

# Dry Eye & Sjögren's Syndrome

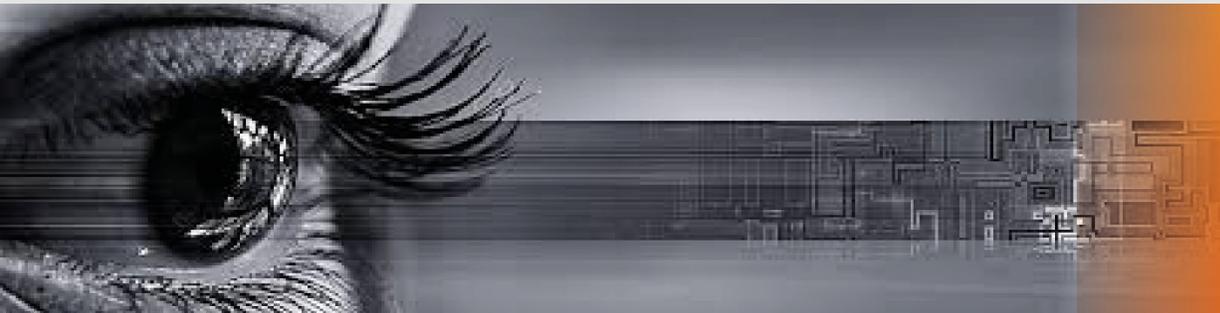
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# Case Scenario Links

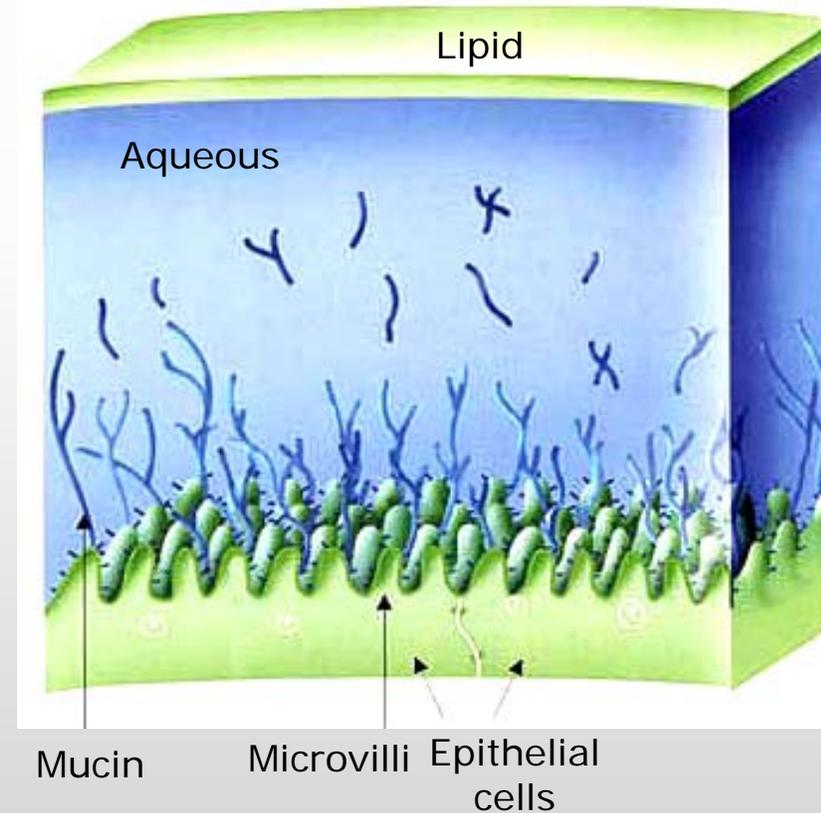
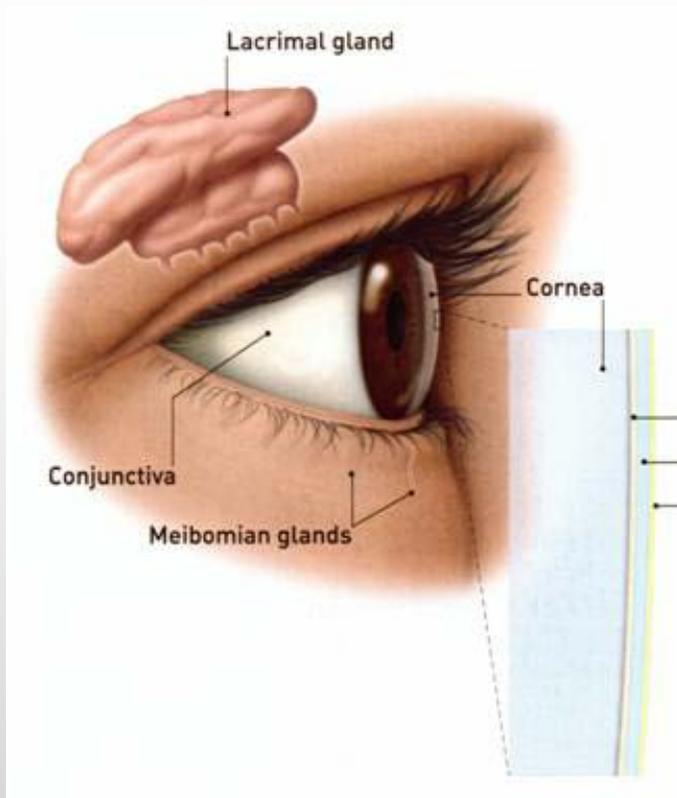
## Dry Eye & Sjögren's Syndrome

