# Rheumatoid Arthritis

## Objectives :

- ★ **Recognize which patient is likely to have RA**
- ★ **Know the different modes of presentation of RA**
- ★ **Develop a plan of investigation and management of RA**

Editing file

**Color index**

Original text
Females slides
Males slides
Doctor's notes [438]
Doctor's notes [439]
Text book
Important
Golden notes
Extra

# Overview

## ◀ Osteoarthritis VS Rheumatoid arthritis (Extra)

- **We will take each disease in a separate lecture, this is just an overview to help you differentiate between them.**

| | Osteoarthritis | Rheumatoid arthritis |
|---|---|---|
| **Pathogenesis** | Mechanical - **wear and tear** destroys articular cartilage **(degenerative joint disorder)** | Chronic, systemic **autoimmune** disease |
| **Predisposing factors** | Major risk factor is **age** (common after 60 years); additional risk factors include obesity and joint trauma. | Associated with **HLA-DR4**, classically arises in women of late childbearing age |
| **Presentation** | - Pain that gets worse with movement and is relieved by rest<br>- **Early morning stiffness** (lasting **LESS** than 30min)<br>- Involves **DIPJs (Heberden nodes), PIPJs (Bouchard nodes)** and 1st CMC but NOT MCP<br>- **Asymmetric** joint involvement<br>- **No systemic** symptoms | - Pain.<br>- **Early morning stiffness** (lasting **MORE** than 1hr) that gets **better with movement**<br>- Swelling in the small joints of the hands and feet.<br>- There's spindling of the fingers caused by swelling of PIPJs and MCP but **NOT DIPJs** or 1st CMC<br>- **Symmetric** joint involvement<br>- **Systemic symptoms** e.g. fever, fatigue, weight loss<br>- Extraarticular manifestations are common* |
| **Joint findings** | - **Osteophytes** (bone spurs)<br>- Joint space narrowing | - **Pannus** (proliferative granulation tissue)<br>- Erosions, cervical subluxation, ulnar finger deviation, swan neck and boutonniere deformities |

* Extraarticular manifestations include **rheumatoid nodules** (fibrinoid necrosis with palisading histiocytes) in subcutaneous tissue and lung (+ pneumoconiosis→ Caplan syndrome), interstitial lung disease, pleuritis, pericarditis, anemia of chronic disease, neutropenia + splenomegaly (**Felty syndrome**), **AA amyloidosis**, Sjögren syndrome, scleritis, carpal tunnel syndrome

# Rheumatoid Arthritis (RA)

## ◀ Introduction

- Rheumatoid arthritis is a chronic **Systemic** inflammatory disease mainly affects synovial joints and tendons. It can affect other systems in the body. Early recognition and treatment can prevent joint destruction and disability.
- Variable expression (the severity and limitations caused by RA is variable)
- RA has a worldwide distribution with a prevalence of 3 %. (Female:male ratio 3: 1)
- Peak age of onset: 25-50 years but could occur at any age, even children 'juvenile type'.
- RA remains a significant cause of disability and mortality and carries a high socioeconomic cost.
- Symmetrical polyarthritis ddx: RA, SLE and seronegative arthritis (We will take each in a separate lecture)

# Rheumatoid Arthritis

## ◀ Etiology

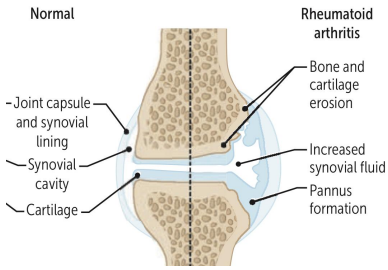
- The exact etiology is **unknown**, but there are factors like genetics, environmental (**smoking**) & infectious components. These factors may cause modification and production of autoantigens (citrulline) by the process of citrullination, leading to the initiation of an autoimmune reaction

**Genetics**: associated with **HLA-DR4**[1] and HLA-DRB1

- **Autoimmune disorder**, associated with IgM autoantibodies against Fc portion of IgG (rheumatoid factor)
- **Environmental** such as **smoking**[2]
- Possible **infectious** component, most likely viral

## ◀ Pathogenesis

Click here for better explanation of the pathogenesis

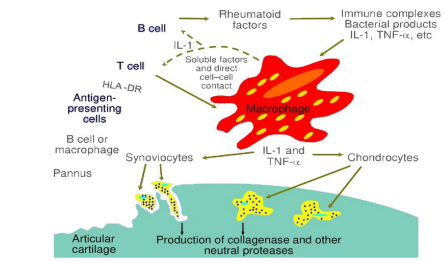



- **The pathology of RA:**
  - **Synovitis** (Joints, Tendon sheaths, Bursae)
  - Vasculitis: widespread cutaneous vasculitis with necrosis of the skin (seen in people with very active, strongly seropositive disease)
  - Subcutaneous Nodules

Synovitis with thickening of the synovial lining → Infiltration by inflammatory cells → Synovium proliferates and grows out over the surface of cartilage

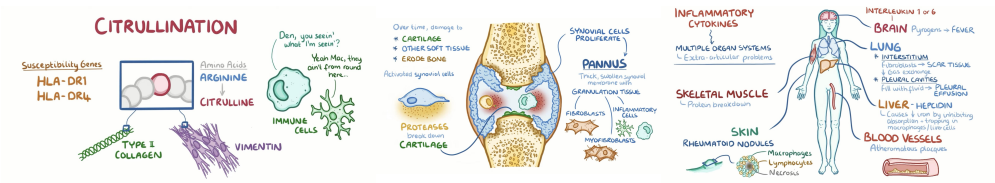
a tumour-like mass called **'pannus'** is produced → Pannus **destroys** the articular **cartilage** and subchondral **bone** → producing **bony erosions** & **joint destruction**

