5th Pruritus Symposium 2016 in Münster, Germany:

News & Highlights

Pereira MP¹, Ständer S¹

1. Department of Dermatology and Center for Chronic Pruritus, University Hospital Münster, Von-Esmarch-Str. 58, 48149 Münster, Germany

Correspondence:
Sonja Ständer, MD
Department of Dermatology and Center for Chronic Pruritus,
University Hospital Münster,
Von-Esmarch-Str. 58,
48149 Münster, Germany
Tel.: +49 251 83 56510
Fax: +49 251 83 52559
Email: Sonja.Staender@ukmuenster.de
PROGRAM

Friday, September 4th 2016

<table>
<thead>
<tr>
<th>Time</th>
<th>Presenter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00am-1:00pm</td>
<td>Workshop Participants</td>
<td>Workshop Pruritus Parameter</td>
</tr>
<tr>
<td>2:30pm</td>
<td>University Rector</td>
<td>Welcome</td>
</tr>
<tr>
<td>2:40pm</td>
<td>T.A. Luger, Münster</td>
<td>Welcome</td>
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<tr>
<td>2:50pm</td>
<td>S. Ständer, Münster</td>
<td>Welcome</td>
</tr>
</tbody>
</table>

Module 1: Neurobiology Update

Special Invited Lecture:

3:00–3:30pm E. Carstens, Davis, USA President, International Forum for the Study of Itch (IFSI) Pain and Pruritus - Interaction or Control?

3:30–3:50pm T.A. Luger, Münster Atopic Dermatitis

3:50–4:10pm M. Schmelz, Mannheim Brain-Nerve-Skin Axis: What’s new?

4:10–4:40pm Coffee Break

Module 2: Updates on Therapies

4:40-5:00pm T.A. Luger, Münster Neurokinin-1 Receptor Antagonists in Pruritus

5:00-5:20pm J. Kupfer, Giessen Mental Induction of Pruritus

5:20–5:40pm P. Staubach, Mainz Magistral Formulations in the Therapy of Chronic Pruritus

5:40–6:00pm B. Pfleiderer, Münster Real-World Analyses of the Treatment Course of Chronic Pruritus in Münster

6:00–6:20pm S. Ständer, Münster Guideline Update: What’s New?

Get Together

Saturday, 5th September 2016

<table>
<thead>
<tr>
<th>Time</th>
<th>Presenter</th>
<th>Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00am</td>
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<td>Welcome</td>
</tr>
</tbody>
</table>

Module 3: Pruritogenic Diseases: Diagnostics and Therapy

9:05-9:30am M. Metz, Berlin Chronic Urticaria

9:30-9:55am A. Kremer, Erlangen CME: Interactive case discussion

9:55-10:20am T. Mettang, Wiesbaden CME: Interactive case discussion

10:20-10:45am E. Weisshaar, Heidelberg CME: Interactive case discussion
### Module 4: Psoriasis and Pruritus

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker(s)</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>11:30-11:35pm</td>
<td>U. Mrowietz, Kiel</td>
<td>Pruritus and Psoriasis</td>
</tr>
<tr>
<td>11:35-11:55pm</td>
<td>A. Tsianakas, Münster</td>
<td>Update on therapy of psoriasis</td>
</tr>
<tr>
<td>11:55-12:15pm</td>
<td>A. Stumpf, Münster</td>
<td>Pruritus and stress</td>
</tr>
<tr>
<td>12:15-12:35pm</td>
<td>T. Mettang, Wiesbaden, D. Nashan, Dortmund</td>
<td>CME: Interactive case discussion</td>
</tr>
</tbody>
</table>

#### 12:35-1:00pm

**General Assembly of the “Arbeitsgemeinschaft Pruritusforschung” (AGP, national Itch Society)**

**until 1:30pm**  
**Lunch**

### Module 5: Patient care in chronic pruritus: Interactive panel discussion

<table>
<thead>
<tr>
<th>Time</th>
<th>Speaker(s)</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:30–1:45pm</td>
<td>E. Pogatzki-Zahn, Münster</td>
<td>Do We Treat Well? Novel Findings About the Interaction Between Pain and Itch</td>
</tr>
<tr>
<td>1:45–1:55pm</td>
<td>S. Steinke, Münster</td>
<td>Panel Talk 1: What Do Patients Want?</td>
</tr>
<tr>
<td>1:55–2:05pm</td>
<td>H.F. Ständer, Bad Bentheim, Dortmund</td>
<td>Panel Talk 2: What Does a Dermatological Practice Offer?</td>
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<tr>
<td>2:05–2:15pm</td>
<td>S. Ständer, Münster</td>
<td>Panel Talk 3: What Does a Specialized Center Offer?</td>
</tr>
</tbody>
</table>

