Heart Disease and Sjögren’s
by Nancy L. Carteron, MD, FAcR

Heart disease remains under-recognized in women. However, the findings of increased risk of heart disease in numerous autoimmune diseases, and the awareness of how heart symptoms differ in women compared to men, are improving the detection of cardiovascular disease in women. Heart disease in Sjögren’s has been studied less than in lupus, rheumatoid arthritis, and psoriatic arthritis. However, there are several published studies that provide a framework to begin to think about the risk and characteristics of heart problems in Sjögren’s.

Case Studies

Bartoloni et al (2015) looked retrospectively at a group of 1,343 Sjögren’s patients with comparison to age matched controls finding heart attack and heart failure were more common in those with Sjögren’s. Hypertension (high blood pressure) and hypercholesterolemia (high lipids) were more prevalent in smoking, obesity and

Ask the Experts
All About Dry Eye

The “Living with Sjögren’s” patient survey, conducted by Harris Poll on behalf of the Sjögren’s Syndrome Foundation (SSF), showed that 92% of Sjögren’s patients suffer from dry eye. Chronic dry eye has two main causes: decreased secretion of tears by the lacrimal (tear-producing) glands and loss of tears due to excess evaporation. Both can lead to ocular surface discomfort, often described as feelings of dryness, burning, a sandy/gritty sensation, itchiness, visual fatigue, sensitivity to light and blurred vision. In Sjögren’s, a person’s white blood cells mistakenly invade moisture-producing glands and affects the entire body, including the lacrimal glands, causing inflammation and reducing secretion,
diabetes, and less prevalent in Sjögren’s. An intriguing observation was that low white blood cell count (leukopenia) was associated with an increased risk of angina. However, this potential correlation will need further study to determine if it is a true correlation.

A meta-analysis of ten published observational studies of 165,291 patients (Yong 2018) found an increased risk of cardiovascular disease and increased artery stiffness in Sjögren’s. A meta-analysis is a statistical analysis that combines results from multiple scientific studies investigating the same question. This type of analysis can be used to identify a reproducible or “true” finding.

An older case-series (Rantapaa-Dahlqvist 1993) looked at 27 consecutive Sjögren’s patients by echocardiogram (ECHO), heart ultrasound. Nine patients (33%) had current or past evidence of pericarditis, which is inflammation of the lining around the heart (pericardium). Four of the nine patients had focal decrease function of the heart muscle (left ventricle), commonly a result of prior ischemia. Ischemia, decreased blood flow to tissue, can lead to damage of the heart muscle and result in decreased ability of the heart to pump oxygenated blood to the body. Ten of the 27 Sjögren’s patients had symptoms of angina, palpitations, dyspnea (shortness of breath), and chest pressure. Thirteen patients reported Raynaud’s, fifteen reported joint pain (arthralgia), and four patients reported having joint inflammation (synovitis). Subsequent studies have suggested a high prevalence (up to 30%) of current or past pericarditis detected by ECHO. However, this commonly does not result in clinical problems.

There have been case reports of myocarditis (heart muscle inflammation) leading to congestive heart failure (CHF), and improvement with steroid treatment over a number of years. Therefore, myocarditis associated with Sjögren’s should be considered in the differential diagnosis of cardiomyopathy and/or new onset CHF. Pulmonary hypertension also occurs in Sjögren’s, as with other autoimmune diseases, particularly lupus and scleroderma. ECHO can screen for elevated right heart pressure, with right heart catheterization study needed to establish the diagnosis. Pulmonary hypertension can lead to heart dysfunction. A Turkish study (Kocab 2014) of 47 Sjögren’s patients utilizing ECHO showed elevated pulmonary artery systolic pressure (PASP); PASP>30 mmHg in 23%, which supports PASP>35 mmHg in 5 patients. PASP<=30 mmHg supports a diagnosis of pulmonary hypertension. The gold
A well-established Sjögren’s disease activity measure, the EULAR Sjögren’s Syndrome Disease Activity Index (ESSDAI) developed by European colleagues in France (Seror 2010) does not include a cardiac disease domain. The ESSDAI has been validated and is currently used in clinical trials for new systemic therapies for Sjögren’s. An opportunity to further capture information regarding cardiovascular findings in Sjögren’s is being missed, given the lack of a cardiac domain in this measure.

