
WELCOME TO
YAZD

Sjögren's syndrome and uncommon presentation

Hamidreza Bashiri, MD, Rheumatologist

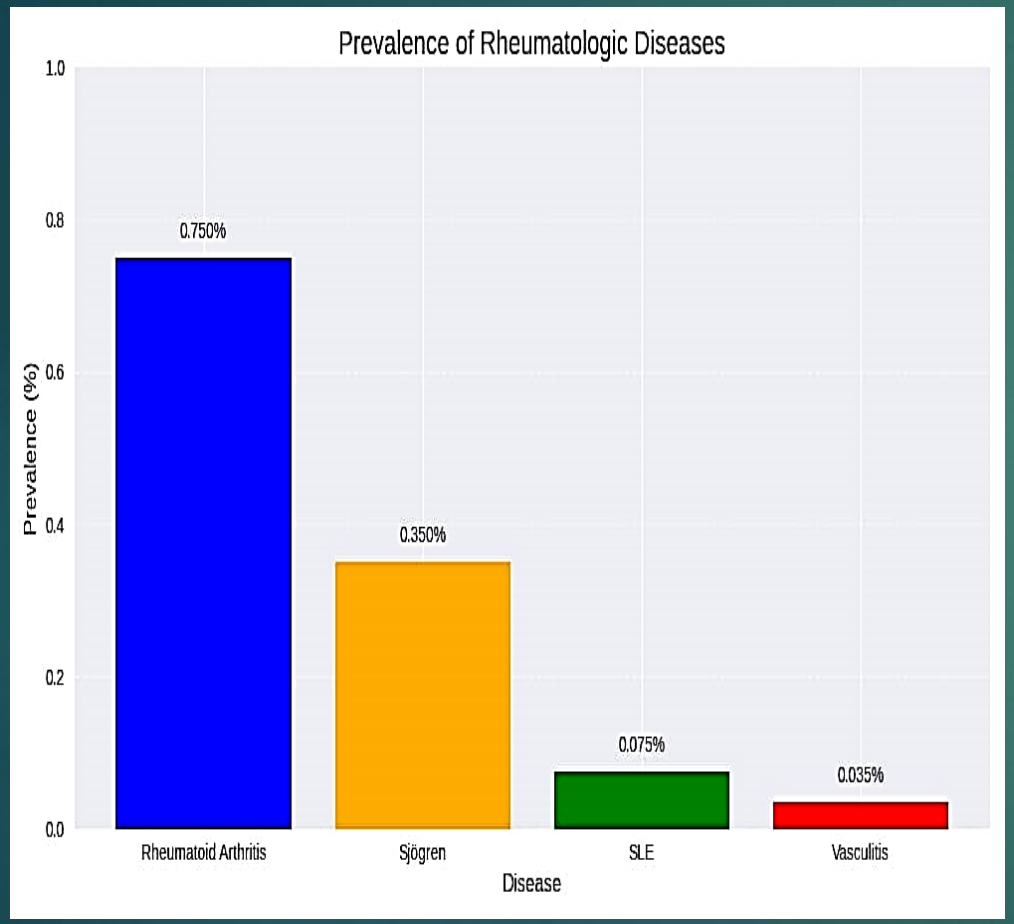
Assistant Professor, Shahid Sadughi University of Medical Sciences

Dec. 2025

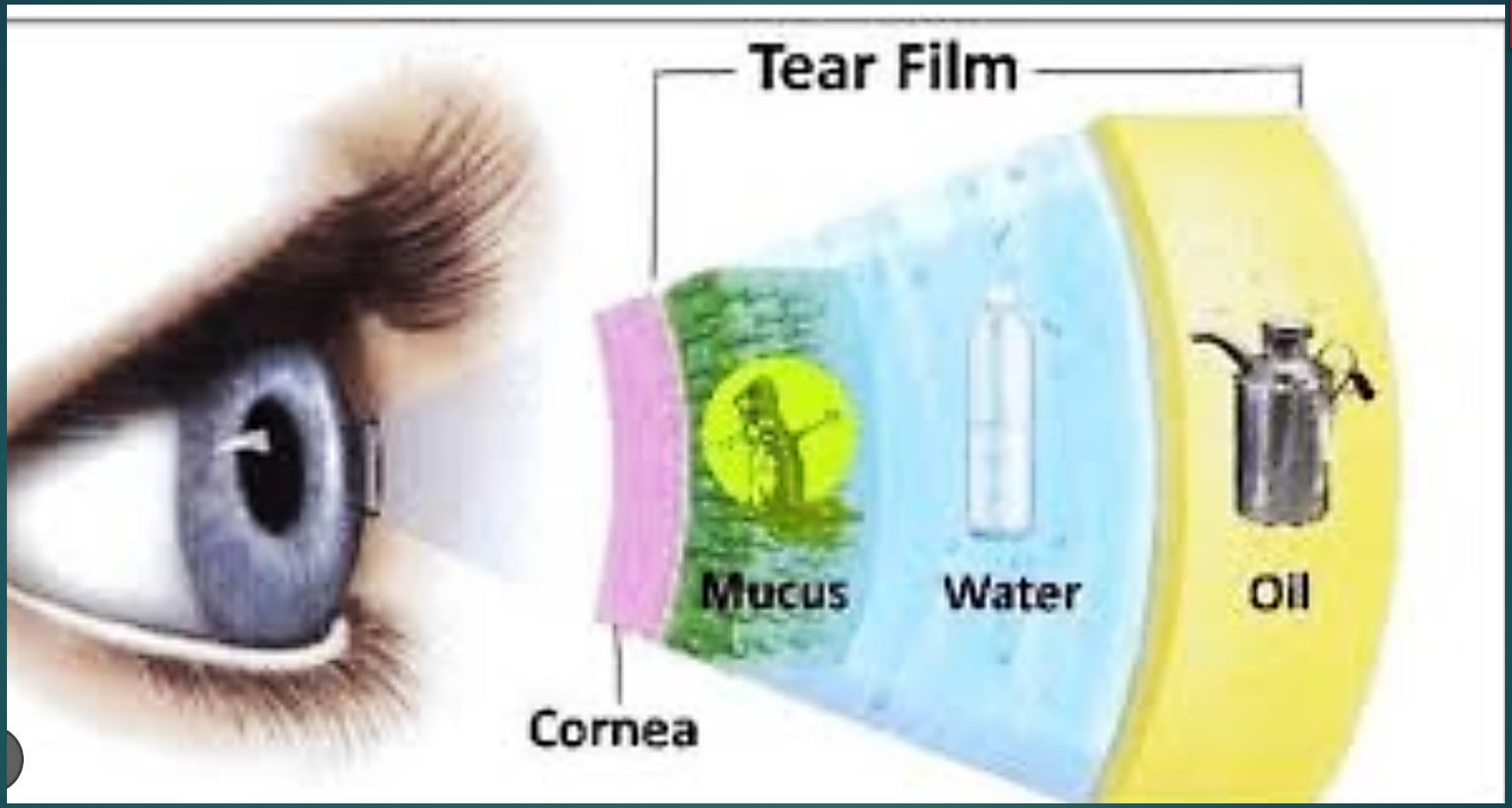
Sjögren's syndrome

- Chronic inflammatory
- Lacrimal and salivary gland function
  - Primary
  - Secondary
- Clinical manifestations
  - Exocrine gland
  - Extra glandular disease(30% to 40%)

- 9:1 female-to-male ratio
- Most commonly in the fourth and sixth decade


Prevalence of Rheumatologic Diseases
Prevalence (%)
1.0
0.8
0.6
0.4
0.2
0.0
0.750%
0.350%
0.075%
0.035%
Rheumatoid Arthritis
Sjögren
SLE
Vasculitis
Disease


SJÖGREN
SLE
VASCULITIS


Tear Film
Mucus
Water
Oil
Cornea

Dry eye

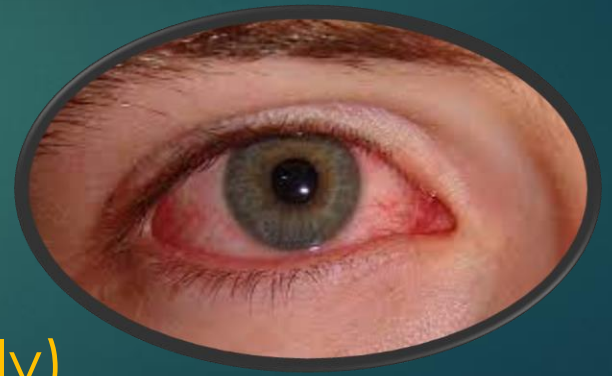
- Reduction in the aqueous component of tears
- Irritation, grittiness, blurry vision
- Insidiously over a period of several years
- often worse in the evening

Inability to cry is not a common symptom

Dry eye

- Photophobia

- Accumulation of thick, rope-like strands (mucus filaments) at the inner canthus(particularly present upon awakening)



- Corneal ulceration and infection of the eyelids
- Anterior and posterior uveitis, scleritis (infrequently)

