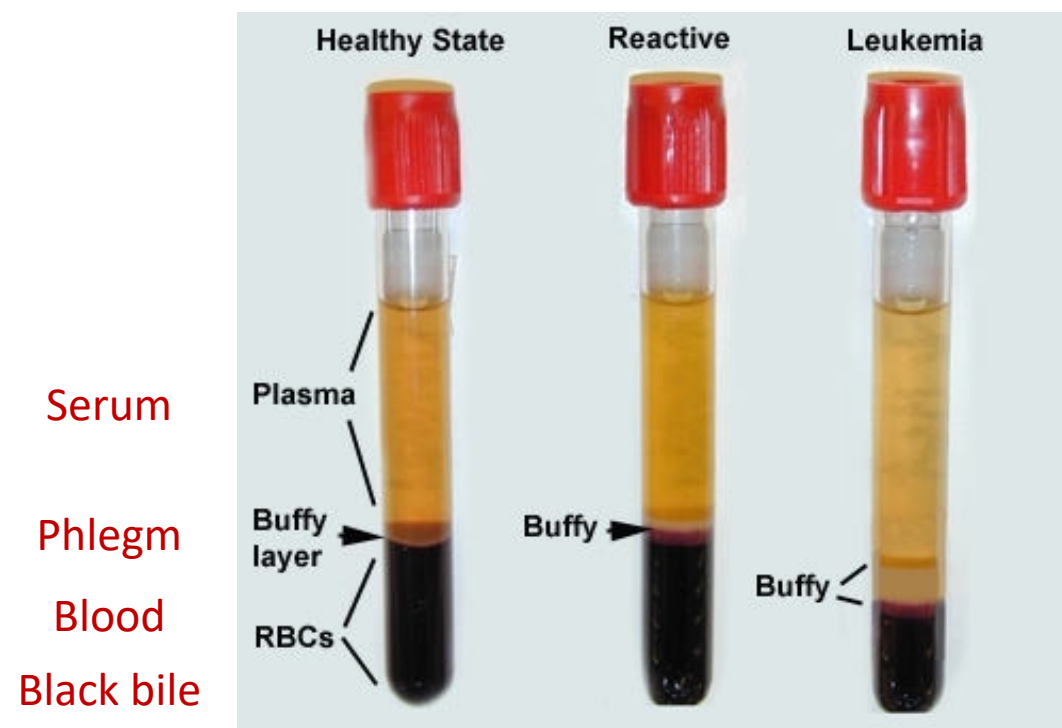
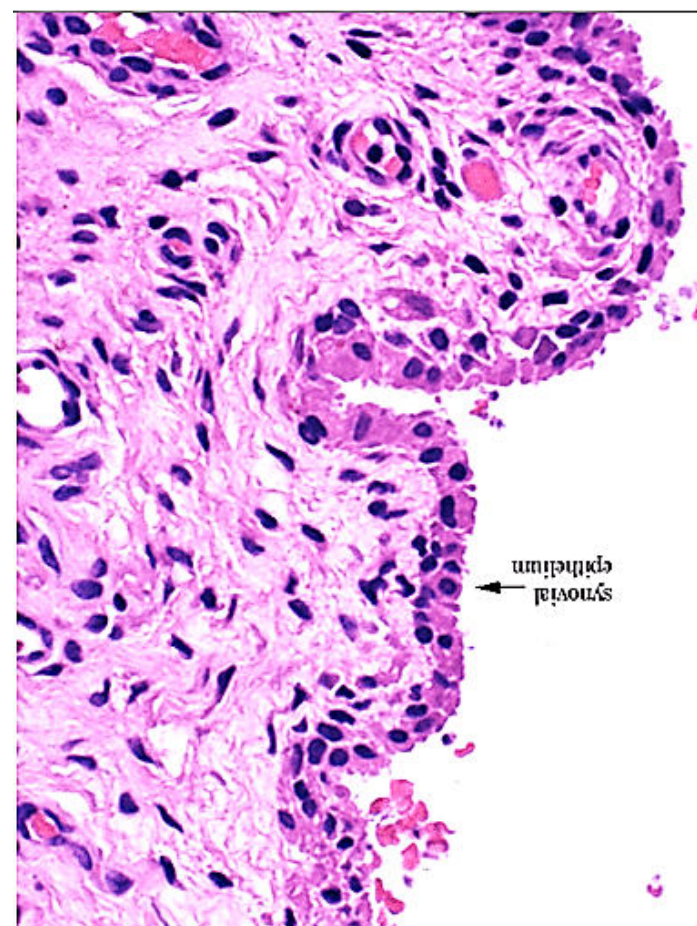
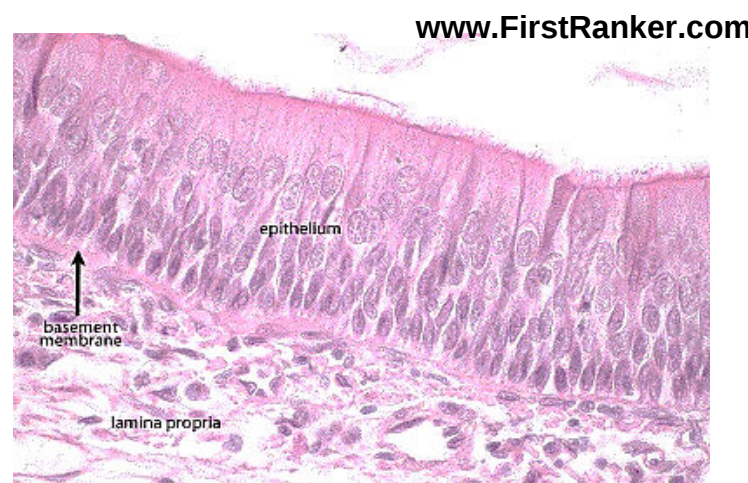
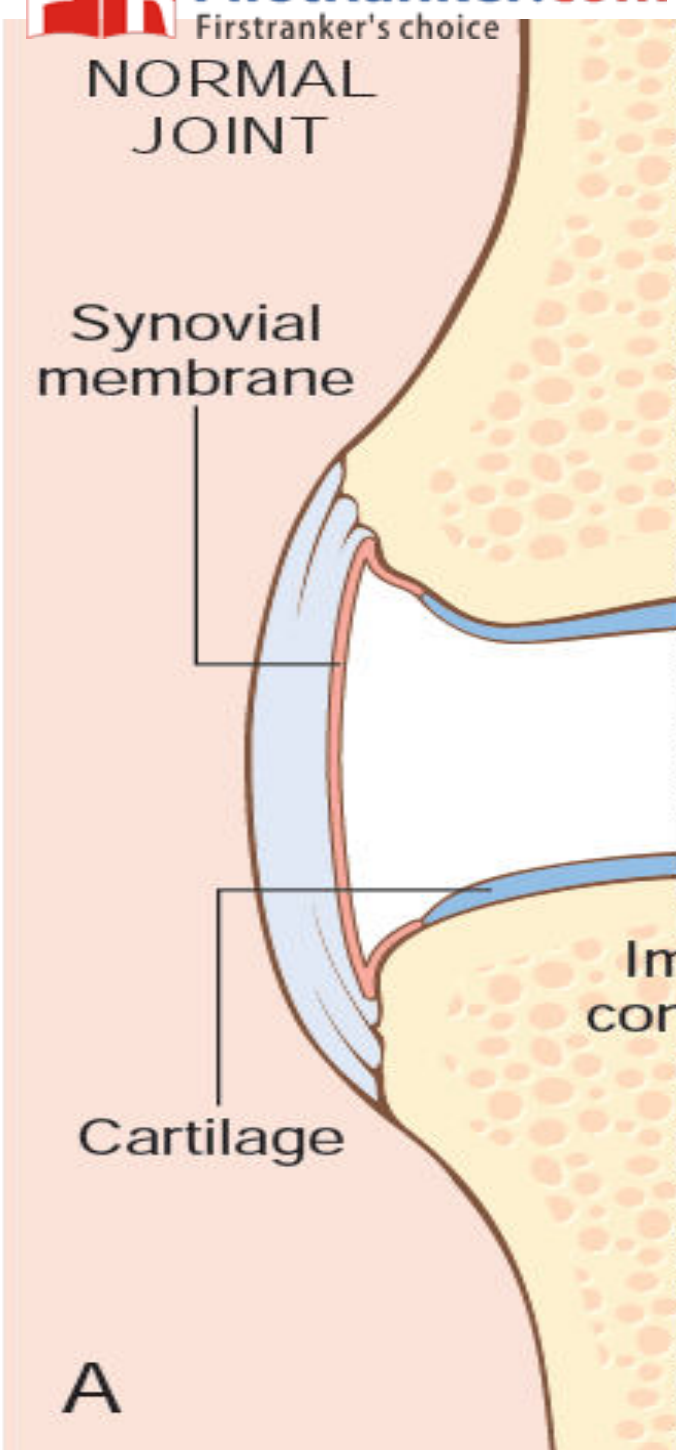


