Sjögren’s syndrome

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History

- The disease name is associated with **Swedish ophthalmologist Henrik Sjögren (**1899-1987).
- In 1930 he discovered women with rheumatism & corneal abrasions who could not produce tears when crying & could not dissolve a lump of sugar in their mouths
- 1933-Published his thesis paper, describing 15 women with lacrimal gland dysfunction leading to ulcerative lesions of the eyes and proposed the term Keratoconjuctivitis Sicca
- Only when his thesis was translated into English in 1943 the name Sjőgren's sy. began to appear in the medical literature.

Introduction

- **Sjögren syndrome** (show-grin) (SS) is a systemic autoimmune chronic inflammatory disorder characterized by lymphocytic infiltrates in exocrine organs.
- Most pts present with **sicca symptoms (Sicca complex),** as xerophthalmia (dry eyes), xerostomia (dry mouth).
- In addition, numerous **extraglandular** features may develop
- Increased risk of **lymphoprolipherative disorders**, predominantly non-Hodgkin`s lymphoma of B-cell origin : in about (5%) of pt.

Ng, Wan-Fai (2016). Sjogren's Syndrome. Oxford University Press. pp. 10–11. ISBN 9780198736950

Sjögren's syndrome may be

1. **Primary** : in the absence of another underlying rheumatic disorder
2. **Secondary**: in association with other autoimmune diseases most frequently RA , SLE or scleroderma.

- These 1ry and 2ry types occur with similar frequency, but the sicca complex seems to cause more severe symptoms in the primary form.
- Classic clinical features of SS may also be seen in infections with certain viruses as hepatitis C virus, HIV, & human T-cell lymphotrophic virus (HTLV) (Sjögrenlike syndromes)

- *Rischmueller M, et al S. Primary Sjögren's syndrome. Best Pract Res Clin Rheumatol. 2016 Feb. 30 (1):189-220.*

Etiology

- Exact etiology is unknown but it is an **autoimmune** disorder under the effect of a combination of genetic, environmental, and several other factors, (as many other autoimmune disorders).
- **Genetic factors** :

1. Association with the human leukocyte antigen: HLA-DR52 in pts with primary SS is about 87%, & in secondary SS is about 30%.
2. High rates of other autoimmune disorders in pts of SS is linked with a genetic predisposition to the syndrome.

*Mattey DL, et al. Association between HLA-DRB1*15 and secondary Sjögren's syndrome in pts with RA.*

J Rheumatol. 2000 Nov. 27(11):2611-6

Etiology (cont.)

- **Hormonal factors**

1. Since SS is associated with a high prevalence in women, sex hormones, especially estrogen, are believed to affect humoral & cell-mediated immune responses affecting susceptibility to the syndrome.
2. Androgens are generally considered to prevent autoimmunity.

Voulgarelis M., Tzioufas A. G. "Pathogenetic mechanisms in the initiation and perpetuation of Sjögren's syndrome".

Nature reviews. Rheumatology. 6: 529–537. doi:10.1038/nrrheum.2010.118

Etiology (cont.)

- **Environmental factors (Possible disease triggers)** :

1. Viral infections, may initiate autoimmunity by molecular mimicry and increase the chances of SS development. Epstein-Barr virus, HIV, hepatitis C, human T-cell lymphotrophic virus 1 , human herpesvirus 6 (HHV-6) and cytomegalovirus may have a role.
2. Sjögrenlike syndromes are seen in patients infected with HIV, HTLV-1, and hepatitis C virus

Fox RI. Sjögren's syndrome. Lancet. 2005 Jul 23-29. 366(9482):321-31

Pathogenesis & Immunology

- After the initial trigger, glandular tissue becomes infiltrated with **lymphocytes**, predominately CD4 T cell →release of **cytokine** IL-1, TNF, and interferon-gamma, →destructive effects on the tissue and interfere with acetylcholine release, → dysfunctional glands
- The term autoimmune Epithelitis is some times used
- Antibodies against Ro and La cellular antigens:

  Ro (SSA): Unknown Function

  La (SSB): Initiation , termination & maturation of RNA-polymerase III transcription

Fan H et al., Mol Cell Biol 1998; 18:3201

Epidemiology

- **In USA**, SS is the 3rd most common rheumatologic dis., behind SLE & RA.
- **In USA**, SS affects 1-3 million people.
- **Worldwide** SS affects 0.1-4% of the population.(This wide range, reflects the lack of uniform diagnostic criteria).
- A few studies show that the **incidence** of SS varies between 3 and 6 per 100,000 per year
- SS occurs in **all** ethnic and racial groups.
- The **female-to-male** ratio is 9:1.

Helmick CG, et al. Estimates of prevalence of arthritis & other rheumatic conditions in the USA. Part I. Arthritis Rheum. 2008 Jan. 58(1):15-25.

Age

- Any age but is most common in **elderly people**.
- Onset typically occurs in the **fourth to fifth** decade of life.
- The **peak age** of onset is 50 years.
- Children and teenagers are **rarely** affected (few case report)
- If so, the **juvenile form of SS is self-limiting**

Harnsberger et al Sjögren's syndrome: diagnosis and therapeutic challenges in the elderly.

Drugs Aging. 2008. 25(1):19-33

Clinical picture

- The clinical presentation of Sjögren syndrome may vary.
- The onset is insidious.
- Diagnosis can be delayed for as long as several years.
- Manifestation may be **glandular and extraglandular**

zioufas AG, Voulgarelis M. Update on Sjögren's syndrome autoimmune epithelitis: from classification to increased neoplasias. Best Pract Res Clin Rheumatol. 2007 Dec. 21(6):989-1010.

Glandular manifestation

- Xerophthalmia (dry eyes) and xerostomia (dry mouth) are the main clinical presentations in adults.
- Bilateral parotid swelling is the most common sign of onset in children.

Extraglandular involvement

- Two general categories:

1. **Periepithelial involvement** :include interstitial nephritis, liver involvement, & bronchiolitis , generally follow a benign course.(Autoimmune Epithelitis)
2. **Extraepithelial involvement** : related to B-cell hyperreactivity, hypergammaglobulinemia, & immune complex formation ,includes palpable purpura, glomerulonephritis, & peripheral neuropathy. These manifestations occur later in the course of SS & are associated with a higher risk of transformation to lymphoma

Schein OD et al. Dry eye & dry mouth in the elderly: a population-based assessment.

Arch Intern Med. 1999 Jun 28. 159(12):1359-63.

Clinical picture (cont.)

