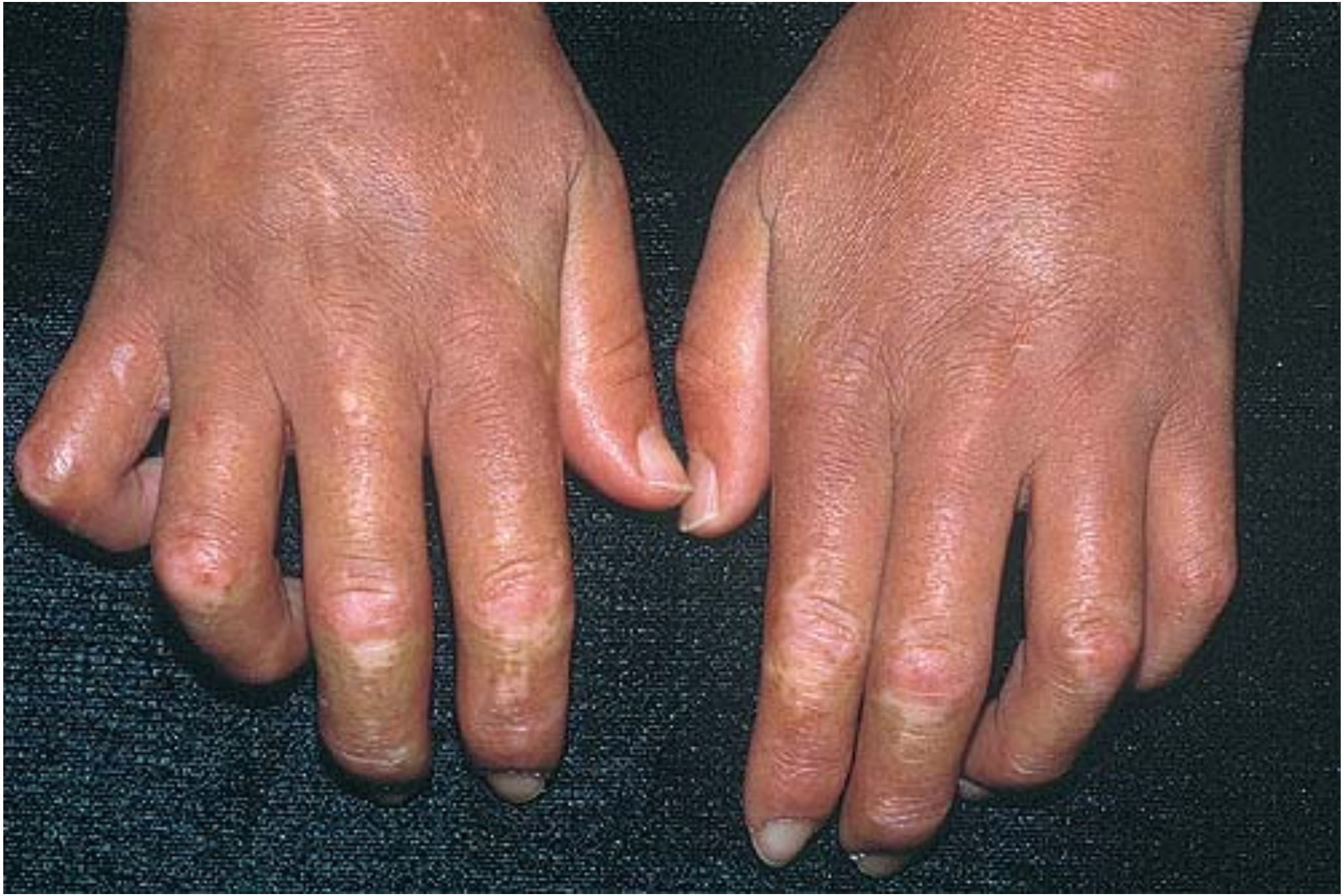


Autoimmune Diseases

Autoimmune Diseases Lecture Objectives

What causes Autoimmune Disease?

- Define tolerance and self-tolerance, and explain why there aren't tons of self-reactive lymphocytes floating around in the body.
- Describe how genetic and environmental factors contribute to causing autoimmune diseases.

Lupus

- Describe the most common clinical findings seen in lupus.
- List the autoantibodies most commonly seen in lupus, and explain how they lead to tissue damage.
- Explain how a FANA is done (and why).
- Describe the typical clinical course and treatment of lupus.

Rheumatoid Arthritis (RA)

- Describe the characteristic clinical and morphologic findings seen in the joints of patients with RA.
- List the systemic findings that can be seen in RA.
- Explain what rheumatoid factor is, and describe how it can be used in the diagnosis of RA.
- Identify the main cause of the tissue damage seen in RA.
- Describe the treatment and prognosis of RA.

Sjögren syndrome

- Explain what we know about the cause of Sjögren syndrome, and identify the autoantibody seen in most patients.
- Describe the clinical findings seen in Sjögren syndrome
- Describe how patients with Sjögren syndrome are treated.

Scleroderma

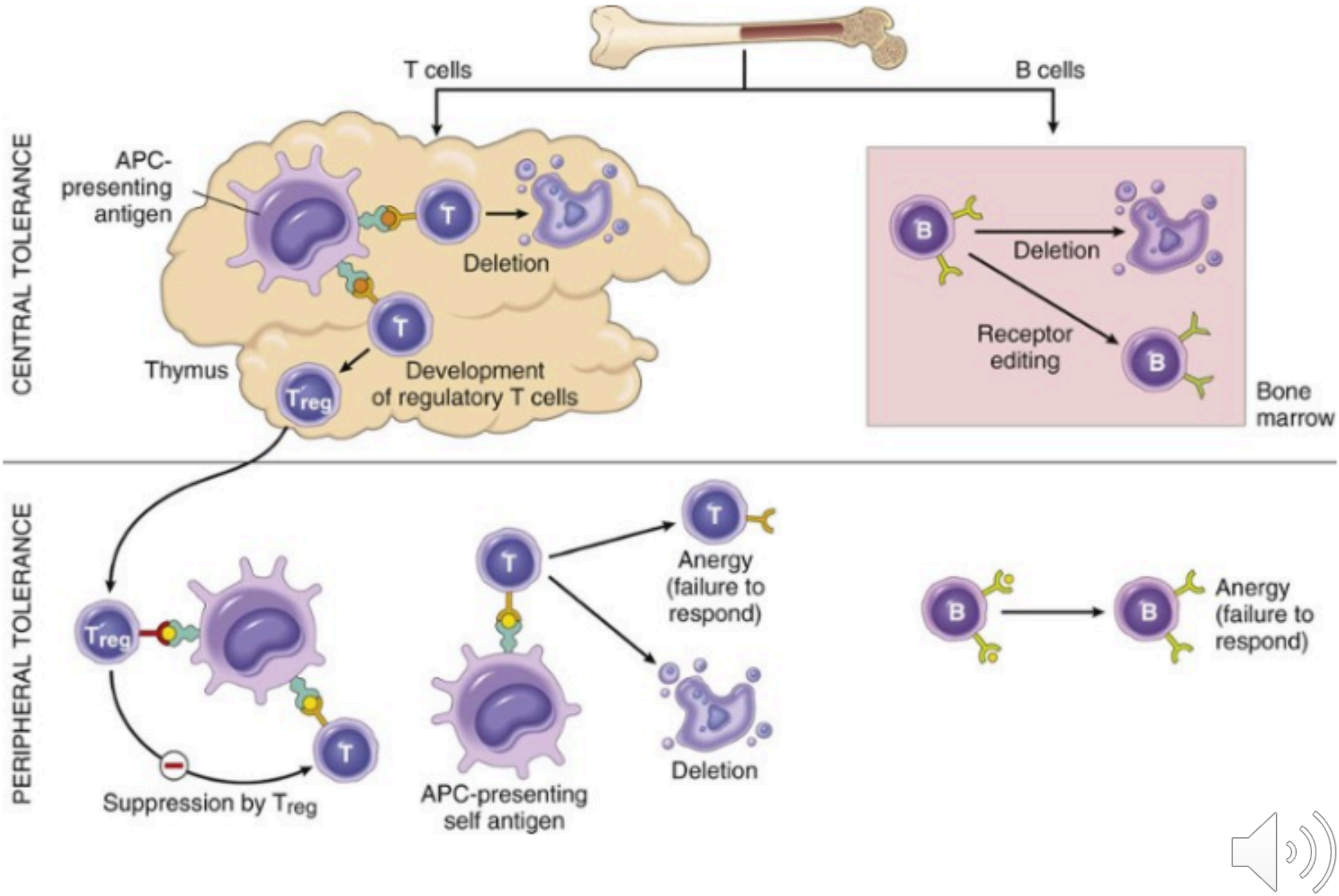
- Explain what we know about the cause of scleroderma, and identify the autoantibody seen in most patients.
- Describe the clinical findings seen in scleroderma.
- Describe the difference between diffuse and limited scleroderma, and explain what CREST syndrome is.
- Describe the overall prognosis for patients with scleroderma.

Immune Diseases Outline

- What causes autoimmune disease?
- Lupus
- Rheumatoid arthritis
- Sjögren syndrome
- Scleroderma

Immunologic Tolerance

- Tolerance = unresponsiveness to an antigen
- Self-tolerance = unresponsiveness to one's own antigens
- In generating billions of B and T cells, some will react against self antigens!
- There are two ways of muzzling these cells: central tolerance and peripheral tolerance

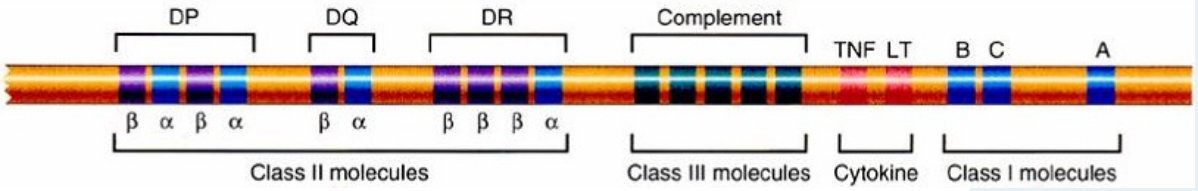

CENTRAL TOLERANCE
T cells
B cells
APC-presenting antigen
T
Deletion
T
Thymus
Treg
Development of regulatory T cells
B
Deletion
Receptor editing
B
Bone marrow
PERIPHERAL TOLERANCE
Treg
T
Suppression by Treg
T
Anergy (failure to respond)
Deletion
APC-presenting self antigen
B
B
Anergy (failure to respond)

What causes autoimmune disease?

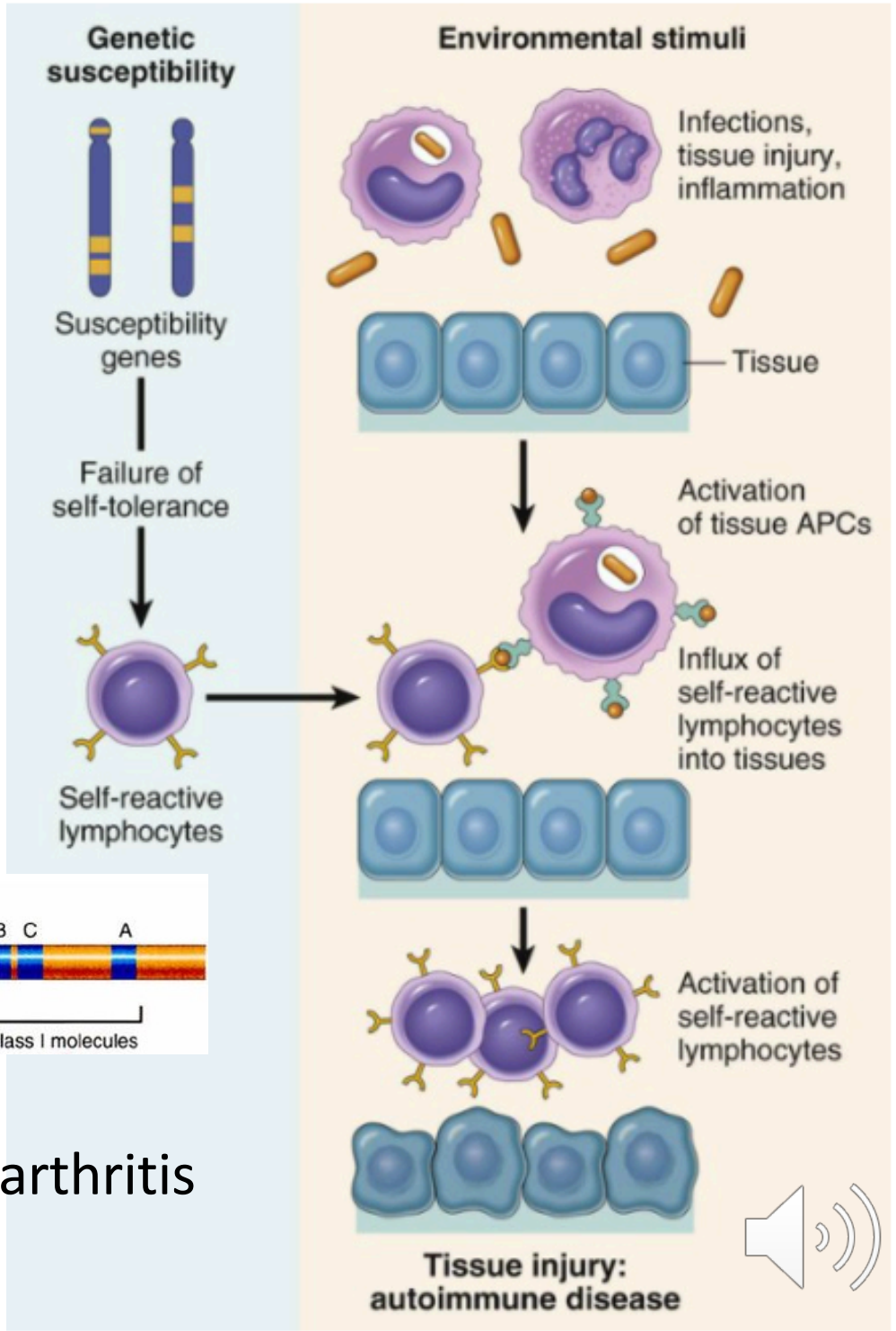
Genes

+

Environment



HLA-DR4: ↑ risk for rheumatoid arthritis



Discoid lupus = skin only

Systemic Lupus Erythematosus

KNOW THIS

- Typical patient: young woman with butterfly rash
- Symptoms unpredictable (relapsing/remitting)
- Multisystem (skin, kidneys, joints, heart)
- Antinuclear antibodies