# Pathogenesis and Pathology of Rheumatoid Arthritis

## “Rheumatoid” : Why?

- Rheum : flow ~ oid: resembling
- Attributed to humors
  - Hippocrates
  - 4 bodily fluids
  - Increased substance flows and settles in joints → rheumatism
  - Paracelsus (1493-1511): substances that could not be passed in urine precipitated in joints, and caused arthritis.
- Autoimmune disease

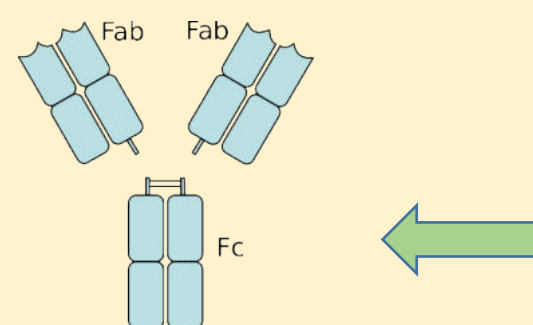




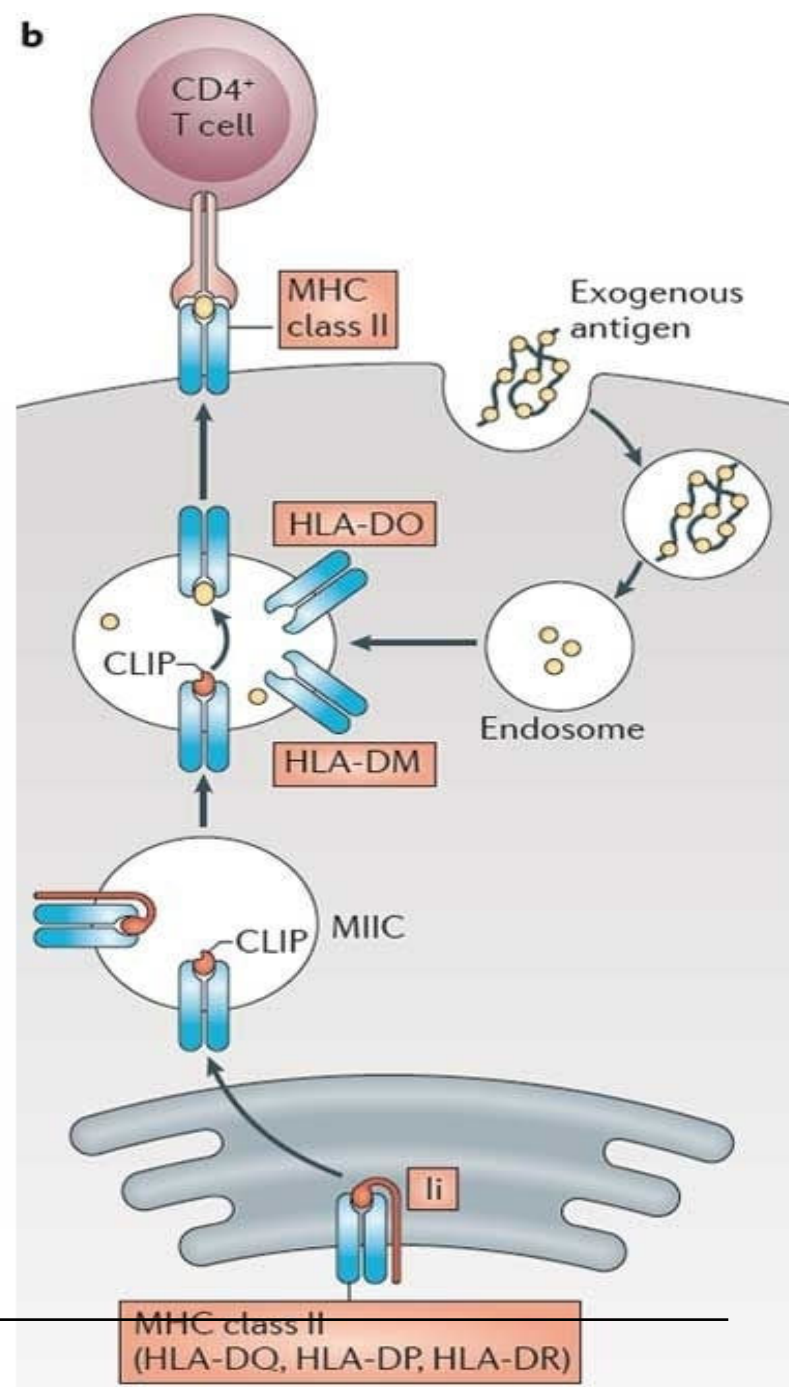
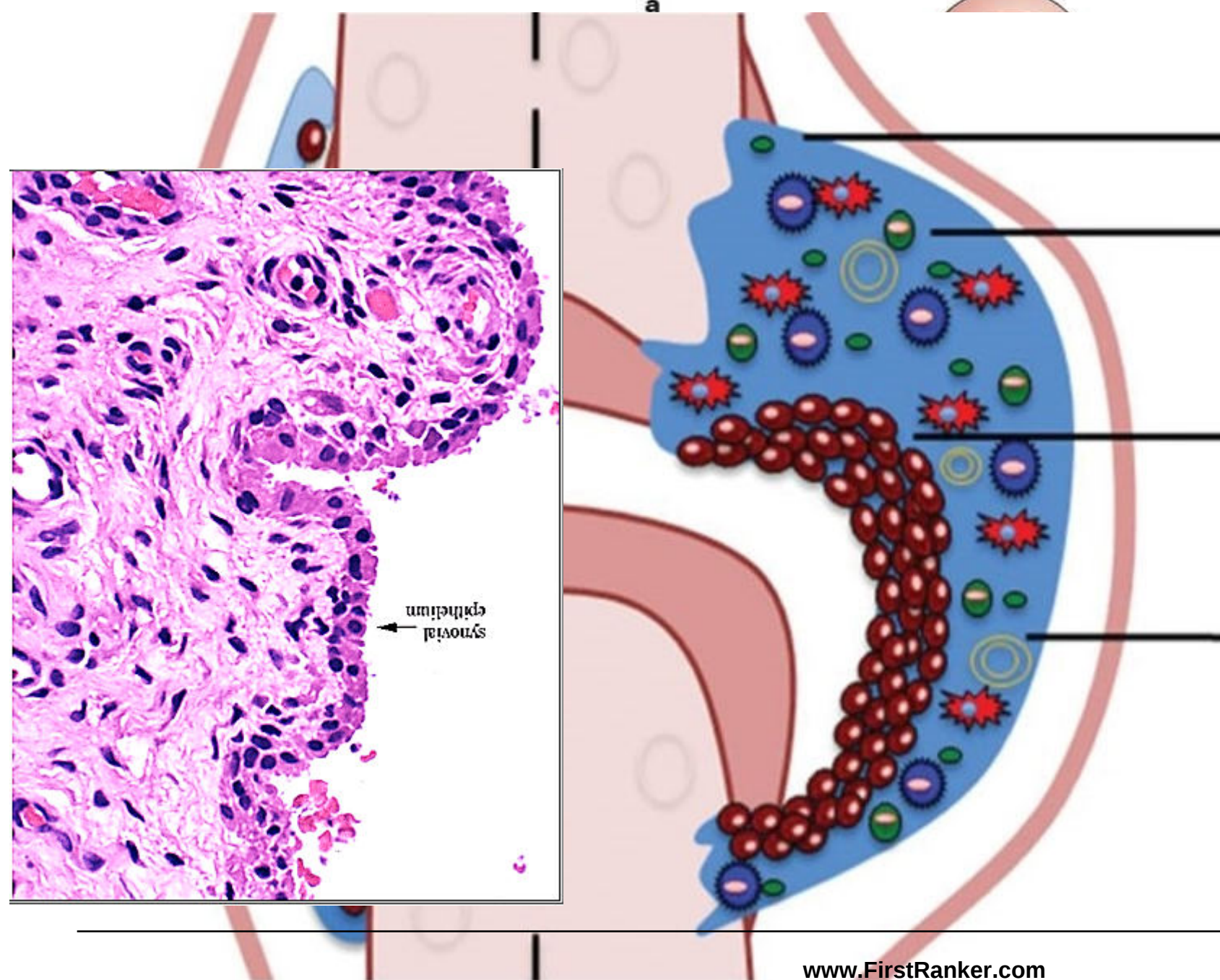
- Where do the antibodies/ Ag-ab complexes come from?
  - Molecular mimicry?
  - Environmental triggers leading to **citrullination** of self proteins? → new epitopes?

