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Sunday, October 15, 2017

Abstract #

1:30-3:30 PM	IFSI Board meeting	
5:00-5:20 PM	**OPENING CEREMONY**	
5:00-5:10 PM	Opening remarks *Jacek C. Szepietowski (Poland)*	
5:10-5:20 PM	Opening remarks IFSI: A successful society for the future *Earl Carstens (USA)*	
5:20-7:00 PM	**Plenary Session** *Chairs: Earl Carstens (USA); Elke Weisshaar (Germany)*	
5:20-5:50 PM	**Bernhard Lecture** Itchy dermatoses in the collection of Wroclaw moulages *Jacek C. Szepietowski (Poland)*	**OP1**
5:50-6:20 PM	**Kuraishi Lecture** Specificity or pattern: implications for clinical itch *Martin Schmelz (Germany)*	**OP2**
6:20-6:50 PM	**Neisser Lecture** Itch and psyche *Mohammad Jafferany (USA)*	**OP3**

Monday, October 16, 2017 AM

8:30-9:00 AM	**Morning session** Hot off the bench: Latest news by young investigators *Chairs: Hermann Handwerker (Germany); Adam Reich (Poland)*	
8:30-8:40 AM	The regulation of pruritus in psoriasis and atopic dermatitis – a possible role for CD26/DPPIV *Eriko Komiya-Suyama (Japan), Ryo Hatano, Haruna Otsuka, Takumi Itoh, Hiroto Yamazaki, Yasushi Suga, Utako Kimura, Taketo Yamada, Mitsutoshi Tominaga, Kenji Takamori, Kei Ohnuma, Chikao Morimoto*	**OP4**
8:40-8:50 AM	Chronic itch in hemodialysis patients: A follow-up study of GEHIS (German Epidemiological Hemodialysis-Itch Study) *Natalie Plewig (Germany), Robert Ofenloch, Thomas Mettang, Elke Weisshaar*	**OP5**
8:50-9:00 AM	Attentional bias to itch-related images in a clinical itch population *Michellie Young (UK), Melanie Burke, Donna Lloyd*	**OP6**
9:05-10:30 AM	**Plenary Session** Neurobiology of Itch *Chairs: Martin Steinhoff (Ireland); Matthias Ringkamp (USA);*	
9:05-09:25 AM	Effects of pruritogens and algogens on rostral ventromedial medullary (RVM) ON and OFF cells *T. Follansbee, Iodi Carstens (USA), Earl Carstens, T. Akiyama, M. Fujii, A. Davoodi, M. Nagamine*	**OP7**
9:25-09:45 AM	How scratching can take its "Toll" on itch, new insights into innate immune mechanisms of peripheral itch sensitisation *Ian McDonald (Ireland), Attila Szöllősi, Imre Szabó Lőrinc, Martin Steinhoff*	**OP8**
9:45-10:00 AM	Preferential activation of subtypes of polymodal nociceptive C-fibers in pigtail monkey following intradermal injection of β-alanine and bovine medullary protein 8-22 *Amanda H Klein, Timothy V Hartke, Matthew Wooten, Gang Wu, Matthias Ringkamp (USA)*	**OP9**
10:00-10:15 AM	Itch as a basic constituent of somatosensation: Evidence for multi-modal capacity of primary C-afferents *Behrang Sharif (Canada), Ariel Ase, Alfredo Ribeiro da Silva, Philippe Séguéla*	**OP10**
10:15-10:30 AM	Sulfated CCK8 induces alloknesis via spinal CCK2 receptor in mice *Mitsutoshi Tominaga (Japan), Fumiya Kusube, Kotaro Honda, Nobuaki Takahashi, Hisashi Naito, Fumiyuki Yamakura, Yasushi Suga, Yasuhiro Tomooka, Kenji Takamori*	**OP11**

11:00 AM-12:30 PM	**Concurrent I** Special Interest Groups (SIGs) *Chairs: Thomas Mettang (Germany); Jacek C. Szepietowski (Poland)*	
11:00-11:15 AM	SIG Sensitive Skin *Laurent Misery (France), Sonja Ständer, Jacek C. Szepietowski, Adam Reich, Joanna Wallengren, Andrea W.M. Evers, Kenji Takamori, Emilie Brenaut, Christelle Le Gal-Ianotto, Joachim Fluhr, Enzo Berardesca, Elke Weisshaar*	**OP12**
11:15-11:30 AM	SIG Scoring itch in clinical trials *Sonja Ständer (Germany), Matthias Augustin, Jacek C. Szepietowski*	**OP13**
11:30-11:45 AM	SIG Questionnaires *Elke Weisshaar (Germany), Jörg Kupfer, Antoinette van Laarhoven, Uwe Gieler, Masutaka Furue, Hidehisa Saeki, Andrea Evers, Gil Yosipovitch*	**OP14**
11:45 AM-12:00 PM	SIG Paraneoplastic itch *Elke Weisshaar (Germany), Thomas Mettang, Sonja Ständer, Frank Brennan, Hong Liang Tey, Gil Yosipovitch*	**OP15**
12:00-12:15 PM	SIG Uremic itch *Thomas Mettang (Germany), Jacek C. Szepietowski, Laurent Misery, Elke Weisshaar*	**OP16**
12:15-12:30 PM	**Discussion**	
11:00 AM-12:30 PM	**Concurrent II** Skin, inflammation and itch *Chairs: Brian Kim (USA); Laurent Misery (France)*	
11:00-11:15 AM	New insights into the pathophysiology of itch during ciguatera fish poisoning *Killian L'Herondelle (France), Laurent Misery, Christelle Le Gall-Ianotto, Réginald Philippe, Matthieu Talagas, Olivier Mignen, Richard Lewis, Raphaele Le Garrec*	**OP17**
11:15-11:30 AM	Intra- and extra-lesional sensitization for non-histaminergic and mechanically-evoked itch in atopic dermatitis *Hjalte Holm Andersen (Denmark), Jesper Elberling, Henrik Sølvsten, Gil Yosipovitch, Lars Arendt-Nielsen*	**OP18**
11:30-11:45 AM	Attenuated activation of endogenous glucocorticoids in keratinocytes induces alloknesis in atopic dermatitis via aberrant artemin production *Akira Matsumoto (Japan), Hiroyuki Murota, Mika Terao, Ichiro Katayama*	**OP19**
11:45 AM-12:00 PM	Neutrophil-somatosensory neuron crosstalk drives acute and chronic itch *Carolyn Walsh (USA), Jamie Schwendinger-Schreck, Jacques Deguine, Emily Brock, Rose Hill, Jessica Wei, Natalie Kelava Kucirek, Karsten Gronert, Greg Barton, Diana Bautista*	**OP20**
12:00-12:15 PM	Cutaneous 4-1BB/4-1BBL signaling induces severe skin inflammation and chronic itch *Stefan Tran, Verena Kupas, Kristian Holz, Marcus Maurer, Thomas A. Luger, Sonja Ständer, Karin Loser (Germany)*	**OP21**
12:15-12:30 PM	Sema3A expression is regulated by calcium/PKC/MAPK/AP-1 signaling axis in normal human epidermal keratinocytes *Yayoi Kamata (Japan), Yoshie Umehara, Azumi Sakaguchi, Yasushi Suga, Mitsutoshi Tominaga, Kenji Takamori*	**OP22**
12:30-2:00 PM	**Lunch and poster viewing I** *Chairs: Elke Weisshaar (Germany), Gil Yosipovitch (USA)*	
2:00-3:30 PM	**Plenary session** New antipruritic treatments *Chairs: Sonja Ständer (Germany); Alan Fleischer (USA)*	
2:00-2:15 PM	Randomized, double-blind, placebo-controlled phase 2 clinical trial of serlopitant effects on multiple measures of pruritus in patients with prurigo nodularis *Sonja Ständer (Germany), Paul Kwon, Thomas A. Luger*	**OP23**
2:15-2:30 PM	Serlopitant for treatment of chronic pruritus: results of a randomized, multicenter, double-blind, placebo-controlled phase 2 clinical trial *Gil Yospovitch (USA), Sonja Ständer, Matthew B. Kerby, James W. Larrick, Andrew J. Perlman, Edward F. Schnipper, Xiaoming Zhang, Jean Y. Tang, Thomas A. Luger, Martin Steinhoff*	**OP24**
2:30-2:45 PM	Recovery of peptidergic epidermal nerve fiber density by Tofacitinib in a mouse model of atopic dermatitis *Kristen Sanders (USA), Kento Sakai, Gil Yosipovitch, Tasuku Akiyama*	**OP25**

2:45-3:00 PM	Crisaborole ointment provides early relief of pruritus in two phase 3 clinical trials in patients with mild or moderate atopic dermatitis *Emma Guttman-Yasky, Gil Yosipovitch (USA), Dedee Murrell, Jon Hanifin*	**OP26**
3:00-3:10 PM	New insights into the anti-pruritic activity of the neurokinin-1 antagonist Aprepitant: partial activation of EGFR signaling in human keratinocytes as a mechanism for reducing erlotinib induced-pruritus *Shawn Kwatra (USA), Cory Nanni, Yevgeniy Semenov, Callie Roberts, Madison Krischak, Madan Kwatra*	**OP27**
3:10-3:20 PM	Efficacy of systemic treatments of psoriasis on pruritus: A systemic literature review and meta-analysis *Emilie Brenaut (France), Chloé Théréné, Thomas Barnetsche, Laurent Misery*	**OP28**
3:20-3:30 PM	Randomized, double-blind, placebo-controlled study of monoclonal anti-IgE antibody omalizumab in the management of pruritus in chronic spontaneous urticaria in the pediatric population. *Barnali Mitra (India), Biju Vasudevan, Reema Solanki, Debdeep Mitra*	**OP29**
4.00-5.30 PM	**Concurrent I** Methods in itch research (clinical) *Chairs: Andrea Evers (The Netherlands); Jörg Kupfer (Germany)*	
4.00-4.20 PM	How to alter placebo and nocebo effects in patients with chronic itch? *Andrea Evers (The Netherlands)*	**OP30**
4.20-4.40 PM	Methods in itch research: Arguments to improve standardization of research methods. *Joerg Kupfer (Germany), Uwe Gieler, Stephanie Kiupel, Christina Schut*	**OP31**
4.40-4.55 PM	Measuring pediatric itch severity: Does personal experience with chronic pruritus influence parent's ability to be proxies? *Grace Lee, Sandy François, Shelby Smith, Caitlin Haydek, James Roberts, Kuang-Ho Chen, Suephy Chen (USA)*	**OP32**
4.55-5.10 PM	Validation of the peak pruritus numerical rating scale: results from clinical studies of dupilumab in adult patients with moderate-to-severe atopic dermatitis *Gil Yosipovitch (USA), Matthew Reaney, Laurent Eckert, Lauren Nelson, Marci Clark, Marius Ardeleanu, Allen Radin, Abhijit Gadkari*	**OP33**
5.10-5.20 PM	12-Item Pruritus Severity Scale: development and validation of new itch severity questionnaire *Adam Reich (Poland), Agnieszka Bożek, Katarzyna Janiszewska, Jacek C. Szepietowski*	**OP34**
5.20-5.30 PM	Clinical bandings of Patient-Oriented Eczema Measure (POEM) scores among Japanese atopic dermatitis patients *Makiko Kido-Nakahara (Japan), Yumi Yasukochi, Takeshi Nakahara, Rie Kuroki, Tetsuya Koga, Toshihiko Mashino, Yuichi Kurihara, Masutaka Furue*	**OP35**
4.00-5.00 PM	**Concurrent II** Methods in itch research (experimental) *Chairs: Glenn Giesler (USA); Roman Rukwied (Germany)*	
4.00-4.15 PM	Methods in experimental itch research – an introduction *Roman Rukwied (Germany)*	**OP36**
4.15-4.30 PM	Re-innervated human skin explant as a model for *in vitro* studies on pruritus *Nicolas Lebonvallet (France), Christelle Le Gall-Ianotto, Cecilia Brun, Thierry Oddos, Laurent Misery*	**OP37**
4.30-4.45 PM	Pharmacological and histochemical characterization of a mouse model of chronic renal failure-associated pruritus *Tsugunobu Andoh (Japan), Shikai Li, Takahito Maki, Daisuke Uta, Yasushi Kuraishi*	**OP38**
4.45-5.00 PM	Depressive behavior manifested in NC/Tnd mice suffering from atopic dermatitis *Kenshiro Matsuda (Japan), Shuichi Yanai, Shogo Endo, Akane Tanaka, Hiroshi Matsuda*	**OP39**
5.00-5.20 PM	Methods in itch research (experimental) *Landon K Oetjen (USA)*	**OP40**
5:30-6:30 PM	**General Assembly Meeting**	
6:30-7:00 PM	**IFSI Board Meeting**	

Tuesday, October 17, 2017

8:30-9:00 AM	**Morning session** Hot off the bench: Latest news by young investigators *Chairs: Toshi Ebata (Japan); Andreas Kremer (Germany)*	
8:30-8:40 AM	Reversing nocebo effects on itch by conditioning with verbal suggestion *Danielle Bartels (The Netherlands), Antoinette van Laarhoven, Michiel Stroo, Kim Hijne Leiden University, Kaya Peerdeman, Rogier Donders, Peter van de Kerkhof, Andrea Evers*	**OP41**
8:40-8:50 AM	Amelioration of atopic-itch sensation in NC/Tnd mice by beta-pinene, the major component contained in distilled Alpinia intermedia Gagnep extracts *Yosuke Amagai (Japan), Tetsuyoshi Hamasaki, Yoshihiro Nomura, Hiroshi Matsuda, Akane Tanaka*	**OP42**
8:50-9:00 AM	Prolonged antipruritic effect of botulinum toxin type A on cowhage-induced itch *Leigh Nattkemper (USA)*	**OP43**
9:05-10:30	**Plenary Session** The wide range of clinical presentations of itch *Chairs: Kenji Takamori (Japan); Gil Yosipovitch (USA)*	
9:05-9:20 AM	An overview of treatment for opioid-induced itch *Kenji Takamori (Japan), Nobuaki Takahashi, Mitsutoshi Tominaga*	**OP44**
9:20-9:35 AM	Pruritus in patients with kidney transplants *Thomas Mettang (Germany), Elke Weisshaar, Jörg Kupfer*	**OP45**
9:35-9:50 AM	Urticaria and itch *Tabi Leslie (UK)*	**OP46**
9:50-10:00 AM	Essential thrombocythemia with aquagenic pruritus: an entity with more agressive clinical and biological profile at the diagnosis and a high morbidity during the follow-up. *Christelle Le Gall-Ianotto (France), Ronan Le Calloch, Aurélie Chauveau, Eric Lippert, Laurent Misery, Jean-Christophe Ianotto*	**OP47**
10:00-10:10 AM	Prevalence and clinical characteristics of pruritus in patients with cutaneous lupus erythematosus *Dominik Samotij (Poland), Justyna Szczęch, Emiliano Antiga, François Chasset, Aleksandra Dańczak-Pazdrowska, Adriana Polańska, Fukumi Furukawa, Carolyn Kushner, Hideo Hashizume, Mohammad Rafiqul Mowla, Aminul Islam, Minoru Hasegawa, Laurent Misery, Takaharu Ikeda, Zygmunt Adamski, Jacek C. Szepietowski, Victoria Werth, Adam Reich*	**OP48**
10:10-10:20 AM	Clinical characteristics of aquagenic pruritus in polycythemia vera *Edyta Lelonek (Poland), Łukasz Matusiak, Tomasz Wróbel, Jacek Kwiatkowski, Jacek C. Szepietowski*	**OP49**
10:20-10:30 AM	Clinical characteristics of pruritus in hidradenitis suppurativa patients. *Lukasz Matusiak (Poland), Justyna Szczęch, Karolina Kaaz, Edyta Lelonek, Jacek C. Szepietowski*	**OP50**
11:15-12:45 PM	**Concurrent I** Patients' perspectives and patient reported outcomes *Chairs: Christian Apfelbacher (Germany); Lidia Rudnicka (Poland)*	
11:15-11:30 AM	Patient-reported outcomes: an introduction *Christian Apfelbacher (Germany), Pauline Nelson*	**OP51**
11:30-11:45 AM	High levels of acting with awareness go along with low levels of itch catastrophizing: First results of a cross-sectional study in patients with atopic dermatitis *Christina Schut (Germany), Kerry Montgomery, Kjell Lüßmann, Andrew Thompson, Uwe Gieler, Christoph Zick, Jörg Kupfer*	**OP52**
11:45 AM-12:00 PM	Do placebo effects work when subjects know that they receive a placebo? Effects of open-label verbal suggestions on itch *Stefanie Meeuwis (The Netherlands), Henriët van Middendorp, Judy Veldhuijzen, Antoinette van Laarhoven, Jan De Houwer, Andrea Evers*	**OP53**
12:00-12:15 PM	A qualitative study to understand patients' perception of the severity of chronic pruritus and its impact on health-related quality of life *Jennifer Theunis, Clementine Nordon, Ylana Chalem, Massimiliano Orri, Jesus Cuervo, Gilles Berdeaux, Marie Auges, Valerie Mengeaud, Laurent Misery (France)*	**OP54**
12:15-12:30 PM	The burden of chronic itch-a questionnaire based evaluation of clinical characteristics, associated morbidity and treatment outcomes in a cohort of patients with chronic pruritus. *Ian McDonald (Ireland), Imre Szabó Lőrinc, Attila Szöllősi, Martin Steinhoff*	**OP55**

12:30-12:45 PM	European EADV network on assessment of severity and burden of Pruritus (PruNet): validation of instruments for itch intensity itch-impaired quality of life in pruritic dermatoses in Europe *Claudia Zeidler (Germany), Philipp Bruland, Claudia Riepe, Inaki Soto, Sabine Steinke, Michael Storck, Martin Dugas, Sonja Ständer*	**OP56**
11:15-12:45 PM	**Concurrent II** Itch and pain *Chairs: Sarah Ross (USA); Uli Zeilhofer (Switzerland)*	
11:15-11:35 AM	Spinal GABA-A receptor subtypes controlling itch *William T. Ralvenius, Elena Neumann, Mario A. Acuña, Martina Pagani, Dietmar Benke, Hendrik Wildner, Uwe Rudolph, Claude Favrot, Hanns Ulrich Zeilhofer (Switzerland)*	**OP57**
11:35-11:55 AM	Opposing effects of cervical spinal cold block on spinal itch and pain transmission *Earl Carstens (USA), Iodi Carstens, T. Akiyama, A. Davoodi, M. Nagamine*	**OP58**
11:55 AM-12:15 PM	Responses single thalamic units to pruriceptive and nociceptive stimuli in the rat. *Glenn Giesler (USA), Brett Lipshetz, Hai Truong, Sergey Khasabov, Donald Simone*	**OP59**
12:15-12:30 PM	Acupuncture for pain management in evidence-based medicine *Taqee Ansari Mohammed (India)*	**OP60**
12:30 AM-12:45 PM	Itch and pain influence on quality of life and sleep disturbances of hidradenitis suppurativa patients *Karolina Kaaz (Poland), Łukasz Matusiak, Jacek C. Szepetowski*	**OP61**
12:45 PM-2:00 PM	**Lunch and poster viewing II** *Chairs: Elke Weisshaar (Germany), Gil Yosipovitch (USA)*	
2:00-3:30 PM	**Concurrent I** Prurigo and other pruritic skin diseases *Chairs: Jeffrey Bernhard (USA); Joanna Wallengren (Sweden)*	
2:00-2:15 PM	Prurigo and other pruritic skin diseases. *Joanna Wallengren (Sweden)*	**OP62**
2:15-2:30 PM	Psoriatic itch 2017 *Jacek C. Szepietowski (Poland)*	**OP63**
2:30-2:45 PM	Novel definition, classification and terminology of chronic prurigo *Manuel Pedro Pereira (Germany), Sabine Steinke, Sonja Ständer*	**OP64**
2:45-3:00 PM	Aprepitant, a NK1-antagonist, administered for 16 weeks reduced itch and supported resolution of skin lesions in a patient with chronic prurigo *Franz J. Legat (Austria), Alexandra Gruber-Wackernagel, Angelika Hofer, Klara Waltner, Peter Wolf*	**OP65**
3:00-3:15 PM	Peripheral effects of targeting the neurokinin 1 receptor in chronic prurigo *Konstantin Agelopoulos (Germany), Falk Rülander, Julia Dangelmaier, Tobias Lotts, Karin Loser, Sonja Ständer*	**OP66**
3:15-3:30 PM	Neurophysiological studies on chronic prurigo *Manuel Pedro Pereira (Germany), Konstantin Agelopoulos, Esther Pogatzki-Zahn, Sonja Ständer*	**OP67**
2:00-3:30 PM	**Concurrent II** New receptors, channels and pathways for itch *Chairs: Ethan Lerner (USA); Yang-Gang Sun (China)*	
2:00-2:15 PM	Neural recruitment and Mrgpr activity are required for the development of a mouse model of atopic dermatitis *Ethan Lerner (USA), Tuanlian Luo, Ehsan Azimi, Vemuri Reddy, Sarina Elmariah*	**OP68**
2:15-2:30 PM	A central feedback neural circuit gates itch-scratching cycle *Yan Gang Sun (China)*	**OP69**
2:30-2:45 PM	TRPV1 regulates PAR-2-evoked intracellular Ca2+ release and inflammatory mediators production in differentiated keratinocytes *Olivier Gouin, Killian L'herondelle, Raphaele Le Garrec, Paul Buscaglia, Olivier Mignen, Christelle Le Gall-Ianotto, Virginie Buhé, Luc Lefeuvre, Laurent Misery, Nicolas Lebonvallet (France)*	**OP70**

2:45-3:00 PM	Spinal release of gastrin releasing peptide (GRP) is required for suprathreshold synaptic activation of GRP receptor (GRPR)-positive neurons *Martina Pagani (Switzerland)*	**OP71**
3:00-3:15 PM	Effects of burn size on post-burn itch and epidermal nerve innervation in mice *Kent Sakai (USA), Kristen Sanders, Gil Yosipovitch, Tasuku Akiyama*	**OP72**
3:15-3:30 PM	Possible role of satellite glial cell derived lipocalin-2 in the pathogenesis of atopic dermatitis *Nobuaki Takahashi (Japan), Mitsutoshi Tominaga, Ryohei Kosaka, Hironori Matsuda, Yasushi Suga, Kenji Takamori*	**OP73**
4:00-5:15 PM	**Concurrent I** Epidemiology of itch and quality of life *Chairs: Suphey Chen (USA); Andrey Lvov (Russia)*	
4:00-4:15 PM	Epidemiological study on the prevalence of itch in Japanese dementia patients *Toshiya Ebata (Japan), Lefkos Middleton, Ryoko Fukuda, Yoshimasa Takase, Nao Taniguchi, Kimitoshi Takemura, Didier LeClercq, Joelle Vaglio, Michel Poncet, Akihiko Ikoma*	**OP74**
4:15-4:30 PM	Pitfalls in pediatric self-reported pruritus severity and quality of life impact *Shelby Smith, Grace Lee, Sandy François, Alix Pijeaux, Kuang-Ho Chen, James Roberts, Suephy Chen (USA)*	**OP75**
4:30-4:45 PM	Quality of life in patients with chronic pruritus: from the conceptual model to items generation *Jennifer Theunis, Clementine Nordon, Ylana Chalem, Massimiliano Orri, Jesus Cuervo, Gilles Berdeaux, Marie Auges, Valerie Mengeaud, Laurent Misery (France)*	**OP76**
4:45-5:00 PM	Chronic itch (CI) in hemodialysis patients: A follow-up study of GEHIS (German Epidemiological Hemodialysis-Itch Study) on incidence and mortality of patients with CI *Katarzyna Grochulska (Germany), Robert Ofenloch, Thomas Mettang, Elke Weisshaar*	**OP77**
5:00-5:15 PM	Prevalence, characteristics and burden of pruritus in chronic dermatoses *Tomasz Hawro (Germany), Katarzyna Przybylowicz, André Ellrich, Max Spindler, Karsten Weller, Sabine Altrichter, Ulrich Reidel, Marcus Maurer, Martin Metz*	**OP78**
4:00-5:15 PM	**Concurrent II** New imaging techniques and other aspects of itch *Chairs: Clemens Forster (Germany); Ichiro Katayama (Japan)*	
4:00-4:15 PM	New methods in brain imaging techniques *Clemens Forster (Germany)*	**OP79**
4:15-4:30 PM	Three dimensional analysis of cutaneous nervous system in pruritic atopic dermatitis and psoriasis skin *Hong Liang Tey (Singapore)*	**OP80**
4:30-4:45 PM	Functional connectivity reveals altered activation of brain areas in chronic cholestatic pruritus *Andreas Kremer (Germany), Theresa Buchwald, Marcel Vetter, Arnd Dörfler, Clemens Forster*	**OP81**
4:45-4:55 PM	Itch Tracker: An application software turning wearable smart devices into a tool to measure nocturnal scratching *Akihiko Ikoma (Japan), Kimitoshi Takemura, Didier LeClercq, Toshiya Ebata*	**OP82**
4:55-5:05 PM	Changes in tactile sensitivity after viewing itch-related images *Michellie Young (UK), Melanie Burke, Donna Lloyd*	**OP83**
5:05-5:15 PM	Keratinocyte derived cortisol regulates itch evoked- allergic cutaneous inflammation *Ichiro Katayama (Japan), Akira Matsumoto, Saori Ochi, Mika Terao, Hiroyuki Murota*	**OP84**
5:20-6:30 PM	**Plenary Session** Future perspectives *Chairs: Earl Carstens (USA); Elke Weisshaar (Germany)*	
5:20-5:40 PM	Future perspectives in treatment of itch *Sonja Ständer (Germany)*	**OP85**
5:40-6:00 PM	Future perspectives in basic research of itch: Mrgpr receptors and the biology of itch *Xingzhong Dong (USA)*	**OP86**
6:00-6:30 PM	**CLOSING CEREMONY**	
6:00-6:15 PM	Handwerker Prize, poster prizes	
6:15-6:30 PM	Closing remarks *Jacek C. Szepietowski (Poland), Earl Carstens (USA)*	

LIST OF POSTERS

PP1: Myeloid GTP-Cyclohydrolase controls itch. Caroline Fischer, Katja Zschiebsch, Annett Häussler, Katrin Watschinger, Irmgard Tegeder

PP2: Histamine is involved in peripheral nerve elongation into epidermis of mice with itching induced by surfactant. Yoshihiro Inami, Atsushi Sato, Hiroshi Ohtsu, Yosuke Mano, Yasushi Kuraishi, Tsugunobu Andoh

PP3: The effects of the NK-1 receptor antagonist netupitant on itch models in mice. Girolamo Calo', Anna Rizzi, Chiara Ruzza, Claudio Pietra

PP4: Optogenetic activation of serotonergic (5-HT) neurons in the rostral ventromedial medulla (RVM) facilitates touch-evoked scratching in a diet-induced chronic dry skin mouse model. Masanori Fujii, Taylor Follansbee, Yuma Yasui, Susumu Ohya, Mirela Iodi Carstens, Earl Carstens

PP5: TRPV channels and post-burn pruritus. Hye One Kim, Yong Won Choi, Jee Hee Son, Yong Se Jo, Bo Young Jung, Chun Wook Park

PP6: Effect of [Leu11]-HK-1-derived peptides on scratching behavior in mice with chronic itch. Hideki Funahashi, Yu Miyahara, Ayaka Haruta-Tsukamoto, Rumi Nakayama-Naono, Toshikazu Nishimori, Yasushi Ishida

PP7: Serotonin receptor subtypes involved in calcium influx in cultured rat dorsal root ganglion neurons. Dan Domocos, Tudor Selescu, Earl Carstens, Mirela Iodi Carstens, Alexandru Babes

PP8: Resistance to serotonin-induced itch in cholestatic mice. Sattar Ostadhadi, Nazgol-Sadat Haddadi, Arash Foroutan, Ehsan Azimi, Sarina Elmariah,, Ahmad-Reza Dehpour

PP9: Global gene expression profiling in prurigo nodularis. Konstantin Agelopoulos, Tobias Lotts, Heike Conrad, Martin Dugas, Sonja Ständer

PP10: Role of cysteinyl leukotrienes and the Cysltr2 receptor in pruriception. Tiphaine Voisin, Amelie Bouvier, Yoshihide Kanaoka, K. Frank Austen, Isaac M. Chiu

PP11: Pharmacological evidence for the involvement of ATP-sensitive potassium channels in chloroquine-induced scratching behavior in mice. Nazgol-Sadat Haddadi, Sattar Ostadhadi, Arash Foroutan, Ahmad-Reza Dehpour

PP12: Modeling of itch sensitization for histaminergic and non-histaminergic itch? – Both UVB- and NGF-induced sensitization selectively increase pain, but not itch, elicited by histamine and cowhage. Silvia Lo Vecchio, Hjalte H. Andersen, Jesper Elberling, Lars Arendt-Nielsen

PP13: Expression Of ubiquitin C-terminal hydrolase L1/PGP9.5 in psoriasis. interplays between axonal nerve terminals snd epidermal keratinocytes in transmission of itch. Piotr Kupczyk, Marcin Hołysz, Mariusz Gajda, Adam Reich, Jacek C. Szepietowski

PP14: Measuring scratching and sleeping behavior besides pruritus intensity. development of a new, all-encompassing pruritus symptoms score – the "Itch-Controlled-Days Score". Sabine Steinke, Henk Wassmann, Frederik Braun, Kirstin Menne, Nani Osada, Laurie Burke, Christine Blome, Claudia Zeidler, Matthias Augustin, Sonja Ständer

PP15: The use of a dermocosmetic to manage pruritus related to skin diseases. an observational study. Sandrine Virassamynaik, Bernard Chadoutaud, Charlène Eydieux, Julie Riviere, Michèle Sayag

PP16: Itch as accompanying symptom in vitiligo. Elkham Karaev

PPI7: Prevalence and magnitude of itch in adolescent atopic dermatitis. Retrospective survey of first-year university students. Yosuke Okuda, Mayuko Tahara, Hiroyuki Murota, Ichiro Katayama, Keiko Yamauchi-Takihara

PP18: Is itch a symptom of cutaneous leishmaniasis? Tizita Yosef Kidane

PP19: Assessment of pruritus among patients with viral hepatitis B and C. Anna Biernacka, Dawid Niżyński, Małgorzata Inglot, Adam Reich

PP20: Descending inhibition of itch and pain in humans – experimental paradigms for assessing endogenous itch inhibition efficacy. Hjalte Holm Andersen, Antoinette van Laarhoven, Jesper Elberling, Lars Arendt-Nielsen

PP21: Pruritus in patients hospitalized in the Department of Dermatology, Jagiellonian University Medical College - a therapeutic approach. Magdalena Spałkowska, Agata Radko, Maciej Nowak, Małgorzata Werynowska, Anna Wojas-Pelc

PP22: Assessment of skin problems among patients with inflammatory bowel disease. is pruritus a major finding? Marta Idzior, Beata Jastrząb, Marta Laskowska, Katarzyna Neubauer, Adam Reich

PP23: Validity and reliability of various instruments for itch intensity measurement in patients with chronic pruritus. a prospective, multicenter study in Korea. Yong Hyun Jang, Gyeong-Hun Park, Byung-Soo Kim, Kap-sok Li, Chang Ook Park, Hye One Kim, Hei Sung Kim, Min Soo Jang, Kyung Duck Park, Eun Jin Doh, Dong Hun Lee, Yang Won Lee, Seong Jin Kim, Do Won Kim

PP24: Evaluation of the clinical characteristics of pruritus in patients with psoriasis using the Japanese version of the 5-D itch scale. Yozo Ishiuji, Yoshinori Umezawa, Norie Aizawa, Sanae Inokuchi, Akihiko Asahina, Koichi Yanaba, Toshiya Ebata, Hidemi Nakagawa

PP25: A Ugandan girl who had to endure thirteen years of itchy rashes without seeing a dermatologist. A case report from the new Gerold Jäger Skin Clinic in Kabale, Uganda. Leo Odongo

PP26: Itch in psoriasis – is age an important factor? Radomir Reszke, Rafał Białynicki-Birula, Jacek C. Szepietowski

PP27: Relationship between pruritus and serum lipocalin-2 in patients with psoriasis. Norie Aizawa, Yozo Ishiuji, Sanae Inokuchi, Koichi Yanaba, Yoshinori Umezawa, Akihiko Asahina, Nobuaki Takahashi, Mitsutoshi Tominaga, Kenji Takamori, Hidemi Nakagawa

PP28: Evaluation of the clinical characteristics of pruritus in patients with dermatomyositis using the Japanese version of the 5-D itch scale. Sanae Inokuchi, Yozo Ishiuji, Norie Aizawa, Koichi Yanaba, Toshiya Ebata, Hidemi Nakagawa

PP29: The need for linguistically and culturally adapted standard questionnaires to assess itch. Preliminary study and perspectives. Deok-Hee Kim-Dufor, Adèle Poulaliou, Laurent Misery

PP30: Detection of presence IgG1-IgG4, IgE, IgA, IgM, C3c, C1q and Fibrinogen deposits under direct immunofluorescence staining in eldery patients with pruritic dermatoses. Natalia Zdanowska, Agnieszka Owczarczyk-Saczonek, Joanna Czerwińska, Martyna Bieniek-Kobuszewska, Waldemar Placek

PP31: Validation of Japanese version of ItchyQoL in chronic pruritus patients. Toshiya Ebata, Yuko Hayakawa, Akishi Momose, Yuko Higaki, Suephy C. Chen

PP32: Differences in factors that drive pruritus quality of life between Asian Americans and other races. Kevin Luk, BS, Alix Pijeaux, BS, Kuang-Ho Chen, PhD, Glenda Wrenn, MD, MSHP, Cassandra Quave, PhD, Sarah Chisolm, MD, Seema Kini, MD, MSCR, Suephy Chen, MD, MS

PP33: Investigating racial disparities in pruritus quality of life in pediatric patients. Alix Pijeaux, Grace Lee, Shelby Smith, Sandy Francois, Kuang-Ho Chen, Suephy Chen

PP34: Does pre-scratching reduce the itch transmission? Ravi Chandra Kopparaju, Chih-Cheng Chen

PP35: The relationship between stress and itch in German university students. Stephanie Kiupel, Joerg Kupfer, Uwe Gieler, Sophia Kottlors, Gil Yosipovich, Christina Schut

PP36: Sumatriptan, the anti-migranous drug, suppresses serotonin-induced itch. The possible involvement of opioidergic system. Nazgol-Sadat Haddadi, Arash Foroutan, Sattar Ostadhadi, Saeed Shakiba, Khashayar Afshari, Maryam Daneshpazhooh, Ahmad-Reza Dehpour

PP37: Defining a Responder on the Peak Pruritus Numerical Rating Scale (NRS) in Patients With Moderate-to-severe atopic dermatitis. detailed analysis from randomized trials of dupilumab. Eric Simpson, Abhijit Gadkari, Laurent Eckert, Matthew Reaney, Marius Ardeleanu, Adeline Abbé, Michael Andria

PP38: Significance of IL-31 expression in skin and in serum in patomechanism of pruritus in CTCLs. Berenika Olszewska, Anton Żawrocki, Marta Malek, Jolanta Gleń, Magdalena Lange, Roman Nowicki, Małgorzata Sokołowska– Wojdyło

PP39: Sumatriptan attenuates CQ-induced scratching through NO-pathway. Khashayar Afshari, Nazgol-Sadat Haddadi, Sattar Ostadhadi, Saeed Shakiba, Arash Foroutan, Ahmad-Reza Dehpour

PP40: Reduction of pruritus in oncological patients receiving EGFRI therapy. Dominika Ragin, Katarzyna Nowacka, Barbara Zegarska

PP41: Lysophosphatidic acid induces itch and pain in humans depending on the mode of application. Margareta Miriam Düll, Lina Wurm, Vivien Ries, Martina Stengel, Peter W. Reeh, Michael J. Fischer, Barbara Namer, Andreas E. Kremer

PP42: Angiolymphoid hyperplasia with eosinophilia – a case of persistent pruritus of the scalp. Patrycja Gajda, Adriana Rakowska, Joanna Czuwara, Mariusz Sikora, Małgorzata Jabłońska

PP43: The problem of the itch in surgical oncology - do we know everything about the prevention, diagnosis and treatment? Katarzyna Nowacka, Maciej Nowacki, Wojciech Zegarski, Dominika Ragin, Barbara Zegarska

PP44: What are pruritogens of chronic kidney disease associated pruritus. Akishi Momose, Michihiro Yabe, Shigetoshi Chiba, Kenjirou Kumakawa, Yasauo Shiraiwa, Tomomi Kusumi, Hiroki Mizukami

PP45: The fatal course of chronic itch (CI). Generalized CI as a first sign of malignancy resembling paraneoplastic sensomotoric neuropathy. Minaya Beigi, Michael Haeberle, Andreas Gschwendtner, Elke Weisshaar

PP46: Functional changes in the cerebral networks for itch and burning pain. Clemens Forster, Verena Vierow, Miriam Rank, Ralf Ringler, Hermann O. Handwerker

PP47: Involvement of spinal microglia in the pathogenesis of imiquimod-induced psoriasis-like dermatitis model mice. Ryohei Kosaka, Mitsutoshi Tominaga, Nobuaki Takahashi, Hironori Matsuda, Yasuhiro Tomooka, Chiharu Nishiyama, Kenji Takamori

PP48: Antipruritic effect of thermal grill illusion on histamine-evoked itch in humans. Daniele Riccio, Mark Brendstrup Bødker, Justina Rusteikaitè, Janne Djernis Christensen, Mia Birkholm Lausten, Anders Lindby Nørgaard Hansen, Hjalte Holm Andersen, Laura Petrini, Lars Arendt-Nielsen, Parisa Gazerani

PP49: Secondary generalized brachioradial pruritus successfully treated with gabapentin. Małgorzata Małek, Laura von Dücker, Sonja Ständer, Dorothée Nashan, Hartmut Ständer

PP50: Morphological and molecular evolutional analyses of itch focused on the gastrin-releasing peptide system in mammals. Keiko Takanami, Keita Satoh, Kazuyoshi Murata, Tatsuya Sakamoto, Hirotaka Sakamoto

PP51: Brachioradial pruritus in a young Caucasian woman as a symptom of cervical radiculopathy. Justyna Szczęch, Adam Reich

PP52: A multinational cross-sectional study on the prevalence and clinical presentation of pruritus in cutaneous lupus erythematosus. an overview. Dominik Samotij, Justyna Szczęch, Emiliano Antiga, François Chasset, Aleksandra Dańczak-Pazdrowska, Fukumi Furukawa, Aminul Islam, Carolyn Kushner, Takaharu Ikeda, Minoru Hasegawa, Hideo Hashizume, Adriana Polańska, Laurent Misery, Mohammad Rafiqul Mowla, Aleksandra Lesiak, Zygmunt Adamski, Jacek C. Szepietowski, Daisuke Tsuruta, Victoria Werth, Adam Reich

PP53: Pilot study of venous ulcer itch. analysis of wound fluid and serum. Julia Paul, Stewart Graham

PP54: The Bibliometrics of Itch. 2017 Update. Melissa McEnery-Stonelake, M.D., Jeffrey D. Bernhard, M.D.

PP55: Treatment of severe atopic dermatitis with omalizumab. Experience of a Portuguese Immunoallergology Department . Rita Aquiar, Ana Mendes, Ana Célia, Fátima Duarte, Estrella Alonso, Amélia Spínola, Elisa Pedro, Manuel Pereira-Barbosa

PP56: Chronic prurigo masks the finding of a bullous pemphigoid. Caroline-Donata Forner, Jan Ehrchen, Claudia Zeidler, Sonja Ständer

PP57: Itch associated with hyperplastic papillomatous skin lesions complicated by squamous cell carcinoma in a patient with Netherton syndrome. Anna Waśkiel, Adriana Rakowska, Tomasz Demkow, Małgorzata Olszewska, Lidia Rudnicka

PP58: Properties of pruritus and related factors among elderly residents of Panti Werdha, public nursing homes in Indonesia. Dianis Wulan Sari, Takeo Minematsu, Mikako Yoshida, Abe Masatoshi, Hiromi Sanada

PP59: Expression of IL-31 in uraemic pruritus. Marta Pelc, Maria Kozioł, Jacek C. Szepietowski

PP60: Differentiated resistance training and exercise treatment for neuropathic itch - a preliminary study. Matthias Fischer, Elke Weisshaar

PP61. A study of pruritus in patients with psoriasis attending dermatology OPD of a tertiary care hospital. Asit Mittal, Manju Meena

PP62: Novel Microneedle Treatment for Keloids. Effects on lesional Volume, Pain and Itch. Hong Liang Tey, Colin Weixuan Tan

PP63: Medical Care of Patients with Chronic Pruritus in the Private Dermatological Practice in Germany – Possibilities and Limitations. Hartmut Ständer, Sonja Ständer

PP64: The burden of aquagenic pruritus in polycythemia vera. Edyta Lelonek, Łukasz Matusiak, Tomasz Wróbel, Jacek Kwiatkowski, Jacek C. Szepietowski

PP65: Endocannabinoid receptor 1 gene polymorphisms have no association with uremic pruritus. Monika Heisig, Łukasz Łaczmański, Adam Reich, Jacek C. Szepietowski

PP66: Mycosis fungoides as the cause of unspecified itching for 4 years. Anastasiia Titenko, Yulia Krinitsina, Viktoria Onipchenko, Vera Pahomova, Irina Sergeeva

PP67: Occupational aspects of scabies. Michael Häberle, Arno Rütten

PP68: Pruritus in patients with acute heart failure. Malgorzata Ponikowska, Jan Biegus, Robert Zymlinski, Jacek C. Szepietowski

PP69: Colonization of skin and mucous membranes by S. aureus in atopic dermatitis patients – is there a link with itch pathogenesis? Leszek Blicharz, Zbigniew Samochocki, Paulina Usarek

PP70: Itch and pain influence on quality of life of atopic dermatitis and psoriasis patients. Karolina Kaaz, Łukasz Matusiak, Jacek C. Szepietowski

PP71: Nodular prurigo as first manifestation of primary biliary cholangitis successfully treated with rifampin and sertraline. Piotr Parcheta, Piotr Stepien, Dorota Zarebska-Michaluk, Beata Krecisz

PP72: Itch in non-melanoma skin cancers. Iwona Chlebicka, Jacek C. Szepietowski

PP73: Gender Disparity in the Psychosocial Effect of Chronic Itch on Children. Sandy François, Grace Lee, Shelby Smith, Alix Pijeaux, Kuang-Ho Chen, James Roberts, Suephy Chen

PP74: Both narrowband-UVB and broadband-UVB are equally effective in reducing itch in chronic pruritus patients. Franz J. Legat, Angelika Hofer, Alexandra Gruber-Wackernagel, Franz Quehenberger, Klara Waltner, Peter Wolf

PP75: ItchyQol assessment in psoriasis vulgaris. Correlation analysis of patient baseline data from a randomized controlled trial (PSORITUS). Sonja Ständer, Karin Loser, Dieter Metze, Jürgen Zimmermann, Thomas A. Luger

PP76: Imperviousness to gender cartoon annotation in self reported pruritus outcomes. Suephy Chen, James Roberts

PP77: «Pseudoallergic» reactions on skin and mucous membrane. is it a psychosomatic phenomenon?. Andrey Lvov, Dmitry Romanov, Anastasia Tereshenko, Svetlana Bobko

PP78: A new tool for modelling stinging test *in vitro*. a comparative evaluation with *in vivo* results using a bacterial polysaccharide. Mehdi Sakka, Raphael Leschiera, Christelle Le Gall-Ianotto, Olivier Gouin, Kilian L'herondelle, Jean-Luc Philbé, Florent Yvergnaux, Thibaut Saguet, Jean-Luc Carré, Laurent Misery, Nicolas Lebonvallet

PP79: Early onset of antipruritic effects with serlopitant for chronic pruritus: post hoc analysis results from a randomized, multicenter, placebo-controlled phase 2 clinical trial: Sonja Ständer, Gil Yosipovitch, Joe Hirman, Paul Kwon

INVITED LECTURES

BERNHARD LECTURE

OP1

ITCHY DERMATOSES IN THE COLLECTION OF WROCLAW MOULAGES

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Itch is regarded as the most common symptom in dermatology. It could be find in many skin diseases, including infectious diseases as well as inflammatory. Wroclaw Department of Dermatology is famous because of its collection of dermatological moulages. During this prestigious Bernhard Lecture some examples of itchy skin diseases documented as moulages of the above mentioned collection will be presented. The use of wax for practical purposes has a long-lasting tradition dating to ancient times. Initially dermatological moulages were produced with the use of plaster moulds, probably because of their lower cost, but in time the need for better quality led to the use of beewax mixture. In the process of constructing the moulage the skin lesions were exactly reproduced by casting. Colour was the only subjective part. The history of Wroclaw moulages dates the times of Albert Neisser, the famous head of the Department of Dermatology (1882–1916). Keizo Dohi, a Japanese physician studing dermatology in Vienna, probably brought the technology of moulages to Wroclaw (Breslau). The vast majority of current collection of moulages was produced by Alfons Kröner who joined the Neisser's department in 1897. The last moulage was made Wroclaw in 1937. The moulages made by Alfons Kröner were considered the best thanks to accuracy. The only flaw was the yellowish tint, which seemed to be result of using poorer quality wax. The current collection of moulages contains of 323 exhibits. Among them there are sevaral dermatoses in which itch is a an important symptom: infections: tinea, impetigo, pruriens pyodermiae; inflammatory diseases: eczema, neurodermatitis, lichen simplex, atopic dermatitis, lichen planus, psoriasis; autoimmune dermatoses: blistering disease, scleroderma and other disorders: acne, Reclinghausen disease, skin cancers.

