Osteoarthritis

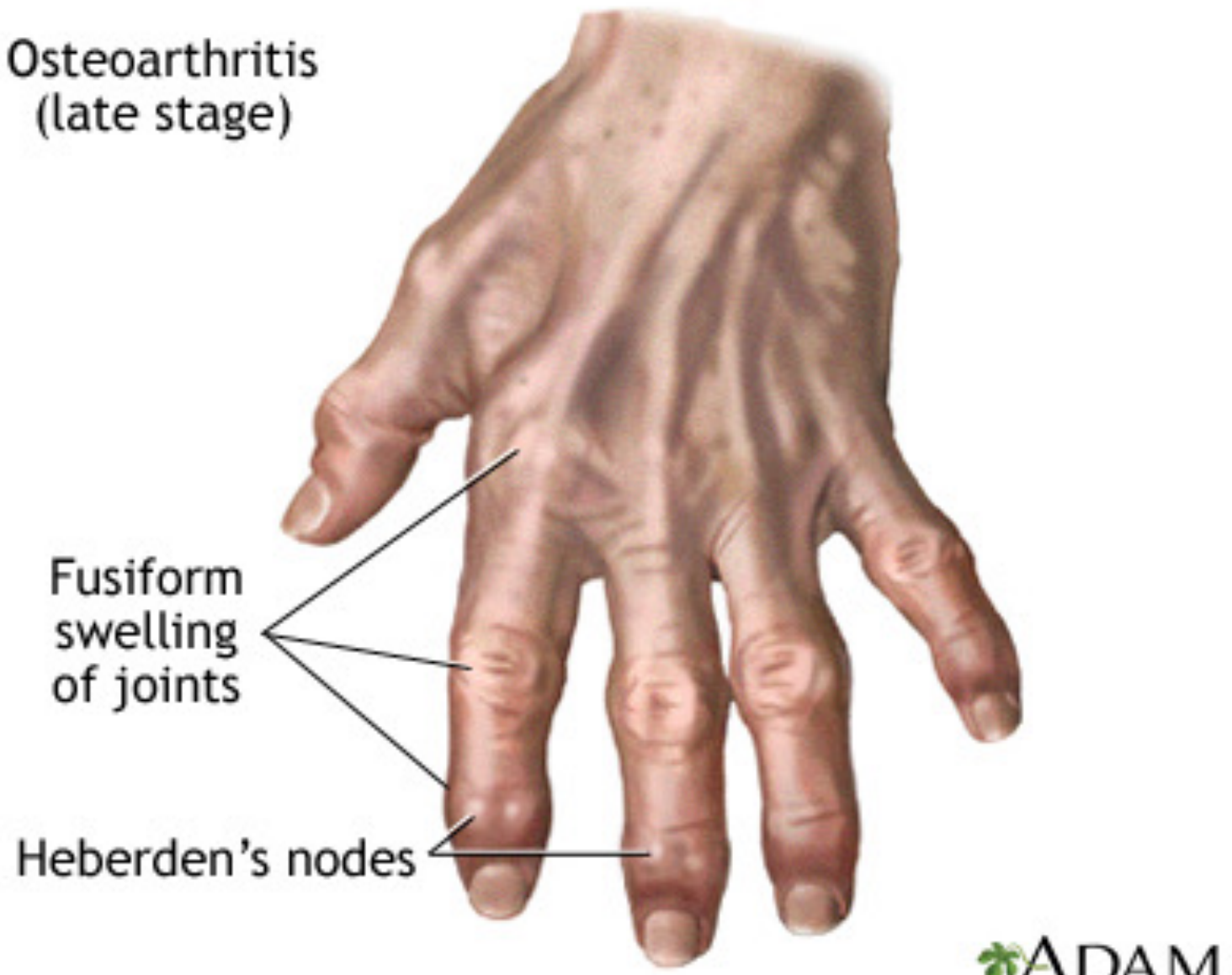
- Most common joint disease
  - Slow progressive degeneration of articular cartilage of weight bearing joints
  - Subchondral bony thickening and bony overgrowths (osteophytes; “spurs”); knobby protrusions at the margins of the distal interphalangeal joints → nontender Haberden’s nodes

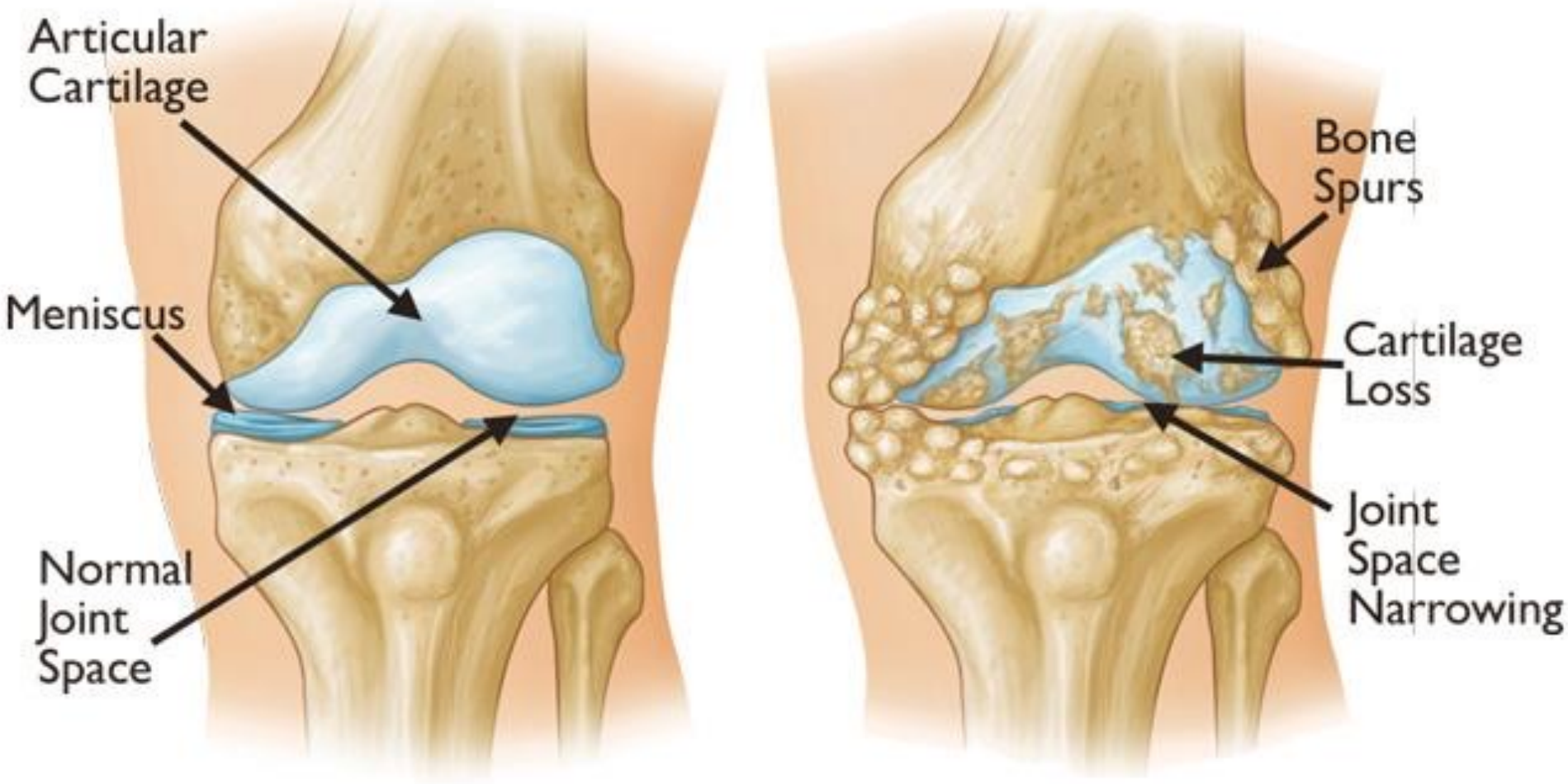
Osteoarthritis

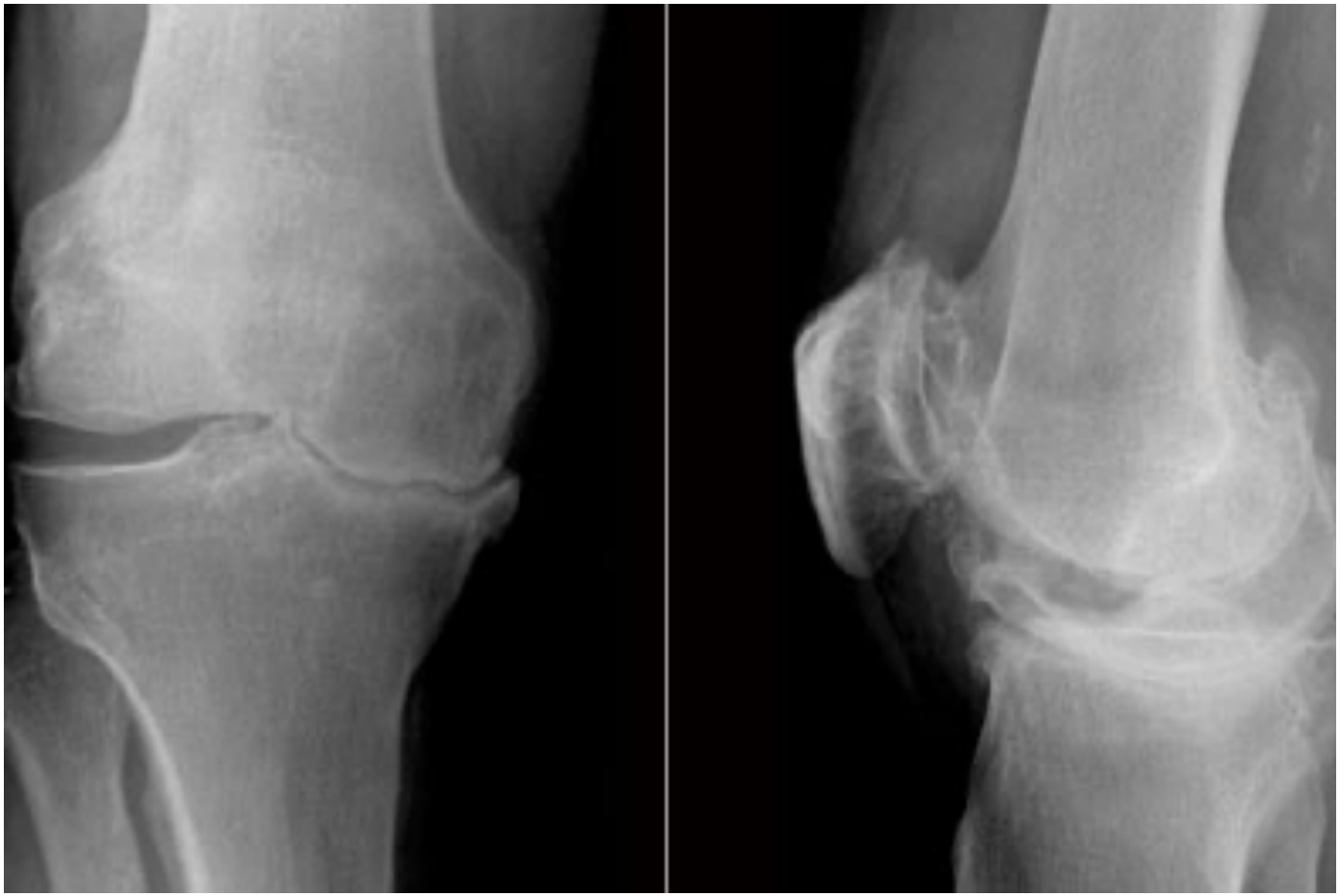
- Primary: defect in cartilage, not an inflammatory disease
  - Men in midlife, somewhat later in women
  - 80% of those over 70 years; nonlinear association
- Secondary: appears at any age in a previously damaged or congenitally abnormal joint (trauma, crystal deposits, infection)
- Knees, hips, cervical and lumbar spine

Osteoarthritis

- Loss of proteoglycans and areas of decreased number of chondrocytes alternating with areas of proliferating chondrocytes with matrix basophilia
- Narrowing of joint space (loss of disk)
- Increased thickness of subchondral bone
  - Fissures, pitting and flaking of cartilage with exposure of bone (eburnated bone)
- Subchondral bone cysts
- Inflammation of the synovium
- Loose bodies in the joint


Osteoarthritis
(late stage)
Fusiform
swelling
of joints
Heberden's nodes
A.D.A.M.


