free communications (FC13–16)**Mechanisms of sensory effects of tacrolimus, *Ulysse Pereira, Nicholas Boulais, Jean-Pierre Pennec, Laurent Misery*Autotaxin is a novel diagnostic marker for intrahepatic cholestasis of pregnancy, *Andreas E. Kremer, Peter H. Dixon, Carrie Ris-Stalpers, Victoria Geenes, Jenny Chambers, Joris A. van der Post, Catherine Williamson, Ulrich Beuers, Ronald P. J. Oude Elferink*BAM8-22 peptide induces histamine-independent sensory responses in humans, *Parul Sikand, Xinzhong Dong, Robert LaMotte*Central modulation of itch by distraction – a functional MRI study, *Astrid Stumpf, Bettina Pfeleiderer, Gudrun Schneider, Gereon Heuft, Martin Schmelz, Ngoc Quan, Phan, Sonja Ständer, Markus Burgmer*15:00–16:30 **Treatments (IP21–24)**Chairs: *Elka Weisshaar and Toshiya Ebata*15:00–15:15 Itch and acupuncture, *Florian Pfab*15:15–15:30 Substance P as a target in chronic pruritus therapy, *Sonja Ständer*15:30–16:30 **Free Communications (FC17–20)**Skin analysis by 5D intravital multiphoton tomography in patients with atopic dermatitis treated with Aprepitant – a case study, *Ngoc Quan Phan, Sonja Ständer, Valentina Dimitrova, Dieter Metze, Stefan W. Schneider, Volker Huck*The effects of an opioid antagonist on the itch-scratch-cycle: A psychophysical and fMRI study, *Clemens Forster, Rebekka Vogelgsang, Verena Vierow, Arnd Dörfler, Hermann O. Handwerker*Topical therapy with a new Cooling Compound® in patients with chronic pruritus, *Matthias Augustin, Ngoc Quan Phan, Christine Blome, Gitta Neufang, Sonja Ständer*16:30–16:45 How effective are placebos and vehicles in relieving the itch of atopic dermatitis: A meta-analysis of published literature, *Alan Fleischer*16:45–17:00 Perspectives in itch treatment, *Gil Yosipovitch*17:00–17:30 **General discussion (IP25–26)**Chairs: *Ethan Lerner and Laurent Misery*17:00–17:15 European guidelines for chronic pruritus, *Elke Weisshaar*17:15–17:30 The bibliometrics of itch, *Jeffrey Bernhard*

POSTERS

PP01: Otis (Option Tool for Itching Scalp): An aid tool for the management of itchy scalps, *Catherine Oliveres-Ghouty; Charles Taieb*

PP02: Development of a questionnaire assessing the burden of pruritus, *Charles Taieb*

PP03: Epidemiology of pruritus in France, *Laurent Misery; Charles Taieb*

PP04: Dandruff and itching: An epidemiological approach in France, *Laurent Misery; Charles Taieb*

PP05: Itching in chronic hand eczema: Results from the carpe registry, *Christian Apfelbacher; Sonja Molin; Elke Weisshaar; Andrea Bauer; Jochen Schmitt; Vera Mahler; Thomas Ruzicka; Peter Elsner*

PP06: Small-fiber neuropathies (SFN): comparison between quantitative sensitivity test (QST) and measurement of density of intra-epidermal nerve fibers (IENF), *Laurent Misery; Anne Pavy-Le Traon; Steeve Genestet; Pascale Marcorelles*

PP07: Psychogenic skin excoriations: The problem is not pruritus..., *Laurent Misery; Myriam Chastaing; Sylviane Touboul; Valérie Callot; Martine Schollhammer; Paul Young; Nathalie Feton-Danou; Sabine Dutray*

PP08: An itchy occupational disease to know in poultry farmers: prurigo due to *Dermanyssus gallinae*, *Brice Loddé; Véronique Bizien-Le Dez; Anne-Marie Roguedas-Contios; Laurent Misery; Jean-Dominique Dewitte*

PP09: Psychogenic itch in dermatologic practice, *Svetlana Bobko*

PP10: Incidence of chronic pruritus and its determinants: results from a population-based study, *Lena Vogelgsang; Uwe Matterne; Christian J. Apfelbacher; Adrian Loerbros; Elke Weisshaar*

PP11: Benefit of a pruritus consultation-hour in a dermatological office – prevalence data of 2009 and 2010 in my office, *Michael Haerberle*

PP12: Dermatologist's ability to primarily diagnose systemic diseases – a case report, *Michael Haerberle*

PP13: Effects of UV-based therapies, corticosteroid ointment and emollients on intraepidermal nerve fibers of acetone-treated mice, *Atsuko Kamo; Mitsutoshi Tominaga; Osamu Negi; Kenichi Taneda; Kenji Takamori; Suhandy Tenggara*

PP14: Evolution of itch in patients with burns: A 12-weeks follow-up study, *Philip Moons; Marjolein Colpaert; Chris Haest; Michael Casaer*

PP15: Intensity and impact on daily life of itching complaints following burns, *Marianne Nieuwenhuis; Marco Bremer; Nancy van Loey*

PP16: Functional itch and psychiatric disorders: continuum of psychodermatological syndromes, *Dmitry Romanov; Andrey Lvov; Svetlana Bobko*

PP17: A case of uremic pruritus and Kyrle's disease: Effective treatment with amitriptyline, *Wei-Sheng Chong; Angeline Yong; Hong-Liang Tey*

PP18: Olopatadine hydrochloride inhibits intraepidermal neurite outgrowth and inflammatory response in an atopic dermatitis mouse model, *Ichiro Katayama; Mostafa Abdel-Atif; Toru Amano; Tadafumi Tamura*

PP19: The impact of pruritic skin diseases on work, classroom, and daily productivity, *Saki Matsui; Hiroyuki Murota; Ichiro Katayama*

PP20: Clinical characterizations of itch in atopic dermatitis and chronic urticaria, *Byung-Soo Kim; Woo-Haing Shim; Margaret Song; Hoon-Soo Kim; Seung-Wook Jwa; Hyun-Chang Ko; Moon-Bum Kim; Seong-Jin Kim; Do-Won Kim*

PP21: Central Itch and neuropathic pain from spinal cord cavernous hemangioma : description of one case, *Nagi Mimassi; Philippe Meriot; France Marchand*

PP22: Profile of itch experience in patients with atopic dermatitis, chronic urticaria and burns: Direct comparison using the Leuven Itch Scale, *Philip Moons; Michael Casaer; Chris Haest; Marie-Anne Morren*

PP23: Measurement of itching: Climimetric properties of the Leuven Itch Scale, *Philip Moons; Michael Casaer; Chris Haest; Marie-Anne Morren*

PP24: Characteristics of itch in the different populations with epidermolysis bullosa using the Leuven Itch Scale, *Julie Snauwaert; Marie-Anne Morren; Philip Moons*

PP25: Mental itch induction in patients with chronic urticaria, *Chris-*

tina Schut; Alexander Claßen; Katharina Reinisch; Uwe Gieler; Jörg Kupfer

PP26: Itch Occurring with chronic wounds, *Julia Paul*

PP27: A qualitative assessment questionnaire for pruritus, *Emilie Brenaut; Karen Talour; Laurent Misery*

PP28: Epidermal and dermal innervation in keloids, *Hong Liang Tey; Ben Maddison; Daren Maruziva; Dudley Ferdinando; Jo Dicks; Gil Yosipovitch*

PP29: Uraemic pruritus vs. Senile pruritus. Incidence and morphological characteristics, *Christian Diehl; Gilda Zurita Salazar; Iliana Caicedo*

PP30: A case with itchy throat: Pollen-food syndrome, *Deren Ozcan; Deniz Seckin*

PP31: Pruritus after hydroxyethyl starch infusion therapy: assessment of a neuropathy, *Emilie Brenaut; Anne Pavy Le Traon; Sebastien Contios; Laurent Misery*

PP32: Topical anti-inflammatory therapies inhibit neural sensitization in patients with atopic dermatitis, *Miyuki Fukuoka; Miwa Hosogi; Yoshiko Miyachi; Akihiko Ikoma*

PP33: Notalgia paresthetica: a two-cohort-study in Brazil and Germany in 65 patients, *Timo Huesmann; Paulo R. Cunha; Mario Huesmann; Tiago Pina Zanelato; Ngoc Quan Phan; Gabriela Maria Abreu Gontijo; Nani Osada; Sonja Ständer*

PP34: The importance of pruritus in lichen planus, *Adam Reich; Kalina Welz-Kubiak*

PP35: Lesional and nonlesional prurigo nodularis skin shows reduced intraepidermal nerve fiber density: a sign of subclinical cutaneous neuropathy? *Britta Schuhknecht; Martin Marziniak; Andrea Wissel; Ngoc Quan Phan; Sonja Ständer*

PP36: An internet web-based questionnaire survey on pruritus of patients with atopic dermatitis in daily life, *Satoshi Takeuchi; Junna Oba; Masutaka Furue*

PP37: Platelet activation as possible indicator of disease activity in chronic urticaria: link with blood coagulation and mast cell degranulation, *Ichiro Katayama; Yoriyoshi Kotobuki; Hiroyuki Murota; Shun Kitaba*

PP38: One third of dermatological out-patients in a private practice suffer from chronic pruritus: a one-week-survey in a consecutive cohort, *Merle Pilz; Sonja Ständer; Hartmut F. Ständer*

PP39: New data on the validation of VAS and NRS in pruritus assessment: minimal clinically important difference and itch frequency measurement, *Adam Reich; Jowita Halupczok; Malgorzata Ramus; Sonja Ständer; Jacek Szepletowski*

PP40: Design of topical cooling agents for itch, *Edward Wei*

PP41: Medical care of chronic pruritus patients: how to efficiently collect patient reported outcomes, *Fleur Fritz; Ngoc Quan Phan; Markus Riek; Bernhard Breil; Matthias Augustin; Martin Dugas; Sonja Ständer*

PP42: Correlation of itch intensity with quality of life, anxiety and depression, *Fleur Fritz; Ngoc Quan Phan; Martin Dugas; Matthias Augustin; Sonja Ständer*

PP43: Dermatophytic Disease and fierce pruritus: About three observations, *Boudghene Stambouli Omar*

PP44: Study on prophylactic impact of ondansetron IV on intrathecal fentanyl-induced pruritus, *Sayed Saed Jahanbakhsh; Baziyar Soha*

PP45: Validation of infrared thermography in serotonin-induced itch model in rats, *Yousef Jasebian; Parisa Gazerani; Frederik Dagnaes-Hansen*

PP46: Epidemiology of scabies to Akram Hospital, about 49 cases in Kinshasa/Drc, *Muteba Baseke; Mangili Aniboti*

PP47: Granzyme A and proteinase-activated receptor 2 are involved in the induction of itch-associated responses to mosquito allergy in mice, *Tsugunobu Andoh; Tasuku Akiyama; Akihisa Enokida; Yasushi Kuraishi*

PP48: Thymic stromal lymphopoietin and tumor necrosis factor-alpha reduces the production of semaphorin 3A in cultured human epidermal keratinocytes, *Suhandy Tenggara; Mitsutoshi Tominaga; Atsuko Kamo; Osamu Negi; Kenichi Taneda; Kenji Takamori*

PP49: Pruritic responses in rat trigeminothalamic tract neurons: Evidence against an itch-specific pathway *Hannah R. Moser; Glenn J. Giesler Jr.*

ABSTRACTS: Special Interest Group Meetings (SIG01–SIG04)**SIG01 OVERVIEW OF QUESTIONNAIRES USED FOR ITCH****Jörg Kupfer; Uwe Gieler***Institute of Medical Psychology, Justus-Liebig-University, Giessen, Germany*

Although pruritus is a widespread phenomenon, only since about 15 years, it was systematically tried to examine different aspects of itch by using questionnaires. These were partly derived from pain research. In the presentation the published questionnaires will be presented shortly. Advantages and disadvantages of individual questionnaires will be discussed from the perspective of our working group. The previously published measurements show strengths and weaknesses in individual aspects. To build up measures through which consensus might be reached and therefore get a widely used test system for a wide range of applications (dermatological or other itchy disorders, clinical and basic research, therapy evaluation both somatic as well as psychosomatic, acute or chronic itching, etc.) we suggest to build two modular test systems (long and short version of a questionnaire). The modules are designed to collect certain aspects of pruritus. Depending on the problem it should be possible to use one or a combination of the modules. Separate modules can thereby be integrated from existing questionnaires. Necessary modules from our point of view would be for example: Strength of itching, time characteristics, affected body surface area, quality, coping, emotional characteristics, possibly a specific therapy evaluation module.

SIG02 QUESTIONNAIRES: USEFUL TOOLS FOR ASSESSING THE MULTIDIMENSIONAL NATURE OF DIFFERENT TYPES OF ITCH**Gil Yosipovitch***Department of Dermatology & Neurobiology and Anatomy, Wake Forest University Baptist Medical Center, Winston Salem, USA*

Chronic itch has a significant impact on the quality of life of millions of patients. Despite it being a common complaint there are few studies describing the use of structured questionnaire for evaluation and measurement of itch and its sensory and affective dimensions. Moreover few studies focus on characterizing itch in different types of itch. This talk provides a summary of our work on assessments of different types of itch and suggests future directions in assessing itch.

HARMONIZATION OF ITCH EVALUATION – REQUISITES FOR ITCH QUESTIONNAIRES FROM JAPANESE EXPERIENCE **SIG03****Masataka Furue; Toshiya Ebata; Akihiko Ikoma; Yoko Kataoka; Hidehisa Saeki; Takahiro Satoh; Kenji Takamori; Satoshi Takeuchi**
Kyushu University, Japan

Itch is an unpleasant and annoying sensation that enormously precipitates severity and duration of skin diseases. Evaluating itch is, therefore, an important procedure to understand and predict the patient's clinical course and outcome. International harmonization of itch measurement is apparently necessary for research and clinical follow-up, however, perceptive and verbal expression of itch sensation is variably influenced by cultural, linguistic and even individual backgrounds including gender. In order to facilitate the discussion of itch evaluation from a Japanese point of view, a Special Interest Group Japan about itch questionnaires (SIGJIQ) was organized by 8 members. Comprehensive discussion was initiated by weighting various aspects of itch recognition such as "Mean itch intensity", "Sleep disturbance", "Maximum score of itch", "Itch duration", "Itch region and area", "Number of itch region", "Itch frequency", "Nature of itch", and "Quality of life". "Mean itch intensity" and "Sleep disturbance" were considered to be an important measure for clinical settings. Further weighting procedure and practical problems about "Visual analogue scale (VAS)" will be reported in details.

CULTURAL ASPECTS AND OTHER ISSUES: WHAT IS IMPORTANT FOR ITCH QUESTIONNAIRES? **SIG04****Elke Weisshaar***University Hospital Heidelberg, Heidelberg, Germany*

Several different questionnaires have been designed and applied in chronic pruritus patients. Some of them were used in different ethnic populations, revealing cultural differences in a number of aspects. Ethnic and regional differences can be explained by different culturally based perceptions of pain and itch, differences in health-related quality of life, diverse life expectancies and by characteristics of the regional health care systems such as reimbursement and access to a specialist. In this lecture, cultural features and other important aspects for itch questionnaires will be discussed.

ABSTRACTS: Invited Lectures (IL01–IL26)

IL01 ITCH IN ADOLESCENTS

Jon Anders Halvorsen

Department of Dermatology, Oslo University Hospital, Norway

Adolescence is characterized by major biological and psychological changes. Itch is an important dermatological symptom among adolescents. The presentation will describe how itch is distributed in a large general population of adolescents in Oslo, Norway, in respect to socio-demographic variables, psychological factors and atopy. The prevalence of itch (“a lot” and “very much”) was 8.8% in a questionnaire-based cross-sectional study of 4,744 adolescents. The prevalence of itch differed across socio-demographic groups: females 11.0%, non-Western 12.3%, low income families 11.3%, and across psychological symptoms: adolescents with mental distress 17.3% and thoughts of suicide 21.1%, and finally across atopic conditions: asthma 15.0%, rhinoconjunctivitis 13.6% and eczema 36.6%. Lastly, itch in adolescents will be briefly discussed in the context of dermatological diseases, systemic diseases, neurological and psychiatric diseases.

IL02 MENTAL INDUCTION OF ITCH

Jörg Kupfer; Christina Schut; Uwe Gieler

Institute of Medical Psychology, Justus-Liebig-University, Gießen, Germany

Introduction: When people are confronted with itch-inducing situations, it is a usual consequence that they experience itch and start scratching. We did some studies to investigate this everyday observation in more detail. We induced itch through audio-visual stimuli and analysed the strength of the induced itch and scratching response. *Methods:* 36 dermatological healthy subjects and 36 patients with atopic dermatitis (AD) participated in each study. We used two videos (control, itch-inducing) in the first study and three (control, itch-inducing: a) crawling insects, b) itchy skin diseases) in the second one. The subjects were recorded while watching the videos. In the statistical analyses the number of scratching-movements and the subjective-perceived itch were the dependent variables. Video-conditions, group membership and psychological variables served as independent variables or predictors. *Results:* Itch-intensity and scratching-movements are increased in AD-patients and healthy controls through our itch-inducing videos. Only in the first study both parameters are higher in patients with AD than in healthy controls. In the first study the increase in scratching could be explained through psychological variables (increased anxiety and decreased agreeableness). In the second study only weak correlations between the dependent and psychological variables occurred. *Discussion:* Possibilities and limitations of audio-visual itch-induction are discussed.

IL03 STRESS AND ITCH IN CHRONIC SKIN DISEASES

Andrea W.M. Evers

Radboud University Medical Centre Nijmegen, The Netherlands

As the stress response involves activation of the HPA axis, which interacts with the immune system, stress-related factors might influence itch severity in chronic inflammatory skin

diseases. In this presentation, we give a short overview of several experimental and prospective studies about the possible relationship between psychophysiological stress factors and itch severity in healthy controls and patients with chronic skin diseases. In these studies, preliminary evidence was found for a relationship between stress factors and the course of itch in chronic skin diseases. Increasing evidence further suggests that the role of stress on itch seem to be particularly relevant during phases of high levels of daily stressors and for patients who report heightened stress levels during a longer period of time. Possible psychophysiological pathways and innovative tailored therapy options will be discussed.

