A guide to the treatment of inflammatory arthritis

Dr Mark Lillicrap
What do you want to get out of this session
A 49 year old female hairdresser comes to see you in your clinic. In addition to her main problem she complains of several weeks of bilateral hand pain, swelling and early morning stiffness that is interfering with her work.

What is the most likely diagnosis:

a) Crystal arthritis  
b) Osteoarthritis  
c) Rheumatoid arthritis  
d) Spondyloarthritis  
e) Systemic lupus erythematosus
NO EARLY MORNING STIFFNESS

EARLY MORNING STIFFNESS

Cup of coffee

Television

Person sweating
NO EARLY MORNING STIFFNESS

DIFFUSE PAIN

Chronic pain syndromes (Fibromyalgia)

Polymyalgia rheumatica
Inflammatory myositis

LOCALIZED PAIN

Joint swelling more likely

Osteoarthritis/arthropathy
Tendinopathy
Bursitis

Joint swelling less likely

Monoarticular

Sepsis
Crystals
Spondyloarthritis

Polyarticular

Rheumatoid
Viral
SLE/CTDs
Spondyloarthritis
Crystals
JOINT PAIN

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Osteoarthritis/arthropathy
Tendinopathy
Bursitis
Rheumatoid arthritis

The American Rheumatology Association
Diagnostic criteria for rheumatoid arthritis (1987)

1. Early-morning stiffness > 1 hour's duration*
2. Arthritis of at least 3 joint types*
   (proximal interphalangeal, metacarpophalangeal, wrist, elbow, knee, ankle, metatarsophalangeal)
3. Arthritis of hand joints*
   (proximal interphalangeal, metacarpophalangeal or wrist)
4. Symmetrical arthritis*
5. Rheumatoid nodules
6. Positive rheumatoid factor
7. Radiographic erosive changes.

* 1-4 must be present for > 6 weeks

Four or more criteria = rheumatoid arthritis
Rheumatoid arthritis

“early morning stiffness that involves the hands”
Rheumatoid arthritis

“early morning stiffness that involves the hands”
Rheumatoid arthritis

“early morning stiffness that involves the hands”
Rheumatoid arthritis – EULAR/ACR - 2010

(1) Patient with at least one joint with *definite* clinical synovitis (swelling)
(2) Synovitis is not better explained by “another disease”

<table>
<thead>
<tr>
<th>JOINT DISTRIBUTION (0-5)</th>
<th></th>
</tr>
</thead>
<tbody>
<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 (large joints not counted)</td>
<td>2</td>
</tr>
<tr>
<td>4-10 small joints (large joints not counted)</td>
<td>3</td>
</tr>
<tr>
<td>&gt;10 joints (at least one small joint)</td>
<td>5</td>
</tr>
</tbody>
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<table>
<thead>
<tr>
<th>SEROLOGY (0-3)</th>
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<tr>
<td>Negative RF AND negative anti CCP</td>
<td>0</td>
</tr>
<tr>
<td>Low positive RF OR low positive anti CCP</td>
<td>2</td>
</tr>
<tr>
<td>High positive RF OR high positive anti CCP</td>
<td>3</td>
</tr>
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<table>
<thead>
<tr>
<th>SYMPTOM DURATION (0-1)</th>
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<tr>
<td>&lt;6 weeks</td>
<td>0</td>
</tr>
<tr>
<td>≥6 weeks</td>
<td>1</td>
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<tr>
<th>ACUTE PHASE REACTANTS (0-1)</th>
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<tr>
<td>Normal CRP AND normal ESR</td>
<td>0</td>
</tr>
<tr>
<td>Abnormal CRP OR abnormal ESR</td>
<td>1</td>
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≥6 = definite RA
A 49 year old female hairdresser comes to see you in your clinic. In addition to her main problem she complains of several weeks of left knee, back and bilateral heel pain with associated early morning stiffness and some intermittent swelling of the left knee.