**Numerous Cellular Interactions Drive the RA Process**

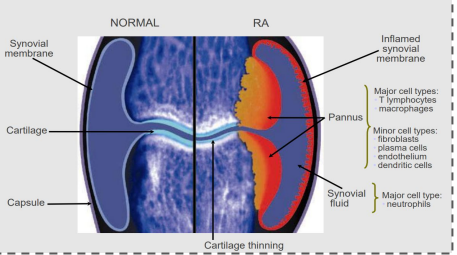



Arend W. *Semin Arthritis Rheum.* 2001;30(suppl 2):1-6.

The interaction between Antigen presenting Cells and HLA-DR4 will activate T cells & B cells. This will lead to the production of Autoantibodies (RF & Anti-CCP "Anti-cyclic citrullinated peptides") as well as the activation of macrophages leading to the production of inflammatory cytokines (TNF-α, IL-1,6,17). This will lead to the activation of the Chondrocytes and Synoviocytes to produce collagenases and other proteases which will cause bone & cartilage destruction.

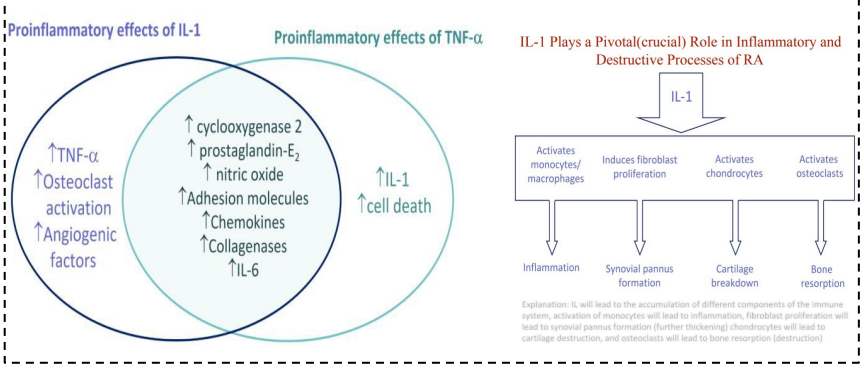



**RA Is Characterised by Synovitis and Joint Destruction**




**Major cell type in the pannus:**
T lymphocytes & macrophages
**Major cell type in the synovial fluid:**
Neutrophils

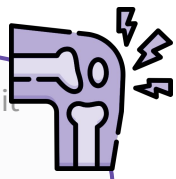
**IL-1** and **TNF-a** Have a Number of Overlapping Proinflammatory Effects:




1-Having HLA-DR4 increases the susceptibility for the development of RA and is associated with a poor prognosis.
2- Environmental stress, such as **smoking & infection**, are thought to promote post-translational modifications.

# Articular features

## ◄ Joint inflammation:



- ➔ Warm **swollen** and **tender** joints usually in a **symmetrical** (important feature to distinguish it from osteoarthritis) pattern
- ➔ **Early morning stiffness** (lasting more than 1hr) that improves with activity
- ➔ **Swelling** in the small joints of the hands and feet.
- ➔ There's **spindling of the fingers** caused by swelling of PIPJs (proximal interphalangeal joint) and MCP (Metacarpophalangeal joints) but NOT DIPJs or 1st CMC
- ➔ RA does not only affect the hands, once you suspect RA you should examine all as the temporomandibular joint, sternoclavicular joint, etc..
- ➔ Baker cysts (synovial cysts in the popliteal fossa) may be present

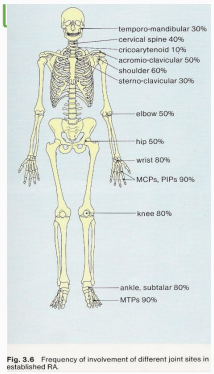


Fig. 3.6 Frequency of involvement of different joint sites in established RA.

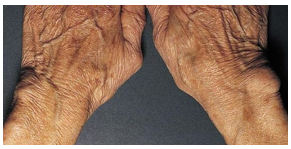
**Joint Involvement On Presentation Of RA:**

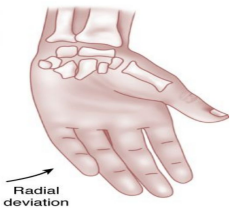
- ➔ **75%** of cases presented with **Polyarticular**:
  - ◆ **60%** of them have only **small** joints of hand & feet involvement
  - ◆ **30%** have only **large** joints involvement,
  - ◆ **10%** have **BOTH** small & large joint involvement.
- ➔ **25%** of cases presented with **monoarticular:**
  - ◆ **50%** of them have **Knee** involvement only.
  - ◆ **50%** have: shoulder, wrist, hip, ankle, or elbow involvement.

If a patient presents with sudden **monoarthritis**, **ALWAYS** consider **septic arthritis** or **infection like TB** (in case of chronic), these must be excluded before the symptoms are attributed to a disease flare-up.