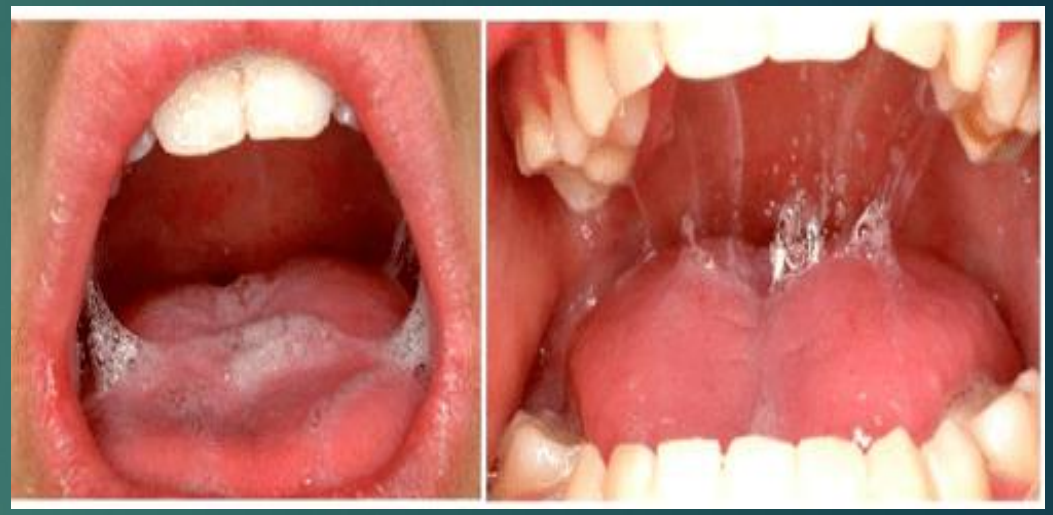
DRY MOUTH

- Directly of oral dryness(xerostomia)

Sticky saliva/ changes both in quality and quantity

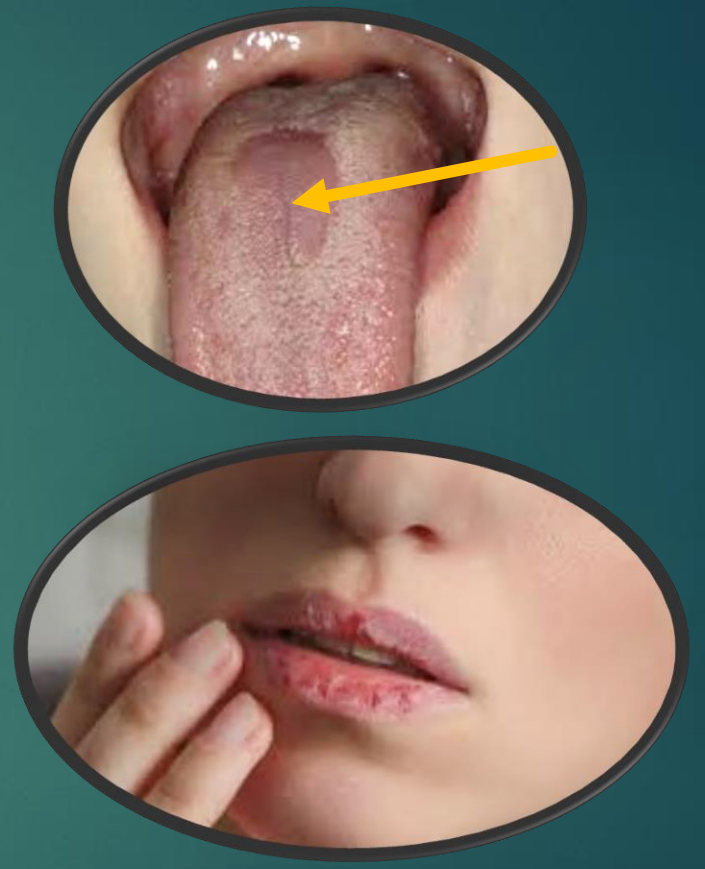
or

- Complications:
  - Adherence of food to buccal surfaces
  - Problems with dentures
  - Changes in taste
  - Inability to eat dry food
  - Speak continuously for long period



DRY MOUTH

- Lingual papillary atrophy
- Dry lip
- Absent sublingual salivary pooling



Complications of salivary hypofunction

- Dental caries (65%)

Primarily affect the cervical root and incisal surface of the teeth

Figure 1. Fissured tongue.

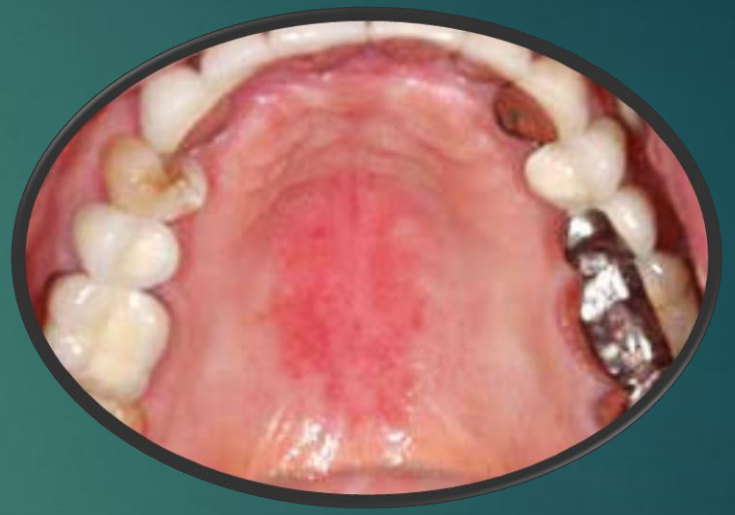
Figure 2. Enamel demineralization.

Figure 3. Class V caries seen commonly in Sjögren's Syndrome (SS).

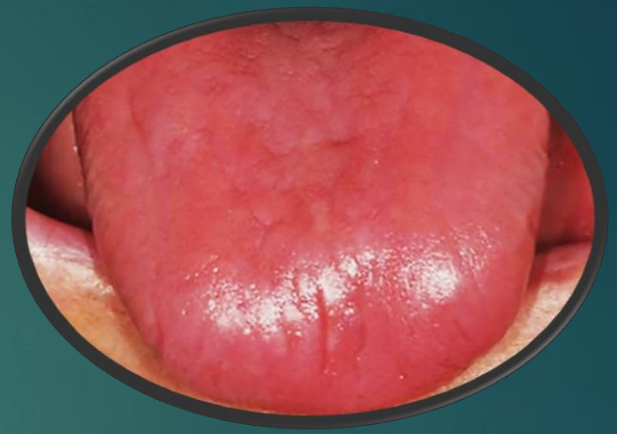
Figure 4. Class VI caries seen commonly in SS.

Oral candidiasis

- One-third of patients
- wearing of dentures
- use of glucocorticoids
- Painful mouth
- Burning sensation
- Sensitivity to spicy or acidic foods
- Diffuse or patchy erythema, typically affecting the hard palate



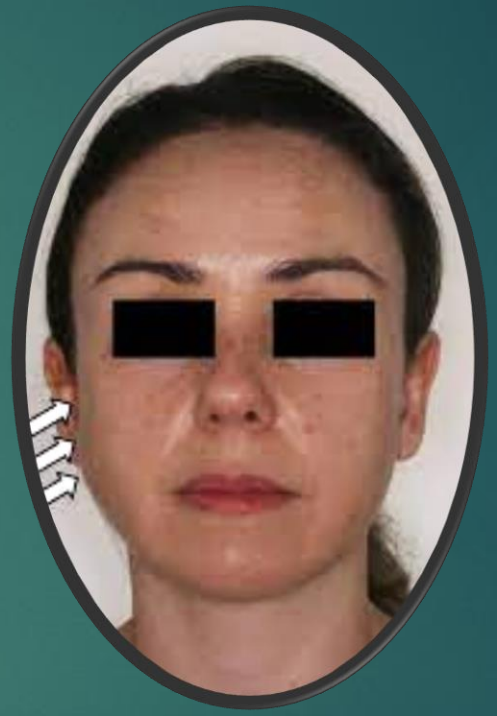
- Loss of tongue papillae



- Angular cheilitis

Salivary and lacrimal gland enlargement

- 20%
- Firm, diffuse, non tender
- Most obvious in the parotid glands
- Chronic or episodic



- Lacrimal gland enlargement is a rare (igG4/sarcoidosis/lymphoma)

EXTRAGLANDULAR ORGAN INVOLVEMENT

- Joint
- Lungs
- Heart
- Gastrointestinal tract
- Kidneys and bladder
- Gynecologic system
- PNS and CNS
- Hematologic abnormalities
- Vascular disease

Some extra-glandular manifestations result from SS itself

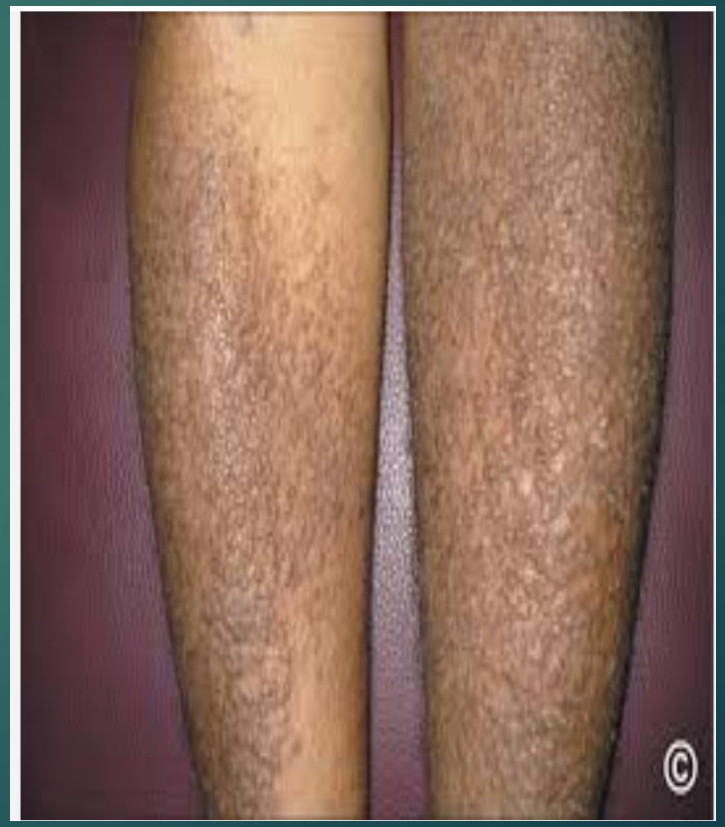
While other result **from others autoimmune disease**:

- Celiac disease
- Autoimmune thyroid disorder

Skin

- xerosis
- Purpura (60%)
- Raynaud phenomenon (13 to 30%)
- Cutaneous vasculitis
- Annular erythema

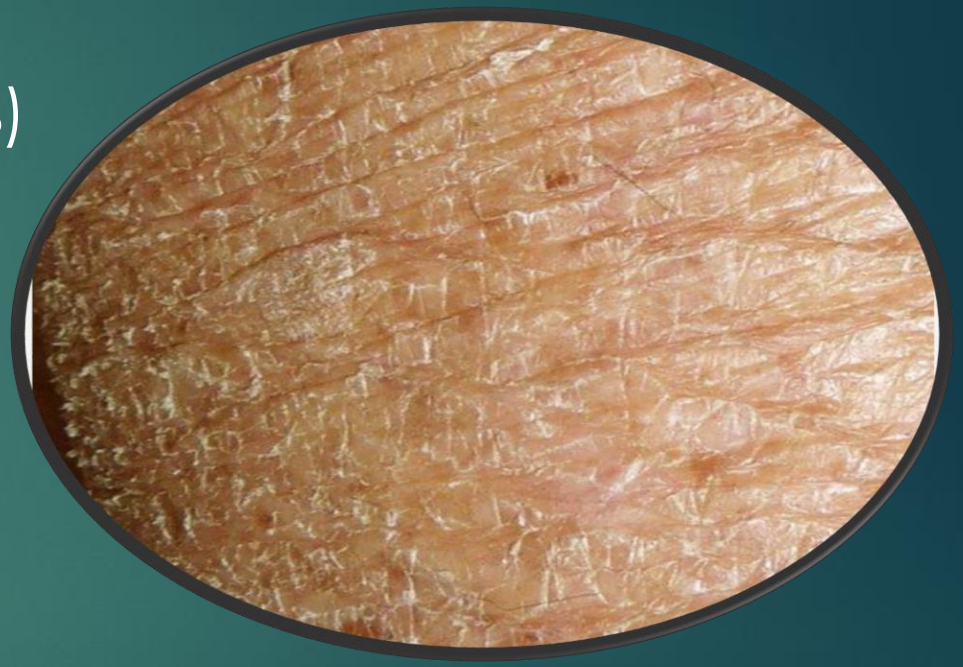
- Erythema nodosum (4%)
- Livedo reticularis
- Lichen planus
- Vitiligo
- Cutaneous amyloidosis



Xerosis

Most common cutaneous features (31-72%)

- Dryness
- Sequela
- Pruritus



lower extremities and axillary

Symptoms tend to be worse in the winter

vasculitis

- One of the rarest(10%)

small-vessel vasculitis

- Palpable purpura is the most common sign, but urticarial lesions, macules, papules, small ulcerated
- lower extremities
- Cryoglobulinaemic vasculitis is the most frequent type

Minority of patients who have medium-sized vessel disease

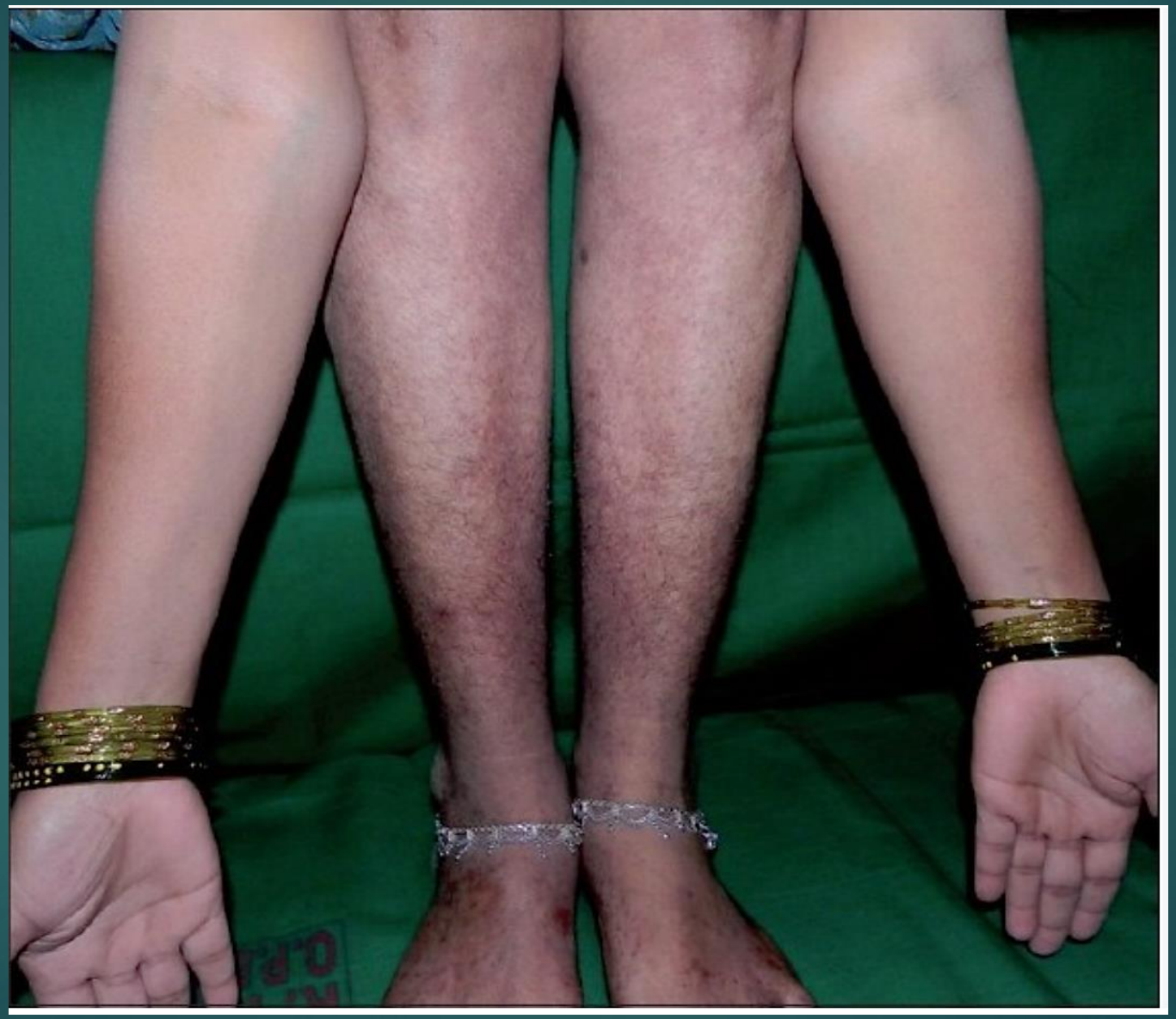
- Extraglandular manifestations(ex, lymphoma)

Benign hyperglobulinemic purpura of Waldenström

- Recurrent purpuric lesions (usually on the lower extremities)
- Elevated (ESR)
- Anemia, leukopenia, normal platelet counts
- Polyclonal hypergamma globulinemia

- Primary: especially in young women
- Secondary: most frequently in SS (RO antigen), RA,SLE

  Rarely in patients with lymphoma and multiple myeloma



Joints

50 %(arthralgia, with or without evidence of arthritis)

- Hands, wrists, and knees
- Symmetric
- Intermittent
- Non erosive on plain radiographs
- Non deforming

RF:40%

ACPA: 5 to 10%

Patients with RF or ACPA defined more severe inflammatory arthritis, which was often erosive

Myopathy

- Mild (1 to 14 %)
- Subclinical
- Insidious onset of proximal muscle weakness

- Significant muscle weakness and marked muscle enzyme elevations together with sicca symptoms may: overlap connective tissue disease

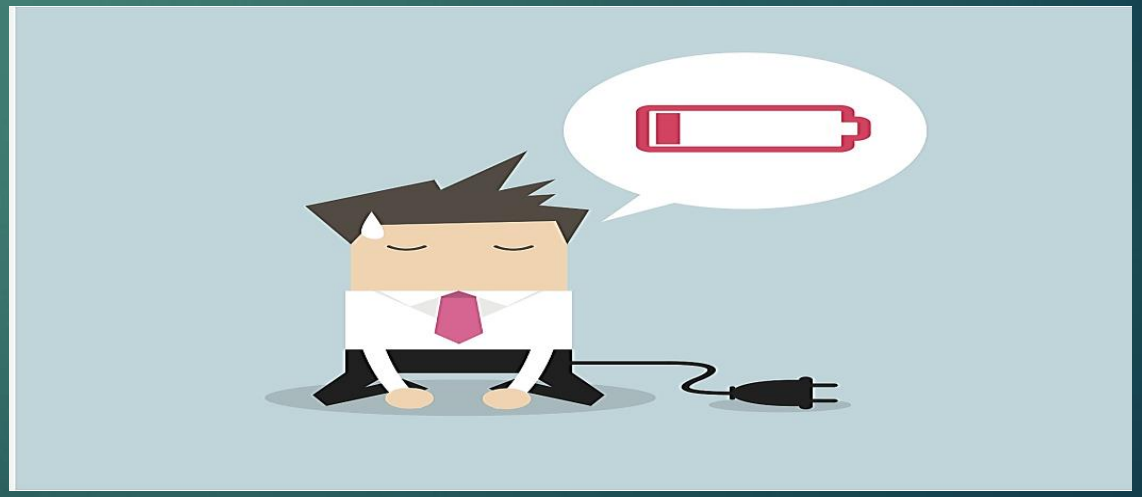
Fatigue and fibromyalgia

Fatigue is one of the most common symptoms

Despite the association of fatigue with systemic disease activity but:

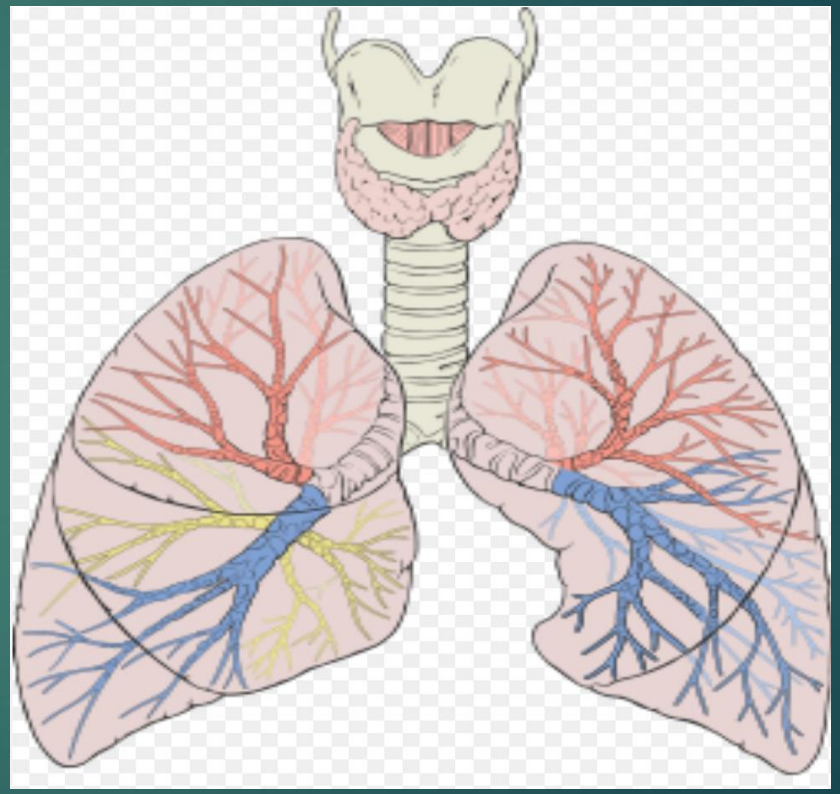
- ✓ Level of proinflammatory cytokines inversely

- sleep disorders
- Depression
- Hypothyroidism
- Fibromyalgia (15 to 31%)



Lungs

- 10 to 20 %have clinically



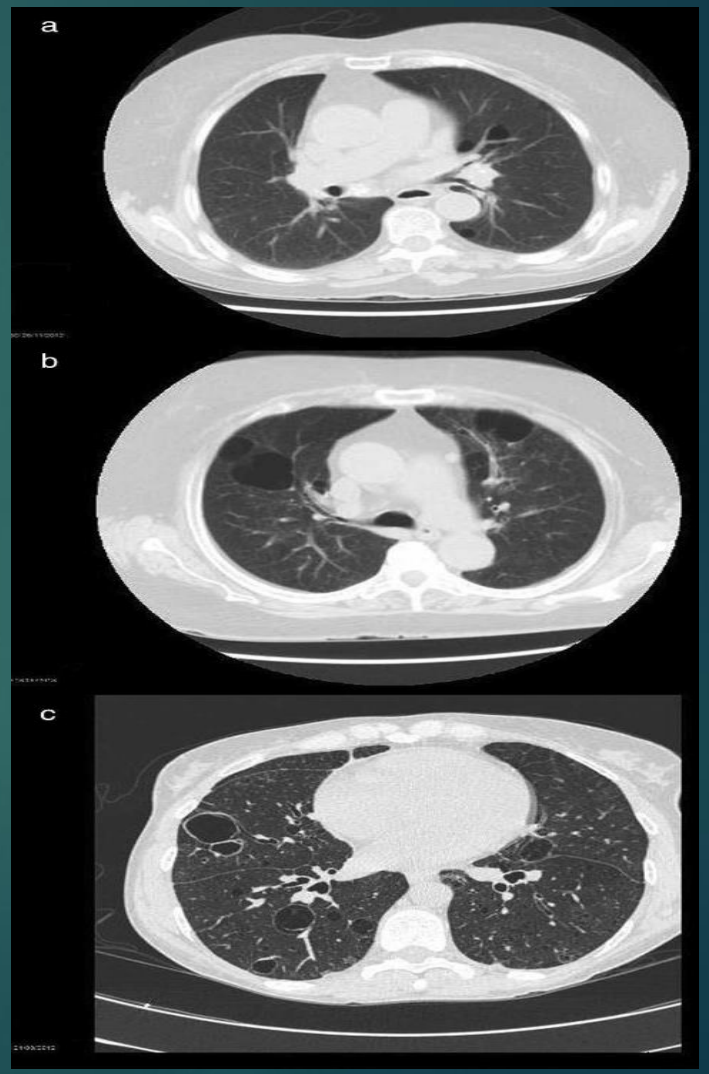
Upper respiratory tract and airways

Upper respiratory tract (large and small airways)

- Nonallergic rhinitis and sinusitis
- Nasal dryness
- Excessive throat clearing
- Dry cough
- Hoarseness

CYSTIC LUNG DISEASE

- Thin-walled lung cyst
- Multiple, bilateral ,middle and lower lung zone
- Often vary in size
- Often asymptomatic
- Older /anti RO(+)
- NO change in the number or size of cyst



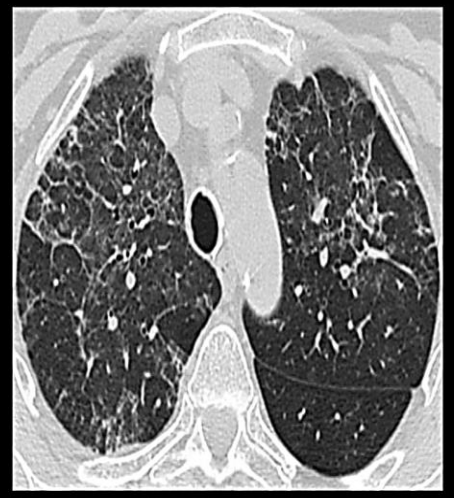
Interstitial lung disease

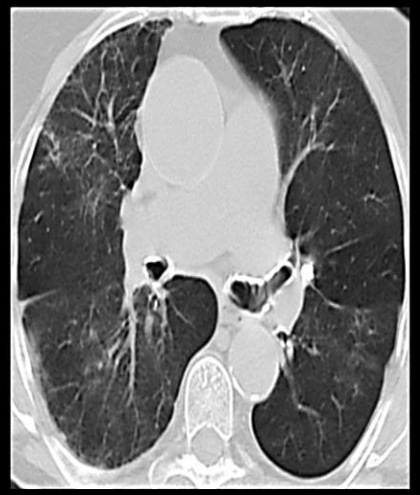
Dyspnea and cough

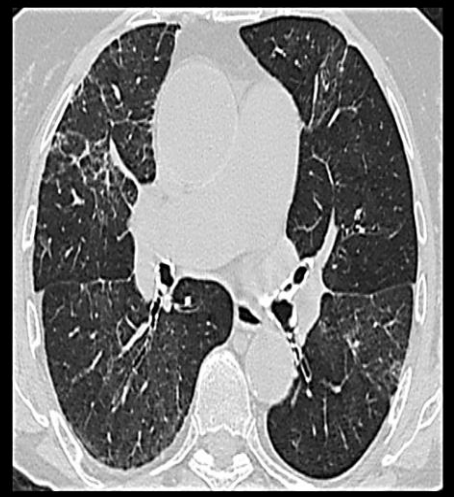
- NSIP is the most common
- Variety of connective tissue diseases and hypersensitivity reactions

- LIP has a strong association
- LIP can be a precursor to a bronchus-associated lymphoid tissue (BALT) lymphoma

