Rheumatoid Arthritis

INTRODUCTION

- Rheumatoid arthritis is a chronic systemic inflammatory disease with symmetrical joint involvement.
- Chronic inflammatory disease that causes pain, swelling, stiffness and loss of function in the joints .
- It is immunologically mediated joint inflammation
- Women affected 2.5times more than men
- Can occur at any age but peaks at 40-50yrs

- The major histocompatibility complex (MHC) molecules, located on T lymphocytes, appear to have an important role in most patients with rheumatoid arthritis.

- HLA is the human version of the major histocompatibility complex (MHC)

- The HLA complex helps the immune system distinguish the body's own proteins from proteins made by foreign invaders such as viruses and bacteria.

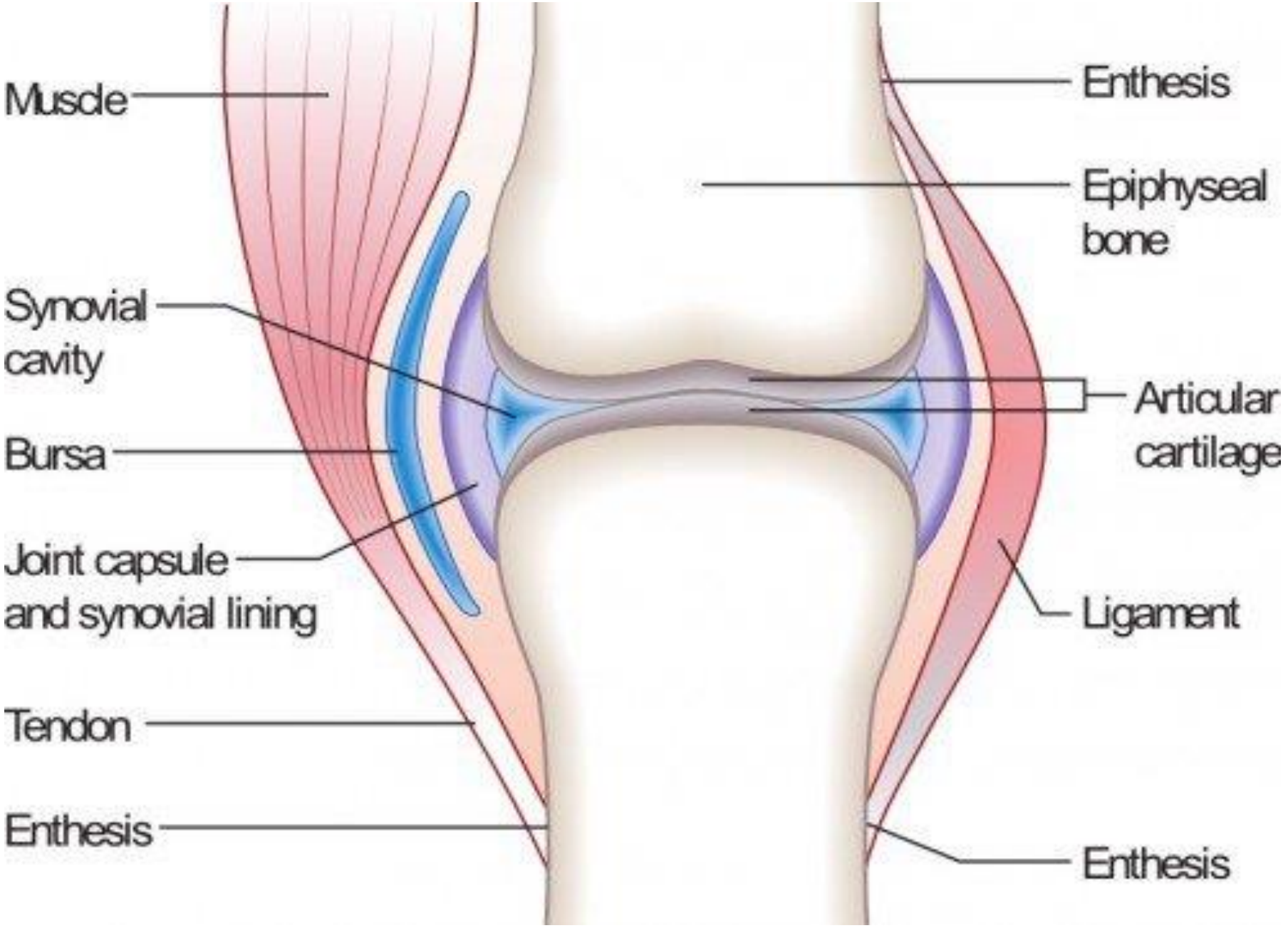
- A majority of patients with rheumatoid arthritis have HLA-DR4, HLA-DR1, or both antigens found in the MHC region.