NEURAL CORRELATES OF DELUSIONAL INFESTATION

IL04

Markus Kölle¹; Peter Lepping², Markus Huber³, Carlos Schönfeldt-Lecuona¹, and Roland W. Freudenmann¹

¹Department of Psychiatry and Psychotherapy III, University of Ulm, Ulm, Germany, ²Glyndwr University and Betsi Cadwaladr University Health Board, North Wales, Wrexham Academic Unit, Technology Park, Wrexham, UK, and ³Department of Psychiatry, General Hospital-Bruneck, Bruneck, Italy

Delusional infestation (DI) is an unspecific psychiatric syndrome that is characterized by the patient's fixed false belief to be infested by some sort of living, or less frequently inanimate pathogens (e.g. bacteria, worms, parasites or “Morgellons”). DI patients often, but not necessarily suffer from chronic “itching” sensations that they explain by the presence of the pathogens in their body. Recent neuroscientific research has provided first, very preliminary evidence that dopaminergic brain regions such as the dorsal “somatic” striatum (putamen) may be macroscopically and/or functionally disturbed in the different forms of DI. Interestingly, this same brain circuit has been involved in other disorders with chronic itching/scratching. A better understanding of the cerebral etiology of the different forms of DI is highly desirable but difficult to achieve in patients with a little insight into their illness and a disease model that excludes their brain.

DRUG-INDUCED PRURITUS

IL05

Jacek C. Szepietowski

Department of Dermatology, Venereology and Allergology, Medical University, Wrocław, Poland

Pruritus is an unpleasant sensation that leads to scratching. In addition to several diseases, the administration of drugs may induce pruritus. It is estimated that pruritus accounts for approximately 5% of all skin adverse reactions after drug intake. Summarizing literature research, for some drugs a clear time-relation has been described and interruption of the drug leads to cessation of pruritus. Pruritus usually lasts less than 6 weeks in this group, fulfilling the definition of acute pruritus. In other drugs, pruritus lasts much longer due to the underlying mechanisms. For example, in hydroxyethyl starch (HES)-induced pruritus, neuronal storage of the substance evokes pruritus, which slowly relieves after degradation of the substance. This can be grouped as chronic pruritus, since it lasts for more than 6 weeks. In ad-

dition, many drugs are described to induce chronic pruritus by unknown mechanisms. In this group of drug-induced pruritus, therapy is very difficult, including the decision to interrupt or change the drug prescription.

IL06 AQUAGENIC PRURITUS IN POLYCYTHEMIA VERA

*Christelle Le Gall-Ianotto; Laurent Misery
Laboratory of Skin Neurobiology, University of Brest, France*

Aquagenic pruritus (AP) is an induced pruritus observed after contact with water at any temperature and is not associated with apparent skin lesions. AP could be an important clinical feature of the hematological disease, polycythemia vera (PV) which is a chronic myeloproliferative disorder resulting from a clonal abnormality of the hematopoietic stem cell inducing the hyperplasia of myeloid cells essentially erythroid. PV is characterized by a unique and recurrent mutation of the tyrosine kinase JAK2 (JAK2V617F) and 30 to 50% of patients complained of AP, that can precede the hemopathy by several years. The pathophysiology of AP in PV remains poorly known. Consequently, the number of treatments proposed is either various as the number of mechanisms suspected to be involved in the AP is high. Among tried treatments, we could include antihistamines, antidepressants, human recombinant interferon (hrIFN), phototherapy or myelosuppressors prescribed for PV. All these treatments demonstrated disappointing results. However, recent studies offer new approaches such as the possible role of circulating basophils or IL-31 and the clinical benefit to use JAK2 or mTOR inhibitors. However, PV-associated AP remains an agonizing and handicapping aspect of the disease and a better understanding of the pathophysiology of AP in PV remains important.

IL07 PRURITUS IN CUTANEOUS T-CELL LYMPHOMAS

*Nicolas Meyer; Carle Paul; Roland Viraben; Laurent Misery
UMR 1037-CRCT and Dermatology Department, Toulouse-Larrey university Hospital, Toulouse, France*

Pruritus has a well-known association with Hodgkin's disease and other nodal lymphomas; indeed it often reveals the disease. Pruritus is also an important symptom of cutaneous T-cell lymphomas. Lymphoma-associated itch is thus both frequent and severe, but its pathophysiology remains unclear. Several data may let us hypothesize that Substance P may be involved. Few studies have evaluated the efficacy of therapeutic agents in the management of cutaneous T-cell lymphoma-related pruritus. The main objective of treatment remains disease control. Pruritus management is generally based on the physician's experience. Treatment is very difficult, especially in Sézary syndrome. We present here both our experience of the management of cutaneous lymphoma-associated pruritus and a review of recently published data.

IL08 PRURITUS AND AMYLOIDOSIS

*Akio Tanaka
Department of Dermatology, Hiroshima University Graduate School of Medicine, Hiroshima, Japan*

Primary localized cutaneous amyloidosis (PLCA) is a chronic pruritic skin disease characterized histologically by focal deposition of amyloid in the papillary dermis. Most cases are sporadic,

but an autosomal dominant family history may be present in up to 10% of cases, consistent with a genetic predisposition in some individuals. Since 2008, 9 pathogenic heterozygous missense mutations in familial PLCA have been identified in the OSMR gene, which encodes oncostatin M receptor beta (OSMR beta), an interleukin-6 family cytokine receptor. OSMR beta is expressed in various cell types, including keratinocytes, cutaneous nerves and nociceptive neurons in dorsal root ganglia; its ligands are oncostatin M and interleukin-31. All pathogenic mutations are clustered in the fibronectin-III repeat domains of the extracellular part of OSMR beta, sites that are critical for receptor dimerization (with either gp130 or IL-31RA), and lead to defective signalling through Jak/STAT, Erk1/2 and PI3K/Akt pathways. Interestingly, a heterozygous missense mutation in the IL31RA gene, which encodes IL-31RA, has also been reported in a Taiwanese familial PLCA. Elucidating the molecular pathology of familial PLCA provides new insight into mechanisms of pruritus in human skin.

PRURITUS IN HUMAN AD-MECHANISMS AND MANagements OF INTRACTABLE ITCH

*Kenji Takamori
Juntendo University Urayasu Hospital, Urayasu, Japan*

Histamine is the best-known pruritogen in human and has been recognized as a main target for antipruritic therapy. However the pruritus for the patients with atopic dermatitis (AD) does not respond to antihistamine treatment. This contradiction may be explained by the following; 1) Participation of pruritogenic mediators other than histamine, 2) Involvement of histamine H4R, 3) Abnormal itch perception by increased intraepidermal nerve densities, 4) Involvement of opioid system in pruritus. Pruritogenic mediators may directly activate itch-sensitive C-fibers. Nerve fibers can also be activated by exogenous mechanical, chemical or biological stimuli, resulting in itch responses. Epidermal hyperinnervation is observed in AD, suggesting that it is partly responsible for intractable itch sensation. Such hyperinnervation is caused by an imbalance of nerve elongation factors e.g. NGF and nerve repulsion factors e.g. Sema3A produced by keratinocytes. Furthermore, we demonstrated that MMP-2 are involved in penetration of nerve fibers into basement membrane. PUVA therapy reduces epidermal hyperinnervation in AD patients by normalization of decreased Sema3A and increased NGF expression in the epidermis, leading to decrease in itch. Sema3A ointment reduces hyperinnervation in epidermis and scratching behavior in AD model mouse. In this session the mechanisms of nerve fibers into epidermis in AD will be discussed.

PRURITUS IN CANINE ATOPIC DERMATITIS

*Thierry Olivry
Center for Comparative and Translational Research, NC State University College of Veterinary Medicine, Raleigh, USA*

Atopic dermatitis (AD) is a chronic relapsing allergic skin disease of dogs with characteristic clinical features, which is associated with IgE antibodies against environmental, food and/or microbial allergens. Pruritus is a cardinal manifestation of canine AD. It is the third most pruritic disease of dogs, and pruritus is rated to be more severe in case of secondary skin infections with *Staphylococcus* or *Malassezia*. In dogs with AD, pruritus manifestations and

IL09

IL10

erythema scores are correlated suggesting that inflammation and itch are part of the same immunological reaction. Randomized controlled trials have established that the pruritus of canine AD responds best to oral and topical glucocorticoids and calcineurin inhibitors (e.g. cyclosporine) while type 1 antihistamines have been shown to provide little relief. In these trials, the improvement in pruritus generally, but not always correlated with that of skin lesions. Because of the similarity in clinical signs, immunopathogenesis and response to pharmacological interventions between human and canine AD, clinical trials enrolling dogs with spontaneous AD provide an excellent model to test antipruritic interventions aimed at relieving human atopic itch.

IL11 ROLE OF PROTEASES, PROTEINASE-ACTIVATED RECEPTORS AND PEPTIDASES IN SKIN INFLAMMATION AND SKIN BARRIER FUNCTION

Martin Steinhoff

Departments of Dermatology and Surgery, UCSF, San Francisco, USA

Although a role of exogenous or endogenous proteases including mast cell tryptase, various trypsin, cathepsins or kallikreins, bacteria-, fungus-, house dust mite-derived proteases is well known, their role and effects in itch are poorly understood. Keratinocytes or immune cells abundantly generate kallikreins (KLK) which play an important role in epidermal homeostasis, barrier function and inflammation. Certain of these effects can be attributed to the activation of a subfamily of G protein-coupled receptors, defined as proteinase-activated receptors (PARs). Understanding the underlying mechanisms regulating PARs and the effects induced by those receptors through proteinases may lead to novel strategies for the treatment of inflammatory skin diseases and pruritus. In the skin, PARs are widely expressed by cells involved in immune responses, inflammation as well as keratinocyte regulation (keratinocytes in an autocrine fashion, endothelium, leukocytes, nerves), thereby controlling epithelial function, endothelial-leukocyte interactions, secretion of inflammatory mediators, and the function of sensory nerves with respect to neurogenic inflammation, pruritus and probably pain. Overexpression of PAR2 in murine keratinocytes leads to a spontaneously increased scratching behavior associated with an atopic-like dermatitis phenotype. Thus, serine proteases can activate PAR2 on keratinocytes which subsequently stimulate primary afferent nerve endings involved in itch transmission implying a role of PAR2 in keratinocyte-nerve communication in pruritic diseases. Modulating proteinase and/or PAR-induced skin function may be a novel tool for the treatment of skin inflammation, barrier dysfunction as well as pruritus, which has an important impact on skin barrier function. Furthermore, we have identified endothelin-converting enzyme-1 (ECE-1) as a key regulator of neuropeptide-induced pruritus and neuronal signaling. ECE-1 modulates ET-1-induced pruritus by prolonging cell signaling in DRG neurons. This review highlights recent advances understanding how proteases, PARs and peptidases control pruritus.

IL12 PRURITUS FROM THE SEA

Laurent Misery

Department of Dermatology, University Hospital, Brest, France

Pruritus (or similar sensations like burnings) can be induced by the venom of many animals from the sea. Its severity is variable.

The most frequent sea-induced pruritus is probably due to jellyfishes and physaliae. Anemones, red sea coral, sponges (Phylum porifera), sea cucumbers can also induce itchy or burning lesions. Swimmer's itch is due to immature schistosomes or anemones. Pruritus could be secondary to common dermatoses like folliculitis, xerosis or eczema. Some dermatoses are specifically aquagenic: aquagenic pruritus, aquagenic urticaria or aquagenic palmoplantar keratoderma. Divers need to know that pruritus is a good symptom of decompression sickness.

NEUROTROPHINS AND ITCH

Martin Schmelz

Department of Anesthesiology and Critical Care Medicine, University of Heidelberg, Mannheim, Germany

Abstract is missing.

IL13

THE MECHANISM BY WHICH CATHEPSIN S TRIGGERS PAR2 ACTIVATION

Vemuri Reddy; Sarina Elmariam; Youping Sun; Ethan Lerner
Massachusetts General Hospital/Harvard Medical School, Boston, USA

Non-histamine itch is mediated by protease-activated receptors, specifically PAR2. This receptor can be activated by cysteine and serine proteases. Serine proteases cleave near the N-terminus of PAR2 to uncover a new N-terminus that interacts with transmembrane domains leading to signal transduction. This activation can be mimicked by synthetic hexapeptides that correspond to the new N-terminus. Whether cysteine proteases shared a similar mechanism of action was not known. We show here that cathepsin S, a cysteine protease, cleaves PAR2 at a site near, but distinct from, that of serine proteases. Hexapeptides based on this distinct cleavage site trigger intact PAR2 as determined by ratiometric calcium imaging and the generation of 2nd messengers. In conclusion, cysteinyl cathepsins activation of PARs is likely a mechanism by which these proteases contribute to both inflammation and itch.

IL14

INHIBITORY NEURONS OF THE DORSAL HORN PLAY A CRUCIAL ROLE IN DAMPENING ITCH

Sarah E. Ross

Department of Neurobiology and The Pittsburgh Center for Pain Research University of Pittsburgh, Pittsburgh, PA, USA

Itch is the least well understood of all the somatic senses, and the neural circuits that underlie this sensation are poorly defined. To address this problem, we are using molecular, genetic and behavioral approaches to dissect the neural circuits that underlie itch. We have identified the first inhibitory neurons in an itch circuit and we show that these neurons are required for normal itch sensation; mice lacking them suffer from dramatically elevated itch leading to severe skin lesions. These neurons are a subset of inhibitory neurons in laminae I and II of the dorsal horn, and we find that the development of these neurons requires a novel Bhlhb5/Prdm8 transcriptional repressor complex that functions in part through the regulation of Cadherin-11. These findings show that loss of inhibition of the spinal cord leads to elevated itch, an idea that may have direct relevance for people suffering from certain types of persistent pathological itch.

IL15

IL16 MRGPRs ARE ITCH RECEPTORS

Qin Liu; Parul Sikand; HaoJui Weng; Kush Patel; Robert LaMotte; Xinzhong Dong
John Hopkins University, Baltimore, USA

Primary sensory neurons in dorsal root ganglia (DRG) play an essential role in generating itch by detecting itch stimuli through their peripheral axons in the skin and sending signals to the spinal cord via their central axons. The lack of identified cell surface receptors in DRG neurons that directly respond to histamine-independent itch stimuli is the major hurdle to develop novel anti-pruritus therapeutics. Mrgprs are a family of G protein-coupled receptors consisting of more than 50 members in the mouse genome. Strikingly, the expression of many Mrgprs is restricted to subsets of small-diameter sensory neurons in DRG but absent in any other tissues. Our analysis of Mrgpr knockout mice together with other evidence suggest that Mrgprs function as novel itch receptors by directly sensing different pruritogens from primary sensory fibers in the skin. Mrgprs are receptors for several pruritogens such as anti-malaria drug chloroquine, peptides SLIGRL, and BAM8-22. BAM8-22, an endogenous peptide, is a specific agonist for human MrgprX1. More importantly, human psychophysical study shows skin application of BAM8-22 induces histamine-independent itch. Thus, BAM8-22 may be an endogenous itch mediator that activates, in humans, MrgprX1, a novel target for potential anti-itch treatments.

IL17 VGLUT2+ NEURONS AND ITCH

Klas Kullander
Department of Neuroscience, Uppsala University, Sweden

Glutamate is an essential transmitter in pain pathways. However, its broad usage in the central and peripheral nervous system has hampered progress in understanding glutamate-based pain transmission. The discovery of vesicular glutamate transporters (VGLUT1-3) has been an essential step in describing specific glutamatergic neuronal subpopulations and glutamate-dependent pain pathways. We have assessed the role of VGLUT2-mediated glutamatergic contribution to pain transmission in primary sensory neurons by conditional targeting of VGLUT2 in various sensory subpopulations. Deletion of VGLUT2 from the entire peripheral nervous system resulted in a significantly decreased, but not completely absent acute nociceptive response of all modalities tested. Moreover, removal of peripheral VGLUT2 dependent glutamatergic transmission caused an incessant scratching behavior. We continued with more specific deletions of VGLUT2 in smaller defined primary afferent subpopulations. Deletion of VGLUT2 in Nav1.8 Cre-positive neurons compromised mechanical pain and NGF-induced thermal hyperalgesia, whereas tactile-evoked sensation, thermal, formalin-evoked, and chronic neuropathic pain were normal. Their spontaneous scratching behavior was normal. In contrast, deletion of VGLUT2 in a subpopulation of neurons expressing the vanilloid receptor (TRPV1) primary afferents resulted in a dramatic increase in itch behavior accompanied by a reduced responsiveness to thermal pain. The increased itch behavior was reduced by administration of antihistaminergic drugs and by genetic deletion of the gastrin-releasing peptide receptor, demonstrating a dependence on VGLUT2 to maintain normal levels of both histaminergic and nonhistaminergic itch. These data establishes that VGLUT2 is a major player in TRPV1 thermal nociception and also serves to

regulate a normal itch response. Together, our data define sets of primary afferents associated with specific sensory modalities and provide useful genetic tools with which to analyze the pathways that are activated by functionally distinct neuronal populations and transmitters.

ROLE OF SPINAL NEUROTRANSMITTER RECEPTORS IN ITCH

Ferda Cevikbas¹; Akihiko Ikoma^{1,2}; Martin Steinhoff¹
¹*Departments of Dermatology and Surgery, University of California, San Francisco, USA and* ²*Department of Dermatology, Kyoto University, Japan*

Recent studies demonstrate that various neuronal receptors in the spinal cord are involved in pruritus. The spinal opioid receptor is one of the best-known examples. Spinal administration of morphine is frequently accompanied by segmental pruritus. In addition to mu-opioid receptor antagonists, kappa-opioid receptor agonists have recently come into usage as novel antipruritic drugs. A very intriguing finding of the recent years suggests that gastrin-releasing peptide receptor (GRPR) in the superficial dorsal horn of the spinal cord as novel pathway of itch-selective neural transmission on central levels. The NMDA glutamate receptor appears to be another potential target for the treatment of itch, especially in terms of central sensitization. Drugs suppressing presynaptic glutamate-release such as gabapentin and pregabalin also reportedly inhibit certain subtypes of itch such as brachioradial pruritus. Our own studies indicate that IL 31RA, the receptor subunit for IL-31, a cytokine dramatically involved in pruritus, plays a pivotal role in the transmission of itch on spinal level. This novel finding suggests that identification of itch-specific receptors and understanding itch-related circuits in the spinal cord will lead to a better understanding and development for treatment of pruritus with all its different facets.