NSIP

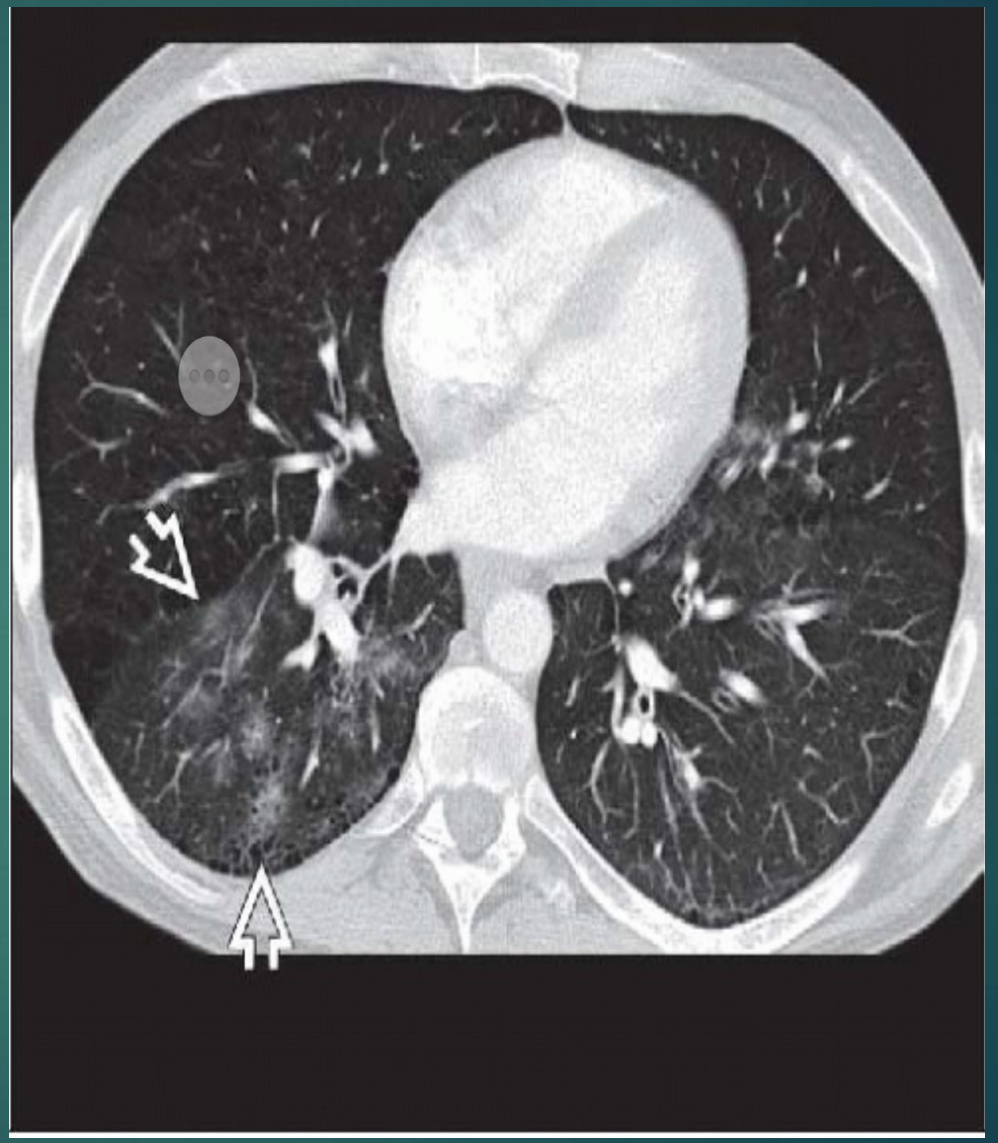






Ground-glass opacities diffusely distributed in both hemithorax; septal thickening, reticular opacities and bronchial ectasias, predominantly distributed in both upper lobes

Findings consistent with NSIP/OP



Heart and cardiovascular system

- May be associated with increased risk for cardiovascular disease
- Acute pericarditis and myocarditis are rare
- Heart block is rare in adult/ not consistently associated with anti-Ro

Gastrointestinal tract

- Dysphagia is common

- Nausea
- Epigastric pain
- Dyspepsia

- Celiac disease may be more prevalent in patients with SS than in the general population(10-fold higher)

Liver- Pancreas

- Hepatic function test abnormalities may be hepatocellular or predominantly cholestatic in pattern(5 to 26%)

- Patients with PBC have an 18 to 38 % prevalence of SS
- clinically overt PBC is 4 % of SS patients
- Autoimmune hepatitis (2%)

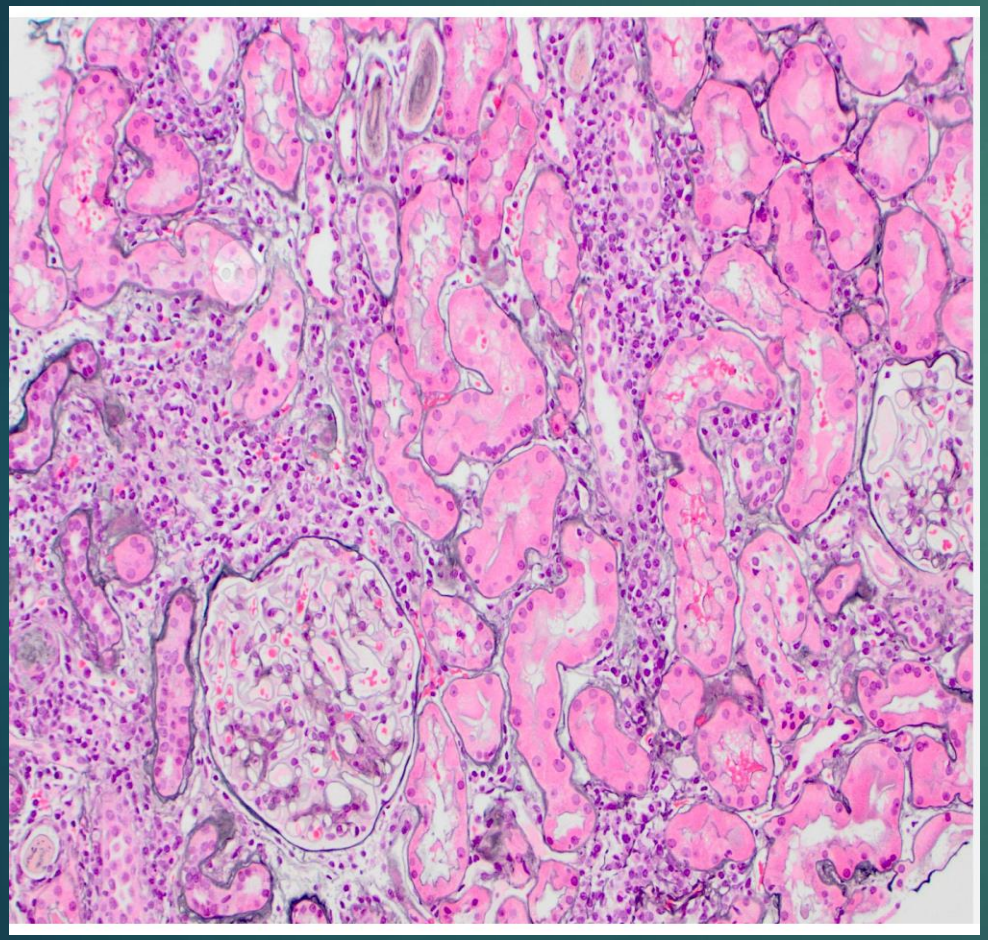
- Involvement of the pancreas would be expected, but is rarely evident clinically

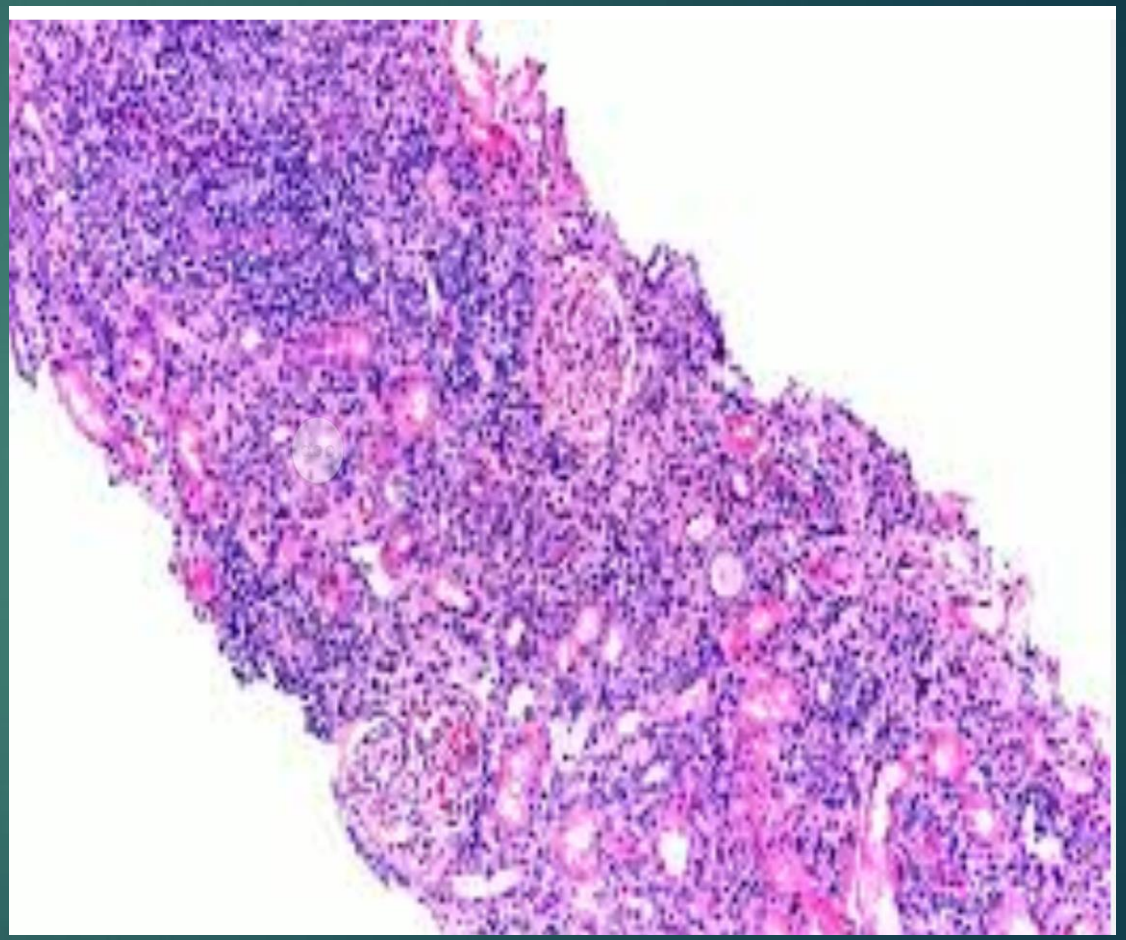
- Sjogren's syndrome can present with recurrent, unexplained gastrointestinal symptoms