- Acute or chronic red eye (Oph01)
- Swollen and tender joints (Rh02)
- SLE / fatigue / pain and swelling in the hands (Rh03)



# The Tear Film

The tear film, which bathes the ocular surface, has a complex structure and composition

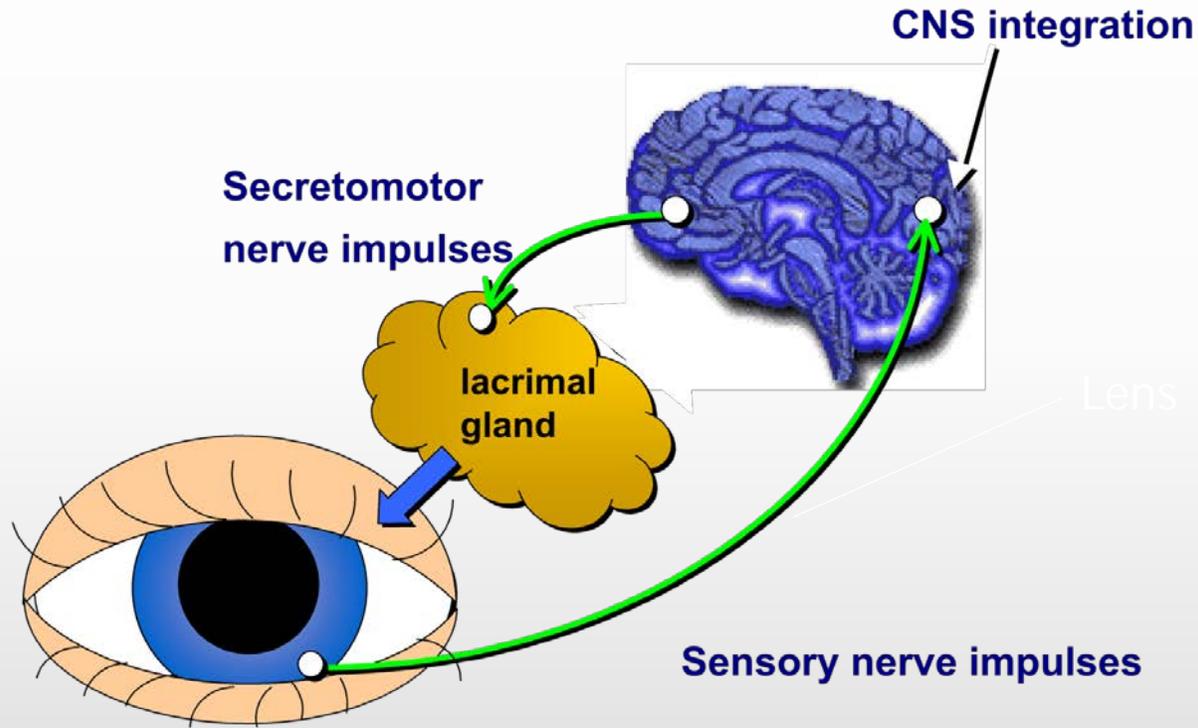


# Tear film functions

- Optical
- Mechanical
- Nutritional
- Defensive

The tear film composition must be maintained within fairly strict limits to maintain a healthy and functional visual system.

