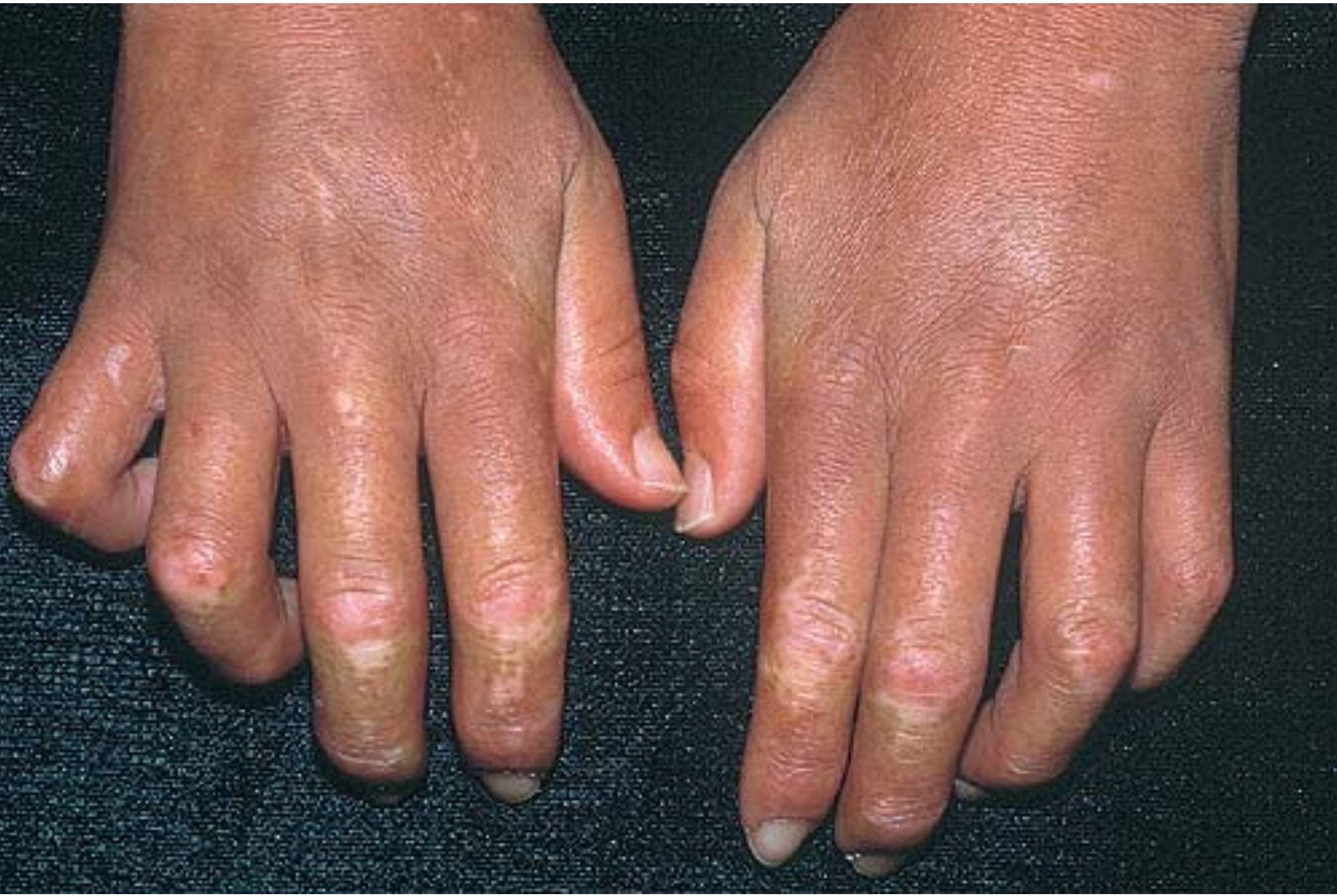


Autoimmune Diseases

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

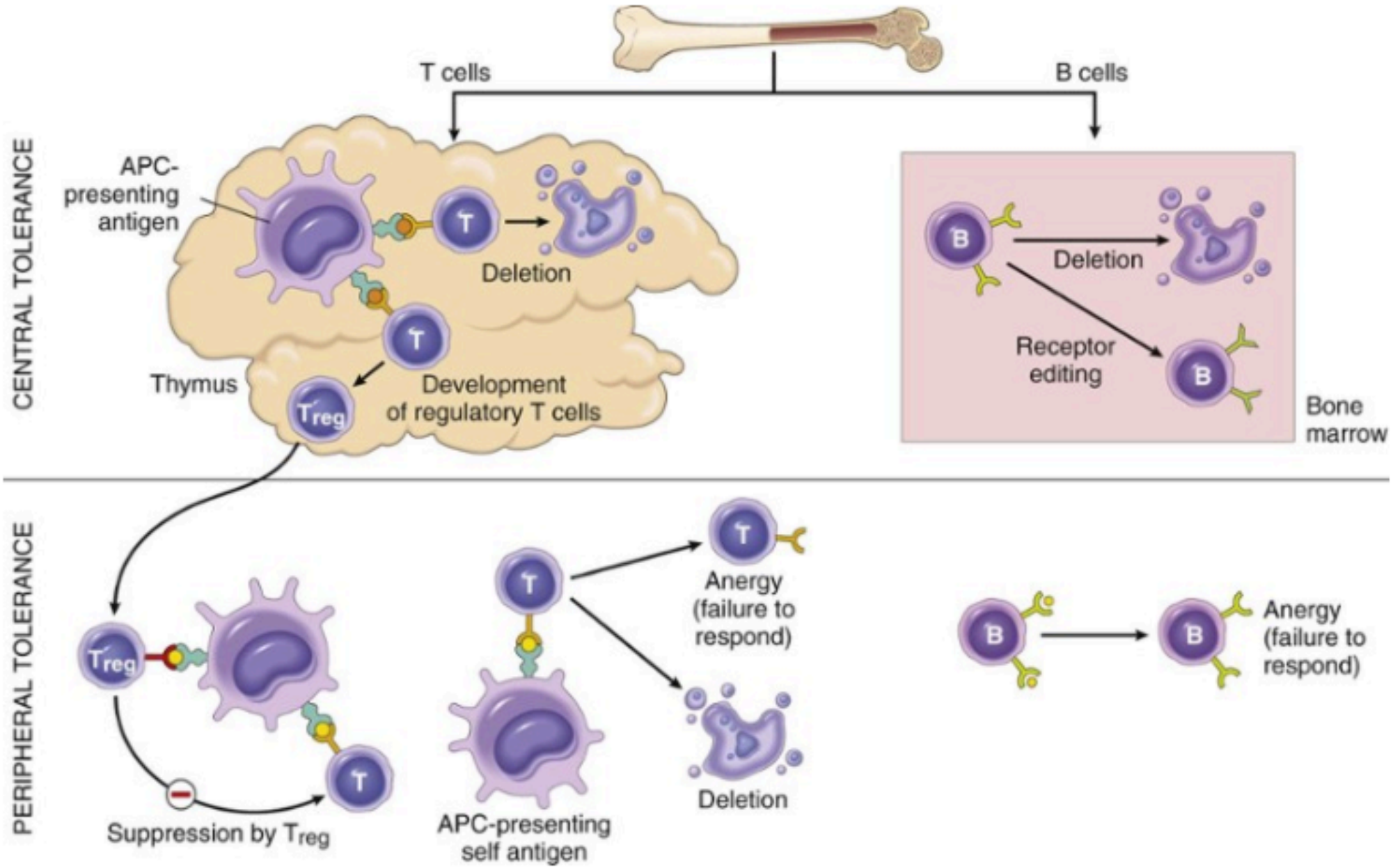
- Explain what we know about the cause of scleroderma, and identify the autoantibody seen in most patients.
- Describe the clinical findings seen in scleroderma.
- Describe the difference between diffuse and limited scleroderma, and explain what CREST syndrome is.
- Describe the overall prognosis for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

Immune Diseases Outline

- What causes autoimmune disease?
- Systemic lupus erythematosus
- 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

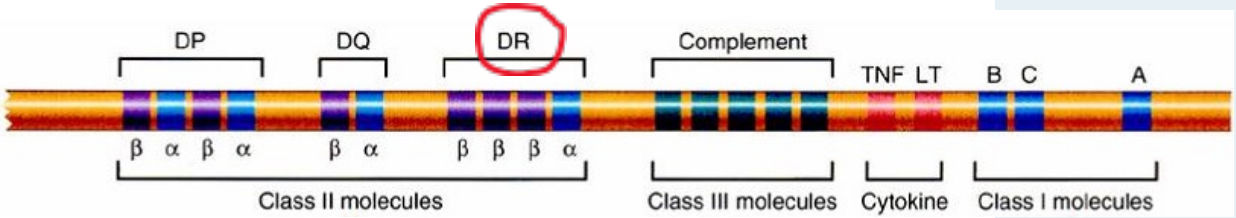

T cells
B cells
CENTRAL TOLERANCE
APC-presenting antigen
T
Deletion
T
Thymus
Treg
Development of regulatory T cells
B
Deletion
Receptor editing
B
Bone marrow
PERIPHERAL TOLERANCE
Treg
T
Suppression by Treg
T
Anergy (failure to respond)
Deletion
APC-presenting self antigen
B
B
Anergy (failure to respond)

What causes autoimmune disease?

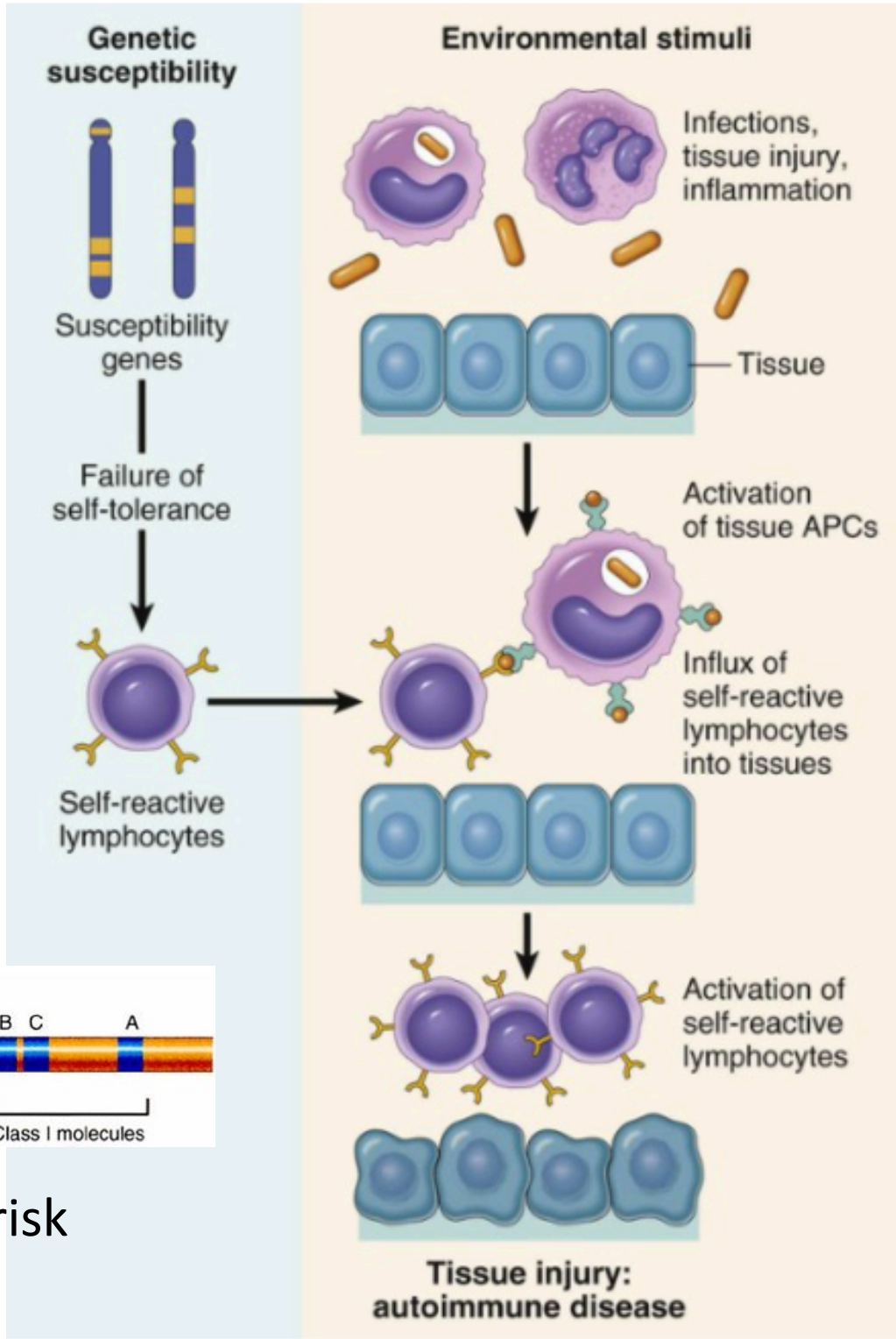
Genes

+

Environment



Example: HLA DR4 = increased risk for rheumatoid arthritis



Systemic Lupus Erythematosus (SLE)