**Conclusion**

Given that heart disease is increased in autoimmune disease, and probably specifically in Sjögren’s, and heart disease in all women may still be under-diagnosed, an increased index of suspicion for cardiovascular disease is warranted in Sjögren’s patients.

**Established risk factors for cardiovascular disease include:**

- High blood pressure
- High lipids
- High glucose/diabetes
- Smoking
- Obesity
- Chronic kidney disease
- Chronic liver disease
- Chronic inflammation

**Risk factors unique to women include:** (Maffei 2019)

- Hormone medications
- Menopause
- Premature ovarian failure
- Endometriosis
- Recurrent pregnancy loss
- Phospholipid antibodies/pro-clotting

**Summary**

- Heart disease and cerebral vascular disease are likely increased in Sjögren’s, and may be under-appreciated
- Severity and chronicity of inflammation likely increases risk

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Continued on page 4 ▼
In addition to myocardial infarction, pericarditis, myocarditis, and pulmonary hypertension can occur.

Many risk factors can be modified: HTN, weight, lipids, smoking, exercise, nutrition.

Unique female risk factors: hormones, primary ovarian failure, phospholipid antibodies.

Discuss cardiovascular risk factor assessment with your PCP, rheumatologist, OBGYN, and cardiologist for further risk-assessment.

Citations

Abrol et al., A Retrospective Study of Long-Term Outcomes in 152 Patients with Primary Sjögren’s Syndrome. Clin Med (Lond) 14:157-164, 2014. (PMID: 24715127)


Wu et al., Increased Risk of Coronary Heart Disease among Patients with Primary Sjögren’s Syndrome. Sci Rep 8:2209, 2018. (PMID: 29396489)

Yong et al., Association between Primary Sjögren’s Syndrome, Cardiovascular and Cerebrovascular Disease. Clinical and Experimental Rheumatol 36:190-197, 2018. (PMID: 29600936)

Ask the Experts

which causes dry eye to be one of the primary symptoms of the disease.

In 2005, Congress officially declared July “Dry Eye Awareness Month” to help educate the public about symptoms and treatment options. In honor of this past Dry Eye Awareness Month, the Foundation is bringing you a few of our most popular dry eye questions from leading experts aimed to promote dry eye education.

Q: “I have heard about sclera contact lenses. Can you tell me about their pros and cons?”

A: Scleral contact lenses (sclerals) are large-diameter rigid contact lenses that, unlike small-diameter rigid contact lenses and soft contact lenses, do not rest on the cornea, which is one of the most sensitive places on the body. Instead, they vault over the cornea and rest on the sclera, the white outer wall of the eye.

Sclerals are made of healthy materials and can be used by optometrists to help improve the health of the ocular surface when dry eye syndrome, due to Sjögren’s and many other conditions, are unable to be managed with Restasis® or artificial tears.

Benefits of scleral lenses

For the surface of the eye:

- People who suffer from dry eye due to Sjögren’s are likely to have at least some damage to the cornea, the front surface of the eye. Scleral lenses create a “pool” of fluid between the back surface of the contact lens and the cornea. This fluid can provide immediate relief from the irritation dry eye causes and, in many cases, allows the corneal surface to heal while the lens is being worn.

- Sclerals allow 2-4 times more oxygen to pass through to your eyes than regular soft contact lenses.

For your vision:

- Many people who have an irregular cornea (due to dry eye disease, keratoconus, corneal transplant, LASIK, RK, PRK, or trauma) also have decreased and/or unstable vision. Scleral lenses mask this irregularity and provide a smooth, round front surface for light to enter the eye.

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**Angina**: a type of chest pain caused by reduced blood flow to the heart. A symptom of coronary artery disease.

**Arrhythmias**: a problem with the rate or rhythm of your heartbeat. It means that your heart beats too quickly, too slowly, or with an irregular pattern.

**Cardiomyopathy**: a disease of the heart muscle that makes it harder for your heart to pump blood to the rest of your body. Cardiomyopathy can lead to heart failure.

**Congenital heart block (CHB)**: is a rare condition that affects the heart’s electrical system, which controls and coordinates its pumping function. In infants affected by this condition, the electrical signal that spreads across the heart and causes it to contract and pump blood, is slowed or completely interrupted.