What is the most likely diagnosis:

a) Crystal arthritis  
b) Osteoarthritis  
c) Rheumatoid arthritis  
d) Spondyloarthritis  
e) Systemic lupus erythematosus
JOINT PAIN

Chronic pain syndromes (Fibromyalgia)

Polymyalgia rheumatica
Inflammatory myositis

Joint swelling more likely

Joint swelling less likely

Monoarticular
Polyarticular

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Osteoarthritis/arthropathy
Tendinopathy
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Sepsis
Crystals
Spondyloarthritis

Rheumatoid
Viral
SLE/CTDs
Spondyloarthriti
Crystals
**JOINT PAIN**

**DIFFUSE PAIN**
- Chronic pain syndromes (Fibromyalgia)
- Polymyalgia rheumatica
- Inflammatory myositis

**LOCALIZED PAIN**
- Joint swelling less likely
- Monoarticular
- Sepsis
- Crystals
- Tendinopathy
- Bursitis
- Polyarticular
- Spondyloarthritides
- Rheumatoid arthritis
- Viral
- SLE/CTDs
- Spondyloarthritis
- Crystals
Spondyloarthritis

- Ankylosing Spondylitis (back stiffness)
- Psoriatic Arthritis (skin and nails)
- Reactive Arthritis (GI or STI)
- Enteropathic Arthritis (IBD)
Spondyloarthritis

Association with HLA-B27
Enthesitis pathologically
Large/medium joints
Oligoarticular presentations
Tendon symptoms
Spinal involvement
NSAID responsive
TNF, IL-17/IL-23
A GUIDE TO CURRENT MANAGEMENT OF SPONDYLOARTHRITIS AND RHEUMATOID ARTHRITIS
Write down on your handout:

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<th>MY NOTES</th>
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<td>Spondyloarthritis</td>
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Rheumatoid arthritis – complicated!

Rheumatoid arthritis - simplified

Adaptive immune response

Innate Immune response

Inflammation & Damage

CYTOKINES
TNF, IL-6, IL-1
IL-15, IL-12

PROSTAGLANDINS
COLLAGENASES
MMPs
Rheumatoid arthritis – simplified more!

Adaptive immune response

Innate Immune response

Inflammation & Damage

CYTOKINES
TNF, IL-6, IL-1
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PROSTAGLANDINS
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Inflammation & Damage

Front line artillery

Inflammatioon & Damage

Officer's mess

BULLETS

RADIO SIGNALS
Rheumatoid arthritis - treatment

Adaptive immune response  Innate Immune response  Inflammation & Damage

CYTOKINES
TNF, IL-6, IL-1
IL-15, IL-12

PROSTAGLANDINS
COLLAGENASES
MMPs

STOP THE BULLETS BEING PAINFUL
Paracetamol
Co-codamol
NSAIDs
Rheumatoid arthritis - treatment

Adaptive immune response

Innate Immune response

Inflammation & Damage

CYTOKINES
TNF, IL-6, IL-1
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PROSTAGLANDINS
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CONTROL THE FRONT LINE ARTILLERY
Steroids

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Paracetamol
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Rheumatoid arthritis - treatment

Innate Immune response

- CYTOKINES
  - TNF, IL-6, IL-1
  - IL-15, IL-12

Adaptive immune response

- PROSTAGLANDINS
  - COLLAGENASES
  - MMPs

Inflammation & Damage

CONTROL THE OFFICERS MESS
- cDMARDs
- Methotrexate
- Leflunomide
- Sulphasalazine
- Hydroxychloroquine

CONTROL THE FRONT LINE ARTILLERY
- Steroids

STOP THE BULLETS BEING PAINFUL
- Paracetamol
- Co-codamol
- NSAIDs
Rheumatoid arthritis - treatment

**Adaptive immune response**
- CYTOKINES
  - TNF, IL-6, IL-1
  - IL-15, IL-12

**Innate Immune response**
- PROSTAGLANDINS
  - COLLAGENASES
  - MMPs

**Inflammation & Damage**
- BLOCK THE RADIO SIGNAL
  - Biologic treatments (-MABs) - bDMARDs
  - JAK inhibitors (-TINIBs) - JAKINIBs

**STOP THE BULLETS BEING PAINFUL**
- CONTROL THE OFFICERS MESS
  - cDMARDs
  - Methotrexate
  - Leflunomide
  - Sulphasalazine
  - Hydroxychloroquine