KNOW THIS

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

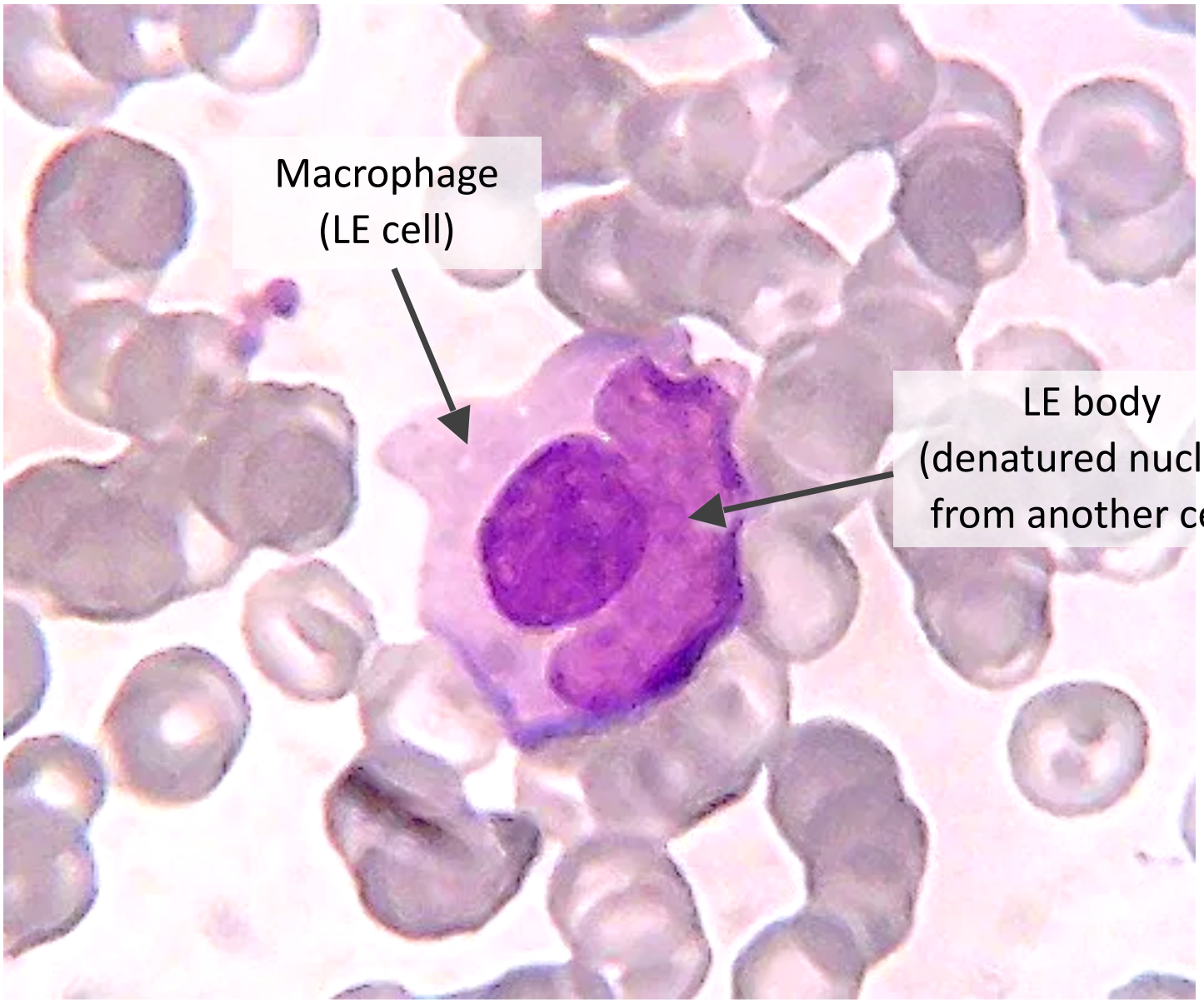
SLE Etiology

Underlying cause

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

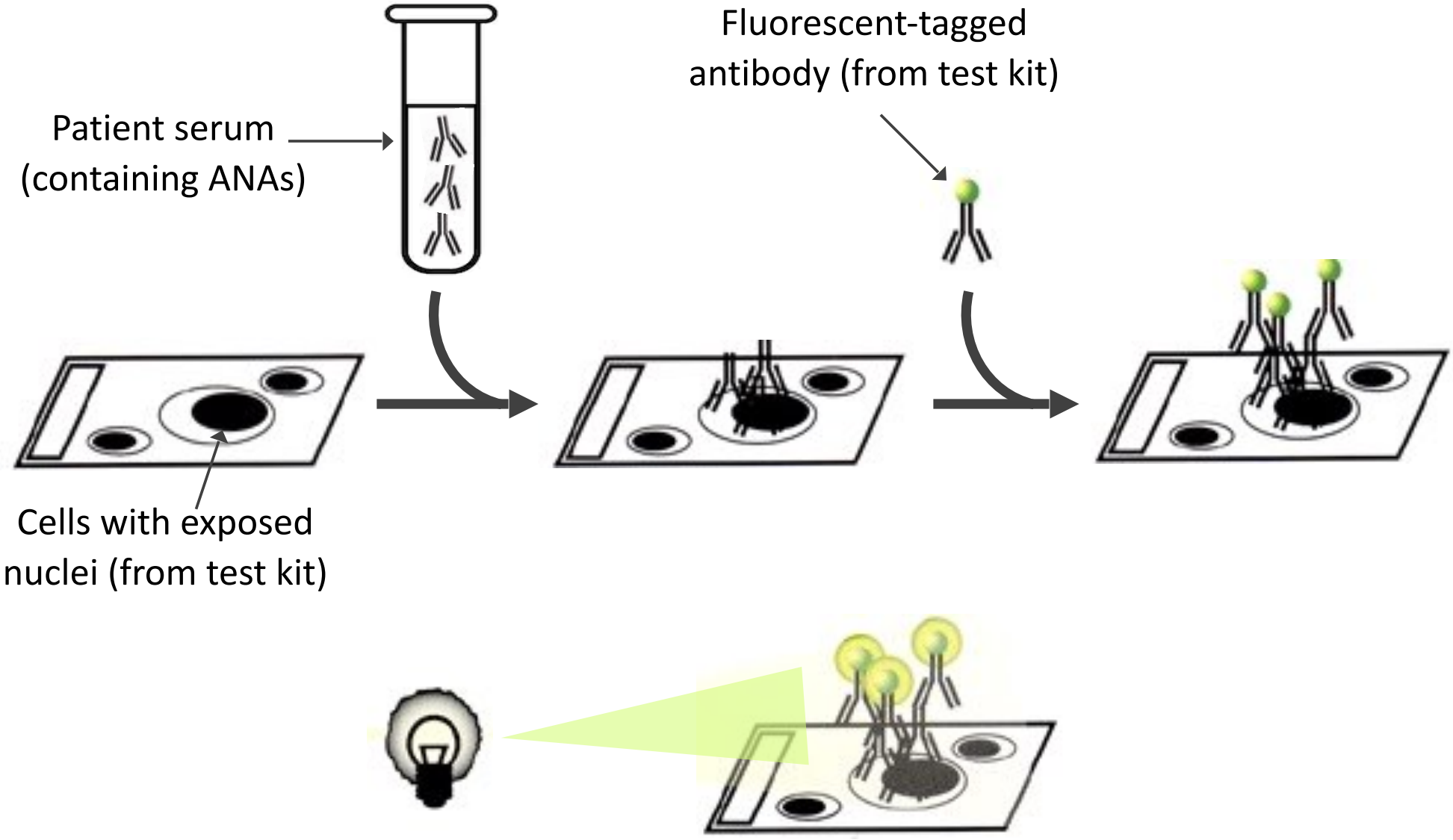
Autoantibodies do the damage

- 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
- Other autoantibodies react with other body tissues too



Lupus erythematosus (LE) cell in bone marrow

Fluorescent antinuclear antibody (FANA) test



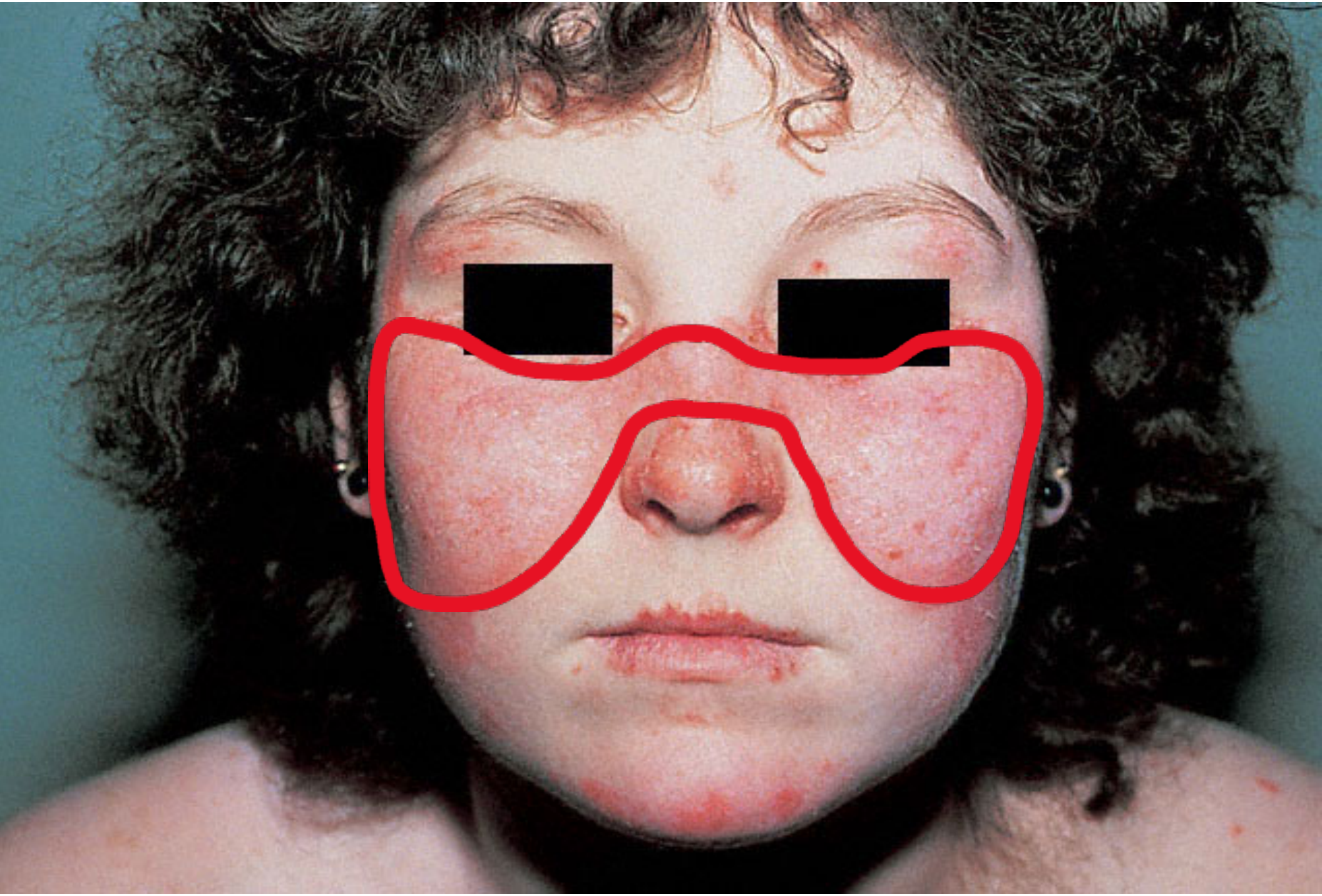
Positive FANA test in SLE

(other AI diseases show different nuclear staining patterns - speckled, etc.)