**Congestive heart failure (CHF)**: occurs when your heart muscle doesn’t pump blood as well as it should. Certain conditions, such as narrowed arteries in your heart (coronary artery disease) or high blood pressure, gradually leave your heart too weak or stiff to fill and pump efficiently.

**Diastolic**: relating to the phase of the heartbeat when the heart muscle relaxes and allows the chambers to fill with blood.

**Dyspnea**: shortness of breath. Often described as an intense tightening in the chest, air hunger, difficulty breathing, breathlessness or a feeling of suffocation.

**Echocardiogram (ECHO)**: heart ultrasound that uses sound waves to produce images of your heart. This common test allows your doctor to see your heart beating and pumping blood.

**Heart palpitations**: the feelings of having a fast-beating, fluttering or pounding heart.

**Myocarditis**: an inflammation of the heart muscle (myocardium). Myocarditis can affect your heart muscle and your heart’s electrical system, reducing your heart’s ability to pump and causing rapid or abnormal heart rhythms (arrhythmias).

**Pericarditis**: swelling and irritation of the pericardium, the thin sac-like membrane surrounding your heart. Pericarditis often causes chest pain and sometimes other symptoms. The sharp chest pain associated with pericarditis occurs when the irritated layers of the pericardium rub against each other.

**Phospholipid antibodies**: when antibodies attack phospholipids, cells are damaged. This damage causes blood clots to form in the body's arteries and veins. (These are the vessels that carry blood to your heart and body.)

**Pulmonary hypertension (PH)**: a type of high blood pressure that affects the arteries in your lungs and the right side of your heart.

**SSA**: Sjögren’s associated antigen A (anti-Ro). About 40-60% of Sjögren’s patients are positive for anti-SSA.

**SSB**: Sjögren’s associated antigen B (anti-La). About 20-30% of Sjögren’s patients are positive for anti-SSB.

**Synovitis**: inflammation of the tissues lining a joint.

**Systolic**: relating to the phase of the heartbeat when the heart muscle contracts and pumps blood from the chambers into the arteries.
Some people are unable to wear other forms of contact lenses and may find that sclerals are more comfortable than the other contact lenses they’ve attempted due to their larger diameters.

Scleral contacts are available for people who need to wear multifocal or bifocal lenses to enhance their near and intermediate-distance vision.

**Comfort**

- The large diameter lens fits under the upper eyelid. This allows the lens to be very comfortable because the edge of the eyelid does not bump over the upper edge of the scleral.
- Since the lens is custom-made for each eye, the edges can be optimized for best comfort on your eye. The scleral acts as a “bandage” to cover any irritating areas on the cornea, in a similar way dry eye irritation is relieved.

**Value**

When properly cared for, sclerals are durable and have a long life of use, providing great value.

**Drawbacks of scleral lenses**

**Measurements and customization**

Special measurements and customization are needed to fit the lens to your eye and visual needs. This fitting process will likely take place over several visits to your optometrist.

**Lens handling**

There is a small learning curve with how to handle the lenses because of their unique attributes. Your optometrist and their staff will coach you on the best technique to get the lenses in and out.

However, the customization process and learning how to handle this special type of contact lens is a small hindrance considering the amazing things they can do for your vision!

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**“Ask the Experts” continued from page 4 ▼**

**Q**

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**Martin O’Donnel, OD**

President/CEO of Vision Source in Holdenville, OK

**Gary Foulks, MD, FACS**

"Ask the Experts" continued from page 4 ▼
Clinical News
Cardiovascular

Sjögren’s-Related Antibodies Associated with Increased Risk for Cardiovascular Disease