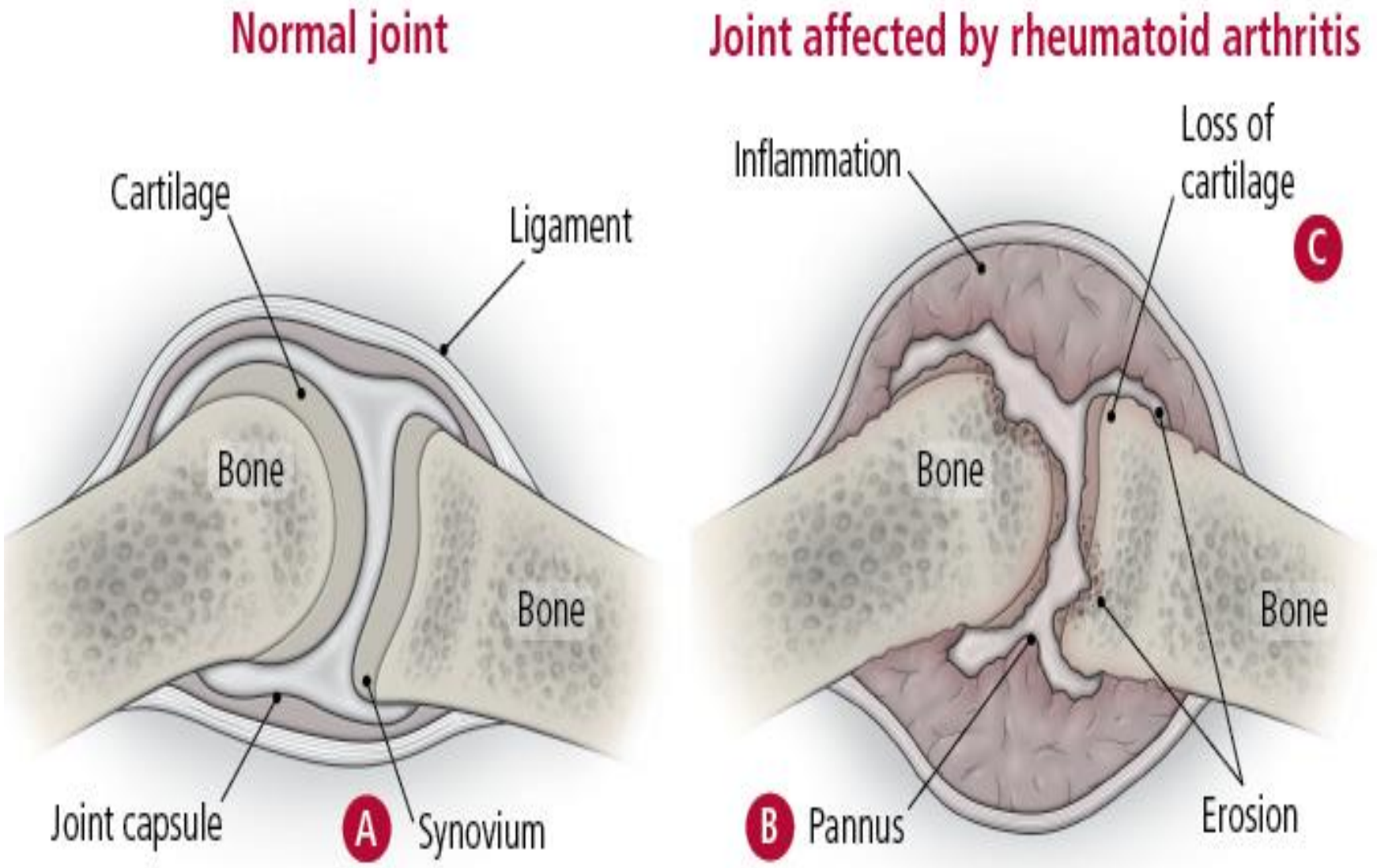
- It's one of a group of disorders in which the body's own immune system turns on itself and starts attacking its own tissue.

