

# Sjögren's Syndrome

## Key Thought Leaders Discuss Sjögren's Syndrome and the Sjö® Diagnostic Test

Moderator

**Paul M. Karpecki, OD, FAAO**

Panelists

**Mile Brujic, OD, FAAO**

**Douglas K. Devries, OD**

**Arthur B. Epstein, OD, FAAO**

**Mel A. Friedman, OD, FAAO**

**Scott G. Hauswirth, OD, FAAO**

**Walter O. Whitley, OD, MBA, FAAO**



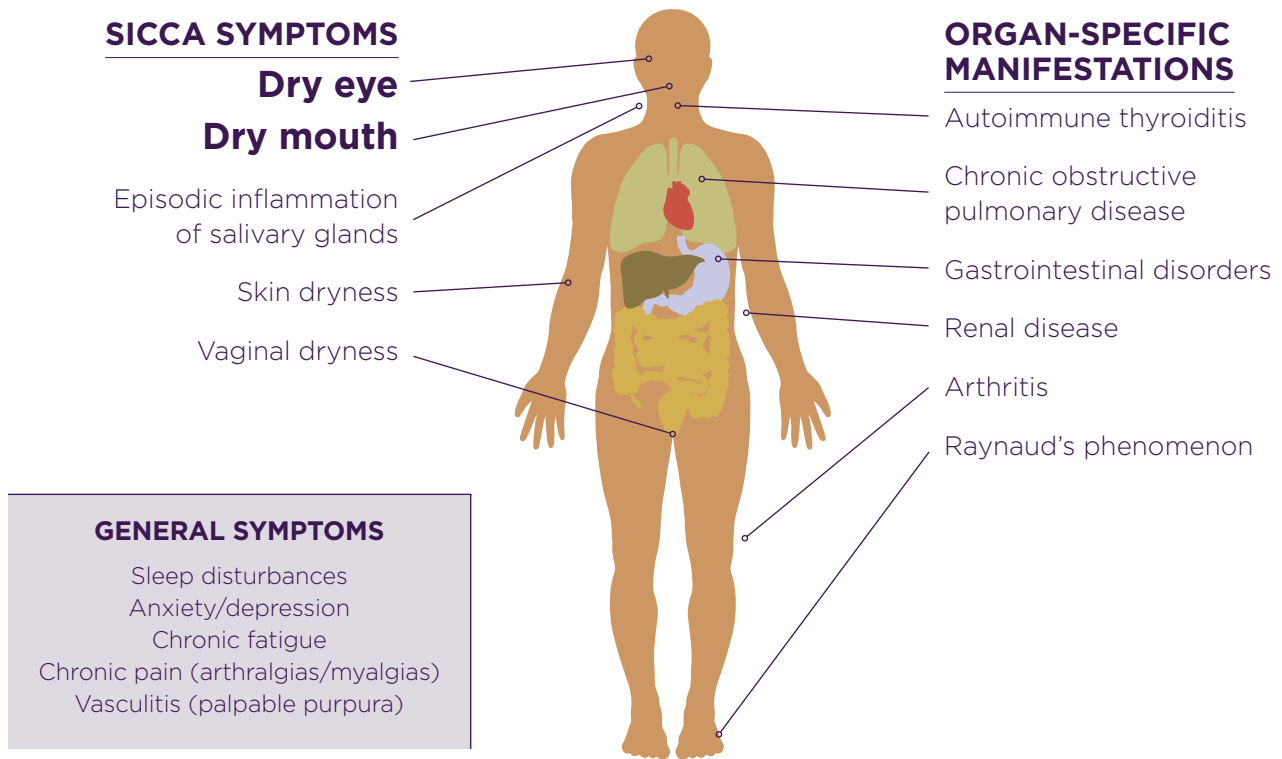


## INTRODUCTION

*Sjögren's syndrome is an insidious autoimmune disease that is characterized by the immune system attacking and gradually destroying moisture-producing glands throughout the body.<sup>1</sup> Patients with Sjögren's syndrome can present with a variety of symptoms, including dry eye, dry mouth, arthralgias, gastrointestinal (GI) disorders, chronic pain, chronic fatigue, and vasculitis, that can become increasingly debilitating as the disease progresses (Figures 1 and 2).<sup>2</sup> Additionally, research has found that patients with Sjögren's syndrome are at a 19 times higher risk of developing non-Hodgkin lymphoma.<sup>3</sup>*

