SJÖGREN'S SYNDROME

Sjögren's Syndrome: Lesser Evil or Hidden Challenge?

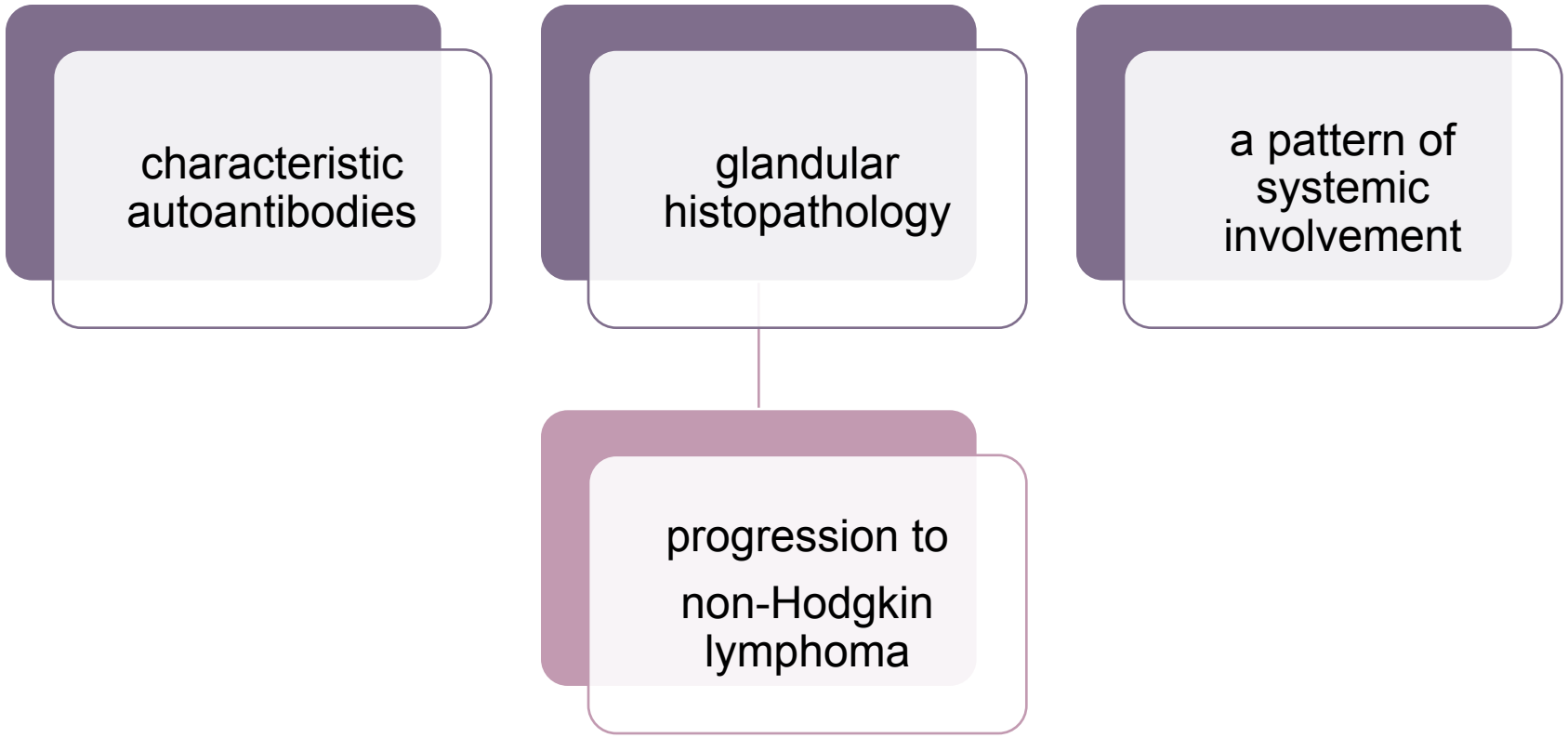
OBJECTIVES

Awareness of Sjögren’s Disease.

Highlight Updated Diagnostic and Treatment Approaches.

Emphasize the Importance of Multidisciplinary Care.

SJÖGREN'S IS A DISTINCT AUTOIMMUNE DISEASE



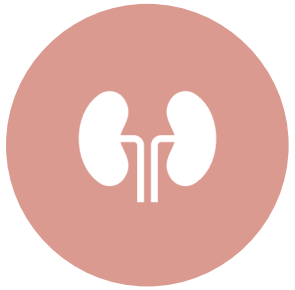
Baer AN and Hammitt KM. Sjögren's Disease, Not Syndrome. *Arthritis Rheumatol.* 2021 Jul;73(7):1347-8. PMID: 33559389.

INTRODUCTION

Chronic autoimmune disorder.

Lymphocytic infiltration of exocrine glands (salivary and lacrimal glands).

Symptoms: Dry mouth (xerostomia) and dry eyes (keratoconjunctivitis sicca).



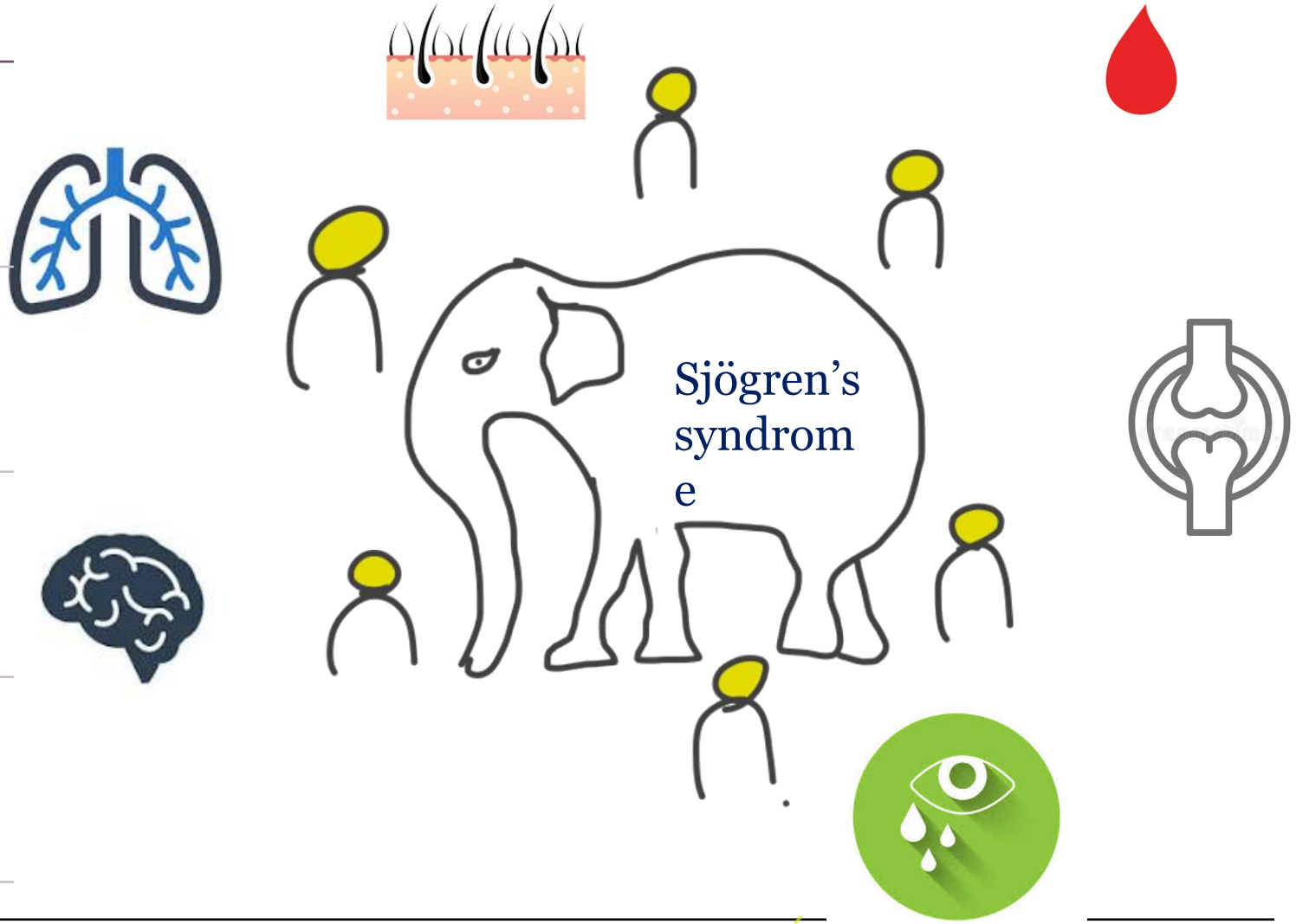
Systemic involvement: Fatigue, joint pain, and organ involvement (lungs, skin, kidneys, CNS).