# Lacrimal functional unit



Dysfunction of any part of the unit can alter the tear film quantity or quality and result in signs and symptoms of dry eye

# Dry Eye Definition

“Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface”

2007 International Dry Eye Workshop (DEWS)

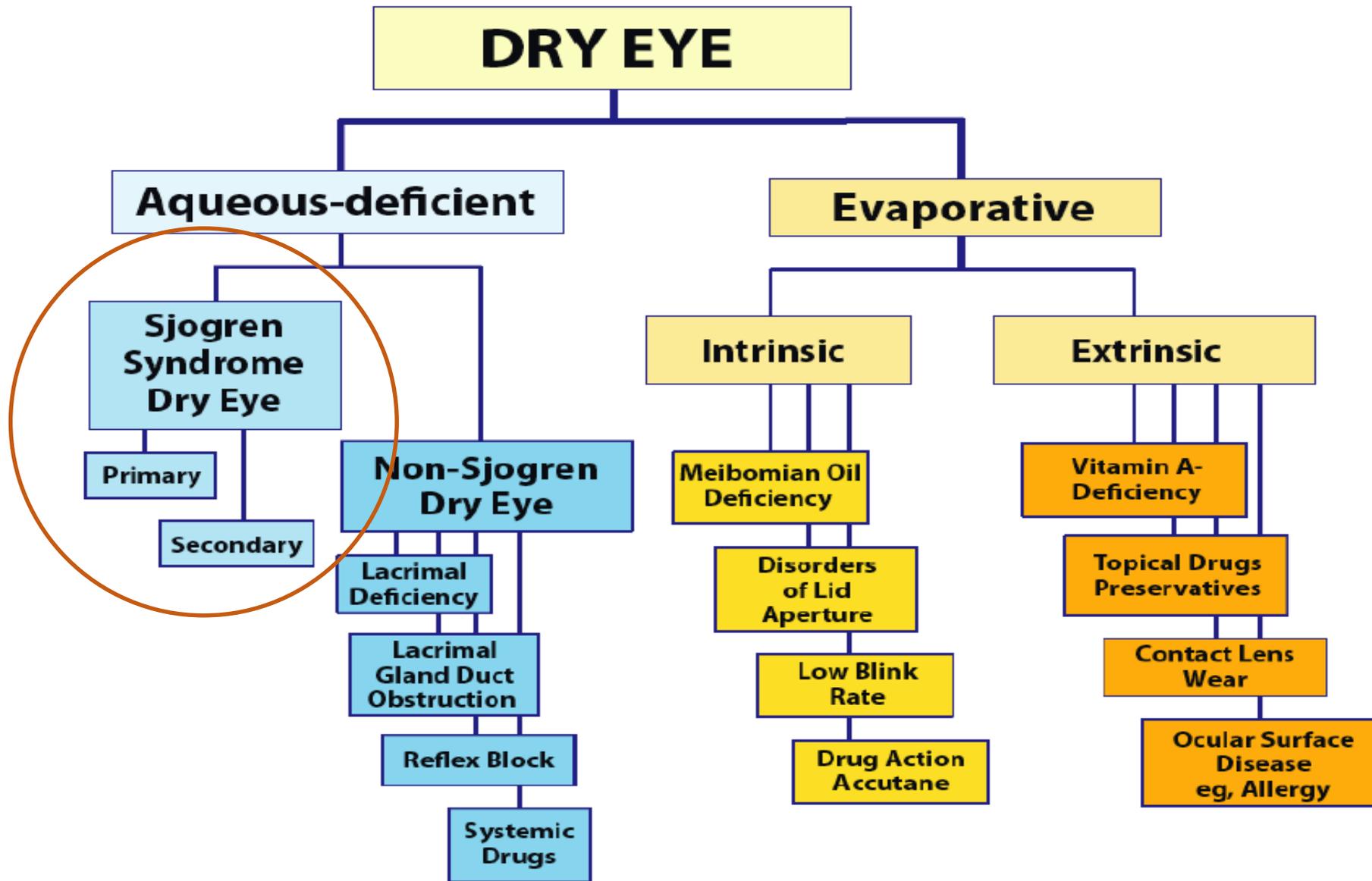
# Dry Eye

- **Symptoms:**

- Dryness, grittiness, irritation, burning, 'feeling of sand in the eye'

- **Prevalence**

- Between 8 and 13% of population affected
- More common with increasing age
- Most common in post-menopausal women
- Environmental conditions and contact lens wear common exacerbating factors