Investigators have noted a marked increase in risk of cardiovascular disease in Ro/SSA- and La/SSB-positive Sjögren’s patients compared to the general population. Sjögren’s patients (n=960) and matched controls from the general population (n=9,035) were identified from the Swedish National Patient Register, with their records being analyzed for myocardial infarction (heart attack), cerebral infarction (stroke) and venous thromboembolism (blood clot). Combined, the groups had hazard ratios (HR) of 1.6 (95% CI 1.2-2.1) for myocardial infarction, 1.2 (95% CI 0.9-1.7) for cerebral infarction and 2.1(95% CI 1.6-2.9) for venous thromboembolism. Compared to the general population, patients positive for both Ro/SSA and La/SSB had a significantly higher risk for both cerebral infarction (HR 1.7, 95% CI 1.0-2.9) and venous thromboembolism (HR 3.1, 95% CI 1.9-4.8). A higher disease duration, ≥10 years in this study, was associated with highest risk for cerebral infarction (HR 2.8, 95% CI 1.4-5.4), while those between 0 and 5 years after diagnosis were at the highest risk for venous thromboembolism (HR 4.7, 95% CI 2.3-9.3). These findings support that monitoring and preventive measures for cardiovascular disease should be considered for this patient group.

Citation

Risk for Venous Thrombosis Identified in Sjögren’s

Investigators have concluded that Sjögren’s patients are potentially at higher risk for venous thrombosis, with interstitial lung disease and anti-SSA positivity increasing that risk. A total of 16 Sjögren’s patients were included in this retrospective study, 14 of which had lower extremity venous thrombosis while the remaining two had jugular vein thrombosis. At admittance, 12 patients had symptoms of dryness and four had pulmonary symptoms. All cases in this study were found to

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have interstitial lung disease and 12 of the 16 cases were anti-SSA positive. Notably, the authors found that patients were negative for antiphospholipid antibodies, which are normally associated with blood clotting in autoimmune populations.

Citation

Sjögren’s Associated with Increased Cardiovascular Morbidity

Investigators have concluded that Sjögren’s is associated with an increase in cardiovascular morbidity and suggest Sjögren’s patients be screened by a cardiologist for cardiovascular comorbidities for preventive interventions as part of a multi-disciplinary approach. In a meta-analysis, it was found that Sjögren’s patients, when compared to controls, were at a significantly increased risk for coronary morbidity (RR=1.34, 95%CI: 1.06-1.38; p=0.01), cerebrovascular morbidity (RR=1.46, 95%CI: 1.43-1.49, p<0.00001), heart failure rate (odds ratio=2.54, 95%CI: 1.30-4.97, p<0.007), and thromboembolic morbidity (RR=1.78, 95%CI: 1.41-2.25, p<0.00001). However, there was no statistically significant increased risk of cardiovascular mortality (RR=1.48, 95%CI: 0.77-2.85, p=0.24). A total of 484 articles were identified from the MEDLINE and COCHRANE databases in addition to abstracts from recent meetings held in the U.S. and Europe. Fourteen of these articles, involving 67,124 Sjögren’s patients, were included in the study.

Citation
You Stood Up!

Celebrating Our Strength: SSF Members Stand Up Around the Country

As the Sjögren’s Syndrome Foundation starts planning for the fall and a new year of events, we want to thank everyone who stepped up by attending, volunteering or donating to one of our events over this past year! Our success is a direct result from you, our amazing volunteers and supporters. Thank you for being a part of our journey to conquer the complexities of Sjögren’s.

The funds you raised allow us to continue providing programs and services, advocating for patients and funding research for the four million people living with Sjögren’s. Together we are working to develop new therapeutics to treat this debilitating disease and transform the future for all patients.

Celebrating the Best of the Best

More than 1,500 patients, family members, friends and healthcare providers joined us to strengthen the fight against Sjögren’s. You raised funds, donated, volunteered and helped us increase awareness by being a part of one of our events.

To help raise funds, these dedicated volunteers write letters, make phone calls, secure sponsors, and use social media to reach their fundraising goals. Thanks to all of your support and hard work, we raised over $200,000 from Foundation events!

A look back at the 2018-2019 SSF National Events:

- Los Angeles Area Walk for Sjögren’s and Health Fair, La Mirada, CA – October 20, 2018
- Austin Area Walk for Sjögren’s and Health Fair, Austin, TX – November 3, 2018
- Team Sjögren’s Goes Turkey, Turkey Trots Nationwide – November 22, 2018
- Team Sjögren’s New Orleans, New Orleans, LA – February 10, 2019
- Phoenix Area Walk for Sjögren’s and Health Fair, Phoenix, AZ – February 23, 2019
- SSF National Patient Conference, Woburn, MA – April 5–6, 2019
- Boston Area Walk for Sjögren’s at the SSF National Patient Conference, Woburn, MA – April 6, 2019
- Tastefully Georgia, Atlanta, GA – April 28, 2019
- Philadelphia Tri-State Area Walk for Sjögren’s and Family Fun Day, Philadelphia, PA – May 4, 2019
- Washington, D.C. Metro Area Walk for Sjögren’s and Health Fair, Reston, VA – May 18, 2019
- Denver Area Walk for Sjögren’s and Family Fun Day, Littleton, CO – June 8, 2019
- Dallas Area Walk for Sjögren’s and Health Fair, Arlington, TX – June 22, 2019

