Highlights of the 16th International Symposium for Sjögren's Disease

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The 16th International Symposium for Sjögren's Disease was held in Egmond aan Zee, the Netherlands, between the 22nd and 25th of April 2024, and chaired by Hendrika Bootsma (University Medical Center Groningen, the Netherlands). The same conference started in 1986, with a different name, and the first call for changing the name Sjögren's syndrome into Sjögren's disease was made by Baer & Hammitt in 2021 (1). This was endorsed by both American and European patient groups. Since then, the name Sjögren's disease has been adopted in >200 scientific publications. In line with this trend, the organising team decided to change the Symposium name to 'International Symposium for Sjögren's Disease'. This 16th edition of the Symposium was attended by more than 300 participants from all over the world, with a central theme of: Looking forward. The main objective of the Symposium was to advance our ability to treat Sjögren's disease, together with all Sjögren's disease-focused clinicians, scientists and patient organisations. Following up on reports of previous meetings (2, 3), the current report describes highlights of the 16th Symposium and focusses on content presented by invited speakers. Submitted abstracts have not been published and were only available to attendees.

Pre-conference workshops

Diagnosing Sjögren's disease (SjD) can be challenging and improving diagnostic accuracy remains an important topic of research. Salivary gland ultrasono-graphy (SGUS) is an emerging, non-invasive imaging technique to detect aberrant morphology of major salivary glands (4). But how does a clinician determine if the SGUS image is typical for SjD, or not? This workshop focused on applying (novel) scoring techniques and imaging modalities in clinical practice.

The theme of the second workshop was SjD-related histopathology 'beyond the focus score'. The focus score is determined via a labial (or parotid) gland biopsy and is part of the classification criteria for SjD (5). A focus is defined as an aggregate of ≥50 lymphocytes and the focus score is the total number of foci per 4 mm^2 salivary gland tissue (6, 7). However, additional histopathological features associated with SjD can be identified in salivary gland biopsies and taking these features into account increases diagnostic accuracy (8). Workshop participants were trained to recognise additional histopathological features in digitalised images of salivary gland tissue.

Opening of the Symposium

The Symposium opened with a keynote lecture on immunomodulatory effects of sex hormones in humans by P. Brodin (Karolinska Institute, Sweden). Brodin presented that testosterone treatment (of subjects undergoing gender-affirming care) reduced anti-viral responses mediated by type-I interferon (IFN). Vice versa, estradiol treatment enhanced type-I IFN responses. As type-I IFN responses are increased in female-predominant, systemic autoimmune diseases like SjD, the presented research may shed new light on the influence of sex hormones on immune responses.

Key points from the Sessions

From a patient's point of view

The first Scientific Session was titled 'From a patient's point of view' and was opened by A. Baer (National Institute of Dental and Craniofacial Research (NIDCR), USA) and K. Hammitt (Sjögren's Foundation, USA). A fictive wonder drug to treat SjD was discussed: SjoGone ('siccakinumab'). By means of this panacea they illustrated the importance of aligning patient and clinician perspectives, for ex-

ample with regards to expectations on efficacy and side effects.

C. Shiboski (University of California San Francisco, USA) was invited to discuss prevention and management of oral complications and highlighted the added value of fluoride treatment to prevent caries. A. Vieira (Sjögren Europe) held an impressive presentation about living with SjD and the aspects that often remain unseen by the outside world. She stressed that patient involvement in research is important to advance our ability to treat SjD. In the same session, J. Koelewijn-Tukker from the Dutch Sjögren's Disease Patient Association (NVSP) shared a new tool to improve communication between patients and care providers called the 'The Sjögren's Symptoms Card and the Positive Health Spider Web'.

Glands and imaging

The next Session on 'Glands and Imaging' was opened by S. Jousse-Joulin (University of Brest, France). She discussed imaging of SjD with special reference to SGUS. Recent progressions in this field include the development of the OMERACT (Outcome Measures in Rheumatology) scoring system to standardise SGUS evaluation across different countries and centres, and implementation of colour Doppler to measure (potentially pathologic) salivary gland vascularisation. The second invited speaker for this session was C. de Paiva (Baylor College of Medicine, USA). This talk focused on the pathology of ocular dryness, and de Paiva showed that interferon-stimulated genes and other immune pathways are similarly upregulated in the conjunctiva of SjD and non-SjD dry eye patients compared to healthy controls. These findings suggest that upregulation of immune pathways in the conjunctiva is linked to dryness and not *per se* to an autoimmune process.

