

Lec 3

(3) Sjögren's Syndrome

Primary Sjögren's syndrome (SS) is a systemic chronic autoimmune disease that targets the exocrine glands. It is characterized by xerostomia (dry mouth), xerophthalmia (dry eyes) which is called **Sicca symptoms**, and is usually accompanied by production of auto-antibodies specific for the **Ro RNA-binding protein**.

Symptoms

- Xerostomia (dry mouth) and xerophthalmia (dry eyes) or sicca symptoms.
- Skin rashes and sensitivity to UV light
- Dry cough or shortness of breath
- Dry throat, lips, or skin and nose
- Feeling tired
- Swelling, pain, and stiffness in your joints with headache.



Epidemiology

SS is a common autoimmune disorder. Prevalence rates vary from approximately 0.5 to 5 percent. Around one-half of all SS cases are primary, with the remainder occurring as secondary SS. In the presence of another autoimmune connective tissue disorder such as RA or SLE, secondary SS is known as the former meaning of primary Sjögren's.

So, **secondary sjögren syndrome** is associated with another underlying rheumatic disease, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA)

Similar to most autoimmune disorders, most cases (approximately 90 percent) occur in **women**, the female-to-male ratio **of Sjögren's syndrome is 9:1**. Peak incidence occurs in the fourth and fifth decades of life. The majority of cases **occur in midlife**; however, the disorder is also seen in children and the elderly.

Etiology

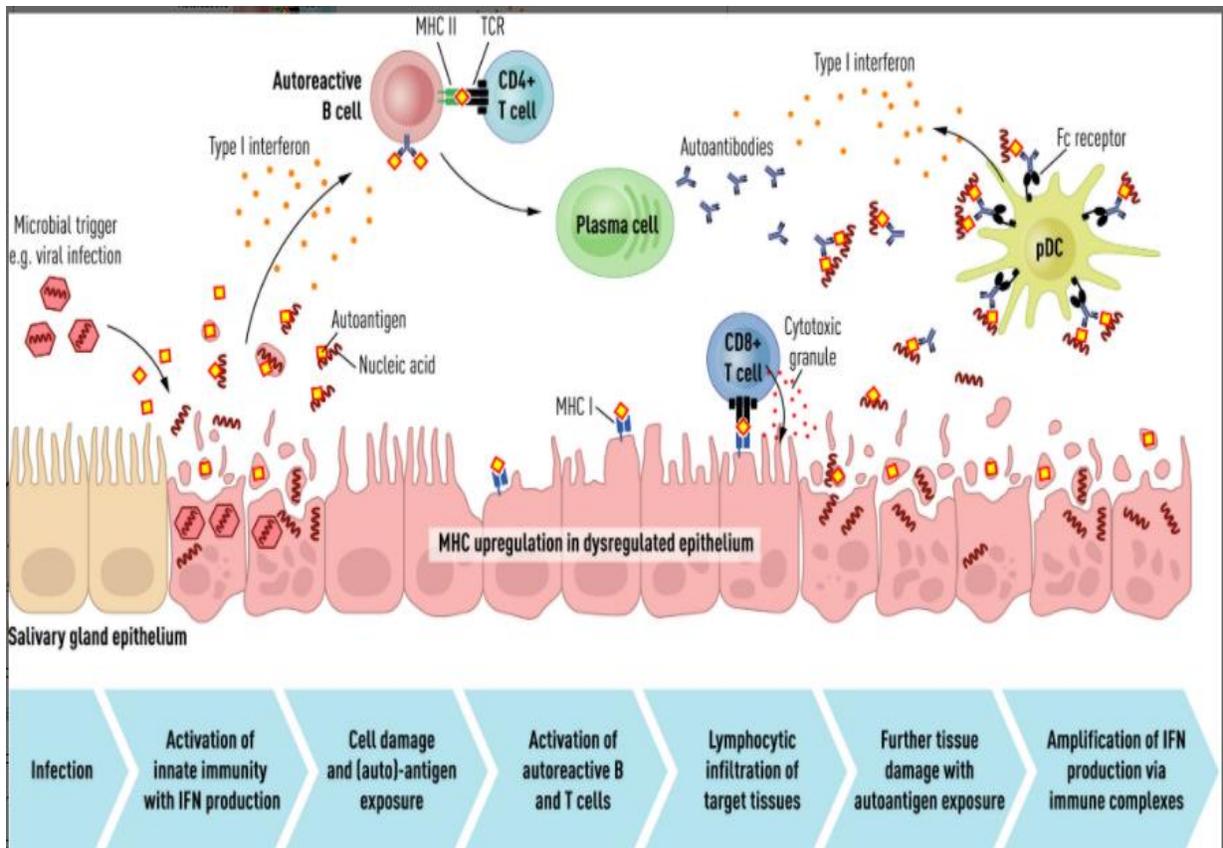
- **Gender:** Female to male 9:1
- **Genetic Marker:**
 - HLA-B8, HLA-DR2, HLA-DR3, and HLA-DR4 is more closely associated related with SS (primary) occurring with Raynaud's phenomenon.
 - * **Raynaud's phenomenon** is a disorder that causes decreased blood flow to the fingers. In some cases, it also causes less blood flow to the ears, toes, knees, or nose
 - HLA-DRw52 is associated with both forms (primary and secondary SS).
- **Antibodies** to the RO antigen.

