Outline of presentation

• Clinical presentation of RA
  – Articular, extra-articular and radiological features

• The immunology of RA

• Diagnosis of RA
  – Classification criteria to aid diagnosis
  – The importance of early diagnosis

• Management of RA – an overview of drug treatment
RA - epidemiology

- Commonest cause of autoimmune inflammatory polyarthritis
- Found in all races with variable prevalence
  - 1 - 2% in Caucasians
  - 0.3 - 0.4% in Chinese
  - Rare in the blacks
- Peak age of onset: 35 - 55 years
- Female : Male = 3 : 1
RA – a erosive synovial disease
RA – a erosive synovial disease

Arthroscopic appearance of a normal joint

Arthroscopic appearance of a rheumatoid joint

Normal synovium | Rheumatoid synovium

Histological appearances of normal and rheumatoid synovium
The immunology of RA
Normal synovium

Rheumatoid synovium

New blood vessels

Infiltrating lymphocytes

Rheumatoid synovium

Proliferating synovial fibroblasts

Other cell populations

Dendritic cells

B lymphocytes

Plasma cells

Mast cells

Osteoclasts

CD68+ macrophage

CD3+ T cells

Mab 67+ Type B synoviocytes

IL-1β

TNFα
CD4
Mø
CD4
Chondrocytes
Cartilage degradation
Joint space narrowing
Synoviocytes
Synovial hyperplasia
Joint inflammation
Osteoclasts
Bone resorption
Bony erosion
Endothelial cells
Neovascularisation
Recruitment of inflammatory cells

DC = Dendritic cell
IL = Interleukin
Mø = Macrophage
RF = Rheumatoid factor
TCR = T cell receptor
TNF = Tumour necrosis factor

Activated T-cell

DR

TCR

DC

CD4

CD4

B

Plasma cell

Antigen presentation

Ig, RF Anti-CCP

Stimulatory

Inhibitory

Unknown antigen

TNFα

Mø

TNFα, IL-6, IL1

Chondrocytes

Synoviocytes

Osteoclasts

Endothelial cells

Cartilage degradation
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Recruitment of inflammatory cells

TNFα

IL-6

Antigen presentation

DC = Dendritic cell
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Soft tissue swelling

RA – Early X-ray changes
RA – Early X-ray changes

Peri-articular osteopenia
RA – Late X-ray changes

Peri-articular erosive lesions
RA – Advanced X-ray changes

Bony destruction with deformities
The progressive course of RA

RA – A chronic, serious, prevalent disease

A global prevalence of around 24 million cases\(^1\)

RA is associated with

- serious comorbidities such as heart disease, infection, and malignancies\(^2\)
- a 5–10 year reduction in life expectancy\(^3\)
- reduced quality of life compared with other serious conditions\(^4\)
- a considerable economic burden\(^4\)

# Classification criteria for RA

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Score</th>
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</thead>
<tbody>
<tr>
<td><strong>Joint involvement</strong></td>
<td></td>
</tr>
<tr>
<td>1 large joint</td>
<td>0</td>
</tr>
<tr>
<td>2-10 large joints</td>
<td>1</td>
</tr>
<tr>
<td>1-3 small joints (with/without large joint involvement)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (with/without large joint involvement)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least 1 small joint)</td>
<td>5</td>
</tr>
<tr>
<td><strong>Serology</strong></td>
<td></td>
</tr>
<tr>
<td>RF and anti-CCP negative</td>
<td>0</td>
</tr>
<tr>
<td>Low +ve RF or low +ve anti-CCP</td>
<td>2</td>
</tr>
<tr>
<td>High +ve RF or high +ve anti-CCP</td>
<td>3</td>
</tr>
<tr>
<td><strong>Acute phase reactants</strong></td>
<td></td>
</tr>
<tr>
<td>Normal CRP and normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP or abnormal ESR</td>
<td>1</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
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\[ \geq 6/10 = \text{Rheumatoid arthritis} \]
The need to diagnosis RA early

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Kraan et al A&R 1998; 1481-8
The need to diagnose RA early

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Kraan et al A&R 1998; 1481-8
The need to treat RA early

Early Disease

- Reversible functional disability
- Irreversible functional disability
The need to treat RA early

Early Disease

Advanced Disease

Functional impairment Level

Early Disease

Advanced Disease

Green: Reversible functional disability

Red: Irreversible functional disability
Conventional drug treatment for RA

• Symptomatic treatment
  – Non-steroidal anti-inflammatory drugs
  – Simple analgesics
• Local corticosteroids

• Disease modifying anti-rheumatic drugs
  – Azathioprine
  – Cyclosporine
  – Hydroxychloroquine
  – IM gold injection
  – Leflunomide
  – Methotrexate
  – Penicillamine
  – Sulphasalazine
CD4+ T cells are activated by interaction with dendritic cells (DCs) presenting antigens, leading to secretion of cytokines such as TNFα, IL-6, and IL-1.

### Key Components:
- **Activated T-cell**
- **DC**: Dendritic cell
- **CD4**: T cell receptor
- **Mø**: Macrophage
- **B**: B cell
- **TNFα**: Tumour necrosis factor alpha
- **IL-6**: Interleukin 6
- **IL-1**: Interleukin 1
- **Ig, RF**: Immunoglobulin, Rheumatoid factor
- **Anti-CCP**: Anti-cyclic citrullinated peptide

### Processes:
- **Stimulatory**
- **Inhibitory**

### Effects:
- **Chondrocytes**
  - Cartilage degradation
  - Joint space narrowing
- **Synoviocytes**
  - Synovial hyperplasia
  - Joint inflammation
- **Osteoclasts**
  - Bone resorption
  - Bony erosion
- **Endothelial cells**
  - Neovascularisation
  - Recruitment of inflammatory cells

**Biologic therapies for RA**
Alternative therapies for RA

- Patients want to try alternative therapies
  - 335/402 patients – alt therapies in the past 1 year
  - 243/335 are current users
  - Mean cost per year = HK$10447 (~US$1400)

- Dietary supplements
  - Vitamins
  - Fish oil
  - Evening primrose oil
  - Green lipped mussels
  - Minerals
- Copper bracelet
- Magnet necklace
- Bee sting

- Scorpions
- Bone setting
- Traditional Chinese Medicine
  - Lingzhi / yunzhi
  - Tu-na
- Qi gong
- Taichi
- Spa / balneotherapy
Summary

• RA is a common chronic autoimmune disease of the joint

• Poorly treated, there is significant morbidity and mortality

• The goal of treatment is to achieve remission

• Early patient identification and treatment is essential

• Multiple treatment regimens are available

• Clinicians should work together to control the disease