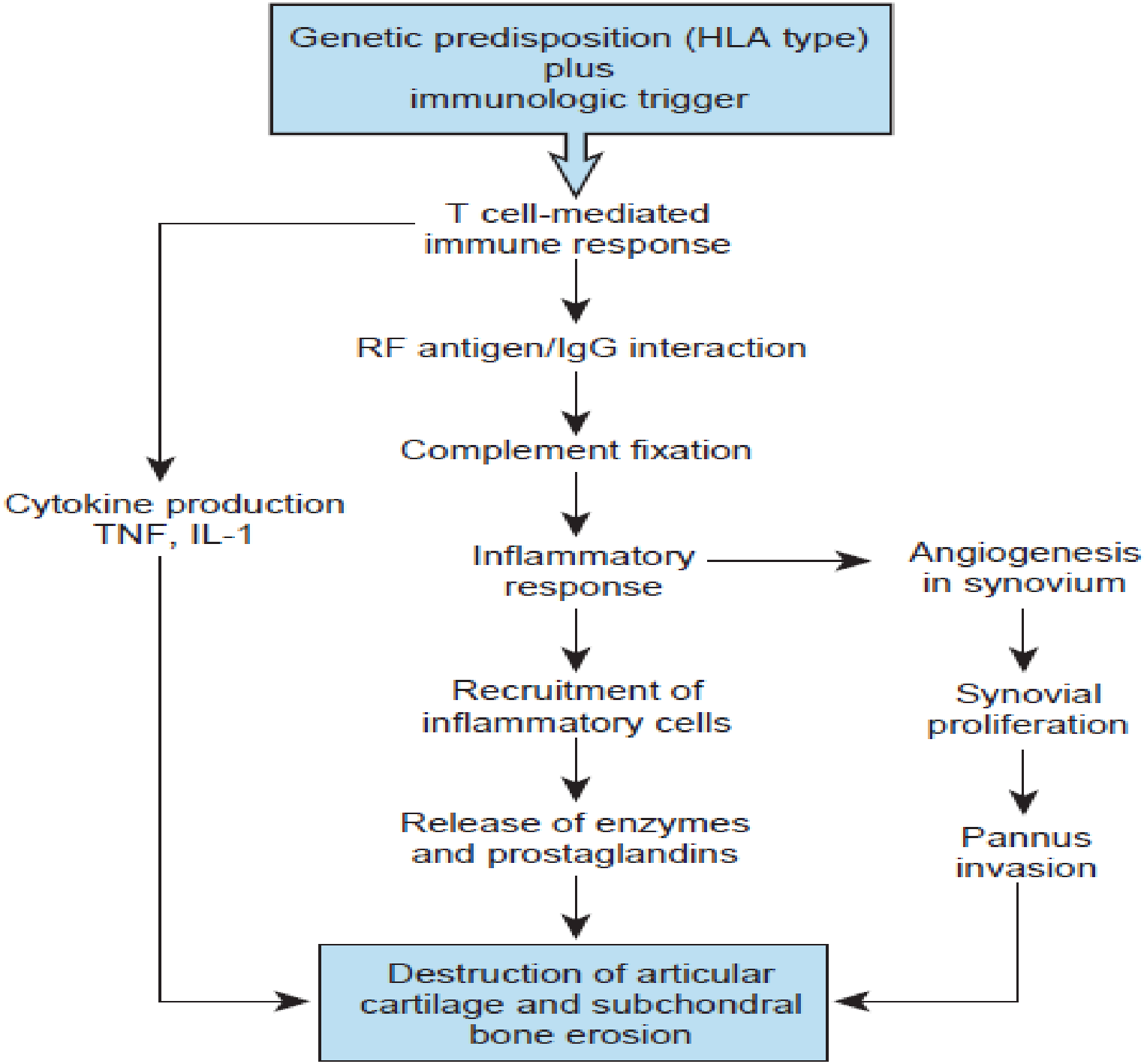
- Although the MHC region is important, it is not the sole determinant, because patients can have the disease without these HLA types.

- Epstien-barr virus, parvoviruses, mycobacteria.