View the upcoming 2019 SSF National Event Calendar on page 15.
Thank you for Supporting a 2018-2019 Walk for Sjögren’s

We are truly grateful to all our Walk for Sjögren’s Sponsors! These sponsors demonstrated a commitment to supporting local Sjögren’s communities across the country, while also generously impacting the overall success of the Walks.

Thank you to our Local Presenting and Major Walk Sponsors

Austin Area Walk for Sjögren’s and Health Fair
- OCuSOFT
- Prisyna

Boston Area Walk for Sjögren’s at the SSF National Patient Conference
- GEICO Philanthropic Foundation
- Eye Eco

Dallas Area Walk for Sjögren’s and Health Fair
- Dr. David Brumbaugh DDS
- Fagadau, Hawk and Swanson, MD
  Eye Physicians and Surgeons
- James and Stacie Thomas
- The Bromberg Family
- The Rubenstein Family

Denver Area Walk for Sjögren’s and Family Fun Day
- Colorado Eye Consultants
- Jim and Joan Walsh Foundation
- Ken and Anne Economou

Los Angeles Area Walk for Sjögren’s and Health Fair
- Eye Eco
- Prisyna

Philadelphia Tri-State Area Walk for Sjögren’s and Family Fun Day
- Bassett Home Furnishings
- Lehigh Valley Plastics
- Leventhal Sutton and Gornstein
- Penn Dry Eye and Ocular Surface Center
  Scheie Eye Institute
- Penn Medicine Valley Forge
- Penn Sjögren’s Center and Division of Rheumatology
- St. Luke United Methodist Church
- The Vivino Family

Phoenix Area Walk for Sjögren’s and Health Fair
- Doctor My Eyes
- Gilbert Center for Family Medicine
- Mayo Clinic
- Spinato’s Pizzeria and Family Kitchen

Washington, D.C. Metro Area Walk for Sjögren’s
- Arthritis and Rheumatism Associates, P.C.
- Ben and Jerry’s Rockville
- Johns Hopkins Jerome L. Greene Sjögren’s Syndrome Center
- NOVA Perio Specialists

Thank you for being a STAR!

Thank you to our Volunteer Walk Committees, Local Walk Sponsors, and a special thank you to everyone who achieved our “Sjögren’s Star Status” by raising over $1,000 for a Walk for Sjögren’s! View our Sjögren’s Stars, on www.sjogrens.org.
Each fall your local United Way, Combined Federal Campaign, state employee, and private employer payroll deduction campaigns begin. We hope you will remember the Sjögren’s Syndrome Foundation when choosing where to allocate your donation. (CFC #10603)

If we are not listed on the contribution form, you usually may write in the Sjögren’s Syndrome Foundation.

Tell your co-workers, friends, and family members how important it is to choose and write in the Sjögren’s Syndrome Foundation on their campaign form, too.

If your employers will not allow you to write in the Sjögren’s Syndrome Foundation, remind them that we are a national non-profit 501(c)3 organization and qualify for most payroll deduction campaigns. If they need more information, please contact the Foundation at 800-475-6473.

Just think – every dollar counts.

Last year alone – thanks to those who chose to give through their employer’s payroll campaign – the Sjögren’s Syndrome Foundation was able to increase its Research and Awareness commitments.
Since January 1, 2017, the European Commission has provided funding of 10 million euros for HarmonicSS, one of the largest research grants ever given for Sjögren’s. This endeavor has 35 participating partners, including 21 clinical centers, eight technical partners, three partners related to public health and two patient associations, the EULAR-PARE and the Sjögren’s Syndrome Foundation.

The vision of HarmonicSS is to create an international network and alliance of partners and cohorts entrusted with the mission of addressing the unmet needs in Sjögren’s in a multidimensional way.