## • Wrist

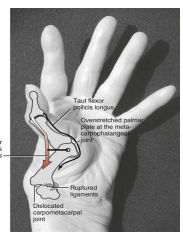
- ○ Synovitis
- ○ **Radial deviation**
- ○ Subluxation and collapse of carpus[2]. Dislocation is complete loss of contact, while subluxation is partial or incomplete dislocation.
- ○ **Prominent ulnar styloid**[2] = piano key sign


**Prominent ulnar styloid**

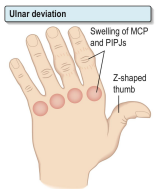



## • Thumbs

- ○ Synovitis
- ○ **"Z" deformity**

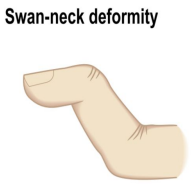


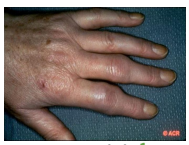
**Z deformity**




## • Proximal Interphalangeal Joints

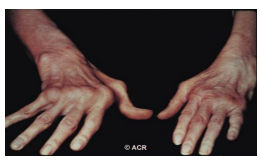
- ○ **Boutonniere/buttonhole deformity:** Fixed flexion[3], flexion of PIPJ and extenison of DIPJ.
- ○ Synovitis
- ○ **Swan neck:** Fixed extension[3], hyperextension of PIPJ and flexion of DIPJ





**Synovitis**[1]

## • Metacarpophalangeal Joints

- ○ Synovitis
- ○ **Ulnar deviation**[4]
- ○ Subluxation



**Important:** So, radial deviation at the wrist and ulnar deviation at the MCPJ

- Ulnar deviation at MCPJ
- Muscle wasting
- Radial deviation at wrist
- "Z" deformity

1. This appearance is called spindling of the digits (swelling of PIPJ). In case an entire finger or toe is swollen, with joint and tendon sheath involvement (Sausage digits/Dactylitis) you must consider psoriatic arthritis (seronegative arthritis) in your differential.
2. Swelling and dorsal subluxation of the ulnar styloid, which causes wrist pain and may cause rupture of the finger extensor tendons, leading in turn to a sudden onset of finger drop of the little and ring fingers predominantly; this needs urgent surgical repair.
3. These deformities cause impairment of hand function.
4. This change leads to unsightly deformity, but function may be preserved once the patient has learned to adapt and pain is controlled.

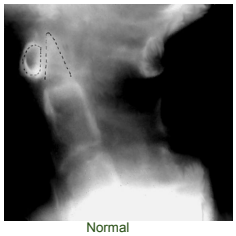
# Articular features

## ◀ Joint involvement & Destruction:

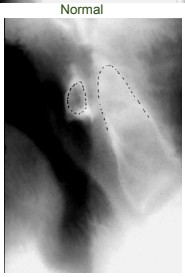
### • Cervical spine

- Painful stiffness of the neck in RA is often muscular, but it may be due to rheumatoid synovitis
- This synovitis leads to bone **destruction**, damages the ligaments and causes atlantoaxial or upper cervical vertebral instability. Particularly at **C1 and C2, which can lead to subaxial subluxation**
- In late RA, difficulty walking that cannot be explained by articular disease, weakness of the legs or loss of control of bowel or bladder may be due to spinal cord compression and is a neurosurgical emergency.
- **MRI is the imaging of choice**, but lateral flexed and extended neck **X-rays** can demonstrate instability.

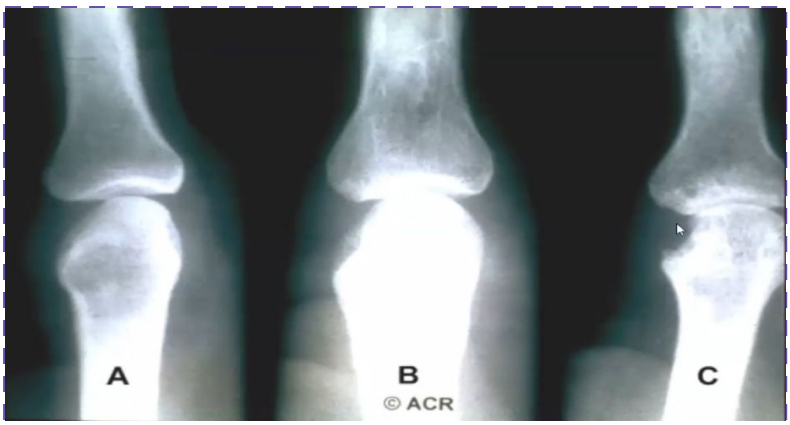
★ **X-RAY Imaging** of the cervical spine in flexion and extension is **recommended** in patients with RA **before surgery** or **upper GI endoscopy** to check for instability (**Cervical subluxation**) and reduce the risk of **cord injury** during **intubation**.



