Rheumatoid Arthritis

RHEUMATOID ARTHRITIS

INTRODUCTION

- This is an autoimmune disease associated with autoantibodies to the Fc portion of immunoglobulin G (rheumatoid factor) and to citrullinated cyclic peptide.
- There is persistent synovitis, causing chronic **symmetrical polyarthritis** with systemic inflammation. Genetically, RA is a heterogeneous group of diseases.

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EPIDEMIOLOGY

- RA has a worldwide distribution affecting 0.5–1% of the population (with a female preponderance of 3 : 1).
- RA remains a significant cause of disability and mortality and carries a high socioeconomic cost.
- It presents from early childhood (when it is rare) to late old age. The most common age of onset is between 30 and 50 years.

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AETIOLOGY

GENETIC FACTORS

Gender- Women, before the menopause, are affected three times more often than men.

Genetic factors- There is a strong association between susceptibility to RA and certain human leucocyte antigen (HLA) haplotypes. There is an increased incidence in first-degree relatives

ENVIRONMENTAL FACTORS

Smoking and other forms of bronchial stress increase the risk of RA

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PATHOGENESIS

- The disease appears to arise from a cell-mediated (T-cell) autoimmune response, but there may be an underlying infectious aetiology.

- Once the T-cell response is triggered, there is a release of cytokines, including interleukins IL-1 and IL-6, and tumor necrosis factor (TNF), (chemo attractants)which cause the inflammatory reaction.

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PATHOGENESIS

- Synovitis occurs when chemo attractants produced in the joint recruit circulating inflammatory cells. Over-production of tumor necrosis factor alpha (TNF-α) leads to synovitis and joint destruction.
- There is inflammation of the soft tissues and synovial hyperplasia, containing lymphocytes and plasma cells. A layer of inflammatory tissue called a ‘pannus’ spreads over the joint surfaces and erodes the subchondral bone, denuding articular cartilage

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PATHOGENESIS

- There is chronic mononuclear cell infiltration and neovascularization.

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PATHOLOGY

RA is characterized by widespread, persistent synovitis of joints, tendon sheaths or bursae.

In RA, the synovium becomes greatly thickened, causing “boggy” swelling around joints and tendons.

Proliferation of the synovium into folds and Fronds can be seen.

Synovium is infiltrated by a variety of inflammatory cells, including polymorphs, lymphocytes and plasma cells.

There is marked vascular proliferation.
Increased permeability of blood vessels and the synovial lining layer leads to joint effusions

This ‘pannus’ of inflamed synovium damages the underlying cartilage by blocking its normal route for nutrition and by the direct effects of cytokines on the chondrocytes.

The cartilage becomes thinned and the underlying bone exposed.

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CLINICAL FEATURES

Typical presentation(approximately 70% of cases)

- **Progressive, symmetrical, peripheral polyarthritis, evolving over a period of a few weeks or months in patients between 30 and 50 years of age.(The disease can occur at any age.)**

- **Less commonly (15%), a rapid onset can occur over a few days (or explosively overnight), with a severe symmetrical, polyarticular involvement, especially in the elderly.**

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CLINICAL FEATURES

- The majority of patients complain of pain and stiffness of the small joints of the hands (MCPs,PIPs) and feet (MTPs).
- The DIPs are usually spared.
- The wrists, elbows, shoulders, knees and ankles are also affected.
- In most cases, many joints are involved, but 10% of patients present with a monoarthritis of the knee or shoulder or with carpal tunnel syndrome.

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CLINICAL FEATURES

- Fatigue is a common complaint. The pain and stiffness are significantly worse in the morning. Sleep is disturbed.
- The joints are usually warm and tender with some joint swelling. There is limitation of movement and muscle wasting.
- Deformities and non-articular features develop if the disease cannot be controlled.

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HANDS AND WRISTS DEFORMITIES DUE TO RA

1. Radial deviation of the wrist
2. Extensor tendon ruptures
3. Ulnar deviation metacarpophalangeal joints
4. Z-deformity of the thumb
5. Boutonnière deformity of the fingers Swan neck deformities
6. Carpal tunnel syndrome

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HANDS AND WRISTS DEFORMITIES DUE TO RA

- PICTURE

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EXTRA-ARTICULAR MANIFESTATIONS OF RA

- Skin – subcutaneous nodules
- Eyes – scleritis, iritis
- Lungs – interstitial lung disease, pleural effusion
- Heart – myocarditis
- Kidneys – nephritis
- Amyloid – lungs, kidneys, heart, bowel
- Compression and vascular neuritis

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American College of Rheumatology criteria for diagnosis of RA

1) Morning stiffness lasting at least 1 hour
2) Active arthritis of three or more joints simultaneously
3) Active arthritis of at least one hand joint (wrist, MCPJ or PIPJ)
4) Symmetrical arthritis
5) Subcutaneous rheumatoid nodules on extensor surfaces,juxta-articular or over bony prominences

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American College of Rheumatology criteria for diagnosis of RA

6) Rheumatoid factor

7) Radiographic changes of periarticular erosions or osteopenia in affected joints, not osteoarthritis

This involves the patient having four of the seven criteria.

On examination there are joint effusions and synovitis. These cause swelling, warmth, erythema and stiffness of the affected joints with pain on movement.

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INVESTIGATIONS

- ESR, CRP- elevated
- Rheumatoid factor-Positive in 80% and ANA at low titre in 30%. Serology reveals ACPA positivity
- Radiology- Deformity, Periarticular erosions, Osteopenia
- Ultrasound and MRI are useful to demonstrate synovitis and early erosions.
- Blood count may show a normochromic, normocytic anemia.

