

Current issues in the Diagnosis and Management of Sjogren's Syndrome

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Primary Sjogren

A systemic autoimmune disease whose characteristic is ocular and salivary involvement, but also includes other organs such as lung (pneumonitis), kidney (interstitial nephritis), and neurological (central and peripheral) and lymphoproliferative features

Goal-1

Correct therapy depends on correct diagnosis

- a) New international criteria
- b) Potential pitfalls in diagnosis

Goals-2

Review the use of
Topical medications
for dry eyes and dry mouth

Goals-3

Review the current guidelines for
diagnosis and therapy
of
extra glandular manifestations

Goals-4

How to empower the patient to
participate in their own care

Epidemiology of Sjogren's

1. Predominately women (9:1) with two ages of median onset
In the 30's and 50's
2. Much of what we call SLE in the older patient is actually Sjogren's syndrome

What causes Sjogren's

A combination of Genetic and
Environmental Factors

From family and twin studies,
approximately 4 genes are required
but even then an environmental factor
is needed

Genetics

1. Most important is HLA-DR, which correlates closely with ANA and anti-SS-A antibody
2. Genes of B-cell activation similar to SLE patients

Environmental

No single agent identified

Viral candidates may include EBV
and coxsackie viruses

Hepatitis C, HIV and HTLV-1 can
mimic

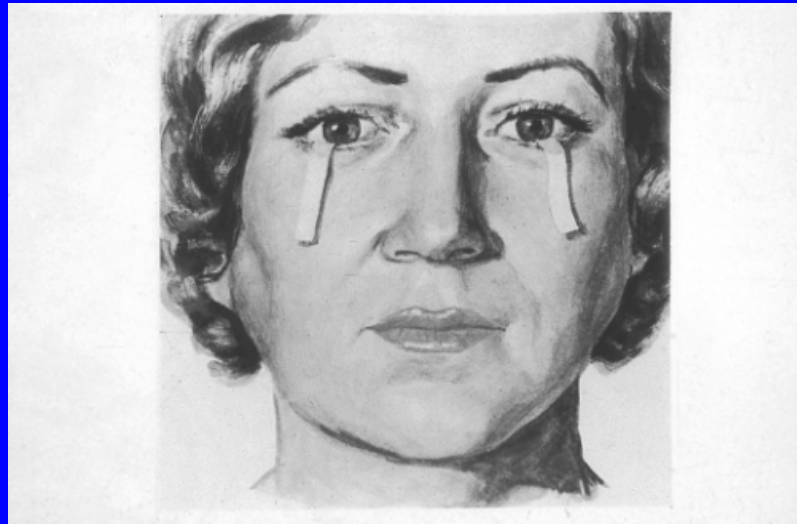
Objective-1

Clinical Issues

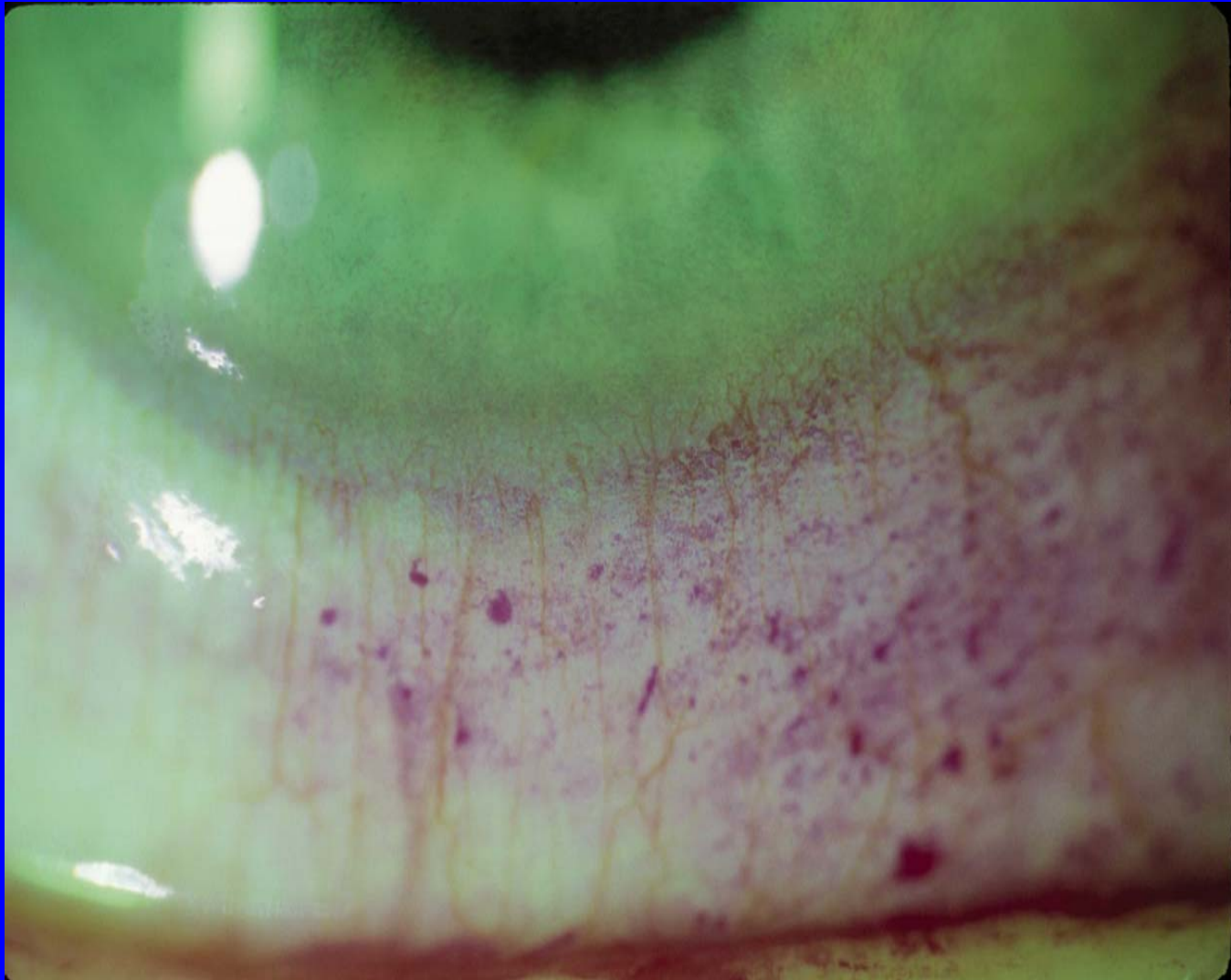
There is good agreement about diagnosis for the patient with florid symptoms of keratoconjunctivitis sicca (KCS), parotid swelling, and high titer ANA with SS-A/SS-B.

