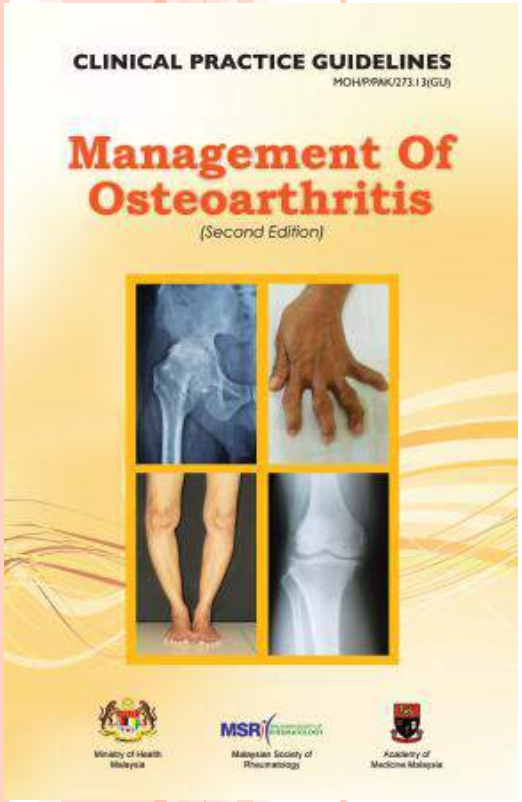


Training of Core Trainers - Epidemiology, Risk Factors & Classification

by

Dr. Siti Aminah Akbar Merican

Family Medicine Specialist

Klinik Kesihatan Seberang Takir

Introduction

- Osteoarthritis (OA) is a progressive joint disease due to failure in repair of joint damage. This may arise as a result of biomechanical, biochemical &/or genetic factors.

- The process may involve one or multiple joints.

- In the Global Burden of Disease 2010 Study, it was estimated that 251 million people suffered from knee OA worldwide.

Epidemiology of OA

- Most commonly used case definition is radiographic OA, symptomatic OA & self-reported OA.

- Symptomatic OA is defined as the presence of the radiographic features of OA in combination with symptoms attributable to it.

- Not all individuals with radiographic OA have concomitant symptoms; thus radiographic OA has the highest prevalence.[Pereira D et a., 2011, level III]

Epidemiology of Hand OA

- Framingham Osteoarthritis Hand OA study:[Haugen IK et al., 2011, level II-2]
  - Mean baseline age was 58.9 years
  - Prevalence was higher in women than men (44.2% vs 37.7%), erosive (9.9% vs 3.3%) & symptomatic (15.9% vs 8.2%)
  - Majority showed progression at 9-year follow up

Epidemiology of Hip OA

- Prevalence of symptomatic hip OA (USA) was 9.2% among adults age >45 with a slight female preponderance. Lawrence RC et al., 2008, level III

- Crude prevalence of radiographic hip OA in Chinese aged 60 - 89 years was 0.9% in women & 1.1% in men. Hip OA was 80 - 90% less frequent than in white persons in the USA. Nevitt MC at al., 2002, level III

Epidemiology of Knee OA-1

- Johnston County OA Project of USA, lifetime risk of developing symptomatic knee OA in at least one knee: Murphy L et al., 2008, level II-2
  - 44.7% (95% CI 40.0% to 49.3%) by age 85 years
  - Higher in those with history of knee injury & increased BMI

Epidemiology of Knee OA-2

- Symptomatic knee OA was:
  - 4.9% among adults age >26 years in the Framingham study[Lawrence RC et al., 2008, level III]
  - 16.7% among adults age >45 in the Johnston County study[Murphy L et al., 2008, level II-2]
  - 12.1% among adults aged >60 in the NHANES III study[Lawrence RC et al., 2008, level III]

Epidemiology of Knee OA-3

- In the Beijing Osteoarthritis Study (>60 years):[Zhang Y et al, 2001, level III]
  - Prevalence of radiographic knee OA was 42.8% in women &d 21.5% in men
  - Symptomatic knee OA occurred in 15.0% of women & 5.6% of men
  - Women in Beijing had a higher prevalence of radiographic knee OA (prevalence ratio=1.45, 95% CI 1.31 to 1.60) & of symptomatic knee OA (prevalence ratio=1.43, 95% CI 1.16 to 1.75) (compared with women of the same age in Framingham)
  - Prevalence of knee OA in Chinese men, similar to white USA counterparts (prevalence ratio of 0.90 for radiographic OA & 1.02 for symptomatic OA)

Epidemiology of Knee OA-4

- In the Community Orientated Program for the control of Rheumatic Disease (COPCORD): Veerapen K et al., 2007, level III
  - 9.3% of adult Malaysians had knee pain & more than half of those examined had clinical evidence of OA
  - Prevalence ranged from 1.1% to 5.6% in the various ethnic groups (study only included those with pain in the past week)
  - Hip pain was less common, with only 2.2% of the study population affected

Non-modifiable Risk Factors

- Advancing age[Blagojevic M et al., 2010, level II-2]
- Female [OR=1.8, 95% CI 1.3 to 2.5 (case-control studies), OR=1.9, 95% CI 1.6 to 2.3 (cohort studies)[Blagojevic M et al., 2010, level II-2]
- Genetic influence on hand & knee OA in women ranges from 39% to 65% ($p<0.001$)[Spector TD et al., 1996, level II-2]
- Presence of Heberden's nodes in hand OA increased the risk for future knee OA (OR=1.4, 95% CI 1.1 to 1.8)[Blagojevic M et al., 2010, level II-2]

Modifiable Risk Factors

- Body mass index (BMI)[Blagojevic M et al., 2010, level II-2]
  - Overweight (BMI 25 to 30 kg/m^2)
    - OR=2.6, 95% CI 2.2 to 3.0 (case-control studies)
    - OR=2.0, 95% CI 1.8 to 2.1 (cohort studies)
  - Obese (BMI >30 kg/m^2)
    - OR=5.5, 95% CI 4.3 to 7.1 (case- control studies)
    - OR=2.4, 95% CI 2.1 to 2.6 (cohort studies)
- Previous knee injury [OR=4.7, 95% CI 3.5 to 6.4 (case-control studies), OR=2.8, 95% CI 1.8 to 4.2 (cohort studies)][Blagojevic M et al., 2010, level II-2]
- Malalignment contributes to the progression of knee OA, mixed results on incidence of progression[Tanamas S et al., 2009, level II-2]

CLASSIFICATION OF OA-1

- By the joint involved, i.e. hand, hip & knee or by aetiology as shown below:-

  - **Primary or Idiopathic**
    - Primary OA includes generalised OA, condition associated with Heberden's nodes & polyarticular disease.
    - Occurs especially in the hand, with a female preponderance & has a high prevalence in first degree relatives.MoH Malaysia, 2002

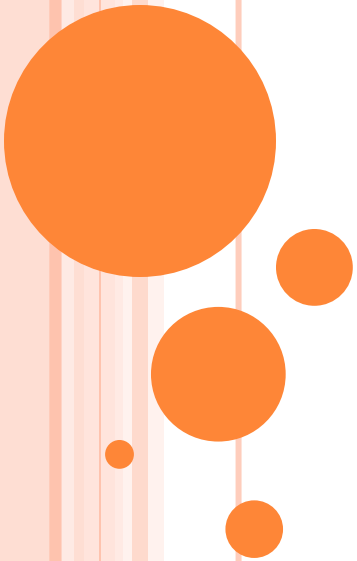
CLASSIFICATION OF OA-2

- **Secondary**
  i. Metabolic such as acromegaly, haemachromatosis & chondrocalcinosis

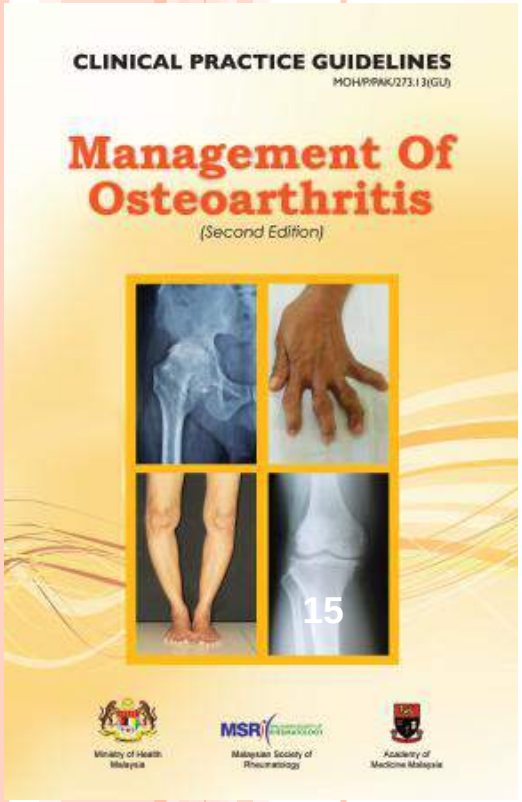
  ii. Anatomic such as slipped femoral epiphysis, Legg-Perthes disease, congenital dislocation of the hip, leg length inequality, hypermobility syndromes & avascular necrosis

  iii. Trauma such as joint injury & fracture through a joint or osteonecrosis

  iv. Inflammatory such as rheumatoid arthritis, psoriatic arthropathy & septic arthrithis



Thank You



TRAINING OF CORE TRAINERS - DIAGNOSIS & INVESTIGATIONS

by

Dato' Dr. Gun Suk Chyn

Consultant Rheumatologist

Hospital Tuanku Jaafar

Diagnosis of OA

- Diagnosed by an overall clinical impression

Symptoms of OA

i. **Joint pain**

- presenting complaint
- insidious in onset, of variable intensity through the day, may be intermittent & relapsing
- increased by joint use & impact & relieved by rest
- night pain in severe OA

Symptoms of OA-2

ii. Stiffness

- occurs after inactivity e.g. EMS or when arising after sitting for a prolonged period
- usually lasts only a few minutes & almost always less than 30 min

Symptoms of OA-3

iii. **Swelling**

- with or without associated warmth & loss of function
- **bony swelling:** in hand OA, hypertrophic bone formation in the IP joint may result in reduced dexterity & difficulty in performing fine movements such as sewing
- OA of the first CMC joint may result in writing difficulties

Symptoms of OA-4

iv. Gait disturbance

- on weight-bearing joints (hip/knee)
- can produce a prominent limp
- impaired function of a weight-bearing joint will cause added stress on the contralateral weight-bearing joint e.g. a patient with impaired right knee function & pain will have difficulty with the left hip & vice versa

Symptoms of OA-5

v. **Loss of muscle bulk**

- inactivity secondary to pain, may lead to significant weakness & loss of quadriceps muscle bulk

vi. **Limb deformity**

- knock knees' (valgus) orn'bowing' (varus)

Symptoms of OA-6

vii. Clicking or grinding sensation

- clicking or grinding sensation with joint motion resulting in discomfort or pain

viii. Instability

- instability in the knee or hip may cause the patient to seek assistance in ambulation e.g. using a cane or crutch

SIGNS OF OA-1

i. Gait - OA of weight-bearing joints, e.g. hip, knee, ankle &/or foot leads to altered gait patterns

ii. Tenderness - tenderness of soft tissues e.g. synovium, capsule, bursae & periarticular muscles, or periosteum at the insertion of capsule or ligaments may be present

iii. Joint swelling - enlargement of the joint due to synovitis, synovial effusion or bone enlargement

SIGNS OF OA-2

iv. Crepitus - grinding, crunching or cracking

v. Limitation of motion - loss of function with reduced motion due to synovitis/effusion or periarticular soft tissue contractures

vi. Deformity - most notable in the IP joints of the hands with enlargement & subluxation

- the first CMC joint
- the knees (varus/valgus) or the hips (shortened extremity)

Deformity may be associated with joint fusion or instability.

Diagnostic Criteria

- The diagnostic criteria for classification of OA are based on the American College of Rheumatology (ACR) criteria

HAND OA

Diagnosis / Criteria	Clinical only 1, 2, 3 + 4a or 4b
1	Hand pain, aching or stiffness
2	Hard tissue enlargement of ≥2 of 10 selected joints (2^{nd} and 3^{rd} DIP, 2^{nd} and 3^{rd} PIP, 1^{st} CMC joints of both hands)
3	Fewer than 3 swollen MCP joints
4a **4b**	Hard tissue enlargement of ≥2 of DIP joints **OR** Deformity of ≥2 of 10 selected joints
Sensitivity **Specificity**	92% 98%

The Diagnostic Criteria for Classification of Idiopathic OA of the Hand Based on the American College of Rheumatology 1990 Criteria

Hip OA

Diagnosis / Criteria	Clinical, Laboratory and Radiographic
	Must have hip pain + at least 2 from 3 of the following
1	ESR <20 mm/hr
2	Femoral and acetabular osteophytes on X-ray
3	Axial joint space narrowing on X-ray
Sensitivity **Specificity**	89% 91%

The Diagnostic Criteria for Classification of Idiopathic OA of the Hip Based on the American College of Rheumatology 1991 Criteria

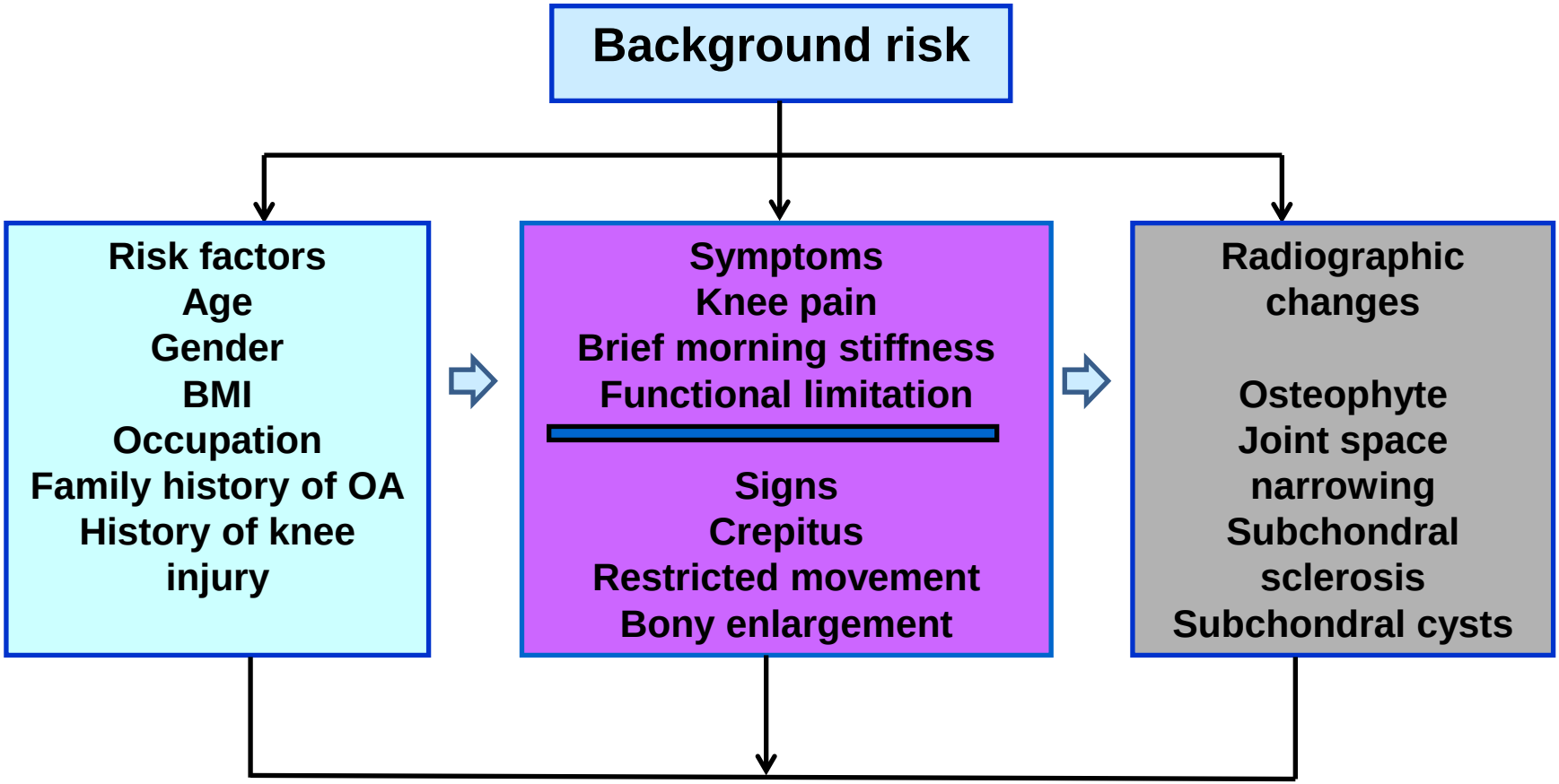
KNEE OA

Diagnosis / Criteria	Clinical and laboratory	Clinical and radiographic	Clinical only	
Must have	Knee pain + At least 5 of 9 of the following	Knee pain + Osteophytes on x-ray + At least 1 of 3 of the following	Knee pain + At least 3 of 6 of the following	
1	Age >50 years	Age >50 years	Age >50 years	
2	Stiffness <30 min	Stiffness <30 min	Stiffness <30 min	
3	Crepitus	Crepitus	Crepitus	
4	Bony tenderness		Bony tenderness	
5	Bony enlargement		Bony enlargement	
6	No palpable warmth		No palpable warmth	
7	ESR <40			
8	RF <1: 40			
9	SF OA			
Sensitivity **Specificity**	92% 75%	91% 86%	95% 69% (if 3/6)	84% 89% (if 4/6)

The Diagnostic Criteria for Classification of Idiopathic OA of the Knee Based on the American College of Rheumatology 1986 Criteria

- Knee OA
  can also be diagnosed using evidence-based recommendations
  by European League Against Rheumatism (EULAR) 2010

Diagnosis of Knee OA



Knee OA can also be diagnosed using evidence-based recommendations by European League Against Rheumatism (EULAR)

INVESTIGATIONS

- Diagnosis of OA is mainly **clinical**
- Blood investigations - ESR/CRP normal
- Synovial fluid analysis - normal & seldom required except to exclude septic, inflammatory & crystal arthropathy

IMAGING

- Plain radiography of the affected joint may be useful to support the diagnosis & assess severity of OA

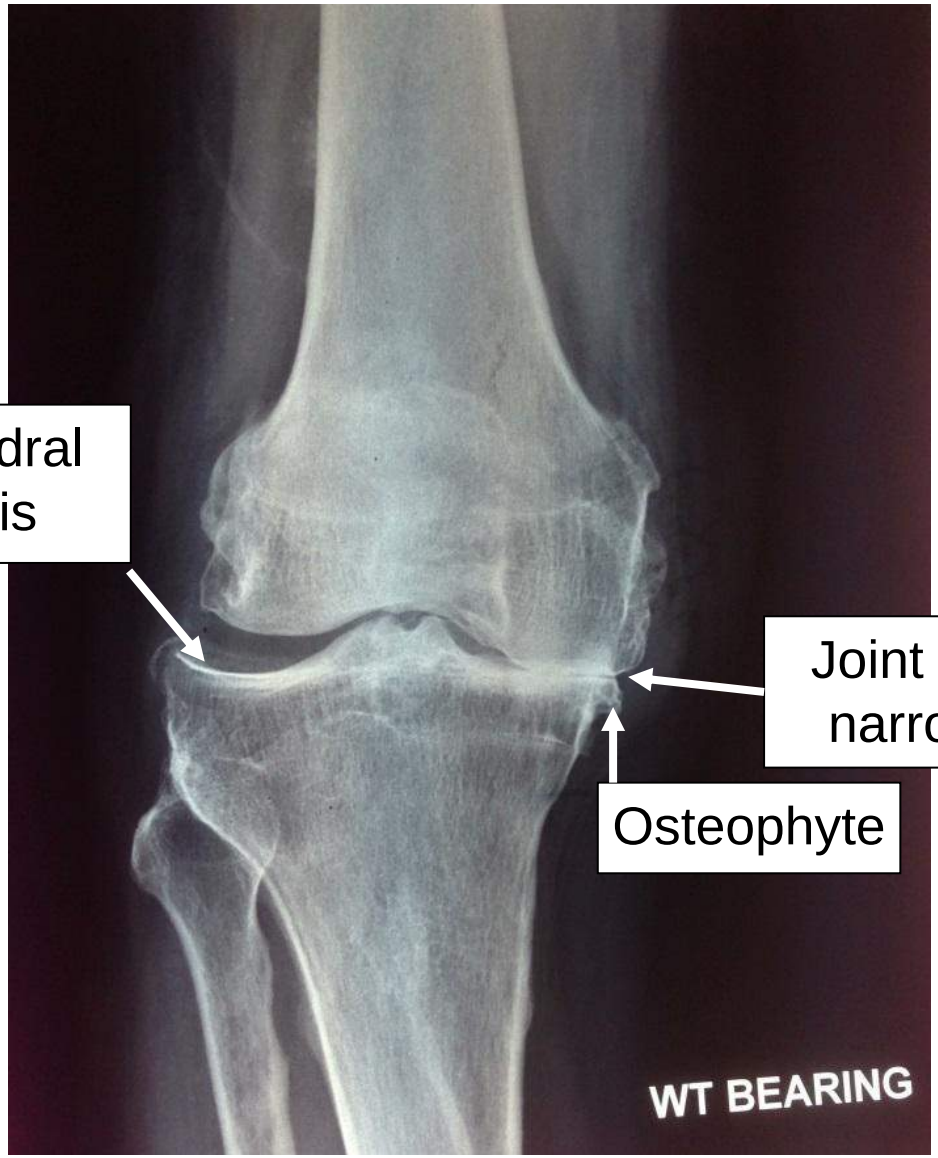
- When radiography is required in hip & knee OA, it should be done in weight bearing position (AP, standing)

Plain Radiograph

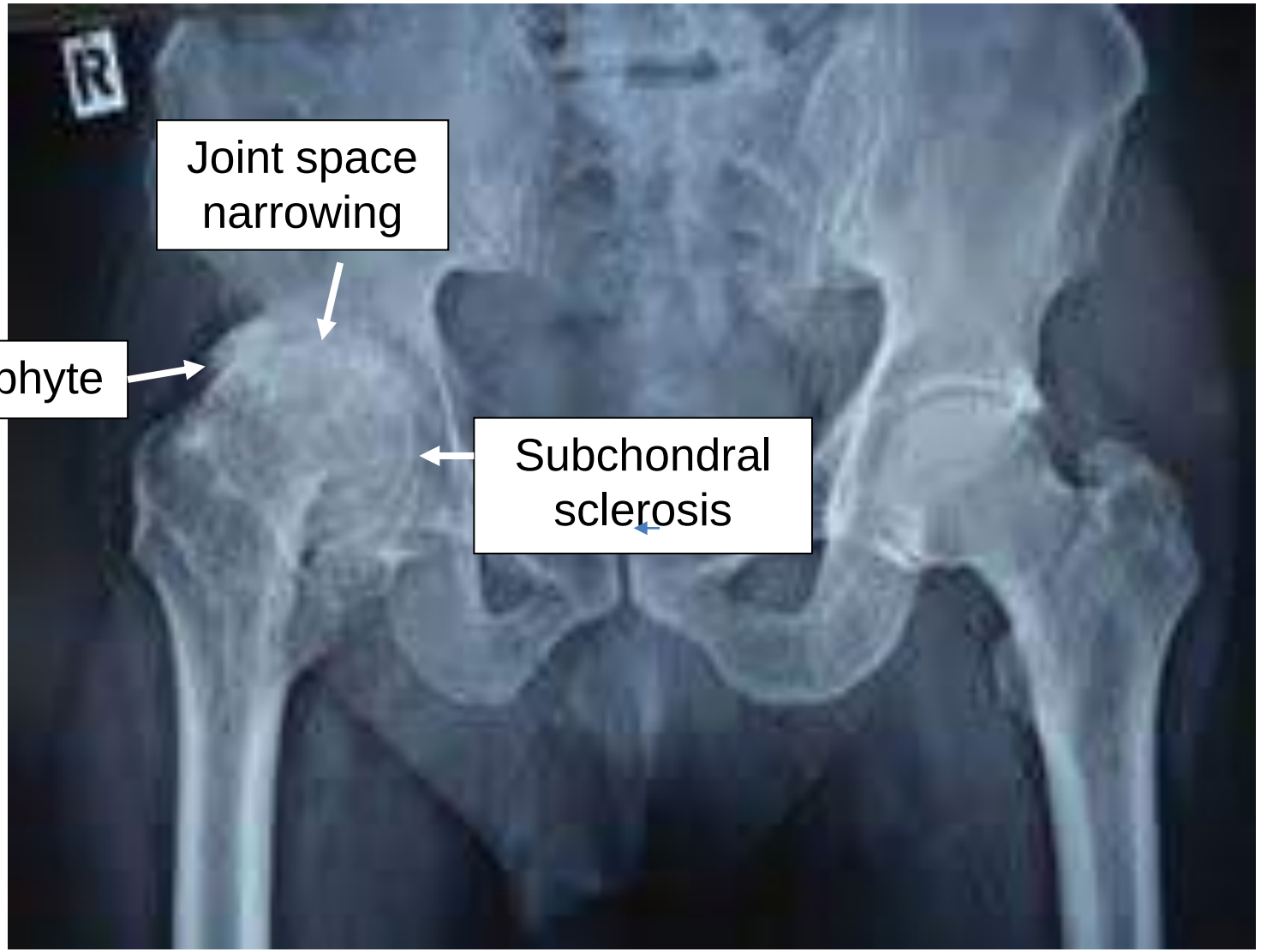
Classical features of OA

- narrowed joint space
- subchondral bone sclerosis
- osteophytes
- subchondral cysts