**Until 3:30pm**  
**Discussion**
5th Münster Pruritus Symposium

The 5th Münster Pruritus Symposium took place from September 16th to 17th, 2016 in Münster, Germany. Organized primarily by Sonja Ständer of the University Hospital of Münster, the symposium is a biannual, German language event allowing for German and other international specialists interested in pruritus research and its clinical management to gather and exchange findings and research. This year, more than 230 clinicians and researchers from 6 different countries and 15 specialties participated. This report aims to present the main highlights and news presented at this forum.

Neurobiology

The scientific block of the program began with a lecture on itch transmission from the skin to the central nervous system by the president of the International Forum for the Study of Itch (IFSI), E. Carstens, from Davis, USA. Peripheral and central sensitization, dysfunction of itch-inhibitory circuits and impairment of descending inhibition may be pathological mechanisms leading to chronic pruritus and are thus possible therapeutic targets. Peripherally, histaminergic itch is TRVP1-dependent, while most kinds of non-histaminergic itch require TRPA1 signaling. At the spinal level, brain natriuretic peptide, gastrin releasing peptide, substance P, glutamate and AMPA receptors appear to be involved in spinal itch modulation. New evidence suggests that scratching suppresses itch by activating inhibitory interneurons. The primary and secondary somatosensory cortex (itch discrimination), premotor cortex, cerebellum and basal ganglia (scratching behavior), insula and anterior cingulate cortex (emotional modulation) and orbitofrontal cortex (goal-directed behavior) are involved in supraspinal central itch processing.

Based on clinical observations, it is known that scratching behavior increases pruritus intensity over time. Gastrin releasing peptide, which is expressed after nerve damage, has been identified as a spinal transmitter for itch. M. Schmelz speculated in his talk that scratching behavior may lead to the rarefaction of intraepidermal nerve fibers and to a spinal, or potentially peripheral upregulation of gastrin-releasing peptide. He suggests that scratching behavior
thus contributes to the maintenance of itch, a theory which has been clinically confirmed by the itch-scratch cycle.

The central processing of itch is another aspect of the neurobiology of pruritus to take into consideration. As reported by E. Pogatzki-Zahn, new findings indicate that descending pain inhibition is impaired in chronic pruritus patients. Interestingly, duloxetine efficacy was found to be higher in pain patients with impaired descending pain inhibition when compared to those with normal functioning inhibitory mechanisms (1). Future studies addressing this issue in chronic pruritus patients are urgently needed.

**Atopic dermatitis**

T. Luger, chair of the Department of Dermatology, Münster, presented the new German guidelines for the management of atopic dermatitis that are currently in press. The importance of a basic care routine consisting of emollients is emphasized in the new guidelines. In recent studies conducted on infants, moisturizing within the first six months following birth was found to significantly reduce the risk of development of eczematous skin lesions, thus representing a cost-effective measure to decrease the incidence of an atopic march (2, 3). Additionally, the new guidelines highlight the importance of a proactive therapy with topical steroids or calcineurin inhibitors. Pimecrolimus (and tacrolimus, based on limited reports) represents a safe and effective treatment option for infants older than 3 months of age (4). There is no evidence of an increased development of skin lymphomas or other skin tumors associated with the use of these agents. New topical compounds for atopic dermatitis have also been found to impact pruritus, including JAK and phosphodiesterase 4 inhibitors (PDE4). The new guidelines, unlike previous ones, do not recommend H1 antihistamines for treating pruritus caused by atopic eczema.

Biologics are regarded as prospective systemic agents for moderate to severe atopic dermatitis (5). In particular, in a randomized controlled trial (RCT) dupilumab, an anti-IL-4/-13 antibody, administered subcutaneously once a week, was found to significantly reduce the severity of eczema and pruritus intensity in patients with AD refractory to conventional treatment (6). Dupilumab is expected to be the first biologic approved for the treatment of
atopic dermatitis. Other future targets include, among others, IL-12/23 antibodies, IL-13 antibodies, H4 antagonists and IL-31 receptor antibodies.