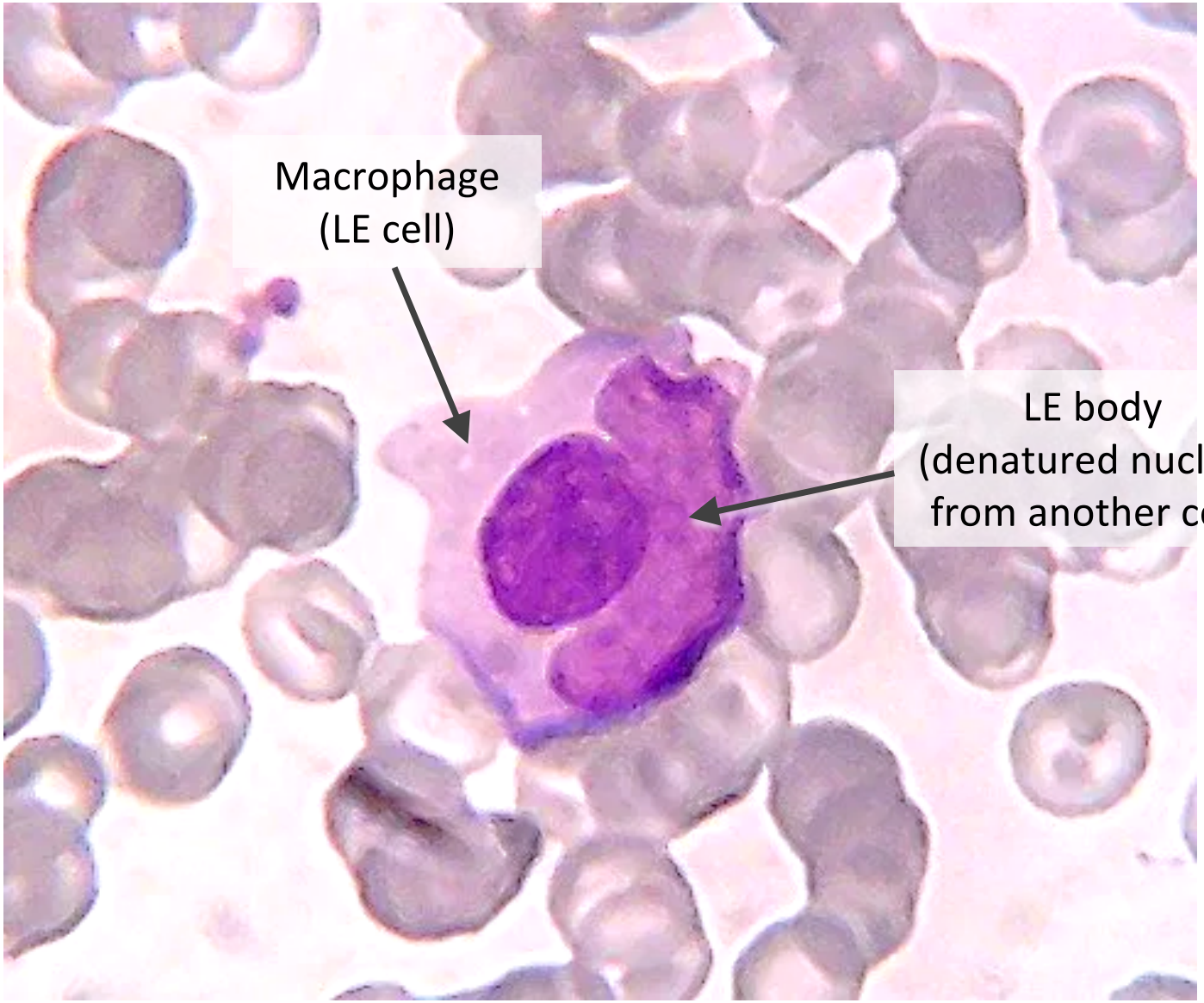
Lupus Etiology

Autoantibodies

- Antinuclear antibodies (ANAs) are present in all patients with lupus
- Most specific ANA: anti-DS DNA
- Anti-RBC, -lymphocyte, -platelet, or –phospholipid antibodies may be present too

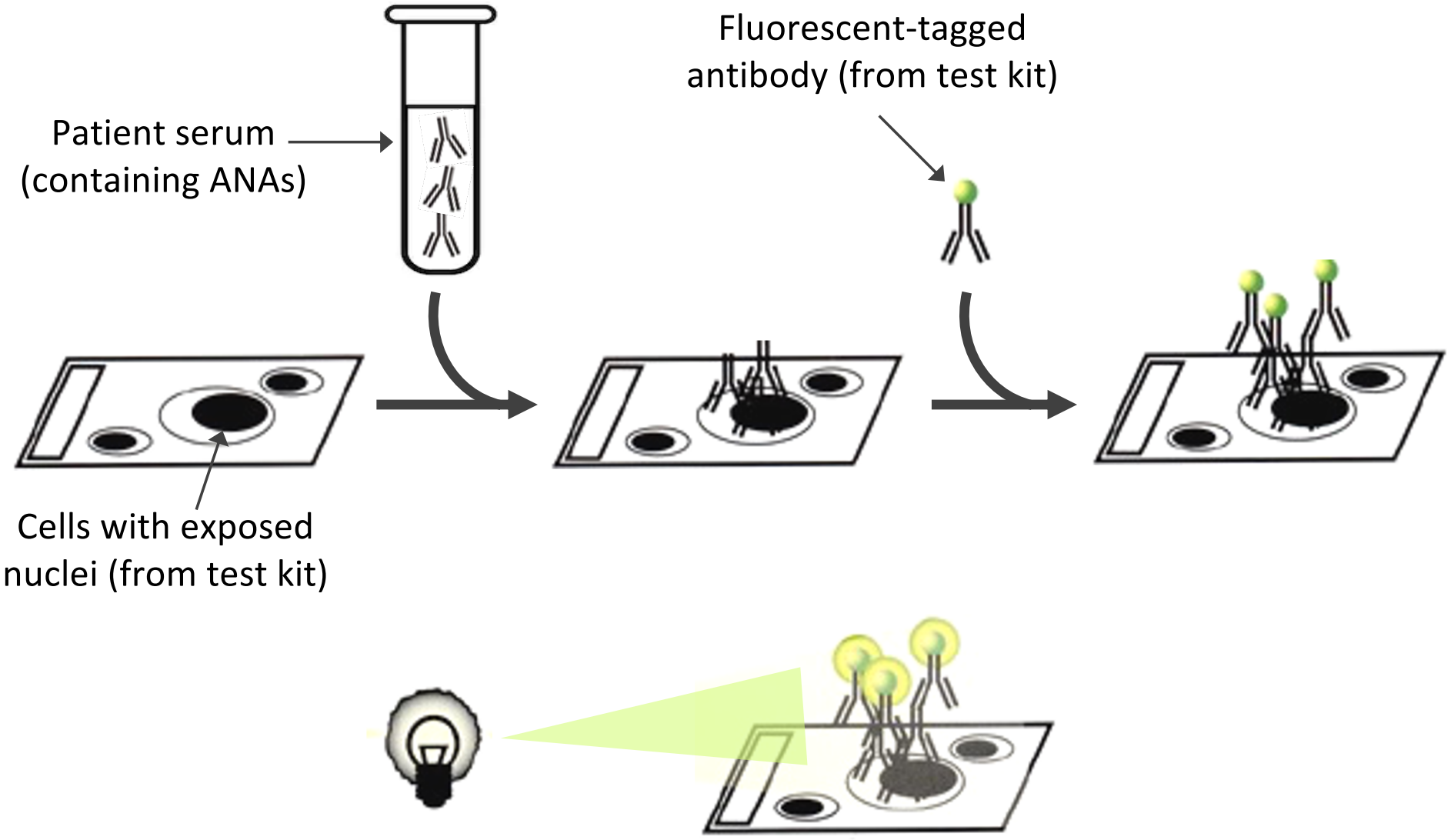
Underlying cause

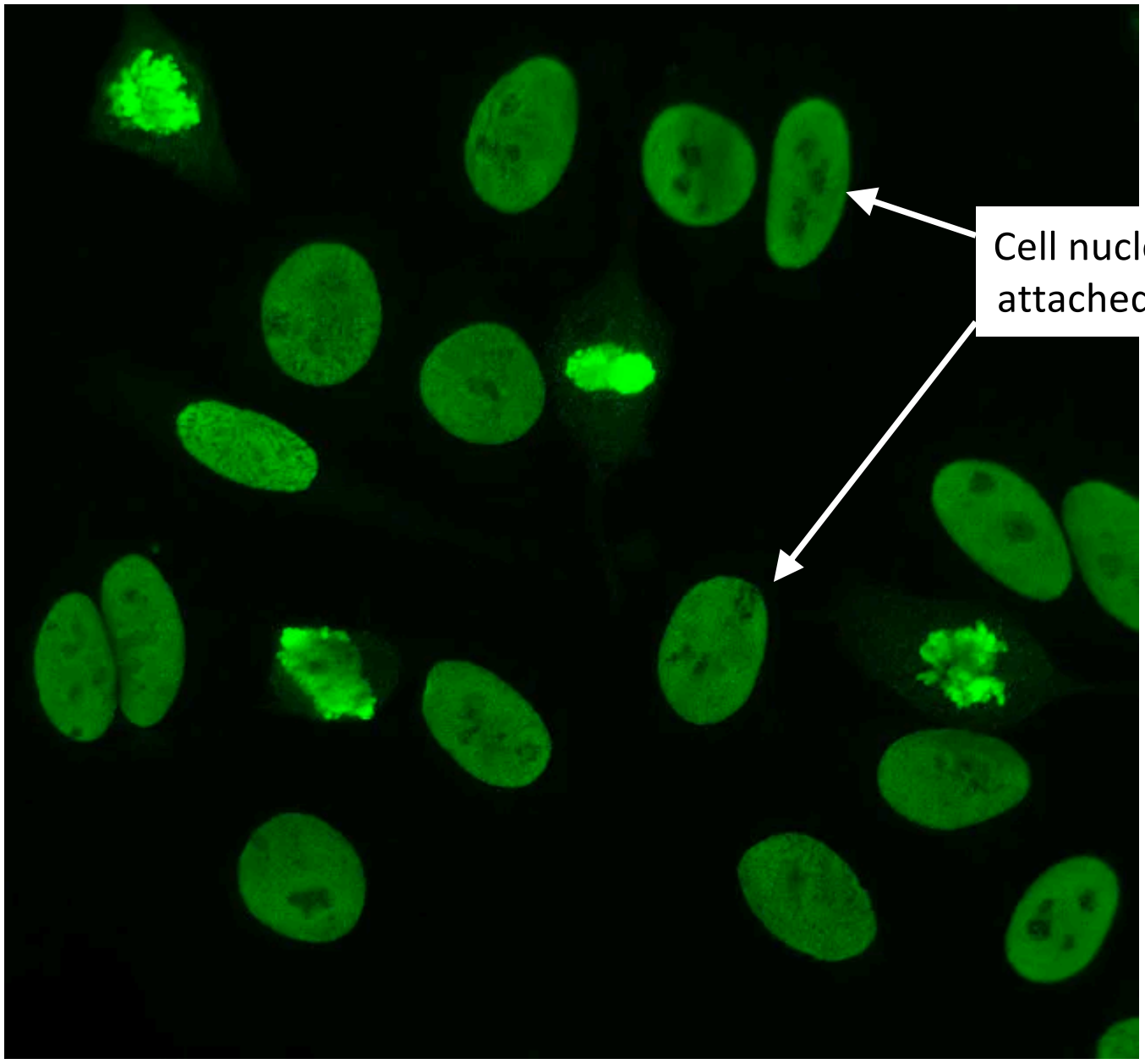
- Genetic predisposition…
- …plus environmental triggers (UV radiation, drugs)



LE (lupus erythematosus) cell

Fluorescent antinuclear antibody (FANA) test





Positive FANA test

What's so bad about having autoantibodies?