PATHOPHYSIOLOGY


Muscle
Enthesis
Epiphyseal bone
Synovial cavity
Articular cartilage
Bursa
Joint capsule and synovial lining
Ligament
Tendon
Enthesis
Enthesis


Normal joint
Cartilage
Ligament
Bone
Bone
Joint capsule
A
Synovium
Joint affected by rheumatoid arthritis
Inflammation
Loss of cartilage
C
Bone
Bone
B
Pannus
Erosion

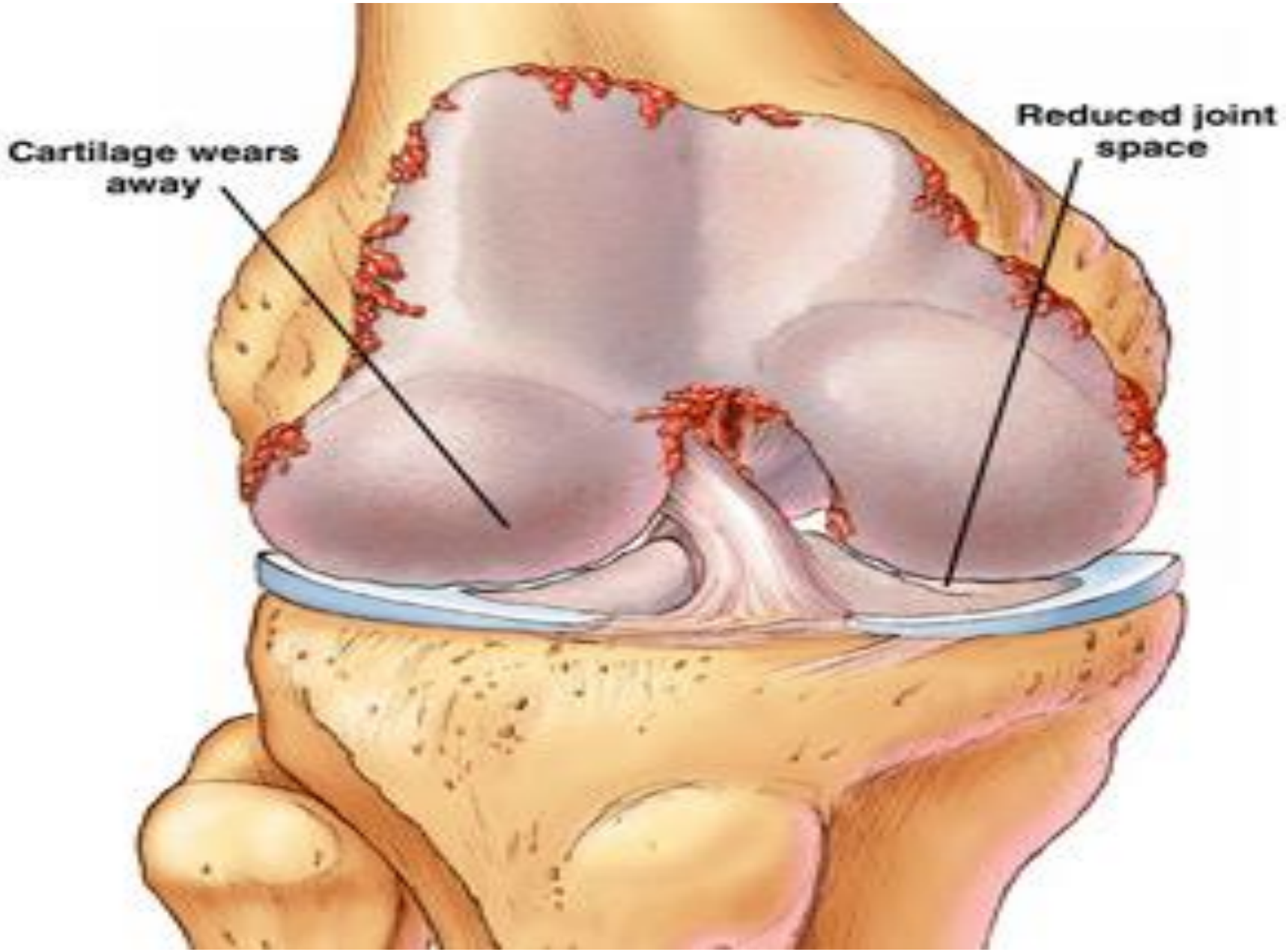

Genetic predisposition (HLA type)
plus
immunologic trigger
T cell-mediated
immune response
RF antigen/IgG interaction
Complement fixation
Cytokine production
TNF, IL-1
Inflammatory
response
Angiogenesis
in synovium
Recruitment of
inflammatory cells
Synovial
proliferation
Release of enzymes
and prostaglandins
Pannus
invasion
Destruction of articular
cartilage and subchondral
bone erosion