In another talk, T. Luger focused on the neurokinin 1 receptor antagonists, a new class of antipruritic agents. The neurokinin-1 receptor is not only expressed in the skin, but also in the central nervous system (7). Substance P is a major ligand and, among other functions, is involved in the modulation of itch (8). New data have established the efficacy of NK1R antagonists not only for the treatment of atopic dermatitis, but also for cutaneous T-cell lymphoma, neoplastic pruritus, neuropathic pruritus and prurigo nodularis (8). Aprepitant, in particular, showed a significant antipruritic effect with only mild side effects in a study including 20 patients with atopic dermatitis and prurigo nodularis (9). Other NK1R antagonists currently being tested in RCTs include tradipitant (Vanda Pharmaceuticals) and serlopitant (Menlo Therapeutics). Both substances show promising results at higher doses.

**Psoriasis**

Itching affects the majority of patients with psoriasis (72%) (10), thus substantially contributing to the severity of the disease (11). Neuropeptides (e.g. substance P and calcitonin gene related peptide) and the nerve growth factor receptor tyrosine kinase A, as well as an imbalance between κ- and µ-opioid receptors, may play a role in the inflammatory process (12). Therapeutically, pruritus decreases with treatment of the psoriasis lesions. In recently published RCTs, apremilast and etanercept were found to significantly improve both pruritus and skin discomfort in psoriasis patients (13, 14). Currently, a plethora of new compounds are being tested in advanced RCTs. According to the PASI score in the LIBERATE trial, treatment with the PD4 inhibitor apremilast resulted in a significant and sustained improvement of disease activity. Recently, attention has shifted to biosimilars, with infliximab being the first biosimilar approved for the treatment of psoriasis, followed by etanercept. Another substance of interest is the IL-17A antagonist secukinumab, which showed efficacy in the treatment of plaque psoriasis in two RCTs (15) and was found to be superior when compared to ustekinumab (16). Studies of
secukinumab on children are currently ongoing. Phase III RCTs investigating an alternative IL-17A antibody, ixekizumab, show high efficacy and a good safety profile. A possible side effect of these compounds is the development of oral candidiasis. The IL-23 blockade is another possible target mechanism, with a phase II RCT suggesting guselkumab as a possible new agent against plaque psoriasis (17).

**Urticaria**

A new online survey study of patients with chronic urticaria indicates that a majority of patients avoid going to their physician because they do not believe they can be helped. As a result, a majority of patients receive substandard care (18). In a diagnostic approach of chronic urticaria, rare diagnoses (e.g. familial cold autoinflammatory syndrome or Muckle-Wells syndrome) should not be forgotten. An underlying inflammatory condition should be screened for with laboratory tests (e.g. a complete blood count or C-reactive protein) (19). Second-generation H1 antihistamines are a recommended therapy for which the dose, if necessary, may be increased up to 4-fold. If symptoms persist for more than 2 weeks, an additional therapy with omalizumab, cyclosporine or leukotriene antagonists is suggested. Systemic steroids should only be used for a short period of time to treat worsening symptoms (19). Recent studies of omalizumab detailed its efficacy in the treatment of chronic idiopathic urticaria (20) and chronic spontaneous urticaria with angioedema refractory to antihistamines (21), as well as other urticarial conditions such as urticaria factitia and cold urticaria.

**New German guidelines for the management of pruritus**

Despite currently being in press, the updated German guidelines for the clinical management of chronic pruritus were also presented (22). Twelve medical societies, as well as chronic pruritus patients, participated in the development of these multidisciplinary guidelines. All decisions were made according to the Delphi method. In the new guidelines, the diagnostic approach is differentiated according to the clinical presentation and pathological findings. It is also emphasized that the incidence of malignancies is higher in patients with pruritus.
beginning within the past 12 months. Sedating antihistamines, leukotriene antagonists, serotonin receptor antagonists and systemic steroids (the latter only for short-term use in very severe cases) are, interestingly, no longer recommended as therapeutic substances. A stepwise therapeutic approach is recommended, beginning with general measures (e.g. emollients for xerosis, topical antiseptic agents for erosive lesions and treatment of accompanying sleep disorders or psychosomatic issues) and higher doses of anti-histamines. Other recommended therapies, depending on the origin of the pruritus, include phototherapy, immunosuppressive drugs (e.g. cyclosporine and methotrexate), anticonvulsants (e.g. gabapentin and pregabalin), antidepressants (e.g. serotonin reuptake inhibitors and tricyclic and tetracyclic antidepressants) and neurokinin-1 receptor antagonists.