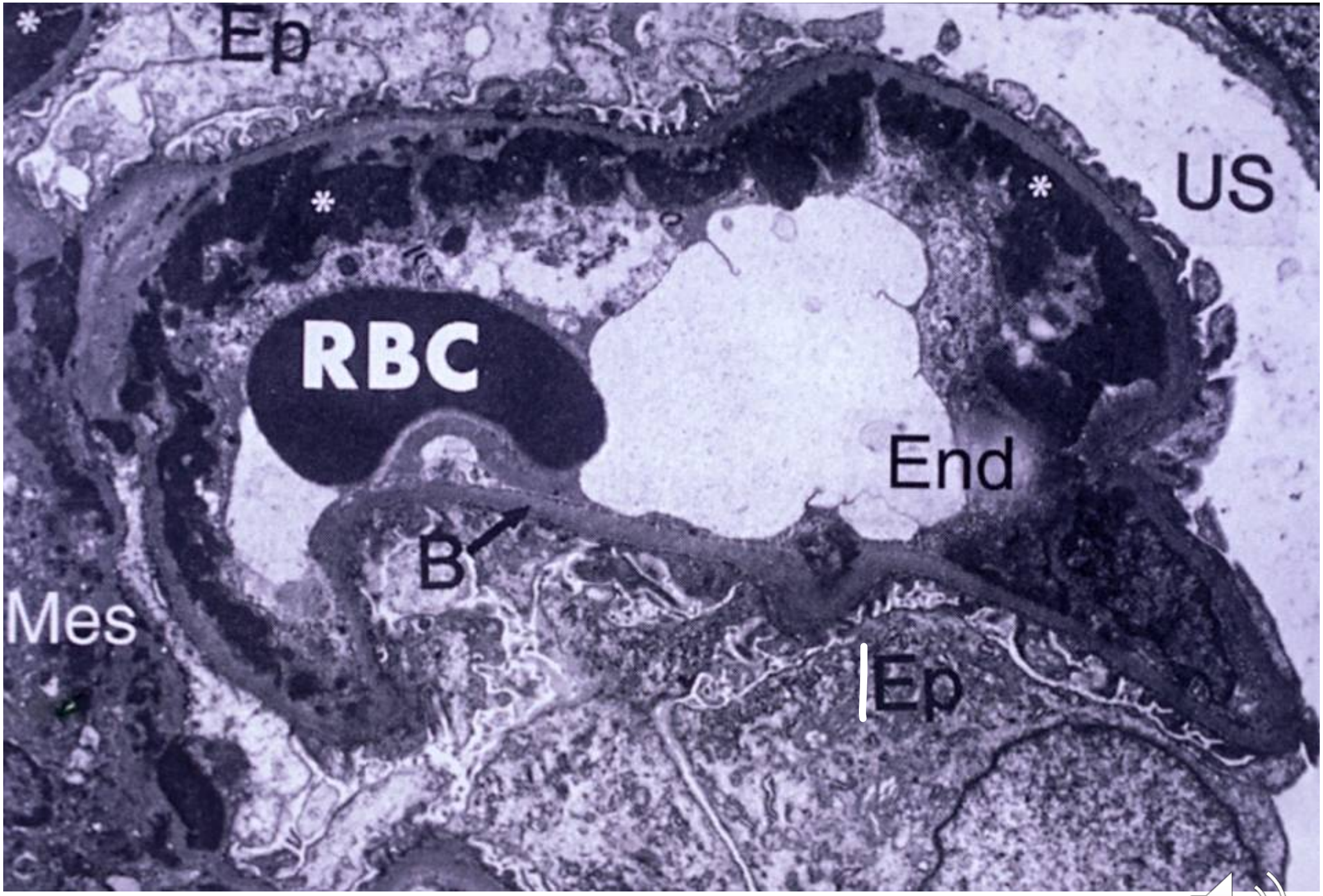
They cause hypersensitivity reactions!

- Form immune complexes (type III)
- Coat cells (type II)

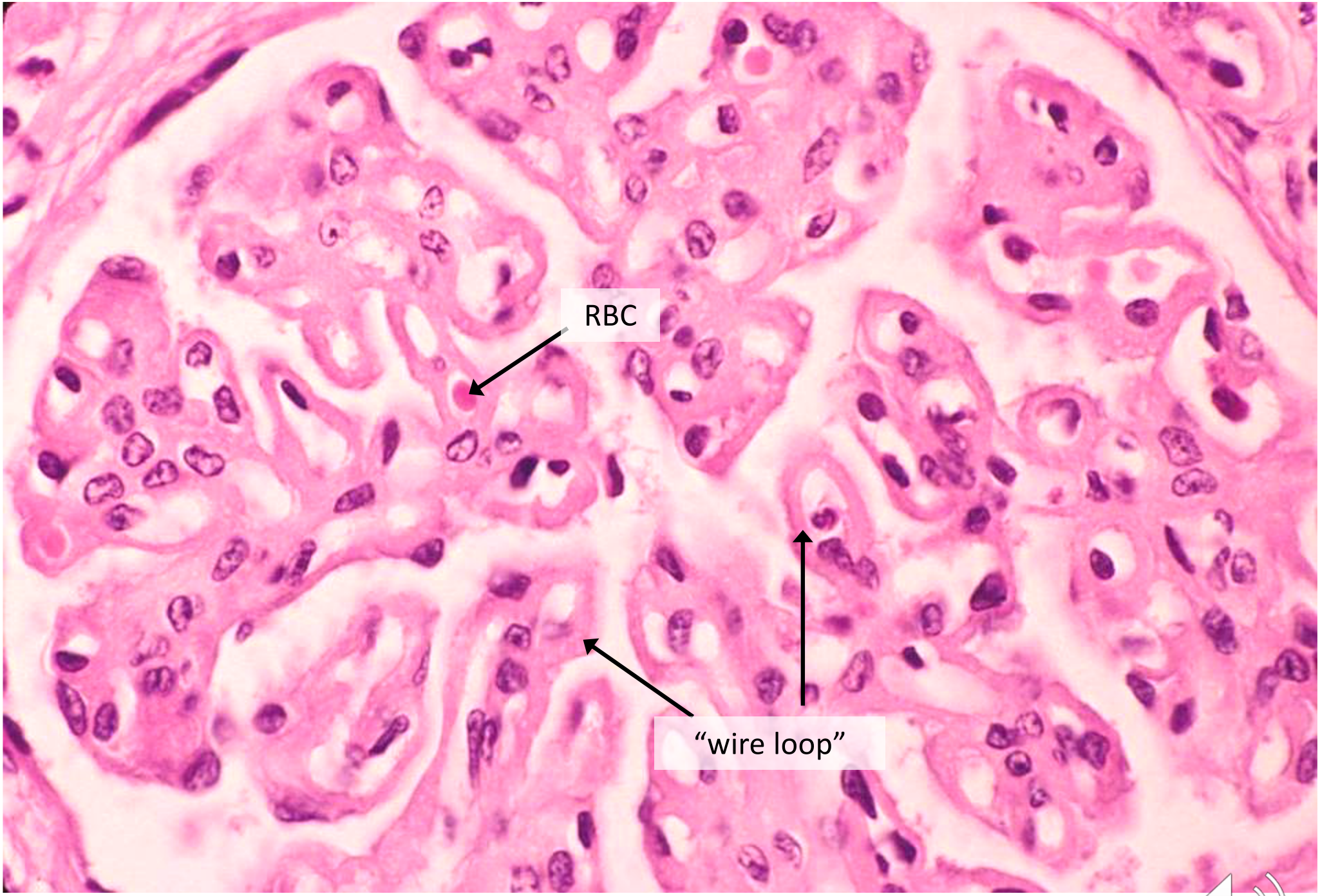
Lupus Signs and Symptoms

Lupus can present in SO many different ways that it's often called "the great imitator."

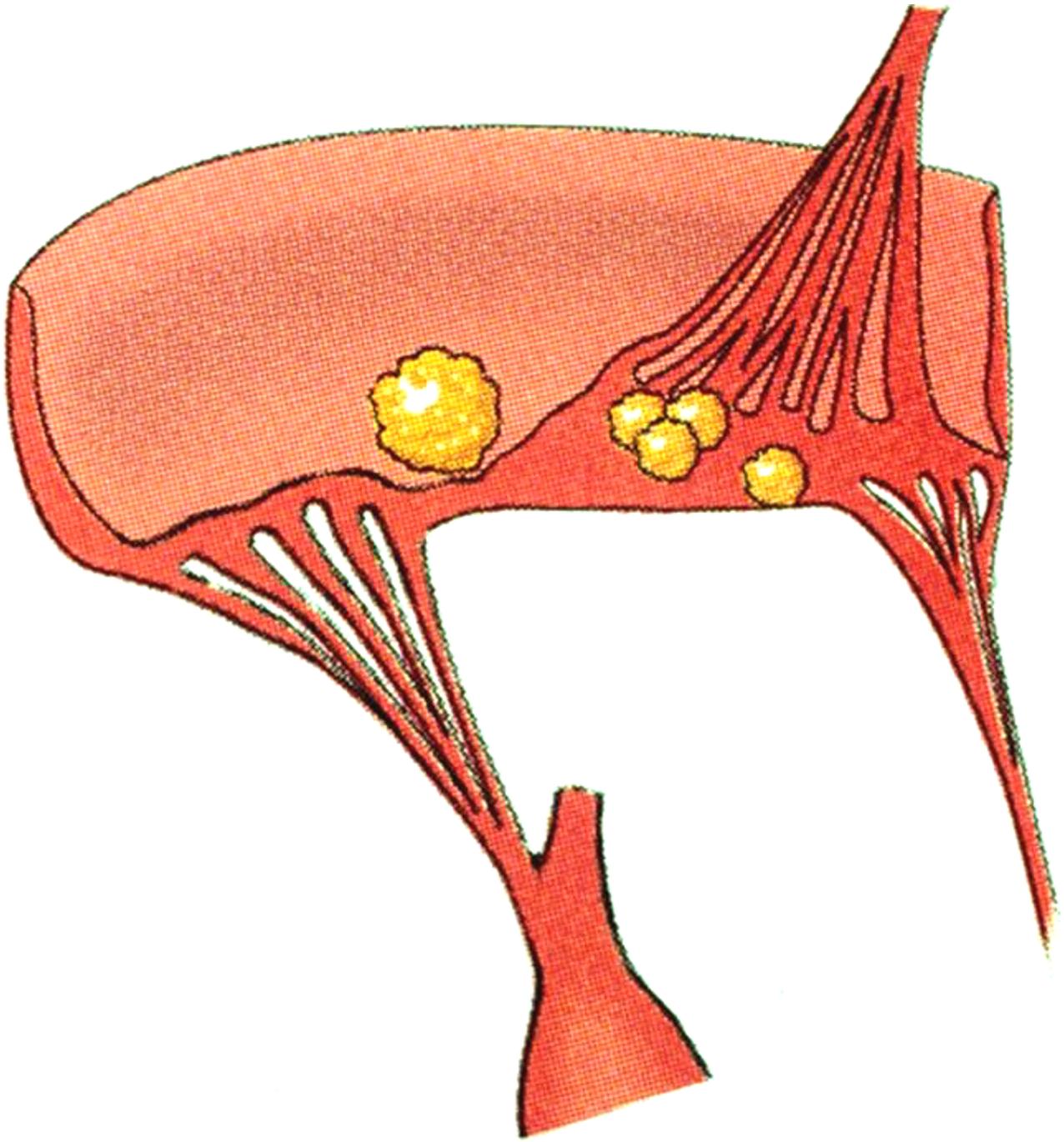
- Unexplained fever
- Fatigue
- Butterfly rash
- Renal failure
- Seizures, psychosis
- Arthritis
- Endocarditis, pericarditis
- Pleuritis



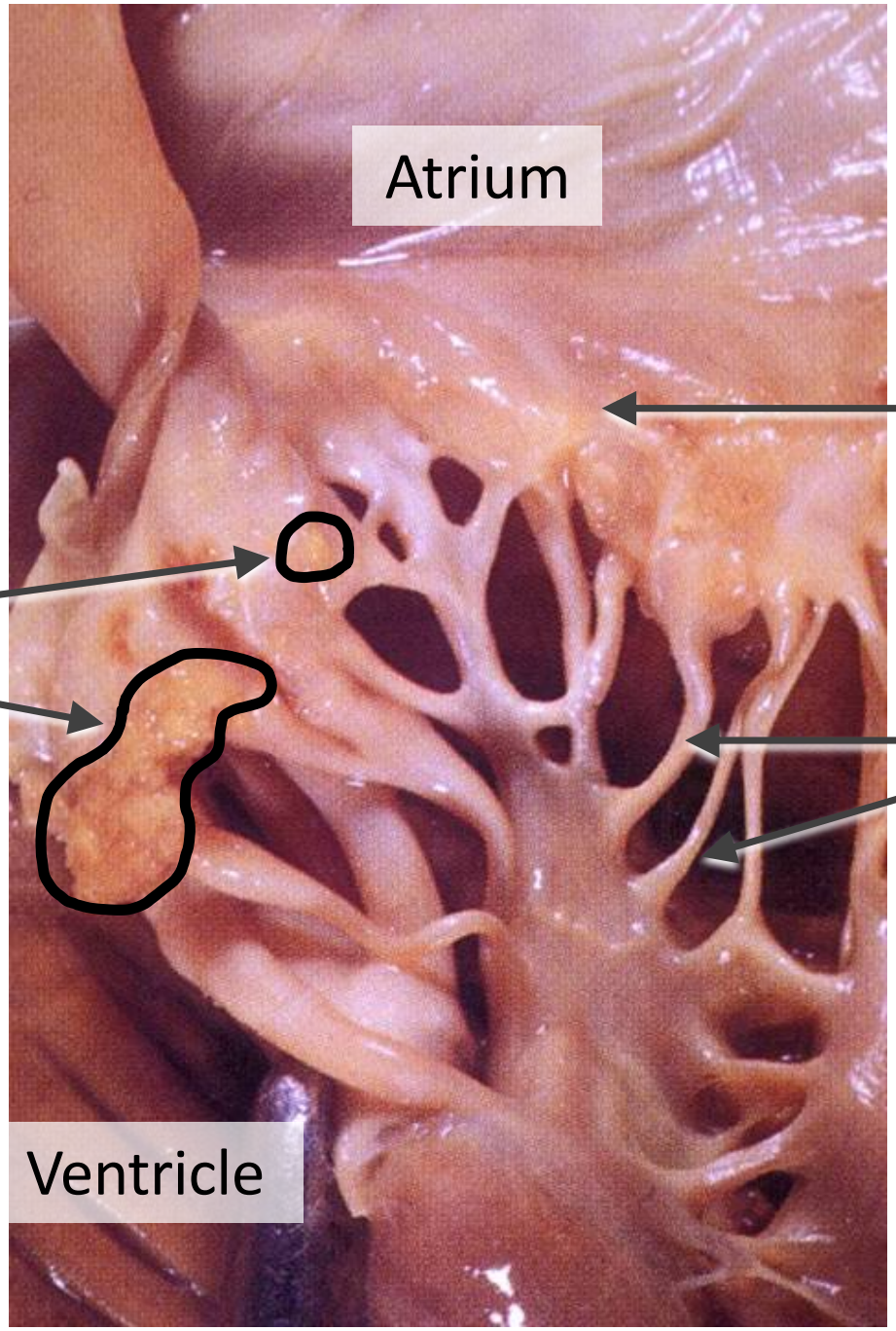
Renal EM in patient with lupus showing subendothelial deposits



