Are You Missing the Early Signs of Sjögren’s Syndrome?

>> What you need to know to help your patients

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Roundtable Participants

Kelly Nichols
OD, MPH, PhD
(Moderator)

Dr. Nichols is FERV Professor at the University of Houston College of Optometry and director of The Ocular Surface Institute clinical research center.

Douglas Devries, OD
Dr. Devries practices at Eye Care Associates of Nevada in Reno and is co-founder of Advanced Vision & Laser Center in Sparks. He also practices at New Eyes in Las Vegas and is an associate clinical professor at Pacific University College of Optometry.

Arthur Epstein
OD, FAAO
Dr. Epstein is co-founder of Phoenix Eye Care in Arizona and director of the Dry Eye Center of Arizona.

Paul Karpecki
OD, FAAO
Dr. Karpecki specializes in corneal disease, particularly ocular surface disease, at Koffler Vision Group in Lexington, Ky.

Katherine Mastrota
MS, OD, FAAO
Dr. Mastrota is center director for Omni Eye Surgery, an optometric referral center in New York City.
Kelly Nichols, OD, MPH, PhD: As many as 4 million people in the United States are believed to be affected by Sjögren’s Syndrome, a chronic, systemic, progressive, autoimmune inflammatory disease. It’s estimated that only 1 million people have been diagnosed, which means up to 75% of those who have the disease may remain undiagnosed.1-3 While these statistics may be surprising to many eyecare practitioners (ECPs), others are even more surprising. For example, it currently takes 4.7 years for a person with Sjögren’s Syndrome to receive an accurate diagnosis.4 This is significant because Sjögren’s is a precursor to other diseases, including lymphoma,5,6 and complications affecting the liver, lungs and thyroid.7 The results of a study conducted at the University of Ioannina School of Medicine in Greece indicated that one in five deaths among patients with primary Sjögren’s Syndrome can be attributed to lymphoma.8 Because the immune response associated with this disease is largely directed at the salivary and lacrimal glands, ocular symptoms are frequently the first to present. Research shows that 1 in 10 people with clinically significant dry eye also have Sjögren’s Syndrome.9 We’re all familiar with the large numbers of patients who come to us seeking relief from the symptoms of dry eye. Many of them may also have Sjögren’s Syndrome, likely undiagnosed. This gives ECPs a unique opportunity to identify patients with this disease early and not only treat its ocular manifestations but also enable patients to seek earlier treatment for its systemic manifestations, which can be multi-system, progressive and debilitating (Figure 1).

Do you think our colleagues have a good understanding of Sjögren’s and its manifestations?

Douglas Devries, OD: I think there’s a lack of in-depth understanding throughout eye care. Arthur Epstein, OD, FAAO: I think there’s an understanding at a basic level that the condition exists, but it has not progressed beyond that. The ramifications aren’t fully understood. I think everyone knows about Sjögren’s, but no one fully understands it.

Figure 1. Areas of the body that may be affected by Sjögren’s Syndrome.
Dry Eye in the Context of Undiagnosed Sjögren’s Syndrome

Dr. Nichols: As we know, a precise determination of the prevalence of dry eye has been elusive. However, an estimated 12.5 million people in the United States, and that may be a conservative estimate, have clinically significant dry eye. Among those, as many as 4 million may have Sjögren’s Syndrome, and most are undiagnosed. As mentioned previously, those numbers translate to one out of every 10 dry eye patients having Sjögren’s. What are your thoughts on this?

Dr. Devries: I find the numbers startling. They tell me that I’m not treating a large percentage of my patients who have Sjögren’s and will experience the consequences but haven’t been diagnosed.

Katherine Mastrota, MS, OD, FAAO: The diagnosis of dry eye is a common one, and perhaps we’re all a bit guilty of lumping all ocular surface disease into the same box, so to speak. We attempt to manage dry eye in a palliative manner, but often don’t think of taking the next step to try and understand whether the cause is something underlying — something more core.

Dr. Epstein: Clearly, a much greater percentage of dry eye patients have Sjögren’s than we tend to believe. It’s tragic that we don’t go to that next level of suspecting it because these patients often progress and become significantly impacted by their dry eye, and then they begin to show the other signs of Sjögren’s.

Dr. Mastrota: Glaucoma patients, too, come to mind. We tend to attribute dry eye in those cases to the medications and the preservatives instead of reminding ourselves that patients can have two conditions at once.