- clinicians should consider Sjogren's syndrome when standard GI workups are inconclusive

Clinical Case Reports, 2025

Kidney





- Interstitial cystitis:(20-fold higher)
  - Dysuria
  - Urinary frequency
  - Nocturia, and urgency

In the absence of a urinary tract infection

Gynecologic symptoms

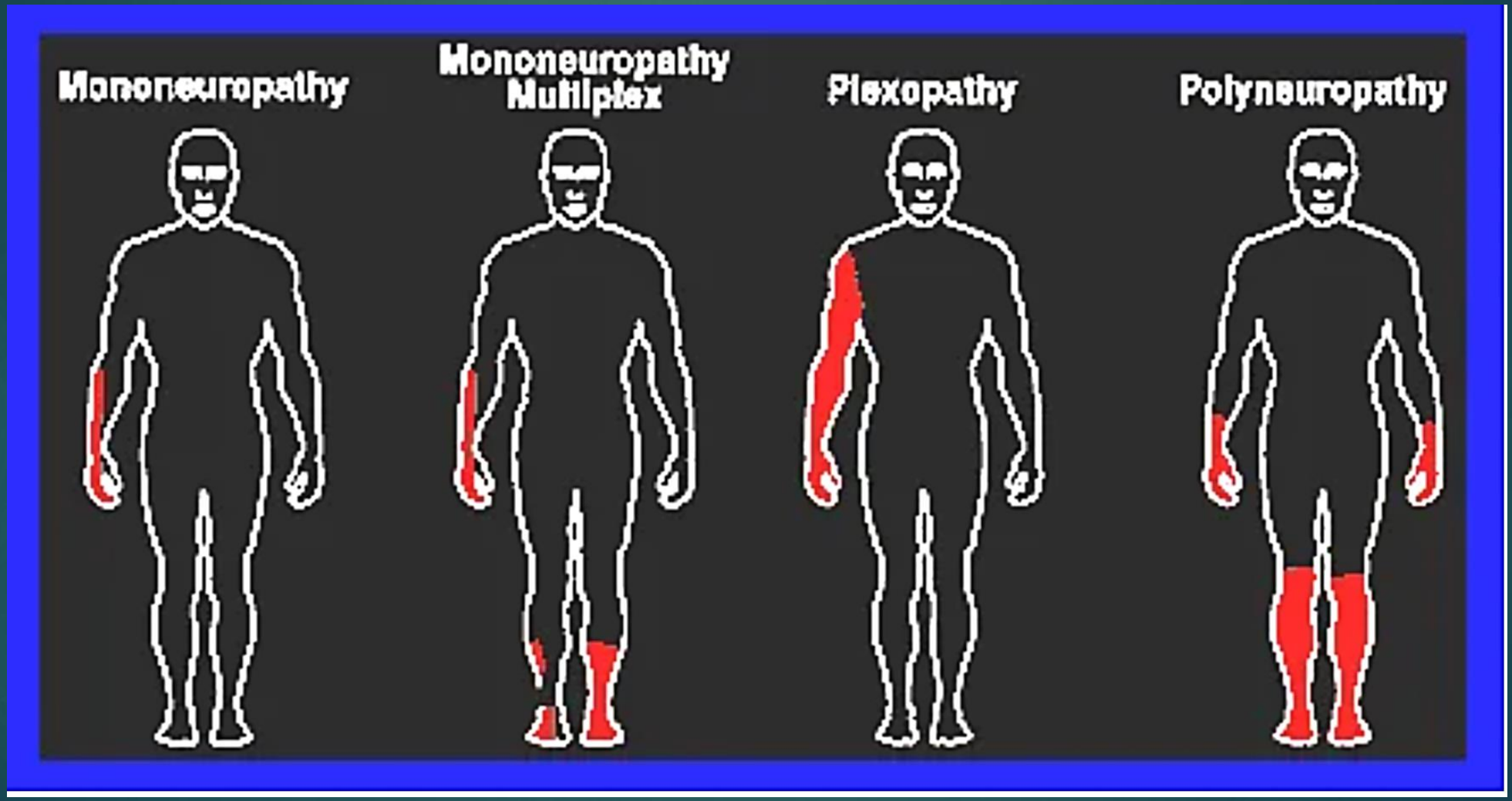
- Vulvovaginal dryness
- Pruritus
- Dyspareunia **(significant source of morbidity)**
  - 40 percent of premenopausal

Neurologic disease

- Variety of neurologic manifestations
- Peripheral nervous system (2 to 25%)
- Both PNS and CNS disease, frequently precede the diagnosis of SS(33-93%)

- Small-vessel vasculopathy /vasculitis
- Dorsal root ganglionitis
- Demyelination
- Myelitis
- Anti neuronal antibodies

Peripheral nervous system



Small fiber neuropathy (A alpha and C fibers)	Large fiber neuropathy (A delta fibers)
Pain and paresthesia	Impaired vibration
Autonomic signs and symptoms	Loss of position sense
Temperature loss	
No weakness	Wasting and weakness of muscles
Normal deep tendon reflexes	Loss of deep tendon reflexes

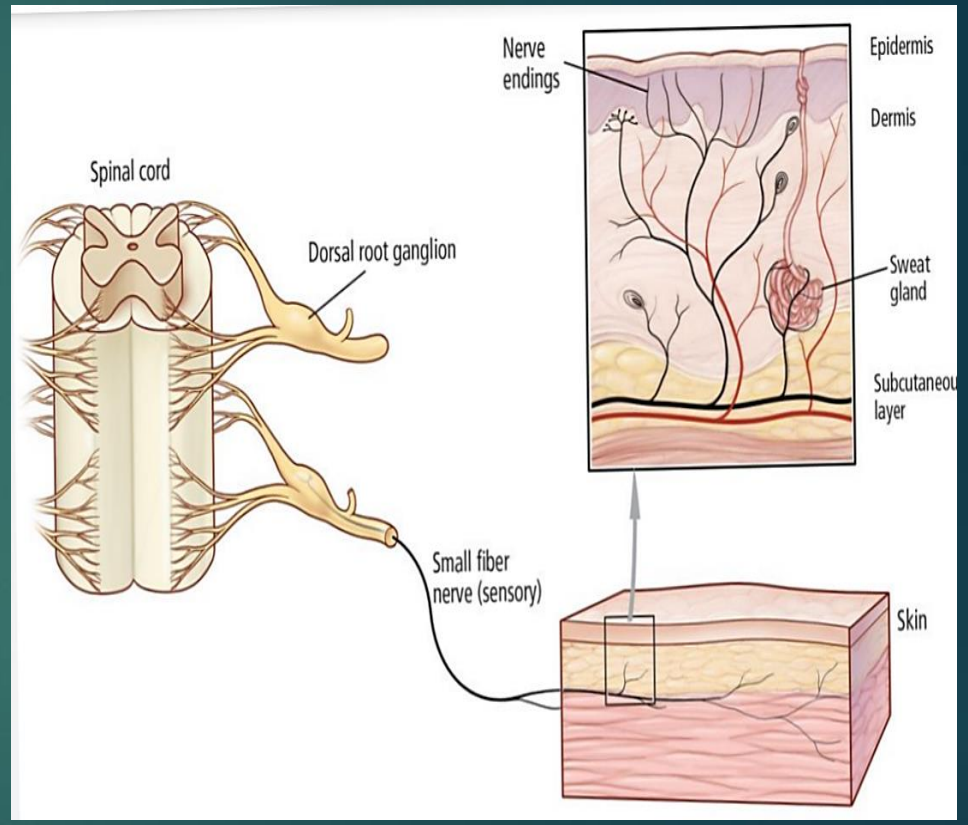
Axonal sensorimotor polyneuropathy

Large myelinated fibers

- Distal paresthesia
- Impairment of light touch and proprioception
- Diminution or loss of D.T.R. particularly in the Achilles tendon
- Muscle weakness, usually mild, primarily affects the toe or foot extensors
- EMG/NCV

