CONQUERING Sjögren's

July/August 2024

July is Dry Eye Awareness Month

Inside this Issue

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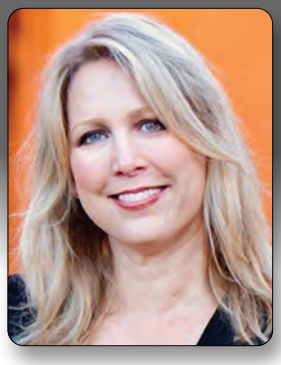
My Eye Surgery Experience with Severe Sjögren's Dry Eye



by Janet Church

I have severe dry eye. I have felt the dryness accelerate over the past 10 years and I suspect this is common for many Sjögren's patients; especially over the age of 55. Several times over the past six years, I have tried to acclimate to a cyclosporine or liftegrast treatment protocol, but the burning and excessive irritation did not allow me to continue. I really wish one of my optometrists or ophthalmologists had prescribed cyclosporine 20 years ago (at diagnosis) when the anti-inflammatory drug may have been tolerable as it may have slowed the progression of my dry eye!

For many years, I used only Systane Ultra eye drops, and then in 2019, I began to occasionally use steroid drops and ointments when I had significant issues. This helped for a while, but steroid use for long-term was not recommended to me due to concerns of increased eye pressure. So, preservative-free Systane Ultra eye drops has been the main therapy for my eyes. Because I have been on hydroxychloroquine since diagnosis 20 years ago, I have seen an ocular specialist every six months for testing to ensure there is no eyesight damage due to the drug. Hydroxychloroquine works well for me, so I am always relieved that my tests are good— 20 years on hydroxychloroquine is a long time.

NOTE: For Sjögren's patients, it is recommended that cyclosporine or lifitegrast is used early to reduce inflammation and slow the progression of dry eye and ocular issues that arise from dry eye, some of which can be serious.

When I moved to Virginia in July 2021 from the West Coast, I selected Dr. Esen Akpek at Johns Hopkins Wilmer Eye Institute to be my doctor and set my appointment in 2022 (I had seen an optometrist before I moved, and I thought I was good to go for at least six months). Although the drive to Johns Hopkins is almost two hours from my home, the extra time to see a Sjögren's expert such as Dr. Akpek was worth it to me as I was having significant issues with dry eye, sight, and pain. Dr. Akpek put me through many tests, including lissamine green dye and slit lamp testing, to look closely at the level of dry eye and determine if there was any ocular damage. To my dismay, the tests showed advancing dry eye with cornea abrasion, nerve damage, and conjunctivochalasis. This last thing— conjunctivochalasis— was a symptom of dry eye of which I had never heard! At this appointment Dr. Akpek placed punctal plugs in my lower ducts and asked that I try cyclosporine again, and then lifitegrast; however, I could not tolerate the pain and irritation. So, she put me on a course of steroids and increased my use of eye drops (serum tears and OTC eye drops). The next visit, I had not improved enough, and so I began the process of getting autologous serum tears and using those with saline drops throughout the day with ointment at night. There was some improvement but still not enough, so we began talking about conjunctivochalasis surgery.

Conjunctivochalasis is when the conjunctiva, the membrane covering your eyeball, loosens and can fold on itself causing ripples and folds in the membrane. These ripples or folds can then trap tears on one side of your eye, prevent tears (or drops) from smoothly covering the entire eyeball, and create very dry areas of the eye that exacerbate conjunctivochalasis causing further damage. It also explained why I felt like I had a soft "something" in my left eye that seemed to improve if I rubbed my eyelid to "smooth it out".

NOTE: In the May/June 2023 issue of Conquering Sjögren's (page 13), Dr. Akpek writes about the conjunctivochalasis surgery I had. It is titled "An Eyeball Tummy Tuck". There are also tips from Dr. Guo on page 6 of this same issue. As a Member of the Foundation, you have access to this issue and past Conquering Sjögren's issues on the member side of the website!

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After a longer period of serum tears and my new punctal plugs in place, I finally agreed to the surgery as my dryness was not improving enough. The key reason I agreed to the "eyeball tummy tuck" is that I was also getting cataracts, and Dr. Akpek will not perform the cataract surgery without the dry eye being under control to support a successful cataract surgery and healthy recovery.

NOTE: In order to obtain the best outcomes from cataract surgery, the procedure should be delayed, if necessary, in order to aggressively manage the dry eye. In addition, all other concurrent ocular surface diseases such as blepharitis, superior limbic keratoconjunctivitis, conjunctivochalasis, or eyelid problems should be addressed well before the cataract removal surgery. From Dr. Akpek's article on cataract surgery on page 5.

Dr. Akpek also mentioned she prefers to perform cataract surgery early on in Sjögren's patients, so it was time I started to make a decision and plan for my eyes. This was in August 2023. I had conjunctivochalasis surgery on my left eye (greater folds and dryness) in December 2023. Essentially, glue is placed on the outer edges of your eyeball and the conjunctiva is then pulled smoothly across your eyeball. The excess membrane is then snipped off. During the surgery we also decided to cauterize my upper tear duct and keep my bottom plug in for the best success. The surgery went well, and I went home and rested. On the second day, the eye coverings were removed. I did have a pretty sore eye for about 4 days until it began improving to where I could read comfortably. By the 8th day, I felt pretty good, and I could tell that my eye felt less dry. I also received the lab results back from the tissue and there was nothing suspicious, but the description of the removed tissues said, "grey keloid-like tissue".

After a month of healing, my left eye felt about the same as my right (in terms of dryness) and I decided NOT to perform the conjunctivochalasis surgery on my right eye. My eyes still feel very dry, but they are healthier, including reduced corneal abrasions.

Now, we are preparing for my cataract surgeries in July with the right eye first. We met to discuss which lenses will be used, and I chose to get back my distance vision and use readers moving forward (Dr. Akpek does not recommend multifocal lenses for Sjögren's patients).

Although my eye dryness has improved with the regimen I have followed, Dr. Akpek is still concerned with the level of dryness as of June. So, I have increased my serum tear use throughout the day, which takes planning since serum tears must be refrigerated at all times. Then 3 weeks before my surgery, I will start a nightly steroid ointment to prepare for the surgery (Dr. Akpek prefers ointment since the steroid eye drops have a preservative that can be drying).