Knee OA – Anteroposterior Standing View



Hip OA – Anteroposterior Standing View

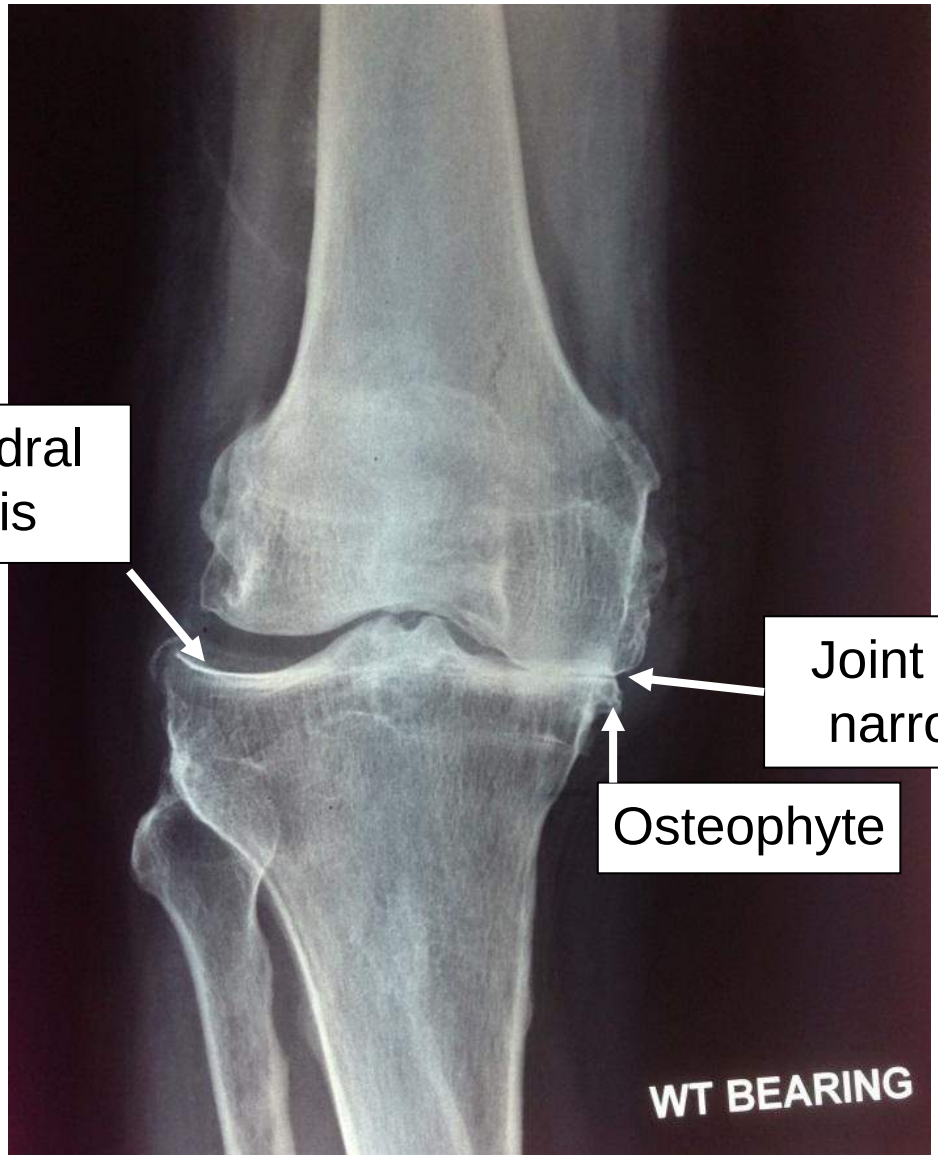


KELLGREN-LAWRENCE GRADING SYSTEM

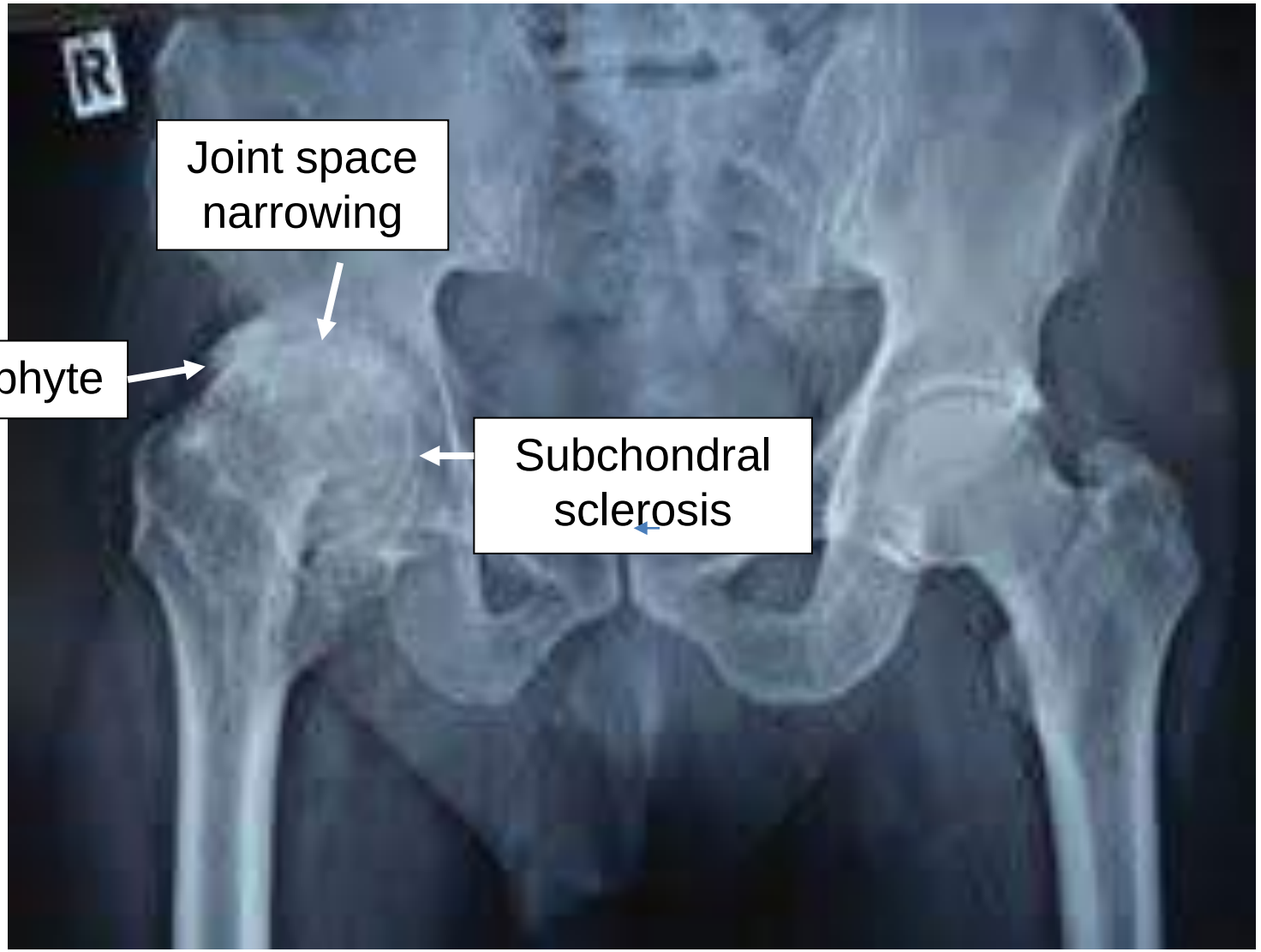
Grade	Description
Grade I	Doubtful narrowing of the joint space, possible osteophytic lipping
Grade II	Definite osteophytes, possible narrowing of the joint space
Grade III	Moderate multiple osteophytes, definite joint space narrowing, some sclerosis, possible deformity of bone ends
Grade IV	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony end deformity.

Adapted: KELLGREN JH, LAWRENCE JS.Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957 Dec; 16(4):494-502.

Knee OA – Anteroposterior Standing View



Hip OA – Anteroposterior Standing View



HAND OA

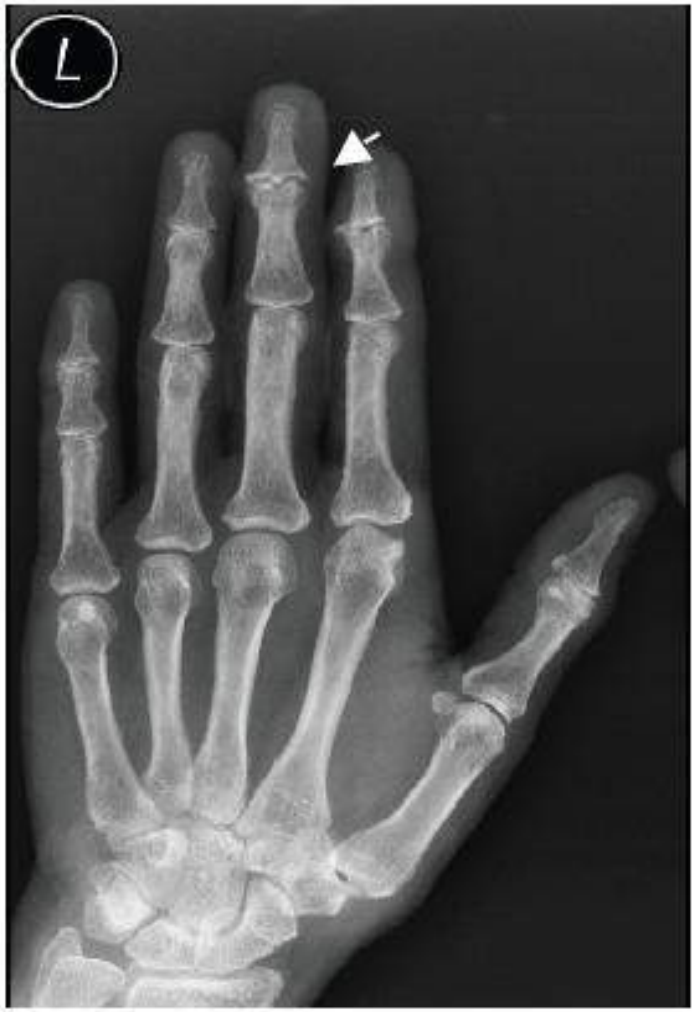


Figure 4. Gull-wing Appearance

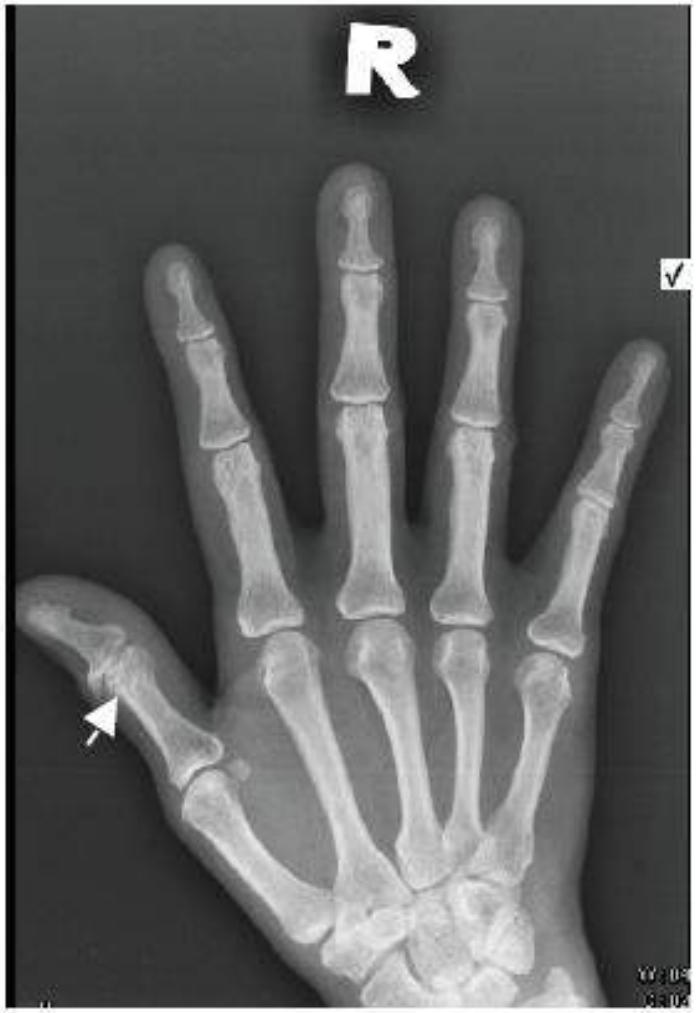
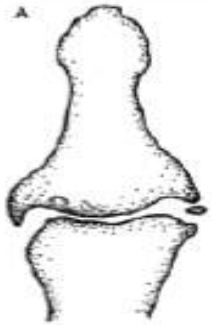
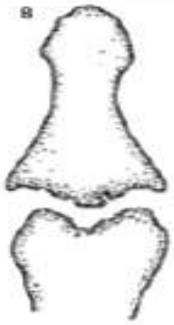
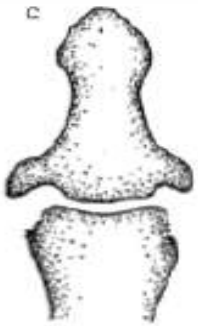
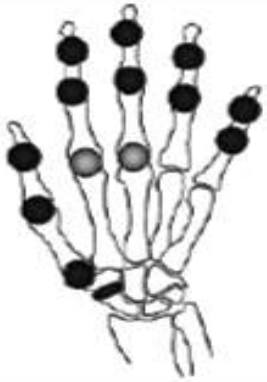
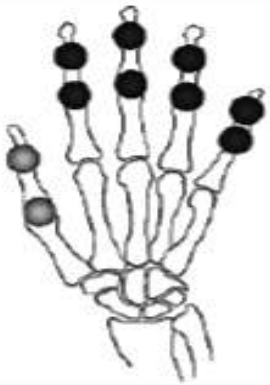
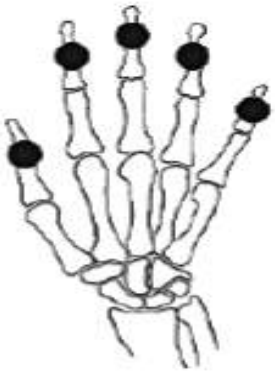
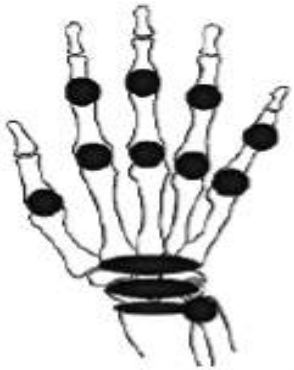


Figure 5. Erosion with Osteophytes

Radiographic Changes of Interphalangeal Joints & Target Sites Involvement of OA & Other Arthritis

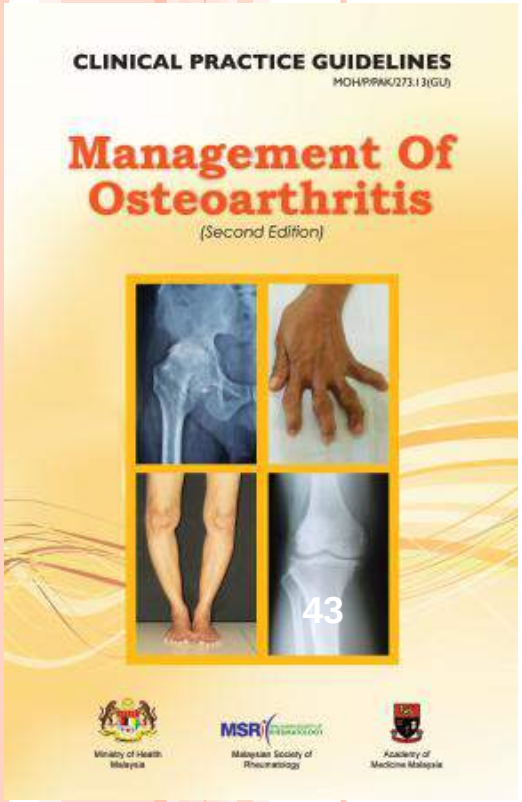
	Osteoarthritis	Erosive OA	Psoriatic Arthritis	Rheumatoid Arthritis
X-Ray changes	 Focal narrowing, marginal osteophyte, sclerosis, osteochondral bodies	 Subchondral erosion	 Proliferative marginal erosion, retained or increase bone density	 Non-proliferative marginal erosion, osteopenia
Target sites				

● Common ● Uncommon

Recommendation 1

- Osteoarthritis should be diagnosed clinically. **(Grade C)**
  - Plain radiographs may be used to support the diagnosis. **(Grade C)**
  - Laboratory investigations may be done to exclude other inflammatory joint diseases. **(Grade C)**

Thank You



Training of Core Trainers - Non-Pharmacological Treatment

by

Dr. Sheela Theivanthiran

Rehabilitation Physician

Hospital Rahabilitasi Cheras

INTRODUCTION

- The management of OA involves a multidisciplinary approach with the aim to relieve symptoms & improve joint function.

- It involves both non-pharmacological & pharmacological approaches.

Non-Pharmacological Treatment

- Patient Education
- Lifestyle Modification
- Physiotherapy
- Occupational Therapy
- Orthoses

EDUCATION-1

- Various types of patient education
- Tailored according to individual needs, goals & functional capabilities
- It should include information[Kao M-J et al, 2012; Coleman S et al., 2012; Hansson EE et al., 2010; Ravaud P et al., 2009 (all level I)]
  - of the diagnosis,
  - nature of the disease, therapeutic options &
  - the importance of ongoing patient participation in the disease management
- A positive attitude is an important goal.

EDUCATION-2

Recommendation 2

- Patient education should form an integral part of osteoarthritis management. **(Grade A)**

Lifestyle Modification

- Lifestyle medicine is defined as the application of environmental, behavioural, medical & motivational principles to the management of lifestyle related health problems. Egger GJ et al., 2007, level III

- Involves initiating & maintaining lifestyle changes

- Focus on weight reduction & physical activity or exercise

Weight Reduction-1

- Obesity is an important modifiable risk factor.

- Weight reduction
  - Beneficial in pain reduction & improvement of function
    Bliddal H et al., 2011, level I; Christensen R et al., 2007, level I; Messier SP et al., 2004, level I

- Each unit of weight loss will result in 4-fold reduction in the load exerted on the knee per step during daily activities. Messier SP et al., 2005, level I

WEIGHT REDUCTION-2

Recommendation 3

- Weight reduction should be emphasised in the management of patients with knee osteoarthritis and who are overweight. **(Grade A)**

PHYSICAL ACTIVITY-1

- Exercise is effective in reducing pain in hip & knee OA.
- The frequency, intensity, duration & rate of progression of exercise can vary.
- The intensity & duration of exercise should increase over time. Fernandes L et al., 2013
- One type of exercise has not been shown to be better than another (strength, aerobic or mixed exercises). Fernandes L et al., 2013

PHYSICAL ACTIVITY-2

- In order to improve adherence, the following are suggested:-
  - Individualised exercise programme
  - Graded type activity
  - Amount of activity based on personal goal setting
  - Feedback on progress
  - Appropriate positive reinforcement
  - Problem solving skills incorporated

PHYSIOTHERAPY

- Physiotherapy can improve muscle strength, balance, coordination & joint mobility. It should be started as soon as possible to improve pain & physical capacity.

EXERCISE-1

- Land-based exercises include:-
  - joint range of movement (ROM), muscle strengthening & low impact aerobic exercises
  - should be supervised & done regularly
  - short term benefits in reducing pain (SMD= -0.40, 95% CI -0.50 to -0.30) & improving physical function (SMD= -0.37, 95% CI =-0.49 to -0.25) in knee OA Fransen M et al., 2008, level I
  - however in hip OA, the benefit is only seen in pain reduction (SMD= -0.38, 95% CI -0.67 to -0.09) but not in physical function (SMD= -0.10, 95% CI -0.51 to 0.32) Fransen M et al. 2009, level I

EXERCISE-2

- Aquatic exercise may be advantageous for OA patients.

- A Cochrane SR showed benefits in hip & knee OA for 3 months:-[Bartels EM et al., 2007, level I]
  - improvement in pain (SMD=0.19, 95% CI 0.04 to 0.35)
  - quality of life (SMD=0.32, 95% CI 0.03 to 0.61
  - however, no statistically significant difference on walking ability
  - aquatic exercise was better than land-based exercises in reducing pain in knee OA (SMD=0.86, 95% CI 0.25 to 1.47)
    - however, there was no effect on walking ability & stiffness

Transcutaneous Electrostimulation (TENS)

- There is a lack of evidence to support the use of TENS for knee OA from the most recent Cochrane SR.[Rutjes AWS et al., 2009, level I]

- However, the ACR 2012 recommends the use of TENS for patients with chronic moderate to severe pain who are not suitable for total knee arthroplasty.[Hochberg MC et al., 2012]

THERMOTHERAPY

- Thermotherapy is commonly used in physical rehabilitation for OA patients.

- ACR recommends the use of thermal agents for hip & knee OA in combination with exercise supervised by a physiotherapist.[Hochberg MC et al., 2012]

- Cold pack usage did not show a significant effect in pain reduction in knee OA (WMD= -1.60, 95% CI -4.53 to1.33).[Brosseau L et al., 2003, level I]

Therapeutic Ultrasound

- Therapeutic ultrasound with high frequency vibrations is a modality used for pain relief in patients with hip & knee OA.

- However, in a Cochrane SR, the effectiveness of this modality in pain reduction & function was inconclusive. Rutjes AWS et al. 2010, level I

PHYSIOTHERAPY

Recommendation 4

- Exercise programmes in hip and knee osteoarthritis must be individualised, supervised and done regularly. **(Grade C)**
- Land-based or aquatic exercise may be used for short-term benefit in osteoarthritis. **(Grade A)**

Occupational Therapy-1

- To improve health, prevent disability & help individuals to achieve their optimum functional level & independence in performing ADL

- People with:-NCC for Chronic Conditions, 2008
  - pain, difficulty & frustration in performing daily activities & work tasks
  - should be referred early to an occupational therapist
  - for splinting, joint protection training & assistive device provision

Occupational Therapy-2

- A NICE-commissioned CPG recommends that:-NCC for Chronic Conditions, 2008
  - assistive devices such as walking sticks & tap turners
  - should be considered as adjuncts to core treatment in OA patients with specific ADL problems
    - It is important to prescribe appropriate assistive device with proper training to the patients.

Joint Protection & Home Exercises (JPE)

- Used in the treatment of hand OA
- JPE increases grip strength significantly by 25% ($p<0.0005$) & global hand function by 65% ($p<0.05$). Stamm TA et al., 2002, level I
- Thumb splints can help to reduce pain in the thumb & improve hand function. NCC for Chronic Conditions, 2008
- Splinting & Joint Protection programme Boustedt C et al., 2009, level I
  - hand OA can give significant decreases in pain & stiffness & improvements in daily activities ($p<0.05$)
- However, there is no evidence to support splinting in knee OA.

Activity of Daily Living (ADL)

- In a RCT, activity modification or instruction in ADL improved pain (MD= -3.21, 95 % CI -3.45 to -0.70) at 6 weeks. Shakoor MA et al., 2007, level I

- Activity modification in performing ADL may be helpful in maintaining proper posture & thus reduce pain & disability.

Rest & Relaxation

- May help in pain control

- The beneficial therapies are:-
  - Jacobson relaxation: improves pain at end of 8-week treatment ($p<0.05$) but the benefit is not sustained[Gay MC et al., 2002, level I]
    - Involves tensing & relaxing of muscles alternately, with the intent of developing awareness of the difference
    - Start from the arm to face working downwards to the shoulders, chest, abdomen, legs & ends with the whole body in complete relaxation
    - The whole cycle can be performed under 20 minutes.

Others

- Music therapy: improves pain at day 1, day 7 & at 2 weeks (end of treatment) (all p=0.001) McCaffrey R et al., 2003, level I

- Guided Imagery Relaxation (GIR): increases Health Related Quality of Life in women with OA (p=0.023) Baird CL et al., 2006, level I

Occupational Therapy

Recommendation 5

- Early referral to occupational therapy may be considered for pain relief and improvement in activities of daily living in osteoarthritis. **(Grade A)**

Orthoses

- Any medical device added to a person's body to support, align, position, immobilise, prevent or correct deformity, assist weak muscles or improve function

- In knee OA, the general purpose is to decrease pain & improve physical function.