*It is estimated that between 2-4 million people have Sjögren's syndrome in the US; however, only 1 million have an established diagnosis. This high incidence of underdiagnosis or misdiagnosis is likely due to the variable and nonspecific nature of the symptoms. Thus, the estimated average time to an accurate diagnosis is 10 years.<sup>1,4</sup> Approximately 1 in 10 cases of dry eye are likely due to Sjögren's syndrome, suggesting that eye care professionals (ECPs), such as optometrists, could be on the frontline of diagnosis.<sup>5,6</sup> The Sjö® Diagnostic Test can be easily implemented by ECPs in their offices. It is the first diagnostic test to incorporate both traditional and proprietary biomarkers. The 3 proprietary biomarkers offer significantly higher sensitivity and specificity than other testing methods, which enables early detection of Sjögren's syndrome.<sup>7</sup> A roundtable of leading optometrists was convened to discuss Sjögren's syndrome and how to incorporate the Sjö® Diagnostic Test into current practice patterns.*

**Figure 1.** Patients with Sjögren's syndrome can present with a wide variety of symptoms. The 2 main symptoms are xerophthalmia and xerostomia, but other common symptoms are arthralgias, chronic pain, chronic fatigue, and gastrointestinal disorders.<sup>2</sup>



**Figure 2.** Corneal staining caused by severe dry eye in a Sjögren's syndrome patient.

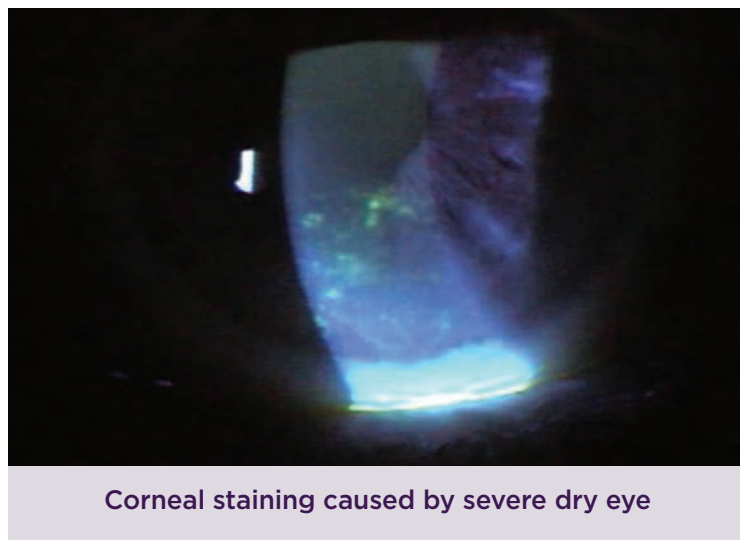


Image courtesy of Arthur B. Epstein, OD, FFAO.