Pathogenetic aspects

During the Symposium, invited talks and oral presentations from abstracts related to 'Pathogenetic aspects' of SjD were divided over two sessions. The first invited speaker was B. Warner (NIDCR, USA), who revealed via spatial transcriptomics of labial salivary gland tissue that epithelial cells interact with CD8+ T cells via expression of major histocompatibility complex (MHC) Class-I. Warner described a population of tissue-enriched Granzyme-K (GZMK) expressing cells termed TteK CD8 cells in salivary gland tissue of SjD patients, and their potential ability to disturb acinar cell homeostasis via disruption of mitochondrial stability. At the same time, he found that seromucous acini were reduced. He further showed that GZMK can be taken up by autologous epithelial cells, resulting in higher levels of cytosolic DNA and IFN activation. The second invited speaker on 'Pathogenetic aspects' was G. Nocturne (University of Paris-Saclay, France). Nocturne presented work on salivary gland organoids to model SjD, showing that organoids can be grown from labial salivary gland cell suspensions derived from SjD patients. Although organoids from both control and SjD salivary glands proliferated in a comparable manner, those derived from SjD biopsies were imprinted with an IFN signature.

Trials and tools

Another session covered recent advances in clinical trials and outcome measures ('tools') for SjD. Dr S. Arends (University Medical Center Groningen, Netherlands) discussed the development and validation of composite outcome measures: Composite of Relevant Endpoints for Sjögren Syndrome (CRESS) and candidate Sjögren Tool for Assessing Response (STAR). Both endpoints consist of five domains: patient-reported symptoms, systemic disease activity, salivary gland, tear gland and serology. These new tools cover disease activity in a broad sense and take clinical heterogeneity into account. Post-hoc analyses of completed trials show a reduced placebo response with CRESS or STAR compared to EULAR Sjögren's syndrome disease activity index (ESSDAI) alone. The Trials and Tools session also included an abstract session where the latest, encouraging results from clinical trials with dazodalibep (CD40L antagonist), iscalimab (anti-CD40 monoclonal antibody), and ianalumab (anti-B-cell activating factor (BAFF) receptor monoclonal antibody) were presented.

Extraglandular involvement

In the Extraglandular Involvement Session, two important manifestations of SjD received specific attention: Dysautonomia and fatigue. B. Goodman (Metrodora Institute, USA) provided an overview of the various clinical expressions of dysautonomia in SjD patients. W-F. Ng (Newcastle University, UK) presented three main mechanisms underlying fatigue in SjD: inflammation, autonomic dysfunction, and depression/anxiety. Ng emphasised that fatigue is often multifactorial and concluded that a holistic approach is needed to address fatigue in SjD patients.

Classification and stratification

To practice precision medicine, the holy grail in modern medicine, different disease subtypes need to be identified. S. McCoy (University of Wisconsin, USA) presented an overview of known SjD endotypes, based on symptoms, clinical and biological manifestations, or a combination of those. Hierarchical clustering consistently separates patients with a high symptom burden from those with a low symptom burden, also when clinical and biological manifestations are included. In addition, McCoy presented work on novel autoantibodies against a peptide from D-aminoacyl-tRNA deacylase (DTD2) in anti-SSA negative SjD patients, a subgroup of SjD patients over which less is understood, which may help in the diagnosis of these patients.

Looking forward

The final Scientific Session was themed 'Looking Forward', to highlight future directions for SjD research. M. Bombardieri (Queen Mary University of London, UK) discussed the role of molecular pathology for (future) patient stratification in SjD. Bombardieri showed that the presence of ectopic lymphoid structures can be used to stratify patients with SjD and that clinical response to rituximab treatment was associated with biomarkers of salivary gland immunopathology.

Outstanding abstracts and young investigator awards

To acknowledge the abstracts that received the highest review score by the International Scientific Committee, an Outstanding Abstract Session was organised. D. Rebel (University Medical Center Groningen, the Netherlands) presented a qualitative study on sexual experience and functioning in female and male patients with primary SjD. C. Lessard (Oklahoma Medical Research Foundation, USA), presented results of a spatial transcriptomics study in human salivary gland tissue, revealing how different glandular cell types may be involved in the pathophysiology of SjD. Y. Nguyen (AP-HP Hospital Beaujon, France) presented a novel patient stratification method based on symptoms, clinical and routine biological data, and showed that different patient clusters were supported by distinct pathophysiological pathways. The fourth speaker in this session was B. Warner (NIDCR, USA), who showed that cGAS-STING pathway activation is a driver of type-I IFN in SjD.

Awards, closing, and 17th ISSjD

The meeting was closed with an awards ceremony. Three highly ranked abstracts presented by early career investigators were selected for a Young Investigator Award: D. Rebel (University Medical Center Groningen, Netherlands), C. Fugmann (Uppsala University, Sweden) and B. Carneiro Cintra (University of Sao Paulo, Brazil). Also, the location of the 17th ISSjD was announced: X. Mariette and his team will organise the next Symposium in Paris, France, in September 2026.

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