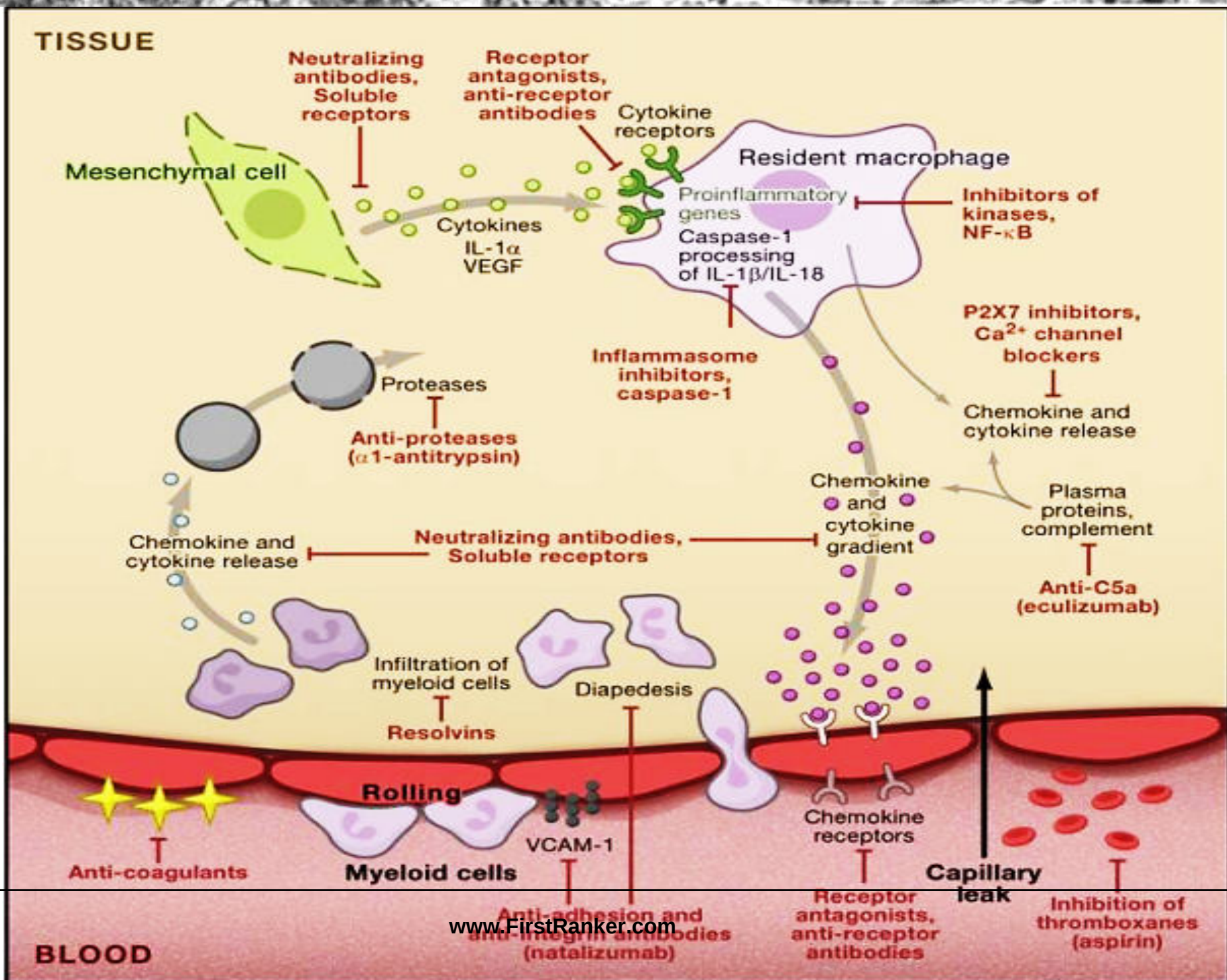
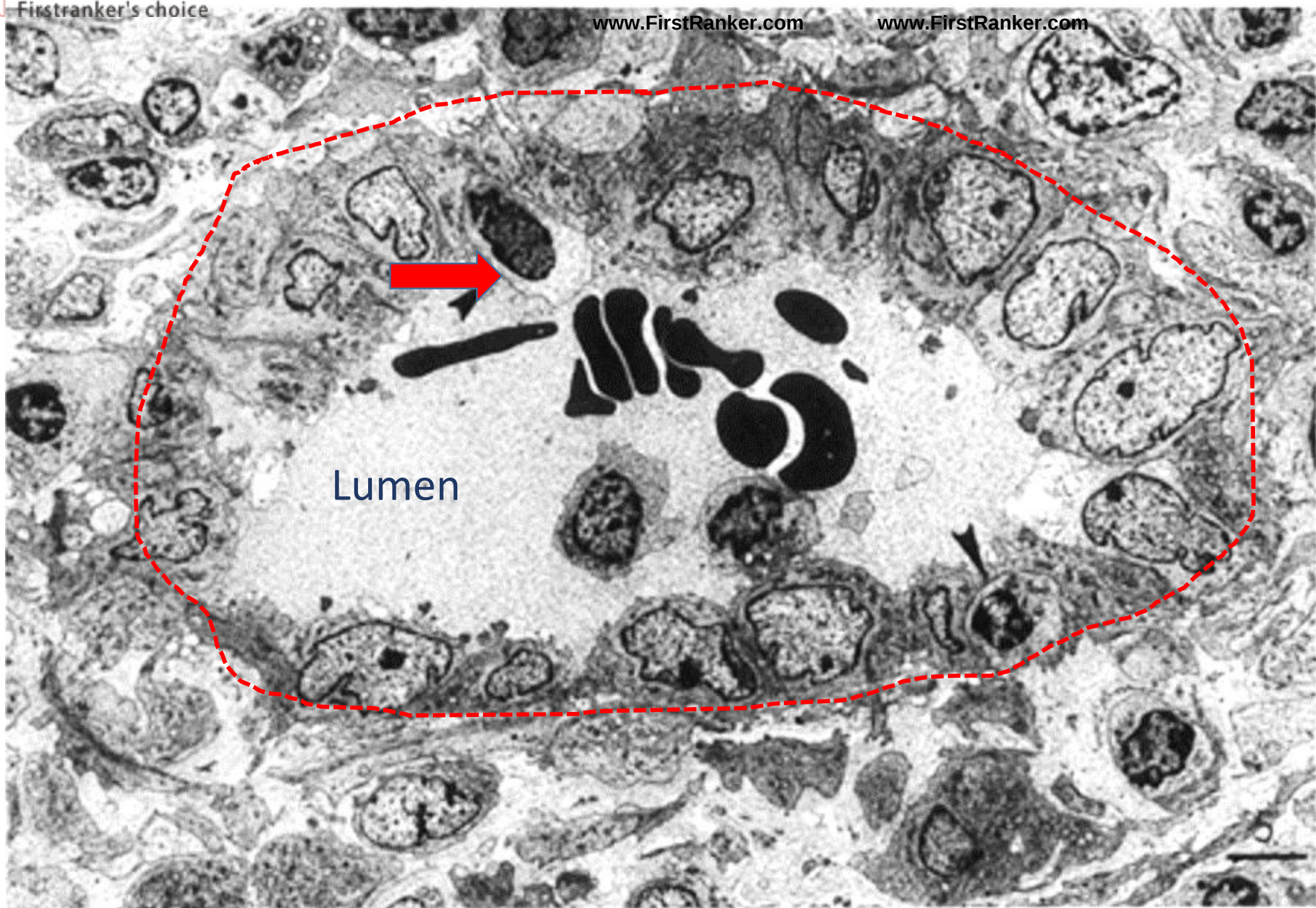
**Anti-ccp** antibodies  
“cyclic citrullinated peptide”