Glomerulus: “wire loop” capillary appearance



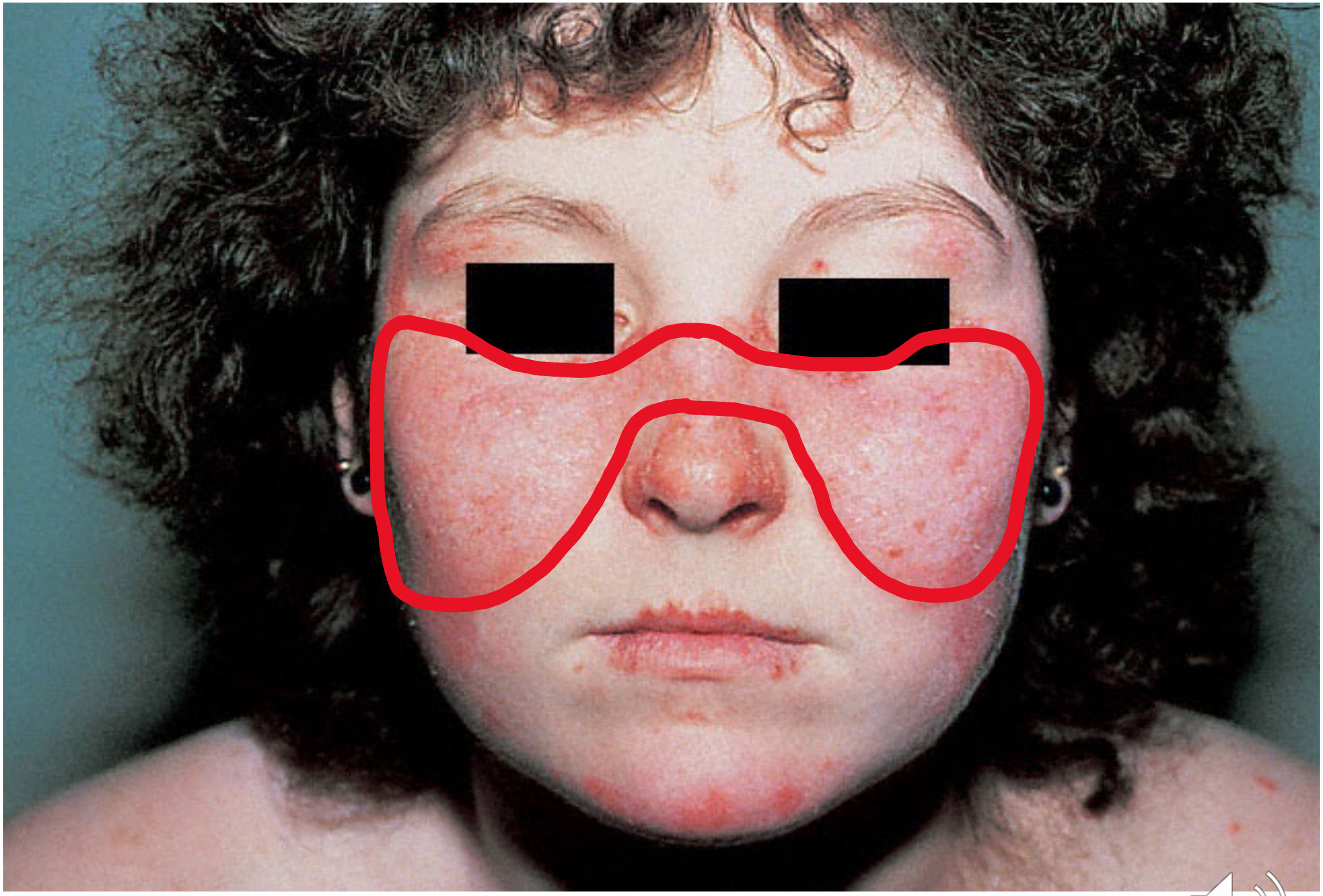
Heart valve: Libman-Sacks lesions



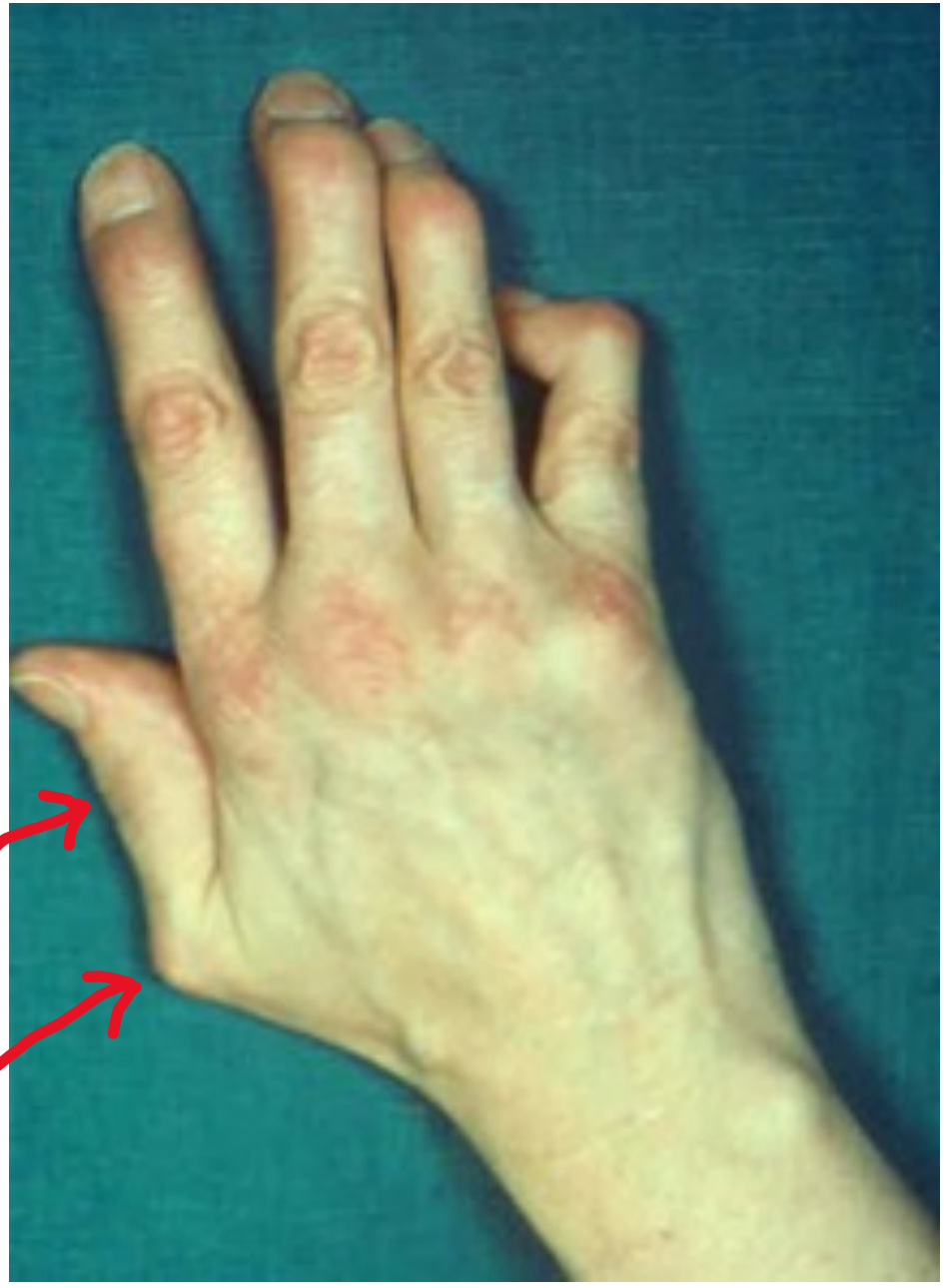
Libman-Sacks lesions

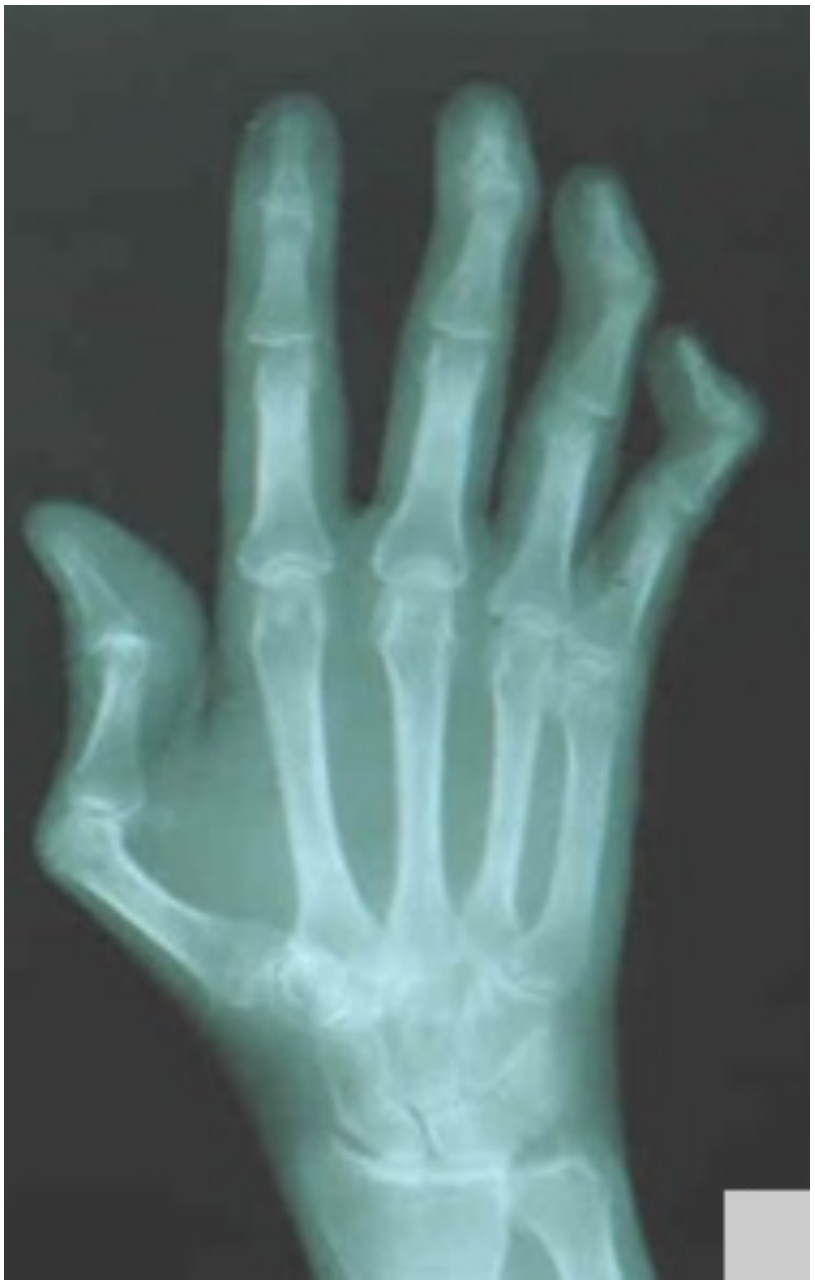
Lupus: Things a Dentist Might See

- Young woman with polyarthritis and a butterfly (or other) skin rash
- Fatigue
- Sensitivity to sunlight
- Headaches, seizures, or psychiatric problems
- Pleuritic chest pain
- Unexplained fever
- Oral lesions (not super common though): nonspecific, red-white, erosive

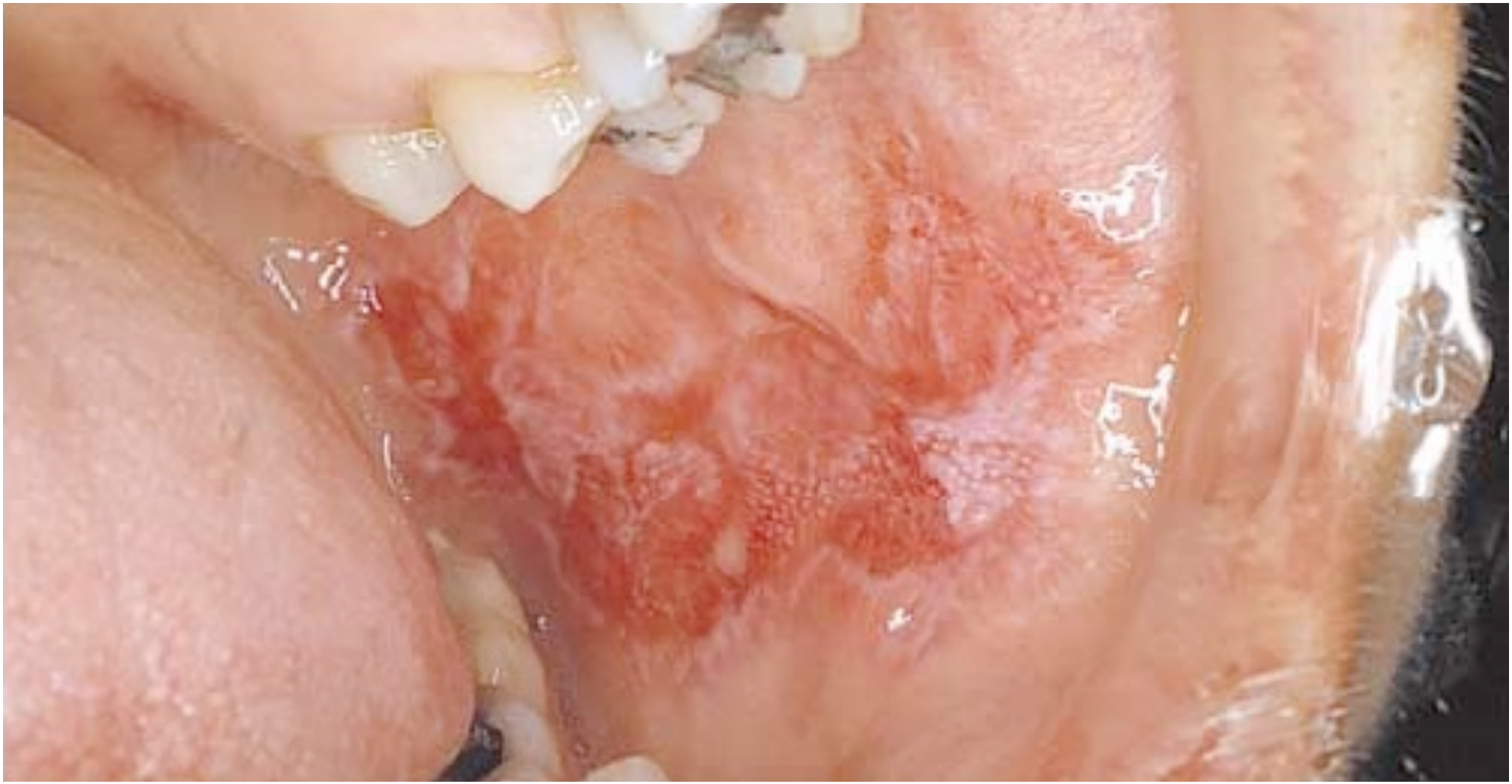


Butterfly rash





Hitch-hiker’s thumb



Non-specific buccal lesion

Lupus Prognosis

- Variable! Some patients have just one or two episodes, rare patients die within months.
- Most patients: relapses/remissions over many years.
- Treatment: rituximab, steroids → anti-inflammatory
  → kills B cells
- 80% 10-year survival
- Most common cause of death: renal failure

Rheumatoid Arthritis

KNOW THIS

- Symmetric arthritis starting in small joints
- May have systemic manifestations
- Rheumatoid factor
- Cytokines (especially TNF) cause damage

RA Etiology

- Genetically predisposed patient
- Something (bug? self-Ag?) activates T cells
- T cells release cytokines:
  - activate macrophages (causing destruction)
  - cause B cells to make antibodies
- Damage is mostly related to cytokines, especially TNF !!