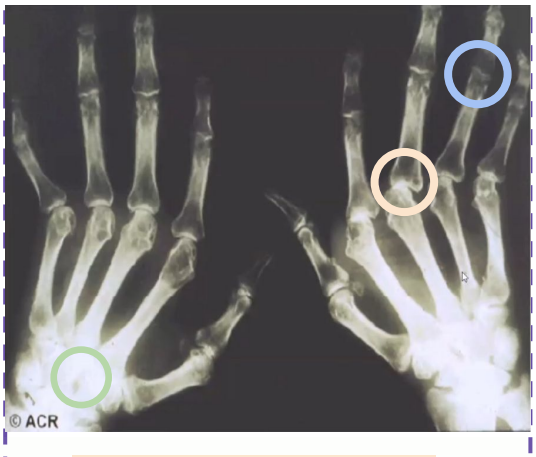
Normal



RA




**A:** X-ray in early disease, we can see the articular surface is intact
**B:** As the diseases progress, we can see some destruction.
**C:** The hypertrophied synovium (Pannus) will invade the bone & cartilage showing Erosion on x-ray




- **Subluxation (partial dislocation) & periarticular osteoporosis or osteopenia**
- **Small erosive changes**
- **You can't differentiate the carpal bones because there is loss of joint cavity**

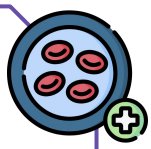
## ◀ Different presentations of RA: (Obj.)

| | |
|---|---|
| **Palindromic** | Palindromic monoarticular attacks last 24-48 h; 50% progress to other types of RA. |
| **Transient** | Disease is self-limiting, lasting <12 months and leaving no permanent joint damage. It is usually seronegative for lgM RF and ACPA. Some of these patients may have undetected postviral arthritis. |
| **Remitting** | There is a period of several years during which the arthritis is active but then remits, leaving minimal damage. |
| **Chronic, persistent** | This is the most typical form; it may be seropositive or seronegative for lgM RF. The disease follows a relapsing and remitting course over many years. Seropositive (plus ACPA) patients tend to develop greater joint damage and long-term disability. They warrant earlier and more aggressive treatment with disease-modifying agents. |
| **Rapidly progressive** | The disease progresses remorselessly over a few years and leads rapidly to severe joint damage and disability. It is usually seropositive (plus ACPA), has a high incidence of systemic complications and is difficult to treat. |

# Extra-Articular features

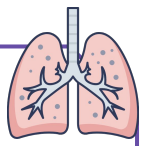
Inflammatory cytokines will go into circulation and lead to other systemic manifestations

## Hematological



- **Felty's syndrome: A triad of Rheumatoid Arthritis + Neutropenia + Splenomegaly**
  - Associated with increased risk of developing **non-Hodgkin lymphoma**
  - **Treatment:** DMARD (**Methotrexate**)
- **Anaemia of chronic disease** is almost universal and is usually **normochromic and normocytic**. It may be iron deficient owing to gastrointestinal blood loss from NSAID ingestion, or rarely haemolytic (Coombs positive). Or due to Liver: production of hepcidin which interferes with absorption of iron and that's why we have anemia of chronic disease.
- There may be a **pancytopenia** due to hypersplenism in Felty's syndrome or as a complication of DMARD treatment.
- A high platelet count indicate an active disease. it just indicate active inflammation, not specific to Rheumatoid arthritis
- Large granular lymphocyte syndrome, **Lymphomas (RA patients are at high risk)**

## Cardiac & Pulmonary

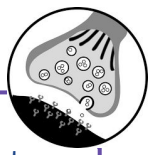


- **Cardiac[1]:** Pericarditis, myocarditis, coronary vasculitis[2], nodules on valves or the conducting system of the heart.
- **Pulmonary:**
  - May present with lung involvement before the articular manifestations
  - Pleuritis, interstitial lung disease[3], bronchiolitis obliterans, arteritis, effusions.
  - **Peripheral, intrapulmonary nodules:** asymptomatic but may cavitate, especially with pneumoconiosis (Caplan's syndrome[4])

## Ocular (rare)

- Sjogren's syndrome (Sicca syndrome): Dry eyes, Dry mouth
- **Episcleritis/scleritis[5]**
- Scleromalacia perforans (Thinning and perforation of the eye)
- Choroid and retinal nodules
- Peripheral ulcerative keratitis

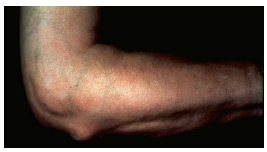
## Neuromuscular



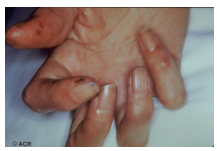
- Entrapment neuropathy
  - Median nerve compression is the most common and bilateral **carpal/Tarsal tunnel syndrome** can occur as a presenting feature of RA
- Peripheral neuropathy
- Mononeuritis multiplex: Involvement of the nerve trunk In case of **rheumatoid vasculitis**

## Others

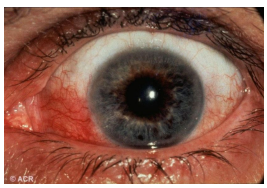
- **Dermatological:** Palmar erythema, **Subcutaneous rheumatoid nodules** over extensor surfaces (pressure areas), vasculitis
- Occasional fever, weight loss, fatigue, malaise
- Lymphadenopathy



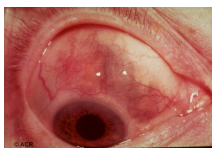
**Subcutaneous nodules**



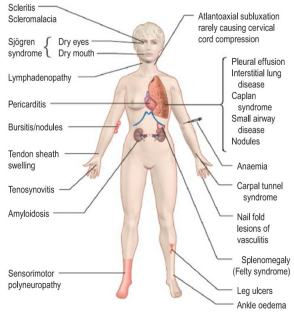
**Small vessel vasculitis**



**Episcleritis**



**Scleritis, Episcleritis, with Scleromalacia**




1. Poorly controlled RA with a persistently raised CRP and high cholesterol **is a cardiovascular risk factor (for IHD and CAD)**, independent of traditional risk factors (i.e. high cholesterol and hypertension). it is like diabetes and hypertension.
2. The most common cause of death in RA is coronary artery disease.
3. There is some evidence that the risk of pulmonary fibrosis is increased by anti-TNF therapy
4. Caplan syndrome: Rheumatoid Arthritis + Pneumoconiosis + Lung nodules
5. The eye involvement in rheumatoid is usually Episcleritis/scleritis. While in seronegative arthritis usually uveitis.