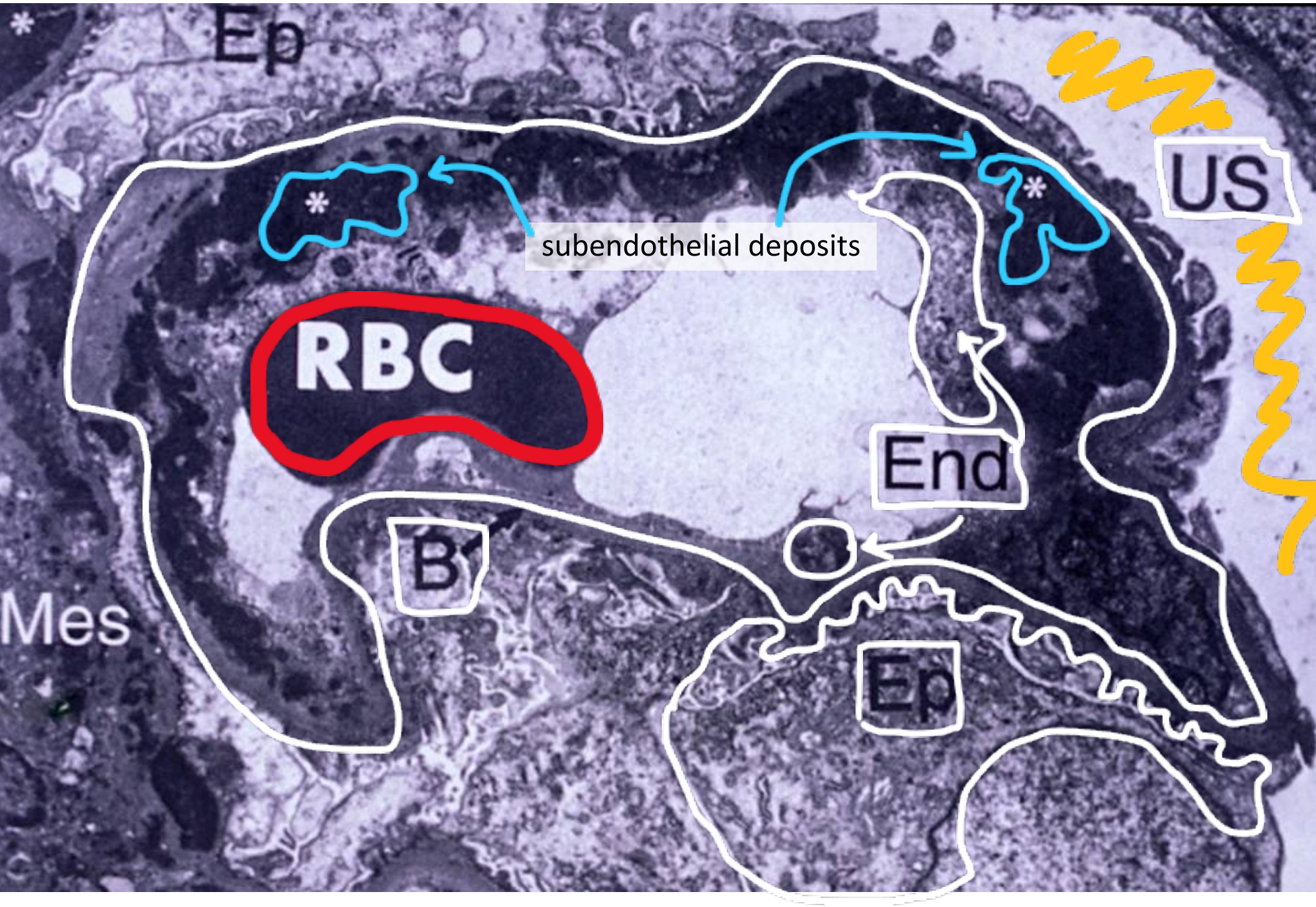
SLE Signs and Symptoms

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

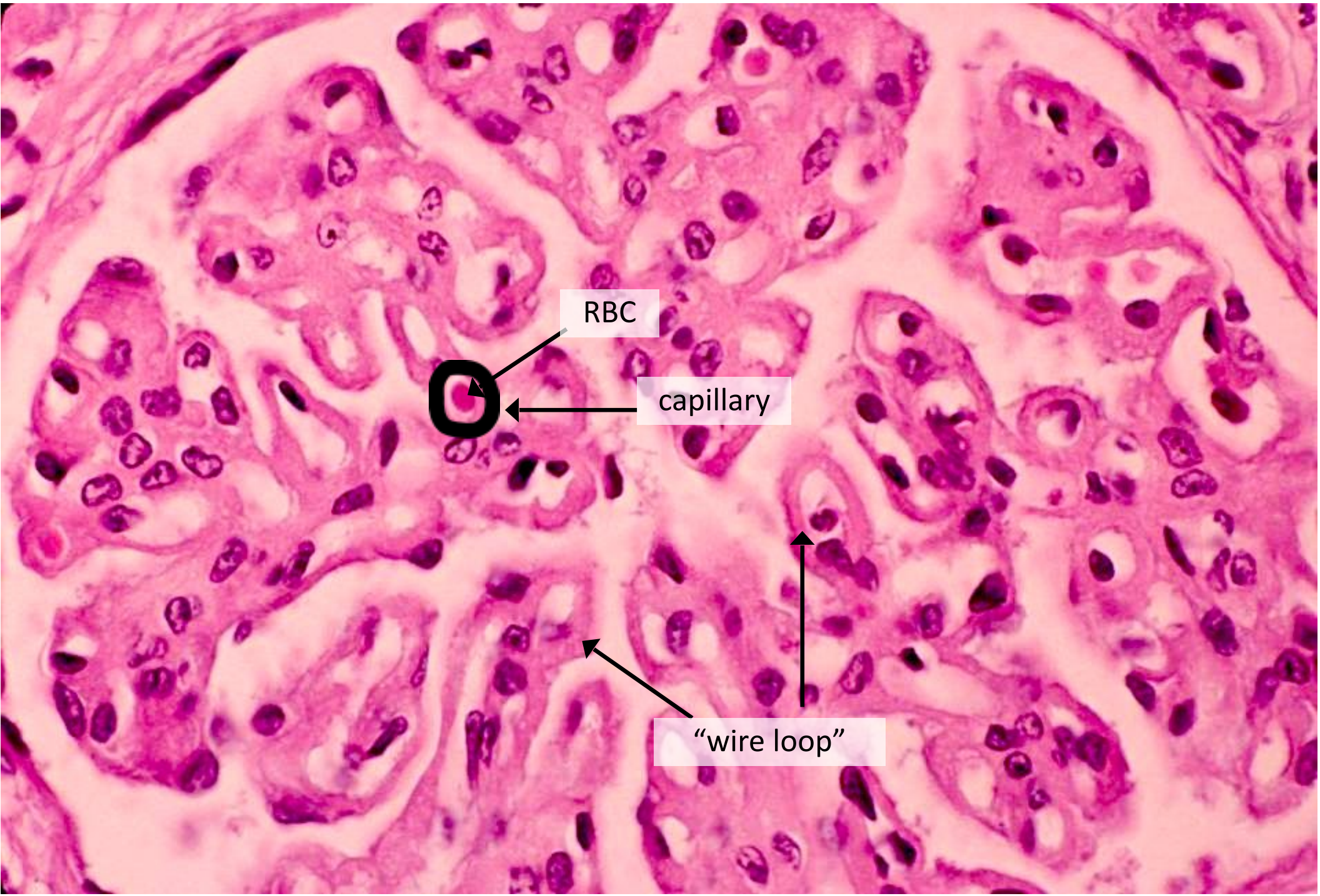
- Unexplained fever
- Fatigue
- Butterfly rash
- Renal failure
- Seizures, psychosis
- Arthritis
- Endocarditis, pericarditis
- Pleuritis
- Non-specific oral lesions