Shoes & Knee Orthoses

- Walking shoes with neutral, contoured orthoses reduce pain & stiffness, & improve function in knee OA at one year ($p<0.001$). Barrios JA et al., 2009, level I

- Knee braces for medial, lateral or patella-femoral OA have not been shown to reduce pain, improve function or quality of life, even though they are widely used. Hunter DJ et al., 2011, level I; Brouwer RW et al., 2006, level I

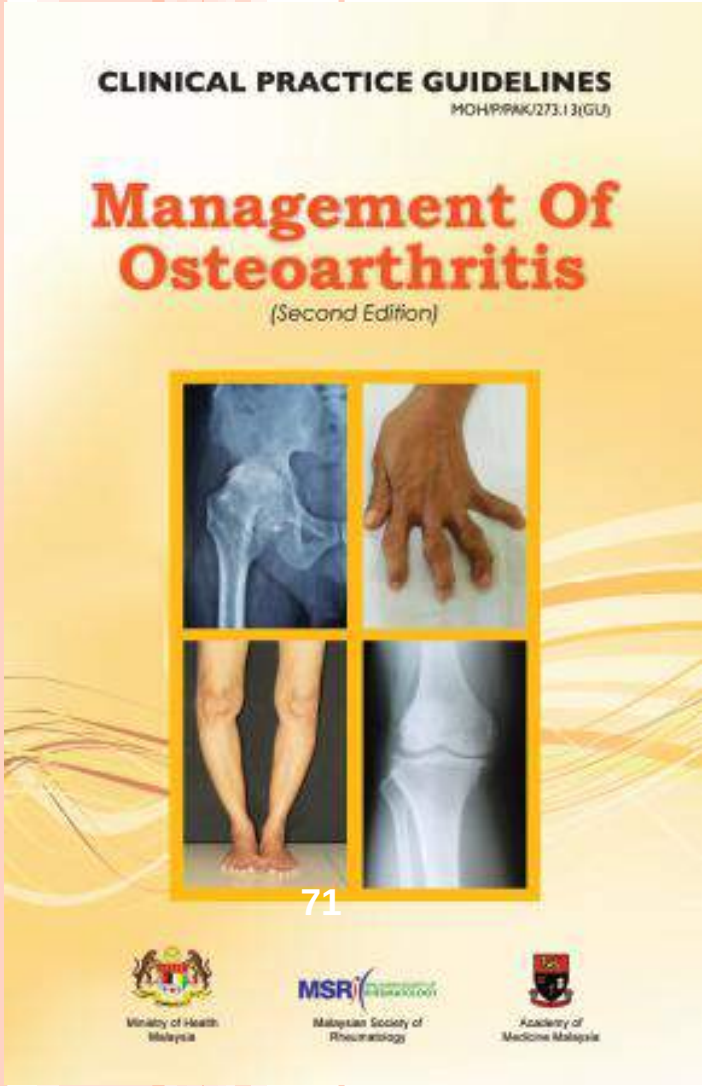
ORTHOSES

- There is insufficient evidence to recommend the use of orthoses in hip OA.

Recommendation 6

- Walking shoes with neutral, contoured orthoses may be offered in:-
  - knee osteoarthritis **(Grade A)**
  - hip osteoarthritis **(Grade C)**
- Knee braces should not be offered in knee osteoarthritis. **(Grade A)**

Thank You



Training of Core Trainers - Pharmacological Treatment (1)

by
Dr. Tan Bee Eng
Consultant Rheumatologist
Hospital Pulau Pinang

INTRODUCTION

1. Oral treatment
    a. Simple analgesics - paracetamol
    b. Weak opioid analgesics - tramadol
    c. Analgesics with anti-inflammatory properties - Non-steroidal Anti-inflammatory Drugs (NSAIDs) & Cyclo-oxygenase-2 (COX-2) Inhibitors
    d. Nutraceutical - glucosamine, chondroitin, diacerein
2. Intra-articular treatment
3. Topical treatment

PARACETAMOL-1

- A mild analgesic

Efficacy in OA:

1. Compared to placebo:
   a) Paracetamol (PCM) was superior to placebo in reduction of overall pain
      - Cochrane SR 2006 assessed the efficacy & safety of acetaminophen vs placebo & vs NSAIDs in OA.[Towheed T et al., 2006, level I]
      - 15 RCTs involving 5986 participants
      - Pain reduction, SMD= -0.13 (95% CI -0.22 to -0.04), NNT=16

PARACETAMOL-2

b) **PCM in the extended release (ER)** formulation was superior to placebo
   - In a 3-month double-blind, placebo-controlled RCT, on moderately severe hip or knee[Altman RD at al., 2006, level I]
   - Acetaminophen ER 650 mg & 1300 mg 3 times daily vs placebo
   - 3 primary end-points:
     - mean change in the WOMAC pain & physical function subscale scores
     - mean patient global assessment of response to therapy at week 12

Results:

- Acetaminophen ER 3900 mg was significantly superior to placebo for all 3 primary end points
- Acetaminophen ER 1950 mg was significantly superior to placebo only with respect to patient assessment of response to therapy

WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index)

- To assess pain, stiffness, & physical function in patients with hip &/or knee OA
- Consists of 24 items divided into 3 subscales:
  - **Pain (5 items):** during walking, using stairs, in bed, sitting or lying, & standing
  - **Stiffness (2 items):** after first waking & later in the day
  - **Physical Function (17 items):** stair use, rising from sitting, standing, bending, walking, getting in/out of a car, shopping, putting on/taking off socks, rising from bed, lying in bed, getting in/out of bath, sitting, getting on/off toilet, heavy household duties, light household duties

PARACETAMOL-3

2. Compared to NSAIDs
   a) NSAIDs were more efficacious than PCM in total WOMAC score (SMD= -0.25, 95% CI -0.39 to -0.11).[Altman RD at al., 2006, level I]

   a) PCM was less efficacious than NSAIDs in overall pain using VAS at rest (WMD= -6.33 mm, 95% CI -9.24 to -3.41) & on walking (WMD= -5.76 mm, 95% CI -8.99 to -2.52).[Lee C et al., 2004, level I]

PARACETAMOL-4

3. A combination tablet of ibuprofen/ paracetamol confers no additional benefit to ibuprofen alone. Doherty M et al., 2011, level I

PARACETAMOL-5

Safety in OA:

- Paracetamol in all formulations is well tolerated & safe

Recommendation 7

- Paracetamol can be used in patients with osteoarthritis. **(Grade A)**
  - It should be used as first-line analgesic in mild to moderate pain. **(Grade C)**

TRAMADOL-1

- A synthetic opioid analgesic

Efficacy:

1. Compared to placebo
   a) Tramadol was more efficacious compared to placebo in reducing pain
      - A SR and meta-analysis in 2007 included 11 RCTs with a total of 1,939 participants who received tramadol or tramadol/paracetamol or placebo or active control[Cepeda MS et al., 2007, level I]
      - Reduced pain (WMD= -8 mm, 95% CI -12.0 to -5.0) & improved stiffness & function (WMD= -0.3 mm, 95% CI -0.5 to -0.2)

TRAMADOL-2

b) Oral controlled-release tramadol is more efficacious in reducing pain & improving physical function

- A double-blind RC cross-over trial comparing the efficacy & safety of oral controlled-release tramadol & placebo in patients with painful OA[Thorne C et al. 2008, level I]

- Treatment: 150 mg daily of CR tramadol or placebo, & were titrated weekly to 200 mg, 300 mg or a maximum of 400 mg once daily
  - After 4 weeks, patients crossed over to the alternate treatment for another 4 weeks
  - All patients who completed the crossover study were eligible to receive open label CR tramadol for 6 months

Result:

- Oral controlled-release tramadol was more efficacious in reducing pain (p=0.0009) & improving physical function (p=0.0205) compared to placebo

TRAMADOL-3

2. Compared to NSAIDs: Tramadol is as efficacious as CR diclofenac
   - Double blind RCT comparing the efficacy of controlled release tramadol & controlled release diclofenac[Beaulieu AD et al., 2008, level I]
   - Treatment:
     - 200 mg CR tramadol, titrated to a maximum of 200 mg, 300 mg or 400 mg per day, or
     - 75 mg SR diclofenac, titrated to 75 mg or 100 mg once daily, or 75 mg twice a day based on pain relief & the presence of side effects
   - Result:
     - Improvements in VAS pain ($p=0.0001$), stiffness ($p<0.0005$) & physical function ($p=0.0001$) scores for both treatments
     - NS differences between the two treatments in the WOMAC subscales, overall pain, pain & sleep, or the clinical effectiveness evaluation

TRAMADOL-4

3. In patients already on NSAIDs for at least 30 days, addition of tramadol/paracetamol combination tablets for 10 days duration is significantly efficacious in managing painful OA compared to those on placebo[Rosenthal NR et al., 2004, level I; Silverfield JC et al., 2002, level I]

   - RCT on add-on therapy: To evaluate the efficacy & safety of adding tramadol 37.5 mg/acetaminophen (APAP) 325 mg combination tablets (tramadol/APAP) to existing therapy for painful OA flare in all & a subset of elderly patients

TRAMADOL-5

Safety & tolerability

1. Tramadol in all formulations show no major or significant adverse events
   - Common side effects are dizziness, nausea, vomiting, constipation & drowsiness.
2. This medication has to be used with caution in the elderly.

Recommendation 8

- Tramadol may be used alone or in combination with paracetamol in patients with osteoarthritis. **(Grade A)**

Other opioids (extra: not covered in current CPG)-1

Cochrane Database of Systematic Reviews 2009 (Nüesch E, Rutjes AW, Husni E, et al. Oral or transdermal opioids for osteoarthritis of the knee or hip. Cochrane Database Syst Rev. 2009 Oct 7;(4):CD003115)

- Randomised or quasi-randomised controlled trials that compared oral or transdermal opioids with placebo in patients with knee or hip osteoarthritis. Excluded studies of tramadol. No language restrictions were applied.

- 10 trials with 2268 participants were included
  - Oral codeine: 3 trials
  - Transdermal fentanyl: 1 trial
  - Oral morphine: 1 trial
  - Oral oxycodone: 4 trials
  - Oral oxymorphone: 2 trials

Other opioids (extra: not covered in current CPG)-2

Results:

- Overall, opioids were more effective than control interventions in terms of pain relief (SMD -0.36, 95% CI -0.47 to -0.26) & improvement of function (SMD -0.33, 95% CI -0.45 to -0.21)
- No substantial differences in effects according to type of opioid, analgesic potency (strong or weak), daily dose, duration of treatment or follow-up
- Adverse events were more frequent in patients receiving opioids compared to control:
  - Pooled risk ratio was 1.55 (95% CI 1.41 to 1.70) for any adverse event, 3.35 (95% CI 0.83 to 13.56) for serious adverse events
  - Withdrawal symptoms were more severe after fentanyl treatment compared to placebo (SMD=0.60, 95% CI 0.42 to 0.79; 1 trial)

Authors' conclusions:

- The small to moderate beneficial effects of non-tramadol opioids are outweighed by large increases in the risk of adverse events.
- Non-tramadol opioids should therefore not be routinely used, even if osteoarthritic pain is severe

NSAIDs & COX-2 Inhibitors-1

- NSAIDs & COX-2 Inhibitors
  - reduce production of prostaglandin by inhibiting the enzyme cyclo-oxygenase
    - vary in their selectivity for inhibiting different types of cyclo-oxygenase
    - COX-2 inhibitors selectively inhibit COX-2
  - provide analgesic & anti-pyretic effects & in higher dose, anti-inflammatory effects

CYCLO-OXYGENASE (COX)

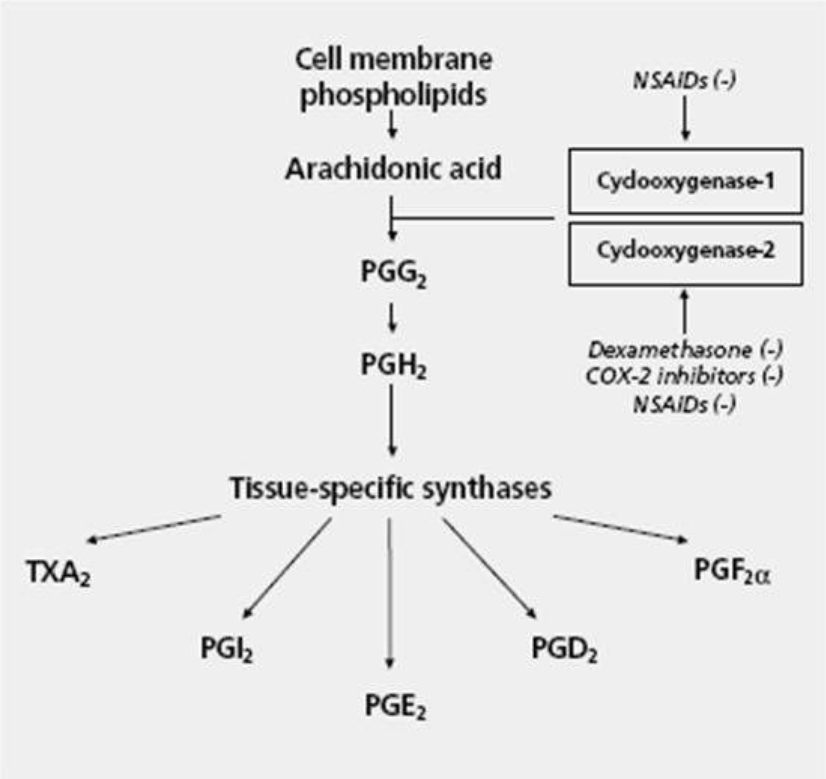


FIGURE 1. Schematic summary of the biosynthetic pathway for eicosanoids derived from arachidonic acid.[9,10]

- The COX-1 isoenzyme is essential for the maintenance of ***normal physiologic states*** in many tissues including the kidney, GIT & platelets
  - COX-1 activation in the gastric mucosa leads to prostacyclin production, which is cytoprotective
  - COX-2 inhibitors selectively inhibit COX-2 & thus improve gastro-intestinal tolerance

NSAIDs & COX-2 Inhibitors-2

Efficacy

- NSAIDs including COX-2 inhibitors were more efficacious than placebo
  - In a meta-analysis of RCT assessing NSAIDs, including COX-2 inhibitors vs placebo in osteoarthritic knee pain[Bjordal JM et al., 2004, level I]
  - 23 trials including 10,845 patients

Results:

- NSAIDs including COX-2 inhibitors were more efficacious than placebo in reducing short-term (2 - 13 weeks) pain intensity (WMD=0.30, 95% CI 0.24 to 0.39) & functional disability (WMD=0.29, 95% CI 0.18 to 0.40)

NSAIDs & COX-2 Inhibitors-3

- Efficacy of NSAIDs vs COX-2 Inhibitors
  - SUCCESS-1 study[Singh G et al., 2006, level I]
  - A total of 13,274 OA patients from 39 countries were randomly assigned to double-blind treatment for 12 weeks
    - celecoxib 100 mg twice daily (BID),
    - celecoxib 200 mg BID, or
    - nonselective NSAID therapy (diclofenac 50 mg BID or naproxen 500 mg BID)
  - Results:

    Celecoxib 100 mg & 200 mg BID were as efficacious as diclofenac 50 mg BID & naproxen 500 mg BID in the treatment of hip, knee or hand OA

NSAIDs & COX-2 Inhibitors-4

Concerns

1. Gastrointestinal (GI) safety

2. Cardiovascular (CV) safety

3. Renal safety

NSAIDs & COX-2 Inhibitors:

GI Safety

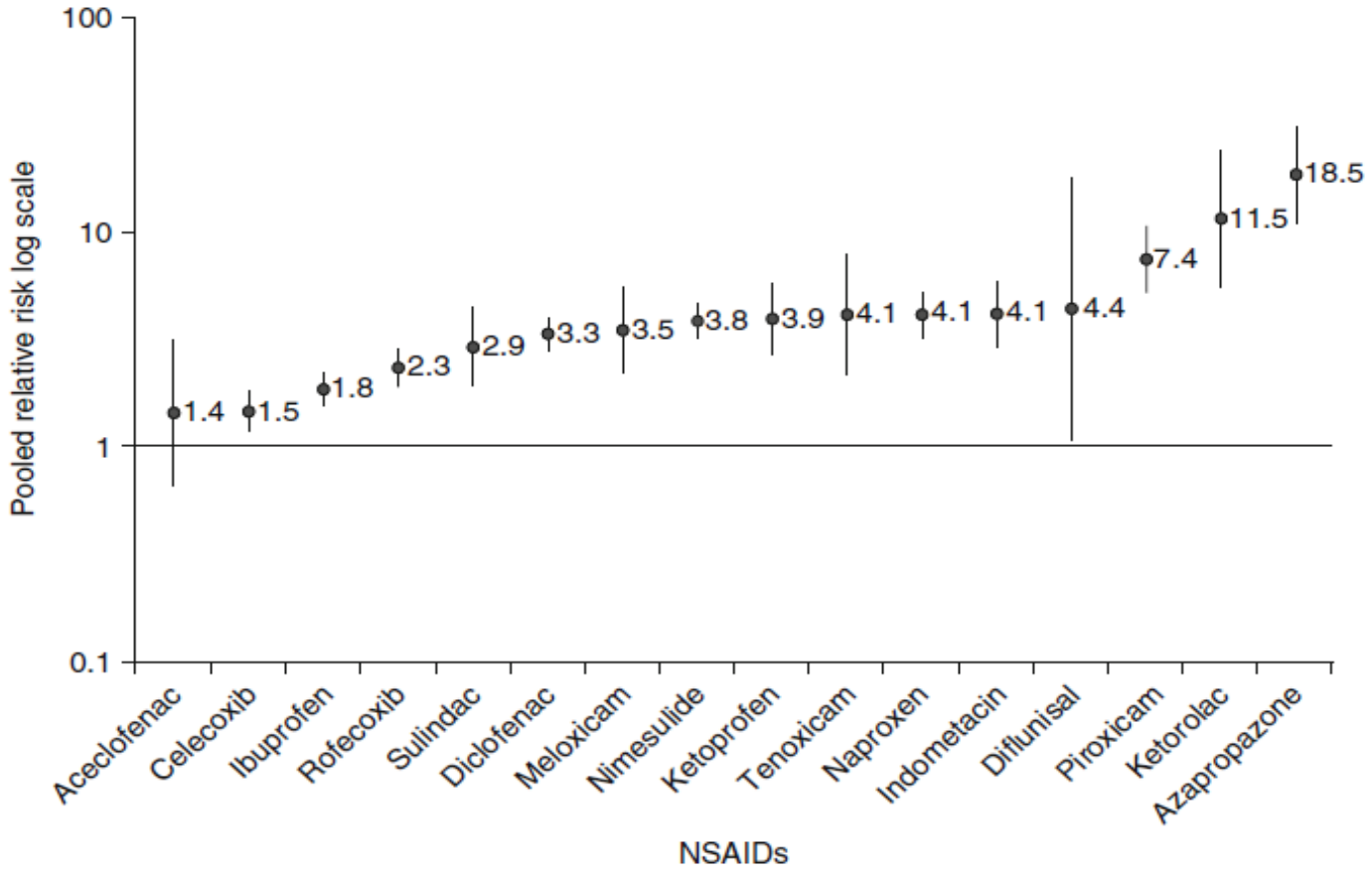
NSAIDs & COX-2 Inhibitors: GI Safety-1

- The RR of upper GI complications of several NSAIDs & celecoxib compared to placebo
  - The SOS Project aimed to conduct a SR & meta-analysis of observational studies to provide summary RR of upper GI complications (UGIC) associated with the use of individual NSAIDs, including selective COX-2 inhibitors. Castellsague J et al., 2012, level II-2

Result:

- The RR of upper GI complications of several NSAIDs & celecoxib compared to placebo ranged from 1.45 to 4.14

NSAIDs & COX-2 Inhibitors: GI Safety-2



NSAIDs & COX-2 Inhibitors: GI Safety-3

- Ulcer complications are seen significantly less frequent in COX-2 inhibitors compared to NSAIDs.[Singh G et al., 2006; Laine L et al., 2007; Hunt RH et al., 2003; Hunt RH et al., 2003 (all level I)]

- Comparing concomitant aspirin & non-aspirin users, the GI complications are significantly less in non-aspirin users (p=0.007).[Singh G et al., 2006, level I]

NSAIDs & COX-2 Inhibitors: GI Safety

Primary Ulcer Prevention

NSAIDs & COX-2 Inhibitors: GI Safety-4

- Proton Pump Inhbitors are effective in the prevention of NSAID-induced endoscopic duodenal & gastric ulcers
  - Cochrane SR 2011[Rostom A et al., 2002, level I]
  - Objectives: To review the effectiveness of common interventions for the prevention of NSAID induced upper GI toxicity
  - 41 RCTs

  Result:
  - PPIs were effective in the prevention of NSAID-induced endoscopic duodenal (RR=0.19, 95% CI 0.09 to 0.37) & gastric ulcers (RR=0.40, 95% CI 0.32 to 0.51) at ≥12 weeks when compared to placebo.

NSAIDs & COX-2 Inhibitors: GI Safety-5

Other findings from the same trial:

- Misoprostol 400 mcg or 800 mcg were effective in reducing the risk of endoscopic ulcers, but less well tolerated, mainly due to diarrhoea.

- Double dose H2RAs & PPIs were effective at reducing the risk of endoscopic duodenal & gastric ulcers [RR=0.44 (95% CI 0.26 to 0.74) & RR=0.40 (95% CI 0.32 to 0.51) respectively] & were better tolerated than misoprostol.

- Standard dose of H2RAs was effective at reducing the risk of duodenal ulcers (RR 0.24, 95% CI 0.10 to 0.57) but not effective at reducing endoscopic gastric ulcer.

- Note: Misoprostol & ranitidine were not included in the CPG
  - Misoprostol was not discussed in the current CPG due to poor tolerance.
  - Double dose H2RAs is needed for gastric ulcer prevention (? Cost-effectiveness, because generic PPIs are cheep and widely available)

NSAIDs & COX-2 Inhibitors: GI Safety

History of GIT Ulcer - Prevention of Ulcer Recurrence

NSAIDs & COX-2 Inhibitors: GI Safety-6

- Lansoprazole significantly reduces the risk of gastroduodenal ulcers recurrence in patients with a definite history of GI ulcers requiring: Sugano K et al., 2012, level I
  - long-term NSAIDs therapy (HR=0.25, 95% CI 0.14 to 0.45)
  - long-term low dose aspirin therapy (HR=0.10, 95% CI 0.04 to 0.23)

What about…

- NSAIDs plus PPI
- COX-2 inhibitors plus PPI

NSAIDs & COX-2 Inhibitors: GI Safety-7

- The risk of GI events is lower in patients receiving celecoxib compared to diclofenac slow release plus omeprazole with HR of 4.3 (95% CI 2.6 to 7.0). Chan FKL et al., 2010, level I

- The risk of recurrent ulcer bleeding is lower in the celecoxib 200 mg BD plus esomeprozole 20 mg BD group compared to the celecoxib 200 mg BD plus placebo group (p=0.0004). Chan FK et al., 2007, level I

NSAIDs & COX-2 Inhibitors:

CV Safety

NSAIDs & COX-2 Inhibitors: CV Safety-1

- Network meta-analysis to analyse the available evidence on CV safety of NSAIDs (including COX-2 Inhibitors)[Trelle S et al., 2011, level I]

- 31 trials in 116,429 patients with more than 115,000 patient-years follow-up

- Naproxen, ibuprofen, diclofenac, celecoxib, etoricoxib, rofecoxib, lumiracoxib or placebo

NSAIDs & COX-2 Inhibitors: CV Safety-2

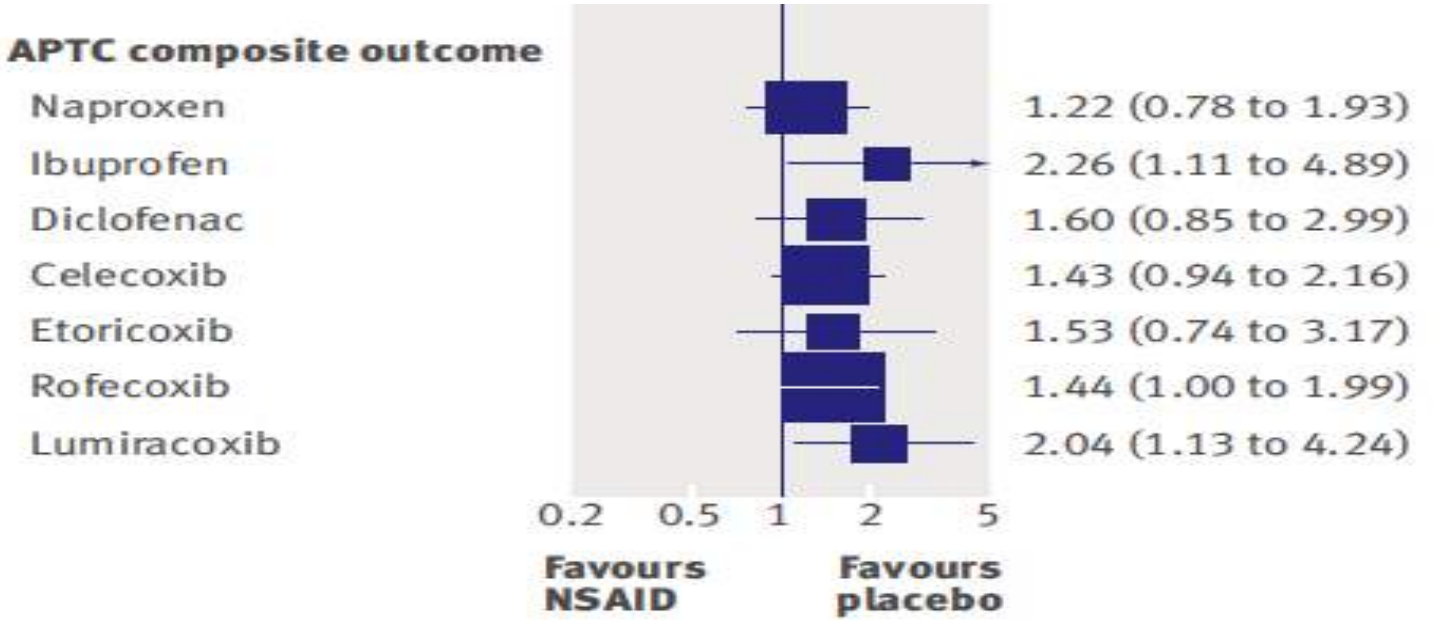


Fig 2| Estimates of rate ratios for non-steroidal anti-inflammatory drugs compared with placebo. NSAID=non-steroidal anti-inflammatory drug; APTC=Antiplatelet Trialists' Collaboration

Naproxen had the lowest Antiplatelet Trialists' Collaboration composite outcome of non-fatal MI, non-fatal stroke or CV death among users of NSAIDs & COX-2 inhibitors (rate ratio=1.22, 95% CI 0.78 to 1.93)

NSAIDs & COX-2 Inhibitors: CV Safety-3

- The numbers of CV thromboembolic events are low in both celecoxib & diclofenac or naproxen groups at 12 weeks [e.g. MI rates: 10 events (0.55/100 patient-years) for celecoxib vs 1 event (0.11/100 patient-years) for NSAIDs] with (p=0.11).[Singh G et al., 2006, level I]
  - Note: the study was not powered to detect such differences

NSAIDs & COX-2 Inhibitors: CV Safety-4

- Long-term etoricoxib use (20 months) is also associated with comparable CV events with that of diclofenac.[Combe B et al., 2009, level I]
  - RCT in 23,504 patients of OA & RA (MEDAL study), with mean treatment between 19.4 - 20.8 months
  - Treatment:
    - OA patients to etoricoxib 90 mg, then to 60 mg once daily vs diclofenac 75 mg twice daily
    - RA patients were randomised to etoricoxib 90 mg once daily or diclofenac 75 mg twice daily
  - Results: irrespective of etoricoxib dose
    - Thrombotic CV risk (HR of etoricoxib to diclofenac) was 0.96 (95% CI 0.81 to 1.15)
    - Maximum average change in SBP with etoricoxib was 3.4 - 3.6 mmHg (DBP: 1.0 - 1.5 mmHg), while diclofenac produced a maximum average change of 0.9 -1.9mmHg (DBP: 0.0 - 0.5 mmHg)

NSAIDs & COX-2 Inhibitors:

Renal Safety

NSAIDs & COX-2 Inhibitors: Renal Safety

- In the Malaysian CPG on Chronic Kidney Disease 2011 in Adults, there was conflicting evidence in the association between chronic NSAIDs usage & the development of CKD.[MoH, 2011]

- However, renal function should be monitored regularly in patients on chronic NSAIDs or COX-2 inhibitors treatment.