KURAISHI LECTURE

OP2

SPECIFICITY OR PATTERN: IMPLICATIONS FOR CLINICAL ITCH

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The main problem for the development of targeted therapy for chronic itch has been a lack of pathophysiologic concepts and identification of specific itch mediators. Recently, new major discoveries in the field of specific mediators and receptors of non-histaminergic itch were made. These include functional markers for primary pruriceptive afferent neurons in rodents (MrgA1, MrgC11, MrgD) and man (MrgX1, MrgD), peripheral mediators that are linked to the itch sensation (IL13, IL31, autotaxin, LPA, TSLP, Cathepsin S) and central transmitters specific for itch processing (B-type natriuretic peptide, gastrin releasing peptide). While most of these potential anti-pruritic targets were developed on the basis of itch-specific approaches along the lines of the specificity theory there are also targets common for nociceptors and pruriceptors such as NK1 antagonists or even sodium channel subtypes such as NaV1.7. Specific mediators for itch have been found in rodents based on the specificity of itch ("labeled line"). However, also nociceptors have a potential role in generating itch ("pattern theory"). Human studies are required to answer the question whether therapeutic targets in humans should be investigated primarily in nociceptors or in specific pruriceptors. While pain and itch behavior in animals can be differentiated operationally, patients report combined itch and pain sensations both in neuropathic pain and neuropathic itch conditions. As pain suppresses pruritus, their concurrent occurrence in patients is unexpected and may suggest common pathophysiological mechanisms of pain and itch processing. Thus, a key problem to be solved in chronic itch patient is the question whether activity in specific pruriceptors or certain patterns of activity in nociceptors is the underlying mechanism.

NEISSER LECTURE

OP3

ITCH AND PSYCHE

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Itch, also referred as pruritus is an unpleasant cutaneous sensation, provoking the desire to scratch. It is an unpleasant subjective sensation responsible for decreased quality of life in a variety of psychodermatological conditions. Comorbid psychiatric conditions including depression and anxiety are frequently associated with itch and scratch cycle. The reciprocal and intricate relationship between psych and itch has been widely studied. The neurobiology of itch involves the complexity of specific mediators, itch-related neuronal pathways and central processing of itch. The connection between itch and psych can be grouped under three headings: pruritic diseases with psychosocial sequel, pruritic diseases aggravated by psychosocial factors and psychiatric disorders causing pruritus. Itch and pain modulation go together in most circumstances and involves various substances including histamine, interleukins, protease-activated receptors, transient receptor potential receptors, opioids, and cannabinoids. The close interaction between keratinocytes and nerve endings modulating pain and itch also play a major role. Management of itch associated with psychosomatic component is directed at underlying cause and adopting a holistic approach to address not only dermatologic and somatosensory aspects but also the cognitive, emotional and psychosocial components. An integrated multidisciplinary team consisting of dermatologist, psychiatrist, psychologist, and social worker, is vital in addressing multifaceted aspects of pruritus.

HOT OFF THE BENCH: LATEST NEWS BY YOUNG INVESTIGATORS

OP4

THE REGULATION OF PRURITUS IN PSORIASIS AND ATOPIC DERMATITIS - A POSSIBLE ROLE FOR CD26/DPPIV

***Eriko Komiya-Suyama**, Ryo Hatano, Haruna Otsuka, Takumi Itoh, Hiroto Yamazaki, Yasushi Suga, Utako Kimura, Taketo Yamada, Mitsutoshi Tominaga, Kenji Takamori, Kei Ohnuma, Chikao Morimoto*

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Psoriasis and atopic dermatitis are chronic inflammatory skin diseases frequently accompanied by itching. Because of limited treatment options for this troublesome symptom, the development

of more effective treatment for pruritus is critically important. CD26 is a 110-kDa, type II transmembrane glycoprotein with known dipeptidyl peptidase IV (DPPIV) in its extracellular domain. CD26 is a T cell costimulatory molecule and plays an important role in T cell biology. In addition to cell surface antigen, a soluble form is present in sera with conservation with DPPIV enzyme activity (sCD26 or sDPPIV). It has been reported that expression levels of DPPIV in keratinocytes of psoriatic skin are increased. However, a mechanistic role of DPPIV enzyme has not yet been elucidated. The aim of this study was to evaluate the clinical significance and the molecular mechanisms of DPPIV enzyme activity in patients with pruritus of psoriasis and atopic dermatitis. We first analyzed levels of sCD26 protein and DPPIV enzyme activity in sera of patients, utilizing a house-made sandwich ELISA. Levels of sCD26 and DPPIV enzyme activity in sera were significantly increased in patients with psoriasis and atopic dermatitis compared to those of healthy normal adults. We next evaluated levels of itch-transmitting neuropeptides including substance-P (SP), which is a substrate for DPPIV enzyme, showing significant increase in sera of psoriasis and atopic dermatitis. Moreover, we found that truncated form of SP (SP5-11) cleaved by DPPIV was significantly increased in both patients. Furthermore, utilizing pruritus model induced by SP intradermal injection, scratching behavior was significantly decreased with treatment of a DPPIV inhibitor. Finally, utilizing Imiquimod-induced psoriasis model and mite extract-induced atopic dermatitis model, scratching behavior was significantly increased in DPPIV overexpressing-mice, meanwhile scratching behavior was significantly decreased with administration of a DPPIV inhibitor. Taken together, our present results study suggests that DPPIV enzyme activity plays an important role in pruritus via truncation of SP, and that regulation of DPPIV enzyme may provide a more treatment option for patients suffer from pruritus.

OP5
CHRONIC ITCH IN HEMODIALYSIS PATIENTS: A FOLLOW-UP STUDY OF GEHIS (GERMAN EPIDEMIOLOGICAL HEMODIALYSIS-ITCH STUDY)

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GEHIS (German Epidemiological Hemodialysis Itch Study) is a representative cross-sectional cohort started in 2013 and including 860 hemodialysis (HD) patients in 25 dialysis units in Germany. We recently showed 25.1% (*n*=217) of HD patients to suffer from current chronic itch (CI). Four years later, in 2017 we performed a follow-up study and contacted all CI patients again to investigate the persistence, course and characteristics of CI. Itching was assessed with the same patient questionnaire about current and previous CI (during the last 3 years), severity of CI (visual analogue scale, VAS). HRQOL (SF-12 questionnaire) and itch-related quality of life (ItchyQoL) were assessed. As this is an ongoing study, results are preliminary and refer to 9 dialysis units containing 212 HD patients being addressed so far. Of those who had previously reported CI (*n*=54), 14.8% (*n*=8) could not be interviewed (e.g. because they had moved to another place or because they were not on dialysis treatment anymore due to transplantation). The following results refer to 46 patients. 45.7% (*n*=21) of those had died in the meantime. Of the remaining 25 patients, 52.4% (*n*=13) were still suffering from CI having a mean age of 66.5 years (SD 11.9 years). First analyses including HRQOL and ItchyQol demonstrate a significant impairment in those still suffering from CI (*n*=13). We compared this group to those who newly acquired CI, lower scores indicating lower HRQOL in the physical subscale of SF-12 (27.9 vs. 37.9) were detected. First analyses of the severity show significantly higher scores in those still suffering from CI compared to those who newly acquired CI (VAS 3.32 vs. 2.88). These new data confirm CI to be a persistent and impairing symptom in hemodialysis patients.

OP6
ATTENTIONAL BIAS TO ITCH-RELATED IMAGES IN A CLINICAL ITCH POPULATION

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Itch-related images have been shown to induce Visually Evoked Itch (VEI) in both healthy and chronic itch populations, although differences in how the effect manifests have been found for the latter group. This study investigated whether these differences are reflected in an attentional bias towards itch images. We tested 30 clinical itch participants (self-reported eczema, psoriasis, etc.) and 30 healthy control participants, using an arrow probe reaction time task combined with eye tracking. Participants viewed pairs of itch and non-itch images for 2000 ms and then reported the direction of an arrow probe presented either congruently or incongruently with the itch image. Participants' reaction times were measured, as well as the direction, number, and duration of saccades towards the itch image. We found an attentional bias in reaction times for the clinical but not the healthy group; clinical participants responded faster on congruent trials, indicating that their attention was directed towards the itch images. Eye tracking also revealed that the clinical group made more saccades towards the itch images, spent longer looking at them, and were more likely to make their first saccade on each trial to the itch image. These effects appear to be primarily driven by images featuring skin damage (scratching, rashes etc.) compared to images featuring irritants. This indicates that VEI provoking images affect clinical groups differently to the healthy population. In clinical participants with a pre-existing propensity to experience itch, the response to viewing itch images may draw upon a top-down attentional mechanism, whereas the creation of VEI in healthy participants may be more reliant on a bottom-up effect with little early processing of the itch content. Understanding these differences will help to elucidate how psychological triggers can affect people with itchy skin conditions and perpetuate the itch-scratch cycle.

NEUROBIOLOGY OF ITCH

OP7
EFFECTS OF PRURITOGENS AND ALGOGENS ON ROSTRAL VENTROMEDIAL MEDULLARY (RVM) ON AND OFF CELLS

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RVM ON- and OFF cells are thought to facilitate and inhibit spinal nociceptive transmission, respectively. However, it is unknown how ON and OFF cells respond to pruritic stimuli or how they contribute to descending modulation of spinal itch signaling. In pentobarbital-anesthetized mice, single-unit recordings were made in RVM from ON and OFF cells identified by their respective increase or decrease in firing that occurred just prior to nocifensive hindlimb withdrawal elicited by paw pinch. Of RVM ON cells, 86% (24/28) were excited by intradermal (id) histamine, 50% by id chloroquine, and 76% by id capsaicin. All units also responded to a scratch stimulus applied adjacent to the hindpaw injection site. Most units were unresponsive to id injec-

tion of vehicle, but still responded to scratching. More variable effects were observed with OFF cells. Id histamine and scratching excited 50% while inhibiting or having no effect in the remainder. Id chloroquine was ineffective in 62% while exciting 15% and inhibiting 23%. Id capsaicin and scratching inhibited 64% while exciting 14% and having no effect in the remainder. These results indicate that ascending pruriceptive signals may activate RVM ON cells to initiate descending facilitation of spinal itch and pain transmission. The mainly inhibitory effect of capsaicin on OFF cells is consistent with decreased descending inhibition to facilitate spinal nociceptive transmission. The mixed effects of pruritogens on OFF cells suggests a more complex descending modulatory effect on spinal pruriceptive transmission that may include descending inhibition (by excitation of some OFF cells) that counteracts descending facilitation (by inhibition of OFF cells and excitation of ON cells).

OP8
HOW SCRATCHING CAN TAKE ITS "TOLL" ON ITCH, NEW INSIGHTS INTO INNATE IMMUNE MECHANISMS OF PERIPHERAL ITCH SENSITISATION

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Itch is the most common symptom in dermatology is associated with significant physical and psychological morbidity. Our understanding of itch however is still far from complete. Toll-like receptors (TLRs) are cellular sensors designed to recognize molecular danger signals associated with exogenous or endogenous threats. Recently TLR3 was found to be significant in the regulation of itch signaling in mice (Liu et al 2012). A detector of double stranded RNA, TLR3 acts as an innate biosensor of viral pathogens, but also responds to endogenous damage associated molecular patterns including RNA released from injured epidermal keratinocytes. We hypothesise that scratching, which leads to epidermal damage and the release of RNA from keratinocytes contributes to the peripheral sensitization of itch in humans via activation of TLR3. *Objective: Aim:* 1) Identify key itch mediators released from keratinocytes following activation of TLR3. 2) Evaluate the expression of TLR3 in chronically scratched skin of patients with nodular prurigo. *Methods:* Normal human epidermal keratinocytes (NHEKs) were treated with the synthetic ligand of TLR3, Poly(I:C) at different concentrations. Secretome analysis was performed at 4 and 24 hours using ELISA. Quantitative RT PCR was preformed to analyse mRNA expression from treated cells. The expression and quantitation of TLR3 in lesional, perilesional and healthy control skin was performed using immunofluorescence. *Results:* Stimulation of NHEKs with Poly (I:C) resulted in the release of IL-6 and Endothelin-1 (ET-1). RT-PCR showed increased mRNA levels of TLR3, TSLP and ET-1 following treatment. Immunofluoresence of skin showed significantly increased expression of TLR3 in the lesional skin of patients with nodular prurigo (mean VAS score 7.5), compared with perilesional (non-scratched) and healthy control skin. *Conclusions:* We have demonstrated that activation of TLR3 in NHEKs results in the release of ET-1. This important mediator of non histaminergic itch in humans known to be increased in lesional skin of nodular prurigo patients (Kido et al 2014). We also found significantly increased expression of TLR3 in lesional skin of nodular prurigo. Therefore TLR3, an innate biosensor may act as an important receptor in the itch-scratch-cycle, responding to injured, scratched epidermal keratinocytes, increasing its expression and triggering itch through ET-1, TSLP and other pro inflammatory cytokines (IL-6).

OP9
PREFERENTIAL ACTIVATION OF SUBTYPES OF POLYMODAL NOCICEPTIVE C-FIBERS IN PIGTAIL MONKEY FOLLOWING INTRADERMAL INJECTION OF B-ALANINE AND BOVINE MEDULLARY PROTEIN 8-22

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In human, intradermal administration of β-alanine (ALA) and bovine adrenal medullary protein 8-22 (BAM8-22) cause the sensation of itch. These pruritogens activate non-overlapping populations of murine DRG neurons that differ in their expression of mas-related G protein-coupled receptors (Mrgprs). In primate, orthologous genes for some Mrgs exist (MrgD-G), whereas others, designated as MrgX1-4, cannot be clearly assigned to any of the MrgA-C subfamilies described in mice. Currently, it is not known what types of cutaneous afferents in primate are activated by ALA, an MrgprD agonist, and BAM8-22, an agonist for murine MrgprC11 and human MrgprX1. Previously, we have shown that two types of heat responses are observed in cutaneous polymodal nociceptive C-fibers when their receptive fields (RF) are exposed to a stepped heat stimulus (49°C, 3s): a quick response (QCs) or a slow response (SCs), and that QC-fibers are preferentially activated by ALA. Whether polymodal nociceptors are activated by BAM8-22 and whether any fiber subclass is preferentially activated is currently not known. Neuronal activity of unmyelinated C fibers innervating the hairy skin was recorded in anaesthetized nonhuman male primates (Macaca nemestrina) using standard teased-fiber techniques. After assessing receptive properties of the afferent fiber under study, two blocks of intradermal injections (each 10 µl) were administered in random order at the RF: one block consisted of extracellular fluid (ECF, the solvent) followed by ALA (90 µg) and another block of BAM8-18 (the inactive truncated peptide, 1 µg) followed by BAM8-22 (1 µg). Neuronal activity was recorded for at least 5 minutes following each injection. We studied a total of 45 C fibers. All of 21SCs and 17/24 QCs responded to BAM8-22, but responses were about 3-fold larger in SCs than in QCs. Only 4/21 SCs but 23/24 QCs responded to ALA, and QC- responses were about 10-fold larger than in SCs. In SCs, responses to BAM8-22 were about 20-fold higher than those induced by ALA, whereas in QCs, responses to ALA were about 2-fold larger than responses to BAM8-22. These results show that QCs and SCs are preferentially activated by ALA and BAM8-22, respectively, and suggest that QCs encode ALA–induced sensations, whereas activity in QCs and SCs likely contributes to encode sensations produced by BAM8-22.

OP10
ITCH AS A BASIC CONSTITUENT OF SOMATOSENSATION: EVIDENCE FOR MULTI-MODAL CAPACITY OF PRIMARY C-AFFERENTS

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Undoubtedly, itch and pain are among the closest modalities of somatosensation. While itch can be described as an unpleasant sensation that leads to scratching behavior, pain is also describable as an unpleasant sensation with the distinction of eliciting withdrawal behavior. Despite significant anatomical and behavioral overlap of pruriception and nociception, the underlying neurophysiological

basis of itch and its relation to pain is still unclear. More specifically, the enigma of how the somatosensory system differentiates itch and pain sensations and triggers distinct fight or flight behaviors remains to be solved. There have been several theories proposed for this discrimination process and one of the most popular ones, in the past decade, is the "labeled line" or "specificity" theory. According to this theory, dedicated components of the somatosensory system, from the periphery to the brain, are specifically specialized for detection, transmission and perception of each sensory modality. Whether this theory can explain all aspects of itch and its discrimination from pain, is currently debated among the scientists studying somatosensory systems. To test the validity of the labeled line theory for itch, we took advantage of a described subpopulation of primary C-fiber pruriceptors that express MrgprA3, the receptor for the itch-inducing compound chloroquine. In order to be able to evaluate the effects of a wide variety of activation conditions, we took advantage of Cre-dependent optogenetic and chemogenetic actuators, selectively expressed on the surface of these MrgprA3+ neurons. Behavioral experiments were performed after complete validation of the heterologous actuators in dorsal root ganglia (DRG) and trigeminal ganglia (TG) neurons. In accordance with previously reported data, our behavioral studies show that chemogenetic activation of these neurons evokes stereotypical itch behavior rather than pain responses. Surprisingly, optical activation of these neurons through ChR2 predominantly induces pain responses and avoidance behaviors rather than scratching. Our results show that *in vivo* a single genetically-defined population of C-fibers can convey itch sensation in certain conditions and pain in others. This calls for novel models to explain how itch and pain are distinctly coded in the mammalian nervous system.

OP11
SULFATED CCK8 INDUCES ALLOKNESIS VIA SPINAL CCK2 RECEPTOR IN MICE

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In the central nervous system (CNS), the neuropeptide cholecystokinin (CCK) is known to act as a neurotransmitter and/or neuromodulator in circumstances such as anxiety, feeding and allodynia. However, the relationship between CCK and spinal itch transmission remains unclear. In our gene expression analysis, increased expression of CCK mRNA was found in the dorsal root ganglia of NC/Nga mice with atopic dermatitis (AD)-like symptoms compared with that in non-AD control mice. Previous studies have also shown that sulfated CCK8 (CCK8S) is distributed widely in the CNS. Therefore, this study was performed to investigate the role of CCK8S in spinal itch transmission. Initially, we examined the effects of intrathecal injection of CCK8S on itch-related scratching behavior in mice. In behavioral analyses, intrathecal injection of CCK8S did not induce scratching bouts in C57BL/6J mice. We next tested whether spinal CCK8S induced alloknesis, namely touch-evoked itch using innocuous von Frey filaments. Intrathecal injection of CCK8S resulted in increased alloknesis scores in treated mice compared to control mice. Pharmacologically, intrathecal injection of L-365,260, a CCK2 receptor (CCK2R) antagonist, significantly attenuated the CCK8S-induced alloknesis, whereas a CCK1R antagonist did not. These findings suggest that CCK8S induced alloknesis via spinal CCK2R. Thus, the CCK8S-CCK2R pathway may be a promising candidate for anti-alloknesis treatment.

SPECIAL INTEREST GROUPS (SIGS)

OP12
SIG SENSITIVE SKIN

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The IFSI special interest group (SIG) on sensitive skin has defined sensitive skin as "a syndrome defined by the occurrence of unpleasant sensations (stinging, burning, pain, pruritus, and tingling sensations) in response to stimuli that normally should not provoke such sensations. These unpleasant sensations cannot be explained by lesions attributable to any skin disease. The skin can appear normal or be accompanied by erythema. Sensitive skin can affect all body locations, especially the face". This is the first international consensual definition. Translations and assessments of instruments of measurement as well as new reviews will be the next steps.

OP13
SPECIAL INTEREST GROUP (SIG): SCORING ITCH IN CLINICAL TRIALS

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Chronic pruritus is a subjective, multidimensional and highly debilitating symptom that is difficult to assess. The SIG Scoring Itch in Clinical Trials (see itchforum.net) was founded in 2008 in order to develop and validate instruments used to make a reliable assessment of its various dimensions. Several instruments assessing the itch intensity (including the ItchyQuant for children), categorization, distribution, qualities and course over time have already been made available for use in clinical trials. The minimal clinically important difference (MCID) has been calculated for both the VAS and NRS. These instruments have also been validated in an electronic form via the ItchApp (provider: arone.com). Novel instruments, including the Patient Global Impression of Change (Dynamic Pruritus Score; DPS), Itch Controlled Days (ICD) and Patient Benefit Index (PBI) have been developed and validated to assess other various parameter. Patient reported questionnaires on reactive conditions ranging from sleep disorders, anxiety, depression and impairment to quality of life have been used in many trials and provide reliable data. In spite of this, the search for objective markers, such as an approach to monitoring cutaneous scratch symptoms or scratch movements, remains ongoing.

OP14
THE SPECIAL INTEREST GROUP (SIG) "QUESTIONNAIRES TO ASSESS CHRONIC ITCH" OF THE INTERNATIONAL FORUM ON THE STUDY OF ITCH (IFSI)

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Chronic itch (CI) is a global disease affecting many patients and has a significant impact on all aspects of patient's life including their well-being. It is complex, difficult to measure and burdensome to patients suffering from CI. The assessment of CI and its associated effects is an important tool of daily clinical practice in itch management. The number of instruments utilized has been constantly growing during the last years. Despite itch being a common complaint, there are few studies describing the use of structured questionnaires for evaluation and measurement of itch and its sensory and affective dimensions. According to the current status of research and clinical experiences there is no single measurement instrument that allows an adequate and comprehensive assessment of CI. In 2011, a Special Interest Group (SIG) on questionnaires to assess chronic itch was founded by several experts and members of the International Forum for the Study of Itch (IFSI) as an interdisciplinary team to integrate knowledge from different disciplines. One goal is to determine which of the various psychometric properties of itch questionnaires offer the greatest utility in the evaluation of CI. A consensus paper addressed the expectations and unmet needs of using itch questionnaires to better assess CI and guide therapy. The SIG is currently working on comparing the content and measurement properties of instruments available and providing a template for questionnaires for future use in different arrangements and modular configurations depending on the underlying disease. Future studies take aim at disease- and population-specific questionnaire validation. In the long-term the questionnaire should serve as a measurement instrument used for clinical practice as well as medical and health research.

OP15
THE SPECIAL INTEREST GROUP (SIG) "PARANEOPLASTIC ITCH" OF THE INTERNATIONAL FORUM FOR THE STUDY OF ITCH (IFSI)

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In 2012, an interdisciplinary interest group of physicians and researchers with a special interest in paraneoplastic itch was founded. A position paper published in 2015 reviewed the current knowledge and aimed to define what can be summarized under the term "paraneoplastic itch (PI)". This term is used to describe itch in patients with both, haematological and solid tumour malignancies. The overall prevalence and incidence is still unclear, however, chronic itch without concomitant skin changes has recently been shown to be a risk factor for having undiagnosed hematologic and bile duct malignancies. Due to the rise of malignant diseases especially in the Western countries this topic is of increasing interest. However, research is hampered by the diverse, multiple and complex pathophysiology of malignant diseases. PI is frequently not recognized and does not receive enough attention by physicians. This may be caused by little awareness of physicians towards this symptom and a lack of diagnostic tests for PI. For the future, we should try to gain more knowledge about PI in terms of pathophysiology, epidemiological data, clinical characteristics and treatment modalities. It would be beneficial to search possible serum markers, to gain more knowledge on PI as a preceding symptom of malignancy and to identify possible risk factors for developing PI.

OP16
THE SPECIAL INTEREST GROUP (SIG) "UREMIC PRURITUS" OF THE INTERNATIONAL FORUM FOR THE STUDY OF ITCH (IFSI)

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In 2013, the special interest group "uremic pruritus" (UP) was founded to improve knowledge and therapeutic options on pruritus in patients with progressed or end-stage renal disease (ESRD). Since then, only a few new papers have appeared shedding light on the pathogenesis and therapy of UP. There are new data available on the prevalence of UP in children on dialysis showing that more young patients are afflicted than assumed before. Data of the GEHIS study in German patients on hemodialysis, a representative study using different prevalence estimates, in contrast, showed that the prevalence of UP is lower than former studies reported. According to the updated DOPPS data there is a decline in the prevalence of patients with severe UP worldwide. Both studies also demonstrated that effective therapies with gabapentin or pregabalin are underutilized. In patients on peritoneal dialysis, the incidence of UP is reported to be lower than in hemodialysis patients, although conflicting data have been reported. After kidney transplantation, a relevant number of patients suffer from pruritus, although it is not clear whether the aetiology of pruritus is similar to that in uraemia. With regard to pathogenesis only little new data has emerged. It is still on debate whether inflammation might play a role in UP. CRP was not increased in patients with UP compared to patients without UP according to GEHIS. Further data of this study hint to a possible neuropathic component most likely caused by neuropathy in HD patients. The impact of skin salt content in uremic pruritus needs to be investigated, as some studies have given hints that salt lowering strategies may lead to lower occurrence of itch in dialysis patients. All this should encourage to consider a possible multifactorial origin of pruritus in HD patients.

SKIN, INFLAMMATION AND ITCH

OP17
NEW INSIGHTS INTO THE PATHOPHYSIOLOGY OF ITCH DURING CIGUATERA FISH POISONING

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Ciguatera fish poisoning (CFP) is the most widespread seafood poisoning caused by the consumption of contaminated tropical fish flesh. This intoxication originates from ciguatoxins (CTXs) which are predominantly responsible of characteristic clinical cutaneous sensory disorders such as cold allodynia and severe pruritus. These toxins are thermostable, resistant to acidic and basic conditions, odourless with no suitable, quick and ready-to-use tool to detect them in intoxicated fish fleshes. With global climate warming, growth of tourism and rise of international trade lead to the spreading of this unsung illness to temperate countries and more and more case reports are notified in non-endemic areas. Hence, ciguatoxins are one of the major potential health issue concerning seafood poisoning. CTXs are potent voltage-gated sodium channel (VGSC) activators but the following molecular mechanisms relating to the sensory disorders are still poorly understood. Previously, using a primary coculture model of sensory neurons and keratinocytes, we showed that Pacific-ciguatoxin-2 is able to induce a voltage-gated sodium channel-dependent release of substance P (SP) and calcitonin gene-related peptide (CGRP). Since these neuropeptides are key mediators involved in itch sensations, this ciguatoxin-induced effect may contribute to explain the sensory disturbances of ciguatera fish poisoning. Here, based on our previous published coculture model, we prospected the role of several molecular targets involved in P-CTX-2-induced SP release. Using calcium imaging experiments performed on monoculture of neurons, we evidenced a striking role of TTX-resistant Na_v channels to keep the intracellular calcium concentration ($[Ca^{2+}]_i$) imbalance within the time. Moreover, we showed the crucial role of calcium influx in the toxin-evoked calcium signal and SP release. Indeed, this is the first time that chronological order of calcium events regarding to cellular signalling, consecutive to VGSCs activation by P-CTX-2, is studied. Taken together, those findings give not only new molecular signalling consecutive to toxin-induced VGSCs activation but also new insights for therapeutic approaches to treat pruritus.

OP18
INTRA- AND EXTRA-LESIONAL SENSITIZATION FOR NON-HISTAMINERGIC AND MECHANICALLY-EVOKED ITCH IN ATOPIC DERMATITIS

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Chronic or episodic severe itch is recurrent in atopic dermatitis (AD). It has been suggested that the non-histaminergic neuronal itch pathway dominate AD itch and induces an "itch-scratch-itch" cycle, which maintains skin lesions, itch and pain. We hypothesized that non-histaminergic neuronal sensitization plays a role in AD, and compared sensitivity to thermal, mechanical, and chemical pruritic stimuli in AD patients and controls. The study included 25 AD patients with chronic itch and 25 healthy controls. Sensory tests were conducted intra-lesionally, extra-lesionally, and in homologous areas of healthy controls and questionnaires on itch characteristics were administered to the patients. Thermal and mechanical quantitative sensory testing (QST) was conducted and conditioned pain modulation efficacy was assessed. Moreover, histamine- and cowhage-provocations were performed and hyperknesis as well as vasomotor reactivity were assessed. AD patients reported their spontaneous itch intensity at 60.7±4.3 ($VAS_{0\text{-}100}$) and their pain intensity at 39.7±5.2 ($VAS_{0\text{-}100}$). Patients experienced significantly increased evoked itch from cowhage both intra- and extra-lesionally, while histamine-evoked itch intensity was not significantly different between groups (a trend toward sensitization was observed intra-lesionally). No differences were found for thermal sensory sensitivity or pain evoked by itch provocations. Patients had increased mechanical pain sensitivity intra- and extra-lesionally and exhibited augmented intra- and extra-lesional sensitivity to mechanically evoked itch, prior to, and after itch provocations. Increased itch following non-histaminergic itch provocations suggests pathway-specific sensitization in AD. The increased susceptibility to mechanically evoked itch and pain, also occurring extra-lesionally, indicates central sensitization mechanisms. Drugs candidates inhibiting the non-histaminergic ($PAR2/TRPA1^+$) itch-pathway are promising for treating AD itch.

OP19
ATTENUATED ACTIVATION OF ENDOGENOUS GLUCOCORTICOIDS IN KERATINOCYTES INDUCES ALLOKNESIS IN ATOPIC DERMATITIS VIA ABERRANT ARTEMIN PRODUCTION

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The enzyme 11beta-hydroxysteroid dehydrogenase-1 (HSD11b1) activates endogenous glucocorticoids in response to local stress and plays an important role in maintaining skin homeostasis. Although decreased epidermal HSD11b1 expression in atopic dermatitis (AD) is thought to cause disruption of the local stress regulation system, involvement of endogenous glucocorticoids in the pathogenesis of AD is unclear. To address this issue, we investigated the impact of local cortisol activation on itch, which is the main symptom of AD. First, we analyzed the distribution of protein gene product (PGP) 9.5-positive nerve fibers in skin of keratinocyte-specific HSD11b1-knockout ($HSD11b1^{fl/fl}$ Krt5-Cre; $HSD11b1^{KCKO}$) mice using immunohistochemistry and 3D imaging. Surprisingly, epidermal nerve fiber sprouting and thickening were observed in skin from $HSD11b1^{KCKO}$ mice in the absence of any skin lesions. $HSD11b1^{KCKO}$ mice frequently showed a scratch response to a light touch to the neck; nevertheless, there was no difference between $HSD11b1^{KCKO}$ and wild-type mice in the number of spontaneous scratching instances. Furthermore, $HSD11b1^{KCKO}$ mice also showed augmented pruritogen-induced alloknesis and hypersensitivity to thermal nociception. Next, we examined cytokines and neurotrophic factors, a humoral factor related to skin innervation from keratinocytes. Artemin (ARTN) production from keratinocytes was promoted in $HSD11b1^{KCKO}$ mice and suppressed by treatment with corticosterone. Then, we performed an immunohistochemical analysis of protein expression in skin biopsy specimens of AD and psoriasis patients. ARTN expression was specifically increased in AD epidermis and the papillary layer, and a significant negative correlation between ARTN and HSD11b1 expression in AD epidermis was observed. Taken together, these results suggest that the deficiency in active endogenous glucocorticoids in keratinocytes increases ARTN production and may contribute to the induction of alloknesis in AD.

OP20
NEUTROPHIL-SOMATOSENSORY NEURON CROSSTALK DRIVES ACUTE AND CHRONIC ITCH

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Eczema is one of the most common chronic itch disorders. Mechanistic studies and therapeutic interventions have focused on the molecular signatures and immune cells found in mature eczematous lesions. However, the molecular and cellular players that contribute to the development of eczema have not been systematically studied.

Here we set out to examine the early changes that occur in the skin during eczema pathogenesis using the Vitamin D mouse model of atopic dermatitis. We find that although a variety of cytokines and innate immune cells infiltrate the skin within the first 5 days of the model, neutrophils are the sole cellular player required for the onset of itch. We used a variety of techniques including transcriptome analysis, qPCR, FACS and mouse behavior to define the molecular interactions between neutrophils and sensory neurons that drive itch behaviors in the development of atopic dermatitis.

OP21
CUTANEOUS 4-1BB/4-1BBL SIGNALING INDUCES SEVERE SKIN INFLAMMATION AND CHRONIC ITCH

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The skin is exposed to the environment resulting in the induction of immune responses. Members of the TNF receptor family regulate cutaneous immunity and the interaction of immune cells with cutaneous nerve fibers is critically involved in the control of immune responses. Since the TNF family receptor 4-1BB and its ligand 4-1BBL are expressed on neuronal as well as immune cells, we hypothesized that 4-1BB/4−1BBL signaling might contribute to cutaneous immunity by regulating the communication of sensory neurons and immune cells. To investigate this we generated transgenic mice overexpressing 4−1BB in the epidermis (4-1BB tg). Interestingly, 4-1BB tg mice spontaneously developed inflammatory skin lesions, which were characterized by irregular acanthosis, fibrosis, collagenosis and massive immune cell infiltrates consisting of mast cells, eosinophils and T cells. Moreover, tg mice showed an increased scratching frequency, thus pointing to the 4−1BB-mediated induction of pruritus. To elucidate the cellular and molecular mechanisms we analyzed the role of mast cells by breeding 4-1BB tg mice to mast cell deficient mutants and could show that mast cells were of minor importance for the pathophysiology of 4-1BB-induced pruritic skin inflammation. Next, we quantified the IL-31 expression in T cells since IL-31 is known to promote neurogenic inflammation. Particularly $CD8^+$ T cells from 4-1BB tg skin produced high levels of IL−31 and by depleting these cells we could demonstrate that the absence of $CD8^+$ T cells completely protected tg mice from developing itch and inflammation. Pruritic skin inflammation requires the interaction of T cells with cutaneous sensory nerve fibers, which generate currents following the stimulation of the itch-related receptor IL-31RA. Hence, we next depleted cutaneous sensory nerve fibers in 4-1BB tg mice by injecting the capsaicin analogue resiniferatoxin (RTX). Notably, RTX significantly down-regulated chronic pruritus and additionally, reduced inflammation. Of note, the depletion of cutaneous sensory nerve fibers also reduced the numbers of IL−31 expressing $CD8^+$ T cells in lesional skin from tg mice. Worth mentioning that 4−1BB/4-1BBL signaling was also up-regulated in cutaneous lesions from patients with pruritic skin diseases, thus strengthening our hypothesis that 4−1BB/4-1BBL signaling might contribute to the communication of the immune system with the peripheral nervous system during the development of itch and inflammation.

OP22
SEMA3A EXPRESSION IS REGULATED BY CALCIUM/PKC/MAPK/AP-1 SIGNALING AXIS IN NORMAL HUMAN EPIDERMAL KERATINOCYTES

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Cutaneous hyperinnervation is involved in itch sensitivity at the periphery. Previously, we reported that epidermal hyperinnervation is mainly caused by an imbalance between nerve elongation factors, including nerve growth factor (NGF), and nerve repulsion factors, such as semaphorin 3A (Sema3A) produced by keratinocytes. However, the regulatory mechanism of endogenous Sema3A is unknown. In this study, we investigated the regulatory mechanism of Sema3A gene in normal human epidermal keratinocytes (NHEK). The 5'-flanking region of Sema3A gene was cloned and a critical region for Sema3A promoter activity within -134 bp from the transcription start site was identified. In this region, transcription factor binding sites including activator protein (AP) -1, retinoid related orphan receptor (ROR) alpha, Sox5/Sox9 and GA-binding protein (GABP) were found. Site-directed mutagenesis of AP-1/ROR alpha site showed significantly lower activity than in an intact case. Although Sema3A promoter activity was up-regulated by 1.4 mM calcium, AP-1/ROR alpha mutant showed unchanged promoter activity in the presence of 1.4 mM calcium. Furthermore, AP-1 and ROR alpha siRNA effectively reduced Sema3A expression compared with control siRNA. Chromatin immunoprecipitation assay revealed AP-1 bound to proximal promoter (-134/-24) in the presence of 0.15 or 1.4 mM calcium. Up-regulation of Sema3A mRNA by 1.4 mM calcium was significantly decreased by AP-1 inhibitor (T-5224). Similarly, it was also decreased by protein kinase C (PKC) inhibitor (Gö6976), MAPK/ERK kinase (MEK) 1/2 inhibitor (PD98059) and jun N-terminal kinase (JNK) inhibitor (SP600125). These results suggest that calcium-induced Sema3A expression in NHEK is mediated by the PKC/MEK1/2/AP-1 and/or PKC/JNK/AP-1 signaling axis in the proximal promoter (-134/-24), and provide a new insight to identify novel antipruritic drug targets.

NEW ANTIPRURITIC TREATMENTS

OP23
RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL OF SERLOPITANT EFFECTS ON MULTIPLE MEASURES OF PRURITUS IN PATIENTS WITH PRURIGO NODULARIS

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Prurigo nodularis (PN) is an intensely pruritic chronic skin condition with suboptimal treatments available. Serlopitant is a neurokinin-1 receptor (NK_1-R) antagonist in development for the treatment of chronic pruritus. A randomized, double-blind, placebo-controlled phase 2 clinical trial assessed the efficacy, safety, and tolerability of serlopitant 5 mg in patients with PN (NCT02196324). Key eligibility criteria were treatment-refractory PN lasting >6 weeks, lesions on multiple body areas, and Visual Analog Scale (VAS) pruritus score ≥70 mm within 72 hours of baseline. Patients were randomized 1:1 to receive serlopitant 5 mg or placebo once daily for 8 weeks; follow-up was 2 weeks. The primary efficacy endpoint was change from baseline in the average itch VAS score. Secondary endpoints included Verbal Rating Scale (VRS); worst-itch VAS; Patient Global Assessment (PGA); Numeric Rating Scale (NRS); Investigator Global Assessment (IGA); and Prurigo Activity Score (PAS). Adverse events (AEs) and clinical and laboratory assessments were evaluated during treatment and follow-up. The efficacy population comprised 127 patients; baseline characteristics were well matched between the treatment groups, as was treatment compliance. Serlopitant produced a statistically significant de-

crease from baseline in pruritus severity compared with placebo when assessed at weeks 2, 4, and 8 ($p \leq 0.05$), as measured by average-itch VAS score. Secondary endpoint results for VRS, PGA, worst-itch VAS, NRS, IGA, and PAS also demonstrated greater improvements in the experience of pruritus with serlopitant over placebo at week 8. Rescue medication was used by a greater proportion of placebo- than serlopitant-treated patients. The most frequently reported treatment-emergent AEs (TEAEs) in the serlopitant group were nasopharyngitis (17.2% serlopitant, 3.2% placebo), diarrhea (10.9% serlopitant, 4.8% placebo), and fatigue (9.4% serlopitant, 6.3% placebo). Most TEAEs were mild or moderate; severe TEAEs were reported for 9.4% and 4.8% of serlopitant- and placebo-treated patients, respectively. There were no meaningful trends in laboratory abnormalities or changes in vital signs, and no deaths. In conclusion, multiple measures of pruritus consistently demonstrated that serlopitant provides greater reduction of pruritus than placebo in patients with PN. Serlopitant was well tolerated and most AEs were mild or moderate; no significant safety signals were detected.