ANIMAL MODELS OF ITCH SENSITIZATION

Earl Carstens
University of California, Davis, USA

Alloknesis is itch evoked by innocuous mechanical stimulation of normal skin adjacent to a site of acute itch, and may also occur along with spontaneous itch and hyperknesis in atopic patients. We developed a mouse model of alloknesis. C57/BL6 mice normally do not respond to innocuous von Frey (vF) stimuli. Following intradermal (id) injection of histamine, vF stimuli evoked hind limb scratch bouts directed to the stimulus. This peaked 20–40 min post-histamine, outlasting “spontaneous” scratching that ceased after 30 min. Touch-evoked scratching was inhibited by naltrexone. Touch-evoked scratching occurred following id injections of 5-HT and a PAR-4 agonist, but not chloroquine or a PAR-2 agonist. In histamine- and touch-sensitive dorsal horn neurons, innocuous vF-evoked responses were enhanced post-histamine. In a model of dry skin pruritus induced by acetone-ether-water (AEW), innocuous vF stimulation adjacent to the AEW treatment area elicited directed hind limb scratching and significantly greater numbers of Fos-immunoreactive superficial dorsal horn neurons. Superficial dorsal horn neurons recorded in AEW-treated mice also exhibit high spontaneous activity and differentially enhanced responses to the PAR-2 agonist but not histamine. Alloknesis, hyperknesis and spontaneous scratching

IL18**IL19**

may reflect differential peripheral and/or central sensitization of itch-signaling pathways.

IL20 ITCH SENSITIZATION IN HUMANS: INFLAMMATORY AND NON-INFLAMMATORY MECHANISMS

Akihiko Ikoma

Department of Dermatology, University of California, San Francisco, USA

Pruritic diseases such as atopic dermatitis are often accompanied by itch sensitization, i.e. alloknesis and hyperknesis, which, besides spontaneous itch, much annoys patients in their everyday life. Regarding itch sensitization, however, neither mechanisms nor therapeutic strategies have been much investigated yet. Our recent studies show that topical anti-inflammatory therapies inhibit alloknesis and pruritogen-mediated hyperknesis in patients with atopic dermatitis, indicating an inflammation-dependent mechanism of itch sensitization. On the other hand, electrically- and mechanically-evoked itch also induce alloknesis in healthy human subjects, suggesting that itch sensitization can be caused in an inflammation-independent manner. Thus, both inflammatory and non-inflammatory mechanisms need to be considered for therapeutic strategies against itch sensitization.

IL21 ITCH AND ACUPUNCTURE

Florian Pfab; Johannes Huss-Marp; Marie Kirchner; Andre Gatti; Ang Li; Jiang Fuqin; Peter Schalock; Georgios Athanasiadis; Heidrun Behrendt; Johannes Ring; Ulf Darsow; Vitaly Napadow

Martinos Center for Biomedical Imaging, Dept. of Radiology, Massachusetts General Hospital, Harvard Medical School, Charlestown, USA

Acupuncture has been shown to exhibit a significant effect on histamine-induced itch in past studies with healthy volunteers. We investigated the effect of acupuncture on allergen-induced itch and skin reaction in 30 atopic eczema patients using a double-blind, randomized, placebo-controlled, crossover trial. Concurrent acupuncture produced a significant abortive reduction of allergen-induced itch. The preventive point-specific effect, after acupuncture, was less robust with regard to itch sensation, but was more effective in suppressing physiological skin prick reactions. A different seven-arm crossover trial in 19 atopic eczema patients used clinically-relevant allergen to induce itch via skin prick test, and contrast real and sham acupuncture with real and placebo anti-histamine (cetirizine). Abortive acupuncture was again the most effective intervention in itch reduction, followed by preventive acupuncture and real cetirizine. A subsequent functional magnetic resonance imaging (fMRI) study was completed to infer potential brain mechanisms of action for acupuncture. Reduction in itch with abortive acupuncture was associated with diminished itch-evoked brain activity in anterior insula, anterior middle cingulate cortex, and several areas of the striatum. Behavioral and physiological effects of acupuncture on experimental itch have been promising. Future large-scale clinical trials are warranted to assess the longitudinal clinical efficacy of acupuncture on the amelioration of itch in atopic eczema.

SUBSTANCE P AS A TARGET IN CHRONIC PRURITUS THERAPY

Sonja Ständer

Competence Center Chronic Pruritus, Department of Dermatology, University Hospital Münster, Germany

Injection of substance P (SP) into the skin induces pruritus by indirect mechanisms such as release of mast cell mediators (e.g., histamine). In keratinocytes, SP stimulates the production of pro-inflammatory cytokines. According to this prominent role of SP in cutaneous pruritus induction, several pruritic diseases such as prurigo nodularis and atopic dermatitis were demonstrated to have increased cutaneous SP-immunoreactive nerve fibers. In this proof of concept study we evaluated if an NK1 antagonist would relieve chronic pruritus. We applied the NK1 antagonist aprepitant 80 mg in a series of 20 patients with chronic pruritus (12 females, 8 males; mean age, 66.7 years) of diverse etiologies for one week. This treatment achieved significant reduction in pruritus ($p < 0.001$, CI 1.913–5.187) in 16/20 patients (80%). The mean value was reduced from VAS 8.4 points (SD \pm 1.7) before treatment to 4.9 points (SD \pm 3.2). Best results were observed in patients with prurigo nodularis and atopic predisposition. The high response rate suggests that a NK1 antagonist is a promising treatment strategy based on the pathophysiology of chronic pruritus. Future controlled trials will have to confirm the efficacy and safety of this novel therapeutic strategy.

HOW EFFECTIVE ARE PLACEBOS AND VEHICLES IN RELIEVING THE ITCH OF ATOPIC DERMATITIS: A META-ANALYSIS OF PUBLISHED LITERATURE

Lindsay G. Sher; Alan B. Fleischer Jr.

Wake Forest University School of Medicine; Winston-Salem, USA

Background: Atopic dermatitis (AD), also known as eczema, is a chronically relapsing skin disease that is common in early infancy and childhood. The major clinical manifestations of AD include pruritus and lichenification of skin. *Purpose:* The goal of this study is to perform a data analysis/meta-analysis to measure the level of pruritus reduction with systemic placebo vs. systemic active treatment, and with topical vehicle (lacking active ingredient) vs. topical active treatment. *Methods:* The incorporation data was based on quality criteria and the selection of specific studies on the treatment of AD. Data sources included electronic searching of MEDLINE, PUBMED, EMBASE, the Cochrane Controlled Clinical Trials Register, the Cochrane Skin Group specialized register of trials, and follow-up references in retrieved articles. A confidence interval was reported to indicate a range of uncertainty for the true treatment effect and thus can be interpreted as the range of values for the treatment effect that is compatible with the observed data. *Results:* The results of metaanalysis of the effect of systemic antihistamines is more clearly defined, and little effect can be demonstrated. Other outcomes will be reviewed in turn. *Conclusions:* Placebo and vehicle controlled trials are critical to our understanding of the true effect of anti-itch therapies.

IL22

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IL24 PERSPECTIVES IN ITCH TREATMENT**Gil Yosipovitch***Wake Forest Baptist Medical Center, Wake Forest, USA*

Pruritus is a multifactorial disease and requires targeted therapy. With better understanding of the pathological mechanisms of itch transmission and processing in different diseases new venues for directed drug therapies evolve. Treatment of specific signaling pathways in the skin involve 2 major types of receptors: G protein receptors such PAR2, Histamine 4 and Mas-related G protein coupled receptors and Transient receptor potential such as vanilloid 1 and 3. In the spinal cord Gastrin-related peptide receptor and Neurokinin 1 serve as potential targets. In the brain, areas that are involved in central sensitization and processing of itch response such as cingulate cortex serve as potential targets. In addition the treatment of pruritus should be tailored for each patient in accordance with the severity of the disease. A multidisciplinary approach involving psychologic and social assistance as well as holistic management is often required for chronic itch sufferers.

IL25 EUROPEAN GUIDELINES FOR CHRONIC PRURITUS**Elke Weisshaar***University Hospital Heidelberg, Heidelberg, Germany*

Chronic pruritus (CP) is a frequent symptom in many skin and systemic diseases as well as in the general population. Its frequency demonstrates a high burden and an impaired quality of life. A group of European experts for chronic pruritus created the European Guidelines for Chronic Pruritus in cooperation with the European Dermatology Forum (EDF) and the European Academy for Dermatology and Venereology (EADV). These guidelines address CP as a symptom. In each form of CP, therapy has to be considered individually. On one side, there is a lack

of controlled randomized trials (ICT) which can be explained by the diversity and complexity of the symptom, the multifactorial aetiology of CP and the lack of well-defined outcome measures. The guidelines focus on therapy of CP considering country-specific treatment modalities including the characteristic features of the health care system. It has to be considered that some topical and systemic therapies can only be performed as “off-label use” and require informed consent. The latest version of the European Guidelines for Chronic Pruritus is presented. <http://www.euroderm.org/edf/images/stories/guidelines/EDF-Guideline-on-Chronic-Pruritus.pdf>

THE BIBLIOMETRICS OF ITCH**Melissa McEneaney-Stonelake; Jeffrey Bernhard***University of Massachusetts Medical School, Worcester, USA*

In 1995 fewer than 40 papers containing itch or pruritus in the title were published; in 2010 there were more than 80. Although use of the word itch has increased steadily since 1965, pruritus still outnumbers it. From 1965–2010, pruritus appeared (as a misspelling) in the title of 30 articles. From 1965, the top 5 sources of itch articles were the Karolinska, Toyoma, Wake Forest, Heidelberg, and Harvard. Kuraishi, Yosipovitch, Andoh, Bergasa, Weisshaar, and Stander published the most itch articles. From 1965–2010, the Lancet and N Eng J Med each published 6 itch articles. Nature published one, Science two. Acta Derm Venereol, Br J Dermatol, J Am Acad Dermatol, Hautarzt, & J Invest Dermatol have published the most itch articles since 1965. Articles published in J Invest Dermatol, Pain, Archives, Br J Dermatol, J Am Acad Dermatol, and ADV had the highest article impact factors. The 5 most frequently cited papers from 1965–2010 were by Hagermark, Schmelz, Andrew, Massry, and Bergasa, each with colleagues. The author with the most citations for articles with pruritus or itch in the title is Hagermark. The next few will be revealed at the congress.

IL26

ABSTRACTS: Free Communications (FC01–FC19)

FC01 INFLUENCE OF NEGATIVE AND POSITIVE EMOTIONS ON THE SENSITIVITY TO ITCH AND PAIN

*Antoinette van Laarhoven; Annika Walker; Oliver Wilder-Smith; Sabine Kroeze; Piet van Riel; Peter van de Kerkhof; Floris Kraaimaat; Andrea Evers
Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands*

While the role of emotions has extensively been studied in pain, less is known about the effect of emotions on the sensitivity to itch. Although there are indications that psychological distress may be related to enhanced itch perception, experimental studies investigating the effects of negative and positive emotions in the sensitivity to itch are lacking. The present study was directed to compare the effects of negative and positive emotions on the sensitivity to itch and pain. Film fragments were used to induce a negative or positive emotional state in healthy female subjects. Itch and pain were induced using the following somatosensory stimuli: electrical stimulation, histamine iontophoresis, and the cold pressor test. Electrical and cold pressor tolerance thresholds were determined as well as levels of itch and pain evoked by the stimuli. Results indicate that emotions can influence not only the perception of pain, but also of itch. Our findings that emotional state may lead to a heightened sensitivity to itch has important consequences for understanding the aetiology and maintenance of sensitization mechanisms, suggesting a vicious circle in which chronic symptoms of itch can result in increased negative emotions and, in turn, increase the itch symptoms.

FC02 IMPACT OF THE 2011 GREAT EAST JAPAN EARTHQUAKE ON PATIENTS WITH SKIN DISEASES – AN EXPERIENCE FROM PARTICIPATING IN A DERMATOLOGICAL SUPPORT GROUP THAT WENT TO THE DISASTER STRICKEN AREAS

*Toshiya Ebata
Department of Dermatology, The Jikei University, Tokyo, Japan*

On 11 March 2011, a 9.0-magnitude earthquake hit northeast Japan causing more than 23,000 to die or become missing. Over 90% of the victims died of drowning caused by the devastating tsunami that occurred shortly after the earthquake. In comparison with casualties from ordinary earthquakes the number of injured was small. However, the extent of the damage caused by the earthquake and tsunami was so enormous that about 100,000 people remain evacuated two months after the earthquake. Many towns were devastated and cannot maintain medical services. From April to June of 2011 the Japanese Dermatological Association (JDA) launched a project to send volunteer dermatologists from all over the country to the damaged regions in order to provide clinical support to evacuees and patients with skin diseases at their homes. The author participated in this project. Of note were the patients with pressure ulcers and chronic itchy skin diseases whose symptoms were seriously exacerbated after the disaster. On the basis of medical examination and interviews

given to these patients and their families the factors that worsened their symptoms will be reported together with a presentation of this project of JDA.

TOPICALLY APPLIED SEMAPHORIN 3A OINTMENT INHIBITS SCRATCHING BEHAVIORS AND IMPROVES SKIN INFLAMMATION IN NC/NGA MICE WITH ATOPIC DERMATITIS

FC03

*Osamu Negi; Mitsutoshi Tominaga; Kenichi Taneda; Atsuko Kamo; Suhandy Tenggara; Kenji Takamori
Institute for Environmental and Gender Specific Medicine, Juntendo University Graduate School of Medicine and Department of Dermatology, Juntendo University Urayasu Hospital, Japan*

Numerous pruritogenic mediators and modulators released in the periphery can directly activate the itch-sensitive C-fibers through specific receptors on the nerve terminal or, alternatively, they can act indirectly by releasing pruritogenic mediators and modulators from other cells. The nerve fibers are also activated by mechanical and chemical stimulations from the external environment, and thereby may elicit itch responses. Histological observations indicate that epidermal nerve fibers are present at higher densities in the skin of patients with atopic dermatitis (AD) than in control individuals. In this study, we investigated antipruritic and antiinflammatory effects of semaphorin 3A (Sema3A) ointment, which is one of nerve repulsion factors, in AD using NC/Nga mice with AD-like phenotype induced by repeated application of *Dermatophagoides farinae* body ointment. Topical application of recombinant Sema3A ointment on atopic NC/Nga mice significantly inhibited the scratching behavior and improved dermatitis score compared with those of control mice. Therefore, these findings may suggest the therapeutic efficacy of Sema3A ointment in pruritus and dermatitis of AD.

GENDER SPECIFIC DIFFERENCES IN ITCH PROCESSING – A FUNCTIONAL MRI STUDY

FC04

*Astrid Stumpf; Markus Burgmer; Gudrun Schneider; Gereon Heuft; Martin Schmelz; Ngoc Quan Phan; Sonja Ständer; Bettina Pfeleiderer
Department of Psychosomatics and Psychotherapy, University Hospital of Münster, Germany*

Background: In contrast to pain studies there is only little knowledge about gender differences in pruritus. Especially gender specific differences in central itch perception and modulation are not examined at all. This is the first fMRI study examining central gender differences in perception and modulation of itch. *Method:* Experimental itch was induced by application of histamine (0.1 mM) via intradermal microdialysis fibers in 33 healthy volunteers (17 females) twice at the left forearm and twice at the left lower leg. Subjects were asked several times to rate itch intensity and urge to scratch and central activation patterns were assessed by fMRI. *Results:* Ratings for itch intensity and urge to scratch were only higher in women in the second leg stimulation. During leg stimulations there was more activity in

emotional areas like cingulate and insular cortex in women than in men. *Conclusion:* Even though itch ratings altered gender dependently only in lower extremities brain regions linked to emotional processing were activated more widespread in females suggesting that itch processing might be different.

FC05 ARTEMIN EXPRESSION IN PRURITIC SKIN DISEASES: HISTOPATHOLOGICAL ANALYSIS

*Megumi Nishioka; Hiroyuki Murota; Ichiro Katayama
Department of Dermatology, Osaka University, Japan*

Recently, we found that substance P-stimulated dermal fibroblasts produced artemin, a member of glial cell line derived neurotrophic factor (GDNF) family, which was found to develop peripheral nerve fiber sprouting. Here, we have explored a potential contribution of artemin to peripheral nerve fiber sprouting in some pruritic skin diseases using immunohistochemical staining method. Artemin staining of normal skin derived from healthy volunteer did not show any positive sign. In contrast, specimens derived from atopic dermatitis skin lesion showed intense staining for artemin in the dermal area. *In situ* hybridization analysis had revealed that the dermal fibroblasts might be a major candidate for source of artemin. Moreover, we will present the results of artemin staining of pruritic skin diseases (e.g. prurigo nodularis, nummular eczema, etc.), and discuss the role of artemin in pathogenesis of pruritic skin diseases.

FC06 EVALUATION OF THE RELATIONSHIP BETWEEN STRESS, PRURITUS AND QUALITY OF LIFE IN LICHEN PLANUS

*Adam Reich; Kalina Welz-Kubiak
Department of Dermatology, Venereology and Allergology,
Wroclaw Medical University, Poland*

Pruritus is one of the major features of lichen planus (LP) and stress is considered as an important pathogenic factor of LP. Our objective was to evaluate relationship between stress and itching in LP and the influence of pruritus on quality of life (QoL). Forty-two consecutive patients (women/men 3:1) with LP were enrolled. A specially designed questionnaire was completed based on anamnesis and physical examination. VAS and the pruritus questionnaire were used for pruritus assessment. Each subject completed the DLQI questionnaire. Stressful life events within one month before skin lesions appearance were identified and assessed with five degree self-assessment scale. The mean severity of itching at the moment of examination was 3.0 ± 2.7 points, and at the most intensive pruritus in the past (Vmax) 7.6 ± 2.3 points. No correlation was found between the stress severity and itch intensity ($p > 0.05$). Severity of itching strongly influenced QoL in LP (DLQI and VASmax.: $p = 0.36$; $p = 0.02$; DLQI and itch questionnaire: $p = 0.69$; $p < 0.001$). Moreover, itching was mentioned by 69% of patients as the most bothersome symptom of LP, followed by the presence of skin changes (45.2% patients). Stress seems not to play important role in modulating pruritus in LP. Itching severity strongly influences the QoL of LP patients.