NSAIDs & COX-2 Inhibitors-5

Recommendation 9

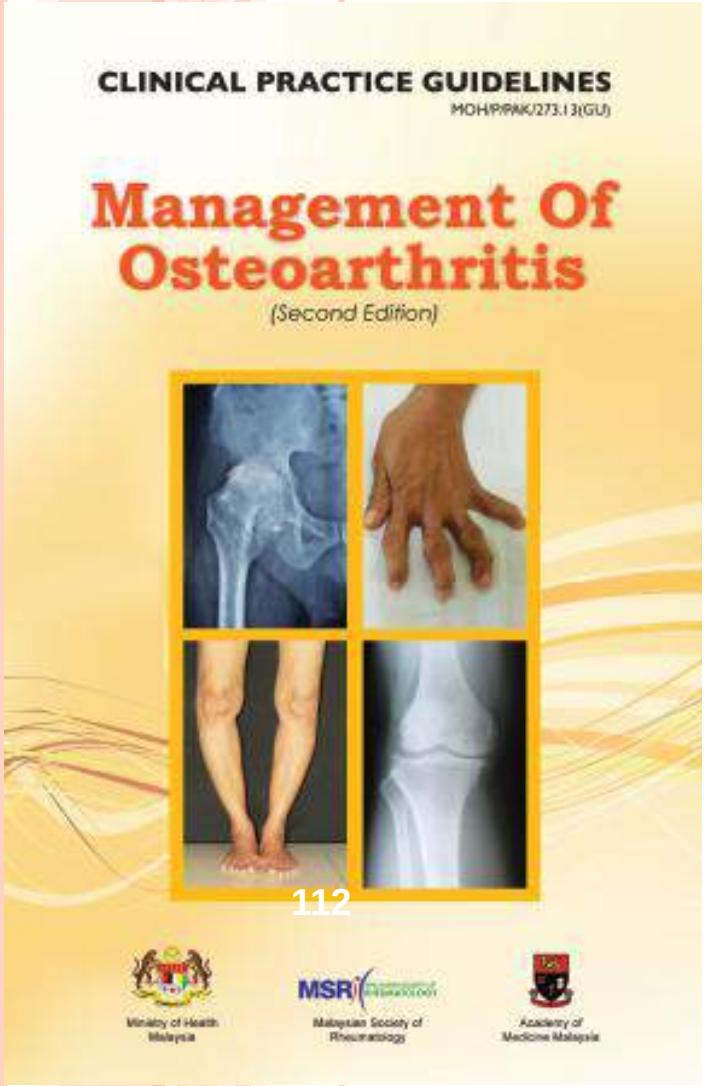
- Non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 (COX-2) inhibitors can be used in the treatment of osteoarthritis. **(Grade A)**
  - In patients with high risk of gastrointestinal (GI) complications, COX-2 inhibitors are preferred to non-selective NSAIDs with proton pump inhibitor (PPI) for primary ulcer prevention. **(Grade A)**
  - In patients with previous GI complications:-
    - NSAIDs or COX-2 inhibitors should be avoided. **(Grade C)**
    - combination of COX-2 inhibitors and PPI may be offered for GI protection if indicated. **(Grade A)**
  - In patients with renal impairment, NSAIDs and COX-2 inhibitors should be used with caution. **(Grade C)**

NSAIDs & COX-2 Inhibitors-6

Note

1. Combination therapy with more than 1 NSAID/ COX-2 inhibitor should never be used.
2. There is no benefit in combination therapy & the incidence of side effects may be additive.
3. Caution is required when prescribing NSAIDs in the elderly & those with hypertension, CV disease, renal or hepatic impairment.
4. Those who are allergic to one NSAID may also be allergic to others.

Thank You



Training of Core Trainers - Pharmacological Treatment (2)

by
Datin Dr. Asmahan Mohamed Ismail
Consultant Rheumatologist
Hospital Raja Perempuan Zainab II

INTRODUCTION

1. *Oral treatment*
   a. *Simple analgesics - paracetamol*
   b. *Weak opioid analgesics - tramadol*
   c. *Analgesics with anti-inflammatory properties - Non-steroidal Anti-inflammatory Drugs (NSAIDs) & Cyclo-oxygenase-2 (COX-2) Inhibitors*
   d. **Nutraceutical – glucosamine, chondroitin, diacerein**
2. **Intra-articular treatment**
3. **Topical treatment**

Nutraceutical

- Glucosamine
- Chondroitin
- Diacerein

GLUCOSAMINE-1

- Amino sugar & prominent precursor in the biochemical synthesis of glycosylated proteins, lipids & glycosaminoglycans
- In general, it is not consistent as structure modifier for OA
- Glucosamine hydrochloride & glucosamine sulfate

GLUCOSAMINE-2

- Efficacy:
  - Glucosamine hydrochloride or its combination with chondroitin sulfate is not efficacious as a structure or symptom modifier.
    Wandel S et al., 2010; Black C et al., 2009; Sawitzke AD et al., 2010; Sawitzke AD et al., 2008 (all level I)

- Efficacy:
  - Glucosamine sulfate 1500 mg per day is more efficacious in pain reduction compared to placebo. Black C et al., 2009, level I; Towheed T et al., 2005, level I
  - Pain relieving effect of glucosamine sulfate can be seen by three months after its initiation. Pavelka K et al., 2002, level I

GLUCOSAMINE-3

- Safety:
  - Glucosamine is well-tolerated & safe. Wandel S et al., 2010; Black C et al., 2009; Towheed T et al., 2005; Sawitzke AD et al., 2010 (all level I)

GLUCOSAMINE-4

Recommendation 10

- Glucosamine sulfate 1500 mg per day may be used as pain relief for knee osteoarthritis. **(Grade C)**
  - Evaluation on pain reduction should be done at three months after initiation of treatment before deciding on its continuation. **(Grade C)**

CHONDROITIN-1

- Chondroitin sulfate is a sulfated GAG which is usually found attached to proteins as part of a proteoglycan

Efficacy:

1. In hip & knee OA
   - Inconsistent pain reliever & disease modifying effect
     Wandel S et al., 2010; Black C et al., 2009; Towheed T et al., 2005; Sawitzke AD et al., 2010; Sawitzke AD et al., 2008; Pavelka K et al., 2002; Dostrovsky NR et al., 2011; Kahan A et al., 2009 (all level I)

CHONDROITIN-2

- Efficacy:

2. In hands OA:

  - Chondroitin sulfate 800 mg as a single dose is more efficacious than placebo in pain reduction, improving hand function & morning stiffness in patients with hand OA. Gabay C et al., 2011, level I

  - Its efficacy as a structural modifier is still debatable. Rovetta G et al., 2004; Rovetta G et al., 2002; Verbruggen G et al. (all level I)

CHONDROITIN-3

- Safety:
  - Chondroitin sulfate is well-tolerated & safe. Gabay C et al., 2011, level I

The efficacy of chondroitin in the treatment of hip or knee OA is inconclusive. It may be beneficial for symptomatic relief in hand OA.

DIACEREIN-1

- Purified anthraquinone derivative
- Inhibits production of interleukin (IL)-1beta which is a major proinflammatory cytokine
- Reduce articular cartilage destruction

DIACEREIN-2

- Efficacy
  - Meta-analysis: Rintelen B et al., 2006, level I
  - Diacerein was slightly more efficacious compared to placebo in
    - reduction of pain [n-wtd pooled Glass score=1.31 (95% CI 0.49 to 2.14)]
    - improvement of joint function [n-wtd pooled Glass score=1.08 (95% CI 0.26 to 1.91)] in knee OA.

DIACEREIN-3

- Efficacy Rintelen B et al., 2006, level I
  - Similar efficacy with NSAIDs in the reduction of pain in knee OA for a duration of 16 weeks [(n-wtd pooled Glass score= -0.01 (95% CI -0.76 to 0.74)]
  - Significant carry-over effect in pain reduction in knee OA compared to placebo [(n-wtd pooled Glass score=2.71 (95% CI 1.32 to 4.10)] & NSAIDs [(n-wtd pooled Glass score=2.27 (95% CI 1.42 to 3.11)] for 16 weeks duration.

DIACEREIN-4

- Safety & tolerability
  - Acceptable safety profile. Rintelen B et al., 2006; Pavelka K et al., 2007; Louthrenoo W et al., 2007; Dougados M et al., 2001 (all level I)
  - The incidence of adverse events such as diarrhoea, abdominal pain, nausea & vomiting is higher compared to placebo ($p<0.01$), most are mild to moderate. Brahmachari B et al., 2009, level I
  - In view of modest efficacy & common adverse events, more studies are warranted to support the use of diacerein in OA.

DIACEREIN-5

Recommendation 11

- Diacerein may be used in the treatment of knee osteoarthritis. **(Grade C)**

Intra-articular Treatment

- Corticosteroid
- Viscosupplementation

Intra-articular Corticosteroids-1

- Cochrane SR of 12 single/double blinded RCTs (n=653) → efficacy & safety of various preparations of IA corticosteroids in the treatment of knee OA. Bellamy N et al., 2006, level I
  - IA corticosteroid offered short-term pain relief at 1 week post-injection in patients with knee OA (WMD in VAS= -21.9 mm, 95% CI -29.9 to -13.9). NNT=3 - 4.
  - The effect continued to be seen at 2 weeks (RR=1.8, 95% CI 1.1 to 3.0) & 3 weeks (RR=3.1, 95% CI 1.6 to 6.0).

INTRA-ARTICULAR CORTICOSTEROIDS-2

Recommendation 12

- Intra-articular corticosteroid may be used for short-term pain relief in an acute exacerbation of knee osteoarthritis. **(Grade A)**

Oral corticosteroid have no role in the treatment of osteoarthritis.

Intra-articular Viscosupplementation-1

- Hyaluronic acid (HA) is a naturally occurring polysaccharide in the synovial fluid.
- Elastoviscosity of synovial fluid
  - The quantity of HA is reduced in the synovial fluid of OA patients
- Viscosupplementation - formulations of HA for IA injection to improve biomechanical function

Intra-articular Viscosupplementation-2

- 2 SRs showed that IA HA maybe beneficial in reducing pain, but the effect sizes were small when compared to placebo.
  - Conflicting results for improvement of physical function.

Rutjes AWS et al., 2012, level I; Bellamy N CJ et al., 2006, level I

INTRA-ARTICULAR VISCOSUPPLEMENTATION-3

- Pharmacoeconomics analysis by NICE (National Collaborative Centre for Chronic Condition, UK) - benefits may be offset by the frequency of the HA injections & other indirect costs.

- NICE does not recommend the use of viscosupplementation in treatment of knee OA. National Collaborating Centre for Chronic Conditions, 2008

Intra-articular Viscosupplementation-4

- Safety:
  - Viscosupplementation is generally well tolerated & with no significant difference in safety profile compared to placebo.[Bellamy N CJ et al., 2006, level I]
  - The risk of overall adverse events is insignificant.[Rutjes AWS et al., 2012, level I]

INTRA-ARTICULAR VISCOSUPPLEMENTATION-5

Due to a lack of supporting evidence, the CPG is unable to recommend the use of viscosupplementation in the treatment of osteoarthritis.

TOPICAL TREATMENT-1

- Topical treatment is an adjunct or alternative to oral NSAIDs for treatment of OA.
- The commonly used topical treatment includes NSAIDs, capsaicin & methylsalicylate.
- Topical analgesics can be in the form of gels, creams & transdermal patches.

TOPICAL TREATMENT-2

- Efficacy: compared to placebo,
  - Topical NSAIDs reduce knee OA pain at week 2 ($p<0.0001$), week 3 ($p<0.0002$)[Niethard FU et al., 2005, level I] & at week 4 to 12 (SMD= -0.33, 95% CI -0.48 to -0.18)[Towheed TE et al., 2006, level I]
  - More efficacious in reducing stiffness of knee OA (SMD in WOMAC stiffness at week 4 to 12=-0.30, 95% CI -0.45 to -0.15)[Towheed TE et al., 2006,level I]
  - Physical function is also significantly improved with topical NSAIDs.[Niethard FU et al., 2005; Towheed TE et al., 2006; Trnavsky K et al., 2004 (all level I)]

TOPICAL TREATMENT-3

- There are no recent studies on the usage of capsaicin & methylsalicylate in OA.

- NICE CPG 2008 recommends that topical capsaicin should be considered as an adjunct to core treatment for knee or hand OA but does not recommend the use of topical methylsalicylate (rubefacients). National Collaborating Centre for Chronic Conditions, 2008

Topical Treatment-4

- Safety:
  - Generally found to be safe in adult with OA in SR of RCTs[Makris UE et al., 2010, level I]
  - The risk of minor skin dryness was higher in topical diclofenac compared to placebo (RR=1.74, 95% CI 1.37 to 2.22).
  - Fewer severe gastrointestinal adverse events were reported in topical NSAIDs compared with oral NSAIDs.

TOPICAL TREATMENT-5

Recommendation 13

- Topical non-steroidal anti-inflammatory drugs may be offered in the treatment of osteoarthritis. **(Grade A)**
  - It may be used as adjunct therapy in mild to moderate pain. **(Grade C)**

Alternative Treatment

- Common alternative treatments that have shown positive results include
  - Acupuncture
  - Avocado Soybean Unsaponifiables(ASU)
  - Ginger

ACUPUNCTURE-1

- Efficacy:
  - Cochrane SR - acupuncture significantly improved pain & function (as assessed by the WOMAC scale) in patients with knee OA compared to sham acupuncture:-Manheimer E et al., 2010, level I
    - SMD= -0.29 (95% CI -0.48 to -0.10) for pain at 3 months & SMD= -0.10 (95% CI -0.21 to -0.01) for pain at 26 weeks
    - SMD= -0.29 (95% CI -0.49 to -0.08) for function at 3 months
    - SMD= -0.29 (95% CI -0.50 to -0.09) for total score at 3 months

ACUPUNCTURE-2

- Safety:
  - No serious adverse events were reported to be associated with acupuncture.
  - Minor side effects were bruising & haematoma.

AVOCADO SOYBEAN UNSAPONIFIABLES-1

- Efficacy:
  - Cochrane SR - ASU provided pain relief & improvement of function compared to placebo in chronic stable OA of the hip & knee:- Little CV et al., 2000, level I
    - SMD= -8.06 (95% CI -11.3 to -4.60) for VAS pain score
    - SMD= -1.69 (95% CI -2.41 to -0.98) for Lequesne index
    - SMD=0.71 (95% CI 0.57 to 0.89) for resumption of NSAIDs

Avocado Soybean Unsaponifiables-2

- Efficacy:
  - Meta-analysis showed improvement in pain in OMERACT III scale (SMD=0.39, 95% CI 0.01 to 0.76) & function in Lequesne index (SMD=45, 95% CI 0.21 to 0.70). Christensen R et al., 2008, level I

Avocado Soybean Unsaponifiables-3

- Safety:
  - ASU had minimal gastrointestinal disturbances & no other serious side effect.

GINGER

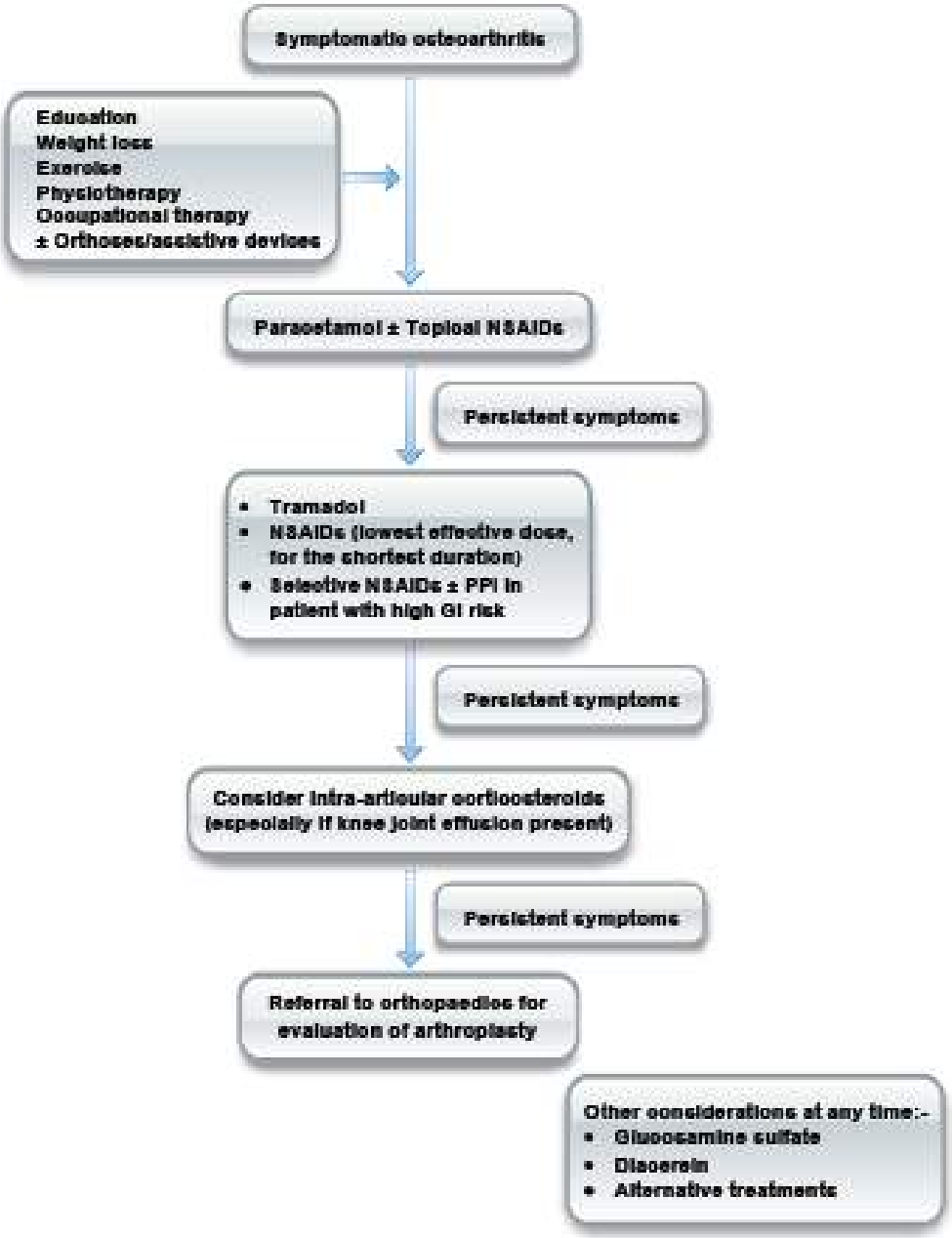
- Efficacy:
  - Small RCT of short duration - ginger extract was significantly more efficacious than placebo but less than ibuprofen ($p<0.005$) in improving pain & function.

- Safety:
  - It was safe without serious side effects. Bliddal H et al., 2000, level I

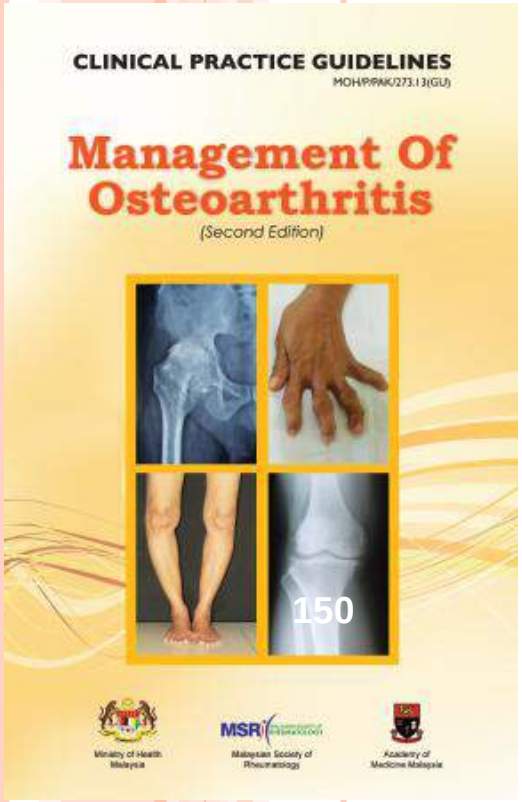
Alternative Treatment

- Acupuncture & avocado soybean unsaponifiables may be used as an adjunct short-term therapy in osteoarthritis. **(Grade A)**

ALGORITHM ON MANAGEMENT OF KNEE & HIP OSTEOARTHRITIS



Thank You



Training of Core Trainers - Surgical Management of OA

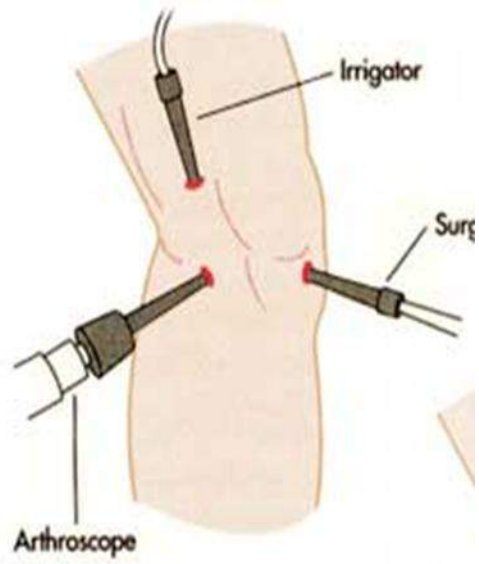
by
Dr. Mohd. Yusof Ibrahim
Consultant Orthopedic Surgeon
Hospital Raja Perempuan Zainab II

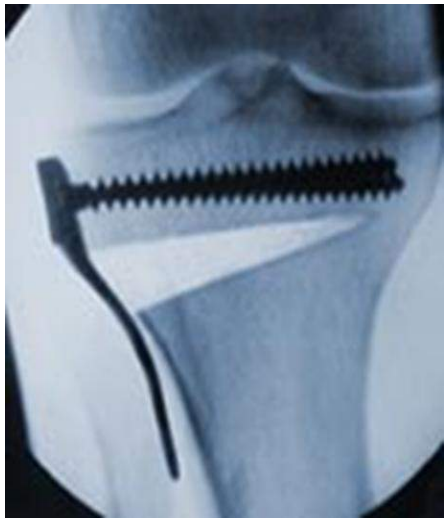
Surgical Management

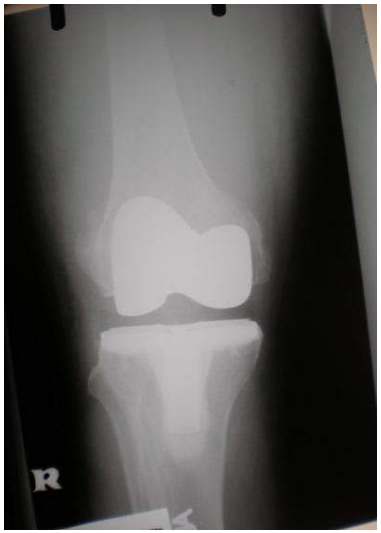
- Considered if symptoms are significant:
  - Pain
  - Limitation of ADL
  - Psychosocial health (psychological well being)
  - Economic impact
  - Recent deterioration

