Rheumatoid Arthritis

G. Pope and Declan Lyons
Chronic systemic inflammatory disease of unknown cause affecting primarily the peripheral joints.

Constitutional symptoms

(fatigue, malaise, morning stiffness)
Genetic:

Assoc. HLA-DR4/DR1.

15%-20% concordance in monozygotic twins.

Infectious agents

e.g. Mycoplasma, EBV, Rubella

Hormonal:
Frequency:

2-3F > M

Incidence 30/100,000

Increases with age: 30-55 peak
Figure 3. Joint frequently affected by rheumatoid arthritis. Less commonly affected are elbows, hips and the neck.
Normal and Arthritic Joints

Figure 1. A normal joint

Figure 2. A joint badly affected by rheumatoid arthritis
Decreased joint space (arrowheads)
Bony erosions (white arrowheads)
Joint deformities (white arrows)
Joint and tendon destruction lead to deformities: ulnar deviation, Z shaped thumb, bouton and swan-neck deformity and subluxation.
- Morning stiffness > 1hr*
- Arthritis hand joints (wrist, MCP or PIP)*
- Arthritis of 3 or > joints simultaneously*
- Symmetrical arthritis*
- Serum RF
- Rheumatoid nodules
- X – ray features typical of RA
• Antibodies (IgM) directed against the Fc portion of IgG

• + 70-80% pts with RA

• Positive predictive value 24% for RA

Faulse +

Sjogren’s 75%
- A post-translationally modified arginine residue
- ELISA anti-CCP

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<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
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<tbody>
<tr>
<td>Anti –CCP</td>
<td>56%</td>
<td>90%</td>
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<tr>
<td>IgM RF</td>
<td>73%</td>
<td>82%</td>
</tr>
<tr>
<td>IgM+ant-CCP</td>
<td>48%</td>
<td>96%</td>
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Extra – articular features
Often over pressure points at extra-articular sites

- They can be fixed to the underlying periosteum or can be freely mobile.

- Present in 30% of patients with Seropositive disease Regress with treatment
• Palpable purpura
• Skin ulceration
• Nailfold infarcts
• Gangrene of the fingers and toes
Pericardial effusions

Pericarditis

Increased mortality from CV:

- Thrombocytosis & ↑ plt adhesiveness
- Intimal hyperplasia
- possible underlying coronary vasculitis
Kidneys

Not commonly affected directly

2° involvement due to meds (eg NSAIDs)

Renal amyloid – green fluorescence in polarized light
Keratoconjunctivitis sicca
Secondary Sjogren’s syndrome
Episcleritis
Scleritis
Scleromalacia perforans
• Carpal tunnel syndrome
• Atlantoaxial subluxation
• Cord compression
• Polyneuropathy predominantly sensory
• Mononeuritis multiplex

The anterior edge of the odontoid process (O) is abnormally separated from the posterior margin of the arch of the atlas (A). Subluxations of the lower cervical vertebral bodies (arrows) are also visible.
• Pleural effusion
• Diffuse fibrosing alveolitis
• Rheumatoid nodules
• Rheumatoid pneumoconiosis (Caplan’s syndrome)
Anaemia due to

- Chronic disease
- NSAID induced GI blood loss
- Hypersplenism
- Suppression of bone marrow function, folate deficiency and haemolysis 2° DMARDs
- Associated pernicious anaemia
<table>
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<tr>
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<th><strong>RA</strong></th>
<th><strong>OA</strong></th>
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<tbody>
<tr>
<td><strong>Worst time</strong></td>
<td>Morning</td>
<td>Evening</td>
</tr>
<tr>
<td><strong>Morning stiffness</strong></td>
<td>Almost always for 1-5 h or all day</td>
<td>Maybe present but duration &lt;45 minutes</td>
</tr>
<tr>
<td><strong>Constitutional symptoms</strong></td>
<td>Usually</td>
<td>Absent unless concommittent disease</td>
</tr>
<tr>
<td><strong>Radiography</strong></td>
<td>MCP, PIP and wrist involvement. Juxta articular OP.</td>
<td>DIP and PIP joints, not usually in wrists</td>
</tr>
<tr>
<td><strong>Joint fluid</strong></td>
<td>WCC 3,000 - 20,000, fluid watery, mucin clot poor</td>
<td>WCC &lt; 3,000, fluid viscous, good mucin clot</td>
</tr>
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Nonpharmacological treatment