1. Sicca symptoms
2. Parotitis
3. Skin manifestation
4. Pulmonary manifestation
5. Gastrointestinal manifestation
6. Hematological manifestation
7. Neurological manifestation
8. Renal manifestation
9. others

1-Sicca symptoms (dry eyes and dry mouth)

- The **most common** symptoms (95% of patients)
- The **incidence increases with age** (more than one third of elderly persons have sicca symptoms)
- Whether this is part of the normal aging process (associated with fibrosis & atrophy observed on some lip biopsy studies) or is due to the accumulation of associated illnesses and medications is unclear.

Mavragani CP, Fragoulis GE, Moutsopoulos HM (Dec 2012). "Endocrine alterations in primary Sjogren's syndrome: an overview". J Autoimmun (Review). 39 (4): 354–8. doi:10.1016/j.jaut.2012.05.011

- **Common medications** that can cause sicca symptoms in any age group include

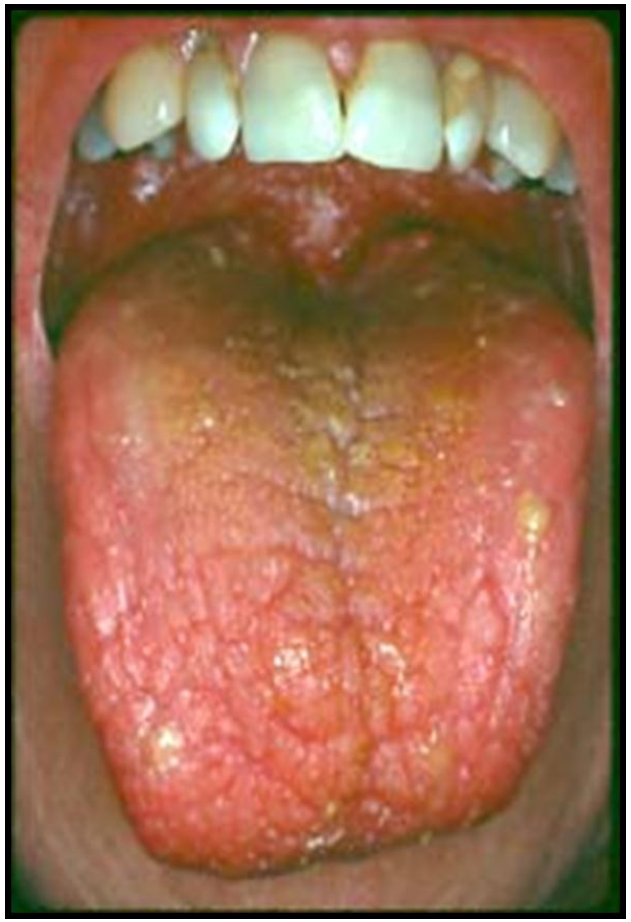
1. antidepressants,
2. anticholinergics,
3. beta blockers,
4. diuretics,
5. antihistamines.
6. Women who use hormone replacement therapy at increased risk of dry eye

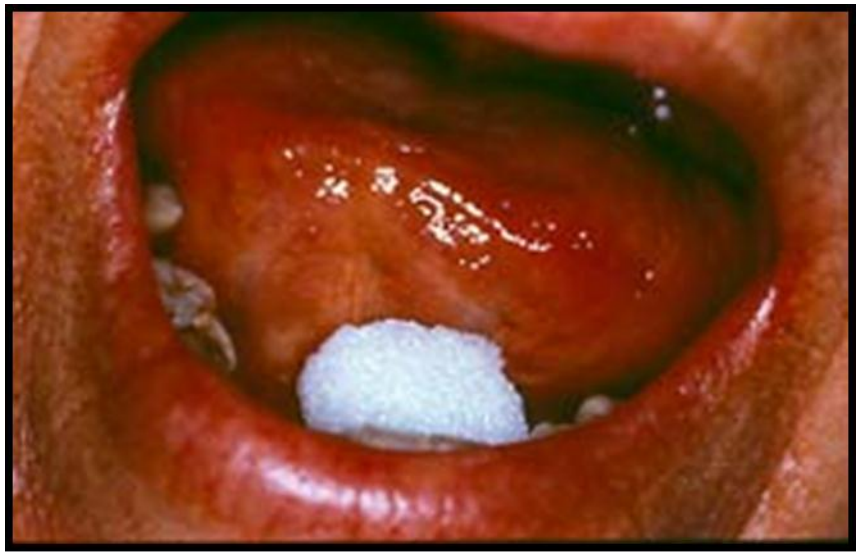
Dry mouth

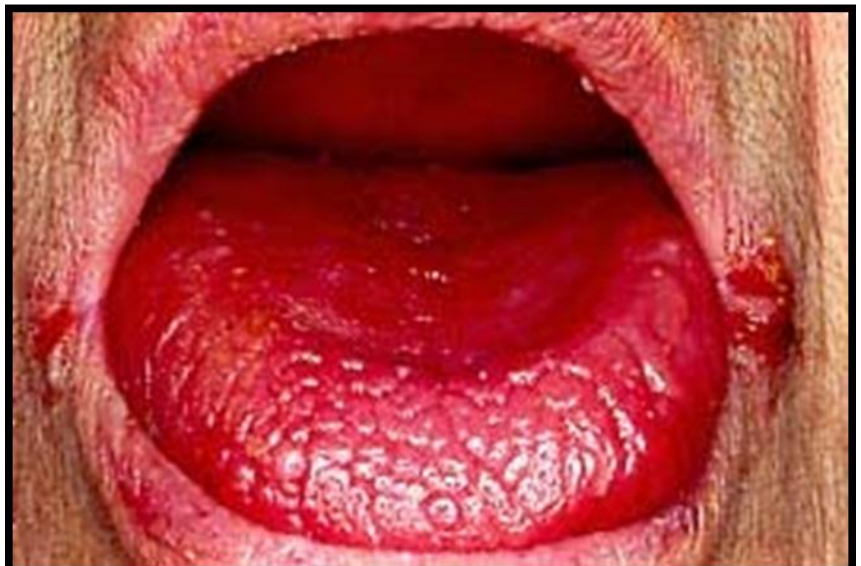
- Inability to eat dry food because it sticks to the roof the mouth
- Putting a glass of water on the bed stand to drink at night (and resulting nocturia)
- Difficulty speaking for long periods of time or the development of hoarseness
- Higher incidence of dental caries
- Altered sense of taste.
- Oral candidiasis with angular cheilitis, causing mouth pain

Soy M, Piskin S. Cutaneous findings in patients with primary Sjogren's syndrome. Clin Rheumatol. 2007 Aug. 26(8):1350-2

Red, and dry tongue .Dental caries - Lips - Red, dry, and Cracks at the corners of the mouth. Chronic oral candidiasis







Dry eyes

- The most common complaint is that of a gritty or FB sensation in the eyes.
- Red, itchy, and painful eye.
- Symptoms typically worsen throughout the day, probably due to evaporation of the already scanty aqueous layer.
- Some pts awaken with difficulty opening their eyes in the morning.
- pts with dry eye should be referred to an ophthalmologist.