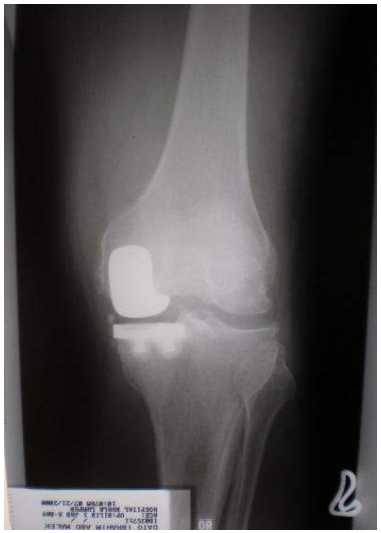
Types of Surgery

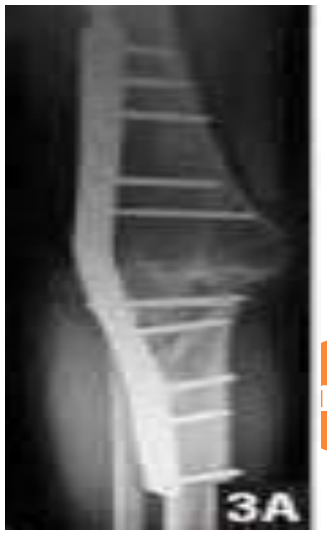
- Arthroscopic surgery
- HTO
- Total Joint Replacement
- Partial Joint Replacement
- Arthrodesis











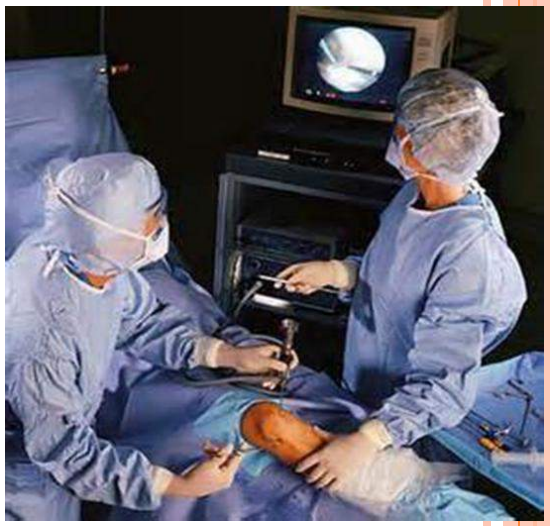
Arthroscopic Surgery (Lavage & Debridement)

- No additional benefit in terms of pain relief & joint function improvement vs optimised physical & medical therapy

  Moseley B, 2009, level I; Kirkley A et al., 2008, level I

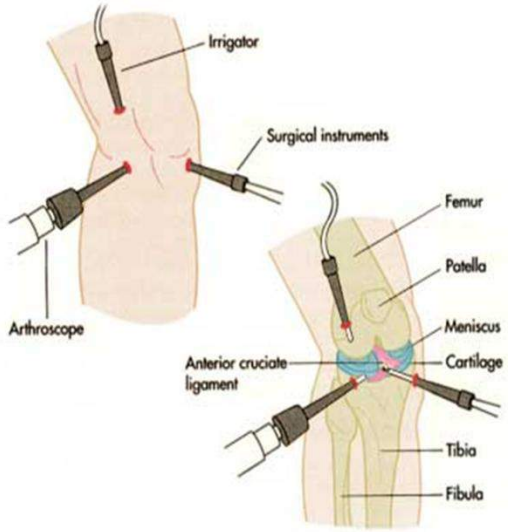
- Indicated in OA a/w mechanical symptoms e.g. locking or symptoms from loose bodies, meniscal tears, unstable cartilaginous flaps

- Inversely proportional to severity of underlying OA



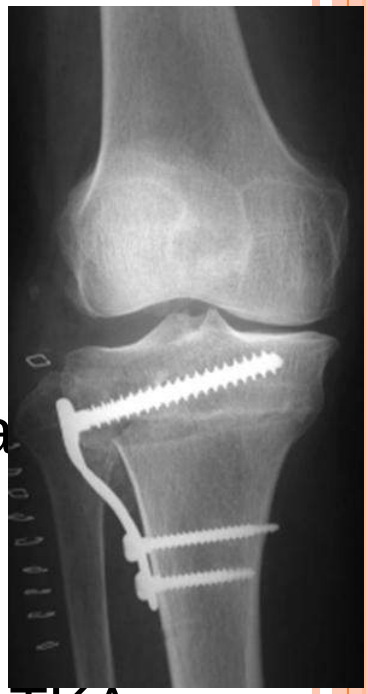
Arthroscopic Procedure

- Ideal for best result:
  - Mechanical symptoms
  - No malalingment
  - Early arthritic change by X-ray
  - MRI evidence of meniscus or structural change



High Tibial Osteotomy (HTO)-1

- In isolated medial compartment knee OA or varus malalingment
  - <50 years old
  - Good knee ROM (>120^0)
  - Realign to correct mechanical axis
  - Load distributed more on normal knee compa



→ Goals:

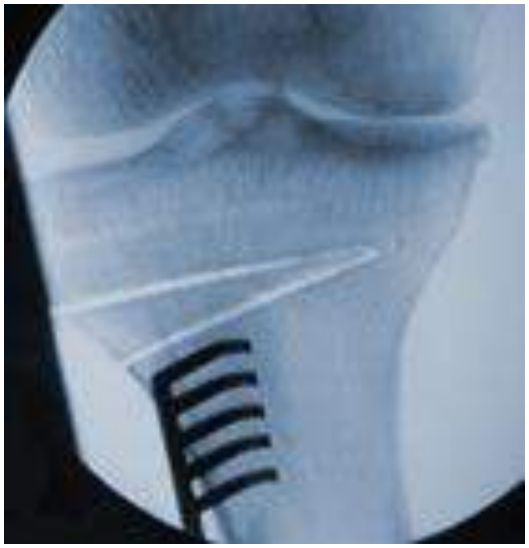
Relief pain, improve function & delay a possible TKA

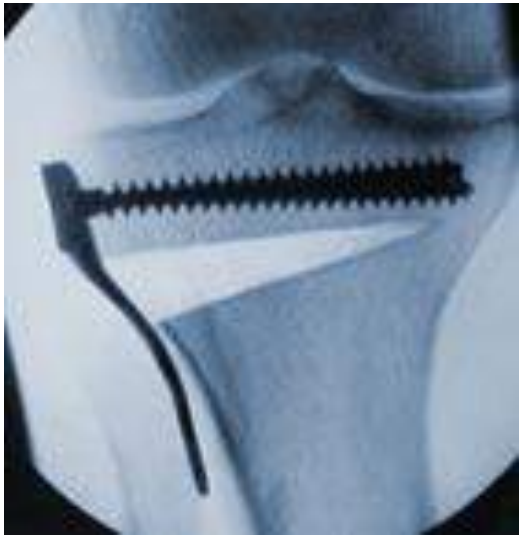
High Tibial Osteotomy (HTO)-2

- Removes a wedge of bone near a damaged joint
  - This shifts weight from the affected compartment to more or healthier cartilage
- A high success rate is predicted when appropriate mechanical alignment is obtained in the properly selected patient.

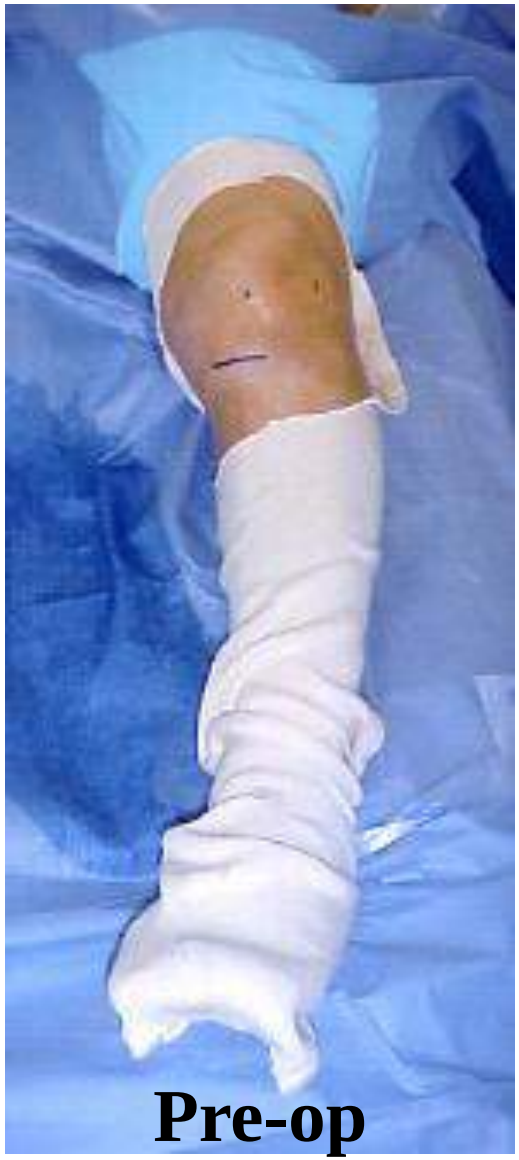
Coventry MB et al., J Bone Joint Surg Am. 1993; Berman AT et al., Clin Orthop Relat Res. 1991; Insall JN et al., J Bone Joint Surg Am. 1984

High Tibial Osteotomy (HTO)-3

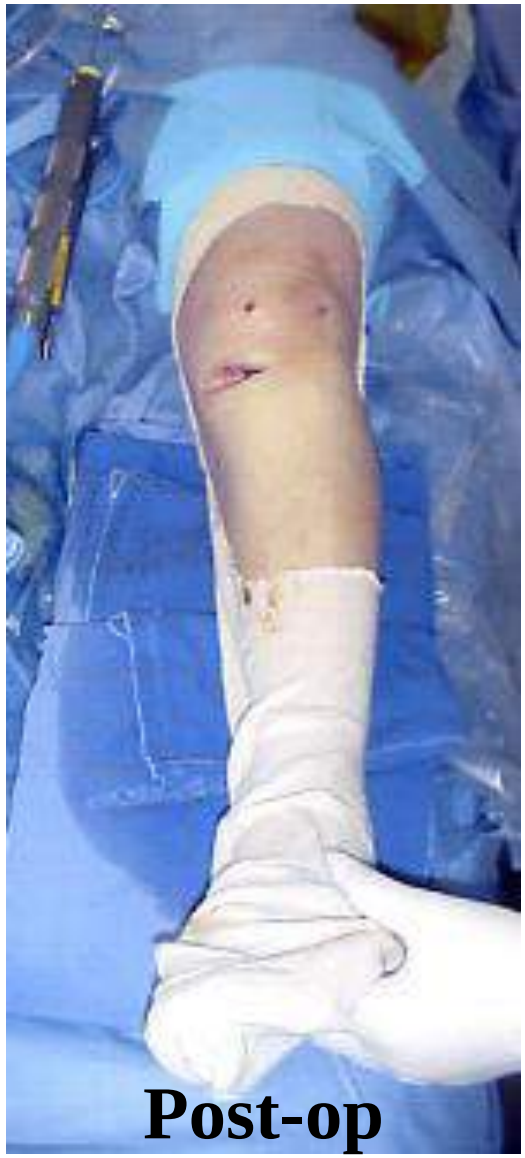




ALIGNMENT CORRECTION



Pre-op



Post-op

Joint Replacement

- Replacement of the diseased joint with artificial joint
- OA is the most common cause for Joint Replacement
- Joints that most commonly replaced:
  - Knee joint
  - Hip joint

  Less common:
  - Ankle joint
  - Shoulder joint
  - Elbow joint

Indications for Joint Replacement

- Pain
- Severe disability
- Deformity
- Limited function (ADL)
- Fail conservative treatment

Goals for Joint Replacement

- Painless joint
- Mobile joint (good range of motion)
- Stable
- Normal function
- Able to perform normal ADL according to age
- Lasting for life

Outcome of Joint Replacement

- Results in dramatic reduction in pain & improvement in ADL

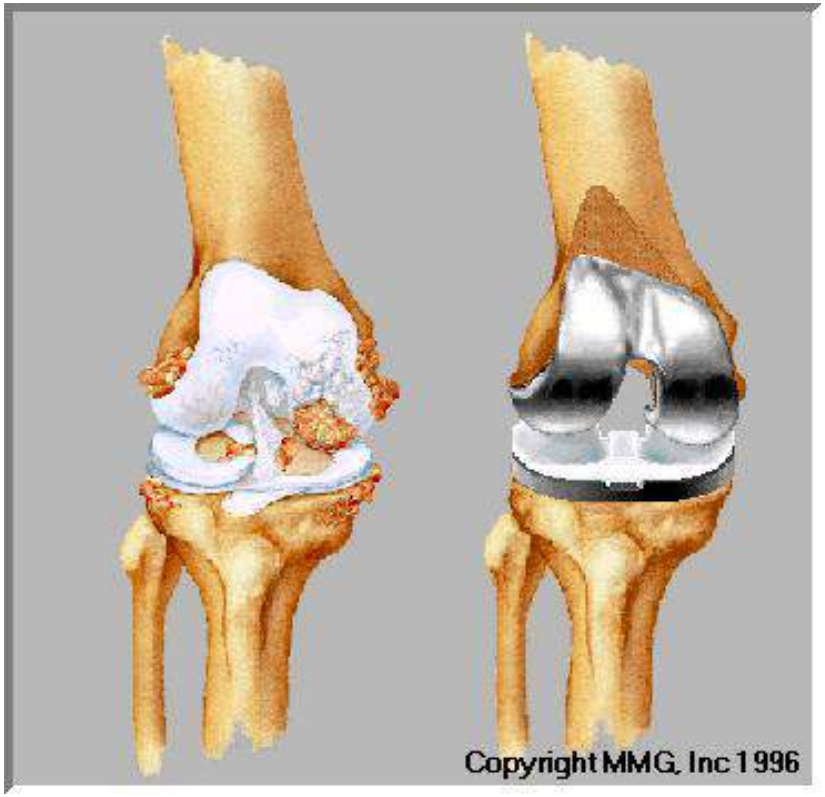
  Health Quality Ontario, 2005, level I

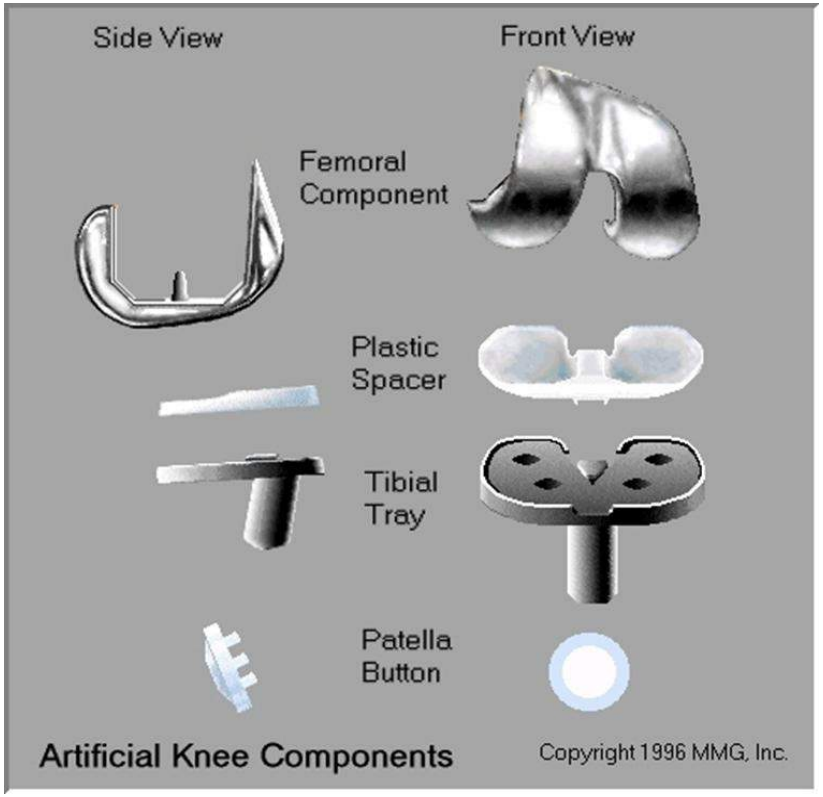
Knee Replacement

- Partial Knee Replacement
  - Unicondylar Knee Replacement
  - Patellofemoral Knee Arthroplasty
  - Bicompartmental Arthroplasty
- Total Knee Replacement (TKR)
  - Simple
  - With stem ± wedge/block augment
  - Mobile bearing
  - Cruciate retaining
  - Posterior stabiliser (PS)

