Modern Review

Review of Modern Literature

In modern scenario, musculoskeletal complaints account for more than 315 million outpatient visits to clinicians per year. In recent surveys of "Centers for Disease Control and Prevention" it is suggested that 33% (69.9 million) of the U.S. population is affected by arthritis or joint disorders. The musculoskeletal symptoms in some patients, may signal the imminence of more serious condition that requires further evaluation or additional laboratory testing so that diagnosis may be confirmed. There are several urgent conditions that must be diagnosed promptly to avoid significant morbid or mortal sequelae. These "red flag" diagnoses include septic arthritis, acute crystal-induced arthritis (e.g., gout), and fracture.

Articular disorders may be characterized by deep or diffuse pain, limited range of motion on active and passive movement, swelling (caused by synovial proliferation, effusion, or bony enlargement), crepitation, instability, "locking," or deformity.

Differentiation between inflammatory and non-inflammatory process:

To establish the diagnosis, the primary object is to identify the nature of the underlying pathologic process. Musculoskeletal disorders are generally classified as inflammatory or non-inflammatory.

Inflammatory disorders may be infectious (infection with Neisseria gonorrhea or Mycobacterium tuberculosis), crystal induced (gout, pseudogout), immune-related [rheumatoid arthritis (RA), systemic lupus erythematosus (SLE)], reactive (rheumatic fever, Reiter's syndrome), or idiopathic. Inflammatory disorders may be identified by the presence of all or some of the four cardinal signs of inflammation i.e. erythema (rubor), warmth (calor), pain

(dolor), and swelling (tumour), systemic symptoms (prolonged morning stiffness, fatigue, fever, weight loss), or laboratory evidence of inflammation [elevated erythrocyte sedimentation rate (ESR) or C-reactive protein, thrombocytosis, anemia of chronic disease, or hypoalbuminemia]. Morning stiffness related to inflammatory disorders (such as RA) is precipitated by prolonged rest, is often several hours in duration, and may improve with activity and anti-inflammatory medications. By contrast, intermittent stiffness associated with non-inflammatory conditions (such as osteoarthritis) is precipitated by brief periods of rest, usually lasts <60 min, and is exacerbated by activity. Non-inflammatory disorders may relate to trauma (rotator cuff tear), ineffective repair (osteoarthritis), neoplasm, or pain amplification (fibromyalgia). Non-inflammatory disorders are often characterized by pain without swelling or warmth, absence of inflammatory or systemic features, minimal or absent morning stiffness, and normal (for age) or negative laboratory investigations.

In reference to these musculoskeletal disorders, Osteoarthritis is most common type of arthritis and also the most common cause of disability with high prevalence in elderly peoples.

OSTEOARTHRITIS

Introduction

Osteoarthritis (OA) is the most common type of arthritis that affect the synovial joints. Its high prevalence, especially in the elderly, and the high rate of disability related to disease make it a leading cause of disability in the elderly. Because of the aging and obesity a major risk factor, OA is increasing in prevalence, and occurrence is on the rise.

Commonly affected joints include the cervical and lumbosacral spine, hip, knee, and first metatarsal phalangeal joint (MTP). In the hands, the distal and proximal interphalangeal joints and the base of the thumb are often affected. Usually spared are the wrist, elbow, and ankle. Ankles are spared because their articular cartilage may be uniquely resistant to loading stresses.

To a greater or lesser extent Osteoarthritis is always characterized by both degeneration of articular cartilage and simultaneous proliferation of new bone, cartilage and connective tissue. The proliferative response result in some degree of remodeling of the joint contour. Previously Osteoarthritis was considered as degenerative joint disorder but now believed to represent a dynamic process in which there is imbalance between cartilage degeneration and regeneration. Osteoarthritis is not a single disease, rather it is the end result of a variety of pattern of joint failure.

It is characterized by slow, progressive, local erosion and later more extensive destruction of articular cartilage, followed by subchondral sclerosis and the formation of large bony spurs or protrusions (osteophytes) at the margins of affected joints. The large weight-bearing joints spine, knees, hips, and the small joints of hands and feet are most often involved. In idiopathic (primary) OA, the most common form of the disease, no predisposing factor is apparent. Secondary OA is pathologically indistinguishable from idiopathic OA but is attributable to an underlying cause.

Definition[64]

a) Osteoarthritis is a degenerative condition affecting the cartilage and weight bearing surfaces, generally of larger synovial joints and leading to long out growths at their margins,

Degeneration of the inter vertebral discs is an analogous process.

b) Osteoarthritis also erroneously called degenerative joint disease, represent failure of a diarthrodial (movable, synovial lined) joint. In idiopathic (Primary) OA, the most common form of the disease, no predisposing factor is apparent. Secondary osteoarthritis is pathologically indistinguishable from idiopathic osteoarthritis, but is attributable to an underlying cause.

c) Osteoarthritis is a degenerative wear and tear process occurring in the joints that are impaired by congenital defect, vascular insufficiency of previous disease or injury. It is by for the commonest variety of arthritis.

Etymology

Osteoarthritis is derived from the Greek word part osteo-, meaning "of the bone", combined with arthritis: arthr-, meaning "joint", and – *itis*, the meaning of which has come to be associated with inflammation. The *–itis,* of osteoarthritis cold be considered misleading – inflammation is not a conspicuous feature. Some clinicians refer to this condition as osteoarthrosis to signify the lack of inflammatory response.

Epidemiology

OA may develop in any joint, but most commonly affects the knees, hips, hands, facet joints and feet. In 2005, it was estimated that over 26 million people in the US had some form of OA[65]. The incidence of hand, hip and knee OA increases with age, and women have higher rates than men, especially after the age of 50 years. A levelling off or decline occurs at all joint sites around the age of 80 years. The age and sex-standardized incidence rate from the Fallon Community Health Plan in Massachusetts (USA) was highest for knee OA 240/100,000

person-years, with intermediate rates for hand OA (100/100,000 person-years) and lowest observed rates for hip OA (88/100,000 person-years)[66] Incidence rates found by the Dutch Institute for Public Health (RIVM) in 2000 were of a similar level. For hip OA, the reported prevalence was 0.9 and 1.6 per 1000 per year in men and women respectively and for knee OA the corresponding figures were 1.18 and 2.8 per 1000 per year in men and women respectively[67]

Racial difference exists in both the prevalence of OA and the pattern of joint involvement. The Chinese in Hong Kong have a lower incidence of hip OA than whites; OA is more frequent in native Americans than in whites. Interphalangeal joint OA and, especially, hip OA are much less common in South African blacks than in whites in the same population. Whether these differences are genetic or are due to differences in joint usage related to life-style or occupation is unknown.

The relation of heredity to OA is less ambiguous. Thus, the mother and sister of a woman with distal interphalangeal joint OA (Heberden's nodes) are, respectively, twice and thrice as likely to exhibit OA in these joints as the mother and sister of an unaffected woman. Point mutations in the cDNA coding for articular cartilage collagen have been identified in families with chondrodysplasia and Polyarticular secondary OA.

Under the age of 55 years, the joint distribution of OA in men and women is similar; in older individuals, hip OA is more common in men, while OA of interphalangeal joints and the thumb base is more common in women. Similarly, radiographic evidence of knee OA and, especially symptomatic knee OA, is more common in women than in men.

Hand OA

The prevalence of radiographic hand OA varies greatly and has been reported to range from 27% to over 80%[68]. Data from the Framingham cohort demonstrated a prevalence of 13.2 percent in men and 26.2 percent in women aged 70 or more years with at least one hand joint with symptomatic osteoarthritis[69] Symptomatic hand OA, as defined by the American College of Rheumatology (ACR) criteria, is however far less common. Its prevalence was found to be 8% in the United States National Health and Nutrition Examination Survey (NHANES III) and 7% in the Framingham cohort. Rates increased among elderly subjects to 13 to 26% for men and women respectively. A study from Teheran showed that the prevalence of hand OA in people aged 40–50 years was 2.2%, rising with age to 22.5% in people aged > 70 years.[70] Interestingly, data from China based on thirteen surveys involving 29,621 adults demonstrated that symptomatic OA of hand was rarely observed irrespective of age or gender[71]

Knee OA

Knee involvement is more common in women, with female-to-male ratios varying between 1.5:1 and 4:1. Prevalence rates for knee OA, based on population studies in the US, are comparable to those in Europe. These studies report that severe radiographic changes affect 1% of people aged 25-34 and this figure increases to nearly 50% in those 75 years and above.

Dutch Institute for Public Health, the prevalence of knee OA in those aged 55 and above was 15.6% in men and 30.5% in women.[72]

Hip OA

Hip OA is less common then either hand or knee OA. The mean prevalence of primary radiographic hip OA in studies from Asia and Africa is 1.4% and 2.8% respectively. These levels are much lower than those seen

in Europe and North America, where the mean prevalence is 10.1% and 7.2% respectively.[73]

Anatomy of Joints

A joint or articulation (or articular surface) is the connection made between bones in the body which link the skeletal system into a functional whole. A joint's function is to bear weight, perform work and exhibit a particular range of motion during movement where two or more bones come together for the purpose of movement. A joint move when the muscles crossing it contract.[74]

Bones are too rigid to bend without being damaged. Fortunately, flexible connective tissues form joints that hold bones together while still permitting some degree of movement, in most cases. A few joints do not permit any movement at all but do provide a great degree of protection.

CLASSIFICATION OF JOINTS

Joints are mainly classified structurally and functionally. Structural classification is determined by how the bones connect to each other, while functional classification is determined by the degree of movement between the articulating bones. In practice, there is significant overlap between the two types of classifications.[75]

Structural classification (binding tissue)

Structural classification names and divides joints according to the type of binding tissue that connects the bones to each other.[76] There are three structural classifications of joints[77]

Fibrous joint – If there is no joint cavity the bones are joined by dense regular connective tissue that is rich in collagen fibers[78]

Cartilaginous joint – There is no joint cavity, the bones are joined together by cartilage.

Synovial joint – The bones are not directly joined – but have a synovial cavity and are united by the dense irregular connective tissue that forms the articular capsule that is normally associated with accessory ligaments.[79]

Functional classification (movement)

Joints can also be classified functionally according to the type and degree of movement they allow[80] Joint movements are described with reference to the basic anatomical planes.[81]

Synarthrosis (IMMOVABLE JOINT) – Permits little or no mobility. Most synarthrosis joints are fibrous joints (e.g., skull sutures). It may be one of three types: suture, gomphosis, synchondrosis.

a) *Suture*

A suture is a fibrous joint composed of a thin layer of dense fibrous connective tissue and unites the bones of the skull. e.g. the coronal suture between the frontal and parietal bones.

b) *Gomphosis*

A gomphosis is a type of fibrous joint in which a cone-shaped peg fits into a socket. Example- articulations of the roots of the teeth with the alveoli (sockets) of the maxillae and mandible.

c) *Synchondrosis*:

A Synchondrosis is a cartilaginous joint in which the connecting material is hyaline cartilage. Most common type of synchondrosis is the epiphyseal plate. Another example is the joint between first rib and sternum.

Amphiarthrosis – Permits slight mobility. Most amphiarthrosis joints are cartilaginous joints (e.g., intervertebral discs). It may be of two types: Syndesmosis, Symphysis.

a) *Syndesmosis*

A syndesmosis is a fibrous joint in which there is considerably more fibrous connective tissue than in a suture. The firbrous connective tissue forms an interosseous membrane or ligament that permits some flexibility and movement. Example- distal articulation of the tibia and fibula.

b) *Symphysis*

A symphysis is a cartilaginous joint in which the connecting material is a broad, flat disc of fibro cartilage. This type of joint is found between bodies of vertebrae.

Synovial joint (also known as a *diarthrosis*) –

A diarthrosis, or freely movable joint, has a variety of shapes and permits several different types of movements. A distinguishing anatomical feature of a diarthrosis is the space, called synovial cavity that separates the articulating bones[82]. Synovial joints can in turn be classified into six groups according to the type of movement they allow[83]: Gliding, hinge, pivot, ellipsoidal, saddle and ball and socket joints.

a) *Gliding Joint*

The articulating surfaces of bones in a gliding joint are usually flat. Only side to side and back and forth movements are permitted. Example- heads and tubercles of ribs glide on bodies and transverse processes of vertebrae, clavicle glide on sternum and scapula.

b) *Hinge Joint*

In a hinge or ginglymus joint, the convex surface of one bone fits into the concave surface of another bone. Example- knee, elbow, ankle and interphalangeal joints etc.

c) *Pivot Joint*

In a pivot or trochoid joint, a rounded pointed surface of one bone articulates within a ring formed partly by another bone and partly by a ligament. The primary movement permitted is rotation. Example- atlas rotates around the dens of the axis, between proximal ends of the ulna and radius.

d) *Ellipsoidal Joint*

In an ellipsoidal or condyloid joint, an oval-shaped condyle of one bone fits in to an elliptical cavity of another bone. Example- joint at the wrist between the radius and carpals. The movement permitted by such a joint is in two planes, side-to-side and back-and-forth.

e) *Saddle Joint*

In a saddle or sellaris joint, the articular surface of one bone is saddle-shaped and the articular surface of the other bone is shaped like a rider sitting in the saddle. Example- joint between the trapezium of the carpus and metacarpal of the thumb.

f) *Ball-and-Socket Joint*

A ball and socket or spheroid joint consists of a ball-like surface of one bone fitted into a cuplike depression of another bone.

Example- shoulder joint and hip joint

GENERAL FEATURE & COMPONENT OF SYNOVIAL JOINT[84]

Synovial joints are most evolved and therefore most mobile type of joints. They possess the following characteristic features;

There articular surfaces are covered with hyaline cartilage. This articular cartilage is avascular, non nervous and elastic. Lubricated with synovial fluid, the cartilage forms slippery surfaces for free movements.

Between the articular surfaces there is a joint cavity filled with synovial fluid. The cavity may be partially or completely subdivided by an articular disc known as meniscus.

The joint is surrounded by an articular capsule which is fibrous in nature and is lined by synovial membrane. Because of its rich nerve supply the fibrous capsule is sensitive to stretches imposed by movements.

The synovial membrane lines the entire joint except the articular surfaces covered by hyaline cartilage. It is this membrane that secretes the slimy fluid called synovial fluid which lubricates the joint and nourishes the articular cartilage.

Varying degrees of movements are always permitted by the synovial joints.

Blood supply of Synovial Joints:

The articular and epiphyseal branches given off by the neighboring arteries form a peri-articular arterial plexus. Numerous vessels from this plexus pierce the fibrous capsule and form a rich vascular plexus in the deeper part of the synovial membrane. The blood vessels of the synovial membrane terminate around the articular margins in a fringe of looped anastomoses termed the circulus vasculosus (circulus articularis vasculosus). It supplies the capsule, synovial membrane and the epiphyses. The articular cartilage is avascular.

After epiphyseal fusion in growing long bones the communications between the circulosus vasculosus and the

end arteries of the metaphysis are established thus minimizing the chances of osteomyelitis in the metaphysis.

Lymphatic drainage of synovial joints:

Lymphatics form a plexus and the subintima of the synovial membrane and drain along the blood vessels to the regional deep nodes.

Stability of synovial joints:

The various factors maintaining the stability at a joint are described below in order of their importance;

Muscles: The tone of different groups of muscles acting on the joint is the most important and indispensable factor in maintaining the stability. Without muscles, the knee and shoulder would have been unstable and the arches of foot would have collapsed.

Ligaments: These are important in preventing any over movement and in guarding against sudden accidental stresses. However they do not help against a continuous strain because once stretched, they tend to remain elongated. In this respect the elastic ligaments (ligament flava and the ligaments of the joints of auditory ossicles) are superior to the common type of white fibrous ligaments.

Bones: They help in maintaining the stability only in firm type of joints like the hip and ankle joints. Otherwise in most of the joints there role is negligible.

Diagnosis of OA

OA can be diagnosed based on structural abnormalities or on the symptoms these abnormalities evoke. Many persons with x-ray evidence of OA have no joint symptoms

Symptomatic OA of the knee (pain on most days of a recent month in a knee plus x-ray evidence of OA in that knee) occurs in approx. 12% of persons age 60 in the United States and 6% of all adults age 30. Symptomatic hip OA is roughly one-third as common as disease in the knee. While radiographically evident hand OA and the appearance of bony enlargement in affected hand joints are extremely common in older persons, most cases are often not symptomatic.

The prevalence of OA correlates strikingly with age. Regardless of how it is defined, OA is uncommon in adults under age 40 and highly prevalent in those over age 60. It is also a disease that, at least in middle-aged and elderly persons, is much more common in women than in men, and sex differences in prevalence increase with age.

Etiology[85,86]

There is no single cause for OA, and the exact etiology for OA is unknown. Osteoarthritis is classified as either primary (idiopathic) or secondary. Among the various structures making up the knee joint, the hyaline joint cartilage is the main target of the harmful influences that cause osteoarthritis and the structure in which the disease begins.

Since a long time, osteoarthritis was neglected and considered simply as degenerative disease. There are so many things which conspire to cause osteoarthritis like genetic predisposition, metabolic and hormonal influence on cartilage, pattern of joint usage, local mechanical success, pre-existing joint disease and specific incidents of cartilage use. There is no single cause of osteoarthritis. In general this may be due to:

A list of etiologies of secondary osteoarthritis of the knee is follows:

Etiologies of secondary osteoarthritis of the knee

- Post-traumatic
- Congenital/malformation
- Malposition (varus/valgus)
- Postoperative
- Metabolic

    i. Rrickets
    ii. Hemochromatosis
    iii. Chondrocalcinosis
    iv. Ochronosis

- Endocrine disorders

    i. Acromegaly
    ii. Hyperparathyroidism
    iii. Hyperuricemia

- Aseptic osteonecrosis

Risk Factors[87, 88]

Joint vulnerability and joint loading are the two major factors contributing to the development of OA. On the one hand, a vulnerable joint whose protectors are dysfunctional can develop OA with minimal levels of loading, perhaps even levels encountered during every day activities. On the other hand, in a young joint with competent protectors, a major acute injury or long-term overloading is necessary to precipitate disease. Risk factors for OA can be understood in terms of their effect either on joint vulnerability or on loading. It can be understood from the image given on next page no.

Systemic Risk Factors

Age:- Age is the most potent risk factor for OA, with prevalence and incidence of disease rising dramatically with age. In some joints, such as the hands, OA occurs in >50% of persons over age 70. Aging increases joint vulnerability through several mechanisms. Whereas

dynamic loading of joints stimulates cartilage matrix by chondrocytes in young cartilage, aged cartilage is less responsive to these stimuli. Indeed, because of the poor responsiveness of older cartilage to such stimulation.

Cartilage thins with age, and thinner cartilage experiences higher shear stress at basal layers and is at greater risk of cartilage damage. Ligaments stretch with age, making them less able to absorb impulses. A combination of all of these factors work in concert to increase the vulnerability of older joints to OA.

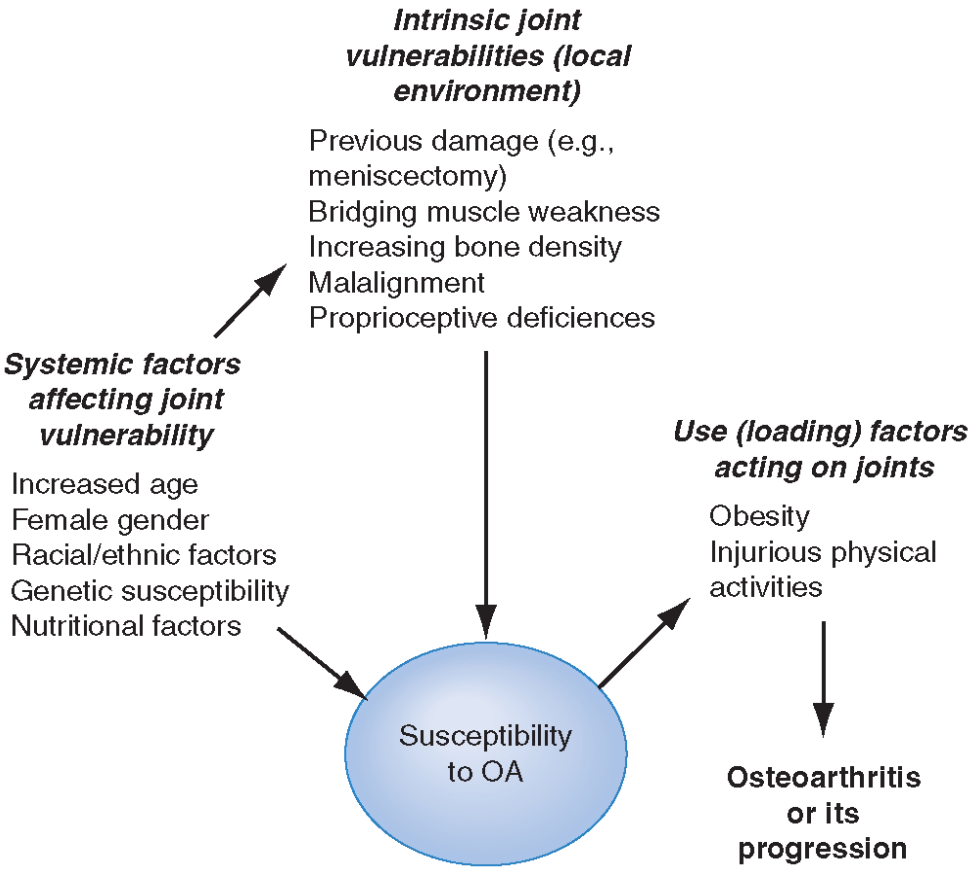


Fig. - *Risk factors for osteoarthritis either contribute to the susceptibility of the joint (systemic factors or factors in the local joint environment) or they increase risk by the load they put on the joint. Usually a combination of loading and susceptibility factors is required to cause disease or its progression.*

Older women are at high risk of OA in all joints, a risk that emerges as women reach their sixth decade. While hormone loss with menopause may contribute to this risk, there is little understanding of the vulnerability of older women's joints to OA.

Risk Factors in the Joint Environment

Some risk factors increase vulnerability of the joint through local effects on the joint environment. With changes in joint anatomy, for example, load across the joint is no longer distributed evenly across the joint surface, but rather shows an increase in focal stress. In the hip, three uncommon developmental abnormalities occurring in utero or childhood, congenital dysplasia, Legg-Perthes disease, and slipped femoral capital epiphysis, leave a child with distortions of hip joint anatomy that often lead to OA later in life.

Major injuries to a joint can also produce anatomic abnormalities that leave the joint susceptible to OA. For example, a fracture through the joint surface often causes OA in joints in which the disease is otherwise rare such as the ankle and the wrist. Avascular necrosis can lead to collapse of dead bone at the articular surface, producing anatomic irregularities and subsequent OA.

Tears of ligaments that protect the joints, such as the anterior cruciate ligament in the knee and the labrum in the hip, can increase joint susceptibility and lead to premature OA. While meniscal tears may increase the risk of OA, meniscectomy operations, including selective ones, increase the risk of later disease.

Another source of anatomic abnormality is **malalignment** across the joint. Varus (bowlegged) knees with OA are at exceedingly high risk of cartilage loss in the medial or inner compartment of the knee, whereas

valgus (knock-kneed) malalignment predisposes to rapid cartilage loss in the lateral compartment.

Loading Factors

Obesity

Three to six times body weight is exerted across the knee during single leg stance. Any increase in weight may be multiplied by this factor to reveal the excess force across the knee in overweight persons during walking. Obesity is a well-recognized and potent risk factor for the development of knee OA and, less so, for hip OA. Obesity is a stronger risk factor for disease in women than in men, and in women, the relationship of weight to the risk of disease is linear, so that with each increase in weight, there is a commensurate increase in risk. Weight loss in women lowers the risk of developing symptomatic disease.

Repeated Use of Joint

There are two categories of repetitive joint use, **occupational** use and **leisure time physical activities**. Workers performing repetitive tasks as part of their occupations for many years are at high risk of developing OA in the joints they use repeatedly. For example, farmers are at high risk for hip OA, miners have high rates of OA in knees and spine, and shipyard and dockyard workers have a higher prevalence of disease in knees and fingers than do office workers. Even within a textile mill, women whose jobs required fine pincer grip [increasing the stress across the interphalangeal (IP) joints] had much more distal IP (DIP) joint OA than women of the same age whose jobs required repeated power grip, a motion that does not stress the DIP joints. Workers whose jobs require regular knee bending or lifting or carrying heavy loads have a high rate of knee OA. One reason why workers may get disease is that during long days at work, their muscles may gradually become

exhausted, no longer serving as effective joint protectors.

Women with increased levels of physical activity, either as teenagers or at age 50, had a higher risk of developing symptomatic hip disease later in life than women who were sedentary. Other athletic activities that pose high risks of joint injury, such as football, may thereby predispose to OA.

Heredity, Genes and Osteoarthritis

Despite its complex clinical expression, it appears that some forms of osteoarthritis have a heritable component.

The most common form of inherited osteoarthritis is primary generalized osteoarthritis (PGOA). PGOA is characterized by the development of Herberdens and Bauchard's nodes and premature degeneration of articular cartilage of multiple joints. The loss of PGOA is concentric and uniform particularly in knee and hips.

Pathology[89]

Pathology is the study of disease by scientific methods. The word pathology came from the Latin words "patho" & "logy". 'Patho' means disease and 'logy' means study, therefore pathology is a scientific study of disease.

Osteoarthritis and Cartilage

Cartilage is a unique tissue with viscoelastic and compressive properties which are imparted by its extracellular matrix, composed predominantly of type II collagen and proteoglycans.

Constituents of Cartilage

- Cellular (chondrocytes): 1 – 2 %
- Liquid phase: 70 – 80 %
- Solid phase: 20 – 30%
  - Collagen: type II and other
  - Proteoglycans: aggrecan and

Under normal conditions, this matrix is subjected to a dynamic remodeling process in which low levels of degradative and synthetic enzyme activities are balanced, such that the volume of cartilage is maintained. In OA cartilage, however, matrix degrading enzymes are overexpressed, shifting this balance in favor of net degradation, with resultant loss of collagen and proteoglycans from the matrix. Presumably in response to this loss, chondrocytes initially proliferate and synthesize enhanced amounts of proteoglycan and collagen molecules. As the disease progresses, however, reparative attempts are outmatched by progressive cartilage degradation. Fibrillation, erosion and cracking initially appear in the superficial layer of cartilage and progress over time to deeper layers, resulting eventually in large clinically observable erosions. OA, in simplistic terms, therefore, can be thought of as a process of progressive cartilage matrix degradation to which an ineffectual attempt at repair is made.

The primary enzymes responsible for the degradation of cartilage are the matrix metalloproteinases (MMPs). These enzymes are secreted by both synovial cells and chondrocytes and are categorized into three general categories: *a) collagenases; b) stromelysins; and, c) gelatinases*. Under normal conditions, MMP synthesis and activation are tightly regulated at several levels. They are secreted as inactive proenzymes that require enzymatic cleavage in order to become activated. Once activated, MMPs become susceptible to the plasma-derived MMP inhibitor, alpha-2-macroglobulin, and to tissue inhibitors of MMPs (TIMPs) that are also secreted by synovial cells and chondrocytes. In OA, synthesis of

MMPs is greatly enhanced and the available inhibitors are overwhelmed, resulting in net degradation.[90]

Pathogensis[91]

The pathology of OA provides evidence of the panarticular involvement of disease. Cartilage initially shows surface fibrillation and irregularity. As disease progresses, focal erosions develop there, and these eventually extend down to the subjacent bone. With further progression, cartilage erosion down to bone expands to involve a larger proportion of the joint surface, even though OA remains a focal disease with nonuniform loss of cartilage.

After an injury to cartilage, chondrocytes undergo mitosis and clustering. While the metabolic activity of these chondrocyte clusters is high, the net effect of this activity is to promote proteoglycan depletion in the matrix surrounding the chondrocytes. This is because the catabolic activity is greater than the synthetic. As disease develops, collagen matrix becomes damaged, the negative charges of proteoglycans get exposed, and cartilage swells from ionic attraction to water molecules. Because in damaged cartilage proteoglycans are no longer forced into close proximity, cartilage does not bounce back after loading as it did when healthy, and cartilage becomes vulnerable to further injury. Chondrocytes at the basal level of cartilage undergo apoptosis.

With loss of cartilage some alterations in subchondral bone, stimulated by growth factors and cytokines, osteoclasts and osteoblasts in the subchondral bony plate, just underneath cartilage, become activated. Bone formation produces a thickening and stiffness of the subchondral plate that occurs even before cartilage ulcerates. Trauma to bone during joint loading may be the primary factor driving this bone response, with healing

from injury (including microcracks) producing stiffness. Small areas of osteonecrosis usually exist in joints with advanced disease. Bone death may also be caused by bone trauma with shearing of microvasculature, leading to a cutoff of vascular supply to some bone areas.

At the margin of the joint, near areas of cartilage loss, osteophytes form. These start as outgrowths of new cartilage and, with neurovascular invasion from the bone, this cartilage ossifies. Osteophytes are an important radiographic hallmark of OA. In malaligned joints, osteophytes grow larger on the side of the joint subject to most loading stress (e.g., in varus knees, osteophytes grow larger on the medial side).

The synovium produces lubricating fluids that minimize shear stress during motion. In healthy joints, the synovium consists of a single discontinuous layer filled with fat and containing two types of cells, macrophages and fibroblasts, but, in OA, it can sometimes become edematous and inflamed. There is a migration of macrophages from the periphery into the tissue, and cells lining the synovium proliferate. Enzymes secreted by the synovium digest cartilage matrix that has been sheared from the surface of the cartilage.

The pathology of OA is not identical across joints. In hand joints with severe OA, for example, there are often cartilage erosions in the center of the joint probably produced by bony pressure from the opposite side of the joint. Bone remodelling is a prominent feature of hand OA, in part because of the thin cartilage in each hand joint. In hand OA, pathology has also been noted in ligament site insertions, which may help propagate disease.

Basic calcium phosphate and calcium pyrophosphate dihydrate crystals are present microscopically in most joints with end-stage OA. Their role in osteoarthritic cartilage is unclear, but their release from cartilage

into the joint space and joint fluid likely triggers synovial inflammation, which can, in turn, produce release of enzymes and trigger nociceptive stimulation.

Sources of Pain

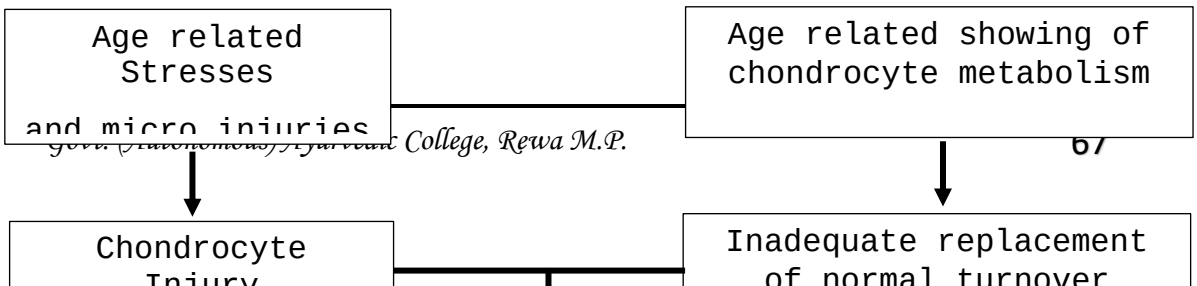
Because cartilage is aneural, cartilage loss in a joint is not accompanied by pain. Thus, pain in OA likely arises from structures outside the cartilage. Innervated structures in the joint include the synovium, ligaments, joint capsule, muscles, and subchondral bone. Sources of pain include synovial inflammation, joint effusions, and bone marrow edema. Osteophytes themselves may be a source of pain. When osteophytes grow, neurovascular innervation penetrates through the base of the bone into the cartilage and into the developing osteophyte.

Pain may arise from outside the joint also, including bursae near the joints. Common sources of pain near the knee are anserine bursitis and iliotibial band syndrome.

Pathophysiology of Osteoarthritis

Articular cartilage is the smooth, white tissue that covers the ends of bones where they come together to form joints. Healthy cartilage in our joints makes it easier to move. It allows the bones to glide over each other with very little friction. Articular cartilage can be damaged by injury or normal wear and tear. It is the long lasting and is probably the last tissue in the body to die, remaining viable for up to 36 hours after death. It is a living rubbery, gel like sponge which is designed to perform two functions i.e. to reduce the friction caused by one bone rubbing against another, and blunt the constant trauma inflicted on bones during everyday life.

Cell injury **Impaired Maintenance**



Cartilage does not contain blood vessels (it is avascular) or nerves (it is aneural). Nutrition is supplied to the chondrocytes by diffusion. It comes from vessels of the underlying bone and some from the synovial membranes which produces synovial fluid. This fluid bathes the cartilage surface and provides some nutrients. The cartilage tissue has very few cells only 1-2 percent which are known as chondrocytes. These cells are embedded in an extracellular matrix which comprises the balance 98-99 percent of the cartilage material. Chondrocytes produce the extracellular matrix. The major constituents of matrix are type -2 collagan, proteoglycans and water (80% of wet weight). Water is essential for not only stock absorption and sponginess but it also carries

nutrients to the cartilage. The proteoglycans attract the whole water and collagen network keep the proteoglycans in place. During adult life, metabolically active chondrocytes continue to synthesis new matrix resulting in a delicate balance between synthesis and degeneration.

If the cartilage is damaged, or if the cartilage chewing enzymes start over reworking, the netting provided by the collagen can become loose and it stretches out and becomes weak. This permits the proteoglycans to lose their grip and they just float away. Thus, the cartilage loses its ability to retain water and absorb shock. This makes it more susceptible cracking, fissuring and complete wearing down. Osteoarthritis is primarily due to break down of articular cartilage with poor repair. Besides the cartilage, the ligaments in and around the joint play a very important part in providing stability to the joint. They along with the capsule keep the bone ends in union and facilitate movements. The synovial membrane lining the joint secrets synovial fluid which nourishes and lubricates the joint. The muscle, besides moving the joint also helps in stabilizing it.

Progression of disease:

The progression of osteoarthritis is highly variable in long term studies it deteriorates with time but improvement is rare. Symptomatic osteoarthritis may progress or may even be arrested. Symptoms don’t correlate well with radiographic progression. Those patients with multiple affected joints have more rapid progression of osteoarthritis in their individual joints. Advanced age of obesity is also associated with a more rapid progression of osteoarthritis.

Classification of Osteoarthritis[92, 93]

A. **Primary osteoarthritis**: this type of osteoarthritis is idiopathic in nature i.e. there is no specific cause for joint breakdown. This occurs in the vast majority of osteoarthritis cases. It may be localized (confined to one or two joints) or generalized (present in three or more joints).

I. Localized osteoarthritis

1. Hands:- Herberden's nodes, Bouchard's nodes (nodal), erosive interphalangeal arthritis (non nodal) Ist carpometacarpal joint.
2. Feet:- Hallux valgus Hallux rigidus, contracted toes (hammer / cookup toes) talonavicular.
3. Knee:
   a. Medial compartment
   b. Lateral compartment
   c. Patellofemoral compartment
4. Hip:
   a. Eccentric (superior).
   b. Concentric (axial, medial)
   c. Diffuse (coxae senilis)
5. Spine:
   a. Apophyseal joints
   b. Intervertebral joints (disks)
   c. Spondylosis (osteoarthritis)
   d. Ligamentous (hyperostosis, foresteir's diseases, diffusion idiopathic skeletal hyperstosis)
6. Other single sites are glenohumoral, acromioclavicular, tibiotalar, sacroiliac, temporomandibular.

II. **Generalized osteoarthritis**: Include three or more areas / joints listed in localized arthritis.

B. **Secondary Osteoarthritis**:

1. Trauma:
   a. Acute
   b. Chronic (occupational, sports)

2. Congenital or developmental:
   a. Localized diseases: Legg-Calve-Perthes, congenital hip dislocation, slipped epiphysis.
   b. Mechanical factors: Unequal lower extremity length, valgus / varus deformity, hypermobility syndromes.
   c. Bone dysplasias: Epiphyseal dysplasia, osteonydhondes-trophy
3. Metabolic:
   a. Ochronosis (alkaptonuria)
   b. Hemochromatosis
   c. Wilson's disease
   d. Gaucher's disease
   e. Chondrocalcinosis
4. Endocrine:
   a. Acromegaly
   b. Hyperparathyroidism
   c. Diabetes mellitus
   d. Obesity
   e. Hyperthyroidism
5. Calcium deposition disease;
   a. Calcium pyrophosphate dehydrate deposition
   b. Apetite arhtropathy
6. Other bone and joint diseases:
   a. Localized: fracture, avascular necrosis, infection, gout.
   b. Diffuse: Rheumatiod (inflammatory) arthritis, Paget's disease.
7. Neuropathic - Charcot disease
8. Miscllaneous:
   a. Frostbite
   b. Caisson disease
   c. Hemoglabinopathies

Theories of the Development of OA[94]

Bio-mechanical theory of Osteoarthritis

The biomechanical theory proposes that excessive joint loading produces altered stresses that derange normal chondrocyte function, leading to an imbalance between matrix mobilisation and synthesis. Thus some areas of cartilage become softened and vulnerable to flaking and fissuring. Chondrocyte injury might further predispose to release of collagenase and other proteases, contributing to the matrix and cartilage break down. The articular alteration might then produce a secondary synovitis with mononuclear cell infiltration leading to release form monocyte or macrophages of inflammatory mediators such as IL-I (mostly beta). These cytokines has the capacity to simulate release of lytic enzymes form chondrocytes and synoviocytes and to inhibit proteoglycans synthesis. The changes in the subchondral bone may also be the consequence of Altered weight – bearing and by weakening the underlying support, predisposes to further cartilage injury. However, whether the bony changes antedate or follow the cartilage injury is uncertain.

Biochemical theory of Osteoarthritis

The biochemical theory places more emphasis on early impairment of the integrity of cartilage by collagenases and other lytic enzymes. This theory proposes that aging or abnormal stresses initiate the injury by inducing a synovitis with the release of enzymes and cytokines, damaging the metabolic integrity of the cartilage, which is then followed by the changes described. The two theories differ only in the events that initiate the changes.

Clinical features[95]

Sign and symptoms of osteoarthritis may be delayed by many years in appearance after the cartilage degeneration

is actually started. The symptoms usually start insidiously in an asymmetric manner.

Limited number of joints are involved in most of the patients. Presenting compliant in osteoarthritis is joint pain which comes on after use and relieved by rest. The most frequently involved joints are spine, hips, knees and hands. The disease is confined to one or only a few joints in majority of the patients. The symptoms are of gradual onset.

1. **Pain**: it is the first manifestation which is first intermittent and aching and is provoked by use of joint and relieved by rest. Sometime pain gets worse, and the joint becomes swollen. As the disease progresses, movement in affected joint becomes increasingly limited, initially as a result of pain and muscular spasm, but later because of capsular fibrosis, osteophytes formation and remodelling of bone. Nocturnal aching pain may be attributable to hyperaemia of the subchondral bone.

   Causes of joint pain in osteoarthritis.

Source	**Mechanism**
Synovium	Inflammation
Subchondral bone	Medullary hypertensionm, microfractures
Osteophytes	Stretching of periosteal nerve endings
Ligaments	Stretch
Capsule	Inflammation, distension
Muscle	Spasm

2. **Stiffness:** Morning stiffness or stiffness of involved joint after a period of inactivity is the prominent features or symptom of OA. It usually lasts less than 30 minutes. Functional impairment in osteoarthritis is highly variable. It depends upon associated muscles wasting and weakness, and on radiological severity of

the disease. Moderate joint stiffness aggravates by rest.

3. **Crepitus**: it is common in knee osteoarthritis and is present in over 90% of patients. Crepitus is due to cartilage loss and joint surface irregularities. Over 50% patients show **Varus** or **Valgus** deformity of legs. OA may involve one joint initially but in later stages it usually involve bilateral joints of knee joints. It may be medial femorotibial, lateral femorotibial or patellofemoral compartment. The involvement of patellofemoral is tested by eliciting pain when patella is compressed against femur on active extension of knee (Shrug test). Fine or coarse crepitus may occur on motion due to friction provoked by narrowing of joint space.
4. **Swelling:** Swelling due to synovial inflammation or synovial effusion occurs in case there is acute episode of osteoarthritis, when patient is already suffering from this disease i.e. in advanced cases. OA may cause joint swelling in those joints that bear weight over a lifetime, such as knees, hips, feet, and spine. Except for the pain in the affected swollen joint, patient usually do not feel sick or tired.
5. **Restriction of Movement:** Capsule fibrolasis, osteophytes, irregularity of articular surface or impaction of loose bodies may decrease the range of motion of joints.
6. **Muscle wasting:** Due to restriction of activity due to pain etc. the muscles of involved joints become wasted and hypotonic. True myopathy is absent.
7. **Deformity**: Mal-alignment of joints e.g. genu valgum may result from irregularities of articular surface of large joints.
8. **Herberden's nodes and Bouchard's Nodes**: Herberden's nodes on dorsal aspect of terminal interphalangeal joints of fingers. The incidence is more in females as compare to males in the ratio of 10:1. The same type of node i.e. pathologically identical nodes when present

over proximal interphalangeal joints are called Bouchard's nodes. It may be symptomless or very painful and associated with paresthesia and stiffness. Often phalanx distal to Herberden's node is flexed or deviated laterally. Occasionally nodes are localized to sites of previous injury to the phalanx.

Grading of Severity: According to progress to the severity of the disease it is graded in to the following four grades (Rao-1985):

Grade – I : Pain, Morning stiffness, Crepitus with normal roentgenogram

Grade – II : Pain, Morning stiffness, Crepitus with marginal osteophytes in roentgenogram

Grade – III : Pain, Swelling, restricted movements, increased crepitus, narrowing of joints space with gross osteoarthritis changes in roentgenogram.

Grade – IV : All the above complaints with heavy crepitus with loose bodies, markedly narrow joints space in radiological films, changes in roentgenogram.

Osteoarthritis of specific joints:[96]

1. **INTERPHALANGEAL JOINTS**: Herberden's nodes, bony enlargements of the distal interphalangeal joints, are the most common form of idiopathic OA. A similar process at the proximal interphalangeal joints leads to Bouchard's nodes. Usually these nodes develop gradually with little or no discomfort, and usually do not interfere significantly with function. But they may present acutely with pain, redness and swelling.

In erosive OA distal and/ or proximal interphalangeal joints of the hands are most prominently affected. Erosive OA tends to be more destructive than typical nodal OA. X-ray evidence of collapse of the sub-chondral plate is characteristic. Deformity and functional impairment may be severe. The synovium is much more

extensively infiltrated with mononuclear cells than in other forms of osteoarthritis.

2. **THUMB BASE:** The second most frequent area of involvement is OA in the thumb base. Swelling, tenderness, and crepitus on movement of the joint are typical. Osteophytes may lead to a "squared" appearance of the thumb base. Pain with pinch leads to adduction of the thumb and contracture of the first web space, often resulting in compensatory hyperextension of the first metacarpophalangeal joint and swan-neck deformity of the thumb.
3. **HIP JOINT**: Congenital or developmental defects (e.g. acetabular dysplasia, Legg-calve-perthes disease, slipped-capital epiphysis) may be implicated in as many as 80% cases of hip OA. 20% of patients will develop bilateral involvement. Pain from hip OA is generally referred to the inguinal area but may be referred to the buttock or proximal thigh. Less commonly hip osteoarthritis present as knee pain, pain can be evoked by putting the involved hip through its range of motion. Flexion may be painless initially, but internal rotation will exacerbate pain. Loss of internal rotation occurs early, followed by loss of extension, adduction, and flexion due to capsular fibrosis and / or buttressing osteophytes.
4. **THE KNEE**: The joints involved in knee osteoarthritis are medial and lateral femorotibial joint and / or patellofemoral joint. Joint movement elicit crepitation. There may be hypertrophy of bone which may be tender. It can be felt by palpation of knee joint. Knock knee which is also called **valgus** deformity is present in osteoarthritis of lateral side of knee joint. Whereas deformity of medial side of knee joint i.e. medial femorotibial joint is called **varus** deformity. The sign of patellofemoral osteoarthritis is pain with manual compression of the patella against the femur during contraction of quadriceps muscle, it is called positive 'shrug' sign.

5. **THE SPINE:** Degenerative disease of the spine can involve the epiphyseal joint, intervertebral disks, and / or paraspinous ligaments. Arthritis of the spine usually occurs due to internal damage to the facet joints. The surfaces of the facet joints are lined with smooth cartilage to allow for movement as the two sides of the joint rub against one another. The combination of the cartilage and the fluid allows the joint to move with little friction. Osteoarthritis (degenerative arthritis) of spine can cause breakdown of cartilage between the facet joints. When the joints move, the lack of the cartilage causes pain as well as loss of motion and stiffness, as they get stiffer they have more back pain. Degenerative disease of the spine can involve the epiphyseal joint, intervertebral disks, and / or paraspinous ligaments. Spondylosis refers to degenerative disk disease.
6. **GENERALIZED OSTEOARTHRITIS**: Generalized OA is characterized by involvement of three or more joints or groups of joints. Heberden's and Bouchard's nodes are prominent. Symptoms may be episodic, with "flare-ups" of inflammation marked by soft tissue swelling, redness and warmth. ESR may be elevated.

Table no. 7

Kellgren-Lawrence (KL) Classification of Osteoarthritis

0	Normal (absence of osteoarthritis)
1	Doubtful narrowing of joint space and possible osteophyte lipping
2	Definite osteophytes and definite narrowing of joint space
3	Moderate joint space narrowing and Moderate multiple osteophytes, some sclerosis and deformity of bone contour
4	Large osteophytes and marked narrowing of joint space, severe sclerosis, and definite deformity

	of bone contour.

Investigation:

Clinical features and radiological features are the basic tools to diagnose osteoarthritis. Intially radiographic findings may be normal but in later stages as the pathology grows following radiological and other changes will occur:

Radiological

X-ray findings

X-ray of affected joint or joints in Antero-posterior and Lateral view may show following features:

Joint space narrowing: Evaluating arthritis usually involves measuring the joint space and judging whether it has narrowed. A weight-bearing x-ray is taken to look for joint space narrowing in the hips and knees.

In osteoarthritis, the joint space narrowing is usually asymmetric. It varies in the different knee compartments of the same knee and surfaces of the hip joint affected. In the knee, joint space narrowing has been linked to loss of articular cartilage. However, meniscal damage also contributes to joint space narrowing. However, it is usually symmetric in osteoarthritis of the finger joints. The wear and tear of osteoarthritis is characterized by joint deterioration and a loss of cartilage.

Osteophytes : An osteophyte is a smooth bony growth or deposit, also referred to as a bone spur. They are also sometimes called osteochondral nodules, osteochondrophytes, and chondro-osteophytes. Technically-speaking, an osteophyte is a fibrocartilage-capped bony outgrowth originating from precursor cells of the

periosteum and growth factors. Osteophytes commonly develop in joints that show signs of degeneration. They are associated with the most common type of arthritis, osteoarthritis. Their presence can serve to distinguish osteoarthritis from other types of arthritis.[97]

Subchondral bone sclerosis: Subchondral sclerosis is a painful condition that affects people who have osteoarthritis. osteoarthritis degrade the cartilage in a joint, it also wears away at the subchondral bone underneath the cartilage.

As the body tries to regrow this bone, it comes back thicker than before, resulting in subchondral sclerosis. It's most likely to be found in later stages of osteoarthritis.

Subchondral sclerosis can cause bone spurs, and in some cases, can reduce motion in the affected joint.[98]

Bony remodelling: OA is associated with early loss of bone owing to increased bone remodelling, followed by slow turnover leading to densification of the subchondral plate and complete loss of cartilage. Early-stage increased remodelling and bone loss, and the late-stage slow remodelling and subchondral densification are important components of the pathogenetic process that leads to OA.

Other findings: In addition to above mentioned findings loose bodies, and calcification linear due to Calcium Pyrophosphate Dihydrate (CPPD) deposition, spotty due to Hydroxyapatite deposition are the other changes.

Advanced Radiological techniques:

Although radiography is the simplest and least expensive imaging technique. It can detect OA-associated

bony features including marginal osteophytes, subchondral sclerosis, and subchondral cysts. Radiography can also determine joint space width (JSW), an indirect surrogate of cartilage thickness and meniscal integrity, but precise measurement of each of these articular structures is not possible by x-ray. Recent MRI based knee osteoarthritis studies have begun to reveal the limitations of radiography. The ability of MRI to image the knee as a whole organ and to directly and three-dimensionally assess cartilage morphology and composition plays a crucial role in understanding the natural history of the disease and in the search for new therapies. Use of the appropriate MRI pulse sequences is crucial to assess the various features of osteoarthritis, and support from experienced musculoskeletal radiologists is necessary for study design, image acquisition, and interpretation.[99]

Laboratory investigations

There is no specific laboratory test to diagnose OA. An examination of synovial fluid from an affected joint is helpful in diagnosis of OA. Tests that may be ordered to rule out other conditions and to evaluate the person's health include:

Rheumatoid factor (RF) and Cyclic citrullinated peptide antibody (CCP) – To help diagnose rheumatoid arthritis (RA) and differentiate it from osteoarthritis; both tests are positive with RA and generally negative in OA.

Synovial fluid analysis – To look for signs of joint infection and to detect monosodium urate (uric acid) crystals that could indicate gout or calcium pyrophosphate crystals that may contribute to joint damage in osteoarthritis. Synovial fluid examination usually shows mild leukocytosis with mononuclear cell predominance. Synovial fluid may show presence of

crystals in 30-70% patients depending upon the technique used. The crystals found most commonly are calcium pyrophostate dehydrate (CPPD) crystals.

Erythrocyte sedimentation rate (sed rate or ESR) – To detect inflammation in the body; ESR will be increased in RA but not in osteoarthritis.

C-reactive protein (CRP) – To detect inflammation and test for the activity of the disease; may be used to help differentiate osteoarthritis and RA; an increased level of CRP occurs in RA but not in osteoarthritis.

Complete blood count (CBC) – To help to evaluate red and white blood cells and hemoglobin; may be ordered to monitor the side effects of some OA treatments.

Comprehensive metabolic panel (CMP) – to help evaluate and monitor kidney and liver function.[100]

Biomarkers of OA: Laboratory markers have received growing attention in recent years, in an attempt to improve diagnosis, assessment of disease activity and severity, and evaluation of therapeutic effects. Many biomarkers have been proposed, in particular those reflecting cartilage and bone turnover and synovitis. Among these, COMP, antigenic keratan sulphate, hyaluronan, YKL-40, type III collagen N-propeptide, and urinary glucosyl-galactosyl pyridinoline appear to be the most promising.[101]

Complications of osteoarthritis[102, 103, 104]

Possible complications of osteoarthritis include:

- Rapid, complete breakdown of cartilage resulting in loose tissue material in the joint (chondrolysis).
- Bone death (osteonecrosis).

- Stress fractures (hairline crack in the bone that develops gradually in response to repeated injury or stress).
- Bleeding inside the joint.
- Infection in the joint.
- Deterioration or rupture of the tendons and ligaments around the joint, leading to loss of stability.
- Pinched nerve (in osteoarthritis of the spine).
- Chondrocalcinosis: Osteoarthritis can also encourage calcium pyrophosphate crystals to form in cartilage. This is called calcification or chondrocalcinosis. Osteoarthritis tends to become more severe more quickly when calcium crystals are present. Sometimes the crystals can shake loose from the cartilage, causing a sudden attack of very painful swelling called acute calcium pyrophosphate crystal arthritis (acute CPP crystal arthritis), a type of calcium crystal disease. The old name acute CPP crystal arthritis was 'pseudogout'.

  Subluxation: Subluxation can also be seen on x-ray as a possible consequence of osteoarthritis. Subluxation is a partial dislocation of a bone.

Differential diagnosis of osteoarthritis.[105]

A differential diagnosis is the distinguishing of a particular disease or condition from others that present similar clinical features. Differential diagnostic procedures are used by physicians and other trained medical professionals to diagnose the specific disease in a patient. Here also Joint symptoms are not only seen in osteoarthritis, but some other disease also exhibit symptoms like OA at some places. So while diagnosing OA such factors should be differentiated for the successful treatment. OA should be differentiated from certain ailment which are expressed below:

i) Chondromalacia Patellae:

It is characterized by anterior knee pain and positive shrug sign, is a syndrome of patellofemoral pain, often bilateral, in teenagers and young adults. It is more common in females than in males. it is also known as “runner's knee,” is a condition where the cartilage on the undersurface of the patella (kneecap) deteriorates and softens. This condition is common among young, athletic individuals, but may also occur in older adults who have arthritis of the knee. Chondromalacia patellae will typically present itself with pain in the knee region, known as patellofemoral pain. Patient may feel sensations of grinding or cracking when bending or extending knee. Pain may worsen after sitting for a prolonged period of time or during activities that apply extreme pressure to knee joints, such as standing for an extended period or exercising.[106]

ii) Ostrochondritis Diseases:

In osteochondritis diseases there is localized avascular necrosis of a segment of the articular surface of the medial condyle of femur. It occurs usually in males during the second decade of life. The predisposing factor may be an injury or impingement against the tibial spine, resulting in thrombosis of the end artery leading to necrosis. One segment of the subchondral becomes necrotic with softening of the overlying cartilage. At a later stage the fragment seprate as a loose body. This leaves a shallow cavity in the articular surface, which eventually is occupied by fibro cartilage. There precise cause in unknown. Initially pain appears from exertion with occasional effusion. The range of motion at the knee joint is usually not affected. However sudden locking with sharp pain may occur if their loose body gets lodged into the joint.

iii) Popliteal cyst:

The semimembranosus bursa that lies between the medial head of gastrocnemius and semimembranosus may become a seat irritative bursitis. The bursa gets distended with fluid, which develops into an elongated fluctuant bursa swelling posteriorly between the planes of these two muscles. A soft cystic swelling close to the medial femoral.

iv) **Baker's cyst:**

Sometimes herniation of the synovial cavity of knee with a fluid sac may occur in the popliteal space. This sac extends backwards at the posterior border of the popliteal space. A soft palpable bulge is present, which becomes more obvious on extending the knee joint. The precipitative factor is the persistent synovial irritation and effusion as occurs in osteoarthritis.

v) **Acute Pyogenic Arthritis**

This condition commonly affects the children. The knee becomes swollen, the overlying skin becomes red and warm compared to the opposite side. The joint is kept in flexed position and even a slight movement will be very much painful.

vi) **Tuberculosis of the knee**

This is a part of the generalized affection and infection is mainly blood born and settles in synovium or in the metaphysic or epiphysis of the femur or the tibia. The limp and aching are early symptoms. Soon there will be swelling in the joint with a slight flexion deformity. At this stage one or more enlarged lymph node in the groin can be felt. In early stage examination of the aspirated effusion or synovial biopsy will be base of diagnosis. In late cases a triple deformity with flexion, posterior subluxation and lateral rotation of the tibia becomes evident with practically no joint space in between.

Prognosis:

In OA, pathological changes tend to either remain stable or worsen. Nevertheless, both rapid progression and spontaneous regeneration have been described and patients often experience improvement in their symptoms irrespective of any underlying pathological change. In general, most mild OA does not progress to sever joint damage. There is some evidence to suggest that the risk factors for progression are different from those for the initiation of OA and more limited evidence suggest the worsening of symptoms.

