433 Teams

MEDICINE

34|Rheumatoid Arthritis and Osteoarthritis

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COLOR INDEX

Slides - Step-Up medicine - Kaplan Notes - Extre explanation - Doctor Notes

Objectives:

By the end of this lecture student should know:

- Pathology,
- Clinical features,
- Laboratory and radiologic changes,
- Line of management of Rheumatoid Arthritis and Osteoarthritis

1/ Rheumatoid Arthritis

RA is unlikely if:

- Joint distribution is not symmetric OR
- DIP is involved OR
- Constitutional symptoms (especially morning stiff- ness) are absent.

General characteristics :

- RA : Sometimes it is called rheumatoid disease because it is not
- confined to joints
- It is a chronic **inflammatory** autoimmune disease involving the
- **synovium of joints.**
- The inflamed synovium can cause damage to cartilage and bone.
- It is a systemic disease that has many extra-articular manifestations
- Variable expression: Disease severity is variable—from moderate restrictions to being confined to a wheelchair or bed.
- Variants of RA:
  - ✓ **Felty'ssyndrome:** Anemia, neutropenia, splenomegaly + RA.
  - ✓ **JuvenileRA:** Begins before 18 years of age. Extra- articular manifestations may predominate (Still's disease) or arthritis may predominate.
- Prevalence about 3%, Worldwide distribution
- The usual age of onset is 20 to 40 years; it is more common in women than in men
- Female : male ratio 3:1
- Peak age of onset: 25-50 years
- Unknown etiology: Etiology is uncertain. It may be caused by an infection or a series of infections (most likely viral), but genetic predisposition is necessary.
- Genetics
- Environmental
- Possible infectious component(viral infections)
- Autoimmune disorder
- **The clinical course of RA can be grouped into four classes of patients:**
  A/ Patient has an acute attack, which subsides, and never has an attack again (10%)
  B/ Undulating course—periods of exacerbations and remissions (20%)
  C/ Patient has periods of exacerbations and "remissions," but "remissions" are really improvements, as patients are symptomatic at all times to some extent (65%)
  D/ Severe, progressive course (5%)

THE PATHOLOGY OF RA:

- Synovitis
  - Joints
  - Tendon sheaths
  - Bursae
- Nodules
- Vasculitis

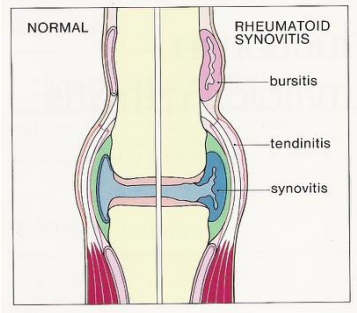
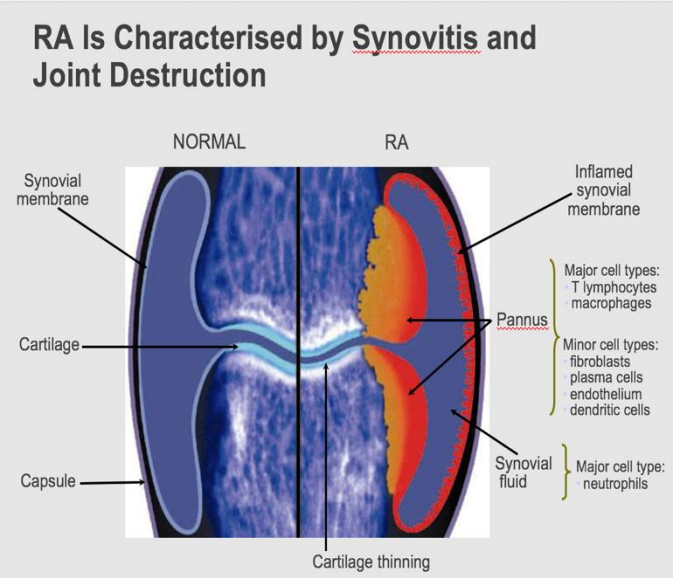
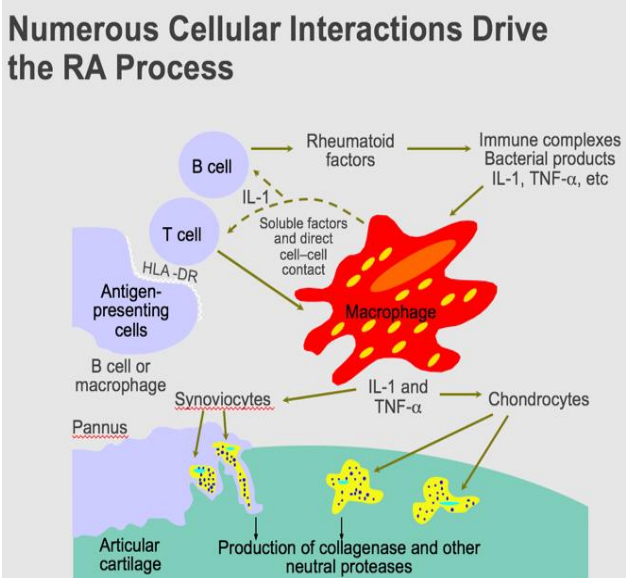
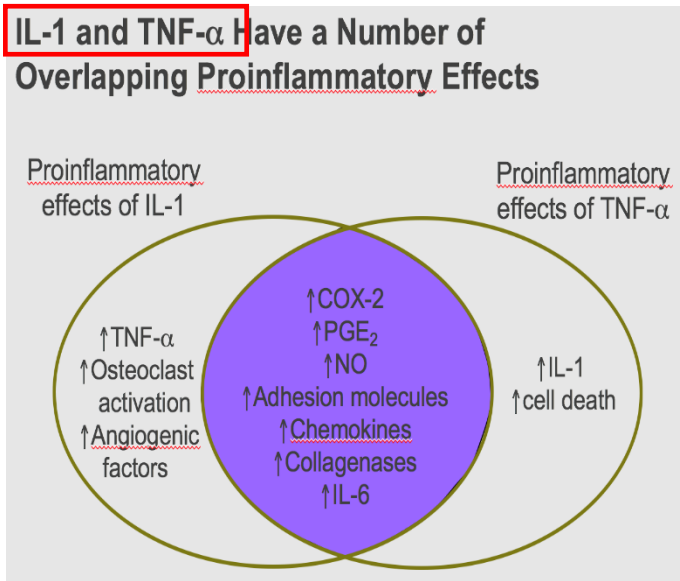