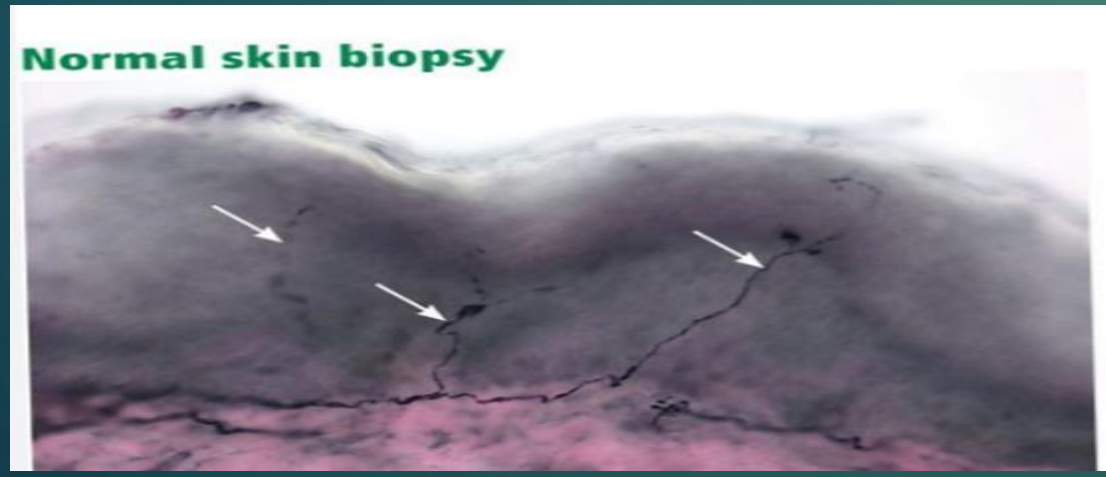
Small-fiber neuropathy

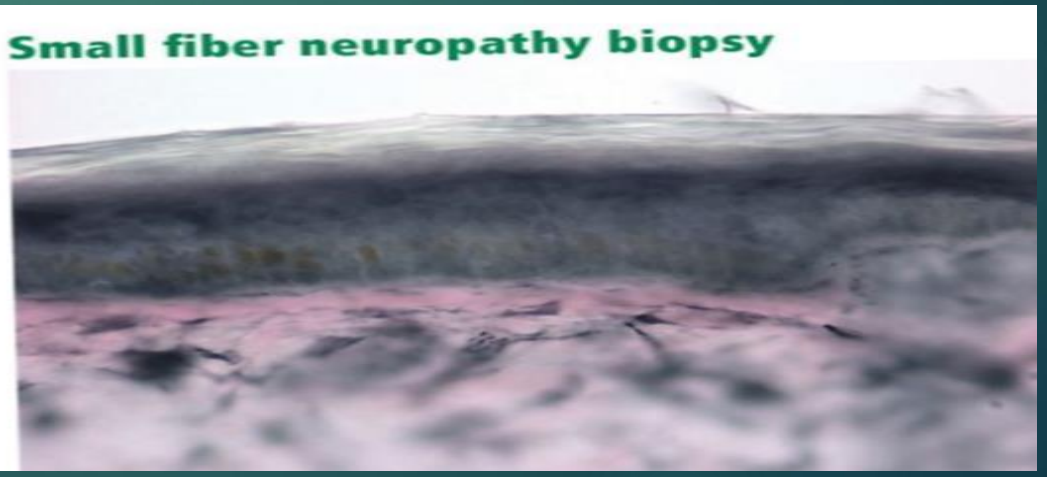
- Painful dysesthesias in the most distal:
- Burning
- Shock-like
- Prickly
- Symmetric
- Asymmetric(dorsal root ganglionitis)



Light touch, proprioception , diminution, loss of deep tendon reflexes are preserved

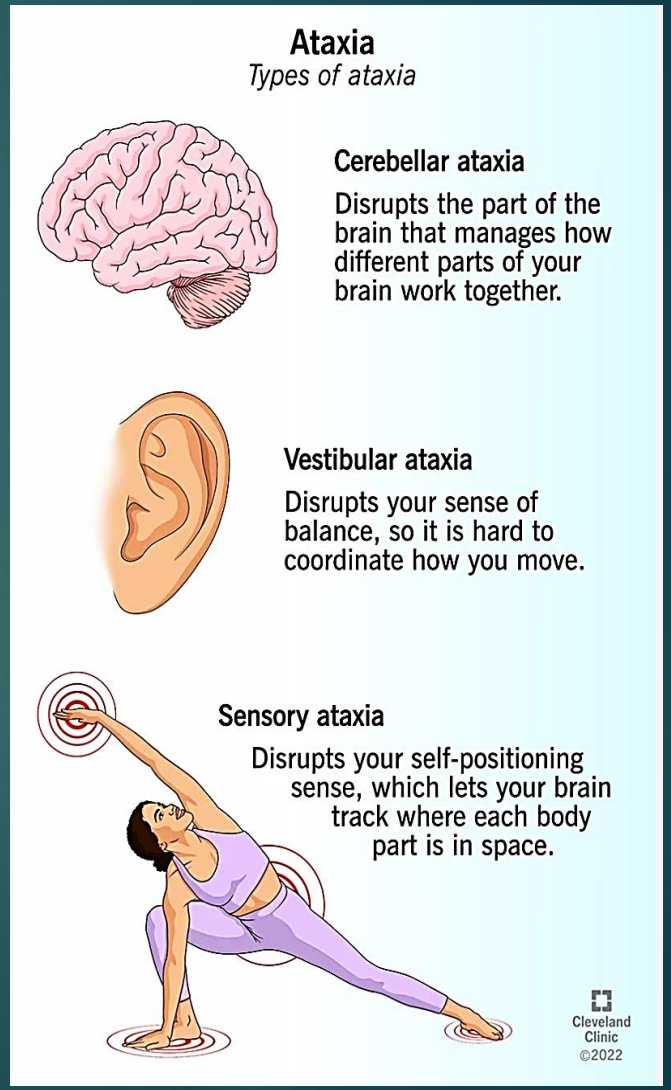
- Lower prevalence of anti Ro
- Male
- No electrophysiologic findings
- Decreased density of epidermal nerve fibers in a skin biopsy





Sensory ataxic neuropathy

- 5%
- Dorsal root ganglionitis
- Asymmetric paresthesia in digits of hand or foot
- Gait ataxia
- Generalized areflexia
- EMG/NCV



Multiple mono neuropathy

- Acute onset
- Tingling or painful dysesthesia in the distal limbs ,Subsequently, motor and sensory symptoms occur episodically and extend to multiple nerve distributions, primarily in the limbs

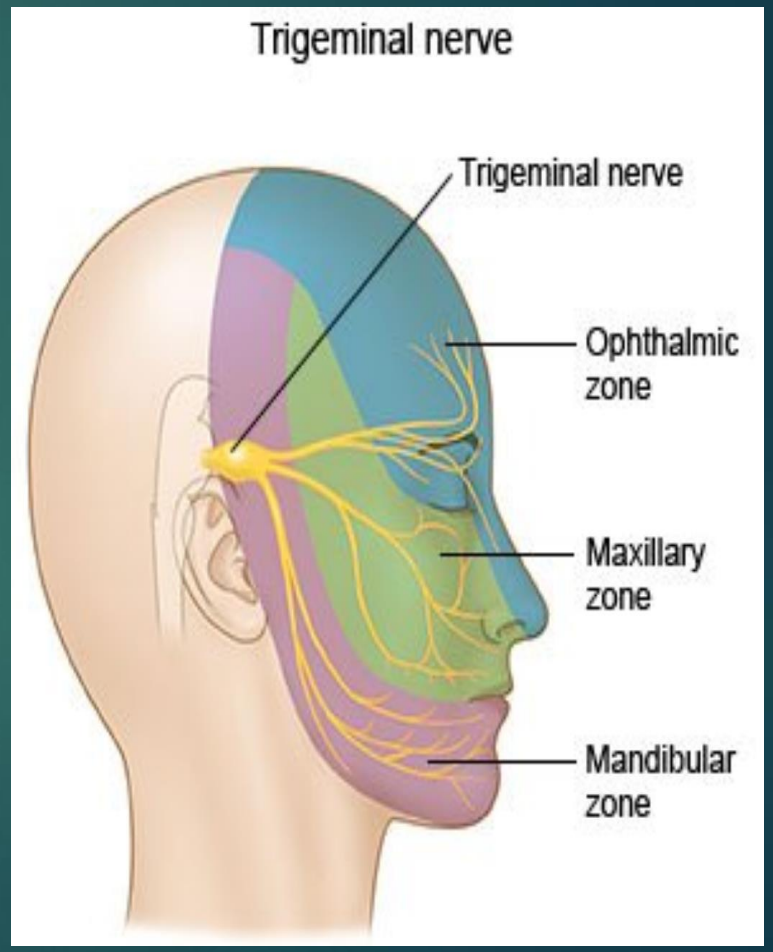
- EMG/NCV:

Axonal damage involving multiple individual nerves in an asymmetric fashion

Trigeminal neuropathy

- Numbness or paresthesia restricted to the trigeminal region
- Usually one side

  Bilateral involvement is more common in SS
- Ophthalmic division is usually spared