Pleiomorphic systemic autoimmune manifestations

glandular manifestations

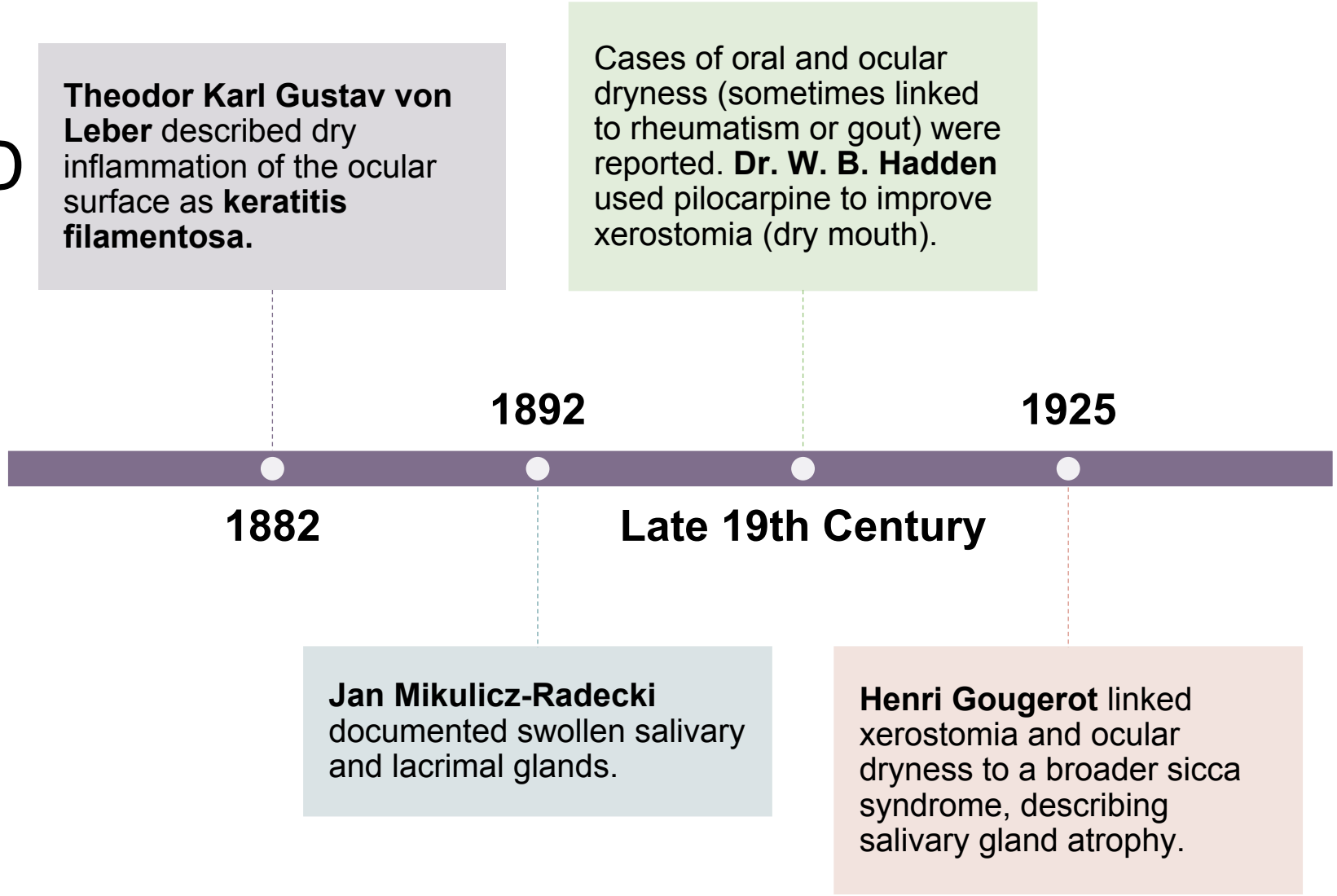
psychosomatic component

possible progression to non-Hodgkin lymphoma



Parisis D, Chivasso C, Perret J, Soyfoo MS, Delporte C. Current State of Knowledge on Primary Sjögren's Syndrome, an Autoimmune Exocrinopathy. J Clin Med. 2020 Jul 20;9(7):2299.

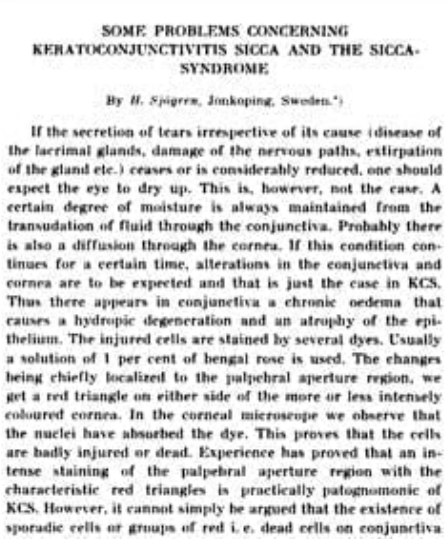
HISTORICAL BACKGROUND



Brito-Zerón P, Baldini C, Bootsma H, Bowman SJ, Jonsson R, Mariette X, Sivils K, Theander E, Tzioufas A, Ramos-Casals M. Sjögren syndrome. Nat Rev Dis Primers. 2016 Jul 7;2:16047. doi: 10.1038/nrdp.2016.47. PMID: 27383445.