The issue in these patients will be therapy
And the extent of extra glandular involvement.

Typical features of dry eyes, dry mouth and swollen glands



Dryness results in the clinical appearance of
keratoconjunctivitis sicca (KCS)
characteristic of Sjogren's syndrome



Severe Xerostomia with dry tongue



Sjogren's syndrome

Eye and Oral Features

1. Most of these patients have a positive ANA with positive Anti-Sjogren's SS-A/SS-B antibodies
2. They have specific needs for the eye and mouth care

Since these patients see many health care
professionals
(ophthalmologists, dentists,
rheumatologists)
their care is expensive and fragmented

We must empower them to be part of
the therapeutic team and even to
educate their health providers

Sjogren's Syndrome- Cervical Dental Caries



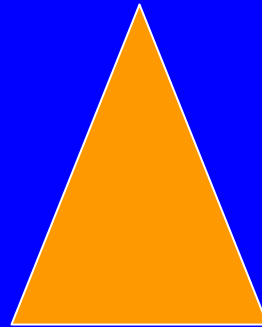
In addition to dry eyes and dry mouth

These patients have signs and symptoms that affect other parts of their body ranging from obvious manifestation of skin vasculitis to vague symptoms of fatigue and cognitive loss

Diagnostic Issues

In the patient with true Sjogren's

Sjogren's syndrome



Extent
Of
Extra glandular
Disease

Therapy
And
Education

Differential Diagnosis: is the Dryness Due to Other Causes

Non Salivary Gland Disease

Drugs-esp.. BP and cardiac
muscle relaxants
antidepressants and
OTC meds for cold
Acute anxiety and depression
Mouth breathing
Central lesions:
Multiple sclerosis
Alzheimer's

Salivary Gland Disease

Hepatitis C
Sarcoidosis
Fatty Infiltrate of Gland
HIV disease
Lymphoma
Cancer of the Salivary Gland
Infection of gland
(TBC, Actinomycosis)
Head & neck radiotherapy