Articular Cartilage
Meniscus
Normal Joint Space
Bone Spurs
Cartilage Loss
Joint Space Narrowing



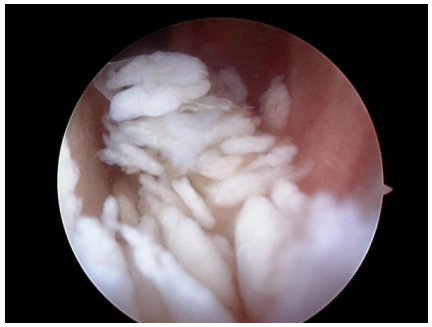
Rheumatoid arthritis

- Systemic chronic inflammatory disease affecting the synovium (IT IS A SYNOVITIS THAT LEADS TO DESTRUCTION AND ANKYLOSIS OF AFFECTED JOINTS)
- Autoimmune disease; 1% world prevalence
- 3:1 women (3^{rd}-4^{th} decade)
- Diarthrodial joints bilaterally
- Remissions and exacerbations
- Heredity; EBV(?)
- HLA-Dw4 haplotype and related B-cell alloantigen

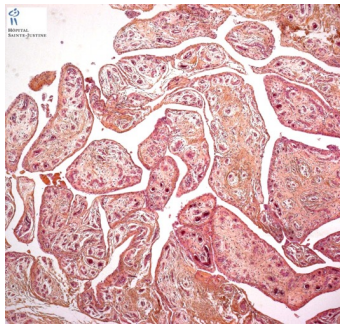
Rheumatoid arthritis

- Starts from the proximal joints of hands and feet then wrists, elbows, ankles, and knees
- Villous hypertrophy of the synovium
- Hyperplasia of the synoviocytes
- Intense lymphoplasmacytic and histiocytic infiltrates
- The synovium forms a cloak (pannus) that fills the in the joint space
- Destructive enzymes and cytokines, and the pannus, destroy the articular surfaces
- Fibrous and bony ankylosis