OP24
SERLOPITANT FOR TREATMENT OF CHRONIC PRURITUS: RESULTS OF A RANDOMIZED, MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL

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Chronic pruritus is a frequently debilitating skin condition, which results in significant morbidity and impaired quality of life. Many current therapies provide inadequate itch relief or can be associated with undesirable safety/tolerability issues; therefore, most are used off label. Here, we report the efficacy and safety results from a phase 2 clinical trial (NCT01951274) of the novel neurokinin-1 receptor antagonist serlopitant vs placebo for the treatment of chronic pruritus. Key eligibility criteria were treatment-refractory pruritus lasting ≥6 weeks and baseline pruritus Visual Analog Scale (VAS) score ≥70 mm. Patients were randomized (1:1:1:1) to receive serlopitant 0.25 mg, 1 mg, 5 mg, or placebo for 6 weeks once daily. The primary efficacy endpoint was the pruritus VAS score percent change from baseline. Adverse events (AEs) and clinical and laboratory assessments were evaluated during treatment and follow-up. The study population included 257 patients (60.7% female; mean age was 43.7 years). Baseline characteristics were comparable between groups. Differences in change from baseline VAS pruritus score were statistically significantly greater with serlopitant 1 mg at weeks 3-6 and 5 mg at weeks 4-6, compared with placebo. At the week 6 efficacy evaluation, the mean (SE) percent change in VAS pruritus scores were –28.3 (4.1) for placebo, –41.4 (4.0; $p=0.022$) for serlopitant 1-mg, and –42.5 (4.1; $p=0.013$) for serlopitant 5 mg. Statistically significant improvements in severity of itch from baseline were also demonstrated using the Numeric Rating Scale – a secondary endpoint – with serlopitant 1 mg and 5 mg at weeks 4, 5, and 6 ($p<0.05$) compared with placebo. The most common treatment-emergent AEs (TEAEs) in the serlopitant groups were somnolence (1.6%, 4.6%, and 4.7% for serlopitant 0.25 mg, 1 mg, and 5 mg, respectively, and 1.6% for placebo) and diarrhea (0%, 6.2%, and 3.2% for serlopitant 0.25 mg, 1 mg, and 5 mg, respectively, and 1.6% for placebo). Most TEAEs were of mild or moderate intensity. Six patients discontinued study drug due to a TEAE. There were no meaningful trends in laboratory abnormalities or changes in vital signs and no deaths. Serlopitant 1 mg and 5 mg provided statistically significant improvement in chronic pruritus VAS score, compared with placebo, and both doses were safe and well tolerated. All TEAEs were of mild or moderate intensity, while no meaningful adverse safety trends were observed.

OP25
RECOVERY OF PEPTIDERGIC EPIDERMAL NERVE FIBER DENSITY BY TOFACITINIB IN A MOUSE MODEL OF ATOPIC DERMATITIS

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The JAK inhibitor Tofacitinib has demonstrated significant antipruritic effects in a phase 2 trial of atopic dermatitis patients. However, the mechanism behind this antipruritic effect is still largely unknown. Dynamic changes in epidermal innervation have been observed in atopic dermatitis and may contribute to chronic itch. Therefore, we investigated whether Tofacitinib affects epidermal innervation in the ovalbumin (OVA) mouse model of atopic dermatitis. Adult male C57BL/6 mice received OVA (100 µg), alum (1 mg), and pertussis toxin (300 pg) on treatment Day 1, followed by OVA (50 µg sc) on Day 5. On Day 7, Alzet osmotic mini-pumps were subcutaneously implanted in the mice. Tofacitinib or vehicle (50% DMSO, 10% PEG 300, and 40% distilled water) was delivered at 15 mg/kg/day. Beginning on Day 14, topical OVA (100 µl, 0.1%) was applied daily by gauze to shaved rostral back skin and covered with a Tegaderm patch. On Days 21 and 28, the patch was removed, and animals were videotaped to assess spontaneous scratching. On both days, Tofacitinib-treated mice displayed significantly inhibited spontaneous scratching compared to vehicle-treated mice. To test for alloknesis, 5 successive innocuous mechanical stimuli were delivered by von Frey monofilament (bending force: 0.7 mN) to random sites along the border of the treatment area. The alloknesis score (0-5) was defined as the number of scratch bouts elicited by the stimulus series. Tofacitinib did not reduce alloknesis score compared to vehicle. To investigate epidermal nerve fiber density (ENFD), mice were perfused on Day 28, and skin was immunostained with antibodies against CGRP, a marker for peptidergic nerves, or P2X3, a marker for nonpeptidergic nerves. Peptidergic ENFD was significantly decreased in the vehicle-treated group compared to naive mice. Tofacitinib significantly increased the peptidergic ENFD, recovering it to naive skin levels. The nonpeptidergic ENFD was significantly increased in the vehicle-treated group compared to naive mice. Tofacitinib did not affect the density of epidermal nonpeptidergic nerves. The re-innervation of peptideric epidermal nerves may activate itch-inhibitory interneurons to suppress itch and contribute to the antipruritic effects of Tofacitinib.

OP26
CRISABOROLE OINTMENT PROVIDES EARLY RELIEF OF PRURITUS IN TWO PHASE 3 CLINICAL TRIALS IN PATIENTS WITH MILD OR MODERATE ATOPIC DERMATITIS

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Introduction: Atopic dermatitis (AD), a chronic inflammatory skin disease that affects children and adults, is characterized by

intense pruritus, regardless of disease severity. Pruritus-induced scratching leads to disease exacerbation that often results in sleep disturbance and reduced quality of life. Quick relief of pruritus is a key treatment goal. Crisaborole topical ointment, 2%, is a novel, nonsteroidal, anti-inflammatory, phosphodiesterase 4 inhibitor for the treatment of mild to moderate AD. A post hoc analysis was performed from 2 identically designed, multicenter, vehicle-controlled, Phase 3 trials evaluating the impact of crisaborole on early relief of pruritus stratified by baseline (BL) disease severity. *Methods:* Global disease severity was measured by the Investigator's Static Global Assessment (ISGA) in patients ≥2 years old with mild (ISGA 2) to moderate (ISGA 3) AD. Patients were randomly assigned 2:1 to receive crisaborole:vehicle twice daily for 28 days. Pruritus was measured on a 4-point scale (none [0] to severe [3]), with improvement defined as a score of none (0) or mild (1) with a ≥1-grade improvement from BL. Early improvement in pruritus was defined as achievement of improvement at day 6. *Results:* Significantly more crisaborole-treated patients than vehicle-treated patients experienced early improvement in pruritus, regardless of BL disease severity (mild AD: 59.5% vs 41.3%; $p<0.001$; moderate AD: 54.7% vs 38.3%; $p<0.001$). At the earliest assessment, at 48 hours, significantly more crisaborole-treated patients with mild AD experienced improvement in pruritus (48 hours: 37.6% vs 26.9%; $p=0.02$). At day 6, mean percentage change from BL in pruritus severity in crisaborole-treated patients with mild AD and in those with moderate AD was significantly greater than that in vehicle-treated patients (mild AD: –42.9% vs –29.2%; $p=0.009$; moderate AD: –40.9% vs –26.1%; $p<0.001$). *Conclusions:* A significant proportion of crisaborole-treated patients experienced early relief of pruritus, regardless of BL disease severity. Additionally, patients treated with crisaborole experienced greater early reduction in pruritus severity than did vehicle-treated patients. Crisaborole may represent a promising, novel, topical AD treatment that can provide much needed early relief of pruritus for patients with mild to moderate AD.

OP27
NEW INSIGHTS INTO THE ANTI-PRURITIC ACTIVITY OF THE NEUROKININ-1 ANTAGONIST APREPITANT: PARTIAL ACTIVATION OF EGFR SIGNALING IN HUMAN KERATINOCYTES AS A MECHANISM FOR REDUCING ERLOTINIB-INDUCED PRURITUS

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Epidermal growth factor-tyrosine kinase inhibitors (EGFR-TKIs), such as erlotinib, are currently used for the treatment of lung and several other cancers. While EGFR-TKI's are effective anti-cancer agents, they produce serious adverse effects on the skin including pruritus and acneiform skin eruptions. Aprepitant, an inhibitor of the Neurokinin 1 receptor (NK1R), is effective in decreasing itch in patients treated with EGFR-TKI's. The goal of the present study is to better understand the mechanism by which NK1R blockade reduces the adverse effects caused by the blockade of EGFR in keratinocytes. While previous studies have suggested a role for mast cells, the role of human keratinocytes remains largely unexplored. Towards this goal, human keratinocyte HaCaT cells were used as a model system to better understand EGFR signaling using Reverse Phase Protein Arrays (RPPA) technology. HaCaT cells were stimulated with and without epidermal growth factor (EGF). The cell lysate from control and EGF-treated HaCaT cells were analyzed by RPPA, which examined expression levels of over 200 proteins/phosphoproteins. Stimulation of HaCaT cells with EGF significantly increased the phosphorylation of several proteins including the following: Akt, EGFR, GSK-3 beta, HER2, HSP27, JNK, MAPK, MDM2, p90RSK, PKC-betaII, PLC-gamma2, Shc, SHP2, Src, and STAT3. The phosphorylation of all of these proteins was blocked when HaCaT cells were stimulated with EGF in the presence of erlotinib. Interestingly, exposure of HaCaT cells to the NK1R blocker aprepitant increased the phosphorylation of EGFR as well as Akt. These results were confirmed in human primary keratinocytes. Taken together, these data suggest that aprepitant may reduce itch and adverse effects of EGFR-TKI's by augmenting EGFR signaling in keratinocytes.

OP28
EFFICACY OF SYSTEMIC TREATMENTS OF PSORIASIS ON PRURITUS: A SYSTEMIC LITERATURE REVIEW AND META-ANALYSIS

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In the course of the last 30 years, several studies have clearly documented that pruritus is a very frequent symptom of psoriasis and its impact on the patients' quality of life. The variety of available systemic treatments for psoriasis is increasing rapidly. Our objective was to assess their efficacy on pruritus based on a systematic literature review. A systematic literature search was performed using PubMed and Trip Database (from January 1990 to September 2016) to find published clinical trials for the treatments of psoriasis, then a meta-analysis was performed. Among 516 articles identified, 35 studies were retained in the systematic review. At baseline, the high prevalence of pruritus (80 to 100%) was confirmed. The meta-analysis included 13 trials using a 0 to 10 itch scale and highlighted that all treatments evaluated had a benefic impact on pruritus. Anti Il-17, JAK inhibitors, adalimumab, and apremilast were all shown to be effective in reducing pruritus in psoriasis with variable effect size magnitudes. Our systematic review highlights that systemic treatments, including UVB phototherapy, improve pruritus in psoriasis but that it is not necessarily correlated with lesion recovering. Nonetheless, these results must be displayed carefully because there are so many variable endpoints in different studies.

OP29
RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY OF MONOCLONAL ANTI-IGE ANTIBODY OMALIZUMAB IN THE MANAGEMENT OF PRURITUS IN CHRONIC SPONTANEOUS URTICARIA IN THE PEDIATRIC POPULATION

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Chronic spontaneous urticaria (CSU) is defined as the spontaneous appearance of itchy wheals, with or without angioedema, persisting for ≥6 weeks. It affects 0.5–1% of the global pediatric population, but it represents a high burden to patients. Children in the age group of 6 to 12 years present frequently with episodic pruritic wheals and oral anti-histamnics are mostly insufficient to prevent a recurrence. Oral steroids and other immune-suppressives although effective temporarily, are associated with a lot of side effects in this age group and are mostly contraindicated. In recent years, monoclonal Anti-IgE antibody 'omalizumab' has been tried in other allergic disorders like atopic dermatitis and bronchial asthma in the pediatric age group, however there are no studies till date of this novel therapeutic regimen in the pediatric age group to control the itching in chronic spontaneous urticaria in the pediatric age group. *Objective:* We sought to evaluate the

efficacy and safety of monoclonal Anti-IgE antibody omalizumab in patients between the group of 6 to 12 years with moderate-to-severe chronic idiopathic urticaria who remained symptomatic despite H1-antihistamine therapy (licensed doses). *Methods:* This was a double-blind, placebo-controlled trial with children between the age group of 6 to 12 years randomized to omalizumab or placebo. We randomly assigned 30 children with comparable baseline age and serum IgE levels to receive four subcutaneous injections, spaced 4 weeks apart, of omalizumab at a dose of 150 mg or placebo, followed by a 16-week observation period. Mean Urticaria activity score (UAS) at baseline was 5.7 points (range, 4–6 points). *Results:* Compared with placebo, omalizumab resulted in a statistically significant reduction in FcεRI expression on basophils and pDC2 ($p<0.001$). UAS and serum IgE levels were significantly reduced in the Omalizumab group as compared to the placebo group both at 16 and 32 weeks. *Conclusions:* Omalizumab diminished clinical symptoms and signs of chronic idiopathic urticaria in children who had remained symptomatic despite the use of approved doses of H1-antihistamines. Chronic spontaneous urticaria (CSU) is a disease with significant morbidity and relative prevalence that has important effects on the quality of life (QoL) of those who suffer from it. Omalizumab is a recombinant humanized anti-immunoglobulin E (IgE) antibody that binds to the Cε3 domain of the IgE heavy chain and prevents it from binding to its high-affinity receptor FcεRI. It has been largely studied in the field of asthma and is currently approved for the treatment of both adult and pediatric (children; >6-year-old) patients. In addition, in recent, well-controlled clinical trials in patients with CSU resistant to antihistamines, add-on therapy with subcutaneous omalizumab significantly reduced the severity of itching, and the number and size of hives, and increased patients' health-related QoL and the proportion of days free from angioedema compared with placebo, with an excellent tolerance. Thus, omalizumab is an effective and well-tolerated add-on therapy for children with CSU who are symptomatic despite background therapy with H1 antihistamines.

METHODS IN ITCH RESEARCH (CLINICAL)

OP30
HOW TO ALTER PLACEBO AND NOCEBO EFFECTS IN PATIENTS WITH CHRONIC ITCH?

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Increasing evidence demonstrates the neurobiological underpinnings and relevance of placebo effects for chronic itch. For example, physical complaints, such as itch or pain, can be effectively altered by placebo effects, due to induction of expectations of a possible beneficial treatment outcome ("Itch already reduces when seeing the itchkiller"). The same is true for nocebo effects which are induced by expectations of a possible unfavorable treatment outcome or side effects. In addition, placebo mechanisms also play a role for immune functioning, such as histamine, through pharmacological conditioning. In the presentations, recent results will be presented to demonstrate the evidence for placebo and nocebo effects in itch as well as innovative methods to induce or change placebo and nocebo effects. The results have direct implications for the treatment of patients with chronic itch. Treatment outcomes might be optimized by using both conscious and automatic strategies of optimizing expectancy effects, for example, by applying conditioning principles for therapy adherence, adding environmental cues to the preferred outcome strategies or replacing regular pharmacological treatments partly by expectancy interventions.

OP31
METHODS IN ITCH RESEARCH: ARGUMENTS TO IMPROVE STANDARDIZATION OF RESEARCH METHODS

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This lecture focuses on two aspects of itch research, where greater standardization of research methods would benefit all stakeholders: Methods to induce itch and measurement of itch (prevalence, chronicity and intensity). Numerous methods of itch induction have been developed during the last years. First of all, the application of substances like cowhage or histamine has to be mentioned. Using the method of direct application on the skin is particularly advantageous because the timing (start and end) of itch can be controlled more easily. In addition, partial invasive procedures such as iontophoresis and skin prick are also used. Some studies have shown that the application of cowhage is one of the most powerful itch-inducing methods. On the other hand, various rather psychologically oriented methods are used to induce itch: The provocation of scratch responses by showing other people scratching (contagious itch), the presentation of auditory or visual (images or videos) stimuli and the presentation of audio-visual stimuli. Especially in patients with chronic itch due to atopic dermatitis or psoriasis, these methods seem to be similarly effective when certain aspects are considered in the study design. In particular, priming on the skin seems to be important to evoke a similar intense itch response to audio-visual stimuli compared to histamine-evoked itch. In addition to chemical and psychological procedures alone, also combinations of both techniques are used. However, because right now there are only first approaches to standardize the use of these methods, study results, even if the same (similar) method to induce itch is used, are hardly comparable. The situation is similar regarding the measurement of itch. Fortunately, standardization with regard to the questions that are used increases. Therefore, it is expected that study results will be more comparable in the future. Nevertheless, epidemiological studies on the prevalence of (chronic) itch revealed very different results (even in the same country) although the questions used were similar or identical. This problem may be caused by missing representativeness of the samples. This will be illustrated by the presentation of German studies. The prevalence of chronic itch is substantially lower if representativeness is given. Conclusions arising from this are discussed.

OP32
MEASURING PEDIATRIC ITCH SEVERITY: DOES PERSONAL EXPERIENCE WITH CHRONIC PRURITUS INFLUENCE PARENT'S ABILITY TO BE PROXIES?

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Background: Chronic pruritus (CP) in pediatric patients is a difficult symptom to measure. The ability of caregivers to accurately rate the severity of itch in children is unknown. The previous experience of caregivers with itch may influence their ability to serve as a proxy for their children. The best duration of recall of itch for children is also unknown. *Methods:* We asked both children and their caregivers to rate the child's itch severity using the ItchyQuant, a cartoon version of the traditional numerical scale used for adults. The scale has been validated in adults and we are in the process of validating in children. The child and the parent both rated the severity of the child's itch within the past 7 days ("last week") as well as the day prior ("yesterday"). The difference between parent and child's ratings was the outcome variable in

a multivariable linear regression model. Parental experience with CP was the primary predictor variable, adjusting for age, race, and gender. *Results:* 231 children ages 6–17 with CP were recruited. In the "yesterday" group, parental experience did not significantly predict the difference in scores. For "last week," parental experience trended significance (beta 1.25, p=0.09), and age significantly predicted the difference in scores (beta 0.26, p=0.03). *Conclusion:* The best duration of recall of itch may be "yesterday" rather than "last week" given the lack of predictors of difference. Parental experience and age influence the difference between child and parent assessment of the child's itch severity, when referring to the previous 7 days. The less the parental experience with CP, the larger the difference in assessment. Also, for every 3-month increase in the child's age, the larger the difference between the parent and child's ratings. Perhaps the parent is more desensitized to the effect of the severity of itch on the child as the child ages. A larger study is needed to understand these differences.

OP33
VALIDATION OF THE PEAK PRURITUS NUMERICAL RATING SCALE: RESULTS FROM CLINICAL STUDIES OF DUPILUMAB IN ADULT PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS

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Objective: To conduct content validation and psychometric assessment of the Peak Pruritus Numerical Rating Scale (PP-NRS) for measuring itch in patients with moderate-to-severe atopic dermatitis (AD). *Methods:* The PP-NRS is a single, self-completed item to assess the intensity of peak (worst) pruritus during the past 24 hours: "On a scale of 0 to 10, with 0 being 'no itch' and 10 being 'worst itch imaginable', how would you rate your itch at the worst moment during the previous 24 hours?" Content validation included interviews with US adults with AD self-reporting moderate-to-severe itch (n=14). Psychometric properties were assessed in a phase 2b (P2b) study (n=379; NCT01859988) and confirmed using pooled data from two phase 3 (P3) studies (n=1,379; NCT02277743, NCT02277769) in moderate-to-severe adult AD patients. Participants completed the PP-NRS once daily through end of treatment (Week 16). The Analysis includes patients receiving ≥1 subcutaneous dose of dupilumab/placebo with ≥1 post-baseline PP-NRS assessment. Patient- and clinician-reported outcome measures (PROs and ClinROs) were used to examine cross-sectional (construct and known-groups validity) and longitudinal (test-retest and sensitivity to change) measurement properties. *Results:* Interview participants interpreted the PP-NRS consistently, and found it relevant, clear, comprehensive, and easy to select a response aligned with their personal rating of peak pruritus in the past 24 hours. In the P2b study, large positive baseline correlations were observed between PP-NRS and measures of similar constructs (Average Pruritus NRS [r=1.00], SCORAD itch VAS [r=0.77], Dermatology Life Quality Index (DLQI) itch item [r=0.67], p<0.01 for all), and weak-to-moderate correlations with measures of different constructs (EASI [r=0.09] and Investigator's Global Assessment (IGA) [r=0.17, p<0.01]). Similar relationships were observed in the P3 studies. The PP-NRS differed predictably and significantly across known groups (p<0.0001) in P2b and P3. Intraclass correlation coefficients of the test-retest analysis were ≥0.95 in P2b and P3. Moderate-to-strong correlations of change were observed on the PP-NRS with PROs (P2b/P3 SCORAD itch VAS r=0.77/0.73; DLQI itch item r=0.66/0.64; PCS r=0.71/0.72) and ClinROs (EASI, r=0.50/0.46; IGA, r=0.50/0.46) (p<0.01 for all). *Conclusions:* Peak Pruritus NRS is a well-defined, reliable, sensitive, and valid scale to assess itch intensity in adult patients with moderate-to-severe AD.

OP34
12-ITEM PRURITUS SEVERITY SCALE: DEVELOPMENT AND VALIDATION OF NEW ITCH SEVERITY QUESTIONNAIRE

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Introduction: Pruritus is a very common subjective symptom, predominantly diagnosed based on patient complaints. A validated assessment of pruritus intensity is an important, but still difficult clinical problem due to a subjective nature of this sensation. *Objective:* The aim of this study was the creation and validation of new itch severity questionnaire. *Material and Methods:* A total of 148 patients (81 women and 67 men) with pruritic dermatoses were asked to assess pruritus intensity using 12-Item Pruritus Severity Score (12-PSS) and Visual Analog Scale (VAS). Patients were also asked to complete the Dermatology Life Quality Index (DLQI) and Hospitality Anxiety and Depression Scale (HADS). Test-retest comparison of 12-PSS was conducted in 102 subjects who completed the itch questionnaire twice with the 3 to 5 day interval. All results were analyzed statistically with Statistica 12.0. *Results:* We have created the 12-PSS assessing pruritus intensity (two questions), pruritus extent (one question) and duration (one question), influence of pruritus on concentration and patient psyche (four questions), and scratching as a response to pruritus stimuli (four questions). A maximum scoring was 22 points. The results showed good consistency (Cronbach α coefficient 0.81) – responses to all single questions significantly correlated with a total scoring. A significant correlation was also observed with VAS (r=0.58, p<0.001) and quality of life level according to DLQI (r=0.53, p<0.001). Test-retest comparison in 102 subjects revealed a good reproducibility of achieved results (ICC=0,72). Significant differences were observed only in three questions, where the second assessment demonstrated significantly lower values. *Conclusions:* The newly developed pruritus severity questionnaire may be used in daily clinical practice in the future.

OP35
CLINICAL BANDINGS OF PATIENT-ORIENTED ECZEMA MEASURE (POEM) SCORES AMONG JAPANESE ATOPIC DERMATITIS PATIENTS

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The Patient-Oriented Eczema Measure (POEM) (score: 0–28) is a self-assessed, repeatable measurement tool for the patients with atopic dermatitis (AD), which consists of seven questions, such as itch, skin dryness and sleep disturbance. With the aim of identifying POEM bands that could be used to aid interpretation of POEM scores when used in daily medical practice and ascertaining whether POEM bandings can be used internationally, we sought to stratify POEM scores into four severity bands, clear, mild, moderate and severe/very severe, by assessing the relationship between POEM and Visual Analogue Scale (VAS), Verbal Rating Scale (VRS) and POEM and Global Question (GQ) in 150 Japanese AD patients. GQ is a question to evaluate their overall AD condition among five different severity grades: clear, mile,

moderate, severe and very severe. POEM showed statistically significant correlations with GQ, VAS and VRS (r=0.7343,0.7364 and 0.7049, respectively, $p<0.01$). The banding for POEM scores with the highest kappa coefficient agreement was chosen as the most appropriate banding: clear=0–2, mild=3–8, moderate=9–18 and severe/very severe=19–28. Among the possible candidates for POEM bandings, this banding was proven to have the most statistically significant correlation of POEM with VAS and VRS (p=0.05-0.001). The banding for POEM scores proposed by Charman, et al. (2013) included five severity bands: 0–2 (clear/almost clear), 3–7 (mild), 8–16 (moderate), 17–24 (severe) and 25–28 (very severe). Our bandings and Charman's turned out be quite similar. POEM is a simple and valuable measure to assess the severity of patients' symptoms and has a potential to become applicable to global clinical trials for AD. However, our banding results being similar but not exactly the same with that of Charman's imply that larger scale of sample analysis is necessary to validate its global use.

METHODS IN ITCH RESEARCH (EXPERIMENTAL)

OP36
METHODS IN EXPERIMENTAL ITCH RESEARCH – AN INTRODUCTION

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The numbers of explorative methods for the study of itch increased remarkably over the past few years. The most obvious model is the administration of itch-inducing substances (pruritogens) in healthy volunteers followed by the recording of magnitude itch sensation. Initially, histamine or histamine releasing substances had been investigated and over decades of research, a growing number of candidates and receptors had been explored and identified to play a central role in itch pathogenesis, such as gastrin-releasing peptides, lysophosphatidic acids, Mas-related G-protein coupled receptors and others. Not only pruritogens but also algogens can be used to evoke experimentally itch. By their means, and employing sophisticated single nerve fibre recordings, the neuronal circuits involved in itch processing could be identified in humans and also animals. Indeed, *in vivo* animal models for itch research attained great steps forward over recent years, comprising for instance the development of atopic dermatitis-like skin lesion models in NC/Nga mice with IgE- and T_H2 cell-associated cytokine IL-31 hyperproduction. Supplementing the methodological port-folio, *in vitro* cell-culture systems also have been introduced, gaining insights into the communication between dermal fibroblasts, atopic keratinocytes and the neuronal network, thus providing an additional tool for studying pathologic itch.

OP37
RE-INNERVATED HUMAN SKIN EXPLANT AS A MODEL FOR IN VITRO STUDIES ON PRURITUS

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In order to study pruritus *in vitro*, we adapted a previously published re-innervated skin explant model by sensory neurons. This model is based on a co-culture between a human skin explant (dermis and epidermis) and sensory neurons from dorsal root ganglia of rats. After several days of co-culture in transwells, we were able to confirm the presence of nerve fibers in the epidermis. We showed by IHC that the major actors of itch (PAR-2, TSLP, TSLP-R, TRPA1, IL31, IL31-R) were present in neurons and epidermal cells. The functionality of the model was assessed by the measurement of TSLP release in the supernatant after incubation with a PAR-2 agonist (SLIGKV-NH_2). In conclusion, our model can be used for studying itch and neurogenic inflammation *in vitro*.

OP38
PHARMACOLOGICAL AND HISTOCHEMICAL CHARACTERIZATION OF A MOUSE MODEL OF CHRONIC RENAL FAILURE-ASSOCIATED PRURITUS

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Chronic renal failure (CRF) is a chronic kidney disease with severe pruritus called uremic pruritus. Although the pruritus is very severe, the underlying mechanisms of the pruritus remain unclear. We have developed a mouse model of CRF-associated pruritus. When mice was given 5/6 nephrectomy, spontaneous scratching was elicited. The scratching was inhibited by mu-opioid receptor antagonist naltrexone, suggesting that the behavior is an itch-related behavior. H_1 histamine receptor antagonist and proteinase-activated receptor 2-neutralizing antibody did not inhibit CRF-associated scratching. Toluidine blue stain of the skin section showed that the number of mast cells did not altered between CRF mice and sham-operated mice. Thus, mast cells may not contribute CRF-associated scratching. It is well known that arachidonic acid metabolites is involved in pruritus. Both TP thromboxane receptor and BLT leukotriene B_4 receptor antagonists attenuated CRF-associated scratching, suggesting that thromboxane A_2 and leukotriene B_4 play an important role in CRF-associated scratching. Interestingly, in skin section of CRF mice, the immunoreactivity of plasma component increased in CRF mice, but not sham-operated mice, was observed on primary afferents. In addition, an intradermal injection of plasma component of CRF mice elicited scratching. These results suggested that plasma component increased in CRF mice is also involved in CRF-associated scratching. Taken together with the above observation, it is considered that the mouse with CRF is useful for the elucidation of the mechanisms of the pruritus and for the development of new anti-pruritic drugs.

OP39
DEPRESSIVE BEHAVIOR MANIFESTED IN NC/TND MICE SUFFERING FROM ATOPIC DERMATITIS

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Background: Depression is one of the psychological disorders complicated in patients suffering from severe atopic dermatitis (AD). However, mechanisms of the pathogenesis and specific mediators of AD-associated depression are poorly understood. To clarify the mechanisms, an animal model suitable for AD is very useful. Therefore, we investigated on AD-associated depression using NC/Tnd mice which spontaneously develop AD-like skin lesions with IgE hyperproducton in the air-unregulated circumstance. Method: Behavioral parameters associated with the depressive disorder were tested in NC/Tnd mice accompanied with various grades of skin lesions. To evaluate depressive behavior, exploratory-, anxiety-, and despair-related behavior and preference were examined by using each general method. Clinical skin severity was scored, and scratching behavior was quantified by using a real time image analyzer, a SCLABA-Real system (Noveltec, Inc., Japan). Sera obtained from mice with severe AD were injected

intravenously into SPF mice without AD symptoms, and immunohistochemistry was performed by using the neural markers of hippocampal neurogenesis including anti-double cortin X antibody (neuroblast marker), and anti-brain lipid binding protein antibody (neural progenitor marker). *Results:* Depressive behavior became obvious relating with aggravation of the clinical aspects of AD in NC/Tnd mice. In the open field test, immobility was significantly prolonged after the onset of AD, whereas partition and rearing behavior were decreased. Sucrose preference was statistically decreased relating with severity of the skin lesions. Prolonged immobility was observed in the tests of tail suspension and forced swimming respectively. On the other hand, SPF NC/Tnd mice without AD did not show any significant changes. The number of neuroblasts in the dentate gyrus was dramatically reduced in NC/Tnd mice with the skin lesions, whereas the number of progenitors was comparable to that in age-matched SPF controls. Intravenous injection of sera obtained from mice with AD not only induced depressive behavior but also decreased the number of neuroblasts. *Conclusion:* These findings clearly demonstrated that NC/Tnd mice suffering from AD developed depressive behavior with impaired hippocampal neurogenesis through the peripheral blood.

OP40

SENSORY NEURONS CO-OPT CLASSICAL IMMUNE SIGNALING PATHWAYS TO MEDIATE CHRONIC ITCH

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Mammals have evolved neurophysiologic reflexes such as coughing and scratching to expel invading pathogens and noxious environmental factors. It is well established that these responses are also associated with chronic inflammatory diseases such as asthma and atopic dermatitis. However, the mechanisms by which inflammatory pathways promote sensations such as itch remain poorly understood. Here, we show that type 2 cytokines directly stimulate sensory neurons in both mice and humans. Further, we demonstrate that chronic itch is dependent on neuronal IL-4Rα and JAK1 signaling. Based on these observations, we show that patients with recalcitrant chronic itch markedly improve when treated with JAK inhibitors in proof-of-concept clinical studies. Thus, signaling mechanisms previously ascribed to the immune system may represent novel therapeutic targets within the nervous system. Collectively, these studies reveal an evolutionarily conserved paradigm in which the sensory nervous system employs classical immune signaling pathways to influence mammalian behavior.

HOT OFF THE BENCH: LATEST NEWS BY YOUNG INVESTIGATORS

OP41

REVERSING NOCEBO EFFECTS ON ITCH BY CONDITIONING WITH VERBAL SUGGESTION

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Background: Nocebo effects are negative treatment effects, unrelated to the treatment mechanism, which are induced by patients' expectations of worsening. Nocebo effects are known to contribute to the experience of itch, however, it has not yet been investigated if nocebo effects can be diminished by positive expectations. In this study, we examined whether nocebo effects on itch can be reduced by positive expectation induction with respect to electrical itch stimuli in healthy subjects. *Methods:* First, negative expectations about itch stimuli were induced in 99 participants by conditioning with verbal suggestion (part 1: induction of nocebo effect). Second, these participants were randomized to either the experimental group or one of the control groups (part 2: reversing nocebo effect). In the experimental group, positive expectations were induced by conditioning with verbal suggestion. In the control groups either the negative expectation induction was continued or an extinction procedure was applied. *Results:* Positive expectation induction resulted in a significantly smaller nocebo effect on itch in comparison with both control groups. Mean levels of itch showed that the nocebo effect was even reversed, signifying a placebo effect. *Conclusions:* The current study is the first to demonstrate that nocebo effects can be reversed by conditioning with verbal suggestion. A better understanding how to diminish and reverse nocebo responses might eventually contribute to increased treatment effectiveness and improved quality of life for patients suffering from chronic itch conditions.

OP42

AMELIORATION OF ATOPIC-ITCH SENSATION IN NC/TND MICE BY BETA-PINENE, THE MAJOR COMPONENT CONTAINED IN DISTILLED ALPINIA INTERMEDIA GAGNEP EXTRACTS

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Background: Alpinia (A.) intermedia, a perennial plant that belongs to the Zingiberaceae family, has been used in folk medicine for a long time in the southern districts of Japan. In this study, we investigated whether b-pinene, a major ingredient contained in the distilled extracts obtained from A. intermedia, suppress the itch sensation and exaggeration of dermatitis in NC/Tnd mice, a spontaneous atopic dermatitis model. *Methods:* Component analyses of the A. intermedia extracts were carried out using headspace gas chromatography-mass spectrometry. b-pinene was topically applied on the skin of NC/Tnd mice, which were maintained under conventional conditions, and parameters including clinical scores, scratching behaviors, and transepidermal water loss was evaluated. Histological analyses of *in vivo* samples were also carried out. The inhibitory effects of b-pinene on the degranulation of bone marrow-derived cultured mast cells (BMCMCs) and neurite outgrowth of dorsal neurite ganglia (DRGs) as well as involving signaling pathways were assessed. *Results:* The component analysis revealed that b-pinene was a major constituent of the A. intermedia extracts. In NC/Tnd mice, we observed that topical application with b-pinene significantly reduced the severity of dermatitis, transepidermal water loss, and scratching behavior. Histological analyses revealed that application of b-pinene significantly decreased the number of cutaneous mast cells as well as density of PGP-9.5-positive neurons in dermis. Adding the b-pinene to cell cultures suppressed degranulation of BMCMCs and neurite outgrowth of DRGs. Signaling analyses revealed that b-pinene strongly suppress Stat6 activation in DRGs. *Conclusion and discussion:* The results of this study indicate that topical application with b-pinene improved the skin condition by suppressing itch sensation and allergic inflammation through Stat6-mediated pathways.

OP43
PROLONGED ANTIPRURITIC EFFECT OF BOTULINUM TOXIN TYPE A ON COWHAGE-INDUCED ITCH

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Background: Botulinum toxin type A (BoNT/A or Botox®)is thought to have an antipruritic effect due to the inhibition of acetylcholine and other pruritic factors, such as substance P and glutamate. Objectives: To test the itch-relieving effect of BoNT/A on cowhage, a non-histaminergic model for chronic itch. *Methods:* In a randomized, single-blind, placebo-controlled trial (NCT02639052) Botox® (BoNT/A; 10 units; Allergan) was intradermally injected in a 4x4 cm test area on the volar surface of arm of 35 healthy subjects (16 males and 19 females; age 26.8±6.8), with a saline control (10 units) injected into the contralateral arm. Thermal sensory parameters (warmth and heat thresholds and heat pain intensity) and itch intensity after cowhage application were examined on the test areas at baseline (before treatment) and then 1 week, 1 month, and 3 months after treatment. *Results:* The intradermal injection of BoNT/A reduced cowhage itch intensity compared to the saline control at 1 week (p<0.0001), 1 month (p<0.0001), and 3 months (p=0.0004). The overall perceived itch (AUC; percent change from baseline) was also decreased versus saline control at 1 week (p=0.016), 1 month (p=0.015), and 3 months (p=0.007). The peak itch intensity was lowered with BoNT/A at 1 week (p=0.0002), 1 month (p=0.0001), and 3 months (p=0.005) compared to the saline treatment. BoNT/A had no effect on thermal thresholds or heat pain intensity. *Conclusions:* One treatment of BoNT/A reduced cowhage itch for at least three months. These results suggest that BoNT/A is a potential long-lasting treatment for localized, non-histaminergic itch.

THE WIDE RANGE OF CLINICAL PRESENTATIONS OF ITCH

OP44
AN OVERVIEW OF TREATMENT FOR OPIOID-INDUCED ITCH

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The μ- and κ-opioid systems play pivotal roles in modulating pruritus in the central nervous system (CNS). Opioid-induced pruritus is a well-known side effect in patients treated for pain with morphine and other μ-opioid receptor (MOR) agonists. In contrast, MOR antagonists (e.g., naloxone and naltrexone) and k-opioid receptor (KOR) agonists (e.g., nalfurafine) have been found to suppress pruritus in patients with systemic diseases, including chronic renal failure and cholestasis. These findings indicate the μ-opioid system induces whereas the κ-opioid system suppresses itch via the CNS. Our previous placebo-controlled, prospective, double-blind study demonstrated that opioid κ-receptor agonist, nalfurafine hydrochloride, effectively reduced intractable pruritus in 337 hemodialysis patients. In addition, our recent open-label study showed that nalfurafine hydrochloride, orally administered to hemodialysis patients at 5 μg per day for 52 weeks, produced long-term suppression of pruritus. Moreover, recently we demonstrated antipruritic efficacy of nalfurafine hydrochloride in chronic liver disease patients with intractable pruritus in a randomized, double-blind study. Experimentally, it is accepted that B5-I neurons, spinal inhibitory interneurons, produce an endogenous k-opioid agonist dynorphin acting as KOR-expressing spinal itch-selective neurons that suppress itch sensation. Meanwhile, peripheral opioid systems may also play important roles in pruritus. For example, topical application of μ-opioid receptor antagonist (e.g. naltrexone) relieved pruritus in atopic dermatitis patients. Our most recent study showed that MOR and KOR were involved in itch-related scratching behavior of imiquimod-induced psoriasis-like dermatitis in mice. In the plenary session, I provide an update and overview on treatment of opioid-induced itch.

OP45
PRURITUS IN PATIENTS WITH KIDNEY TRANSPLANTS

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Background: Uremic pruritus is a frequent and often tormenting symptom in patients on dialysis. According to former studies pruritus disappears after kidney transplantation. To readdress this topic we investigated patients who had previously received a kidney transplant and analysed possible correlations between pruritus and a series of clinical and laboratory findings in those patients with a functional graft without the need of dialysis. *Methods:* Patients who had received a kidney transplant from 1976 to 2014 whose follow-up took place in a single centre were asked to complete a questionnaire regarding pruritus. Additionally, clinical and laboratory parameters routinely and periodically obtained as well as current medication were recorded. Correlations were calculated using appropriate statistical tools. *Results:* 74 of 132 patients on routine follow-up after kidney-transplantation agreed to fill in the questionnaire. 8 of these 74 patients reported to suffer from a dermatosis and were excluded from the analysis. 11 pat. of the remaining 66 (16.7%) reported to suffer from chronic itch. The median of the intensity of itch the day of the interview was 2 (range 0-7) on a numeric rating scale from 0 to 10. Most often itch appeared on the extremities (9 of 11), the back (3 of 11) and neck (4/11). No association could be found between the prevalence of pruritus and the time since transplantation. Additionally, there was no association between the history of itch before (ie. while on dialysis) and after transplantation. The intensity of itch correlated with transplant-function (CKD-epi), serum-creatinine and haemoglobin levels. All patients suffering from itch were on beta-blockers, none of these patients had alpha-blockers. *Conclusion:* A substantial proportion of patients with functioning kidney-transplant suffer from chronic itch although to a minor intensity. There seems to be no association between history of itch during time on dialysis and after transplantation, suggesting a different pathogenesis of itch in transplant patients. Whether the use of beta-blockers does play a role in itch of transplant patients should be evaluated in a larger cohort.

OP46
URTICARIA AND ITCH

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Chronic urticaria (CU) is a disease characterized by pruritic weals, angioedema or both, lasting for 6 weeks or longer. It has an estimated 1% worldwide prevalence. Quality of life is often severely affected, since the associated itching can disturb sleep, disrupt or restrict activities, and cause social embarrassment. A primary effector of urticaria is the mast cell, which releases hista-

mine when activated by stimuli that may be either immunological or non-immunological. Histamine acts predominantly on H1 and H2 receptors, with H1 receptor stimulation leading to a neuronal reflex mechanism that causes itch. There are several guidelines which outline the classification, diagnosis and management of CU. The latest European guidelines categorise CU into two subtypes; Chronic spontaneous urticaria (CSU), which is endogenous and occurs without provocation, and chronic inducible urticaria (CIndU), where symptoms are induced by a demonstrable stimulus. Diagnosis for CSU is made by taking a thorough history, as well as blood tests that may exclude an underlying disease. CIndU can be confirmed with provocation tests. Differential diagnosis includes urticarial vasculitis and autoinflammatory disease, in addition to various cutaneous diseases. Assessment tools for the severity of CU include the Urticaria Activity Score over 7 days (UAS7), Itch Severity Score (ISS), and the CU-2QoL, a disease-specific measure of quality of life impairment. The European, UK and US guidelines for CU all have some variation in their step-wise procedures for managing the disease. All recommend that second generation antihistamines are the mainstay first-line treatment, and dosages may be increased by up fourfold. A number of add-on treatments are available for patients with CU refractory to antihistamines. The European guidelines now recommend that the monoclonal anti-IgE antibody, omalizumab, should be the next line of treatment, followed by ciclosporin or montelukast. Short courses of systemic corticosteroids may be use as a rescue treatment for acute exacerbations, however long-term use is not recommended. Potential future treatments for CU include H4 receptor antagonists, as well as other anti-IgE and anti-IL-1 biologics.

OP47

ESSENTIAL THROMBOCYTHEMIA WITH AQUAGENIC PRURITUS: AN ENTITY WITH MORE AGRESSIVE CLINICAL AND BIOLOGICAL PROFILE AT THE DIAGNOSIS AND A HIGH MORBIDITY DURING THE FOLLOW-UP

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Polycythemia vera (PV) and essential thrombocythemia (ET) are myeloproliferative neoplasms in which arterial or venous thromboses and phenotypic evolutions (leukemia, myelofibrosis) are the most recurrent complications. Aquagenic pruritus (AP), induced by water contact, is a typical symptom of PV. However, we showed recently that it also present in ET withdifferent clinical characteristics from those observed in PV patients. In 2008, the presence of AP in PV was associated with a lower risk of arterial thrombosis. So, it seemed particularly interesting to analyze the clinical impact of the presence of AP in ET patients for such a risk. For this, the biological and clinical data of 396 ET patients followed in our hospital was used (Observatoire Brestois des NEoplasies myéloprolifératives database, OBENE, NCT02897297). So, 42 (10.6%) of our 396 patients suffered from AP. Interestingly, their median age at diagnosis was younger (51.6 vs 63.8 yr, p<0.0001). Furthermore, they presented more symptoms as erythrocytosis, hyperviscosity, constitutional symptoms and splenomegaly (p<0.01). ET with AP were more proliferative (more polycythemic but less thrombocythemic, p<0.04 each) and were more difficult to treat (2.2 vs 1.1 treatment lines, p=0.005). Concerning the occurrence of thrombotic events (arterial or venous) at diagnosis, no significant difference between groups was found. In contrast, there were more thrombotic events during the follow-up in group with AP (30.9 vs 17.2%, p=0.03). The artery/vein rate of thrombotic events was also different (50/50 vs 2/3:1/3, p<0.05). Furthermore, 1/3 of ET with AP had phenotypic evolutions (PV or secondary myelofibrosis) against 13.8% in the other group (p=0.0007). Concerning the overall survival of the patients, we noted that ET with AP have a lower rate of death (11.9 vs 32.5%, p=0.006) in spite of a longest follow-up (12.1 vs 7.7 years, p=0.002). AP is not only a PV symptom, but is also present in ET. Furthermore, ET with AP were more proliferative, more symptomatic at diagnosis but had also higher risk of thrombosis and phenotypic evolution than ET without AP. Despite that, these patients have a higher overall survival. So, the presence of AP in patients with ET characterizes patients with high risk of morbidity (thromboses, phenotypic evolution). The systematic determination of the presence of AP in ET patients at diagnosis should permit to better identify these patients for a better management and follow-up.