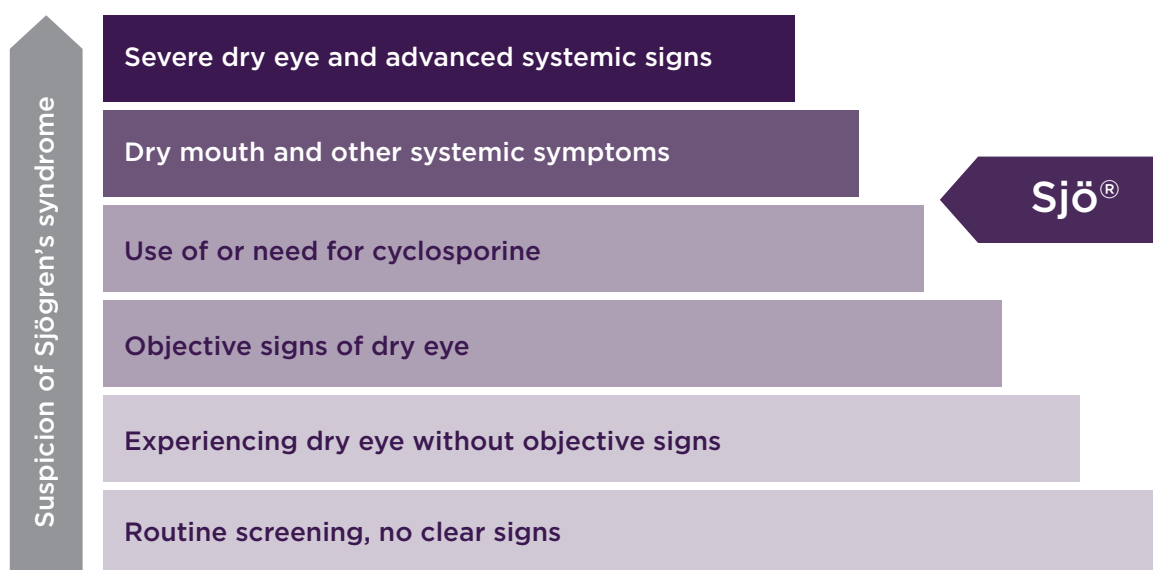
## WHEN TO CONSIDER SJÖGREN'S SYNDROME

**Paul M. Karpecki, OD, FAAO:** My clinic is primarily 90% ocular surface disease, and I recently had my staff pull all the cases with a 710.2 code, which encompasses keratoconjunctivitis sicca, secondary to Sjögren's syndrome. It turns out that we have over 300 such patients, so that's a big part of my practice, and they come from all over the country. It seems that once you have success with a few Sjögren's syndrome patients, they tell others and all of a sudden you go from 50 patients to 200. Given the potential number of patients, are there certain signs and symptoms that push you to consider Sjögren's syndrome in a dry eye patient?

**Mile Brujic, OD, FAAO:** I think we have to be somewhat sensitive to who we are testing. The perfect example of what I mean is if the patient is a 22-year-old female who is taking isotretinoin and presenting with dry eyes, I would not test her because I know exactly why she has dry eyes. But, if a patient presents with either significant signs or symptoms that can't be easily explained, I start to consider Sjögren's syndrome. One scenario is if a patient reports extreme dryness, with +2 to +3 diffuse corneal staining, damaged meibomian glands, or just a rough-looking ocular surface with no obvious cause, I will start to think of Sjögren's syndrome.

A second scenario is a combination of what I am seeing, what I am hearing the patients

**Figure 3.** Algorithm of signs that may push a clinician to consider Sjögren's syndrome. The Sjö® Diagnostic Test can fit into clinical practice when there is a greater suspicion of Sjögren's syndrome, such as when dry eye patients are refractive to cyclosporine treatment or have concomitant dry mouth or systemic symptoms.



say, and their systemic presentation. For example, if a patient comes in with a mild-to-moderate dry eye along with 2 or more diffuse rheumatologic issues that they may have been self-treating, such as stomach symptoms, loss of mental acuity, or chronic fatigue, then I start questioning them a little bit more, and I order the Sjö® Diagnostic Test (Figure 3).

**Mel A. Friedman, OD, FAAO:** In my practice, we like to take care of patients with the totality of healthcare and try to get ahead of the disease. One example is a 75-year-old female patient that came into the office with complaints of arthritic type pains, xerostomia, dryness of eyes, etc. For the last 10 years, her primary care physician was treating her for degenerative joint disease, but we suspected Sjögren's syndrome, so I ordered the Sjö® Diagnostic Test. She came up with huge rheumatology factors, indicating rheumatoid arthritis, so I referred her to a rheumatologist and the results have been encouraging.

It should be noted that GI disturbance is a big symptom in Sjögren's syndrome, and I don't know how many people even realize or start thinking about GI symptoms in conjunction with dry eye. I can tell you that my practice has definitely started asking about Crohn's disease, colitis, etc, in relation to dry eye, which we never used to do.

Also, I just wanted to point out that an easy and cheap test for xerostomia is to have the patient eat a soda cracker in front of you. Watch how the patient eats it, and if he or she has difficulty swallowing, that could be a sign of dry mouth.

**Scott G. Hauswirth, OD, FAAO:** Similar to everyone here, I am interested in identifying Sjögren's syndrome patients early and initiating treatment as early as possible. In order to identify potential Sjögren's syndrome patients, as part of my dry eye questioning, I also ask about chronic fatigue, chronic pain, and occasional dry mouth, and I think that has made a difference in increasing the capture of earlier-stage Sjögren's syndrome patients. If the patient has any 2 of these 3 symptoms, I include autoimmune issues and Sjögren's syndrome as part of my differential diagnosis. The Sjö® Diagnostic Test is designed to pick up autoantibodies at a much earlier stage, so we're able to diagnose younger patients who may not yet be positive with the Ro and La autoantibody tests. So, with the inclusion of the Sjö® Diagnostic Test in our diagnostic process, it just makes sense to order it sooner than with the panel we have traditionally used.

