Inflammatory lesions of the joints (ARTHRITIS)

1- Osteoarthritis (OA)

It is the most common joint disorder. It is a frequent, part of aging and is an important cause of physical disability in persons older than 65 years of age. The fundamental feature of osteoarthritis is **degeneration of the articular cartilage**.

Types:-

I- Primary OA : more common, osteoarthritis appears insidiously with age and without apparent initiating cause. In such cases the disease usually is oligoarticular (i.e., affecting only a few joints), with the joints of the hands, knees, hips, and spine most commonly affected.

II- Secondary OA : represent less than 5% of cases when osteoarthritis strikes in youth, there is typically some predisposing condition, such as previous trauma, developmental deformity, or underlying systemic disease such as marked obesity. often involves one or several predisposed joints.

Gender has some influence; knees and hands are more commonly affected in women, whereas hips are more commonly affected in men.

PATHOGENESIS

Normal articular cartilage performs two functions:

(1) Along with the synovial fluid, it provides virtually friction-free movement within the joint.

(2) In weight-bearing joints, it spreads the load across the joint surface in a manner that allows the underlying bones to absorb shock and weight.

These functions require the cartilage to be elastic (i.e., to regain normal architecture after compression) and to have high tensile strength. These attributes are provided by proteoglycans and type II collagen, respectively, both produced by chondrocytes.

The articular cartilage constantly undergoes matrix degradation and replacement. Normal chondrocyte function is critical to maintain cartilage synthesis and degradation; any imbalance can lead to osteoarthritis, there is an imbalance in the expression, activity, and signaling of cytokines and growth factors that results in degradation and loss of matrix.

Chondrocyte function is affected by a variety of influences:- genetic factors, increasing bone density, as well as sustained high estrogen levels.

MORPHOLOGY

1- Vertical and horizontal fibrillation and cracking of the matrix occur as the superficial layers of the cartilage are degraded. Eventually, full-thickness portions of the cartilage are lost.

2- The subchondral bone plate is exposed and is smoothened and burnished by friction, giving it the appearance of polished ivory (bone eburnation).

3- Small fractures can dislodge pieces of cartilage and subchondral bone into the joint, forming loose bodies (joint mice).

4- The fracture gaps allow synovial fluid to be forced into the subchondral regions to form fibrous walled cysts.
5- Bone outgrowths develop at the margins of the articular surface called **osteophytes**.

2- Suppurative Arthritis

Bacteria can seed joints during episodes of bacteremia results in a suppurative arthritis. Any bacteria can be causal:

- Hemophilus influenzae predominates in children younger than 2 years of age,
- S. aureus is the main causative agent in older children and adults
- Gonococcus is prevalent in older adolescents and young adults.
- Patients with sickle cell disease are prone to Salmonella infection at any age.

The classic presentation is one of sudden onset of pain, redness, and swelling of the affected joint(s), with restricted movement of the joint. Fever, leukocytosis, and elevated ESR are common.

3- Rheumatoid Arthritis

It is a chronic inflammatory disorder of autoimmune origin that principally attacks the joints, producing a nonsuppurative proliferative and inflammatory synovitis progresses to the destruction of the articular cartilage and, in some cases ankylosis (adhesion) of the joints. Extra articular lesions may occur in the skin, heart, blood vessels, and lungs.

Pathogenesis

Genetic predisposition and environmental factors contribute to the development and chronicity of the disease. The pathologic changes are mediated by antibodies against self-antigens and inflammation caused by cytokines, predominantly secreted by CD4+ T cells.

The genetic evidence of RA is demonstrated through high chance of disease in those with HLA-DQ alleles.

CD4+ T helper (TH) cells may initiate the autoimmune response in RA by reacting with a microbial or a chemically modified self-antigen.