# Sjögren's Syndrome

- Chronic, systemic, inflammatory, auto-immune disorder characterised by lymphocytic infiltration of the exocrine organs
- Affects 0.1 - 4% of the population, no race predilection
- More common in females; ratio of 9:1
- Onset typically in 30's or 40's
- Characteristically presents with sicca symptoms:
  - Xerophthalmia (dry eye)
  - Xerostomia (dry mouth)
  - Parotid gland enlargement
  - Extraglandular features e.g. arthralgia, RA, Raynaud's phenomenon, lymphoma

# Sjögren's Syndrome

- Primary SS occurs in the absence of an underlying rheumatic disorder  
1° SS = Dry Eye + Dry Mouth
- Secondary SS is associated with an underlying rheumatic disease, such as SLE, RA, or scleroderma.  
2° SS = Dry Eye + Dry Mouth + Connective Tissue Disease
- Treatment typically centres around symptom management, but patients require monitoring for potential lymphoma development
- Morbidity is mainly associated with decreased exocrine organ function, and mortality with associated conditions such as SLE /RA.
- Patients with primary SS who do not develop a lymphoproliferative disorder have normal life expectancy

# Pathophysiology

- Not fully understood
- Believed that environmental or endogenous antigens can trigger a self-perpetuating inflammatory response in susceptible individuals
- Genetic associations
- Sex hormones believed to play a role
- Viruses may be responsible for triggering onset (e.g. HIV)

# 'Vicious circle'

- Structural and functional changes in the lacrimal (and salivary) glands, result in reduced aqueous production
- Tear hyperosmolarity, as a proinflammatory stimulus, induces an inflammatory cascade on the ocular surface
- This causes an immune response in the ocular surface epithelium, and local cytokine and metalloproteinase production
- The end result is damage to the epithelium, already vulnerable from poor tear film protection, evidenced as epithelial erosions, surface irregularity and impaired vision

# Clinical findings

- History of ocular sicca symptoms (n.b. not exclusive to SS)
- History of oral sicca symptoms (eating / speaking difficulties)
- Dryness of other mucosal surfaces
- Parotitis / visibly enlarged parotid glands
- Extra-glandular involvement

# Symptoms related to extra-glandular involvement

- Cutaneous symptoms (including dryness, pruritus, Raynaud's)
- Pulmonary symptoms (e.g. xerotrachea leading to dry cough or recurrent bronchitis)
- GI symptoms due to pharyngeal/oesophageal dryness (difficulty swallowing, reflux)
- Cardiac symptoms (e.g. pericarditis)
- Neurological symptoms (e.g. peripheral neuropathy, distal paresthesia, trigeminal / facial nerve palsies)
- Renal symptoms (secondary to interstitial nephritis)
- Debilitating fatigue

# Ocular examination

(requires Ophthalmology referral)

- Ocular redness  
(conjunctival hyperaemia,  
limbal redness)
- Dullness of the corneal reflex  
(due to surface irregularity)



# Ocular examination

Blepharitis or meibomian gland dysfunction (eyelid disease) can also exist, affecting the tear lipid layer. This requires treatment with lid hygiene and warm compresses.



**Blepharitis**



**Meibomian gland dysfunction (MGD)**

# Ocular examination

- Poor tear film stability (tear break up in  $<10$  sec abnormal)



- Mucous strands (filamentary keratitis)

# Ocular examination

- Reduced tear production (reflex tearing) indicating lacrimal gland insufficiency (Schirmer test)



A normal result is a wetted length of  $> 10\text{mm}$  in 5 minutes. A wetted length of  $< 5\text{mm}$  in 5 minutes is considered abnormal.

To best evaluate lacrimal gland function, the test should be performed *without* topical anaesthesia.

# Ocular examination

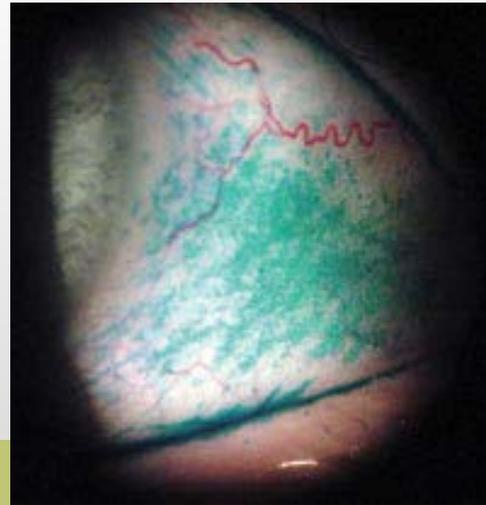
## Ocular surface staining

- Rose bengal or Lissamine green will stain primarily dead/devitalised cells (and cells without mucous cover)
- Fluorescein will highlight areas of epithelial cell loss