- CONTROL THE FRONT LINE ARTILLERY
  - Steroids

- STOP THE BULLETS BEING PAINFUL
  - Paracetamol
  - Co-codamol
  - NSAIDs
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<td>infliximab and inflectra, etanercept (enbrel and benepali), adalimumab (humira and imraldi), golimumab, certolizumab</td>
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<tr>
<td>Anti-B-cell</td>
<td>rituximab</td>
</tr>
<tr>
<td>Anti-IL-6</td>
<td>tocilizumab, sarilumab</td>
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<tr>
<td>CTLA4-Ig</td>
<td>abatacept</td>
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-TINIB (Jakinib) treatments - RhA

<table>
<thead>
<tr>
<th>Medication</th>
<th>JAK Inhibitor(s)</th>
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</thead>
<tbody>
<tr>
<td>Baracitinib</td>
<td>JAK1 and JAK2 inhibitor</td>
</tr>
<tr>
<td>Tofacitinib</td>
<td>JAK1 and JAK3 inhibitor</td>
</tr>
<tr>
<td>Upadacitinib (in review)</td>
<td>JAK1 inhibitor</td>
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A 49 year old female hairdresser (who presents with 3 months of polyarthritis of the hands) is diagnosed with new onset rheumatoid arthritis.

What is the most appropriate initial treatment:

a) NSAID of your choice
b) Steroid tablets (+/- NSAID)
c) Steroid tablets and cDMARD (+/- NSAID)
d) Steroid tablets and cDMARD (+/- NSAID) and biologic DMARD
Treat to Target – Remission induction

Disease Activity Score in 28 joints (DAS28)

DAS28 = >5.1  Severe disease
DAS28 = 3.2 – 5.1  Moderately active disease
DAS28 = 2.6 – 3.2  Mildly active disease
DAS28 = <2.6  Disease remission

Rheumatoid arthritis - treatment risks

**Adaptive immune response**
- CYTOKINES
  - TNF, IL-6, IL-1
  - IL-15, IL-12
- PROSTAGLANDINS
  - COLLAGENASES
  - MMPs

**Innate Immune response**

**BLOCK THE RADIO SIGNAL**
- Biologic treatments (-MABs) - bDMARDs
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**STOP THE BULLETS BEING PAINFUL**
- Paracetamol
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**CONTROL THE OFFICERS MESS**
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**CONTROL THE FRONT LINE ARTILLERY**
- Steroids

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- NSAIDs
Rheumatoid arthritis - treatment risks

CYTOKINES
TNF, IL-6, IL-1
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PROSTAGLANDINS
COLLAGENASES
MMPs

Adaptive immune response

Innate Immune response

Inflammation
& Damage

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**CONTROL THE FRONT LINE ARTILLERY**
Steroids

**STOP THE BULLETS BEING PAINFUL**
Paracetamol
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NSAIDs

**CYTOKINES**
TNF, IL-6, IL-1
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**PROSTAGLANDINS**
COLLAGENASES
MMPs

**STOP THE BULLETS BEING PAINFUL**
Rheumatoid arthritis - treatment risks

- **Adaptive immune response**
- **Innate Immune response**
- **Inflammation & Damage**

**CYTOKINES**
- TNF, IL-6, IL-1
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**PROSTAGLANDINS**
- Collagenases
- MMPs

**BLOCK THE RADIO SIGNAL**
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**CONTROL THE FRONT LINE ARTILLERY**
- Steroids

**STOP THE BULLETS BEING PAINFUL**
- Paracetamol
- Co-codamol
- NSAIDs

1.5x
Anti-TNF versus non-biologic DMARDs

Increased risk of infection:

**Serious infections**
Hazard Ratio 1.2 (95% CI 1.1 – 1.5)  
*Rheumatology 2011; 50:124-131*

**Septic arthritis**
Hazard Ratio 2.3 (95% CI 1.2 to 4.4)  
*Ann Rheum Dis 2011;70:1810-1814*

**Skin Infections and Herpes Zoster**
Hazard Ratio Skin - 1.4 (95% CI 0.9-1.8)  
Hazard Ratio Herpes Zoster -1.8 (95% CI 1.2-2.8)  
*Ann Rheum Dis 2013;72:229-23*

No increased risk of venous thromboembolism  
*Ann Rheum Dis 2011; 70: 1831-4*

No increased risk of malignancy  
*Arth Care Res 2010;62: 755-63*

No increased mortality  
*A&R 2010; 62: 3145-3153*
Rheumatoid arthritis

Early morning stiffness of hands
New classification criteria  
(diagnose earlier)
Treat to target
Treat aggressively and early to prevent damage
Use combination treatments from start
All the main treatments increase infection risk
If in doubt stop the treatments during admission
Spondyloarthritis

- Ankylosing Spondylitis (back stiffness)
- Psoriatic Arthritis (skin and nails)
- Reactive Arthritis (GI or STI)
- Enteropathic Arthritis (IBD)
Spondyloarthritis/PsA – simplified

Adaptive immune response | Innate immune response | Inflammation & Damage

CYTOKINES
TNF, IL-17, IL-23
IL-12

PROSTAGLANDINS
COLLAGENASES
MMPs

RADIO SIGNALS
BULLETS

Officers mess | Front line artillery | Inflammation & Damage
Spondyloarthritis/PsA – simplified more!

Adaptive immune response

Innate Immune response

Inflammation (BUT NOT) Damage (usually)

CYTOKINES
TNF, IL-17, IL-23
IL-12

PROSTAGLANDINS
COLLAGENASES
MMPs

RADIO SIGNALS

BULLETS

Officers mess

Front line artillery

Inflammation & Damage
Spondyloarthritis/PsA - treatment

Adaptive immune response

Innate Immune response

Inflammation

(BUT NOT)
Damage 
(usually)

STOP THE BULLETS
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NSAIDs

PROSTAGLANDINS
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Spondyloarthritis/PsA - treatment

Adaptive immune response

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Inflammation
(BUT NOT)
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(usually)

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CONTROL THE FRONT LINE ARTILLERY
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Spondyloarthritis/PsA - treatment

Adaptive immune response

Innate Immune response

Inflammation

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CONTROL THE FRONT LINE ARTILLERY
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Co-codamol
NSAIDs

CONTROL THE OFFICERS MESS
cDMARDs
Leflunomide
Sulphasalazine
Apremilast
Spondyloarthritis/PsA - treatment

Adaptive immune response → Innate Immune response → Inflammation

**BLOCK THE RADIO SIGNAL**
- Biologic treatments (-MABs) - bDMARDs
- JAK inhibitors (-TINIBs) - JAKINIBs

**CONTROL THE OFFICERS MESS**
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**CONTROL THE FRONT LINE ARTILLERY**
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- NSAIDs

**CYTOKINES**
- TNF, IL-17, IL-23
- IL-12

**PROSTAGLANDINS**
- COLLAGENASES
### Biologic DMARD treatment - PsA

<table>
<thead>
<tr>
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<tr>
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Spondyloarthritis/PsA - treatment risks

Adaptive immune response

Innate Immune response

Inflammation & Damage

**BLOCK THE RADIO SIGNAL**

Biologic treatments (-MABs) - bDMARDs

JAK inhibitors (-TINIBs) - JAKINIBs

**CONTROL THE OFFICERS MESS**

cDMARDs

Leflunomide

Sulphasalazine

Apremilast

**CONTROL THE FRONT LINE ARTILLERY**

Steroids

**STOP THE BULLETS BEING PAINFUL**

Paracetamol

Co-codamol

NSAIDs

**CYTOKINES**

TNF, IL-17, IL-23

IL-12

**PROSTAGLANDINS**

COLLAGENASES

**STOP THE BULLETS BEING PAINFUL**

Paracetamol

Co-codamol

NSAIDs
A 49 year old female hairdresser (who presents with 3 months of recurrent monoarthritis of the left knee and some enthesitis of the plantar fascia) is diagnosed with new onset Psoriatic arthritis.

What is the most appropriate initial treatment:

a) NSAID of your choice
b) Steroid tablets (+/- NSAID)
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d) Steroid tablets and cDMARD (+/- NSAID) and biologic DMARD
Key take home points

Spondyloarthritis/Psoriatic arthritis
Asymettrical presentation
Enthesitis/tendonitis
Different cytokine profile to RhA (IL-17/IL-23 axis)
Treat with escalating treatment
PsA is less likely to cause damage
Still treat to target
Similar algorithm to RhA
All the main treatments increase infection risk
If in doubt stop the treatments during admission
Write down on your handout:

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