HISTORICAL BACKGROUND

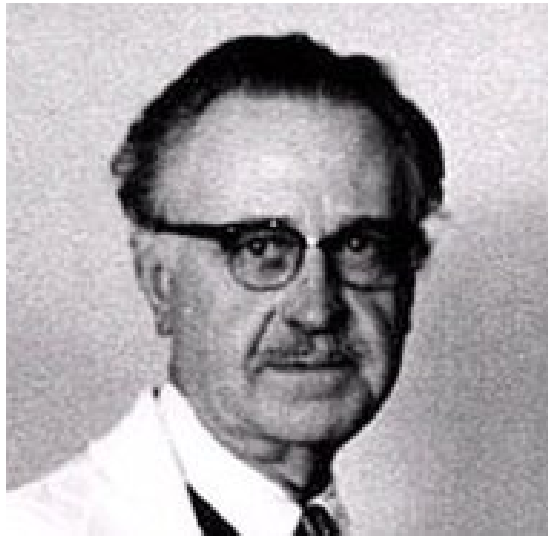
- **1930: Henrik Samuel Conrad Sjögren**
- Swedish ophthalmologist (1899–1986).
- He identified it as "**a general disease**," establishing it as a **distinct nosologic entity**.



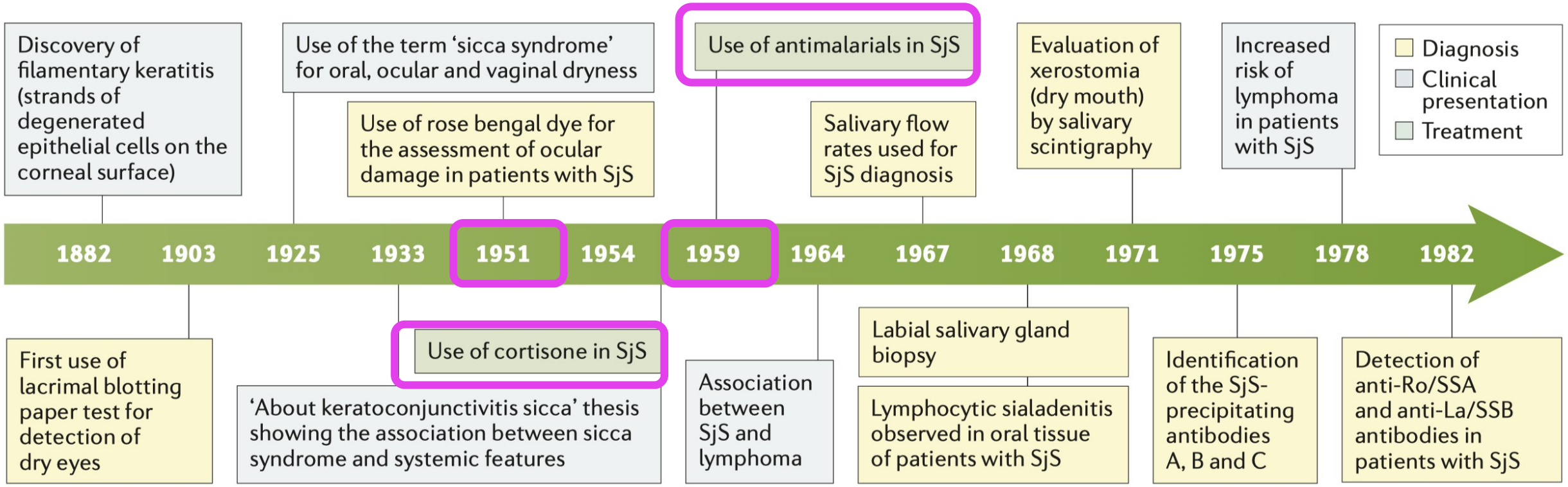
SOME PROBLEMS CONCERNING
KERATOCONJUNCTIVITIS SICCA AND THE SICCA-SYNDROME

By *H. Sjögren*, Jonkoping, Sweden.*)

If the secretion of tears irrespective of its cause (disease of the lacrimal glands, damage of the nervous paths, extirpation of the gland etc.) ceases or is considerably reduced, one should expect the eye to dry up. This is, however, not the case. A certain degree of moisture is always maintained from the transudation of fluid through the conjunctiva. Probably there is also a diffusion through the cornea. If this condition continues for a certain time, alterations in the conjunctiva and cornea are to be expected and that is just the case in KCS. Thus there appears in conjunctiva a chronic oedema that causes a hydropic degeneration and an atrophy of the epithelium. The injured cells are stained by several dyes. Usually a solution of 1 per cent of bengal rose is used. The changes being chiefly localized to the palpebral aperture region, we get a red triangle on either side of the more or less intensely coloured cornea. In the corneal microscope we observe that the nuclei have absorbed the dye. This proves that the cells are badly injured or dead. Experience has proved that an intense staining of the palpebral aperture region with the characteristic red triangles is practically patognomonic of KCS. However, it cannot simply be argued that the existence of sporadic cells or groups of red i. e. dead cells on conjunctiva



Brito-Zerón P, Baldini C, Bootsma H, Bowman SJ, Jonsson R, Mariette X, Sivils K, Theander E, Tzioufas A, Ramos-Casals M. Sjögren syndrome. Nat Rev Dis Primers. 2016 Jul 7;2:16047. doi: 10.1038/nrdp.2016.47. PMID: 27383445.



1998
Salagen® (pilocarpine hydrochloride)

2000
Evoxac® (cevimeline)

2009
NeutraSal®

Brito-Zerón P, Baldini C, Bootsma H, Bowman SJ, Jonsson R, Mariette X, Sivils K, Theander E, Tzioufas A, Ramos-Casals M. Sjögren syndrome. Nat Rev Dis Primers. 2016 Jul 7;2:16047. doi: 10.1038/nrdp.2016.47. PMID: 27383445.

2017 BSR

2020 eular

2024 BSR

BRITISH SOCIETY FOR RHEUMATOLOGY

The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome

Recommendation

EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies

Rheumatology, 2025, **64**, 409–439
https://doi.org/10.1093/rheumatology/keae152
Advance access publication 16 April 2024
Guidelines

British Society for Rheumatology RHEUMATOLOGY OXFORD

Guidelines

British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease

Elizabeth J *et al* British Society for Rheumatology guideline on management of adult and juvenile onset Sjögren disease, *Rheumatology*, Volume 64, Issue 2, February 2025, Pages 409–439, https://doi.org/10.1093/rheumatology/keae152

Elizabeth J. *et al.* The British Society for Rheumatology guideline for the management of adults with primary Sjögren's Syndrome, *Rheumatology*, Volume 56, Issue 10, October 2017, Pages e24–e48

amos-Casals M, Brito-Zerón P, Bombardieri S On behalf of the EULAR-Sjögren Syndrome Task Force Group*, et al* EULAR recommendations for the management of Sjögren's syndrome with topical and systemic therapies *Annals of the Rheumatic Diseases* 2020;**79:**3-18.

UNDERSTANDING SJÖGREN'S /

Sjögren's Syndrome to Sjögren's Disease: Why the Name Changed

> International Sjögren's patient and medical community has officially changed the disease name from *Sjögren's Syndrome* to *Sjögren's Disease*!