Temporal staining of the conjunctiva also has a very high association with Sjögren's syndrome. Barbara Caffery's research showed that patients who had a greater temporal conjunctival staining pattern had a high association with Sjögren's syndrome, so I have been looking at that lately.<sup>8</sup> Another potential early sign is the pattern of corneal staining and tear meniscus height. In my experience, patients with more circular, confluent staining may be more likely to test positive for Sjögren's syndrome, as well as those who have a decreased tear meniscus height.

I have also started to look at the pattern of corneal staining in patients with Sjögren's



syndrome. What I have found is that patients who have more circular confluent staining will probably test positive for Sjögren's syndrome. Finally, a really thin tear meniscus might be another potential sign of Sjögren's syndrome that you should consider evaluating since you have fluorescein in there.

**Douglas K. Devries, OD:** I practice at a referral center and I get some of the more challenging and complex cases in ocular surface diseases. For instance, similar to what Dr. Brujic discussed, when I see patients with dry eye and dry mouth, Sjögren's syndrome comes to mind. Also, when there are no obvious underlying causes or explanations and the patients' symptoms are recalcitrant to treatment, I start to consider Sjögren's syndrome. In addition, when the signs, symptoms, and severity just don't make sense, I again consider testing for Sjögren's syndrome. If a dry eye patient has a history of any autoimmune disease or symptoms of any autoimmune disease, not just Sjögren's syndrome, I will order the Sjö® Diagnostic Test. If the test results come back negative, yet positive for other autoimmune factors, the patient will benefit from a referral to a rheumatologist and view it as comprehensive care.

I want to point out one of the other things that I have noticed in my Sjögren's syndrome patients, which is that they often develop

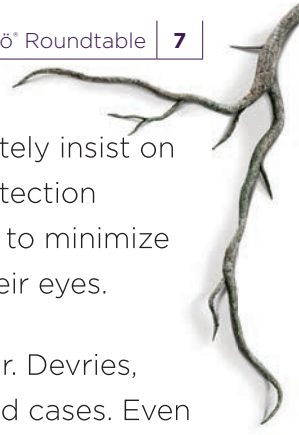
conjunctivochalasis at a much earlier age. When I notice a young patient has developed conjunctivochalasis, I test for Sjögren's syndrome, and I usually get a pretty high rate of positivity with those patients.

**Arthur B. Epstein, OD, FAAO:** My practice is tightly focused on dry eye; I would estimate that 70% of what I see is dry eye. In addition to reiterating what everyone has already said, I want to add that one of the things I learned from diagnosing so many patients is that young, otherwise asymptomatic, fairly normal patients, may have fairly high positivity for the proprietary biomarkers in the Sjö® Diagnostic Test. Previously, I was hesitant to refer someone for traditional Sjögren's syndrome testing because patients do not want to go through a biopsy, and traditional testing mechanisms are out of my sphere of control. However, my trigger for ordering the Sjö® Diagnostic Test is much lower than it was for the traditional testing because the testing is easy.

I agree with Drs. Brujic and Devries that the biggest thing that prompts me to consider Sjögren's syndrome is when things do not quite add up: a young person with much more severe symptoms or someone with a family history who suddenly develops dry eye at a young age. In addition, similar to others here, we are definitely testing more of our younger patients than before because the Sjö® Specimen Collection Kit is so easy to use.

**Walter O. Whitley, OD, MBA, FAAO:** I practice at a dry eye center and what I have found is that every patient is a little bit different.





Similar to many here, I usually start to think about the possibility of Sjögren's syndrome when a patient presents with symptoms of dry mouth or if the patient's signs and symptoms just do not make sense. With Sjö® testing, we get additional information that may help to diagnose the patient at an early stage. So why not do it and get the information earlier?

## TREATMENT PATTERNS FOR SJÖGREN'S SYNDROME

**Dr. Karpecki:** I feel that our colleagues often approach innovations with an attitude of, "It gives me an answer, but I do not know what to do with that diagnosis, so why should I test for it?" Even if they understand the significance of Sjögren's syndrome, they may not understand how to approach it. So, let's talk about what you do after you diagnose a patient with Sjögren's syndrome. How does that diagnosis change the way you manage the patient?

**Dr. Devries:** After a diagnosis, I don't allow a long time for staging and ramping up treatment. Instead, I refer the patient to a rheumatologist and start very aggressive treatment, especially if the patient is a 35- or 40-year-old who has tested positive. Even though the dry eye may not be really advanced, you know it will eventually progress, so I get much more aggressive a lot faster.