Rose bengal staining



Lissamine green staining



# Oral examination:

(ensure regular dental care)

- Visibly reduced sublingual salivary pool
- Tongue may stick to tongue depressor
- Frequent dental caries. Periodontal disease / tooth loss
- Tendency to develop oral candidiasis.
- ENT exam for bilateral parotid gland enlargement
- Sialometry / sialochemistry

# Joint examination

- Arthritis may be a component of SS
- Symmetric, polyarticular, inflammatory arthritis suggests underlying RA or a connective-tissue disease such as SLE or scleroderma.
- One third of patients with RA have Sjögren's syndrome.

# Differential diagnoses

- Ig-related Amyloidosis
- Bulimia
- GVHD
- Pancreatitis
- Polymyositis
- RA
- Salivary Gland Tumours
- Sarcoidosis
- Scleroderma
- SLE
- TB

# Work-up

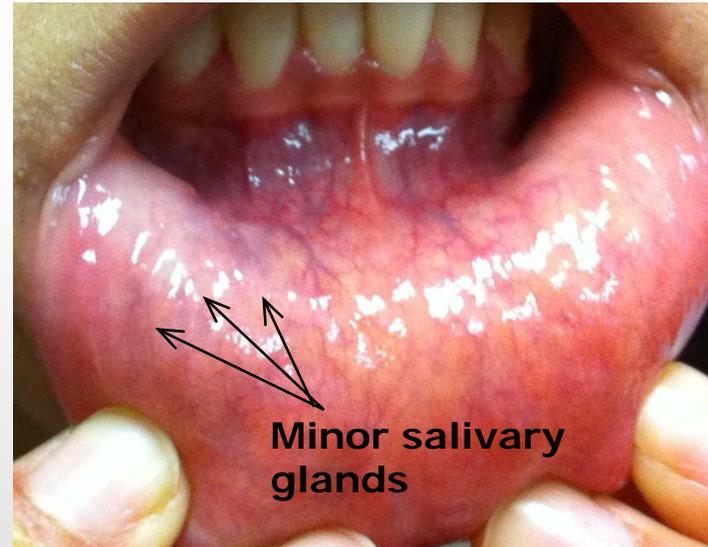
## Immunological work-up includes:

- RF – positive in most patients with SS
- ANA – typically present in patients with SS
- Anti-SSA/Ro – found in  $\approx$  50% of patients (75% with 1° SS and 15% with 2° SS)
- Anti-SSB/La – present in 40-50% of patients with 1° SS

*n.b. titers of these antibodies do not reflect disease activity*

# Minor salivary gland biopsy

- Biopsy of the minor salivary glands of the lower lip is the single most useful test to confirm the diagnosis of SS.
- A 1.5 to 2cm incision of normal-appearing mucosa allows for the harvesting of 5 or more salivary gland lobules.
- Histopathological findings (H&E) include focal lymphoid infiltration of minor salivary glands



# Classification Criteria

**American-European Consensus criteria for diagnosis of 1° SS: 4 of 6 positive responses to criteria below (must include no. 5 or 6)**

1. Ocular symptoms (dry eye)
2. Oral symptoms (dry mouth)
3. Ocular signs (abnormal Schirmer without anaesthesia; < 5mm in 5 min / ocular surface staining)
4. Oral signs (abnormal sialometry; unstimulated salivary flow <1.5 mL in 15 min)
5. Positive minor salivary gland biopsy
6. Positive anti-SSA or anti-SSB antibody results

# Classification Criteria

- 2° SS is diagnosed in presence of:
  - a connective tissue disease
  - symptoms of oral or ocular dryness, plus
  - criterion 3, 4 or 5 (ocular/oral signs or positive biopsy)
- For 1° SS, application of these criteria has yielded a sensitivity of 97.2% and a specificity of 48.6%
- For 2° SS, application of the criteria yielded a sensitivity of 64.7% and specificity of 97.2%

# Treatment of dry eye: Level 1

- **Level 1** - Mild symptoms, no corneal signs
  - Artificial tear supplements
    - tailor viscosity to symptom severity
    - if instilled > 4 times per day, use non-preserved drops
  - Modify environmental conditions
    - increase relative humidity
    - avoid windy conditions
  - Avoid anticholinergic / antihistamine medications