DIFFERENTIAL PROCESSING OF COWHAGE AND HISTAMINE ITCH IN HEALTH AND DISEASE. INSIGHTS INTO BRAIN PROCESSING OF CHRONIC PRURITUS REVEALED BY ARTERIAL SPIN LABELING FMRI **FC07**

*Alexandru Papoiu; Robert Coghill; Robert Kraft; Gil Yosipovitch
Wake Forest School of Medicine, Wake Forest, USA*

Cowhage induced itch represents a PAR2-mediated form of non-histaminergic itch that activates a distinct spinothalamic pathway. Recent findings suggest that chronic itch could be mediated at least in part by PAR2 receptors and endogenous proteases, therefore cowhage itch could serve as a model for chronic pruritus. We have previously showed that in healthy individuals there are common patterns of brain activation induced by cowhage and histamine itch, but also certain notable differences. We extended our comparative study of brain processing of these two itch modalities in 31 patients with different types of chronic itch. Preliminary analyses in chronic itch patients suggest these two itch modalities are processed differently in chronic itch states. The patterns of brain activations induced by cowhage and histamine itches in various types of chronic itch patients will be presented. Investigating the differential brain processing of these two forms of itch in various chronic itch states provides a new angle for advancing our understanding of the cerebral processing of itch.

EXPRESSION PROFILES OF THERMO-TRP CHANNELS IN CHRONIC PRURITUS **FC08**

*Heike Benecke; Julia Wördehoff; Tobias Lotts; Martin Marziniak; Thomas A. Luger; Hanns Hatt; Sonja Ständer
Department of Cell Physiology, Ruhr-University Bochum,
Bochum, Germany*

Patients suffering from chronic pruritus show a broad clinical variation in experiencing itch. Around 23% of patients experience additional thermal sensations (warm and cold). The present study was designed to investigate the cutaneous expression of temperature sensing transient receptor potential (Trp) channels in the skin of pruritus patients. Initially, pathological thresholds for cold and heat were determined by the method of quantitative sensory testing (QST). Skin biopsies of patients and healthy volunteers were subjected to RNA extraction and cDNA synthesis. Thermo-Trp channel expression was analyzed by the quantitative RealTime PCR technique including specific intron-spanning primers. Our investigation focused on general differences between healthy controls and pruritus patients and more particularly on a potential linkage between pruritus sub-phenotypes and distinct expression patterns. All thermo-Trp channels were detected in the analyzed skin biopsies with TrpV1 always showing the highest expression level. Comparative analysis revealed a weak but significant increase in TrpV1 and TrpV3 RNA transcript levels in pruritus patients over the healthy control group. However, expression profiles between both pruritus subgroups did not show significant differences. We therefore suggest that apart from TrpV1 also TrpV3 may be involved in the pathophysiology of the symptom pruritus at least in patients with abnormal thermal perception.

FC09 A ROLE OF MATRIX METALLOPROTEINASE-8 IN DERMAL NERVE GROWTH: IMPLICATIONS FOR POSSIBLE APPLICATION TO PRURITUS INVOLVING SKIN NERVE FROM IN VITRO MODELS

Mitsutoshi Tominaga; Suhandy Tenggara; Atsuko Kamo; Kenji Takamori

Institute for Environmental and Gender Specific Medicine, Juntendo University, Urayasu, Japan

Cutaneous nerve density is related to abnormal itch perception in dermatoses, such as atopic dermatitis and xerosis. However, the mechanisms underlying elongation of dermal nerve fibers within interstitial collagen matrix are poorly understood. Here, a culture system of rat dorsal root ganglion neurons consisting of type I collagen and a Boyden chamber containing a nerve growth factor (NGF) concentration gradient was used. Nerve fibers penetrating into type I collagen gel were observed in the presence of the NGF concentration gradient. Levels of matrix metalloproteinase-8 (MMP-8) mRNA and protein were increased in the cultured neurons and the conditioned medium, respectively. The nerve fiber penetration was dose-dependently inhibited by MMP-8 blockers. Moreover, MMP-8 immunoreactivity was partially localized at growth cones in NGF-responsive nerve fibers. Semaphorin 3A stimulation also showed the opposite effects on these NGF-dependent events. Intriguingly, MMP-8 expression was upregulated by type I and III collagens, which are substrates for this enzyme. These results suggested that MMP-8 is involved in sensory nerve growth within interstitial collagen matrix through modulation by axonal guidance molecules and/or extracellular matrix components. These findings provide insight into the development of pruritus involving skin nerve density.

FC10 FUNCTIONAL DIFFERENTIATION BETWEEN HISTAMINE AND COWHAGE ITCH IN HUMANS

Roman Rukwied; Benjamin Weinkauff; Martin Dusch; Jasper van der Ham; Justus Benrath; Matthias Ringkamp; Martin Schmelz

Department of Anaesthesiology, Medical Faculty Mannheim, Heidelberg University, Germany

Following peripheral nerve block of the lateral femoral cutaneous nerve (LFCN) by ultrasound-guided, injection of 3 ml Naropin® 1% we selectively assessed in 8 subjects mechano-sensitive and mechano-insensitive nociceptors. 30 min after blockade the sensory LFCN territory was mapped mechanically and electrically. We identified areas being sensitive to transcutaneous electrical but insensitive to mechanical stimuli (“differential anaesthetic zone”). In this zone we explored heat pain thresholds, axon-reflex flare (LDI) and sensation (VAS) upon pH4, cowhage and histamine stimulation. No heat pain-thresholds could be determined in the differential zone. We recorded reduced pain ratings upon intradermal pH4 (20 µl) injections (48+9 vs. 79+6 VAS in normal skin) but no difference in flare development (6.5+0.8 cm² vs. 6+1.2 cm²). Histamine iontophoresis caused pruritus in the area of differential sensitivity in 5 of 8 subjects (26+14 VAS). Cowhage spicules did not provoke any sensation, contrasting cowhage-itch in normal skin (29+11 VAS). LFCN block caused a differential anaesthetic area to mechanical, thermal, and electrical stimuli. Histamine, but not cowhage, provokes itch in areas selectively insensitive to mecha-

nical stimuli. Mechano-insensitive nociceptors are sufficient to induce histamine-itch, whereas mechano-sensitive (polymodal) nociceptors are essential for cowhage-induced itch.

PUNCTATE CHEMICAL STIMULATION WITH HISTAMINE AND CAPSAICIN ACTIVATES A SUBSET OF POLYMODAL NOCICEPTORS IN MONKEY

FC11

Matthias Ringkamp; Jasenka Borzan; Kaitlin Schaefer; Timothy Hartke; Richard Meyer

Department of Neurosurgery, Johns Hopkins School of Medicine, Baltimore, USA

Active cowhage spicules produce the sensation of itch by activating mechanosensitive nociceptors. Punctate chemical stimulation by inactive cowhage spicules loaded with capsaicin or histamine also produces itch and pain sensations in human subjects, suggesting that they activate the same types of primary afferent nociceptors. We tested this hypothesis by studying the responses of unmyelinated nerve fibers in monkey to heat-inactivated cowhage spicules coated with histamine (10 mg/ml) or capsaicin (200 mg/ml) solution. Single-fiber activity in unmyelinated nociceptive afferents was recorded from cutaneous nerves innervating hairy skin in the anesthetized monkey. Receptive fields of mechanically-sensitive afferents were tested with a stepped heat stimulus (49°C, 3 s), and afferents classified as either quickly adapting (QC) or slowly adapting (SC). Of the 34 mechanosensitive C fibers studied, 2 were unresponsive to this heat stimulus, 14 were QCs and 18 SCs. Most QCs and SCs responded to histamine loaded spicules, but the responses were significantly larger in QCs. All QCs responded to capsaicin loaded cowhage spicules, compared to only 4/18 SCs. The capsaicin response was significantly greater in QCs than SCs. We conclude that QC polymodal nociceptors may be responsible for mediating the pain and/or itch sensations associated with punctate applications of histamine and capsaicin.

WARMING ENHANCES SEROTONIN-EVOKED ITCH VIA TRPV4

FC12

Tasuku Akiyama; Margaret Ivanov; Masaki Nagamine; Mirela Carstens; Akihiko Ikoma; Ferda Cevikbas; Jon Levine; Martin Steinhoff; Earl Carstens

Neurobiology, Physiology & Behavior, UC Davis, USA

Warming the skin often aggravates itch in patients with itchy dermatitis, but the underlying mechanism is largely unknown. Here we show that TRPV4, a warm-sensitive cation channel expressed in skin cells and sensory neurons, plays an important role in the enhancement of 5-HT-evoked itch by skin warming. In WT mice, the number of scratch bouts evoked by 5-HT, but not histamine, was significantly greater when the chamber temperature was 28°C compared to 25°C (skin temperatures of 33.7 and 36.4°C, respectively). TRPV4KO mice exhibited significantly fewer 5-HT-evoked scratch bouts compared to WT, while there were no differences in numbers of scratch bouts elicited by histamine, PAR-2 agonist or chloroquine. Calcium imaging revealed that the incidence of responses to application of 5-HT, but not other pruritogens, was significantly lower in DRG cells from TRPV4KO compared to WT mice. The responses to 5-HT, but not histamine were significantly enhanced when the

bath temperature of the perfusion chamber was maintained at 35°C compared to 33°C. Levels of 5-HT in the skin are known to increase under conditions of increased vascular permeability associated with skin diseases. Under these conditions, warmer skin temperatures may evoke itch due to a decrease in threshold for 5-HT-evoked itch signaling.

FC13 MECHANISMS OF SENSORY EFFECTS OF TACROLIMUS

Ulysse Pereira; Nicholas Boulais; Jean-Pierre Pennec; Laurent Misery

University of Western Brittany, Laboratory on Nervous Factors and Tissular Structuration, Brest, France

Tacrolimus is an immunosuppressant drug currently used for the treatment of atopic dermatitis and pruritus. This topical therapy is effective and safe, but transient burning, stinging and itch are frequently reported. In order to understand the mechanisms underlying these burning sensations, we examined the impact of tacrolimus on substance P (SP) release in an *in vitro* model of cutaneous neurogenic inflammation. Because phosphorylation of TRPV1 (transient receptor potential subtype vanilloid 1) plays a role in the induction of pain, we investigated whether tacrolimus regulates the phosphorylation state of TRPV1. Finally, we used macro-patch to evaluate the impact of tacrolimus on voltage-gated calcium currents of sensory neurons. Here we show that tacrolimus was able to induce initial SP release by extracellular calcium influx and inhibited SP release induced by capsaicin after 1, 24 and 72 h of pretreatment. Analysis of TRPV1 phosphorylation by western blot confirmed the capacity of tacrolimus to favour phosphorylation. Electrophysiological study showed inhibitory effects on calcium currents. Hence, the efficiency of tacrolimus on pruritus, as well as sensory side effects, could be explained by a direct effect on neurons through an effect on calcineurin, possibly by a desensitization of TRPV1 and calcium currents through the PIP2 regulation pathway.

FC14 AUTOTAXIN IS A NOVEL DIAGNOSTIC MARKER FOR INTRAHEPATIC CHOLESTASIS OF PREGNANCY

Andreas E. Kremer¹; Peter H. Dixon²; Carrie Ris-Stalpers³; Victoria Geenes²; Jenny Chambers²; Joris A. van der Post³; Catherine Williamson²; Ulrich Beuers¹; Ronald P. J. Oude Elferink¹
¹Tytgat Institute for Liver and Intestinal Research and Department of Hepatology & Gastroenterology, Academic Medical Center, University of Amsterdam, The Netherlands, ²Maternal and Fetal Disease Group, Institute of Reproductive and Developmental Biology, Imperial College London, London, United Kingdom, and ³Department of Obstetrics and Gynaecology, Academic Medical Center, Amsterdam, The Netherlands

Introduction: Intrahepatic cholestasis of pregnancy (ICP) is a cholestatic disorder characterized by pruritus, elevated aminotransferases and fasted bile salts which is in contrast to other pruritic disorders of pregnancy associated with an increased risk of adverse fetal outcomes. We have recently identified increased autotaxin activity in women with ICP. Here, we studied whether serum autotaxin could distinguish ICP from other diagnoses. **Methods:** Autotaxin activity, bile salts and transaminases were measured enzymatically in sera of pregnant women with ICP

($n=43$), other pruritic disorders of pregnancy ($n=15$), HELLP-syndrome and (pre-)eclampsia ($n=17$), pregnant ($n=44$) and healthy controls ($n=219$). **Results:** ATX activity was increased in women with ICP ($p<0.0001$) compared to other pruritic disorders of pregnancy, HELLP-syndrome, pre-eclampsia, and pregnant controls. With a cut-off value of 30.0 nmol/ml*min, autotaxin had a sensitivity of 88% and specificity of 93% in diagnosing ICP from other pruritic disorders and a sensitivity of 80% and specificity of 85% from HELLP-syndrome and pre-eclampsia. Longitudinal studies revealed that autotaxin activity strongly rose in the third trimester of pregnancy. Autotaxin displayed no circadian rhythm and was not influenced by oral food intake. **Conclusion:** Autotaxin activity represents a highly sensitive and specific diagnostic tool in distinguishing ICP from other disorders of pregnancy.

BAM8-22 PEPTIDE INDUCES HISTAMINE-INDEPENDENT SENSORY RESPONSES IN HUMANS

Parul Sikand; Xinzhong Dong; Robert LaMotte
Department of Anesthesiology, Yale University School of Medicine, New Haven, USA

The mechanisms underlying histamine-independent itch are of clinical importance as many types of chronic itch are poorly treated with antihistamines. The bovine adrenal medulla 8-22 peptide (BAM8-22), is a potent activator of Mas-related G protein-coupled receptors (Mrgprs), and induces scratching in mice in a Mrgpr-dependent manner. To study the sensory responses induced by BAM8-22 in humans, peptide-soaked heat-inactivated cowhage spicules were tested in the volar forearm of fifteen healthy volunteers. BAM8-22 produced predominantly itch, accompanied by pricking/stinging and burning. The sensations were occasionally accompanied by one or more mechanically evoked dysesthesias, namely alloknesis, hyperknesis, and hyperalgesia. The sensations and dysesthesias were similar to those produced by spicules containing histamine. But unlike histamine spicules, BAM8-22 spicules produced no wheal or neurogenic flare. The inactive truncated BAM8-18 peptide, produced weak or no sensations and no dysesthesias. Pretreatment with a topical antihistamine cream blocked histamine-induced sensations, dysesthesias and skin reactions but not the sensations and dysesthesias evoked by BAM8-22. Thus, BAM8-22 evokes itch, nociceptive sensations and cutaneous dysesthesias in humans by a histamine-independent mechanism. Hence, BAM8-22 may be an endogenous itch mediator in humans and its receptor, the MrgprX1, a novel target for potential anti-itch treatments.

CENTRAL MODULATION OF ITCH BY DISTRACTION – A FUNCTIONAL MRI STUDY

Astrid Stumpf; Bettina Pfeleiderer; Gudrun Schneider; Gereon Heuft; Martin Schmelz; Ngoc Quan Phan; Sonja Ständer; Markus Burgmer
Department of Psychosomatics and Psychotherapy, University Hospital of Münster, Germany

Background: The central processing of itch is not completely understood. In contrast to pain studies there are no studies concerning the central effect of distraction. This is the first fMRI study that examines the central modulation of experi-

FC15

FC16

mental itch by distraction. *Method:* Experimental itch was induced by application of histamine (0.1 mM) via intradermal microdialysis fibers in 33 healthy volunteers (17 females) twice at the left forearm and twice at the left lower leg. After 90 s during each condition the subjects were distracted by a stroop task over 90 s. Subjects were asked several times to rate itch intensity and urge to scratch and central activation patterns were assessed by fMRI. *Results:* Distraction by stroop task reduced the urge to scratch but not the itch intensity. During the distraction task activation of the insula, thalamus and the periaqueductal grey was increased, all cerebral areas important in central inhibition of pain. *Conclusion:* Itch and pain seem to have similar inhibition pattern especially concerning the urge to scratch. The itch sensation and the urge to scratch seem to be different itch dimensions.

FC17 SKIN ANALYSIS BY 5D INTRAVITAL MULTI-PHOTON TOMOGRAPHY IN PATIENTS WITH ATOPIC DERMATITIS TREATED WITH APREPITANT – A CASE STUDY

Ngoc Quan Phan; Sonja Ständer; Valentina Dimitrova; Dieter Metzger; Stefan W. Schneider; Volker Huck
Clinical Neurodermatology and Competence Center for Chronic Pruritus, Department of Dermatology, University Hospital Muenster, Germany

Intravital multiphoton tomography (5D-IVT) is a new tool for non-invasive *in vivo* analysis of human skin. Experimental studies showed that substance P and its receptor neurokinin 1 (NK1) are involved in induction of pruritus and inflammation. In our study, we investigated the antipruritic potency and changes in the human epidermis analysed by 5D-IVT in the longitudinal course of a 4-week monotherapy with the NK1-receptor antagonist aprepitant in patients with atopic dermatitis (AD). After 4 weeks, maximum VAS was reduced from mean 9.15 to 6.35. Focusing on the skin metabolism at the stratum corneum/stratum granulosum interface in these patients in comparison to non treated patients and healthy subjects, we observed a normalised cell metabolism. These findings correlated with the SCORAD which revealed a mean improvement from 70.85 to 53.05. Thus, our findings suggest antipruritic and anti-inflammatory effects of aprepitant in AD. Application of 5D-IVT allows a deeper understanding of the individual disease development and the improved management of the therapeutic intervention in clinical application and approves a non-invasive *in vivo* imaging of human skin. Further studies will evaluate the application of the 5D-IVT technology as a diagnostic tool and to monitor the therapeutic efficacy.