Dr. Devries: I would imagine many early Sjögren’s patients get dismissed as being perimenopausal.

Dr. Nichols: That is possible given that 9 out of 10 Sjögren’s Syndrome patients are women.10 Can you recall a male patient with Sjögren’s in your practice? They do exist.

Dr. Epstein: It’s rare, but I also wonder if their presentation is milder than in females, perhaps a more delayed onset, which could make the disease more likely to be missed.

Dr. Nichols: I had a male patient who had cancer, so his cancer treatments very likely caused his dry eye. But he could just as easily have had Sjögren’s. He said to me at one point, “I’m a firefighter, and I beat cancer, but this dry eye is going to bring me down.”

Dr. Epstein: The patients I’ve had with diagnosed Sjögren’s Syndrome have had severe ocular manifestations and were miserable.

Dr. Mastrota: Also, dry eye patients often travel from practice to practice searching for relief when treatments aren’t working. They continue to be uncomfortable and unhappy. It begins a cycle of misery for these individuals.

### TABLE 1: The Sjö test, which incorporates novel biomarkers for Sjögren’s Syndrome, can be administered in an optometry office.

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Type</th>
<th>Diagnostic Characteristics</th>
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<tbody>
<tr>
<td>SS-A (Ro)</td>
<td>Traditional</td>
<td>Expressed in approximately 70% of patients and typically appears later in the course of the disease than novel biomarkers</td>
</tr>
<tr>
<td>SS-B (La)</td>
<td>Traditional</td>
<td>Expressed less frequently than Ro and typically appears later in the course of disease than novel biomarkers</td>
</tr>
<tr>
<td>Antinuclear Antibody (ANA)</td>
<td>Traditional</td>
<td>Expressed in about 70% of Sjögren’s Syndrome patients</td>
</tr>
<tr>
<td>Rheumatoid Factor Levels (IgG, IgA, IgM)</td>
<td>Traditional</td>
<td>Found in many rheumatic conditions and is not unique to Sjögren’s Syndrome</td>
</tr>
<tr>
<td>Salivary Protein-1 (SP-1)</td>
<td>Novel, proprietary</td>
<td>Provides greatest specificity and sensitivity for early Sjögren’s Syndrome</td>
</tr>
<tr>
<td>Carbonic Anhydrase (CA6)</td>
<td>Novel, proprietary</td>
<td>Offers additional sensitivity for an early diagnosis</td>
</tr>
<tr>
<td>Parotid Secretory Protein (PSP)</td>
<td>Novel, proprietary</td>
<td>Expressed around the same time as CA6 for early diagnosis</td>
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Being able to make a diagnosis earlier can empower patients to better manage their condition.

Dr. Epstein: We recognize the complexity of dry eye patients more than ever before, which enables us to better address their problems. It would be great if they could be diagnosed and managed properly at any doctor’s office.

Reducing Time to Diagnosis

Dr. Nichols: Earlier detection of Sjögren’s could certainly help reduce the distress, both ocular and systemic, that patients experience. The Sjögren’s Syndrome Foundation has a goal to reduce the time to diagnosis, currently 4.7 years, by half in the next 5 years. What can ECPs do?

Dr. Devries: Our history/intake forms are a good place to start. They could include questions related to dry mouth and systemic problems that manifest with Sjögren’s, such as aches and pains and extreme fatigue. Incidentally, in my experience, many of my Sjögren’s patients also have conjunctival chalasis.

Dr. Epstein: I take a structured approach with dry eye patients, looking for associated rheumatoid conditions, which is part of my intake form.

Dr. Nichols: Do you find patients are aware of words like Sjögren’s, rheumatoid arthritis, lymphoma, lupus, and so on?

Dr. Epstein: Yes. Those who’ve been through the system are much more self-educated than they’ve been in the past. I also think it’s important to pay attention to how patients present. Do they appear to have arthritis? About half of Sjögren’s patients have another autoimmune disorder, such as rheumatoid arthritis, lupus or systemic scleroderma. How do they shake your hand? Do their hands seem to be extremely cold, which could be an indication of Sjögren’s-related Raynaud’s disease? Did they bring a cup of water into the exam?

Dr. Nichols: Patients with those types of symptoms are already advanced in the Sjögren’s disease process. We would like to be able to determine earlier which patients are likely to go down that road — before they do.