As part of this aggressive plan, I would not hesitate to put Sjögren's syndrome patients on autologous serum or add an amniotic membrane at a much earlier stage. Of course, patient education is one of the most

important aspects. We immediately insist on some type of environmental protection and eyewear that is really going to minimize the environmental impact on their eyes.

**Dr. Brujic:** Personally, I am like Dr. Devries, more aggressive, even in the mild cases. Even in the absence of significant symptoms, I would start them on long-term cyclosporine or something similar to help maintain a more normal ocular surface. Aggressive treatment and education can help patients be more compliant since they understand what's going to happen.

**Dr. Friedman:** I think aggressive treatment also helps build confidence in the doctor, and the patient feels like he or she has received an immediate response. I treat the same way as everyone else; more aggressive when the patient tests positive for Sjögren's syndrome. The more severe the form of dry eye, the more aggressive you have to be.

**Dr. Hauswirth:** I agree with the previous comments, but I think the biggest change that has occurred in my practice is my dialogue with the patient. I tend to be fairly aggressive with dry eye treatments anyway; however, the presence of Sjögren's syndrome really changes the game plan. It is more than just dry eye; it is an aggressive systemic disorder, which has a much larger impact, and it requires a completely different conversation than other forms of dry eye.

**Dr. Devries:** Do you have that conversation at the time you order the Sjö® Diagnostic Test? Because that is what I do. I say, "I really would

like to know this information because it will change the course of how aggressive we get. If the test results are negative, suggesting that you do not have Sjögren's syndrome, that is great and I will be relieved; however, if your test results are positive, then we know how to deal with it appropriately."

**Dr. Hauswirth:** Exactly. My practice has physician assistants that actually perform the test, so when I schedule that, I will say to the patient, "We are going to get some blood work done. This is going to basically help me understand really how severe this is, whether it is just your eyes or if it is really a systemic condition, which is going to necessitate participation from other healthcare providers, like rheumatologists, dentists, etc." This way, the patients know I am already looking ahead to who else we can get to help them out.

**Dr. Whitley:** In line with a much more aggressive approach to treatment, I think that Sjögren's syndrome is a perfect place to use punctal occlusion because we know the patient doesn't have enough secretions in the first place.

**Dr. Epstein:** It's funny that you should mention punctal plugs. I rarely use punctal plugs, but one of the few times where I think they actually make sense is in Sjögren's syndrome patients.

**Dr. Karpecki:** I agree. In my practice, patients with either Sjögren's syndrome or neurotrophic corneas typically get punctal plugs, in addition to therapy, at some point

in the course of management. A diagnosis of Sjögren's syndrome does change my therapy in other ways, as well. The rheumatologic or systemic component has to be managed in order to effectively treat the dry eye. I find that if you try to work on the eyes in a person who has an untreated autoimmune condition, there is just not as much improvement as you would expect. To optimize the chances of success, you have to have the systemic treatment, in addition to topical therapy.

In my experience, you can also treat the dry mouth symptoms with oral cevimeline 30 mg TID.

I have also found that it is important to be much more aggressive with treatment and educate patients that these are long-term treatment plans. I think it requires a very different approach to treatment, even though there might be overlap with other forms of dry eye.

## HOW AND WHEN TO REFER SJÖGREN'S SYNDROME PATIENTS

**Dr. Karpecki:** When you suspect Sjögren's syndrome, when does the rheumatology consult come in? I think we are all going to agree that you get a rheumatologist involved pretty quickly after the test results come in, but the second part of the question is, how has the rheumatology response been to referrals?

**Dr. Brujic:** For me, education has been the most important thing. When I had my first positive Sjö® Diagnostic Test, I picked up the phone and told the rheumatologist



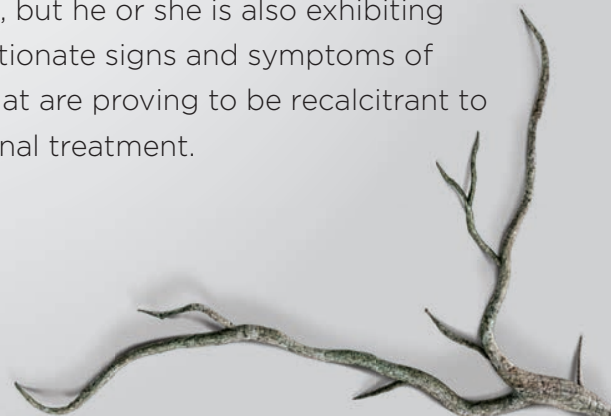
that I was going to be sending this person to him because of the Sjö® Diagnostic Test results. First of all, he had no idea about the 3 proprietary markers and he wanted to see the published papers about the markers. After I emailed them to him, he accepted the patient and we have grown the relationship from there, but rheumatologists definitely want to see the published work and want to understand the data behind the proprietary markers.