The prognosis of osteoarthritis is not necessarily bad. But older people commonly have comorbidities. Marked disability is less as compare to Rheumatoid arthritis, symptoms may be quite severe and limit activity considerably. This is especially true to involvement of hips, knees and cervical spine. Although there is no cure, proper treatment may greatly relieve symptoms and there may be improved function of joints.

Treatment[107, 108]

The goals of the treatment of OA are to alleviate pain and minimize loss of physical function. To the extent that pain and loss of function are consequences of inflammation, of weakness across the joint, and of laxity and instability, the treatment of OA involves addressing each of these impairments. Comprehensive therapy consists of a multimodality approach including nonpharmacologic and pharmacologic elements.

Patients with mild and intermittent symptoms may need only reassurance or nonpharmacologic treatments. Patients with ongoing, disabling pain are likely to need both non-pharmacotherapy and pharmacotherapy.

Non-pharmacotherapy

Since OA is a mechanically driven disease, the mainstay of treatment involves altering loading across

the painful joint and improving the function of joint protectors, so they can better distribute load across the joint. Ways of lessening focal load across the joint include

(1) Avoiding activities that overload the joint, as evidenced by their causing pain;

(2) Improving the strength and conditioning of muscles that bridge the joint, so as to optimize their function; and

(3) Unloading the joint, either by redistributing load within the joint with a brace or a splint or by unloading the joint during weight bearing with a cane or a crutch.

Reduce weight: Each pound of weight increases the loading across the knee three to six fold. Weight loss may have a commensurate multiplier effect, unloading both knees and hips. Thus, weight loss, especially if substantial, may lessen symptoms of knee and hip OA.

In hand joints affected by OA, splinting, by limiting motion, often minimizes pain for patients with involvement either in the base of the thumb or in the DIP or proximal IP joints. With an appropriate splint, function can often be preserved.

Weight-bearing joints such as knees and hips can be unloaded by using a cane in the hand opposite to the affected joint for partial weight bearing.

Exercise: The development of weakness in muscles that bridge osteoarthritic joints is multifactorial in etiology. First, there is a decline in strength with age. Second, with limited mobility comes disuse muscle atrophy. Third, patients with painful knee or hip OA alter their gait so as to lessen loading across the affected joint, and this further diminishes muscle use. Fourth, "arthrogenous inhibition" may occur, whereby contraction of muscles bridging the joint is inhibited by a nerve afferent feedback loop emanating in a swollen and stretched joint capsule; this prevents maximal attainment of voluntary maximal strength. Since adequate muscle

strength and conditioning are critical to joint protection. One of the cardinal elements of the treatment of OA is to improve the functioning of muscles surrounding the joint.

At least for knee OA, trials have shown that exercise lessens pain and improves physical function. Most effective exercise regimens consist of aerobic and/or resistance training, the latter of which focuses on strengthening muscles across the joint. Physicians should reinforce the exercise prescription at each clinic visit, help the patient recognize barriers to ongoing exercise, and identify convenient times for exercise to be done routinely. The combination of exercise with calorie restriction is especially effective in lessening pain.

Patellar taping: Osteoarthritis of the patellofemoral compartment can cause severe pain. Which aggravate with kneeling, squatting, climbing of stairs, medial taping of patella can reduce the pain significantly.

Thermal modalities: Application of heat to the osteoarthritis joint may reduce pain and stiffness.

Tidal irrigation of knees: Copious irrigation of the osteoarthritis knee through a large bore needle, flushing out fibrin, cartilage shards, and other debris, has been reported to provide months of comfort for some patients where joints has been refractory to analgesics, NSAIDS.

Pharmacotherapy

While nonpharmacologic approaches to therapy constitute its mainstay, pharmacotherapy serves an important adjunctive role in OA treatment. Available drugs are administered using oral, topical, and intraarticular routes.

Acetaminophen, Nonsteroidal Anti-Inflammatory Drugs (NSAIDs), and COX-2 Inhibitors

Acetaminophen (paracetamol) is the initial analgesic of choice for patients with OA in knee, hip, or hands. For some patients, it is adequate to control symptoms, in which case more toxic drugs such as NSAIDs can be avoided. Doses up to 1 g 4 times daily can be given according to following:

Table no. 8

Table – Pharmacologic Treatment for Osteoarthritis		
Treatment	Dosage	Comments
Acetaminophen	Up to 1 g qid	Prolongs half-life of warfarin
NSAIDs[a]		Take with food. High rates of gastrointestinal side effects, including ulcers and bleeding, occur. Patients at high risk for gastrointestinal side effects should also take either a proton-pump inhibitor or misoprostol.[b] There is an increased concern about side effects (gastrointestinal or bleeding) when taken with acetylsalicylic acid. Can also cause edema and renal insufficiency.
Naproxen	375–500 mg bid	
Salsalate	1500 mg bid	
Ibuprofen	600–800 mg 3–4 times a day	
Cyclooxygenase-2 inhibitors	100–200 mg/d	High doses are associated with an increased risk of myocardial infarction and stroke. Can cause edema and renal insufficiency.
Celecoxib		
Opiates		Common side effects include dizziness, sedation, nausea or

		vomiting, dry mouth, constipation, urinary retention, and pruritis. Respiratory and central nervous system depression can occur.
Capsaicin	0.025–0.075% cream 3–4 times a day	Can irritate mucous membranes.
Intraarticular injections		
Hyaluronans	Varies from 3 to 5 weekly injections depending on preparation	Mild to moderate pain at injection site. Controversy exists re: efficacy.
Steroids		

a. NSAIDs denotes nonsteroidal anti-inflammatory drugs.
b. Patients at high risk include those with previous gastrointestinal events, persons 60 years, and persons taking glucocorticoids. Trials have shown the efficacy of proton-pump inhibitors and misoprostol in the prevention of ulcers and bleeding. Misoprostol is associated with a high rate of diarrhea and cramping; therefore, proton-pump inhibitors are more widely used to reduce NSAID-related gastrointestinal symptoms.

Since synovial Inflammation is likely to be a major cause of pain in patients with OA, local anti-inflammatory treatments administered intraarticularly may be effective in ameliorating pain, at least temporarily. Glucocorticoid injections provide such efficacy, but work better than placebo injections for only 1 or 2 weeks. There is no evidence that repeated glucocorticoid injections into the joint are dangerous. Hyaluronic acid injections can be given for treatment of symptoms in knee and hip OA.

Surgery

When medical therapies have failed and the patient has an unacceptable reduction in their quality of life and ongoing pain and disability, then at least for knee and hip OA, total joint arthroplasty is indicated.

For knee OA, several operations are available. Among the most popular surgeries, at least in the United States, is arthroscopic debridement and lavage.

For patients with knee OA isolated to the medial compartment, operations to realign the knee to lessen medial loading can relieve pain. These include a high tibial osteotomy, in which the tibia is broken just below the tibial plateau and realigned so as to load the lateral, nondiseased compartment, or a unicompartmental replacement with realignment.

The ultimate sugery for OA of knee is knee replacement that can be indicated with certain precautions.

Correction of Malalignment

For patients with knee OA isolated to the medial compartment, operations to realign the knee to lessen medial loading can relieve pain. These include a high tibial osteotomy, in which the tibia is broken just below the tibial plateau and realigned so as to load the lateral, non-diseased compartment, or a unicompartmental replacement with realignment.

Ultimately, when the patient with knee or hip OA has failed medical treatment modalities and remains in pain, with limitations of physical function that compromise the quality of life, the patient should be referred for total knee or hip arthroplasty.

Cartilage Regeneration

Chondrocyte transplantation has not been found to be efficacious in OA, perhaps because OA includes pathology of joint mechanics, which is not corrected by chondrocyte transplants. Similarly, abrasion arthroplasty (chondroplasty) has not been well studied for efficacy in OA, but it produces fibrocartilage in place of damaged hyaline cartilage. Both of these surgical attempts to regenerate and reconstitute articular cartilage may be more likely to be efficacious early in disease when joint malalignment and many of the other non-cartilage abnormalities that characterize OA have not yet developed.