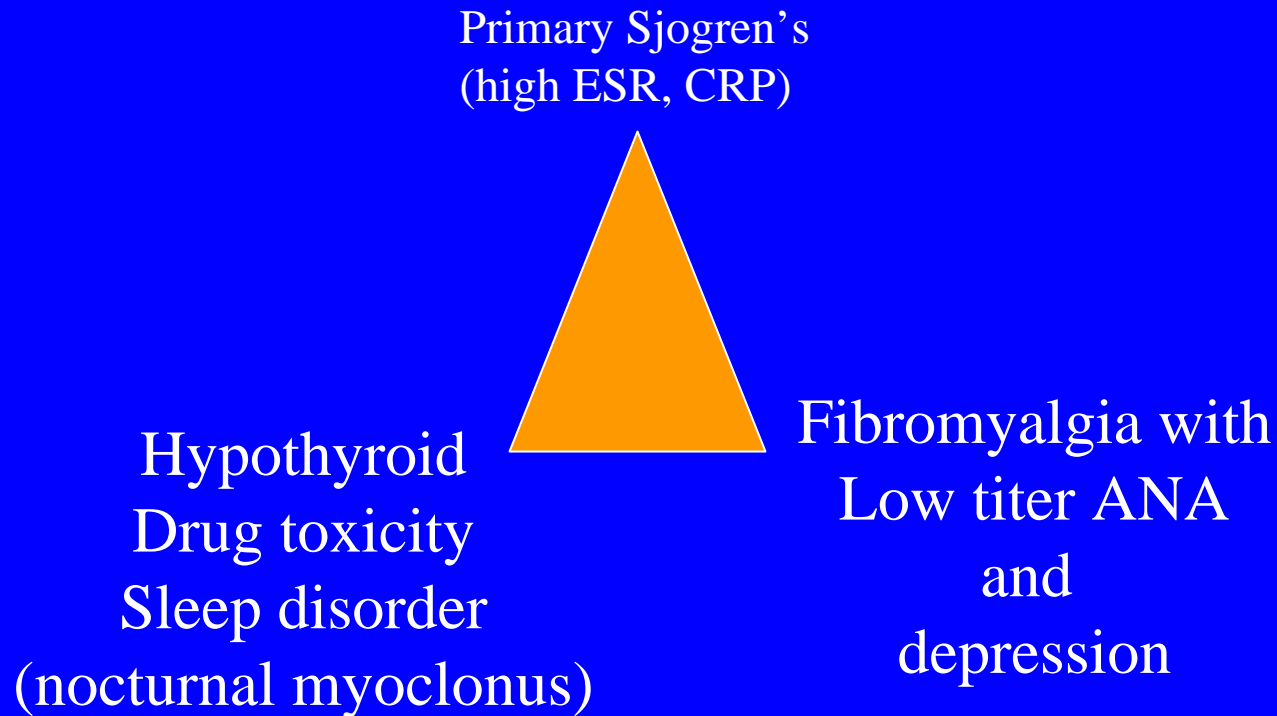
Objective-2

Clinical Issues

The most difficult and common questions involve the diagnosis and treatment of the patients with vague complaints of dryness, fatigue, cognitive dysfunction, arthralgias and low titer ANA

Objective-3

Clinical Issues of Diagnosis of fatigue



Issues in Diagnosis-1

Past confusion over criteria

San Diego criteria (0.5% incidence) versus

Original EEC criteria (5% incidence)

Now clarified

With new proposed international

criteria

Issues in Diagnosis-2

Submitted criteria (11/01) by International
SS advisory board

Will require either

A positive minor salivary gland biopsy

Or

Antibody against SS-A (Ro)

New international criteria-1

1. Ocular Symptoms

2. Oral Symptoms

3. Salivary gland function

(flow rate by flow rate, scan, or sialography)

AND

4. Histopathology (focus score > 1)

5. Autoantibody to SS-A or SS-B

New international criteria-2

New Criteria for SS (cont'd)

Exclusions

Pre-existing lymphoma, sarcoid

Hepatitis B or C

Drugs with Anticholinergic side effects

(measurements of tear/saliva with patient off drug for 3 half lives)

Caution in interpreting studies on clinical associations published during past several years- since results will depend on the inclusion criteria

For example:

- A) On disease associations (esp. liver-as hepatitis C now now an exclusion)
- B) “Primary” Fibromyalgia patients now excluded

How good are our tests?