Rheumatoid factor

IgM antibody directed against IgG

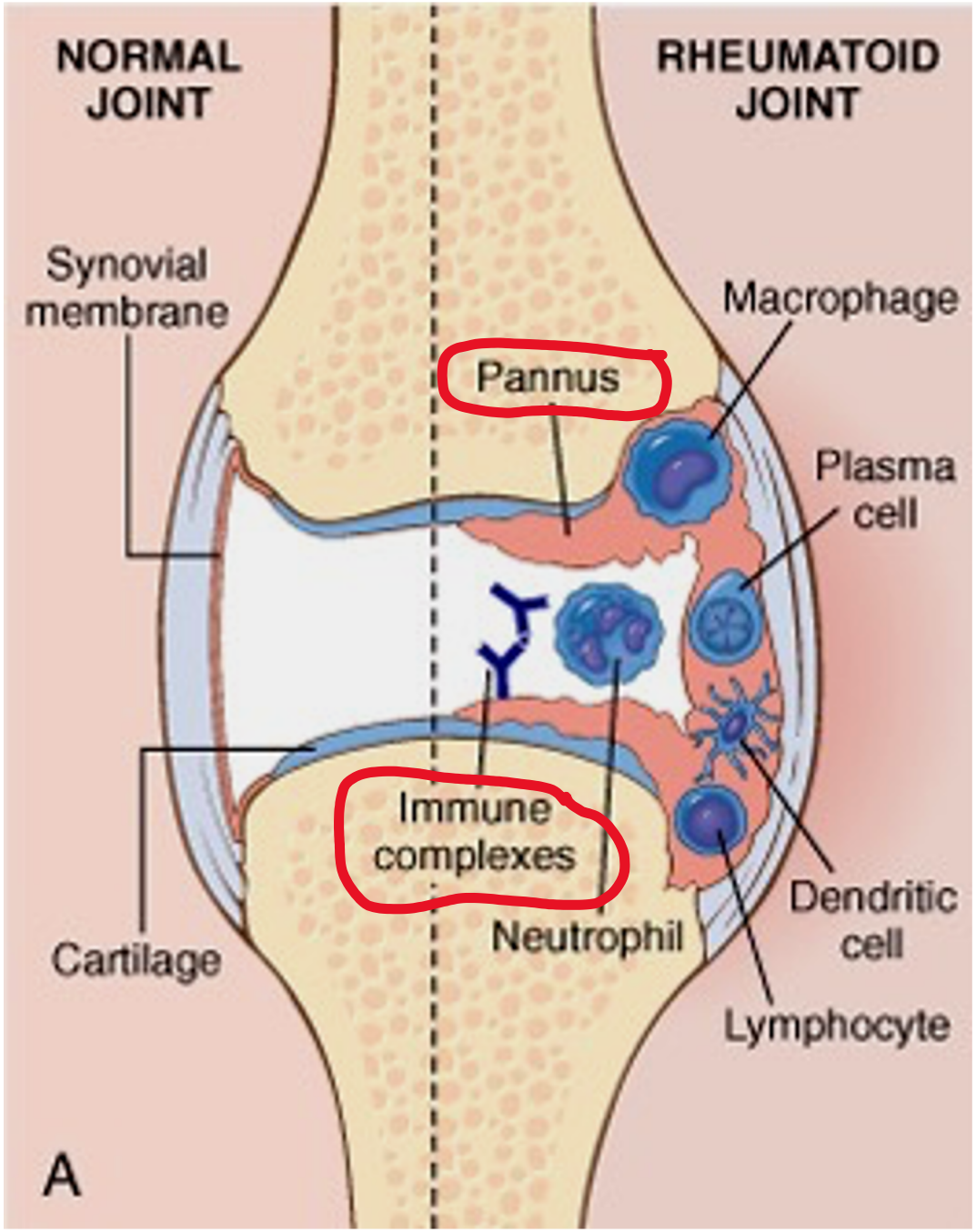
Present in 80% of patients

RA Signs and Symptoms

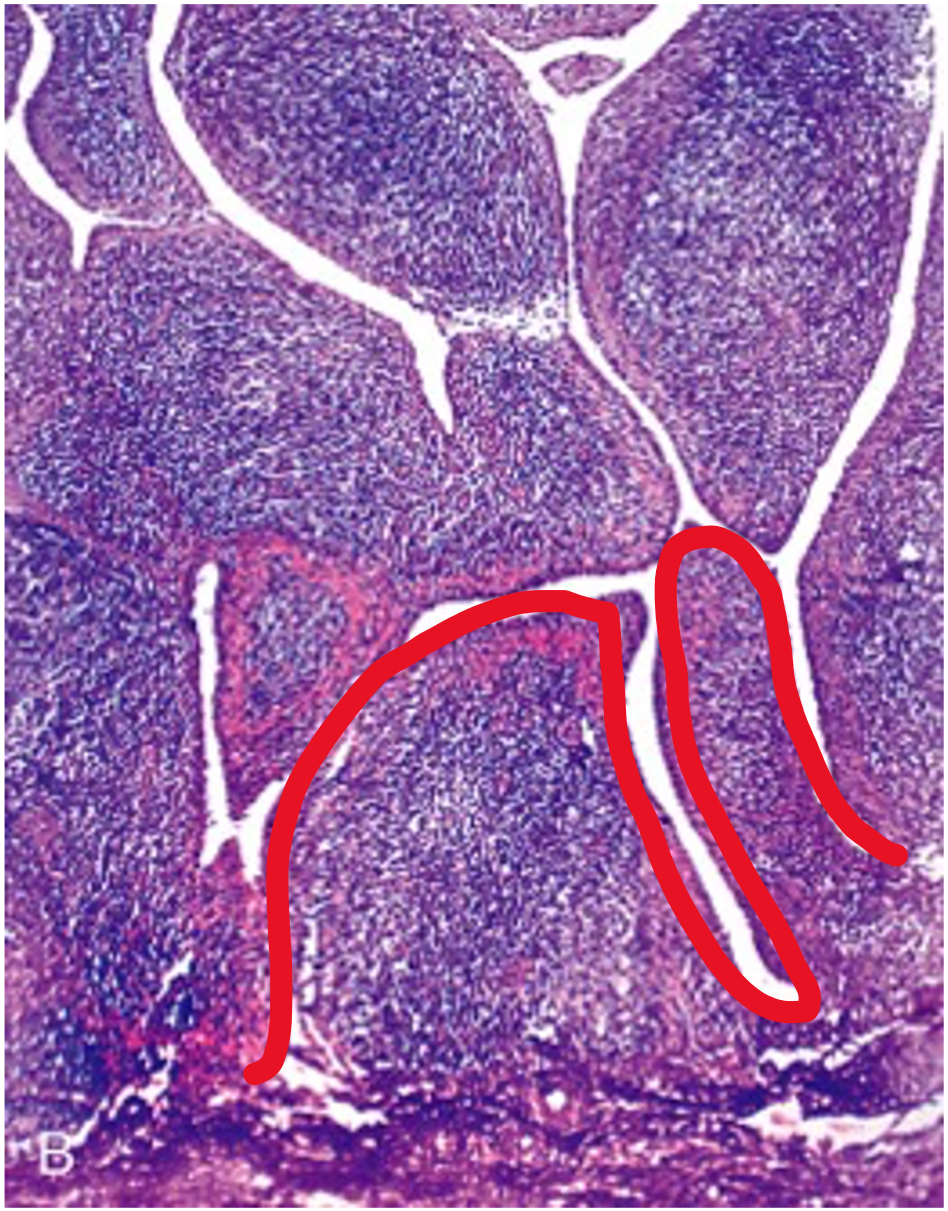
- Arthritis
- Fever, fatigue
- Pericarditis
- Pleuritis
- Eye changes
- Rheumatoid nodules on forearms

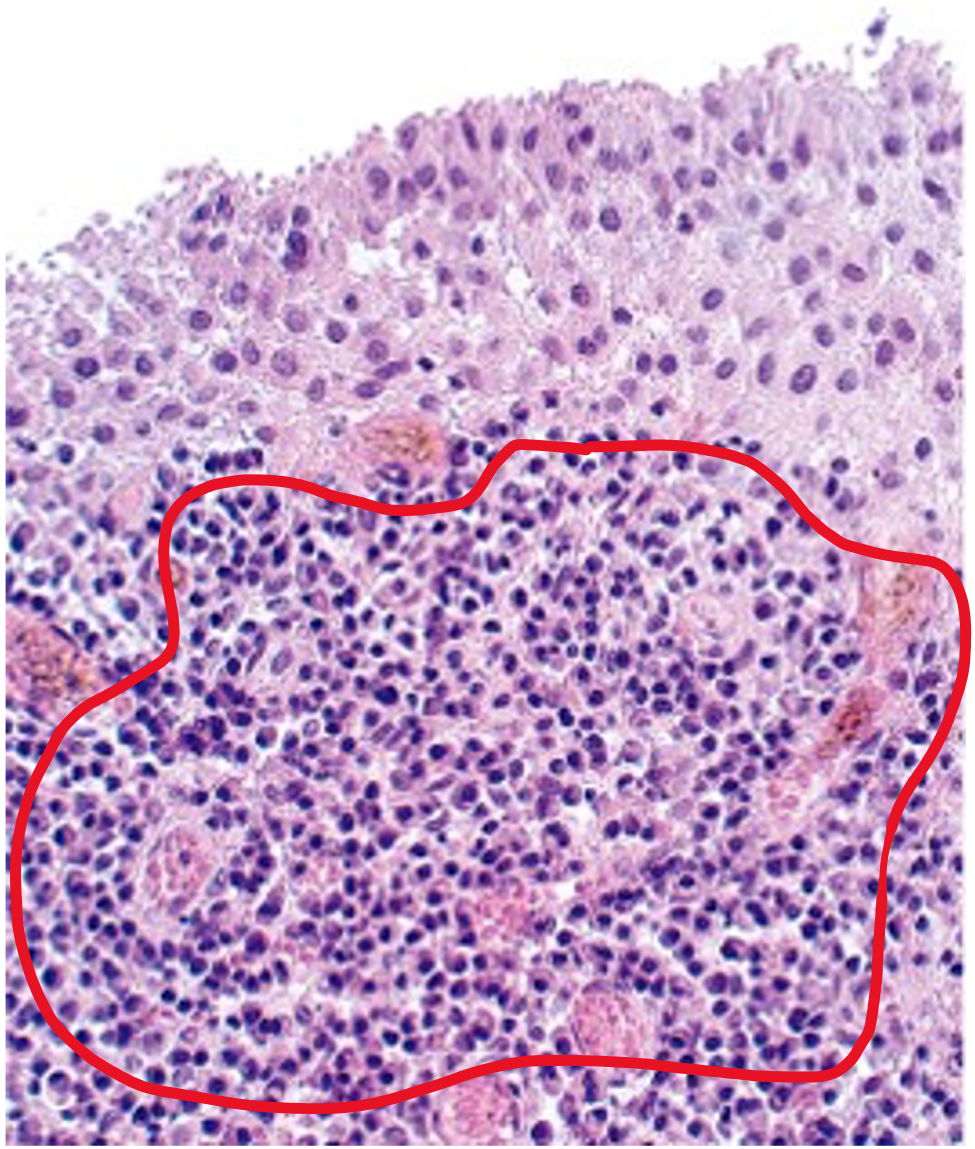
Characteristic Features of Arthritis in RA

- Mainly small joints (hands), but also knees, elbows, shoulders
- Symmetric; characteristic hand features
- Chronic synovitis with pannus formation:
  - synovial cell proliferation
  - inflammation
  - granulation tissue