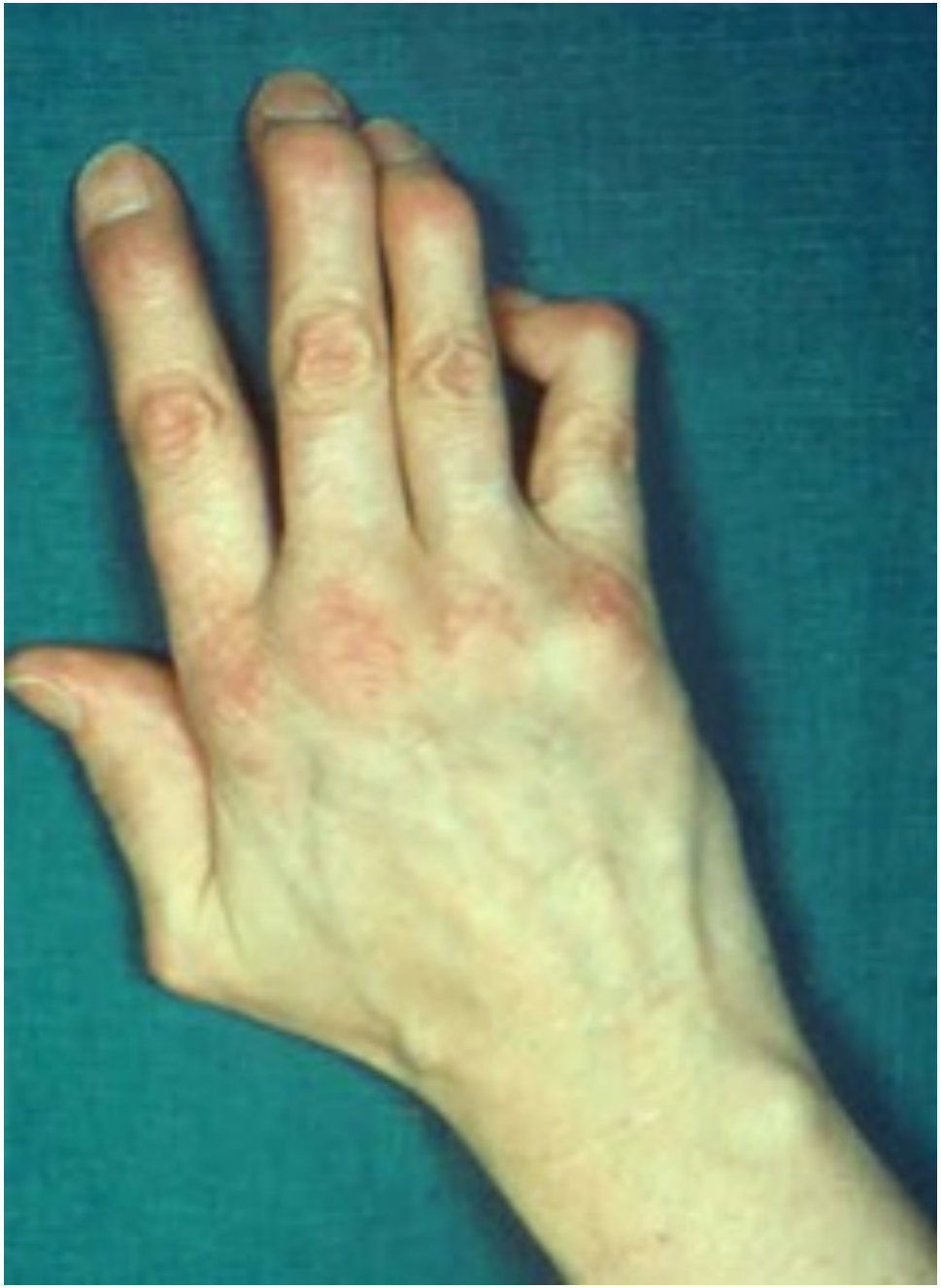
Butterfly rash

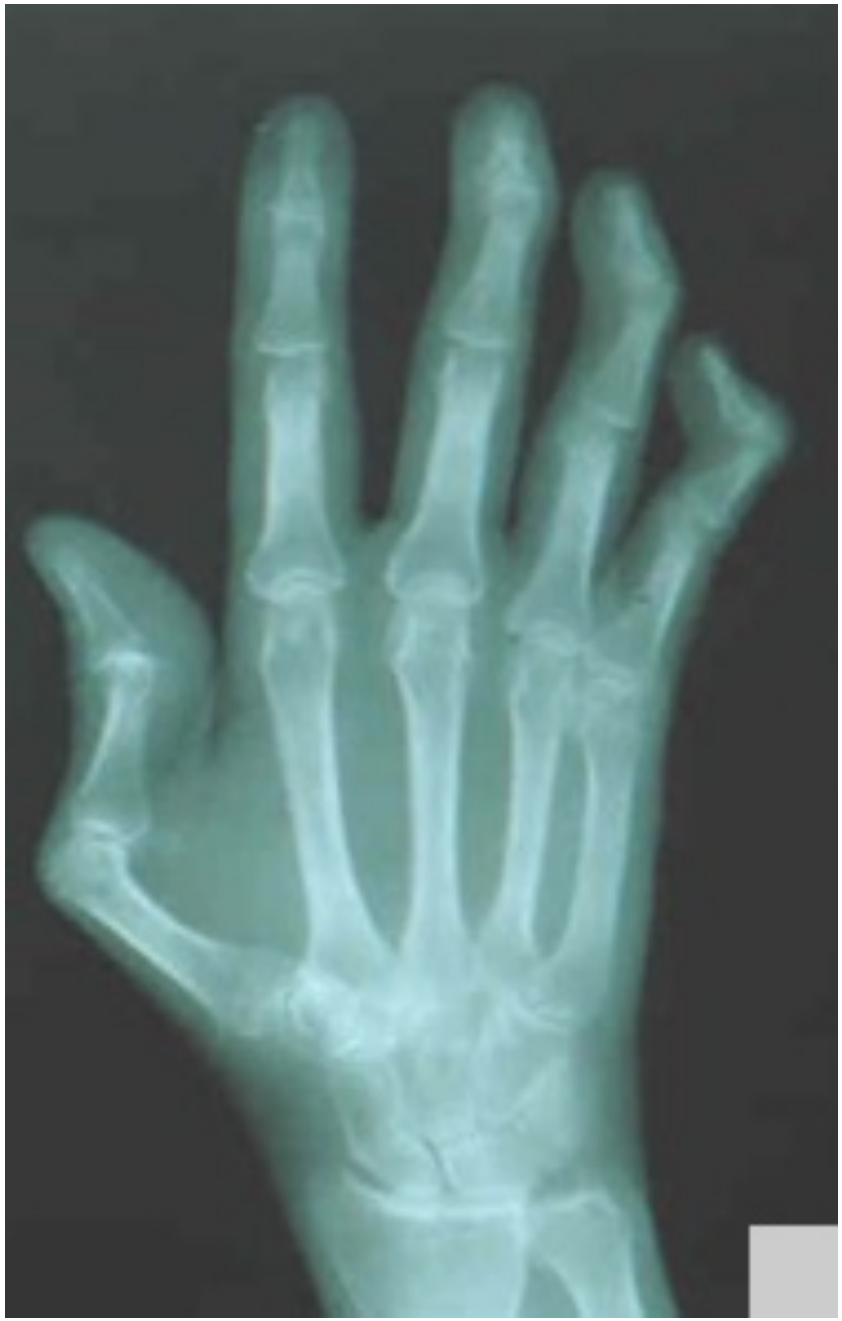


Renal EM in patient with lupus showing subendothelial deposits

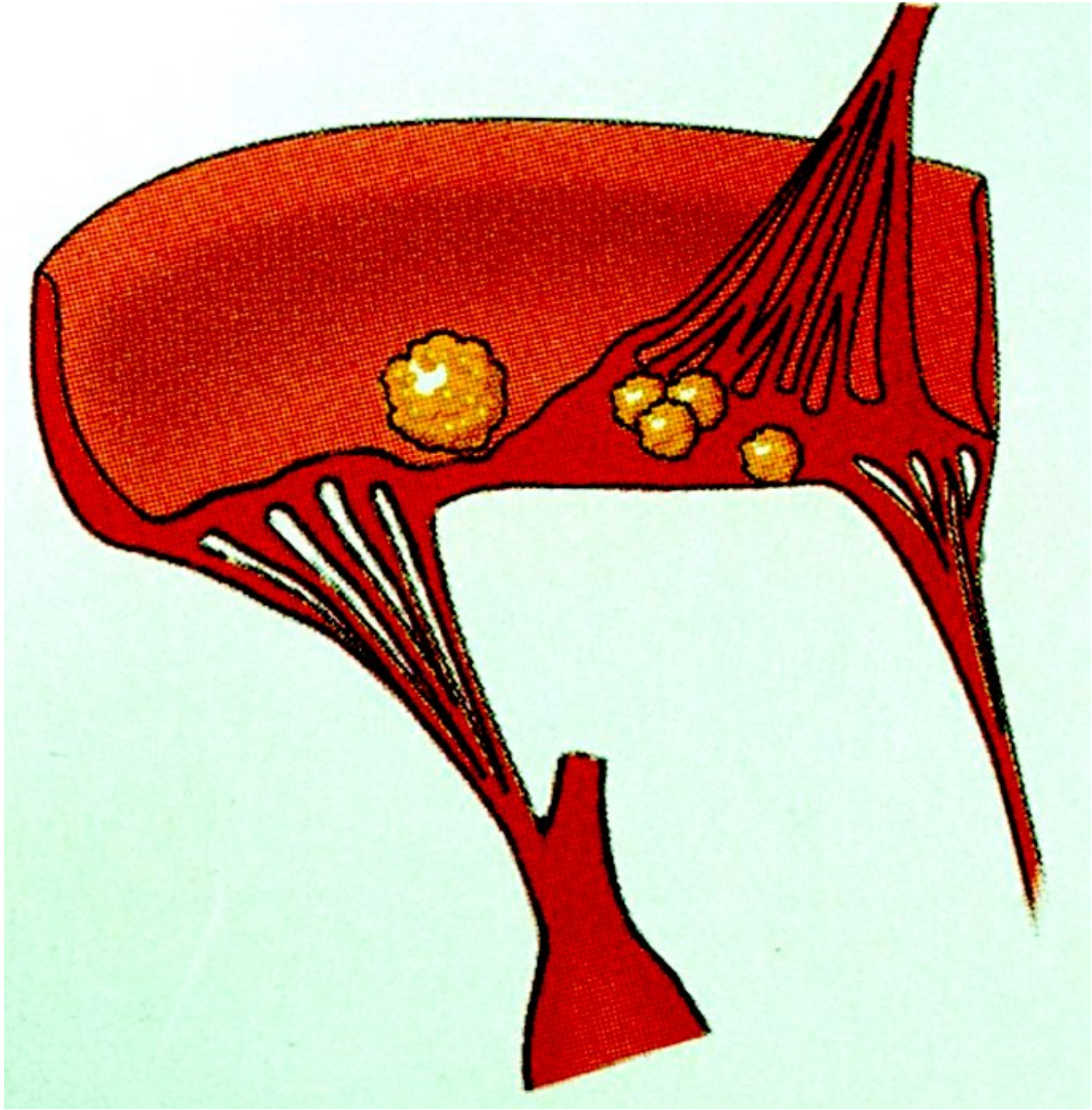


Glomerulus: “wire loop” capillary appearance

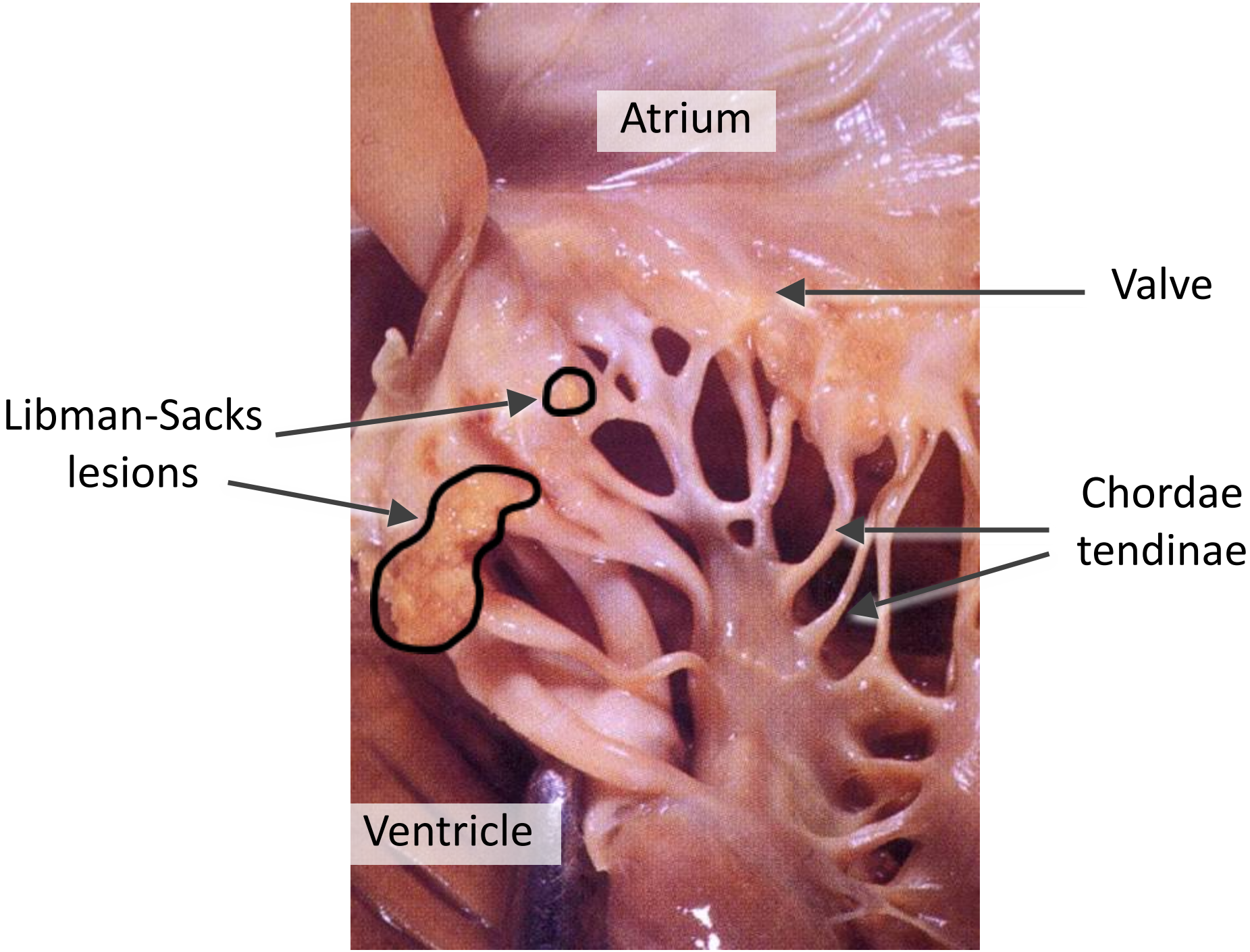




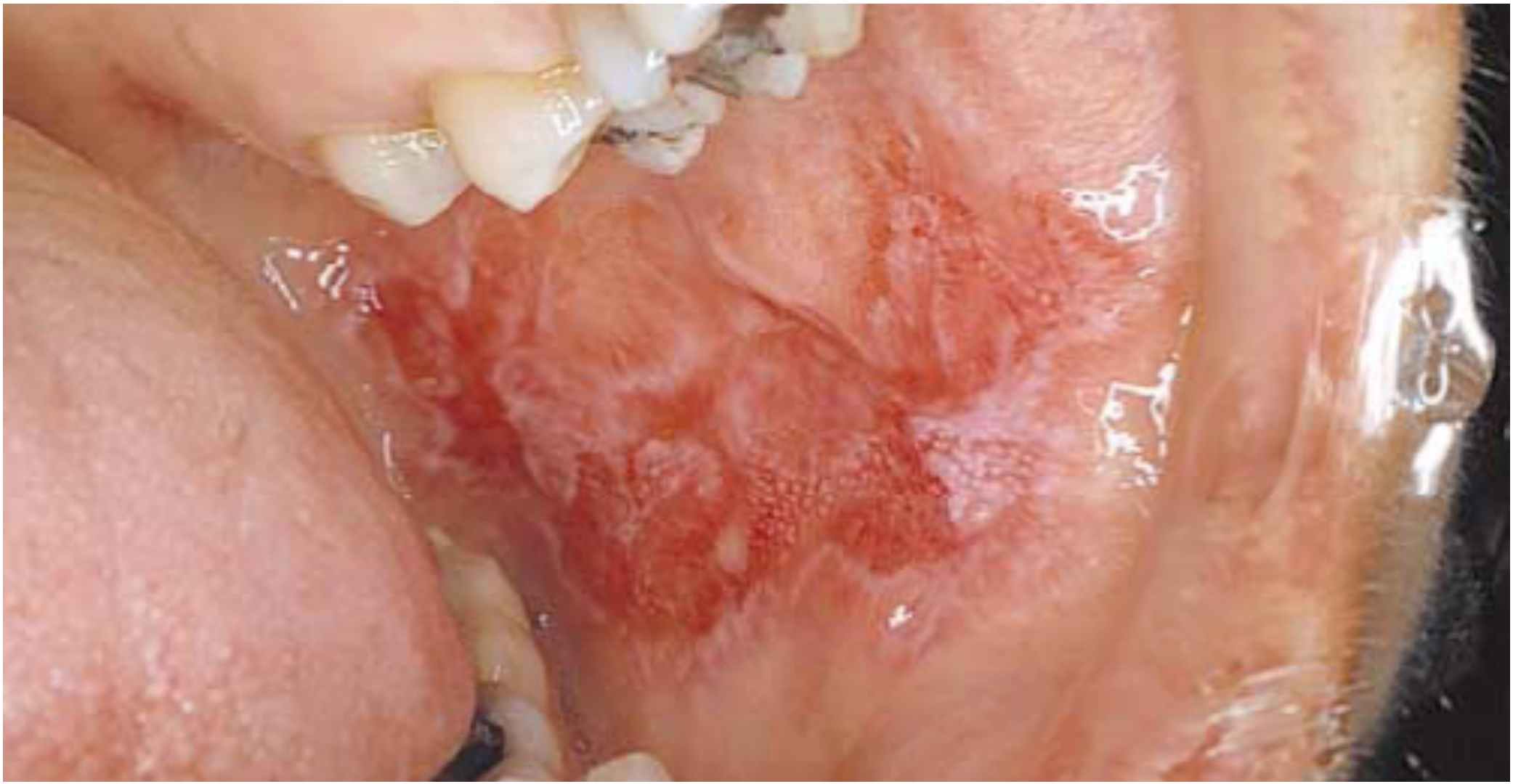
Arthritis: Hitch-hiker’s thumb



Endocarditis: Libman-Sacks lesions



Libman-Sacks lesions



Non-specific buccal lesion

SLE: 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

SLE Prognosis

- Variable! Some patients have just one or two episodes, rare patients die within months.
- Some patients have a limited form involving just skin.
- Most patients: relapses/remissions over many years.
- Treatment: rituximab, steroids
- 80% 10-year survival
- Most common cause of death: renal failure