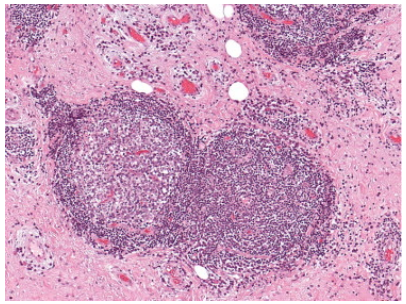
- Rice bodies



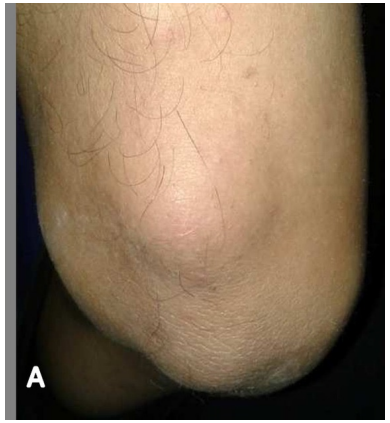
- Hyperplastic synovium and Pannus

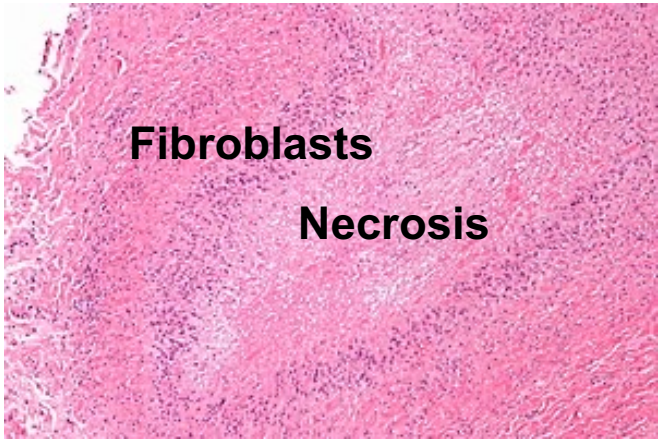


- Allison-Ghormley bodies



Rheumatoid nodules



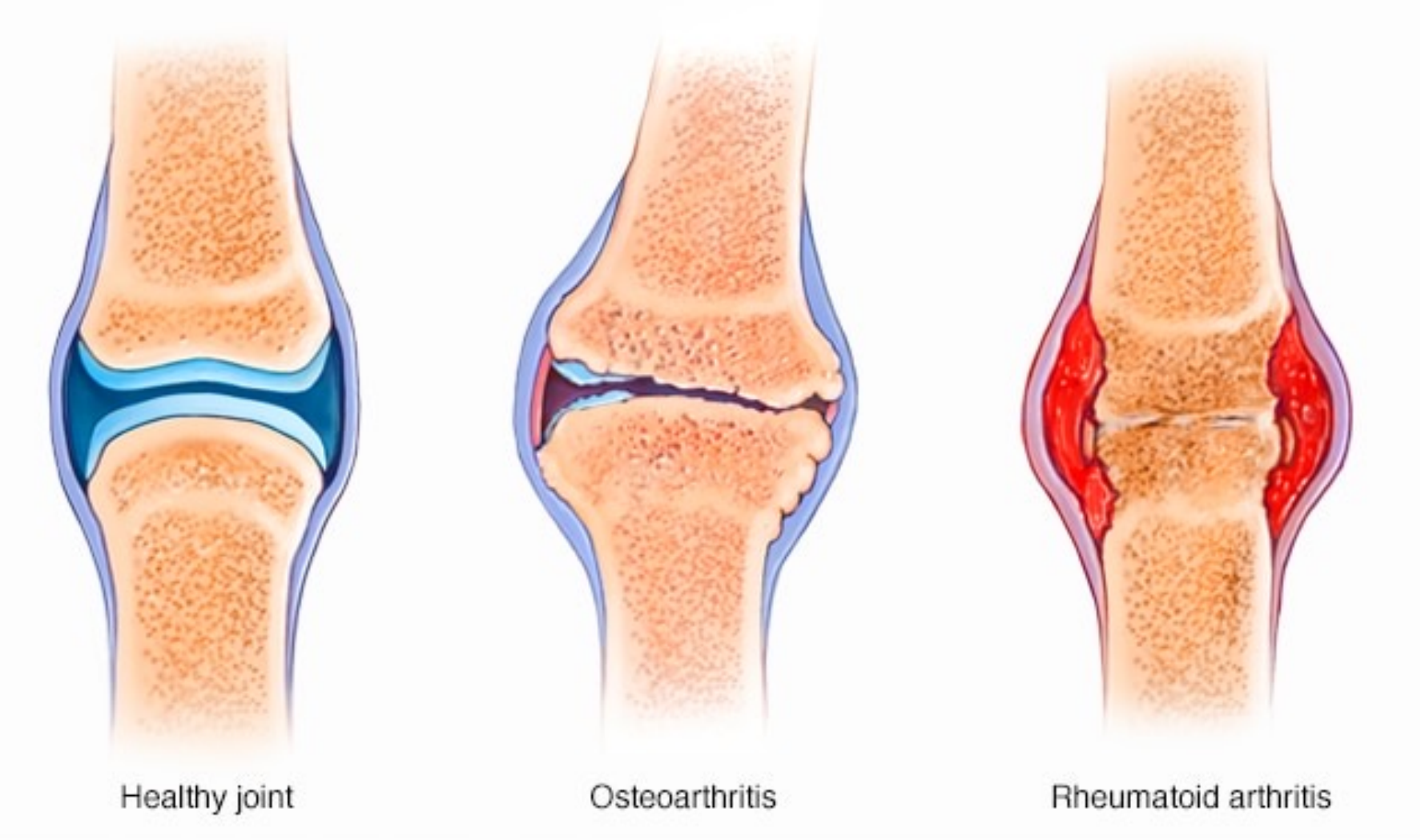


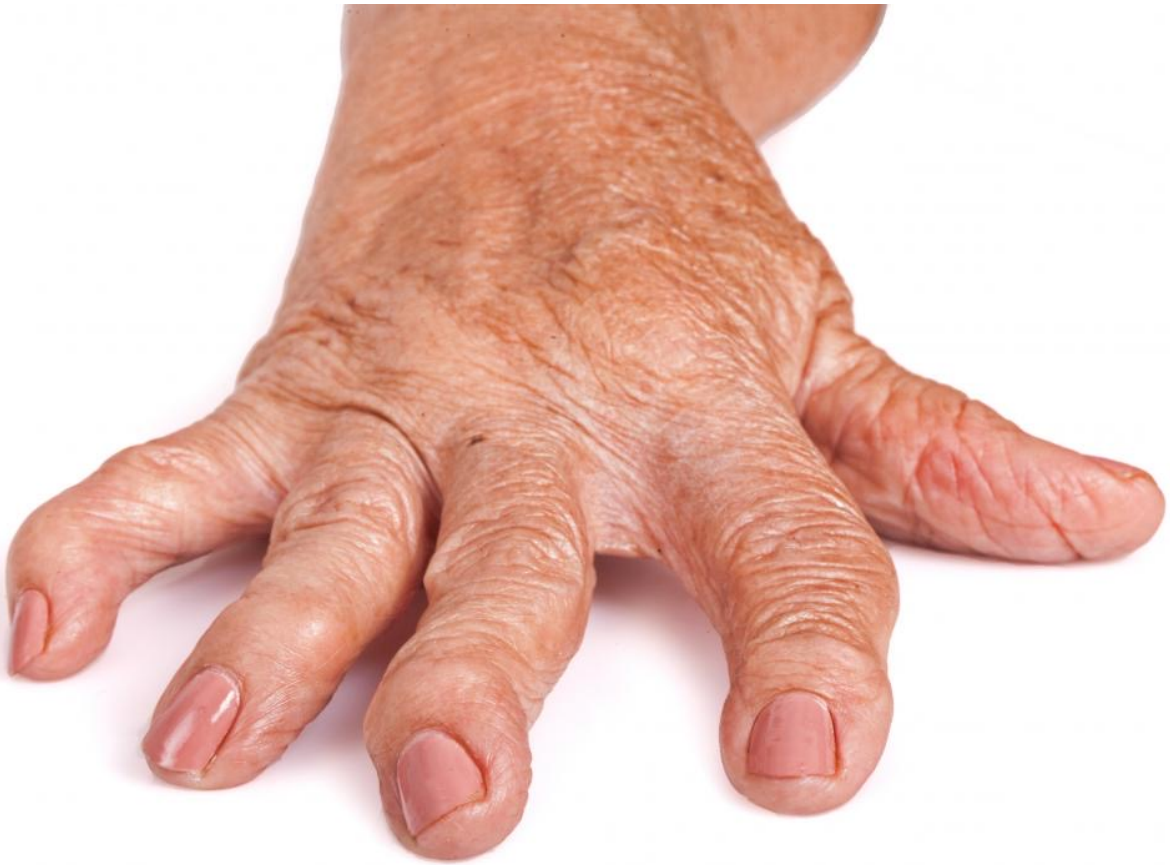
Non-joint manifestations

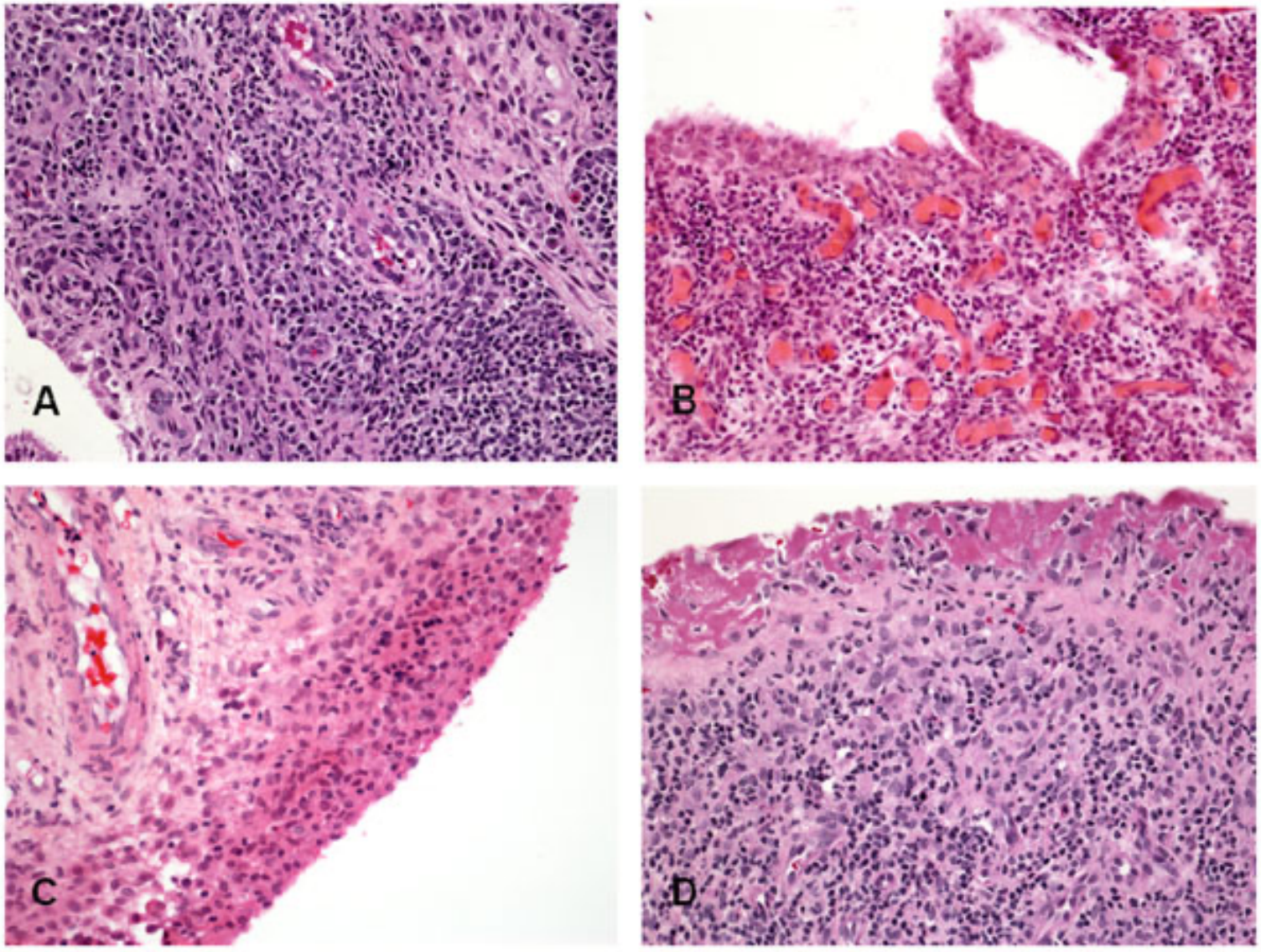
- Rheumatoid nodules in subcutaneous tissue
- Vasculitis
- Fibrosing inflammatory lesions of the lungs, pleura, pericardium, myocardium, peripheral nerves, and eyes.

Theory of Pathogenesis

- Genetically susceptible patient; HLA-DR4
- Infection? Prime suspect is EBV; mycoplasma, mycobacteria
- Inflammatory synovitis initiates and autoimmune response with formation of Abs
  - CD4+ are activated → release of IL-1 and TNFalpha → lysis of cartilage
- Autoantibodies against IgG and production of the rheumatoid factor (usually IgM, IgA, IgE and IgG); 20% of patients are RF negative
- Deposits of immune complexes in the synovium
- Activation of complement cascade
- Inflammation
- Activation of macrophages
- Homing of T cells
- Secretion of cytokines



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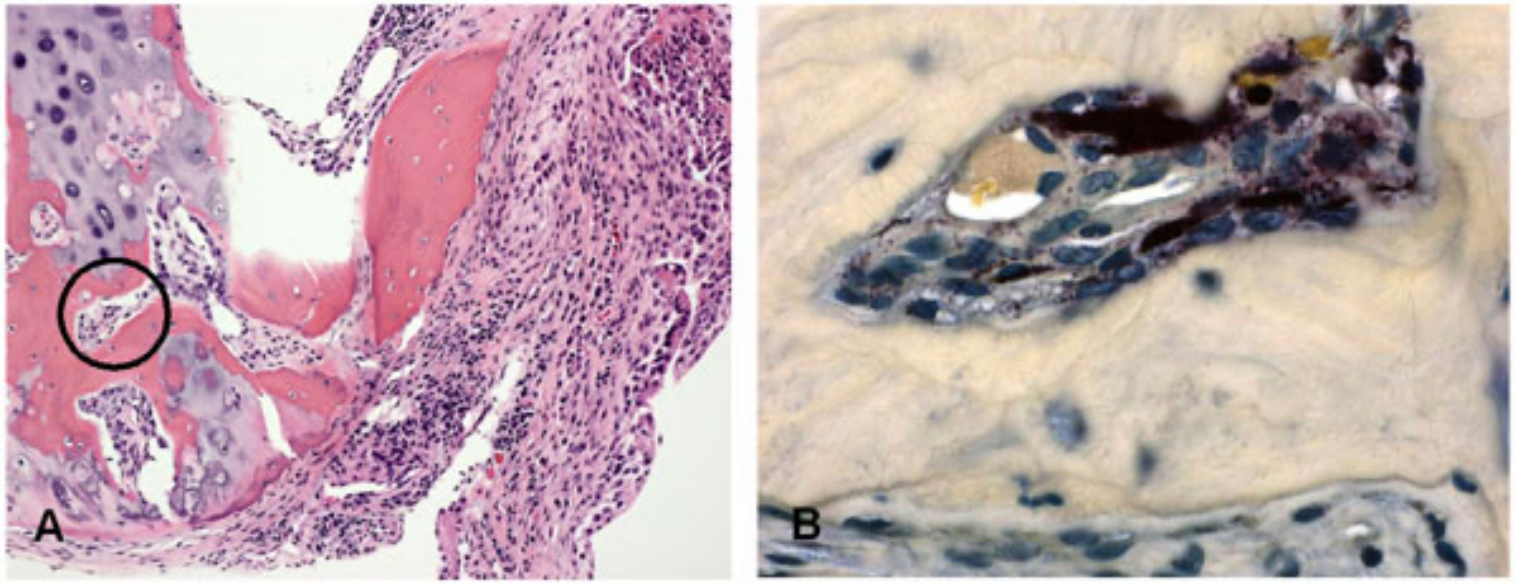
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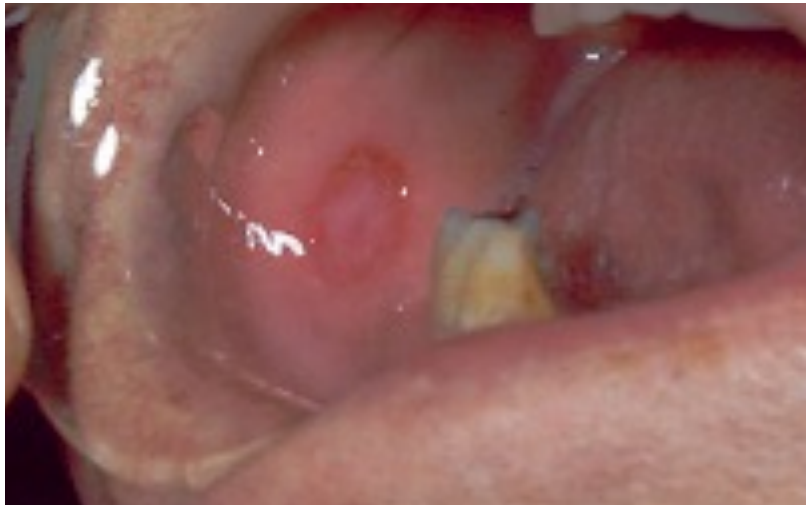
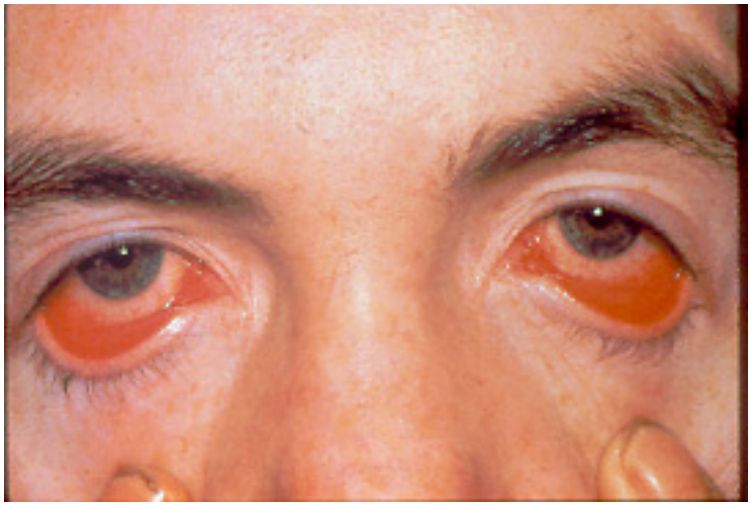
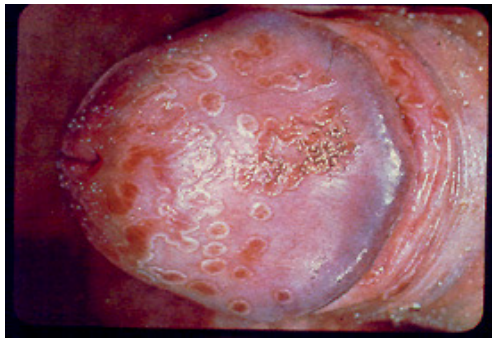
Spondyloarthropathy

- Used to be a type of RA
- NOW comprises a group of diseases
  - Ankylosing spondylitis
    - Vertebral column & sacroileac joints, young men
  - Reactive arthritis (Reiter syndrome)
    - Polyarthritis, conjunctivitis, non-gonococcal urethritis, oral lesions
  - Psoriatic arthritis
  - Arthritis and inflammatory bowel disease (enteropathic arthritis)
    - Crohn's dz, ulcerative colitis

Reactive arthritis







Gout

- Hyperuricemia
  - It is necessary for gout, but only a few fraction of hyperuricemic people develop gout
- Idiopathic
- Predisposing factors: alcohol, obesity
- Most cases occur in men; Almost never in women before menopause
- Attacks of acute arthritis triggered by crystallization of urates in joints
- Asymptomatic intervals
- Eventual development of chronic tophaceous gout and arthritis

Primary gout

- Hyperuricemia in the absence of other disease
  - Asymptomatic hyperuricemia can precede gout
- Impaired secretion by kidneys

Secondary gout

- Hematopoietic pathologic conditions
  - Leukemias
  - Lymphomas
- After chemotherapy
- Alcoholism

Clinical features

- Acute gouty arthritis
  - Painful
  - Involves one joint initially, then polyarticular
  - Podagra (painful, red metatarsophalangeal joint)
- Tophaceous gout
  - Development of tophi
    - Chalky, cheesy, yellow-white, pasty deposits of monosodium urate crystals
  - Helix and antihelix of ear
  - Achilles tendon

