# Musculoskeletal Diseases

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## Musculoskeletal diseases

- Osteoarthritis (OA)
- Rheumatoid arthritis (RA)
- Gout

## Useful websites: Health professionals

- American College of Rheumatology  
  [www.rheumatology.org](http://www.rheumatology.org)
- Australian Rheumatology Association  
  [www.rheumatology.org.au](http://www.rheumatology.org.au)
- Osteoarthritis Research Society International  
  [www.oarsi.org](http://www.oarsi.org)

## Useful websites: Patients

- Arthritis Foundation – USA  
  [www.arthritis.org](http://www.arthritis.org)
- Arthritis Australia  

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**OSTEOARTHRITIS**
Useful references


Epidemiology

- Most prevalent rheumatic disease
- Enormous disability and loss of productivity
  - Second only to cardiovascular disease
- Prevalence and severity increases with age
- Degree of OA almost universal > 75 years
- True incidence unknown
- Women more often affected
  - Especially nodal OA

Risk factors

- Obesity
  - ↑ed body weight strongly associated with hip, knee and hand OA
  - ↑ risk of eventual prosthetic joint replacement
- Occupation, sports and trauma
  - Repetitive use or injury
- Genetic factors
  - Heredity plays a role
- Osteoporosis inversely correlated with OA

Pathophysiology

- Primarily disease of joint cartilage
- Cartilage: low-friction surface covering bone ends
  - Lubrication during movement
  - Shock absorbency
  - Load support and joint stability

Normal joint

Pathophysiology

- Cartilage composition
  - Water
  - Chondrocytes: control synthesis and degradation of cartilage
  - Collagen: tensile strength, maintenance of shape
  - Proteoglycans: provide the "stuffing material"
- OA is the progressive loss of joint cartilage
  - Failure of chondrocytes to maintain balance between cartilage formation and destruction
  - Loss of cartilage exposes underlying bone leading to microfractures and osteophytes
## Clinical Features
- Phenomenon of normal aging
- Primarily affects weight-bearing joints
  - Hips
  - Knees
  - Hands
- Not inflammatory by nature

## Symptoms
- Pain
  - Deep, aching pain
  - Worse on motion and weight bearing
  - Improves with rest
- Stiffness
  - Resolves with motion, recurs with rest
  - Usually < 30 minutes duration
  - Instability of weight bearing joints
  - Limited motion

## Clinical Signs
1. Hands: Heberden’s and Bouchard’s nodes
2. Knees: One of most commonly affected joints
3. Hips: Usually in older individuals
4. Spine: Commonly lumbar spine
5. Feet
6. Other: bony proliferation, crepitus, muscle atrophy, joint effusions
7. One or multiple joints, asymmetrical

## Hand OA

### Heberden’s nodes

### Bouchard’s nodes
Laboratory findings

- No specific test
- ESR normal or slightly elevated
- Rheumatoid factor negative
- Haematological and biochemical surveys usually normal
- No systemic manifestations

Radiological findings

- Early in disease
  - X-ray changes often absent
- Progression of OA
  - Narrowing or complete loss of joint space
  - Sclerosis and cysts in adjacent bones
  - Osteophytes: bony overgrowth
- Late OA
  - Effusions, abnormal alignment

Knee osteoarthritis

American College of Rheumatology Guidelines

“The goals of osteoarthritis (OA) management are to control pain and other symptoms, minimise disability, and educate the patient about the disease and its therapy”

Management

Goals of management of the patient with OA include:

- Education of patient, carers and relatives
- Relieve symptoms such as pain, stiffness and immobility
- Preserve joint motion and function by limiting disease progression
- Minimise disability

How we achieve the goals...

Treatment approach individualised to include:

1. Patient education
2. Physiotherapy
3. Occupational therapy
4. Dietary considerations
5. Pharmacological therapy
6. Surgery
### 1. Patient education
- Education for patient’s family, friends, other carers
- Arthritis Foundation Self-Management Programs
  - Decreased joint pain
  - Frequency of arthritis-related visits to the doctor
  - Increases in physical activity and overall improvement in quality of life

### 2. Physiotherapy
- Heat or cold treatments
  - Heat useful prior to exercise
- Exercise programs
  - Maintain range of motion
  - Relieve pain
  - Reduce muscle spasms
  - Include aerobic, range of motion exercise, muscle strengthening exercise, hydrotherapy

### 3. Occupational Therapy
- Assistive devices for ambulation (canes, walkers)
- Patellar taping (for knee OA), appropriate footwear and bracing
- Assistive devices for activities of daily living

