RHEUMATOID ARTHRITIS

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RHEUMATOID ARTHRITIS

- RA is a chronic multisystem disease of unknown cause
- characteristic feature of RA is persistent inflammatory synovitis
- usually involving peripheral joints in a symmetric distribution.
- potential of the synovial inflammation to cause cartilage damage and bone erosions and subsequent changes in joint integrity is the hallmark of the disease.

EPIDEMIOLOGY

- prevalence of RA is approximately 0.8% of the population
- women > men (3X)
- prevalence increases with age
- RA is seen throughout the world
- affects all races
- onset is most frequent during the 4th and 5th decades
- 80% of all patients developing the disease between the ages of 35 and 50

ETIOLOGY

UNKNOWN

GENETICS

ENVIRONMENTAL

GENETICS

Family studies indicate a genetic predisposition

- HLA-DRB1 alleles
- HLA-DR4
- 70% with classic or definite RA express HLADR4
- Asian Indians - there is no association between the development of RA and HLA-DR4.
- In these, there is an association between RA and closely related HLA-DR1

GENETICS

genes outside the HLA complex also contribute

- genes controlling the expression of the antigen receptor on Tcells, immunoglobulin heavy and light chains
- polymorphisms in the tumor necrosis factor (TNF) and the interleukin (IL) 10 genes
- region on chromosome 3 (3q13)

ENVIRONMENTAL FACTORS

Climate

Urbanization

Cigarette smoking

PATHOLOGY

- Earliest lesions in rheumatoid synovitis
- Micro vascular injury
- Increased number of synovial lining cells
- Perivascular infiltration with mononuclear cells
- Synovium becomes edematous
- Protrudes into the joint cavity as villous projections