The disease name
Sjögren's Syndrome
has officially changed to
Sjögren's Disease!

A
A

Symptoms +

https://sjogrens.org/understanding-sjogrens/sjogrens-syndrome-to-sjogrens-disease-why-the-name-changed

WHY NAME CHANGED?

Systemic Nature:

Severity:

Alignment:

Awareness:

https://sjogrens.org/understanding-sjogrens/sjogrens-syndrome-to-sjogrens-disease-why-the-name-changed

CLINICAL PRESENTATION

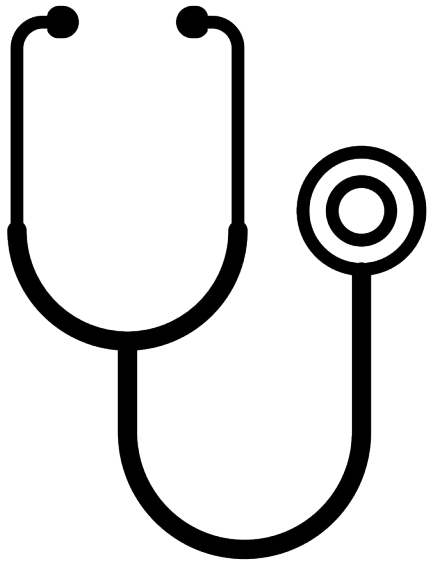
Glandular Symptoms:

- Dry mouth (xerostomia).
- Dry eyes (keratoconjunctivitis sicca).
- Parotid gland enlargement.

Extraglandular Symptoms:

- Fatigue, joint pain, skin rashes, Raynaud's phenomenon.
- Pulmonary, renal, or neurological involvement.

DIAGNOSTIC CRITERIA

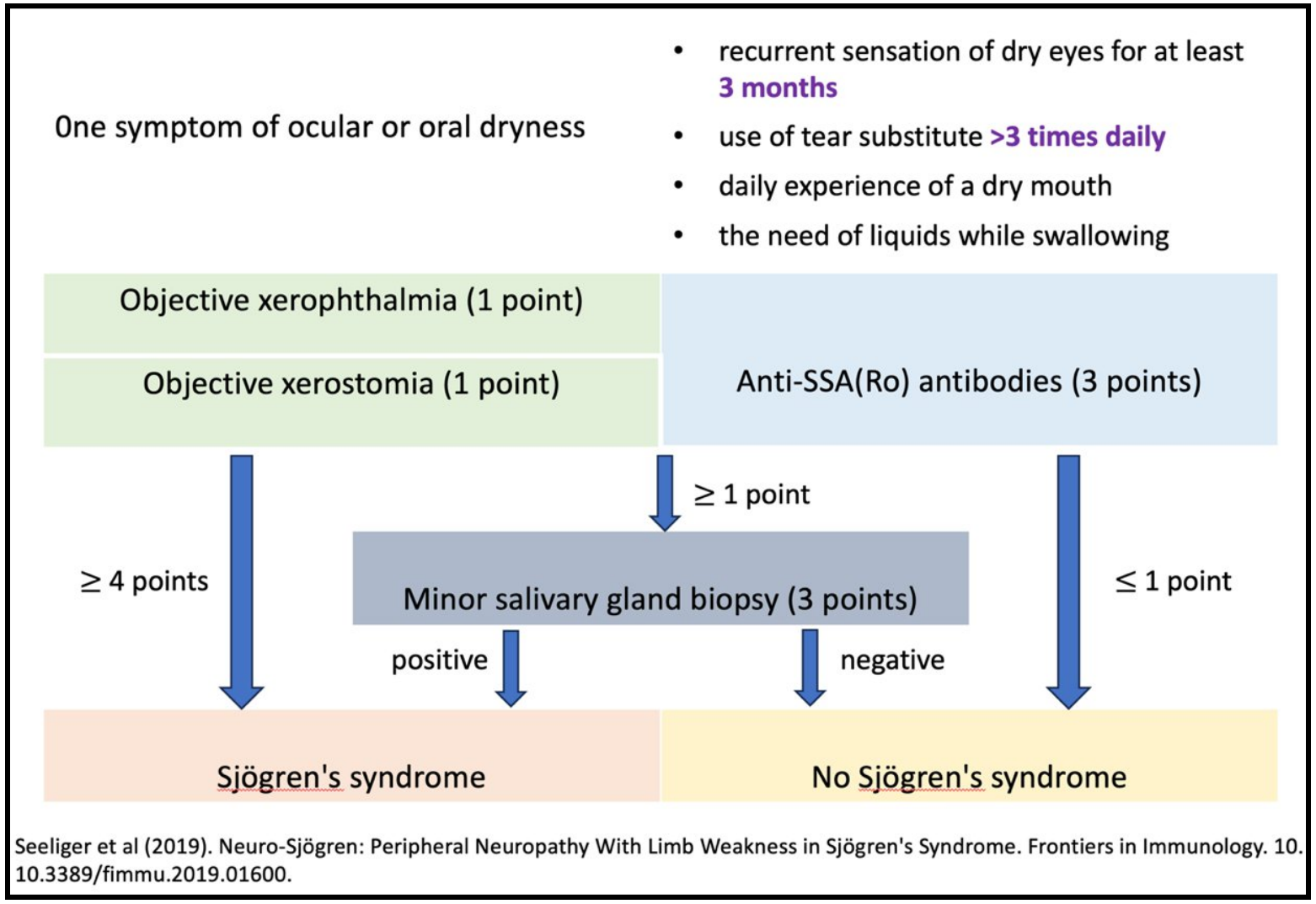


2016 ACR/EULAR Classification Criteria:

- Ocular symptoms (e.g., dry eyes for >3 months).
- Oral symptoms (e.g., dry mouth for >3 months).
- Objective tests for dry eyes (Schirmer’s test, Ocular Staining Score).
- Objective tests for dry mouth (salivary flow rate).
- Labial salivary gland biopsy.
- Positive anti-SSA/Ro antibodies.

Shiboski CH, Shiboski SC, Seror R, et al. 2016 American College of Rheumatology/European League Against Rheumatism Classification Criteria for Primary Sjögren's Syndrome: A Consensus and Data-Driven Methodology Involving Three International Patient Cohorts. *Arthritis Rheumatol*. 2017;69(1):35-45. doi:10.1002/art.39859

2016 ACR/EULAR CLASSIFICATION CRITERIA:



Seeliger et al (2019). Neuro-Sjögren: Peripheral Neuropathy With Limb Weakness in Sjögren's Syndrome. Frontiers in Immunology. 10. 10.3389/fimmu.2019.01600.

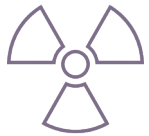
DIAGNOSTIC WORKUP

Clinical Evaluation:

Detailed history and physical examination.

Laboratory Tests:

Autoantibodies (anti-SSA/Ro, anti-SSB/La, ANA, RF).
Inflammatory markers (ESR, CRP).
Salivary and tear function tests.



Imaging Studies:

Salivary gland ultrasound, MRI, or scintigraphy.

Histopathology:

Labial salivary gland biopsy.