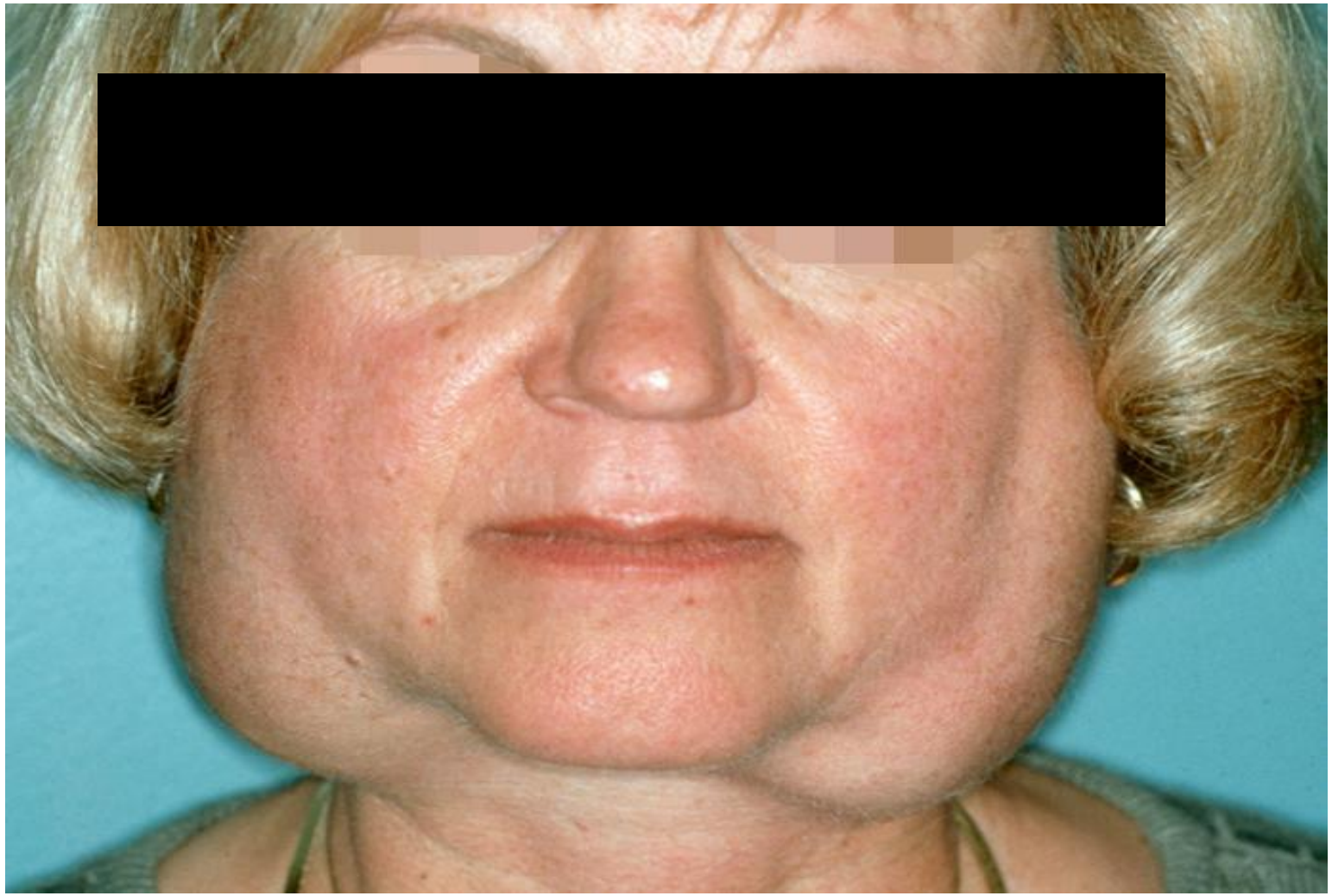
Schaumberg DA, et al. Hormone replacement therapy and dry eye syndrome. JAMA. 2001 Nov 7. 286(17):2114-9

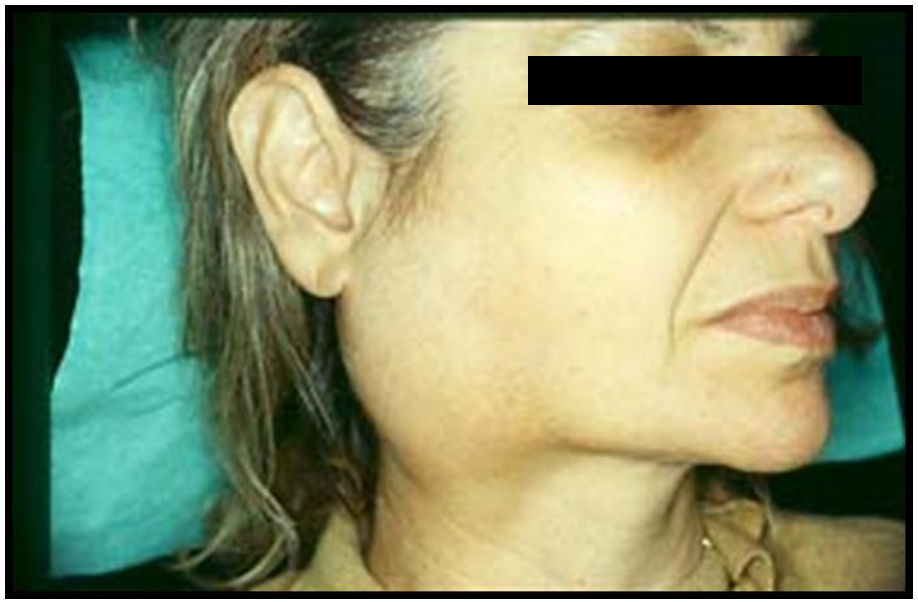
2-Parotitis (30% of pts)