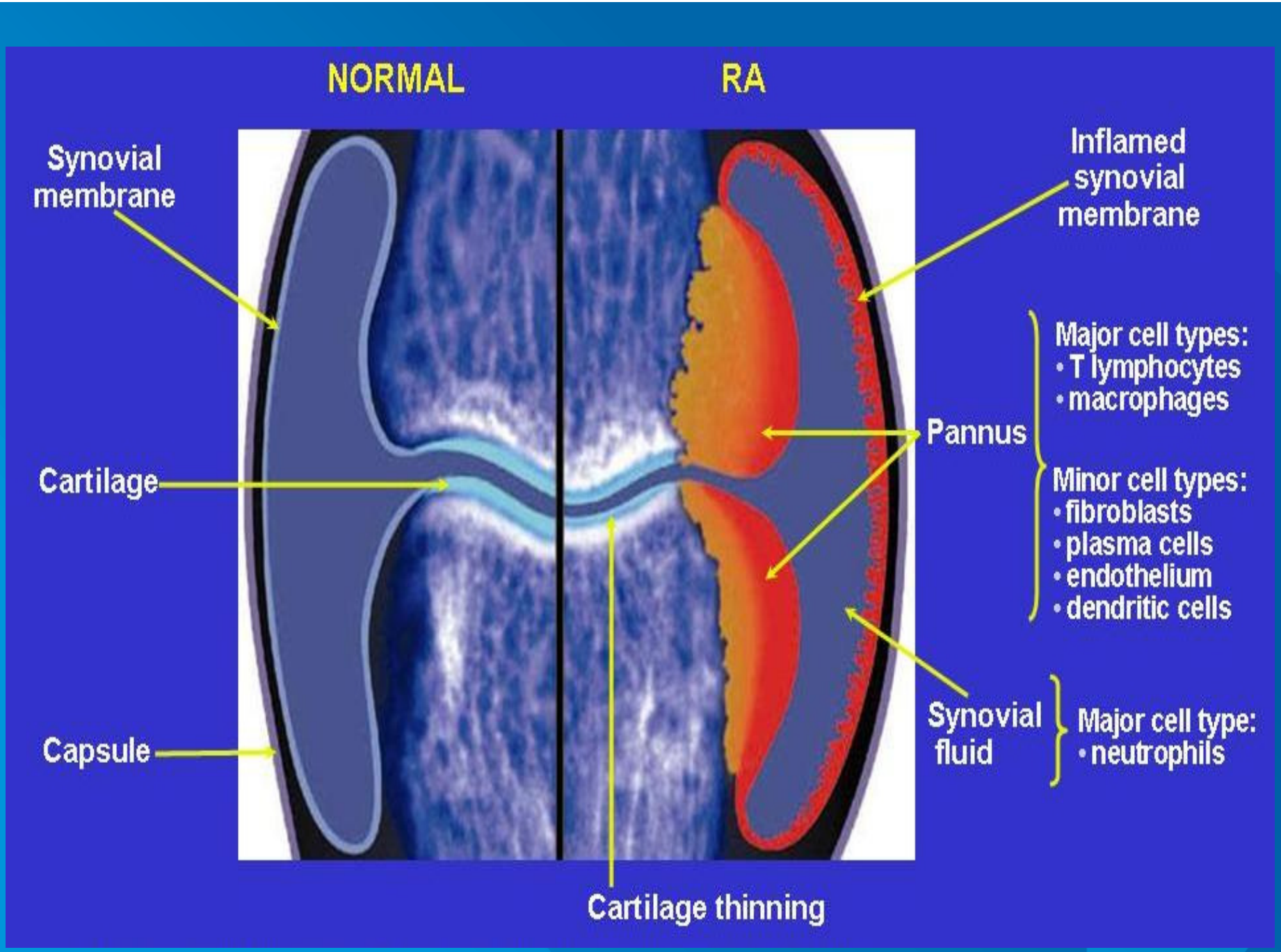
PATHOLOGY

Normal joint

- synovial membrane (macrophage and fibroblast-like cells)
- fibrous joint capsule
- synovial fluid
- cartilage covers articular surface

RA joint

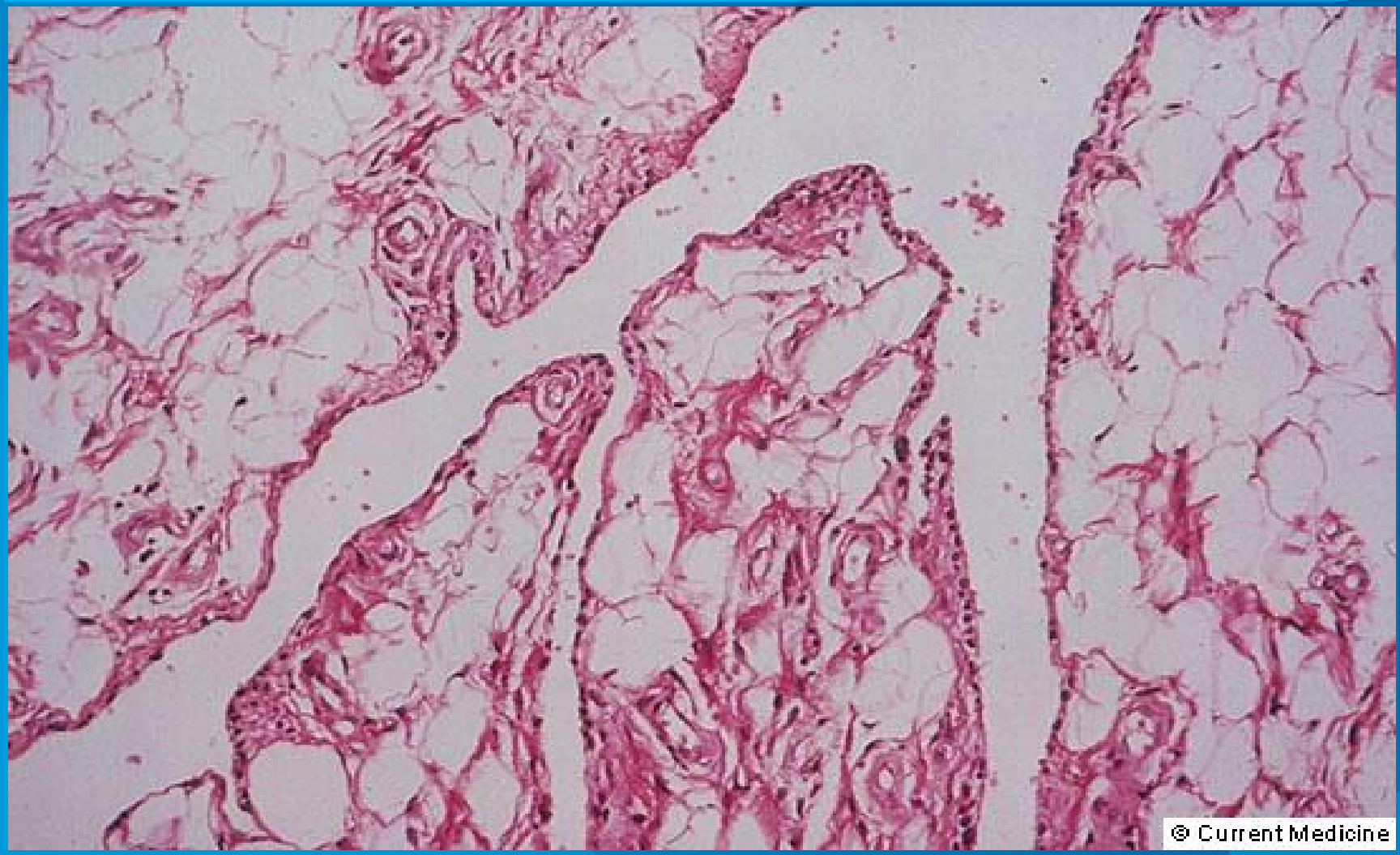
- SM hyperaemic, congested
- synovial cell proliferation and villous hypertrophy
- SM infiltration by lymphocytes, macrophages
- Vascular pannus at cartilage-synovium junction
- increased volume and cellularity of SF
- atrophy of supporting muscles
- osteopaenia of surrounding bone