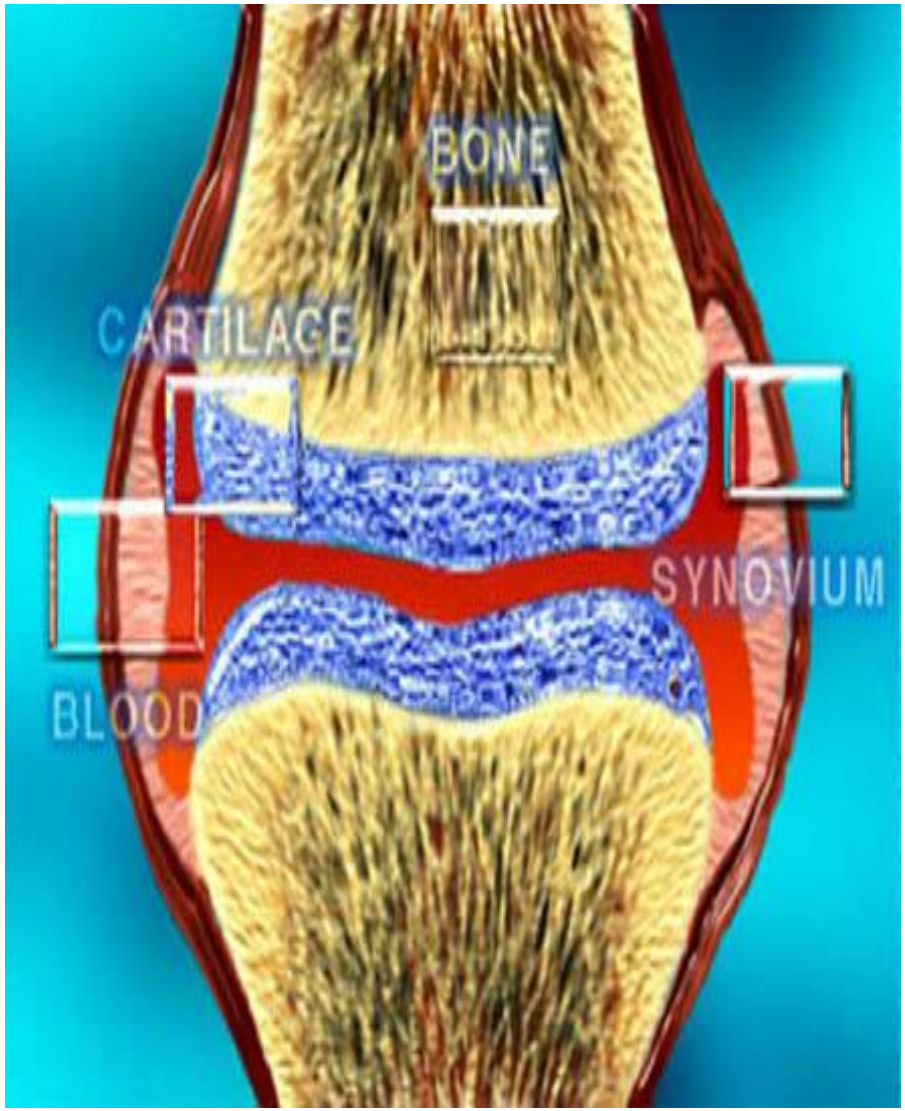
- Rheumatoid arthritis is considered to be a self-immune response to an unknown antigen and the antibody formed against rheumatoid arthritis is (rheumatoid factor), which is Immunoglobulin M (IgM).

- Chronic inflammation of the synovial tissue lining the joint capsule results in the proliferation of this tissue.