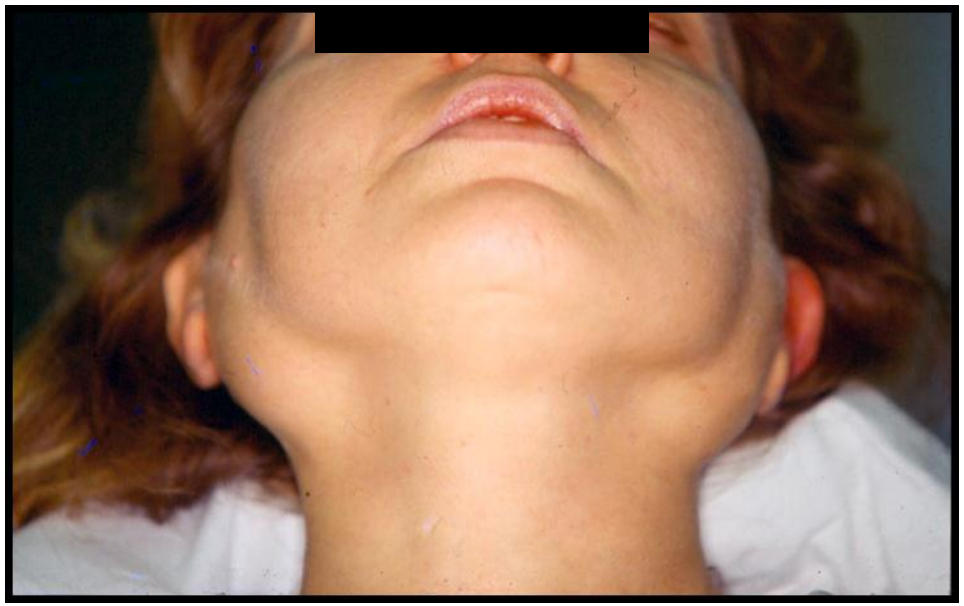
- History of recurrent parotitis, may be bilateral.
- Parotid enlargement may be asymptomatic & discovered on examination.

Fox RI, Liu AY. Sjögren's syndrome in dermatology. Clin Dermatol. 2006 Sep-Oct. 24(5):393-413.

parotitis





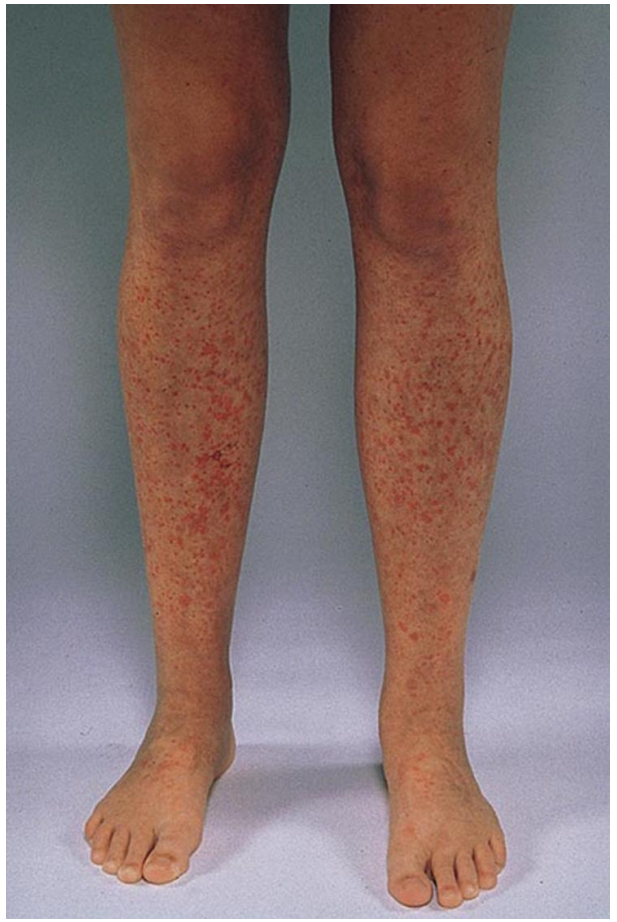


3-Skin manifestation (50% of pts)

Nonvasculitic: Dryness (xeroderma), Eyelid dermatitis & Pruritus

Vasculitis: as purpura, in pts with hypergammaglobulinemia or cryoglobulinemia.

Raynaud phenomenon in about 20% of pts.



Vasculits

4-Pulmonary manifestation

- Prevalence of clinically significant lung disease in SS is (9–20%) but when investigated , prevalence increases to (43% and 75%)
- CT scan abnormalities are found in (34–50%) of patients
- Dry cough (60%) due to dryness of the tracheobronchial mucosa (xerotrachea)
- Dry cough may precede SS diagnosis by several years.
- Dyspnea (30%) due to interstitial lung disease (ILD) that is usually mild

Parambil JG et al . Interstitial lung disease in primary Sjögren syndrome. Chest. 2006 Nov. 130(5):1489-95.

4-Pulmonary manifestation (cont.)

- Some studies recommend that when SS is known, ILD screening should be done & vice versa
- Recurrent bronchitis (35%) , pneumonitis (25%) , bronchiolitis (12%) or bronchiectasis (50%)
- Rare respiratory complications such as amyloidosis or pulmonary hypertension may occur.
- High risk of pulmonary embolism in SS pts

Dalavanga YA, et al. Lymphocytic alveolitis: a surprising index of poor prognosis in patients with primary Sjogren's syndrome. Rheumatol Int 2006; 26: 799–804

5-Gastrointestinal manifestation (24%)

- Dryness of the pharynx & esophagus leads to difficulty with swallowing , gastroesophageal reflux and esophagitis.
- Rarely, pts develop acute or chronic pancreatitis, & malabsorption
- In pts with gastritis, H. pylori infection should be sought because of its association with gastric lymphomas.
- Delayed gastric emptying, causing early satiety, upper abdominal discomfort, nausea, and vomiting.
- Primary biliary cirrhosis , autoimmune hepatitis or IBD (13%).

Ebert EC. Gastrointestinal and hepatic manifestations of Sjogren syndrome. J Clin Gastroenterol 2012; 46: 25–30

6-Haematological manifestations (40%)

- The most serious manifestation
- Anemia, cytopenias, monoclonal gammopathies and cryoglobulinaemia
- Lymphoprolipherative disorders, predominantly non-Hodgkin's lymphoma of B-cell origin in (5 %) of pts.
- The increased prevalence of B-cell malignancies suggests that SS may be a boundary disease between autoimmunity & lymphoproliferation
- Some studies recommend that features of SS should be looked for in all pts with immune cytopenias

Manganelli P et al Clin Exp Rheumatol. 2006 Jul-Aug;24(4):438-48.