DIFFERENTIAL DIAGNOSIS

1. Rheumatoid arthritis (RA).
2. Systemic lupus erythematosus (SLE).
3. Fibromyalgia.
4. Chronic fatigue syndrome.
5. Medication side effects (e.g., anticholinergic drugs).

CHALLENGES IN DIAGNOSIS

Overlap with other autoimmune diseases.

Atypical presentations (e.g., extraglandular symptoms without dryness).

Variability in autoantibodies (not all patients test positive for anti-SSA/Ro).

EMERGING DIAGNOSTIC TOOLS

- **Biomarkers:** Research ongoing for early diagnosis and monitoring.
- **Advanced Imaging:** Elastography, contrast-enhanced ultrasound.

KEY POINTS

- Multidisciplinary approach required (clinical evaluation, lab tests, imaging, histopathology).
- Early and accurate diagnosis is crucial for treatment and preventing complications.
- Advances in diagnostic tools and criteria continue to improve management.

DISEASE ACTIVITY MEASUREMENT TOOL

1	Constitutional	N	L		M	7	Renal	N	L	M	H
		0	3		6			0	5	10	15
2	Lymphadenopathy	N	L	M	H	8	Muscular	N	L	M	H
		0	4	8	12			0	6	12	18
3	Glandular	N	L		M	9	PNS	N	L	M	H
		0	2		4			0	5	10	15
4	Articular	N	L	M	H	10	CNS	N	L		H
		0	2	4	6			0	10		15
5	Cutaneous	N	L	M	H	11	Hematological	N	L	M	H
		0	3	6	9			0	2	4	6
6	Pulmonary	N	L	M	H	12	Biological	N	L		M
		0	5	10	15			0	1		2

<5 low	≥ 5 to ≤13 Moderate	≥14 High	≥3 improvement

eular | EUROPEAN ALLIANCE OF ASSOCIATIONS FOR RHEUMATOLOGY

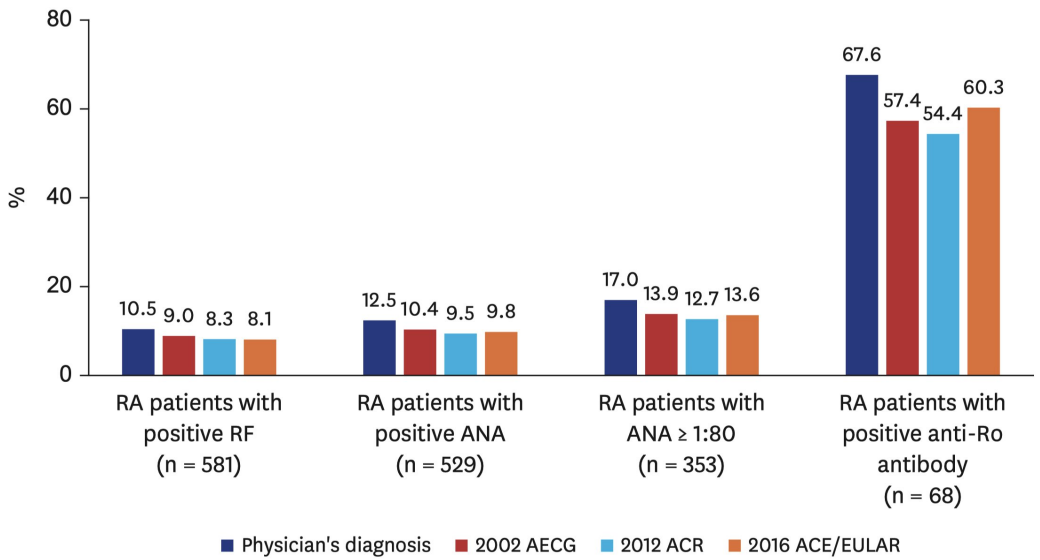
- **ESSDAI (EULAR Sjögren's Syndrome Disease Activity Index):**
  - Measures systemic involvement.
  - Helps tailor treatment based on disease severity.

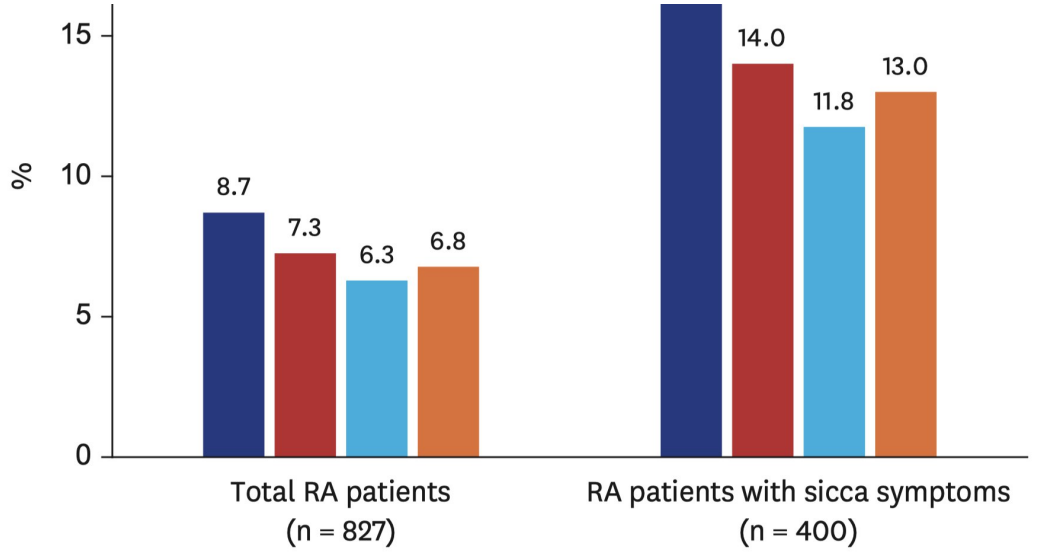
Seror, R., Bowman, S. J., Brito-Zerón, P., & the EULAR Sjögren's Task Force. (2015). EULAR Sjögren's syndrome disease activity index (ESSDAI): A user guide. *RMD Open, 1*(1), e000022. https://doi.org/10.1136/rmdopen-2014-000022

SJOGREN SYNDROME VS OTHER AUTOIMMUNE DISEASES

The prevalence of SS in SLE patients ranged from 9% and 19%.

The prevalence of SS among RA patients has been reported to be as high as 55%.

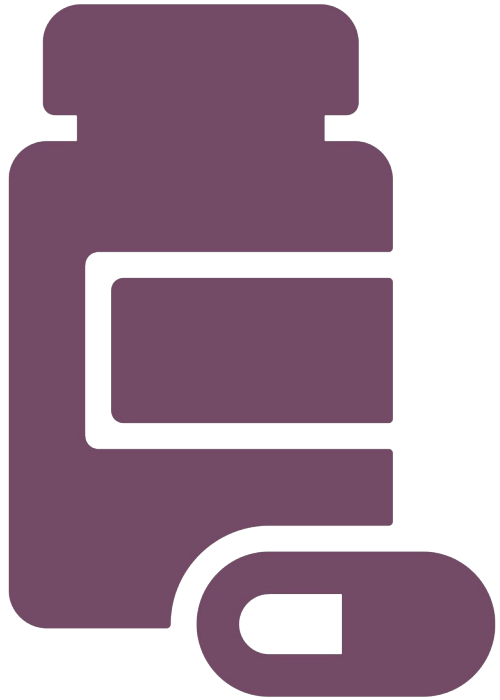




Kim, Hyoungyoung et al. "The Prevalence of Sjögren's Syndrome in Rheumatoid Arthritis Patients and Their Clinical Features." Journal of Korean Medical Science vol. 35,45 (2020): e369.