Fig. 3.3 The three major sites of rheumatoid synovitis.

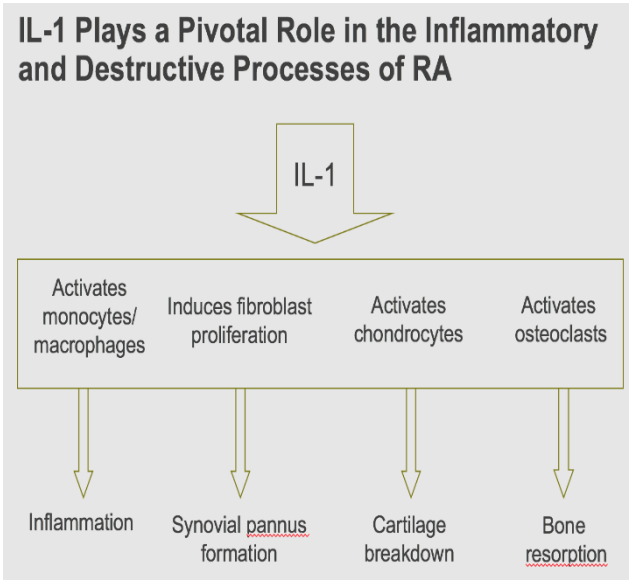




"Trigger > activation of the T&B cells, Rheumatoid factor and autoantibodies >proteolytic enzymes, cytokines, ILs and TNF are produced> inflammation and synovial pannus formation, cartilage breakdown and bone resorption."



Pannus= part of the thickened synovia that will invade the cartilage and bone (will show in x-ray as erosion)



Clinical features:

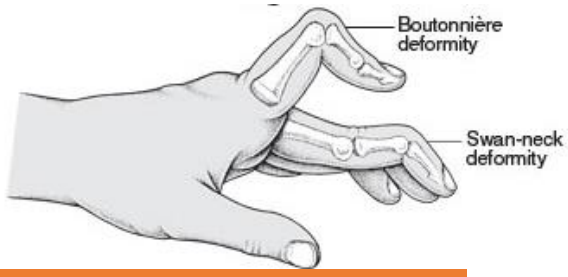
Joint inflammation(Inflammatory polyarthritis): Tender, warm swollen joints is the most common sign(soft tissue swelling)**, Symmetrical pattern**(the classical picture is symmetrical arthritis but may start with one joint) **—can involve every joint in the body except the DIP"destal inter phalangeal" joints.**

a. Pain on motion of joints/tenderness in joints

b. Joints commonly involved include **joints of the hands (PIP, MCP) and wrists,** knees, ankles, elbows, hips, and shoulders.

c. Characteristic hand deformities

- Ulnar deviation of the MCP joints
- Boutonnière deformities of the PIP joints (PIP flexed, DIP hyperextended)
- Swan-neck contractures of the fingers (MCP flexed, PIP hyperextended, DIP flexed)



JOINT INVOLVEMENT ON PRESENTATION OF RA	
Polyarticular(symmetrical) 75%	**Monoarticular 25%**
Small joints of hands and feet 60%	Knee 50%
Large joints 30%	Shoulder, Wrist, Hip, Ankle and Elbow 50%
Large and Small joints 10%	

1. **Constitutional symptoms can be prominent (Fatigue, occasional fever, malaise)**

✓ **Morning stiffness** (present in all patients)—improves as the day progresses

✓ Low-grade fever, weight loss

✓ Anemia(normocytic normochromic), Fatigue can be prominent because this is a systemic disease.

2. **Cervical spine involvement is common at C1–C2 (subluxation and instability),but it is less common in the lower cervical spine.**

✓ Instability of the cervical spine is a potentially life-threatening complication of RA. Most patients do not have neurologic involvement, but if they do, it can be progressive and fatal if not treated surgically.

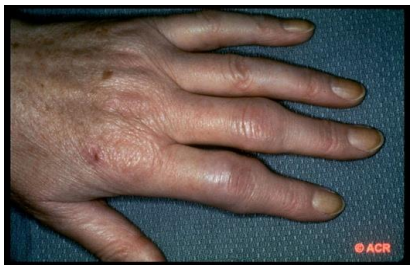
✓ This is seen in 30% to 40% of patients. All patients with RA should have cervical spine radiographs before undergoing any surgery (due to risk of neurologic injury during intubation).

3. **Cardiac involvement may include pericarditis, pericardial effusions, conduction abnormalities, and valvular incompetence.**
4. **Pulmonary involvement—usually pleural effusions; interstitial fibrosis mayoccur**
5. **Ocular involvement—episcleritis or scleritis**
6. **Soft tissue swelling (rather than bony enlargement)**
7. **Drying of mucous membranes: Sjögren's xerostomia**
8. **Subcutaneous rheumatoid nodulesover extensor surfaces may also occur in visceral structures—e.g., lungs, pleura, pericardium**

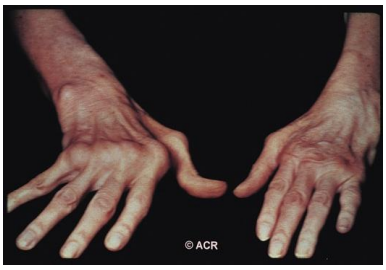
✓ Pathognomonic for RA

✓ Nearly always occurs in seropositive patients (i.e., those with rheumatoid factor [RF])

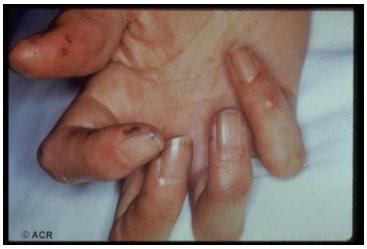
Articular features seen in the Rheumatoid Hand	
WRIST: Synovitis, Prominent ulnar styloid, Subluxation **(Partial dislocation)** and collapse of carpus and Radial deviation**(the angle will be lost with the deviation).**	**PIPs:**Synovitis and Fixed flexion or extension deformities (Swan neck (MCP flexed, PIP extended, DIP flexed)or boutonniere deformity(PIP flexed DIP extended)) (RA doesn't affect DIPs)
MCPs: Synovitis, Ulnar deviation and Subluxation.	**THUMBS:**Synovitis and 'Z' deformity(hyperextension of the interphalangeal joint, fixed flexion and subluxation of themetacarpophalangeal joint and gives a "Z" appearance to the thumb) .



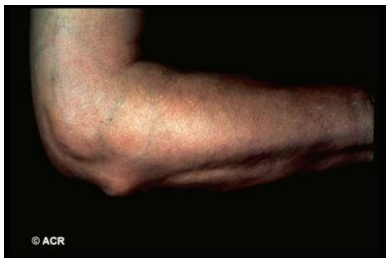
Swelling of interphalangeal joints (spindle shape)



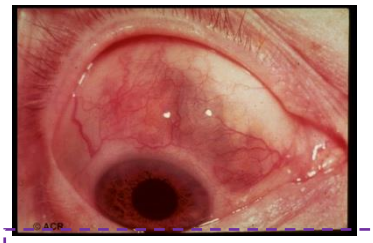
Radial deviation at the wrist, ulnar deviation at MCP and muscle wasting with prominent styloid process +Z deformity.



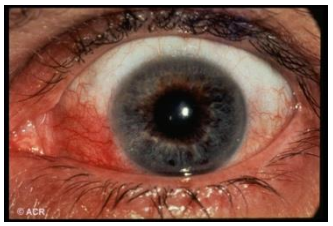
Small vessels vasculitis



Subcutaneous nodule



Episcleritis (blood vessels congestion) pigmentation of the choroid due to thinning of the sclera.



Episcleritis + scleritis

Extra-articular Manifestations in Rheumatoid Arthritis (it is usually common in patients with long standing seropositive"presence of RF in the serum" disease)	
Constitutional symptoms	Malaise Anorexia, Some Weight Loss, Fever
General(because it is systemic)	fatigue, lymphadenopathy
cutaneous	• Skin becomes thin and atrophic and bruises easily • Vasculitic changes/ulcerations involving fingers, nail folds(vasculitiscausing rashes) • Subcutaneous **rheumatoid nodules**usual site on bony prominence(elbows, sacrum, occiput)—**pathognomonic for RA** • palmar erythema

Pulmonary	• Pleural effusions (verycommon)—**pleural fluid characteristically has very low glucose** and low complement • Pulmonary fibrosis—with a restrictive pattern on pulmonary function tests and a honeycomb pattern on CXR • Pulmonary infiltrates • Rheumatic nodules in lungs (similar to those on skin)—cancavitateor become infected pleuritis, interstitial lung disease(in the form of fibrosis),bronchiolitis obliterans, arteritis
cardiac	• Rheumatic nodules in valve or heart—can lead to conduction disturbances (heart block and bundle branch block) • Pericarditis—in 40% of patients with RA • myocarditis, coronary vasculitis • Pericardial effusion
Eyes	• episcleritis /Scleritis • Scleromalacia—softening of the sclera(thinning and perforation of sclera); if not treated may perforate, leading to blindness • Choroid and retinal nodules • Dry eyes (and dry mucous membranes in general); may develop Sjögren's syndrome(dryness of salivary and lacrimal glands), amyloidosis(deposition of amyloid in the tissue,Kidneys are not primarily involved & there is no glomerulonephritis like SLE *Involvement of the kidneys is due to amyloid deposition (any chronic inflammatory process may lead to amyloidosis)
Nervous system	• Mononeuritic multiplex—infarction of nerve trunk Patient cannot move the arm or leg; implies systemic vasculitis, which is a bad sign. • Entrapment neuropathy(compression like carpal tunnel syndrome), peripheral neuropathy. • Cervical cord compression can result from atlantoaxial joint subluxation, which makes procedure like endotracheal intubation contraindicated.
Felty's syndrome	• Triad of RA, neutropenia, and splenomegaly • Also anemia, thrombocytopenia, and lymphadenopathy • Associated with high titers of RF and extra-articular disease • Increased susceptibility to infection • Usually occurs fairly late in the disease process
Blood	• Anemia of chronic disease: Mild, normocytic, normochromic anemia • Thrompocytosis. • Large granular lymphocyte syndrome, lymphomas
Vasculitis	A microvascular vasculitis—can progress to mesenteric vasculitis, PAN, or other vascular syndromes

Diagnosis:

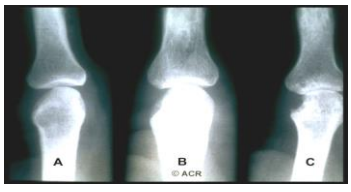
The diagnosis is based on the use of clinical criteria; there is no single test or finding that will diagnose RA.

Diagnostic criteria—need 4 of the following diagnostic criteria.

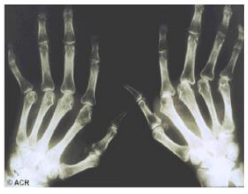
- ✓ Morning stiffness (>1 h) for 6 weeks
- ✓ Swelling of wrists, MCPs, PIPs for 6 weeks
- ✓ Swelling of 3 joints for 6 weeks
- ✓ Symmetric joint swelling for 6 weeks
- ✓ RF positive or anti-cyclic citrullinated peptide

- Morning stiffness, symmetrical joint involvement, and nodules are no longer needed for diagnosis of RA.

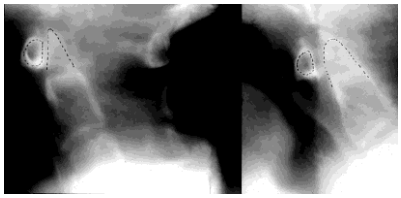
- serology**Anti-CCP**(anti cyclicciterenated peptide. Very specific to RA (rarely + in other condition but not that sensitive) A positive anti-CCP antibody is highly specific for RA and can occur before clinical onset of the disease) is more specific than Rheumatoid factor RF(IgM that is done routinely in lab, It is not specific and can be +v in SLE and non rheumatologiacal condition like hepatitis, endocarditis) (if it's high it's associated with more severe diseases).
- Hematology : CBC (anemia of chronic illness, thrombocytosis because of the active inflammation), ESR (high), Raised C- reactive protein.
- Biochemistry: LFT(before medication because some medications used in treatment may affect liver like methotrexate), Renal profile(as a baseline because NSAIDs may affect kidney function).
- Radiography: Joints, Spines, Chest.



-Erosion due to invasion of the pannus.
-A, B & C are erosive change in RA.
-The more erosion means the more early and aggressive disease



Joint destruction and periarticular osteopenia around the joints (this differentiates RA from psoriasis)



Cervical spine involvement (Atlantoaxial subluxation)

- however, X-ray abnormalities and nodules are not necessary for the diagnosis of RA.

The 2010 ACR / EULAR classificationcriteria for rheumatoid arthritis

Target population (Who should be tested?): Patients who

1) Have at least 1 joint with definite clinical synovitis (swelling)
2) With the synovitis not better explained by another disease

Add **A–D**; a score of 6/10 is needed to classify patient as having definite RA

RF: rhumatoid factors.

ACPA: Anti–citrullinated protein antibody.

A. Joint involvement	
1 large joint.	**0**
2-10 large joints	**1**
1-3 small joints (with or without involvement of large joints)	**2**
4-10 small joints (with or without involvement of large joints)	**3**
3-10 joints (at least 1 small joint)	**5**
B. Serology (at least 1 test result is needed for classification)	
Negative RF and negative ACPA	**0**
Low-positive RF or low-positive ACPA	**2**
High-positive RF or high-positive ACPA	**3**
C. Acute-phase reactants (1 test result is needed for classification)	
Normal CRP and normal ESR	**0**
Abnormal CRP or abnormal ESR	**1**
D. Duration of symptoms	
6 weeks	**0**
>6 weeks	**1**

- ***If both RF and ACPA are negative, consider diagnoses other than RA***
- ***Patients with diagnosis of RA who have a positive RF, ACPA, or both are at a higher risk of developing erosive joint damage—early treatment with DMARDs is indicated.***

Treatment :

None of the nonsteroidal anti-inflammatory drugs (NSAIDs) have been shown to be better than aspirin in RA, but they have fewer GI side effects.

- There is no single NSAID superior to other agents, and the newer agents have not been shown to have a decreased incidence in toxicity (GI, renal, etc.).
- Cyclooxygenase 2 (COX-2) inhibitors are a type of NSAID which selectively blocks the COX-2 enzyme at the site of inflammation. The benefit of COX-2 inhibitors is that they do not inhibit COX-1, an enzyme that helps with the production of the protective stomach lining. The nonselective (traditional) types of NSAIDs block both COX-2 and COX-1, which can lead to increased risk for gastrointestinal side effects (bleeding, etc.).
- Because of the increased risk of MI, both rofecoxib and valdecoxib have been recalled; currently only celecoxib is available.
- Other drugs in RA:

✓ Glucocorticoids (usually for short courses only)

✓ Disease-modifying agents: antimalarials, gold, sulfasalazine, methotrexate (MTX), and tumor necrosis factor (TNF) receptor inhibitors.

Disease-Modifying Antirheumatic Drugs (DMARDs):

- Much of the joint damage that ultimately leads to disability occurs early in the course of the disease, so early treatment with DMARDs is critical.

- ✓ Hydroxychloroquine
- ✓ Sulfasalazine
- ✓ Methotrexate
- ✓ Leflunomide
- ✓ Gold
- ✓ Azathioprine

- DMARDs have dramatically reduced the need for cervical spine surgery in RA patients.
- Control symptoms.
- No immediate analgesic effects.
- Can delay progression of the disease (prevent/slow joint and cartilage damage and destruction).
- Effects generally not seen until a few weeks to months.

Hydroxychloroquine	Sulfasalazine	Methotrexate
• **Mild non-erosive disease** • **combinations** • **200 mg bid** • **eye exams**	• 1 gm bid - tid • CBC, LFTs • onset 1 - 2 months	• most commonly used drug • fast acting (4-6 weeks) • po, SQ - weekly • CBC, LFTs

- Combination therapy with first-line drugs (methotrexate, hydroxychloroquine,and sulfasalazine) produces higher remission rates.
- Methotrexate is the main-stay of therapy. Leflunomide has the same efficacy as methotrexate.

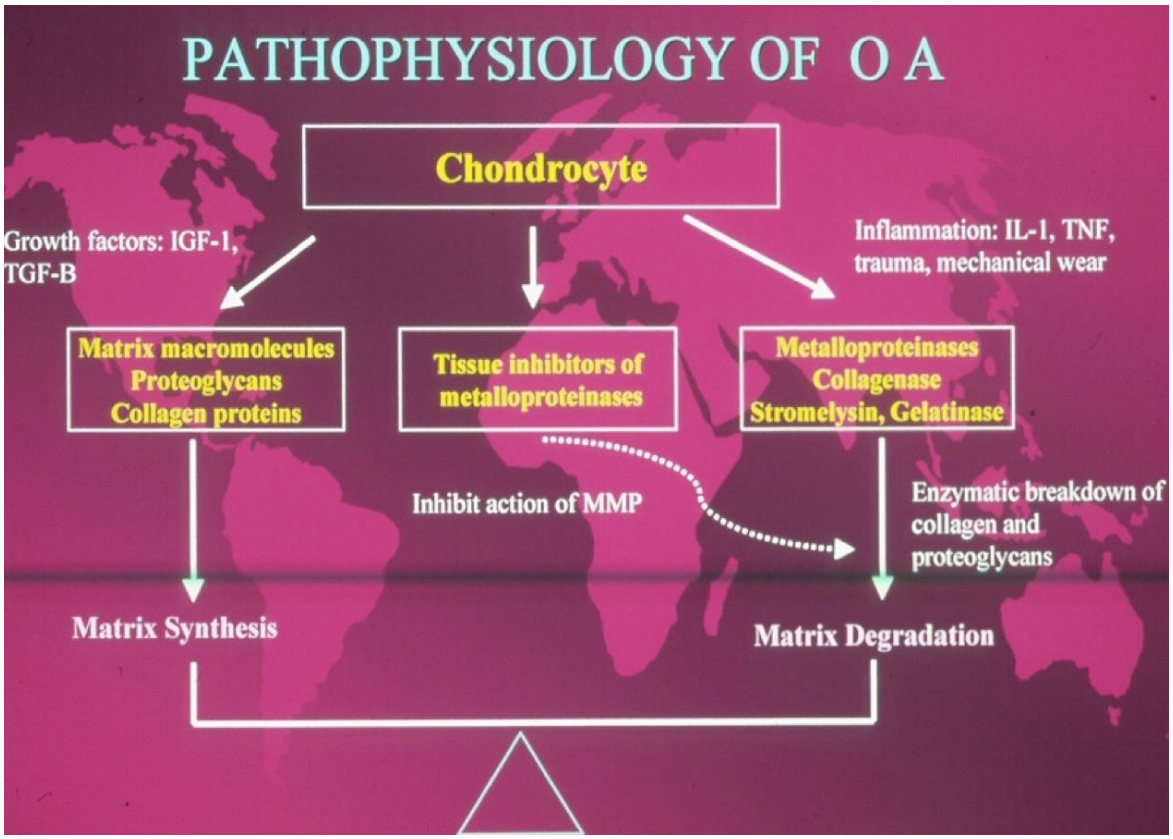
Poor prognostic indicators in RA
• High RF titers • Subcutaneous nodules
• Erosive arthritis • Autoantibodies to RF

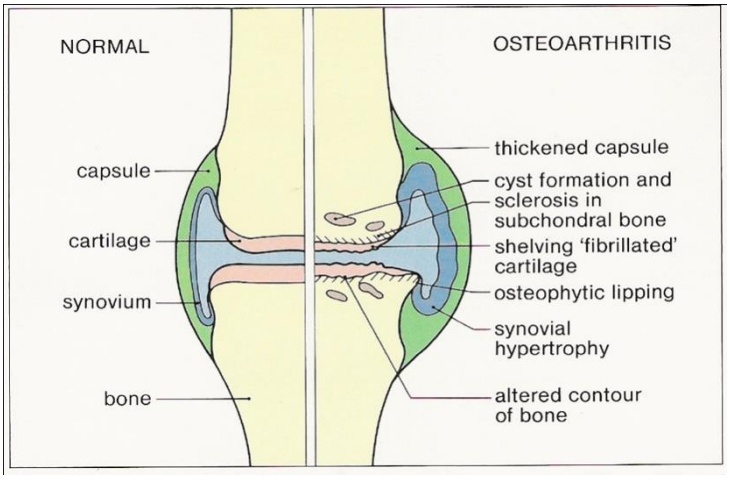
	Rheumatoid arthritis	Osteoarthritis
Swelling	Soft	Bony
Pathological features of joints	Pannus invasion of cartilage	Osteophytic bony outgrowths

2/ Osteoarthritis

Definition:

Osteoarthritis (OA) is the most common joint disease in humans. The target tissue in OA is articular cartilage. There is destruction of cartilage along with secondary remodeling and hypertrophy of the bone. OA, unlike RA, is not an inflammatory disease. it's a degenerative disease of the cartilage





Multifactorial etiology of OA

(Etiology is not known but there are biomechanical factors)

- Joint instability
- Age
- Hormonal factors
- Trauma
- Altered biochemistrylike hemochromatosis
- Inflammation
- Genetic predisposition
- ? Others

Symptoms and signs of OA :

- Pain – worse on use of joint
- Stiffness – mild after immobility
- Loss of movement
- Pain on movement/restricted range
- Tenderness (articular or periarticular)
- Bony swelling
- Soft tissue swelling
- Joint crepitus

To differentiate between OA and RA: In OA there are no systemic manifestations like fever and weight loss.

Diagnosis: Made on clinical and x-ray findings.

RADIOLOGICAL FEATURES OF OA:

- Narrowing of joint space (Because the cartilage is loss)
- Osteophytosis (osteophyte formation as part of repair)
- Altered bone contour
- Bone sclerosis and cysts
- Periarticular calcification
- Soft-tissue swelling

Treatment:

- Aimed at reducing pain and maintaining mobility, since there is no cure for OA.
- **Nonpharmacological Measures.** Reduction of joint loading can be achieved by correction of poor posture and weight loss. Physical therapy and exercise programs should be designed to maintain range of motion, strengthen periarticular muscles, and improve physical fitness.
- **Drug Therapy.** Therapy is palliative because no agent has been shown to change the natural course of the disease. Although limited studies have claimed a chondroprotective effect of certain NSAIDs, well-done studies have not documented such an effect. NSAIDs should only be used to alleviate pain.
- In double-blinded placebo trials, there was no difference in relief of joint pain among acetaminophen (4,000 mg/d), analgesic doses of ibuprofen (1,200 mg/d), and anti-inflammatory doses of ibuprofen (2,400 mg/d). Although the first drug to use for pain in OA is acetaminophen, it is reasonable to prescribe analgesic doses of NSAIDs if there is no relief with simple analgesics. Cautious dosing should be prescribed in elderly patients because they are at highest risk for the side effects associated with NSAIDs, especially GI (ulcers, hemorrhage, etc.). COX-2 inhibitors may be used in patients who are at high risk for GI complications (only available agent is celecoxib).
- Another modality that has been shown to benefit patients with OA is the use of capsaicin cream, which depletes local sensory nerve endings of substance P. Some patients do feel local burning.
- Orthopedic surgery and joint arthroplasty is reserved for cases in which aggressive medical treatment has been unsatisfactory, especially if the patient's quality of life has been decreased.
- Intraarticular injection of hyaluronic acid has been approved for treatment of knee OA that hasn't responded to pharmacologic treatment. Despite this, the efficacy of hyaluronic acid has been questioned since a large clinical trial failed to demonstrate superiority over intraarticular injections of saline. Similarly glucosamine and chondroitin sulfate are not routinely used in the treatment of OA since in 4 recent randomized, double blind trials both of these agents were no more effective than placebo.
- Also, clinical trial results based on analysis of x-rays suggested the possibility of glucosamine being chondroprotective. Since the radiologic methods employed in the trial were limited, there was concern about the interpretation of such data. A current multicenter trial sponsored by the National Institutes of Health is under way in order to address this question.

MCQs

1)A 40-year-old woman complains of 7 weeks of pain and swelling in both wrists and knees. She has several months of fatigue. After a period of rest, resistance to movement is more striking. On examination, the meta-carp phalangeal joints and wrists are warm and tender. There are no other joint abnormalities. There is no alopecia, photosensitivity, kidney disease, or rash. Which of the following is correct?

a. The clinical picture suggests early rheumatoid arthritis, and a rheumatoid factor and anti-CCP (anticycliccitrullinated peptide) should be obtained.

b. The prodrome of lethargy suggests chronic fatigue syndrome.

c. Lack of systemic symptoms suggests osteoarthritis.

d. X-rays of the hand are likely to show joint space narrowing and erosion.

e. An aggressive search for occult malignancy is indicated.