# Investigations & Classification

## ◀ Investigations

### Hematological

- **CBC:** Anemia of chronic disease **(Normochromic normocytic anemia),** thrombocytosis. You may see leukopenia if the patient is on methotrexate or iron deficiency anemia if the pt is using NSAIDs
- **ESR and CRP:** Usually high in active disease, useful in monitoring treatment

### Biochemistry

- Liver function test (**LFT**)
- **Renal profile:** Because the medications can cause side effects, so you should have a baseline before you start.

★ **Aspiration of the joint** may be needed if an effusion is present. The aspirate looks cloudy owing to white cells. **In a suddenly painful joint**, septic arthritis should be suspected. Indicated if septic arthritis is suspected or to rule out other differentials e.g (gout)

### Radiological (X-ray)[1]

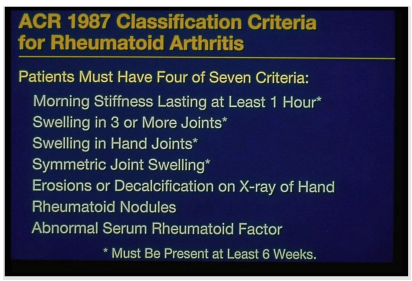
- **Joints:** Do x-ray to look for any subluxations, Swelling in early disease and later joint narrowing and erosions.
- **Spines:** Cervical spine x-ray
- **Chest:** For lung involvement or effusion

### Serology

- Rheumatoid factor (**RF**): IgM[2] . May be raised in another diseases (not specific)
- Anti-citrullinated peptide antibodies (**ACPA/Anti-CCP**)[3]

**Anti-CCP** is **more specific but still not diagnostic** for RA.
**High titer** of **RF** or **Anti-CCP** is associated with more susceptibility to **extra-articular** manifestations (like lung involvement or vasculitis)

## ◀ The 2010 ACR/EULAR classification criteria for rheumatoid arthritis:




- In the old criteria (1987) a score of 4/7 is diagnostic, however this classification has been disregarded now. why? because it contains erosions as a criterion, but you should NEVER wait for erosion to happen, but rather try to prevent it at all costs by medications
- Target population Patients **(who should be tested?)**:
  - Who have **at least 1 joint** with definite clinical **synovitis** (Swelling) Not explained by other disease..
  - With the synovitis not better explained by another disease.
- The cut-off point for RA is at **≥6 points.** Patients can also be classified as having RA if they have both typical erosions and longstanding disease previously satisfying the classification criteria.

**2010 criteria:** You aren't required to memorize it

| Criteria | Points |
|---|---|
| **1. Joint involvement** | **0–5** |
| 1 medium to large joint | 0 |
| 2–10 medium to large joints | 1 |
| 1–3 small joints (large joints not counted) | 2 |
| 4–10 small joints (large joints not counted) | 3 |
| >10 joints; at least one small joint | 5 |
| **2. Serology** At least 1 result is needed for classification | **0–3** |
| Negative RF and negative ACPA | 0 |
| Low positive RF or low positive ACPA | 2 |
| High positive RF or high positive ACPA | 3 |
| **3. Acute-phase reactants** | **0–1** |
| Normal CRP and normal ESR | 0 |
| Abnormal CRP or abnormal ESR | 1 |
| **4. Duration of symptoms** | **0–1** |
| <6 weeks | 0 |
| ≥6 weeks | 1 |

1. In severe disease, extensive imaging of joints may be required. MRI is the technique of choice, especially for the knee and cervical spine
2. **IgM RF** is not diagnostic of RA and its **absence does not rule the disease out**; however, it is a useful predictor of prognosis. A persistently high titre in early disease implies more persistently active synovitis, more joint damage and greater disability eventually, and justifies earlier use of DMARDs. The term 'seronegative RA' is used when the standard tests for IgM RF are persistently negative. These patients tend to have a more limited pattern of synovitis.
3. ACPAs are usually present with RF in RA. They are better predictors of a transition from early transient inflammatory arthritis to persistent synovitis and early RA.

# Complications and Management

## Complications

### Amyloidosis

- **RA is the most common cause of secondary AA amyloidosis.**
- AL amyloidosis causes a polyarthritis that resembles RA in distribution and is also often associated with **carpal tunnel syndrome** and **subcutaneous nodules**.
- Amyloidosis causing **proteinuria**, **nephrotic syndrome** and chronic kidney disease.
  So, if a rheumatoid patient presented with proteinuria, edema, etc. consider amyloidosis.