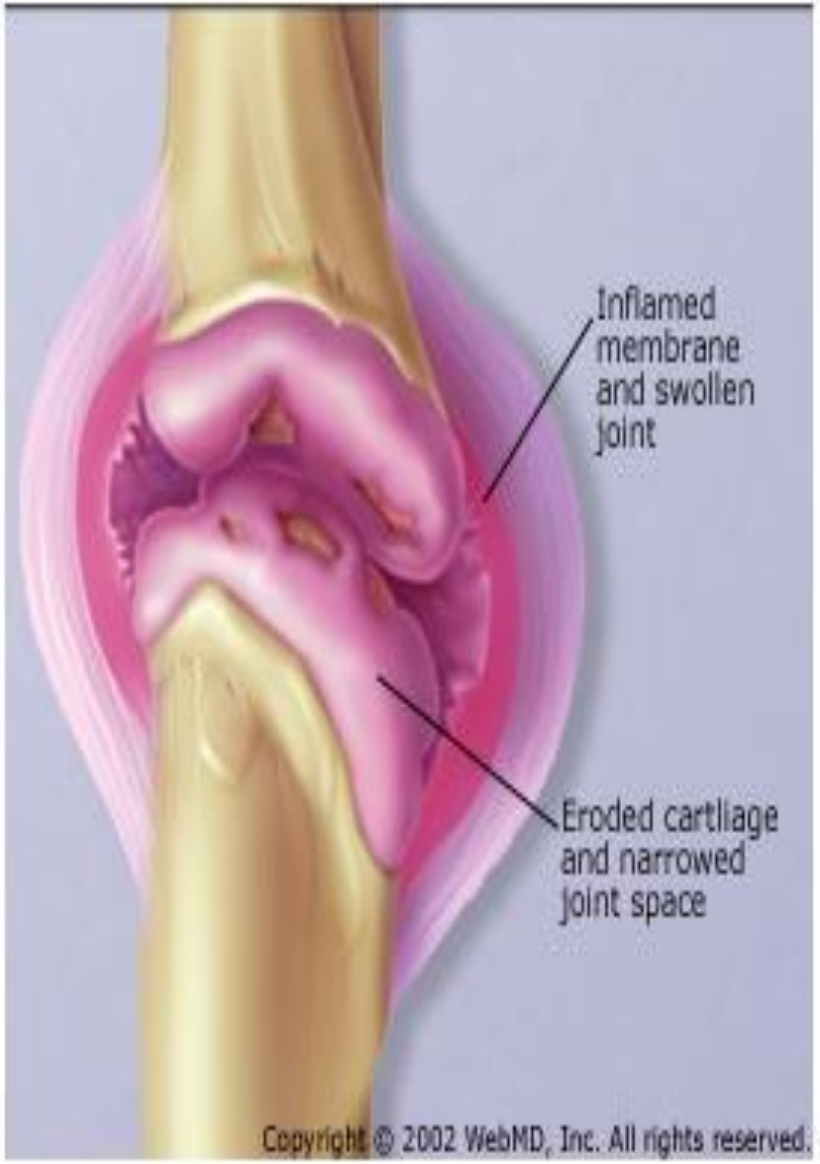
- The inflamed, proliferating synovium (multiplication of parts or cell division) characteristic of rheumatoid arthritis is called *pannus*.

- This pannus invades the cartilage and eventually the bone surface, producing erosions of bone and cartilage and leading to destruction of the joint.