NORMAL
RA
Synovial membrane
Inflamed synovial membrane
Major cell types:
• T lymphocytes
• macrophages
Pannus
Cartilage
Minor cell types:
• fibroblasts
• plasma cells
• endothelium
• dendritic cells
Synovial fluid
Major cell type:
• neutrophils
Capsule
Cartilage thinning

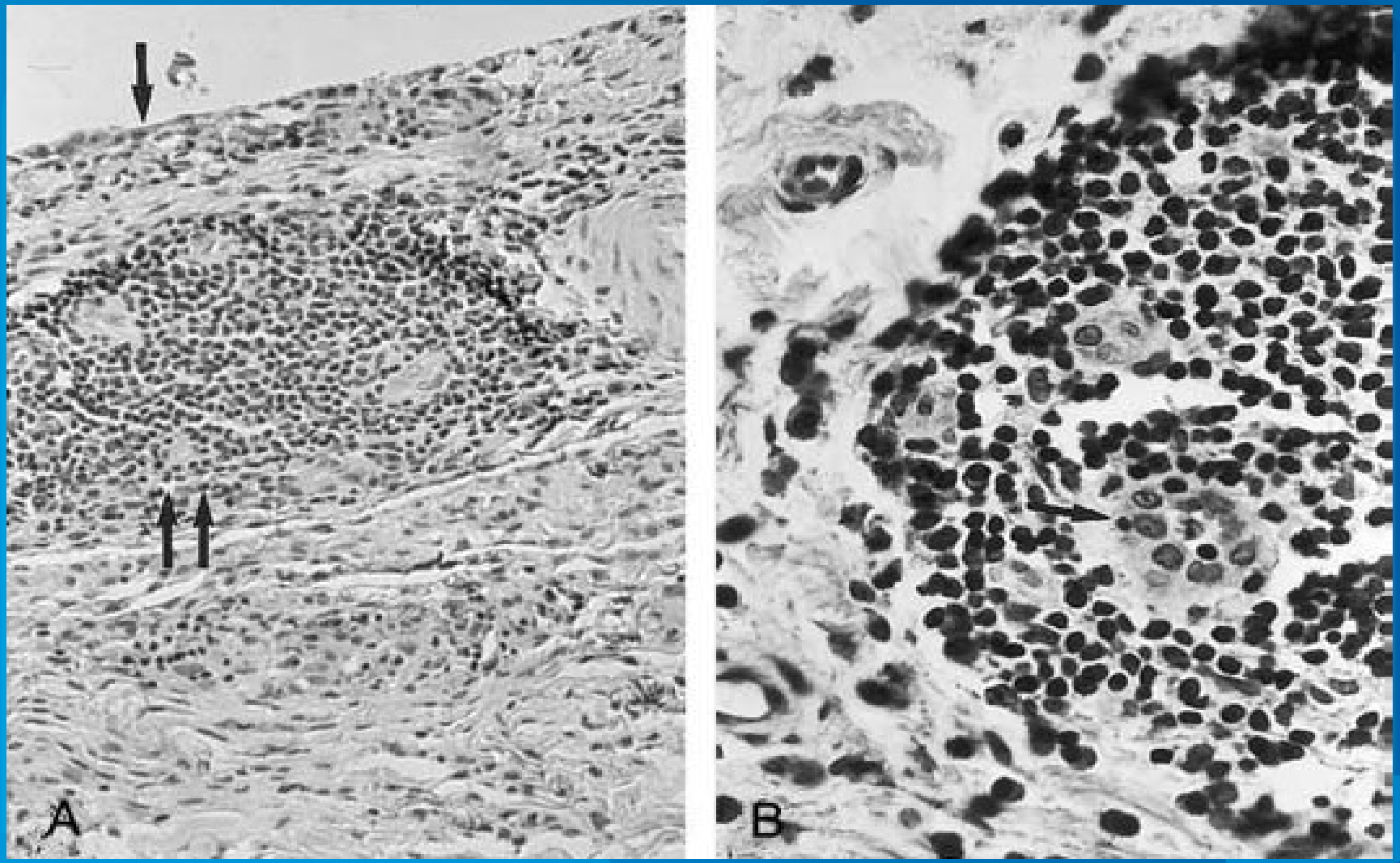
Light microscopic examination

- hyperplasia and hypertrophy of the synovial lining cells
- microvascular injury, thrombosis, neovascularization
- infiltration with mononuclear cells, often in aggregates around small blood vessels
- predominant infiltrating cell is CD4 T cells
- variable numbers of B cells. antibody-producing plasma cells, activated mast cells, activated fibroblasts, activated mesenchymal stromal cells

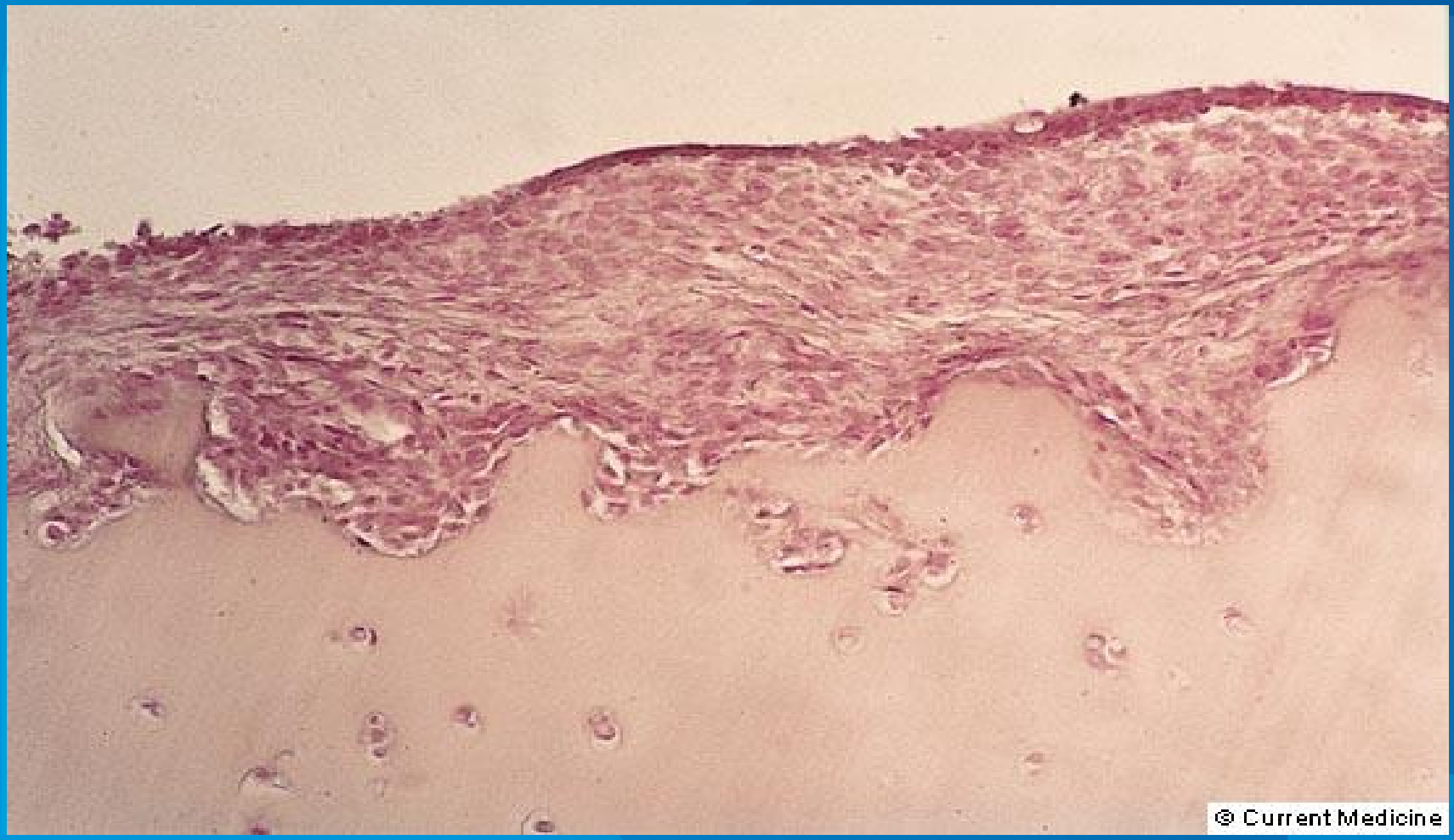
NORMAL ARTICULAR SYNOVIUM



HISTOLOGY OF RHEUMATOID SYNOVITIS



INVASIVE PANNUS

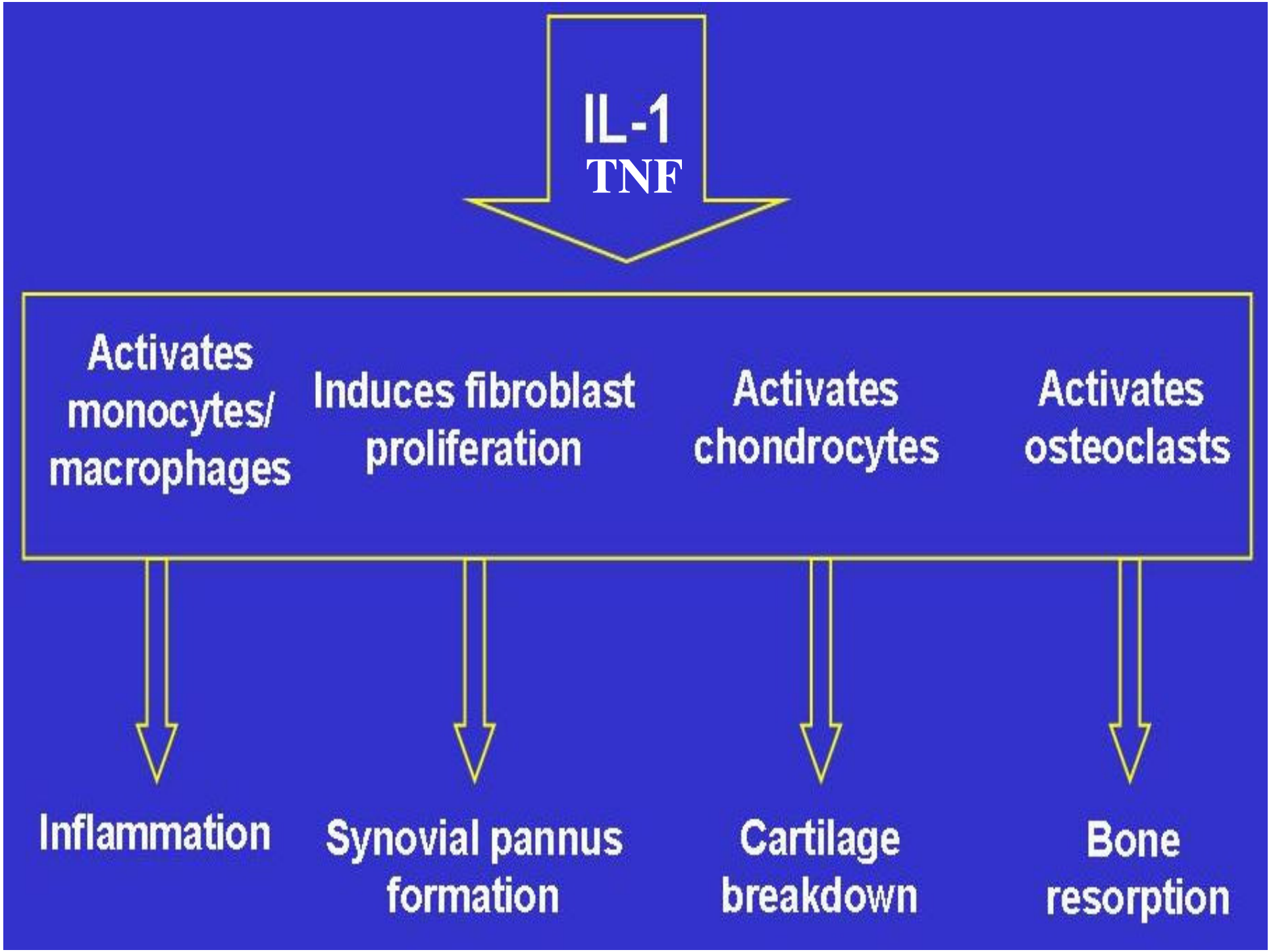


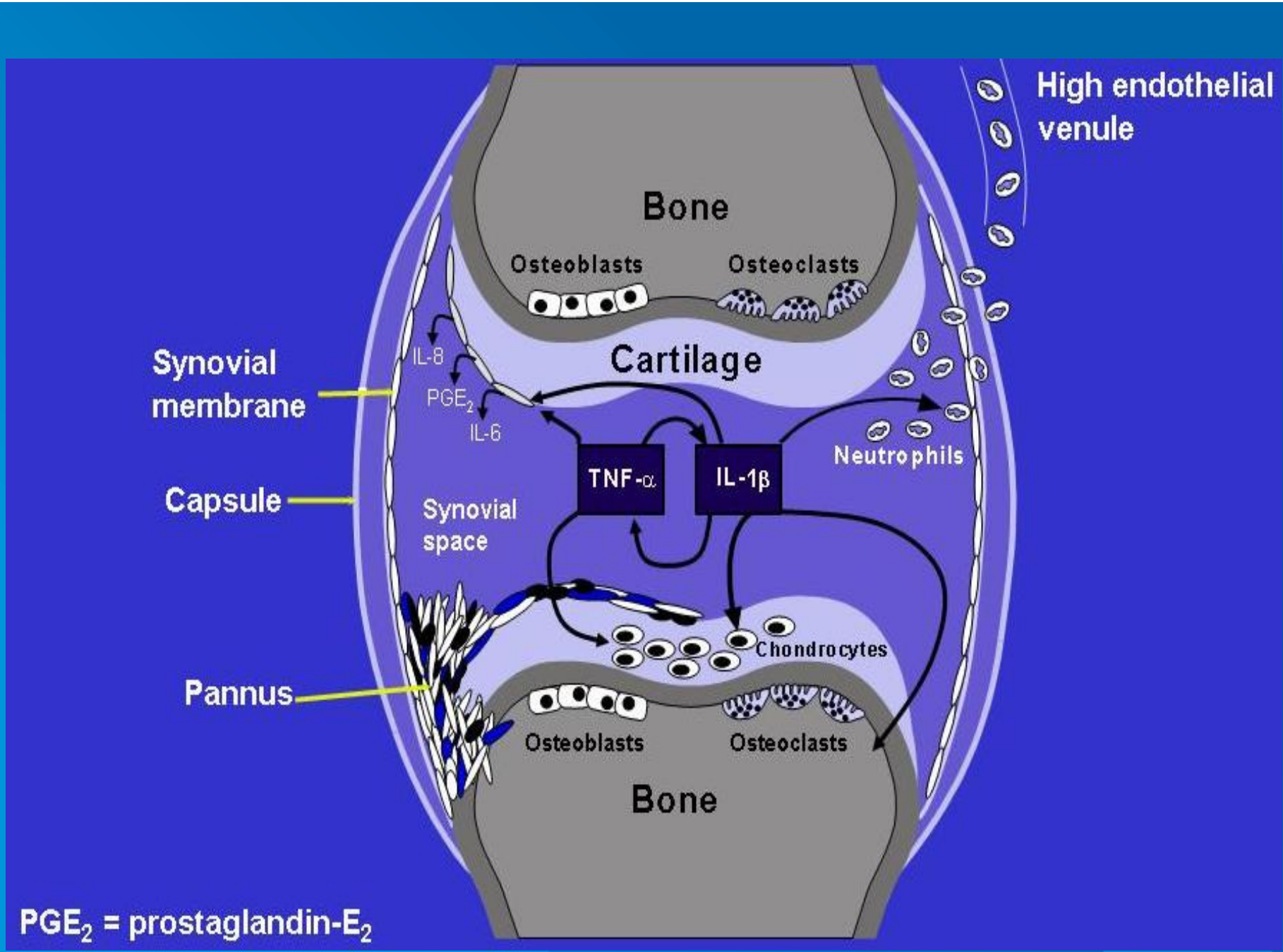
PATHOLOGIC FINDING

- chronic synovitis with pannus formation
- pannus erodes cartilage, bone, ligament, tendons
- this vascular granulation tissue is composed of proliferating fibroblasts, small blood vessels, and a variable number of mononuclear cells and produces a large amount of degradative enzymes, including collagenase and stromelysin, that may facilitate tissue damage.
- In acute phase effusion and other manifestations of inflammation are evident
- In the later stages ankylosis of the joint
- In both the acute and chronic phase, there may be widespread inflammation of the tissues, significant joint destruction

IMMUNOPATHOLOGY

- Aggregates of T-cells, macrophages and plasma cells in SM
- SF contains mainly neutrophils
- Pro (TNFα, IL1, IL6) and anti-inflammatory (IL10, TGFβ) cytokines within joint
- Interplay between immune cells and cytokines generates inflammation and joint damage


IL-1
TNF
Activates monocytes/ macrophages
Induces fibroblast proliferation
Activates chondrocytes
Activates osteoclasts
Inflammation
Synovial pannus formation
Cartilage breakdown
Bone resorption


High endothelial venule
Bone
Osteoblasts
Osteoclasts
Cartilage
Synovial membrane
IL-8
PGE2
IL-6
Capsule
Synovial space
TNF-α
IL-1β
Neutrophils
Chondrocytes
Pannus
Osteoblasts
Osteoclasts
Bone
PGE2 = prostaglandin-E2

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