### Septic arthritis (Monoarticular)

- In immunosuppressed patients, the affected joints may not display the typical signs of **inflammation** with accompanying **fever** found in patients with an intact immune system
- It has significant **morbidity** and **mortality** **(medical emergency)**.
- Risk factors: Prosthetic joints, pre-existing joint disease
- Treatment is with systemic **antibiotics**[1] and **drainage**
- The most common organism is **S. aureus**
  - **MSSA:** Flucloxacillin + drainage
  - **MRSA:** Vancomycin + drainage

## Factors predicting poor prognosis

1. Older **age**
2. **Female** sex
3. **Symmetrical** small joint involvement
4. Morning stiffness **>30 min**
5. **>4** swollen joints
6. Normochromic normocytic anaemia
7. Cigarette **smoking**
8. **Comorbidity**
9. C-reactive protein **>20** g/dl
10. **Positive** rheumatoid factor (**RF**) and anti-citrullinated peptide antibodies (**ACPA**)
11. Early erosive damage (On x-ray, US, MRI)

## Treatment

### 01

**Treatment Goals:**

- Relieve pain.
- Reduce inflammation.
- Prevent/slow joint damage.
- Improve functioning and quality of life.

### 02

**Treatment approaches:**

- Lifestyle modification: such as weight reduction and smoking cessation
- **Rest:** **JUST** During active phase. not prolonged rest as it is may lead to stiffness and muscle wasting.
- Physical and occupational therapy
- Medications & surgery (repair or replacement). or correction of deformity

**Box 18.28 Management of rheumatoid arthritis**

- Establish the diagnosis clinically.
- Use NSAIDs and analgesics to control symptoms.
- Try to induce remission with i.m. depot methylprednisolone 80–120 mg if synovitis persists beyond 6 weeks.
- If synovitis recurs, refer to a rheumatologist to start DMARDs and consider combinations of sulfasalazine, methotrexate and hydroxychloroquine. Give a second dose of i.m. depot methylprednisolone or oral steroids.
- Refer for physiotherapy and general advice through a specialist team.
- As improvement occurs, as measured by less pain, less morning stiffness and reduced acute-phase response, tail off steroids and possibly reduce drugs.
- If no better, use anti-TNF-α therapy or other biological agent.

*DMARDs, disease-modifying anti-rheumatic drugs; TNF-α, tumour necrosis factor alpha.*

### 03

**Rationale for the Early Treatment of RA:**

- **Erosions** develop **early** in the disease course
- Destruction is **irreversible**.
- Disease activity is strongly associated with joint destruction later in the disease course.
- **Early treatment** can **slow** down or prevent radiographic **progress**
- Disease activity must be suppressed maximally in its early stages to prevent destruction and preserve function.

1. Suspected **Gram +ve**? 1st line is **vancomycin, with clindamycin** or cephalosporin second line. Suspected **Gram- negative**? 1st line is **3rd Gen. cephalosporin** with IV ciprofloxacin second line. In confirmed (MSSA) primary options include flucloxacillin alone or combined with fusidic acid or gentamicin, while penicillin-allergic patients should receive clindamycin or a 3rd Gen. cephalosporin. In cases of (MRSA), vancomycin is the drug of choice. Antibiotics should be altered according to sensitivities. Drainage of the joint and/or arthroscopic joint washouts are required in all cases.

# Management

## NSAIDs

| Drug name | **Aspirin**<br>**Ibuprofen - Ketoprofen - Naproxen** | **Celecoxib - Etoricoxib**<br>Selective **COX-2** Inhibitors (less GI side effects) |
|---|---|---|
| **Uses** | • **1st line to relieve pain** and inflammation. **NO ROLE** in preventing the progression<br>• Paracetamol is the analgesic of choice in pregnancy (Paracetamol is not an NSAID)<br>• Use in **combination** with a **DMARD** | |
| **Side effect** | • If **GI side-effects** are prominent, or the patient is over 65, add a PPI | |

## Corticosteroids

| | |
|---|---|
| **General info** | • Low dose use if **NSAIDs do not provide adequate pain relief or during flares**<br>• Short-term treatment may be appropriate but **avoid** long-term use.<br>• Used as a bridge when waiting for DMARDs to take effect; DMARDs are much slower in onset of action than steroids.<br>• Sometimes if 1 or 2 joints are active, we may give local injections, provided that we excluded septic arthritis.<br>• Corticosteroids are the most common cause of secondary osteoporosis, Therefore, concomitant vitamin D and bisphosphonates are necessary to reduce fracture risk in patients expected to be on corticosteroid therapy for more than 3 months' duration. |

## Disease-Modifying Antirheumatic Drugs (DMARDs)

Click here for a summary of all DMARDs

| Drug name | **Methotrexate** |
|---|---|
| **General info** | • **Methotrexate is the 1st line & Gold standard DMARD**<br>★ **MUST be part of the initial therapy with NSAIDS**<br>• **Monitoring requirement (CBC, LFTs)** bc it causes liver toxicity, lung fibrosis and bone marrow suppression. Can also lead to stomatitis and oral ulcers<br>• **MOA:** Inhibits **DNA synthesis** and cell division. |
| **Uses** | • Should be initiated **early** (at the time of diagnosis) to control symptoms. **No immediate analgesic effects**. So, begin treating With NSAID while waiting for DMARDs to take effect (~6 weeks).[1]<br>• Once the **effect is evident**, **gradually** taper and discontinue NSAIDs and continue DMARDs.<br>• **Can delay progression of the disease** (prevent/slow joint and cartilage damage and destruction)<br>• Should **not** be used in **pregnancy** and conception should be delayed until women have been off the drug for 3-4 months (Davidson's) (in kumar it's 6 weeks) because it's teratogenic. For women who wants to get pregnant have to stop the drug at least 3 months before stop contraceptive |
| **Alternatives to Methotrexate** | • **Hydroxychloroquine** It requires **eye examinations** every 6 months because of the risk of visual loss due to **retinopathy**. **Used in mild non-erosive disease.**<br>• **Sulfasalazine:** used as first line in young females of reproductive age , requires blood monitoring is because of the risk of leukopenia, thrombocytopenia and bone marrow toxicity. (CBC, LFTs)<br>• Both **hydroxychloroquine** and **sulfasalazine** are **safe in pregnancy.**<br>• **Leflunomide, Azathioprine** (especially if there are severe extra-articular manifestations, like lung involvement or vasculitis. You may also use other drugs like cyclophosphamide)<br>• For both (Leflunomide & Azathioprine) monitor CBC, LFTs. |

1. In early RA, the combination of at least one swollen joint for more than 6 weeks with no prior injury, no associated history or family history of spondyloarthritis or associated conditions such as psoriasis, and a positive ACPA test is the best way to select patients for earlier treatment to avoid joint damage.