Gout

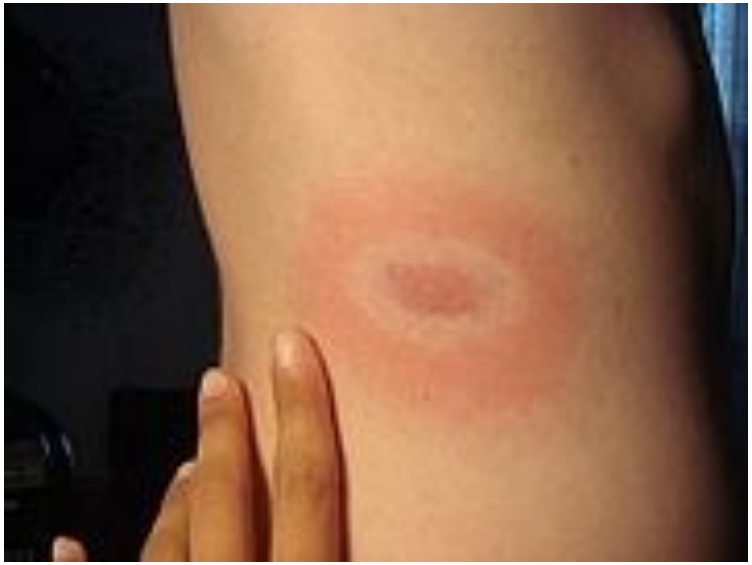
- Pathology
  - Formation of granulomas with needle-shaped crystals
- Renal failure, urate stones
- Treatment
  - Colchicine
    - Prophylactic
  - Probenecid & sulfinpyrazone
    - Interfere with urate resorption
  - Allopurinol
    - Inhibitor of enzyme that converts the xanthine and hypoxanthine to uric acid

Pseudogout

- Chodrocalcinosis
- Calcium pyrophosphate crystals deposits in joints
- Older individuals
- No gender, race predilection
- 30-60% prevalence
  - There is a hereditary form
- Can cause significant joint damage
  - Knees, wrists, elbows, shoulders, ankles

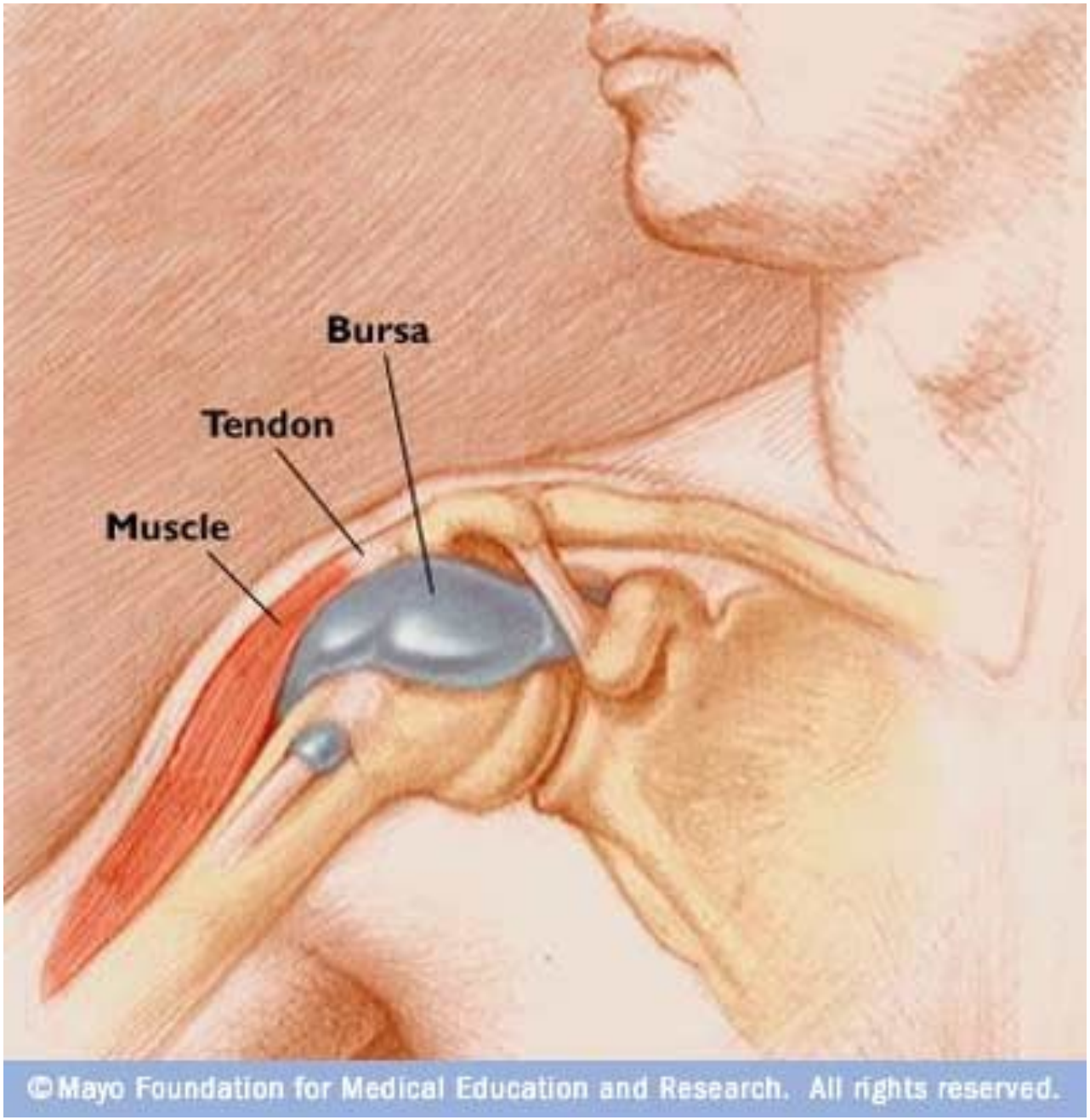
Lyme disease

- Ring-like rash at the site of the bite
  - Erythema chronicum migrans
- Migratory joint pain and subsequent oligoarthritis



Bursitis

- Inflammation of the bursa
  - elbow, shoulder, knee
- Fibrous thickening of the bursa wall
- Tendency to double-fault in tennis and develop a bad slide in golf

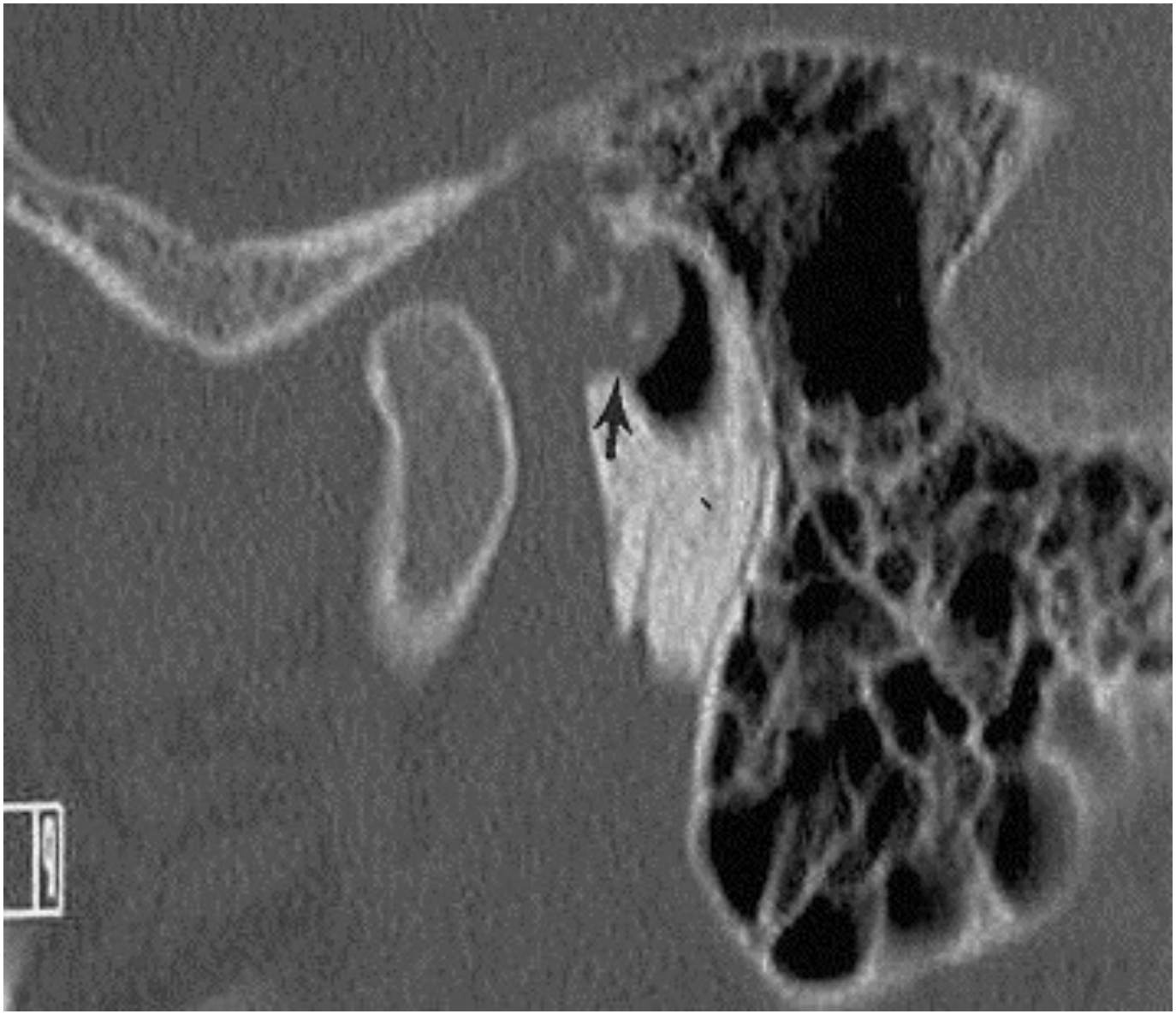


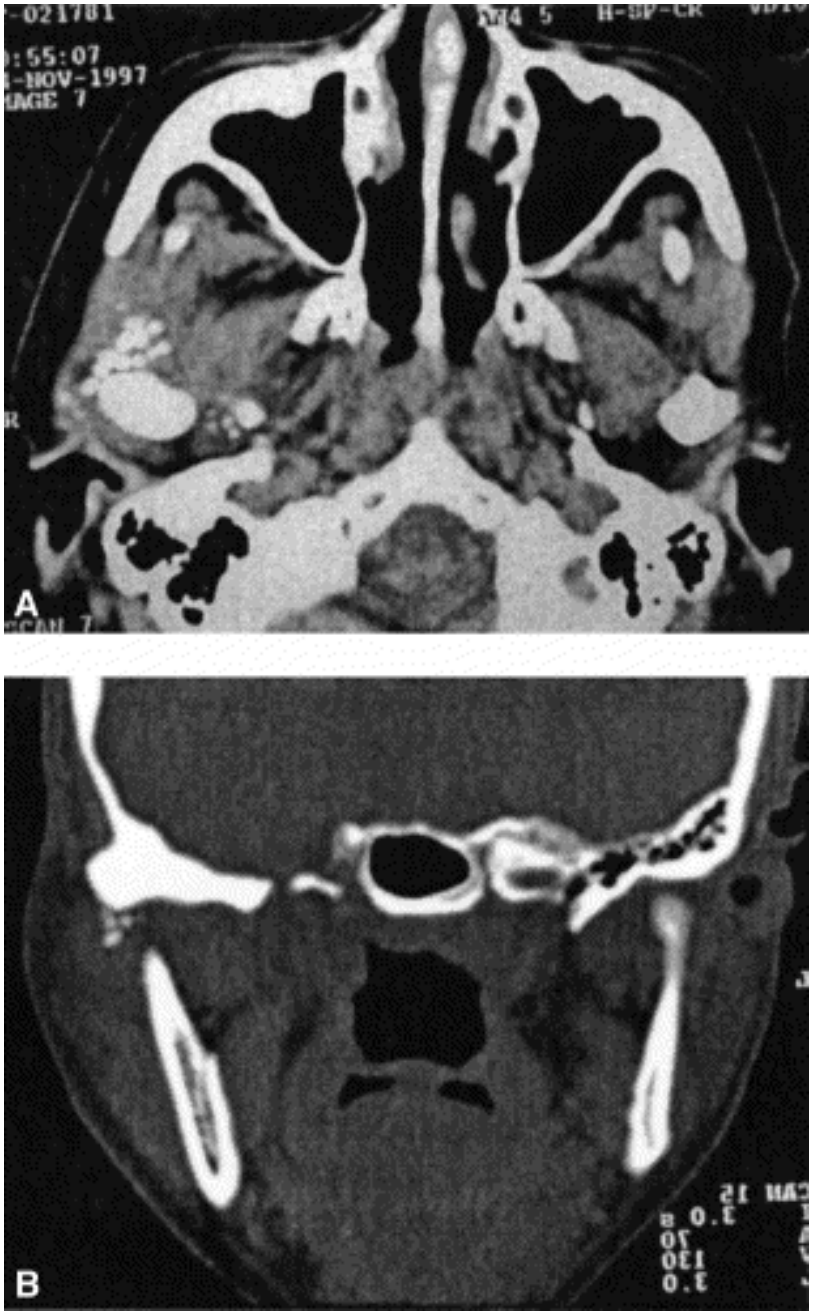
Tumors and Tumor-like Conditions

- Ganglion cyst: Wrist; connective tissue cyst; near the joint capsule or the tendon sheath
- Synovial cyst: herniation of synovium through the joint capsule (Baker cyst; popliteal fossa)
- Pigmented villonodular tenosynovitis
  - Knee, hip, ankle, pain
- Giant cell tumor of tendon sheath
  - Painless mass; wrist; Most common soft tissue tumor of the hand