The T cells produce cytokines that stimulate other inflammatory cells to effect tissue injury:

- ✓ IFN-γ from TH1 cells activates macrophages and synovial cells.
- ✓ IL-17 from TH17 cells recruits neutrophils and monocytes.
- ✓ TNF and IL-1 from macrophages stimulate resident synovial cells to secrete proteases that destroy hyaline cartilage.

In RA, complexes of antibodies with citrullinated fibrinogen, type II collagen, α-enolase, and vimentin deposit in the joints.

About 80% of patients have serum IgM or IgA autoantibodies that bind to the Fc portions of their own IgG. These autoantibodies are called ***rheumatoid factor*** and may also deposit in joints as immune complexes, although they are not uniformly present in all patients with RA and can be found in patients without the disease. The most

specific antibody for rheumatoid arthritis is anti-CCP (cyclic citrullinated peptide) antibody.
The inflammation localizes to the joint, recruiting macrophages and triggering activation and/or proliferation of synovial cells, chondrocytes, and fibroblasts. The production of proteolytic enzymes and cytokines contributes to the destruction of cartilage through increased osteoclast activity.

Morphology
RA typically manifests as symmetric arthritis principally affecting the small joints of the hands and feet.
Grossly: the synovium becomes edematous, thickened, and hyperplastic, covered by delicate and bulbous villi.
Histologic features include:
(1) synovial cell hyperplasia and proliferation;
(2) Dense inflammatory infiltrates of CD4+ helper T cells, B cells, plasma cells, dendritic cells, and macrophages.
(3) Increased vascularity resulting from angiogenesis.
(4) Neutrophils and aggregates of organizing fibrin on the synovial and joint surfaces.
(5) Osteoclastic activity in underlying bone, allowing the synovium to penetrate into the bone, causing periarticular erosions and subchondral cysts.

- **pannus**: a mass of edematous synovium, inflammatory cells, granulation tissue, and fibroblasts that grows over the articular cartilage and causes its erosion. In advanced untreated cases the pannus can bridge the bones to form a fibrous ankylosis, which may later ossify as a bony ankylosis.
- **Rheumatoid nodules** are an infrequent manifestation of RA and typically occur in subcutaneous tissue including the forearm, elbows, occiput, and lumbosacral area. Microscopically, they resemble necrotizing granulomas.

Arthritis of Metabolic Origin (Gout)

Deposition of monosodium urate (MSU) crystals in tissues, especially the joints due to hyperuricemia; related to overproduction or decreased excretion of uric acid which derived from purine metabolism and is excreted by the kidney.
Primary gout (90% 0f the cases) is the most common form; etiology of hyperuricemia is unknown.
Secondary gout (10%) is seen in those with
1. Leukemia and myeloproliferative disorders-Increased cell turnover leads to hyperuricemia.
2. Renal insufficiency- decreased renal excretion of uric acid
Presents as painful arthritis of the great toe (podagra)

- ☒ MSU crystals deposit in the joint, triggering an acute inflammatory reaction.
- ☒ Alcohol or consumption of red meat may precipitate arthritis.

Chronic gout leads to:

l. Development of tophi :which is white, chalky aggregates of uric acid crystals with fibrosis and giant cell reaction in the soft tissue and joints.
2. Renal failure- Urate crystals may deposit in kidney tubules (urate nephropathy).

Pathogenesis

Most cases of gout are characterized by a primary overproduction of uric acid. Less commonly, hyperuricemia occurs because of decreased renal excretion of urate. Whatever the cause, increased levels of uric acid in the blood and other body fluids (e.g., synovium) lead to the precipitation of monosodium urate crystals which act as chemotactic for inflammatory cells and can also activate complement. This leads to a local accumulation of neutrophils and macrophages in the joints and synovial membranes; and release a mediators such as IL-1, IL-6, and TNF which can directly activate synovial cells and cartilage cells to release proteases (e.g., collagenase) that cause tissue injury.
The resulting acute arthritis typically remits in days to weeks, even if untreated. Repeated bouts, however, can lead to the permanent damage seen in chronic tophaceous arthritis.