Antibody-derived drug that kills B cells

Rheumatoid Arthritis

KNOW THIS

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

RA Etiology

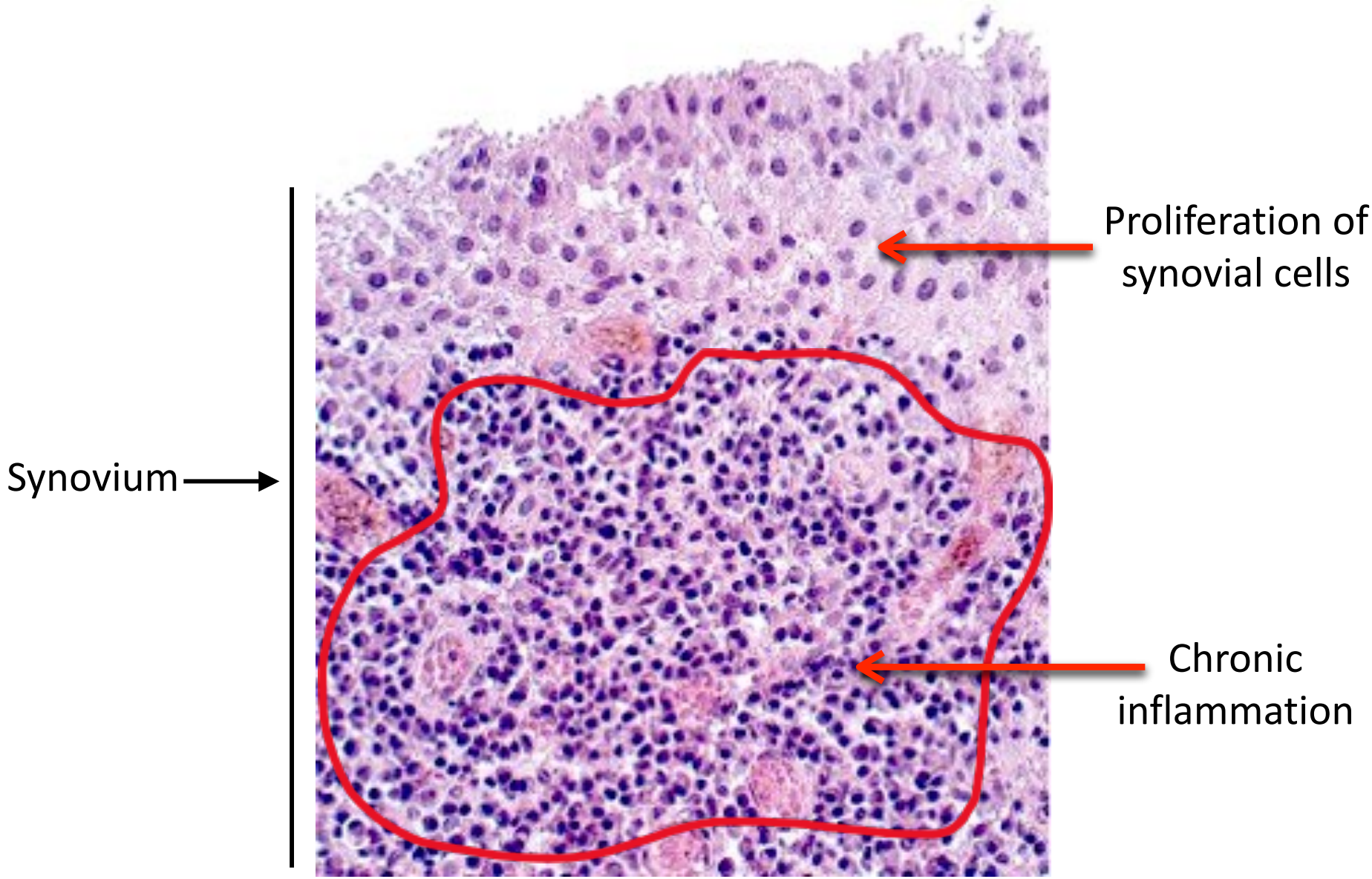
- Genetic predisposition + environmental trigger
- CD4+ T cells react against some joint antigen, and then:
  - Stimulate inflammation
  - Cause B cells to make antibodies (like rheumatoid factor, an IgM antibody directed against IgG that's present in most patients) and cytokines.
- The cytokine TNF (tumor necrosis factor) causes most of the damage in RA!
  - Stimulates even more inflammation
  - Tells synovial cells to make cartilage-damaging proteases

RA Signs and Symptoms

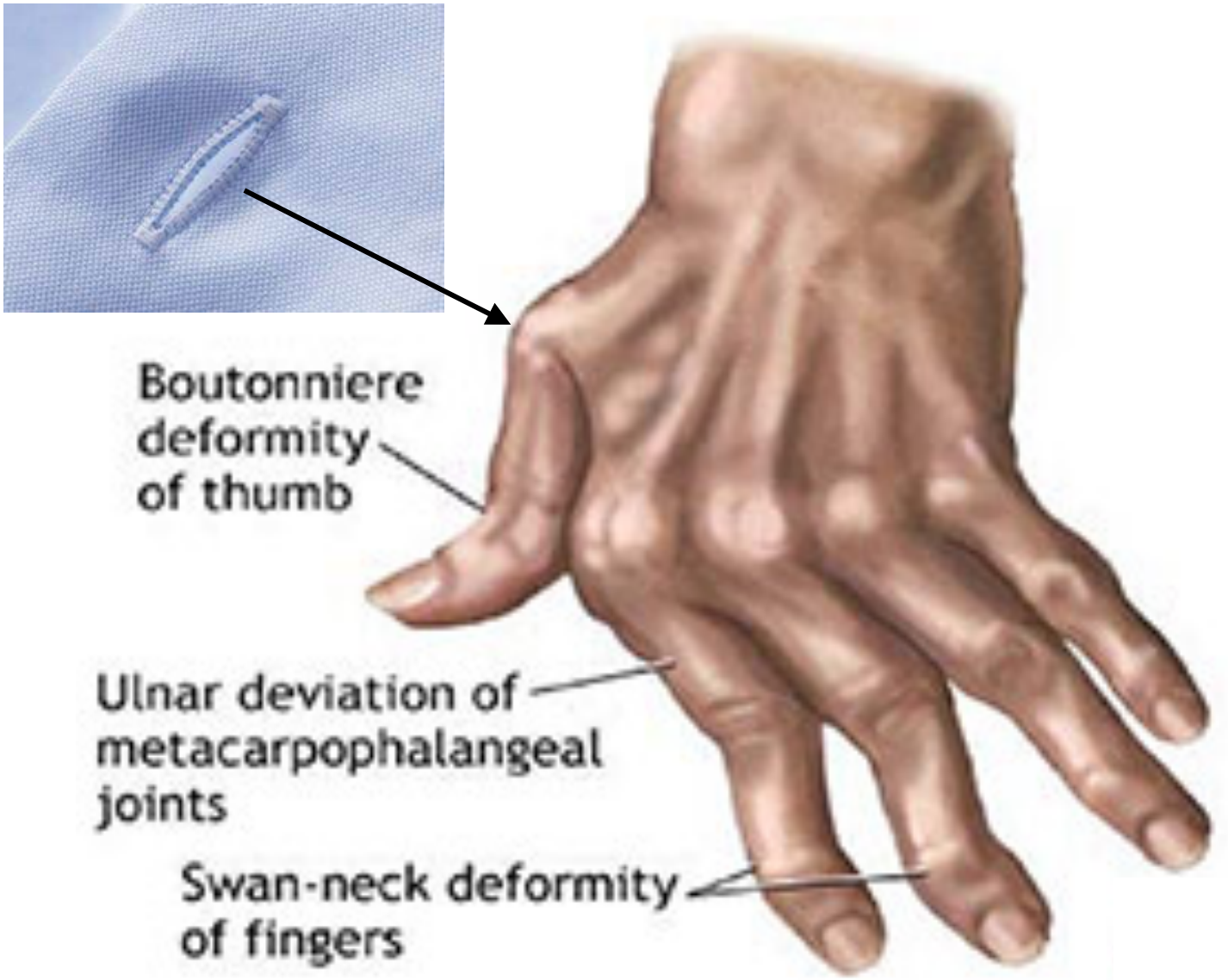
- Arthritis
- Rheumatoid nodules
- Fever, fatigue
- In severe cases, inflammation of other organs (heart, lungs, eyes…)