Synovial Chondromatosis

- 18-75 years (median 45)
- More frequent in women in contrast with other joints
- Pain (82%) , swelling (65%), combination (50%), crepitus
- X-ray: Loose irregular radiopaque bodies
- Treatment: Removal of loose bodies, some surgeons do total synovectomy



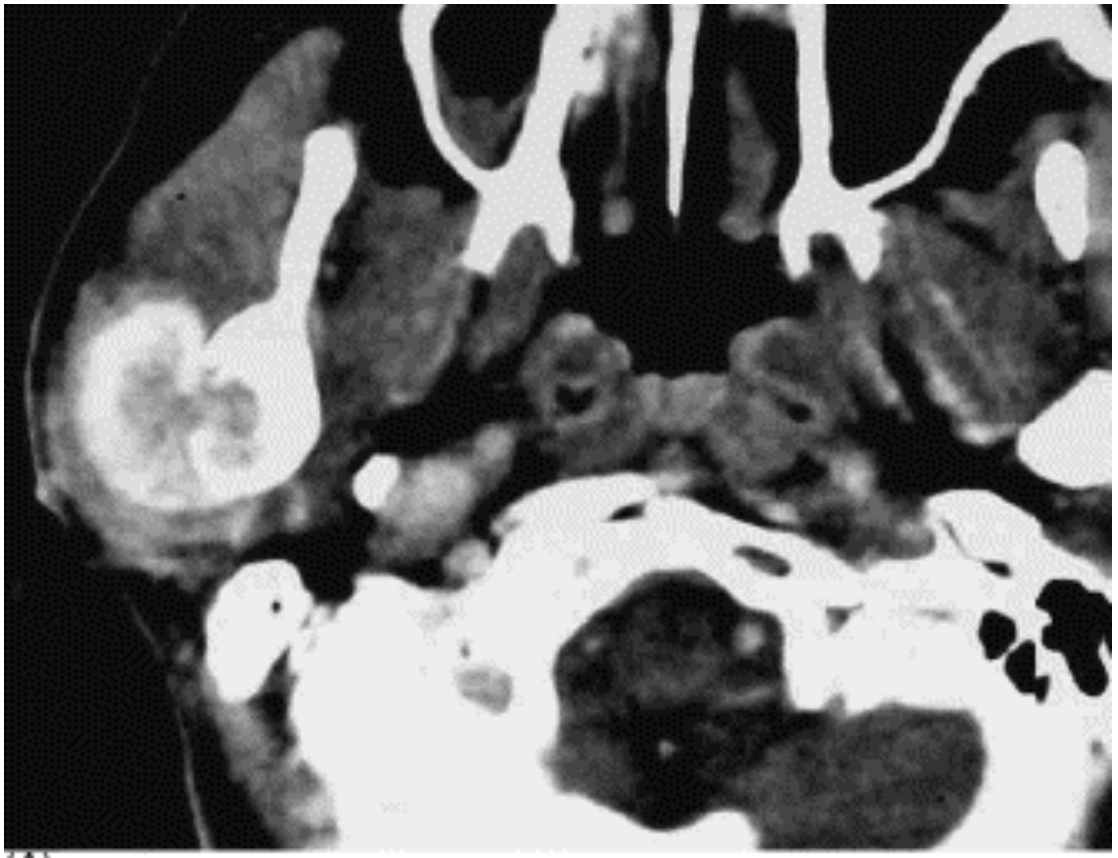

A
B

Osteochondroma

- Most frequent neoplasm of bone
- Cartilage capped bone projection
- Metaphysis
- Condylar is rare; coronoid even rarer
- Median age ~40 for condylar
- ~2F:M

Pigmented villonodular synovitis

- Uncommon
- 10-70 years
- Patients are rarely younger than 30
- Average age 43.7
- Slight female predominance
- Swelling, pain
- Bone erosion
- Diffuse or localized; diffuse can be very aggressive
- Inflammation, giant cells, hemosiderin, regular mitoses



(A)

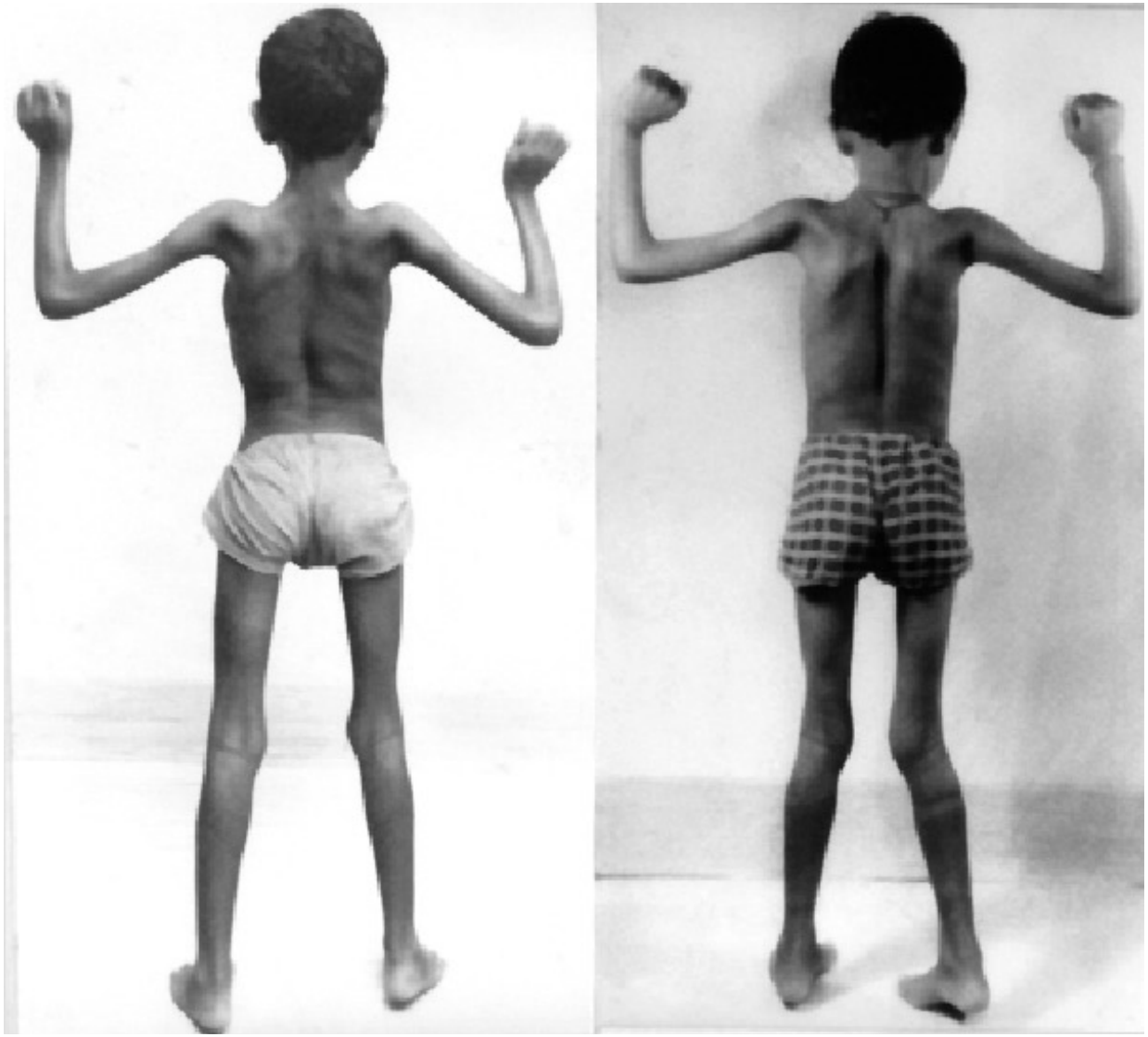
Ganglion and synovial cyst

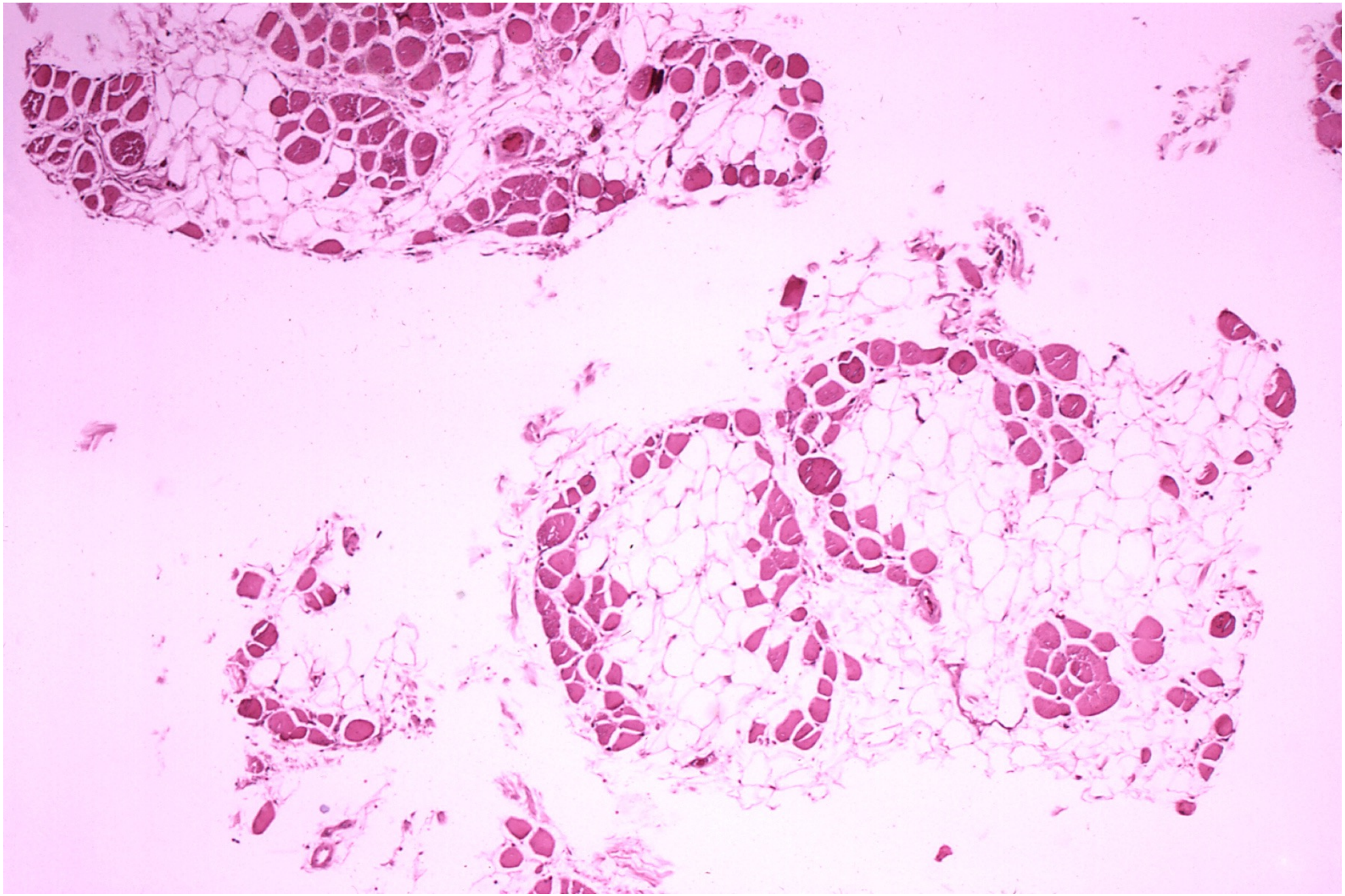
- Confusion with the name
- Ganglion is a pseudocyst: myxoid degeneration; does not have synovial lining
- Synovial cyst: lined by cuboidal to flattened cells
- Preauricular swelling, pain