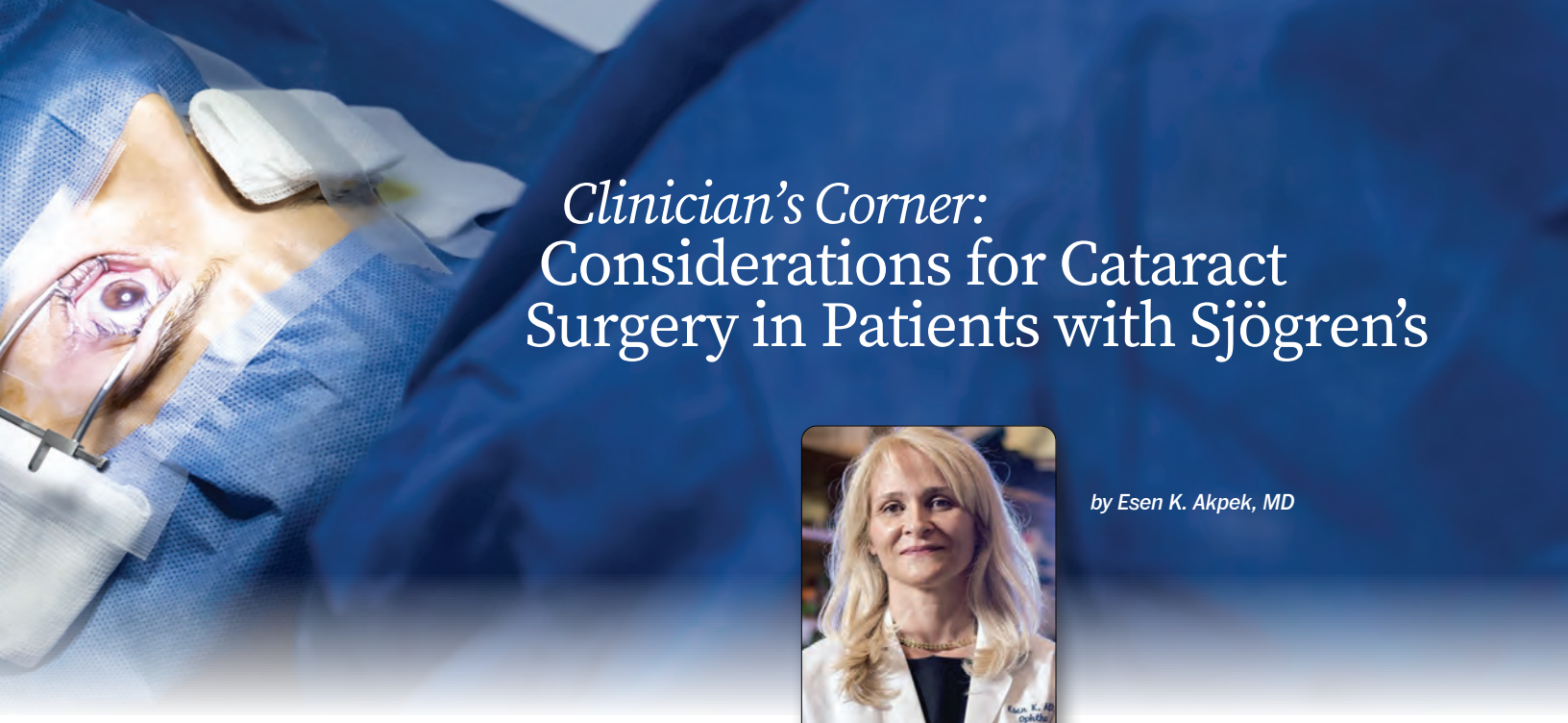
Once my right eye heals from the surgery, we will test my vision again so we can tweak the lens for my left eye (my dominant eye) to get the best vision based on my preferences and Dr. Akpek's recommendation. During this surgery, we will also cauterize my right eye's upper tear duct. I will let you know how the cataract surgery goes and if there are any specific details that may help others get ready for eye surgery.

Eye surgery is a bit unsettling, and I was surprised to learn about this symptom and issue of "conjunctivochalasis". I hope my experience helps you and your eye care provider consider this symptom and best prepare for any eye surgery. Consider taking my article, Dr. Akpek's cataract surgery article, and the conjunctivochalasis article to your provider. I know most Sjögren's patients do not have access to experts such as Dr. Akpek, but I hope these articles can help educate your provider to support the most successful surgeries for YOU! ■

Do we have your current e-mail address?

If you want to receive all the latest updates from the Sjögren's Foundation, then you should make sure we have your most up-to-date e-mail address! The Foundation is starting to share more information via e-mail, from news about the Foundation and Sjögren's, to information about the latest treatments and medicines, to local Support Group updates and more. So contact us at info@sjogrens.org to be certain we have your latest e-mail address in our database, and then keep an eye out in your Inbox for Sjögren's news.

Just like all information you give the Foundation, your e-mail address will remain private and will never be given or sold to an outside organization.



Clinician's Corner: Considerations for Cataract Surgery in Patients with Sjögren's

by Esen K. Akpek, MD

Concurrent dry eye and cataract is common due to overlapping epidemiology since both conditions affect older individuals. The presence of dry eye in patients presenting for cataract surgery is frequently underappreciated by the evaluating surgeon, leading to undermanagement of the condition preoperatively. Significant corneal epithelial micro-erosions can create an irregular corneal surface, which may impact vision and cause decreased contrast sensitivity– the difficulty perceiving and distinguishing objects or patterns with subtle differences in contrast. This can complicate assessing the significance of the cataract on the patient's vision-related quality of life. In addition, if not addressed prior to surgery, the punctate micro-erosions of the cornea (visualized as punctate staining of the corneal surface with fluorescein dye) will likely worsen causing post-operative patient dissatisfaction due to ocular discomfort and blurred vision.

Unfortunately, the importance of dry eye may not always be recognized by the patients presenting for cataract evaluation. Patients may be unaware of the relation and fail to mention that they have a prior diagnosis of dry eye. Particularly, the individuals with serious dry eye, such as patients with Sjögren's, may only notice fluctuation or blurring of vision and may not complain of dryness or eye pain. This is due to corneal nerve damage because of the ongoing ocular surface inflammation leading to reduced corneal pain sensation. Because cataracts also cause vision problems, the surgeon may not necessarily suspect the presence of dry eye, unless informed by the patient. Therefore, it is important to see a qualified cataract surgeon who will perform a thorough ocular surface evaluation, particularly staining of the cornea and conjunctiva using vital dyes even in the absence of any patient reported ocular dryness of discomfort symptoms.

In order to obtain the best outcomes from cataract surgery, the procedure should be delayed if necessary, in order to aggressively manage the dry eye. In addition, all other concurrent ocular surface diseases such as blepharitis, superior limbic keratoconjunctivitis, conjunctivochalasis, or eyelid problems should be addressed well before the cataract removal surgery.

The following can be helpful tips for the patients seeking cataract removal surgery as well as the cataract surgeons:

- Review of medical history and medications can be helpful to raise a red flag to perform detailed dry eye evaluations, even in the absence of prior diagnosis of dry eye or patient reported symptoms.
- Presence of micro-erosions of the corneal epithelium can lead to inaccurate biometry for intraocular lens implant measurements and calculations, which subsequently lead to unexpected post-operative refractive errors. Therefore, these need to be identified and managed pre-operatively, as recommended by the American Society of Cataract and Refractive Surgery.
- Patients with Sjögren's- related dry eye will not get the benefits of multifocal intraocular lens implants because of higher order aberrations and decreased contrast sensitivity. Patients with autoimmune diseases and dry eye receiving multifocal intraocular lens implants frequently complain of significant visaul symptoms such as halos, glare, starburst, or distortion. Traditional monofocal

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implants, monofocal implants with extended depth of focus or monofocal astigmatism correcting toric lens implants would work well.

- It is important to keep the cornea moist during the surgical procedure by coating it with high concentration hyaluronic acid containing ophthalmic viscoelastics rather than balanced salt solution drops. This will prevent washing away the precious mucin layer of the pre-corneal tear film due to frequent drop instillation during surgery.
- Minimizing post-operative drop regimen by injecting an intracameral (anterior chamber of the eye) antibiotic and inserting a steroid containing tear duct plug at the completion of surgery could help reduce the inevitable post-operative worsening of dry eye findings.
- Post-operative topical non-steroidal anti-inflammatory drops can worsen dry eye by reducing blink rate which increases the tear film evaporation and by reducing tear production through numbing of the ocular surface. They should be used judiciously and only when indicated, with a preference for preparations that have the least drop frequency and the lowest levels of benzalkonium chloride preservatives.
- In cases where dry eye is especially very severe, use of post-operative amniotic membrane grafting over the cornea immediately at the completion of the surgery could be helpful. Although, because the membrane is semi-transparent, the visual improvement will be delayed for about a week, until the membrane dissolves.
- Lastly, in the post-operative period, patients with Sjögren's- related dry eye should be monitored more closely to ensure the healing of the eye without any corneal or conjunctival complications. ■

