Tracking Disease Activity and Progression
in Sjögren's Disease

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> ***"Monitoring for new symptoms or signs of progression is so important in Sjögren's disease. Systemic complications can progress silently, and by the time they become obvious, we've often missed the opportunity to intervene."***
>
> — Erin Siceloff, PA-C

OBJECTIVE: Understand the importance of regular, comprehensive assessment in Sjögren's disease and how advanced practice providers (APPs), as frontline clinicians, play a valuable role in tracking disease activity and progression to inform ongoing monitoring and management.

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Erin Siceloff was compensated for her time by Novartis Pharmaceuticals Corporation.

Sjögren's disease is more than dryness[1]

Sjögren's is a systemic autoimmune disease that can be serious and progressive[2-5]

Sjögren's disease (SjD) is often recognized for its hallmark sicca symptoms, with approximately 90% of patients reporting oral and/or ocular dryness.[6] SjD can extend beyond dryness; it is a systemic disease that can cause inflammation or damage across multiple organ systems, including the joints, skin, lymph nodes, lungs, and brain.[1,7-9]

To better understand disease burden, clinicians should consider the broader systemic impact of SjD[3]

The EULAR Sjögren's syndrome disease activity index (ESSDAI) can support this approach by organizing systemic activity into measurable domains, helping clinicians identify less obvious manifestations and assess overall disease activity as low, moderate, or high.[10]