### 4. Dietary considerations
- For the overweight patient, dietary counseling is important
  - Especially patients with hip or knee OA
- Excess weight:
  - Increases biomechanical load on weight-bearing joints
  - Contributes to progression of disease
  - Causes contraction of muscles stabilising the joint
  - Obese patients have poorer outcome following joint replacement surgery

### 5. Pharmacological therapy
- Considered an addition to non-pharmacological measures
  - Paracetamol (increase to 4g/day)
  - Topical NSAIDs, capsaicin, rubefacients
  - NSAIDs and COX-2 selective agents
  - Glucosamine and chondroitin
  - Intra-articular corticosteroids and hyaluronan
  - Opioid analgesia

**PARACETAMOL**
## Paracetamol

- Analgesic agent
- First line drug according to 2000 ACR Guidelines
- Better tolerated than the NSAIDs and may be as effective
  - Especially in mild-to-moderate disease
- Recent study has challenged the role and efficacy of paracetamol in knee OA


### Is paracetamol effective?

Systematic review: Towheed TE et al. Acetaminophen (paracetamol) for osteoarthritis. Cochrane Review 2005

- Seven placebo controlled RCTs; five showed superior efficacy and similar safety profile
- Pooled analysis: statistically significant improvement in pain over placebo
- Overall: short-term analgesic potential of paracetamol is accepted
- **Key is adequate dosing: 4g/day**

## Paracetamol safety profile

- **Hepatotoxicity**
  - Very rare at therapeutic doses
  - Associated with malnourished states and pre-existing hepatic impairment (especially EtOH)
- Potential interaction with warfarin

## TOPOCAL NSAIDS, CAPSAICIN AND RUBEFACIENTS

### Topical NSAIDs

- NSAIDs:
  - Diclofenac – Voltaren
  - Ibuprofen – Nurofen
  - Ketoprofen – Orudis
  - Piroxicam – Feldene

### Topical capsaicin and rubefacients

- Capsaicin: topical analgesic
  - Regular use, up to two weeks for effect
- Rubefacients: counter-irritants
  - Deep-Heat
  - Metsal
  - Goanna Arthritis Cream
Topical NSAIDs, capsaicin or rubefacients

- May be used but relatively expensive
- Has been scepticism regarding efficacy
  - ? rubefacient only
- Systematic review (BMJ 1998;316:333-8)
  - Topical NSAIDs provide effective pain relief that seems comparable with systemic NSAIDs - SHORT TERM DATA ONLY
- May avoid the need for an oral NSAID in high risk patients - safer than systemic agents

Topical NSAIDs, capsaicin or rubefacients

- Achieve low systemic levels
- Very safe – no association with GI bleeding
- May be sufficient in milder disease
- OA – may be less useful if multiple, large joint involvement
- Add on if regular paracetamol inadequate
- European guidelines: Topical NSAIDs on par with oral agents
- America: Not reimbursable; largely disregarded in guidelines

NSAIDs and selective COX-2 inhibitors

<table>
<thead>
<tr>
<th>NSAID</th>
<th>COX-2 Selective INHIBITOR</th>
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<tbody>
<tr>
<td>Aspirin</td>
<td>Celecoxib</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Meloxicam</td>
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<tr>
<td>Ibuprofen</td>
<td>Parecoxib</td>
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<td>Indomethacin</td>
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<tr>
<td>Ketoprofen</td>
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<tr>
<td>Naproxen</td>
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<td>Piroxicam</td>
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Mechanism of Action

Cyclooxygenase inhibition

Constituent pathway
- Impaired gastric cytoprotection
- Antiplatelet effects

Inducible pathway
- Anti-inflammatory
- Analgesia

Efficacy

- Long held belief that OA is not inflammatory
- Despite this, NSAIDs recommended
- But more recent evidence suggests inflammatory component (presence of synovitis)
- Contribute to pain and disease progression
Efficacy

- The various NSAIDs display comparable analgesic and anti-inflammatory efficacy
- Systematic review: studies of NSAIDs in OA found no evidence to support a ranking of NSAID efficacy

Efficacy

- ACR 2000: NSAIDs add-on for patients who fail to obtain adequate relief with paracetamol
- However, recent literature suggest NSAIDs may be better for symptom relief in large joint OA
  - RCT plus two ‘surveys of preference’
  - Future research may lead to change in order of preference

Adverse effects

- Gastrointestinal (dose related)
- Antiplatelet effect (conventional NSAIDs)
- Renal impairment (NSAID and COX-2 inhibitor)
- Salt and water retention
- Bronchospasm