Summer Sun Safety

by Mona Z. Mofid, MD, FAAD

Ultraviolet (UV) radiation emitted from the sun and other light sources (such as some fluorescent lights) can alter immune function and lead to an autoimmune response in the body and in the skin. Skin rashes and disease flares in Sjögren's patients can result as well as ocular sensitivity and pain. In Sjögren's, sun sensitivity is associated with the autoantibody SSA/or Ro. To avoid reactions to UV light, try the following tips:

- Protect your skin and eyes through use of sunscreen, sunglasses, ultraviolet light-protective clothing, hats, and non-fluorescent lighting.
- Use sunscreen that protects against both UVA and UVB rays. Doctors now recognize the dangers of UVA light in addition to those of UVB.
- Look for the words "broad spectrum," which often are used to mean protection from both UVA and UVB light. Note that SPF ratings refer only to UVB rays. In the U.S., a "star" rating on products is coming into increased use to help consumers figure out how much UVA protection is provided. A European rating referred to as "PFA" measures UVA protection.
- Use plenty of sunscreen! Most people only use about 1/3 the recommended amount of sunscreen. This reduces the benefit of the SPF rating.
- Use a higher number SPF sunscreen.
- Remember that water, humidity and sweating decrease sunscreen effectiveness and mean you must reapply your sunscreen.
- Wear sun-protective clothing. It is designed to protect your skin from UVA and UVB rays, is more reliable than sunscreen, does not wash off or need to be reapplied, can be washed and dried quickly, and, compared to sunscreen, is not known to cause skin reactions.
- Don't forget to wear sunscreen on areas not covered by sun-protective clothing, such as the neck and ears. Consider purchasing UV-protective car and home window films (which come in clear) and tinting.
- Wear good UV-protective eye lenses and sunglasses.
- Seek the shade when outside.
- Investigate whether UV-protective clothing and eyewear, window shields, and sunscreens are eligible for reimbursement under your insurance plan or Flexible Health Care Spending Account.

Announcing a new Sjögren's Patient Support Community – Join Today!

The Sjögren's Foundation is excited to announce a new Sjögren's Patient Support Community. In partnership with Inspire, a leading provider of online health communities, we invite you to join this community where patients can connect, share tips, ask symptom questions, and learn from one another virtually.

Inspire has been supporting online patient communities since 2006. Through the years they have built over 250 communities that focus on relevant health topics. This partnership will allow those with multiple and overlapping diseases and health challenges to find peer support all in one place. Other topic communities of particular interest to Sjögren's patients may be:

- Autoimmune Disease
- Arthritis
- Dysautonomia Support Network
- Fibromyalgia
- Lupus Connect
- Scleroderma
- Peripheral Neuropathy
- Psoriasis
- Headaches and Migraines
- Multiple groups for GI Issues
- Multiple groups for lung diseases like Pulmonary Fibrosis
- And MANY more!

Additionally – the Inspire platform will allow us to bring you "Ask the Expert" sessions. During the designated "Ask the Expert" weeks, a Sjögren's expert will engage in the community to answer your questions. Session topics will be on a range of symptoms and challenges that patients face, such as general Sjögren's Management, Oral, Ocular, Neurological symptoms and more!

Scan this code to join the Sjögren's Patient Support Community or visit https://www.inspire.com/groups/sjogrens

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Awareness Never Looked So Good – Featuring You!

Help Us Spread Sjögren's Awareness this Summer

Sjögren's Pen

Did you know an estimated 4 million Americans suffer with Sjögren's? This is NOT a rare disease! The Sjögren's Foundation is constantly working to raise awareness of this disease through education, research, and advocacy. All year long we tell you about our efforts on social media, but we know we are not the only ones working to raise awareness.

This summer, we want to highlight YOU- whether you are a patient, friend or loved one of a patient, or a medical provider- and how you are helping spread awareness of Sjögren's! Whether you are wearing your Sjögren's t-shirt, sharing information or holding up one of our templated signs– YOU are helping Sjö the world that Sjögren's is serious, systemic and prevalent. Share your stories and pictures with the Foundation for a chance to be featured on our Facebook and Instagram!

FInd out more information at: https://info.sjogrens.org/summer-awareness
or scan the QR code
on the right

Sjögren's Car Magnet

Sjögren's Shopping Tote

Research Outcomes Series-
Sjögren's Grant Recipients

Anat Galor, MD, MSPH (2017/2018 Pilot Research Award Grantee; renewed 2018/2019)

Professor of Ophthalmology
University of Miami | Bascom Palmer Eye Institute

Title

Recent Advances in Sjögren's Therapies and Potential Future Prospects

Authors

Shyamal Raolji, BS & Anat Galor, MD, MSPH

Author's scientific summary:

Over the years, we have explored the relationship between **gut dysbiosis** and Sjögren's (SjD) associated Dry Eye (DE) manifestations. The premise for these investigations stemmed from **epidemiological**

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Editor's brief summary

The Galor research group has worked over the past three years on determining the relationship between autoimmune dry eye, specifically in Sjögren's, and the gut **microbiome** (the composition of microbes- bacteria, virus, and fungi- that live naturally in the body).

In two different studies, they found that the composition of bacteria in the gut—specifics found in the author's scientific summary— differs in individuals with autoimmune dry eye compared to controls that do not have an autoimmune condition. Furthermore, they found that the gut microbiome is **heterogeneous** among several different studies, including theirs, and that this may be due to disease-related definitions that differ among studies. These two studies are important for establishing a link between autoimmune dry eye and the microbiome and describing study heterogeneity to limit variability of future data.

It has been shown in previous studies that the use of prebiotics and probiotics as well as **fecal microbial transplantation (FMT)** can modify the gut microbiome. In a third study, the Galor research group investigated whether microbiome modification by FMT of an individual without an autoimmune condition (considered a "healthy" donor) could change the microbiome of an individual with autoimmune dry eye and improve dry eye conditions. The microbiome of the autoimmune dry eye patients changed temporarily and was more similar to the donor's microbiome. Some subjects reported improved gastrointestinal and dry eye conditions, but overall, their dry eye metrics and **T-cell profiles** did not change significantly.

Even though FMT showed a temporary and minimal effect for patients, this study influences the development of future studies that look at providing better microbiome modulation- maybe through **synthetic biology**. Overall, the Galor research group has contributed to more information about the link between dry eye and the gut, which provides foundational work needed for developing therapies for dry eye in autoimmune disease patients.

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studies that linked gut microbiome signatures to autoimmune diseases.[1,2] For examples, studies in 2008 by Vaahtovudo et al. and in 2013 by Scher et al. found that individuals with rheumatoid arthritis (RA) had an increased abundance of ***Prevotella copri*** (*P. copri*) and a decreased abundance of ***Bifidobacteria*** and ***Bacteroides*** in the gut.[3,4] Lending biological relevance to this association, individuals with RA were also found to have unique IgG/IgA antibody reactivity to *P. copri* as compared to individuals with other forms of arthritis such as psoriatic arthritis (PsA).[3,4]

Based on these data and the frequent co-existence of SjD and RA, we investigated whether we could identify unique microbiome signatures in individuals with SjD associated DE compared to controls. In a 2020 study[5], we examined gut microbiome signatures from 21 individuals (mean age 60±8.8 years, female 67%, 5 Item Dry Eye Questionnaire (DEQ5) 11.6±4.8, Ocular Surface Disease Index (OSDI) 41.2±22.6, Schirmer score 8.1±6.1mm), 13 of whom met the 2016 American College of Rheumatology (ACR) criteria for Sjögren's (SjD DE) and 8 with DE symptoms and early SjD marker positivity or aqueous tear deficiency who did not meet ACR criteria (non-SjD DE), and 21 male controls who had no medical conditions or autoimmune diseases (provided by OpenBiome, Cambridge, MA; mean age 26±5.6 years).