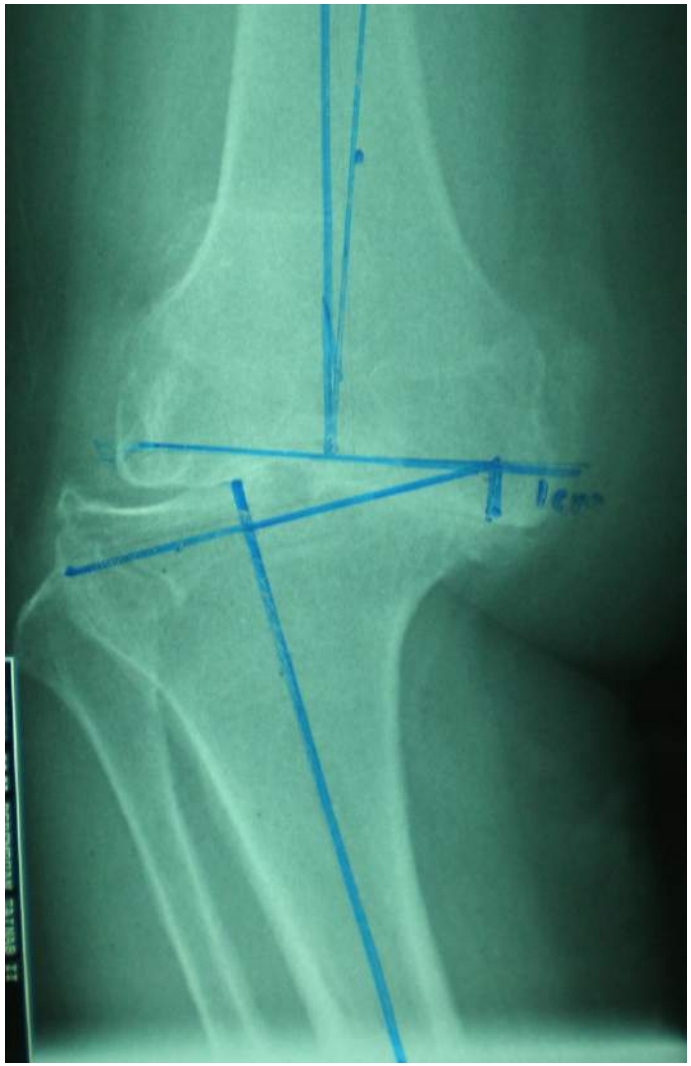

Total Knee Implant

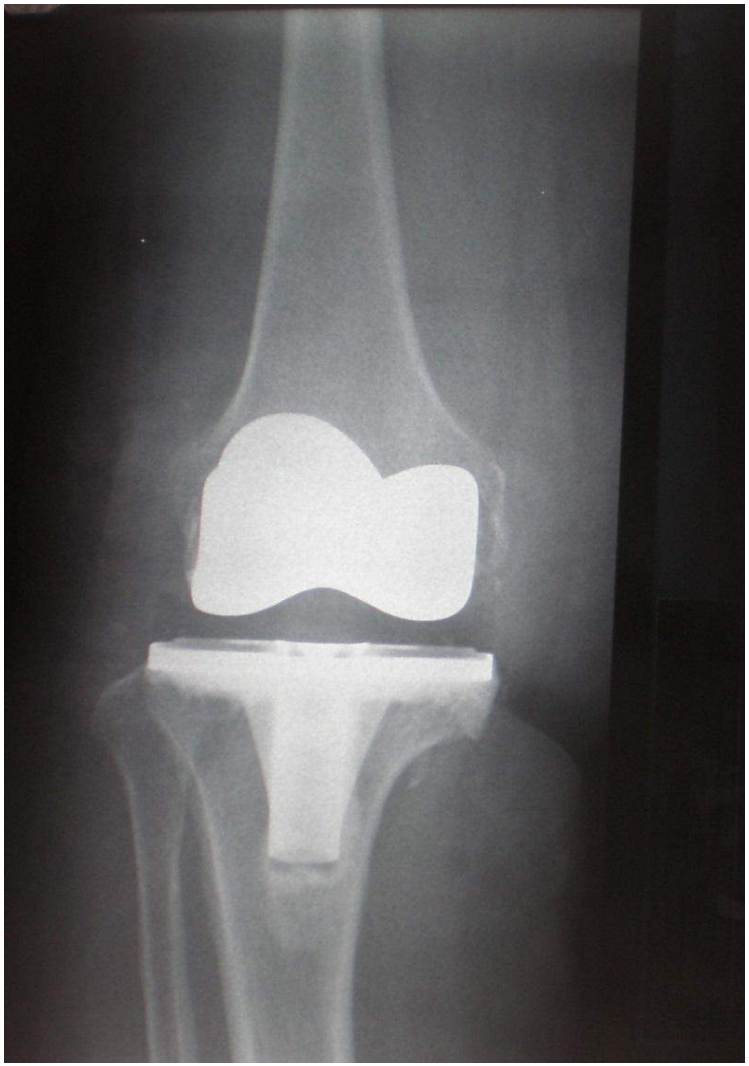
TOTAL KNEE REPLACEMENT-1



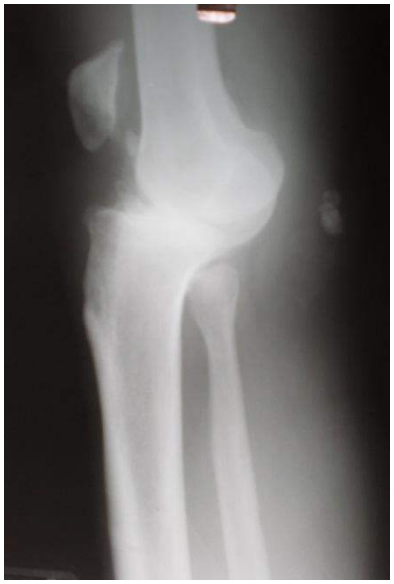


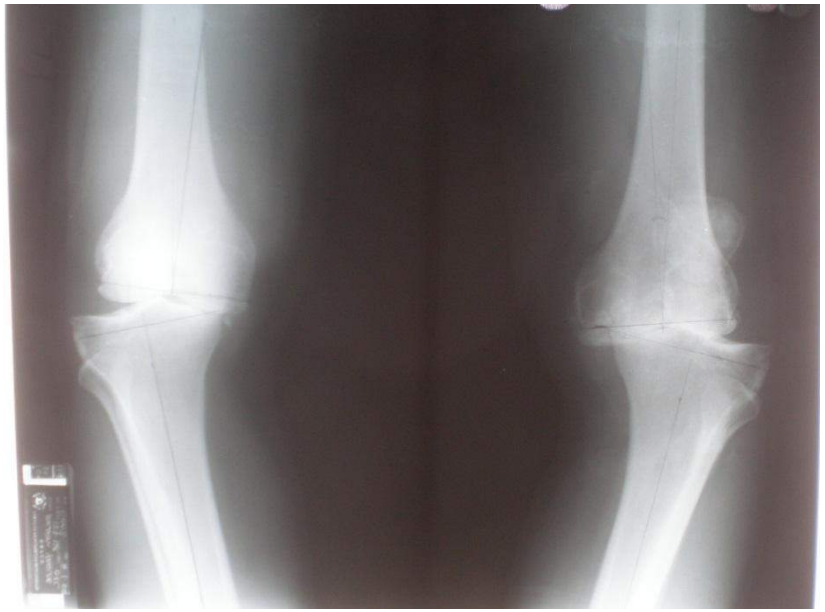
Total Knee Replacement-2

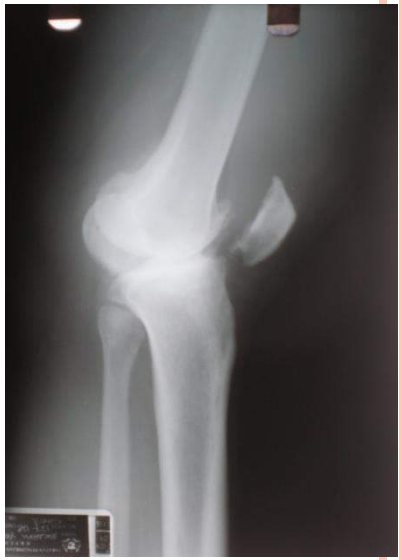


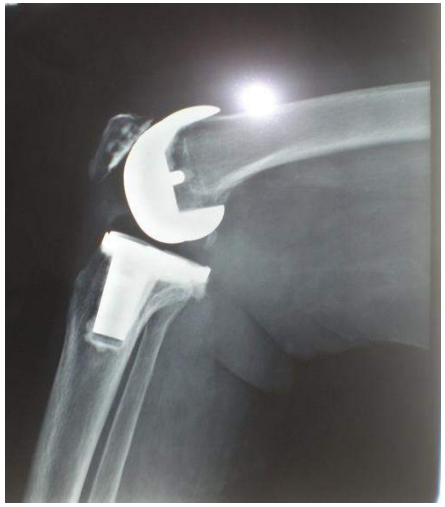


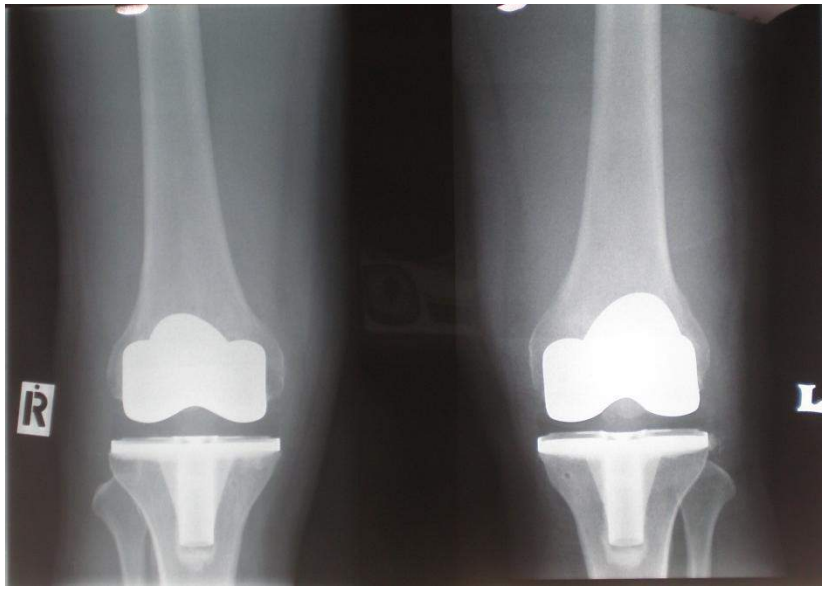
Stable & Functional Knee Joints

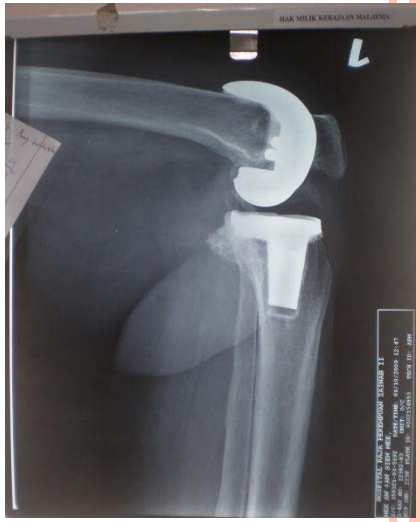




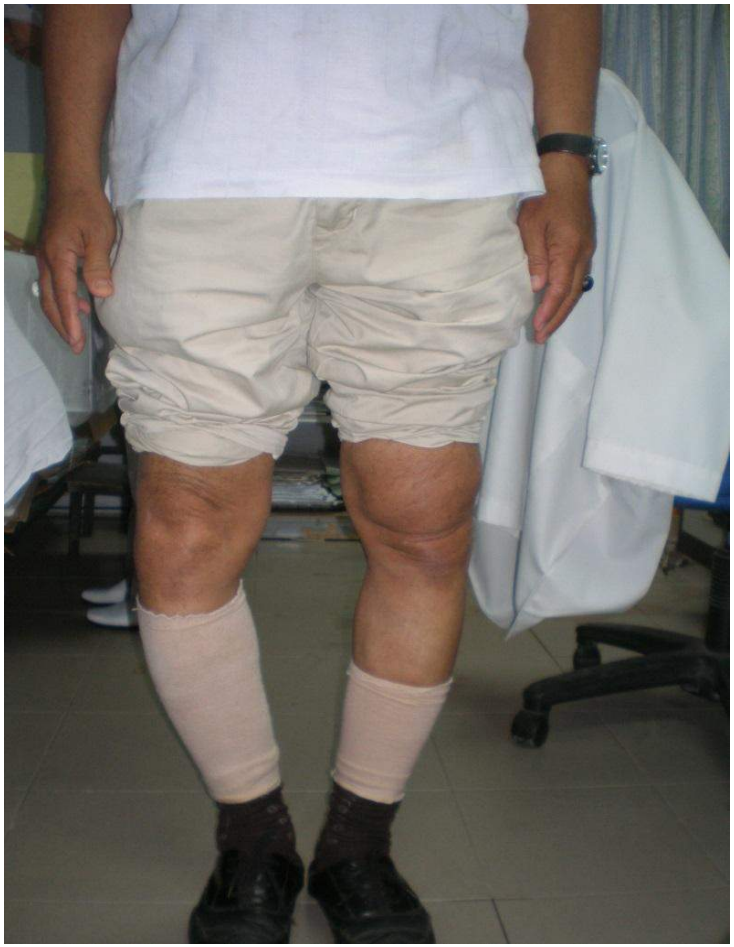


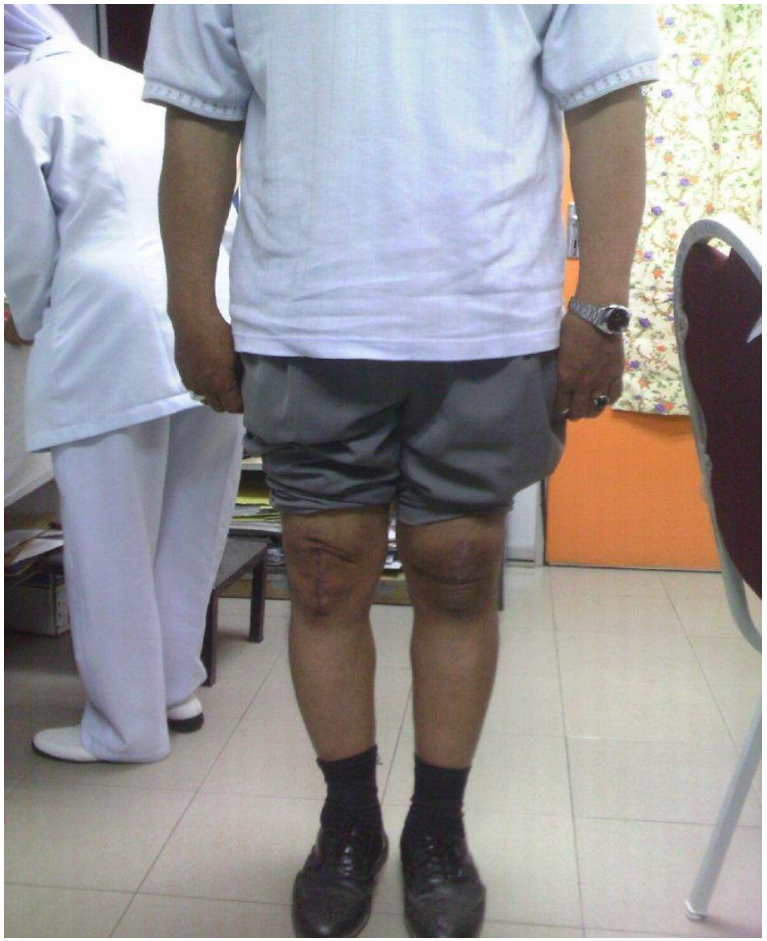






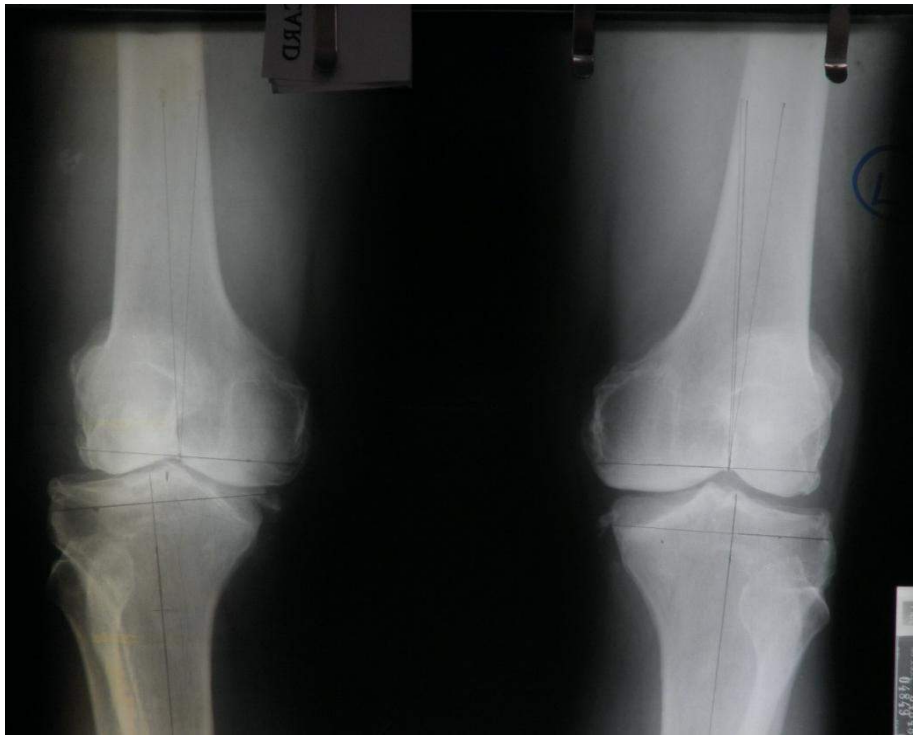
Correction of Deformity-1



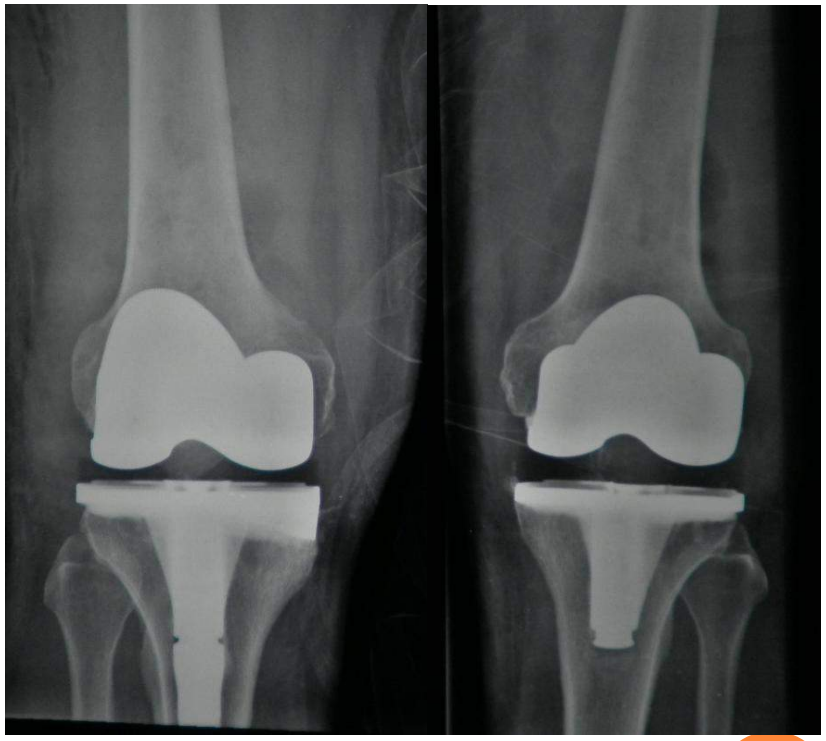


Total Knee Replacement (TKR)

Before operation

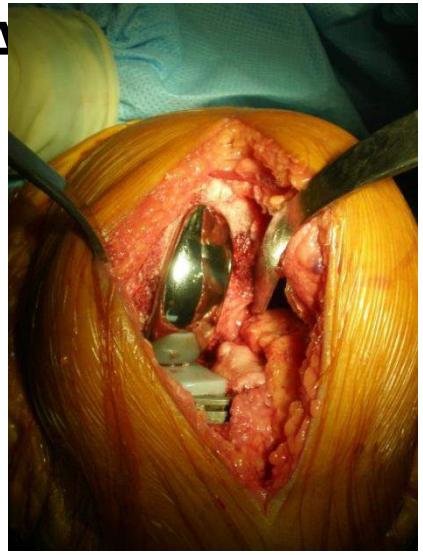


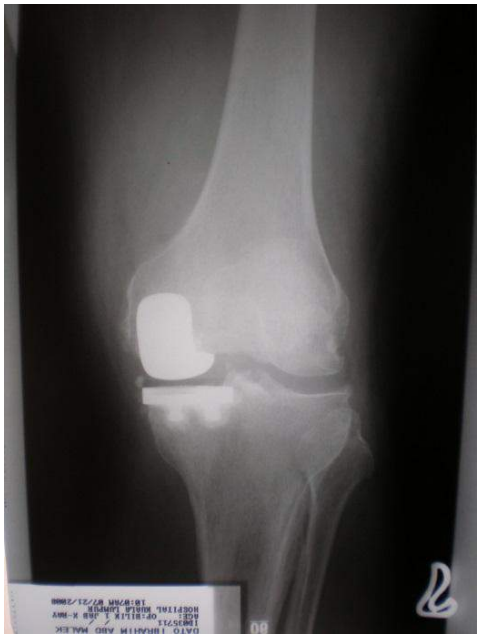
After operation



Unicompartmental Knee Repla

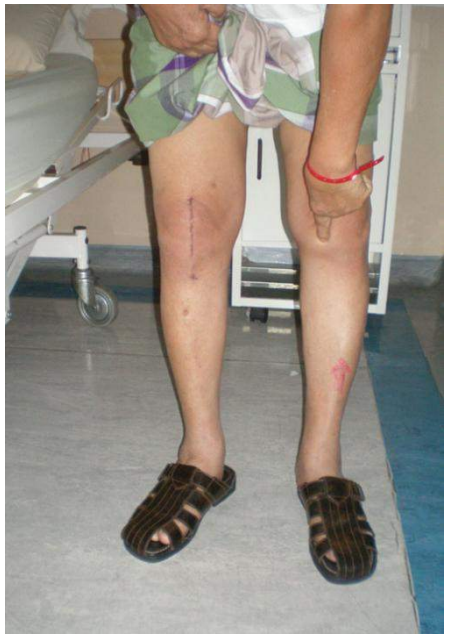
- Advantages:
  - Better ROM
  - More normal kinemetics
  - Proprioception
  - More rapid recovery (MIS)
  - ↓ Cost





Unicompartmental Knee Replacement-2

- Unicompartmental OA
- Intact contralateral compartment
- Localised pain
- Intact ACL & PCL
- Correctable deformity <10
- ROM >105



- Survival at 10 years is 85%

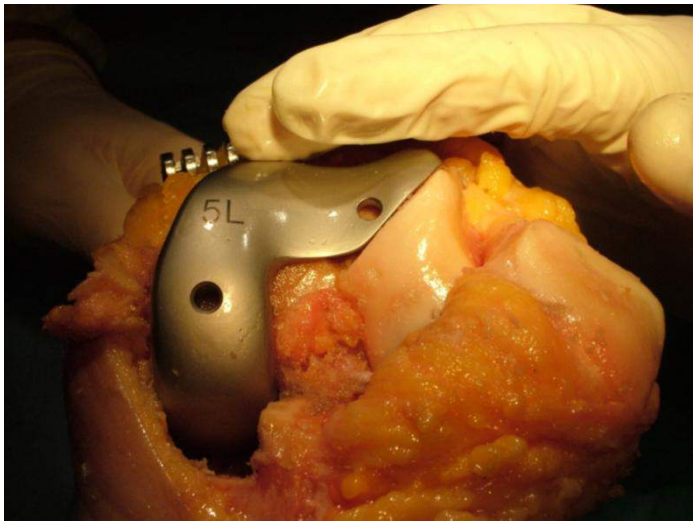
Spahn G et al., 2013, level I; Singapore MoH, 2007

Bicompartmental Knee Arthroplasty-1

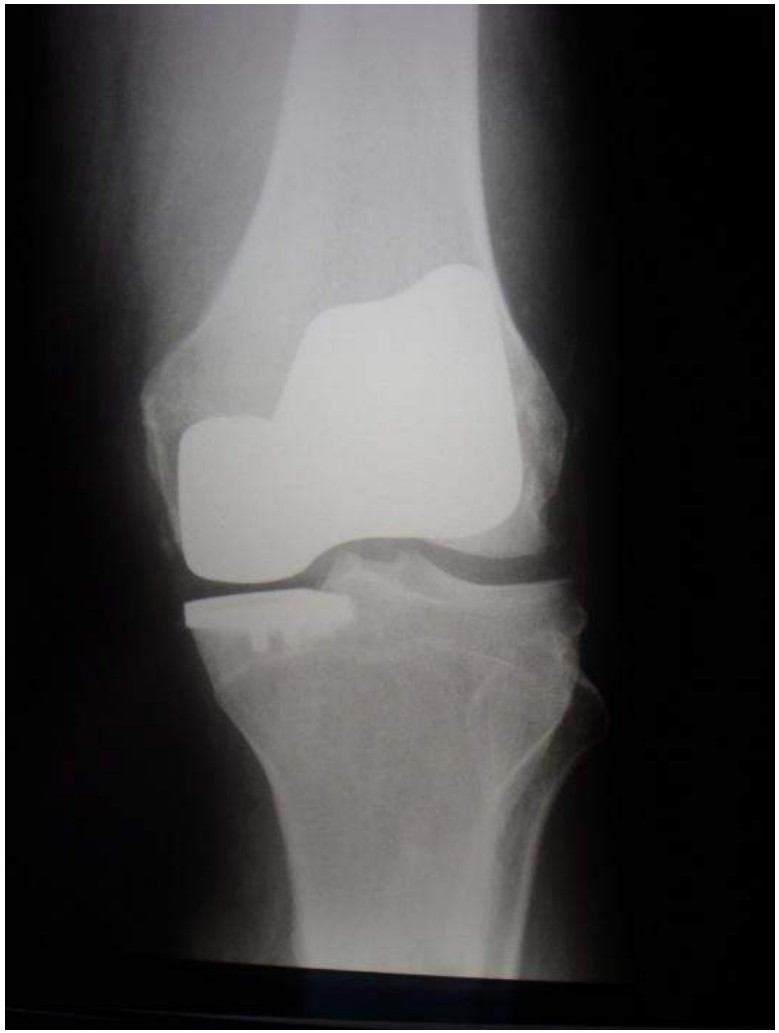
- Indications:
  - Relatively young patient with patelofemoral knee OA + medial or lateral compartment OA

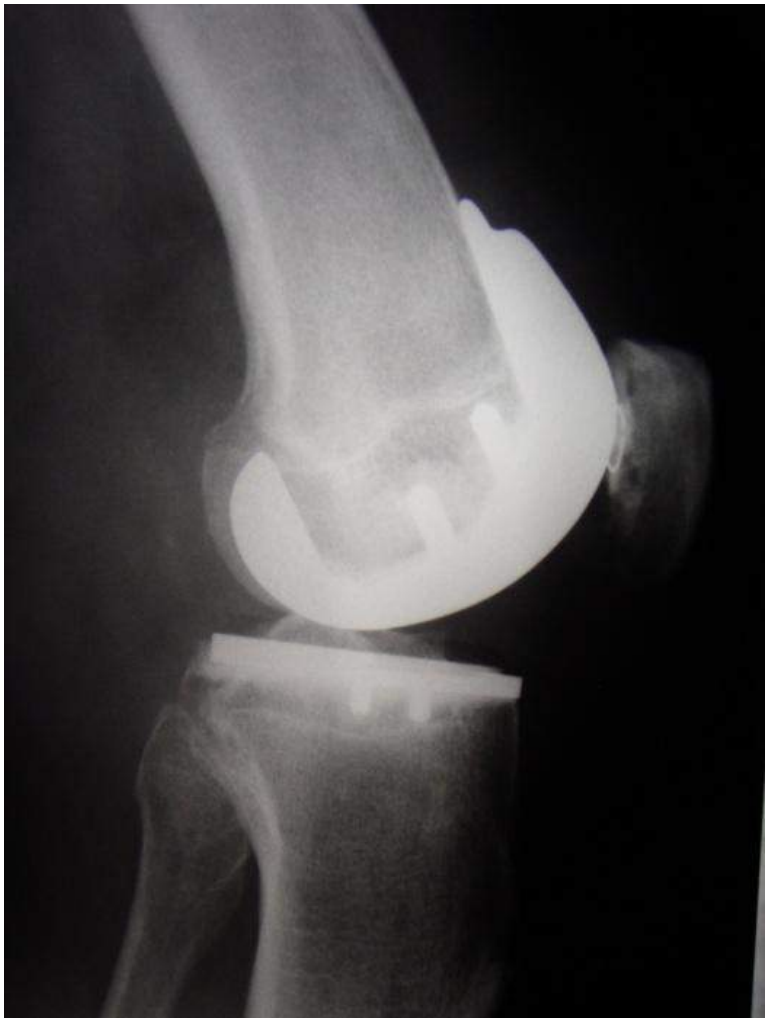
Bicompartmental Knee Arthroplasty-2

- Save both cruciate ligament
- Advantages:
  - Offer a degree of bone preservation
  - Kinemetics
  - ROM & proprioception



Bicompartmental Knee Arthroplasty-3

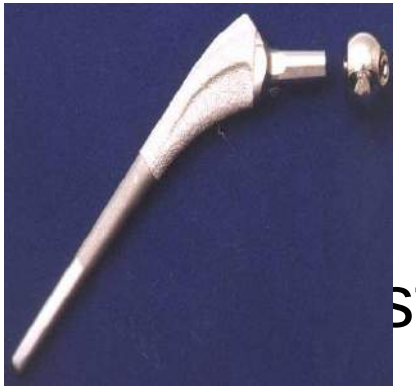




Hip Arthroplasty

- Hemiarthroplasty
  - Thompson
  - Austin Moore
- Bipolar hemiarthroplasty
- Total hip arthroplasty (THR)

Total Hip Replacement (THR)-1



- Indication:
  - Similar with TKR
- 80% of THR in Canadian stry is due to OA.

  Canadian Institute for Health Information, 2009, level III
- With the advancement of implant design, metallurgy & surgical techniques, THR is also indicated in younger patients with severe hip OA (1^0 or 2^0).

Total Hip Replacement (THR)-1

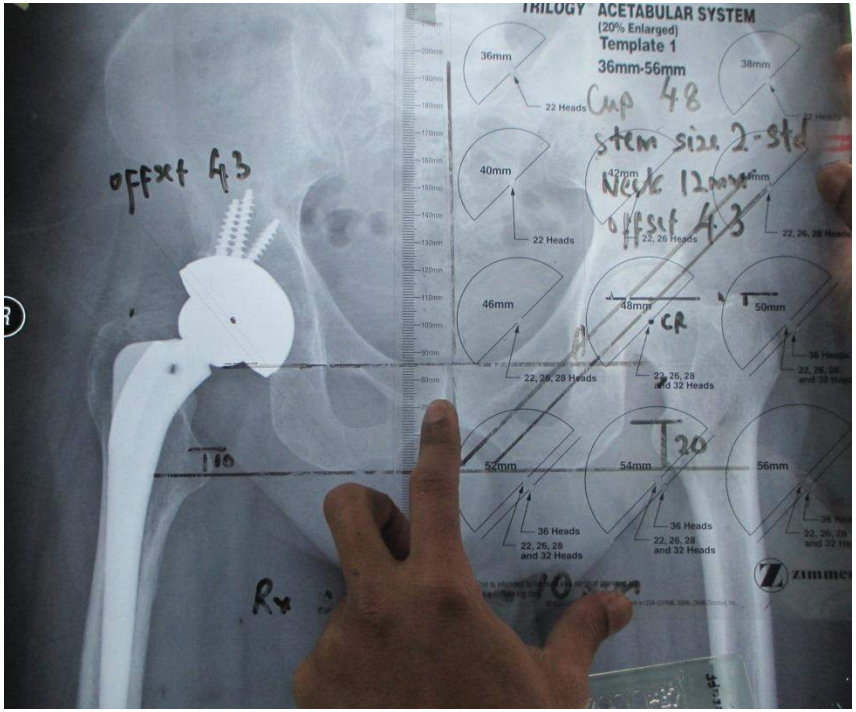
- Types of THR
  - Cemented
  - Uncemented
  - Hybride
  - Reverse hybride

- Types of material for articulation
  - Metal on PE
  - Metal on ceramic
  - Ceramic on ceramic

PRE-OPERATIVE PLANNING

…. an essential ingredients for a successful THR….