Pathogenesis

- Microbial triggers, such as viral infections, initiate disruption of the salivary gland epithelium and induce production of type I IFN, thus creating an inflammatory microenvironment with autoantigens released and exposed on dying cells.
- Antigen-presenting cells then process and present viral and self-antigens, which leads to activation of autoreactive T and B cells with activation of plasma cells to produce Ab.

- Autoreactive T cells induce tissue damage via secretion of cytotoxic granules, thus further disrupting the epithelium and causing amplified exposure of autoantigens.
- Immune complexes formed between autoantibodies and autoantigens bind receptors on Plasmacytoid dendritic cells (pDCs), this due to type-I IFN production.
- In turn (بدوره), type-I IFNs drive autoantibody production through promoting differentiation and activation of the autoreactive B cells.
- Through this process, a self-perpetuating cycle of autoimmunity is created. IFN, interferon, plasmacytoid dendritic cells (pDCs), MHC, major histocompatibility complex (MHC), T-cell receptor (TCR).

***plasmacytoid dendritic cells** : type of immune cells that secreted large quantities of type-1 interferon (IFNs) in response to a viral infections.



Criteria for SS Classification

1. Ocular symptoms

- Dry eyes for more than 3 months
- Foreign-body sensation
- Use of tear substitutes more than 3 times per day

2. Oral symptoms (Xerostomia)

- Feeling of dry mouth
- Recurrently swollen salivary glands
- Frequent use of liquids to aid swallowing

3. Ocular signs (Conjunctivitis Sicca)

- ✓ Schirmer test performed without anesthesia (<5 mm in 5 min)
- ✓ Positive vital dye staining results

4. Oral signs

- Abnormal salivary scintigraphy(التصوير الومضي) findings
- Abnormal parotid sialography (تصوير اللعاب) findings
- Abnormal sialometry(قياس الغدد اللعابية) findings (unstimulated salivary flow <1.5 mL in 15 minutes)

5. Positive anti–SSA or anti–SSB antibody results

6. Positive minor salivary gland biopsy findings

Laboratory diagnosis:

- 1- **ANA (Anti-Nuclear Antibody):** About 70% of Sjögren’s patients have a positive ANA test result.
- 2- **RF (Rheumatoid Factor):** In Sjögren’s patients, 60-70% have a positive RF.
- 3- **SS-A (or Ro) and SS-B (or La):** these are the marker antibodies for Sjögren's. 70% of Sjögren’s patients are positive for SS-A and 40% are positive for SS-B (these may also found in lupus patients).

4- **ESR.**

5- **IGs (Immunoglobulins):** These are normal blood proteins that participate in immune reactions and are usually elevated in Sjögren's patients.

6- **The ophthalmologic (eye) tests include:**

- **Schirmer Test:** Measures tear production.
- **Rose Bengal and Lissamine Green:** Eyedrops containing dyes that an eye care specialist uses to examine the surface of the eye for dry spots.

The dental tests include:

- Salivary Flow (تدفق اللعاب):** Measures the amount of saliva produced over a certain period of time.
- Salivary scintigraphy(التصوير الومضائي اللعابي):** A nuclear medicine test that measures salivary gland function. (لقياس وظيفة الغدة اللعابية)
- Salivary gland biopsy(خزعة للغدة اللعابية):** (usually in the lower lip) Confirms inflammatory cell (lymphocytic) infiltration of the minor salivary glands.

Differential diagnosis of Sjögren syndrome:

- Medications that cause sicca symptoms.
- Gingivitis/periodontitis
- Oropharyngeal candidiasis
- HIV, HCV infections
- SLE similar to SS
- RF, Scleroderma and dermatomyositis that called Secondary Sjögren syndrome.
- Primary biliary cirrhosis