We found that individuals with DE (both SjD and non-SjD) exhibited alterations in their gut microbiome compared to healthy controls, as detected using **16S rRNA sequencing**. While in both groups, the dominant phyla were ***Firmicutes*** and Bacteroidetes, individuals with DE (both SjD and non-SjD) had decreased *Firmicutes* (-1.1 fold) and increased **Proteobacteria** (+3.0 fold), **Actinobacteria** (+1.7 fold), and **Bacteroidetes** (+1.3 fold) compared to controls. Furthermore, **Faith's phylogenetic diversity analysis** demonstrated an increased diversity in SjD DE cases compared to controls (13.57 ± 0.89 vs 10.96 ± 0.76, p = 0.02).[5] This study demonstrated microbiome differences in individuals with autoimmune DE (SjD and non-SjD) and younger, healthy controls.

In a follow up study in 2022, we expanded our analysis and examined individuals with autoimmune DE without a secondary autoimmune disease (e.g., individuals with RA, lupus excluded). We enrolled 20 individuals with DE symptoms and/or signs (mean age 61±12.8 years, female 30%, DEQ-5 15.2±3.4, OSDI 55.1±22.8, Schirmer 7.1±5.2mm); 19 individuals had markers to either anti-carbonic anhydrase 6 (CA6), anti-parotid secretory protein (PSP), or anti-salivary protein 1 (SP-1) at a level >20 EU/ml but no other autoimmune conditions (early markers) and 1 individual met SjD criteria. In contrast with our prior study, we recruited 20 gender and age matched individuals without DE symptoms or signs from the same population (mean age 59±11.7 years, female 35%, DEQ-5 4.8±3.8, OSDI 14.2±12.3, Schirmer 20.4±9.2 mm) and analyzed the gut microbiome using deep RNA sequencing. Similar to our prior analysis, the dominant phyla in all participants were *Firmicutes* and Bacteroidetes. We identified five genera and 32 species that were significantly different between cases and controls. Of the five genera, ***Sneathia***, ***Pyramidobacter***, ***Parascardovia***, and ***Veillonella*** had significantly higher abundances in cases compared controls. Among the 32 identified species, 27 were more abundant in cases versus controls, with 10 belonging to the ***Lactobacillus*** genus and four to the *Bifidobacterium* genus.[6] When comparing our results to prior studies, some differences were noted, including no difference ***Faecalibacterium*** in the current study while reduced abundances were noted in previous studies, including our own.[5,7] Also divergent from prior studies,[5,8] no differences in **α-diversity** were noted between the groups. Prior studies have found both increased[5] and decreased diversity[8] in cases with autoimmune DE versus controls. These data highlight the **heterogeneity** of gut microbiome findings across studies and suggest that some differences may stem from disease related definitions.

Based on *epidemiological* studies, we next wanted to explore the concept of disease modulation through gut microbiome modification, which can be achieved through diet, pre- and probiotics, or fecal microbial transplant (FMT). Based on data in ulcerative colitis,[9] we investigated the safety of FMT in individuals with autoimmune DE. For the study, we recruited 10 individuals (mean age 60.4±4.2 years, female 70%) with DE symptoms and signs (DEQ5 15.3±3.3, OSDI 48±22, Schirmer 11.3±6.5mm), 5 who met full SjD criteria and 5 individuals with antibodies to CA6, PSP, or SP-1 (early markers).[10] When analyzing baseline gut microbiome signatures, some similarities were noted compared to our first study,[5] with cases having a higher α-diversity compared to the donor (provided by Openbiome). Additionally, cases showed decreased levels of *Faecalibacterium, Prevotella*, and ***Ruminococcus*** genera, and increased levels of ***Alistipes***, ***Streptococcus***, and ***Blautia*** genera. When comparing our microbiome results with prior studies, both similarities and differences were noted. For example, we noted a decreased abundance of *Prevotella*, whereas prior studies, including our own, found increased *Prevotella* in individuals with autoimmune DE[5] and SjD.[11] Furthermore, our findings of increased *Alistipes* abundance coincides with the findings of some[11] but not all,[8,12] studies. In agreement with prior studies,

we found higher *Blautia*[7] and lower *Faecalibacterium* abundance,[5,7,8] lower *Ruminococcus* genera,[5,8] and increased *Streptococcus*,[7,8] in cases compared to controls.

After providing a baseline microbiome sample, all individuals underwent two FMT, delivered by enema, from the same healthy donor, one week apart. No adverse symptoms or signs were reported by participants. After the two FMT enema sessions eight out of the 10 subjects displayed shifts in their microbiome compositions toward that of the donor, although these changes were temporary as most reverted to their original host microbiome during the three-month observational period.[10] Interestingly, five individuals reported subjective symptom improvements in both gastrointestinal and dry eye conditions three months post-FMT. However, dry eye metrics and T cell profiles did not significantly change over time.[10] Moving forward, FMT is likely not the most elegant way to modify the microbiome as the transplanted material is heterogenous between donors and more targeted approaches are being investigated.

Synthetic biology is one such approach that has emerged as a promising avenue. Synthetic biology can be classified into two main categories: use of "unnatural molecules" to mimic complex natural bodily behaviors and "natural molecule" manipulation to achieve an intended result.[13] Based on this understanding, and prior research that demonstrated the probiotic effects of *Lactobacillus acidophilus*, as well as *L. acidophilus* surface layer proteins' (Slp) protective (SlpA) and inflammatory (SlpB) effects, Lightfoot et al. conducted a study to explore the effects of SlpA modulation on T-cell induced colitis in mice.[14-16] In the study, mice were split into four groups: 1) ones that received no treatment (PBS), 2) ones subjected to the wild-type strain of *Lactobacillus acidophilus*, 3) ones exposed to a strain expressing solely SlpA, and 4) ones treated with isolated/purified SlpA.

Mice were orally **gavaged** once with their respective treatment prior to induction of colitis. Mice were then gavaged again one day later, and once a week for four weeks. The results showed that mice in the control and wildtype groups developed colitis as indicated by weight loss, bloody diarrhea, intestinal epithelial erosions, and decreased colon length in addition to displaying increased proinflammatory markers such as IL-1B, IL-6, TNF-α, IFN-γ. On the other hand, mice treated with modified bacteria or SlpA alone experienced weight gain and did not experience bloody diarrhea, cecal and colonic atrophy, or increased gut permeability, indicating a beneficial effect on barrier integrity and function. Additionally, mice treated with modified bacteria or SlpA showed reduced IFN-γ and CD4+ T cell levels.[15] This data supports the potential therapeutic role of modified microbes in addressing the signs of autoimmune disease. More data, however, is needed before this technology can be applied to humans with autoimmune DE.