- To put the implant as to restore biomechanics of hip joints. This will:-
  - improve function
  - reduce wear
  - reduce aseptic loosening



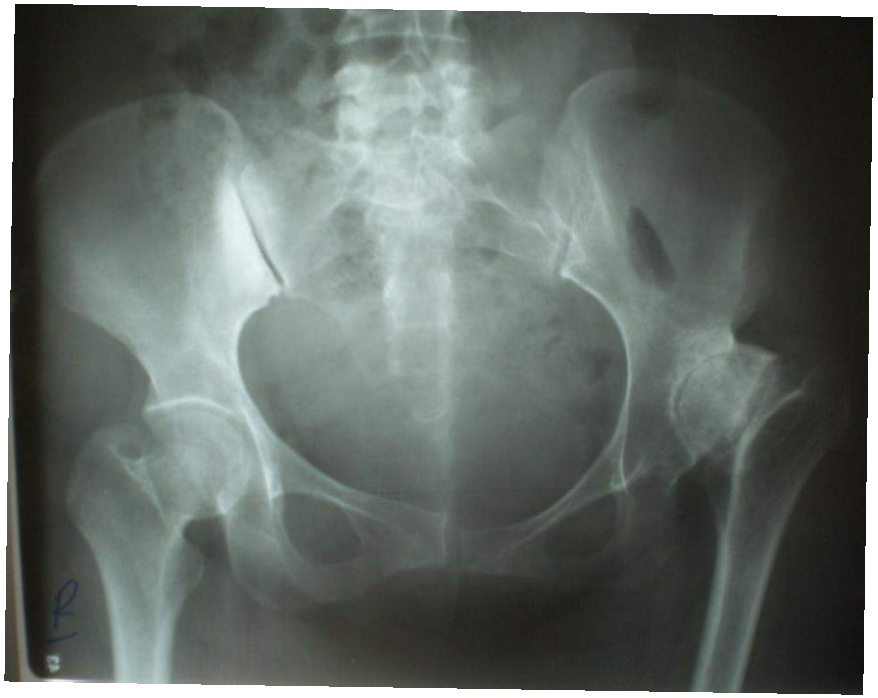
Charnley J, Springer-verlag 1979

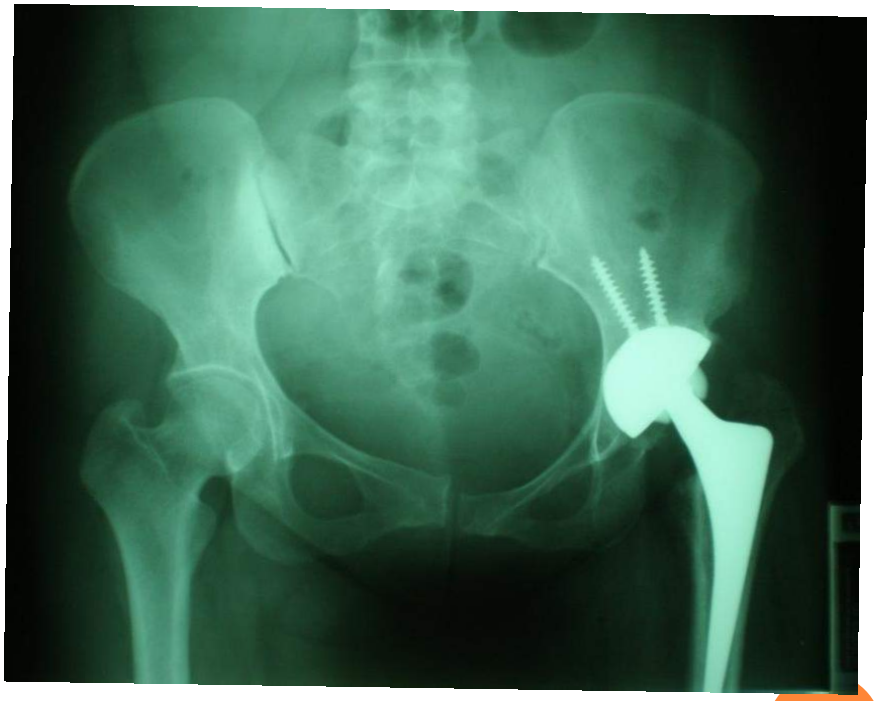
Salkalkala DP. Clin Orthop;

388:125- 134, 2001

Total Hip Replacement (THR)-2

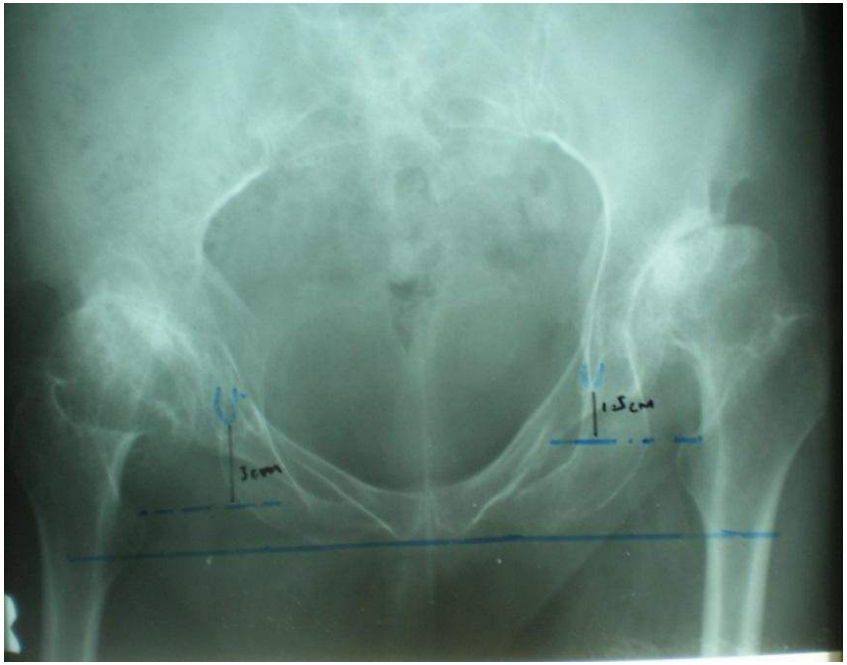
Unilateral THR for Unilateral OA

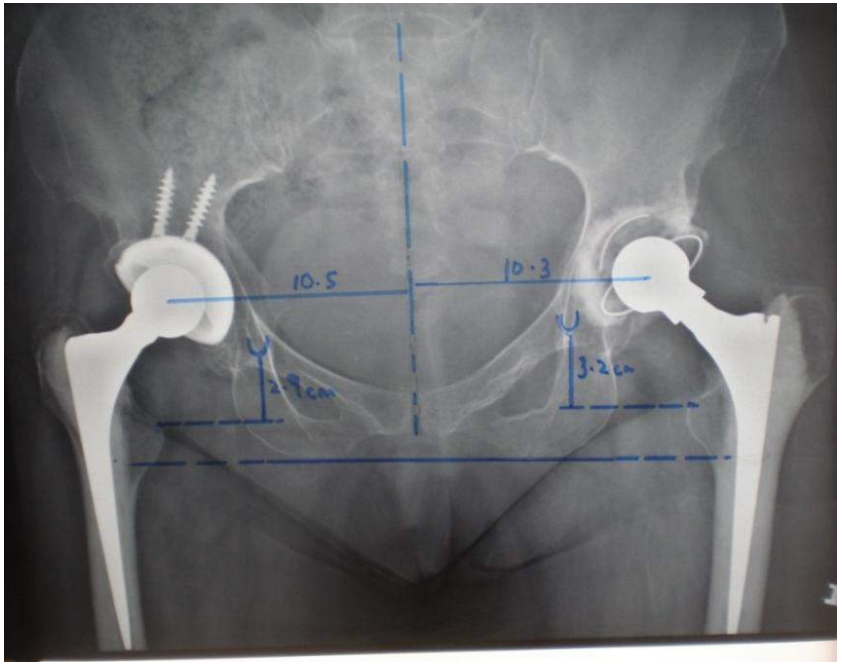




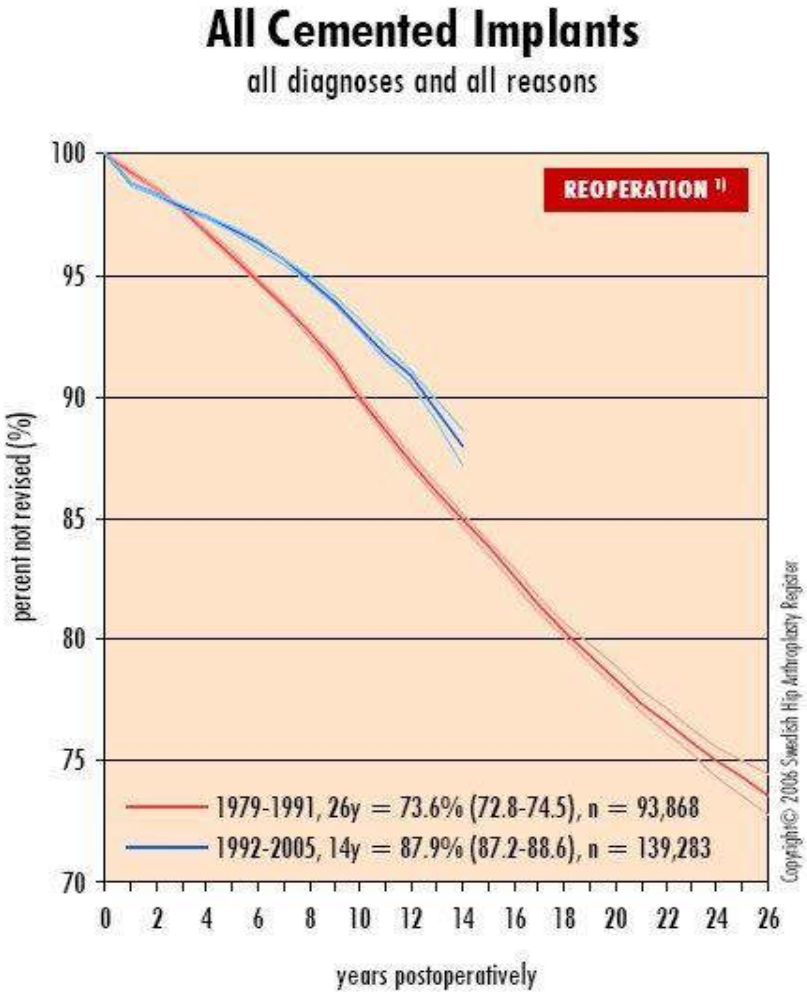
Total Hip Replacement (THR)-3

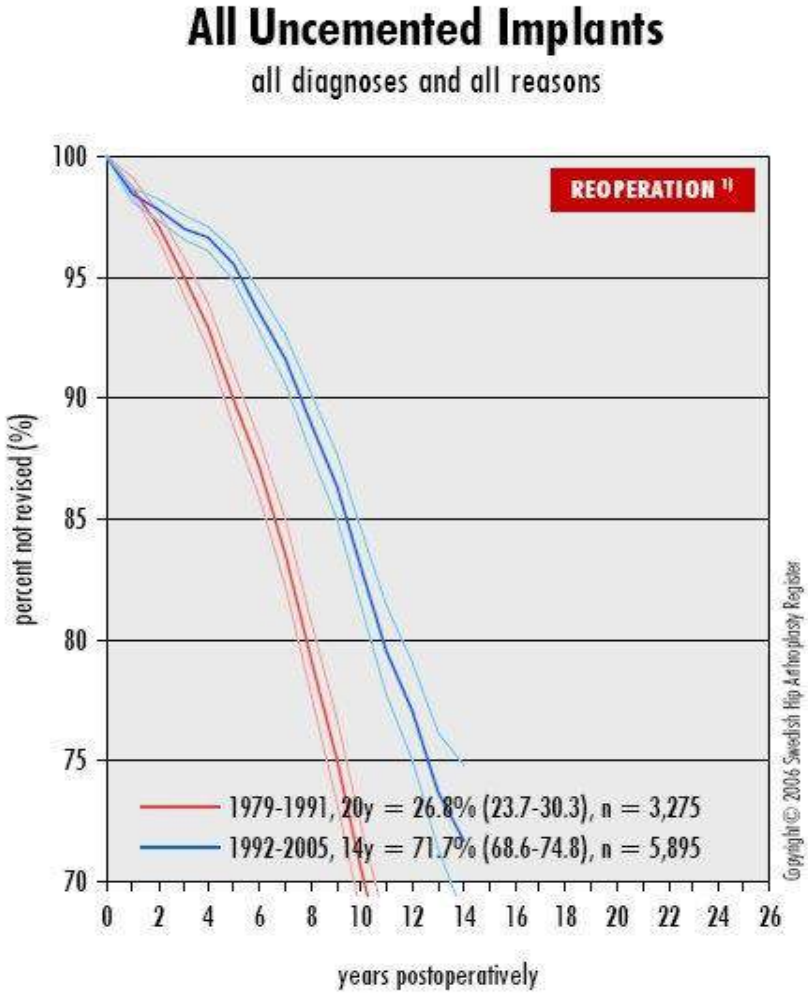
Bilateral THR



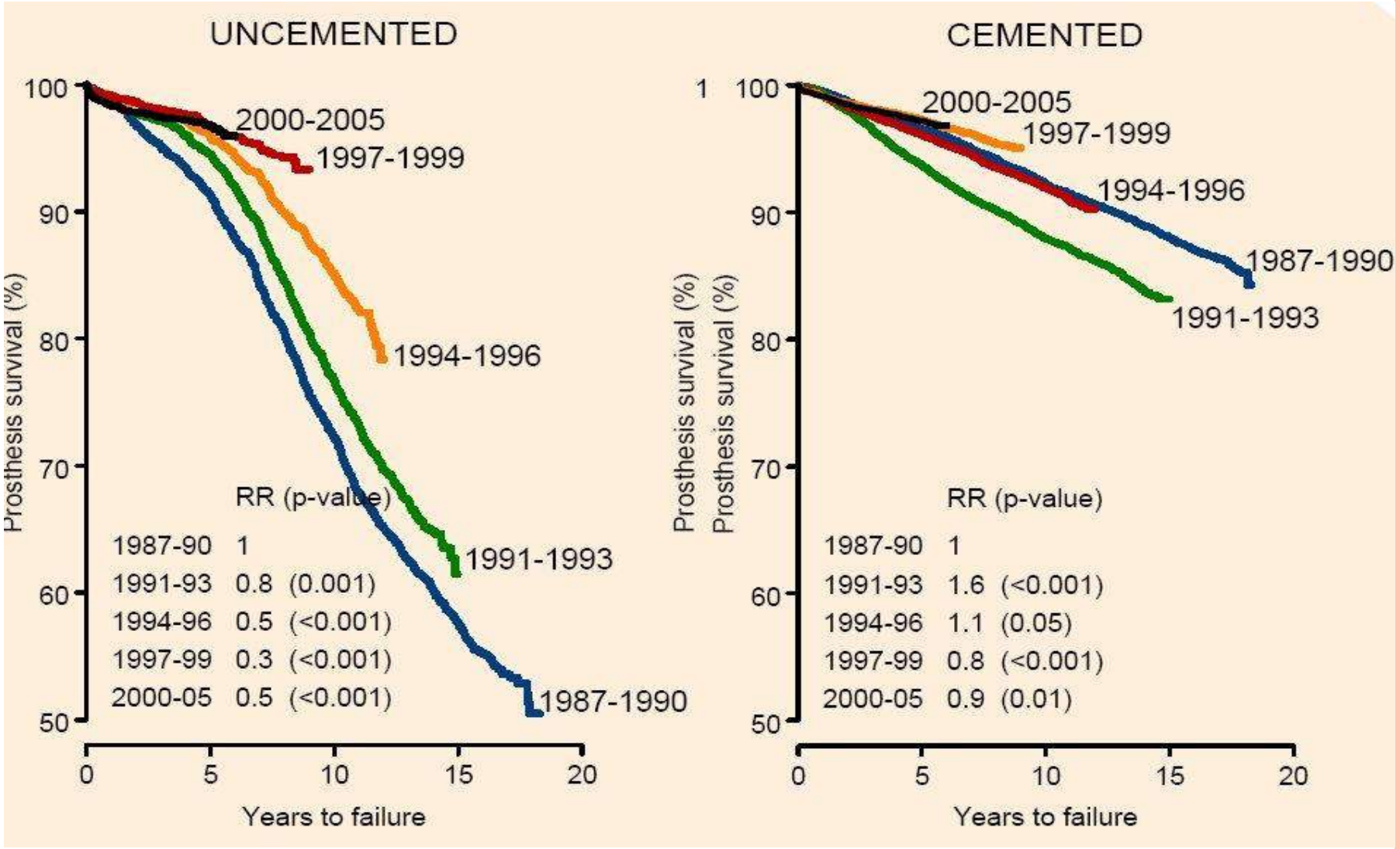


How long implant can last?
Swedish Hip Registry



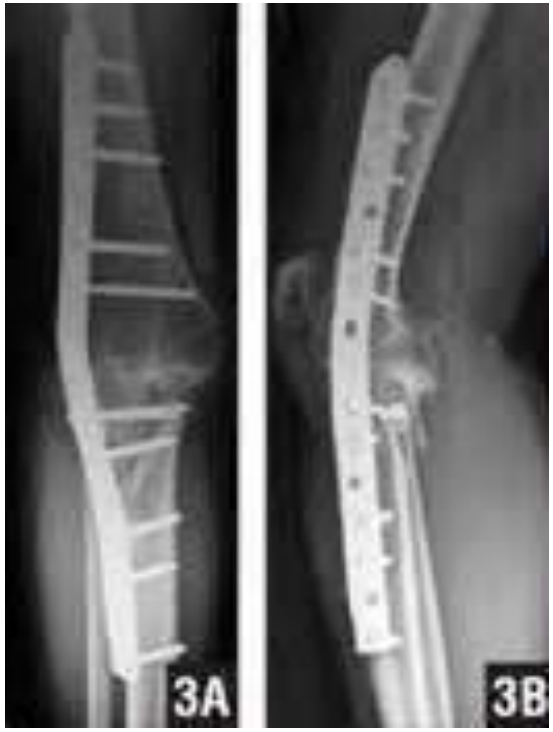


How long implant can last
Swedish Hip Registry



Joint Arthrodesis-1

- Aim
  - To fuse the diseased joint in optimal position
  - Originally used for TB joint in pre-antibiotic era



JOINT ARTHRODESIS-2

Indications:

- Young active labourer with unilateral painful OA
- Severe OA with combined ligamentous injury
- Uncontrolled septic arthritis & complete joint destruction
- Failed and/or infected arthroplasty

Advantages:

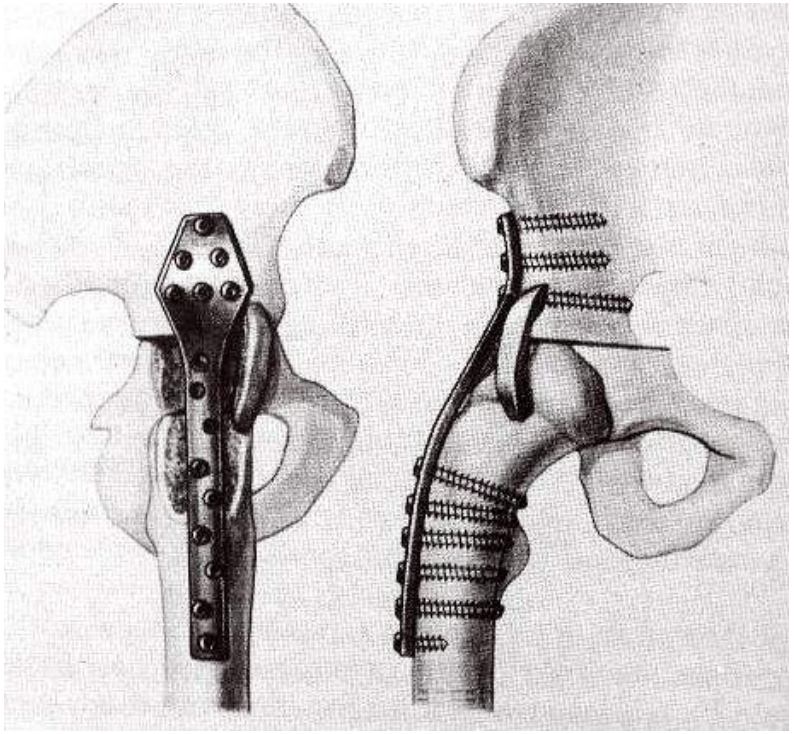
- Stable pain free knee allowing long-term ambulation

Disadvantages:

- Stiff joint
- Abnormal gait after surgery
- Late back pain
- Conversion to TKR or THR give unpredictable result

JOINT ARTHRODESIS-3

- Increase in energy expenditure during ambulation of 30%



Recommendation 15

- Arthroscopic lavage and debridement should not be offered as a treatment in osteoarthritis (OA) of the knee except in selected conditions*. **(Grade A)**
- Joint Replacement should be offered to patients with severe OA. **(Grade A)**

Recent Advances

a. Intra-articular stem cells

- MaHTAS TR - limited evidence on benefits in articular cartilage repair

  Health Technology Assessment Section (MaHTAS), 2013

b. Autologous Chondrocytes Implantation

- Lack of evidence to be used in treatment of 1^0 OA

c. Platelet Rich Plasma

- Preliminary short term result showed some benefit in early OA. No further improvement after 6 months.

  Spakova T et al., 2012, level III; Kon E et al., 2010, level II-2

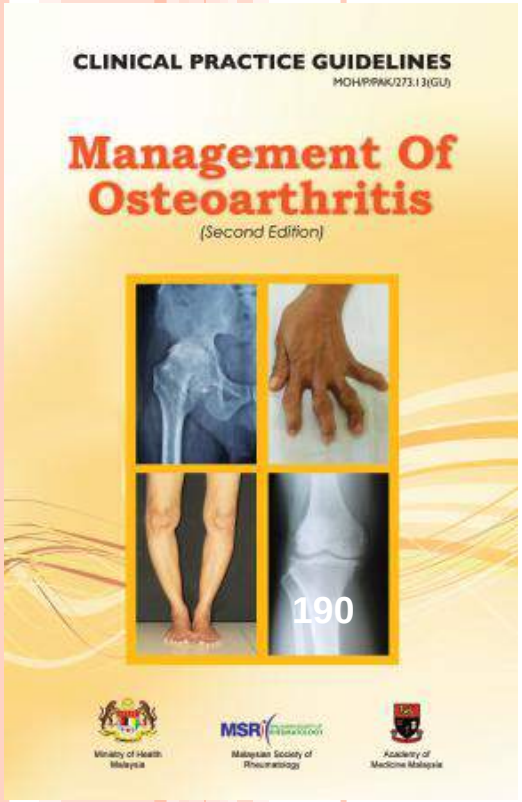
Due to a lack of available evidence, the CPG is unable to recommend the use of intra-articular stem cells, autologous chondrocyte implantation or platelet-rich plasma in the treatment of osteoarthritis.

Referral

Recommendation 16

- Referral of osteoarthritis cases to either rheumatology or orthopaedic clinic should provide the following information:-
  - Diagnosis
  - Severity and its impact on activity of daily living
  - Co-morbidities that might require further medical assessment
  - Relevant investigation results and current medications **(Grade C)**

Thank You



TRAINING OF CORE TRAINERS – CASE STUDY 1

by

Dr. Habibah Mohamed Yusoof
Consultant Rheumatologist, Hospital Selayang
Dr. Rosaida Hj. Mohd. Said
Consultant Gastroenterologist, Hospital Ampang &
Dr. Norhayati Hussein
Rehabilitation Physician, HRC

History

- Mrs. SH, 65 year-old lady
- Food caterer
- Leads a sedentary lifestyle, poor dietary habits
- Overweight
- PMH: DM, Hypertension for 7 years

- Chief complain: bilateral knee joint pain past 1 year

Question 1

- What further questions should you ask?
- What are relevant risk factors for her presenting medical problem?

ANSWER 1

- Further questions to ask:
  - Pain : use related
    : gets worse during the day
    : minimal morning stiffness (<30 min)
    : after inactivity
  - Decrease range of motion of knee joints
- Risk factors for OA:

RISK FACTORS

Non-modifiable	Modifiable
• Advancing age • Female • Genetic • Heberden's nodes in hand OA	• Body mass index (BMI) >25 kg/m^2 • Previous knee injury • Joint malalignment

Question 2

- What are the relevant clinical findings that will aid in making the diagnosis?

Answer 2

- Relevant clinical findings:
  - General examination
    - Body weight, Body Mass Index (patients's BMI=31)
  - Joint examination
    - Joint instability
    - Bony enlargement
    - Restricted movement
    - Crepitus
    - Variable swelling &/or instability

Diagnosis

- A clinical diagnosis of OA is supported by the presence of:
  - typical symptoms
  - physical findings
  - ±laboratory results
  - imaging features

Classic clinical criteria

- Presence of knee pain plus at least 3 of the following 6 clinical characteristics:
  - Greater than 50 years of age
  - Morning stiffness for <30 minutes
  - Crepitus on active motion of the knee
  - Bony tenderness
  - Bony enlargement
  - No palpable warmth

(sensitivity & specificity for OA of 95% & 69% respectively)

The Diagnostic Criteria for Classification of Idiopathic OA of the Knee Based on the American College of Rheumatology 1986 Criteria

c. Knee OA

Diagnosis / Criteria	Clinical and laboratory	Clinical and radiographic	Clinical only	
Must have	Knee pain + At least 5 of 9 of the following	Knee pain + Osteophytes on x-ray + At least 1 of 3 of the following	Knee pain + At least 3 of 6 of the following	
1	Age >50 years	Age >50 years	Age >50 years	
2	Stiffness <30 min	Stiffness <30 min	Stiffness <30 min	
3	Crepitus	Crepitus	Crepitus	
4	Bony tenderness		Bony tenderness	
5	Bony enlargement		Bony enlargement	
6	No palpable warmth		No palpable warmth	
7	ESR <40			
8	RF <1: 40			
9	SF OA			
Sensitivity **Specificity**	92% 75%	91% 86%	95% 69% (if 3/6)	84% 89% (if 4/6)

ESR=erythrocyte sedimentation rate RF=rheumatoid factor

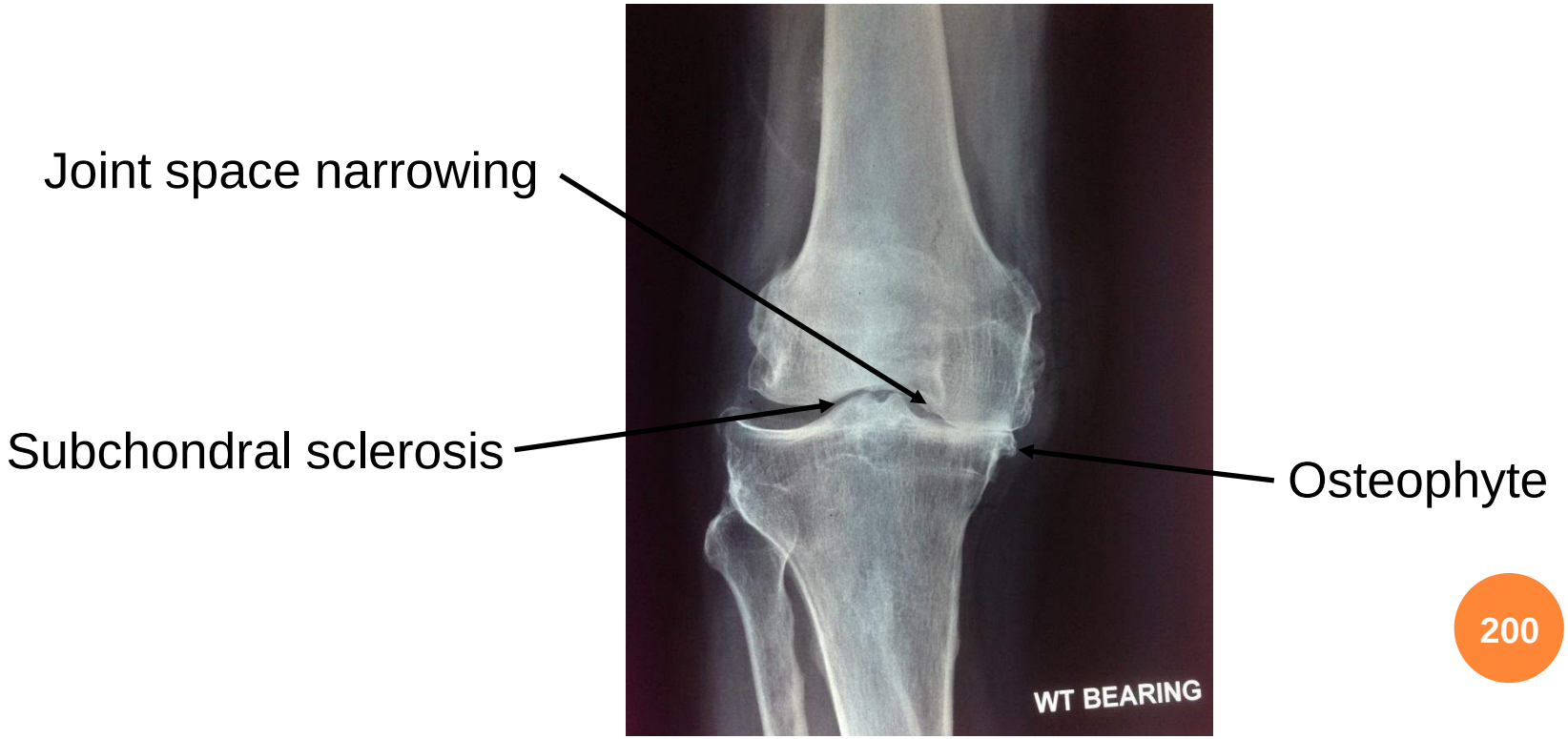
SF OA=synovial fluid signs of OA (clear, viscous or white blood cell count <2,000/mm^3)

Question 3

- Which diagnostic studies are appropriate?