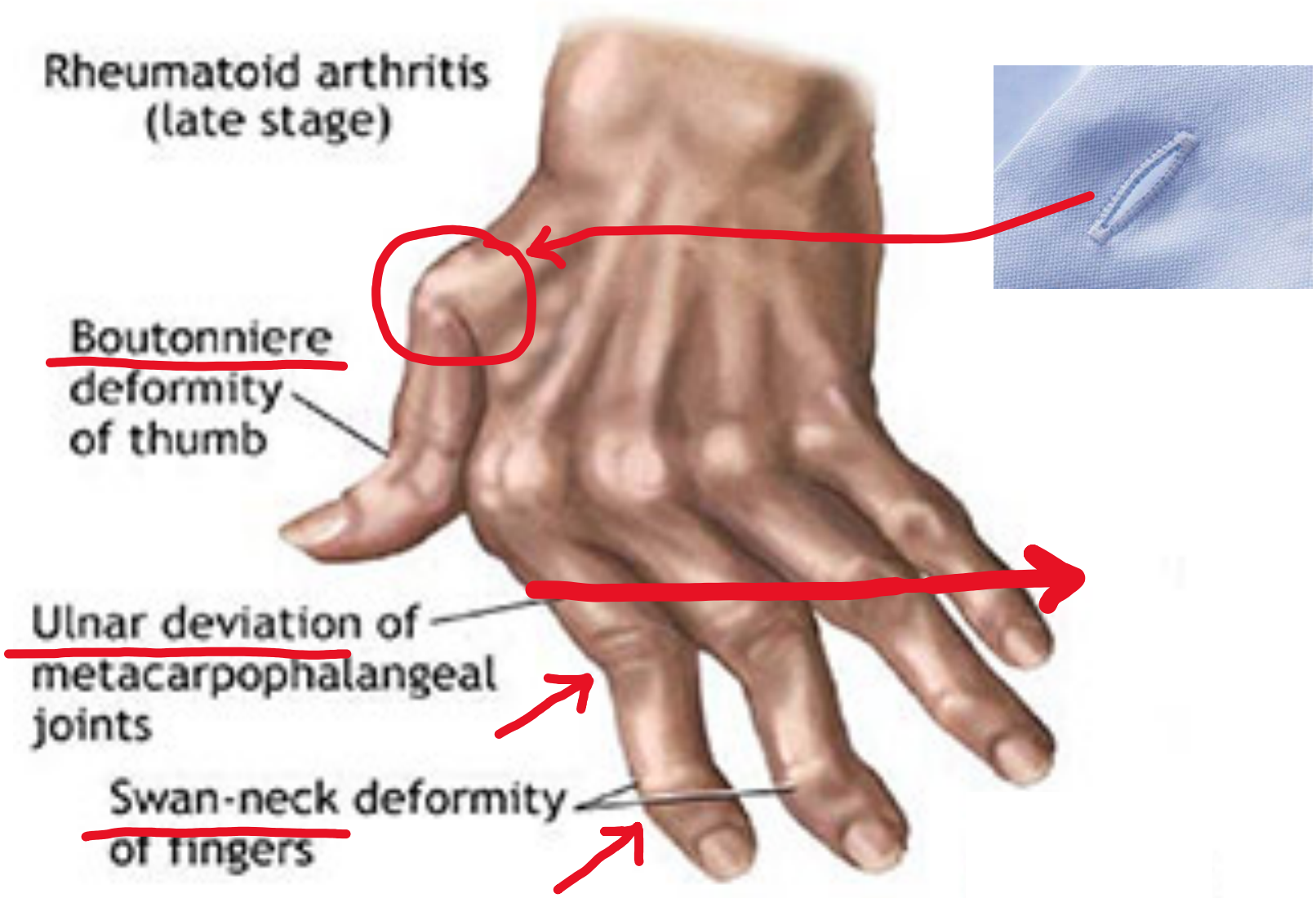


Rheumatoid arthritis joint lesion

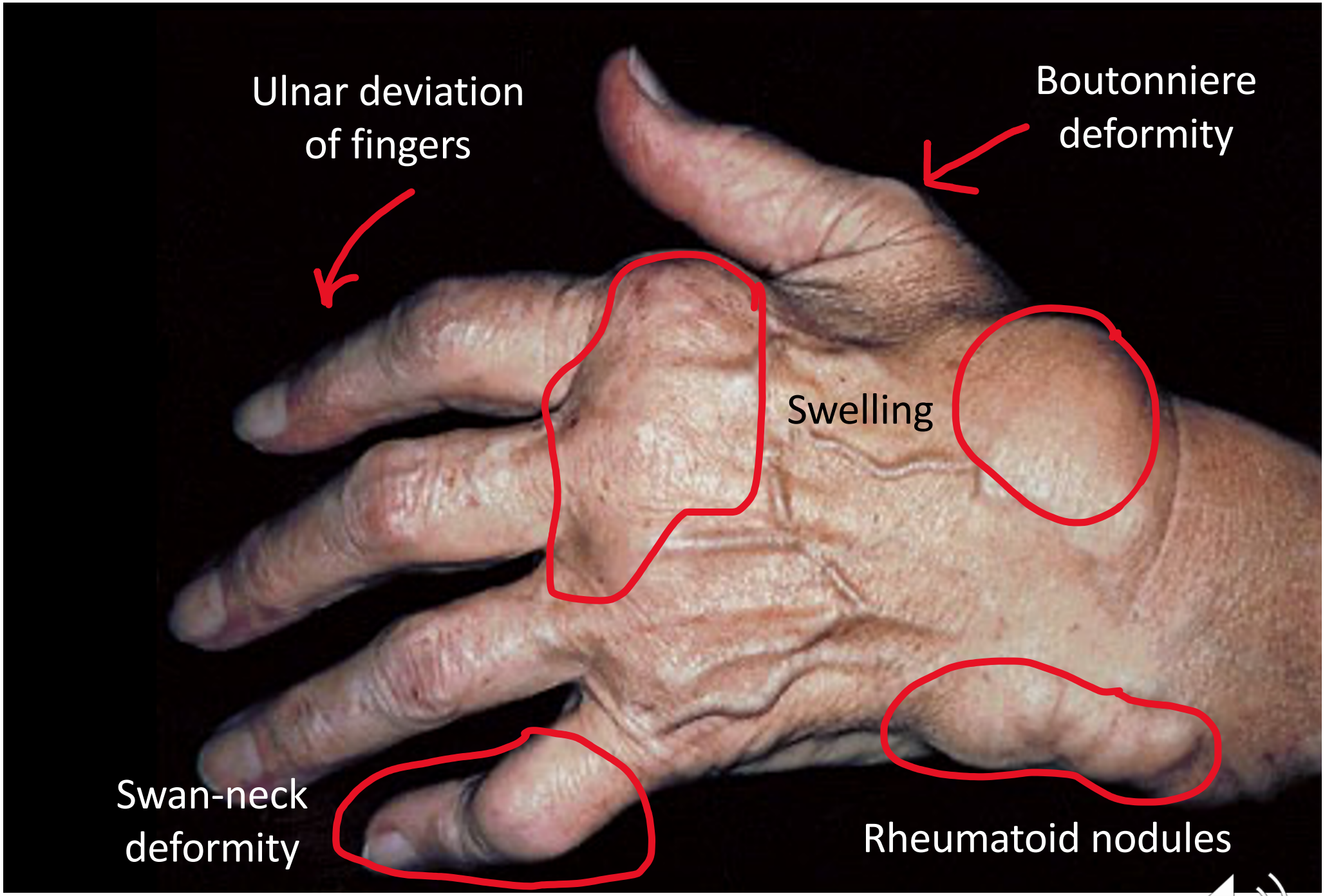




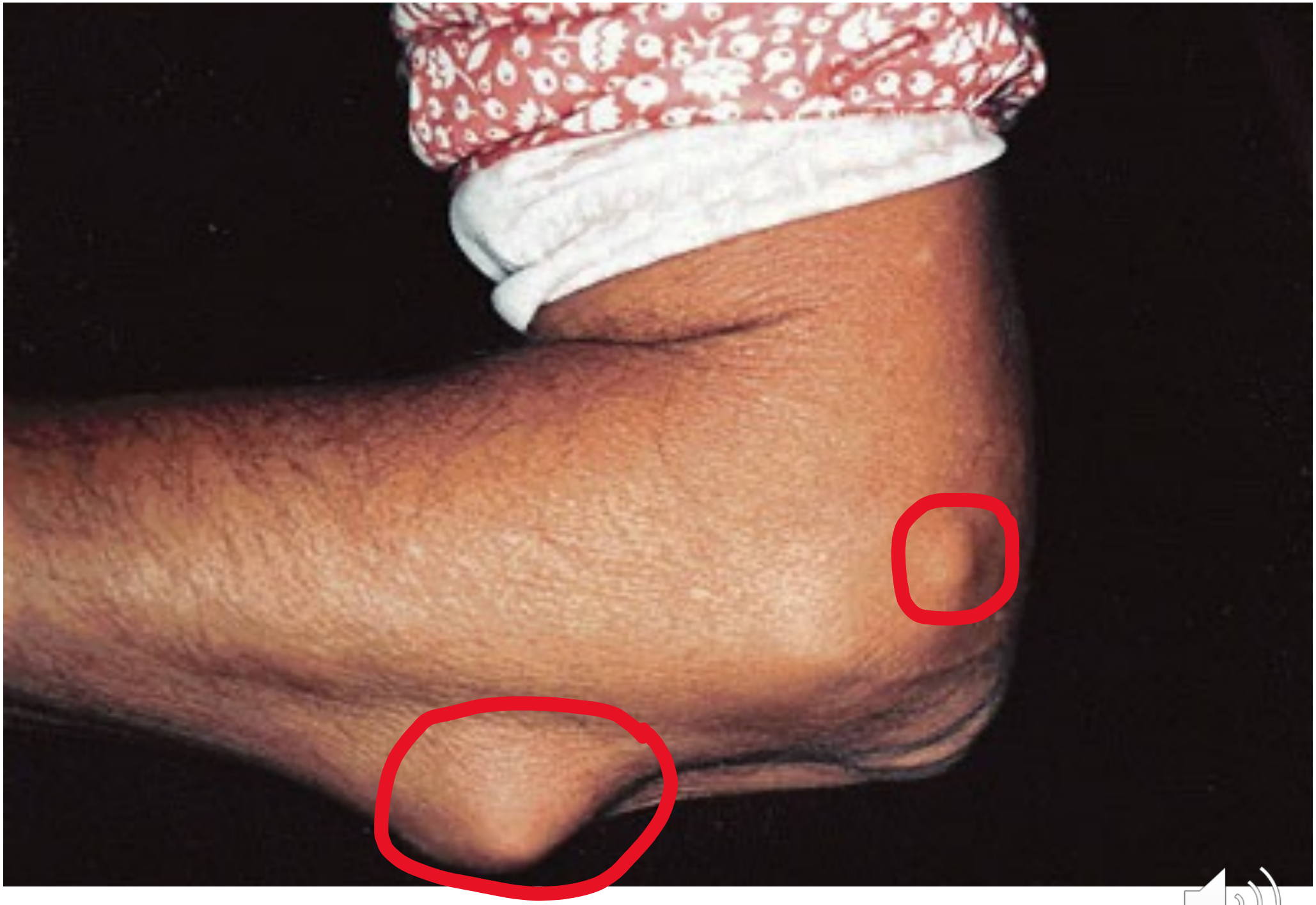
Rheumatoid arthritis: villi (L) and lymphoid aggregates (R)



Rheumatoid arthritis joint deformities



Rheumatoid arthritis joint deformities



Rheumatoid nodules

RA: Things a Dentist Might See

- Female patient with joint pain, swelling
- Fingers: ulnar deviation, swan-neck deformities, boutonniere deformity
- Rheumatoid nodules

RA: Prognosis

- Most patients have chronic disease course with progressive joint destruction and disability
- Lifespan shortened by 10-15 years
- Treatment: steroids, anti-TNF agents

Sjögren Syndrome

KNOW THIS

- Inflammatory disease of salivary and lacrimal glands
- Dry eyes, dry mouth
- T cells destroy glands
- Increased risk of lymphoma

Sjögren Etiology

- Genetic predisposition, environmental trigger
- CD4+ T cells directed against cells in glands
- Autoantibodies
  - ANAs → Anti-SS-A, anti-SS-B antibodies present in 90% of patients!
  - RF

Sjögren Signs and Symptoms

Salivary and lacrimal glands

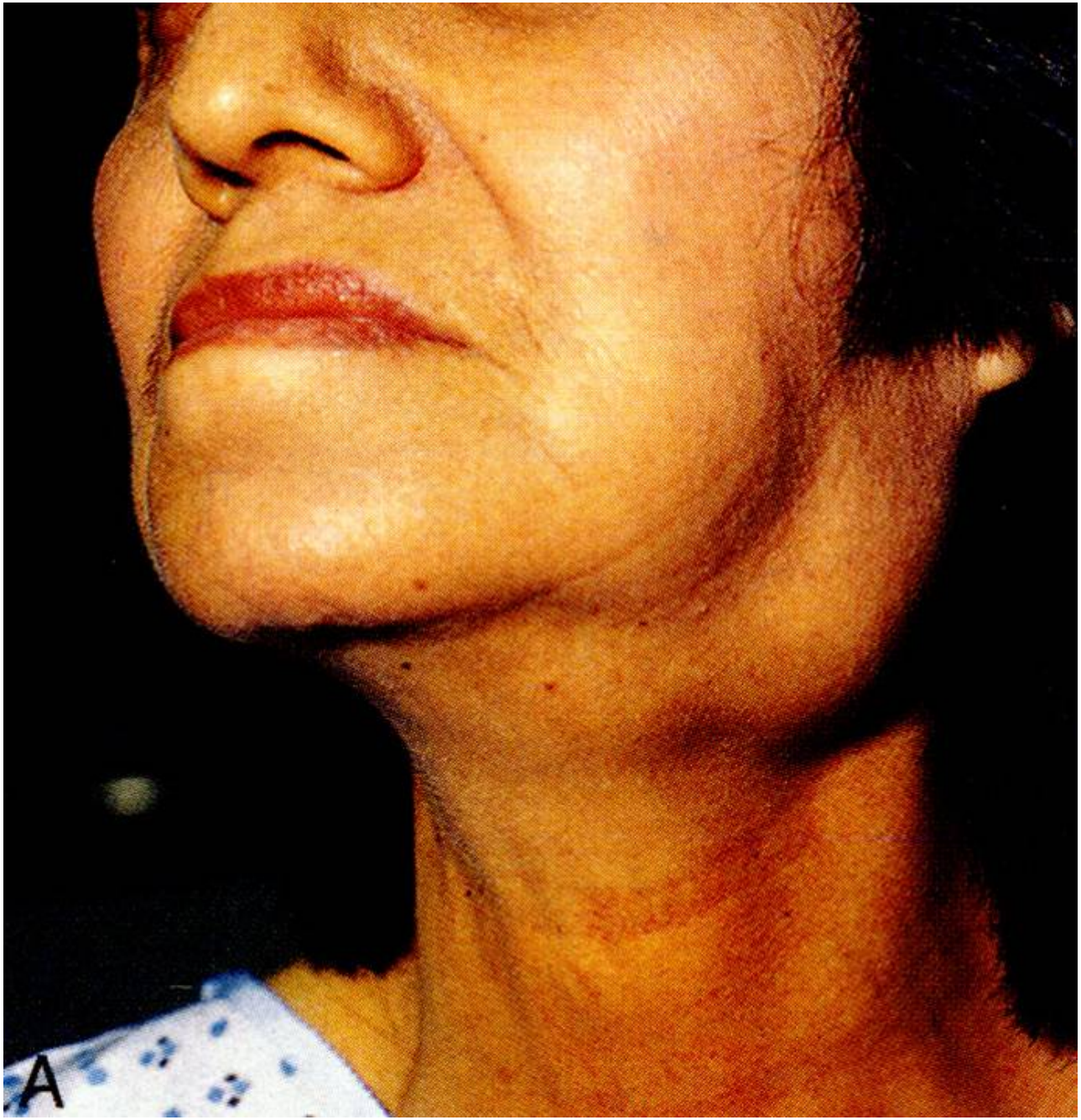
- enlarged, inflamed
- dry eyes, dry mouth
- 40x increased risk of lymphoma!