Risk factors for patients taking NSAIDs

<table>
<thead>
<tr>
<th>Risk of upper GI complications</th>
<th>Risk of renal complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age = 65+ years</td>
<td>Elevated serum creatinine</td>
</tr>
<tr>
<td>Comorbid medical problems</td>
<td>Age = 65+ years</td>
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<tr>
<td>Use of oral glucocorticoids</td>
<td>Hypertension</td>
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<tr>
<td>Use of anticoagulants</td>
<td>Congestive heart failure</td>
</tr>
<tr>
<td>Previous history of PUD</td>
<td>Use of ACE inhibitors</td>
</tr>
<tr>
<td>Previous history of upper GI bleeding</td>
<td>Use of diuretics</td>
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</tbody>
</table>

Avoiding GI complications...

- Heirarchy of GI risk with all NSAIDs
  - High risk: ketoprofen, piroxicam
  - Lowest risk: selective COX-2s, ibuprofen, diclofenac
- Patient with no GI risk factors: use conventional NSAID
- Patient with GI risk factors: use low risk (including selective COX-2s)

Avoiding GI complications...

- BUT the absolute reduction in serious GI complications with selective COX-2s is modest
- Safer to use NSAID + gastroprotective agent
  - Misoprostol or PPI
Renal complications

- All NSAIDs (selective or non-selective) are associated with renal impairment
- Selective COX-2s hold no advantage
- Beware the “triple whammy”
  - NSAID + ACEI + diuretic

Cardiovascular effects

- All NSAIDs (selective or non-selective) are associated with hypertension and fluid retention
- Conventional NSAIDs inhibit COX-1 therefore antiplatelet
- Selective COX-2 inhibitors: not antiplatelet so low dose aspirin or other anti-platelet must be continued for patients with cardiovascular risk factors
- AND evidence accumulating that inhibition of COX-2 may be prothrombotic

Glucosamine and chondroitin

- Naturally occurring components of joint cartilage
- Paracetamol, NSAIDs and corticosteroids not disease modifying
- Glucosamine and chondroitin: proposed to stop and possibly reverse degenerative process in OA
  - Glucosamine: may stimulate proteoglycan synthesis or inhibit degradation of existing cartilage
  - Chondroitin: may stimulate cartilage synthesis or inhibit enzymes that degrade cartilage

What is the role of glucosamine in OA?

- McColl G. Glucosamine for OA of the knee Aust Prescr 2004;27:6103 (excellent review)
- Symptom modifiers vs structure modifiers
- 2005 Cochrane Review
  - 20 studies
  - Collective improvements in pain and function
  - Three to six weeks to provide benefit
  - Well tolerated
  - May result in long-term slowing of disease progression (radiologic evidence)
  - Possible increase in insulin resistance
- Product quality can vary

INTRA-ARTICULAR CORTICOSTEROIDS AND HYALURONAN
**Intraarticular corticosteroids**

- Joint aspiration followed by depot injection of corticosteroid into inflamed joints
  - Effective if 1 or 2 joints affected
  - Up to 6 wks decreased pain, increased function
- Generally not monotherapy
- Low risks if appropriate sterile technique applied
- Effective short-term treatment

**Hyaluronans**

- High molecular weight glycosaminoglycans normally found in cartilage and synovial fluid
  - Joint aspiration followed by intraarticular injection
  - Increase viscosity within joint fluid by replacing natural hyaluronans – shock absorber
  - Pain relief in knee OA may last months
- Hylans in Australia: marketed for knee OA (Synvisc® and Fermathron®)

**OPIOID ANALGESIA**

**Opioid analgesics...**

...when all else fails

**6. Joint replacement surgery**

- Joint replacement common in end stage disease
- Improved surgical options are the major advance in management of severe OA
### Treatment summary

- Non-pharmacologic therapy is the foundation of the care plan
  - Encourage ongoing regular exercise and other non-drug measures
- Based on safety, efficacy and cost, regular paracetamol (4g/day) should be tried initially for pain relief
  - Continue non-drug measures
- Based on effect on disease progression, glucosamine may be commenced at any time
- Topical NSAID, capsaicin or rubefacient for small joint and limited involvement (at any time)

### Treatment summary continued…

- If further analgesia is required:
  - Add low dose short acting NSAID on prn basis
  - Consider intra-articular injection of corticosteroid particularly if one or two joints affected
- If further analgesia is needed, use a higher dose of NSAID on a regular basis
- If this is inadequate, consider joint replacement or an oral opioid analgesic