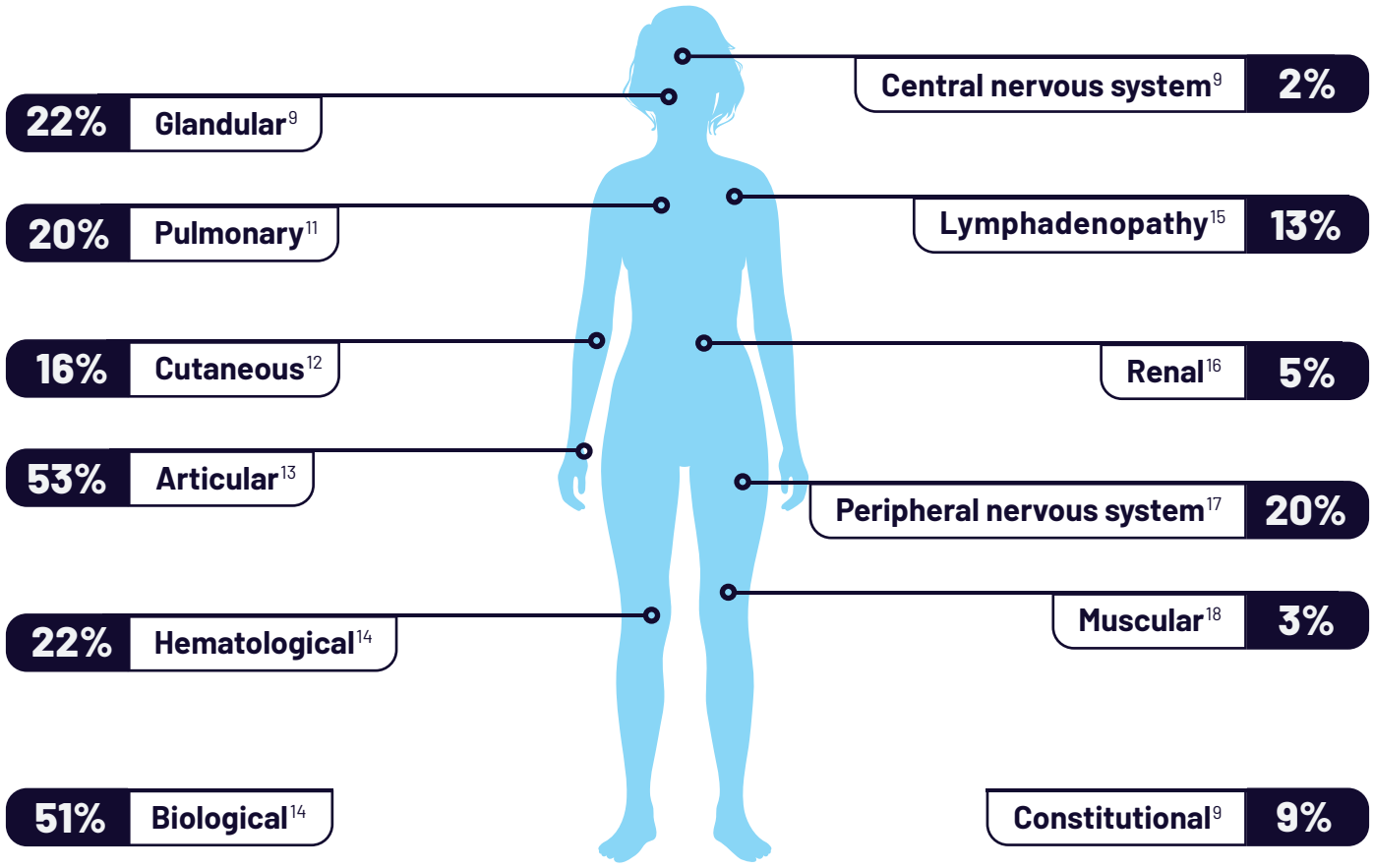


Figure 1. Prevalence of systemic involvement across 12 ESSDAI domains.

EULAR, European Alliance of Associations for Rheumatology.

The heterogeneous nature of SjD calls for regular, comprehensive assessments[3]

Progression in SjD is highly variable[2]

Some patients may have a slow, relatively stable disease course, while others may experience worsening symptoms or develop new systemic manifestations.[2] Because disease progression is unpredictable and varies across patients, **ongoing assessment should consider not only dryness factors, such as salivary and lacrimal gland function, but also systemic manifestations, including joint pain and organ involvement.** EULAR recommendations for the management of SjD note that the frequency of ongoing monitoring should be tailored based on their level of systemic disease activity.[3]

Monitor Patients With Systemic Disease Activity

- **Watch for worsening of existing symptoms**
- **Identify new symptoms or systemic manifestations**
- **Screen for lymphoma**

Experts Recommend*

Low Systemic Disease Activity
Monitor less frequently, such as every 6 to 12 months

High Systemic Disease Activity
Monitor more frequently

Figure 2. Recommendations for individualized patient monitoring and frequency.[3,14,19]

> ***"Treatment and management strategies are really different in patients with mild disease versus patients with more severe disease."***
>
> — Erin Siceloff, PA-C

*Based on the 2019 EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies.

Looking beyond the physical exam to uncover hidden disease activity

Critical indicators of disease can lie beneath the surface

The heterogeneity of SjD can make disease progression difficult to predict and may complicate assessment if evaluation is focused only on classic sicca symptoms.[2,3] **Ask clear, targeted questions and encourage deeper discussion to better understand the full impact of the disease on your patients' lives (Figure 3).**

ESSDAI-based questions* can help reveal hidden disease activity

Glandular domain
Have you noticed any swelling in your face or neck?

Articular domain
Have you had pain in your hands, wrists, ankles, and feet in the past 4 weeks?

Pulmonary domain
Have you been experiencing shortness of breath or a persistent cough?

Renal domain
Have you noticed any changes in your urine color or volume?

Figure 3. Sample questions to help assess 4 of the 12 ESSDAI domains.[20]

Click here to learn how the ESSDAI assesses systemic disease activity in patients with SjD

In addition to targeted questioning, blood testing for biomarkers can help detect subclinical systemic disease activity **(Table 1)**.[20] Together, thoughtful questioning and biomarker assessment can support a more comprehensive understanding of disease burden and help inform ongoing monitoring and management.

> ***"Not everything is going to show up on physical exam, so sometimes you have to ask the right questions and look at the right labs to understand what's going on."***
>
> — Erin Siceloff, PA-C

Biomarker	Abnormal levels† that may identify subclinical systemic disease activity
IgG level	• ≥16 g/L, or a recent decrease of IgG level (<5 g/L)[20]
Blood cell counts (of autoimmune origin only)	• Neutropenia (<1500/mm^3)[20] • Anemia (<12 g/dL)[20] • Thrombocytopenia (<150,000/mm^3)[20] • Lymphopenia (<1000/mm^3)[20]
Cryoglobulins	• Presence of cryoglobulins[20]
Complement levels	• Hypocomplementemia (C4 or C3)[20]

Table 1. Biomarkers that can help identify subclinical systemic disease activity. These biomarkers are captured in the biological and hematological domains of the ESSDAI score and can be tracked in clinical practice.[20]

*Each domain requires a thorough evaluation of Sjögren's disease-related signs and symptoms, guided by detailed definitions to determine the level of disease activity. In some cases, laboratory or imaging assessments may also be necessary to accurately assign an ESSDAI score. †Lab values may vary.
C3, complement component 3; C4, complement component 4; Ig, immunoglobulin.

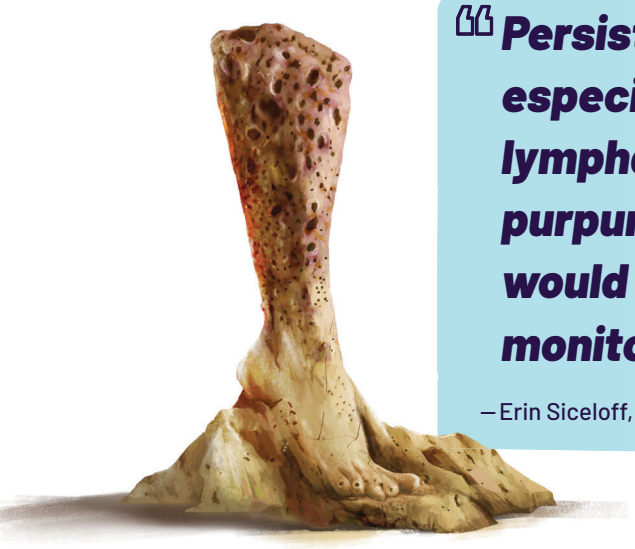
Biomarkers and clinical features can help indicate the level of systemic disease activity and the likelihood of disease progression[21]

Certain phenotypes have been associated with a higher risk of progression to systemic manifestations, including a high focus score, the presence of germinal centers, rheumatoid factor positivity, cryoglobulinemia, low complement levels (C3/C4), and male gender.[21]

Features such as swollen salivary glands, lymphadenopathy, and cutaneous involvement, including palpable purpura, have also been associated with an increased risk of lymphoma in patients with SjD.[22] **Biomarkers and observable clinical factors can help build a more complete picture of disease burden, support risk stratification, and guide decisions about follow-up and monitoring.**

Biomarker or clinical factor	Risks associated with systemic disease activity
Prolonged inflammation in the salivary glands	• Associated with irreversible damage, atrophy, or fibrosis that may lead to impaired salivary gland function[4,23]
Moderate or high disease activity (ESSDAI ≥5)	• **4× increased** odds of lymphoma vs patients with ESSDAI <5[24,‡] • **5× increased** odds of chronic pulmonary disease compared with those with ESSDAI <5[25,§] • **10× increased** odds of myocardial infarction compared with those with ESSDAI <5[25,§]
Consistently high IgG levels over a 3-year period	• **~2× increased** risk of developing systemic organ involvement and irreversible organ damage at 3 years compared with patients with Sjögren's disease who have consistently normal IgG levels[26]
Cytopenias	• Up to **16× increased** odds of lymphoma[14]
Skin involvement, especially palpable purpura; Cryoglobulinemia; Lymphopenia; Low complement levels, especially C4	• Increased odds of lymphoma[14,27-29] · Skin involvement: **up to 16 times** · Cryoglobulinemia: **up to 22 times** · Lymphopenia: **up to 16 times** · Hypocomplementemia: **up to 40 times**

Table 2. Factors that may increase the risk associated with systemic disease activity.