2)A 48-year-old woman complains of joint pain and morning stiffness for 4 months. Examination reveals swelling of the wrists and MCPs as well as tenderness and joint effusion in both knees. The rheumatoid factor is positive, antibodies to cyclic citrullinated protein are present, and subcutaneous nodules are noted on the extensor surfaces of the forearm. Which of the following statements is correct?

a. Prednisone 60 mg per day should be started.

b. The patient should be evaluated for disease-modifying antirheumatic therapy.

c. A nonsteroidal anti-inflammatory drug should be added to aspirin.

d. The patient's prognosis is highly favorable.

e. The patient should receive a 3-month trial of full-dose nonsteroidal anti-inflammatory agent before determining whether and/or what additional therapy is indicated.

3)A 60-year-old man complains of pain in both knees coming on gradually over the past 2 years. The pain is relieved by rest and worsened by movement. The patient is 5 ft 9 in tall and weighs 210 lb. There is bony enlargement of the knees with mild warmth and small effusions. Crepitation is noted on motion of the knee joint bilaterally. There are no other findings except for bony enlargement at the distal interphalangeal joint. Which of the following is the best way to prevent disease progression?

a. Weight reduction

b. Calcium supplementation

c. Total knee replacement

d. Long-term nonsteroidal anti-inflammatory drug (NSAID) administration

e. Oral prednisone

Answers:

1- a 2- b 3- a

1) The clinical picture of symmetrical swelling and tenderness of the metacarpophalangeal (MCP) and wrist joints lasting longer than 6 weeks strongly suggests rheumatoid arthritis (RA). Rheumatoid factor, an immunoglobulin directed against the Fc portion of IgG, is positive in about two-thirds of cases and may be present early in the disease. The history of lethargy or fatigue is a common prodrome of RA. The inflammatory joint changes on examination are not consistent with chronic fatigue syndrome; furthermore, patients with CFS typically report fatigue existing for many years. The MCP-wrist distribution of joint symptoms makes osteoarthritis very unlikely. The x-ray changes described are characteristic of RA, but would occur later in the course of the disease. Although arthritis can occasionally be a manifestation of hematologic malignancies and, rarely, other malignancies, the only indicated screening would be a complete history and physical examination along with a CBC.

2)The patient has more than four of the required signs or symptoms of RA, including morning stiffness, swelling of the wrist or MCP, simultaneous swelling of joints on both sides of body, subcutaneous nodules, and positive rheumatoid factor. Subcutaneous nodules and anti-CCP antibodies are poor prognostic signs for the activity of the disease, and disease-modifyingantirheumatic drugs (DMARDs) such as methotrexate, antimalarials, sulfasalazine, leflunomide, anti-TNF agents, or a combination of these drugs should be instituted. Methotrexate has emerged as a cornerstone of most disease-modifying regimens, to which other agents are often added. Low-dose corticosteroids (e.g., prednisone 7.5 mg a day or less) have recently been shown to reduce the progression of bony erosions and, although controversial, are useful additions to DMARD therapy. High-dose steroids, however, Should be avoided. Use of anti-inflammatory doses of both aspirin and nonsteroidal together is not desirable because it will increase the risk of side effects. Given the aggressive nature of this woman’s rheumatoid arthritis and negative prognostic signs, use of DMARDs is indicated. Significant joint damage has been shown by MRI to occur quite early in the course of disease.

3) The clinical picture of pain in weight-bearing joints made worse by activity is suggestive of degenerative joint disease, also called osteoarthritis. Osteoarthritis may have a mild to moderate inflammatory component. Crepitation in the involved joints is characteristic, asis bony enlargement of the DIP joints. In this overweight patient, weight reduction is the best method to decrease the risk of further degenerative changes. Aspirin, other NSAIDs, or acetaminophen can be used as symptomatic treatment, but these agents do not affect the course of the disease. The long-term use of NSAIDs is limited by potential side effects, including renal insufficiency and gastrointestinal bleeding. Calcium supplementation is relevant for osteoporosis, but does not treat osteoarthritis. Oral prednisone would not be indicated. Intra-articular corticosteroid injections may be given two to three times per yearfor symptom reduction. Knee replacement is the treatment of last resort, usually when symptoms are not controlled by medical regimens and/or activities are severely limited.

Done By:

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Hussain Alsalman	Aisha Alsafi
Faroq Abdulfattah	Areej Alwahaib