To conclude, over the years, our 3 studies, as well as the work of countless others, have continued to elucidate the relationship between the gut microbiome and immune-mediated DE, with a focus on SjD. Our studies highlight that gut microbial alterations have been observed in individuals with autoimmune DE, but that heterogeneity has been noted across studies, perhaps with differences noted by autoimmune DE sub-type. As such, future studies are needed to examine microbiome signatures within autoimmune sub-types (SjD, SjD with other autoimmune diseases, early markers) in multiple compartments (gut, skin, ocular surface), study their complex interactions with the immune system, and investigate strategies for microbiome modulation. Overall, the hope is that a better understanding of the gut-eye axis will provide a foundation for improved therapeutic strategies in SjD. ■

References:

1. Jacobs, J.P. and J. Braun, Immune and genetic gardening of the intestinal microbiome. *FEBS Lett*, 2014. 588(22): p. 4102-11.
2. McHardy, I.H., et al., Integrative analysis of the microbiome and metabolome of the human intestinal mucosal surface reveals exquisite inter-relationships. *Microbiome*, 2013. 1(1): p. 17.
3. Scher, J.U., et al., Expansion of intestinal Prevotella copri correlates with enhanced susceptibility to arthritis. *Elife*, 2013. 2: p. e01202.
4. Vaahtovuo, J., et al., Fecal microbiota in early rheumatoid arthritis. *J Rheumatol*, 2008. 35(8): p. 1500-5.
5. Mendez, R., et al., Gut microbial dysbiosis in individuals with Sjogren's syndrome. *Microb Cell Fact*, 2020. 19(1): p. 90.
6. Goodman, C.F., et al., Case-Control Study Examining the Composition of the Gut Microbiome in Individuals With and Without Immune-Mediated Dry Eye. *Cornea*, 2022.
7. de Paiva, C.S., et al., Altered Mucosal Microbiome Diversity and Disease Severity in Sjogren Syndrome. *Sci Rep*, 2016. 6: p. 23561.
8. Cano-Ortiz, A., et al., Connection between the Gut Microbiome, Systemic Inflammation, Gut Permeability and FOXP3 Expression in Patients with Primary Sjogren's Syndrome. *Int J Mol Sci*, 2020. 21(22).
9. Moayyedi, P., et al., Fecal Microbiota Transplantation Induces Remission in Patients With Active Ulcerative Colitis in a Randomized Controlled Trial. *Gastroenterology*, 2015. 149(1): p. 102-109 e6.
10. Watane, A., et al., Fecal Microbial Transplant in Individuals With Immune-Mediated Dry Eye. *Am J Ophthalmol*, 2022. 233: p. 90-100.
11. Moon, J., et al., Gut dysbiosis is prevailing in Sjogren's syndrome and is related to dry eye severity. *PLoS One*, 2020. 15(2): p. e0229029.
12. Wang, F., et al., The composition and function profile of the gut microbiota of patients with primary Sjogren's syndrome. *Clin Rheumatol*, 2023. 42(5): p. 1315-1326.
13. Benner, S.A. and A.M. Sismour, Synthetic biology. *Nat Rev Genet*, 2005. 6(7): p. 533-43.

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"Research" *continued from page 11* ▼

14. Konstantinov, S.R., et al., S layer protein A of Lactobacillus acidophilus NCFM regulates immature dendritic cell and T cell functions. Proc Natl Acad Sci U S A, 2008. 105(49): p. 19474-9.

15. Lightfoot, Y.L., et al., SIGNR3-dependent immune regulation by Lactobacillus acidophilus surface layer protein A in colitis. *EMBO J*, 2015. 34(7): p. 881-95.

16. Slover, C.M. and L. Danziger, Lactobacillus: a Review. Clinical *Microbiology Newsletter*, 2008. 30(4): p. 23-27.

Types of bacteria in this study

Gram-positive

Parascardovia and *Bifidobacteria* genera in Phylum Actinobacteria; Firmic*utes, Faecalibacterium, Veillonella, Lactobacillus, Streptococcus, Blautia*, and *Ruminococcus* genera in Phylum Bacillota

Gram-negative

Prevotella, Bacteroides, and *Allistipes* genera in Phylum Bacteroidota also known as Bacteriodetes; Phylum Proteobacteria; *Sneathia* genus; *Pyramidobacter* genus

Note

If genera are in the same phylum, they share common fundamental characteristics, but may have evolved different characteristics over time.

Glossary

16S rRNA sequencing– laboratory method that enables identification and analysis of the entire microbial community within a sample by comparing ribosomal RNA sequences

α–diversity– describes the species diversity (richness) within a community

Epidemiological– relating to the incidence, distribution, and control of diseases

Faith's phylogenetic diversity analysis– a test to determine the diversity (or differences) between organisms

Fecal Microbial Transplantation– procedure in which stool from a "healthy" donor is placed into another patient's intestine; also called fecal microbiota transplantation or stool transplantation

Gavage– forced feeding by a tube inserted into the stomach through the mouth

Genera– a group of organisms that share more similarities than those in a phyla (See definition of phyla)

Gut dysbiosis– imbalance of microbes in the intestines that usually causes symptoms

Heterogeneous– different in content; in the case of study heterogeneity, it denotes the variability in outcomes that goes beyond what would be expected (or could be explained) due to measurement error alone

Microbiome– the composition of microbes– bacteria, virus, and fungi– that live naturally in the body

Phyla– a group of organisms with a certain degree of morphological or developmental similarity or as a group of organisms with an evolutionary relationship

Synthetic biology– a multidisciplinary field of biotechnology that involves engineering the genetic material of organisms—such as viruses, bacteria, yeast, plants, or animals—to have new characteristics

T-cell profiles– Used to examine the characteristics, function, frequencies, and subsets of T cells. T cells play a vital role in the immune response, and can mistakenly attack a person's own cells in autoimmune diseases. Specifically, there is an increase in infiltrating T cells in the salivary glands of patients with Sjögren's.

Living with Sjögren's: Dry Eye

For Dry Eye Awareness month, we wanted to take another look at the data related to dry eye and eye-related conditions and symptoms from our 2021 *Living with Sjögren's* patient survey.

Briefly, the Foundation developed the *Living with Sjögren's* patient survey to gain insight and better understand the physical, mental, emotional, and financial impact of Sjögren's. The Foundation published a summary of major findings that provides a comprehensive analysis of the survey findings. This summary of major findings can be accessed at: https://sjogrens.org/living-with-sjogrens/patient-survey-results.

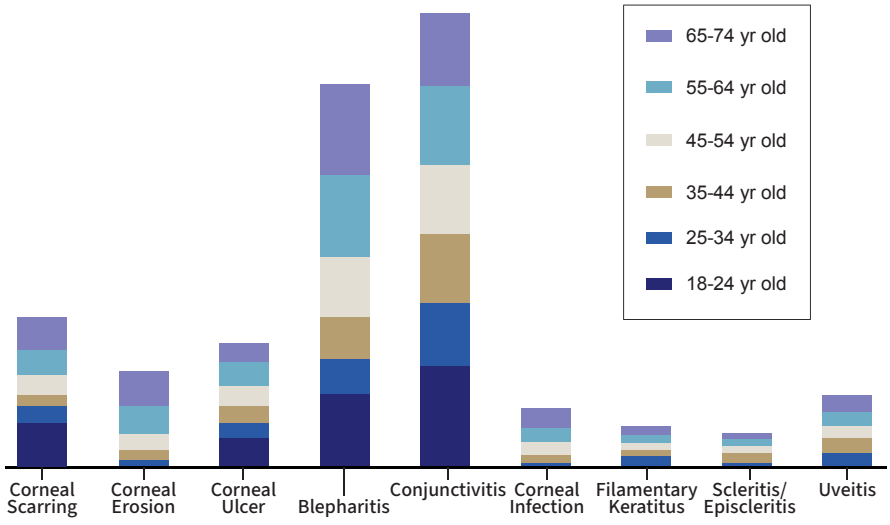
From the original analysis, we learned that 95% of patients experience dry eye symptoms and 94% of patients report having been diagnosed with dry eye. Patients experience a wide variety of symptoms. Most respondents stated that eight of these symptoms have a major or moderate impact on their life, including: fatigue (79%); dry eyes (75%); dry mouth (73%); joint pain (65%); trouble sleeping (64%) eye discomfort (60%); muscle pain (56%); and brain fog (54%). Over fifty percent of all respondents reported experiencing the most prevalent 21 symptoms (including dry eyes and eye pain) within the prior 12 months.