TREATMENT OVERVIEW

- Tailored to organ-specific severity using **ESSDAI**.
- Systemic therapies for moderate to severe disease activity (**ESSDAI >5**).
- Therapeutic response: **Reduction of ≥3 points in ESSDAI** score.



CORTICOSTEROIDS

- Not recommended for routine treatment.
- Used for significant organ manifestations (**ESSDAI ≥14**).
- Minimum dose and duration to control active systemic disease.

CSDMARDS

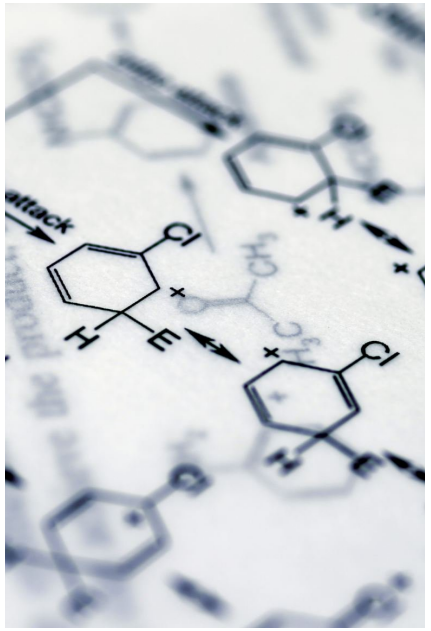
- Glucocorticoid-sparing agents.
- No evidence supporting one agent over another.
- High rates of adverse events (41-100%).

HYDROXYCHLOROQUINE

- Maximum dose of 6 mg/kg.
- Recommended for skin, joint disease, and fatigue.
- Monitor for clinical/biological response; stop if no response after 12 months.

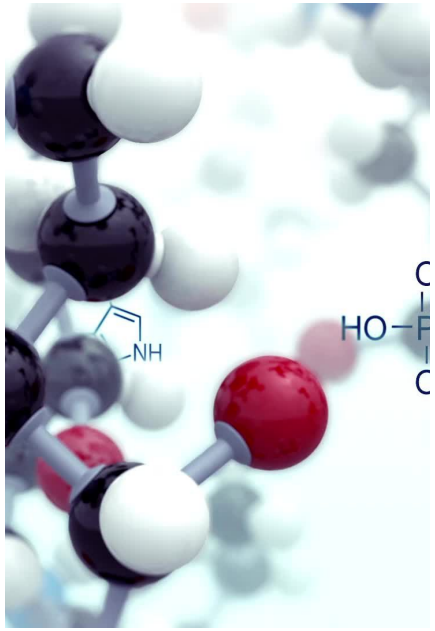
METHOTREXATE

- Recommended for inflammatory arthritis.
- Commonly used in combination with other therapies



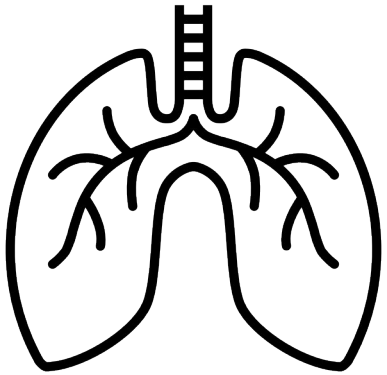
AZATHIOPRINE

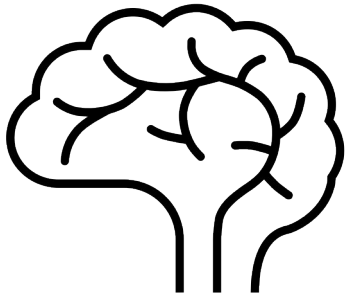
- Not routinely recommended.
- May be considered in systemic complications.

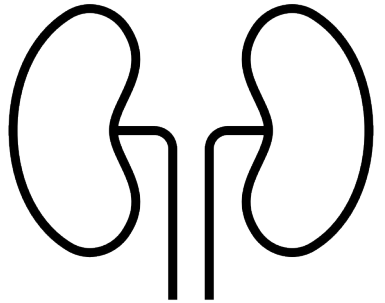


MYCOPHENOLATE MOFETIL AND CYCLOPHOSPHAMIDE

- May be considered in organ-threatening systemic complications such as CNS, renal, or lung disease.







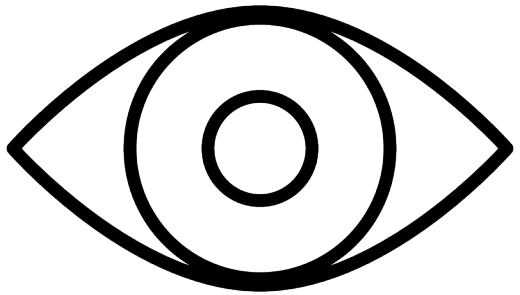
BIOLOGICS

- **Rituximab:** Targets B cells, used in severe or refractory cases.
- Other biologics under investigation.

MULTIDISCIPLINARY APPROACH

- Role of rheumatologists, ophthalmologists, dentists, other specialists and GPs.
- Importance of coordinated care for optimal outcomes.
- Case management and patient-centered care models.

MANAGEMENT OF DRY EYE



- **Evaluation:** Symptom assessment, clinical signs, diagnostic tests.
- **Management Strategies:**
  - Environmental modifications.
  - Topical therapies (artificial tears, gels, ointments).
  - Anti-inflammatory treatments (corticosteroids, cyclosporine).
  - Advanced therapies (punctal occlusion, autologous serum drops).

ORAL DRYNESS

Mild dysfunction

- Nonpharmacological stimulation (eg, sugar-free acidic candies, lozenges, xylitol, sugar-free chewing gum)

Moderate dysfunction

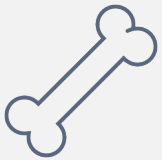
- Pharmacological stimulation (eg, pilocarpine, cevimeline; anetholtrithione, bromhexine, N-acetylcysteine)

Severe dysfunction

- Saliva substitution

MANAGEMENT OF ARTICULAR INVOLVEMENT

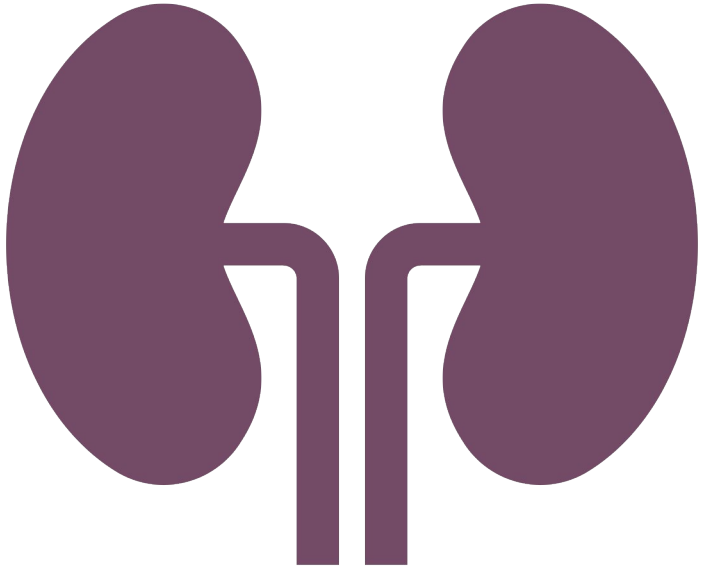
Low ESSDAI: NSAIDs, hydroxychloroquine.