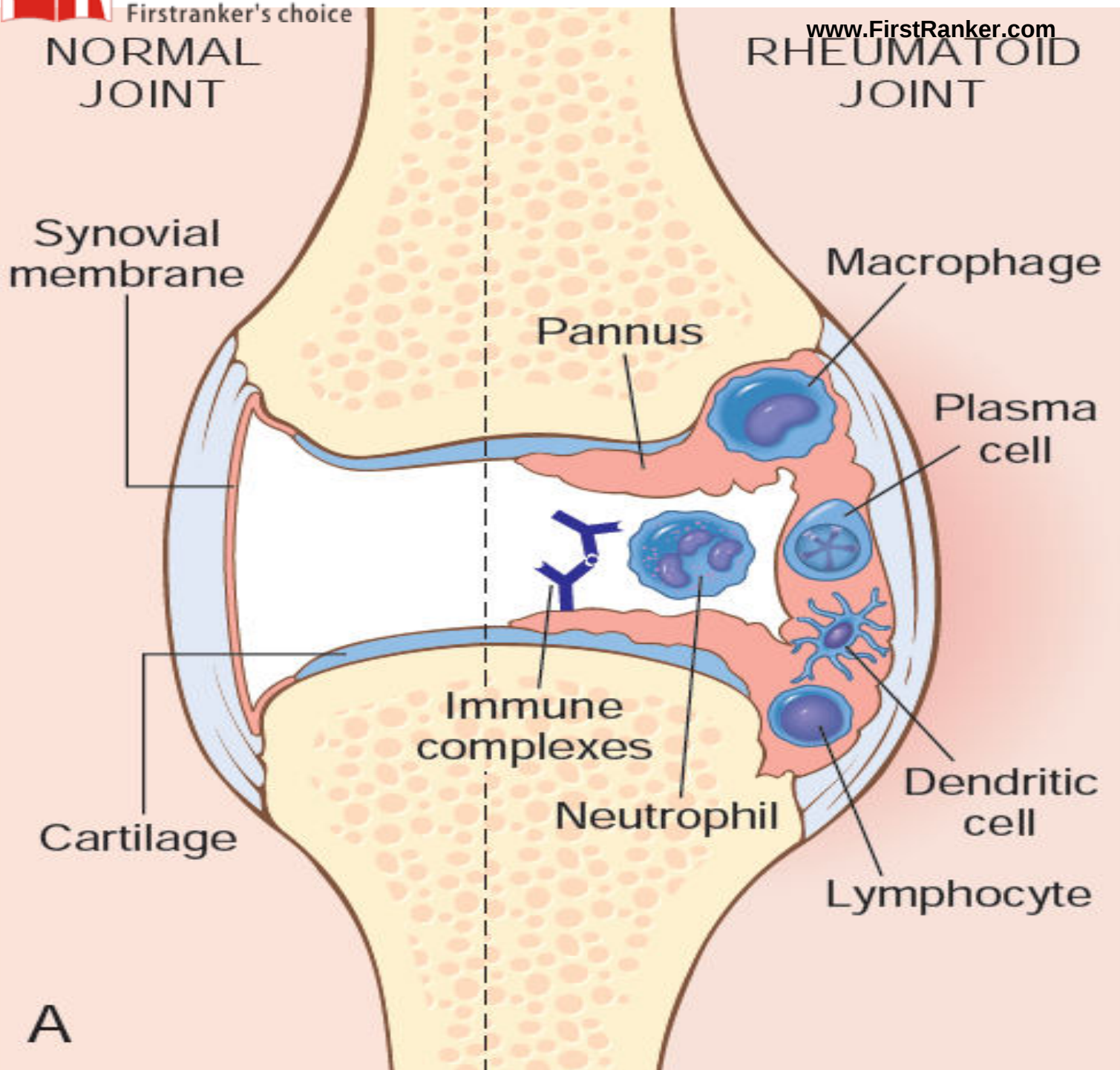
- Rheumatoid factor  
(autoantibody against **Fc** portion of IgG)



- HLA-DRB1** alleles present arthritogen?







• What do the Antigen antibody complexes contain?

- Citrullinated fibrinogen
- Enolase
- Collagen
- Vimentin

• Why are some joints affected more commonly than others?

## SUMMARY

50% risk attributable

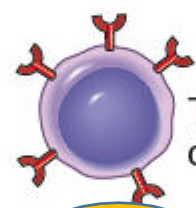
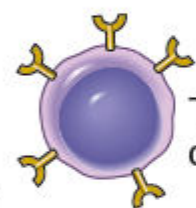
Susceptibility genes (HLA, other)

Environmental factors (e.g., infection, smoking)

Failure of tolerance, unregulated lymphocyte activation

Enzymatic modification (e.g., citrullination) of self protein

T and B cell responses to self antigens (including antigens in joint tissues)



IL-17

IFN $\gamma$



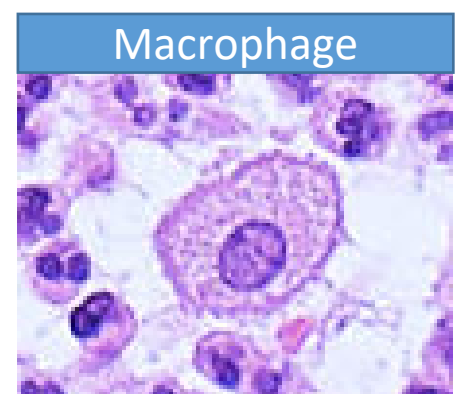
Fibroblasts  
Chondrocytes  
Synovial cells

Proliferation

Release of collagenase, stromelysin, elastase, PGE $_2$ , and other enzymes

TNF $\alpha$

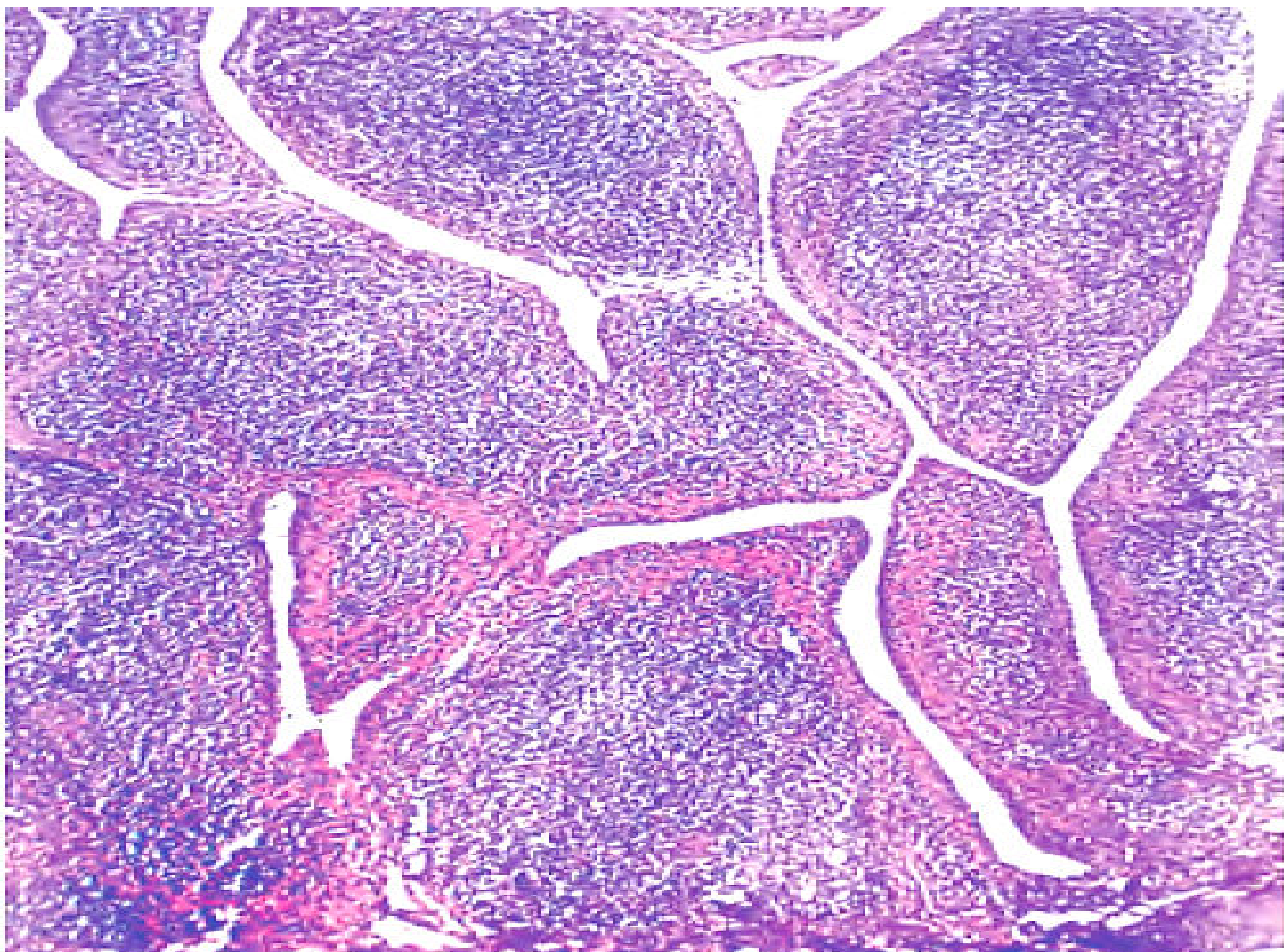
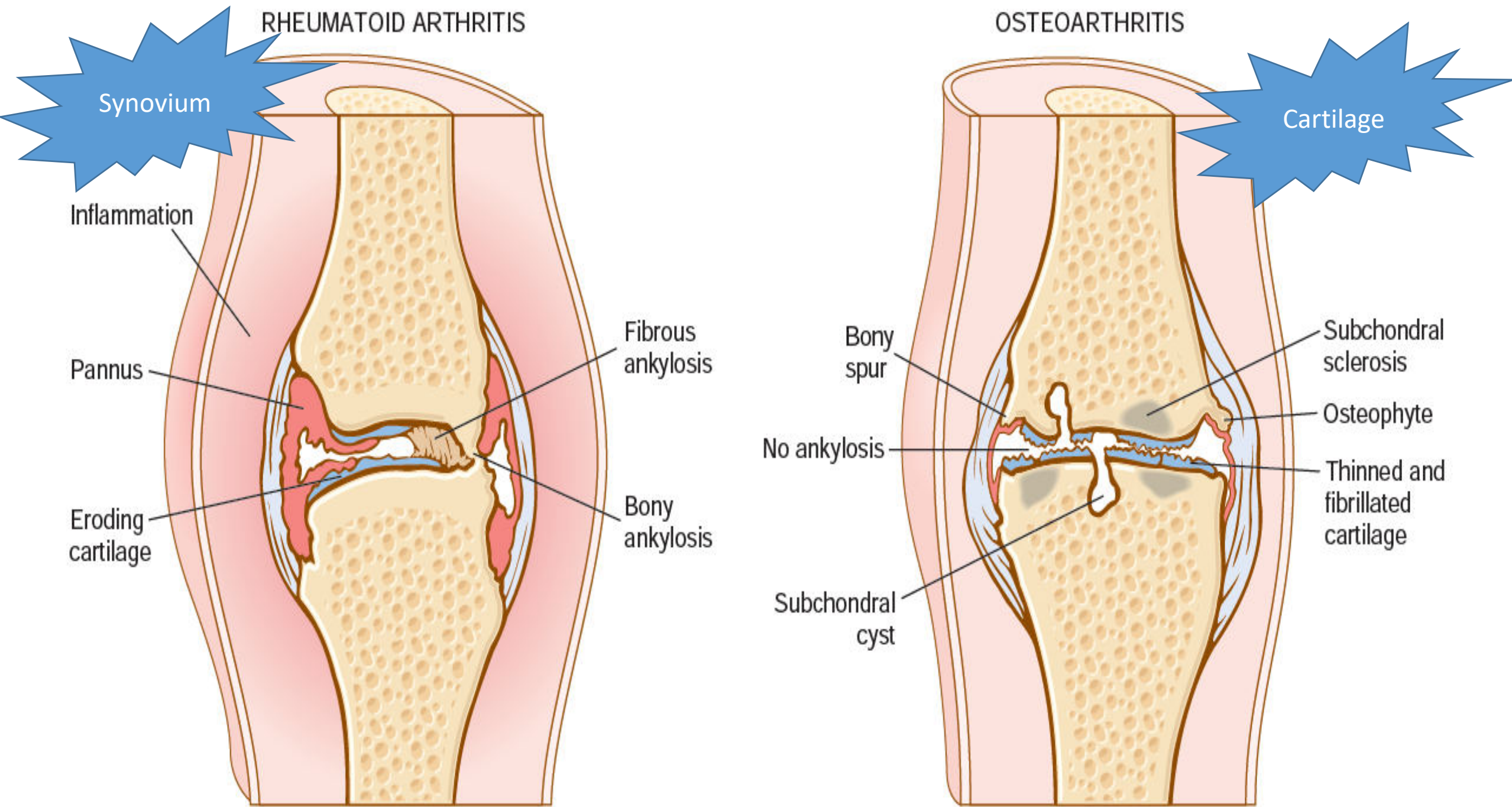
IL-1



Pannus formation; destruction of bone, cartilage; fibrosis, ankylosis

RHEUMATOID ARTHRITIS

OSTEOARTHRITIS

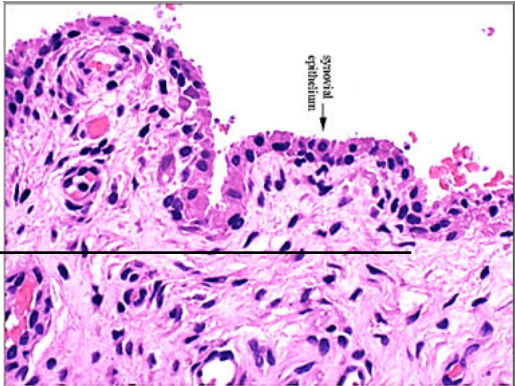


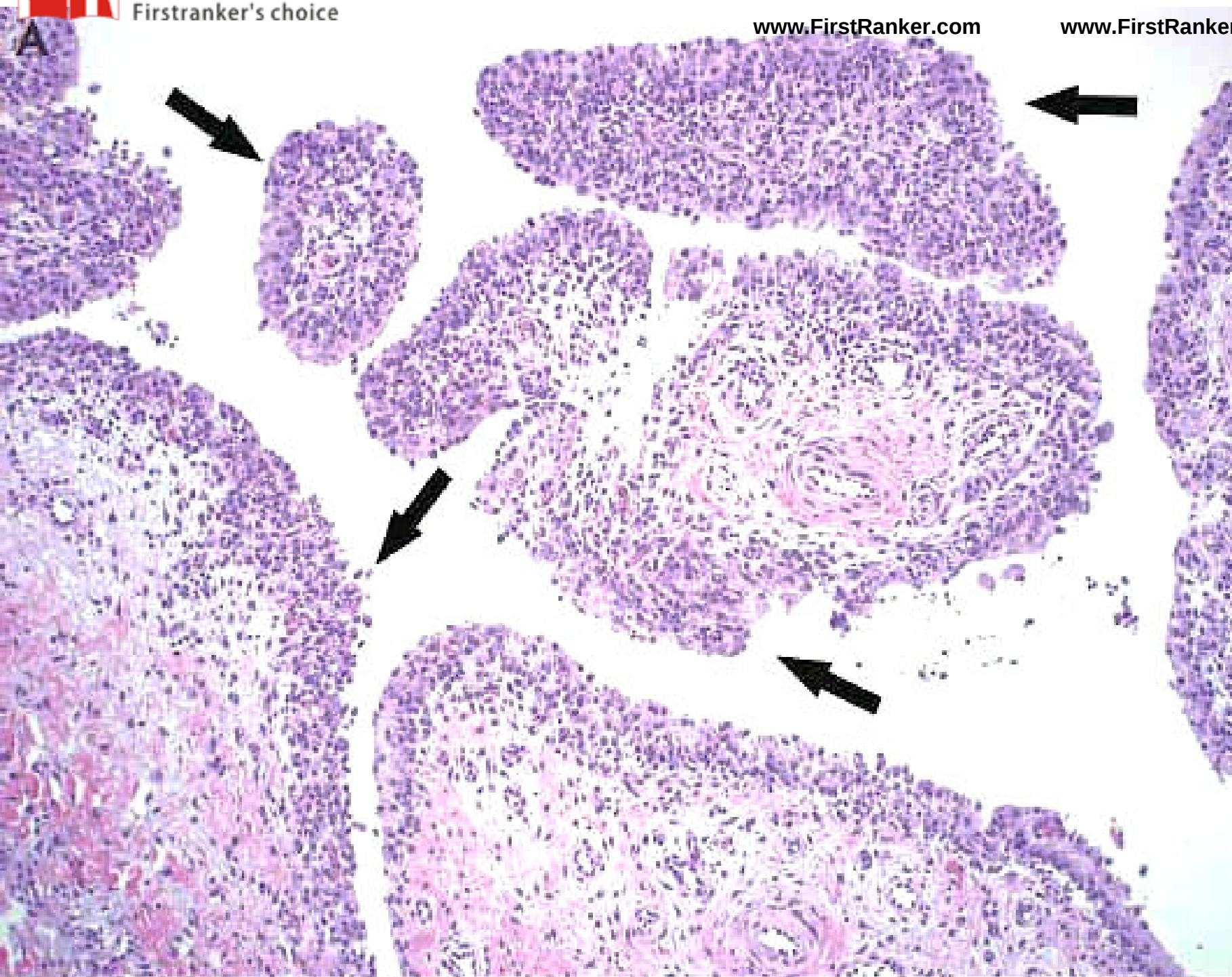