OP48

PREVALENCE AND CLINICAL CHARACTERISTICS OF PRURITUS IN PATIENTS WITH CUTANEOUS LUPUS ERYTHEMATOSUS

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Various inflammatory skin diseases are accompanied by pruritus of various severity. However, data on pruritus in patients suffering from cutaneous lupus erythematosus (CLE) are very limited. This multicenter, prospective, cross-sectional study was undertaken to evaluate the prevalence and clinical characteristics of pruritus in patients with CLE. The study was based on the questionnaire assessing sociodemographic data, clinical subtypes of CLE, as well as various clinical aspects of pruritus, including its intensity, accompanying experiences, influence on psyche as well as treatment modalities used by patients to alleviate it. Skin lesion severity was assessed with CLASI, while systemic symptoms were assessed with SELENA-SLEDAI. The study was approved by Ethic Committee of Wroclaw Medical University. A total of 61 completed and verified questionnaires were included for preliminary analysis. Three (4.9%) patients had acute CLE (ACLE), 14 (22.9%) subacute CLE (SCLE) and 43 (70.5%) had chronic CLE (CCLE). One (1.6%) patient presented clinical features of both ACLE and CCLE. Mean activity according to CLASI was 6.0±5.6 while mean damage was 3.3±4.2 points. Pruritus was reported by 46 (75.4%) patients. In contrast, pain within skin lesions was experienced by only 8 (13.1%) of CLE patients. The maximum pruritus severity measured with Numeric Rating Scale (NRS) was 5.5±2.4 points, being the most severe in generalized ACLE, but the differences were not statistically significant. Most commonly pruritus affected scalp (n=22; 47.8%), nose (n=16, 34.8%) as well as the rest of the face (n=19; 31.1%) and arms (n=15; 24.6%). Significant correlation was observed between Activity CLASI score and maximum (r=0.39, p<0,01) as well as average pruritus

intensity (r=0.32, p=0.02). Such relationship was not observed for pain. No relationship was also found between severity of systemic symptoms and reported pain or itch intensity. Based on our results we may conclude that pruritus is relatively frequent, but often overlooked symptoms in patients with CLE. Further studies are needed to better characterize its clinical characteristics and verify the efficacy of various treatment modalities.

OP49
CLINICAL CHARACTERISTICS OF AQUAGENIC PRURITUS IN POLYCYTHEMIA VERA

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Background: Aquagenic pruritus (AP) is one of the main clinical features of polycythemia vera (PV). Despite it was described more than three decades ago, the knowledge about its clinical characteristic and management still remains scarce. Objectives: This study was undertaken to analyze clinical characteristics of AP and its associations with laboratory results. *Material and Methods:* The study group consisted of 102 patients with molecularly confirmed PV with the mean age of 66.9±12.7 years. Demographic data, data on disease history, PV status and treatment modalities were collected. Pruritus intensity was evaluated with visual analogue scale (VAS), verbal rating scale (VRS) and a 4-item Itch Questionnaire. Moreover, various clinical features of AP (including localization, quality, descriptors) and the most common factors responsible for its aggravation or alleviation were examined. Participants underwent also basic laboratory tests. *Results:* AP was observed in 41.1% individuals. The mean duration of AP was 6.6±8.6 years and its onset was noticed in the majority of sufferers before the PV diagnosis (52.4%). The mean AP intensity was assessed as 4.8±1.9 points (VAS) and 6.0±2.9 points (4-item Itch Questionnaire). One third of patients with AP avoided any contact with water. Sleep disturbances, were observed among 16.7% AP patients. Of note, negative correlations between hemoglobin, hematocrit and pruritus severity were found. Antipruritic treatment was received only by 3 patients without any clinical improvement. *Conclusions:* AP seems to be an entity of neglected importance among PV sufferers with HGB and HCT serving as major contributors of its intensity.

OP50
CLINICAL CHARACTERISTICS OF PRURITUS IN HIDRADENITIS SUPPURATIVA PATIENTS

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Background: The growing body of research has indicated pruritus as an important hidradenitis suppurativa (HS) feature. Objectives: This study was undertaken to evaluate the pruritus and additonally pain among HS patients. *Material and Methods:* The study group consisted of 103 (50 females, 53 males) HS patients with the mean age of 35.6±13.2 years. The disease severity was assessed as 38.0±36.5 points, 9.2±4.6 points and 42/47/14 according to HSS (Hidradenitis Suppurativa Score), HSSI (Hidradenitis Suppurativa Severity Index) and Hurley I/II/III staging, respectively. Pruritus and pain intensity were evaluated with visual analogue scale (VAS), numeric rating scale (NRS) and a 4-item Itch Questionnaire. DLQI was also implemented to assess the QoL issues. Moreover, various clinical features of pruritus and the most common factors responsible for its aggravation or alleviation were examined. *Results:* The pruritus within last seven days before examination was reported among 41.7% of HS patients, whereas pain was observed in 77.5% individuals. The pruritus severity was assessed as 5.0±2.1 points, 5.5±2.3 points, and 4.6±1.9 points (for VAS_{max}, NRS_{max} and 4-item Itch Questionnaire, respectively). The pain intensity was evaluated as 7.3±2.4 points (VAS_{max}) and 7.5±2.5 points (NRS_{max}). Pruritus was observed predominantly in buttocks area (90% of pruritic lesions) and armpits (83% and 87% of pruritic lesions). With except for buttocks, pain was distributed quite equally between armpits, inguinals, abdomen, chest and anogenital area. The presence of pruritus neither had an impact on QoL assessed with DLQI, nor did it show interaction with the pain in this regard. The pain presence was a crucial contributor (p=0.002), even more important than disease severity (p=0.04). Nonetheless, the pruritus intensity correlated significantly with DLQI. The pain intensity correlated negatively with QoL assessed with DLQI and additionally with disease severity. The majority of patients described their itch as burning (46.5%), stinging (25.6%) or tickling (18.6%). The most common factors exacerbating itch intensity were increased sweating, heat and physical activity. The pain was reported as the most troublesome symptom of HS consecutively outpacing exudation, pruritus, appearance and smell. *Conclusions:* In patients with HS, in addition to pain, the pruritus of mild-to-moderate intensity is not uncommon symptom associated with the disease adversely affecting the quality of life.

PATIENTS' PERSPECTIVES AND PATIENT REPORTED OUTCOMES

OP51
PATIENT-REPORTED OUTCOMES: AN INTRODUCTION

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A patient-reported outcome (PRO) is defined as any report of the status of a patient's health that comes directly from the patient, without interpretation of a clinician or anyone else. The measurement of PROs has become an important component of outcomes assessment in clinical research, observational health services research and - more recently - in routine healthcare. Examples of PROs include instruments that measure health-related quality of life (HRQOL) such as the ItchyQoL, symptoms or treatment satisfaction. The measurements generated by PRO measures need to be valid and relevant for patients, healthcare professionals and other stakeholders. This will only be achieved if the development and validation is done in a robust way. The development of a PRO is a multi-step process, involving a content validity phase and a psychometric testing phase. In this process, it is important to consider all measurement properties of the PRO of interest. According to the consensus-based taxonomy of the COSMIN (COnsensus-based Standards for the selection of health Measurement Instruments) group, these are: content validity including face validity, reliability, responsiveness, internal consistency, structural validity, measurement error, hypothesis testing, criterion validity, cross-cultural validity. Aspects of feasibility such as patient comprehensibility, interpretability or completion time also need to be assessed. When we think about PRO validation, we often think about the psychometric phase, for instance testing test-retest reliability (stability of the measurements over time) by calculating an intra-class correlation coefficient. While PRO studies often give detailed reports of the psychometric testing of PROs, those that adequately report on content validation are less prominent. In the content validity phase in which a PRO is created, three steps are important: (1) definition of a conceptual model; (2) generation of content in terms of items in relation to that model; and (3) cognitive interviewing to ensure

feasibility of the measure. Thus, the development and validation of PRO measures for patients with chronic itch as in other clinical fields is complex and not restricted to psychometrics alone. It requires a mixed-methods approach with appropriate application of quantitative and qualitative research and the requisite multidisciplinary expertise to conduct each phase well.

OP52
HIGH LEVELS OF ACTING WITH AWARENESS GO ALONG WITH LOW LEVELS OF ITCH CATASTROPHIZING: FIRST RESULTS OF A CROSS-SECTIONAL STUDY IN PATIENTS WITH ATOPIC DERMATITIS

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Theoretical background: Mindfulness, defined as paying attention to the present moment on purpose and without judging, leads people to react consciously instead of automatically. Mindfulness interventions have been shown to have positive effects on the skin, quality of life and stress in patients with psoriasis. Moreover, recently, naturally occuring levels of mindfulness have been shown to be related to anxiety, depression, quality of life and skin shame in patients with different skin diseases. Whether, naturally occuring levels of mindfulness are also related to itch catastrophizing in patients with the chronic itchy skin disease atopic dermatitis (AD), is investigated with this study for the first time. *Methods:* 109 ND-patients (44 male, 65 female; mean age: 45±13 years) filled in the Comprehensive Inventory of Mindfulness Experiences (CHIME) and the Itch Cognition Questionnaire (ICQ) during the first week of their stay at a rehabilitation clinic on Borkum, Germany. In addition, the average itch intensity during the last two weeks prior to the stay at the clinic was measured by a visual analogue scale (VAS 0–10). *Results:* Correlation analyses revealed that the mindfulness scales „acting with awareness", „accepting and non-judgemental orientation" and „decentering and non-reactivity" significantly negatively correlated with itch catastrophizing [acting with awareness: r=–0.368; $p \leq 0.001$; accepting and non-judgemental orientation: r=–0.196; $p=0.044$; decentering and non-reactivity: r=–0.230; $p=0.018$]. The regression analysis showed that after controlling for age, gender, illness durination and itch intensity during the last two weeks, an additional 11.1% of the variance of itch catastrophizing was explained by „acting with awareness" [F (2/76) = 24.789; $p \leq 0.001$]. *Discussion:* This study was the first to show that different facets of mindfulness are negatively related to itch catastrophizing in patients with AD, whereby acting with awareness showed the strongest correlations with itch catastrophizing. It is striking that this facet of mindfulness also showed the strongest correlations with psychological burden in patients with different skin conditions in a previous study. In our point of view, it would therefore worth to investigate whether certain mindfulness techniques aiming to especially increase acting with awareness are able to reduce not only itch related cognitions, but also scratching in itch inducing situations.

OP53
DO PLACEBO EFFECTS WORK WHEN SUBJECTS KNOW THAT THEY RECEIVE A PLACEBO? EFFECTS OF OPEN-LABEL VERBAL SUGGESTIONS ON ITCH

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Negative and positive outcome expectancies, induced by verbal suggestions, have been shown to influence subjective symptoms such as itch. Although most experimental studies on placebo and nocebo effects have only informed participants following participation that they received an inert substance (closed-label placebo/nocebo), there is a growing body of literature that suggests that placebo effects can occur even when it is known that a given substance is inert (open-label placebo). An experimental study was conducted to investigate the effects of open-label positive verbal suggestions on itch. It was expected that open-label positive verbal suggestions would reduce itch following a validated itch-inducing histamine test. Healthy volunteers ($n=92$) were randomized to either an experimental or a control group. Itch was evoked experimentally during a single laboratory session by histamine iontophoresis. In the experimental group, participants were told that the test would elicit little itch and received information on how expectations could influence itch (i.e. open-label positive verbal suggestions), whereas in the control group, no suggestions were given. Open-label verbal suggestions were found to affect itch expectations in this study, but not induced itch. Additionally, within the experimental group only, lower post-verbal suggestion expected itch was significantly associated with lower self-reported itch. These results offer support for open label placebo efficacy in itch. Future research might focus on strengthening the verbal suggestions used in the current study, for example by using more explicit explanations of the role of expectations in itch. Further identifying the role of expectations in itch could provide new knowledge on how to optimize treatment effects in chronic itch.

OP54
A QUALITATIVE STUDY TO UNDERSTAND PATIENTS' PERCEPTION OF THE SEVERITY OF CHRONIC PRURITUS AND ITS IMPACT ON HEALTH-RELATED QUALITY OF LIFE

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Objectives: To understand how patients suffering from Chronic Pruritus (CP) perceive the severity of CP and its impact on health-related quality of life (HRQoL). *Methods:* A preliminary conceptual framework was developed after a systematic literature review. It was revised based on qualitative data generated by patients suffering from CP (underlying skin condition were psoriasis, atopic dermatitis, scalp seborrheic dermatitis, urticaria or none, in elderly people) during focus groups (FG). Participants' verbatim were textually reported into transcript, which were thematically analyzed using qualitative content analyses (inductive approach). *Results:* Nineteen participants from one dermatological center in France were interviewed through 3 FG sessions. The severity of CP was reported in terms of: (*i*) intensity of itch (sensation type and scratching response), (*ii*) duration, and (*iii*) extension. Subdomains of interest for HRQoL were organized into: (1) sleep and fatigue; (2) coping and anticipation; (3) sexual life; (4) emotions and cognitions; (5) concentration; (6) daily activities; (7) cognitions attributed to others; (8) social relations; and (9) time spent. These sub-domains of interest were consistent across all skin conditions. Saturation of concepts was reached after the second FG. *Discussion:* A comprehensive and clinically sound conceptual framework of CP severity and its impact on patients' HRQoL has been achieved through structured literature review and focus groups.

OP55

THE BURDEN OF CHRONIC ITCH-A QUESTIONNAIRE BASED EVALUATION OF CLINICAL CHARACTERISTICS, ASSOCIATED MORBIDITY AND TREATMENT OUTCOMES IN A COHORT OF PATIENTS WITH CHRONIC PRURITUS

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Itch is the most common symptom in dermatology having a significant impact on patient's quality of life. With new treatment options on the horizon it is important to clinically differentiate patients, evaluating itch independently and with objective measures. *Aims:* 1) Characterize clinical features of itch in a cohort of patients attending the dermatology department. 2) Evaluate the impact of itch on quality of life, sleep and mental health. 3) Evaluate the efficacy of treatments as reported by patients. *Methods:* Patients with a diagnosis of prurigo nodularis (PN), atopic dermatitis (AD), psoriasis (PSO) and pruritus of undetermined origin (PUO) were recruited from the dermatology OPD of SVUH. A pruritus questionnaire incorporating the itch VAS was developed. DLQI, PSQI and HADS were also used. *Results:* 73 patients were recruited. Itch was a symptom for more than 5 years in 62.67%. 45.9% reported "always" feeling itchy. 36.49%, the largest group reported bedtime as the most bothersome time. Heat and stress were the commonest exacerbating factors. The mean VAS was 6.69 indicating moderate to severe itch. This was greatest in patients with PN (7.50) and lowest in patients with psoriasis (5.89) with a significant difference in severe and very severe itch between the two groups (83.3% vs 47.2%, $p<0.05$). VAS was found to be a significant predictor of DLQI, PSQI, and HADS. Importantly it remained a significant predictor of DLQI independent of PASI (regression coefficient B=1.881, $p<0.05$). 77.73% of patients had abnormal sleep patters (PSQI score > than 5). The mean PSQI was highest in patients with PUO and lowest in patients with psoriasis. 34.7% of patients had a borderline or abnormal HADS for anxiety. This was proportionally greatest in patients with PN (50%). Most patient's felt that topical and systemic treatments were only partially effective (71.67% and 72.73% respectively). Phototherapy was reported to be the most efficacious treatment overall. *Conclusion:* In this patient cohort itch was found to be a chronic symptom. There was significantly less severe itch in patients with psoriasis where it had less impact on sleep than the other groups. Measurement of itch by VAS was an important predictor of DLQI in all groups and was independent of PASI. Systemic and topical treatment efficacy remains partial for most patients. This highlights the unmet medical need in pruritus treatment and the need for its evaluation independent of other disease measures.

OP56

EUROPEAN EADV NETWORK ON ASSESSMENT OF SEVERITY AND BURDEN OF PRURITUS (PRUNET): VALIDATION OF INSTRUMENTS FOR ITCH INTENSITY ITCH-IMPAIRED QUALITY OF LIFE IN PRURITIC DERMATOSES IN EUROPE

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Pruritus is a frequent symptom of many dermatoses and leads to a restriction of quality of life. There are currently no uniform procedures for measuring the symptom itself and its consequences in patients' life within Europe. For this reason PruNet was founded, which comprises 31 experts from 15 countries. In a consensus conference, pruritus-specific instruments were evaluated and selected for the validation study using a Delphi process. The chosen questionnaires, itch intensity scales (including visual analog scale, numeric rating scale and verbal rating scale), the ItchyQoL and 5PLQ (both tools for measuring the impairment of quality of life in patients with chronic pruritus), were translated into national languages and were digitized for tablet application. Validation took place in a dermatological collective in Germany, Poland, Austria, Switzerland, Spain, France, Turkey, Russia and Italy for 4 weeks. A total of 552 (> 50/center) patients with contact dermatitis, prurigo nodularis, psoriasis vulgaris, lichen planus or mycosis fungoides/Sézary syndrome and pruritus >3 on the NRS were included. Following the COSMIN checklist, we analyzed the data from all countries. All questionnaires showed an excessive consistence, an excellent reproducibility, a good concurrent and convergent validity. The acceptance of instruments was high among patients and physicians involved. By validation of itch specific tools, a harmonization is given. This is not only important in daily routine to improve the care of patients with itchy dermatoses, but also in clinical trials to establish urgently needed new therapeutics in order to better compare clinical data.

ITCH AND PAIN

OP57

SPINAL GABA-A RECEPTOR SUBTYPES CONTROLLING ITCH

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Chronic itch affects about 10% of the general population. Chronic itch is in most cases histamine-independent and does as such not respond to classical antipruritic compounds. Previous work by different groups has demonstrated that the relay of itch signals is under the tight control by inhibitory circuits of the spinal dorsal horn, which use GABA and/or glycine for synaptic inhibition. Using a battery of $GABA_A$ receptor point mutated mice, we found that specific pharmacological targeting of alpha2 and alpha3$GABA_A$ receptors reduces acute histaminergic and non-histaminergic itch in mice. Systemic treatment with an alpha2/alpha3$GABA_A$ receptor selective modulator alleviated acute and chronic oxazolone-induced itch in mice, and chronic itch in dogs sensitized to house dust mites. Transsynaptic circuit tracing, immunofluorescence and electrophysiological experiments suggest that spinal alpha2 and alpha3$GABA_A$ receptors as likely molecular targets underlying the antipruritic effect. Our results indicate that drugs targeting alpha2 and alpha3$GABA_A$ receptors are well-suited to alleviate itch, including non-histaminergic chronic itch, which is a particularly difficult to treat condition.

OP58

OPPOSING EFFECTS OF CERVICAL SPINAL COLD BLOCK ON SPINAL ITCH AND PAIN TRANSMISSION

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Inactivation of descending pathways enhanced responses of spinal dorsal horn neurons to noxious stimuli, but little is known

regarding tonic descending modulation of spinal itch transmission. To study effects of cervical spinal cold block on responses of dorsal horn neurons to itch- and pain-evoking stimuli, single-unit recordings were made from superficial dorsal horn neurons in pentobarbital-anesthetized mice. 64 units were tested (46% wide dynamic range-type, 54% nociceptive-specific). Cold block had no effect on mechanically-evoked responses. Ten units' responses to noxious heat were significantly enhanced during cold block, while 6 units' responses were reduced and 18 unaffected. 26 units responded to mustard oil (AITC), with a further significant increase in firing during the 1-min period of cold block beginning 1 min after AITC application. Activity during cold block was significantly greater compared to the same time period of control responses to AITC in the absence of cold block (n=39). Id histamine excited 17 units. Cold block starting 1 min after id injection of histamine caused a marked decrease in firing. The histamine-evoked response during and following cold block was significantly lower compared to control histamine-evoked responses in the absence of cold block (n=57). A similar but weaker depressant effect of cold block was observed for dorsal horn unit responses to chloroquine (n=26), for which chloroquine-evoked activity during cold block was lower compared to control responses in the absence of cold block (n=25). These results indicate that spinal chemonociceptive transmission is under tonic descending inhibitory modulation, while spinal pruriceptive transmission is under an opposing, tonic descending facilitatory modulation.

OP59
RESPONSES SINGLE THALAMIC UNITS TO PRURICEPTIVE AND NOCICEPTIVE STIMULI IN THE RAT

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Comparatively little is known about processing of pruriceptive information in the brain. Indeed, no studies have been performed in which the responses of individual thalamic neurons have been examined to itch-producing stimuli. We characterized the responses of more than 50 thalamic neurons in rats activated by mechanical stimulation of the cheek. Responses of these neurons to pruriceptive stimuli that included intradermal injections of serotonin (5-HT), chloroquine, beta alanine and histamine were determined. Response by these neurons to nociceptive stimuli (pinching of the skin and injection of capsaicin) were also examined. Seventy-eight percent of thalamic neurons were activated by at least one pruriceptive stimulus. Forty-three percent of such pruriceptive neurons were recorded in the ventral posterior medial nucleus (VPM), 40% in posterior triangular nucleus (PoT) and smaller fractions in other posterior thalamic nuclei. More than 44% of pruriceptive neurons were activated only by noxious mechanical stimuli (HT), 39% were activated by innocuous and noxious mechanical stimuli (WDR). A small number of neurons that responded only to innocuous mechanical stimuli were activated by pruriceptive stimuli. Eighty-six percent of pruriceptive neurons were activated by injection of histamine, 52% by 5-HT, 49% by beta alanine, and 31% by chloroquine. Twenty-four percent of examined neurons were activated by a single pruritogen, 22% by two pruritogens, 19% by three and 11% by all four. These results indicate that 1) surprisingly, more than three-fourths of thalamic neurons that responded to mechanical stimulation of the cheek were also activated by injection of one or more of the tested pruritogens; 2) the overwhelming majority of pruriceptive thalamic neurons were also activated by nociceptive stimuli; and 3) pruriceptive thalamic neurons were most frequently located in either VPM or PoT.

OP60
ACUPUNCTURE FOR PAIN MANAGEMENT IN EVIDENCE-BASED MEDICINE

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Pain is an enormous and prevalent problem that troubles people of all ages worldwide. The effectiveness of acupuncture for pain management has been strongly verified by large randomized controlled trials (RCTs) and meta-analyses. Increasing numbers of patients with pain have accepted acupuncture treatment worldwide. However, some challenges exist in establishing evidence for the efficacy of acupuncture. A more applicable and innovative research methodology that can reflect the effect of acupuncture in the settings of daily clinical practice needs to be developed Pain is "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. The previous experience of acupuncture research studies are invaluable for researchers to recognize the limitations and challenges of research designs and would help to move the field forward in future research. For example, the design of an adequate sham control, involvement of skilled and experienced acupuncturists, adequate outcome measures in the clinical trials, and the discovery of physiological effects of acupuncture . in basic science are all important tasks for acupuncture researchers to address and solve. Challenges and future directions of acupuncture research for pain conditions in EBM High-quality RCTs and meta-analysis have increasingly produced robust evidence of the effectiveness of acupuncture for pain conditions, although nonspecific physiologic response to the needle insertion and the nature of holistic character of acupuncture treatment lead to many challenges in the research designs that reflect the daily clinical acupuncture practice, an individual patient data meta-analysis was conducted by Andrew et al to evaluate the effectiveness of acupuncture for four types of chronic pain: back and neck pain, osteoarthritis, chronic headache, and shoulder pain. The result reflects that acupuncture was superior to sham acupuncture controls and to the usual care controls in all four chronic pain conditions.

OP61
ITCH AND PAIN INFLUENCE ON QUALITY OF LIFE AND SLEEP DISTURBANCES OF HIDRADENITIS SUPPURATIVA PATIENTS

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Background: Hidradenitis suppurativa (HS) is a chronic, inflammatory, debilitating and suppurative disease of the hair follicle manifested by painful abscesses, fistules and scarring lesions. HS has great impact on patients' quality of life. *Objectives:* This study was undertaken to evaluate the influence of itch and pain on quality of life of hidradenitis suppurativa patients. *Material and Methods:* The study group consisted of 108 (51 females, 57 males) HS patients with the mean age of 36.3±12.1 years. The mean disease severity was assessed as 34.8±32.1 points, 9.0±4.4 points and 50/49/9 according to HSS (Hidradenitis Suppurativa Score), HSSI (Hidradenitis Suppurativa Severity Index) and Hurley I/II/III staging, respectively. Itch and pain intensity were evaluated with visual analogue scale (VAS). The quality of life was assessed by DLQI. Moreover, sleep abnormalities were estimated with Athens Insomnia Scale (AIS), Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). *Results:* During the course of disease and within three last days subjective symptoms were experienced by the following group of patients: itch – 66/108 (61.0%) vs. 61 (56.5%) patients and pain – 93/108 (86.0%) vs. 88/108 (81.5%) patients, respectively.

The mean and maximal severity of itch and pain within three last days were assessed as: itch – 4.1±2.9 points, 5.0±2.1 points and pain – 4.9±2.9 points, 7.3±2.4 points, respectively. The mean QoL was assessed as 13.0±8.0 points. The scores for particular sleep abnormalities questionnaires were 5.4±4.3 points, 6.4±3.6 points and 6.1±3.9 points with regard to AIS, PSQI and SSE, respectively. The severity of itch and pain significantly correlated with scores obtained by the AIS (R=0.44, p=0.004) and (R=0.39, p=0.001), respectively. Moreover, the disease severity assessed with HSSI significantly correlated with scores obtained by the AIS (R=0.22, p=0.03). Decreased QoL assessed with DLQI correlated positively with scores obtained with AIS and PSQI ($p \leq 0.0001$ for both correlations). *Conclusions:* Decreased quality of life and sleep disturbances in hidradenitis suppurativa patients seem to be an underestimated problem and could be related to pain and itch experienced during the course of disease.

PRURIGO AND OTHER PRURITIC SKIN DISEASES

OP62
PRURIGO AND OTHER PRURITIC SKIN DISEASES

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Prurigo is a clinically accepted entity of itching papular or nodular lesions scattered on skin sites that can easily be scratched. Histologically, the hyperkeratotic nodules present with a reduced density of intraepithelal nerve fibers and an increased number of hypertrophic dermal sensory nerve fibers. The pathologic nerve fibers may fire spontaneously to produce itch. There are many exogenous and endogenous triggers of itch in prurigo. Toxic agents deposited in the skin by parasites, bacteria or topically or orally administered drugs can induce itch. In susceptible individuals, ultraviolet light can induce changes in epidermal innervation that result both in itch generally and in prurigo lesions. Prurigo occurs sometimes in atopic patients or during pregnancy. An umbilicated type of prurigo may be associated with some internal diseases like renal failure, diabetes mellitus or collagen disorders. Malabsorption due to gluten enteropathy, anorexia nervosa or fasting can also induce special types of prurigo. T-cell lymphoma and visceral neoplasias are the most common malignancies associated with prurigo. Some forms of prurigo may be secondary to scratching which destroys epithelial innervation mechanically leading to pathologic firing of damaged nerve fibers. Emotional factors can also influence the perception of itch and scratching. There are some specialised forms of prurigo with ethnic preference, like prurigo pigmentosa in Japan, actinic prurigo (a chronic photodermatitis found predominantly in native North and South American Indians) or "papular eruptions in black men." Topical treatment options are: corticosteroids (preferentially administered under occlusive dressings or intralesionally), calcineurin receptor inhibitors, cannabinoid receptor agonist, UVB, cryotherapy, capsaicin or bath photochemotherapy. Systemic regimens involve use of PUVA, methotrexate, cyclosporin A, arotinoid acid, azathioprine, chloroquine, dapsone, minocycline or naltrexone. Psychopharmaca targeting transmitters of mood which deteriorate prurigo may be useful. Clinical trials of drugs using substance P antagonist and interleukin 31 antibody seem promising in treatment of itch. Combined sequential treatments for generalised, therapy-resistant cases need to be tailored to the exacerbations that occur and to maintenance treatment in order to enable the patient to withstand the intolerable itch.

OP63
PSORIATIC ITCH 2017

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Itch is the most common symptom in dermatology. Mild to severe itch accompanies numerous skin disorders including, but not limited to atopic dermatitis, eczema, psoriasis, lichen planus, mycosis fungoides, Psoriasis is a chronic inflammatory skin diseases, affecting 1–3% of general population. For a long time psoriasis was considered as a non-pruritic dermatosis. The current 2017 knowledge shows that itch is a very prevalent symptom of psoriass found in 70-80% of patients suffering from this disease. Itch may be limited to psoriatic plaques, but in about 30–40% of patients may also affect uninvolved skin. The mean severity of pruritus assessed according to visual analog scale (VAS) is slightly above the five points, indicating that most patients suffer from pruritus of moderate severity. Recently it has been documented that itch is the most bothersome symptom of psoriasis and is most important factor contributing to the disease severity. Patients present decreased well-being status, they are more depressed and they have higher level of stigmatization. The pathogenesis of psoriatic itch is still not completely clear and several possible factors may contribute to its appearance and exacerbation. One may consider increased innervation density and abnormal neuropeptides homeostasis as well as disturbed peripheral opioid system. There is no gold standard to treat psoriatic itch. According the European guideline resolution of skin lesion is crucial for the itch elimination. Therefore, new biological therapies have been evaluated and it is clear that they are of benefit for patients with psoriatic itch. However, the holistic approach, including psychological support should be offered to this group of subjects.

OP64
NOVEL DEFINITION, CLASSIFICATION AND TERMINOLOGY OF CHRONIC PRURIGO

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Prurigo exists as a term for over two centuries, but has been used for many years without well-defined criteria. Due to the multitude of possible clinical manifestations, including papular, nodular, plaque-type or umbilicated types, a variety of terms has been associated with prurigo leading to confusion in the dermatological routine care and in the scientific literature. Aiming to achieve a consensual definition, classification and terminology for chronic prurigo, twenty-four European experts of the Task Force Pruritus (European Academy of Dermatology and Venereology) met at the Department of Dermatology and Center for Chronic Pruritus, University Hospital Münster on February 3rd, 2017. The Delphi Method was used for the voting and consensus was reached when an agreement across ≥75% of the participants was achieved. Experts considered chronic prurigo a distinct disease with its own pathophysiological mechanisms and clinical presentation. 'Chronic prurigo' was chosen as an umbrella term condensing the various presentations of this disease. These may indicate different disease stages with papular prurigo often developing into nodular prurigo and ultimately to plaque-type prurigo and thus artificial separations are avoided by using this generic term. Main criteria for the diagnosing chronic prurigo include (*i*) suffering from chronic pruritus for at least 6 weeks, (*ii*) evidence of prolonged scratching in the medical history or upon physical examination and (*iii*) the presence of pruriginous lesions. Regarding its pathophysiological mechanisms, the original cause for the itch underlying the CPG may be of various origins (dermatological, systemic, neurological,

psychiatric/psychosomatic, multifactorial or unknown). However, even after treatment of the underlying cause of the itch, CPG may persist due to the development of chronicity processes. Especially the itch-scratch cycle that ensues plays an important role. Therefore, these chronicity processes should be targeted when treating patients with CPG in order to achieve an improvement of the symptoms. Dermatologists should embrace this novel definition, classification and terminology of chronic prurigo in order to facilitate the communication among clinicians, scientists and patients.

OP65
APREPITANT, A NK1-ANTAGONIST, ADMINISTERED FOR 16 WEEKS REDUCED ITCH AND SUPPORTED RESOLUTION OF SKIN LESIONS IN A PATIENT WITH CHRONIC PRURIGO

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Chronic prurigo (CPR) results from the development of an "itch-scratch cycle", with chronic pruritus (CP) (> 6 weeks) and repeated scratching eventually leading to pruriginous papules, nodules and/or plaques. To date, medications with additional antipruritic effects are available only off-label for the treatment of CP or CPR. Substance P and its neurokinin-1 (NK1) receptor are believed to play an important role in the pathophysiology of itch. Aprepitant, a NK1 antagonist, licensed for the treatment of nausea and vomiting during highly emetic chemotherapy, was reported to have antipruritic effects in prurigo nodularis during short-term use. However, long-term itch reduction is required to clear pruriginous skin lesions in CPR. We treated a male patient (73 years) suffering for more than 20 years from recalcitrant CPR, with permanent itch and pruriginous nodular skin lesions on his extremities and trunk, with aprepitant 80 mg/day for 16 weeks. Beside emollients with menthol, urea, and polidocanol, antipruritic treatments including topical corticosteroids, tacrolimus, and capsaicin, as well as oral antihistamines were clinically ineffective. Over the years, he repeatedly received UVB, UVA1, oral and bath-PUVA therapies. Finally, after 2 months of saltwater plus narrowband (NB)-UVB, pruritus was still 4.7 on the VAS (0=no itch, 10=worst imaginable itch) and extensively excoriated pruriginous skin lesions were still present. Within 2 weeks of daily aprepitant 80mg, pruritus weakened from 4.7 to 3.3 (34% reduction) and was 3.0 after 6 weeks. We then added NB-UVB three times per week and after further 4 weeks topical corticosteroids, once daily for 2 weeks and then every other day for 2 weeks. This further reduced itch to 2.2. Eventually, due to the high costs of aprepitant, we reduced its dose to 80 mg every other day and stopped it after 2 weeks completely. From that time point on, treatment was continued with NB-UVB, intermittent topical corticosteroids, and additional daily topical calcipotriol. Within further 8 weeks itch was reduced to 0.5 and only very few excoriations remained. In conclusion, while various previous treatments were insufficient to permanently reduce itch in this patient, it appears that the long-term (16 weeks) aprepitant treatment was capable of "breaking the itch-scratch cycle", eventually paving the way for additional UV and topical treatments to become effective in reducing itch and pruriginous lesions in this patient.

OP66
PERIPHERAL EFFECTS OF TARGETING THE NEUROKININ 1 RECEPTOR IN CHRONIC PRURIGO

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Blocking the neurokinin 1 receptor (NK1R) in chronic pruritus has recently been shown to reduce pruritus intensity. Both, central effects involving spinal dorsal horn neurons and peripheral effects involving cutaneous components are discussed as underlying mechanisms. In human skin NK1R may initiate several inflammatory reactions like mast cell activation and expression of pro-inflammatory cytokines by keratinocytes. Within this study we therefore investigated *in vivo* and *in vitro* peripheral effects mediated by the NK1R antagonists aprepitant and casopitant. For the *in vivo* study 13 patients suffering from the chronic prurigo subtype prurigo nodularis (PN) received an oral four weeks treatment with aprepitant (80 mg/d). Clinical and immunohistochemical parameter were assessed before and after treatment. Furthermore expression of NK1R and activation of potential downstream targets were measured. Studies were continued *in vitro* using keratinocytes (HaCaT, NHEKs). Cells were stimulated using the NK1R activating substance P (SP) with or without pre-treatment with aprepitant or casopitant. Again, the effect of NK1R antagonism on downstream molecules was assessed. Treatment with aprepitant reduced significantly pruritus intensity in PN patients. This was not reflected by histological changes what may be due to the short treatment period. Immunohistochemistry revealed altered expression of some inflammatory marker suggesting a peripheral therapeutic effect. Epidermal NK1R expression was higher in PN patients compared to matched healthy controls (n=10); after treatment with aprepitant it increased even more. We speculate that the upregulation may be needed to overcome at least in parts the long lasting blockage by aprepitant. First analyses of NK1R antagonism in keratinocytes *in vitro* revealed no effect on expression of pro-inflammatory cytokines. Additionally we analysed downstream molecules which can be activated by NK1R and found Erk1/2 to be affected. SP induced activation/phosphorylation of Erk1/2 was significantly reduced by both, aprepitant and casopitant. This was confirmed *in vivo* as 7 of 9 PN patients showed reduced Erk1/2 phosphorylation after treatment with aprepitant. In sum, altered receptor expression and reduced MAPK activation *in vivo* and *in vitro* suggests a peripheral mechanism on keratinocytes for the observed antipruritic effect of NK1R antagonism.

OP67
NEUROPHYSIOLOGICAL STUDIES ON CHRONIC PRURIGO

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Chronic prurigo (CPG) is a highly burdensome condition, which has gained interest in recent years. Recently European experts of the EADV Task Force Pruritus reached a consensus on the clinical definition and terminology of CPG. However, the underlying pathophysiological mechanisms remain unclear and need further clarification. For peripheral itch transmission, both mechano-insensitive C-fibers (C_{MI}) activated by histamine and mechano- and heat sensitive C-fibers (C_{MH}) activated by cowhage play a central role. We compared patients with CPG (n=40) and healthy controls (n=40) in their response to cutaneous stimulation with cowhage, histamine and a negative control (NaCl) at the volar forearm. CPG patients, but not healthy controls, showed enhanced itch intensity after stimulation with cowhage in comparison to histamine (p<0.01). Additionally the maximal itch intensity after cowhage stimulation was significantly higher in CPG patients compared to controls (p<0.05), arguing for peripheral sensitization of C_{MH}-fibers. The intraepidermal nerve fiber density was reduced in CPG patients (n=21) compared to healthy controls (n=27). In spite of this finding, quantitative sensory testing revealed in an earlier study no differences in thermal detection

thresholds between patients (n=8) and controls (n=12; p=0.68) and thus no impairment of C-fiber function was observed. As we could demonstrate in a previous study a normalization of the intraepiderrnal nerve fiber density after healing of the prurigo lesions, we speculate that the prolonged scratching activity, and not an endogenous neuropathy, is responsible for the structural but not functional neuronal alterations observed in CPG. Peripheral sensitization of C_{MH}-fibers and structural neuronal alterations due to prolonged scratching may contribute to the perpetuation of the pruritus and of the CPG.

NEW RECEPTORS, CHANNELS AND PATHWAYS FOR ITCH

OP68
NEURAL RECRUITMENT AND MRGPR ACTIVITY ARE REQUIRED FOR THE DEVELOPMENT OF A MOUSE MODEL OF ATOPIC DERMATITIS

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Atopic dermatitis is characterized by chronic inflammation and severe itch. In addition to defective barrier function and immune dysregulation, altered neural innervation and neurogenic inflammation play less well-characterized but important roles in disease pathogenesis. Performing serial *in vivo* imaging of fluorescently-labeled peripheral sensory neurons in mice during the evolution of an allergic eczema, we show that cutaneous nerves function as precursors to the allergic process. Within hours of antigen exposure, neuropeptidergic fibers begin to pathfind and expand their arbors while vascular and immune changes follow. Neural activity was required for the maintenance of nascent fibers and development of inflammation. We identify Mrgpr signaling as an essential regulator of early neural responses to allergens, priming cellular feedback loops that drive allergic eczema and scratching. Our data provide critical insights regarding the temporal sequence of key cellular events in atopy pathogenesis and prompt a shift in the therapeutic paradigm for its management.

OP69
A CENTRAL FEEDBACK NEURAL CIRCUIT GATES ITCH-SCRATCHING CYCLE

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Itch triggers scratching behavior, which in turn leads to widespread itchiness. Uncontrollable itch-scratching cycles result in serious skin and deep tissue damage in patients with chronic itch. Itch signal processing is known to be under tonic inhibitory control at the spinal level, but the neural circuit mechanism promoting the itch-scratching cycle remains elusive. The fact that stress enhances or induces itchiness points to a top-down positive feedback circuit in gating spinal itch processing. Here we report that a group of tachykinin 1 (Tac1)-expressing glutamatergic neurons in the periaqueductal gray (PAG) of the mouse facilitate the itch-scratching cycle, through positive-feedback dis-inhibition of spinal neurons expressing gastrin-releasing peptide receptor (GRPR), the key relay neurons for itch sensation. Activity of Tac1-expressing neurons in the PAG was elevated during itch-induced scratching behavior. Suppressing the activity or ablation of these Tac1-expressing neurons greatly impaired itch signal processing. Consistently, selective activation of these Tac1-expressing neurons induced robust spontaneous scratching behavior by removing the inhibition of spinal itch processing via the rostral ventromedial medulla (RVM) inhibitory neurons that are known to inhibit spinal interneurons. These results establish that the Tac1-expressing neurons in the PAG play a key role in gating itch-scratching cycles, through feedback regulation of itch processing in the spinal cord.

OP70
TRPV1 REGULATES PAR-2-EVOKED INTRACELLULAR CA2+ RELEASE AND INFLAMMATORY MEDIATORS PRODUCTION IN DIFFERENTIATED KERATINOCYTES

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The activation of PAR-2 in keratinocytes enhances inflammation through a $Ca2^{+}$-dependent cytokines expression and release such as TSLP. However, studies only used primary keratinocytes from the basal stratum of the epidermis to analyze the role of PAR-2 in inflammatory process and itch. We investigated the involvement of PAR-2 in the intracellular calcium signaling pathways in differentiated keratinocytes and consequently inflammatory genes modulation. Calcium imaging recordings in Ca^{2+}-free medium showed that PAR-2 agonist peptide (SLIGKV) evoked calcium release from endoplasmic stores, which was totally inhibited by the specific PLC antagonist (U73122). The InsP3R (xestospongin C) and TRPV1 antagonist (AMG9810) impaired PAR-2-evoked Ca^{2+} release partially but totally when they were associated. Using RT-qPCR to study the inflammatory cytokines RNA expression, we demonstrated that SLIGKV induced a 13-folds up-regulation of the TSLP expression and by 2-folds expression of IL1-β, TNF-α and CXCL2. PAR-2-mediated cytokines up-regulation in the keratinocytes was abolished with PAR-2 antagonist (GB83). In addition, the blockage of TRPV1 with specific antagonists (AMG9810, SB366791 and capsazepin) or with siRNA knockdown of TRPV1 impaired PAR-2-mediated gene expression. Our findings demonstrated for the first time that PAR-2 promotes skin inflammation in the differentiated keratinocytes through PLC-dependent Ca^{2+} release by both IP3 and TRPV1 channels release and consequently inflammatory genes expression.