Moderate/High ESSDAI: Glucocorticoids, immunosuppressive drugs, biologics.

MANAGEMENT OF RENAL INVOLVEMENT

- **Tubular Involvement:** Correct metabolic acidosis, electrolyte imbalances.
- **Glomerulonephritis:** Glucocorticoids, immunosuppressive agents, or biologics.

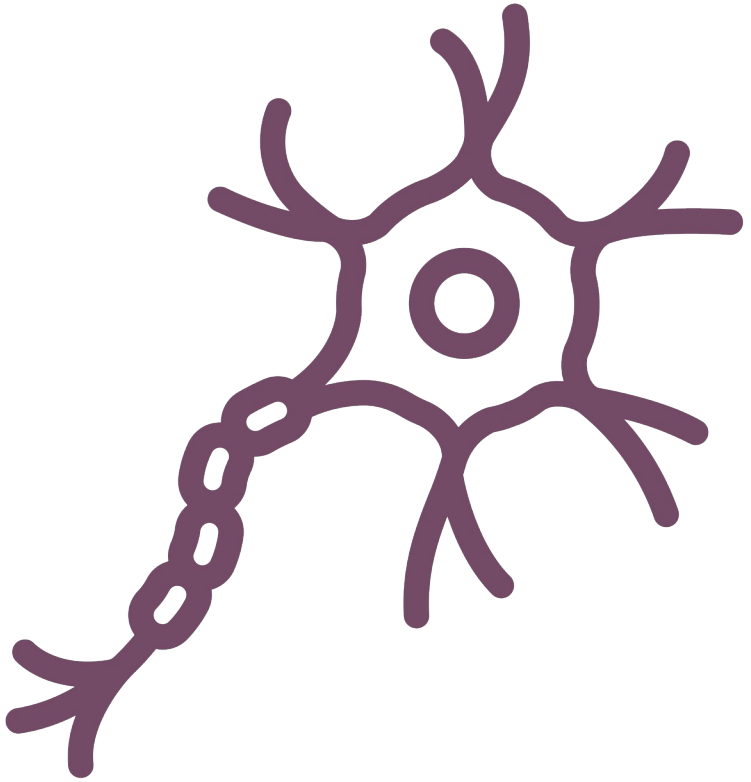


MANAGEMENT OF CNS INVOLVEMENT

- **CNS Vasculitis:** Glucocorticoids, cyclophosphamide, or rituximab.
- **Neuromyelitis Optica Spectrum Disorder (NMOSD):** Glucocorticoids, rituximab.
- **MS-Like Disease:** Disease-modifying therapies (e.g., interferons, glatiramer acetate).

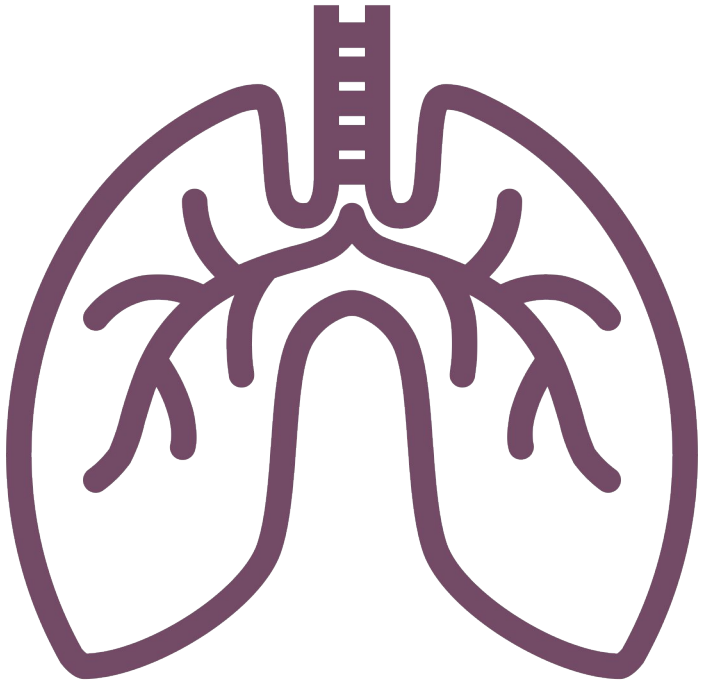
MANAGEMENT OF PERIPHERAL NEUROPATHY

- **Multineuritis:** Glucocorticoids, immunosuppressive drugs.
- **Axonal Polyneuropathy:** Symptomatic treatment, pulse methylprednisolone, or rituximab.
- **Ganglionopathy:** IVIG, rituximab.

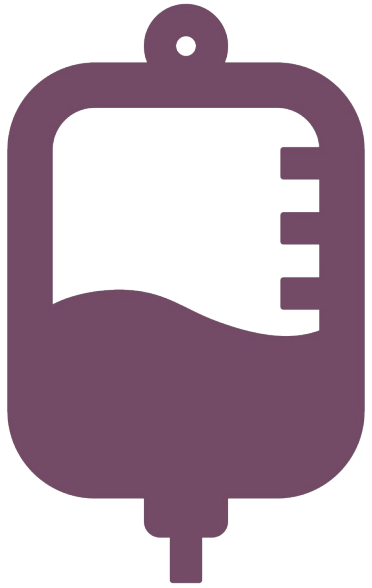


MANAGEMENT OF INTERSTITIAL LUNG DISEASE (ILD)

- **Initial Assessment:** Functional capacity, HRCT, PFTs.
- **Management:** Corticosteroids, mycophenolate mofetil, or antifibrotic therapy.
- **Refractory Cases:** Rituximab, cyclophosphamide, or lung transplant.