Skeletal Muscle Pathology

Duchene muscular dystrophy

- X-linked
- Pelvic and shoulder girdles
- Deletion of gene that encodes dystrophin (*DMD*)
  - Dystrophin is made in the heart and skeletal muscle
  - Also in neurons in the hippocampus
- Degeneration of muscles, impaired repair, fibrosis, fibrofatty deposits
- Elevated serum creatinine kinase
- Steroid treatment
- Death form respiratory insufficiency, cardiac arrhythmia, 10-15 years of age wheel chair-bound



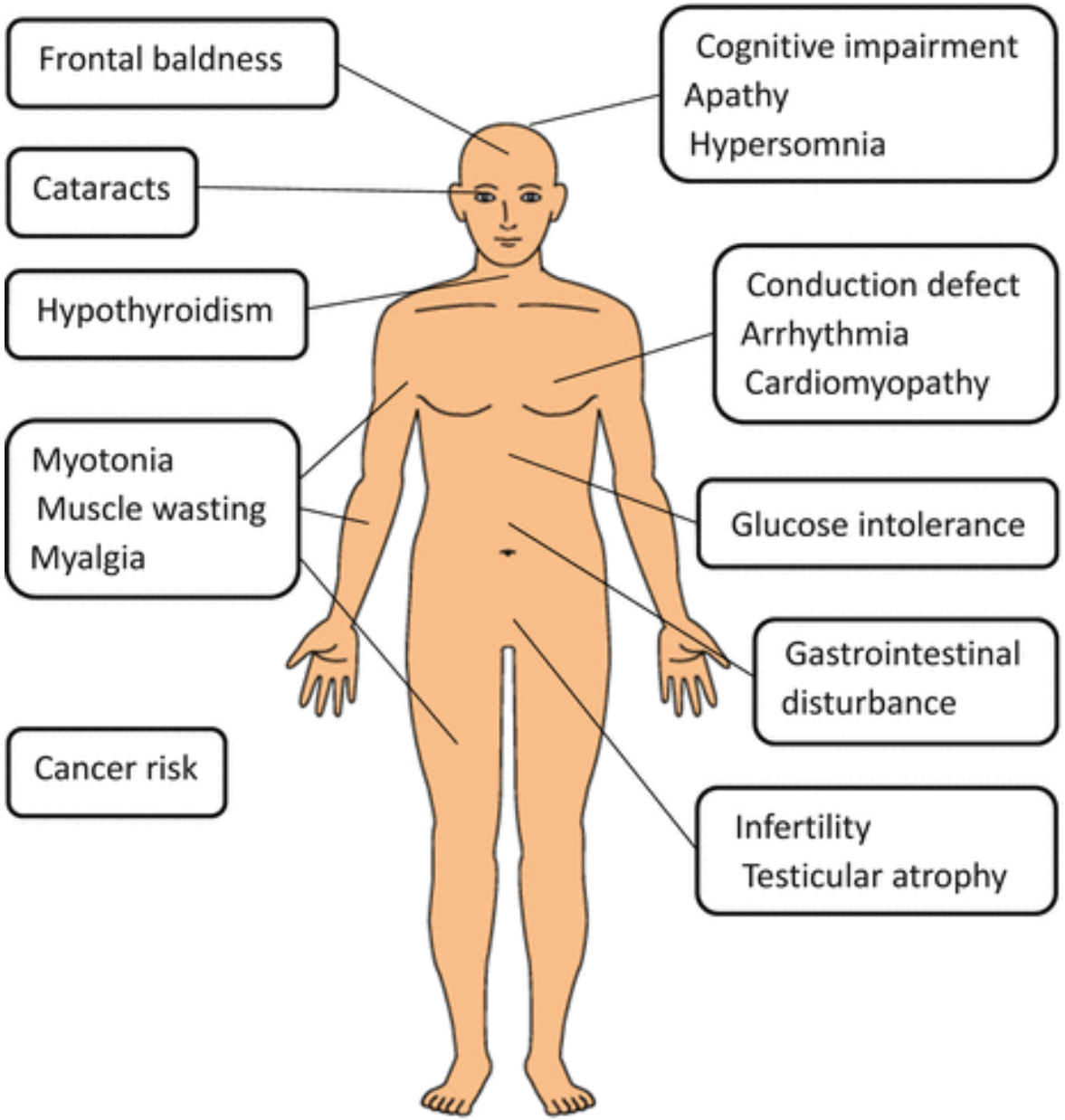


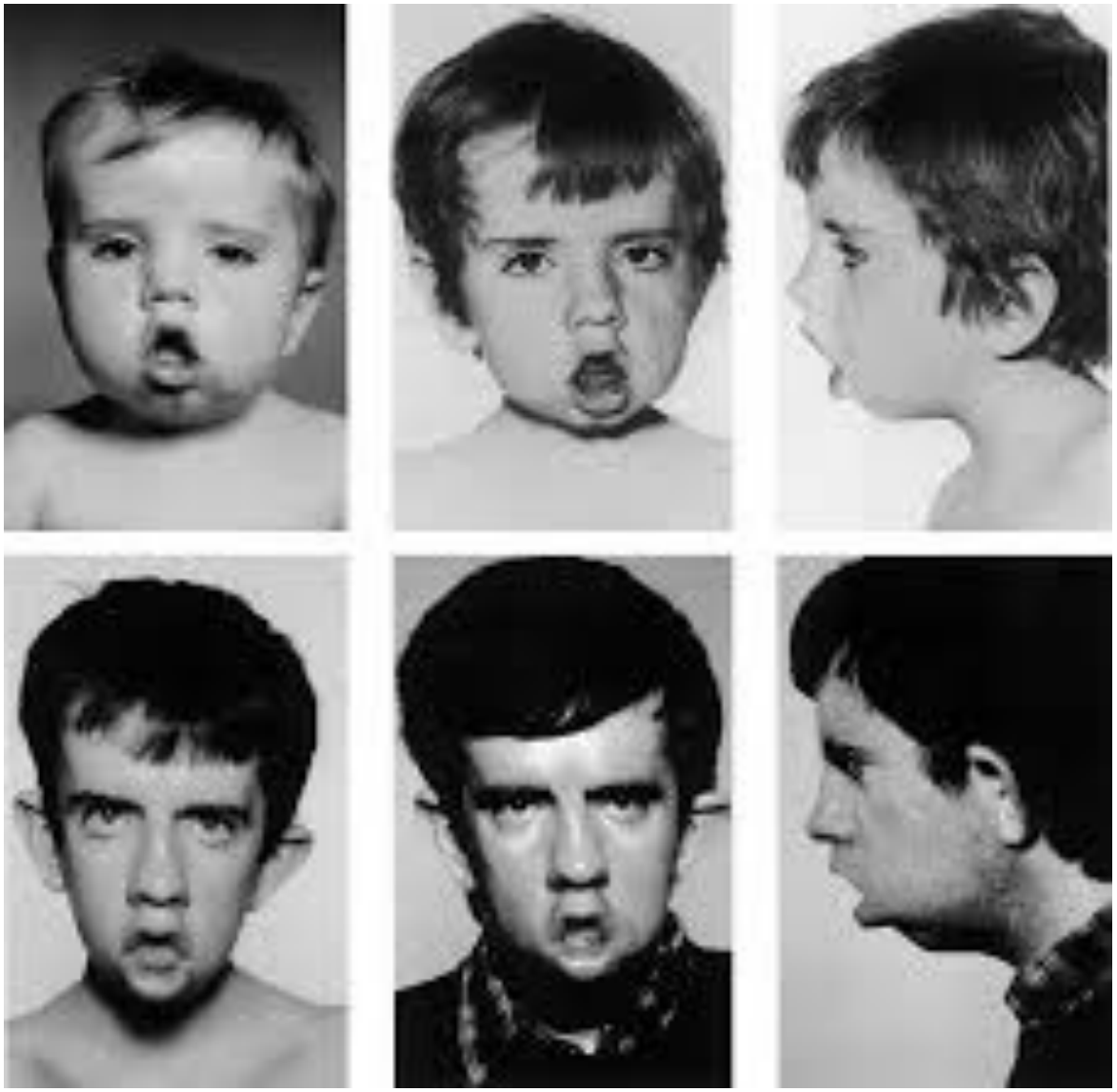
Myotonic dystrophy

- AD
- Most common form of adult MD
- Sustained muscular contractions and rigidity
- Progressive muscle weakness and wasting
- Chromosome 19
- Atrophy of type I and hypertrophy of type II fibers
- Anticipation
  - Earlier age of onset and increased severity in successive generations

Myotonic dystrophy

- Three clinical groups
  - Congenital
  - Adult: facial and jaw muscles, ptosis
  - Late: minimal symptoms


Frontal baldness
Cataracts
Hypothyroidism
Myotonia
Muscle wasting
Myalgia
Cancer risk
Cognitive impairment
Apathy
Hypersomnia
Conduction defect
Arrhythmia
Cardiomyopathy
Glucose intolerance
Gastrointestinal disturbance
Infertility
Testicular atrophy