OP71
SPINAL RELEASE OF GASTRIN RELEASING PEPTIDE (GRP) IS REQUIRED FOR SUPRA-THRESHOLD SYNAPTIC ACTIVATION OF GRP RECEPTOR (GRPR)-POSITIVE NEURONS

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Gastrin releasing peptide (GRP) and its cognate receptor (GRPR) have been identified as important components in spinal cord pruriceptive-processing. However, the functional aspects of spinal itch-processing circuits are not well understood. Here, we combined electrophysiological and optogenetic approaches to functionally characterize GRP- and GRPR-positive neurons and to study their synaptic connectivity as well as modulation by GRP. We performed whole-cell patch-clamp recordings from GRP and GRPR neurons in acute spinal cord slices to characterize their intrinsic biophysical properties and firing patterns. We found that GRP neurons constitute a rather homogenous population with 92% of cells showing initial bursting firing. GRPR neurons were more heterogeneous comprising delayed (64%) and non-delayed (36%) firing subpopulations. We also found that delayed-firing GRPR neurons had significantly hyperpolarized resting membrane potentials (RMP), lower input resistances (Ri) and higher rheobase compared to GRP neurons. These characteristics are consistent with delayed-firing GRPR cells being glutamatergic

neurons involved in integrating and transmitting the spinal itch information. We then characterized the synaptic connectivity between GRP- and GRPR-positive neurons in slices prepared from GRP-ChR2 GRPR::eGFP mice and found that GRP neurons were synaptically connected to GRPR neurons. Under baseline conditions, light stimulation of ChR2-expressing GRP cells induced subthreshold responses in GRPR neurons. Application of 300 nM GRP caused a slow depolarization of delayed-firing GRPR neurons, which often resulted in ongoing action potential firing after several minutes. Moreover, in the presence of exogenous GRP, the same light stimulation paradigm triggered action potential firing in GRPR delayed neurons. Our results represent a detailed physiological characterization of GRP- and GRPR-cells involved in spinal pruriceptive processing and suggest that GRP boosts the functional output from spinal itch-processing circuits.

OP72
EFFECTS OF BURN SIZE ON POST-BURN ITCH AND EPIDERMAL NERVE INNERVATION IN MICE

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The majority of burn patients suffer from chronic itch, which is often resistant to antihistamine treatment. This post-burn itch involves sensitization of itch-signaling pathways, leading to ongoing itch and alloknesis (touch-evoked itch), but the underlying mechanisms behind post-burn itch are largely unknown. To this end, we developed a model of post-burn itch by inducing scald burn injury in adult C57BL/6 mice (exposing an area of the shaved back skin to boiling water). Because patients with larger burn surface areas exhibit more severe itch, we presently investigated if different sizes of burn injury (7 mm or 10 mm diameter) affect the time course of post-burn itch in mice. We further tested whether a histamine H1R antagonist inhibits post-burn itch in mice and whether the density of intraepidermal fibers is altered in the scald burn model. To assess spontaneous scratching, we videotaped mice on Days 0, 1, 3, 5, 7, 10, 14, 21, and 28 after the scald burn. The 7 mm scald burn caused a transient increase in spontaneous scratch bouts that declined within 14 days. The 10 mm scald burn caused two phases of post-burn itch: counts of spontaneous scratch bouts increased transiently on Days 1, 3, and 5, returned to the basal level by Day 10, and increased again on Days 14, 21, and 28. To test for alloknesis, a weak von Frey filament (VF; 0.7 mN), which does not elicit any scratch response in naïve C57BL/6 mice, was repeatedly applied to post-burn skin on Days 0, 1, 3, 5, 7, 14, 21, and 28. The presence or absence of evoked hindlimb scratch bouts was noted. VF-evoked scratching increased significantly on Days 1 and 3 in the 7 mm model and Days 21 and 28 in the 10 mm model. The histamine H1 receptor antagonist chlorpheniramine was tested on Day 22 but did not inhibit spontaneous scratching or alloknesis, suggesting that non-histaminergic itch pathways are involved in late-phase post-burn itch. Finally, post-burn skin was dissected and immunostained with Protein Gene Product 9.5 antibody to label nerve fibers. A reduction of epidermal nerve fiber density in both the burn site and adjacent skin was observed in the 10 mm scald burn model on Day 28. Reduced epidermal nerve fiber density may contribute to post-burn itch through disinhibition of itch (reduction of pain signals). This new animal model appears to be useful for investigations of post-burn itch and sensitization of itch-signaling pathways.

OP73
POSSIBLE ROLE OF SATELLITE GLIAL CELL DERIVED LIPOCALIN-2 IN THE PATHOGENESIS OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a chronic inflammatory skin disease with intractable itch. Dorsal root ganglion (DRG) plays an important role in signal transduction of itch. It was recently reported that interaction between DRG neurons and satellite glial cells (SGC) is involved in pain modulation. However, the role of SGC in induction of dermatitis and itch remains unclear. In this study, we examined whether SGC derived lipocalin-2 (LCN2) is involved in the induction of dermatitis and itch-related behavior in AD model NC/Nga mouse. AD-like symptoms were induced by application of Dermatophagoides farinae body (Dfb) twice a week for 3 weeks. LCN2 gene and protein expression in DRG of AD-NC/Nga mice was higher than that of control NC/Nga mice. Immunohistochemical analysis revealed that LCN2 was co-localized with GLAST, a marker of SGC, in DRG. LCN2-immunoreactive SGC was significantly increased in the DRG of AD-NC/Nga mice. In addition, expression level of LCN2 mRNA in the DRG was significantly increased faster than in the spinal cord during the process of induction of AD-like dermatitis in NC/Nga mice. Intrathecally administrated anti-LCN2 antibody (1 μg/5 μl) twice a week for 3 weeks at the same time as induction of AD-like dermatitis in NC/Nga mice reduced dermatitis score without inhibiting scratching behavior. This is supported by finding that intrathecal administration of recombinant mouse LCN2 (1 μg/5 μl) did not induce scratching behavior in NC/Nga mice. These results suggest that SGC derived lipocalin-2 is involved in the pathogenesis of dermatitis in AD-NC/Nga mice.

EPIDEMIOLOGY OF ITCH AND QUALITY OF LIFE

OP74
EPIDEMIOLOGICAL STUDY ON THE PREVALENCE OF ITCH IN JAPANESE DEMENTIA PATIENTS

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Itch is common in the elderly. Previous epidemiological studies show the prevalence of itch in a range from 7 to 37.5% with greater than 20% in most cases. However, itch has not been studied in dementia patients, since the broadly-used self-evaluation scales are not applicable in this population. We conducted a study focusing on itch in 148 dementia patients who are receiving medical care in nursing homes or at home. For the self-evaluation of itch we asked the subjects whether they had itch or not at present and asked them to rate their itch on numerical rating scale (NRS). For the objective evaluation of itch by others, their caregivers evaluated the presence and extent of scratching behavior and we evaluated the extent of scratch marks by calculating the body surface area where scratch marks exist. We also evaluated the severity of skin dryness and sought its correlation with the extent of scratching and frequency of skin care using moisturizer. The prevalence of itch in the surveyed dementia patients was 37.8% according to self-evaluation of itch, whereas nearly 50% according to scratch evaluation by others. The higher the dementia severity was, the larger percentage of patients could not answer whether they had itch or not, or rate the severity of itch. Over 30% of those who denied having itch scratched according to the observation by others. Over 70% had dry skin, the severity of which positively correlated to the level of scratching. In conclusions, subjective evaluation is not sufficient and objective evaluation should be applied to

understand the status of itch in dementia patients. Skin dryness is an important factor associated with itch in dementia patients.

OP75
PITFALLS IN PEDIATRIC SELF-REPORTED PRURITUS SEVERITY AND QUALITY OF LIFE IMPACT

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Introduction: The ability of children to convey a self-report of itch severity can be challenging as their cognitive levels may drastically vary within a small age range. In response to these challenges, we have created the ItchyQuant and pediatric versions of the ItchyQol, illustrated scales to measure itch severity and quality of life impact of pruritus in children, respectively. A mixed method approach was undertaken to assess the feasibility of these scales in younger children. *Methods:* Children with itch > 6 weeks, between ages 4–7 years, were asked to rate their itch severity on the ItchyQuant scale and estimate the quality-of-life impact on the cartoon-annotated ItchyQoL. Parents also estimated their child's itch severity and were asked if they agreed with the child's response. Standardized questions were asked by the interviewer to assess ability to comprehend the duration of recall (last week). *Results:* Ninety-seven children with chronic pruritus were recruited. A combination of interviewer observations and data collection showed three key differences between 4–5-year-olds and 6–7-year-olds. First, 4–5-year-olds were 40% more likely (30% vs. 75% and 36% vs. 75%) to answer questions about the days of the week incorrectly compared to the 6–7-year-olds, demonstrating a lack of understanding of time. Second, interviewers noted that younger children were 16% (18% vs. 2%) more likely to struggle with comprehending questions on the ItchyQoL. 4–5-year-olds were also 9% more likely (12% vs. 3%) to be deemed hyperactive or distracted during the process. Finally, parents agreed with their child's itch severity rating almost 20% less (64% vs. 45%) in the younger group. *Conclusion:* Our initial investigation has demonstrated that the current version of the cartoon-annotated ItchyQoL is likely too complex for 4–5-year-old patients, while appropriate for the 6–7-year-olds. As a result, we have implemented changes to account for these cognitive differences by reducing the number of items on the ItchyQoL, while also eliminating questions pertaining to the prior week. We will begin a pilot study with 4–5-year-old patients to test the validity of this new tool.

OP76
QUALITY OF LIFE IN PATIENTS WITH CHRONIC PRURITUS: FROM THE CONCEPTUAL MODEL TO ITEMS GENERATION

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Objectives: To develop a patient-reported questionnaire, measuring the severity of Chronic Pruritus (CP) and its impact on health-related quality of life (HRQoL). *Methods:* A three-step approach was followed: (1) a Conceptual Framework (CF) was developed using a systematic literature review and experts' interviews, to render the relevant domains for severity and HRQoL; (2) the CF was updated following Focus Groups with 19 patients; (3) a pool of items was generated for each domain of interest, and their comprehensibility was tested during cognitive debriefing with patients (semi-structured interviews; *n*=21). *Results:* 155 articles were reviewed to develop the preliminary CF addressing 16 domains of HRQoL and 7 of severity, and which was clinically validated by 2 medical experts. Patients' verbatim showed some relevant differences on severity, between clinical and patients' perspectives. Moreover, a new domain of interest was revealed: the time spent anticipating and thinking about CP. A preliminary version of the questionnaire was drafted and refined after cognitive debriefing sessions. The final version includes 50 items. *Discussion:* A first version of this patient-reported questionnaire was developed following international guidelines and namely, using patients' interviews. This questionnaire will measure the severity of CP and its impact on HRQoL in a comprehensive manner.

OP77
CHRONIC ITCH (CI) IN HEMODIALYSIS PATIENTS: A FOLLOW-UP STUDY OF GEHIS (GERMAN EPIDEMIOLOGICAL HEMODIALYSIS-ITCH STUDY) ON INCIDENCE AND MORTALITY OF PATIENTS WITH CI

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GEHIS (German Epidemiological Hemodialysis Itch Study) is a representative cross-sectional cohort conducted in 2013. It contains a total of 860 hemodialysis (HD) patients in 25 dialysis units in Germany. We showed that 25.1% (*n*=217) of HD patients suffered from current chronic itch (CI). In 2017, four years later, all 860 HD patients are currently contacted again to investigate the number of new itch cases (incidence) in this cohort. We aim to provide data on the incidence and prevalence of CI in this follow-up study, and to identify its determinants based on cross-sectional and longitudinal analyses. Previous research supports the observation that CI is a poor prognostic marker for patients on HD, however, this is now investigated in a representative cohort of HD patients for the first time. Patients' characteristics and CI were assessed with the same patient questionnaire as in 2013 investigating e.g. current and previous CI (during the last 3 years), severity of CI (visual analogue scale, VAS). As this is an ongoing study, results are preliminary and refer to 9 dialysis units containing 212 HD patients being addressed so far. Of those, 46.7% (*n*=99) had died in the meantime and 11.3% (*n*=24) could not be contacted (e.g. because they had moved to another place or because they were not on dialysis treatment anymore due to transplantation). 89 HD patients were investigated, 60.7% of those were male and the mean age was 69.0 years (SD 12.4). In 11.2% (*n*=10) CI had developed in the past year, while 13.5% (*n*=12) reported not to suffer from CI anymore, resulting in a one-year prevalence of 25.8%. The mortality rate was 45.7% in the group suffering from CI in 2013 compared to 54.9% in the group without CI, no differences between sexes were found. Interestingly, this effect was pronounced in patients aged younger 70 years (32.7% mortality in the non-CI group vs. 19.0% in the CI group) while the mortality in patients aged 70 years or older was equal between groups. First results refer to an increased incidence of CI in younger HD patients. Preliminary analyses hint to a difference in mortality between HD patients with and without CI in younger age groups but further analyses are needed to see if this can be confirmed in the whole cohort.

OP78
PREVALENCE, CHARACTERISTICS AND BURDEN OF PRURITUS IN CHRONIC DERMATOSES

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Many dermatological conditions are associated with pruritus and in some of them itch is a hallmark symptom. Crucial data on its

prevalence, characteristics including distribution patterns and burden are still missing for many dermatoses. Here, we have analyzed prevalence, characteristics of chronic pruritus, including its distribution patterns (body heatmaps), burden of chronic pruritus on quality life and the presence of suicidal thoughts in different dermatoses. Unselected patients with active dermatoses, that can be, reportedly, associated with pruritus and control patients with angioedema filled out the study questionnaire including questions on pruritus presence, localization, characteristics and the quality of life, quality of sleep, sexuality, and suicidal ideations. 880 in- and out-patients of dermatology university department with 18 different dermatological diagnoses returned completed questionnaires. Pruritus in the disease course/current pruritus were reported by 100%/77% patients with chronic spontaneous urticaria (143), 88%/73% psoriasis (138), 100%/91% atopic dermatitis (AD, 128), 100%/78% chronic inducible urticaria (76), 100%/96% prurigo (75), 65%/47% cutaneous T cell lymphoma (68), 78%/56% mastocytosis (54), 100%/86% pruritus on unaffected skin (30), 45%/28% parapsoriasis en plaque (29), 39%/31% cutaneous B cell lymphoma (26), 100%/67% bullous pemphigoid (15), 82%/64% lichen planus patients (11). The most intense maximal pruritus was reported by patients with pruritus on unaffected skin (mean ± SD of maximum visual analogue scale = 8 ± 1.4), followed by AD (7.5 ± 2.2). Suicidal thoughts due to pruritus were reported by many patients with itchy skin diseases, ranging from 0% in parapsoriasis en plaque to 19% in patients with pruritus on unaffected skin and to 22% in patients with lichen planus. Taken together, we have visualized, for the first time, the localization of pruritus in patients from large variety of dermatological diseases. Together with itch intensity, the results show a characteristic pattern of pruritus for many diseases. This can lead to a better understanding of the pathophysiology of itch in these diseases, help in the development of better treatment options and can lead to a better management of our patients. Patients presenting at a dermatological department should be asked for the presence of pruritus, and in individuals reporting about chronic pruritus it should be inquired whether suicidal thoughts exist.

NEW IMAGING TECHNIQUES AND OTHER ASPECTS OF ITCH

OP79
NEW METHODS IN BRAIN IMAGING TECHNIQUES

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Since more than 20 years functional magnetic resonance imaging (fMRI) has been used to image regional cerebral blood flow (rCBF). Stimulus related changes of the rCBF have been regarded as markers of regions that are involved in the cerebral processing of the respective perception. This technique based on the BOLD (blood oxygenation level depended) signal identified brain regions which generate the sensation of itch. They were compare with regions that have been described to be involved in the suppression of itch or are activated by pain. It turned out that there is a strong overlap of the affected brain areas during these experiences, although it is obvious that they clearly evoke qualitatively different sensations. It was discussed that this overlap is due to the neural basis of itch that for many years has been considered as sub-modality of pain and is elicited by weak activations of the nociceptors. From this, it was not surprising that similar cerebral regions were detected. Beside this intensity model population coding was proposed where itch uses its own pathway to the brain. An itchy stimulus activates "pruriceptive nociceptors" which then transmit their activity to a common network for pain and itch. The pivotal question remained: How does the brain code the different qualities if not by a pattern of activated brain areas? The conclusion was that different temporal activity patterns within a functional brain network code the perception quality. Indeed, fMRI connectivity analyses showed that during resting state (no stimulus, no mental task) a "default mode network" could be detected which refers to a pattern of co-activation across the brain regions included in this network. The related connectivity was measured by correlation analyses of the BOLD signals. During the processing of a stimulus the pattern of co-activation changed. New approaches for analyzing the correlations of BOLD signals pursue stimulus related changes within such a network. Further, they seem to have the potential to detect changes within cerebral networks due to a chronic painful or pruritic input. In the presentation a short overview will be given about this technique, how it can be used to identify itch related brain network and its changes due to chronic conditions. Preliminary findings from patients suffering from chronic pruritus will be compared with those from healthy subjects. The limitations of this method will be discussed.

OP80
THREE DIMENSIONAL ANALYSIS OF CUTANEOUS NERVOUS SYSTEM IN PRURITIC ATOPIC DERMATITIS AND PSORIASIS SKIN

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Intra-epidermal nerve fibre (IENF) count in skin biopsies have been used as a reflection of the innervation density of itch-transmitting C nerve fibres in the skin. It is of interest to determine the changes in IENF densities in pruritic conditions such as atopic dermatitis and psoriasis, but previous studies have reported conflicting results. The conventional method of determining IENF count is by assessing the number of PGP9.5-positive nerve fibres crossing the basement membrane per unit length in 50 µm-thick histological sections. However, such an approach is 2-dimensional and is limited by the thickness of the section examined. We hereby adopt a 3-dimensional approach to such an analysis. 12 atopic dermatitis and 10 psoriasis patients with an average itch score of >3/10 over the prior 1 week were recruited. Skin biopsies from lesional and non-lesional areas were obtained, together with biopsies at corresponding body sites in 10 healthy volunteers. Immunostaining of PGP9.5-positive nerves in the biopsy, followed by optical clearing and 3D imaging of tissue sections up to 450 µm was performed. The epidermis was then segmented from the 3D image, followed by filament tracing of IENF. Analysis of neural density and characteristics of the neural network, such as filament length, number of dendrite branches and dendrite straightness, were then performed. Preliminary analyses suggest that there were significant differences in the innervation densities and neural characteristics in the itchy atopic dermatitis and psoriasis lesions compared to non-lesional skin and skin from healthy volunteers. This novel method enables us to study the cutaneous nervous system in a comprehensive 3D manner and serves as a platform in future studies to better identify itch receptors co-localising with nerve fibres.

OP81
FUNCTIONAL CONNECTIVITY REVEALS ALTERED ACTIVATION OF BRAIN AREAS IN CHRONIC CHOLESTATIC PRURITUS

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Introduction: Pruritus is a frequent symptom of hepatobiliary disorders particularly those with cholestatic features. Although various substances including bile salts, endogenous opioids, and

lysophosphatidic acid have been controversially discussed as potential peripheral pruritogens, the central mechanism involved in itch sensation in cholestatic pruritus remains elusive. *Methods:* 23 patients with primary biliary cholangitis or primary sclerosing cholangitis were investigated in this study. These patients were divided into two groups, those patients suffering from spontaneous pruritus (SP, n=9) and those without pruritus (WP, n=14). Baseline itch intensity was quantified using a questionnaire and a visual analogue scale. Functional magnetic resonance imaging (fMRI) scans were using a classical connectivity fMRI-design with EPI sequences to BOLD signal changes. The first fMRI sequence was free from stimulation to detect the default mode (DM) network. During the second and third fMRI sequence mild heat pain and itch stimuli (histamine iontophoresis) were applied. After each run sensory qualities were assessed by questionnaire. Individual mean BOLD time courses were extracted from the seed regions left posterior insula cortex (lpIC) for exploring an "input" network and the PAG for exploring the "output" network. Pearson's correlation coefficients were calculated between the seed regions and other regions in a whole brain study. In a 2nd level analysis contrasts were calculated between the two patient groups. *Results:* During the DM situation higher functional connectivity (FC) was found within the SP group in the "input" network of the lpIC to anterior parts of the insular cortex of both hemispheres and to the secondary somatosensory cortex S2, while FC to frontal areas was weaker in the SP group. Also the output network was enhanced in SP (FC of the PAG to thalamus, caudate body and limbic system). During histamine FC in the input networks were enhanced in both groups, however, FC values were smaller in SP. FC of the output network increased more strongly as compared to DM in SP within limbic regions while in WP only FC to PAG modulating areas (ACC, IC, BA10) were enhanced. *Conclusion:* The DM network seemed to be violated in SP probably due to the continuous pruritic input. Accordingly changes within the networks due to an additional pruritic stimulus are less pronounced in SP as compared with subjects who are not suffering from spontaneous itch.

OP82
ITCH TRACKER: AN APPLICATION SOFTWARE TURNING WEARABLE SMART DEVICES INTO A TOOL TO MEASURE NOCTURNAL SCRATCHING

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Background/objective: Itch is difficult to objectively evaluate. Previous studies of actigraphy demonstrated potentials of accelerometers in watch-type devices to help objective evaluation of itch severity through measurement of scratching. We have developed an application software (app), named Itch Tracker, that can be installed to broadly-used smartwatches and used to measure scratching during night. Clinical studies were conducted to validate the app's reliability. *Methods:* Two proof-of-concept studies using the smartwatch in which the software is installed were carried out. In the first study, a total of five patients with atopic dermatitis who had moderate or severe itch were hospitalized for one night for video-monitoring and smartwatch-recording of scratching during night. With the records from the video and smartwatch compared, the sensitivity and positive predictive value (PPV) of the software were studied. In the second study, twenty patients with atopic dermatitis and ten healthy volunteers participated to record nocturnal scratching at home for seven consecutive days. The correlation of scratching time with the skin severity and self-evaluated itch severity was studied. *Results:* In the first study, the average sensitivity and PPV were 84.6% and 90.2%, respectively. There was a statistically-significant positive correlation between smartwatch-detected and video-captured scratching time per hour (r=0.90, p<0.001). There was no significant difference in scratching duration between the dominant and non-dominant arm. In the second study, the severity of the lesions (EASI) well correlated with smartwatch-detected scratching (r=0.71, p<0.001), but not with the self-evaluated itch severity or sleep disturbance. There was no statistically-significant correlation between smartwatch-detected scratching time and self-evaluated itch severity or sleep disturbance. *Conclusion:* The app has been proven to have a high validity and reliability in measuring scratching.

OP83
CHANGES IN TACTILE SENSITIVITY AFTER VIEWING ITCH-RELATED IMAGES

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Visually Evoked Itch (VEI) is the phenomenon whereby itch-related images can create sensations of itch in the absence of any physical stimulation. It has been suggested that changes in skin sensitivity are involved in the creation of these sensations; this study used the Somatic Signal Detection Task (SSDT; Lloyd et al., 2008) to investigate whether viewing itch or non-itch images affected participants' tactile sensitivity. In the SSDT, participants detect the presence of a near-threshold vibration presented on the left index finger on 50% of trials. A LED flashes on 50% of trials, which increases the likelihood of both the correct detection ('hits') and misperception ('false alarms') of the vibration. 40 right-handed participants (with no pruritic skin conditions) viewed a block of itch and a block of non-itch images (counterbalanced between participants) interspersed with the SSDT. Their sensitivity threshold was measured before each block which was used to set the stimulus intensity for the SSDT. Participants also rated the itchiness of the images and their scratching behaviour was observed. We found that performance on the SSDT significantly differed between the itch and non-itch conditions. The hit rate was higher for the itch block, both with and without the light. Participants showed greater sensitivity during the itch block than the non-itch block, which suggests their tactile perception was enhanced following exposure to itch images. There was little difference in false alarm rates, which indicates that no change in their response criterion occurred; viewing either set of images did not create a greater propensity to report feeling a vibration overall. Participants' itchiness ratings and scratch frequency were both higher during the itch block, which is consistent with the presence of VEI. This indicates that the creation of VEI corresponds with a change in tactile sensitivity. Viewing itch images appears to prime participants to perform better at detecting a tactile stimulus, without creating a bias towards reporting its presence more frequently overall. This may be because these images prompt participants to pay greater attention to their skin and what is happening to it. This lends weight to an explanation of VEI based on altered sensory thresholds for detecting itch.

OP84
KERATINOCYTE DERIVED CORTISOL REGULATES ITCH-EVOKED ALLERGIC CUTANEOUS INFLAMMATION

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Topical glucocorticoid (GC) is commonly used for the management of allergic skin diseases such as atopic dermatitis (AD). However, serious topical steroid withdrawal syndrome with accelerated itch sensation is occasionally observed shortly after the cessation of chronic use of GC, even in now days. We previously reported that long-term epicutaneous application of GC and its withdrawal induced severe scratching behavior after challenge with DNFB in sensitized mice in contrast to control mice. In this

model, the expression of preprotachykinin-A (PPT-A) mRNA, a precursor of substance P (SP), and inducible nitric oxide synthase (iNOS) mRNA in mice was observed both of those molecules are known to induce itch. In order to evaluate the factors responsible for the augmented scratching behavior, we injected various cytokines (IL-1α, IL-2, IL-3 and TNF-α) subcutaneously into the ear of DNFB contact-sensitized mice before DNFB challenge. Among the cytokines, only IL-3 and TNF-α significantly increased scratching behavior in DNFB contact dermatitis mice. Furthermore, PPT-A mRNA was only expressed in mice pre-injected with IL-3 before challenge, but not in those pre-injected with other cytokines. Our recent studies suggest that oxidative stresses, such as UV-irradiation or exposure to haptens or chemicals induce active cortisol via conversion from inactive cortisone by activation of 11β-hydroxysteroid dehydrogenase type 1 (11βHSD1) in the skin. Cortisol derived from keratinocytes, which are exposed to environmental stimuli, is speculated to minimize damage of the skin in a homeostatic fashion. Decreased expression of 11βHSD1 in keratinocytes has been found in AD and leads to the impairment of the innate host defense response. (Terao M et al. Am J Pathol. 2016 ;186(6):1499-510). More recently, we presented that increased scratching behavior to chloroquine (CQ) , a ligand to Mas related G protein-coupled receptor A3(MrgprA3) is observed in K5 HSD11b1 KO mice(cKO), compared with WT (Matsumoto A, Murota H et al.). Long term application of topical GC and its abrupt withdrawal might modify 11βHSD1 expression in the skin and accelerate itch associated skin inflammation. Taken together, stress might disrupt homeostasis of the skin not only by impairing barrier function of horny layer but also by affecting local innate immune response in AD.

FUTURE PERSPECTIVES

OP85
FUTURE PERSPECTIVES IN THE TREATMENT OF ITCH

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The understanding of the mechanisms behind chronic pruritus (CP) has increased in the past several years; accordingly CP is increasingly becoming considered an indication in clinical trials. According to the online portal clinicaltrials.gov, more than 280 active study centers are currently recruiting for this indication, most of which are located in the USA (*n*=95) and Europe (*n*=77) and are evaluating new substances for various types of CP such as uremic pruritus, atopic dermatitis, psoriasis, chronic prurigo and epidermolysis bullosa. Two therapeutic concepts can be distinguished by analyzing the utilized substances. On one hand, new substances are examined for the influence of specific, mainly inflammatory-based disease mechanisms (e.g. blocking of cytokines) in the acute phase of diseases, during which any changes to the pruritus as a symptom of a disease and primary endpoint are recorded. Atopic dermatitis and its therapies with antibodies against interleukin (IL)-31 or IL-4/IL-13 receptors are a representative example for this. On the other hand, central mechanisms for neuronal transmission, induction and perception of pruritus are addressed in the trials and CP of a systemic cause is selected as the primary endpoint. CP in chronic kidney disease has thus won recognition as a representative indication. Current trial results have shown promising results for mu antagonists/kappa agonists, neurokinin-1 receptor antagonists, nerve growth factor (NGF) antagonists, phosphodiesterase E4 inhibitors and histamine 4 receptor antagonists.

OP86
FUTURE PERSPECTIVES IN BASIC RESEARCH OF ITCH: MRGPR RECEPTORS AND THE BIOLOGY OF ITCH

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Primary sensory neurons in dorsal root ganglia (DRG) play an essential role in generating itch by detecting painful and itchy stimuli through their peripheral axons in the skin and sending signals to the spinal cord via their central axons. We identified a large family of G protein-coupled receptors in mice called Mrgprs. Many of these receptors are exclusively expressed in distinct subsets of DRG neurons. We found that several Mrgprs function as novel receptors by directly sensing variety of itchy substances including peptides, drugs, amino acids, and proteases. Importantly, the mouse works have been confirmed by human psychophysical studies. We have genetically labeled and manipulated Mrgpr-expressing neurons in DRG and demonstrated for the first time that there is a labeled line in DRG for itch coding. On the other hand, itch coding in the spinal cord is likely not mediated by labeled line. Besides DRG neurons, we are also interested in how mast cells, a type of innate immune cells found in many tissues, are involved in itch. In addition, we have developed imaging techniques which allow us to monitor DRG neuronal activities *in vivo* and unveil novel itch mechanisms.

POSTERS

PP1
MYELOID GTP-CYCLOHYDROLASE CONTROLS ITCH

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GTP cyclohydrolase (Gch1) governs the production of the enzyme cofactor, tetrahydrobiopterin (BH4), which is essential for biogenic amine synthesis, bioactive lipid metabolism and redox coupling of nitric oxide synthases (NOS). Inhibition of Gch1 or its knockout in nociceptive neurons reduces nociception in various models. While these previous studies addressed neuronal Gch1, we asked here if Gch1 of myeloid immune cells contributed to pain and itch. Hence, we studied behaviour and myeloid cell functions in lysozyme M Cre-mediated myeloid specific Gch1 knockout (LysM-Gch1$^{-/-}$) and overexpressing mice (LysM-Gch1-HA). Knockout or overexpression had no effect on nociceptive behaviour in various models including formalin, paw inflammation and sciatic nerve injury, but LysM driven Gch1 knockout reduced, and its overexpression increased the itching response in histamine and non-histamine evoked itch models. The anti- and pro-itching effects were mediated by inhibition, respective increase, of histamine and serotonin release from mast cells, contributed by respective changes of nitric oxide, but did not involve hydrogen peroxide production. Diaminohydroxypyrimidine (DAHP)-mediated Gch1 inhibition provided even stronger itch suppression, mediated by additionally augmenting itch-suppressing bioactive lipids in the skin, a function of BH4-dependent AGMO. Together, these loss- and gain-of-function experiments of myeloid-specific Gch1 show that itch in the mouse partly depends on Gch1/BH4-dependent serotonin and histamine release and AGMO-dependent bioactive lipid mediators.

PP2
HISTAMINE IS INVOLVED IN PERIPHERAL NERVE ELONGATION INTO EPIDERMIS OF MICE WITH ITCHING INDUCED BY SURFACTANT

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The repetitive act of washing your skin with soaps can lead to cutaneous sensory hypersensitivity symptoms. This enhances itchiness and is induced by several stimuli. However, the mechanism and the factors associated with cutaneous sensory hypersensitivity induced by soaps remain unclear. Sodium dodecyl sulphate (SDS) is a synthetic surfactant commonly found in laundry detergents, dish detergents and shampoos. In addition to the increase of the expression of histamine-synthesizing enzyme histidine decarboxylase (HDC) and the concentration of histamine in the epidermis, our previous report has shown that repeated applications of SDS to mouse shaved skin increased the density of intraepidermal nerve fibers. These findings suggest that histamine may contribute to the induction of neuronal sprouting into the epidermis. In this study, we investigated the role of histamine on SDS-induced neuronal sprouting into the epidermis. The repeated SDS exposure increased the elongation of peripheral nerve fibers into the epidermis in wild type mice, but not in HDC knockout mice. In both wild type and HDC knockout mice, the expression of nerve growth factor was increased and that of nerve repulsion factors semaphorin 3A was decreased. The application of histamine increased the total length and the maximum length in small-sized, but not large-sized, mouse dorsal root ganglion neurons. Therefore, these results suggest that histamine plays an important role in intraepidermal nerve fiber elongation in murine skin treated repeatedly with SDS.

PP3
THE EFFECTS OF THE NK-1 RECEPTOR ANTAGONIST NETUPITANT ON ITCH MODELS IN MICE

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Spinal NK-1 receptors play an important role in itch transmission and NK-1 antagonists demonstrated antipruritic properties in preclinical as well as clinical studies. For example, the NK-1 antagonist aprepitant has been shown in small studies to be effective for treating chronic and malignancy-associated pruritus. Netupitant is a selective, long lasting and brain penetrant NK-1 receptor antagonist utilized in chemotherapy-induced nausea and vomiting therapy in combination with the 5-HT$_3$ antagonist palonosetron. Thus, the aim of this study was the investigation of the putative antipruritic action of netupitant in mice. Pruritogenic substances with different mechanism of action were injected intradermally (i.d.) in the rostral part of the mouse back and the number of bouts of scratching were counted for 30 min. Substance P (10–100 nmol), cloroquine (10–200 nmol), deoxycholic acid (25–250 µg), and compound 48/80 (1–50 µg) elicited dose dependent pruritogenic effects. From these dose response studies, equieffective doses, approximately promoting 100 bouts of scratching in 30 min, were selected to be challenged against netupitant 10 mg/kg p.o. (2 h pretreatment). The results showed that netupitant reduced in a statistically significant manner the pruritogenic effect of all substances but not compound 48/80. This latter effect suggests that mast cells are not the cell target for the action of SP and that there is no involvement of NK-1 receptor signaling in the scratching behavior elicited by compound 48/80 in mice. In conclusion these results suggest that NK-1 receptor selective antagonist netupitant is worthy of development as innovative drug for treating non histaminergic itch.

PP4
OPTOGENETIC ACTIVATION OF SEROTONERGIC (5-HT) NEURONS IN THE ROSTRAL VENTROMEDIAL MEDULLA (RVM) FACILITATES TOUCH-EVOKED SCRATCHING IN A DIET-INDUCED CHRONIC DRY SKIN MOUSE MODEL

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In atopic dermatitis, innocuous mechanical stimuli (e.g., contact with wool) often elicit itch sensation (called alloknesis), thus contributing to persisting itch. RVM is a brainstem region containing 5-HT neurons descending to the spinal cord. Although the descending RVM 5-HT neurons are well known to contribute to pain modulation, their role in alloknesis remains unclear. In this study, using optogenetics, we examined the effects of selective activation of RVM 5-HT neurons on touch-evoked scratching and thermal pain sensitivity in a chronic dry skin mouse model. We have previously shown that hairless mice fed a special diet containing no polyunsaturated fatty acids and no starch develop atopic dermatitis-like pruritic dry skin (M. Fujii et al., Exp.

Dermatol., 24:108-13, 2015). When this special diet was given to C57BL/6 mice, similar dry skin conditions were induced. Alloknesis was assessed using 0.7 mN von Frey filaments applied to the shaved back skin. The low-threshold mechanical stimulation of the skin frequently evoked site-directed scratching in special diet-fed C57BL/6 mice with dry skin, although rarely in normal mice. To selectively induce a light-activated channel channelrhodopsin-2 (ChR2) in RVM 5-HT neurons, we micro-injected a Cre-inducible adeno-associated virus carrying ChR2 gene into the RVM of Fev-Cre mice in which Cre is expressed in central 5-HT neurons and then an optic fiber was implanted just above the RVM. Blue light (20 Hz, 5 ms pulses) was delivered via the implanted optic fiber during behavioral testing. Consequently, the optogenetic stimulation significantly increased touch-evoked scratching in special diet-fed dry skin mice. On the other hand, pain-related thermal response (measured by Hargreaves test) was significantly decreased by the stimulation. Therefore, the present results suggest that under chronic dry skin conditions activation of RVM 5-HT neurons facilitates touch-evoked itch, while inhibiting thermal pain.

PP5
TRPV CHANNELS AND POST-BURN PRURITUS

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Background: Post-burn pruritus is a common distressing sequela of burn wounds. Empirical antipruritic treatment often fails to have a satisfactory outcome because the mechanism has not been fully elucidated. Transient receptor potential (TRP) channels are considered to be related to pathway of pruritus. *Methods:* Sixty-five burn patients with (n=40) or without (n=25) pruritus were investigated, including skin biopsies. Keratinocytes and fibroblasts from those samples were separated. Immunohistochemical staining for TRPV3 and TRPA1; and immunofluorescence staining for TSLP, TSLPR, loricrin, involucrin, β–SMA, and TGF-α, were performed on samples of burn scars and normal skin. Real-time PCR and western blotting were done. We measured intracellular Ca^{2+} levels in keratinocytes from scars with or without pruritus, following TRPV3 activation and blocking, and measured the effects of PAR2 agonist on TRPV3 function. Expressions of TSLP after TRPV3 activation in keratinocytes were measured by western blotting and real-time PCR. *Results:* In immunohistochemical and immunofluorescence staining, TRPV3, TSLP, and TSLPR stained more intensely the epidermis of the burn scars of post-burn-pruritus patients, than that of non-pruritic-burn patients. Real time-PCR showed that mRNA of TRPV3 and TSLP were significantly more abundant in keratinocytes from pruritic burn scars than in keratinocytes from non-pruritic burn scars. In addition, mRNA and protein levels of PAR2, NK1R, TSLP, and TSLPR were also significantly increased in pruritic burn scars. With TRPV 3 activation, intracellular Ca^{2+} concentrations were more significantly increased in keratinocytes from pruritic burn scars than in those from non-pruritic ones. In keratinocytes from pruritic burn scars, PAR2 activation markedly potentiated opening of TRPV3 channels. TRPV3 activation itself resulted in little increase of Ca^{2+} influx with PAR2 inhibition in keratinocytes. In keratinocytes from all samples, PLC-β, PKA, PKCs, and PKD inhibitor markedly reduced intracellular Ca^{2+} level by TRPV3 activation, as well as by PAR2 activation. TRPV3 activation also increased mRNA and protein expression of TSLP in keratinocytes. *Conclusions:* In conclusion, we confirmed that TRPV3 of keratinocytes and PAR2, NK1R, TSLP, and TSLPR were highly expressed in pruritic burn scars. In addition, it seemed that PAR2 sensitized TRPV3 channels with PKA, PKC, PKD signaling pathways. It also seemed that TRPV3 activation induced TSLP expression.

PP6
EFFECT OF [LEU11]-HK-1-DERIVED PEPTIDES ON SCRATCHING BEHAVIOR IN MICE WITH CHRONIC ITCH

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Hemokinin-1 (HK-1) is a mammalian tachykinin peptide consisting of 11 amino acids. Recently, we demonstrated that the pretreatment with [Leu^{11}]-HK-1, in which Met at the C-terminal of HK-1 was replaced by Leu, produced a decrease in scratching induced by both intrathecal administration of HK-1 and intradermal injection of some pruritogens such as histamine or serotonin. However, it is not clarified whether [Leu^{11}]-HK-1-derived peptides, in which a part of amino acids was replaced of by D-tryptophan (D-Trp), change the effective duration on scratching behavior in mice with chronic itch. Therefore, to clarify the effect of [Leu^{11}]-HK-1-derived peptides in mice with chronic itch, [Leu^{11}]-HK-1 or [D-Trp^{9}]-[Leu^{11}]-HK-1 was intrathecally injected after painting of diphenylcyclopropenone on the nape. Scratching in mice with chronic itch was attenuated by administration of [Leu^{11}]-HK-1 until 30 minutes, while the effect lasted until 24 hours after intrathecal injection of [D-Trp^{9}]-[Leu^{11}]-HK-1. These results indicate that D-Trp in [Leu^{11}]-derived peptides plays a crucial role in the effective duration on scratching behavior in mice with chronic itch.

PP7
SEROTONIN RECEPTOR SUBTYPES INVOLVED IN CALCIUM INFLUX IN CULTURED RAT DORSAL ROOT GANGLION NEURONS

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Serotonin (5-HT) mediates both pain and itch in the peripheral nervous system. Our aim was to identify the specific 5-HT receptor subtypes expressed in the rat dorsal root (DRG) and trigeminal (TG) ganglion neurons. We used calcium microfluorimetry and the patch clamp technique to investigate the action of 5-HT in primary cultures of rat sensory neurons. DRG and TG were dissected out from adult male Wistar rats and dissociated neurons were cultured on glass coverslips. After 24 h, the cells were loaded with Calcium Green-1 AM and imaged while being chemically stimulated using a fast-exchange superfusion system. The calcium responses to 5-HT (50 μM) were classified as transient and sustained according to their kinetics. The selective 5-HT3 antagonist granisetron (1 μM) completely inhibited transient responses while the 5-HT3 agonist SR 57227 (1–10 μM) elicited similar responses in the same neurons. The non-selective agonist 5-Carboxamidotryptamine (5-CT, 50 μM) induced only sustained responses, solely in neurons that were sensitive to 5-HT. The same kinds of responses were elicited by the 5-HT1A and 5-HT7 agonist 8-OH-DPAT (10 μM) but were not inhibited by the 5-HT7 antagonist SB269970 (1–10 μM). The 5-HT1A receptor antagonist WAY-100,635 (100 nM) was able to irreversibly inhibit the sustained responses evoked by 5-HT. As 5-HT1A is a metabotropic receptor, we investigated the intracellular pathways leading to the sustained calcium influx. The broad-spectrum Transient Receptor Potential channel blocker Ruthenium Red did not inhibit the sustained responses. Nor did the more selective antagonists: CIM 0216 (1 μM), A967079 (5–10 μM) and HC-067047 (0.5 μM) for TRPM3, TRPA1 and TRPV4 respectively. The adenylyl cyclase activator forskolin (10 μM) or the cAMP analog, 8-Br-cAMP (10 μM) did not affect the sustained responses to 5-HT. Voltage clamp experiments were carried out in

5-HT-sensitive DRG neurons pre-selected with calcium imaging, and revealed only transient currents (5-HT3-like) at a holding potential of -80 mV. These currents were inhibited by granisetron (10 nM). In conclusion, our results suggest that the transient responses are mediated by the 5-HT3 ion channel while the sustained responses are likely mediated by the 5-HT1A metabotropic receptor. This is supported by the inhibitory effect of WAY-100,635 and by the calcium influx elicited by 8-OH-DPAT and 5-CT.

PP8

RESISTANCE TO SEROTONIN-INDUCED ITCH IN CHOLESTATIC MICE

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Introduction: Cholestatic itch can be severe and significantly impair the quality of life of patients. Serotonin system is implicated in cholestatic itch; however, the pruritogenic properties of serotonin have not been evaluated in cholestatic mice. Here, we investigated the serotonin-induced itch in cholestatic mice. *Methods:* Cholestasis was induced by bile duct ligation (BDL). Serotonin, sertraline or saline were administered intradermally to the rostral back area in BDL and sham-operated (SHAM) mice, and itch was assessed by quantification of hind paw scratching bouts towards the injection site over one hour after treatments. *Results:* Bile duct ligated mice had significantly increased scratching responses to saline injection on the 7th day after surgery. Additionally, serotonin or sertraline significantly induced scratching behavior in BDL mice compared to saline at day 7 after surgery, while it did not induce itch at day 5. The scratching behavior induced by serotonin or sertraline was significantly less in BDL mice compared to SHAM mice. Likewise, the locomotor activity of BDL or SHAM mice was not significantly different from un-operated (UNOP) mice on 5th and 7th day, suggesting that the scratching behavior was not affected by motor dysfunctions. *Conclusion:* Despite the potentiation of evoked itch, a resistance to serotonin-induced itch is developed in cholestatic mice.

PP9

GLOBAL GENE EXPRESSION PROFILING IN PRURIGO NODULARIS

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Prurigo nodularis (PN) is a subtype of chronic prurigo (CPG). It is characterized by continuous scratching that leads to multiple itchy nodules. Although CPG shows a high negative impact on daily life quality, effective therapies are still not available. A deeper insight into affected pathways and involved genes may help to define new therapeutic targets. Therefore, we performed global gene expression profiles in PN patients and matched healthy controls (HC). Biopsies from 5 PN patients (lesional = PL; healthy/non-lesional = PH) and 5 HCs (healthy = HH) were included. Expression profiles were generated using Affymetrix Human Gene 1.0 ST Arrays. Due to the small sample size data processing was done using the R/Bioconductor package limma. Deregulated genes were defined with an absolute log2-fold change >1 and a p-value < 0.05. For pathway analysis we made use of Reactome, a free open source database. A first analysis revealed 276 deregulated genes (DEG) between PL and PH, 376 DEGs between PL and HH and only 58 genes were found to be differentially expressed between PH and HH. Different settings for overlapping DEGs like PL/PH vs. HH (n=9) and PL vs. PH/HH (n=223) were calculated. Pathway analysis revealed DEGs of the latter comparison to be enriched in various pathways like signalling by interleukins, signalling by NGF, formation of the cornified envelope and others. Further analyses of the data are underway and may provide an even deeper knowledge of molecules and pathways involved in PN pathology.

PP10

ROLE OF CYSTEINYL LEUKOTRIENES AND THE CYSLTR2 RECEPTOR IN PRURICEPTION

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Itch is associated with allergic skin diseases such as atopic dermatitis with few effective treatments. The molecular and cellular mechanisms underlying pruriceptor neuron activation and sensitization in allergic conditions are not well understood. Cysteinyl leukotrienes (Cys-LTs) are eicosanoid lipid mediators released by immune cells that play a prominent role in lung inflammation in asthma and skin inflammation in atopic dermatitis. Here we investigate the role of Cys-LTs and their signaling through the Cysltr2 receptor in itch. LTC4 synthase (LTC4S) is the enzyme that initiates the production of three Cys-LTs: LTC4, LTD4, and LTE4. LTC4 and LTD4 have been found to signal through the type 1 cys-LT receptor (Cysltr1) or type 2 receptor (Cysltr2) with different affinities. Using transcriptional profiling analysis of somatosensory neurons, we find that Cysltr2 is highly enriched in pruriceptor neurons that co-express IL31ra and Nppb. We hypothesize that neuronal Cysltr2 acts to detect Cys-LTs in the skin released by immune cells during allergic inflammation. We first test whether Cys-LTs activates sensory neurons and produces itch-associated behaviors in mice. Using calcium imaging, we show that LTC4 activates a subpopulation of sensory neurons that also responds to capsaicin. Intradermal cheek injection of LTC4 triggers scratching in mice, and this itch behavior is decreased in Cysltr2-/- mice. N-methyl LTC4 (NMLTC4), the nonhydrolyzable form of LTC4, also induced neuronal activation and itch dependent on Cysltr2. By contrast, LTD4 did not produce itch or neuronal activation. We are testing the functional relevance of this signaling pathway in mouse models of atopic dermatitis and skin inflammation. Our study implicates LTC4 as a relevant endogenous ligand for triggering pruriceptor neurons through Cysltr2 to produce itch.

PP11

PHARMACOLOGICAL EVIDENCE FOR THE INVOLVEMENT OF ATP-SENSITIVE POTASSIUM CHANNELS IN CHLOROQUINE-INDUCED SCRATCHING BEHAVIOR IN MICE

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Introduction: Chloroquine (CQ) evokes itch in human and scratching behavior in rodents through a histamine-independent pathway. Chloroquine directly excites peripheral sensory neurons which convey itch signals to the central nervous system. It has been revealed that ATP-sensitive potassium channels (K_{ATP} channels) are important in regulating neuronal excitability. Thus, we aimed to investigate the involvement of K_{ATP} channels in CQ-induced itch which may also reveal a linkage between metabolic state of cells and itch. *Materials and Methods:* Intradermal (id) injection of CQ at dose of 400 µg/site induced the scratching behavior. The K_{ATP}

channel openers, diazoxide (DZX) and minoxidil (MIN), and a K_{ATP} channel blocker, glibenclamide (GLI), were administered intraperitoneally (IP) before CQ. Then, itch was assessed by quantification of hind paw scratching bouts towards the injection site. Quantitative reverse transcription-PCR (qRT-PCR) was also used to investigate the possible changes in dermal expression of Kcnj8 and Kcnj11, the genes encoding the K_{ATP} channels. *Results:* Either DZX (10 mg/kg, IP) or MIN (10 mg/kg, IP) significantly attenuated CQ-induced scratching behavior in mice. Moreover, pretreatment with GLI (3 mg/kg, IP) significantly reversed the anti-pruritic effects of DZX and MIN. Our findings of qRT-PCR analysis also show that the expression of Kcnj8 is decreased after CQ injection. *Conclusion:* We suggest that K_{ATP} channels are involved in CQ-induced itch.

PP12
MODELING OF ITCH SENSITIZATION FOR HISTAMINERGIC AND NON-HISTAMINERGIC ITCH? – BOTH UVB- AND NGF-INDUCED SENSITIZATION SELECTIVELY INCREASE PAIN, BUT NOT ITCH, ELICITED BY HISTAMINE AND COWHAGE

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Itch sensitization to pruritic chemical provocations and mechanical stimuli has been found in patients with chronic itch, e.g. atopic dermatitis. The precise mechanisms behind such itch sensitization are unclear as is the circumstances influencing the ability of inflammatory perturbations to cause pain and/or itch sensitization as well as spontaneous itch and pain. We used two well-established human models of nociceptive sensitization to explore how pre-established unspecific inflammation (induced by epidermal UVB-damage) and non-inflammatory neurotrophic pain sensitization (induced by intradermal NGF-injections) altered sensitivity to chemical (histamine and cowhage) and mechanically-evoked itch. For the UVB experiment, 20 healthy volunteers (10F/10M) were included. Six volar forearm spots (2cm in diameter) were irradiated with increasing UVB-doses (up to 2 x minimal erythemal dose) and two spots acted as controls. For the NGF-experiment 16 healthy volunteers (5F/11M) were included and 2 µg of NGF were injected (4x50 µl blebs in 2 cm diameter areas) into both volar forearms, while saline were used as control. Pain sensitivity measurements were conducted to validate models. Subsequently, itch was evoked using histamine (1%) and cowhage spicules in the primary hyperalgesic areas and itch/pain was scored on a visual analog scale. Hyperknesis was measured with von Frey filaments. Both the UVB- and the NGF-model induces robust primary painful hyperalgesia ($p<0.01$) and mild hyperknesis ($p<0.05$), but neither of the models increases itch rating to chemical itch provocations. Contrarily, significant increases specifically for pain ratings were observed. This suggests that these models do not appropriately mimic itch sensitization of inflammatory dermatoses and that rather distinct and perhaps prolonged inflammatory processes are involved in clinically observed itch sensitization.

PP13
EXPRESSION OF UBIQUITIN C-TERMINAL HYDROLASE L1/PGP9.5 IN PSORIASIS: INTERPLAYS BETWEEN AXONAL NERVE TERMINALS SND EPIDERMAL KERATINOCYTES IN TRANSMISSION OF ITCH

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Introduction: Itch is unpleasant sensation occurring in psoriasis, multisystem immunegenetic skin disease. Itch transmission is mediated via skin C-fibers, axonal terminals of dorsal root ganglion (DRG) neurons. However, in chronic skin neuroinflammation enhanced transmission of itch might by induced not only by outgrowing and disordering nerve terminals, but additional modulate via abnormal activity of neuro-immune-endocrine cells: fibroblasts, Langerhance, melanocytes, and keratinocytes. For identification and distribution of skin nerve fibers, as well neuro-immune-endocrine cells protein gene product 9.5 (PGP9.5), biochemically Ubiquitin C-terminal hydrolase L1 (UCHL1) is commonly used. UCHL1 gene and PGP9.5 protein (UCHL1/PGP9.5 system) belongs to the deubiquitinase enzyme (DUBs) family, which is responsible for cleave of C-terminal peptide adducts as well as N-terminally conjugated ubiquitin from substrate proteins. UCHL1/PGP9.5 is widely expressed in the Central Nervous Sysytem (CNS), while its disorders are linked with neurodegeneration, cancer, impaired immune functions, tissue injury and pain-related sensations. It seems that disordered interplays between neuronal and non-neuronal cells via common UCH-L1/PGP9.5 expression might control skin neuro-immune-endocrine status and escalate itch. *Material and Methods:* The 20 skin punch biopsies from non-lesional and lesional site of the skin were obtained from psoriasis patients and 20 normal skin of healthy individuals. Gene expression was performed using real-time PCR, whereas protein level was estimated by immunofluorescence microscopy. *Results:* Fluorescence microscopy imaging demonstrate impaired distribution of PGP9.5 nerves in non-lesion and lesions itchy skin (basing on VAS score) comparing to skin without itch and control group. Additionally, significant relations between non-neuronal PGP9.5 expression within basal keratinocytes and suprabasal keratinocytes with itch were also observed. In contrast, real-time PCR gene expression results demonstrate significant downregulation of UCHL1 mRNA in non-lesional and lesional skin in itchy group compare to skin without itch and control group. *Conclusions:* We believed, that this unusual and impaired expression pattern between UCHL1 transcript and its protein PGP 9.5 may demonstrate new findings about peripheral innervations and neuro-immune-endocrine cells in molecular aspect of psoriatic itch.

PP14
MEASURING SCRATCHING AND SLEEPING BEHAVIOR BESIDES PRURITUS INTENSITY: DEVELOPMENT OF A NEW, ALL-ENCOMPASSING PRURITUS SYMPTOMS SCORE – THE "ITCH-CONTROLLED-DAYS SCORE"

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Background: Besides pruritus intensity different associated symptoms as sleeping or scratching behavior have been shown to affect the disease burden and quality of life of chronic pruritus (CP) patients. A newly developed questionnaire aimes to measure a variety of pruritus-relevant symptoms and to evaluate the control of pruritus within clinical routine and research. *Methods:* Within the development part of the study structured patient interviews helped to identify the parameters defining an itch controlled day (p= 89 CP patients). After item generation, feasibility-check and item reduction, the Itch-Controlled-Days (ICD) questionnaire

was created with nine items on pruritus intensity, sleeping and scratching behavior. The score was tested and validated in 60 patients. *Results:* Retest-reliability was excellent (Cronbach's alpha >0.95; intraclass correlation coefficient > 0.9; Cohen's kappa >0.8). Spearman-Rho correlation analysis and Mann-Whitney-U testing showed moderate to strong convergence of pruritus intensity values (VAS, VRS, NRS) and quality of life (ItchyQoL, DLQI) (all $p<0.01$). The 9 items of the ICD questionnaire allow to calculate a score from 0 to 22. *Conclusion:* The measurement of different pruritus- relevant symptoms within one single score helps to assess the itch control easily and systematically.

PP15
THE USE OF A DERMOCOSMETIC TO MANAGE PRURITUS RELATED TO SKIN DISEASES: AN OBSERVATIONAL STUDY

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Introduction: Pruritus is defined as an unpleasant sensation resulting in an urge to scratch. Pruritus is the most common symptom in dermatology, affecting over one-third of the world population. Pruritus may be occasional or chronic, local or widespread, and related to various skin diseases such as atopic dermatitis, psoriasis and urticaria. It is sometimes related to cutaneous dryness, as is the case for senile pruritus. The Skin Relief™ technology associated to enoxolone were developed to have a significant action on pruritus. It inhibits the release of pruritic mediators like Thymic Stromal Lymphopoietin, Nerve Growth Factor and histamine. And so, it reduces nerve fibre activation. In this context, the was to assess the efficacy of an antipruritic spray to quickly calm the itching including Skin relief™ technology. This product was tested in 4 dermatological diseases: atopic dermatitis, psoriasis, chronic urticaria and senile pruritus. *Material/Methods:* An observational, prospective and multicentre study was performed in Poland including 120 patients (30 subjects in each group). The product was sprayed many times as needed on the body and face during 21 days. Efficacy assessments on pruritus were performed at D0 and D21 by using 5-D pruritus scale (5 to 25), by scoring itching sensations and skin conditions with numerical scale (0 to 9). Tolerance was also assessed. *Results:* The analyzed population included 118 subjects (63 males and 55 females) with a mean age of 41 years old (±27). The product was applied 2.5 times a day on average. A significant decrease of 5-D pruritus scale (–40%) and sensations of itching (–63%) was observed between D0 and D21. In parallel, a significant improvement of skin conditions: dryness (–52%), roughness (–53%), scales (–58%), suppleness (+26%). It relieves pruritus in 21 seconds on average and the effect lasts half a day in 56% of subjects. The majority of the subjects were very satisfied by the product (98% of patients). And, the product was well-tolerated in 99.2% of subjects. *Conclusions:* This study confirms the interest to use an antipruritic spray in chronic skin diseases: atopic dermatitis, psoriasis, chronic urticaria and senile pruritus. This product can be considered as effective, safe and easy to use.

PP16
ITCH AS ACCOMPANYING SYMPTOM IN VITILIGO

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Purpose of research: Identification of the prevalence rate and basic characteristics of pruritus in the patients with vitiligo. *Material and Methods:* Material used in this research included ambulatory cards and application-questionnaires of the patients with various forms of vitiligo, referred for medical care in the first quarter of 2017. *Results of research:* The ambulatory cards and application-questionnaires were obtained from 124 patients with vitiligo, of them 118 (95%) patients noted skin pruritus as accompanying symptom in disease. Of 118 patients men were 39 (about 33%), women – 79 (about 67%). Localized form of vitiligo occurred in 101 patients, generalized form – in 17 patients. Fifty-six patients noted appearance of pruritus at the basis of occurrence of depigmented spots, in 38 patients the pruritus appeared before and in 24 patients after formation of vitiligo focuses. Localized form of pruritus was revealed in 115 patients, generalized form was found only in 3 at the age of 44, 53 and 55 years. The gradually progressive skin pruritus was noted in 97 patients, in 21 patients the pruritus was found rarely. Episodic pruritus appearance was observed in 85 patients, cyclicity was noted in 33, at the same time 78 patients observed intensification/appearance of pruritus at the night or after nervous-psychological stress. Analysis of the accompanying disease revealed 58 patients suffering from anemia of various stage of severity, 47 – with pathology of endocrine system (all 3 patients with generalized pruritus suffered due to diabetes mellitus), 24 – from diseases of hepatobiliary system, and 12 from diseases of urinary excretive system and others. On the background of the basic disease treatment 85 patients noted disappearance of pruritus, in 33 the treatment of vitiligo had no influence of the elimination of skin pruritus. *Conclusion:* Thus, on the basis of vitiligo the pruritus mostly frequent occurred in females, developed on the background of depigmentation, expressed looking like episodic, limited, gradually intensifying form and disappeared on the basis of the main disease treatment.

PPI7
PREVALENCE AND MAGNITUDE OF ITCH IN ADOLESCENT ATOPIC DERMATITIS: RETROSPECTIVE SURVEY OF FIRST-YEAR UNIVERSITY STUDENTS

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Recent epidemiological studies revealed the increased number of adolescent subjects with atopic dermatitis. The picture of Japanese adolescent subjects with atopic dermatitis is poorly understood. Thus, we conducted the questionnaire survey to investigate the prevalence of Japanese adolescent subjects with atopic dermatitis, and to evaluate the magnitude of itch in 1st-year university students with atopic dermatitis. On 2016, 1st-year students of our university answered the self-completed questionnaire about both the past history of allergies and the demographic factors in a retrospective manner. Finally, 3,135 sheets were effectively analyzed. In total, 13.2 % of students had a history of diagnosed as atopic dermatitis. Nearly half of the subjects with atopic dermatitis had the protracted clinical course since childhood. At the health examination of 1st-year students, all students with atopic dermatitis got clinical examination by specialist in dermatology. Magnitude of itch was evaluated by visual analogue scale. Magnitude was somewhat lower than we expected, probably because of their successs in university entrance exam.

PP18
IS ITCH A SYMPTOM OF CUTANEOUS LEISHMANIASIS?

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Cutaneous leishmaniasis is a parasitic infection caused by different species of the obligate intracellular protozoa Leishmania. This disease is transmitted through the bite of an infected female

sandfly. It occurs in a variety of clinical forms depending on the subspecies of the Leishmania involved, and the immunological status of the host. In addition to the classical clinical presentation, which is usually non itchy entity, several unusual and atypical clinical features of the disease are being reported these days. In this report, I describe a rare variant of cutaneous leishmaniasis initially associated with itch, resembling squamous cell carcinoma-like leishmaniasis. This case report alerts to the existence of atypical forms of cutaneous leishmaniasis. In our case, the lesion of the patient clinically mimicked squamous cell carcinoma and were associated with itch. It should be kept in mind that the wide spectrum of clinical variants of cutaneous leishmaniasis can occur and icth, although rarely, may be a symptom of the disease.

PP19
ASSESSMENT OF PRURITUS AMONG PATIENTS WITH VIRAL HEPATITIS B AND C

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Introduction: Itching is an unpleasant subjective sensation that leads to scratching. It is a common symptom of skin diseases but may also occur in various systemic diseases. *Objective:* The aim of the study was the clinical characteristics of itch accompanying viral hepatitis B and C. *Material and Methods:* Screening was performed among 110 people infected with HBV, HCV or both. A total of 22 (20%) patients aged 25–68 years with pruritus were included for further analysis. The study was based on an questionnaire containing questions about general health, duration of liver disease and its clinical picture, accompanying illnesses, medications and pruritus. *Results:* In the analyzed group, 9 patients ere diagnosed with type B hepatitis, whereas in 13 hepatitis type C was stated. The duration of liver disease ranged from 3 to 22 years. In 15 (68.2%) patients liver cirrhosis was documented; one (4.5%) patient suffered from hepatocellular carcinoma. The most common site of pruritus was the trunk (n=13, 59.1%), generalized pruritus was observed in 3 (13.6%) patients. Secondary skin lesions were found in 14 (63.6%) people. The most common period of pruritus occurrence was night and evening, the least common pruritus was noted in the morning. *Conclusions:* Pruritus affects about one fifth of patients with viral hepatitis, most commonly in those subjects with long-term disease duration and significant liver failure.

PP20
DESCENDING INHIBITION OF ITCH AND PAIN IN HUMANS – EXPERIMENTAL PARADIGMS FOR ASSESSING ENDOGENOUS ITCH INHIBITION EFFICACY

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Endogenous descending pain inhibition is reduced in chronic pain states signified by lowered conditioned pain modulation (CPM) efficacy. In parallel, patients with chronic itch may exhibit decreased endogenous descending inhibition of itch (CIM) and pain, but little is known about descending inhibition of itch and techniques to evoke conditioned modulation of itch. We systematically assessed CPM and CIM of experimentally elicited itch and pain. Twenty-six healthy volunteers were tested. Conditioning stimulations comprised cold pressor-induced pain and histamine-evoked itch. Test stimuli were conducted with electrical paradigms designed to evoke itch or pain. Five conditions were investigated; 1) itch modulation by contralateral itch; 2) itch modulation by contralateral pain; 3) itch modulation by ipsilateral pain; 4) pain modulation by contralateral pain (i.e. a standard CPM-paradigm; positive control condition), and 5) pain modulation by contralateral itch (negative control condition). Conditioning itch stimulation did not significantly affect the mean itch ratings (although an insignificant trend was observed), however, the mean itch intensity was significantly decreased by both contra- and ipsilaterally applied conditioning pain stimulation, signifying a pain-evoked CIM-effect. Mean pain ratings were significantly reduced by the conditioning pain stimulus, but not by the conditioning itch stimulus. Descending itch inhibition could not be significantly evoked by conditioning itch stimulation, but can be efficiently evoked with conditioning pain stimulation. These results suggest a hierarchical prioritization in favour of pain-induced central descending inhibition of both itch and pain in humans. Future studies assessing endogenous inhibition efficacy of itch in patients with chronic itch could favourably apply a design assessing pain-evoked itch modulation ("pain inhibiting itch" paradigm).

PP21
PRURITUS IN PATIENTS HOSPITALIZED IN THE DEPARTMENT OF DERMATOLOGY, JAGIELLONIAN UNIVERSITY MEDICAL COLLEGE - A THERAPEUTIC APPROACH

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Introduction: The presence of pruritus is common in dermatological patients. The treatment of itch involves moisturizing agents, as well as topical and systemic drugs. Antihistamines are often effective in treating the itch sensation, however the age- and concomitant disease-related limitations should be taken into consideration when implying the treatment. *Aim:* The aim of the study was to assess the range of the problem of pruritus and to highlight the need for special cautions that should be taken during the treatment of this symptom.*Material and Methods:* We analyzed clinical data of 310 patients hospitalized in the Department of Dermatology, Jagiellonian University Medical College in Krakow, Poland between January and March 2016. 102 of 310 patients (32.9%) presented with pruritus – 66 women and 36 men, aged 18–86. *Results:* The most common group of patients with pruritus were middle-aged (35–64 year old) individuals (45%), followed by elderly patients (31.4%). The most common cause of itch were allergic diseases (45.1%), most commonly atopic dermatitis (15.7%). 50% of patients were treated with oral antihistamines (1st and/or 2nd generation). Localized pruritus was observed in 75.5% of patients, generalized in 24.5%. 35.5% of patients described pruritus as severe. Intensity of pruritus was higher in patients with generalized than with localized itch (56% vs 29%; p=0.013) and those patients received antihistamines more commonly (64% with intense pruritus vs 42% with nonintense; p=0.04). Elderly patients received topical treatment and have been treated with other systemic drugs more often (97% vs 81% for topical treatment; p=0.035; 44% vs 23% for other drugs; p=0.03). Elderly subjects had significantly higher levels of creatinine, urea and glucose (p<0.05 each). *Conclusions:* Antihistamines are frequently used in the management of pruritus. However, in the group of elderly patients more caution should be taken when implying such treatment. Use of antihistamines requires careful assessment of the

risk of pharmacological interactions and their effects on central nervous system. The choice of the drug and its dosage should be adjusted to the hepatic and kidney function.

PP22
ASSESSMENT OF SKIN PROBLEMS AMONG PATIENTS WITH INFLAMMATORY BOWEL DISEASE: IS PRURITUS A MAJOR FINDING?

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Introduction: Patients with inflammatory bowel diseases (IBD) often requires prolonged immunosuppression. Such treatment may result in various dermatological complications as itching which can be very heavy for patients. *Objective:* The aim of this study was to analyze the prevalence of dermatological conditions in patients with IBD with special emphasis on pruritus. *Materials and Methods:* The study included patients with IBD hospitalized in gastroenterological department. All patients underwent a thorough medical history and physical examination. Based on achieved data the stratified questionnaire evaluating their skin condition, and previous treatment was completed by investigators. All data were analyzed statistically. *Results:* The results showed that questionnaire is a valuable research tool which allow to identify significant dermatological problems in patients with inflammatory bowel disease. About 20% of patients with IBD suffered from pruritus (19.5%), which the third most common dermatological ailment in this population of patients after xerosis (46.5%) and hair loss (20.9%). Patients also stressed the need for dermatological consultations during diagnosis and treatment of IBD. *Conclusions:* Such "trivial" problem as itching might be neglected by the gastroenterologist or GP but it can be very problematic for patient. It is the reason why patients with IBD require proper evaluation of skin problems and the dermatologist should be included in the diagnostic and therapeutic team supervising patients with IBD

PP23
VALIDITY AND RELIABILITY OF VARIOUS INSTRUMENTS FOR ITCH INTENSITY MEASUREMENT IN PATIENTS WITH CHRONIC PRURITUS: A PROSPECTIVE, MULTICENTER STUDY IN KOREA

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Background: Despite its high prevalence and significant impact on quality of life, a valid assessment of chronic pruritus remains elusive due to its subjectivity and multifactorial nature. Various tools have been used over time to provide a more reliable and accurate evaluation of pruritus. Pruritus intensity can be measured using the Visual Analog Scale (VAS), Numeric Rating Scale (NRS), Verbal Rating Scale (VRS), and various multidimensional questionnaires including Itch Severity Scale (ISS). However, to date, no single method has been recognized as a gold standard. *Objective:* In this study, we evaluated validity and reliability of VAS, NRS, VRS and ISS and relation to a pruritus-specific quality of life instrument, IcthyQoL. *Methods:* A total of 419 patients with chronic pruritus (215 males, 214 females, mean age 46.58 years) recorded their pruritus intensity on VAS (100-mm line), NRS (0–10), VRS (four-point) and ISS scales. Re-test reliability was analyzed after three hours. In addition, IcthyQoL survey was conducted on all patients. *Results:* Correlation of VAS, NRS and VRS by Spearman's correlation coefficient showed statistically significant high values. ISS showed a low intercorrelation validity with these three tools. However, ISS correlated strongly with IchyQoL compared to VAS, NRS, and VRS. Statistical correlation of the three hours' difference was also the highest in ISS. Re-test reliability of VAS, NRS and VRS was similar and lower than ISS. *Conclusion:* Since pruritus is a subjective symptom of multifactorial trait, its assessment may be challenging. The best way to assess the itch intensity should be studied.

PP24
EVALUATION OF THE CLINICAL CHARACTERISTICS OF PRURITUS IN PATIENTS WITH PSORIASIS USING THE JAPANESE VERSION OF THE 5-D ITCH SCALE

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The prevalence of pruritus in the patients with psoriasis has ranged from 64% to 97%. Pruritus leads the patients with psoriasis to scratch and it may trigger new eruptions. Thus, the management of pruritus is important to avoid aggravation of psoriasis by scratching. It is needed to assess pruritus in the psoriatic patients for the choice of appropriate treatments. Currently, only a few resources are available to measure pruritus. However, these scales do not obtain the multidimensional aspects of pruritus. The 5-D itch scale is a new simple self-administered questionnaire. It consists of five sections that measure duration, degree, direction, disability and distribution of itching. To examine the clinical characteristics of pruritus in patients with psoriasis using the Japanese version of the 5-D itch scale. A total of 69 patients with psoriasis (44 men and 25 women), all between 23 and 80 years of age, participated in this study (mean±SD; 54.6±15.6). The Japanese version of the 5-D itch scale was administered to these patients. In addition, we evaluated the disease severity and quality of life (QOL) by the severity of psoriasis (psoriasis area and severity index [PASI]) and the dermatology life quality index (DLQI), respectively. The mean and standard deviation of 5-D score was 10.1±4.3 with the scores ranging between 5 and 22. The mean PASI score was 6.4±7.3 with the scores ranging between 0 and 28. Our data are currently under analysis and will be expected to give the characterization and correlation of pruritus, the disease severity and QOL in Japanese patients with psoriasis. The 5-D is a reliable, multidimensional measure of itching that has been validated in patients with psoriasis. The 5-D should be useful as a new tool for the evaluation of psoriatic pruritus.

PP25
A UGANDAN GIRL WHO HAD TO ENDURE THIRTEEN YEARS OF ITCHY RASHES WITHOUT SEEING A DERMATOLOGIST: A CASE REPORT FROM THE NEW GEROLD JÄGER SKIN CLINIC IN KABALE, UGANDA

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Background: Gerold Jäger skin clinic in Kabale is an initiative of Dr. Leo Odongo, a 33-year-old Ugandan trained dermatologist who, in the last five months, has been doing voluntary work of establishing the fourth university skin clinic in Uganda, where he is currently volunteering as a dermatologist in Kabale Regional Referral Hospital in South-Western Uganda. Uganda has less than fifteen trained dermatologists. The clinic is named after Prof. Dr. Gerold Jäger, who established the field of dermatology in Uganda and who also supervised Dr. Odongo´s Master´s degree Dissertation in Dermatology. We report here about a 13 -year-old girl who has suffered from the itch without getting access to a dermatologist until she was rescued by the new skin clinic in Kabale. *History:* A 13-year-old girl in whom the mother reports very itchy recurrent rashes on the body since early childhood. The itchy rash was later associated with itchy eyes. No history of asthma. However, there is positive family history of atopy. Mother sought treatment for the girl from many health workers, none of whom was a dermatologist. She was then given wrong advice and wrongly stopped from eating several food items. She was advised to smear herbal products, cow ghee and cow milk on the girl as remedy. Despite all these, the itchy rashes kept on recurring with increasing itch and discomfort for the girl. The mother was then told of the new clinic that had been opened in Kabale where she brought the girl to us for treatment. *Findings on physical examination:* We found the girl had dryness of skin with multiple scratch marks on the trunk and extremities with the face less affected. There was marked lichenification at the flexure surfaces (especially the antecubital fossae and the popliteal fossae). Atopic dermatitis was diagnosed. We treated the girl with two-weeks course of topical betamethasone ointment 0.1% applied twice daily. We recommended stoppage of use of herbal products, ghee and cow milk application on the girl's skin and resumption of eating of the foods she had been wrongly stopped from eating. We reviewed the girl after two weeks of treatment and she had marked improvement in her symptoms. Itching had ceased completely and her quality of life had improved greatly. *Conclusion:* In our respective capacity we can all contribute something to the care of people who are tormented with itch. With the voluntary work of Dr. Leo Odongo, the girl was rescued from the torment of itch.

PP26
ITCH IN PSORIASIS – IS AGE AN IMPORTANT FACTOR?

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Introduction: The suspected lifespan of the population has increased in recent years. Itch is the most common symptom in dermatology present in the majority of patients with psoriasis. As the frequency of chronic itch increases with the age, it will constitute important issue in elderly patients suffering from this common dermatosis. *Objective:* To assess detailed itch characteristic in patients with psoriasis vulgaris with a special emphasis on age status. *Material and Methods:* The study included 67 consecutive inpatients hospitalized in the Department of Dermatology, Venereology and Allergology, Wroclaw Medical University due to psoriasis vulgaris. A detailed history was taken. A physical examination of the skin including the evaluation of Psoriasis Area and Severity Index (PASI), Body Surface Index (BSA) and Physician's Global Assessment (PGA) was performed. The presence of chronic itch was assessed, including the location, severity, variation during the day, influencing factors and impact on daily activities and sleep. Dermatology Life Quality Index (DLQI) and 6 Item Stigmatization Scale (6ISS) questionnaires were filled by the patient. A statistical analysis was performed. *Results:* Among 67 patients, 31.3% were women and 68.7% were men. The mean age was 55.5±15.3 years; 70.1% of participants were aged less than 65 years, while 29.9% were aged 65 and over. The mean time of the onset of disease was 19.5 years, whereas the mean PASI, BSA and PGA scores were 15.9, 32% and 2.1, respectively (no statistical differences between groups aged below 65 years and over 65 years; p=0.68; p=0.92; p=0.80; respectively). Chronic pruritus was present in 71.6% patients; no differences were observed between age groups. The mean pruritus intensity in the last 3 days was 5.7 points; no differences were observed between age groups (5.6 vs. 6.1 points; respectively; p=0.46). In patients aged 65 and over cold ambient temperature reduced the itch intensity statistically more common than in individuals aged below 65 (86.7% vs. 24.2%; respectively; p=0.01); the mood decrease due to itch was also more prevalent in the former age group (73.3% vs. 60.6%; respectively; p=0.02). *Conclusion:* Itch is a common and relevant phenomenon in people suffering from psoriasis vulgaris. In the majority of aspects its characteristic did not differ according to the age group, while several aspects of itch were different, implying that aging may influence clinical features of itch in psoriatic subjects.

PP27
RELATIONSHIP BETWEEN PRURITUS AND SERUM LIPOCALIN-2 IN PATIENTS WITH PSORIASIS

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Background: Lipocalin-2 (LCN2) is a member of the highly heterogeneous secretory protein also known as neutrophil gelatinase-binding lipocalin (NGAL). It is mainly secreted from activated neutrophils and is known to be associated with neurodegeneration, cancer metastasis and inflammatory responses. It has been reported that serum LCN2 concentration increases in psoriasis patients, and decreases in patients with atopic dermatitis. A previous study also shows that astrocyte-derived LCN2 is involved in enhancement on spinal itch in the mouse model of atopic dermatitis. Recently the relationships between serum LCN2 concentration and pruritus have been reported in patients with psoriasis. Objective: This study was performed to examine the correlation between serum LCN2 level and pruritus in psoriasis or in atopic dermatitis patients. *Methods:* Serum LCN2 concentrations were measured in psoriasis patients, atopic dermatitis patients and healthy controls using enzyme-linked immunosorbent assay (ELISA). The itch intensity was assessed with visual analog scale (VAS), and the disease severity was measured by psoriasis area and severity index (PASI) and scoring atopic dermatitis (SCORAD). Correlation was examined between serum LCN2 with VAS, PASI and SCORAD. *Results:* Serum LCN2 concentrations were significantly elevated in psoriatic patients and atopic dermatitis patients compared to healthy controls. In the psoriatic patients, serum LCN2 concentrations were significantly correlated with VAS, but not with PASI. In contrast, there was no correlation between serum LCN2 concentration and VAS, SCORAD in atopic dermatitis patients. *Conclusion:* These findings suggest that LCN2 is associated with the pruritus of psoriasis patients. Serum LCN2 levels may be a useful clinical marker for pruritus assessment in the patients with psoriasis.

PP28
EVALUATION OF THE CLINICAL CHARACTERISTICS OF PRURITUS IN PATIENTS WITH DERMATOMYOSITIS USING THE JAPANESE VERSION OF THE 5-D ITCH SCALE

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Dermatomyositis (DM) is a type of idiopathic inflammatory myopathy. The pathogenesis is considered to be microangiopathy affecting skin and muscle. The cutaneous manifestations of DM are the most important symptoms of this disease. The skin signs are various such as heliotrope rash, Gottron's papules, paronychium erythema, poikiloderma, the V-neck sign, the shawl sign, cuticular overgrowth, mechanic's hands, photosensitivity and so on. Pruritus is one of the cardinal symptoms that DM patients often complain. It is known to significantly affect daily life and correlates with a worse quality of life. To evaluate pruritus is very important to improve their quality of life. However, the precise characteristics of pruritus in patients with DM are unknown. The aim of current study is to evaluate the clinical characteristics of pruritus in patients with DM. Pruritus was assessed by Japanese version of 5-D itch scale. The 5-D itch scale is a new simple self-administered questionnaire. It consists of five sections that measure duration, degree, direction, disability and distribution of itching. Recently, DM has been categorized into several disease subsets based on the various myositis-associated autoantibodies such as anti-Jo-1 antibody, anti-Mi-2 antibody, anti-transcriptional intermediary factor 1 gamma (TIF1γ) antibody, anti-melanoma differentiation-associated gene 5 product (MDA5) antibody. We examine the relationship between pruritus and myositis-associated autoantibodies. In addition, DM is associated with internal malignancy. We also examine the relationship between pruritus and the presence of internal malignancy. Our data are currently under analysis and will be expected to give the prevalence and characterization of pruritus in Japanese patients with DM.

PP29
THE NEED FOR LINGUISTICALLY AND CULTURALLY ADAPTED STANDARD QUESTIONNAIRES TO ASSESS ITCH: PRELIMINARY STUDY AND PERSPECTIVES

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Itch is defined as an unpleasant sensation leading to the need to scratch. Nonetheless, the meaning is not necessarily the same depending on languages, cultures and historical periods. For patients and even doctors, it is not always evident to differentiate itch from close sensations such as pain, burning, tingling, tickling, prickling, tightness or stinging, and it is not obvious that the borders between these sensations are the same in all languages. The presented study is a preliminary framework for the creation of standard and validated questionnaires considering cross-cultural and linguistic adaptations. Twenty-seven languages classified into 6 language families are included in our study. The adequate understanding of the sensations experienced by patients is undeniably crucial in the patient-doctor relationship and indispensable for clinical trials, investigations into quality of life, psychological studies and pathophysiological research. The presented preliminary study confirms the need and proposes a method for the creation of standard and validated questionnaires. The next step will be a study with interviews of patients that would describe their symptoms in their own language in order to validate translations of questionnaires in all studied languages.

PP30
DETECTION OF PRESENCE IGG1-IGG4, IGE, IGA, IGM, C3C, C1Q AND FIBRINOGEN DEPOSITS UNDER DIRECT IMMUNOFLUORESCENCE STAINING IN ELDERY PATIENTS WITH PRURITIC DERMATOSES

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Background: Pruritic dermatoses of the eldery pose a diagnostic and therapeutic challenge. Prodromal phase of bullous pemphigoid (BP) should be considered in patients with extensive pruritus and skin lesions of polymorphic appearence and urticaria-like plaques, eczema-like papules and dermatitis herpetiformis-like lesions. Early recognition of prodromal BP may decrease progression of the disease. While the pathogenicity of IgG autoantibodies to BP 180 kDa has been demonstrated in BP, the role of IgE autoantibodies remains unclear. *Objectives:* The purpose of the study was to assess the presence of tissue-bound IgG1-IgG4, IgE, IgM, IgA, C3c, C1q and fibrinogen deposits in eldery patients with various pruritic dermatoses who had never experienced clinically apparent blisters, and their correlation with distinct clinical features. *Materials and Methods:* In this retrospective study we assessed the presence of IgG1-IgG4, IgE, IgM, IgA, C3c, C1q and fibrinogen deposits as detected by direct immunofluorescence microscopy of skin biopsy speciemens obtained from 33 eldery patients (>60 years old). Clinical features at time of diagnosis were noted. Patients with acute or chronic, mild to intense pruritus, who had never experienced blisters and patients who didn't have any other known dermatological disorder were included to the study. *Results:* IgG1-IgG4 and IgE deposits were present in 1 patient and were localized in epidermis. Deposits of IgG2 and IgG3, IgG4, IgE in dermoepidermal junction were present in 1 patient. Deposits of IgE in epidermis were found in 3 patients, IgM and C1q in 4 patients. Deposits of C3c and C3c, IgG1 and fibrinogen were present in 1 patient. The most common clinical presentation was itch with no skin lesions (14 patients), prurigo nodularis-like lesions (8 patients), urticaria-like lesions (5 patients), eczema-like lesions (3 patients), dermatitis herpetiformis-like lesions (2 patients) and lichen planus-like lesions (1 patient). *Conclusion:* Our findings show that presence of tissue-bound IgG1-IgG4, IgE, IgA, IgM, C3c, C1q and fibrinogen deposits provide additional information in some patients, Prospective studies indicating correlation between presence of circulating IgE and IgG with tissue-bound deposits of autoantibodies are needed, same as designation of specificity of autoantibodies with distinct clinical features and course of disease.

PP31
VALIDATION OF JAPANESE VERSION OF ITCHYQOL IN CHRONIC PRURITUS PATIENTS

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Chronic pruritus (CP) has such a negative impact on quality of life (QoL) of the patients. Hence, it is important to monitor the extent of QoL impairment in the course of treatment of CP. ItchyQoL is the first pruritus-specific QoL instrument developed in 2008 and widely used in the English and German speaking countries. We here report a validation of the Japanese version of ItchyQoL (ItchyQoL-JPN). ItchyQoL-JPN was created through the standard protocol including backward translation. A total of 100 adult patients with

CP (atopic dermatitis 68, uremic pruritus 18, other dermatitis 6, prurigo 4, chronic urticarial 4) participated in the study to test reliability, validity and responsiveness of ItchyQoL-JPN. Reliability was demonstrated by internal consistency (Cronbach alpha: 0.81) and test-retest reproducibility (intraclass correlation coefficient: 0.89, $p<0.001$). ItchyQoL-JPN showed face and content validity. Convergent validity was demonstrated by positive correlation of ItchyQoL-JPN with itch intensity measured with a visual analogue scale (VAS, 0=no itch and 10=the worst itch imaginable) (r=0.46, $p<0.001$) and Skindex-16 (r=0.85, $p<0.001$), a widely used QoL instrument of skin diseases in Japan. Changes in ItchyQoL-JPN over the course of 2 to 3months correlated well with changes in VAS (r=0.70, $p<0.001$) showing a good responsiveness. The results from the present study suggest that ItchyQoL-JPN may make it possible to evaluate the QoL impairment of the Japanese patients with CP.

PP32
DIFFERENCES IN FACTORS THAT DRIVE PRURITUS QUALITY OF LIFE BETWEEN ASIAN AMERICANS AND OTHER RACES

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Racial disparities in pruritus quality of life (QoL) have been reported. Our data from a veterans population indicated that non-whites have greater pruritus-specific QoL impact. Asian or Pacific Islanders (API) more commonly report certain pruritic conditions and seek medical care for pruritus, but the etiology of this disparity remains unclear. API are traditionally grouped into one population or grouped as "Other", but are in reality a heterogeneous group. We investigated potential factors mediating this disparity in an API population of 43 itchy and 29 non-itchy subjects. Surveys assessing QoL (ItchyQoL) and itch severity were given to itchy subjects, and demographics and medical distrust to all subjects. The API group had a mean itch severity score of 4.19 (SD 2.62), which is lower than that of the veterans (5.2, SD 2.3). As in the veteran group, itch severity was a significant predictor of QoL. However, in the API group, years since immigration was an additional predictor for functional impact, and sex for emotional impact ($p < 0.05$). As in the veterans group, itch had disproportionately higher emotional rather than functional or symptomatic impact on QoL among API. Statistically significant differences in individual ItchyQoL item means between itchy API and veterans of different races were also found among all three subscales. Qualitatively, we found certain ItchyQoL items to be drivers under each subscale. APIs had higher concern for scratching and seasonal aggravation for symptomatic impact; sleep disturbance for functional impact; and concern that their pruritus would last forever for emotional impact. Finally, we found differences in medical system distrust between itchy and non-itchy subjects; compared to the non-itchy API, itchy subjects felt less comfortable telling their physicians "anything" (Z –2.34, p=0.019). Interestingly, itchy API more strongly disagreed that "their physicians pretended to know something he/she did not know" (Z –2.55, p=0.011) or "if a mistake was made in their treatment, their doctor would try to hide it from them" (Z –2.08, p=0.037). Despite a small homogenous cohort, these preliminary results merit further exploration of potential differences between API ethnicities and related sociocultural factors that may mediate these disparities in pruritus.