Miscellaneous

Workshop: Pruritus parameters

The 7th consensus workshop of the Pruritus Parameters Initiative took place shortly before the symposium, where the preliminary results of the PruNet project, a pan-European study aiming to validate assessment instruments in 16 countries, were presented (I. Soto Rey, Münster and F. Legat, Graz). The pruritus intensity (visual analogue scale) and quality of life (ItchyQol) were regarded as the most important parameters requiring assessment. Standardized questionnaires are currently being validated throughout the participating countries (23). The first results of the Itch-free Days Scale validation study, showing a high test-retest reliability, were presented. This instrument assesses scratching behavior and sleep disturbances, in addition to itch intensity (S. Steinke, oral communication). Furthermore, a new questionnaire is being developed for patients suffering from pruritus due to primary biliary cholangitis and will require future validation (A. Kremer, oral communication).

Pruritus and stress

A new study suggests that negative emotions can have a substantial effect on pruritus intensity and affirms the importance of cognitive therapies for treating chronic itch (24). New data (A. Stumpf, oral communication) suggests that stress
influences pruritus both biologically (e.g. altered immune response, altered neuropeptide and hormone activity and aberrant parasympathetic response) and psychologically (e.g. coping strategies and social isolation). J. Kupfer reported on analyses related to atopic dermatitis patients who were subjected to a structured educational program, while the association between the pruritus intensity and psychosocial parameters were analyzed. Interestingly, research on pruritus intensity revealed surprising correlations between women and their level of education.

Interactive session
Several case reports on chronic pruritus patients were presented in an interactive fashion to the audience and detailed chronic pruritus as a result of dermatological (e.g. Grover’s disease), systemic (e.g. Hodgkin’s lymphoma, follicular lymphoma, iron deficiency and Helicobacter pylori infection), neuropathic (e.g brachioradial pruritus), autoimmune, genetic and drug-induced conditions. Through interaction with the audience, it became apparent that secondary skin lesions due to scratching may mislead attending physicians into misdiagnosing a dermatosis as the cause of the pruritus, when in fact a systemic disease is the true underlying cause.

Patient needs
The importance of patient reported outcomes was greatly emphasized. Patient needs, in particular, were the subject of much discussion. A recently published study established that these vary according to gender, age, disease category (e.g. inflammatory skin condition and chronic scratch lesions), itch intensity and quality of life (25).

Cooperation between dermatology offices and specialized centers
Pruritus is the most frequent symptom presented in dermatology practices (26). Close cooperation between specialized centers and dermatological offices is essential for the management of chronic pruritus patients. Dermatology offices can offer patients a quicker appointment and work together with local physicians of other specialties, thus decreasing the volume of patients, and
consequently the waiting time, in specialized centers. In dermatological practices, a comprehensive medical history (e.g. using standardized questionnaires) and the basic diagnostic procedures (histology, direct immunofluorescence, blood tests) should be taken and the first therapeutic measures (basic skin care, topical therapy, antihistamines) initiated before the patient is referred to a specialized center (H. Ständer, oral communication).

*Prurigo Nodularis League*

The Prurigo Nodularis League (PNL), founded in 2014, is a network of international experts, physicians, researchers and affected patients who aim to improve basic and clinical research and raise awareness of prurigo nodularis, a rare but debilitating disease. More information on the activities of the PNL can be found on prurigo-nodularis.net or facebook.com/PrurigoNodularisLeague. Participants expressed interest in the results of current trials on different substances such as κ-opioid agonists/μ-opioid-antagonists, NK1R antagonists and certain antibodies.

**Conclusion**

Chronic pruritus is a condition with high incidence and a complex pathophysiology, diagnostic approach and therapeutic management. It is necessary to hold more national and international conferences and forums for researchers and clinicians interested in chronic itch in order to gain more valuable knowledge on its various complicated dimensions.
References:


