BEYOND DRYNESS:

The Hidden Impact of Systemic Manifestations in Sjögren's Disease

Featuring expert insights from

Eric Anderson, MD, RhMSUS

> ***Sjögren's disease is more than just dry eyes and dry mouth; it is a systemic autoimmune disease that can dramatically affect the lives of our patients. Many patients are suffering from manifestations beyond sicca that may be underappreciated or misattributed to other causes, leading to delays in diagnosis and treatment.***
>
> - Eric Anderson, MD, RhMSUS

Dr Anderson was compensated for his time.

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Sjögren's disease is a systemic autoimmune disease that can be serious and progressive[1–4]

Don't be misled by its common symptoms—Sjögren's disease can be a serious systemic condition with implications that can extend far beyond dryness.[5]

A hallmark feature of Sjögren's disease is the presence of sicca symptoms, including dry eyes and dry mouth.[6] Over 90% of patients report sicca symptoms. In addition, patients may experience vaginal dryness, fatigue, pain, and depression.[7-9] **Additionally, 30% to 40% of patients experience systemic manifestations beyond sicca, which can occur in the joints, skin, lymph nodes, or other organ systems** (Figure 1).[6,8,10] Patients may face severe systemic manifestations that can significantly impact long-term health and lead to reduced life expectancy.[11]

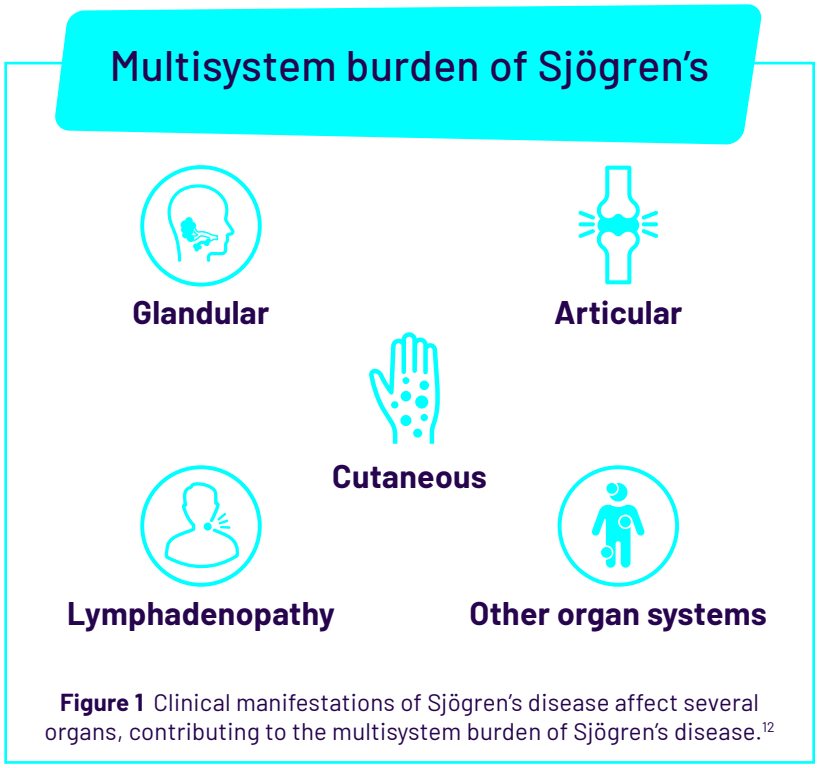

Figure 1 Clinical manifestations of Sjögren's disease affect several organs, contributing to the multisystem burden of Sjögren's disease.[12]

Sjögren's disease is a prevalent systemic autoimmune disease affecting between 1 and 4 million individuals in the United States, with a prevalence of 0.5% to 1.0%.[13] Sjögren's predominantly affects women, with a female-to-male ratio of approximately 9:1. Initial symptom onset is most commonly observed between the ages of 45 and 55 years (Figure 2).[5]

In the United States **up to 4 million** people are affected

Affects an estimated **0.5% to 1.0%** of the population

Ratio of **~9:1** females to males

Usual age of **45 to 55 years** for symptom onset

Figure 2 Sjögren's disease prevalence, gender distribution, and age of onset.[5,13]

> ***One of the hardest things for my patients with Sjögren's disease is that they often suffer silently. Friends and family cannot directly see the impact of their dryness or the pain in their joints that may not be swollen. This can cause our patients significant difficulty in maintaining a job or even finding joy in their hobbies.***
>
> - Eric Anderson, MD, RhMSUS

The heterogeneity of Sjögren's disease demands a broader clinical lens

The heterogeneity of Sjögren's disease often makes progression unpredictable. No two patients present with the same manifestations.[1] Existing symptoms can worsen, and in some patients, new manifestations can emerge over time.[14] **Survey findings highlight the extensive symptom burden associated with Sjögren's and its significant impact on patients' daily functioning and overall quality of life** (Figure 3).[15]

Patients with Sjögren's disease experience a
wide range of symptoms

Surveyed patients experiencing symptoms in the past 12 months, %

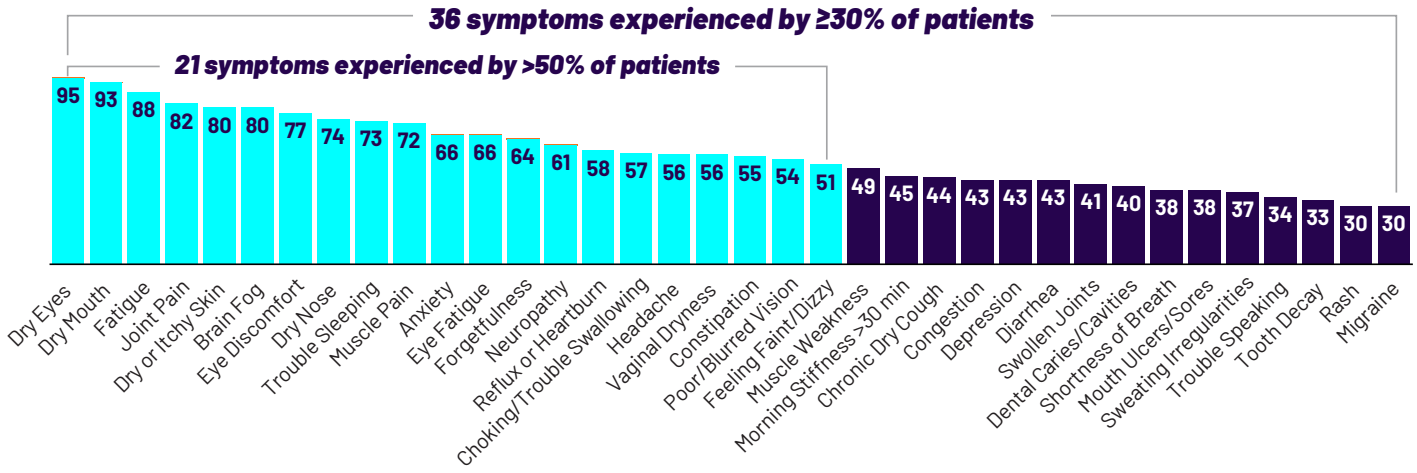

Figure 3 Results from a survey conducted by the Sjögren's Foundation in 2021 showing the range of symptoms experienced by adult patients with self-reported Sjögren's disease (N=3622).[15]

> ***Sjögren's disease is a whole-body disease and sometimes patients will not report dryness as their initial manifestation. I recently saw a woman in her 40s who was referred for worsening paresthesia. She had never really thought she had dry eyes or dry mouth but reported frequent tearing during our initial evaluation. Her Schirmer's testing and her unweighted unstimulated salivary flow rate were both concerning for underlying Sjögren's disease. While her anti-Ro/anti-La testing were negative, we did a minor salivary gland biopsy that was positive for Sjögren's disease. We need to be aware of these other manifestations, as sometimes the path to a diagnosis is not as clear.***
>
> - Eric Anderson, MD, RhMSUS

Sjögren's disease may extend far beyond dryness[5]

The manifestations of Sjögren's can affect multiple systems and may present at diagnosis or emerge over time (Figure 4).[1] Without timely diagnosis and intervention, symptoms can worsen and new organ involvement may emerge. **This underscores the need for early, individualized management to prevent disease progression and reduce the risk of long-term complications.**[1]