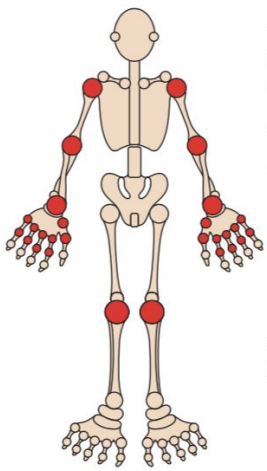
# Management cont.

| If not improving, use: Biologic Response Modifiers | |
|---|---|
| **General info** | **Before using any drug** (especially **anti-TNF**) we have to **exclude** infections like latent **TB** by screening with a **p**urified **p**rotein **d**erivative (**PPD = Mantoux test**) |
| **Drugs** | - **TNF Inhibitors: Etanercept, infliximab**, Adalimumab.<br>➔ **first line** as DMARDs for those **not responding** to methotrexate or **intolerant** of methotrexate. They are often used initially in combination with methotrexate to prevent disease progression. **Contraindicated** in **CHF.**<br>➔ TNF inhibitors are **safe** in **pregnancy**. Even some can be used out to 6 months of pregnancy<br>- **IL-6 receptor inhibitor :** Tocilizumab.<br>- **T-Cell costimulation modulator:** Abatacept.<br>- **Anti-CD20:** Rituximab |

| Others | |
|---|---|
| **Physiotherapy** | • Effective in maintaining the range of motion.<br>• Strengthening of muscles, Prevent contractures, Prevent deformities.<br>• Maintain activities of daily living. |
| **Occupational therapy** | • Education of patients in the use of daily living activities<br>• Prevention of joint contractures and deformities. |
| **Surgery** | • Surgery has a useful role in the long-term approach to patient management but is less frequently needed as therapeutic disease control becomes more effective.<br>• Its main objectives are prophylactic, to prevent joint destruction and deformity, and reconstructive, to restore function.<br>• Rarely we do synovectomy, if the patient is not responding to treatment |

## ◀ Calculation of the Disease Activity Score 28 (DAS28)

- DAS28 is widely used to assess disease activity, response to treatment and need for biological therapy.
- It involves counting the number of swollen and tender joints in the upper limbs and knees, and combining this with the ESR and the patient's assessment of the activity of their arthritis on a visual analogue scale, where 0 indicates no symptoms and 100 the worst symptoms possible.
- This data are entered into a calculator to generate a numerical score. The higher the value, the more active the disease



**Calculation**
- Count swollen joints
- Count tender joints
- Measure erythrocyte sedimentation rate*
- Note patient global health assessment (1–100)
- Enter data into calculator: www.4s-dawn.com/das28

**Interpretation**
- >5.1 High activity
- 2.6–5.1 Moderate activity
- <2.6 Remission

# Juvenile Idiopathic Arthritis (JIA)



- **Definition:** Juvenile (Childhood) forms of psoriatic arthritis, rheumatoid arthritis, and other undifferentiated forms of inflammatory arthritis
- **Epidemiology:** has a similar prevalence of diabetes, one in each thousand child might have JIA
- Usually, patients have a phenotype that differentiate this disease from adulthood disease.
- Such very common phenotype is uveitis.
- Oligoarthritis is the most common form of JIA
- ANA is usually +ve in JIA patients.
- **Management:** complex and requires expert medical teams. Generally, first line is methotrexate.
- Early management can prevent joint deformities until the patient reaches adulthood, when the disease usually fades.

## ◀ DDx of RA and the main characteristics of other diseases

- **The diagnosis of Rheumatoid arthritis can be very challenging in real practice**
- **Diseases don't read books, any disease can have any presentation**

| Disease | Distinguisher (Reference: Current Medical Diagnosis And Treatment, 2022) |
|---|---|
| **Osteoarthritis** | Not associated with constitutional symptoms, relieved by rest, usually asymmetrical and has minimal signs of articular inflammation. usually a disease of the elderly |
| **Gout** | Monoarticular and intermittent |
| **Spondyloarthritis** | Sacroiliac joint and spine involvement |
| **Acute Viral Arthritis** | Resolves within weeks, Seronegative |
| **SLE** | Malar rash, Alopecia, Photosensitivity, glomerulonephritis, very high ANA |
| **Granulomatosis with polyangiitis** | preferentially involves larger joints, usually spares the small joints of the hand, accompanied by severe headache |
| **Rheumatic fever** | Migratory in nature, high ASO titer, prompt response to aspirine |
| **Paraneoplastic Syndromes** | Finger clubbing, palmar fasciitis, Negative rheumatoid factor with S&S suggestive of hormon-like secretions |
| **Psoriatic arthritis** | Affects the DIP, whereas RA spares the DIP |