Dry Eye and Eye-Related Conditions

We dove deeper into what other eye-related symptoms and conditions our patients with a dry eye diagnosis might have. Approximately 44% of patients reported being diagnosed with dry eye and at least one other eye-related condition that includes blepharitis, conjunctivitis, corneal scarring, corneal erosions, corneal ulcers, uveitis, filamentary keratitis, and scleritis/episcleritis. Approximately one-quarter (25%) of respondents reported having dry eye and one other eye-related condition, nine percent (9%) of patients have dry eye and two eye-related conditions, and 10% of patients reported having three or more eye-related conditions.

Dry Eye and Eye-Related Conditions by Age Group

Among patients with dry eye and at least one eye-related condition, blepharitis (21%) and conjunctivitis (20%) were the most frequently reported diagnosed conditions. Among the 18– to 24-year-old population, the reported incidence of blepharitis (28%) and conjunctivitis (20%) was as common as in older groups, suggesting that even our younger persons with Sjögren's should have eye examinations for these conditions. The reported frequency of eye-related conditions increases with age group. Twice as many patients aged 45- to 54 reported corneal conditions like corneal scarring (5.58%) and corneal erosion (4.40%) compared to the 35- to 44-year-old population (2.95% and 2.62%, respectively). Three times as many 65- to 74-year-old patients reported



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Conquering Sjögren's One Step at A Time!

Join us in a Fall Walk as we celebrate 40 years of Progress!

Walk for Sjögren's is a national awareness and fundraising program that takes place across the country every spring and fall. But the walks are so much more! They are an amazing series of events where patients build community together, interact with Sjögren's experts, educate family and friends, and raise funds for important initiatives and research. This year, we are commemorating 40 years of Sjögren's progress with our theme: Conquering Sjögren's, One Step at a Time!

Join us at one of our fall virtual events! We had a great set of spring walks and look forward to seeing you in the fall. If you're interested in attending and would like to learn more, start by attending the July 11th Fall Walks Kick-off Rally at 7:30 pm ET and/or please contact Jessica Levy at jlevy@sjogrens.org, visit **events.sjogrens.org**, or scan the QR code below.

Fall 2024 – Walk for Sjögren's Calendar

July	**Virtual Fall Walks Kick-off** *Thursday, July 11, 2024 (7:30 pm ET/ 4:30 pm PT)*
September	**Virtual Texas Walk for Sjögren's** *Saturday, September 28, 2024 (10:00 am CT)*
October	**Virtual Northeast Walk for Sjögren's** *Saturday, October 19, 2024 (10:00 am ET)* **Virtual West Coast Walk for Sjögren's** *Saturday, October 19, 2024 (10:00 am PT)*

events.sjogrens.org

Celebrating 40 Years

CONQUERING SJÖGREN'S ONE STEP AT A TIME

We would like to thank our National Sponsors for their support

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Clinical News

Neurology

Factors Affecting Severity of Autonomic Dysfunction in Sjögren's Patients

The severity of autonomic dysfunction increased with both age and dual-positive biopsy and autoantibody status. This Taiwan-based clinical study included 299 SjD patients and 30 age-matched controls.

Heart rate variability (HRV) parameters were compared between SjD patients and controls to determine the extent of autonomic dysfunction. Total power index (4.98 ± 1.29 vs. 5.54 ± 1.21, p =0.022) and vagal activity (4.95 ± 1.33 vs. 5.47 ± 1.19, p = 0.041) were significantly lower in SjD patients compared to controls. Sympathetic modulation (44.13 ± 17.99 vs. 44.50 ± 17.53, n.s.) and the balance of HRV (1.60 ± 1.23 vs. 1.65 ± 1.33, n.s.) were similar in SjD patients.

SjD patients were stratified into two groups by age: ≤50 years (n=111) and >50 years (n=188), and then HRV parameters of each group were compared with the control group. Similarly, as compared to controls, the total power index (5.78 ± 1.30 vs. 4.68 ±1.19, p <0.001) and vagal activity (4.70 ± 1.26 vs. 5.37 ±1.34, p =0.007) were significantly lower in the >50 years group compared to those ≤50 years.

Patients who were dual-positive for anti-SSA/Ro or anti-SSB/La autoantibodies and a lip biopsy had significantly higher R-R interval variation (696.10 ±975.41, p <0.05 and scored higher for dryness (8.10±1.45, p <0.05) based on ESSPRI scores.

Citation

Lin HC, Yen CM, Chen WS, et al. Unveiling the age-related dynamics in Sjögren's syndrome: Insights from heart rate variability and autonomic function. *Int J Rheum Dis*. 2024;27(3):e15088. doi:10.1111/1756-185X.15088

Rheumatology

Hyperactivation of B Cells in Childhood Sjögren's

B-cell hyperactivation and a distinct B-cell phenotype were identified in a retrospective study of patients with childhood onset SjD (cSjD). Biological samples from 17 patients with cSjD were obtained from a biobank with an additional, six samples of peripheral blood mononuclear cell (PMBC) taken at diagnosis and before immunosuppressive treatment to evaluate B-cell phenotype, and ten plasma samples taken before any treatment to evaluate BAFF (B-cell activating factor) levels. PMBC samples (n=12) were also evaluated after treatment initiation (patient samples treated with rituximab were excluded) to determine TFH (T follicular helper cells) and B-cell autoreactivity. All samples were age-matched with controls.

There was a significant reduction in the frequency of unswitched memory B cells and an expansion of atypical B cells and PD1hi CXCR5- T peripheral helper cells. There was no difference in B-cell alterations after treatment. Levels of BAFF were higher in cSjD patients before treatment than controls. BAFF levels correlated with total IgG (R2 = 0.67, p=0.0068) and anti-Ro antibodies (R2 = 0.44, p=0.037). There was no correlation in BAFF levels with disease severity measured with ESSDAI scores. However, BAFF levels positively correlated with the transitional B cell subset (R2 = 0.81, p=0.0056).

To determine the defectiveness of B cell tolerance checkpoints, the frequencies of ANA+ B cells within the subset of transitional, naïve, unswitched memory, switched memory, and plasmablast compartment were analyzed. The frequency of ANA+ transitional (p <0.001), unswitched memory (p <0.001), and plasmablast (p <0.01) B cells were significantly higher in cSjD patients than controls. Overall, this study shows evidence of B-cell hyperactivation and impairment of B-cell tolerance checkpoints in cSjD patients.

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"Clinical News" *continued from page 15* ▼

Citation

Lin HC, Yen CM, Chen WS, et al. Unveiling the age-related dynamics in Sjögren's syndrome: Insights from heart rate variability and autonomic function. *Int J Rheum Dis*. 2024;27(3):e15088. doi:10.1111/1756-185X.15088

Disease Duration Affects the Clinical Phenotype of Sjögren's

Sjögren's (SjD) patients with longer disease duration were determined to have an increased prevalence of sicca symptoms, fatigue, and joint pain, and an increased positivity rate of autoantibodies associated with SjD. This study consisted of 952 SjD patients who were stratified into three groups based on their disease duration, defined as time span between age of onset and age of diagnosis: short (<5 years), moderate (≥5 years and <10 years), and long (≥ 10 years). SjD patients with long disease duration were matched to other grouped SjD patients by age at disease diagnosis and age at disease onset.

Those categorized as having long disease duration (20%) had a significantly higher prevalence of dry mouth (p <0.001), dry eyes (p <0.001), fatigue (p <0.001), arthralgia (p <0.001), and dental caries (p <0.001) than SjD patients with a shorter disease duration (<10 years). Anti-SSA/Ro60 (p <0.05), anti-SSA/Ro52 (p <0.05), and anti-SSB/La (p <0.05) were also higher in those with long disease duration after matching for age of onset and diagnosis. The prevalence of dry mouth, dry eyes, fatigue, arthralgia, dental caries, and autoantibodies (anti-SSA/Ro60, Ro52, anti-SSB/La, ANA) increased with disease duration.