"Persistent parotid gland enlargement—especially if it's unilateral, and lymphadenopathy, or things like palpable purpura—those are clinical signs that would make me pay closer attention and monitor a patient more carefully."

—Erin Siceloff, PA-C

‡Based on patients who developed mucosal-associated lymphoid tissue lymphoma more than 3 years after the ESSDAI measurement.[24]
§Based on the ESSDAI score measured at the most recent visit.[25]

Although chronic inflammation does not always result in organ damage, morphological changes are irreversible once they occur[23,30]

Systemic manifestations of SjD can significantly affect long-term health and may contribute to reduced life expectancy **(Figure 4)**.[31]

Interstitial Lung Disease

Up to 20% of patients with SjD have interstitial lung disease[32]

Cardiovascular Impact

34% increased risk of coronary morbidity and a 46% increased risk of cerebrovascular morbidity compared with the general population[33,*]

Lymphoma

10 to 44 times higher risk in patients with SjD than in healthy individuals[14]

50% **Increased risk of mortality** among patients with SjD compared with the general population[34,†]

Figure 4. Systemic complications and increased morbidity and mortality in SjD.

> ***In Sjögren's disease, being proactive rather than reactive matters.***
>
> —Erin Siceloff, PA-C

*Based on a systematic review and meta-analysis assessing cardiovascular morbidity in patients with SjD (14 studies; N=67,124).[33]

†Based on a systematic review and meta-analysis assessing all-cause mortality risk in patients with SjD (14 studies; N=14,584).[34]

Key Takeaways for Advanced Practice Providers

SjD is more than dryness — it is a serious, systemic autoimmune disease that can progress over time and may lead to irreversible organ damage if not recognized early[1-5,23,30]

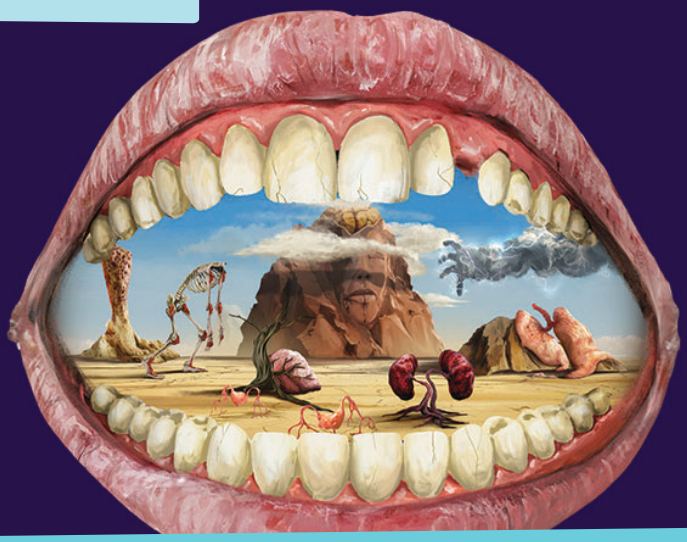
Sicca symptoms alone may not reflect total disease burden — assessment should consider the broader impact of SjD on the whole patient[3,29]

Regular, comprehensive assessment can help APPs better understand disease activity and support ongoing monitoring and management[3,30]

Biomarkers, clinical factors, and an ESSDAI-based review of systems can help uncover manifestations beyond classic sicca symptoms[21,30]

"Sjögren's disease can affect a patient's quality of life far beyond what a lab abnormality alone may show, so I try to take a comprehensive approach that considers patient-reported symptoms, labs, and other objective findings."

— Erin Siceloff, PA-C



Discover additional insights from APPs on scoring disease activity in **Sjögren's disease**

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