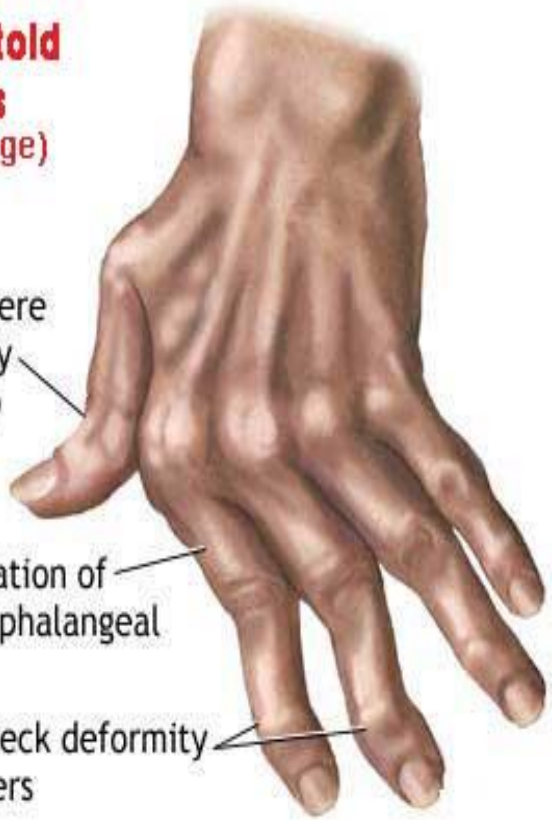

Cartilage wears away
Reduced joint space

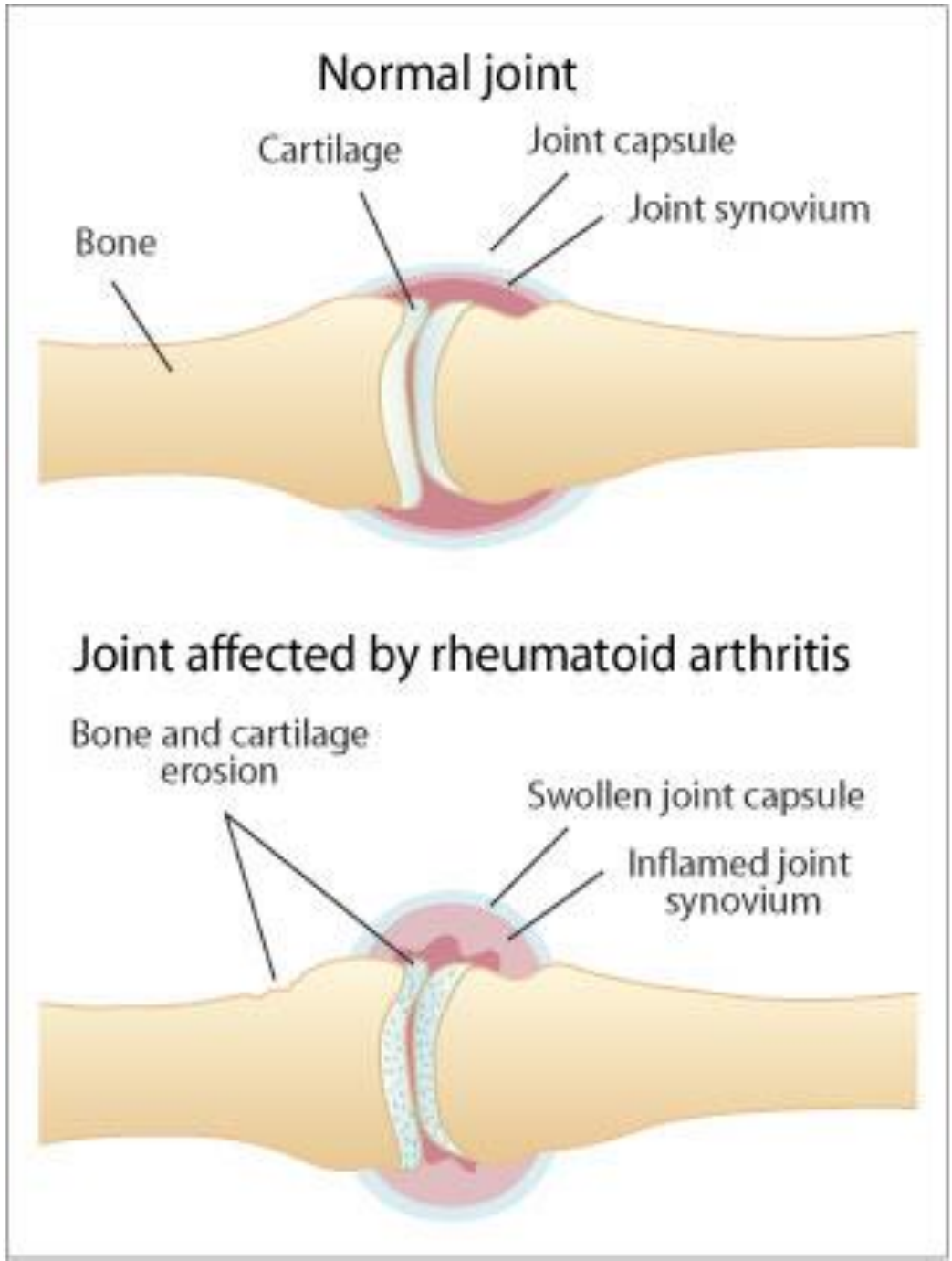


Rheumatoid Arthritis



Rhematoid Arthritis
(Late stage)





- The immune system has both
  - humoral (B -Lymphocytes) and
  - cell-mediated (T-lymphocytes) functions.

- The humoral component is necessary for the formation of antibodies.

- These antibodies are produced by plasma cells.

- Most patients with rheumatoid arthritis form antibodies called *rheumatoid factors*.

- *Rheumatoid factors have not been identified* as pathogenic, nor does the quantity of these circulating antibodies always correlate with disease activity.

- Seropositive patients tend to have a more aggressive course of their illness than seronegative patients.

- Immunoglobulins (IgM) can activate the complement system

- The complement system amplifies the immune response by encouraging chemotaxis, phagocytosis, and the release of lymphokines by mononuclear cells, which are then presented to T lymphocytes.

- The processed antigen is recognized by MHC proteins on the lymphocyte, which activates it to stimulate the production of T and B cells.

- The proinflammatory cytokines tumor necrosis factor (TNF), interleukin-1 (IL-1), and interleukin-6 (IL-6) are key substances in the initiation and continuance of rheumatoid inflammation.