The lip biopsy and the
the ANA and anti-SS A antibody
are often considered “specific” tests
but they are not specific

Pitfalls in diagnosis-1

A) Positive ANA does not mean Sjogren's or SLE

These tests are sensitive but not specific

(only about 1:100 patients with ANA 1:320 will have SS or SLE)

B) anti SS-A antibody more specific-but
differences between detection kits

The ANA is sensitive but not specific

The ANA should not be used as a screen
for Sjogren's or SLE

but to confirm a clinical diagnosis

ANA 1:80 present in 20% of normals
(esp. in fibromyalgia patients)

This is important since some aggressive physicians have actually treated fibromyalgia patients for their fatigue with cyclophosphamide thinking that it was CNS vasculitis

Even the Gold standard of lip biopsy is often misread by pathologists

On review of outside biopsies diagnosed as Sjogren's syndrome, over half (32/60) were reclassified on review.

Vivino, F.B., I. Gala, and G.A. Hermann, *Change in final diagnosis on second evaluation of labial minor salivary gland biopsies*. J Rheumatol, 2002. **29**(5): p. 938-44.

Part of the confusion is that patients complain of dry eyes/mouth and rheumatologists talk about antibodies

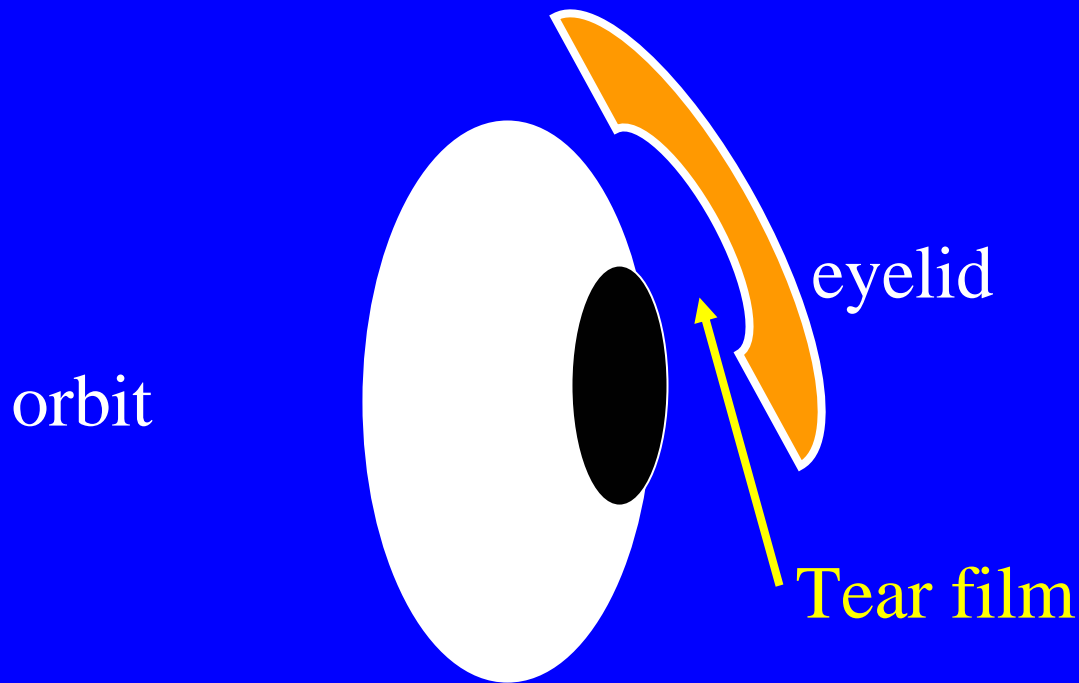
Why do patients complain of dry eyes and dry mouth?