**Dr. Hauswirth:** I think that you have to find the right rheumatologist. For instance, we have a rheumatologist that we refer to on a regular basis. At the beginning of the relationship, the rheumatologist actually came to our practice and sat down with me to talk about how we were going to structure referrals. Also, we provided the rheumatologist with information about the Sjö® Diagnostic Test. Altogether, I think taking these steps definitely helped a lot with building a successful relationship between our practices.

**Dr. Karpecki:** Like Drs. Hauswirth and Brujic, I, too, like to provide rheumatologists with information about Sjögren's syndrome and the Sjö® Diagnostic Test, specifically, in regard to the higher risk of non-Hodgkin lymphoma in the Sjögren's syndrome patient population.<sup>3</sup> Once, I sent a letter to a local rheumatologist referring a possible Sjögren's syndrome patient and cited the statistics about non-Hodgkin lymphoma. The rheumatologist immediately called me back to discuss the data, which started a 2-way referral system.

**Dr. Friedman:** I've found that, for most of our local rheumatologists, there is usually a 2-month waiting period. To facilitate the referral process, we like to make the appointments for the patients and get them set up with the rheumatologists as soon as possible. When considering referrals for patients with Sjögren's syndrome, one primarily thinks of rheumatologists. However, in my practice, it has become a mandatory protocol to refer to not just a rheumatologist, but also to an oncologist. Evidence suggests that Sjögren's syndrome patients are at a much higher risk of developing non-Hodgkin lymphoma.<sup>3</sup> Therefore, it is imperative that the primary ECP realizes the responsibility that he or she has when managing patients with Sjögren's syndrome.

**Dr. Devries:** When a patient has a positive result from the Sjö® Diagnostic Test, I will facilitate a referral to a rheumatologist, if the patient is not already established with one. As an ECP, you will initially have to establish a rapport with local rheumatologists and, as pointed out by my colleagues at this roundtable, explain the findings because many rheumatologists have not been exposed to the proprietary biomarkers that are measured by the Sjö® Diagnostic Test. I will also explain to rheumatologists that the patient is not just testing positive for Sjögren's syndrome, but he or she is also exhibiting disproportionate signs and symptoms of dry eye that are proving to be recalcitrant to conventional treatment.



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## CONCLUSIONS

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**Dr. Karpecki:** Any concluding thoughts about why ECPs should integrate the Sjö® Diagnostic Test into their practice?

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**Dr. Whitley:** For some patients, the Sjö® Diagnostic Test gives an answer to all the symptoms they have been experiencing and they are relieved. They are just grateful to finally have an answer.

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**Dr. Friedman:** Well, for me, it is the results that I have seen after the diagnosis is made. I have had patients go from 20/50, 20/60, 20/100 visual acuity to 20/25 visual acuity after treatment. So it is worth being aggressive, making the right diagnosis, and getting everyone involved because you can get good results.

Also, for practitioners that truly believe in taking care of the whole body, the Sjö® Diagnostic Test fits right into that philosophy because, sometimes, it isn't just dry eye. By diagnosing and managing Sjögren's syndrome, you are really managing the patient's total well-being.

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**Dr. Epstein:** I agree that Sjögren's syndrome and the Sjö® Diagnostic Test are important for those practitioners who want to open up small practices wherever they can and be successful. These practitioners are going to need a holistic approach that is integrated into the local healthcare community, but Sjögren's syndrome and the Sjö® Diagnostic Test are also going to appeal to practitioners who already have a practice and want to get more involved in a specialty. The Sjö® Diagnostic Test is an easy way to start specializing in dry eye.

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**Dr. Devries:** I feel that integrating the Sjö® Diagnostic Test into a practice elevates the overall level of care that ECPs can provide to their patients, which, most importantly, may result in better outcomes for those patients.

Overall, there is one thing that everyone has kind of been alluding to but no one has actually expressed in so many words. Because of the Sjö® Diagnostic Test, optometry is in a position of diagnosing a chronic disease with significant morbidity and with long-term consequences. A diagnosis of Sjögren's syndrome has a massive impact on the patient, and optometrists are definitely in the position to help diagnose and manage these patients.

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