Characteristic Features of Arthritis in RA

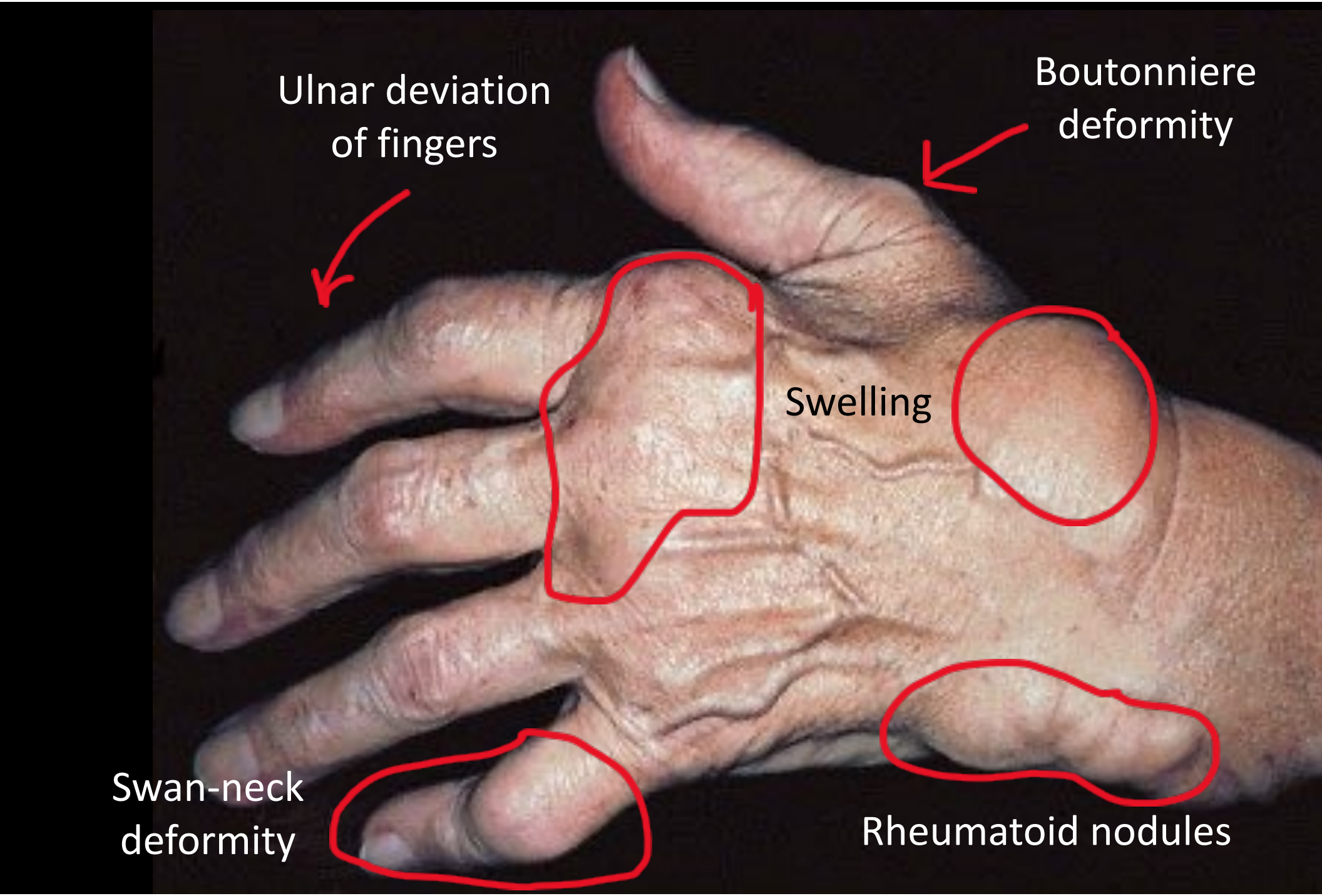
- Mainly small joints (hands), but also knees, elbows, shoulders
- Symmetric; characteristic hand features
- Chronic synovitis (inflammation of synovium, which lines the joint cavity)
  - synovial cell proliferation
  - chronic inflammation



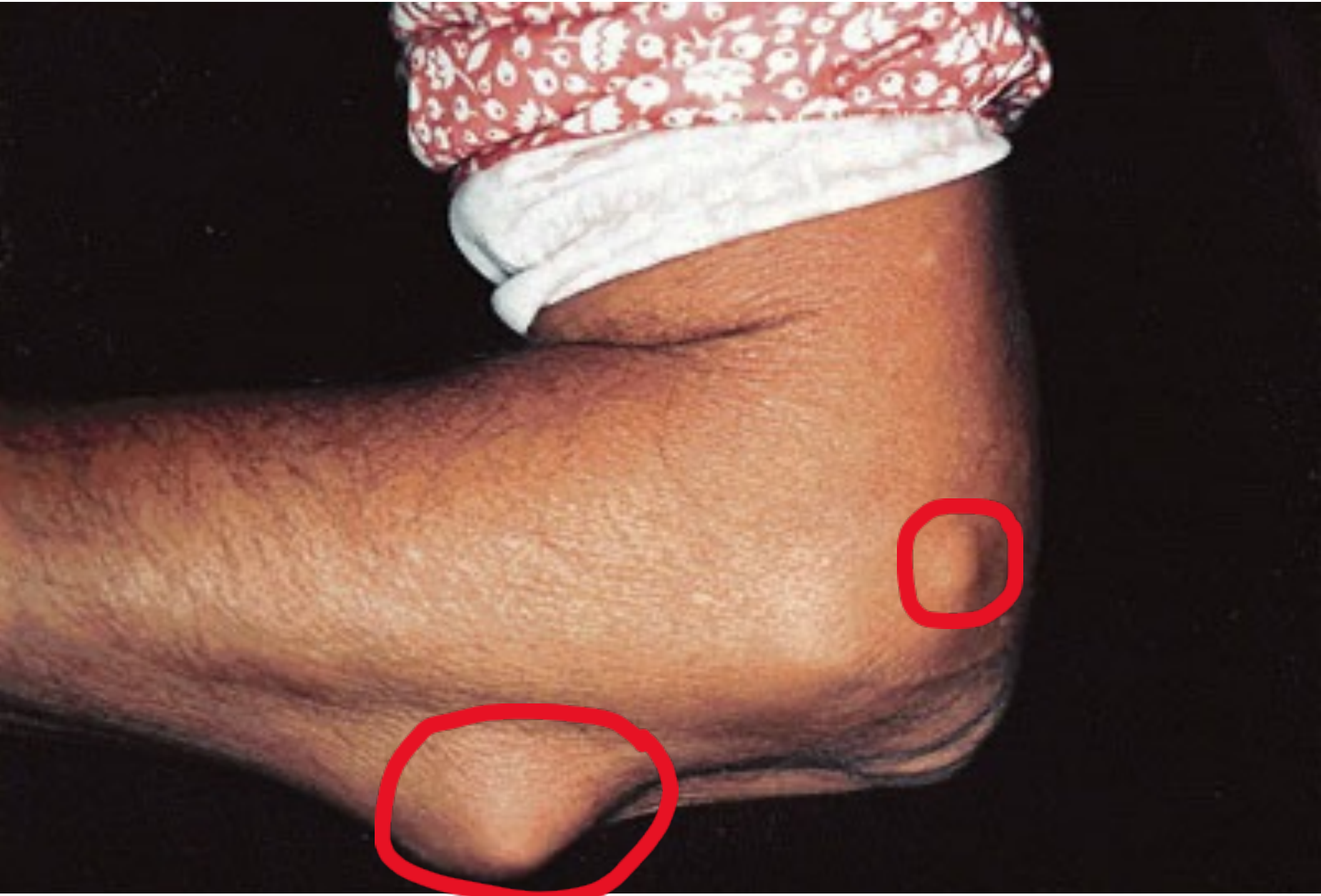
Rheumatoid arthritis: synovitis



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 react against cells in salivary, lacrimal glands
- Autoantibodies
  - ANAs
  - RF

ANAs → Anti-SS-A, anti-SS-B antibodies present in 90% of patients!

Sjögren Signs and Symptoms

Salivary and lacrimal glands

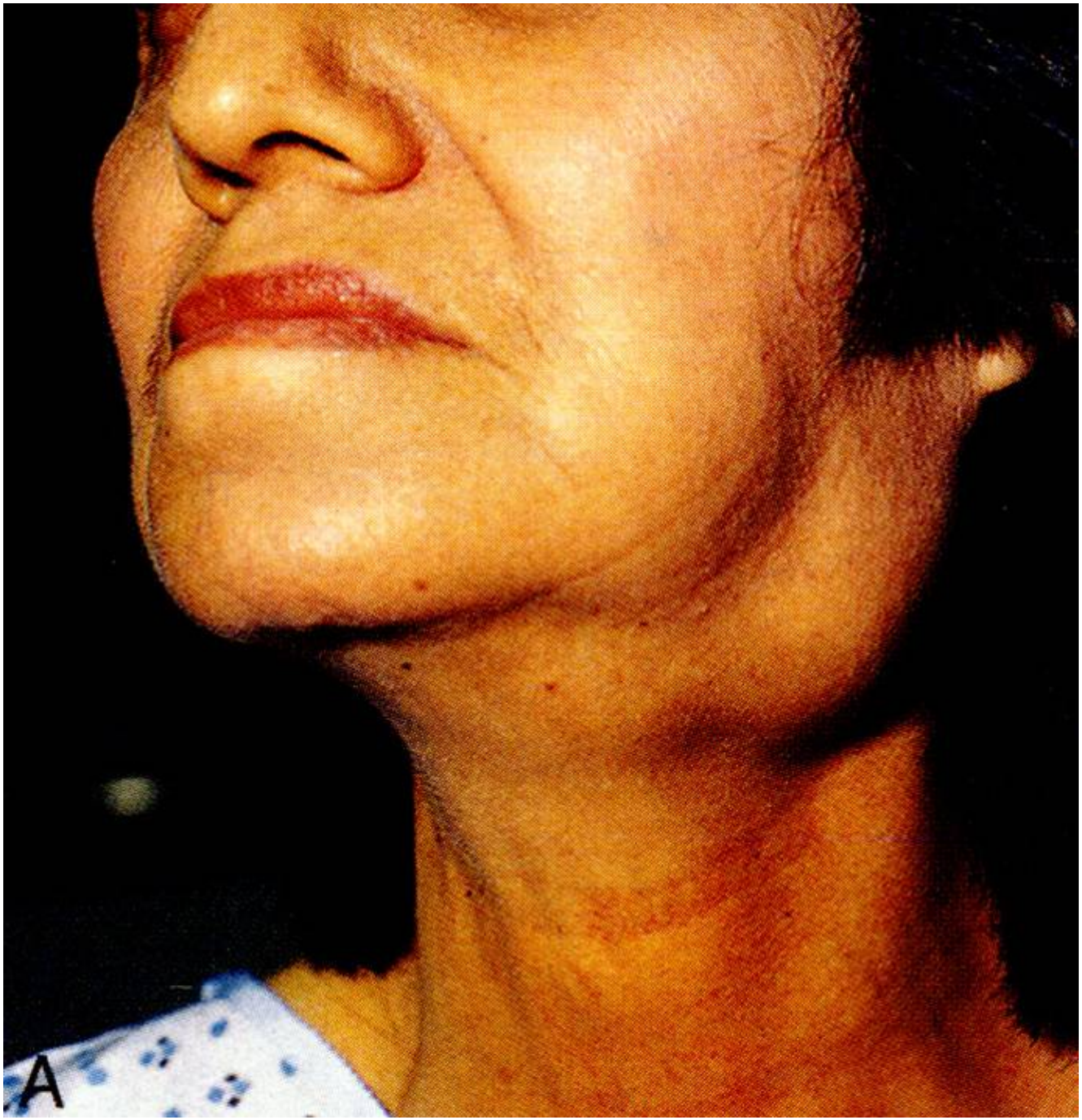
- enlarged, inflamed
- dry eyes, dry mouth
- 40x increased risk of lymphoma!

