Lecture No. 4

Sjögren's syndrome

Sjögren's syndrome (SS) is a systemic chronic inflammatory disorder characterized by lymphatic infiltrates in exocrine organs (lacrimal and salivary glands). Sjögren's syndrome predominantly effects females (female:male ratio 9:1) in their fourth and fifth decades of life. It was named after the Swedish ophthalmologist Henrik Sjögren's after he reported 19 cases of keratoconjunctivitis in 1933.1 The hallmark feature of SS is deficient tear and saliva production due to lymphocytic infiltration of the salivary and lachrymal glands leading to xerostomia (dry mouth) and xerophthalmia (dry eyes). In addition, SS can involve any organ system and present with a wide spectrum of clinical features.

There are two type of Sjögren's syndrome

- **Primary Sjögren's syndrome** (when the disease occurs alone) is a systemic autoimmune disease that targets the exocrine glands. It is characterized by xerostomia (dry mouth), xerophthalmia (dry eyes).
- **Secondary Sjögren's syndrome** is defined as the former definition of primary Sjögren's in the presence of another autoimmune diseases such as RA, SLE, Scleroderma, and polyarteritis nodosa.

Etiology and Pathogenesis

A number of factors play a role in the development of Sjögren's syndrome

1. Endogenous factors [**HLA-B*8-DRB1*03 ((B8 DR3) and hormones (estrogens)**].
2. Exogenous factors [**viruses (herpes and retrovirus)**].

The pathogenesis of SS is still largely unknown. In a genetically predisposed individual, various environmental factors, such as viral infections, may lead to epithelial cell activation and a protracted inflammatory response with features of autoimmunity. The actual trigger of glandular dysfunction is assumed to be a viral infection. Epithelial cells in the infected gland present viral antigens. This attracts T cells, which infiltrate the glandular tissue and cause a local inflammatory reaction, resulting in damage to glandular tissue. The T cells activate the glandular epithelium and, most importantly, B cells. This results in excessive, uncontrolled B-cell proliferation, which initially manifests in the peripheral blood as hypergammaglobulinemia in association with presence of immune complexes.

Clinical features

The principle feature of Sjögren's syndrome is autoimmune destruction of exocrine gland, most prominently the lacrimal and salivary glands, but also glands at other sites including respiratory mucosa and vagina. The disease commonly affects eyes, mouth, parotid gland, lung, kidney, skin and nerves system. Most individuals with Sjögren's syndrome present with sicca symptoms, such as xerophthalmia (dry eyes), xerostomia (dry mouth), and parotid gland enlargement. Other xeroses such as dry skin and dry vaginal mucosa leading to irritation and dyspareunia may also occur. In addition, numerous extra glandular features may develop, such as arthralgia, arthritis, pulmonary disease, leucopenia, anemia, lymphoadenopathy, neuropathy, renal tubular acidosis and lymphoma.