Systemic disease

- fatigue
- arthralgia/myalgia
- Raynaud phenomenon
- vasculitis
- peripheral neuropathy

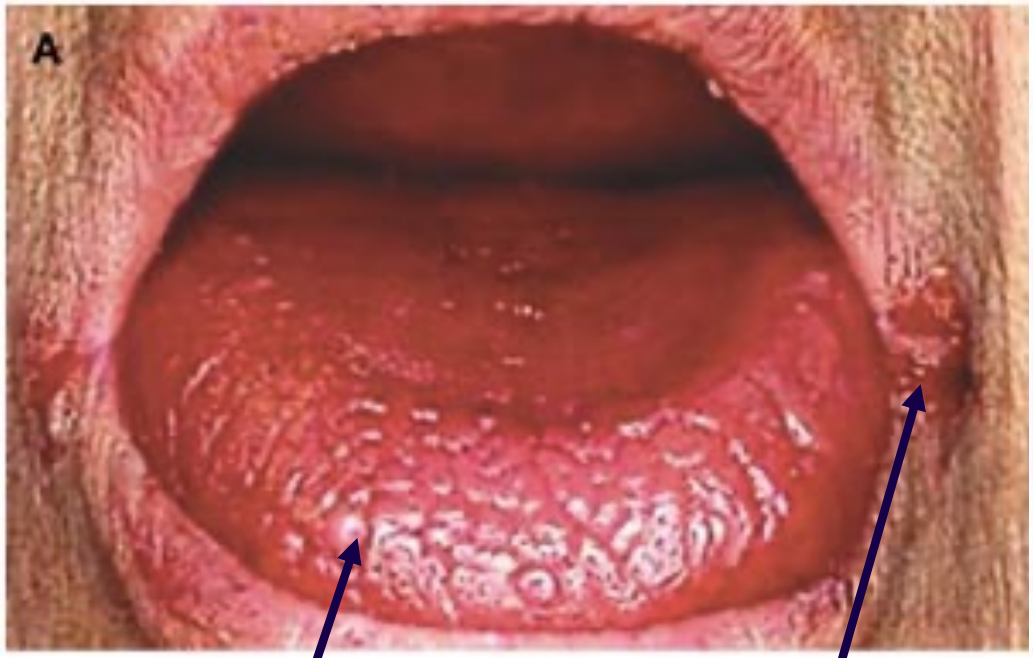
Sjögren: Things a Dentist Might See

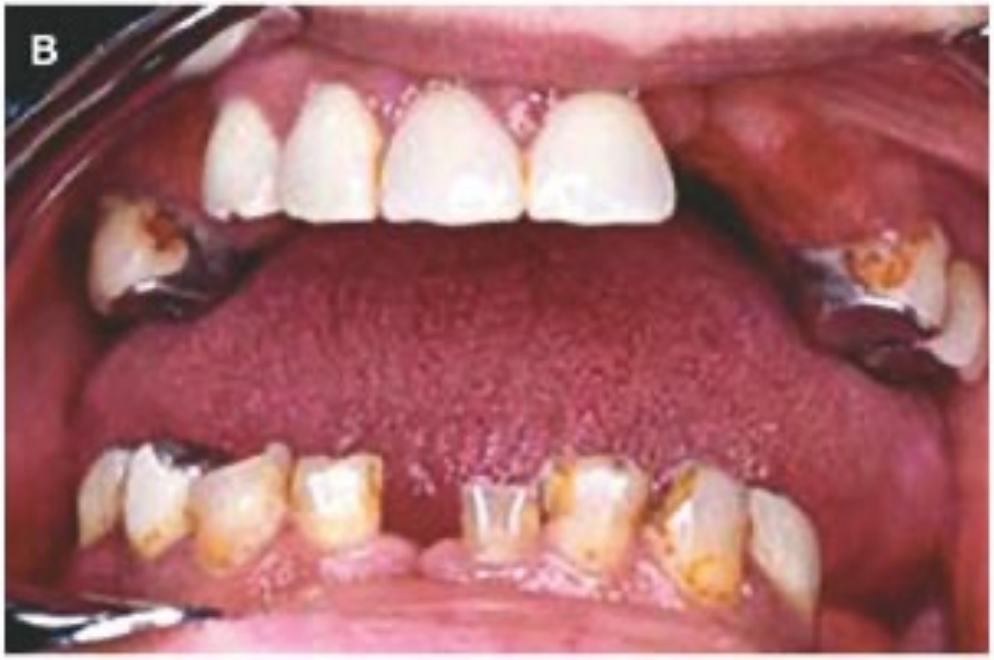
- Female between 35-45
- Enlarged salivary glands
- Raynaud phenomenon
- Keratoconjunctivitis sicca (dry eyes)
- Oral changes:
  - xerostomia (dry mouth)
  - mucosal atrophy
  - candidiasis
  - mucosal ulceration
  - caries
  - taste dysfunction



Sjögren syndrome: salivary gland enlargment

Oral changes in Sjögren Syndrome





atrophic papillae, deeply fissured epithelium

angular cheilitis

missing teeth and multiple caries

Sjögren Treatment

- Treatment is mostly supportive and symptom-based
- Oral treatment: adequate hydration, scrupulous dental hygiene, cholinergic agents (stimulate saliva release), frequent dental exams
- Eye treatment: lubricating solutions, surgical procedures
- Systemic symptom treatment: steroids, other immunosuppressive drugs

Scleroderma (Systemic Sclerosis)

KNOW THIS

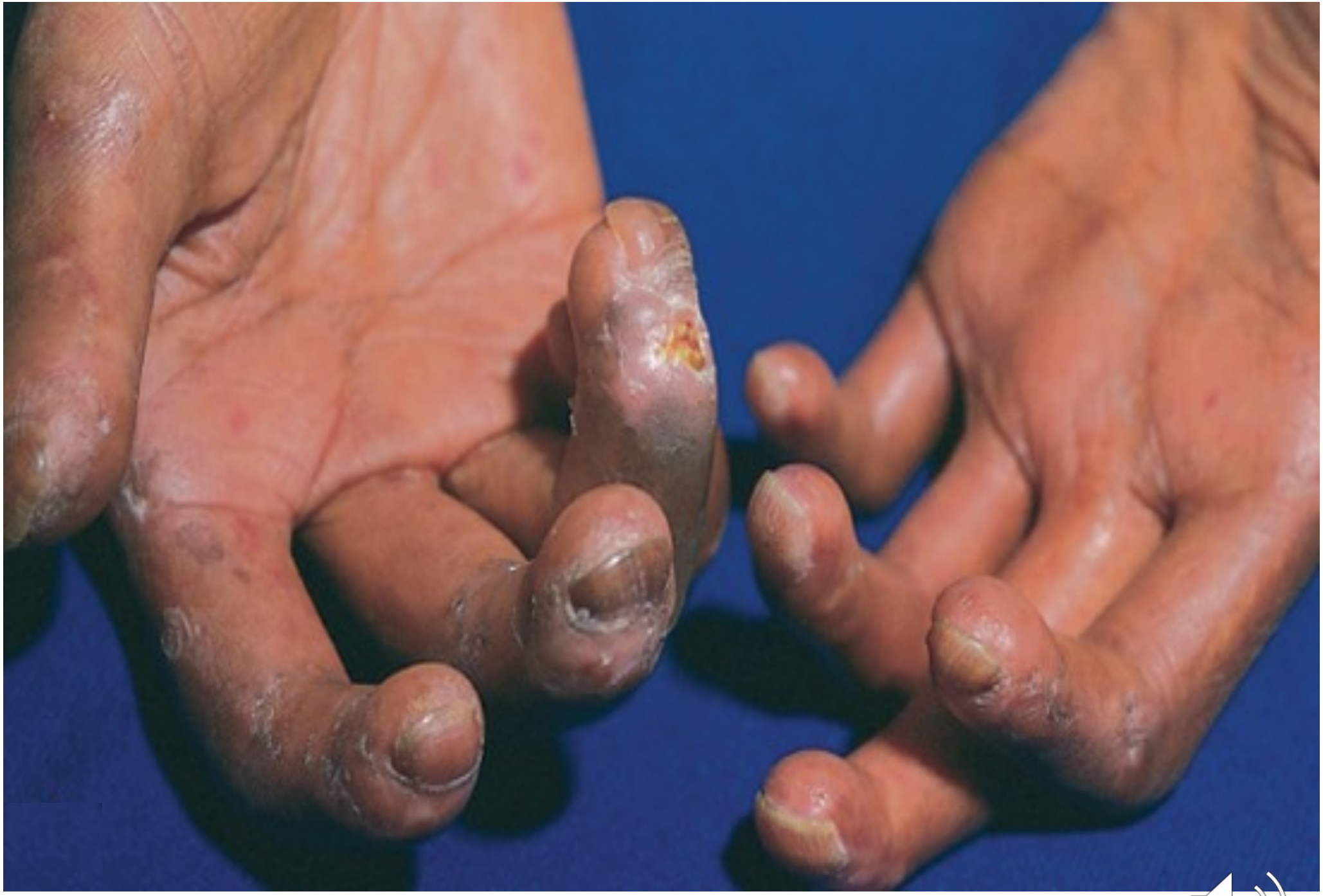
- Excessive fibrosis in skin and viscera
- Claw hands
- Mask-like face
- Diffuse and limited types

Scleroderma Etiology

- CD4+ T cells accumulate for some reason
- T cells release cytokines that activate mast cells and macrophages, which release fibrogenic cytokines
- B cell activation also occurs but doesn't play major role
- Autoantibody: anti-Scl 70

Scleroderma Signs and Symptoms

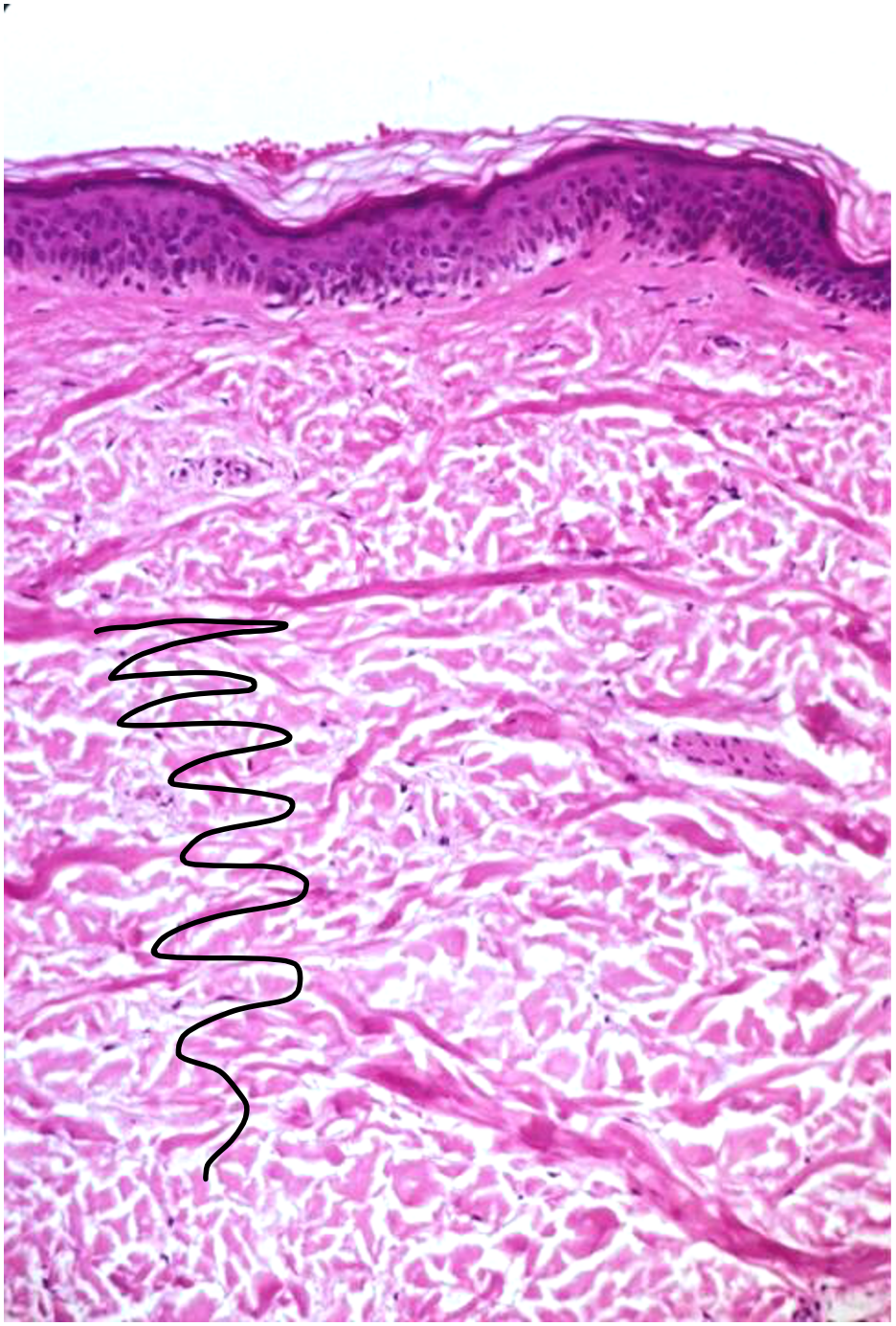
- Skin: diffuse, sclerotic atrophy. Fingers first.
- GI: “rubber-hose” esophagus
- Lungs: fibrosis, pulmonary hypertension
- Kidneys: narrowed vessels, hypertension
- Heart: myocardial fibrosis