Systemic disease

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

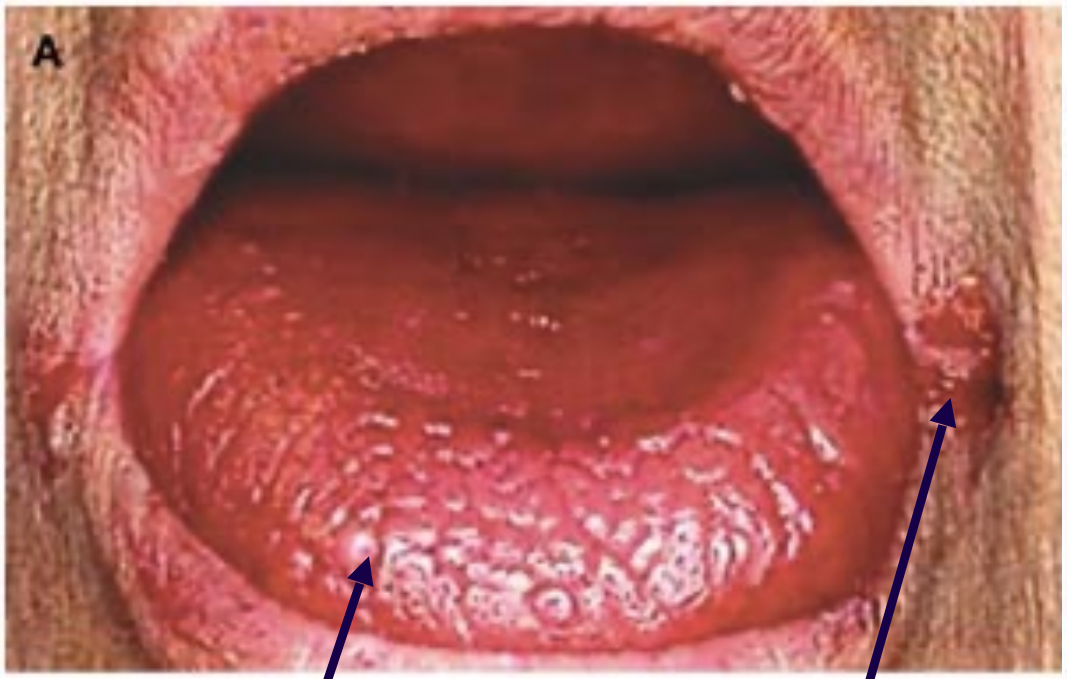
Sjögren: Things a Dentist Might See

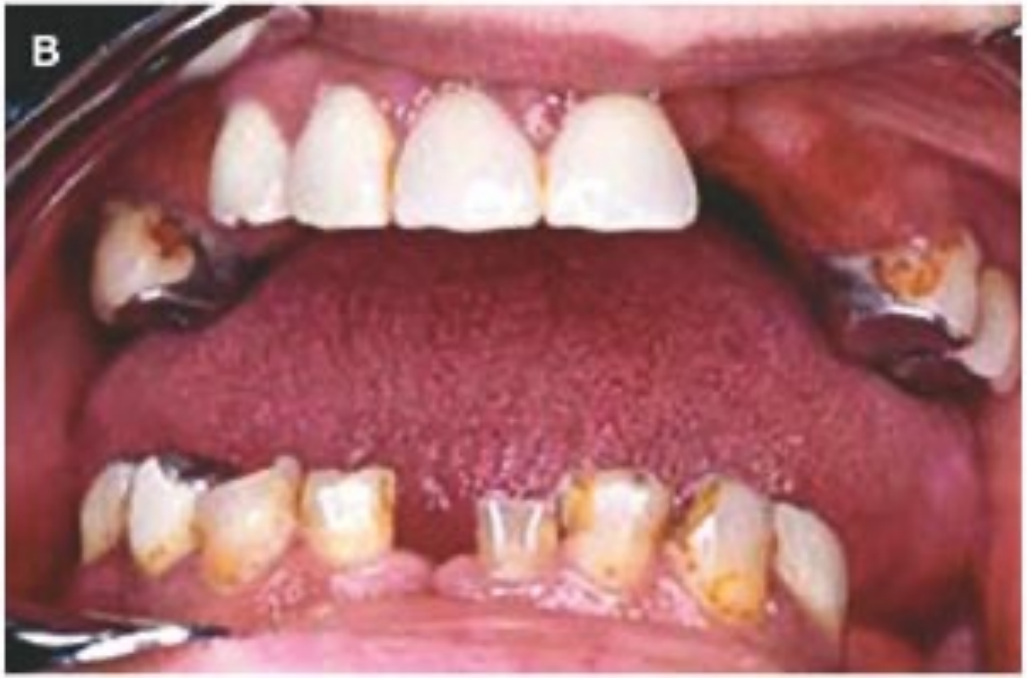
- Female between 35-45
- Enlarged salivary glands
- Raynaud phenomenon
- Keratoconjunctivitis sicca (dry eyes)
- Oral changes:
  - xerostomia (dry mouth)
  - mucosal atrophy
  - candidiasis
  - mucosal ulceration
  - caries
  - taste dysfunction



Sjögren syndrome: salivary gland enlargement

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

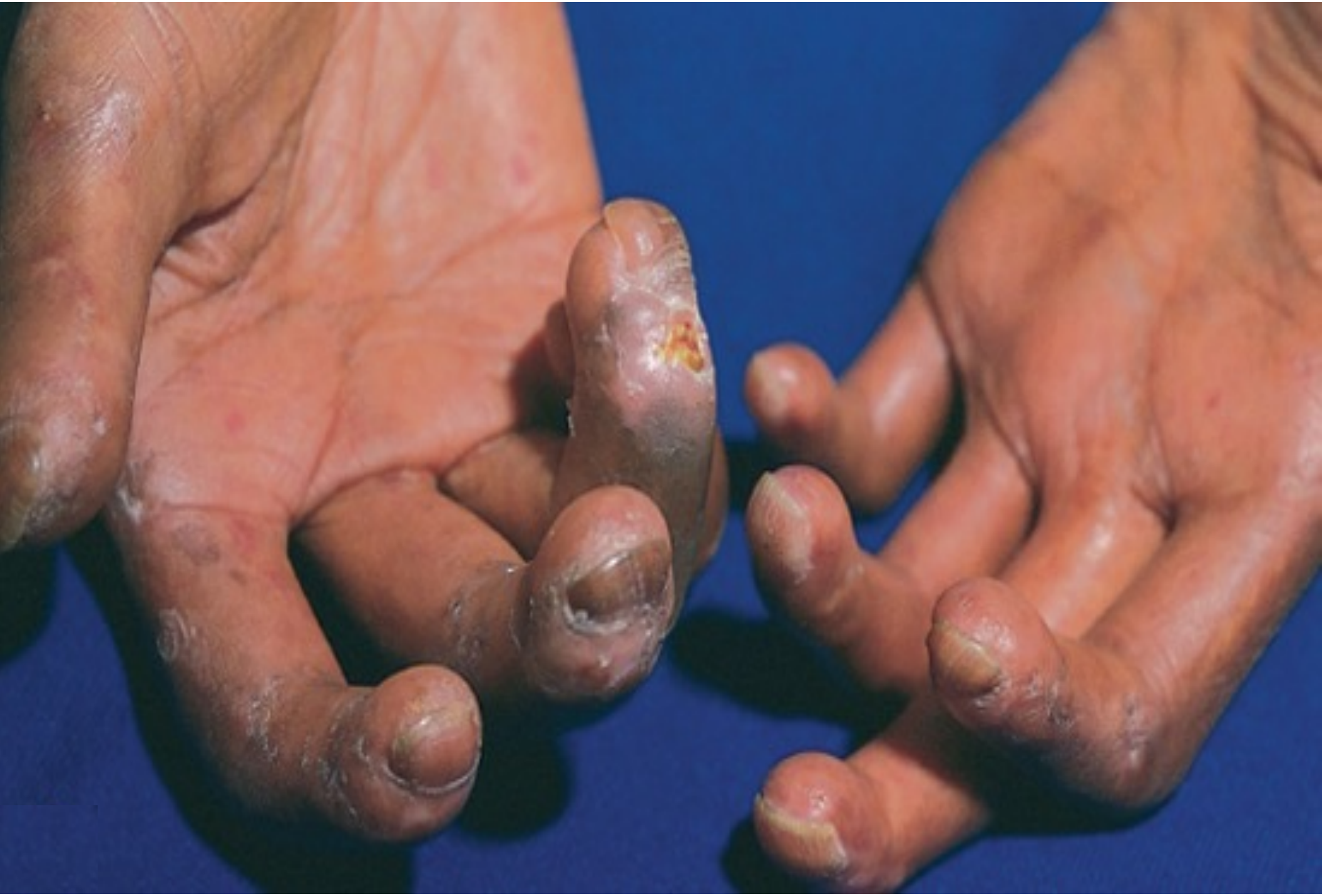
Scleroderma Etiology

- CD4+ T cells accumulate, and activate macrophages
- Macrophages release cytokines that stimulate collagen production (“fibrosis”)
- B cell activation also occurs but doesn’t play major role
- Autoantibody: anti-Scl 70

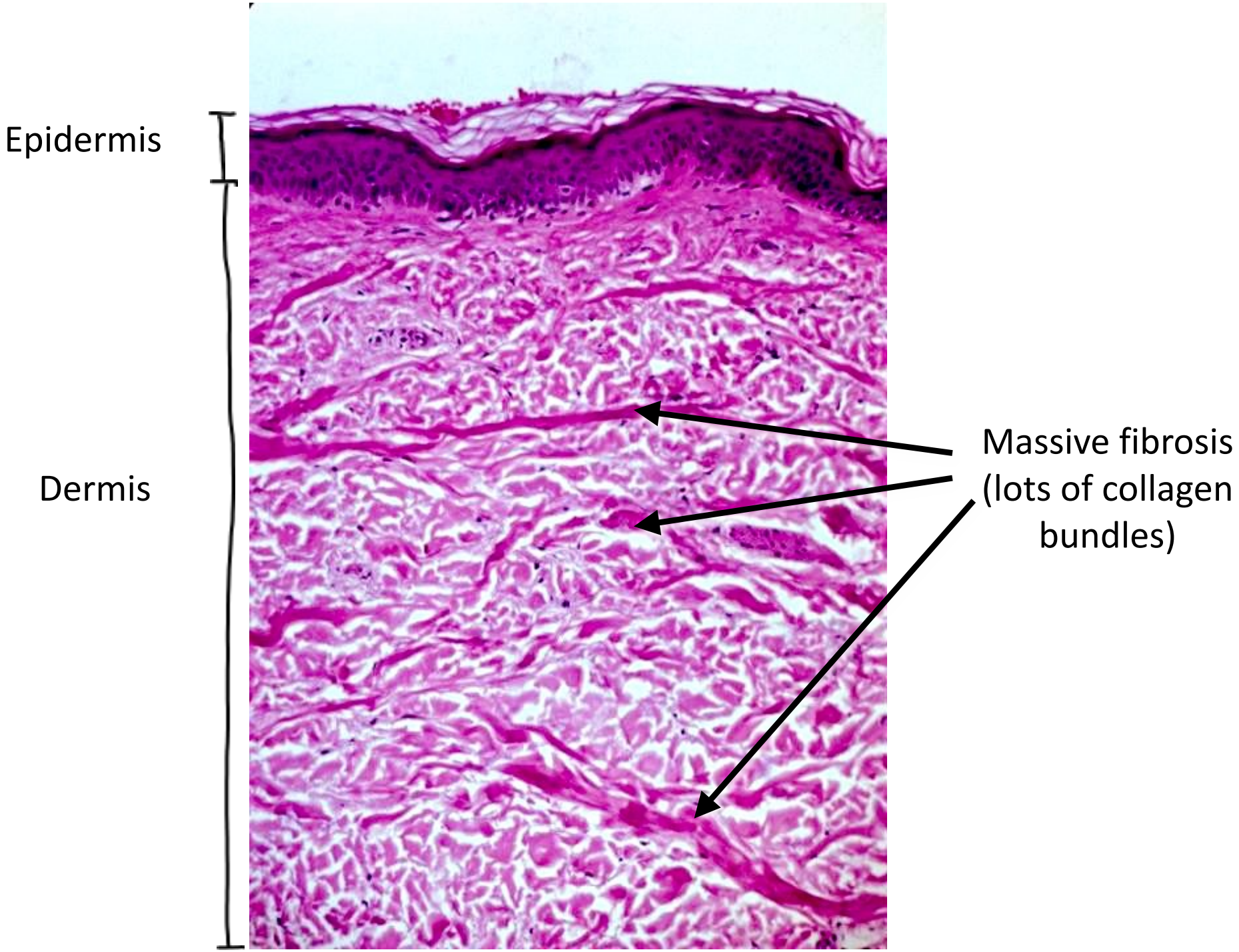
Scleroderma Signs and Symptoms

(Sclerosis = fibrosis)

