Rheumatoid Arthritis

- A systemic, inflammatory, autoimmune, polyarticular arthritis, usually of peripheral joints, characterised by joint destruction and deformity. It can also have extra-articular manifestations.
- More common in women (3:1) and can present at any age; peak age of onset 55y.
- Detected early, full remission can be achieved in >80% of patients, preventing joint damage and disability.
- If treatment is started <6m after initial symptoms, monotherapy is more likely to be effective.
- Patients with RA are at higher risk of cardiovascular disease, especially if RF/antiCCP +ve, disease >10y, extra-articular manifestations. Remission of disease with active treatment reduces these risks.

Features of inflammatory arthritis	Differential diagnosis of RA	Extra-articular features of RA
• Acute or subacute onset • Worse with rest and improved by exercise • Nights disturbed by pain • Morning stiffness lasting >30min • Systemic symptoms may be present, particularly fatigue • Squeeze test +ve (pain on squeezing across MCPJs/MTPJs) • Soft, boggy, tender swelling around joints (synovitis)	• Osteoarthritis • Gout • Seronegative arthritides (psoriatic arthritis, ankylosing spondylitis, IBD) • Septic arthritis (especially if monoarthritis) • Viral arthritis (rubella, parvovirus, Hep B) • Reactive arthritis (postinfective: throat, gut, STI) • Connective tissue disease (SLE) • PMR • Fibromyalgia • Others: sarcoidosis, thyroid disease, infective endocarditis, paraneoplastic syndromes, multiple myeloma, hemochromatosis	**Eyes:** Sjogren's syndrome, scleritis, episcleritis **Skin:** leg ulcers, rashes; **Rheumatoid nodules:** skin, eyes, lung, heart, vocal cords; **CNS:** peripheral nerve entrapment, polyneuropathy, mononeuritis multiplex, atlanto-axial subluxation **Resp:** pleural involvement, fibrosis, obliterative bronchiolitis; **CVS:** CVD, pericardial effusions, myocarditis/valvulitis, vasculitis; **Anaemia; Kidney involvement; Liver:** mild hepatomegaly, abnormal LFTs; **Orthopaedic:** carpal tunnel syndrome, tendon rupture, cervical myelopathy, osteoporosis, tendon rupture, deformities and functional impairment **Depression/Anxiety/social impact/fatigue** **Other:** thyroid disorder, osteoporosis, splenomegaly, susceptibility to infections, lymphadenopathy **Complications of drug treatment:** GI side effects (NSAIDs), increased risk of infection (glucocorticoids, DMARDs), liver toxicity (methotrexate), osteoporosis (glucocorticoids)

Diagnosis of Rheumatoid Arthritis – ultimately a CLINICAL DIAGNOSIS!

History suggests inflammatory arthritis

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Physical examination to check for synovitis, not just arthralgia (use GALS screening examination initially and then focussed examination based on findings/history – see 'Joint Pain' guideline)

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Synovitis present?

- **no** → Consider alternative diagnoses
  - If level of suspicion for RA high, discuss with consultant and ensure careful follow-up to monitor
  - Avoid checking RF if no synovitis
  - **If diagnosis in doubt, discuss with consultant**
- **yes** → Investigations: CBC, ESR, CRP, RF
  Consider Xray if synovitis of hands/feet
  Calculate EULAR score

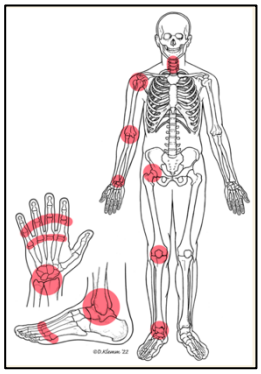
EULAR score ≥6
(or suggestive features on Xray: periarticular osteopenia, joint space narrowing, bone erosions; or signs of late disease)

Likely RA
Discuss with consultant
(note if RF-ve but still a high EULAR score, careful consideration of seronegative arthropathies)

EULAR score <6
- Consider alternative diagnosis (see 'Joint Pain' guideline)
- If high level of suspicion for RA, but RF negative, **discuss with consultant** (arrange for anti-CCP)
- Ensure careful follow-up to monitor

ACR/EULAR 2010 Classification Criteria for RA	
JOINT INVOLVEMENT (tenderness/swelling suggestive of active synovitis with no better alternative diagnosis e.g. SLE, psoriatic arthritis, gout)	
1 large joint	0
2-10 large joints	1
1-3 small joints (+/- involvement of larger joints)	2
4-10 small joints (+/- involvement of larger joints)	3
>10 joints (at least one small)	5
SEROLOGY	
Negative RF and negative anti-CCP	0
Low positive RF or low positive anti-CCP	2
High positive RF or high positive anti-CCP (3x upper limit of normal)	3
ACUTE PHASE REACTANTS	
Normal CRP and ESR	0
Abnormal CRP and ESR	1
DURATION OF SYMPTOMS	
<6 weeks	0
≥6 weeks	1

Large joints = shoulders, elbows, hips, knees, ankles
Small joints = hands, feet, wrists **(except DIPJs and big toe)**



Typical pattern of joint involvement in RA

Goal of treatment is complete remission using DMARDs, **without** NSAIDs or corticosteroids

Initial management of Rheumatoid Arthritis

1. **Pre-treatment investigations:**
   - Creatinine (eGFR)
   - Baseline CBC, ALT and AST if going to prescribe methotrexate
   - HbA1c, urine protein if other CV risk factors
2. **DMARD** – start as soon as possible after diagnosis. Choose 1st-line based on severity of disease & patient wishes – discuss carefully:

Hydroxychloroquine (HCQ)	Methotrexate (MTX)
Advantages: does not require much monitoring and so does not require as many clinic visits or blood tests as with MTX (therefore cheaper) *Disadvantages:* may not control symptoms, can lead to retinopathy, especially at higher doses and if taken over a long period (prevalence 7.5% if taking >5years) **Given the challenges of monitoring and potential side effects of MTX, AIC Kijabe Hospital recommends trialling HCQ alone as first line therapy in *most* adult cases.** *Other details:* it can take 6-12 weeks before benefits are seen *Dosing:* start with 200mg once daily; titrate gradually until symptoms controlled to a maximum dose of 400mg OR 5mg/kg/day (whichever is lower)	*Advantages:* Gold standard for 1st-line therapy in RA; more likely to achieve control than HCQ *Disadvantages:* Common side effects: loss of appetite, nausea, GI upset, headaches, fatigue, hair loss. Rare but serious side effects: liver toxicity/jaundice, pulmonary toxicity (cough, chest pain, sob), signs of infection, bleeding problems, severe skin/mouth rash. Requires regular monitoring, especially in the first few months. This will make it more expensive than HCQ. *Other details:* Only taken **once weekly** (very important not to take more often). Folic acid is taken once weekly to reduce risk of side effects. Symptoms should improve within 3-6 weeks after starting MTX, but it could take 12+ weeks to see the full benefit. Usually, in this context, a trial of HCQ is worth trying first, but consider MTX if severe disease or high risk of progression (anti-CCP +ve and/or erosions on Xray at baseline) and if patient can commit to and afford, monitoring. *Dosing:* start with 10mg PO once weekly (+ Folic acid 5-10mg once weekly, taken the day after MTX); titrate until symptoms controlled every 2-6 weeks (depending on severity) to a maximum dose of 25mg once weekly. Warn of **RED FLAG SYMPTOMS** and to return to clinic if: sore throat, fever, unexplained bruising, bleeding, rashes, mouth ulcers, cough/DIB, nausea or vomiting. *Monitoring:* 2-weekly CBC, Creat, ALT and AST until on a stable dose for 6w; then monthly CBC, Creat, ALT and AST for 3m; then 3-monthly for duration of treatment with methotrexate. (See DMARD guideline for details.) All patients taking methotrexate should be **discussed with consultant** at every visit

3. **Adjunctive treatment** - NSAID or corticosteroid for initial symptom control
   a) NSAIDs 1st-line choice if suitable (check baseline creatinine/eGFR) + omeprazole 20mg OD
      Use at adequate doses (unless contraindicated) e.g. ibuprofen 600mg QID; celecoxib 200mg BD; meloxicam 15mg OD
   b) Corticosteroids, especially if severe symptoms e.g. prednisolone 10-15mg OD (limited benefit higher doses) +/- PPI if high risk
4. **Check for CV risk factors** and manage accordingly
5. Start **patient education**
6. Arrange review in 2 weeks

Follow-up and long-term management of RA

1. **History & Physical Examination**
   - Check symptoms, compliance, functional status (fatigue is significant in up to 50%)
   - Screen for depression, anxiety (PHQ2 and GAD2)
   - Cardiovascular risk – check risk factors, BMI, BP
   - Examine for signs of active disease or complications
2. **Investigations**
   - Monitoring if taking MTX
   - Annual creatinine/eGFR; annual HbA1c if other risk factors
   - Annual retinopathy screen if taking HCQ
3. **Plan**
   - **Titrate medication**
     - Titrate DMARD until complete remission. If no improvement by 8 weeks, **discuss with consultant.**
     - Aim to stop NSAIDs/corticosteroids as rapidly as clinically feasible (taper corticosteroids if taken >2 weeks). If patient is requiring long-term use of NSAID/corticosteroid, then DMARDs need increasing! **Discuss with consultant**
     - If disease is not controlled by first DMARD at maximum tolerated dose, check compliance, review diagnosis (see Joint Pain guideline) and **discuss with consultant**. (May need to either switch to MTX, if started with HCQ, or to take two DMARDs).
     - If disease is well-controlled and there is a **flare of symptoms** - check compliance. **Discuss with consultant.** Consider increasing dose of DMARDs; may require short-term NSAID/corticosteroid.
   - **Continue patient education**
   - **Immunisations** – recommend pneumococcal vaccine (only required once in lifetime), annual flu vaccine and to keep up-to-date with Covid vaccines
   - **Physiotherapy +/- occupational therapy** as indicated
   - Arrange follow-up as indicated. Ensure patient aware of red-flag symptoms

Patient education

- Nature of disease
- Need for long-term treatment and follow-up in order to control symptoms and to prevent disability
- Side effects of medication
- Red flag symptoms
- How to spot a flare
- Exercise/physio
- Healthy lifestyle to reduce CV risk factors
- Immunisations

Direct to on-line information if relevant

Discuss with consultant

- EULAR score ≥6
- EULAR score <6 but high clinical suspicion for RA
- Diagnosis unclear
- Any patient taking MTX
- Side effects of treatment
- No response to DMARD by 8w
- If unable to wean of steroids/NSAIDs
- If disease well-controlled but flare of symptoms

References: JAMA 2018;320(13):1360; BMJ 2016;352:i387; UpToDate accessed 12/1/24; 2010 RA classification criteria: an ACR/EULAR collaborative initiative. Arthritis Rheum. 2010 Sep;62(9):2569-81. doi: 10.1002/art.27584. PMID: 20872595; Polyarticular Joint Pain in Adults, AAFP, *January 2023; Volume 107, Number 1*;