THE EFFECTS OF AN OPIOID ANTAGONIST ON THE ITCH-SCRATCH-CYCLE: A PSYCHOPHYSICAL AND FMRI STUDY

FC18

Clemens Forster; Rebekka Vogelgsang; Verena Vierow; Arnd Dörfler; Hermann O. Handwerker
Institute of Physiology I, University of Erlangen, Germany

While μ -opioid agonists inhibit pain, itch is augmented. Accordingly, a μ -antagonist like Naltrexon should decrease the itch. In this double-blind study itch evoked by histamine, cowhage or capsaicin was compared with Naltrexon and placebo pre-treatment, respectively. The itching substances were applied using native cowhage spicules or inactivated spicules loaded with histamine or capsaicin. After the itch sensation had developed four passive scratch bouts were given to modulate the sensations. During the psychophysical session the subjects continuously rated the itch on a visual analogue scale and completed a questionnaire with 24 items describing sensory qualities. The same protocol was used while the cerebral processing of itch was analyzed using fMRI. The psychophysical results showed a more displeasing character of the scratch bouts after Naltrexon in particular during the capsaicin stimuli. Under Naltrexon most of the activated brain clusters were similar to those of the placebo condition. In pACC the scratch response to capsaicin and histamine was stronger under placebo, whereas in the sACC a more negative BOLD response was encountered after the scratch bouts. Somewhat higher scratching responses to histamine were also found bilaterally under placebo in the thalamus and in S1.

TOPICAL THERAPY WITH A NEW COOLING COMPOUND® IN PATIENTS WITH CHRONIC PRURITUS

FC19

Matthias Augustin; Ngoc Quan Phan; Christine Blome; Gitta Neufang; Sonja Ständer
CV Derm, German Center for Health Services Research in Dermatology, Department of Dermatology, University Clinics of Hamburg, Germany

Cooling the skin by menthol quickly relieves itch and is often used by chronic pruritus patients. In a vehicle-controlled, double-blind study, 36 patients were treated with a lotion containing a newly developed cooling substance Cooling Compound® (CC) (group 1: 22 female, 14 men; mean age 54.3 years) and 35 patients with the same lotion without CC (group 2: 25 female, 10 men, mean age 56.9 years). The lotion was applied twice daily for 4 weeks. Patients underwent thorough clinical investigation, and pruritus, life quality (DLQI) and patient-relevant benefit were assessed, the last with the help of the Patient Benefit Index Pruritus (PBI-P) questionnaire. Pruritus intensity assessed by global rating, reduction in percent and 5-point Likert scale and DLQI showed significant improvement in group 1 ($p < 0.05$). In this study, high concentrations of CC were used. As a consequence, intense cold sensation lead more often to adverse side effects in group 1 (with CC) such as extreme feelings of cold and burning on mucosa (group 1: 68.6% vs. group 2: 14.6%). Overall, both groups tolerated the lotions well. In summary, treatment of dry, pruritic skin with Cooling Compound® reduces chronic pruritus of different origins.

ABSTRACTS: Poster Presentations (PP01–PP49)**PP01 OTIS (OPTION TOOL FOR ITCHING SCALP): AN AID TOOL FOR THE MANAGEMENT OF ITCHY SCALPS***Catherine Oliveres-Ghouty; Charles Taieb
Paris, France*

Objective: Design a tool to guide disease management available to all pharmacists and non-dermatologist health professionals in order to provide a solution for the patient. *Material and Methods:* The development of the questionnaire followed a rigorous methodological process. The questionnaire was then administered to a representative sample of 1,703 French subjects. *Results:* In France, 21.49% suffers from an itchy scalp. Amongst subjects who reported itching in the last 7 days during their interview, 22.9% said their itching was exclusively on their scalp, 52.5% on their body (not-the-scalp) and 24.6% experienced itching both on their body-and-scalp. Amongst subjects who reported itchy scalps, 34.9% also reported excessive desquamation from the scalp, which orients treatment towards management of seborrheic dermatitis (SD). For 60.66% of those suffering from itchy scalps, the diagnosis of SD cannot be given due to a lack of dandruff. Analyzing these subjects' 3S score showed sensitive scalps in 48.9% of cases, (11.8%:very sensitive scalp). For this last group, the health professional should not only provide the patient with immediate relief, but should also refer them to their dermatologist for additional investigations. *Discussion:* This questionnaire available to non-dermatologist health professionals will allow for rapid patient management and referral to dermatologists for those who require more detailed diagnosis.

PP02 DEVELOPMENT OF A QUESTIONNAIRE ASSESSING THE BURDEN OF PRURITUS
*Charles Taieb**Public Health, Pierre Fabre, Boulogne, France*

Introduction: In a difficult economic context, the public health burden is increasingly often a legitimate concern for health authorities. *Objective:* To explore the handicap, in the largest sense, generated by pruritus (scratching or itching) using a questionnaire to express the burden of the symptom on the daily life of patients. *Equipment and methods:* The questionnaire was developed following a strict methodological process, involving a multidisciplinary team incorporating various players who are involved in the treatment of patients and caring for their families. A review of the literature and discussions with the children and their families were conducted in order to identify the concepts related to the pathology. *Result:* Exploratory assessments showed that the concept of burden could be structured around 2 modules: frequency and severity for the first module; daily life, family and personal relationships, work and psychological impact for the second module. A first analysis managed to reduce these items to 29 whilst conserving the 2 modules but making it easier to use the analysis. *Conclusion:* Several existing questionnaires attempt to assess one or other of these components; the BOSIP (Burden-of-Scratching-Itching-and-Pruritus) questionnaire takes them all into consideration in order to explain every angle of the handicap generated.

EPIDEMIOLOGY OF PRURITUS IN FRANCE*Laurent Misery; Charles Taieb
CHU Brest, France*

Objective: The epidemiology of pruritus is not well known, as it has been subject to little study in France. This is therefore the main objective of this study. *Methods:* A representative sample of the population was taken by the CSA-Health-Institute. 1,703 subjects completed a questionnaire on itching, its frequency and intensity. *Results:* The prevalence of pruritus is 29.8%. For 3.5% of the population asked, itching is frequent, whereas 13% rarely experience itching. Incidence of itching was 9.5%. The evening and night are the times at which itching is most intense. The scalp, back, legs and arms are the most frequently itchy areas of the body, with 47.5%, 32.1%, 28.4% and 25% subjects reporting them, respectively. Nine percent would rate their itching as intense or unbearable. Forty percent of subjects found their itching to be more intense when lying down or at rest. Ninety percent of subjects felt their itching on the surface, and 9% deeper under the skin. *Discussion:* Pruritus affects around one third of the French population over a period of 1 year, and 10% in the last week. These statistics are similar to those gained from studies in Norway and Germany. The intensity is of course variable, but pruritus is nevertheless an undeniable public health issue.

DANDRUFF AND ITCHING: AN EPIDEMIOLOGICAL APPROACH IN FRANCE*Laurent Misery; Charles Taieb
CHU Brest, France*

Objective: To evaluate the prevalence of dandruff in France. *Methods:* A representative sample (1,703 subjects) of the French population was taken by the CSA-Health-Institute. Those surveyed took a questionnaire. *Results:* In France, 16.5% reported excessive desquamation of the scalp, commonly known as dandruff. 58.15% of subjects with dandruff reported a sensitive or very sensitive scalp. Sixty-eight percent of those who reported dandruff complained of itching (on any area of the body). Amongst those who did not have dandruff, these figures stood at 21.5% and 25.9%, respectively. Excluding itchy scalp, the prevalence of itching is 41% with dandruff vs 26%. Itchy scalps affect 51% of the subjects with dandruff vs 15% ($p < 0.001$). *Discussion:* The prevalence of dandruff appears to be significantly high among the French population. This does not determine a diagnosis: Generally seborrheic dermatitis, but also psoriasis, eczema and other conditions. It is useful to note that subjects who claimed to have dandruff were more likely to also have pruritus. As pruritus is a symptom generally linked to dandruff of the scalp, its presence on other areas of the body is more surprising. Is this caused by sensitivity to pruritus (central or peripheral) or is pruritus a symptom of sensitive skin in other areas?

PP03**PP04**

PP05 ITCHING IN CHRONIC HAND ECZEMA: RESULTS FROM THE CARPE REGISTRY

Christian Apfelbacher; Sonja Molin; Elke Weisshaar; Andrea Bauer; Jochen Schmitt; Vera Mahler; Thomas Ruzicka; Peter Elsner

Institute of Epidemiology and Preventive Medicine, University Regensburg, Germany

The aim of the CARPE (German acronym: Chronisches Handekzem-Register zum Patienten-Langzeitmanagement) registry is to investigate characteristics and treatment modalities in patients affected by chronic hand eczema (CHE) in Germany. Here, we present data on itching and the relationship of itching with health-related quality of life (HrQoL) and severity of CHE. Patients with CHE are prospectively assessed by means of a dermatological examination and a patient questionnaire. Itching is assessed by the physician in four categories (none, moderate, average, severe) and severity of CHE is measured by a physician global assessment (PGA) as severe, moderate, mild, almost clear, clear. Quality of life is measured by the Dermatology Life Quality Index (DLQI). 853 patients were included for analysis, of whom 18.4% reported no, 25.9% moderate, 34.0% average and 21.3% severe itching. Mean DLQI scores rose in a linear manner with itching intensity. Severity of hand eczema was also associated with itching. 46.8% of patients with severe hand eczema reported itching, compared to 16.1% with moderate, 14.3% with mild, 8.3% with almost clear and 7.7% with clear hand eczema. The vast majority of patients with CHE report itching. The intensity of itching is associated with both the degree of HrQoL impairment and the severity of CHE.

PP06 SMALL-FIBER NEUROPATHIES (SFN): COMPARISON BETWEEN QUANTITATIVE SENSITIVITY TEST (QST) AND MEASUREMENT OF DENSITY OF INTRA-EPIDERMAL NERVE FIBERS (IENF)

Laurent Misery; Anne Pavy-Le Traon; Steeve Genestet; Pascale Marcorelles

Department of Dermatology, University Hospital, Brest, France

SFN are characterized by pruritus and other abnormal sensations on endings than become more diffuse in a second time. Because electromyography does not show any abnormality, QST is an excellent technique to perform diagnosis. We compared QST to the study of density of IENF after immunostaining of PGP9.5 after skin biopsies. Nine patients (8 women and 1 man, mean age: 60 years) with a clinical diagnosis of SFN were included in the study. Electromyography was normal. QST showed decreased cold sensitivity in all cases, decreased thermo-algesic sensitivity (3 cases) and decreased vibratory sensitivity one time. The number of distal IENF was decreased 8 times. In the last case, the diagnosis of psychogenic pruritus was made. QST is an excellent tool for diagnosis of IENF but is too long and too expensive. Analysis of IENF allows to discriminate SFN from psychogenic disorders or simulation, is less expensive and more rapid. Both studies need an expert team.

PSYCHOGENIC SKIN EXCORIATIONS: THE PROBLEM IS NOT PRURITUS...

Laurent Misery; Myriam Chastaing; Sylviane Touboul; Valérie Callot; Martine Schollhammer; Paul Young; Nathalie Fetton-Danou; Sabine Dutray

Psychodermatology Group, French Society of Dermatology, France

Psychogenic excoriations are also called neurotic excoriations, dermatillomania or skin picking syndrome. After definition of diagnostic criteria, a study on the psychiatric profiles of outpatients with psychogenic excoriations and the circumstances around these excoriations' creation was performed. Although data must be interpreted cautiously because our study was performed with only 10 patients, the study provides interesting data about the onset of psychogenic excoriations, the absence of pruritus, the behaviour of picking, and comorbidity. Common or specific characteristics were identified according to cases. The majority of patients associated first excoriations with personal problems. Four patients related abuse in childhood or adolescence. This study confirms that skin picking is an impulsive reaction and does not belong to the obsessive-compulsive disorders: impulsivity is defined by ineffective or failing control resulting in uninhibited behaviour.

AN ITCHY OCCUPATIONAL DISEASE TO KNOW IN POULTRY FARMERS: PRURIGO DUE TO DERMANYSSUS GALLINAE

Brice Loddé; Véronique Bizien-Le Dez; Anne-Marie Roguedas-Contios; Laurent Misery; Jean-Dominique Dewitte
Department of Occupational Health and Environmental Diseases, University Hospital, Brest, France

Diseases due to bites of *Dermanyssus gallinae* are rarely reported in medical literature. The case of an occupational prurigo in relation with skin contacts of this acarid introduces our research on specificities of transmittable diseases through this vector. A 44-year-old man had a skin rash with papules and itch on exposed areas at every time he was at work in a poultry farm. At the same time he has seen red poultry mite on these areas. Exploration found sensitization to *Dermanyssus pteronyssimus* which is an acarid very close to *Dermanyssus gallinae* at the beginning of this occupational prurigo. By analysing literature there are few similar occupational cases meanwhile transmittable diseases especially bacteriological ones could be caused by the bites of infected *Dermanyssus gallinae*. We report an occupational case of prurigo due to bites of *Dermanyssus gallinae* in a poultry farm. This case seems to be particular even though transmittable diseases are major health risks of the bites of this acarid eventually infected.

PSYCHOGENIC ITCH IN DERMATOLOGIC PRACTICE

Svetlana Bobko
Moscow, Russia

Introduction: Itch is one of the most common symptoms in dermatologic practice. The problem of psychosomatic itch is very actual. *Material and Methods:* 25 patients with severe itch (22 women, 3 men, mean man age 55.28±14.94, itch

duration 4.852 ± 4.66) were examined by dermatologist, psychiatrist, psychologist within the work of psychodermatological group in dermatologic department. Dermatologic, systemic and psychotropic therapy was conducted taking into consideration dermatologic diagnosis, psychosomatic disorders. *Results:* There were the following diagnosis: Dermatitis Artefacta Syndrome ($n=2$); Skin Picking Syndrome ($n=10$), somatoform itch ($n=13$). Variety of sensations described as itch are demonstrated in different nosologies. Itch at the beginning of Dermatitis Artefacta Syndrome could cause massive autoaggressive behavior resulted in disfiguring atrophic face scars. Dermatologist noticed differences in such groups of patients: itch duration, localization, intensity, presence of excoriations, skin findings that demanded individual approach of diagnostic and treatment. *Conclusions:* According to psychiatric diagnosis (from anxious and depressive till delusional disorders and tactile hallucinosis) adequate psychotropic drugs were prescribed, mainly neuroleptics, with positive dynamics of mental disorders and sensations. Complex psychodermatological approach for itch studying and recommended psychopharmacological treatment seem to be actual for such patients.

PP10 INCIDENCE OF CHRONIC PRURITUS AND ITS DETERMINANTS: RESULTS FROM A POPULATION-BASED STUDY

Lena Vogelgsang; Uwe Matterne; Christian J. Apfelbacher; Adrian Loerbroks; Elke Weisshaar
Department of Clinical Social Medicine, Occupational and Environmental Dermatology, University Hospital Heidelberg, University of Heidelberg, Germany

Aim of the study: Pruritus is the most common symptom in dermatology. While previous studies have suggested a considerable prevalence of chronic pruritus (>6 weeks) in the general population, data on its incidence and determinants in the community are lacking. *Method:* A total of 1,189 participants of our previous cross-sectional pruritus prevalence study agreed to be contacted for future studies. Following a maximum of three contact attempts, of those 1,189 individuals 0.12% ($n=15$) died between baseline and follow-up. Of those alive ($n=1,174$), 80.1% ($n=941$) participated at follow-up in a follow-up study about 1 year after baseline. Participants completed a questionnaire covering occurrence of chronic pruritus, its characteristics as well as anamnestic, social and psychological variables. *Results and Conclusion:* The 1-year incidence of chronic pruritus in the general population was found to be 7.2%. Bivariate analyses found several factors, such as dry skin, to be associated with the prevalence of chronic pruritus. This is the first study investigating the incidence of chronic pruritus and its determinants at the population level. Knowledge about the risk factors for chronic pruritus may inform the development of preventive interventions.

PP11 BENEFIT OF A PRURITUS CONSULTATION-HOUR IN A DERMATOLOGICAL OFFICE – PREVALENCE DATA OF 2009 AND 2010 IN MY OFFICE

Michael Haeblerle
Dermatological Office, Kuenzelsau, Germany

Although pruritus is considered to be a common problem, only a few studies have examined its prevalence in patients consul-

ting a dermatologist in a private office. 488 individuals were included in a retrospective study of all pruritus patients between 01/01/2009 and 12/31/2010. The mean age was 52 years. All 488 patients complained of itching within the past 7 days. This study revealed a variety of diagnoses: 1) Dermatological diseases 227, 46.5%; psoriasis 110, 22.53%; atopic eczema 70, 14.34%; others 47, 9.63%. 2) Hepatic diseases 86, 17.6%. 3) Renal diseases 56, 11.5%. 4) Psychiatric diseases 48, 9.8%. 5) Neurological diseases 33, 6.8%; small fiber disease 22, 4.5%; brachioradial pruritus 11, 2.3%. 6) Pruritus in pregnancy 12, 2.5%. 7) Hematologic diseases 6, 1.2%. 8) Others 20, 4.1%.

DERMATOLOGIST'S ABILITY TO PRIMARILY DIAGNOSE SYSTEMIC DISEASES – A CASE REPORT

Michael Haeblerle
Dermatological Office, Kuenzelsau, Germany

In 12/10 an 81-year-old woman presented with strong pruritus which did not respond to scratching. She had no other complaints. Her face was pale. She had not consulted any physician for years and did not take any medication. Blood analysis showed gamma-GT 1077 U/l, GOT 146 U/l, GPT 326 U/l, Bilirubin 3.1 mg/dl. She was hospitalized immediately. A lymph node metastasis of an ovarian cancer was diagnosed to constrict the cholelith. Gastroenterological intervention and chemotherapy lead to relief within a few weeks. 05/11 the patient presented in my office with moderate pruritus, but in good condition. Since 2006 a pruritus consultation-hour has been established in my dermatological office in Kuenzelsau, a rural town with a population of 15,000 in southern Germany. My office covers an area roamed by appr. 100,000 inhabitants. Regional general practitioners in the Hohenlohekreis recommend my special pruritus consultation-hour due to own promotional activities. Hepatic diseases are the most common cause of consultation beside dermatoses. Lysophosphatidic acid is responsible for the pruritus due to cholestasis which has been shown by Kremer. The presented case report is a good example for the dermatologist's ability to primarily diagnose systemic diseases.