Laboratory finding

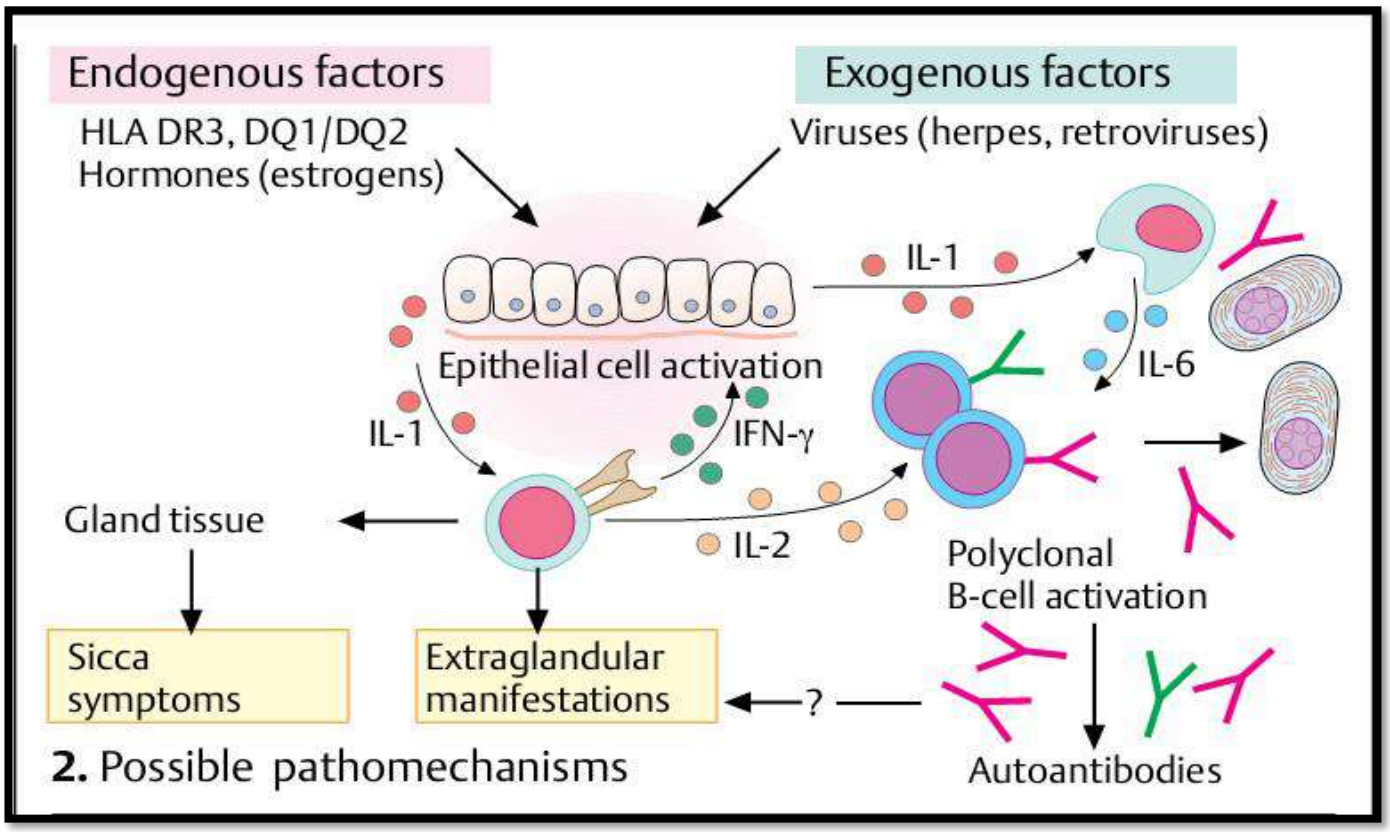
The most important diagnostic tests for Sjögren's syndrome are

1. **Schirmer's test:** Lachrymal function can be assessed by the Schirmer's test to quantify the amount of tear production, a slip of sterile filter paper is placed over the lower eyelid, failure to produce sufficient tears within 5 min wet 10 mm of the paper suggest defective tear production, then this is positive for Sjögren's syndrome.
2. **Erythrocyte sedimentation rate (ESR)** is elevated in 80% of patients.
3. **C reactive protein (CRP)** is also elevated in patients.
4. **Rheumatoid factor (RF)** is present in 52% of cases of primary-type Sjögren's syndrome and in 98% of secondary-type cases.
5. **Complete blood count (CBC)** shows anemia and leucopenia.
6. **Autoantibodies**
    - **Anti-SS-A (anti-Ro) and anti-SS-B (anti-La)** are present in most cases of primary-type Sjögren's syndrome. While anti salivary duct antibodies are present in most cases of the secondary type. Anti-Ro/SS-A antibodies are found in over 70% of patients with SS, but are also frequently found in SLE and other autoimmune diseases even in the absence of oral or ocular dryness. Anti-La/SS-B is more specific; it is present in 50% of patients with primary SS or SS/SLE but is rarely seen in other diseases. The pathogenic role of these antibodies is not yet defined except in newborns born to women with anti-

Ro/SS-A and/or anti-La/SS-B antibodies. These antibodies can cross the placenta and bind to Ro and La antigens located on the cell surface of fetal myocardial tissue, leading to fetal heart block.

- **Antinuclear antibodies (ANA)** of the speckled type are present in most cases of primary Sjögren's syndrome.
- In recent years, research has focused on identifying antibodies more specific for SS, such as anti-a-fodrin and anti-muscarinic acetylcholine receptor antibodies, but the results have been controversial. The major stimulus for saliva production is the binding of acetylcholine to muscarinic acetylcholine receptors. The hypothesis that oral and ocular dryness could result from antibodies antagonizing the muscarinic acetylcholine receptor-3 is intriguing.

7. **Creatinine clearance** may be diminished in up to 50% of patients.
8. **Rose Bengal, fluorescein and lissamine green staining** are performed on an outpatient basis to the detection corneal and conjunctival damage due to dryness.
9. **Salivary gland evaluation** is done by collection of unstimulated saliva or salivary scintigraphy.



2. Possible pathomechanisms