7-Neurologic manifestation (8-40%)

- Myelopathy, fits & encephalopathy (5-10%)
- Sleep disorder (15%), anxiety (20%) or depression (40%)
- Other causes of these symptoms, including concomitant SLE & multiple sclerosis should be excluded
- Sensory (distal paresthesias) or motor, peripheral neuropathy, 35%
- Cranial neuropathies can develop, particularly , optic neuropathy, trigeminal neuropathy, or facial nerve palsy.
- Mononeuritis multiplex due to vasculitis.
- Progressive weakness & paralysis due to hypokalemia caused by RTA

Mori K, et al. The wide spectrum of clinical manifestations in Sjögren's syndrome-associated neuropathy.

Brain. 2005 Nov. 128:2518-34

8-Renal and urological manifestation (4%)

- Renal calculi, type I renal tubular acidosis (distal) with hypokalaemic metabolic acidosis.
- Nephrogenic diabetes insipidus, and hypokalemia can occur secondary to tubular damage caused by tubulointestitial nephritis
- All types of glomerulonephritis may occur and is usually attributable to another disorder, such as SLE or mixed cryoglobulinemia
- Interstitial cystitis, with symptoms of dysuria, frequency, urgency, and suprapubic pain

Leppilahti M, et al. Interstitial cystitis-like urinary symptoms among patients with Sjögren's syndrome: a population-based study in Finland. Am J Med. 2003 Jul. 115(1):62-5

9- other manifestation

- Nasal dryness can result in discomfort and bleeding (18%).
- Dry vagina (10%), which can lead to dyspareunia, vaginitis, and pruritus.
- Fatigue (70–80%), arthralgia & non erosive arthritis(40%)
- Recurrent miscarriages or stillbirths (5%)
- History of venous or arterial thrombosis. These are related to the presence of antiphospholipid antibodies (5%)
- Pericarditis and pulmonary hypertension

Launay D,etal . Pulmonary arterial hypertension: a rare complication of primary Sjögren syndrome: report of 9 new cases and review of the literature. Medicine (Baltimore). 2007 Sep. 86(5):299-315

Secondary Sjogren syndrome

- Secondary SS is usually mild, and sicca symptoms are the main feature.
- Symptoms of the primary basic disease predominate
- 2 ry SS does not modify the prognosis or outcome of the basic disease.
- Manifestations of 2 ry SS include the following:

1. Salivary gland swelling
2. Lung involvement
3. Nervous system involvement
4. Renal involvement
5. Raynaud phenomenon
6. Lymphoproliferative disorders

Prajs K, et al. Polyarteritis nodosa and Sjögren's syndrome: overlap syndrome. Rheumatol Int. 2010 May 18

Complications

- Infections: as dental infections, eye infections, bronchitis, and vaginitis.
- Lymphoma (5%) & parotid tumors (2%) (hard parotid enlargement)
- Primary biliary cirrhosis : (5%)
- women with anti-Ro/SSA & anti-La/SSA antibodies who become pregnant, have an↑ rate of neonatal lupus erythematosus with congenital heart block (4%).
- Heart block can also occur in SS pts later in life, in adulthood, and their serological examination may reveal antibodies against Purkinje fibers
- Vasculitis and Type I cryoglobulinemia

- *Manthorpe, A; Wirestrand, LE (November 2004). "Late neonatal lupus erythematosus onset in a child born of a mother with primary Sjögren's syndrome". Ann. Rheum. Dis. 63 (11): 1496–7. doi:10.1136/ard.2003.014944. PMC 1754813. PMID 15479901.*

Sjogren Syndrome Workup

- No single test is sufficiently sensitive or specific in the diagnosis
- The condition is properly diagnosed when the results of various tests are simultaneously positive and when subjective symptoms and serologic abnormalities are present
- Investigation include

1. laboratory,
2. Ophthalmologic test & staining,
3. Salivary flow (sialometry) , sialography & salivary scintigraphy
4. Salivary gland biopsy

1-laboratory

- Elevated ESR in (80%) & anemia in (50 %)
- Presence of anti-Ro/SSA and anti-La/SSB
- ANA in (70%) & RF in (60-70%)
- Serum protein electrophoresis :monoclonal gammopathy
- Anti–alpha-fodrin antibody (reliable diagnostic marker of juvenile SS)
- Creatinine clearance may be diminished in up to (50%) of patients
- IGs (Immunoglobulins) are usually elevated.

Masaki Y et al. Proposal for a new clinical entity, IgG4-positive multi-organ lymphoproliferative syndrome: Analysis of 64 cases of IgG4-related disorders. Ann Rheum Dis. 2008 Aug 13.

Anti-Ro/SSA,

- Antibodies against Ro/SSA are found in approximately (70% of pts with primary SS and 15% of pts with secondary SS).
- Thus, the absence of anti-Ro/SSA antibodies does not exclude the diagnosis of SS.
- Also antibodies against Ro/SSA are present in 50% of pts with SLE and are sometimes found in healthy individuals.
- Thus, the presence of antibody against Ro/SSA cannot by itself be used to establish a diagnosis of Sjögren syndrome

Anti-La/SSB

- Antibodies against La/SSB are present in 40-50% of pts with primary SS
- Also present in 15% of patients with SLE.
- Finding antibodies against La/SSB in pts without antibodies against Ro/SSA is unusual, but this combination has occurred in pts with primary biliary cirrhosis and autoimmune hepatitis.
- Titers of anti-Ro/SSA & anti-La/SSB antibodies do not reflect dis. activity

Complete Blood Count (CBC)

1. Anemia of chronic disease is present in 50% of pts.
2. Pernicious anemia may be associated with the atrophic gastritis.
3. An abnormal WBC count, especially with an abnormal differential count, should prompt concerns for a lymphoreticular malignancy.
4. Leukopenia occurs in up to 42% of patients.
5. Although a low platelet or WBC count can occur in pts with primary SS , the finding should also prompt consideration for coexisting SLE.