Dr. Epstein: As the first point of contact for many of these patients, ECPs can be the first to recognize something more significant is going on in connection with their ocular status and direct them to the proper specialist.

In addition, it’s important to recognize that the classic presentation of Sjögren’s in the eyecare office is typically aqueous-deficient dry eye. However, both aqueous-deficient and evaporative dry eye can be associated with inflammation affecting all layers of the tear film. Meibomian gland disease can be present, too. Being cognizant of this opens up more possibilities for us in terms of patient management. Dry eye is a complex, challenging diagnostic entity, and we need to keep an open mind throughout the process.

Dr. Mastrotota: Part of the challenge is that dry eye symptoms may improve or worsen in cycles or remain stable.

Dr. Nichols: Yes, and Sjögren’s is a dynamic disease as well. Symptoms don’t always present concurrently and tend to be cyclical. Patients may have periods during which they experience significant pain and irritation and periods where they feel normal and appear clinically normal.

“Patients may have periods during which they experience significant pain and irritation and periods where they feel normal and appear clinically normal.”

— Kelly Nichols, OD, MPH, PhD

New Test Improves Diagnostic Sensitivity and Specificity

Dr. Nichols: Unfortunately, the serology testing traditionally used to diagnose Sjögren’s doesn’t have very high sensitivity and specificity, so it isn’t likely to detect disease early. New research has identified additional biomarkers — salivary protein-1 (SP-1), carbonic anhydrase (CA6) and parotid secretory protein (PSP) — that appear to improve the speed and consistency of diagnosis (Table 1).

This new knowledge has been incorporated into the Sjö test, which was approved by the FDA in November 2013. The test includes the traditionally used biomarkers plus (SP-1), (CA6) and (PSP), and has exhibited high sensitivity and specificity of more than 95%. The Sjö test can be administered in-office via a blood sample obtained with a finger prick.

How do you think this test could be incorporated into optometric practice?

Dr. Epstein: The increased sensitivity and specificity is a major step forward, and the test is far more accessible to us as clinicians, which I think is a massively important step. I could see it easily becoming part of my armamentarium for patients who have moderate to severe dry eye, and perhaps even for those who have mild but progressive...
Collaboration Among Specialties Crucial to Helping Sjögren’s Patients

By Paul M. Karpecki OD, FAAO

Even with new diagnostic tests that allow primary eyecare providers to determine the presence of Sjögren’s syndrome, the role of rheumatologists and other healthcare providers hasn’t diminished. To improve the quality of life of Sjögren’s patients, each specialty must contribute to the management of the systemic component of the disease, ensure optimal communication on behalf of the patient and monitor for life threatening co-morbidities.

Systemic Disease Management

Patients with ocular manifestations of a systemic disease rarely experience complete resolution of ocular symptoms until the systemic disease is controlled. In patients with primary or secondary Sjögren’s syndrome, although it’s essential to address the health of the ocular surface, these patients often have an autoimmune dysfunction, such as rheumatoid arthritis (RA) or systemic lupus erythematosus, which must be controlled as well. In many patients, the ocular symptoms will only improve fully once the RA or lupus is treated and controlled.

Communication

Optometry must take a ‘seat at the table’ for all patients who have systemic diseases with ocular manifestations. We must establish strong communication lines with other healthcare providers, so patients can benefit from each practitioner’s area of expertise. Remember, too, that good communication can lead to increased referrals to optometric practices that manage a high number of patients with advanced ocular surface diseases.

Monitoring for Life-threatening Conditions

Research shows that the incidence of non-Hodgkins lymphoma in patients with Sjögren’s Syndrome is very high. Kassan and colleagues’ first document-ed this link in 1978 when it was found that patients with SS keratoconjunctivitis sicca (KCS) had a 43.8 times greater incidence of lymphoma compared to age- and gender-matched controls in the general population.

Also, the average age of onset of Sjögren’s is in the late 40s, so these patients, mostly female, will likely require ongoing systemic follow-up. It’s imperative that we work with rheumatologists or internal medicine specialists to ensure that patients are aware of this link and their doctors are monitoring them yearly.

Secondary Sjögren’s is related to an autoimmune or connective tissue disorder. Thus, all patients with secondary Sjögren’s will have associated diseases, including RA or lupus, that require systemic management.