Multiple comparisons showed that the prevalence of interstitial lung disease (ILD) (padjusted <0.05) was higher in SjD patients with shorter disease duration (<10 years) and that the prevalence of leukopenia was lower (padjusted <0.05). After matching for age at disease diagnosis, those categorized as having a long disease duration still had a lower prevalence of ILD (p <0.001) and a higher prevalence of leukopenia compared to controls (p <0.008). After matching for age of disease onset, there were no significant differences in prevalence of ILD and leukopenia between disease duration groups. These data show that clinical phenotypes of SjD are correlated with disease duration despite age-related comorbidities.

Citation

Zhang Y, Yang JY, Chen JQ, et al. Disease duration affects the clinical phenotype of primary Sjögren syndrome: A medical records review study of 952 cases. *J Clin Rheumatol*. Published online February 23, 2024. doi:10.1097/RHU.0000000000002076

Higher Sjögren's Disease Activity Associates with Risk of Cardiovascular Diseases, Chronic Pulmonary Disease, and Monoclonal Gammopathy

Comorbidities that contribute to mortality were analyzed in patients with Sjögren's (SjD) who had a high ESSDAI score (≥ 5) and higher disease activity was associated with peripheral vascular disease, myocardial infarction, chronic pulmonary disease, and monoclonal gammopathy. The study cohort consisted of 111 patients with SjD and were compared to 194 patients with sicca as controls. Electronic health record data was obtained from the University of Wisconsin.

SjD patients had an increased prevalence of monoclonal gammopathy (p <0.001, which was still significant after controlling for age (OR =16.631, 95% CI [2.08-133.31], p =0.008). Patients were then stratified by disease severity into two groups (ESSDAI <5 and ESSDAI ≥5) at diagnosis and at their most recent assessment. Logistic regression analyses were performed to determine associations with disease severity of the two groups at baseline and recent assessment. There was a significant difference in patient age with ESSDAI ≥5 compared to patient age with ESSDAI <5 at diagnosis (62 ± SD 11 years vs. 57 ± SD 11 years; p = 0.04). Monoclonal gammopathy had a higher prevalence in the ESSDAI ≥5 group compared to ESSDAI <5 (n=7, 16.67% vs. n=5, 5%; p = 0.04). At time of diagnosis, SjD patients with ESSDAI ≥5 were three times more likely to have chronic pulmonary disease (age adjusted OR = 3.79, 95% CI [1.35-10.60], p =0.003) and ten times more likely to have peripheral vascular disease (age adjusted OR =10.42, 95% CI [1.17-93.06], p =0.01).

The prevalence of chronic pulmonary disease for SjD patients with ESSDAI ≥5 increased at time of recent assessment compared to time of diagnosis and these patients were five times more likely to have chronic pulmonary disease compared to SjD patients with ESSDAI <5 (OR= 5.75, 95% CI [1.85-17.89], p =0.001). SjD patients with ESSDAI ≥5 at recent assessment were also ten times more likely to have a myocardial infarction than SjD patients with ESSDAI <5 (OR= 10.06, 95% CI [1.17-86.65], p =0.01).

Overall, these findings support that disease severity increases the risk of chronic pulmonary disease and peripheral vascular disease, and over time, increases the risk of myocardial infarction.

Citation

Bohman BR, Dowds HS, Blagogee TE, Ike RW, Hansen KE, McCoy SS. Sjögren's disease activity associates with cardiovascular disease and monoclonal gammopathy: a university cohort study of disease activity and comorbidities. *Clin Rheumatol*. 2024;43(3):1093-1101. doi:10.1007/s10067-024-06890-y

Anti-Ro/La Seronegative is a Distinct Subtype of Sjögren's

A distinct subtype of Sjögren's (SjD) was identified in SjD patients who are seronegative for SjD autoantibodies (anti-Ro and/or anti-La), characterized by reduced systemic manifestations, exocrine gland dysfunction, and less B lymphocyte activation, compared to patients who test positive for SjD autoantibodies (seropositive). The study cohort consisted of 192 seropositive (82.8%) and 40 seronegative (17.2%) patients with SjD.

Seronegative SjD patients were older (56.50 years (50.00-63.75) vs. 48.00 years (39.00-58.00); p <0.000) and were more likely to have an ESSDAI score < 5 (32.50% vs. 15.63%; p = 0.013) compared to seropositive SjD patients. Symptoms related to glandular dysfunction, including xerostomia (80.00% vs. 57.80%; p =0.009) and xerophthalmia (62.50% vs. 44.80%; p =0.041) were also more prevalent in seronegative SjD patients compared to seropositive SjD patients.

While serum levels of ESR were lower in seronegative SjD patients compared to seropositive SjD patients, platelet count (265.0 (205.25-310.75) x 109/L vs. 218.5 (162.50-272.75) x 109/L; p =0.003), serum total bilirubin (10.85 (7.48-15.40) x U/L vs. 8.00 (5.90-10.90) x U/L; p=0.005), and creatine kinase (62.00 (33.75-103.25) x U/L vs. 48.00 (30.00-67.75) x U/L; (p=0.026) were significantly higher.

In parameters associated with B lymphocyte infiltration, seronegative SjD patients had significantly lower levels of gamma globulin (30.10 (26.50-35.00) g/L vs. 32.80 (28.95-37.95) g/L; p =0.012), immunoglobulin G (IgG) (14.20 (12.20-15.70) g/L vs. 17.45 (13.83-21.45) g/L; p =0.000), and immunoglobulin A (2.47 (1.87-3.50) g/L vs. 2.98 (2.26-3.93) g/L; p =0.027) compared to seropositive SjD patients. Seropositive SjD patients had significantly higher ANA (95.30%, n= 183 vs. 55.00%, n=22) and RF (95.30%, n= 183 vs.10.00%, n= 4) positivity compared to seronegative SjD patients.

Histological examination of labial glands showed there was more lymphocytic infiltration (100.00% vs. 79.80%; p =0.002) and IgG deposition (p =0.014) in seronegative SjD patients compared to seropositive SjD patients. No difference in T cell or B cell lymphocytic infiltration of the labial gland between seronegative or seropositive SjD patients was found.

These findings support seronegative (anti-Ro/La) as a distinct subtype of SjD.

Citation

Lan J, Deng C, Huang H, et al. Seronegative primary Sjögren's syndrome, a distinct subtype of primary Sjögren's syndrome in Chinese patients. *BMC Rheumatol*. 2024;8(1):15. Published 2024 Apr 16. doi:10.1186/s41927-024-00384-9

Reproductive Health

Sjögren's and Adverse Pregnancy Outcomes

Patients who are pregnant and have Sjögren's (SjD) were determined to be at an increased risk for a variety of adverse pregnancy outcomes. This umbrella review included 32 systematic reviews of 709 studies that analyzed data on 16 adverse pregnancy outcomes in 12 autoimmune diseases, including SjD. Of the total number of included studies, only 15 primary studies from two systematic reviews included the reporting of adverse pregnancy outcomes associated with SjD patients, including miscarriage, preterm birth, fetal loss, still birth, and low birth weight.

There was a significantly higher risk of miscarriage in patients with SjD (8.85 relative risk (RR) (3.10-25.26) compared to controls. Patients with systemic lupus erythematosus (SLE) (OR 4.90 (3.10-7.69)) and rheumatoid arthritis (RA) (OR 1.32 (1.21-1.43)) also had a significant association with miscarriage. There was no significant association with stillbirth in women with SjD (OR 1.05 (0.37-2.97), but there was a significantly higher risk for those with SLE (OR 16.90 (3.02-94.40)) and RA (OR 1.99 (1.17-2.06)). The odds were also significantly higher for preterm births and low birth weight in patients with SjD and SLE.