Additional test considerations

- High alkaline phosphatase level - consider primary biliary cirrhosis
- Elevated transaminase levels - Consider the possibility of hepatitis C, which can be associated with sicca symptoms,
- Low bicarbonate level - Consider evaluating patients for type I (distal) renal tubular acidosis;
- Hypokalemia - can also be observed in pts who have Sjögren syndrome without renal tubular acidosis

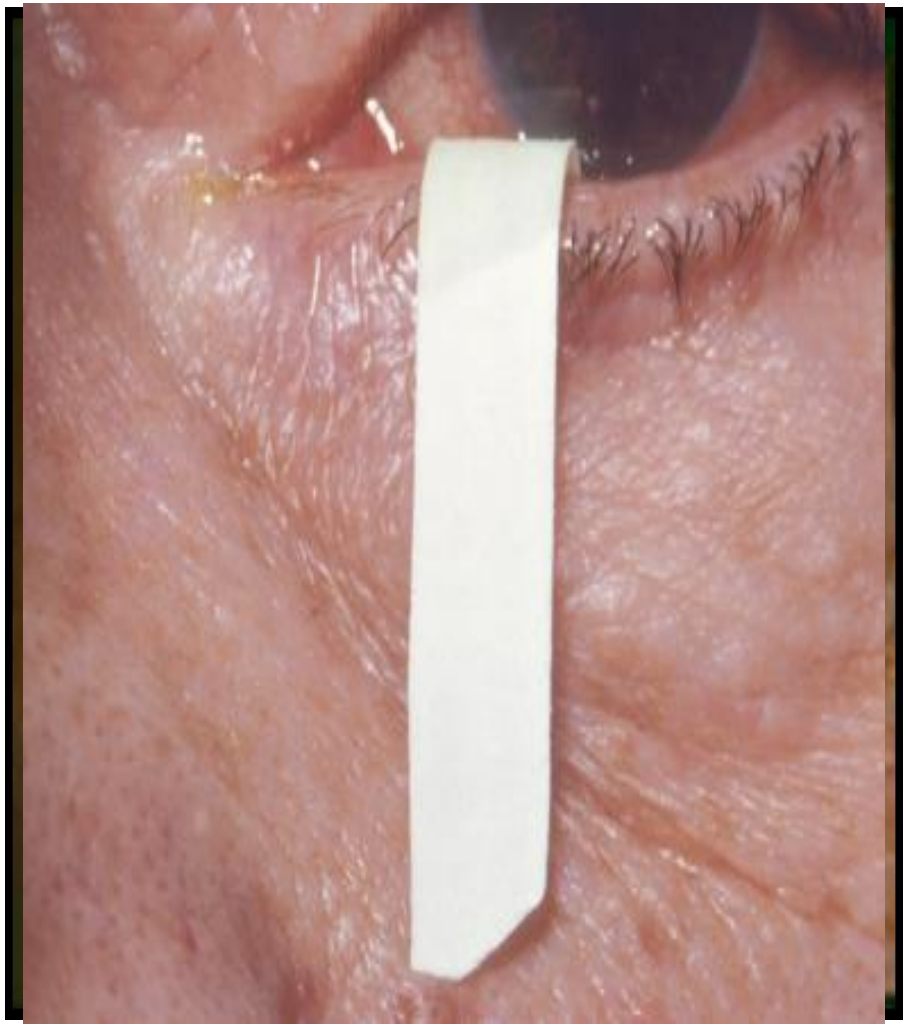
Montaño-Loza AJ, et al. Abnormal hepatic biochemistries and clinical liver disease in patients with primary Sjögren's syndrome.

Ann Hepatol. 2007 Jul-Sep. 6(3):150-5.

2-Ophthalmologic tests :

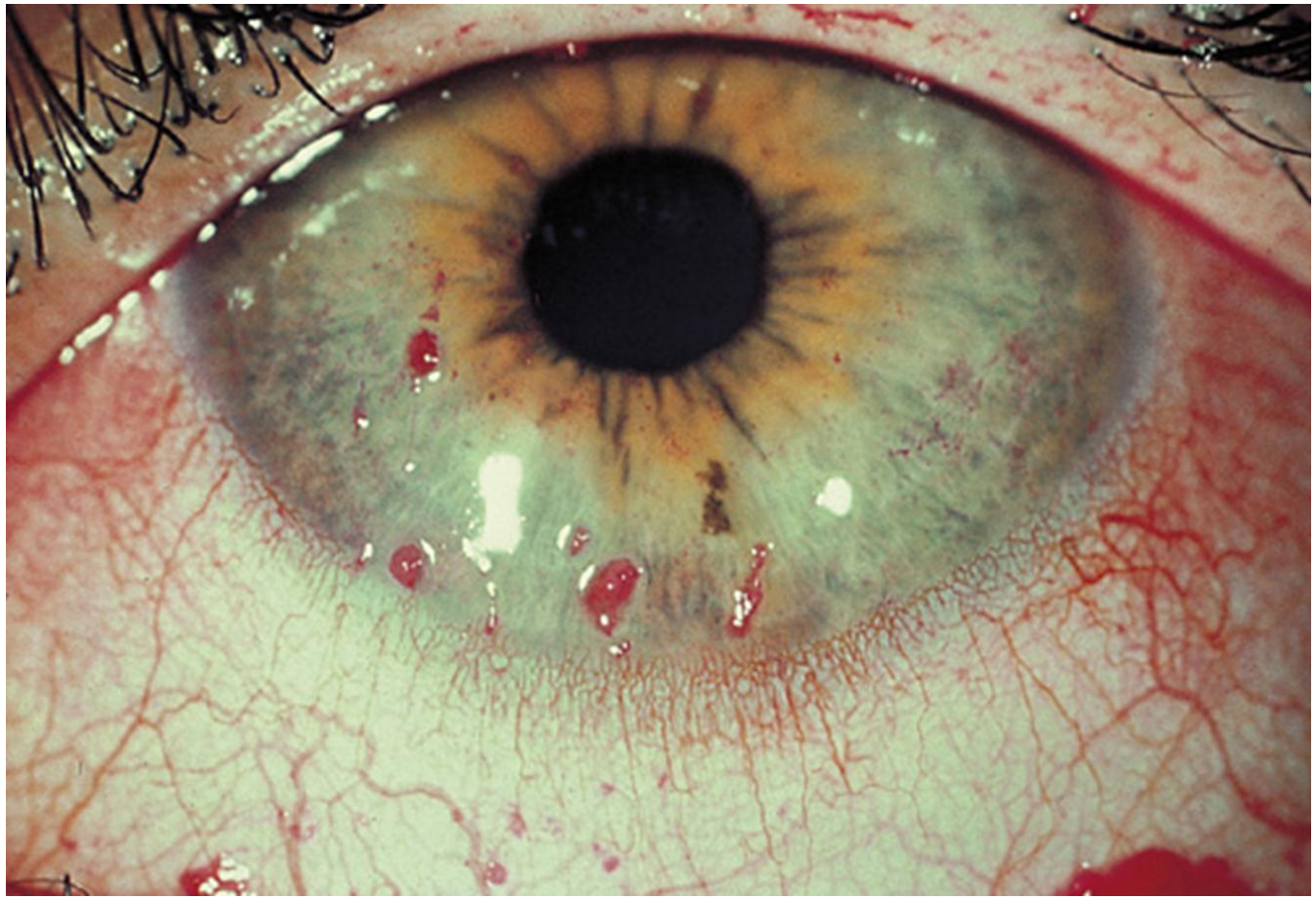
- Schirmer Test : Measures tear production.
- Rose Bengal : Eyedrops containing dyes that an eye care specialist uses to examine the surface of the eye for dry spots.
- Lissamine green staining works similarly but is less irritating to the eye.
- Fluorescein staining can be used to detect corneal damage.