PP33
INVESTIGATING RACIAL DISPARITIES IN PRURITUS QUALITY OF LIFE IN PEDIATRIC PATIENTS

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Introduction: Racial disparities in the quality of life (QoL) impact of chronic pruritus (CP, >6 weeks) have previously been reported in adults, with non-whites reporting worse QoL impact even after adjusting for itch severity. Although racial disparities in CP prevalence have been described in children, differences in QoL impact remain unclear. This study investigates racial differences in QoL impact in children with CP. *Methods:* 8-17 year olds with CP were recruited from the Emory Clinic (n=153). Subjects completed the pediatric ItchyQoL, a 35-item survey that measures the symptomatic, emotional, and functional QoL impact of itchy skin in children (validation pending). Race was reported by guardian, and subsequently categorized as "Black" or "Nonblack". *Results:* A total of 153 patients were recruited of which 89 were Nonblack. Nonblack children were nearly 3 times more likely to report having felt different from other kids their age, because of itchy skin, compared to Black children (Odds Ratio 2.9; 95% CI 1.258–6.981). In none of the other ItchyQoL items did nonblack children significantly differ from blacks. Interestingly, when race was categorized as "White" and "Nonwhite", there were no significant differences in any of the items. *Conclusion:* The fact that nonblack children were more likely to feel different from peers than black children may be due to the high prevalence of atopic dermatitis in black children. Black children would see that their friends itch as much as they do. The fact that categorization of White vs. Nonwhite did not yield differences suggest that the Hispanic and Asian populations may not differ significantly from Whites in their QoLimpact. Further investigation is indicated to elucidate possible etiologies for these initial findings, such as cultural perception and social implications of itch in children.

PP34
DOES PRE-SCRATCHING REDUCE THE ITCH TRANSMISSION?

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Itch is an unpleasant sensation caused by pruritogen transmitted by sensory neurons to the spinal dorsal horn and then to higher brain center, which eventually induces the desire to scratch. The act of scratching and variable noxious counter stimuli like noxious heat and painful sensations relieve the itch sensation. However, it is not clear whether the noxious stimuli prior to injection of pruritogen could effectively reduce the itch sensation. Here we observed antipruritic effect produced by brief noxious stimuli applied on mouse skin prior to pruritogen. This effect was accomplished by We demonstrated that application of noxious stimuli (e.g., passive scratching) on the nape skin of mild anesthetized prior to prutrinogen could significantly reduce itch response. Similar itch reduction was observed in the nape and cheek skin models, when intradermal injection of capsaicin was given prior to prutinogen. The antipruritic effect produced by brief noxious stimuli lasted for more than 20 minutes. We further demonstrated that passive scratching of mice led to phosphorylation of ERK in cervical DRG neurons and enhanced c-Fos expression in lamina II of the cervical spinal dorsal horn. Taken together, noxious stimuli prior to pruritogen challenges are effective to diminish itch responses by neural modulation at the spinal cord level, although possible involvement of supraspinal control cannot be excluded.

PP35

THE RELATIONSHIP BETWEEN STRESS AND ITCH IN GERMAN UNIVERSITY STUDENTS

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Background: Attending university is often accompanied by different stressors like taking exams or financial strain. In addition, itch and stress are related in patients with atopic dermatitis. A recent US-study found that stress and itch are linked in university students. However, the previous study did not differentiate between students with and without skin diseases and with acute or chronic itch. Therefore, the aim of the current study is to investigate whether the relationship between stress and itch differs between these groups. *Methods:* 794 students (135 male) filled in a web-based version of the Perceived Stress Questionnaire (PSQ) to measure perceived stress during the last month and a modified version of the Self-Reported Skin Questionnaire (SRSQ) to measure different skin symptoms, including itch. Itch intensity during the last four weeks was measured by a visual analog scale ranging from 0–10. Correlation analyses were conducted to investigate the relationship between stress and itch intensity in students with and without skin diseases and acute or chronic itch. *Results:* In 252 students, itch did not occur during the last month (35 with skin disease). Of the students who reported itch, 442 had acute itch (139 with skin disease), 100 had chronic itch (66 with skin disease). We found a significant relationship between stress and itch intensity in students who had no skin disease and acute itch (r=0.196; p=0.002) as well as in students who had no skin disease, but reported chronic itch (r=0.367; p=0.033). The correlation between stress and itch intensity in students who have been diagnosed with a skin disease and had chronic itch was not significant (r=0.166; p=0.186). Also, the relationship in students with a clinical diagnosis of a skin disease and acute itch was not significant (r=0.053; p=0.57). *Discussion:* This study investigated the relationship between stress and itch in German students, differentiating between students with and without skin diseases and with acute or chronic itch. Interestingly, we only found significant relationships between stress and itch intensity in students without a skin disease, no matter if they had chronic or acute itch. The finding that stress and itch intensity were not related in students with a skin disease could partly be explained by the fact that we did not distinguish between itch related and non-itch related skin diseases.

PP36

SUMATRIPTAN, THE ANTI-MIGRANOUS DRUG, SUPPRESSES SEROTONIN-INDUCED ITCH: THE POSSIBLE INVOLVEMENT OF OPIOIDERGIC SYSTEM

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Introduction: Serotonin (5-hydroxytryptamine or 5-HT) is a neurotransmitter in itch. In Addition, impaired serotonin signaling is linked to variety of itch conditions. Intradermal injection of 5-HT induces scratching behavior in mice through stimulation of 5-HT receptors. Previous studies have demonstrated that activation of 5-HT1B/1D receptors inhibits neurotransmission. Therefore, we investigated if sumatriptan, a selective 5-HT1B/1D receptors agonist, has inhibitory effects on serotonin-induced itch in mice. *Materials and Methods:* Serotonin was injected intradermally into the rostral back of mice, and itch was assessed by quantification of hind paw scratching bouts towards the injection site. Then, the effect of sumatriptan, GR-127935, a selective 5-HT1B/1D receptors antagonist, and opioid receptor antagonists on 5-HT-induced itch was assessed. *Results:* Intradermal and intraperitoneal administration of sumatriptan significantly reduces 5-HT-induced scratching behavior in mice. While intradermal injection of GR-127935 reverses the anti-pruritic effects of sumatriptan. In addition, our findings show that intradermal and intraperitoneal naltrexone (NTX), a non-specific opioid receptor antagonist, and methylnaltrexone (MNTX), a peripherally acting opioid receptor antagonist, significantly decrease the 5-HT-induced scratching behavior. Additionally, combined treatment with sub-effective doses of sumatriptan and an opioid receptor antagonist, naltrexone, decreases 5-HT-evoked scratching activity. *Conclusion:* Sumatriptan inhibits 5-HT-induced itch by activating the peripheral 5-HT1B/1D receptors. Moreover, peripheral opioid receptors have role in serotonin-induced itch, and anti-pruritic effects of sumatriptan seem to involve the peripheral opioid system. Thus, 5-HT1B/1D receptors agonists may be useful to treat a variety of pathologic itch conditions with impaired serotonergic system.

PP37

DEFINING A RESPONDER ON THE PEAK PRURITUS NUMERICAL RATING SCALE (NRS) IN PATIENTS WITH MODERATE-TO-SEVERE ATOPIC DERMATITIS: DETAILED ANALYSIS FROM RANDOMIZED TRIALS OF DUPILUMAB

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Rationale: To empirically derive estimates of responder definitions for the Peak Pruritus Numerical Rating Scale (NRS) in moderate-to-severe atopic dermatitis (AD), and to apply these to determine benefit of dupilumab on itch. *Methods:* Responder definition estimates were computed using anchor- and distribution-based methods from a phase 2b randomized study of dupilumab (NCT01859988). The anchor-based analysis used the following anchors at Week (W) 16: 1-point improvement on the Pruritus Categorical Scale (PCS); patients achieving 50%−74%, 75%−89%, 90%−100% improvement in Eczema Area and Severity Index (EASI) (EASI 50−74, EASI 75−89, EASI 90−100, respectively); patients achieving an Investigator's Global Assessment (IGA) score of ≤1 (IGA 0/1), or an IGA improvement of ≥2 points. For the distribution-based method, one half-SD of the mean Peak Pruritus NRS score at baseline was used. Post-hoc cumulative distribution functions (CDFs) of Peak Pruritus NRS at W2 and W16 were plotted for patients with moderate-to-severe AD receiving dupilumab 300 mg every week (qw) (n=462) or every other week (q2w) (n=457), or placebo (n=460) using data from two phase 3 randomized, double-blind, placebo-controlled trials of dupilumab (SOLO 1: NCT02277743; SOLO 2: NCT02277769). *Results:* The responder definition estimate based on the patient-reported PCS was 2.6; estimates based on clinician-reported anchors (EASI and IGA) ranged from 2.2 to 4.2, with the highest estimates derived from the most stringent clinical criteria (EASI 90–100 and IGA 0/1). The one-half SD estimate was much lower at 0.76. In SOLO 1, the CDF plots showed clear separation between the two dupilumab groups and the placebo group across the full range of observed response thresholds (W2: −4 to 0; W16: −8 (dupilumab q2w)/ −7 (dupilumab qw) to 0). In SOLO 2, a similar separation was

observed (W2: −5 to 0; W16: −7 to 0). Across both phase 3 trials, more dupilumab- vs placebo-treated patients were classified as responders at W2 and W16 using thresholds derived from the phase 2b study. Treatment groups had similar rates of treatment-emergent adverse events (TEAEs) (SOLO 1: 65%–73%; SOLO 2: 65%–72%). Commonly-occurring TEAEs were AD exacerbations and injection-site reactions. *Conclusions:* Peak Pruritus NRS response can be defined as a reduction of ≥3–4 points. The CDFs demonstrate that dupilumab had a clinically meaningful impact on itch in moderate-to-severe AD patients.

PP38
SIGNIFICANCE OF IL-31 EXPRESSION IN SKIN AND IN SERUM IN PATOMECHANISM OF PRURITUS IN CTCLS

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Primary cutaneous T-cell lymphoma (CTCL) is a chronic disease accompanied by persistent pruritus which responds poorly to antihistamines and therefore significantly reduces quality of life. Diagnosing especially early stage of mycosis fungoides (MF) is difficult as it resemble inflammatory dermatoses such as atopic dermatitis or eczema. Not only the pathogenesis of the disease but also the pathomechanism of pruritus in CTCL in not fully understood. Due to unclear and conflicting reports about role of IL-31 in pathogenesis of pruritus accompanying CTCL, we ought to develop the subject of IL-31 in CTCL. We conducted research over study group of 51 patients with MF and 40 healthy volunteers. Majority of CTCLs were diagnosed at the time of collecting skin biopsies and blood specimens. Expression of IL-31 was evaluated in formalin-fixed paraffin-embedded biopsy specimens from CTCL patients and healthy individuals by means of immunohistochemical staining. Serum IL-31 levels in CTCL patients were determined by the enzyme-linked immunosorbent assay methodology. The IL-31 serum and skin level was significantly higher in CTCL patients than in control group. We found lack of significant difference in IL-31 serum and skin level between pruritic and non-pruritic MF patients and no correlation between IL-31 serum , skin level and pruritus severity. Due to our conflicting results that are not in line with current state of knowledge about role of IL-31 in pruritus in CTCL, we decided to repeat the research. Four years after garnering samples and data we were able to verify diagnoses once more and conduct research over a solid group of CTCL patients. We investigated the correlation between the IL-31 skin levels, IL-31 serum levels, pruritus and stage of the disease.

PP39
SUMATRIPTAN ATTENUATES CQ-INDUCED SCRATCHING THROUGH NO-PATHWAY

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Introduction: Chloroquine (CQ) induces histamine-independent itch in human and mice. We recently reported the role of intradermal nitric oxide (NO)/ cyclic guanosine monophosphate (cGMP) pathway in CQ-evoked scratching behavior in mice. Chloroquine stimulates neuronal nitric oxide synthase (nNOS) activity to over-producing NO in the skin. Sumatriptan, the 5-hydroxytryptamine 1b/1d receptors (5-HTR1b/1d) agonist, is used to treat migraine and cluster headaches. According to previous studies, sumatriptan inhibits NOS activity and inhibits neurotransmission. Thus, we investigated the effect of sumatriptan on CQ-induced scratching behavior. *Materials and Methods:* The rostral back model of itch was used. Chloroquine was injected intradermally into the nape of the neck and scratching behavior was evaluated by measuring the number of bouts in 30 minutes. Then, the effect of local and systemic administration of sumatriptan on scratching behavior was assessed. Finally, sub-effective doses of sumatriptan and a non-selective NO synthase inhibitor, L-N-nitro arginine methyl ester (L-NAME), was administered before intradermal CQ. *Results:* Intraperitoneal and intradermal administration of sumatriptan attenuates CQ-induced itch which reversed by intradermal GR-127935, the selective 5-HTR1b, and 5-HTR1d antagonist. Co-administration of sub-effective doses of sumatriptan and L-NAME significantly decreased the scratching behavior. *Conclusion:* Sumatriptan suppresses CQ-induced itch by activating 5-HT1b/1d receptors. This effect probably mediates through NO pathway.

PP40
REDUCTION OF PRURITUS IN ONCOLOGICAL PATIENTS RECEIVING EGFRI THERAPY

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EGFR inhibitors are targeted agents used for treatment of malignancies characterised by overexpression of EGF receptor. e.g. colorectal, pancreatic and breast cancer, non-small cell lung cancer or head and neck cancer. Due to the impact on differentiation and growth of epithelial cells, EGFR inhibitors induce a number of side effects, including pruritus. While treating with EGFRI, pruritus usually occurs during the first three months of therapy in approximately half of the patients. Itching is most likely associated with the EGFRI drugs due to their influence on substance P activation, which is one of the major neuromediators of pruritus. Itching may accompany xerosis, a side effect which often occurs during the treatment. It is likely to be located in areas affected with papulopustular rash - the most common side effect of EGFRI treatment. Pruritus is unlikely to require EGFRI dose alteration or a drug change. Nevertheless, it significantly decreases QoL of the patients. As a result, it is vital to reduce itching using topical and systemic treatment and to instruct patients on the proper skin care. Basic management is focused on decreasing the pruritus by regaining the proper structure of the epidermal barrier. Cosmetics rich in greasing and moisturizing components, as well as emollients, should be used. Delivering physiological lipid mixtures, substances with occlusive properties and humectants would diminish transepidermal water loss. Cosmetics which dehydrate and irritate the skin, such as retinoids, alkaline soaps or alcohol containing mixtures, should be excluded. Moreover, patients are expected to avoid overexposure to the UV, synthetic clothing and perfumes. Depending on the severity of pruritus, different recommendations for reducing itching of various etiologies exist. Topical steroids or 1–3% menthol are commonly used, yet first of all, topically applied drugs aimed at reducing the coexisting papulopustular rash should be selected. Antihistamines and lidocaine applied topically are probably not efficient enough, thus they are not recommended. Systemic treatment includes non-sedating second-generation antihistamines. Research is being conducted on efficiency of antiepileptic agents in providing pruritic relief.

PP41

LYSOPHOSPHATIDIC ACID INDUCES ITCH AND PAIN IN HUMANS DEPENDING ON THE MODE OF APPLICATION

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Introduction: Hepatobiliary disorders involving cholestasis are frequently accompanied by pruritus. Lysophosphatidic acid (LPA) has recently been identified as potential mediator of this agonizing symptom. Serum levels of the LPA forming enzyme ATX correlated with itch intensity in pruritic patients and intradermal injection of LPA induced scratching behaviour in mice. This study aimed to further investigate the involvement of LPA and bile salts in itch signalling using psychophysics and microneurography. *Methods:* Psychophysical testing and microneurography were performed on 32 healthy volunteers and 22 cholestatic patients with primary biliary cholangitis and primary sclerosing cholangitis. LPA and the bile salts, taurocholate (TC) and taurolithocholate (TLC), were applied intradermally via heat-inactivated cowhage spicules or intradermal injections. Histamine, capsaicin and the vehicle SIF served as control applications. The flare reaction was determined by laser Doppler imaging. Sensitization and desensitization of nerve endings by LPA were tested using thermal, mechanical and electrical stimuli. Electrophysiological recordings of single primary C-fibres were performed in healthy human subjects at the peroneal nerve. *Results:* In psychophysics, focal application of LPA caused itch (mean±SEM; 1.4±0.4 vs. 0.3±0.2; $p<0.001$), whereas the injection of LPA induced dose-dependent pain and heat hyperalgesia. Neither the TRPV1 inhibitor BCTC nor the TRPA1 blocker A967079 reduced LPA-mediated symptoms. In some patients with PBC and PSC, LPA injection caused itching instead of pain. LPA induced a sensitization to heat, while responses to cold, mechanical and electrical stimuli remained unchanged. In contrast, neither TC nor TLC induced any substantial sensation in healthy volunteers and cholestatic patients. In microneurography, human nociceptors, mechano-sensitive (CM, n=22 of 34) and mechano-insensitive (CMi, n=9 of 11), were both activated by LPA injection. While CM were excited rather weakly, medium or strong responses to the injection could be observed in few fibres, mainly histamine-responsive CMi. *Conclusion:* LPA activated human nociceptors and produced itch and pain in humans depending on the mode of application. Presumably the focal activation of nociceptors according to the spatial contrast theory accounts for the itch sensation. A small subgroup of nociceptors, i.e. histamine-responsive CMi, could be further involved in LPA mediated perceptions.

PP42

ANGIOLYMPHOID HYPERPLASIA WITH EOSINOPHILIA – A CASE OF PERSISTENT PRURITUS OF THE SCALP

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Background: Angiolymphoid hyperplasia with eosinophilia (ALHE) is an uncommon benign vascular and inflammatory disorder that typically occurs in young adults. ALHE usually presents as a group of several red-brown or violaceous papules or small nodules localized on the head or neck, and the ears area. A probably role in the pathogenesis of the disease is a mechanical injury. *Objective:* We report a rare case of ALHE in a 38-year-old female with several nodules involving the occipital and parietal area with accompanying persistent pruritus. *Case report:* The first violaceus nodules in the occipital area appeared in 2011 and they spontaneously resolved after a few months. Since 2014, progressively increasing nodular lesions with a maximum diameter of 1 cm in the occipital and parietal region with concomitant persistent pruritus not responding to topical steroids and cryotherapy. *Results:* In the physical examination a number of nodular lesions were found in the scalp, strongly bleeding after mechanical irritation. The trichoscopy showed nodules with a normal hair-shafts and cloud-vessels on a homogenous pink background. Histopathological examination revealed clusters of proliferating capillaries and cellular infiltrate, localized around the blood vessels, composed mainly of lymphocytes and large number of eosinophils. Triamcinolone injections of 10 mg/ml were used for the treatment. A significant reduction of the pruritus was achieved, which stopped appearance of new skin lesions and partial resolve of the previous ones. *Conclusion:* ALHE is considered an atypical vascular tumor but numerous factors suggest that it is an unusual reactive process. In our case, the disease was most likely stimulated by persistent itch. Reduction of the pruritus stopped the progression of the disease.

PP43

THE PROBLEM OF THE ITCH IN SURGICAL ONCOLOGY - DO WE KNOW EVERYTHING ABOUT THE PREVENTION, DIAGNOSIS AND TREATMENT?

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Introduction: The surgical oncology is stiill developing. In recent years a significant number of new and innovative treatment alike diagnostic options has been introduced into the clinic. Beside the still obtained better prognostic and general overcome results there is stiil a big need to create in this specific medical speciality a new types and forms of suportive care and treatment options. To the one of such problematic fields in current surgcal oncology becomes the still not fully resolved problem of the Itch in oncologic patients. *Aim:* The aim of this study was to anylze the general incidence of itch in surgical oncology patients alike possible diagnostic and therapeutic options developed globaly to resolve this problem.Additionaly we have assed the possible future development ways and new creating ideas which could be important in nexy years. *Material and Methods:* In this study we have performed an comperhesive review analyzis of scientific papers, recomendations and gudelines reffering to the problem of the itch in surgical oncology. In this study we have collect also the clinical data from the reference center for surgical oncology of patients in which the problem of the itch has been diagnosed. Our material concerned the time period of 2002 and 2017. During our analyzis we have also searched the informations about possible development in this problematic field. *Results:* In this study we have presented the most common types of cases in which itch has been reported and which should be imortant in futher dermatological deliberations in the field of surgical oncology. The most common and detailed materials has been found using the open scientific data bases. *Conclusion:* The problem of the itch in surgical oncology patients is still important and not fully resolved. More specific scientific analyzis and targeted programs should be performed in the future.

PP44

WHAT ARE PRURITOGENS OF CHRONIC KIDNEY DISEASE ASSOCIATED PRURITUS

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In peripheral mechanism of pathophysiology of chronic kidney disease (CKD) associated pruritus (CKD-aP), the pruritogens, the modulators and the receptors of CKD-aP are important. To date, many pruritogens originated keratinocyte, macrophage/monocyte, mast cell, lymphocyte and so forth in the skin of patients with many skin diseases (e.g., atopic dermatitis) have been discovered. This study was undertaken to analyze the expressions of pruritogens in the skin of CKD patients with and without CKD-aP. The study included 16 subjects on CKD stage 5 (10 with CKD-aP and 6 without pruritus) from 2004 to 2006, 23 subjects (13 with CKD-aP and 10 without pruritus) from 2007 to 2009, 29 subjects (14 with CKD-aP and 15 without pruritus) from 2010 to 2012 and 20 subjects (10 with CKD-aP and 10 without pruritus) from 2013 to 2016. The degree of pruritus was scored with Shiratori's classification of itch in japan. Skin samples were obtained at the forearm or elbow during formation of the arteriovenous fistula surgeons. The expression of pruritogen in the skin was studied with immunohistochemistry. The expressions of acethylcholine (Ach), nerve growth factor (NGF), histamine, interleukin 6 (IL-6), β-endorphin, adenosine triphosphate (ATP), substance P, vasoactive intestinal peptide (VIP), leukotriene B4 (LTB4) and calpain in the skin were studied as pruritogens. The expressions of Ach, NGF, β-endorphin, IL-6 and calpain were positively stained in the skin of CKD patients with and without CKD-aP. But, there was no difference in the intensity of expressions of Ach, NGF, β-endolphin, IL-6 and calpain between studied groups. This study indicates that the unique pruritogens of CKD-aP may not exist and that the receptors are more important than pruritogen in peripheral mechanism of pathophysiology of CKD-aP.

PP45

THE FATAL COURSE OF CHRONIC ITCH (CI): GENERALIZED CI AS A FIRST SIGN OF MALIGNANCY RESEMBLING PARANEOPLASTIC SENSOMOTORIC NEUROPATHY

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Malignancies can be accompanied by paraneoplastic syndromes or symptoms. They can be caused by an indirect effect of malignancy and may be the first sign of an underlying malignancy. "Paraneoplastic itch" is used to describe itch in patients with haematological and/or solid tumour malignancies. Paraneoplastic neurological syndromes (PNS), defined as a group of rare neurological disorders, may occur. We present a 68-year-old male who developed chronic itch (CI) on normal looking skin (head, arms, shoulder, thighs) in December 2015. CI was of burning, stinging and sharp character and was suspected as possible neuropathic itch. The patient's history revealed a good response of CI to a course of systemic corticosteroids applied once. He was advised to get a full body check-up (Internal Medicine, Neurology) which he was reluctant to do. Four months later he had lost 10 kg of weight and developed nausea, vomiting and neurological symptoms. Electroneurography revealed a severe sensomotoric polyneuropathy. To detect a potential underlying malignancy, imaging examinations (e.g. chest X-ray, ultrasound of the abdomen, pelvis CT scan) and lumbar puncture were performed. While imaging showed no evidence of a tumour, lumbar puncture revealed the presence of Anti-Hu antibodies, the most frequently identified paraneoplastic antibodies. Therefore, a close follow-up scheme was set up to detect the underlying malignancy. In November 2016, mediastinal lymph node biopsy proved lymph node metastasis by a large cell neuroendocrine carcinoma (LCNEC) which is a rare subgroup of high grade neuroendocrine tumors, typically of pulmonary origin. The diagnosis requires the presence of a neuroendocrine pattern and a positive staining with neuroendocrine markers (chromogranin A, synaptophysin, CD 56) in immunohistochemistry which was demonstrated in our case. However, the primary carcinoma location was never detected in our patient. In spite of chemotherapy, the patient died in April 2017. It is most likely that CI was the first paraneoplastic symptom, triggered by the neuroendocrine tumour. The most probable cause of paraneoplastic symptoms is an indirect effect through various mediators including immune and humoral mechanisms. A falsely initiated immune reaction could also explain the good response of CI to a therapy with systemic steroids. It should be remembered that CI without concomitant skin changes followed by neurological symptoms can be caused by a yet undiagnosed malignancy.

PP46

FUNCTIONAL CHANGES IN THE CEREBRAL NETWORKS FOR ITCH AND BURNING PAIN

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From many functional imaging studies a general notion evolved that the processing of painful or itchy input is based on activity changes in cerebral networks. In this study we focused on the modulation of those networks using functional imaging in combination with functional connectivity (FC) analyses. According to our hypothesis the behavior of the resting state network is changed during itch and pain. For pain the skin of the right forearm of 18 healthy subjects was pretreated by topical application of capsaicin (0.05% for 30 minutes). This lead to heat pain by temperatures of less than 50°C due to thermal hyperalgesia. The stimulation temperature was 1°C above the individual pain threshold. Itch was induced by iontophoresis of histamine into the skin of the volar forearm. In two fMRI sessions itch and pain were assessed using a connectivity fMRI-design with EPI sequences. The first run was free from stimulation to detect the default mode network. During the second fMRI sequence itch or pain stimuli were applied, respectively. The 2nd session was not earlier than 2 weeks later. Individual mean MRI (BOLD) time courses were extracted from the seed regions left posterior insula for exploring an "input" network and the PAG for exploring the "output" network. Pearson's correlation coefficients were calculated between the seed regions and other regions in a whole brain study. In a 2nd level analysis contrasts were calculated between resting state and itch or pain conditions. Under itch the FC with the posterior insular cortex predominantly increased to frontal areas (BA8, BA9, BA45). In BA8 and BA45 the changes were also correlated with the individual ratings of itch. The FC with the PAG increased within pACC, subgenual parts of the ACC, and the left amygdala, while the connectivity decreased to the caudate body and the frontal lobe (BA 6). Under pain the FC of the posterior insula increased with many brain regions but decreased with the PAG, indicating a negative feedback between endogenous pain inhibition and cortical pain input. Enhanced FC was found of the PAG with medial frontal regions (BA 10), posterior parts of the anterior cingular cortex (pACC) and the left amygdala while the coupling decreased to the

thalamus and S2 (BA 40). Besides the interesting result indicating a negative feedback between pain input (but not itch input) and output of the pain control system, our results indicate that cerebral networks processing pain and itch are not identical.

PP47
INVOLVEMENT OF SPINAL MICROGLIA IN THE PATHOGENESIS OF IMIQUIMOD-INDUCED PSORIASIS-LIKE DERMATITIS MODEL MICE

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Intractable itch is a symptom of psoriasis that impairs patients' quality of life, for which existing treatment is largely ineffective. Recent studies have revealed the involvement of spinal glial cells, such as microglia and astrocytes, in the sensitization and enhancement of itch in atopic dermatitis-like model mice. However, the roles of spinal glial cells in psoriatic itch remain unclear. Therefore, this study was performed to investigate the roles of spinal microglia and astrocytes in the pathological process of psoriatic itch using an imiquimod (IMQ)-induced psoriasis-like dermatitis model mouse (IMQ-treated mice). C57BL/6J mice received daily topical application of IMQ to their rostral back skin for five days. They exhibited worsening scores of dermatitis and increased scratching behavior and transdermal water loss (TEWL) in a time-dependent manner, with these values reaching a peak at day 4 or day 5. Our immunohistochemical analyses showed morphological changes of spinal microglia in the IMQ-treated mice compared with that in control mice. Hypertrophied microglia were transiently increased from day 2 to day 3. These findings suggest that spinal microglia are associated with the pathological process of psoriasis.

PP48
ANTIPRURITIC EFFECT OF THERMAL GRILL ILLUSION ON HISTAMINE-EVOKED ITCH IN HUMANS

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Itch is an unpleasant sensation that causes a desire to scratch. An effective and safe treatment for itch is still lacking. It is known that counter-stimuli including noxious thermal stimuli can inhibit itch. Recently, central neuronal processing underlying this inhibition has been elucidated. Noxious thermal stimuli, however, can lead to skin damage and therefore would not be suitable at clinic. Therefore, it would be optimal to use counter stimuli within non-noxious thermal range. This can be achieved by using thermal grill illusion (TGI). Hence, the aim of this pilot study was to investigate the effect of mixed temperatures (not noxious thermal stimuli of 18°C and 41°C) produced by a custom-made thermal grill on histamine-evoked itch in healthy volunteers. The effect of cold application alone (18°C) on itch intensity was also investigated. Histamine dihydrochloride (1.0%, Allergopharma, Reinbek, Germany) was applied in 8 healthy subjects (age 24±0.38 years) with a standard skin prick lancet on the volar forearm. Itch intensity was recorded over time for up to 15 minutes on a visual analogue scale (VAS 0–10, 0 no itch, 10 worst itch imaginable). TGI significantly reduced the itch intensity ($p<0.05$), while innocuous cold application alone did not show any significant effect ($p>0.05$). This is the first report presenting the itch-relieving effect of thermal grill on histamine-evoked itch model in humans. It is therefore proposed that thermal grill would be beneficial in itch relief at clinic. Further studies are planned in our group to test this hypothesis with application of a newly developed mobile thermal grill device.

PP49
SECONDARY GENERALIZED BRACHIORADIAL PRURITUS SUCCESSFULLY TREATED WITH GABAPENTIN

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Brachioradial pruritus (BRP) is a rare type of chronic pruritus that is usually localized at the dorsolateral part of the arms. We report on 79-year-old man who suffered from severe pruritus located on the dorsolateral sides of both arms occurring after an apoplectic stroke. After some years of different topical treatments, systemic corticosteroids and antihistamines without success, pruritus became even worse and generalized to the whole body. No underlying disease for the generalization could be found. Quality of life was reduced and sleeping was disturbed; NRS was 8-10. Intraepidermal nerve fiber density of the lower leg was significantly reduced. Therefore we started a systemic treatment with gabapentin which could be slowly increased up to 1200 mg/d. This therapy was well tolerated and the NRS reduced to 3. This case report shows for the first time that an apoplectic stroke can trigger brachioradial pruritus which subsequently generalized. The neuropathic nature of the pruritus was demonstrated via intraepidermal nerve fiber density. Gabapentin was an effective and well tolerated therapy in the patient. It could be speculated that an earlier systemic therapy with gabapentin could probably have prevented the secondary generalization of the pruritus.

PP50
MORPHOLOGICAL AND MOLECULAR EVOLUTIONAL ANALYSES OF ITCH FOCUSED ON THE GASTRIN-RELEASING PEPTIDE SYSTEM IN MAMMALS

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Gastrin-releasing peptide (GRP) is a 29-amino acid peptide in rodents and 27 residues in primates. We focused on GRP as an itch neuronal marker in the somatosensory system. We found that GRP was expressed in the small-sized primary afferents and projected to the caudal part of the spinal trigeminal nucleus and all level of the spinal dorsal horn in rats. These findings suggested that GRP is an important neuropeptide for itch transmission not only in the spinal somatosensory system but also in the trigeminal somatosensory system. GRP receptor mRNA and protein were expressed in the regions where GRP immunoreactive fibers appeared to terminate in rats. Immunoelectron microscopy showed that GRP-positive terminals contain many clear round vesicles and dense-cored vesicles. Furthermore, we used 3-dimentional scanning electron microscopy (3-D SEM) combined with immunohistochemistry to analyze the 3-D ultrastructure of the itch-mediating synaptic formation in the spinal dorsal horn. The 3-D SEM analysis revealed that GRP terminals connected with many postsynaptic components than we expected. These results suggest that neural networks

controlling the itch transmission are extraordinary complex in the spinal cord. Next, we had the question of how organism acquires the itch sensation during evolution and why we possess an unpleasant itch sensation. To address these questions, we utilized the phylogenetic and comparative analyses using Asian house musk shrews, mice, rats and macaque monkeys. We found that the deduced amino acid sequence of GRP-10 which is a possible C-terminal-fragment of mature GRP had highly been conserved among mammals. Immunohistochemical analysis showed that the expression and distribution of GRP were consistent across mammals such as primitive eutherians, rodents, and primates. These results suggest that this system may be a conserved property for itch-mediating function in mammals.

PP51
BRACHIORADIAL PRURITUS IN A YOUNG CAUCASIAN WOMAN AS A SYMPTOM OF CERVICAL RADICULOPATHY

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Brachioradial pruritus is a rare pruritic condition, described for the first time by Waisman in 1968. Up to date the etiology of this disease remains unclear, however, this type of pruritus is frequently classified as neurologic itch. We report a 29-year-old Caucasian woman suffering from pruritus of the upper arms affecting the skin overlying the proximal head of the brachioradialis muscles. First symptoms of the disease appeared 10 years before admission to the hospital. Patient reported presence of severe itch with periodically visible pruritic papules on the upper arms. Clinically, all skin lesions were assessed as secondary to scratching. According to patient history, pruritus exacerbations were connected with sun exposure. Although the patient was a young woman, she also complained about severe pain of cervical spine. Magnetic resonance of cervical spine revealed a pressure on a dural sac at then level if C6/C7. In addition, herniated discs at C3/C4 and C5/C6 level were described. Patient started pregabalin treatment with significant improvement of the symptoms within several weeks. Our case presentation further supports the idea that brachioradial pruritus is an example of neuropathic itch related to the damage of nervous system at the level of cervical spine.

PP52
A MULTINATIONAL CROSS-SECTIONAL STUDY ON THE PREVALENCE AND CLINICAL PRESENTATION OF PRURITUS IN CUTANEOUS LUPUS ERYTHEMATOSUS: AN OVERVIEW

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Pruritus is an important symptom frequently accompanying various inflammatory skin conditions. Some recent data have indicated, that it may also be associated with autoimmune connective tissue diseases, including systemic sclerosis, dermatomyositis and cutaneous lupus erythematosus (CLE), however, studies on the true prevalence and clinical characteristics of pruritus in CLE are very limited. For that reason we have organized a multinational, prospective, cross-sectional study in order to precisely assess the prevalence, intensity, and clinical characteristics of pruritus in adult patients suffering from various subtypes of CLE. We have selected centers from various continents with special interest in CLE diagnostics and treatment to cover possible differences between races and climate including Europe (6 centers), North America (1 center) and Asia (5 centers). As the first step of the study we have developed a questionnaire assessing various aspects of pruritus as well as including sociodemographic data, data on the subtypes of CLE and severity of cutaneous (with CLE Area and Severity Index) as well as systemic symptoms (SELENA-SLEDAI). The subjects' well-being and health-related quality of life was determined using Dermatology Quality of Life Index (DLQI) and EuroQol Five Dimensions Questionnaire (EQ-5D). The preliminary questionnaire was sent to participating centers for comments. After including all comments we have prepared a final version of the questionnaire which was approved by Local Ethic Committee. Subsequently, it was sent to all participating centers along with an electronic database file to facilitate the data caption. Preliminary data from the study will be presented during the congress.

PP53
PILOT STUDY OF VENOUS ULCER ITCH: ANALYSIS OF WOUND FLUID AND SERUM

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Purpose/Hypothesis: We aimed to use metabolomics for biochemical profiling of wound fluid and serum from persons with venous ulcers that itched compared to those that did not. We hypothesized that using metabolomics we would identify significant differences in the metabolome of biomatrices, increasing our overall understanding of the biochemistry of wound related itch, while uncovering potential biomarkers for those at greatest risk of developing itch. *Background:* Venous ulcer itch is a recognized clinical problem which has been inadequately characterized and which can result in great distress for persons with chronic venous ulcers. The pathophysiology and etiology of wound-related itch have not been determined. *Methods:* Specimens of wound fluid and serum were obtained from 21 patients with venous ulcers (14 male, 16 white, age range 47–85 years). The sample was divided between case (itch, n=10) and controls (no itch, n=11) based on self-report. Wound assessments and patient interviews were conducted for comparison of wound characteristics between persons with and without wound-related itch. Metabolomic analysis of serum was conducted using targeted mass spectrometry coupled with liquid chromatography (LC-MS/MS; Biocrates p180) and proton nuclear magnetic resonance spectroscopy (1H NMR). Wound fluid was analyzed using LC-MS/MS (Biocrates p180). *Results:* Intensity of wound-related itch episodes ranged from 2 to 10 (mean=8). Selected compounds converged to form predictive models of itch for wound fluid (p<0.3) and serum (p<0.2). Logistic regression for wound fluid produced a predictive algorithm with AUC = 0.919,

using concentrations of citrulline, threonine, serine and asparagine. Pathways significantly perturbed in wound fluid include methane, cyanoamino acid, and sulfur metabolism. ROC analysis was used to produce a model for serum using betaine and PC ae C424, with a predictive accuracy of 82.6%. Pathways significantly perturbed in serum include glycolysis/gluconeogenesis, nitrogen metabolism, and tyrosine metabolism. *Conclusion:* This study demonstrates the potential of using metabolomics for identification of those at risk of developing venous ulcer itch while increasing our understanding of the pathophysiology of wound related itch. A more comprehensive understanding of how and why some patients develop itch will allow us to develop therapeutic agents for strategic intervention.

PP54

THE BIBLIOMETRICS OF ITCH: 2017 UPDATE

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In 1834, only 1 article about itch/pruritus was published (Lancet, 1834, 23, 59–62); this number has increased substantially to a high of 198 articles in 2015. Pruritus continues to be used more frequently than itch in article titles. The common misspelling - pruritis – still manages to evade correction from time to time. During 2015–2016, Acta Dermato-Venereologica again published the largest number of itch articles, followed by Current Problems in Dermatology, Handbook of Experimental Pharmacology and Scientific Reports. Schmelz and colleagues' 1997 paper was the most cited itch article during 2015–2016 (J Neurosci, 1997, 17, 8003–8008), whereas Foster and colleagues published the most cited itch article of papers published in 2015–2016 (Neuron, 2015, 85, 1289–1304). During 2015–2016, itch papers appeared twice in Nature Communications, twice in Nature Medicine, 8 times in Pain, twice in PNAS, once in Science, and not at all in Lancet, Nature or NEJM, for a total of 15 total published in key journals, as compared to 10 papers during 2011–2012. Yosipovitch, with 2,201 total citations, is the most cited author of itch articles overall, followed by Schmelz and Kuraishi. Yosipovitch is the author with the highest h-index, which measures an author's cumulative impact.

PP55

TREATMENT OF SEVERE ATOPIC DERMATITIS WITH OMALIZUMAB: EXPERIENCE OF A PORTUGUESE IMMUNOALLERGOLOGY DEPARTMENT

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Introduction: Controlling severe eczema is not always possible despite the optimization of therapy. Omalizumab is associated with improvement in cutaneous symptoms and quality of life (QoL) in patients (pts) with atopic dermatitis (AD). This study aims to evaluate the efficacy and QoL of pts under omalizumab. *Methods:* Pts with severe AD refractory to the recommended therapy, were evaluated for treatment with omalizumab. The clinical response was assessed by the therapy used and by the questionnaires: SCORAD (Scoring Atopic Dermatitis) and DLQI (Quality of Life-Dermatology Index). Data from SCORAD and DLQI at 12 months (T12) were compared with the initial treatment phase (T0). Data were analyzed using SPSS, version 17®, p-value <0.05. *Results:* 24 atopic patients (14 men) with severe AD, mean age 31 years. Total IgE 8835 (2296–21691) KU/l. All patients were given montelukast 10 mg/day, topical and oral corticosteroids, topical calcineurin inhibitors and anti-H1 antihistamines. 7 patients sensitized to Dermatophagoid mites underwent Immunotherapy (IT) for 16 (6–36) months prior to treatment without clinical improvement. 12 patients receiving cyclosporine, 2 patients with azathioprine, and 1 with Ig G unresponsive. Omalizumab was administered sc, 300–600 mg every 2 weeks in an average of 16 (12–73) months. From the comparison between T0 and T12 it was found that the medication was reduced in dose and in the number of drugs, systemic corticosteroid therapy was suspended without clinical re-referral and the mean SCORAD increased from 65.5 (T0) to 28.5 (T12). 15 of 24 patients had a complete improvement (65.2%) and 6 (26.1%) patients had a partial response, although the mean treatment time from initiation of treatment to initial improvement was variable. 1 patient (4.3%) did not improve. There were no systemic adverse reactions and 1 patient had exuberant local reaction Analysis of the DLQI score showed that cutaneous pathology. has a moderate-severe QoL effect in 12 out of 24 pts, ie in 50% of pts. In T12 the AQLQ showed that AD had a moderate effect on patients' QoL (mean score of 6.6) compared to T0 (mean score of 21), which had an extremely severe impact on QoL. QoL did not show a significant correlation with duration of Omalizumab, p=0.04. *Conclusion:* Omalizumab was effective in the treatment of AD and appears to be a safe alternative when patients with severe AD are refractory to other therapies. The treatment demonstrated an improvement in QoL in patients' perception.

PP56

CHRONIC PRURIGO MASKS THE FINDING OF A BULLOUS PEMPHIGOID

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Chronic prurigo (CPG) is a severe disease which might be triggered by a variety of diseases such as dermatological, but also systemic, neurological, psychiatric/psychsomatic, multifactorial disorders or unknown causes. All these diseases have in common to induce pruritus which results in scratching of the skin finally establishing a chronic itch-scratch-cycle leading to CPG. To illustrate this, we present a case of a 61-year-old female patient with CPG for more than 6 years. In addition to itch, she reported experiencing burning and painful sensations in the skin triggered by warmth. The CPG was initially localized at the left foot; however, a few months later, it became generalized to the remaining integument. Additionally, the patient reported a highly intense pruritus (10/10 on the visual analog scale). On inspection the whole integument displayed pruriginous nodules; other lesions such as blisters were not present. Concomitant diseases included stomach ulcers, chronic pancreatitis and spondylosis with chronic pain. A histological examination revealed alterations typically found in CPG. Direct immunofluorescence showed IgG and C3 deposits in the basal membrane, while the indirect immunofluorescence showed an IgG titer of 1:8,000, thus leading to the diagnosis of bullous pemphigoid. Previous therapy consisted of azathioprine 50 mg daily (this discontinued due to pancreatitis), minocycline 200 mg daily and doxycycline 200 mg daily. Under a cyclic therapy with intravenous methylprednisolone 500 mg for 3 days every four weeks and over 1.5 years and dapsone 100 mg daily the bullous pemphigoid was controlled and antibodies could no longer be detected. However, the CPG and the associated pruritus persisted. We initiated a therapy with cyclosporine and naloxone intravenous. Due to this, the pruritus intensity decreased from initial 10 to 1. This case report demonstrates that chronic prurigo is a disease which can be triggered by other pruritic diseases as in this case bullous pemphigoid. Once CPG is established, the therapy of the underlying etiology is not sufficient to cure CPG. This needs an own approach. However, our case also advocates thorough diagnostics of CPG patients in order to unmask potential associated diseases.