The partners, working together, have created and maintain an electronic platform with open standards and tools, enabling the secure storage, governance, analytics, access control and controlled sharing of information. The overall idea of the HarmonicSS project is to bring together large, well-characterized European cohorts of Sjögren’s patients. Additionally, after taking into consideration the ethical, legal, privacy and IPR issues for sharing data from different countries we are working to interlink and harmonize them in the cloud as an integrated Sjögren’s cohort. Upon harmonization, services for big data mining governance and visual analytics will be integrated to address the unmet needs identified for Sjögren’s. To this end, the electronic platform is created to:

- Provide a training tool for non-specialized physicians and patients.
- Perform genetic data analytics in an attempt to compare the different genotypes of patients within the clinical picture.
- Develop a stratification model by defining the different phenotypes of the disease.
- Validate existing biomarkers and discover novel ones.
- Identify models of lymphomagenesis, as lymphoma is the worst outcome of the disease.
- Formulate clinical practices for patients and physicians.
- Develop salivary gland ultrasonography image segmentation.
- Search and suggest health policies related to Sjögren’s and evaluate their implementation.

The users of the HarmonicSS platform are clinicians, researchers undertaking basic and translational research, health policy makers and patient associations.

I wish to emphasize and recognize the highly important contributions of the patient associations, particularly EULAR-PARE and the Sjögren’s Syndrome Foundation. One big success has been EULAR-PARE creating a chapter of Sjögren’s patient advocates from all over Europe, named SS Europe. Last but not least, these partners have made great contributions in helping to disseminate the results of this important project.
Audio talks of the most popular talks from our 2019 SSF National Patient Conference in Woburn, Massachusetts, are now available with the follow-along PowerPoint presentation printouts.

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<td>Understanding Blood Changes and Lab Results by Alan N. Baer, MD</td>
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<tr>
<td>Ocular Manifestations of Sjögren’s by Esen K. Akpek, MD</td>
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<td>How Sjögren’s Can Impact the Central Nervous System by Edward A. Maitz, PhD</td>
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<td>Nutrition, Wellness and Autoimmune Disease by Lauri Lang, RDN, LDN</td>
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Shipping and Handling:
- Audio Download: FREE
- CD: $7 for first item + $1 for each additional item

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SSF EVENT CALENDAR

To learn more about SSF events, please visit www.sjogrens.org or contact Jessica Levy at (301) 530-4420 ext. 218 or email jlevy@sjogrens.org.

SEPTEMBER
Team Sjögren’s Philadelphia
Sunday, September 15, 2019
Philadelphia, Pennsylvania

OCTOBER
Los Angeles Area Walk for Sjögren’s
Saturday, October 19, 2019
La Mirada Community Regional Park

NOVEMBER
One Day Sjögren’s Patient Conference
Saturday, November 2, 2019
Hilton Garden Inn Cleveland-Downtown

Austin Area Walk for Sjögren’s
Saturday, November 9, 2019
Round Rock Premium Outlets

Feature Study:
Do you suffer from Dry Eye?
A Sjögren’s and Dry Eye Study may be happening in your area.
To learn more call: (919) 353-5938 or email csherry@tearsolutions.com
Visit: www.TearSolutions.com

Clinical Trials in Sjögren’s

The SSF now has a section on its website devoted to clinical trials in Sjögren’s. Visit www.sjogrens.org/home/about-sjogrens/clinical-trials-whatsinvolved.
World Sjögren’s Day

Each July 23rd, the SSF joins with Sjögren’s organizations around the world to celebrate World Sjögren’s Day, which commemorates the birthday of Dr. Henrik Sjögren, a Swedish ophthalmologist who first identified the disease in 1933.

World Sjögren’s Day is an opportunity to recognize advancements made in Sjögren’s this past year and the incredible progress the SSF has made on behalf of Sjögren’s patients. More importantly, it is a way to help raise awareness of this complex disease and funds for future research.

Thank you to everyone who helped celebrate World Sjögren’s Day by sharing your story or donating to the Foundation’s research efforts. Together, we are transforming the future for all Sjögren’s patients!

Visit www.sjogrens.org to learn more about the World Sjögren’s Day 2019!