It is important to recognize that symptoms can only be interpreted as part a functional unit that involves a neuroendocrine circuit

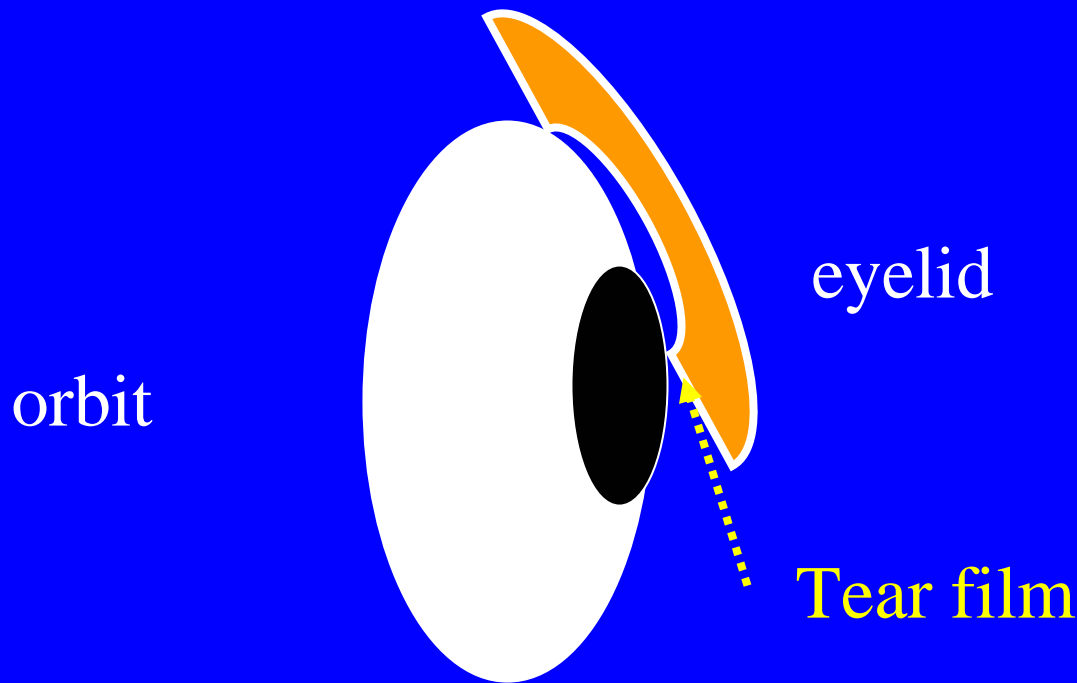
They are describing the sensation
of increased friction

As the eyelid traverses the orbit
Or the tongue moves around the
buccal mucosa

Normally the upper eyelid
glides over the globe on a coating called the tear film
composed
of water, protein, mucins