Physio /OT/Podiatrist

Surgery

Pharmacological treatment
Hips last longer and the prosthesis can be revised, this is less well developed for knees thus the procedure should be deferred until the patient is >70yrs.
• Arthralgia

• > 3 inflamed/swollen jts

• No extraarticular disease

• Neg Rheumatoid factor

### Severe
- >20 inflamed jts
- extra artic disease
- Raised ESR or CRP
- + RF and/or anti-citrinullated peptide antib
- Xray evidence of jt invol.
**NSAIDS**

Symptom relief/ not retard jt destruction

GI and renal toxicity S.E.

**Prednisolone**

Adverse effects of

- osteoporosis (Ca + vitD +bisphosphonates)
- hyperglycemia
- hypertension
↓ progression/destruction and loss of function

↓ need for other anti inflammatory or analgesic meds.

Initiation <3/12 with established dx RA, who remains symptomatic despite adequate doses of NSAIDs or active disease
- Methotrexate (MTX)
- Sulfasalazine (SSZ)
- Hydroxychloroquine
- Leflunomide
- Azathioprine
- Gold salts

MTX and SSZ are the most active in terms of frequency of
<table>
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<tr>
<th>Adverse event</th>
<th>Treatments</th>
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<tr>
<td>Liver and bone marrow toxicity</td>
<td>MTX, SSZ, leflunomide, azathioprine, gold, D-p.</td>
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<tr>
<td>Renal toxicity</td>
<td>Cyclosporin A, iv gold</td>
</tr>
<tr>
<td>Pneumonitis</td>
<td>MTX</td>
</tr>
<tr>
<td>Allergic skin rxns</td>
<td>Gold, SSZ</td>
</tr>
<tr>
<td>Autoimmunity</td>
<td>SSZ</td>
</tr>
<tr>
<td>Infections</td>
<td>Azathioprine, Cyclosporin A</td>
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<tr>
<td>Ocular toxicity</td>
<td>Antimalarials</td>
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Developed following recognition of TNF-α

+ IL-1 as central pro-inflammatory cytokines in RA.

Bind TNF and prevent its interaction with its receptors.

Expensive – not recommended until at least one xenobiotic
Adverse RXNs:

drug induced lupus-like syndromes,
demyelinating disorders
BM suppression.
Malignancies
Latent TB/ infections
75% continue having some joint pain, swelling and flare-ups

5% develop severe disease with extensive disability

20% always have very mild rheumatoid arthritis

Figure 4. How people with rheumatoid arthritis are likely to be affected
Poor prognosis

• Insidious polyarticular onset

• Male sex

• Advanced age

• Extra-articular manifestations

• Functional disability at one year after start of disease

• Substantially raised concentration of rheumatoid factors

• Presence of HLA-DR4
• Excess mortality associated with severe RA parallels that of 3-vessel CAD or Stage IV Hodgkins

• Co-morbidities which contribute to this excess

Cardiovascular disease

Infections esp. pulmonary, skin & joint

GI blood loss

Lymphoproliferative disorders
• Figure 5. (A), Pelvic X-ray in Early Stage Disease. A pelvic roentgenogram of a patient with classic seropositive rheumatoid arthritis was taken early in the course of the disease. (B), Pelvic X-ray: Four Years Later. Another roentgenogram taken 4 years later demonstrates marked acetabular protrusion and resorption of the femoral heads, both of which are characteristic of the disease.
In clinical trials 30-70% of patients achieve partial response according to the ACR’s disease activity score.

In practice, meds are manipulated to reduce disease activity as much as possible. Options are:

1. Increase the dose
2. Switch to a different DMARD
3. Initiate combination therapy
1. PMR

2. Fibromyalgia – Fatigue, musculoskeletal aching and difficulty sleeping but usually sharply defined areas of tenderness ‘trigger points’ at the base of the neck, back and adjacent to large joints can be found.

3. Underlying malignancy.

4. Reactive or undifferentiated arthritis – polyarthritis and constitutional symptoms but no joint destruction and spontaneous remission within 6-12 months