Sjögren's Syndrome: The Forgotten Autoimmune Disease

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DISCLOSURES
I have no relevant financial relationships with commercial interests
All medications discussed are being used 'off-label': None of the medications discussed today are FDA approved for the purposes suggested

EPIDEMIOLOGY PRIMARY SJÖGREN'S
- Prevalence: 1.5-3.9/100,000 population
- 3rd most common autoimmune connective tissue disease
- If we include 2ndary SS it is the most common
- Yet hear more of lupus, scleroderma and dermatomyositis
- 90% are women
- Most common age to develop 40-50 years old

MAKING A DIAGNOSIS

EUROPEAN-AMERICAN CONSENSUS GROUP DIAGNOSTIC CRITERIA
1. Positive salivary gland biopsy OR positive SSA OR positive SSB serology AND
2. Three Objective Clinical Signs (Below) AND
3. Four Subjective Clinical Symptoms (Below)
EULAR OBJECTIVE CLINICAL SIGNS

• A. Ocular
  1. Schirmer’s test <=5mm in 5 minutes
  2. Rose Bengal >= 4 on van Bijsterveld’s score
• B. Oral
  1. Positive minor salivary gland biopsy

EULAR OBJECTIVE CLINICAL SIGNS

• C. Salivary Gland Involvement
  1. Unstimulated whole salivary flow <= 1.5ml/15 min
  2. Parotid sialography with diffuse sialectasias without obstruction
  3. Salivary scintigraphy showing delayed uptake/excretion
• D. Autoantibodies
  1. Ro (SS-A) or La (SS-B) antigens

EULAR CLINICAL SYMPTOMS

• Ocular
  1. Daily, persistent, troublesome dry eyes > 3 months
  2. Recurrent sensation of sand or gravel in the eyes
  3. Use of tear substitutes > tid
• Oral
  1. Daily dry mouth > 3 months
  2. Recurrent or persistent swollen salivary glands as an adult
  3. Frequently drink liquids to aid in swallowing dry food

ALWAYS CHECK FOR MEDICATIONS

• Antihistamines and decongestants
• Anti-diarrheal. (e.g. loperamide)
• Diuretics, combined alpha-beta blockers like labetalol, ACE-inhibitors, calcium channel blockers
• Antipsychotics; Antidepressants (Amitryptaline, nortryptaline, SSRI); Tranquilizers
• Muscle relaxants (e.g. flexeril)

SJÖGREN’S SKIN

• 150 patients with primary Sjögren’s syndrome
• 48% with Raynaud’s and PSS had dilated capillaries
  • pericapillary haemorrhages and capillary thrombosis were absent
DERM

• Xerosis
• Itch
• Atopic
• SCLE
• Photosensitivity
• Calcinosis
• Raynaud’s (30%)

SCLE AND PHOTOSENSITIVITY IN SJÖGREN’S

• 30% of Sjögren’s patients have photosensitivity
• 6-15% have rash clinically and histopathologically consistent with subacute cutaneous lupus

PHOTOPROTECTION

• Fibroblasts from connective tissue patients have been shown in-vitro to be more sensitive to not only UVB but also UV-C (254 nm), and UV-A (320 to 400 nm)
• SPF relates exclusively to the ability of a sunblock to extend the minimal erythema dose time which is a result of UVB exposure.

ANA

• Ro is poorly represented on Hep-2 cells and so sometimes ANA negative but Ro+ although Ro is a nuclear antibody

SICCA SYMPTOMS

• Dry eyes
• Dry mouth

DRY EYE THERAPY

• Most common response to treating dry eyes from physicians is to tell patient to use eye drops
• Most patients have thought of this on their own
• Myriad of products available
WHAT DO WE NEED TO KNOW?

• “Dry Eyes” are not always “dry”
• “Tears” are not just “water”

“Dry Eyes”

• Manifest in myriad different report of symptoms
  • Dryness
  • Grittiness
  • Inability to see contact lenses
  • Changes in vision
  • Tearing
  • In part these symptoms are clues of what has gone wrong and how to fix it

TEARS ARE MORE THAN JUST WATER

HOW DO WE FIX DRY EYES?

1. Increase functional tears
   - Depends on what layer, or layers of tear film is affected
     if multiple layers
   - Depends if it is just volume, or also composition of layer
     that is affected
   - Depends on why layer is deficient
   - Depends if it is basal or reflex tear production or both

2. Decrease tear loss
   - Reduce or eliminate tear drainage
   - Reduce evaporation (25% of tear loss)

3. Fully evaluate
   - Medications
   - Herbals, supplements
   - Timing of medications
   - Address environmental or behavioral factors
**TEAR HISTORY**

- Take a tear history which should include:
  - Sensation
  - Timing
  - Quality of tears

**SYMPTOMS**

- Tearing can be:
  - Reduced basal secretion
  - Loss of lipid layer so low surface tension
  - Blocked outflow from puncta

**SYMPTOMS**

- Tearing 2/2 Reduced basal secretion
- - HIS TORY HELPS
  - As no reflex tearing at night eyes are dry first thing, tears develop as day goes on

**SYMPTOMS**

- Tearing 2/2
  - Loss of lipid layer so low surface tension
  - Blocked outflow from puncta

  - PHYSICAL EXAM HELPS

- Tearing 2/2 Loss of lipid layer so low surface tension
  - Look for inflamed
  - or blocked meibomian glands

- Tears should flow out from puncta
  - Look for blocked puncta
TEARING FROM REDUCED BASAL SECRETION

- As no reflex production at night pills taken at night affect eyes more
- Night time eye protection is essential
  - Humidifier in bedroom
  - Protective eyewear
- Night-time eye protection
- Prevents evaporation