EFFECTS OF UV-BASED THERAPIES, CORTICOSTEROID OINTMENT AND EMOLLIENTS ON INTRAEPIDERMAL NERVE FIBERS OF ACETONE-TREATED MICE

Atsuko Kamo; Mitsutoshi Tominaga; Osamu Negi; Kenichi Taneda; Kenji Takamori; Suhandy Tenggara
Institute for Environmental and Gender Specific Medicine, Juntendo University, Tokyo, Japan

UV-based therapies, as well as corticosteroid ointments and emollients, have anti-pruritic effects in various skin diseases. The anti-pruritic mechanism of these agents may be partly due to inhibition of intraepidermal nerve growth, but these effects have not been fully characterized. We therefore examined the anti-nerve growth effects of these therapies in acetone-treated mice. Acetone-induced intraepidermal nerve growth was significantly decreased in mice treated with heparinoid in emollients, and psolaren ultraviolet A-beta-methasone valerate (PUVA-BV), narrowband ultraviolet B (NB-UVB) and excimer lamp in UV-based therapies. Heparinoid, PUVA-BV, and NB-UVB tended

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to normalize the abnormal expression of nerve growth factor and semaphorin 3A in the epidermis, but excimer lamp had no effect on them. These results suggest that UV-based therapies, especially NB-UVB and excimer lamp, and heparinoid in emollients may be effective therapeutic methods for pruritus involving epidermal hyperinnervation.

PP14 EVOLUTION OF ITCH IN PATIENTS WITH BURNS: A 12-WEEK FOLLOW-UP STUDY

Philip Moons; Marjolein Colpaert; Chris Haest; Michael Casaer
Center for Health Services and Nursing Research, Katholieke Universiteit Leuven, Belgium

Introduction: Itching following burns is a common problem. Previous studies are often lacking valid and reliable assessment methods; and longitudinal research is scarce. We investigated different dimensions of itch during the wound healing process. *Methods:* Sixty-four patients with burns (median TBSA=0.55%; 61% males) were included in a longitudinal study. Patients filled-out the Leuven Itch Scale (LIS) at 4, 8, and 12 weeks post-burn. The LIS assesses 9 aspects of itch, experienced over the past 4 weeks. For the frequency, duration, severity, distress, and consequences of itching, subscale scores (range: 0–100) were calculated. *Results:* Itch occurred in 71% of patients at 4 weeks, 47% at 8 weeks, and 25% at 12 weeks post-burn (Cochran's $Q=12.545$; $p=0.006$). The mean itch frequency score was 36.6 ± 26.9 , 27.3 ± 29.3 and 14.6 ± 25.4 ($F=4.906$; $p=0.009$) at 4, 8 and 12 weeks, respectively. The mean itch duration score was 41.4 ± 21.2 , 25.5 ± 22.1 and 14.3 ± 17.8 ($F=6.096$; $p=0.004$). The mean itch severity score was 31.0 ± 25.7 , 30.0 ± 23.9 and 22.9 ± 18.5 ($F=0.363$; $p=0.70$). The mean itch distress score was 31.5 ± 30.1 , 28.7 ± 24.7 and 24.9 ± 20.8 ($F=0.203$; $p=0.82$); and the mean itch consequence score was 11.0 ± 16.5 , 12.1 ± 14.1 and 6.2 ± 4.9 ($F=0.406$; $p=0.67$), respectively. *Conclusions:* The frequency and duration of itch significantly decreased during the first 12 weeks post-burns. No significant evolutions were found for itch severity, distress and consequences.

PP15 INTENSITY AND IMPACT ON DAILY LIFE OF ITCHING COMPLAINTS FOLLOWING BURNS

Marianne Nieuwenhuis; Marco Bremer; Nancy van Loey
Association of Dutch Burns Centres, Burn Centre Martini Hospital, Groningen, The Netherlands

Introduction: Rationale A growing body of research documents the high frequency rates of post burn itching. However, there is little additional information, e.g. regarding possible differences in intensity in different body parts, the role of injury depth, and the impact of itching on daily living in patients with burns. *Methods:* Consecutive patients admitted to five burn centres completed the Burns Itch Questionnaire (BIQ) at 3 months post burn. This is a 20-item questionnaire inquiring after intensity and occurrence of itching, and impact on daily life. Items are scored on a 10-point Likert scale (0=no itch to 9=most severe itch). We collected additional data regarding demographic and injury characteristics. *Results:* We obtained data for 167 persons. Patients were on average 40 years old, 19% was female. Mean TBSA was 13%. Eighty-eight patients (53%) had itch complaints. Ninety percent of these patients reported itch in superficial burn surface areas, 47% experienced (also) itching in grafted areas, and 33%

reported itching of donor sites. Itching had the highest intensity in grafted burns. Overall itch and itch frequency were negatively correlated with age. *Conclusion:* Itching complaints are most frequent in superficial burn injury, but the highest intensity of itching is reported in grafted areas.

FUNCTIONAL ITCH AND PSYCHIATRIC DISORDERS: CONTINUUM OF PSYCHODERMATOLOGICAL SYNDROMES

Dmitry Romanov; Andrey Lvov; Svetlana Bobko
Moscow, Russia

Background: Itch unexplained by any dermatological or somatic cause is considered as functional. It is usually noted that there are associated psychiatric disorders. However there is no precise knowledge on the set of distinct psychiatric disturbances accompanied with functional itch and peculiarities of pruritus in them. As a result little is known about preferable psychiatric medications for these disorders. Objective. Development of typology of psychodermatological syndromes represented with functional itch and elaboration of differentiated treatment approaches. *Methods:* Psychopathological and dermatological observation of 83 patients (62 women, mean age 49.1 ± 17.1 years) seeking medical help for functional itch in dermatological clinic. *Results:* Functional itch was associated with epileptic syndrome ($n=2$, 2.4%), delusional parasitosis ($n=13$, 15.7%), circumscribed hypochondriasis ($n=4$, 4.8%), obsessive-compulsive disorder ($n=11$, 13.2%), impulse-control disorder ($n=12$, 14.5%), conversional disorder ($n=15$, 18.1%), somatoform disorder ($n=26$, 31.3%). Functional itch differed phenomenologically across the psychodermatological syndromes. It was the initial and persistent presentation and could be considered as a predictor designating the future course of disease. Differentiated recommendations for psychotropic treatment were elaborated. *Conclusion:* Functional itch is a heterogeneous phenomenon developing within a variety of psychiatric disorders which form a continuum from epileptic/psychotic to neurotic level requiring different psychopharmacological approaches.

A CASE OF UREMIC PRURITUS AND KYRLE'S DISEASE: EFFECTIVE TREATMENT WITH AMITRIPTYLINE

Wei-Sheng Chong; Angeline Yong; Hong-Liang Tey
National Skin Center, Singapore

Uremic pruritus is a common problem for patients with chronic renal failure. Kyrle's disease, on the other hand, is a rare disorder of keratinization classified among the perforating dermatoses and is associated with diabetes mellitus, hepatic abnormalities and congestive heart failure. We present a case of uremic pruritus and Kyrle's disease in a 64-year-old Chinese male with poorly controlled type 2 diabetes mellitus. He presented with intractable generalized itch and extensive excoriated nodules over his trunk and lower limbs. Histology of one of the nodules was consistent with Kyrle's disease. His condition was unresponsive to prednisolone and he experienced drowsiness and bipedal oedema to gabapentin. He was tried on Amitriptyline 10mg at night and there was a marked decrease in itch intensity within 1 week, followed by progressive flattening of skin lesions. To our knowledge, this is the first report of the successful treatment of uremic pruritus with amitriptyline.

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PP18 OLOPATADINE HYDROCHLORIDE INHIBITS INTRAEPIDERMAL NEURITE OUTGROWTH AND INFLAMMATORY RESPONSE IN AN ATOPIC DERMATITIS MOUSE MODEL

Ichiro Katayama; Mostafa AbdEl-latif; Toru Amano; Tadafumi Tamura

Department of Dermatology, Osaka University, Osaka, Japan

Control of itch is an important issue in the treatment of atopic dermatitis (AD). Itch is mediated by a variety of pruritogens, including histamine, and promoted by neurite outgrowth in the epidermis of AD patients, likely due to release of nerve growth factor. We investigated the effects of orally administered olopatadine hydrochloride (olopatadine) on itching, itching mediators and neurotogenic action in a mouse model. NC/Nga mice were treated topically with dermatophagoides farinae body (Dfb) extract to induce AD-like lesions, twice weekly for 4 weeks. Mice were treated concomitantly with oral administration of olopatadine, distilled deionized water, or topical tacrolimus in the last 2 weeks. Olopatadine significantly suppressed scratching, improved the dermatitis score, inhibited neurite outgrowth, and decreased the elevated inflammatory markers, growth factors, and histamine content in the lesional skin and serum concentration of Dfb-specific IgE. Notably, olopatadine treatment increased semaphorin 3A expression in the epidermis. Our study confirms the pleiotropic effects of olopatadine, such as inhibition of inflammation and neurite extension into the epidermis.

PP19 THE IMPACT OF PRURITIC SKIN DISEASES ON WORK, CLASSROOM, AND DAILY PRODUCTIVITY

Saki Matsui; Hiroyuki Murota; Ichiro Katayama

Department of Dermatology, Osaka university, Japan

Allergic diseases-related symptoms have been recognized to exert a negative impact on the social and economic situation via impairing the patient's work productivity. In this study, we had evaluated the impact of pruritic skin diseases on work, classroom, and daily productivity using WPAI-AS measure, and the effect of taking anti-histamine for 1 month on this measurement result. At the same time, intensity of itch and patient's quality of life were assessed. Pruritic skin diseases resulted in significant impairment of work, classroom, and daily productivity. The severity of overall work impairment in atopic dermatitis, urticaria, and prurigo was higher than for other diseases analyzed. However, classroom activity was more adversely affected in patients with urticaria relative to other diseases. All pruritic diseases in this study negatively impacted daily activity to a similar degree. Impaired productivity was significantly improved in patients taking non-sedative antihistamines for 1 month. These results indicate that pruritic skin diseases reduce patient productivity at work, in the classroom, and during daily activities, and that non-sedative antihistamines may offer an advantage over sedative antihistamines for alleviating certain negative consequences of these skin diseases.

PP20 CLINICAL CHARACTERIZATIONS OF ITCH IN ATOPIC DERMATITIS AND CHRONIC URTICARIA

Byung-Soo Kim; Woo-Haing Shim; Margaret Song; Hoon-Soo Kim; Seung-Wook Jwa; Hyun-Chang Ko; Moon-Bum Kim; Seong-Jin Kim; Do-Won Kim

Department of Dermatology, School of Medicine, Pusan National University, Busan, Korea

Itch is an essential feature of atopic dermatitis (AD) and chronic urticaria (CU). Therefore, understanding and managing itch are prerequisite for the treatment of AD and CU. However, in the respect of pathophysiology, itch in AD can be distinguished from that in CU. Unlike urticaria, histamine is not considered to be a major pruritogen in AD. In fact, many other pruritogens such as tryptase, kallikrein 7, interleukin-2, 31, substance P, nerve growth factor, μ -opoids, prostaglandin E2, thromboxane A2 are related to the provocation of itch in AD. On the basis of pathophysiological differences of itch between AD and CU, it could be assumed that clinical characterizations of itch may also be differentiated. Thus, we conducted a current study to clarify the clinical difference of itch in AD and CU using a structured questionnaire based on McGill pain questionnaire.

CENTRAL ITCH AND NEUROPATHIC PAIN FROM SPINAL CORD CAVERNOUS HEMANGIOMA: DESCRIPTION OF ONE CASE **PP21**

Nagi Mimassi; Philippe Meriot; France Marchand
Pain Clinic, University Hospital Brest, France

Central itch with central neuropathic pain are reported in one patient suffering from a cervical spinal cavernous hemangioma. These disabling symptoms evolved for several months. The patient, without skin or systemic disease or drug intake, was suffering from an ongoing dysesthesia and left leg burning pain. The quality of dysesthesia was essentially itching. Itch was more intense and undesirable than burning pain. No muscle atrophy or motor deficit are observed. Restricted movement is noted. MRI of brain and spinal cord showed a C6 spinal cavernous hemangioma. No surgical procedure. Patient was treated with pregabalin and SNARI. Itch is notably improved. On the contrary, burns persist despite treatment. This observation confirm that a spinal cord lesion can modify via, probably, microglia, second order neuron and cytokines, in skin, sensory neurons and non neural cell types implicated in itch pathophysiology. In spinal cord, several types of receptors are involved in neuropathic pain and itch. We discuss the location of the cavernoma, the pathways of sensibility at this level and different spinal receptors involved in the itch from central origin.

PROFILE OF ITCH EXPERIENCE IN PATIENTS WITH ATOPIC DERMATITIS, CHRONIC URTICARIA AND BURNS: DIRECT COMPARISON USING THE LEUVEN ITCH SCALE **PP22**

Philip Moons; Michael Casaer; Chris Haest; Marie-Anne Morren
Center for Health Services and Nursing Research, Katholieke Universiteit Leuven, Belgium

Aim: Itch occurs in various patient populations. A direct comparison of the itch experience across different populations is lacking. We comprehensively investigated the profile of the itch experience in patients with atopic dermatitis (AD), chronic urticaria (CU) or burns. *Methods:* Patients with AD ($n=63$), CU ($n=41$) and burns ($n=46$) completed the Leuven Itch Scale (LIS). The LIS allows to calculate subscale scores for itch frequency, duration, severity, distress, and consequences, each of

which ranges from 0 to 100. A higher score represents a bigger itch problem. **Results:** Itch occurred in 96.8% of patients with AD; 95% in CU; and 55.6% in burns. For the three groups, the mean itch frequency score was 74.2 ± 21.0 , 55.0 ± 24.2 and 30.6 ± 31.9 (Kruskal-Wallis = 50.6; $p < 0.001$), respectively. The mean itch duration score was 54.9 ± 27.9 , 55.6 ± 26.5 and 44.4 ± 19.2 (Kruskal-Wallis = 2.3; $p = 0.31$). The mean itch severity score was 59.5 ± 21.0 , 48.0 ± 25.4 and 36.2 ± 25.1 (Kruskal-Wallis = 16.5; $p < 0.001$). The mean itch distress score was 67.2 ± 20.6 , 51.6 ± 29.9 and 32.9 ± 30.2 (Kruskal-Wallis = 23.4; $p < 0.001$); and the mean itch consequence score was 45.1 ± 16.9 , 28.9 ± 17.5 and 13.0 ± 19.5 (Kruskal-Wallis = 38.7; $p < 0.001$), respectively. **Conclusions:** In patients with AD, the frequency, severity, distress and consequences of itch were significantly higher compared to patients with CU or burns. The LIS allows to comprehensively describing profiles of the itch experience in different patient populations.

PP23 MEASUREMENT OF ITCHING: CLINIMETRIC PROPERTIES OF THE LEUVEN ITCH SCALE

Philip Moons; Michael Casaer; Chris Haest; Marie-Anne Morren

Center for Health Services and Nursing Research, Katholieke Universiteit Leuven, Belgium

We evaluated the validity, reliability and responsiveness of the Leuven Itch Scale (LIS), a new instrument to measure itching in diverse patient populations. It measures frequency, duration, severity, circumstances, distress, location, sensory perceptions, consequences and management of itching. **Methods:** The LIS was evaluated in consecutive studies. Content validity was judged by 10 experts. Face validity was measured through interviews with 8 burn patients. Clinimetric evaluation was undertaken in patients with burns ($n = 46$), atopic dermatitis ($n = 63$) and chronic urticaria ($n = 41$). **Results:** The very low proportion of invalid scores in most items confirmed content validity. All hypotheses on relations with other variables could be accepted, confirming construct validity. For validity evidence on internal structure, a moderate positive significant correlation was found between itch frequency versus itch distress, and between itch frequency versus itch severity. As hypothesised, a strong correlation was found between itch severity and distress. Test-retest reliability showed a moderate to almost perfect agreement for about half of the items. For responsiveness, the LIS did not suffer from floor or ceiling effects, and detected changes in itch frequency in patients with burns. **Conclusions:** The LIS is a useful and clinimetrically sound instrument that can be used in trials assessing the effectiveness of treatments for pruritus.

PP24 CHARACTERISTICS OF ITCH IN THE DIFFERENT POPULATIONS WITH EPIDERMOLYSIS BULLOSA USING THE LEUVEN ITCH SCALE

Julie Snauwaert; Marie-Anne Morren; Philip Moons
UZ Leuven, Belgium

Aim: Itch is a common, but understudied problem in patients with epidermolysis bullosa (EB). With the Leuven Itch Scale (LIS), we measured the characteristics of itch in the 3 major forms of EB: EB simplex (EBS) ($n = 12$), junctional EB (JEB) ($n = 3$), dystrophic EB (DEB) ($n = 5$). **Methods:** The LIS was filled out

by patients who were either followed-up at our hospital ($n = 7$) or recruited by the Belgian patients' organization ($n = 13$). The LIS allows to quantify the extent of itch by summarizing the different aspects of itch (frequency, duration, severity, distress, consequences, surface area). **Results:** Itch occurred in 16/20 patients (80%); EBS 75%; JEB 100%; DEB 80%. The mean itch frequency score in these three groups was 33.3 ± 30.8 ; 75 ± 0.0 ; and 60.0 ± 33.5 (Kruskal-Wallis = 5.1; $p = 0.076$), respectively. The itch duration score was 22.2 ± 44.1 ; 22.2 ± 38.5 ; and 41.7 ± 41.9 (Kruskal-Wallis = 1.8; $p = 0.41$). The mean itch severity score was 31.2 ± 12.6 ; 75.0 ± 5.0 ; and 61.3 ± 23.9 (Kruskal-Wallis = 9.3; $p = 0.009$). The mean itch distress score was 29.7 ± 16.2 ; 78.7 ± 2.3 ; and 62.5 ± 33.0 (Kruskal-Wallis = 7.2; $p = 0.027$). The mean itch consequences score was 19.2 ± 19.2 ; 46.2 ± 3.5 ; and 39.2 ± 30.2 (Kruskal-Wallis = 3.9; $p = 0.14$). The mean surface area score was 8.8 ± 7.8 ; 31.5 ± 2.3 ; and 51.3 ± 28.8 (Kruskal-Wallis = 10.5; $p = 0.005$). **Conclusions:** As expected, itch is a common problem in patients with EB. Patients with more severe forms, like DEB and JEB, experience itch more prominent in the different areas that are measured by the LIS.