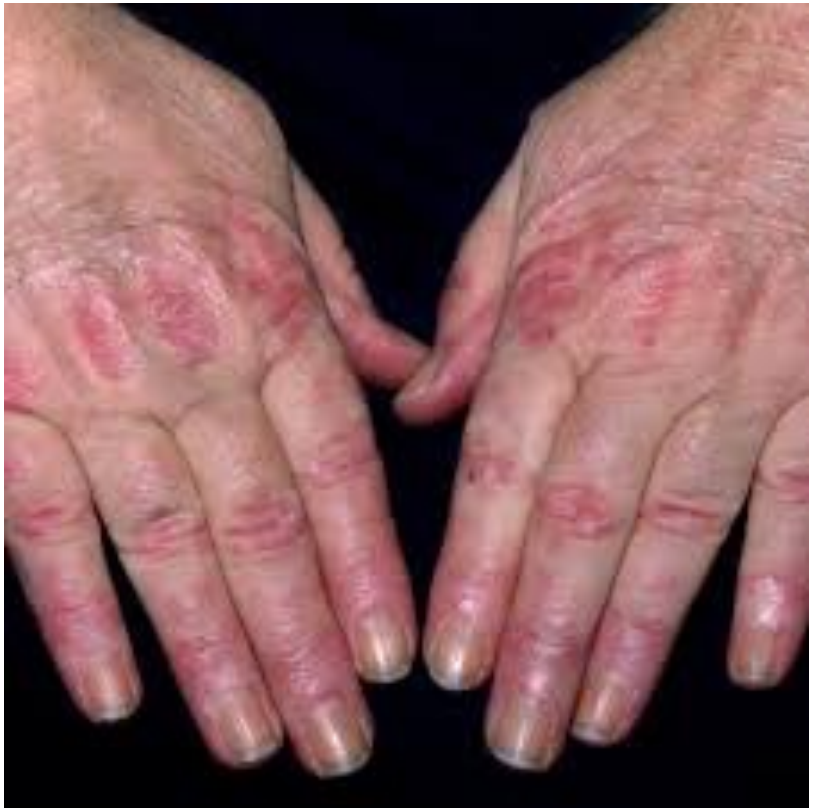


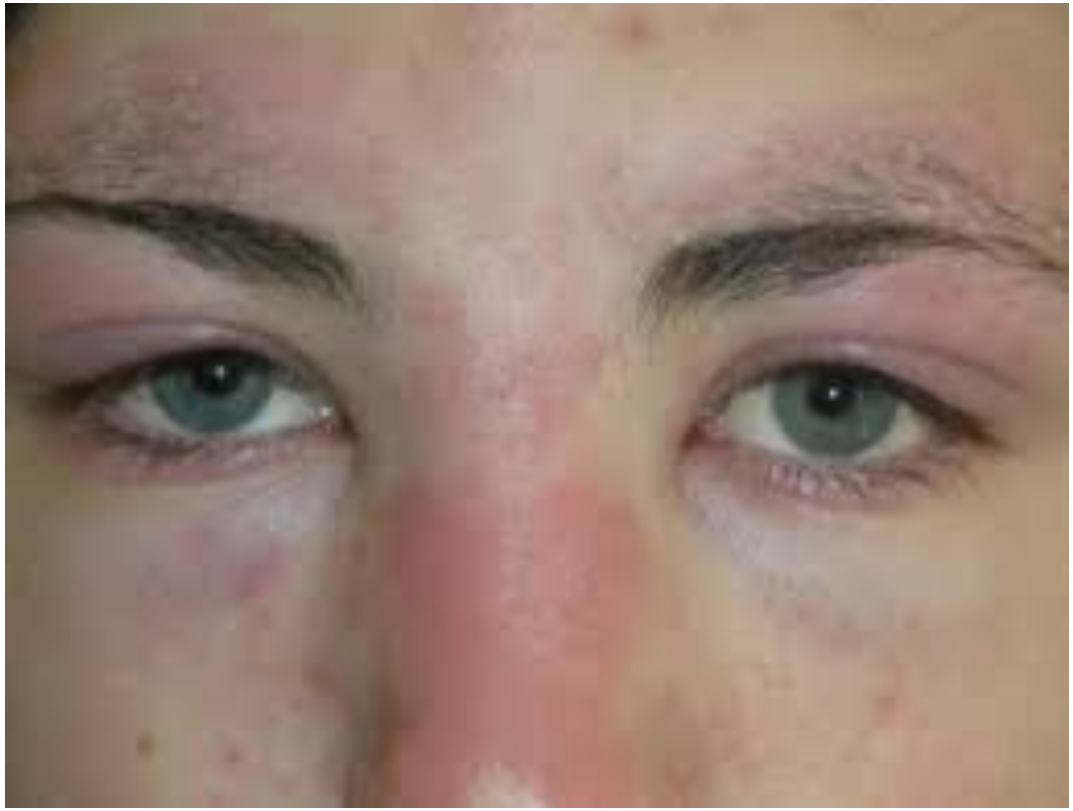
Autoimmune Myopathies

- Dermatomyositis
  - Complement mediated cytotoxic Abs against microvasculature of muscle
  - Distinctive skin rash
    - Face and eyelids and on knuckles, elbows, knees, chest and back
    - The rash, which can be itchy and painful
    - It is often the first sign of dermatomyositis.
  - Muscle weakness
    - Muscles closest to the trunk, such as those in your hips, thighs, shoulders, upper arms and neck
  - Inflammatory myopathy

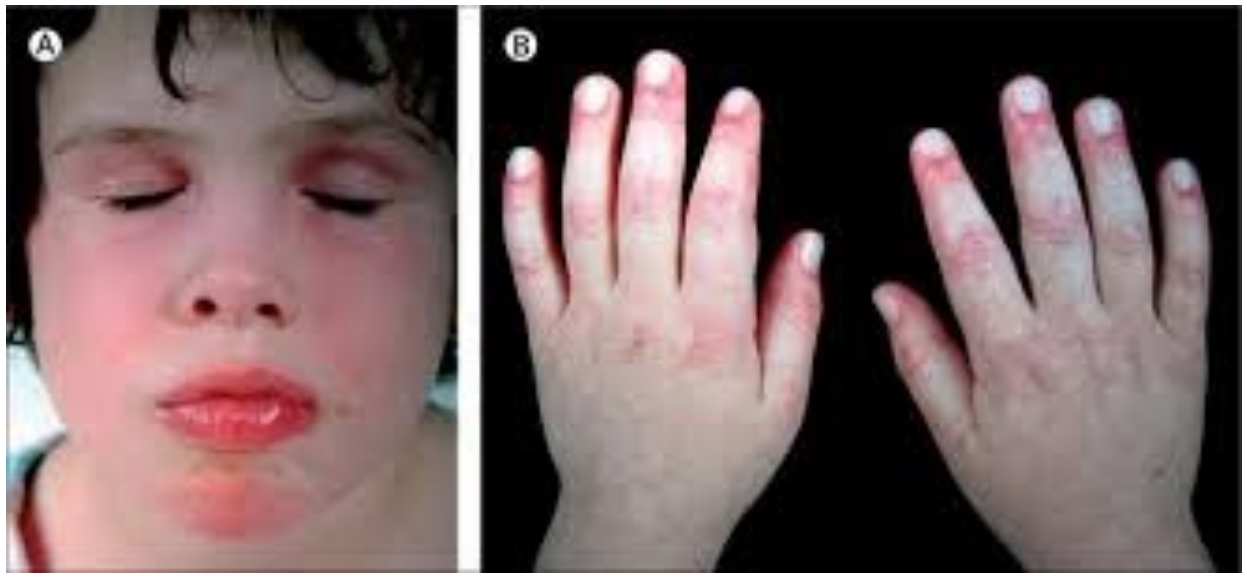
Dermatomyositis - Complications

- Dysphagia
  - Muscles in your esophagus are affected
  - Weight loss and malnutrition
  - Aspiration pneumonia
- Shortness of breath
- Increased risk for cancer
  - Cervix, lungs, pancreas, breasts, ovaries and gastrointestinal tract
  - Raynaud's phenomenon
    - Cold and numb toes, fingers, ears and redness of the skin
- Calcium deposits
  - Muscles and skin (tumor calcinosis)





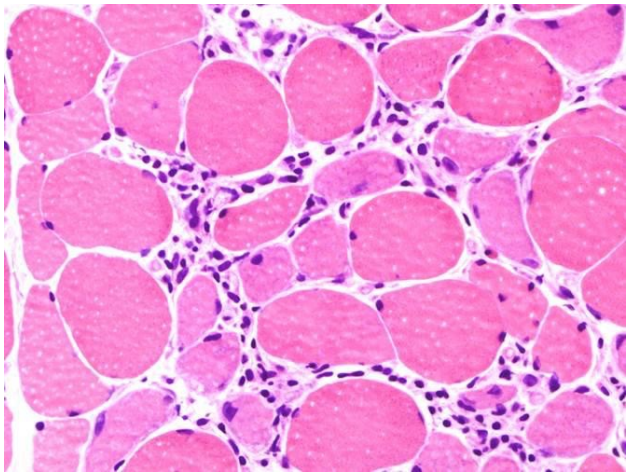
Dermatomyositis



Gingival and periungual juvenile dermatomyositis

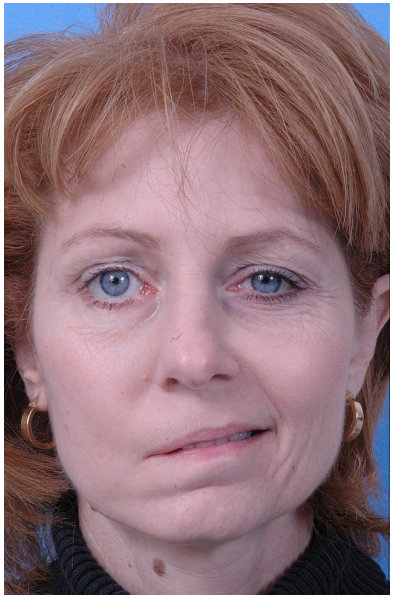
Autoimmune Myopathies

- Polymyositis
  - Direct damage by cytotoxic T cells
  - Inflammation of the muscles or associated tissues, such as the blood vessels that supply the muscles



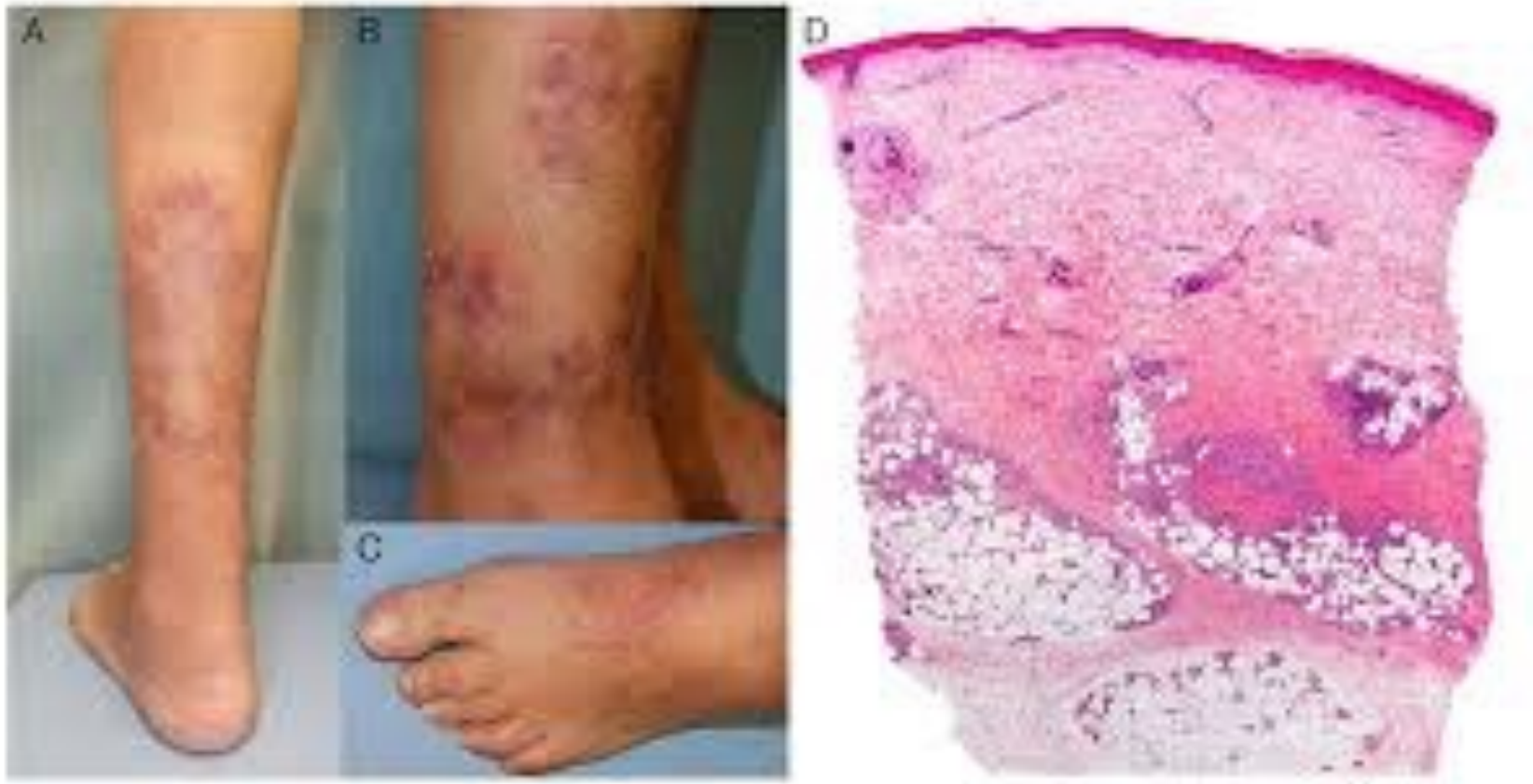
Autoimmune Myopathies

- Myasthenia Gravis (serious muscle weakness)
  - Muscular fatigability caused by circulating Abs to acetylcholine receptor at the myoneural junction
  - Extraocular muscles, swelling muscles, extremities
  - Patients can develop other autoimmune diseases
  - 40% patients have thymoma
  - 75% of remaining thymic hyperplasia
  - Removal of thymus can be curative