Papillae

Synovial hyperplasia

Lymphoid follicles

Normal Synovium

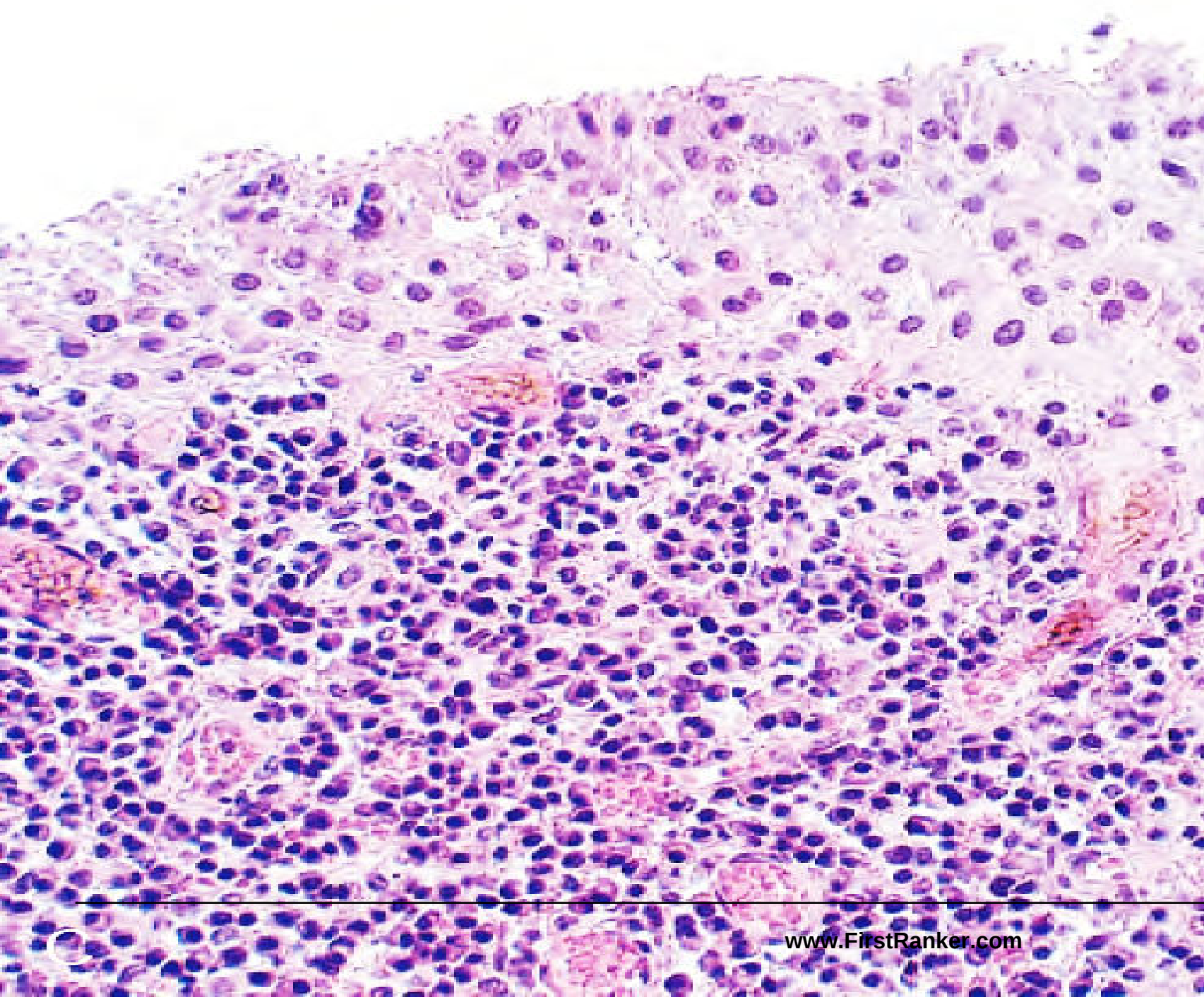
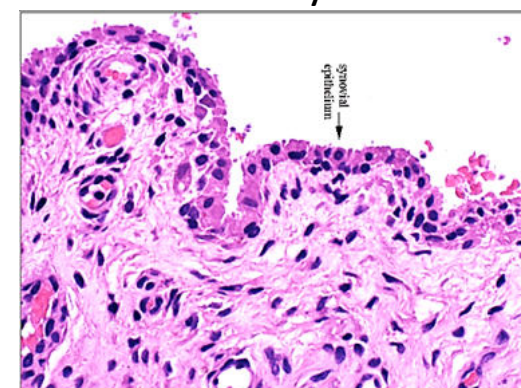