PP25 MENTAL ITCH INDUCTION IN PATIENTS WITH CHRONIC URTICARIA

Christina Schut; Alexander Claßen; Katharina Reinisch; Uwe Gieler; Jörg Kupfer
Institute of Medical Psychology, Justus-Liebig-University, Gießen, Germany

Introduction: Itch can be induced mentally through audiovisual stimuli. Furthermore mental itch is higher in patients with atopic dermatitis (AD) compared to healthy controls. So far this result has not been investigated in other skin-patients. Thus the aim of this study is to examine whether itch can be induced in patients with chronic urticaria (CU) through audiovisual material and whether it is increased in comparison to controls. **Methods:** Thirty-six CU patients and 36 controls are video-recorded while watching three videos (each 9:30 min) in a randomized order: a video with crawling insects (animal-video; AV), a video on skin-diseases (SV) and a control-video on skin as a communication-organ (CV). Scratching behavior and perceived itch are assessed as dependent variables. **Results:** Preliminary results (10 CU patients and 21 controls) indicate that perceived itch increases in CU patients as well as in healthy controls while watching the AV or SV compared to the CV. One striking result is that itch-increase evoked through the SV appears to be lower in CU patients than in healthy controls. **Discussion:** In a next step the itch increase will be compared between different groups of skin patients. Additionally psychological variables will be considered as predictors of itch increase.

PP26 ITCH OCCURRING WITH CHRONIC WOUNDS

Julia Paul
PhD Candidate, College of Nursing, Wayne State University, Detroit, USA

Background: Itch associated with wounds is recognized clinically, but is not well described in the literature. Wounds can be perpetuated by scratching in response to itch. The Theory of Wound Itch derived from Levine's Principles of Conservation provides a theoretical framework for this study. **Purpose:**

To examine the phenomenon of itch associated with chronic wounds. Research questions are: (a) What is the frequency, timing, duration and intensity of itch related to chronic wounds? (b) What are the characteristics of wounds that itch? (c) What treatments do participants use to manage wound itch? (d) How does wound itch affect quality of life for these participants? (e) What is the relationship between wound itch and pain? *Methods:* The study is cross-sectional, descriptive and correlational. 200 participants were recruited from a hospital-affiliated wound care center. Participants were interviewed with structured interview tools, and their wounds were assessed. *Results:* Data collection has just been completed. Data analysis with descriptive and parametric statistics is in progress. *Conclusion:* Findings of this study will increase general knowledge of wound itch and its impact on persons with chronic wounds.

PP27 A QUALITATIVE ASSESSMENT QUESTIONNAIRE FOR PRURITUS

Emilie Brenaut; Karen Talour; Laurent Misery
Department of Dermatology, University Hospital of Brest, France

Our aim was to develop a questionnaire for semiological analysis of pruritus and then use it in order to highlight the semiological particularities according to the dermatitis responsible for pruritus. The questionnaire was built in 6 sections: chronology, effects of treatment, characteristics of the pruritus and/or associated symptoms, intensity, disruption to daily activities and characteristics of the scratching. There was no overall score. The questionnaire was tested with 150 patients presenting with acute or chronic pruritus. The most frequent diseases were: eczema (40 patients), psoriasis (19), scabies (19), atopic dermatitis (18) and urticaria (16). The first analyses showed a good response rate with few unanswered questions. The time for completion was 5 min. In the literature, few teams have used questionnaires to evaluate pruritus by targeting one type of dermatitis, particularly atopic dermatitis with the "Eppendorf Itch Questionnaire". Created through analogy with previous ones, our questionnaire is based above all on the qualitative (the description) rather than the quantitative (the intensity) aspect. We will make use of the responses when we have enough participants to highlight the semiological characteristics according to the dermatitis. At the moment, we have only performed a French version of this questionnaire.

PP28 EPIDERMAL AND DERMAL INNERVATION IN KELOIDS

Hong Liang Tey; Ben Maddison; Daren Maruziva; Dudley Ferdinando; Jo Dicks; Gil Yosipovitch
National Skin Centre, Singapore

Background: Itch in keloids is common but the mechanism is unknown. *Aims:* 1) Examine whether innervation of keloids in the epidermis and dermis is different from healthy skin. 2) Determine if there is a difference in innervation between the central and peripheral regions of keloids and if any difference correlated with pain and itch sensory scores. *Method:* Keloid specimens from 13 patients who underwent excision and healthy skin from 9 age- and site-matched controls were collected. The itchy and painful regions of keloids were marked out before excision was

performed. Peripheral and central biopsies were performed on the excised keloids. The keloidal and control specimens were stained with Protein Gene Peptide 9.5. Confocal microscopy and a bespoke image analysis algorithm were used to analyze the images. *Results:* A trend towards a lower epidermal nerve fiber density was found in keloids compared to controls ($p=0.11$) and this difference was greater when itchy keloids were compared to controls ($p=0.069$). There were no differences in nerve fiber density and distribution between central and peripheral regions of the keloids. *Conclusion:* A trend towards a lower epidermal nerve density was observed in keloids and this is more pronounced in keloids which are itchy.

URAEMIC PRURITUS VS. SENILE PRURITUS. INCIDENCE AND MORPHOLOGICAL CHARACTERISTICS

PP29

Christian Diehl; Gilda Zurita Salazar; Iliana Caicedo
Universidad Nacional de Córdoba Argentina - CIFAC Guayaquil, Ecuador

Pruritus is an important symptom in patients with skin disease and systemic disease. It could change the skin characteristics and affect the life of the patient. In patients under hemodialysis, pruritus and dry skin are frequent. Aged people can develop pruritus, in some case, but aging also produces on the skin typical changes that cannot be avoided, such as the loss of epidermal hydration, strength and elasticity of skin; sebaceous glands produce a lesser quantity of sebum, and others change. In the Ecuador, this is the first study about pruritus in hemodialysis patients and aged people performed with the Cutometer MPA 580. We examined a total of 75 patients, 25 haemodialysis patients, 25 were aged people (> 70 years) and 25 people constituted the control group. The skin dryness were assessed by clinical and bioengineering methods; moreover measurement of stratum corneum hydration using Corneometer was assessed, such as transepidermal water loss using TEWL probe, sebum production with Sebumeter and skin pH with pH-meter. We used two skin places for our measurements: one area in the forearm and another one in an area with pruritus without laceration. Our results are presented in this lecture, and compared with published literature.

A CASE WITH ITCHY THROAT: POLLEN-FOOD SYNDROME

PP30

Deren Ozcan; Deniz Seckin
Department of Dermatology, Baskent University Faculty of Medicine, Ankara, Turkey

Pollen-food syndrome (PFS), is an IgE-mediated allergic reaction, characterized by oropharyngeal itch, throat tightness or tingling of lips which occurs upon ingestion of certain fresh fruits or vegetables in pollen-sensitized individuals. Although diagnosis relies heavily on clinical history, allergy testing is required to elucidate the nature of sensitization. A 36-year-old woman presented with a one-year history of oropharyngeal itch and erythema that appears particularly following ingestion of kiwi. Her past medical history was unremarkable except for diagnosis of acute urticaria with unknown cause. On dermatologic examination, soft palate was hyperemic and dermatographism was positive. Skin prick testing yielded a positive reaction with birch and grass pollens but not with the food panel which

did not include kiwi. Total IgE level was normal. The possible diagnosis was PFS and prick-by-prick test with kiwi is planned. Avoidance of kiwi ingestion and treatment with levocetirizine resulted in alleviation of the symptoms. Understanding the nature of cross-reactivity between pollen and foods has resulted in greater understanding of various clinical presentations in daily dermatology practice. In patients having non-specific oral mucosal symptoms such as itchy throat, the presence of food and pollen allergy should be investigated and PFS should be included in the differential diagnosis.

PP31 PRURITUS AFTER HYDROXYETHYL STARCH INFUSION THERAPY: ASSESSMENT OF A NEUROPATHY

Emilie Brenaut; Anne Pavy Le Traon; Sebastien Contios; Laurent Misery

Department of Dermatology, University Hospital, Brest, France

A 75-year-old woman presented with generalised pruritus without primary skin lesions. Her past medical history included a heart rhythm disorder, a fracture of the right humerus with two operations. It was generalised, precipitated by heat, and scratching induced pain. Pruritus appeared a few weeks after the second surgical operation. We suspected pruritus induced by HES and have confirmed that she received intravenous infusion of HES after the second operation. A functional evaluation of the peripheral nervous system was performed. Quantitative sensory testing (QST) showed an increased threshold of cold sensitivity at the extremities, and a dramatic increase in vibratory sensitivity. The threshold of thermo-algetic sensitivity was within normal limits. Quantitative sudomotor axon reflex test or QSART was reduced on the leg, which confirmed a small-fibre neuropathy of the sympathetic fibres. Electromyographic evaluation also revealed a sensitive neuropathy. The pathophysiology of HES-associated pruritus is not fully understood, it can be associated with HES tissue deposition, in particular in Schwann cells of cutaneous nerves. To our knowledge, there are no reports in the literature regarding the functional exploration of pruritus induced by HES. Our case suggests that pruritus induced by HES is probably caused by small-fibre and large-fibre neuropathy.

PP32 TOPICAL ANTI-INFLAMMATORY THERAPIES INHIBIT NEURAL SENSITIZATION IN PATIENTS WITH ATOPIC DERMATITIS

Miyuki Fukuoka; Miwa Hosogi; Yoshiki Miyachi; Akihiko Ikoma

Department of Dermatology, Graduate School of Medicine, Kyoto University, Japan

Several studies have suggested a major role of neural sensitization in chronic itch like in chronic pain. For example, patients with atopic dermatitis feel more intense itch by histamine application in their skin lesions, although, in contrast, the sensitivity to histamine in their unaffected skin area is less than in healthy people's skin. The effect of topically applied anti-inflammatory therapies on neural sensitization has never been reported as far as we know. In this study, the effect of topically applied bethamethasone-17-valerate ointment (BV) on histamine and serotonin-induced skin reactions such as flare and itch as well as spontaneous itch, allodynia and skin conditions was evaluated

in patients with atopic dermatitis. We also investigated quantitative change of nerve fibers and receptor expressions after the treatment by means of immunohistochemical staining and quantitative PCR with biopsy specimens obtained from patients and healthy volunteers. We observed increased expression of histamine receptors in the mRNA level in the skin lesion of patients, which did not change significantly after treatment, although histamine-induced itch decreased significantly. This finding indicates the possibility of change in receptor function rather than in receptor number after treatment.

PP33 NOTALGIA PARESTHETICA: A TWO-COHORT-STUDY IN BRAZIL AND GERMANY IN 65 PATIENTS

Timo Huesmann; Paulo R. Cunha; Mario Huesmann; Tiago Pina Zanelato; Ngoc Quan Phan; Gabriela Maria Abreu Gontijo; Nani Osada; Sonja Ständer

Department of Dermatology, University Hospital Münster, Germany

Notalgia paresthetica is a rare form of neuropathic pruritus at the back. The aim of this retrospective two-center study was to describe the clinical, histological and radiological results in a consecutive collective. A total of 65 patients (49 f, 16 m; mean 56.2 years) were examined. Notalgia paresthetica was localized in 56.9% of patients in the upper left quadrant, in 56.9% in the upper right quadrant, in 10.8% in the lower right quadrant, and in 16.9% in the lower left quadrant. Skin investigation showed in 42 patients (64.6%) scratch lesions, in 52 patients (80.0%) a hyperpigmentation. Only 4 patients (6.2%) had no skin lesions. Histologically, the presence of epidermal single cell necrosis (36.9%), epidermal hyperpigmentation (40.0%), dermal hyperpigmentation (43.0%), amyloid (6.1%) and the absence of any abnormal findings (3.1%) were found. The intraepidermal nerve fiber density was significantly ($p < 0.05$) lower in the pruritic than in the non-lesional area. Radiological examinations showed in 32.3% of patients a spinal stenosis. In 15.7% of patients only, localization of stenosis correlated with the dermatomal localization of pruritus. The significant reduction of the intraepidermal nerve fibers suggests that a damage of the peripheral nerves is a more important factor in notalgia paresthetica than spinal changes.

PP34 THE IMPORTANCE OF PRURITUS IN LICHEN PLANUS

Adam Reich; Kalina Welz-Kubiak

Department of Dermatology, Venereology and Allergology, Wrocław Medical University, Poland

Pruritus is one of the major features of lichen planus (LP) and stress is considered as an important pathogenic factor of LP. Our objective was to evaluate relationship between stress and itching in LP and the influence of pruritus on quality of life (QoL). Forty-two consecutive patients (women/men 3:1) with LP were enrolled. A specially designed questionnaire was completed based on anamnesis and physical examination. VAS and the pruritus questionnaire were used for pruritus assessment. Each subject completed the DLQI questionnaire. Stressful life events within one month before skin lesions appearance were identified and assessed with five degree self-assessment scale. The mean severity of itching at the moment of examination was

3.0±2.7 points, and at the most intensive pruritus in the past (Vmax) 7.6±2.3 points. No correlation was found between the stress severity and itch intensity ($p>0.05$). Severity of itching strongly influenced QoL in LP (DLQI and VASmax.: $\rho=0.36$; $p=0.02$; DLQI and itch questionnaire: $\rho=0.69$; $p<0.001$). Moreover, itching was mentioned by 69% of patients as the most bothersome symptom of LP, followed by the presence of skin changes (45.2% patients). Stress seems not to play important role in modulating pruritus in LP. Itching severity strongly influences the QoL of LP patients.

PP35 LESIONAL AND NONLESIONAL PRURIGO NODULARIS SKIN SHOWS REDUCED INTRAEPIDERMAL NERVE FIBER DENSITY: A SIGN OF SUBCLINICAL CUTANEOUS NEUROPATHY?

Britta Schuhknecht; Martin Marziniak; Andrea Wissel; Ngoc Quan Phan; Sonja Ständer
Department of Dermatology, University Hospital Münster, Germany

Prurigo nodularis (PN) shows increased numbers of dermal nerve fibers. Investigation of epidermal nerves was pending as of yet. Biopsies taken from lesional, interlesional and non-lesional skin of 58 PN patients of diverse origin were immunostained for protein gene product (PGP) 9.5. The intraepidermal nerve fiber (IENF) density per millimeter was determined and compared in 20 healthy volunteers. All biopsies showed significantly decreased IENF density ($p<0.001$) regardless of patients' age, origin of PN, intensity or quality of pruritus. Lowest levels of IENF were found in lesional skin (mean 4.638 IENF/mm), followed by interlesional (mean 5.156 IENF/mm) and nonlesional (mean 7.86 IENF/mm) skin as compared to normal skin of healthy volunteer controls (mean 12.2 IENF/mm). Hypoplasia of epidermal sensory nerves in lesional and interlesional skin independently of clinical parameters is a new finding in PN and suggests involvement of epidermal nerves in PN pathophysiology. It cannot be ruled out that reduced IENF is due to repeated scratching. However, the presence of hypoplasia in nonlesional PN skin suggests presence of a subclinical small fiber neuropathy.

PP36 AN INTERNET WEB-BASED QUESTIONNAIRE SURVEY ON PRURITUS OF PATIENTS WITH ATOPIC DERMATITIS IN DAILY LIFE

Satoshi Takeuchi; Junna Oba; Masutaka Furue
Department of Dermatology, Kyushu University Hospital, Japan

Background: Controlling pruritus and scratching is important in the treatment of atopic dermatitis (AD) because scratching exacerbates dermatitis. It is therefore reasonable for clinicians to know occasions causing pruritus in daily life of AD for better communication and disease control. **Methods and Patients:** We conducted an internet web-based questionnaire survey on pruritus in daily life in 503 patients with AD (female:male = 346:157) who visited our open accessible, patient-oriented educational website for AD and its treatment from October 2007 to February 2008. **Results:** In the survey, 52.3% of the responders suffered from recent unendurable daytime pruritus, and 73.2% of the responders experienced predicament sleeping caused by pruritus. Occasions

of sweating, bathing, wearing synthetic fiber-, wool- or hemp-made clothes, and climbing under covers often cause pruritus in the patients, and patients tend to feel pruritus particularly when they are nervous, displeased, busy, or rather vacant and free by contraries. Topical corticosteroids and emollients were immediately potent after application whereas tacrolimus and oral antihistamins tend to act slower in controlling pruritus of AD. **Conclusions:** This survey visualized current occasions of feeling pruritus of AD in daily life and may help to better communicate with patients and give patient instructions in daily clinic.

PP37 PLATELET ACTIVATION AS POSSIBLE INDICATOR OF DISEASE ACTIVITY IN CHRONIC URTICARIA: LINK WITH BLOOD COAGULATION AND MAST CELL DEGRANULATION

Ichiro Katayama; Yori-hisa Kotobuki; Hiroyuki Murota; Shun Kitaba
Department of Dermatology, Graduate School of Medicine, Osaka University, Japan

Purpose: It has been growing attention that blood coagulation cascade is activated during the urticarial attack. Elevated plasma D-Dimer and prothrombin fragment 1+2. Final product of coagulation cascade, thrombin has been thought to be one candidate to induce mast cell degranulation as well as complement fragment or PAF. However, involvement of platelet in urticaria is poorly investigated. **Patient and Method:** In this study, we studied the relationship of plasma level of platelet factor IV, β thromboglobulin, D-Dimer, prothrombin Fr. 1+2 and disease activity of 23 patients with chronic urticaria. **Results:** Elevated plasma level of platelet factor IV, (13/23) and β thromboglobulin (15/23) were observed in the patients with chronic urticaria and returned to normal level after the usual anti-histamine therapy. Relapse of platelet activation was observed with recurrence of urticaria. Some cases showed clinical response to anti-platelet drug. **Conclusion:** Platelet activation was thought to be possible disease activity indicator in chronic urticaria. Platelet-derived factor with or without blood coagulation products might induce mast cell degranulation in chronic urticaria.