LIPID LAYER LOSS

- Address underlying meibomian dysfunction
- Exogenous supplementation

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MEIBOMIAN DYSFUNCTION

- Optho consult
- STOP PRESERVED EYE DROPS – block meibomian
- Warm compress
- Eyelid massage to remove debris
  - Index finger to outer corners pull eyelid taught, ring finger to gently massage along lid edge

MEIBOMIAN DYSFUNCTION

- Trial scrub with 1:1 dilated Johnson’s baby shampoo on cotton tip applicator
- Or commercially available lid scrubs OCU SOFT LidScrubs or Novartis EyeScrub
MEIBOMIAN DYSFUNCTION

• Restasis
• Doxycycline 200mg Po BID x 3 months for meibomian inflammation

LIPID LAYER LOSS

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• Exogenous supplementation

LIPID LAYER LOSS

• Address underlying meibomian dysfunction
• Exogenous supplementation

EXOGENOUS SUPPLEMENTATION

• Myriad of products available
• Indeed, not all ‘drops’

AVOID

• Avoid preserved tears but if do use always less than 4x/day (block meibomian glands)
• Avoid benzalkonium chloride and thimerosal which exacerbate (more common in generics)

WHEN LIPID LAYER LOW LOOK FOR:

• Want ones with oils so e.g. Refresh Endura is castor oil based
• Gels best for nighttime use
• Ointments better but cause blurring
# Aqueous Layer

- Sticky secretions in morning suggest loss of aqueous but not mucin component
- As no reflex production at night pills taken at night affect eyes more
- Artificial Tears should have lower viscosity (often labelled “light”)

## Artificial Tears

- Patient education: [www.dryeyezone.com](http://www.dryeyezone.com)
- May need to mix and match to achieve optimal control
- Patients need to have flexibility in frequency and form depending on environment they are in at that moment

## How Do We Fix Dry Eyes?

2. Decrease tear loss
   - Reduce or eliminate tear drainage
   - Reduce evaporation (25% of tear loss)

## Punctal Plugs to Stop Drainage

- Tears should flow out from puncta
HOW DO WE FIX DRY EYES?

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BLINKING IS IMPORTANT

• 25% of tear loss through evaporation
• Protective eyewear night or day
• Blinking redistributes lipid layer
• Computer or TV use leads to 90% reduction in blink rate
• Need to take breaks every 20 minutes

SICCA SYMPTOMS

• Dry eyes
• Dry mouth

“Dry Mouth”

• May or may not complain of ‘dry mouth’
• May complain of changes in taste
• May complain of being unable to tolerate hot or spicy foods

EXAM

• Parotid gland enlargement
• Salivary pool
• Tongue
• Other mucous surfaces

EXAM – PAROTID GLANDS

• Not my patient - most patients will not be this obvious
• Old facial photos can be helpful in noting changes
EXAM – SALIVARY POOL

- Ask patient to swallow then look under tongue for salivary pool
- Normal refill within 30 seconds
- However, sometimes subjective dry mouth out of proportion to volume loss
- Reduced sulfating of MUC5B more closely correlated with subjective “dry mouth” than fluid volume

EXAM – TONGUE

- Often papillae atrophy, smoother tongue

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OTHER MUCOUS SURFACES

- Steroids, antibiotics, distracted immune system and mucosa without biofilm (transferrin, calprotectin, histatins, defensins)
- More prone to oral candida — always CHECK oral mucosa every visit

CANDIDAL INFECTIONS

- White thrush less common - look for macules erythema tongue palate buccal and angular cheilitis

CANDIDAL INFECTIONS

- Can be harder to treat due to poor environment
- Also if low saliva secretion ORAL FORMS DO NOT WORK WELL AS MEDICINE NOT RE-SECRETED
  - washes have insufficient time in contact
  - use topicals eg nystatin vaginal tablet sucked in mouth

SALIVA SUBSTITUTES

- Come in rinses, lozenges, gels and sprays
- Higher viscosity intended to reduce need for re-application
- Higher pH to neutralize acids
- Some contain bactericidal agents to reduce caries
MEDICATIONS Proven in dry mouth, not statistically significant for dry eyes

- Pilocarpine 5mg 4 times daily
- Cevimeline 30mg 3 times daily (better tolerated as targets M3 over cardiac M2 receptors)
  - Can lead to hyperhidrosis, polyuria, flushing, headache
  - Caution in patients with heart arrhythmias, CV disease, Parkinson’s, COPD
  - do not use in uncontrolled asthma, narrow angle glaucoma

DERM

- Xerosis
- Itch
- Atopic
- SCLE
- Photosensitivity
- Calcinosis
- Raynaud’s (30%) *Vaginal dryness
- Sweet’s
- Pulmonary
- Pregnancy - neonatal lupus, congenital heart block
- Vasculitis
- Hairloss
- Small fiber polyneuropathy
- Erythromelalgia

Summary

- Often onset 40-50s women
- Always get Ro/La even if ANA negative
- Clues are sudden onset severe dryness and asteatotic dermatitis
- May also report Raynaud’s and photosensitivity
- Ro+ with SCLE does not only mean SLE

Summary

- Look at their capillary nailfolds
- Look at meibomian glands, punctal blockage, and salivary pool
- Take a full dry eye/dry mouth history
- In designing treatment regiment remember neither tears nor saliva are “just water”

PATIENT RESOURCES

- https://www.sjogrens.org/
- http://www.sjogrenssyndromesupport.org/
- https://scholar.google.com/
- http://www.dryeyezone.com