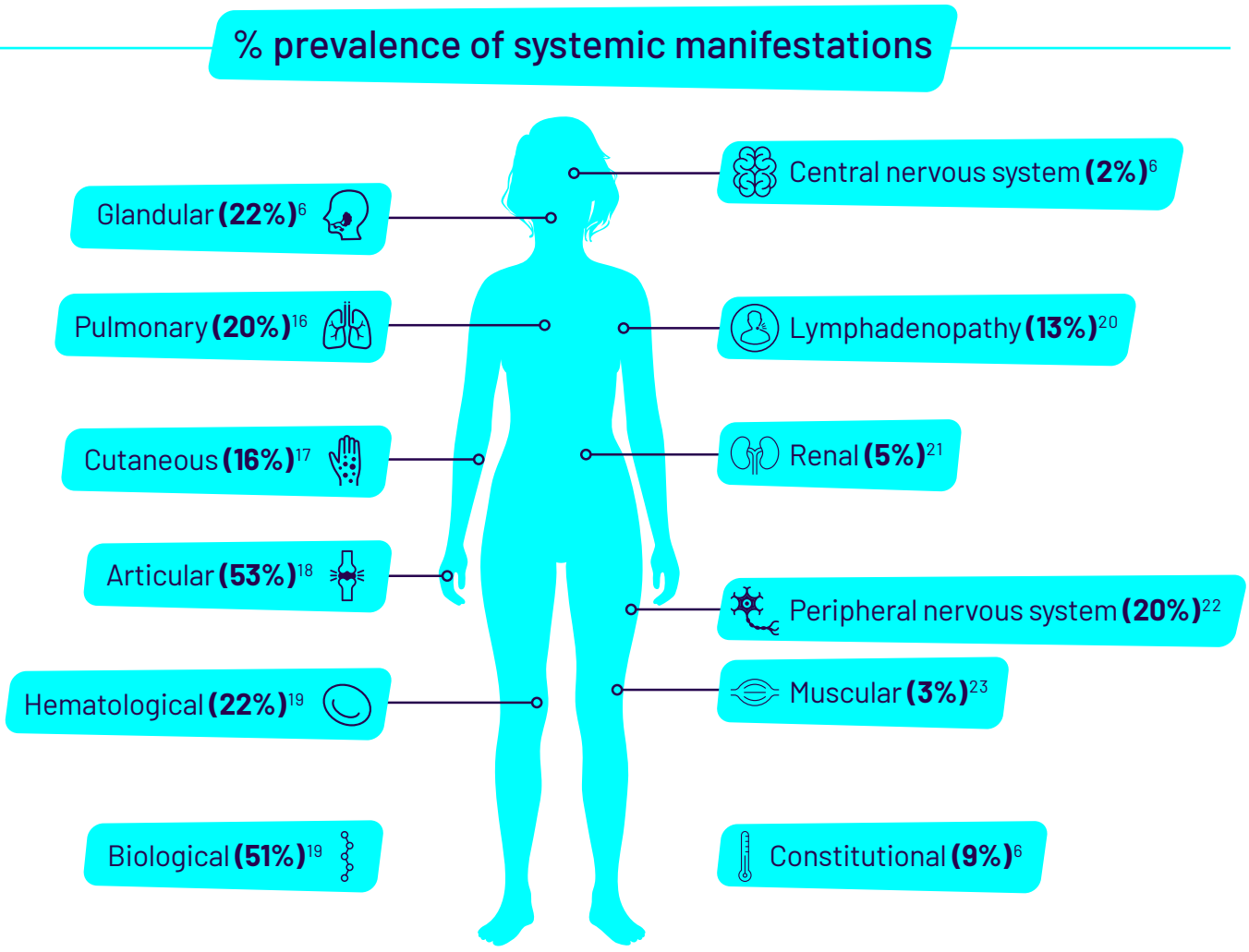

Figure 4 Systemic manifestations can affect multiple domains in patients with Sjögren's disease.

> ***When I am assessing established or suspected patients with Sjögren's disease, I perform a detailed review of systems to ensure I am assessing for additional organ involvement beyond their sicca symptoms. I pay particular attention to any new pulmonary, neurologic, or cutaneous complaints, as these may be signs of more serious organ involvement and require additional evaluation and treatment.***
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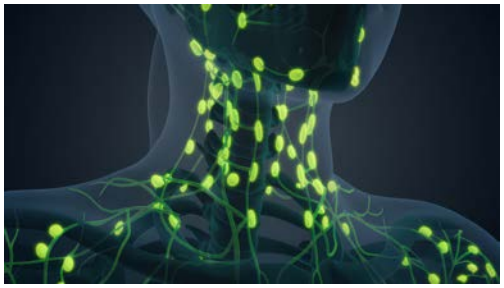
> - Eric Anderson, MD, RhMSUS

Patients with Sjögren's may face serious systemic manifestations that can significantly impact long-term health[11]

Complications of Sjögren's disease can be ***irreversible***[11,24]



Patients with Sjögren's have a 10- to 44-fold increased risk for lymphoma compared with healthy individuals.[25]

Up to 20% of patients with Sjögren's disease have interstitial lung disease (ILD).[26] Among those with ILD, up to 61% exhibit a nonspecific interstitial pneumonia pattern.[27]