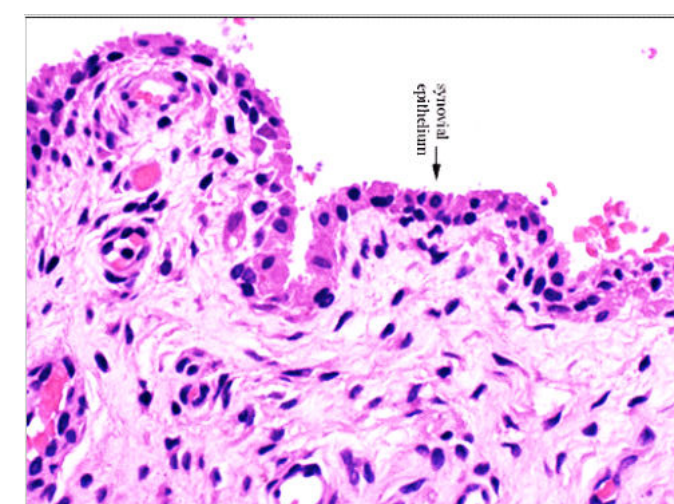
papillae

Synovial hyperplasia

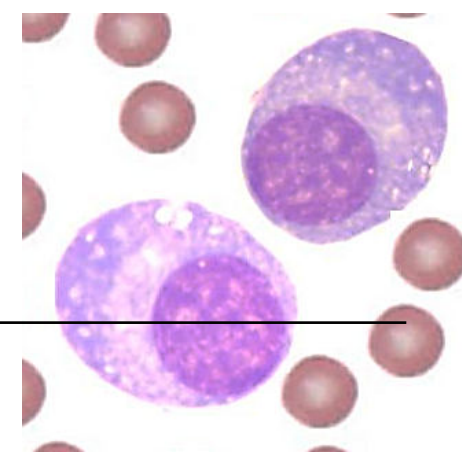
Normal Synovium

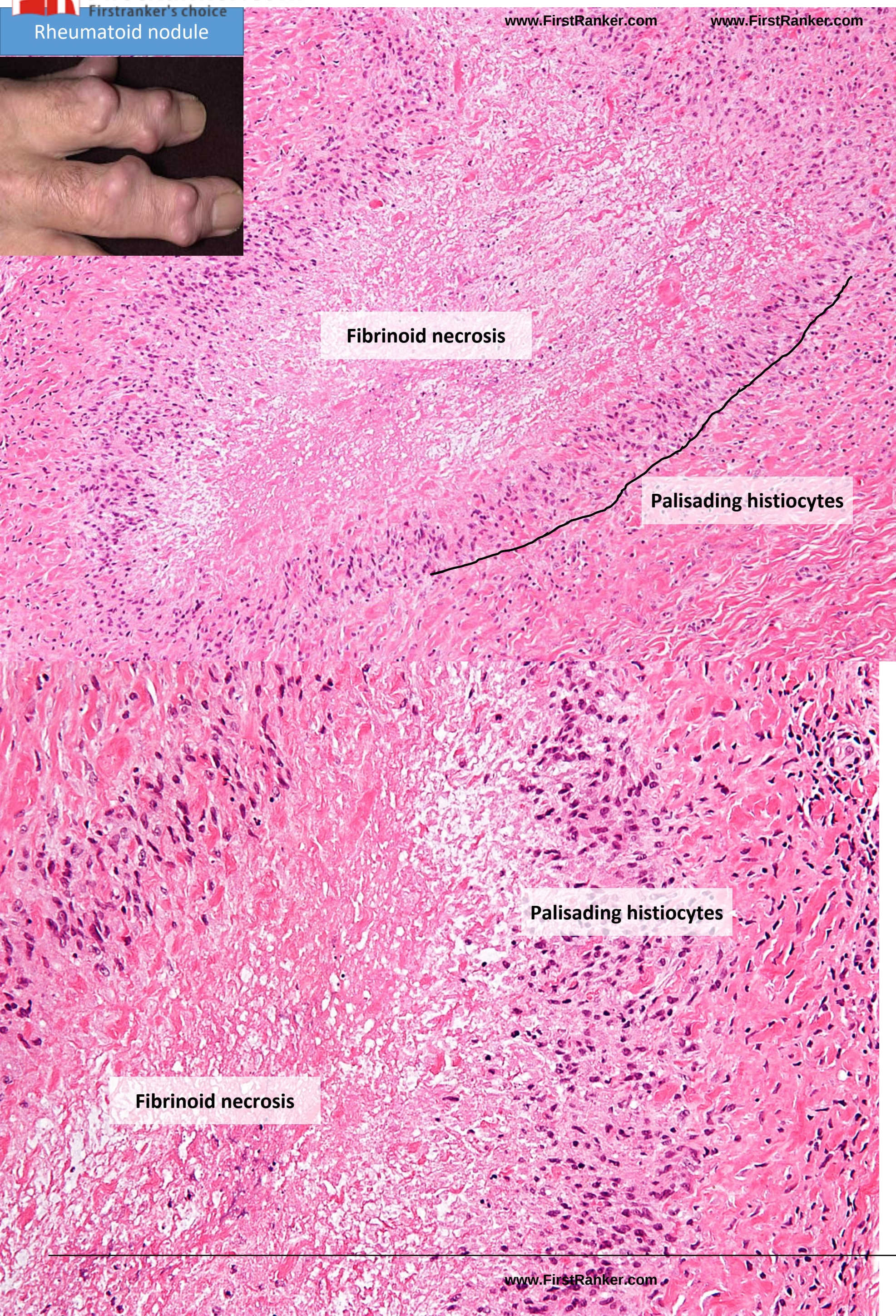


Synovial hyperplasia



Plasma cells





# Points to remember

- Anti – ccp antibodies
- Rheumatoid factor
- HLA-DRB1 **alleles**
- Pannus formation
  - Synovial hyperplasia, lymphoid follicles, plasma cells
  - Fibrin
- Rheumatoid nodule
  - Necrosis with palisading histiocytes
- Differences between Rheumatoid and Osteoarthritis

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