Musculoskeletal disorders

Rheumatoid Arthritis (RA)

Introduction / Epidemiology

- Rheumatoid arthritis is a chronic, systemic, autoimmune inflammatory disorder primarily affecting the synovial joints, leading to joint destruction, deformity, and disability.

Epidemiology:

- **Prevalence**: ~0.5–1% of the global population.
- **Age of onset**: Common between **30–50 years**, though it can occur at any age.
- **Gender ratio**: **3:1 female predominance**.
- **Geographic variation**: More prevalent in developed countries, possibly due to lifestyle and genetic factors.
- **Genetic factors**: Associated with **HLA-DR4 and HLA-DR1** alleles.

Etiopathogenesis

Etiology (multifactorial):

1. **Genetic predisposition:**
   - HLA-DR4/DR1 alleles.
2. **Environmental triggers:**
   - Smoking (most established risk factor).
   - Infections (Epstein-Barr virus, Mycoplasma, Parvovirus B19).
   - Hormonal influence (estrogens may enhance immune response).
3. **Autoimmune mechanism:**
   - Loss of tolerance leads to **autoantibody production** (e.g., Rheumatoid Factor and anti-CCP antibodies).
   - These immune complexes deposit in synovium → activate complement → chronic inflammation.

Pathogenesis:

1. **Antigen-presenting cells (APCs)** present self-antigens to **CD4+ T cells**.
2. **Cytokine release**: TNF-α, IL-1, IL-6, IL-17.
3. Recruitment of macrophages, B-cells → **pannus formation**.
4. **Pannus**: Granulation tissue that erodes cartilage, bone, and tendons.
5. **Joint destruction** and deformity over time.

Clinical Features / Symptoms

Articular manifestations:

- **Symmetrical, polyarticular joint pain**.
- Morning stiffness > 1 hour.
- **Most commonly involved joints**: MCPs, PIPs, wrists, knees, ankles, MTPs.
- **Joint swelling, tenderness, warmth**.
- **Late deformities**: Swan-neck, boutonniere, Z-deformity of thumb, ulnar deviation.

Extra-articular manifestations:

- **Rheumatoid nodules** (subcutaneous, extensor surface).
- **Pulmonary**: interstitial fibrosis, pleuritis.
- **Cardiac**: pericarditis, increased atherosclerosis.
- **Ocular**: scleritis, keratoconjunctivitis sicca (dry eyes).
- **Hematological**: anemia of chronic disease, Felty's syndrome (RA + splenomegaly + neutropenia).
- **Neurological**: entrapment neuropathies (e.g., carpal tunnel syndrome).

Diagnosis & Investigations

Clinical criteria (ACR/EULAR 2010):

- Joint involvement, serology (RF, anti-CCP), acute phase reactants (ESR/CRP), and symptom duration.

Laboratory Tests:

- **Rheumatoid factor (RF)**: positive in ~70–80% (not specific).
- **Anti-cyclic citrullinated peptide (anti-CCP)**: more specific (~95%).
- **ESR & CRP**: elevated in active disease.
- **CBC**: normocytic normochromic anemia.
- **LFTs, RFTs**: baseline before starting DMARDs.

Imaging:

- **X-rays**: joint space narrowing, periarticular osteopenia, erosions.
- **MRI/Ultrasound**: early synovitis and erosions.

Treatment Goals / Therapeutic Objectives

- Reduce inflammation and pain.
- Prevent or slow joint damage.
- Preserve joint function and mobility.

- Improve quality of life.
- Achieve clinical remission or low disease activity.

Non-Pharmacological Therapy

- **Patient education**.
- **Physical therapy**: ROM exercises, muscle strengthening.
- **Occupational therapy**: assistive devices to improve function.
- **Diet**: anti-inflammatory diet (omega-3 fatty acids).
- **Psychological support**: stress reduction, support groups.
- **Smoking cessation**.