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INVESTIGATIONS

- 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.
- Doppler ultrasound is a very effective way of demonstrating persistent synovitis when deciding on the need for DMARDs or assessing their efficacy.
- Other investigations will depend on the clinical picture,

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FACTORS PREDICTING A POOR PROGNOSIS FOR RA

- Older age and Female sex
- Symmetrical small joint involvement
- Morning stiffness >30 min
- >4 swollen joints
- Cigarette smoking Co-morbidity
- C-reactive protein >20 g/dL
- Positive rheumatoid factor and anti-citrullinated peptide antibodies

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Management

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

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MANAGEMENT

- 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.

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MANAGEMENT

- If no better, use anti-TNF-α therapy or other biological agent.DMARDs, disease-modifying anti-rheumatic drugs; TNF-α, tumour necrosis factor alpha.

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DRUG THERAPY FOR RA

Non-steroidal anti-inflammatory drugs and coxibs

1.Used to relieve night pain and morning stiffness in addition to disease-modifying drugs.
2.Gastrointestinal side-effects are prominent.

Corticosteroids

1.The early use of corticosteroids slows down the course of the disease.
2.Corticosteroids are the most common cause of secondary osteoporosis and the risk of fracture is increased by them.
3.Intra-articular injections, Intramuscular depot injections, Oral corticosteroids are used as options

Disease-modifying anti-rheumatic drugs

1.These have been shown to reduce inflammation, joint swelling and plasma acute phase reactants, and to slow the development of joint erosions as well as irreversible damage.

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DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

DRUG	PHARMACOLOGY	SIDE EFFECTS AND CONTRAINDICATIONS
Methotrexate	• Remains the anchor drug in RA therapy, • A screening history, chest X-ray and an interferon gamma release assay (IGRA) in high-risk patients are performed to exclude tuberculosis. • Initial pneumococcal and annual influenza vaccinations are given	Should not be used in pregnancy and conception should be delayed until women have been off the drug for 6 weeks. SE- Nausea ,Oral ulcers ,Diarrhea Abnormal liver bio-chemistry ,neutropenia, thrombocytopenia, renal impairement, Pulmonary fibrosis(rare)

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DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

DRUG	PHARMACOLOGY	SIDE EFFECTS AND CONTRAINDICATIONS
Methotrexate	Full blood counts and liver biochemistry should be monitored. Methotrexate usually works within 1–2 months. The starting weekly dose of 7.5–10 mg orally is increased up to 15– 25 mg as necessary to reduce disease activity.	Oral folic acid reduces side-effects but may also lessen efficacy.

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DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

DRUG	PHARMACOLOGY	SIDE EFFECTS AND CONTRAINDICATIONS
Sulfasalazine	It is well tolerated and can be used during pregnancy. The usual starting dose of 500 mg per day is increased to a maintenance dose of 2–3 g per day. Around 50% of patients respond in the first 3–6 months, but efficacy can be lost	Blood monitoring is obligatory because of the risk of leucopenia and thrombocytopenia. SE- Nausea ,Oral ulcers Abnormal liver bio-chemistry ,neutropenia, thrombocytopenia,

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DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

DRUG	PHARMACOLOGY	SIDE EFFECTS AND CONTRAINDICATIONS
Hydroxychloro-quine	A dose of 200–400 g daily is well tolerated. It is used alone in mild disease or commonly as an adjunct to other DMARDs.	Retinopathy is extremely rare, Rheumatologists arrange an initial check of macular function with an Amsler chart and further reviews annually, as retinopathy is irreversible.

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DISEASE-MODIFYING ANTI-RHEUMATIC DRUGS

DRUG	PHARMACOLOGY	SIDE EFFECTS AND CONTRAINDICATIONS
Leflunomide	This DMARD exerts an immunomodulatory effect by blocking clonal expansion of T cells. Dose of 20 mg daily (10 mg if diarrhoea is a problem) is used.	Diarrhoea diminishes with time. Blood monitoring is obligatory (full blood count, platelets, liver biochemistry) SE- Abnormal liver bio-chemistry ,neutropenia, thrombocytopenia

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BIOLOGICAL THERAPIES

TNF-A BLOCKERS

- These agents are more expensive than traditional DMARDs so they are used after at least two DMARDs (usually sulfasalazine and methotrexate) have failed.
- They are usually given in combination with methotrexate to reduce loss of efficacy due to anti-drug antibody formation

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BIOLOGICAL THERAPIES

TNF-A BLOCKERS

- Etanercept
- Adalimumab
- Infliximab
- Certolizumab pegol
- Golimumab

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PHYSICAL MEASURES

- Input is required from the multidisciplinary team
- Physiotherapists advise a combination of rest for active arthritis and exercises to maintain joint range and muscle power. Exercise in a hydrotherapy pool is popular and effective.
- Occupational therapists help to manage activities of daily living despite the arthritis.
- Podiatry, footwear advice and psychological support should also be offered

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SURGICAL MANAGEMENT OPTIONS

- Arthrodesis
- Joint replacement,
- Excision arthroplasty(excision of radial head)
- Tenosynovectomy (to prevent tendon rupture)
- Tendon transfer and interposition grafting (for tendon rupture)

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PROGNOSIS

A poor prognosis is indicated by:

- a clinical picture of an insidious rather than an explosive onset of RA, female sex, increasing number of peripheral joints involved and the level of disability at the onset
- Blood tests showing a high CRP/ESR, normochromic normocytic anemia, and high titers of ACPA and of RF
- X-rays with early erosive damage
- **Prognosis can be altered with early DMARD therapy .**