PP57

ITCH ASSOCIATED WITH HYPERPLASTIC PAPILLOMATOUS SKIN LESIONS COMPLICATED BY SQUAMOUS CELL CARCINOMA IN A PATIENT WITH NETHERTON SYNDROME

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Introduction: Netherton syndrome is a rare autosomal recessive disorder in the group of inherited ichthyoses. The case of the disease is serine protease inhibitor Kazal- type 5 (SPINK5) gene mutations which result in absence or, rarely, decreased expression of the encoded protein lymphoepithelial Kazal-type-related inhibitor (LEKTI) in the epidermis and stratified epithelia. Netherton syndrome is characterized by congenital ichthyosiform dermatitis, linearis circumflexa, atopic diathesis and trichorrhexis invaginata („bamboo hair"). Cases of patients with Netherton syndrome with associated hyperplastic papillomatous skin lesions or non-melanoma skin cancers were described in the literature. *Aim:* We present a patient with Netherton syndrome and hyperplastic papillomatous skin lesions associated with itch and complicated by squamous cell carcinoma. *Case report:* An 18-year-old patient with Netherton syndrome was referred to our hospital. Ichthyosiform erythroderma appeared immediately after birth and persisted throughout his life. At the age of 8, itching, hyperplastic papillomatous skin lesions occurred in the groin area and have been growing progressively. Nodular skin lesions on the scrotum developed at the age of 14 and wide excision was performed immediately. Histopathological examination of the surgical specimen revealed cytopathic effect related to Human Papillomavirus (HPV) infection and confirmed diagnosis of squamous cell carcinoma. During admission, the patient had scaling erythroderma involving the entire skin surface. Complete loss of scalp hair, eyebrows and eyelashes was observed. Hyperplastic papillomatous skin lesions were presented in the genitoanal area. The anogenital lesions were associated with itch (5 in VAS, 5 points in Itch questionnaire). Laboratory investigations revealed increased serum level of total IgE (732 IU/ml). Emollients were recommended to reduce itch. *Conclusion:* In patients with Netherton syndrome treatment strategies should include the control of itch.

PP58

PROPERTIES OF PRURITUS AND RELATED FACTORS AMONG ELDERLY RESIDENTS OF PANTI WERDHA, PUBLIC NURSING HOMES IN INDONESIA

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Background: Pruritus is a crucial problem in aging societies. In the bedridden and cognitively impaired elderly patients, it is difficult to assess cases of pruritus due to the lack of macroscopic abnormalities. The purposes of this study were to explore the skin properties related to pruritus and to identify the factors associated with them. *Methods:* This cross-sectional study was conducted in Panti Werdha, public nursing homes for elderly in Indonesia. Basic characteristics and itching data were obtained by interview, and skin properties including barrier function and inflammation were direct examination by skin blotting, skin microscopy, stratum corneum (SC) hydration, and skin pH. The pruritus-related skin properties and associated factors including basic characteristics and skincare behaviors were analyzed. *Results:* The average participant age was 74 years. Prevalence of itching on whole body was 69.1%, and 50.3% of those manifesting itching on the left forearm diagnosed pruritus. SC hydration, skin pH, albumin, nerve growth factor β (NGFβ), skin with hair, skin with scales, and skin with sweat gland were related with pruritus (p = 0.007, 0.012, <0.001, <0.001, 0.049, <0.001 and <0.001, respectively). SC hydration and skin pH were associated with clothing change frequency (β =0.135 and β=–0.137, p <0.05). Albumin was associated with age (β=–0.130, p = 0.044). NGFβ was associated with cumulative lifetime sun exposure at work (β=0.145, p=0.026) and bathing duration (β=–0.151, p=0.022). Skin microscopy; skin with hair was associated with age (AOR 0.5, 95% CI 0.3–0.9) and sex (AOR 1.8, 95% CI 1.0–3.2). Skin with scales was associated with bathing frequency (AOR 0.3, 95% CI 0.1–0.8). Skin with sweat gland was associated with bathing frequency (AOR 3.3, 95% CI 1.3–8.0). *Conclusion:* Albumin and NGFb in skin blotting were possible indicators of skin assessment method for pruritus.

PP59

EXPRESSION OF IL-31 IN URAEMIC PRURITUS

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Uraemic pruritus is a bothersome symptom in about 40% of patients undergoing dialysis therapy. Its etiopathogenesis remains not fully explained. In recent years attention has been paid to the role of interleukin 31 (IL-31) in the pathogenesis of chronic pruritus, especially in patients with atopic dermatitis. Preliminary studies suggest elevated serum IL-31 levels in patients suffering from uraemia. Therefore, this research project aims to determine the expression of IL-31 in the skin of patients with uraemic itch. The study was based on archived collection of biopsy material (21 skin biopsies from adult patients with pruritus and 20 biopsies of patients free from itching in chronic kidney disease). IL-31 expression was demonstrated by immunohistochemistry using commercially available IL-31 antibodies. There was no significant difference in overall IL-31 expression between patients with and without pruritus. However, significant difference (p=0.02) was noted in the distribution of IL-31 expression in both studied groups. IL-31 expression showed two patterns being expressed through the whole epidermis and mainly in the suprabasal layers of the epidermis. In patients with uraemic pruritus IL-31 expression was significantly more common (p=0.01) across the whole epidermis than limited to the suprabasal layers of the epidermis. No significant relationship between IL-31 expression and sex, age of patients and hemodialysis duration was found. A trend towards the relationship of IL-31 expression and severity of itch assessed according to visual analog scale (VAS) was noted (p=0.09). In conclusion it seems that IL-31 expression is more pronounced in patients with uraemic pruritus compared to those free from this symptom, but there is a need for further studies to clarify the exact role of IL-31 in uraemic pruritus.

PP60

DIFFERENTIATED RESISTANCE TRAINING AND EXERCISE TREATMENT FOR NEUROPATHIC ITCH - A PRELIMINARY STUDY

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Neuropathic itch means localized chronic itch (CI) with stinging, burning and sharp sensations usually affecting the corresponding dermatomes of the skin. Secondary generalization of CI has been described. A high correlation between changes seen on magnetic resonance tomography (MRT) such as nerve compression or da-

mage due to e.g. spinal pathology, degenerative changes and the symptoms of localized CI like brachioradial pruritus (BRP) was demonstrated. Exercising involving a non-pharmacologic active range of motion and strengthening of muscles as well as stretching muscles is a main strategy of treating neuropathic pain caused by e.g. herniated disc. Improvement of notalgia paresthetica (NP), another variant of neuropathic itch, by exercises was described in a case report. Potential explanations include changes of affected muscles by either shortening or lengthening of muscles being involved, reduction in the angle of affected nerves and reducing the pressure on nerves by extension of the spine. Effective therapies for neuropathic itch are limited and non-pharmacological treatments are lacking. Recently, strength training was introduced as a so-called differentiated resistance training and exercise treatment focusing on the spine. By combining new results of sports science with itch research, a preliminary study was started to investigate the effect of differentiated resistance training and exercise treatment of the spine (focusing on the back) for treating neuropathic itch. As a first step, the training design has the patients passively loosening up soft tissue (muscles and fascia) around the cervical and thoracic spine and actively warming up the shoulder girdle as a preparation for the actual strength training. Step two requires the patients to go through a series of resistance training exercises, such as lateral flexion, flexion and extension of the cervical spine, scapula elevation and depression, as well as scapula retraction, full extension of the spine (erector spinae) and arm adduction (latissimus dorsi). The primary outcome measure is itch (severity, quality, itch-related quality of life (ItchyQol)). The secondary outcome measures are general well-being (SF SF-12), muscle strength and mobility. We present the design, development and progress of a training program for neuropathic itch and report results of the first patients.

PP61
A STUDY OF PRURITUS IN PATIENTS WITH PSORIASIS ATTENDING DERMATOLOGY OPD OF A TERTIARY CARE HOSPITAL

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Objective: To assess the burden of pruritus in patients suffering from psoriasis . *Materials and Methods:* All the consecutive newly diagnosed patients of Psoriasis not on any anti psoriasis treatment were included in the study. A detailed history and examination was performed to know the extent and severity of psoriasis using Psoriasis Area Severity Index (PASI) score. The global assessment of pruritus was done by using preformed questionnaire and itch assessment scales (Four-item itch questionnaire and Behaviour rating scale). *Results:* Total 150 patients (91M, 59F) were enrolled. 91 patients were having plaque type, 32- guttate, 14 sebo-psoriasis (3 exclusively scalp involvement) , 8 - palmoplantar, 1 – pustular, 1- erythroderma. Age at presentation ranged from 2 years to 76 years. 101 patients were having mild psoriasis (PASI $\leq$ 10) whereas 49 patients were having moderate to severe psoriasis (PASI > 10). 130/150 (86.67%) patients were having pruritus of variable severity. 20 patients had no pruritus at all and their major concern was unsightly appearance of lesions and associated dryness. According to Four-item itch questionnaire (FIIQ) out of a maximum score of 19, following pruritus scores were recorded:

Score 3 4 5 6 8 9 10 11 14 15 16 17 18
No of Pt 5 22 52 21 3 5 7 3 2 2 3 3 1

According to BRS (max 5) following score were observed:

BRS Score 0 1 2 3 4
No of Pt 20 48 50 30 2

There was no significant association found between Pruritus score and severity of Psoriasis, duration of Psoriasis, morphological patterns of Psoriasis, and site of Psoriasis.

PP62
NOVEL MICRONEEDLE TREATMENT FOR KELOIDS: EFFECTS ON LESIONAL VOLUME, PAIN AND ITCH

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Background: Itch and pain are common symptoms of keloids and significantly impact the quality of life of patients. Current therapeutic options are limited. The first-line option is intra-lesional corticosteroid injections which, due to the sensitivity of keloids, is painful and precludes treatment in many patients. Other available therapies are limited by cost, inconvenience and a lack of acceptability or tolerability. We developed triamcinolone-embedded dissolving microneedles as a novel therapy for keloids. We aim to determine the effects of a 1-month therapy on keloidal size, pain and itch. *Materials and Methods:* The study was a single-blind, intra-individual controlled 8-week clinical trial. Patients with keloids on the trunk or limbs with a diameter of 1-2cm and at least 1cm apart were recruited. Two keloids were treated with either (*i*) once-daily, self-administered injections with triamcinolone-loaded, dissolving hyaluronic acid microneedles or (*ii*) control with no intervention. For the intervention group, subjects were to stop treatment after 4 weeks. Evaluations were performed at baseline, 4 weeks and 8 weeks. Outcome measures were (*i*) volume of the keloids objectively determined by a 3-dimensional scanner and (*ii*) pain and itch scores on numerical scales. *Results:* Twenty-eight patients (24 males) were recruited but one defaulted. Preliminary analyses revealed that the mean keloid size was significantly reduced in the intervention group after 4 weeks of treatment. The mean reduction in size in the intervention group was also significantly greater than that in the control group. At 8 weeks (after stopping treatment for 4 weeks), the mean size in the intervention group increased to near that at the baseline. With respect to pain and itch, the intervention group demonstrated progressive and significant lower scores at 4 and 8 weeks compared to baseline. There were no side effects registered. *Conclusions:* Treatment with triamcinolone-embedded dissolving microneedles resulted in significant reduction in the size and pain and itch scores of keloids.

PP63
MEDICAL CARE OF PATIENTS WITH CHRONIC PRURITUS IN THE PRIVATE DERMATOLOGICAL PRACTICE IN GERMANY – POSSIBILITIES AND LIMITATIONS

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Chronic pruritus has a high point prevalence of 36.2% and can be considered a frequent symptom in the private dermatological practice. The medical care of these patients can be based on the revised S2k German Guideline for Chronic Pruritus what was completed in 2016. Under the current healthcare policies and economic conditions of the private dermatological practice in Germany, it is challenging to follow the therapy recommendations of the guideline as therapies require experience and are frequently off-label. A collaboration with specialists or itch centers is desirable. Another area can be easily followed such as for example a structured establishment of the patient medical history via pruritus questionnaires, intensity scales or questionnaires for quality of life. This simple procedure provides a time-saving, standardized basis for additional diagnostics and serves as a basis for cooperation with a specialized center. Furthermore, a basic examination and appropriate blood tests, microbiological swabs and skin biopsies could be performed in the practice, where it is also possible to

commence basic stage 1 therapeutic measures in accordance with the German Guideline. Nonetheless, further measures require the support of a specialized center and, in the private practice, can only be implemented in individual cases. Innovative approaches such as teledermatological techniques will facilitate the collaboration between care givers.

PP64
THE BURDEN OF AQUAGENIC PRURITUS IN POLYCYTHEMIA VERA

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Background: Aquagenic pruritus(AP) has significant influence on sufferers' quality of life (QoL). *Material and Methods:* This study analyzed an impact of AP on patient well-being among 102 patients with polycythemia vera (PV). Pruritus intensity was evaluated with visual analogue scale (VAS), verbal rating scale (VRS) and a 4-item Itch Questionnaire. Moreover, psychosocial aspects of AP were assessed with Hospital Anxiety and Depression Scale (HADS), EQ-5D and itch-specific QoL questionnaire (ItchyQoL). *Results:* AP of mean duration 6.6±8.6 years and intensity assessed as 4.8±1.9 points (VAS) was present in 42/102 individuals. The prevalence of depression and anxiety among AP patients was 23.8% and 9.5%, respectively. The depression was more frequent in AP group (vs. non-AP). Moreover, AP sufferers had higher HADS-anxiety scoring than patients without pruritus (p=0.005). The negative correlation between AP duration and EQ-5D-VAS was found. The ItchyQol score of 37.3±12.3 points was influenced by AP extent (p=0.01) and duration of its episodes (p=0.02). *Conclusions:* Summarizing, AP means an additional burden in PV patients negatively influencing their QoL

PP65
ENDOCANNABINOID RECEPTOR 1 GENE POLYMORPHISMS HAVE NO ASSOCIATION WITH UREMIC PRURITUS

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Uremic pruritus (UP) is a common symptom in hemodialysis patients. Its etiology is still not fully understood and that is why there is no specific treatment. The endocannabinoid system plays a role in many pathological conditions. Moreover, there is reliable evidence on the association between cannabinoid system and pruritus. We aimed to evaluate weather genetic variations in the endocannabinoid receptor 1 (CNR1) gene can affect UP. The rs12720071, rs806368, rs1049353, rs806381, rs10485170, rs6454674, and rs2023239 polymorphisms of the CNR1 gene were genotyped in 159 hemodialysis patients and 150 healthy controls using two multiplex polymerase chain reactions the mini-sequencing technique. No statistically significant relationship was found in any of the evaluated genotypes between patients with and without UP, even after excluding patients with diabetes and dyslipidemia. There were no differences between patients with UP and the control group. However, in the group of all HD patients a significantly higher incidence of GA genotype and lower incidence in GG genotype in the polymorphism rs806381s was revealed versus the control group (p=0.04). It seems that polymorphisms of the CNR1 gene are not associated with uremic pruritus.

PP66
MYCOSIS FUNGOIDES AS THE CAUSE OF UNSPECIFIED ITCHING FOR 4 YEARS

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In dermatological practice, patients suffering from chronic unspecified pruritus are often found. The first diagnosis is usually scabies, hives, atopic dermatitis. Lymphomas of the skin are also accompanied by intense itching, however, the diagnosis in most cases is stopped up to several months and even years. We present a clinical case of a patient suffering from chronic itching for 4 years with a wide range of differential diagnosis A woman, born in 1937, first applied to the Novosibirsk Regional Dermatology and Venerology Clinic in January 2013 with complaints of intense skin itching. On examination, the skin is clean. A year later, in July 2014, against a background of itching, rashes appeared in the form of inflammatory papules on the skin of the thighs, the flexural surfaces of the elbow joints, the abdomen. The diagnosis of allergic dermatitis was established, treatment with antihistamines was prescribed, the effect was not given. During the year, the itching persisted, the patient was diagnosed with chronic eczema, atopic dermatitis, but the traditional therapy for these diseases was ineffective. By the end of 2015, the rashes took the form of a universal erythroderma accompanied by intense itching. A histological examination of the skin showed a picture of chronic dermatitis. In March 2016, a diagnosis of clinical cutaneous lymphoma was made on the basis of a clinical picture, but repeated skin biopsy again indicated chronic dermatitis. A bone marrow biopsy with no pathological abnormalities. In November 2016, the board issued a diagnosis of clinical cutaneous lymphoma, a lymph node biopsy was performed, which showed a lymphoproliferative disease. In February 2017, a fungal mycosis T4N2MxB0 with total skin lesions, with affected axillary lymph nodes, characterized by slow progressing course was diagnosed. This clinical case demonstrates that cutaneous lymphomas can mimic many benign dermatoses at the clinical and histological levels. If the patient has an intense itch that does not lend itself to traditional therapy, for a long time, doctor should think about the diagnosis of cutaneous lymphoma.

PP67
OCCUPATIONAL ASPECTS OF SCABIES

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Ten employees and 6 residents with dementia in an old folks home simultaneously developed itching rashes, especially on the abdomen and arms. Scabies was diagnosed by dermatoscopy and biopsy. One seniorresident, who had moved from another nursing home 6 months earlier, was identified as the source of the infection. She had been treated for eczema of some months. Elderly people suffering from dementia need a regular procedure, transferring them from bed to armchair and back, twice daily, by lifting. Intensive skin contact is inevitable during this procedure, which explains clinical signs on abdominal skin. Overall, 18 elderly care nurses, 6 contact persons und 10 residents were examined for scabies. Clinics were organized at 6 am, 1 pm and 9 pm in order to cover all shifts. Topical therapy was performed using 5% permethrin in a greasy ointment. Immediate notification to local health authorities of outbreaks of infections diseases is mandatory as required by German legislation. A sophisticated strategy is essential: The dermatologist, management, staff and the health authorities establish a time schedule for examinations, treatments, follow-ups, quarantine period and informative meetings. The chain of infection must to be interrupted as soon as

possible. Staff rotation is interrupted, and all affected persons must be treated simultaneously. Contaminated textiles must be washed at 60°C, protective clothing is provided for the staff. Handouts are helpful for cooperation. Statutory accident insurance provides compensations for infected staff members as required by German legislation. Scabies is listed as an occupational disease (BK 3101).

PP68
PRURITUS IN PATIENTS WITH ACUTE HEART FAILURE

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Background: Pruritus is a common and distressing symptom, often complicating non-dermatological systemic diseases such as chronic kidney disease, hepatobiliary or hematological disorders. As previously reported (Niklasson O et al, Br J Dermatol 2015;172:1541-6.) pruritus was postulated to also be common among patients with stable, chronic heart failure (HF) with the prevalence of itching at some point at 3-month follow-up period reaching 40%. *Objectives:* Our study was set-up to investigate the prevalence of pruritus in patients admitted to the Department of Cardiology due to acute HF. We also aimed to provide clinical characteristics of patients reporting pruritus and explore potential underlying causes. *Material and Methods:* We prospectively recruited 87 consecutive patients with acute HF (65 (74.7%) men, mean age: 67±5 years, left ventricular ejection fraction: 36±5%) who received standard cardio-vascular therapy and were studied before hospital discharge. Pruritus was assessed using the visual analogue scale (VAS), numeral rating scale (NRS), specially constructed questionnaire regarding connection between pruritus and cardiac disease, therapy and other factors, as well as Dermatology Life Quality Index (DLQI). *Results:* The prevalence of itching during the entire cardiac disease was 16% (14 out of 87 subjects). From that group 10 out of 14 patients reported itch occurring during the last 3 days – in those subjects pruritus was scored at 5.4 on VAS and 5.5 on NRS. The remaining 4 subjects stated that itching occurred at some point in the past during the entire cardiac disease, but not at the present hospitalization. In the majority (71%) of patients pruritus was limited to a certain area of the skin, mostly lower and upper limbs (50%). Noteworthy, 9 out of 16 patients that experienced itching had increased level of bilirubin and half of this group suffered from anemia. Both these factors are proven to contribute to the development of pruritus. Based on our study and clinical experience we do not see a significant connection between pruritus and HF.

PP69
COLONIZATION OF SKIN AND MUCOUS MEMBRANES BY S. AUREUS IN ATOPIC DERMATITIS PATIENTS – IS THERE A LINK WITH ITCH PATHOGENESIS?

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Introduction: Pathogenesis of itch in atopic dermatitis (AD) remains unclear. Nevertheless, altered microbiome composition is proposed as one of the factors contributing to epithelial barrier damage, increased local and systemic inflammation and intensification of pruritus. Numerous reports suggest that both skin lesions and other regions of the human body show selective expansion of *S. aureus* and simultaneous reduction of other components of the natural microflora. Indeed, *S. aureus* strains can be a source of local and systemic factors that potentially exacerbate skin inflammation and itch. *Aim of the study:* To assess the relation between *S. aureus* colonization and itch severity in AD. *Methods:* A total of 33 patients (19 males/14 females, mean age = 31 years) with AD were enrolled in the trial. Every subject presented for an interview and clinical examination (confirmation of AD diagnosis, disease severity assessment based on SCORAD scale). Swabs were taken from lesional and non-lesional skin and from anterior nares. Bacterial cultures on Chapman media were then performed. Morphologically distinct colonies were identified with the help of mass spectrometry. Additionally, a professional microbiologist assessed concentration of *S. aureus* colonies in the cultures (a scale of 0-3 points). Control group consisted of 33 sex- and age-matched healthy individuals. Results were analyzed statistically. *Results:* Overall percentage of cultures positive for S. aureus in the study group was 64% for anterior nares (vs 11% in control group), 79% for lesional skin and 58% for non-lesional skin (vs 6% in control group). We aimed to establish the association between results of microbiological tests and selected parameters of the SCORAD scale related with itch (excoriation and subjective evaluation of sleep loss and pruritus). Patients colonized by *S. aureus* showed higher values of these parameters. Spearman correlation ratio was also calculated to assess the impact of colony concentration on the intensity of the symptoms. Rho was remarkably high for excoriation. In case of subjective parameters rho reflected moderate correlation with colony concentration of *S. aureus*. *Conclusions: S. aureus* colonization of AD patients is associated with increased pruritus. Furthermore, colonization intensity is positively correlated with SCORAD scale parameters expressing itch. Our research suggests that new therapeutic and prophylactic measures are needed to improve itch control in atopic eczema.

PP70
ITCH AND PAIN INFLUENCE ON QUALITY OF LIFE OF ATOPIC DERMATITIS AND PSORIASIS PATIENTS

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Background: Atopic dermatitis (AD) and psoriasis (Ps) are common chronic, inflammatory and recurrent skin diseases. They both are accompanied by subjective symptoms, such as itch and pain. AD and Ps have great impact on patients' quality of life. Sleep is a important, active process of lives of human. *Objectives:* This study was undertaken to evaluate the influence of itch and pain on quality of life of atopic dermatitis and psoriasis patients. *Material and Methods:* The study group consisted of 100 (42 females, 58 males) AD patients with mean age of 39.2±15.4 years and 100 (39 females, 61 males) Ps patients with mean age 44.1±15.8 years. The mean disease severity was assessed as 33.6±10.7 points and 13.5±8.4 points according to SCORAD (Scoring Atopic Dermatitis) and PASI (Psoriasis Area Severity Index), respectively. Itch and pain intensity were evaluated with visual analogue scale (VAS). The quality of life was assessed by DLQI. Moreover, sleep abnormalities were estimated with Athens Insomnia Scale (AIS), Pittsburgh Sleep Quality Index (PSQI) and Epworth Sleepiness Scale (ESS). *Results:* During the course of disease and within three last days subjective symptoms were experienced by the following group: AD: itch – 100% vs. 100% patients; pain – 43% vs. 38% patients and Ps: itch – 95% vs. 95% patients and pain – 18% vs. 16%, respectively. The mean itch and pain severity within three last days was estimated as: AD: 7.1±2.7 points and 5.3±2.9 points and Ps: 6.4±2.8 points and 1.2±3.0 points, respectively. The mean QoL was assessed as: AD: 16.4±7.9 points and Ps: 12.8±7.5 points. The scores for particular sleep abnormalities questionnaires were 10.5±5.5 points, 8.3±4.2 points and 7.9±4.8 points in AD and 7.4±5.2 points, 8.1±4.8 points and 7.1±4.8 points in Ps,

with regard to AIS, PSQI and ESS, respectively. The severity of itch significantly correlated with scores obtained by the AIS (r=0.44, $p<0.001$) and (r=0.34, $p<0.001$), ESS (r=0.35, $p<0.001$) and (r=0.24, $p=0.014$), for AD and Ps respectively. Moreover, decreased QoL correlated significantly with severity of itch and pain AD (r=0.45, $p<0.001$), (r=0.36, $p=0.026$) and Ps (r=0.32, $p<0.001$), (r=0.5, $p<0.001$), respectively. *Conclusions:* Itch can affect the quality of sleep of AD and Ps patients. Improving sleep quality of dermatological patients may improve their quality of life.

PP71
NODULAR PRURIGO AS FIRST MANIFESTATION OF PRIMARY BILIARY CHOLANGITIS SUCCESSFULLY TREATED WITH RIFAMPIN AND SERTRALINE

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Primary biliary cholangitis (PBC) is an immune-mediated chronic cholestatic liver disease with a slowly progressive course Prurigo nodularis is characterized by extremely pruritic nodules with well-defined clinical symptoms and histopathological findings. Disorder is caused by a variety of pathomechanisms Pruritus is one of the most difficult symptoms to treat in the course of PBC. Often, it can be severe and refractory to multiple treatments, and significantly affects the quality of life of the patient There is evidence to suggest that rifampicin is an effective treatment for pruritus in patients with chronic cholestatic liver disease. It is used as a second line of therapy in the PBC. Rifampicin can cause hepatitis in about 7% of patients treated for cholestatic liver disease. Serotonin is fourth line agent in PBC. Antipruritic effect has been demonstrated in a case series. We report the case of a 42-year-old woman present with pruritic papules and nodules on her legs, arms and trunk developed over the past 2 years. After wide spectrum of diagnostic procedures we found significant elevation liver and cholestatic enzymes, IgM and AMA antibodies. Skin biopsy confirmed nodular prurigo. Patient was examined and reffered do Infectious Diseases Department. Diagnosis of PBC was conifrmed. We start therapy with rifampin 150 mg once daily with amelioration of the itch. After 4 weeks of therapy, patient developed hepatotoxicity. Due to side effect, rifampin was stoped. The patient then received 50 mg sertraline once daily with rapid and significant improvement.

PP72
ITCH IN NON-MELANOMA SKIN CANCERS.

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Itch is one of the most important symptoms in dermatology. Its presence has been proven in many diseases which during many years were defined as non-itching disorders. However there are not many studies examining prevalence, intensity, type, duration this important symptom in patients with BCC and SCC. The authors of this study exam correlation between intensity of itch and type of cancer, age of patients, location of lesion and previous treatment. The mterial are patients treated because of non-melanoma skin cancer (NMSC) in Ward of Plastic Surgery in Department of Dermatology, Venereology and Allergology, Wroclaw Medical University between June 2016 and May 2017. For the analysis were included 175 patients operated because of NMSC (89 women and 86 men). In 90.3% the histological diagnosis was BCC. Itching in lesion was reported in 37% ptients with BCC (45% male patients but only 29%f emale). 61%patients with SCC reported itch and/or pain. It seems there is relationship between presence and intensity of itch and superficial type of BCC, extrafacial location and males.

PP73
GENDER DISPARITY IN THE PSYCHOSOCIAL EFFECT OF CHRONIC ITCH ON CHILDREN

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Background: Dermatologic conditions can have a significant impact on the quality of life (QoL) but little is known about the psychosocial effects of chronic itch on children. Moreover, there is published literature regarding greater emotive expressivity of girls vs. boys. We hypothesized that girls would demonstrate higher emotional impact from chronic pruritus than boys. *Methods:* Children between the ages of 6–17 who experience chronic itch (6 weeks or longer) were recruited and administered a panel of surveys including pediatric versions of the ItchyQoL, a self-report of the QoL impact from chronic pruritus. There is a younger child (6–7 years) and older child (8–17 years) version that we are currently validating. For this analysis, only the items related to emotional impact were analyzed. Proportions were used to determine distinctive emotional concepts. Chi-square and Fisher's exact test were used to assess the possible difference between genders in the two age groups. *Results:* There were 67 (6–7 year-olds) with 29 boys and 38 girls and 164 (8–17-year-olds) with 102 girls and 62 boys. For the 6–7 year-olds, 34 % expressed sadness, 30% were mad and 15% were scared due to their itchy skin. For the older children, 23% were sad, 33% were angry and 12% were scared. Of note in the older group, 65% were frustrated, 50% were driven crazy and 39% were embarrassed by their itchy skin. Between genders, there was no significant difference in the 6–7 age group. For the 8–17 age group, girls were more embarrassed ($p= 0.02$) and more worried ($p=0.03$) than boys. *Conclusion:* A third of the younger group was saddened and scared due to their chronic itch; a lower percentage of (pre)adolescents expressed those feelings. A third of all subjects voiced anger and the majority of (pre)adolescents experienced frustration. There were no gender differences in the younger group. In the (pre)adolescent group, girls expressed more embarrassment and worry than boys. It should be noted that certain concepts tested were specific to each age group; frustration, driven crazy and embarrassment were not tested in the younger group. These findings give us insight on the emotional aspects elicited from chronic pruritus in children. Emotional support tailored to these concepts may be helpful, paying particular attention to embarrassment and worry in older girls. A larger scaled study is needed to further assess these concepts.

PP74
BOTH NARROWBAND-UVB AND BROADBAND-UVB ARE EQUALLY EFFECTIVE IN REDUCING ITCH IN CHRONIC PRURITUS PATIENTS

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Chronic pruritus (CP) (> 6 weeks) significantly reduces the patients' quality of life. Repeated scratching and development of an "itch-scratch cycle" may lead to chronic prurigo (CPR) with pruriginous papules and nodules. Treatment of CP is difficult and, to date, there are no licensed treatments for CP or CPR. Phototherapy with broadband (BB)-UVB has previously been shown to reduce CP in patients with renal insufficiency (RI). In recent years, however, due to superior efficacy of narrowband (NB)-UVB over BB-UVB in the treatment of psoriasis, atopic dermatitis, and vitiligo, NB-UVB has almost completely replaced BB-UVB in phototherapy units and private dermatological offices. Though, clinical experience suggests NB-UVB to be effective in reducing pruritus e.g., in patients with RI or CPR, there has not

been a study comparing it with BB-UVB. Thus, we investigated the effects of BB-UVB versus NB-UVB in reducing pruritus in patients with CP. 49 patients consented and were randomly assigned to BB-UVB or NB-UVB. After testing for individual minimal erythema dose (MED) with the respective light source, patients were whole-body UV-treated 3x per week for 6 weeks in equally looking BB-UVB or NB-UVB cabins (starting dose 50% MED, UV-dose increments 20% per week). Before, weekly during, and at the end of treatment, patients evaluated their pruritus using a visual analogue scale (VAS) ranging from 0 (=no itch) to 10 (=worst imaginable itch). 38 patients with CP (23F, 15M; median age 65y, range 20–85 years) received at least 4 weeks of UV-treatment (BB-UVB: 18; NB-UVB: 20) and were eligible for final evaluation. Of these 38 patients, 35 had either CPR or secondary scratch lesions, and 3 had no skin lesions. BB-UVB reduced pruritus VAS from 6.05 (2.2–10) to 2.10 (0–7.5) (median reduction 67.2%), and NB-UVB from 6.75 (1.1–10) to 1.20 (0–8.7) (median reduction 80.7%). Testing for non-inferiority (equality range up to 20% of the relative treatment effect, asymptotic Wilcoxon-Mann-Whitney Test) indicated that NB-UVB was not inferior to BB-UVB in the ability to reduce pruritus (p=0.0037). In conclusion, NB-UVB proofed to be equally effective as BB-UVB in reducing pruritus in CP patients and both phototherapeutic modalities showed very strong antipruritic activity at a grade (itch reduction by 70–80%) that is hardly reached by any other treatment option available nowadays. Thus, like in other conditions NB-UVB can also be administered in CP patients with great overall efficacy.

PP75
ITCHYQOL ASSESSMENT IN PSORIASIS VULGARIS: CORRELATION ANALYSIS OF PATIENT BASELINE DATA FROM A RANDOMIZED CONTROLLED TRIAL (PSORITUS)

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Background: Pruritus is a frequent complaint in psoriasis vulgaris (PV) and has impact on the quality of life (QoL) of patients. The DLQI is a standard instrument commonly used in psoriasis. DLQI is discussed to show correlations of QoL with the pruritus intensity in psoriasis. So far no data are available on use of an itch-specific QoL instrument, ItchyQol, in PV. *Methods:* Patients with moderate to severe PV and intense pruritus were assigned to treatment with Secukinumab within a randomized controlled trial (PSORITUS). The present correlation analysis comprised assessment of PSORITUS baseline data including the results of the ItchyQol questionnaire, itch intensity VAS, comorbidities and demographic data. *Results:* 130 patients with PV were included: 46 (34.5%) females; age range 24–75 years, median: 49 years. Patients suffered since 18.5 years (median) from PV; 13.8% had psoriasis arthritis. PASI was 20.9 (median), VAS worst 24 h was 8.1 (median); VAS average 24 h was 7.2 (median). ItchyQol score ranged from 33 to 110 with a mean of 78.7 (SD 17.4; median: 83); DLQI ranged from 3.0 to 30 (mean: 17.8, SD 7.9; median: 18.5). ItchyQol showed moderate to strong correlations with VAS worst, VAS average, and DLQI. The multiple linear regression analysis showed significant dependency of QoL as measured by ItchyQol for parameter as follows: female gender (estimate of 5.81 ItchyQol-points worse QoL than males), VAS average 24 h, duration of PV and health-related patient needs as measured by the Patient Need Questionnaire (part of Patient Benefit Index). *Conclusion:* ItchyQol assessment demonstrated that patients with psoriasis vulgaris are highly burdened by pruritus. Itch intensity and ItchyQol are correlating with each other influencing patient's needs and treatment expectations.

PP76
IMPERVIOUSNESS TO GENDER CARTOON ANNOTATION IN SELF REPORTED PRURITUS OUTCOMES

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The ItchyQuant and the pediatric versions of the ItchyQoL are cartoon-annotated in an attempt to assist young children to understand the concepts behind self-rated itch severity and quality of life (QoL) impact of chronic pruritus (CP, itch lasting >6 weeks). A cartoon of a young boy dominates both the ItchyQuant and ItchyQoL, leading to worry that girls may not relate to the instruments. In this study, we sought to discern any gender differences in the internal consistency and central tendencies (mean, median, etc.) of the ItchyQOL. *Method:* The ItchyQuant and ItchyQoL were administered to 6–7-year-old and to 4–5-year-old children with CP. Internal consistency for the ItchyQoL was calculated using Cronbach's alpha across all children in a given age cohort and then separately by gender within that same age cohort. Differences in central tendency between genders were evaluated using an ANOVA for comparison of means, a Wilcoxon Rank Sum test, and a test of the mean number of scores per gender group which were above the overall median score (i.e., a median test). Correlation between ItchyQuant and ItchyQoL scores were explored for each gender using Spearman rank order correlations. A p-value <0.05 was considered statistically significant. *Results:* 70 6–7-year-old (32 boys and 38 girls) and 33 4–5-year-old (13 boys and 20 girls) completed the instruments. The ItchyQoL's Cronbach's alpha did not differ substantially between boys, girls, and overall (0.81, 0.86, and 0.84, respectively) in the 6–7-year-old group. The overall mean for boys and girls was 5.59 and 5.37, which was not significantly different according to an ANOVA. The Rank Sum test did not reveal significant differences, nor did the median test (51% vs 49% above the median score). The ItchyQuant scores correlated with the ItchyQoL significantly and similarly between boys and girls (0.56 and 0.49, p<0.01 for both). In the 4–5-year-old age group, analogous results were found. *Conclusion:* Although the majority of the items in the ItchyQoL and the ItchyQuant were depicted by cartoons of young boys, there does not appear to be a gender difference in the ItchyQOL properties of interest when aggregated over items. It appears that girls can relate the instrument to themselves as well as boys.

PP77
«PSEUDOALLERGIC» REACTIONS ON SKIN AND MUCOUS MEMBRANE: IS IT A PSYCHOSOMATIC PHENOMENON?

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The variety of skin sensations associated with mental disorders is rather wide and cause problems in diagnostics and treatment. Recently the application of patients with complains on itch of the skin and mucous membrane becomes more and more often. Glossalgia and glossopyrosis or Burning mouth syndrome is associated with dysgeusia, paresthesia, dysesthesia, xerostomia, among the therapeutic approaches clonazepam, psychotherapy, capsaicin and gabapentin are mentioned in literature (Liu YF. et al., 2017, Vellappally S., 2016). Skin with a greater density of epidermal innervation is more susceptible for the development of cutaneous sensory disorder (Gupta M.A. et al., 2013). Burning mouth syndrome may be associated with higher scores for depressive and anxiety symptoms (Davies S.J. et al., 2016). In 2016-2017 17 patients (average age 41.94 years old) applied with complains on different sensations of the skin and mucous membrane without or

with rash on skin. The patients were consulted by allergologists and other specialist and directed to our center. Dermatovenereologist and psychiatrist in detail examined the patients. Among the diagnosis 8 patients had glossalgia, 5 patients had urticaria, 2 patients – somatoform itch and 2 patients – amplified itch at the base of atopic dermatitis. Psychiatric equivalents of itch and other sensations (burning, tingling, tickling, pricking, prickling, tightness, stinging and others) were widely presented and were the sign of different psychodermatological interventions. The manifestation of rash as a variant of psychogenic «pseudoallergic reactions» in form of urticum, papules was noticed. The use of psychotropic drugs (antipsychotics and others) is necessary in such cases and shows its efficacy.

PP78

A NEW TOOL FOR MODELLING STINGING TEST IN VITRO: A COMPARATIVE EVALUATION WITH IN VIVO RESULTS USING A BACTERIAL POLYSACCHARIDE

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Stinging test is an *in vivo* classic protocol that evaluates sensitive skin and tests molecules, actives, formula or ingredients on soothing sensation. In practice, stinging test is made using lactic acid at 10 or 5 percent % placed on nasolabial fold right and left of the face of volunteers. After begin a stinging sensation, a placebo is deposited on one side and potential soothing on the other side. To predict the probable soothing sensation of a product before *in vivo* testing and to modelize effect on the skin, we developed a culture and co-culture model based on acid lactic test and substance P (SP) release using human keratinocytes and PC12 cells. In order to predict a calming effect, we used a bacterial polysaccharide present in Fucogel® in *in vivo* stinging test and our *in vitro* model. Keratinocytes and PC12 cells were placed on a 96-wells plate. PC12 cells were differentiated using NGF for 3 days and keratinocytes were maintained one day in proliferation medium before application of lactic acid or polysaccharide or both. Firstly, ideal concentration of acid lactic (10%, 5%, 1%, 0.5%, 0.4%, 0.3%, 0.2%, 0.1%, 0.07%, 0.04%, 0%) has been determined to release SP without cytotoxicity on keratinocytes and PC12 cells. We showed a release of SP for all conditions with lactic acid. The release of SP was significant from 0.1% of lactic acid without toxicity for PC12 cells and keratinocytes. When pH was neutralized, lactic acid doid not provoke SP release. On keratinocytes, 0.1% lactic acid induced a cytosolic calcium entry whereas prior pH neutralization did not. At these concentrations of lactic acid, 0.1% of polysaccharide induced a significant decrease of SP release on two cellular types and in co-culture without modified the pH of the medium. *In vivo*, stinging test associated with Fucogel® application was followed by a decrease by 30% of prikling intensity versus placebo on 19 women volunteers from 21 to 69 years old. Our *in vitro* model is ethically interesting and is adapted for cosmetic ingredients screening because there is no animal experimentation. Furthermore, Fucogel® has an interesting soothing activity revealed by *in vivo* stinging test and our new *in vitro* stinging test based on SP release.

PP79

EARLY ONSET OF ANTIPRURITIC EFFECTS WITH SERLOPITANT FOR CHRONIC PRURITUS: POST HOC ANALYSIS RESULTS FROM A RANDOMIZED, MULTICENTER, PLACEBO-CONTROLLED PHASE 2 CLINICAL TRIAL

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Introduction: Chronic pruritus, a prevalent symptom of a variety of underlying conditions, can significantly impact quality of life. Many chronic pruritus therapies have limited efficacy, and some are associated with undesirable safety/tolerability issues. Immediate relief of itch is an initial treatment goal for chronic pruritus. The neuropeptide substance P and its receptor, neurokinin 1 receptor (NK_1-R), play a role in the pathogenesis of chronic pruritus. The NK_1-R antagonist serlopitant was shown to provide statistically significant improvement in chronic pruritus when given once daily for 6 weeks compared with placebo and was safe and well tolerated in a phase 2 clinical trial (NCT01951274). Here, we show evidence that the onset of antipruritic effects with serlopitant begins in the first few days of initiating treatment. *Material/Methods:* Key eligibility criteria were treatment-unresponsive or -refractory pruritus lasting ≥6 weeks and baseline itch Visual Analog Scale (VAS) score ≥7. Patients were randomized 1:1:1:1 to receive serlopitant 0.25 mg, 1 mg, 5 mg, or placebo. After a loading dose of 3 tablets at baseline, patients took 1 tablet daily for 6 weeks. Change from baseline on study days 1 to 14 was analyzed, with the difference in average change from baseline between the serlopitant and placebo groups tested using a t-test. *Results:* Two hundred fifty-seven patients were randomized to serlopitant 0.25 mg (n=64), 1 mg (n=64), or 5 mg (n=65), or placebo (n=64); baseline characteristics were comparable. The mean change from baseline VAS itch score was significantly greater with serlopitant 1 mg beginning on day 2 and 5 mg beginning on day 3 than with placebo. The antipruritic effects of serlopitant were sustained to week 6; the percentage change from baseline VAS itch score was significantly greater with serlopitant 1 mg (–41.4; p=0.022) and 5 mg (–42.5; p=0.013) at week 6 compared with placebo (–28.3). *Conclusions:* Serlopitant provided statistically significant improvement in chronic pruritus beginning as early as day 2 with the 1 mg dose and day 3 with the 5 mg dose compared with placebo. The improvements in the experience of pruritus with serlopitant were sustained to week 6 with the 1 mg and 5 mg doses.