Pharmacological Therapy

A. First-line drugs: Disease-Modifying Anti-Rheumatic Drugs (DMARDs)

Drug	Dose	Duration	Mechanism	Notes
Methotrexate (MTX)	7.5–25 mg weekly	Lifelong	Inhibits dihydrofolate reductase → ↓ lymphocyte proliferation	Gold standard, monitor LFTs, CBC
Hydroxychloroquine	200–400 mg/day	Long-term	Inhibits antigen presentation, ↓ TLRs	Safe in pregnancy
Sulfasalazine	1–3 g/day in divided doses	Long-term	Inhibits prostaglandin synthesis	Can cause rash, GI upset
Leflunomide	10–20 mg/day	Long-term	Inhibits pyrimidine synthesis	Monitor liver enzymes

B. Biologic DMARDs (used if unresponsive to traditional DMARDs)

Drug	Type	Mechanism
Etanercept, Infliximab, Adalimumab	Anti-TNF agents	Bind TNF-α
Tocilizumab	IL-6 receptor inhibitor	↓ Inflammation
Rituximab	Anti-CD20	B-cell depletion
Abatacept	CTLA-4 analog	Inhibits T-cell activation

Note: Require screening for **latent TB**, **hepatitis B**, and **baseline CBC/LFTs**.

C. NSAIDs and Corticosteroids (for symptom relief)

- **NSAIDs**: Ibuprofen, Naproxen – reduce pain but do not prevent disease progression.

- **Glucocorticoids**:
  - Low-dose oral (e.g., prednisolone 5–10 mg/day) during flare-ups.
  - Intra-articular steroids for mono/oligoarticular flare.
  - Long-term use discouraged due to adverse effects.

Individualized Patient-Specific Therapeutic Plan

Factor	Considerations
Age	Elderly → avoid MTX if renal function reduced; prefer hydroxychloroquine
Comorbidities	Hepatic (avoid leflunomide), renal (adjust MTX), diabetes (avoid steroids)
Pregnancy	Avoid MTX, leflunomide. Use hydroxychloroquine, sulfasalazine
Allergies	Switch to biologics if DMARD allergy
TB history	Avoid TNF inhibitors unless latent TB treated

Controversies / Special Considerations

- **Early aggressive treatment** vs. step-up therapy.
- **Biologics vs. traditional DMARDs**: biologics are effective but costly and risk infections.
- **JAK inhibitors** (e.g., tofacitinib): newer oral option, but safety concerns (cardiovascular, malignancy).
- **Vaccination**: must be up-to-date **before** starting immunosuppressives.
- **Biosimilars**: newer cheaper alternatives to branded biologics – still under study.

Monitoring Therapy

Parameter	Frequency
CBC, LFT, RFT	Every 2–4 weeks initially, then 8–12 weeks
ESR/CRP	Monthly to assess disease activity
Disease Activity Scores: DAS28	Every visit
Chest X-ray / TB screening	Before biologics
Eye exam (hydroxychloroquine)	Baseline, then annually after 5 years

Adverse Effects & Their Management

Drug	Adverse Effects	Management
Methotrexate	Hepatotoxicity, stomatitis, bone marrow suppression	Folic acid 5 mg/week, monitor LFTs

Hydroxychloroquine	Retinopathy	Annual eye exams
Sulfasalazine	GI upset, rash	Dose titration, hydration
Biologics	Infections (TB, fungal)	Screen before use, stop during infections
Steroids	Osteoporosis, hyperglycemia	Use shortest duration, calcium + vitamin D, bisphosphonates

Follow-up and Patient Counseling

Follow-up:

- Every 1–3 months during active disease
- Every 3–6 months during stable phase
- Monitor side effects, adherence, comorbidities

Counseling:

- Educate about disease nature and need for lifelong management
- Importance of adherence and regular monitoring
- Discuss family planning and contraception (MTX is teratogenic)
- Vaccinations: Influenza, pneumococcal, hepatitis B, shingles (live vaccines avoided in biologics)
- Lifestyle modification: Smoking cessation, exercise, weight management

Osteoarthritis (OA)

Introduction / Epidemiology

- Osteoarthritis is a chronic, progressive, degenerative joint disorder characterized by the loss of articular cartilage, subchondral bone remodeling, osteophyte formation, and mild synovial inflammation, leading to joint pain, stiffness, and functional limitation.

Epidemiology:

- Most common form of arthritis worldwide.
- **Prevalence** increases with age; affects ~10–15% of individuals over 60 years.
- **Gender**:
  - Men are more affected <50 years.
  - Women more affected >50 years (especially postmenopausal).

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