Schirmer test



A filter paper is placed in the lower conjunctiva, and the amount of tearing on the filter paper is recorded. Normal wetting is greater than 15 mm after 5 minutes, whereas a definitive positive result is less than 5 mm after 5 minutes. This test is not specific. yielded a sensitivity of 42% and a specificity of 76% for Sjögren syndrome

Keratoconjunctivitis sicca (rose bengal test) in SS



3-Salivary Flow (Sialometry)

- Measures the amount of saliva produced over a certain period of time usually in 15 min.(basal and after stimulation)
- Method of collection (passive drainage , suction/aspiration or spitting)
- Basal secretion: normal 0.4 mil/min & hyposcreation ≤ 1.5mil/15min
- It is a good measure to establish xerostomia, but the findings are not specific

Suction cup used in

Salivary flow rate (**Sialometry**)

Sialography and Scintigraphy

- **Sialography** : radiopaque material is injected into the salivary glands. Sialography is useful to exclude the presence of obstructions or strictures, but the same finding of Sjögren syndrome is seen in various other diseases and is therefore not specific to SS
- **Salivary scintigraphy**, the uptake and secretion of sodium technetium-99m (99m Tc) to detect the salivary flow rates. However, the finding of low flow rates is not specific to SS .
- Positive findings on either sialography or scintigraphy fulfill a criterion for diagnosis by the **American-European Consensus Group.**

Vitali C, et al. Classification criteria for Sjögren's syndrome: a revised version of the European criteria proposed by the American-European Consensus Group. Ann Rheum Dis. 2002 Jun. 61(6):554-8.

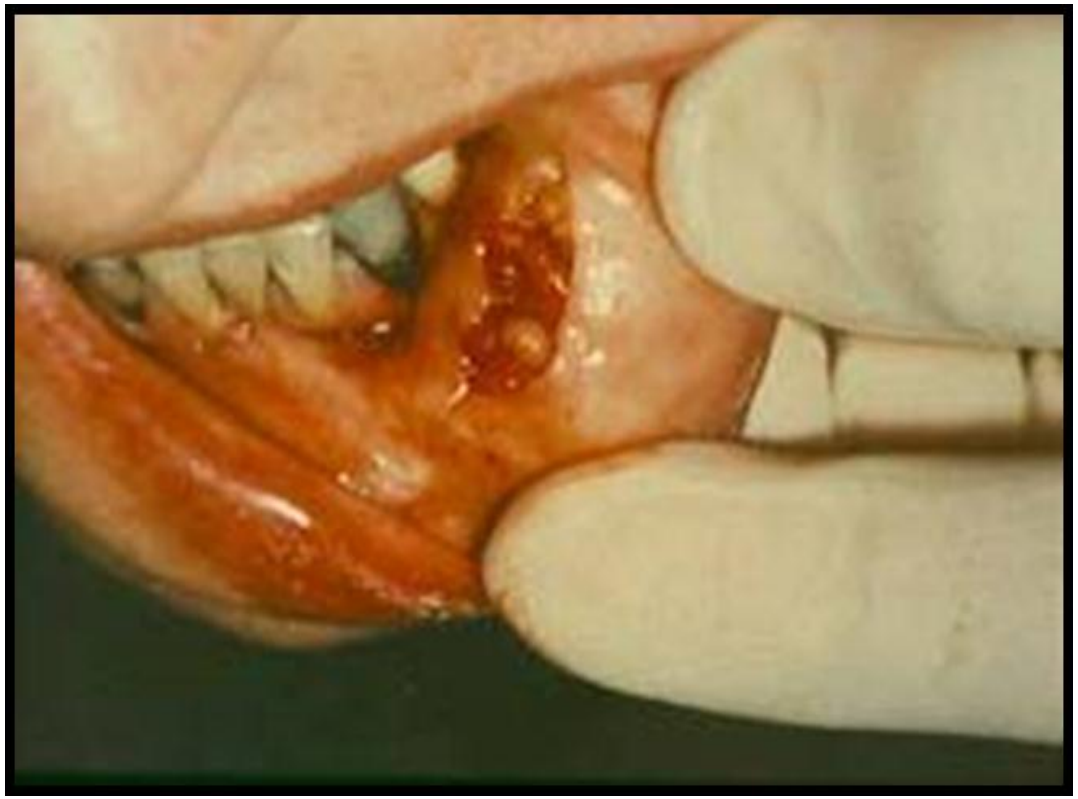
Biopsy

- Minor salivary gland biopsy currently is the best single test to establish a diagnosis of Sjögren syndrome
- However it is not mandatory, used only if the diagnosis is in doubt
- An incision is made on the inner aspect of the lower lip and some minor salivary glands are removed for examination
- Biopsy show lymphocytic infiltration of the glands.
- At least 4 salivary gland lobules should be obtained for analysis.
- Biopsy can also help to detect lymphoma & sarcoidosis.

Langerman AJ,et al. Utility of lip biopsy in the diagnosis and treatment of Sjogren's syndrome.