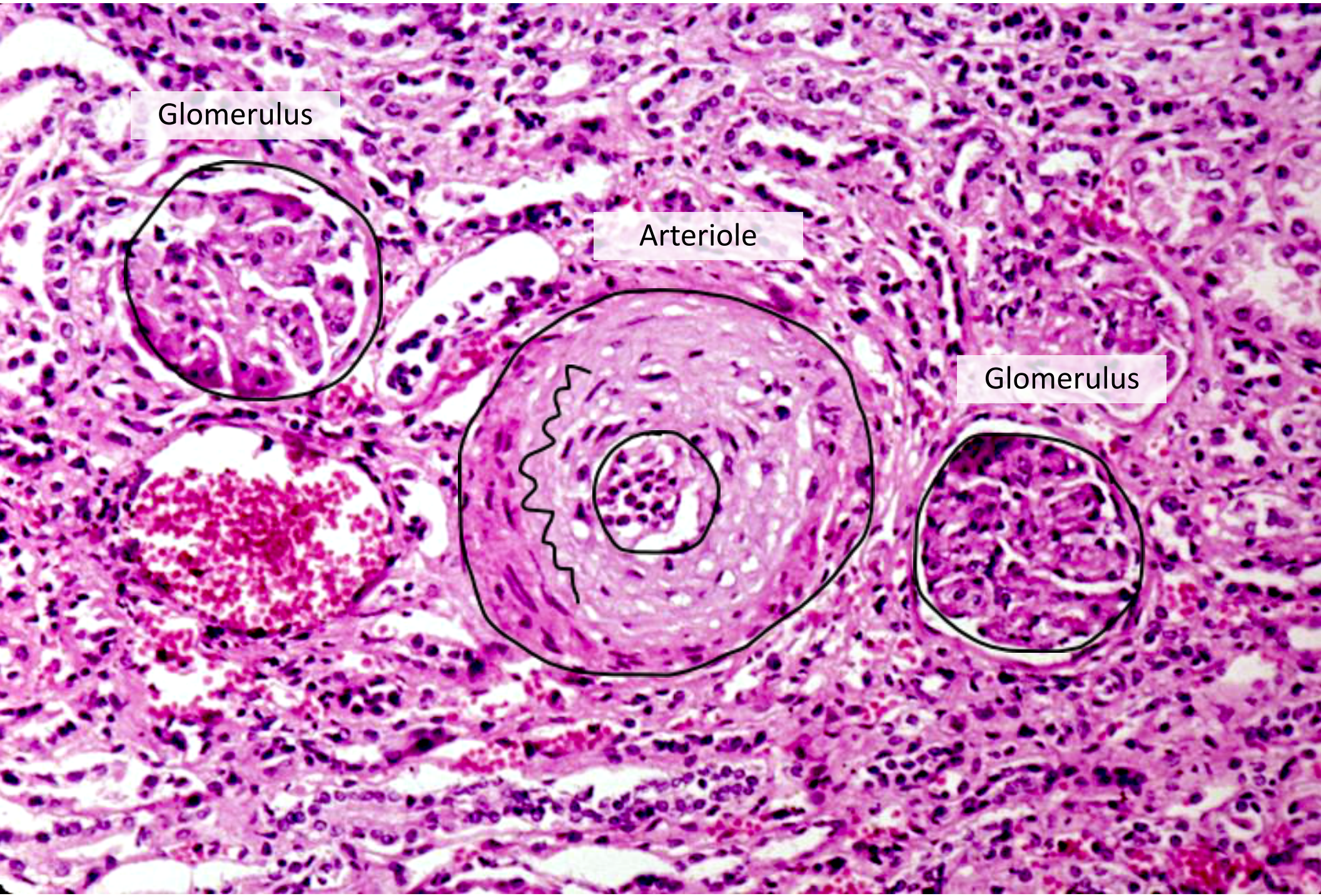
- Skin: diffuse, sclerotic atrophy. Fingers first.
- GI: “rubber-hose” esophagus
- Lungs: fibrosis, pulmonary hypertension
- Kidneys: narrowed vessels, hypertension
- Heart: myocardial fibrosis



Scleroderma: claw hands



Scleroderma: sclerotic skin



Scleroderma: narrowed renal vessel

Limited vs. Diffuse Scleroderma

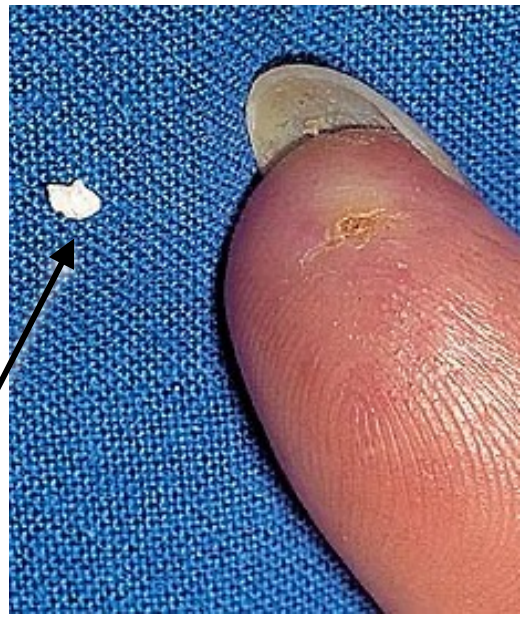
Limited Scleroderma

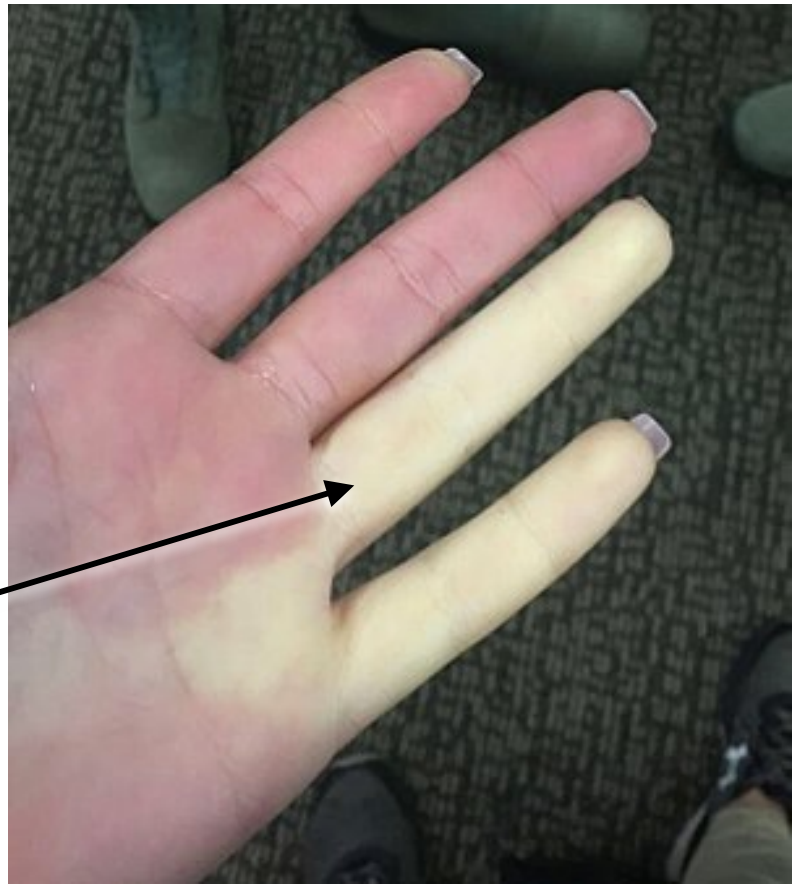
- Mild skin involvement
- Late visceral involvement
- Benign course

Diffuse Scleroderma

- Widespread skin involvement
- Early visceral involvement
- Rapid course

CREST Syndrome (considered “limited”





Calcinosis

Raynaud phenomenon

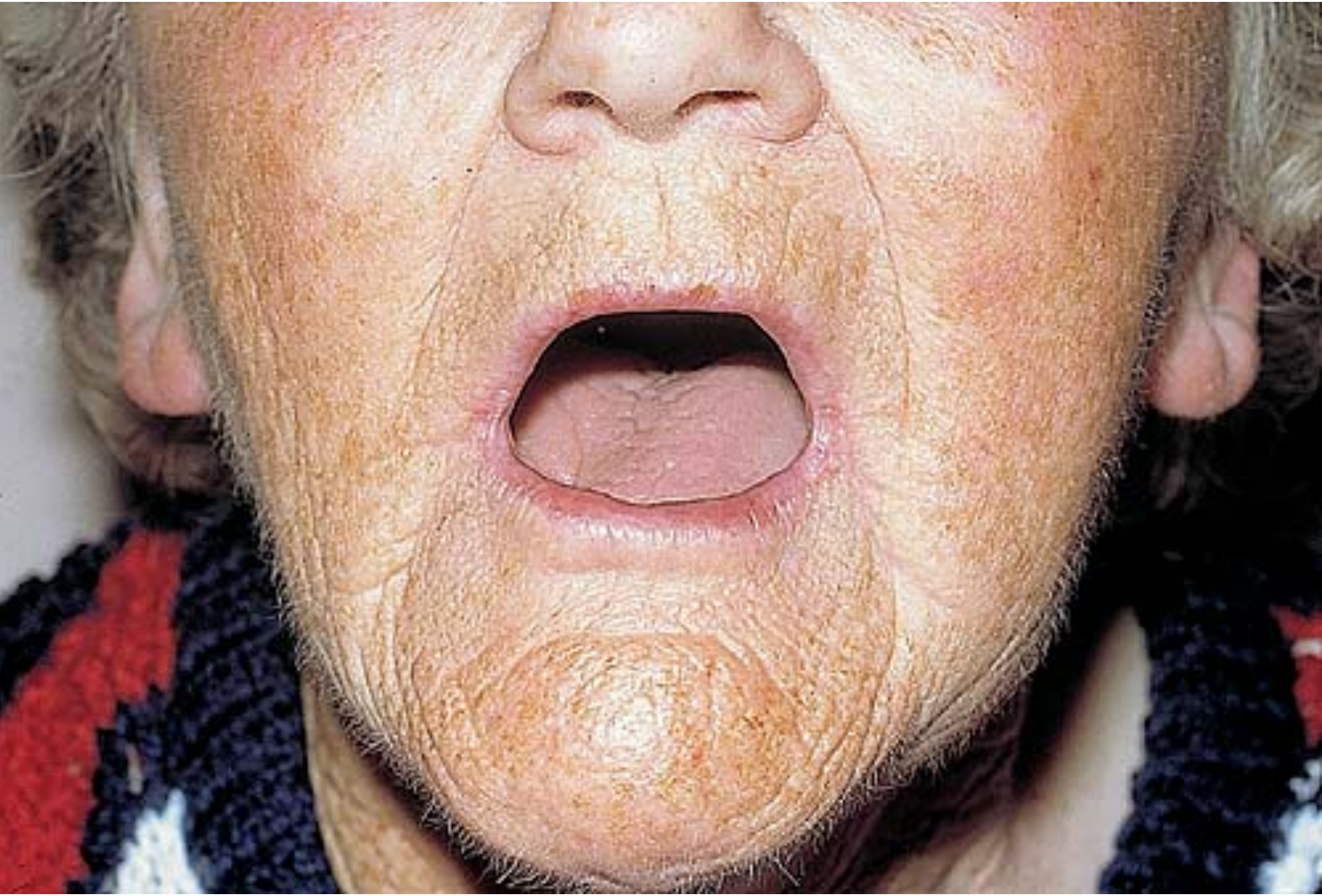
Esophageal dysmotility

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%