- Lymphocytes may be either B cells (derived from bone marrow) or T cells (derived from thymus tissue).

- Activated T cells produce cytotoxins, which are directly toxic to tissues, and cytokines, which stimulate further activation of inflammatory processes and attract cells to areas of inflammation.

- **Vasoactive substances** also play a role in the inflammatory process.
- Histamine, kinins, and prostaglandins are released at the site of inflammation.
- These substances increase both blood flow to the site of inflammation and the permeability of blood vessels.

- These substances cause the edema, warmth, erythema, and pain associated with joint inflammation and make it easier for granulocytes to pass from blood vessels to the site of inflammation.

- Loss of cartilage may result in a loss of the joint space.

- The formation of chronic granulation or scar tissue can lead to loss of joint motion or bony fusion (called *ankylosis).*

- **Rheumatoid arthritis progresses in 3 stages:-**

  1 st Stage - Swelling of the synovial lining, causing, pain, warmth stiffness, redness and swelling around the joint.

  2 nd Stage - Rapid division and growth of cells, or pannus, which causes the synovium to thicken.

  3 rd Stage - The inflamed cells release enzymes that might damage, bone & cartilage, often causing the involved joint to loose its shape and alignment, causing more pain and loss of movement.

C L I N I C A L PRESENTATION

SYMPTOMS

- Joint pain and stiffness of more than 6 weeks' duration.
- May also experience fatigue, weakness, low-grade fever, and loss of appetite.
- Muscle pain and afternoon fatigue may also be present.
- Joint deformity is generally seen late in the disease.
- Tenderness with warmth and swelling over affected joints usually involving hands and feet.
- Distribution of joint involvement is frequently symmetrical.

- Stiffness and muscle aches (myalgias) may precede the development of joint swelling (synovitis).

- During disease flares, the onset of fatigue begins earlier in the day and subsides as disease activity lessens.

EXTRA-ARTICULAR INVOLVEMENT

- RHEUMATOID NODULES (on extensor surfaces of elbows, forearms, and hands)
- VASCULITIS (Invasion of blood vessel walls by inflammatory cells)
- PULMONARY COMPLICATIONS (pleural effusion,fibrosis)
- OCULAR MANIFESTATIONS (keratoconjunctivitis)
- CARDIAC INVOLVEMENT (pericarditis)
- FELTY'S SYNDROME (splenomegaly and neutropenia)
- OTHER COMPLICATIONS (Lymphadenopathy)

Rheumatoid arthritis and Osteoarthritis differences

Rheumatoid arthritis	Osteoarthritis
Usually begin b/w ages 25–50 years	Usually begins after age 40 years
Autoimmune response affecting the synovial membrane leads to joint destruction	Biomechanical: Leads to loss of cartilage matrix
Develops within weeks or months	Develops slowly, over many years
Usually symmetrical, primarily affects small joints, may involve large joints like elbow	Usually affects weight bearing joints such as knee, hip, lower spine, may be uni or bilateral.
Signs of inflammation present	Pain begins with the use of joints, inflammatory signs are less common
Morning stiffness often >1 hour	Morning stiffness usually lasts <20 minutes
Generalized symptoms, such as fatigue, weight loss and anemia may be present	Does not cause a general feeling of unwellness
More common in females	Commonly found in both male and females
Osteophytes absent	Osteophytes may be present
Rheumatoid factor (RF) frequently present	Rheumatoid factor (RF) absent

Characteristics of rheumatoid arthritis and osteoarthritis (2)		
Characteristic	**Rheumatoid arthritis**	**Osteoarthritis**
Age at which the condition starts	It may begin any time in life.	It usually begins later in life.
Speed of onset	Relatively rapid, over weeks to months	Slow, over years
Joint symptoms	Joints are painful, swollen, and stiff.	Joints ache and may be tender but have little or no swelling.
Pattern of joints that are affected	It often affects small and large joints on both sides of the body (symmetrical), such as both hands, both wrists or elbows, or the balls of bothfeet.	Symptoms often begin on one side of the body and may spread to the other side. Symptoms begin gradually and are often limited to one set of joints, usually the finger joints closest to the fingernails or the thumbs, large weight-bearing joints (hips, knees), or the spine.
Duration of morning stiffness	Morning stiffness lasts longer than 1 hour.	Morning stiffness lasts less than 1 hour. Stiffness returns at the end of the day or after periods of activity.
Presence of symptoms affecting the whole body (systemic)	Frequent fatigue and a general feeling of being ill are present.	Whole-body symptoms are not present.