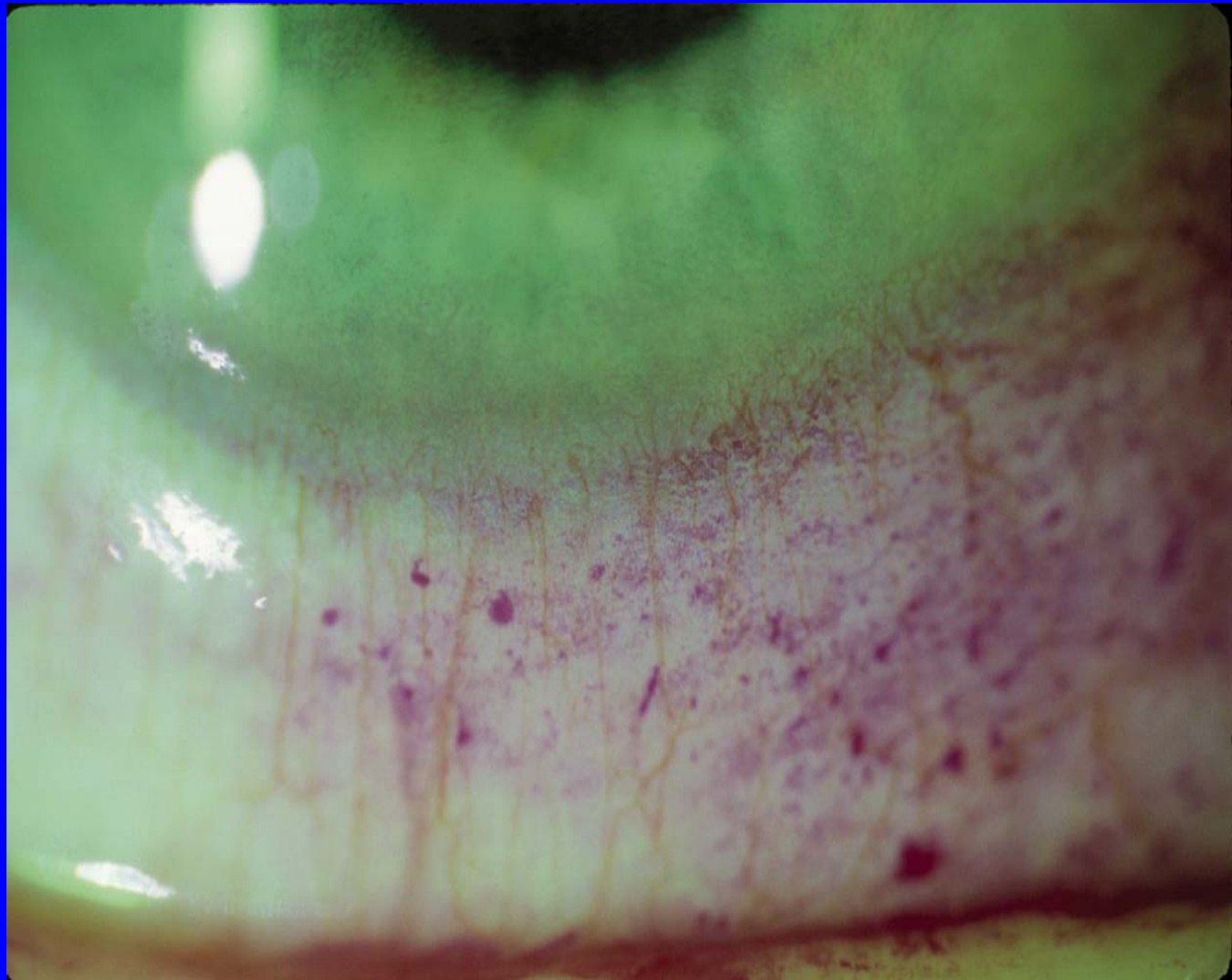


When the tear film is inadequate,
The upper lid sticks to the surface of the orbit and
Actually pulls of the surface layer of the ocular
surface



The
Sjogren's
patient is
describing
increased
friction as
the upper
lid moves
over the globe

Dryness results in the clinical appearance of
keratoconjunctivitis sicca (KCS)
characteristic of Sjogren's syndrome



In Sjogren's syndrome

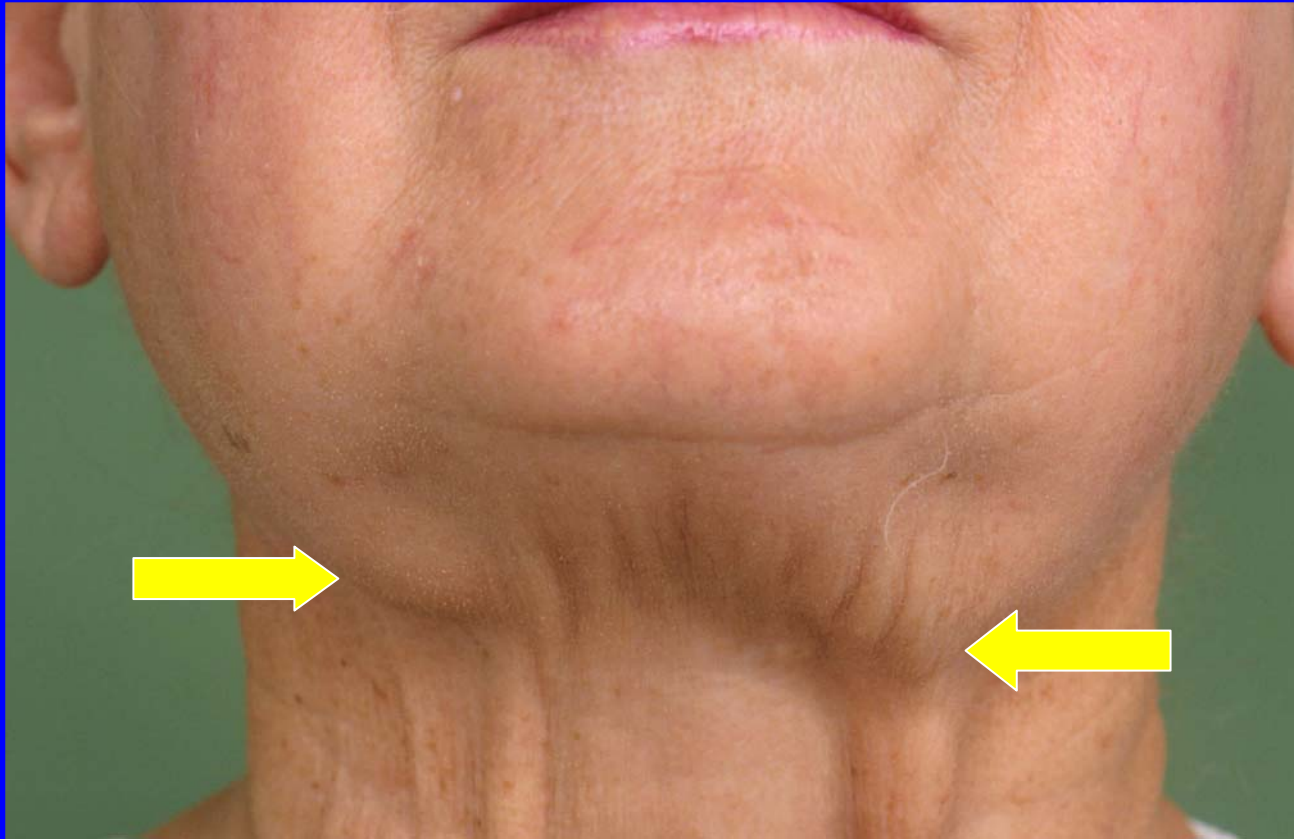
A similar deficiency in the saliva increases the friction as the tongue moves around the mouth in order to swallow or talk