Overall, patients with Sjögren's experience

Nearly 50%
increased risk in mortality*

compared with the general population, according to a meta-analysis of 14 studies[28]

Greater mortality risk was associated with[28]

- Older age
- Male gender
- Vasculitis
- ILD
- Low complement levels
- Positive anti-La/SSB
- Cryoglobulinemia

> ***Sometimes these serious manifestations have more subtle presentations. I usually check complement levels, inflammatory markers, urine studies, and CBC/CMP at each of my visits to watch for any new changes that could be a tip-off for worsening disease. I screen for lymphoma annually. I ask about changes in functional status, difficulty speaking or singing to assess for developing pulmonary involvement. Early identification and treatment of these more severe manifestations is important to reduce the risk of long-term organ damage in our patients with Sjögren's disease.***
>
> - Eric Anderson, MD, RhMSUS

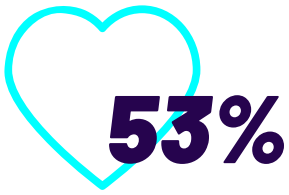
CBC, complete blood count; CMP, comprehensive metabolic panel; SSB, Sjögren's syndrome type B.

*Based on a systematic review and meta-analysis assessing all-cause mortality risk in patients with Sjögren's disease (N=14,584).

Sjögren's disease **is a constant presence that impacts quality of life**[7]

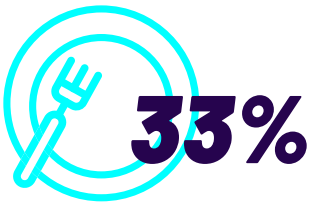
Sjögren's disease can also affect the ***emotional*** and ***social well-being*** of patients[29]

Fatigue in Sjögren's disease can be profound, making it difficult to concentrate, and is often associated with depression and anxiety.[30] Additionally, approximately 50% of patients report disruption in their sex life, social activities, or ability to work.[7]



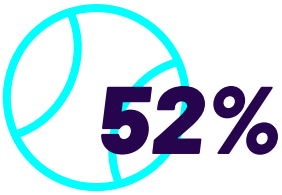
53%

report a negative impact on their **sex life**[7,*]



33%

report an impaired **ability to enjoy food** or a need to make dietary adjustments (36%)[15,†]



52%

report participating in **hobbies, social activities, and extracurricular activities**, which were frequently negatively impacted by Sjögren's disease[7,*]

49%

report their **job, career, or ability to work** were frequently negatively impacted by Sjögren's disease[7,*]

> ***I try to assess the impact my patient's symptoms have on their ability to care for themselves, their families, maintain work, and meaningfully participate in the things that bring them joy. If they cannot do these things, this is an opportunity for intervention.***
>
> – Eric Anderson, MD, RhMSUS

*Based on the 2016 "Living with Sjögren's Disease" survey assessing demographics, symptoms, quality of life, cost, and treatment in adult patients with Sjögren's disease (N=2961).

†Based on the 2021 "Living with Sjögren's" survey assessing the variety, severity, and quality of life impact of symptoms in adult patients with Sjögren's disease (N=3622).

Introducing “sicca plus,” a framework to identify patients eligible for biologic therapy

Sicca PLUS

If a patient with sicca symptoms is also experiencing 1 or more signs of systemic organ involvement, it may be time to consider a biologic therapy. Signs of organ involvement may include inflammatory joint disease, swollen glands, lymphadenopathy, cutaneous, or other organ involvement.

Currently, there are no approved therapies targeting the underlying pathogenesis of Sjögren’s disease or slowing the disease progression.[31] A more comprehensive approach to patient care is needed to do more for your patients with “sicca plus”—one that considers not just dryness factors, such as salivary flow and tear production, but also other factors, including fatigue, joint pain, organ involvement, and overall disease activity.[2]

> ***Diagnosing someone with Sjögren’s disease is only the beginning of their journey. For far too long we have been limited to symptomatic sicca management and ‘borrowed’ treatments with mixed results for more serious manifestations. We are in desperate need of treatments that can assess the multidomain nature of Sjögren’s disease that we can confidently prescribe to our patients.***
>
> - Eric Anderson, MD, RhMSUS

> ***Sjögren's disease is a systemic autoimmune disease that can significantly affect our patients in ways beyond dryness. Understanding and identifying these other manifestations is crucial to help improve outcomes for our patients with Sjögren's disease.***
>
> - Eric Anderson, MD, RhMSUS

UNCOVER THE POTENTIAL SYSTEMIC IMPACT of Sjögren's

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