# Summary

## Rheumatoid Arthritis

| | |
|---|---|
| **Etiology** | Unknown could be :<br>1. Genetic 2. infectious 3. environmental 4.Autoimmune |
| **Features** | **Articular features:**<br>• Wrist (Radial deviation)<br>• Metacarpophalangeal Joints (Ulnar deviation)<br>• Thumbs ("Z" deformity)<br>• Proximal Interphalangeal Joints (Swan neck, boutonniere deformity))<br>• Cervical spine (Do X-ray imaging before any procedure)<br>**Extra-articular features:**<br>• Felty's syndrome (RA + Neutropenia + Splenomegaly)<br>• Cardiac: RA is a cardiovascular risk factor<br>• Pulmonary: Interstitial Lung Disease<br>• Neuromuscular: Carpal Tunnel syndrome<br>• Dermatological: Subcutaneous nodules mostly in the pressure areas |
| **Investigations** | Anti-CCP is more specific than RF |
| **Treatment** | **NSAIDs**<br>• **1st line to relieve pain** and inflammation. **NO ROLE** in preventing the progression<br>**Corticosteroids**<br>• During flares or if NSAIDs do not provide adequate pain relief<br>**Methotrexate**<br>• **Best initial** and **Gold standard** in managing RA. it Inhibits **DNA synthesis** and cell division.<br>• initiated **early** (at the time of diagnosis) to control symptoms. **No immediate analgesic effects (~6wks)**<br>• **Can delay progression of the disease**<br>**Anti-TNF**<br>• For those **not responding** to methotrexate or **intolerant** of methotrexate.<br>• **Before using any drug** we have to **exclude** infections like latent **TB** by screening with a **PPD** |
| **Factors predicting poor prognosis** | 1. Older **age**<br>2. **Female** sex<br>3. **Symmetrical** small joint involvement<br>4. Morning stiffness **>30 min**<br>5. **>4** swollen joints<br>6. Normochromic normocytic anaemia<br>7. Cigarette **smoking**<br>8. **Comorbidity**<br>9. C-reactive protein **>20** g/dl<br>10. **Positive** rheumatoid factor (**RF**) and anti-citrullinated peptide antibodies (**ACPA**)<br>11. Early erosive damage (On x-ray, US, MRI) |

# Lecture Quiz

**Q1: A 45-year-old woman presents to the rheumatology outpatient clinic with a three month history of stiff hands and wrists. She mentions that the pain is particularly bad first thing in the morning. On examination, the wrists, metacarpophalangeal joints and proximal interphalangeal joints are swollen and warm. A diagnosis of rheumatoid arthritis is suspected. Which of the following investigations is most specific for confirming the diagnosis?**

A- X-rays
B- Rheumatoid factor levels
C- Anti-citrullinated peptide antibody (anti-CCP) levels
D- C-reactive protein
E- Erythrocyte sedimentation rate

**Q2: A 40-year-old woman presents to the rheumatology outpatient clinic with a three month history of stiff hands and wrists. She mentions that the pain is particularly bad first thing in the morning. On examination, the wrists, metacarpophalangeal joints and proximal interphalangeal joints are swollen and warm. A diagnosis of rheumatoid arthritis is suspected. Blood tests for rheumatoid factor return as positive. What is the most appropriate management?**

A- Non-steroidal anti-inflammatory drugs (NSAIDs)
B- Intramuscular depot injection of methylprednisolone plus NSAIDs
C- Anti-TNF therapy
D- Intramuscular depot injection of methylprednisolone plus NSAIDs and methotrexate and sulfasalazine
E- Physiotherapy

**Q3: A 55-year-old woman presents to her GP with shortness of breath and dry cough. The symptoms began a few months ago and have progressed. She has a past medical history of rheumatoid arthritis, diagnosed ten years earlier. On respiratory examination, there are bibasal fine inspiratory crackles on auscultation. What is the most likely cause of her symptoms?**

A- Pulmonary oedema
B- Consolidation
C- Pleural effusions
D- Pulmonary fibrosis
E- Intrapulmonary nodules

**Q4: A 30-year-old woman presents to accident and emergency with worsening stiffness in the hands, wrists and feet. She mentions that the pain has been particularly bad in the mornings. On examination, there is a palpable spleen. Initial blood tests reveal a low neutrophil count and a raised C-reactive protein. The most likely diagnosis is**

A- Felty's syndrome
B- Reactive arthritis
C- Still's disease
D- Infectious mononucleosis
E- Serum sickness

**Q5: A 40-year-old woman complains of pain and swelling in both wrists and ankles for 7 weeks. She has several months of fatigue. Morning stiffness impairs her activities for approximately 2 hours. OTC naproxen provides temporary relief. On examination, the metacarpophalangeal (MCP) joints and wrists are warm and tender; there is slight tenderness to pressure over the ankles and metatarsophalangeal (MTP) joints as well. All other joints are normal. There is no alopecia, photosensitivity, kidney disease, or rash. Which of the following is correct?**

A- The clinical picture suggests early rheumatoid arthritis (RA), and a rheumatoid factor and anticyclic citrullinated peptide (anti-CCP) should be obtained.
B- The prodrome of lethargy suggests chronic fatigue syndrome (CFS).
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.

Answers: Q1:C | Q2:A | Q3:D | Q4:A | Q5:A

Answers Explanation File!

# GOOD LUCK !

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