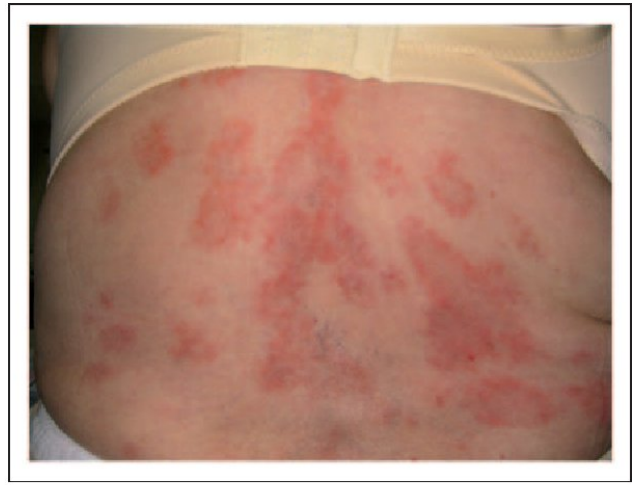
MANAGEMENT OF HEMATOLOGICAL INVOLVEMENT

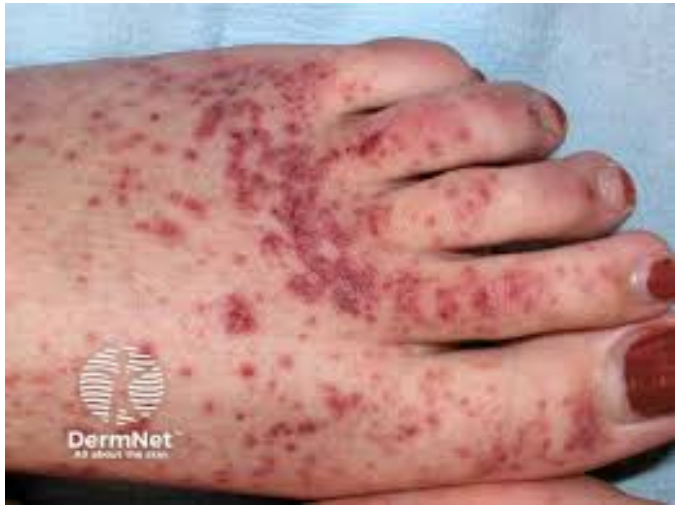


- **Neutropenia:** G-CSF for recurrent infections.
- **Immune Thrombocytopenia:** Glucocorticoids, rituximab.
- **Hemolytic Anemia:** Glucocorticoids, IVIG, or rituximab.

MANAGEMENT OF CUTANEOUS INVOLVEMENT

- **Annular Erythema:** Topical glucocorticoids, hydroxychloroquine.
- **Cutaneous Vasculitis:** Hydroxychloroquine, glucocorticoids, or immunosuppressive agents.

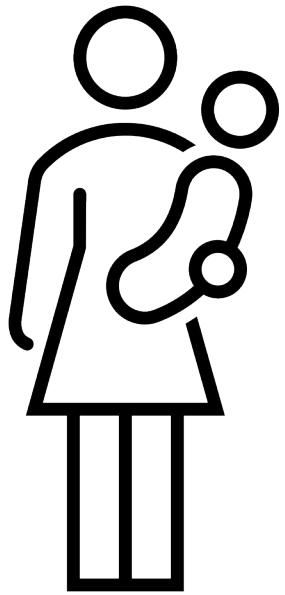




https://dermnetnz.org/topics/sjoegren-syndrome

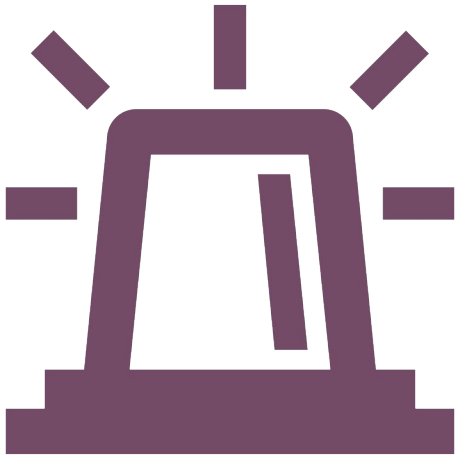
Brito-Zerón, Pilar et al. “Annular erythema in primary Sjögren’s syndrome: description of 43 non-Asian cases.” *Lupus* 23 (2014): 166 - 175.

SJÖGREN'S SYNDROME AND PREGNANCY



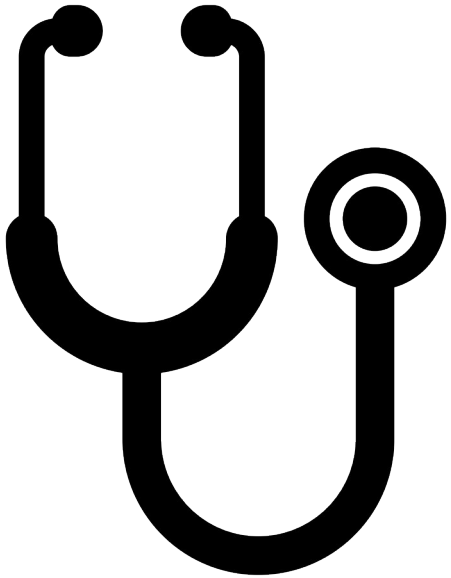
- **Impact on Pregnancy:** Increased risk of fetal loss, neonatal lupus, congenital heart block.
- **Pre-Pregnancy Counseling:** Stabilize disease activity, adjust medications.
- **Pregnancy Care:** Low-dose aspirin, hydroxychloroquine, fetal monitoring.

RISK OF LYMPHOMA



- **Lymphoproliferative Disorders:**
  - Persistent swelling of the salivary or lacrimal glands.
  - Unexplained lymphadenopathy (swollen lymph nodes).
  - B symptoms (fever, night sweats, weight loss).
  - Elevated beta-2 microglobulin or monoclonal gammopathy on lab tests.
  - Low level of complement C4 alone or together with low levels of C3.

RED FLAGS FOR REFERRAL TO A RHEUMATOLOGIST



- Persistent sicca symptoms.
- Systemic symptoms (fatigue, joint pain, vasculitis).
- Abnormal lab findings (autoantibodies, elevated inflammatory markers).
- Organ involvement (lung, kidney, CNS).
- Sjogren associates (RA, SLE and DM)
- Unclear diagnosis
- Risk of lymphoma.

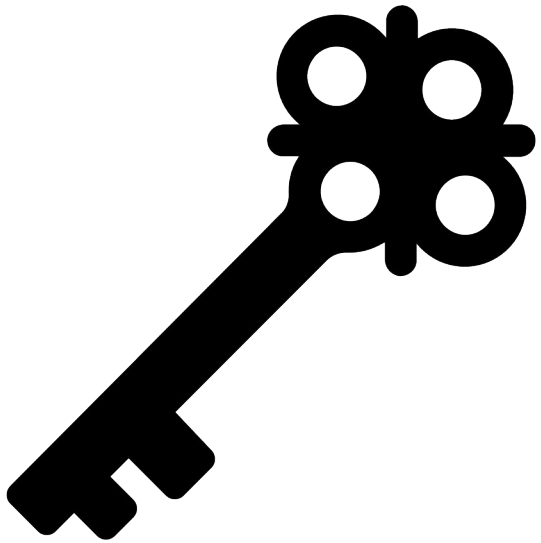
EMERGING THERAPIES

- **Biologics:** New B-cell targeting therapies.
- **JAK Inhibitors:** Under investigation for systemic involvement.
- **Stem Cell Therapy:** Early-stage research for severe cases.

PATIENT EDUCATION AND SUPPORT

- Importance of patient education on disease management.
- Support groups and resources for patients
- Lifestyle modifications to improve quality of life.

KEY TAKEAWAYS



- Sjogren syndrome is a systemic autoimmune disease with glandular and extraglandular manifestations.
- Early diagnosis and tailored treatment are crucial.
- Multidisciplinary care and patient education improve outcomes.

Thank You