Dentists should also be included in the treatment of patients with Sjögren’s, because associated salivary gland dysfunction can lead to a wide range of oral manifestations.

Understanding any systemic disease, providing effective communication and monitoring for life-threatening conditions is critical to managing Sjögren’s patients. Fortunately, new point-of-care diagnostic capabilities will allow us to make an accurate diagnosis earlier, so we can be more confident in managing the disease.

References


Strategies for Patients with Sjögren’s Syndrome

Dr. Nichols: Current Preferred Practice Pattern guidelines include treatment options for Sjögren’s-associated dry eye such as topical lubricants, topical cyclosporine, autologous serum, topical corticosteroids, punctal occlusion and systemic secretagogues. As with other forms of dry eye, the overall goal of therapy is to normalize the tear film, decrease inflammation, improve lacrimal function and facilitate epithelial healing. Treating the ocular symptoms of Sjögren’s can help to prevent lacrimal gland degradation.

Do you treat dry eye patients differently if you know they have Sjögren’s?

Dr. Mastrota: Yes, and I surmise intuitively we all would. We know what is likely coming down the line, and we want to slow down that train any way we can. The earlier we can intervene in order to break the cycle of inflammation, the better.

Dr. Devries: Referral to a rheumatologist is important, too, and the Preferred Practice Pattern notes that.

Dr. Nichols: When you’re managing patients who have dry eye and known Sjögren’s, what are some of the strategies you use?

Dr. Devries: I tend to be aggressive. I put patients on cyclosporine (Restasis,
What you need to know to help your patients

Allergan) the first time I see them. I recommend they use moisture chamber goggles to manage the environmental conditions. For many patients, I also utilize compounded androgen ointment and have them use omega-3 creams. I frequently use autologous serum as well. That involves a blood draw, which is spun down into a serum and sent to a compounding pharmacy to be mixed with balanced salt solution and put into small eye drop vials. Patients use the drops every few hours over an 8-week period, which gives the eye a chance to heal by utilizing the growth factors and trans-growth factors in the serum. It’s not a panacea, but it’s rare that I don’t see some kind of a positive result. For patients with severe, unresolved punctate epithelial keratitis, I may use an amniotic membrane.

Even though these measures are aggressive, patients with Sjogren’s and severe dry eye are very good with compliance because they’ve been so uncomfortable and their symptoms have affected their lives so dramatically.

**Dr. Epstein:** Scleral lenses and bandage contact lenses can also be helpful. Mindful of meibomian gland function, I think preserving whatever aqueous is left on the eyes is critically important. Interestingly, I use very little Restasis for most patients, but for this group I use it fairly frequently.

**Dr. Nichols:** We mentioned the importance of referring patients with a diagnosis of Sjögren’s to a rheumatologist. Perhaps a dental referral is something that also shouldn’t be overlooked.

**Dr. Epstein:** I wonder whether most optometrists co-manage directly with dentists or whether the rheumatologist coordinates it?

**Dr. Nichols:** The dental loop is definitely an interesting concept. Why wouldn’t we be working with the dentists in our communities on this? It seems like an easy connection to make.

### A New Way to Help Our Dry Eye Patients

**Dr. Nichols:** We’ve learned a great deal about dry eye in the past 10 years. We’re putting together a much more global picture of how best to manage this group of patients. A key component is ruling in or ruling out potential underlying etiologies, and the new Sjö test should be a big help in regard to Sjögren’s and therefore a great service to our patients.

**Dr. Devries:** I’m very excited about this test. Immediately, it makes me think of my most challenging cases of dry eye, where, for example, patients just aren’t responding to treatment like I would expect or are progressing for no apparent reason. The test will give them a quick answer, which is what they need and want. When doctor and patient are armed with that information, we can move on to setting expectations and doing what we need to do to provide relief to our patients and protect them as much as possible from further damage.

**Dr. Epstein:** Sjögren’s patients pretty much define what I feel I’ve dedicated most of my life to. They’re among the patients who need us the most. Anything I can do to recognize what they need, initiate treatment earlier, and be part of a team that can help them more effectively is very exciting to me.

**Dr. Nichols:** Further improving our care of dry eye patients is a common goal for all of us. Being able to also identify patients in our practices who have undiagnosed Sjögren’s Syndrome is a step of major importance.

### References


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