The decrease in saliva leads to acceleration of dental decay and other infections such as oral candidiasis

The Sjogren's Syndrome with swollen parotid gland

The concern is infection or
lymphoma

Sjogren's Syndrome - Diffuse Submandibular Salivary Gland Enlargement



Sjogren's Syndrome - Ascending Salivary Gland Infection



Sjogren's Syndrome - Investigations

MRI



If you order an MRI

1. Ask for MRI -sialography (this is just a fat suppression view to visualize the ducts). It takes only 5 minutes more and no risk
2. Have the MRI printed out on CD and give copy to patient for their record

Although the systemic manifestations can occur in Sjogren's as in SLE, there are some subtle differences

Extraglandular manifestations

Sjogren's syndrome

Skin-hyperglob purpura.....

Lung-interstitial pneumonitis

Renal-interstitial nephritis...

Cardiac-pulmonary hypertension..

Hematologic--lymphoma....

Neurologic-peripheral neuropathy

Esophageal-dysphagia and tracheal reflux

SLE

Skin-leukocytoclastic vasculitis

Lung-pleural effusions

Renal-glomerulonephritis

Cardiac-pericarditis

Hematologic-ITP, hemolytic anemia

Neuropathy-mononeuritis multiplex

Systemic therapy-1

In general, similar to SLE
Steroids work and the question is how
to get the patients off steroids

Systemic therapy-2

Usually start with
hydroxychloroquine or methotrexate
for rash or arthralgias

Systemic therapy-3

For severe visceral vasculitis,
still use cyclophosphamide (pulse)

But try to use less than 6 cycles
and then try

Leflunomide, mycophenolic acid
anti-CD20 (Rituxin)

Systemic therapy-4

Recent preliminary report that infliximab
(Remicade)

Published (Steinberg, 2003)

But a larger multicenter trial

Presented at American College of
Rheumatology

Did not show benefit of TNF inhibitor

How can we educate and make the patient part of the therapeutic team

In an era of decreased time for patient contact, we must utilize the internet and support groups as a backbone.

The internet can be source of either information or mis-information unless we help create useful sites.

What should be on an Internet site?

We need to ask Patients what they want and need-

- a) medications and procedures
- b) insurance issues
- c) Hot “Links” to other relevant sites

But not all patients are computer literate?

Determine if physicians and patients
can work through local libraries,
where high school students can fulfill
“civic service” by setting up sites and
serving as resources to maintain sites.

Summary-1

1. New diagnostic criteria are developed that should diminish confusion in clinical practice and in the research literature
2. There is variability in reading minor salivary gland biopsies and interpretation of positive ANA's

Summary-2

Sjogren's syndrome has clinical features and treatment that are generally similar to SLE

But the Sjogren's patient has particular needs in terms of the medications they tolerate and particular disease manifestations.