PP38 ONE THIRD OF DERMATOLOGICAL OUTPATIENTS IN A PRIVATE PRACTICE SUFFER FROM CHRONIC PRURITUS: A ONE-WEEK-SURVEY IN A CONSECUTIVE COHORT

Merle Pilz; Sonja Ständer; Hartmut F. Ständer
Department of Dermatology, University of Münster, Germany

The frequency of pruritus in dermatological patients is unknown. To investigate this, 385 patients with dermatological diseases (178 males, 207 females; mean age 45.7 years; SD 22.7 years; median, 47 years) presenting within one week in a private practice in a rural area were asked to fill in a pruritus questionnaire. Forty-eight patients refused the participation. Among the remaining 337 patients, 124 patients (36.8%) had pruritus. 112 patients (90.3%; 33.2% of all patients) had chronic pruritus. 78.2% stated that the symptom is frequently to continuously present during day and night time. 33% of patients experienced moderate to severe impairment of the quality of life while 51.6% of patients feel a moderately and high emotional burden. Sleep loss was reported by 27.5%. Only 62.9% searched dermatological advice

because of the symptoms. 54.0% patients had consulted a GP before. 73.4% had an antipruritic pretreatment as follows: 26.6% used topical and 3.2% systemic OTC measures while 56.5% had prescribed topical and 10.5% systemic therapies. In summary, chronic pruritus is frequent among dermatological patients. Among these patients, the emotional burden is higher than the loss of sleep or impairment of the quality of life. Interestingly, 54% consulted a GP before and 73% had a pretreatment.

PP39 NEW DATA ON THE VALIDATION OF VAS AND NRS IN PRURITUS ASSESSMENT: MINIMAL CLINICALLY IMPORTANT DIFFERENCE AND ITCH FREQUENCY MEASUREMENT

Adam Reich; Jowita Halupczok; Małgorzata Ramus; Sonja Ständer; Jacek Szepietowski
Department of Dermatology, Venereology and Allergology, Wrocław Medical University, Poland

Introduction: Objective measurement of pruritus still remains an important clinical issue. *Objective:* The aim of this study was to determine the minimal clinically important difference (MCID) for VAS and NRS, and to estimate the most convenient pruritus assessment frequency. *Materials and Methods:* Fifty-seven inpatients with dermatological pruritus were recruited. All patients were asked to assess their pruritus with VAS, NRS and VRS in various clinical settings. *Results:* The mean change of VAS and NRS was 3.0 ± 2.2 and 3.0 ± 2.0 if pruritus improved; 2.5 ± 1.8 and 2.7 ± 1.5 if was the same, 2.0 ± 1.5 and 2.0 ± 1.5 , if got worse. Twice and trice daily assessment showed higher internal consistency than once daily pruritus measurement (Cronbach- α coefficient: VAS: 0.97, 0.96 and 0.91; NRS: 0.97, 0.97 and 0.92, respectively). Twice daily assessment showed the highest correlation with the global pruritus estimation: VAS: 1x/day: $\rho=0.33$, 2x/day: $\rho=0.47$, 3x/day: $\rho=0.12$; NRS: 1x/day: $\rho=0.34$, 2x/day: $\rho=0.49$, 3x/day: $\rho=0.16$. *Conclusions:* Based on the achieved results we assumed that the MCID for VAS and NRS in pruritus assessment depends on the direction of change and is equal to 3.0 points, if pruritus improved, and 2.0 points, if it becomes worse. Twice daily assessment of itch severity seems to be the most reliable frequency of pruritus evaluation.

PP40 DESIGN OF TOPICAL COOLING AGENTS FOR ITCH

Edward Wei
University of California, Berkeley, USA

Menthol and cooling by abstraction of heat relieves itch (Patel and Yosipovitch, *Skin Ther Letter* 2010; 15: 5–9). This observation serves as a rationale for study of coolants for pruritus. Here, many chemicals were screened on philtrum skin by topical application and measuring coolness intensity and duration. The goal was to find substances that elicit refreshing cool for at least several hours, are easy to formulate for target delivery, and have potency and reasonable safety profile. Icilin, a known cooling agent, dropped out of contention because it is difficult to formulate and does not readily penetrate keratinized skin. Several N-alkylcarbonyl amino acid esters showed promise, the primary candidate being p-menthoyl-D-Ala-O-n-propyl ester (Av-27). Av-27, 5 mg/ml in Aquaphor[®] ointment or propanediol, applied to philtrum skin will produce cooling for 1.5 to 1.8 h

at a dose of ~ 0.015 mg/cm². When overt cooling disappeared, antipruritic action is still prolonged. The TRP-M8 ion channel is linked to cooling and alcohols interfere with receptor activation. Remarkably, it was found that, among the standard alcohols used for dermatological formulations, the R-enantiomer of 1,2-propanediol solvent exerted the least degree of interference with cooling sensations.

MEDICAL CARE OF CHRONIC PRURITUS PATIENTS: HOW TO EFFICIENTLY COLLECT PATIENT REPORTED OUTCOMES

Fleur Fritz; Ngoc Quan Phan; Markus Riek; Bernhard Breil; Matthias Augustin; Martin Dugas; Sonja Ständer
Institute of Medical Informatics, University Hospital Münster, Germany

Information about quality of life is valuable for physicians, patients and researchers. However, the documentation during routine medical care is not common. We aimed to develop an efficient method to collect patient reported outcomes (PRO) data within the electronic health record (EHR) and make it available for secondary use. Three relevant questionnaires for pruritus patients (DLQI, HADS and VAS) were implemented in the local hospital information system. A web-based application was developed to allow patients to complete the questionnaires themselves, using an iPad. Data is then imported into the EHR. PROs are now regularly documented and are available in the EHR for purposes of treatment, communication and research. For example, the overview of the DLQI during the course of treatment is now visible and high HADS scores lead to request forms for psychosomatic consultation. In the pruritus department some 200 forms are filled in per month resulting in 78% completeness of forms. Data quality is high by checking the number of answered questions during completion and using automatic score calculations. For research questions accumulated data can be exported in an excel format. Documenting QoL in the EHR is feasible, clinically accepted and provides data for medical treatment and clinical research.

CORRELATION OF ITCH INTENSITY WITH QUALITY OF LIFE, ANXIETY AND DEPRESSION

Fleur Fritz; Ngoc Quan Phan; Martin Dugas; Matthias Augustin; Sonja Ständer
Institute of Medical Informatics, University Hospital Münster, Germany

VAS is the most commonly used tool for the assessment of itch intensity. The association of VAS with quality of life, depression and anxiety parameters is pending. During one year (February 2010 until March 2011) 1,524 patients with chronic pruritus (623/41% male, 901/59% female; age 9–94 years with mean 60 years, SD 15 years) completed questionnaires regarding 100 mm VAS, DLQI and HADS. For all four parameters (VAS, DLQI, HADS-A, HADS-D) the scores were grouped into four severity classes. The association of (grouped and non-grouped) VAS with DLQI, HADS-A and HADS-D was evaluated using the Chi-square and Kruskal-Wallis test. Both tests showed a significant association of VAS with DLQI, HADS-A and HADS-D, respectively ($p < 0.0005$). A cross tabulation of grouped data showed that a low VAS was strongly associated with low DLQI

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and HADS scores (groups 1 and 2). DLQI and HADS scores in groups 3 and 4 (i.e. high and extreme severity) coincided with (highest) VAS to some degree, although not equally well. Highest DLQI and HADS scores were frequently associated with intermediate VAS in groups 2 and 3. Itch intensity assessed using VAS correlated with quality of life as well as with anxiety and depression.

PP43 DERMATOPHYTIC DISEASE AND FIERCE PRURITUS: ABOUT THREE OBSERVATIONS

Boudghene Stambouli Omar

Department of Dermatology, Faculty of Medicine, University Aboubakr Belkaid Tlemcen, Algeria

Dermatophytic disease (DD) is a chronic visceral cutaneous dermatophytosis caused by dermatophytes ordinary crossing the skin barrier. We present three cases of dermatophytic disease (two males and one female presenting previously unreported giant cutaneous horns. A squamous erythroderma. Lichenified in some parts with a fierce pruritus. Multiple papulonodules, especially at the level of the trunk, a partial alopecia of the body hair and scalp which is squamous and presents purulent and ulcerated nodosities, a complete onychomycodystrophia. A polyadenopathy with important and fistulized ganglions on the neck, armpits and groins. *Trichophyton violaceum* is isolated from superficial samples (squames, nails and hair) and deep samples (nodules and adenopathies) (for two patients) and *Trichophyton rubrum* is isolated (for one patient). The DD remains a disease with a limited prognostic in spite of the introduction of new anti-fungal therapies (imidazole derivatives, terbinafin) with an immuno-stimulating purpose (transfer factor tried by hironaga, interferon). Is the decrease of the cellular immunity against the dermaophytes transmitted in an autosomic recessive way, or is it secondary to the dermatophytic infection which occurs on a genetically predisposed field?

PP44 STUDY ON PROPHYLACTIC IMPACT OF ONDANSETRON IV ON INTRATHECAL FENTANYL-INDUCED PRURITUS

Sayed Saed Jahanbakhsh; Bazyar Soha

Anesthesia Department of Emam-Reza Hospital, Mashhad University of Medical Sciences, Iran

Introduction: Adding opioids to local anesthetic solutions leads to enhanced anesthesia and provide postoperative analgesia. Spinal opioids have some side effects, though. One of them is pruritus. Ondansetron (5HT₃-receptors agonist) has whelming effect on itching. *Objectives:* We designed a randomized, double-blinded, placebo-controlled study to evaluate prophylactic impact of ondansetron (IV) on intrathecal fentanyl-induced pruritus. *Method:* 207 ASA I-II-III patients candidated for pelvic or lower limb operations had undergone spinal anesthesia (10–15 mg hyperbaric bupivacain and 25 µg fentanyl intrathecal) and were divided randomly into two groups: Case (ondansetron 8 mg IV) and Control (normal-salin 2cc IV). Systolic blood pressure, pulse rate and side effects were documented in 5 min, 10 min, 30 min, 60 min and every one hour till 6 h after operation. Patients were asked about existence, severity and site of pruritus 2 and 6 h after operation. *Results:* Incidence and severity of pruritus

were significantly lower in ondansetron group. The incidence of PONV in placebo group was higher ($p < 0.05$). The incidence of other side effects were the same in both group. *Conclusion:* Ondansetron reduces the incidence and severity of interathecal fentanyl-induced pruritus (specially in dermatoms T6-L1) and PONV. However, it makes no change in systolic blood pressure, pulse rate, block time, painless duration and incidence of urinary retention and backache.

PP45 VALIDATION OF INFRARED THERMOGRAPHY IN SEROTONIN-INDUCED ITCH MODEL IN RATS

Yousef Jasemian; Parisa Gazerani; Frederik Dagnaes-Hansen
Department of Medical Microbiology and Immunology, Aarhus University, Denmark

The number of scratching bouts is generally used as a standard method in animal models of itch. The aim of the present study was to validate the application of infrared thermography (IR-Th) in a serotonin-induced itch model in rats. Adult Sprague-Dawley male rats ($n = 24$) were used in 3 consecutive experiments. The first experiment evaluated vasomotor response (IR-Th) and scratching behavior (number of bouts) induced by intradermal serotonin (10 µl, 2%). Isotonic saline (control: 10 µl, 0.9%) and Methysergide (antagonist: 10 µl, 0.047 mg/ml) were used. The second experiment evaluated the dose-response effect of intradermal serotonin (1%, 2% and 4%) on local temperature. The third experiment evaluated the anesthetized rats to test the local vasomotor responses in absent of scratching. Serotonin elicited significant scratching and lowered the local temperature at the site of injection. A dose-response relationship of serotonin and local temperature changes was found by IR-Th. There was a significant negative correlation between temperature and number of scratching bouts. Vasoregulation at the site of serotonin injection occurred in the absent of scratching reflexes. In conclusion, IR-Th is a reliable, non-invasive, and objective method for assessment of serotonin-induced itch model in rat. This method may prove benefits in studying pruritus and antipruritic agents.

PP46 EPIDEMIOLOGY OF SCABIES TO AKRAM HOSPITAL, ABOUT 49 CASES IN KINSHASA/DRC

Muteba Baseke; Mangili Aniboti

University Clinics, University of Kinshasa, Republic of Congo

Introduction: Scabies is a contagious skin disease cosmopolitan and has an increasing impact in the world. It is caused by a mite, *Sarcoptes scabiei*, mandatory human parasite living in the epidermis, where he dug furrows in the stratum corneum. *Objectives:* To determine: The prevalence of scabies, scabies The distribution according to: age and sex. *Methods:* Retrospective study over a period of 2 years from January 2009 to January 2011 Akram hospital centers. Data were entered on Excel 2007, SPSS Windows version 13 was used for analysis. *Results:* Forty-nine cases of scabies have been reported, 384 patients with all kinds of skin diseases were recorded representing an incidence of 12.7%, 57% are female and 43% male; patients aged 24–47 years are most affected with 63.2%. *Conclusion:* Scabies appears as a major health problem in Kinshasa with a frequency of 12.7% of dermatoses with a predilection for subjects aged 24 to 47 years or 63%.

PP47 GRANZYME A AND PROTEINASE-ACTIVATED RECEPTOR 2 ARE INVOLVED IN THE INDUCTION OF ITCH-ASSOCIATED RESPONSES TO MOSQUITO ALLERGY IN MICE

Tsugunobu Andoh; Tasuku Akiyama; Akihisa Enokida; Yasushi Kuraishi

Department of Applied Pharmacology, Graduate School of Medicine and Pharmaceutical Sciences, University of Toyama, Toyama, Japan

We have shown that itch of mosquito allergy is caused by histamine-independent mechanisms and involves CD4⁺ T cells increased in the skin of sensitized mice. Considering that protease and proteinase-activated receptor (PAR) are involved in itch, this study investigated whether proteinase and PAR, especially PAR2, would be involved in itch of mosquito allergy in mice. The serine proteinase inhibitors nafamostat mesilate and 4-(2-aminoethyl)benzenesulfonyl fluoride hydrochloride attenuated mosquito allergy-induced scratching. The peptidic PAR2 antagonist FSLLY-NH₂ and anti-PAR2 antibody also suppressed the allergic scratching. Challenge with mosquito allergens released serine proteinase(s) in the skin of sensitized mice. CD4⁺ T cells isolated from the skin of sensitized mice expressed the serine proteinase granzyme A, but not granzyme B and C. An intradermal injection of granzyme A elicited scratching in naive mice, which was inhibited by anti-PAR2 antibody. These results suggest that mosquito allergy-induced itch is mediated at least partly by granzyme A secreted from CD4⁺ T cells and PAR2 receptors.

PP48 THYMIC STROMAL LYMPHOPOIETIN AND TUMOR NECROSIS FACTOR-ALPHA REDUCES THE PRODUCTION OF SEMAPHORIN 3A IN CULTURED HUMAN EPIDERMAL KERATINOCYTES

Suhandy Tenggara; Mitsutoshi Tominaga; Atsuko Kamo; Osamu Negi; Kenichi Taneda; Kenji Takamori
Institute for Environmental and Gender Specific Medicine, Juntendo University Graduate School of Medicine, Tokyo, Japan

Epidermal hyperinnervation are observed is atopic dermatitis (AD), suggesting that it is partly responsible for the intractable itch. The hyperinnervation is probably controlled by nerve elongation and repulsive factors, produced by keratinocytes. Semaphorin 3A (Sema3A) which is one of the nerve repulsion factors, is expressed in epidermal layer of normal human skin

while the expression is downregulated in AD patients. However, the downregulation mechanisms of Sema3A in AD are still unknown. *Objectives:* This study was performed to investigate the downregulation mechanisms of Sema3A in the atopic skin using cultured normal human epidermal keratinocytes (NHEK). *Method:* Effect of calcium concentrations and cytokines on expression of Sema3A proteins in cultured NHEK were examined by Western blot analysis. *Results:* The production of Sema3A proteins was increased during keratinocytes differentiation. Meanwhile, the Sema3A production in NHEK cultures in high-calcium serum free medium was decreased in the presence of thymic stromal lymphopoietin (TSLP) or tumor necrosis factor (TNF)-alpha. *Conclusion:* TSLP or TNF-alpha may lower nerve repulsive action in the epidermis of AD through downregulation of Sema3A production in the differentiated keratinocytes.

PRURITIC RESPONSES IN RAT TRIGEMINOTHALAMIC TRACT NEURONS: EVIDENCE AGAINST AN ITCH-SPECIFIC PATHWAY

Hannah R. Moser, Glenn J. Giesler Jr.

Department of Neuroscience, University of Minnesota, Minneapolis, USA

In rodents, intradermal cheek injection of pruritogens or algogens elicits hindlimb scratching or forelimb wiping, respectively, indicating a difference in the way these types of information are processed by the nervous system. We hypothesize that the trigeminothalamic tract is responsible for carrying information about facially-applied pruritogens to the brain. To test this, we have recorded from antidromically-identified trigeminothalamic tract neurons in the trigeminal nucleus caudalis of anesthetized rats during application of various pruritogens and algogens to facial receptive fields. A subset of trigeminothalamic tract cells shows a significant increase in firing rate upon injection of serotonin, which has been shown to elicit scratching when applied to the rat cheek. We have also identified a population of neurons which responds to histamine. Some cells respond to both serotonin and histamine, and all cells also respond to nociceptive mechanical, thermal, and/or chemical stimuli (e.g. capsaicin). To date, no cell has shown a significant response to cowhage, consistent with findings that rats do not exhibit significant scratching or wiping to this stimulus. Our data do not support the existence of an itch-specific pathway in the trigeminal system, suggesting a role for differential pattern or population coding.

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