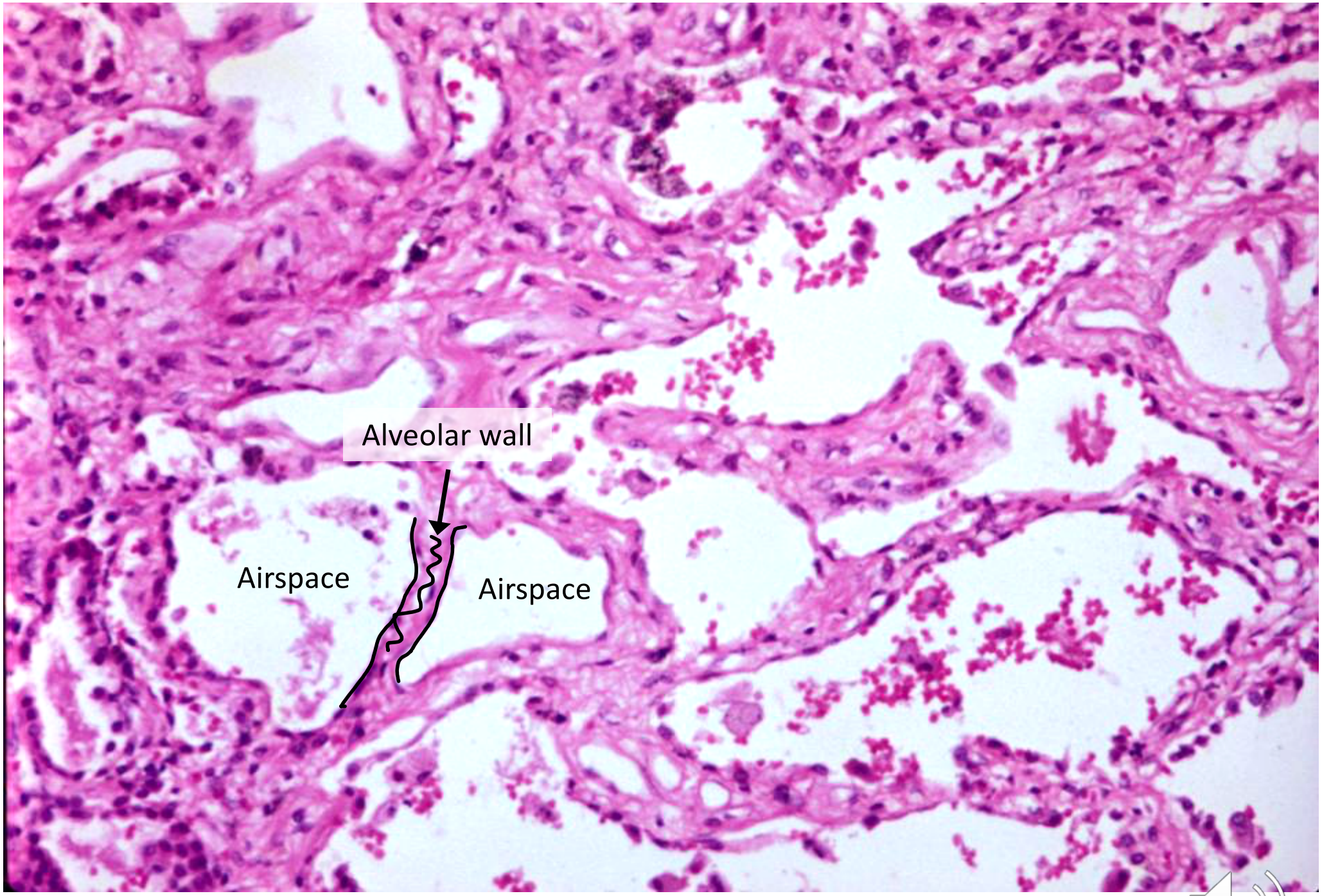
Scleroderma: claw hands

Epidermis

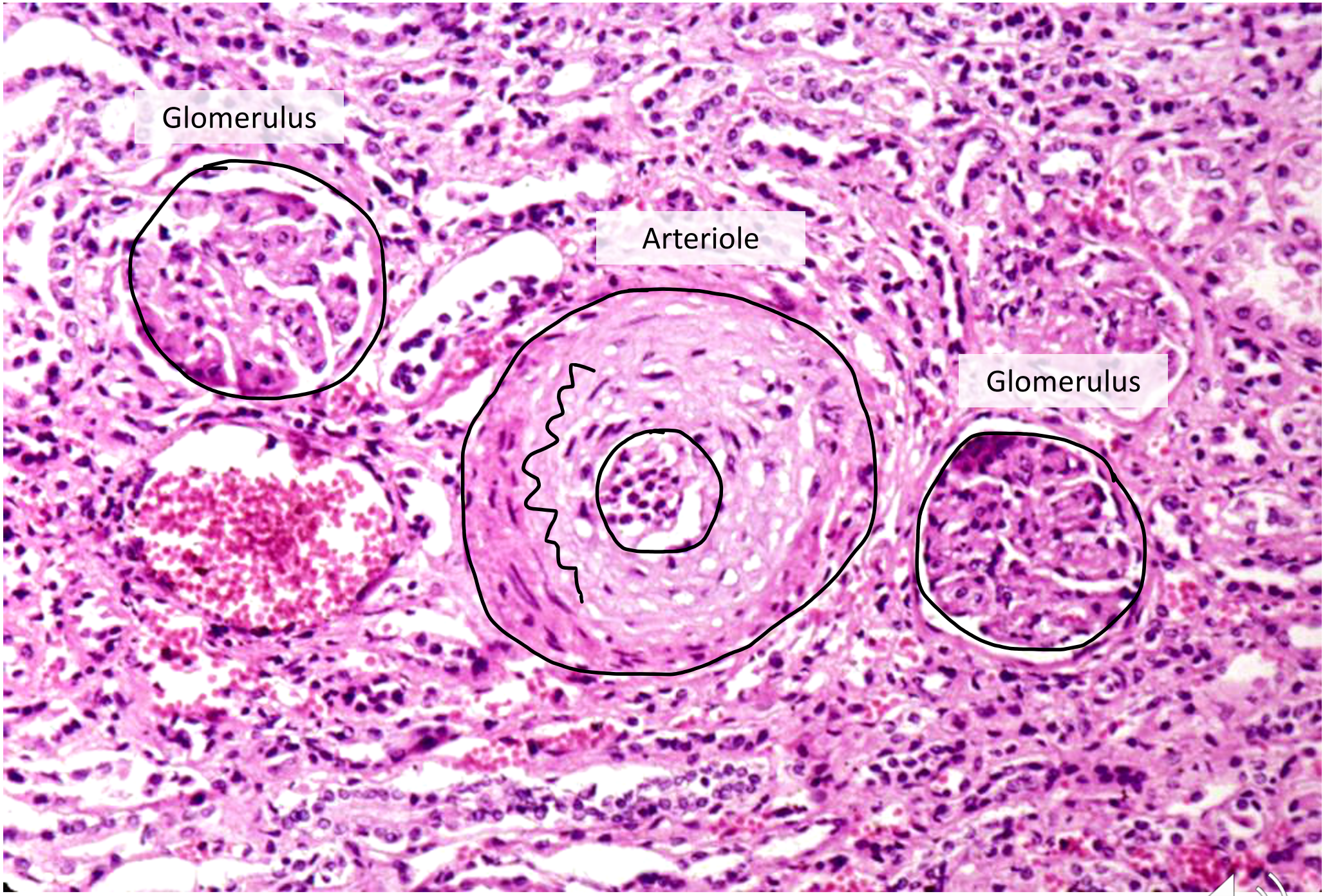
Dermis



Scleroderma: sclerotic skin



Scleroderma: fibrosis in alveolar walls



Scleroderma: narrowed renal vessel

Limited vs. Diffuse Scleroderma

Limited Scleroderma

- Mild skin involvement
- Late visceral involvement
- Benign course

Diffuse Scleroderma

- Widespread skin involvement
- Early visceral involvement
- Rapid course

CREST Syndrome

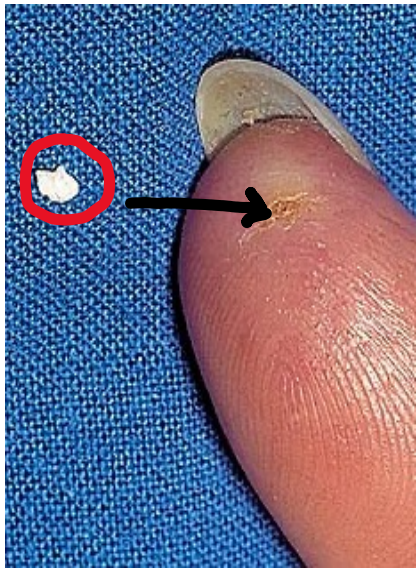
Calcinosis

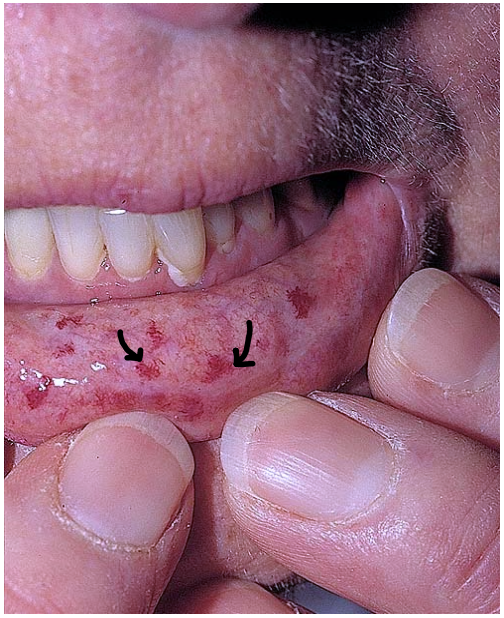
Raynaud phenomenon

Esophageal dysmotility

Sclerodactyly

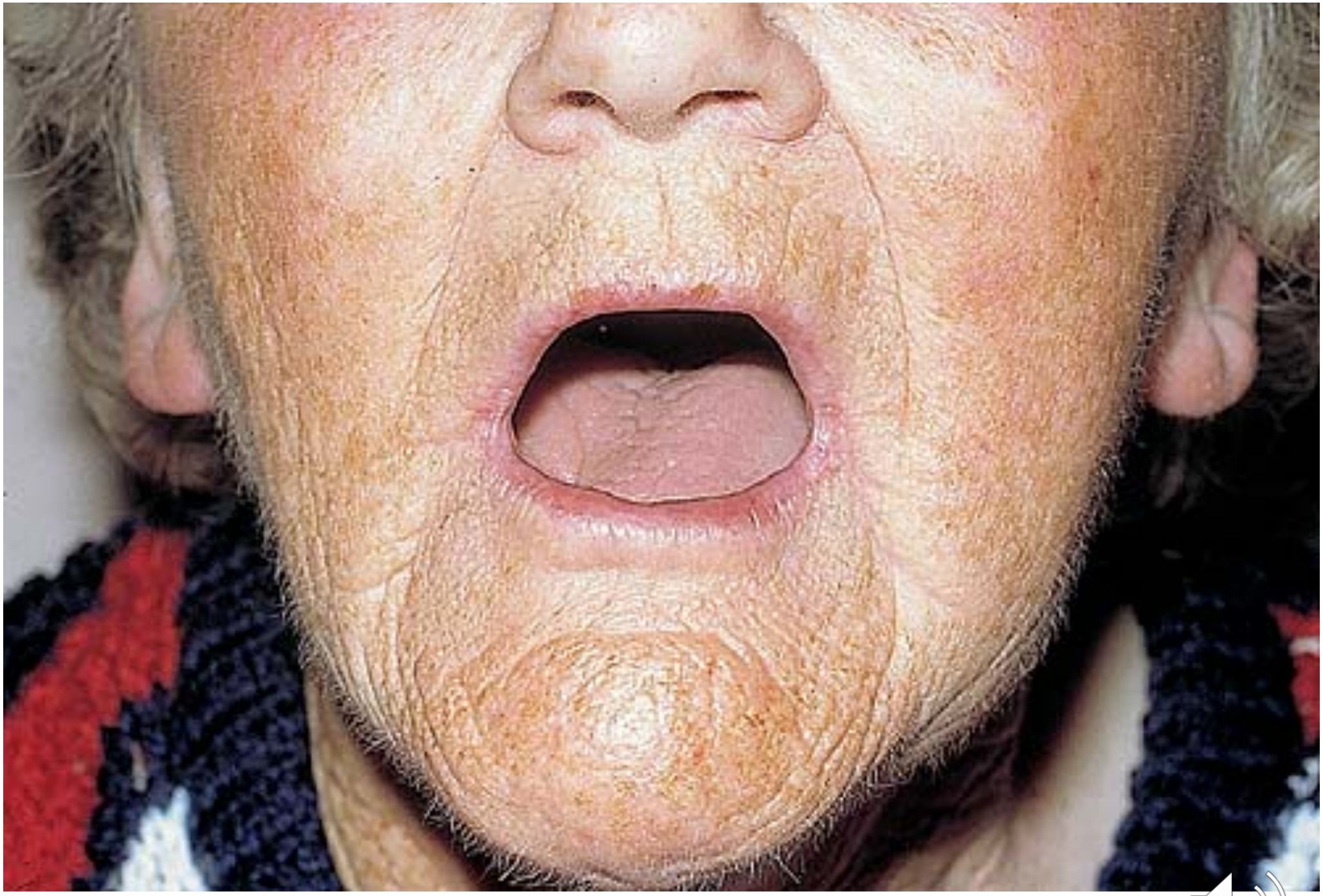
Telangiectasia





Scleroderma: Things a Dentist Might See

- Female between 50-60
- Raynaud phenomenon
- Stiff, claw-like fingers
- Mask-like face
- Difficulty swallowing
- Dyspnea, chronic cough
- Difficulty getting dentures in



Scleroderma: restricted mouth opening

Scleroderma Prognosis

- Steady, slow, downhill course over years
- Limited scleroderma may exist for decades without progressing
- Diffuse scleroderma is more common and has worse prognosis
- Overall 10-year survival = 35-70%