These findings support that women who are pregnant and have SjD, particularly those with SLE and/or RA, should consult with their doctors as they are at risk for several adverse pregnancy outcomes. Of the 15 primary studies included, none reported on gestational hypertension, gestational diabetes mellitus, pre-eclampsia, caesarean section, small for gestational age, or intrauterine growth restriction, suggesting large knowledge gaps compared to other autoimmune diseases included in this umbrella review.

Citation

Singh M, Wambua S, Lee SI, et al. Autoimmune diseases and adverse pregnancy outcomes: an umbrella review. *BMC Med*. 2024;22(1):94. Published 2024 Mar 5. doi:10.1186/s12916-024-03309-y

Oral

Use of Electronic Dental and Health Record Data to Predict Sjögren's

Two regression models were created to predict Sjögren's (SjD) diagnosis using both electronic health record (EHR) and dental record (EDR) data or EHR data alone, where both models were found to be good predictors of SjD diagnosis. EHR and EDR data were obtained from the Indiana Network for Patient Care and Indiana University School of Dentistry, respectively. The EHR/EDR data were examined three years prior to SjD

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diagnosis for SjD cases and matching non-SjD controls. There were 129 SjD cases and 371 controls with linked EHR and EDR data.

A conditional logistic regression model was used to determine the clinical and dental risk factors associated with SjD diagnosis. The study found that EHR data containing usage of lubricating throat drugs (OR = 14.97 [2.70-83.06]), dry mouth (OR = 6.19 [2.14-17.89]), pain in joints (OR = 2.54 [1.34-4.76]), tear film insufficiency (OR = 27.04 [5.37-136]), and rheumatoid factor (OR = 6.97 [1.94-25.12]) were associated with an increased risk of SjD diagnosis.

In the EDR data, surgical dental procedures (OR = 2.33 [1.14-4.78]) were associated with increased risk of SjD diagnosis while diagnostic dental procedures (OR = 0.45 [0.20-1.01]) were associated with a decreased risk. Both multivariable prediction models overlap in the variables chosen except for surgical and diagnostic dental procedures added in the EHR/EDR model. The EHR predictive model had a C-index of 0.811 (95% CI = 0.750-0.872) while the EHR-EDR predictive model had a C-index of 0.834 (95% CI = 0.775-0.893), suggesting that adding EDR data improves predictability of SjD diagnosis.

Citation

Mao J, Gomez GGF, Wang M, Xu H, Thyvalikakath TP. Prediction of Sjögren's disease diagnosis using matched electronic dental-health record data. *BMC Med Inform Decis Mak*. 2024;24(1):43. Published 2024 Feb 9. doi:10.1186/s12911-024-02448-9

Longevity of Dental Restorations in Sjögren's Predicted by Electronic Health and Dental Record Data

Electronic health record (EHR) and dental health record (EDR) data determined that patients with Sjögren's (SjD) experienced a significantly shorter time to dental restoration failure compared to matched controls. The study cohort was comprised of 102 SjD cases and 42 matched controls with at least one direct dental restoration that spanned over 15 years of treatment history. The 102 SjD cases consisted of 21 positive SjD cases, 57 negative SjD cases, and 24 uncertain SjD cases based on clinical findings, where negative SjD cases had less severe clinical findings compared to positive and uncertain SjD cases. EHR and EDR data were obtained from the Indiana Network for Patient Care and Indiana University School of Dentistry, respectively.

The study found 529 direct dental restorations in SjD cases and 140 direct dental restorations in controls. Cox regression models analyzed the differences between SjD cases and controls for time to direct restoration failure and several covariates including demographics, medical or dental insurance, medical diagnosis, medication use, preventive dental visits per year, and number of tooth surfaces. SjD cases (Hazard ratio (HR)= 2.99, 9% CI [1.48-6.03]; p = 0.002) and positive SjD cases (HR = 3.30, 95% CI [1.49-7.31]; p = 0.003) showed significantly shorter time to direct dental restoration failure compared to controls. Only number of tooth surfaces had a significant influence on survival time of direct dental restorations, where restorations with two or more surfaces failed faster than single-surface restorations (HR = 1.74, 95% CI [1.115-2.710]; p = 0.015). After controlling for number of tooth surfaces, SjD cases were 2.76 times more likely to experience a direct dental restoration failure compared to controls (HR = 2.76, 95% CI [1.37-5.57]; p = 0.005).

Many of the cases included in this study have less than 1 preventive dental visit per year and with the significant number of direct dental restoration failures, management and evaluation plans should be implemented as part of the dental procedure planning. ■

Citation

Gomez GGF, Wang M, Siddiqui ZA, et al. Longevity of dental restorations in Sjogren's disease patients using electronic dental and health record data. BMC Oral Health. 2024;24(1):203. Published 2024 Feb 7. doi:10.1186/s12903-024-03957-9

"Dry Eye" continued from page 13 ▼

these conditions as compared to 35- to 44-year-olds (9.38% and 9.52%, respectively).

The proportion of older patients reporting three or more eye-related conditions is approximately two and three times greater, respectively, among 55- to 64-year-olds (7.99% and 65- to 74-year-olds (9.22%) when compared to 35- to 44-year-olds (3.61%).

Dry Eye and Eye-Related Symptoms

Those patients with a dry eye diagnosis were also more likely to have eye fatigue (67% vs. 29%), eye discomfort (79% vs. 33%), and poor, blurred vision (55% vs. 30%) compared to respondents who were not diagnosed with dry eye. The proportion of patients reporting headaches (56% vs 52%) and migraines (30% vs 24%) with a dry eye diagnosis was only slightly higher among patients with dry eye diagnosis than among those without.

The main takeaway from this analysis is that if you or your doctor suspect Sjögren's, then it is important to prioritize and monitor your eye health— early and over time— with an ophthalmologist. ■

IN MEMORIAM

In Memory of Heidi Ann Burke
John Burke

In Memory of Jacquelyn Crosby
Debra Smith

In Memory of Marlene Dunham
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World Sjögren's Day

AMGEN

Doubling Down on Donations for World Sjögren's Day– Amgen will Match up to $40,000 for 40 years of Progress!

Help us Celebrate World Sjögren's Day on July 23rd by donating to the Sjögren's Foundation. Amgen, a corporate sponsor, will generously match up to $40,000 of donations made in honor of World Sjögren's Day. This year's Amgen match is an increase from last year to $40,000 to celebrate our 40th anniversary.

Why do we celebrate July 23rd as World Sjögren's Day?

World Sjögren's Day was created to commemorate the birthday of Dr. Henrik Sjögren, the Swedish ophthalmologist who discovered Sjögren's.

In 1929, Dr. Sjögren met a patient who complained of dry eyes, dry mouth, and joint pain. Each of these symptoms were already well known, but it was the combination of them that Dr. Sjögren noticed and decided to investigate. Dr. Sjögren could have dismissed his patient that "just had dry eyes", but his open mind led him to the discovery of an unknown clinical entity that was later named after him.

World Sjögren's Day celebrates the man who has helped all patients find answers to their health questions. As many Sjögren's patients still have a hard time getting diagnosed, World Sjögren's Day is a great opportunity for you to have your voice heard. We encourage you to celebrate this day by using your voice and educating those close to you that Sjögren's is serious, systemic, and prevalent.

Please consider giving a donation in honor of World Sjögren's Day. Your support has allowed researchers to build on Dr. Sjögren's work, making the recent scientific breakthroughs in the field possible.

Together we can conquer the complexities of Sjögren's!

If you would like to make a donation, please visit www.sjogrens.org/world-sjogrens-day-donations or scan the QR code to the left.