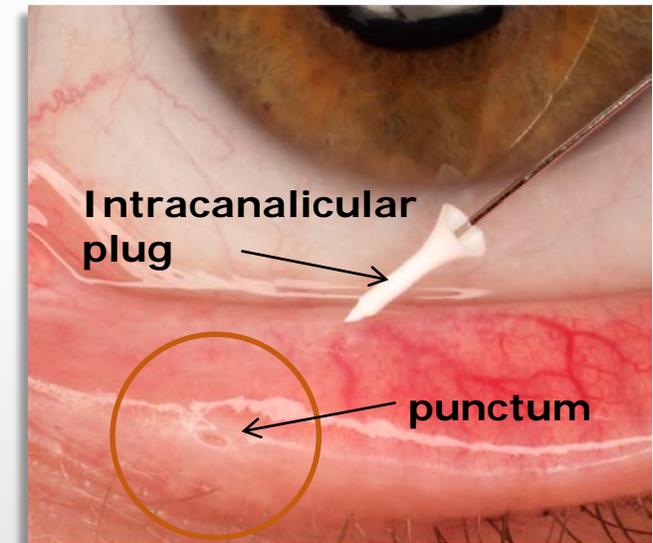
# Treatment of dry eye: Level 2

- **Level 2** - moderate-severe symptoms with tear film / visual signs, or mild ocular surface staining
- **Level 1 treatments plus:**
  - Unpreserved tears or gels ± ointments at night-time
  - Topical steroids (restricted course due to side effects risk)
  - Cyclosporine A (Restasis (US) / local pharmacy preparation)
  - Nutritional supplements (EFAs)



# Treatment of dry eye: Level 3

- **Level 3** - Severe symptoms with marked corneal changes or filamentary keratitis
- **Level 2 treatments plus:**
  - Tetracyclines (low dose, long course)
  - Autologous / allogeneic serum tears
  - Punctal occlusion (to retain tears)
  - Acetylcysteine to break down mucous strands



# Treatment of dry eye: Level 4

- **Level 4** - Extremely severe symptoms with altered lifestyle, or severe corneal staining, erosions, or conjunctival scarring
- **Level 3 treatments plus:**
  - Systemic anti-inflammatory therapy including acetylcysteine
  - Topical Vitamin A
  - Caution for permanent punctal occlusion
  - Moisture chamber glasses

# Treatment of dry mouth

- Sip water frequently
- Sugar-free lemon drops to stimulate saliva
- Artificial saliva (variable patient tolerance)
- Humidifiers for symptomatic relief
- Regular dental visits
  - fluoride treatment
  - special toothpaste
- Topical anti-fungals as required for candidiasis

# Treatment of joint pain

- Arthralgias
  - NSAIDs
  - Hydroxychloroquine
- Rheumatoid arthritis
  - Likely to require other disease-modifying medications (under direction of rheumatologist)

n.b. Cyclophosphamide used to treat serious systemic manifestations of SS has been associated with increased risk of lymphoma development

# Multidisciplinary care of SS

- **Physician** (to provide overall perspective)
  - **Rheumatologist** (management of connective tissue disease)
  - **Ophthalmologist** (management of ocular surface manifestations)
  - **ENT specialist** (minor salivary gland / parotid biopsies)
  - **Dentist** (for oral prophylaxis and treatment)
- ± Renal physician, chest physician, haematologist, oncologist

# Common SS medications

- Cholinergic parasympathomimetics (muscarinic agonists) (e.g. oral pilocarpine, cevimeline (US))
- Artificial tears
- Artificial saliva agents
- Disease modifying agents (e.g. hydroxychloroquine)
- Immunosuppressants (e.g. cyclophosphamide)
- Immunomodulators (e.g. cyclosporin A)

# Complications of SS

- Typically SS patients undergo outpatient reviews 3 – 6 monthly to check for complications
  - Emergence of related disorders (e.g. SLE)
  - Parotid gland infections
  - Parotid tumours
  - Pseudolymphomas / lymphomas
  - (18x increased risk of NHL in SS)

# Take home message

- SS has a generally good prognosis
- Prognosis more closely aligned with any associated disorders (e.g. SLE)
- Patient education and support is essential
  - Do not underestimate the impact SS, as a chronic condition, can have on daily life
  - Teach patient avoidance tactics and self-care strategies to help manage the symptoms associated with their dry mucosal surfaces
  - Support groups: Sjögren's Syndrome Society of NZ

[www.sjogrensnewzealand.co.nz](http://www.sjogrensnewzealand.co.nz)

# The End

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