Polyarteritis Nodosa

- Men
- Small and medium size arteries
- Vasculitis
- Decreased blood supply to organs
- Implicated
  - Hepatitis B (~30%)
  - Sulfa drugs, penicillin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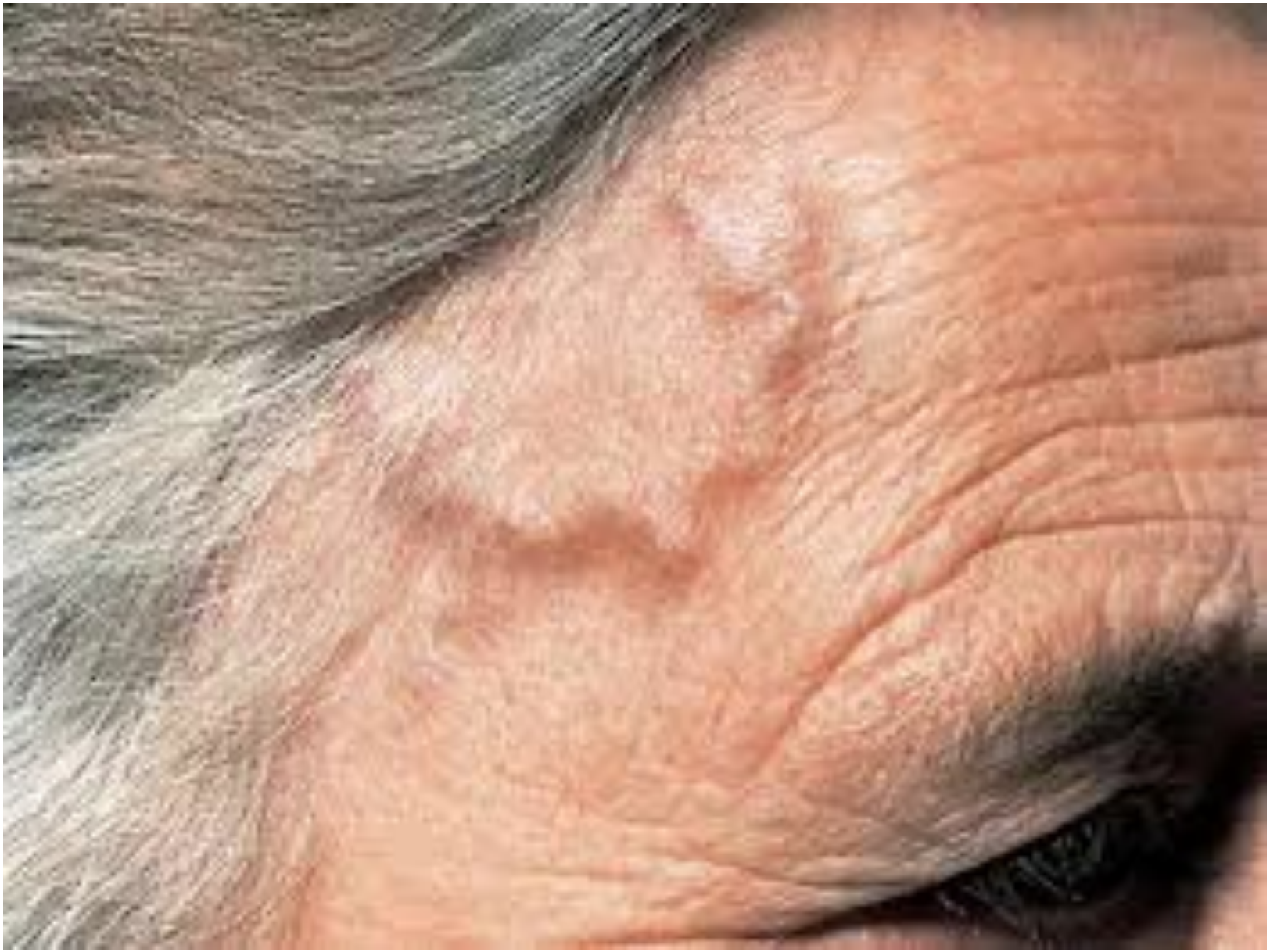
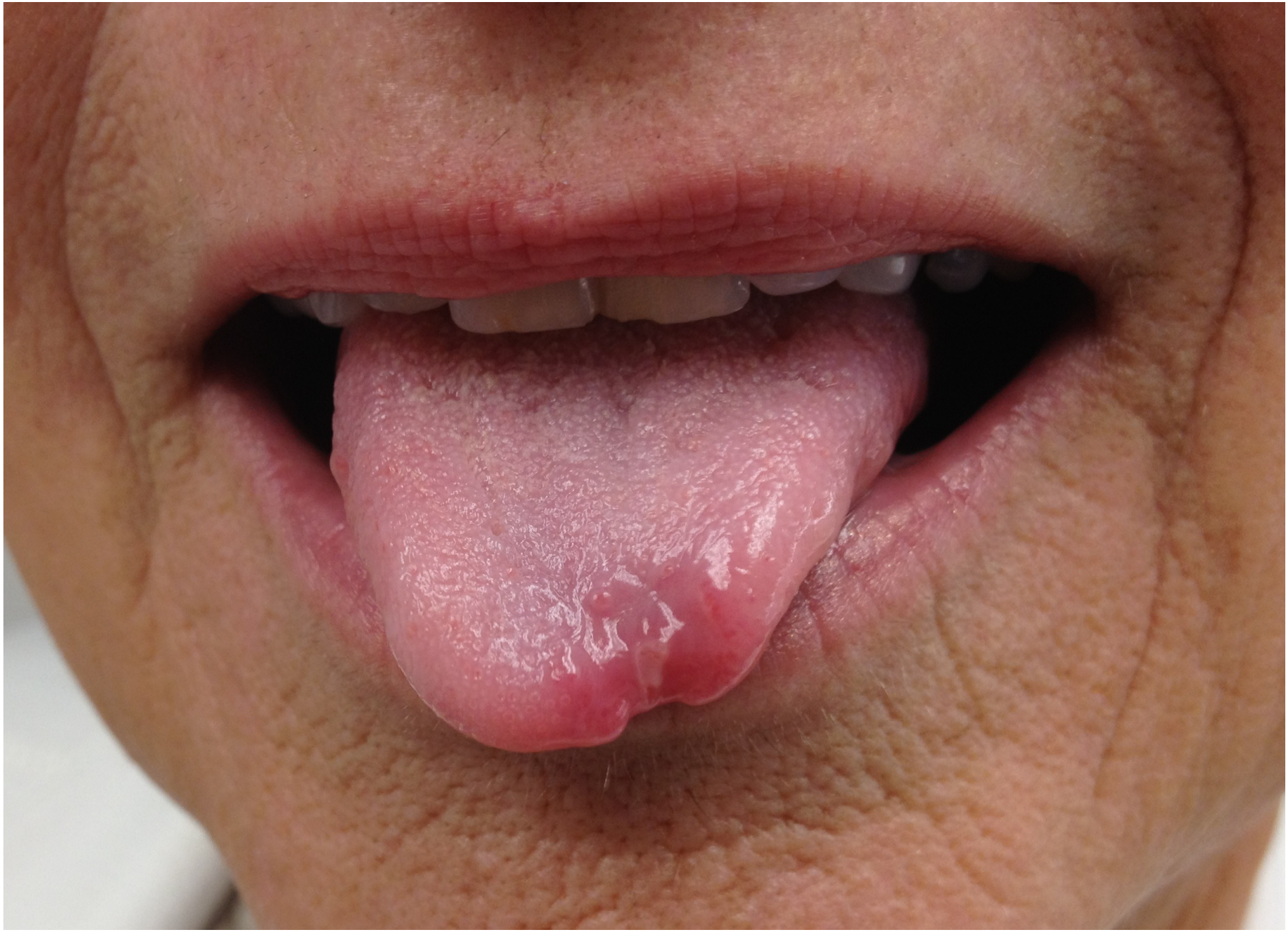
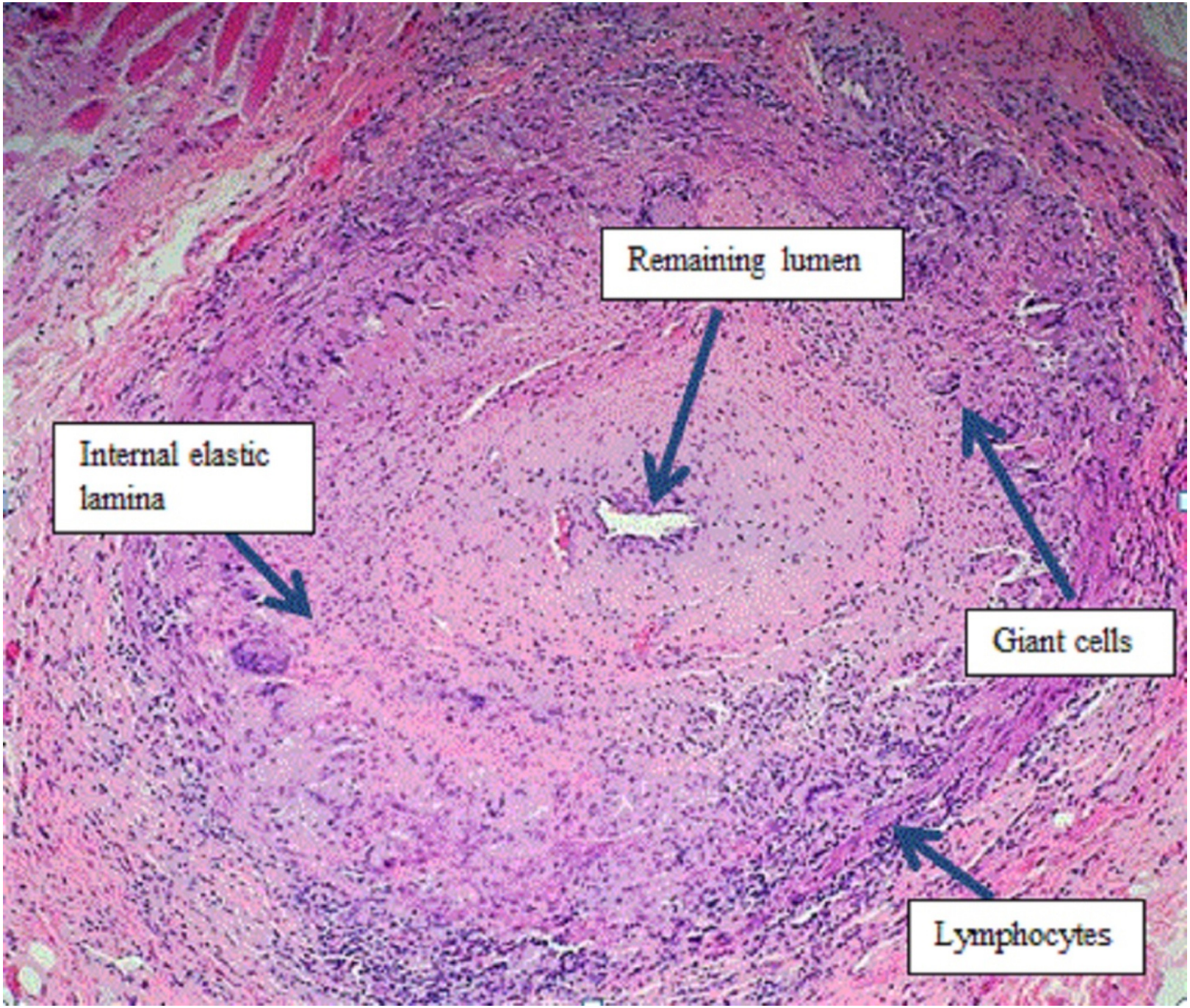
Temporal Arteritis

- Inflammation of large arteries
- Temporal artery and other arteries
- Headache, visula changes
- Confirmatory biopsy
- If untreated can lead to blindness






Remaining lumen
Internal elastic lamina
Giant cells
Lymphocytes