Laryngoscope. 2007 Jun. 117(6):1004-8

Salivary gland biopsy



Classification criteria

- American-European Consensus Group classification (2007)
- ACR classification (2012)

American-European Consensus Group classification :The criteria are:

1. **Ocular symptoms** - Dry eyes for more than 3 months, foreign-body sensation, use of tear substitutes more than 3 times daily
2. **Oral symptoms** - Feeling of dry mouth, recurrently swollen salivary glands, frequent use of liquids to aid swallowing
3. **Ocular signs** - Schirmer test performed without anesthesia (< 5 mm in 5 min), positive vital dye staining results
4. **Oral signs** - Abnormal salivary scintigraphy findings, abnormal parotid sialography findings, abnormal sialometry findings (unstimulated salivary flow < 1.5 mL in 15 min)
5. **Positive minor salivary gland biopsy findings**
6. **Positive anti–Ro/SSA or anti–La/SSB antibody results**

American-European Consensus Group classification (cont.)

- These **criteria allow a diagnosis** of SS in pts without sicca symptoms or without doing a biopsy.
- **Diagnosis of primary SS** requires at least four of the criteria; in addition, either criterion number 5 or criterion number 6 must be included.
- SS can be diagnosed in pts who have **no sicca symptoms** if three of the four objective criteria are fulfilled

Langegger C, et al. Use of the European preliminary criteria, and the American-European criteria for diagnosis of primary Sjögren's Syndrome in daily practice: a retrospective analysis.Rheumatol Int. 2007 Jun. 27(8):699-702.

- **Secondary SS** is diagnosed when, in the presence of a CTD , symptoms of oral or ocular dryness exist in addition to criterion 3, 4, or 5.
- Application of these criteria has yielded a **sensitivity** of 97.2% and a **specificity** of 48.6% for the diagnosis of **1ry SS**. The **sensitivity** is 64.7% and **specificity** is 97.2% for **2ry SS**
- **Subjective criteria** : ocular symptoms and oral symptoms
- **Objective critiria** : ocular signs, salivary gland involvement, histopathology, or autoantibodies

Exclusion criteria

- Include any of the following:

1. Past head-and-neck irradiation
2. Hepatitis C virus infection
3. Acquired immunodeficiency syndrome (AIDS)
4. Prior lymphoma
5. Sarcoidosis
6. Graft versus host disease
7. Use of anticholinergic drugs

ACR classification criteria

- These classification criteria were developed to improve specificity of criteria used for diagnosis
- This high specificity makes the ACR criteria more suitable for application in situations in which misclassification or misdiagnosis may present a health risk.
- They were accepted by the ACR as a provisional criteria set in 2012

Shiboski SC, et al. American College of Rheumatology classification criteria for Sjögren's syndrome:

Arthritis Care Res (Hoboken). 2012 Apr. 64(4):475-87

According to the ACR criteria, the diagnosis of SS requires at least 2 of the following 3 findings:

1. **Positive serum** anti-Ro/SSA and/or anti-La/SSB antibodies or positive RF & antinuclear antibody titer of at least 1:320
2. **Ocular staining score** of at least 3
3. Presence of **focal lymphocytic sialadenitis** with a focus score of at least 1 focus/4 mm 2 in labial salivary gland biopsy samples

- Application of these criteria has yielded a **sensitivity** of 93% and a **specificity** of 95% for the diagnosis of SS **(for both primary and secondary forms of SS).**

Treatment

- No curative agents for SS exist, only symptomatic treatment
- In 2ry SS, treatment is based on ttt of the basic disease
- Depending on the problems, pts with SS may need consultation of

1. Rheumatologists,
2. Ophthalmologists,
3. ENT physicians.
4. Nephrologist
5. Pulmonologist
6. Hematologist/oncologist
7. Dentist

Treatment (cont.)

- **Dry mouth** : parasympathomimetic as pilocarpine, side effects include sweating, abdominal pain, flushing and increased urination.
- **Dry Eyes** :artificial tears, cyclosporine eye drops & pilocarpine
- **Arthralgias and arthritis** :NSAIDs, steroids, Hydroxychloroquine or disease-modifying antirheumatic drugs (DMARDs) such as methotrexate or immunosuppressive drugs & sometimes IVIG .
- **ILD** : steroids & immunosuppressive agents, as cyclophosphamide.
- **Long-term anticoagulation**: in pts with vascular thrombosis
- **Rituximab (anti-CD20)** in sever extraglandular manifestation
- **Surgical Therapy** : seal the tear ducts that drain tears (punctal occlusion).

Summary of the Sjögren's Syndrome Foundation (SFF) Guidelines (2016)

- Published in the United States with the following **goals**

1. Symptom palliation
2. Prevention of complications
3. For rheumatologists, proper selection of pts for immunosuppressive therapy

Dry mouth

Recommendations (and their strength) for SS pts with dry mouth include :

1. Topical fluoride should be used for caries prophylaxis (strong)
2. Saliva can be increased through, sugar-free lozenges and/or chewing gum, & the prescription medications pilocarpine & cevimeline (weak)

Musculoskeletal pain recommendation :

1. Hydroxychloroquine (HCQ); first-line treatment
2. Methotrexate
3. HCQ plus methotrexate
4. Short-term steroids(15 mg or less a day for 1 month or less) long-term steroids (≤15 mg/d for more than 1 month) may be useful,
5. Leflunomide
6. Sulfasalazine
7. Azathioprine (may be a better choice than leflunomide or sulfasalazine in patients with major organ involvement)
8. Cyclosporine

Fatigue

- The only strongly recommended treatment of fatigue was exercise.
- Hydroxychloroquine may be considered in selected situations

Dry eye

- For dry eye disease, recommendations vary according to the severity of eye involvement, (need ophthalmological evaluation)
- Artificial tears, gels, ointments in mild cases
- Anti-inflammatory therapy with pulse steroids or cyclosporine in moderate cases
- Systemic anti-inflammatory medication or permanent punctal occlusion in sever cases

Biological Therapies

- The guidelines advise **against** use of tumor necrosis factor–alpha (TNF-α) inhibitors to treat sicca symptoms in pts with **primary SS**.
- If TNF-α inhibition therapy is used for rheumatoid arthritis or other related overlap conditions in pts with **2 ry SS**, monitor for the following:

1. Lymphoma and other malignancies (risk for non-Hodgkin is elevated)
2. Serious infections, including tuberculosis
3. Invasive fungal infections
4. Hepatitis B reactivation
5. Hepatotoxicity
6. Cytopenias

Rituximab

- Rituximab may be considered as a therapeutic option for the following indications in patients with primary SS

1. Keratoconjunctivitis sicca (KCS)
2. Xerostomia
3. Cryoglobulinemia associated with vasculitis
4. Severe parotid swelling
5. Inflammatory arthritis
6. Pulmonary disease
7. Peripheral neuropathy, especially mononeuritis

THANK YOU