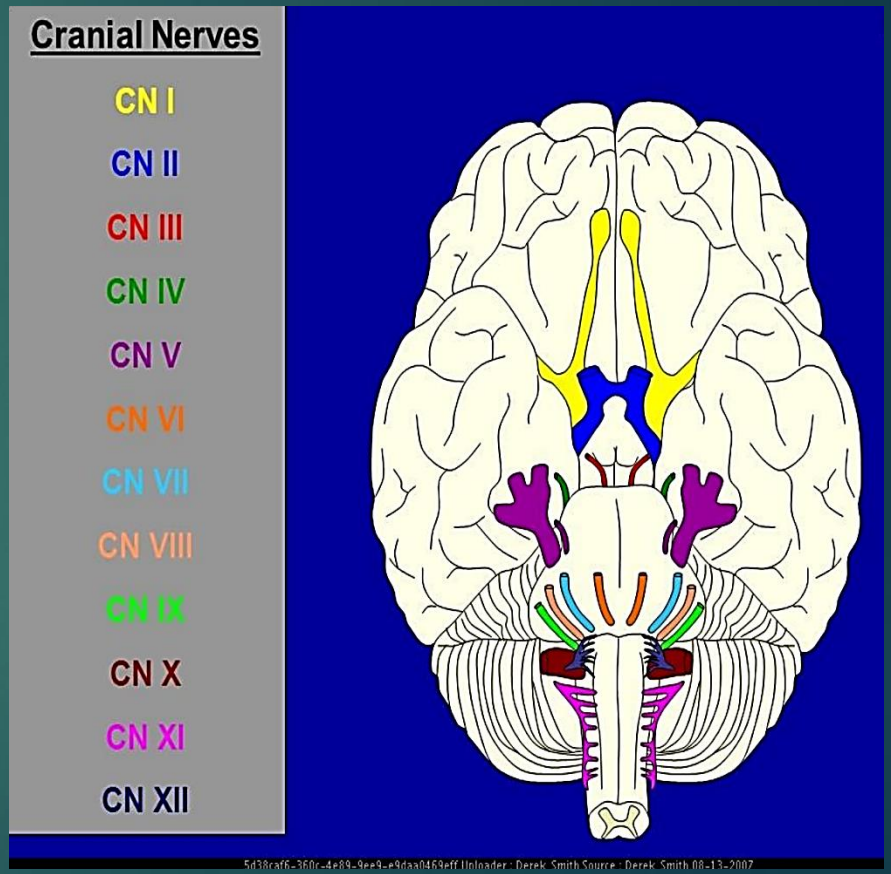


Multiple Cranial Neuropathy

Six cranial nerves may be involved in an individual patient

- Most commonly affected are VII (Bell palsy)

Contrast enhance MRI and CSF evaluation



Central nervous system

- Any part of the brain or spinal cord
  - Asymptomatic MRI lesion
- Nonspecific T2-weighted white matter usually in absence of focal neurologic sign
- Correlate more with age and cardiovascular risk factor

- Optic neuritis:
  - Usually monocular, visual loss, eye pain
  - May be the presenting symptom

- Transverse myelitis:
  - Acute
  - Longitudinally extensive myelopathy(greater than three vertebral segments)
  - Most often located in the cervical spinal cord

Neuromyelitis optica spectrum disorders(NMOSD)

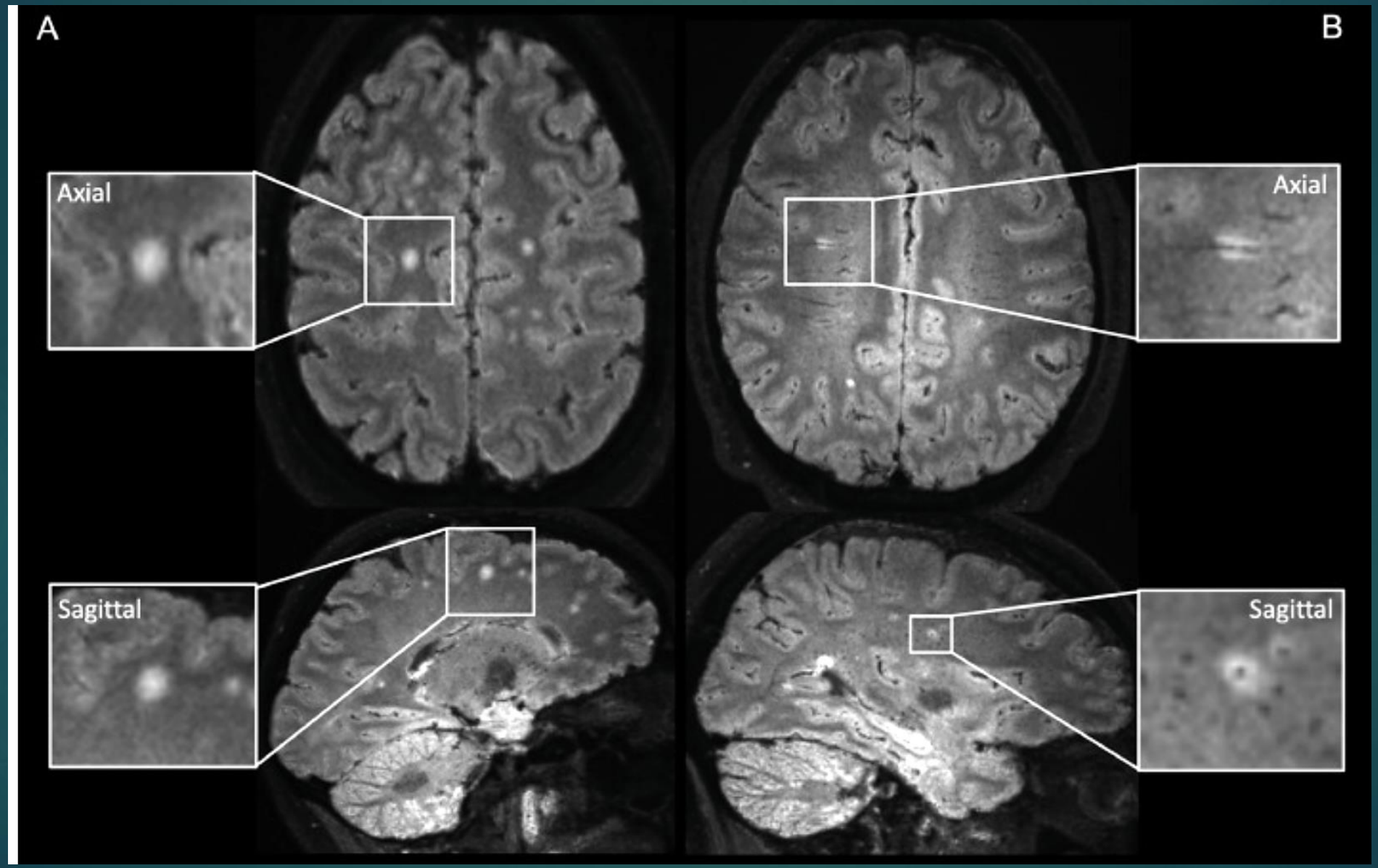
- Transverse myelitis and optic neuritis is often associated with antibodies to aquaporin-4

- NMOSD is not a direct manifestation of SS but rather an overlap of two distinct autoimmune disease

Multiple sclerosis-like

- Same demographics as SS
- SS-associated myelopathy may instead be misdiagnosed with M.S
- Linkage between the two disease has been controversial

- Vein traversing centrally through the lesions (central vein sign)


A
B
Axial
Axial
Sagittal
Sagittal

- Alternative diagnoses such as MS or NMOSD have be excluded before attributing symptom and finding to SS

- PATIENTS WITH THESE SYNDROMES BE EVALUATED ACCORDING TO THEIR SYNDROM PRESENTATION, REGARDLESS OF WHETHER THEY HAVE A DIAGNOSIS OF SS OR NOT

Cognitive Dysfunction

- Poor memory and concentration("brain fog“)
- Rang from subtle cognitive impairments to frank dementia
- In most case the symptoms are mild

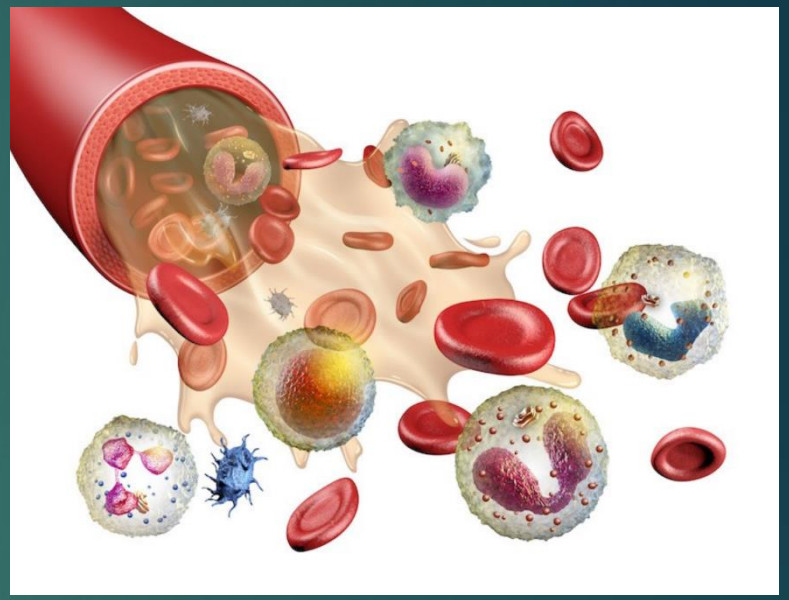
Patients should be evaluated :

- Thyroid dysfunction
- Vitamin B12 deficiency
- Sleep distrubances
- Affective disorders
- Medication side effects

Hematologic manifestations

- Abnormal counts in any cell line
- More than one cell line

- New development of a cytopenia in a patient with established SS can be an early sign of underlying lymphoma



Normochromic, normocytic anemia:

- 20%
- Anemia is usually mild

Leukopenia:

- 12 to 22%
- Mild
- Differential W.B.C most often normal

Mild thrombocytopenia (50,000 -150,000):

- 5 to 13 %
- Severe thrombocytopenia is rare, in contrast to SLE

Take home message

In the diagnostic labyrinth of systemic diseases, when a clinical presentation resists attribution to more familiar culprits, one must not forget to invite *Sjõgren*'s syndrome to the differential diagnosis party—it has a knack for showing up unannounced, often disguised in the most unexpected costumes.