Answer 3

- Laboratory tests in knee OA:
  - No specific laboratory tests for knee OA
  - To rule out other causes
- Radiographic features in knee OA:



KELLGREN-LAWRENCE GRADING SYSTEM

The Kellgren-Lawrence grading system is the most widely used radiological classification to identify and grade OA (refer to **Table 5**).

Table 5. Kellgren-Lawrence Grading System

Grade	Description
Grade I	Doubtful narrowing of the joint space, possible osteophytic lipping
Grade II	Definite osteophytes, possible narrowing of the joint space
Grade III	Moderate multiple osteophytes, definite joint space narrowing, some sclerosis, possible deformity of bone ends
Grade IV	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony end deformity.

Adapted: KELLGREN JH, LAWRENCE JS.Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957 Dec; 16(4):494-502.

European League Against Rheumatism (EULAR)

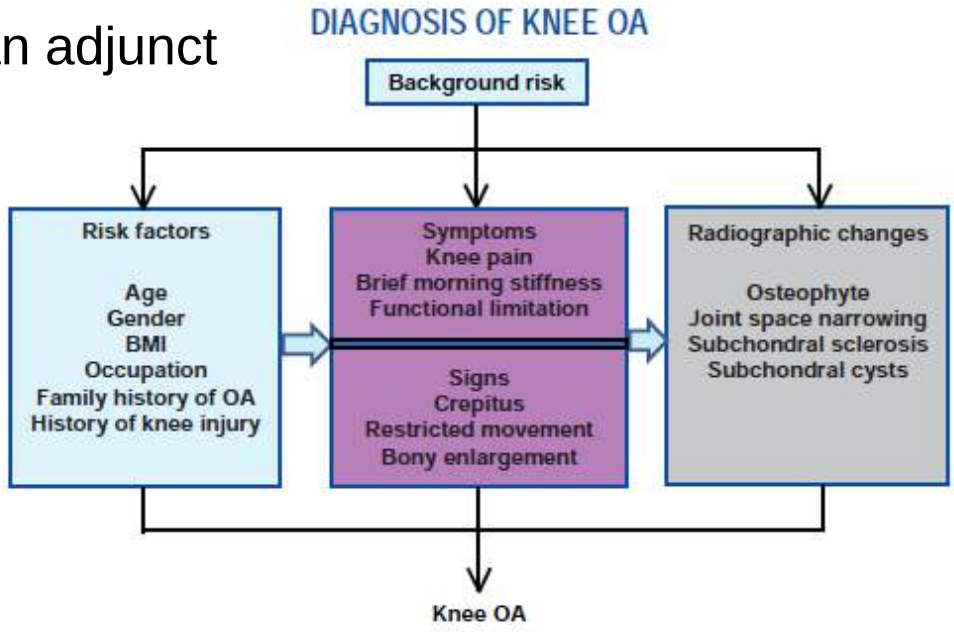
A. Background risk (the population prevalence of knee OA)

B. Risk factors (such as age, gender, BMI & occupation)

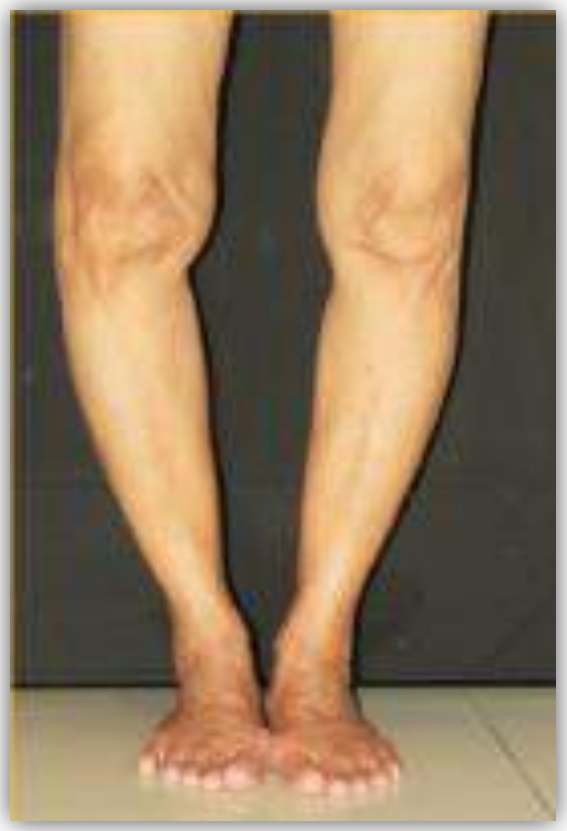
C. Symptoms (persistent knee pain, brief morning stiffness & functional limitation)

D. Physical examination (crepitus, restricted movement & bony enlargement)

E. Plain radiographs as an adjunct



Management of Knee OA

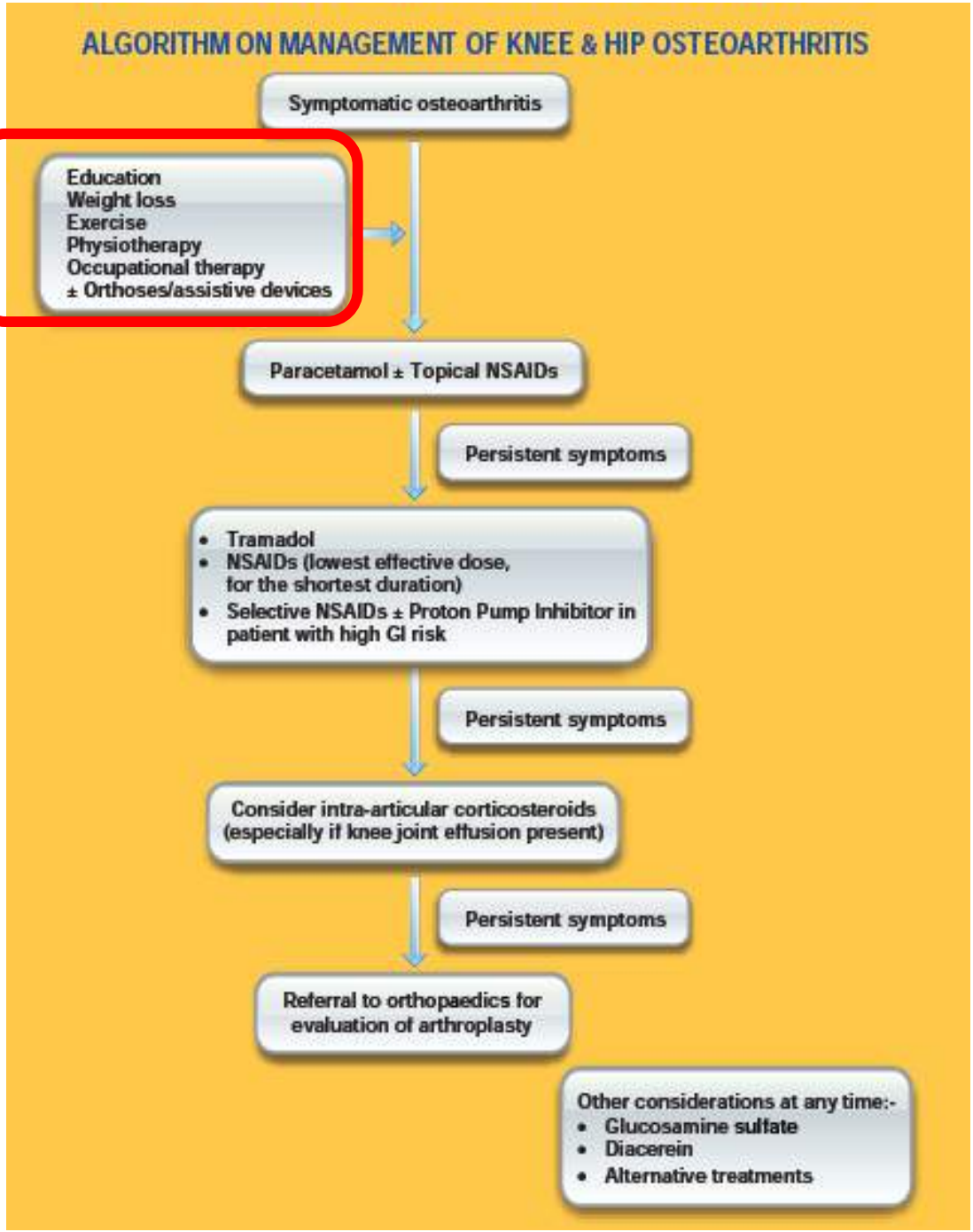


QUESTION 4

- “…Dr…saya tak suka makan ubat…Ada cara lain tak…’

- Mrs. SH opts not to not take any medications for her bilateral knee pain. She prefers to practice non-pharmacological approach.

- What non-pharmacological treatment approaches can you offer to the patient?


ALGORITHM ON MANAGEMENT OF KNEE & HIP OSTEOARTHRITIS
Symptomatic osteoarthritis
Education
Weight loss
Exercise
Physiotherapy
Occupational therapy
± Orthoses/assistive devices
Paracetamol ± Topical NSAIDs
Persistent symptoms
Tramadol
NSAIDs (lowest effective dose, for the shortest duration)
Selective NSAIDs ± Proton Pump Inhibitor in patient with high GI risk
Persistent symptoms
Consider intra-articular corticosteroids (especially if knee joint effusion present)
Persistent symptoms
Referral to orthopaedics for evaluation of arthroplasty
Other considerations at any time:-
Glucosamine sulfate
Diacerein
Alternative treatments

Answer 4

- Non-pharmacological treatment approaches in the management of knee OA is:
  1. Patient education
  2. Lifestyle modification: weight reduction, physical activity
  3. Physiotherapy
  4. Occupational therapy
  5. Orthoses

Patient Education

- Patient education is an important non-pharmacological approach in the management of OA.

- There are various types of patient education programmes & each have to be tailored according to the individual needs, goals & functional capabilities.

Question 5

- What are the important components of patient education in management of OA?

ANSWER 5

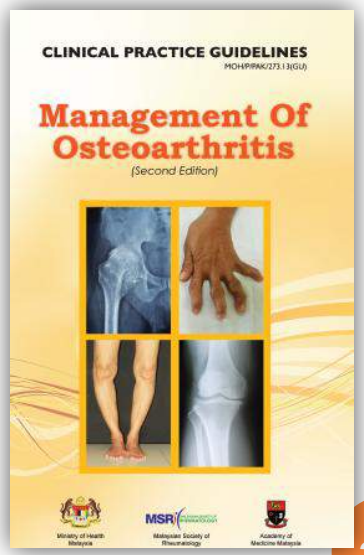
- Patients who have an understanding of the disease tend to cope better & report less pain.

- Components of patient education should include :

1. Information of the diagnosis
2. Nature of the disease
3. Therapeutic options
4. Importance of ongoing patient participation in the disease management

Recommendation 2

- Patient education should form an integral part of osteoarthritis management. (**Grade A**)



Question 6

- What are the main emphasis on lifestyle modification when managing individuals with OA?

ANSWER 6

- Lifestyle modifications involves INITIATING & MAINTAINING lifestyle changes.

- Main emphasis on lifestyle modifications should focus on:
  1. Weight reduction
  2. Physical activity/exercise

Question 7

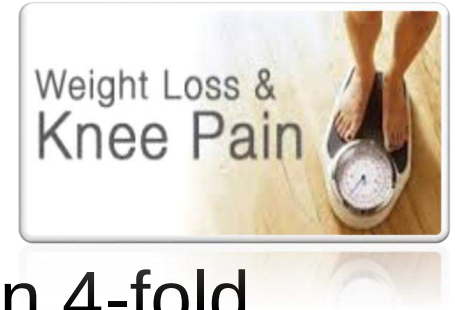
- The patient has been advised to reduce her weight to a better desired BMI.

- What is the impact of weight loss on knee OA?

Answer 7

- Obesity is an important modifiable risk factor for the development & progression of knee OA.

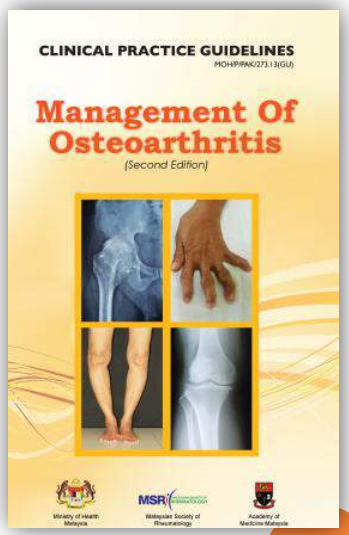
- Weight reduction is beneficial in:
  - Pain reduction
  - Improvement of function



- Each unit of weight loss will result in 4-fold reduction in the load exerted on the knee per step during daily activities.

Recommendation 3

- Weight reduction should be emphasised in the management of patients with knee osteoarthritis and who are overweight. **(Grade A)**



QUESTION 8

- *“ ...Dr…macamana saya nak bersukan bila lutut ini asyik sakit….baru gerak sikit, lutut saya dah jadi sakit….”*

- The patient demonstrates obvious displeasure upon hearing your suggestion that she should exercise.

- What are the benefits of physical activity on individuals with knee OA?
- How can you improve her adherence to physical activity?

Answer 8

- Emphasize to the patient that appropriate exercise is effective in reducing knee OA.
- Exercise will need to be tailored accordingly.
- Exercise frequency, intensity, duration & rate of progression varies.

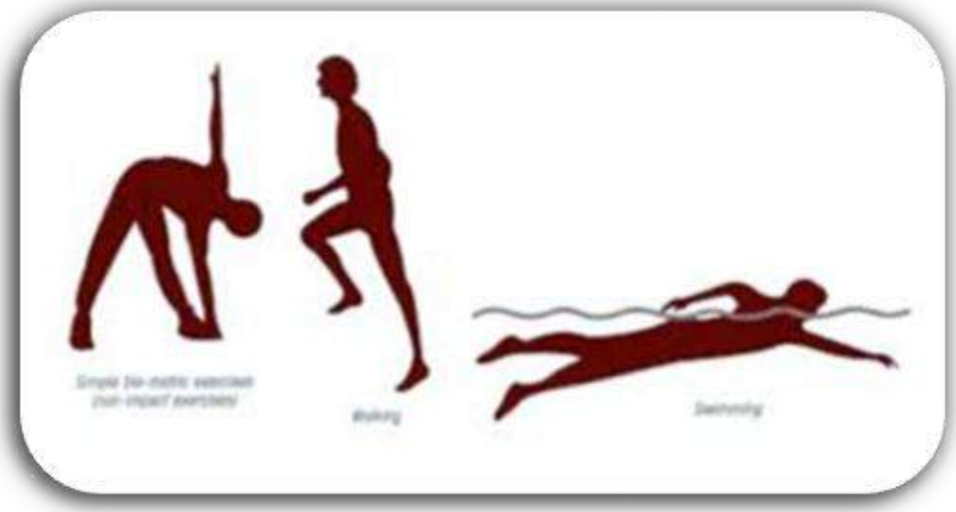
Answer 8

- Adherence is important in ensuring sustainable lifestyle modifications.

- Strategies to improve adherence to physical activity:-
  - Individualised exercise programme
  - Graded type activity
  - Feedback on progress
  - Positive reinforcement
  - Incorporate of problem solving skills

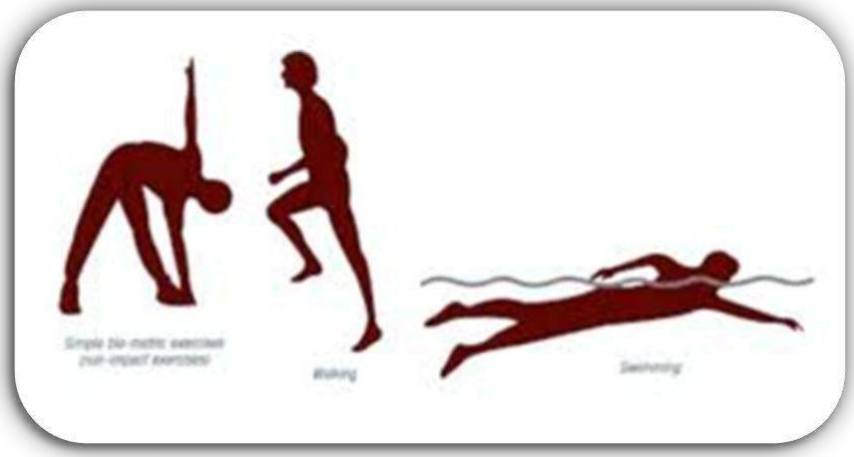
QUESTION 9

- What are the physiotherapy interventions that can be offered as part of the non-pharmacological management of OA?



Answer 9

- These interventions are proven to be beneficial to individuals with OA:
  - Land-based Exercise
  - Aquatic Exercise
  - Thermotherapy



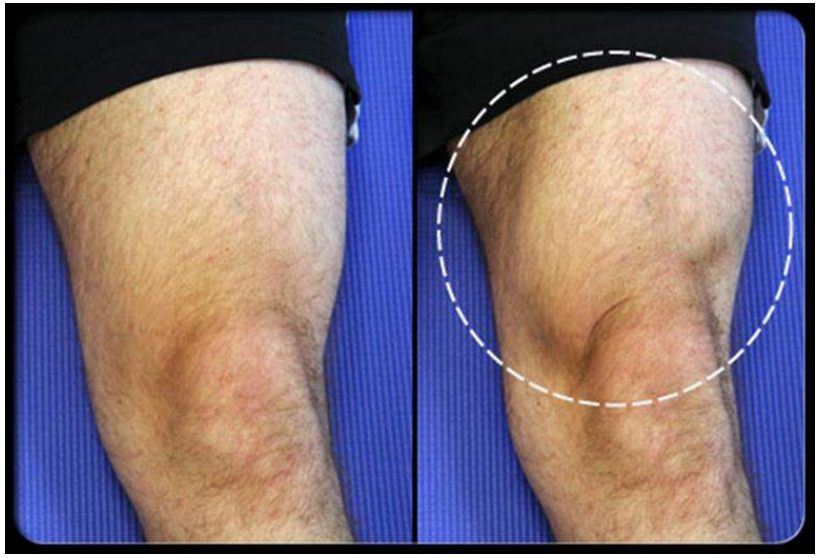
Question 10

- What types of land-based exercise are beneficial in management of OA?

- What are the benefits of land-based exercise for the patient with knee OA?

Answer 10

- Land-based exercises include:
  - Flexibility exercise: Range of movement (ROM), stretching exercises
  - Muscle strengthening: Quadriceps strengthening
  - Low impact aerobic exercises e.g. walking, bicycling, etc.



QUADRICEPS STRENGTHENING EXERCISE

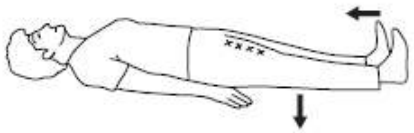


Figure A

Lie flat in bed with your legs straight. Bend your ankles & push the back of your knees down firmly against the bed. Hold for 5 seconds, then return to the original position & relax.

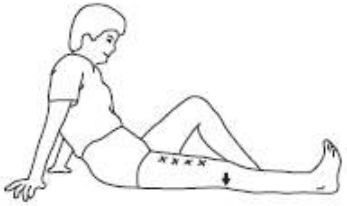


Figure B

Sit on a firm flat surface with one leg bend & keep the other leg straight. Bend your ankle & push the back of your knees down firmly against the bed. Hold for 5 seconds, then return to the original position & relax.

Figure C

Lie flat in bed with a rolled towel/small cushion under your knee. Bend your ankle & push the back of your knee down firmly against the rolled towel/ small cushion (keep knee on the towel/ cushion). Hold for 5 seconds, then return to the original position & relax.

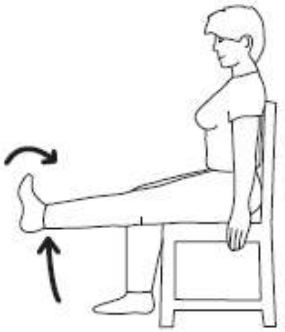


Figure D

Sit on a chair. Straighten your knee & bend your ankle. Hold for 5 seconds, then return to the original position & relax.

Answer 10

- For a patient with knee OA, land-based exercise has short term benefits in:
  - Reducing pain
  - Improving function

Question 11

- The patient was told by her friend that swimming is good for knee pain relief.

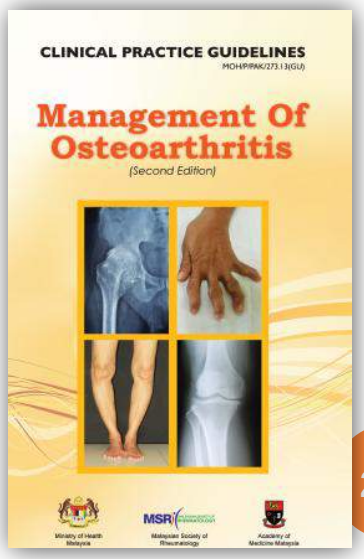
- How does swimming help in the management of OA?

Answer 11

- Aquatic exercise may be advantageous for patients with OA.
- Aquatic exercise have been shown to show benefits in knee & hip OA by:
  - Improvement in pain
  - Improvement in quality of life
- For knee OA, aquatic exercise is better than land-based exercise in reducing knee pain.

Recommendation 4

- Exercise programmes in hip and knee osteoarthritis must be individualised, supervised and done regularly. **(Grade C)**
- Land-based or aquatic exercise may be used for short-term benefit in osteoarthritis. **(Grade A)**



QUESTION 12

- You plan to refer Mrs. SH to the physiotherapist for physical therapy & to the occupational therapist. She asks for the reason for referral to the occupational therapist.

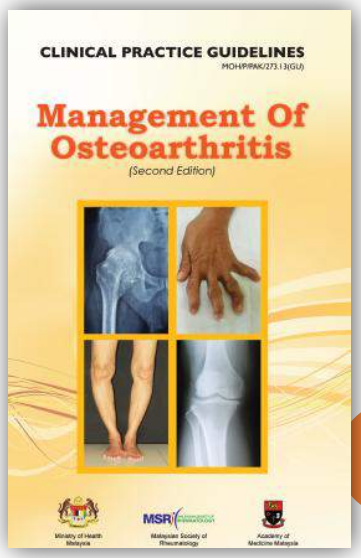
- What is the role of occupational therapy in the management of knee OA?

Answer 12

- Role of occupational therapy in management of OA include:
  - Activity modification including joint protection technique
  - Provision of assistive device e.g. mobility aids
  - Pain control via relaxation technique: Jacobson Relaxation, Guided Imagery Relaxation

Recommendation 5

- Early referral to occupational therapy may be considered for pain relief and improvement in activities of daily living in osteoarthritis. **(Grade A)**



Question 13

- The patient's daughter asks you whether heat packs or ice packs can help to reduce her mother's knee pain.

- What is your advice on the use of heat packs or ice packs?
- Which mode of pain relief will you recommend?

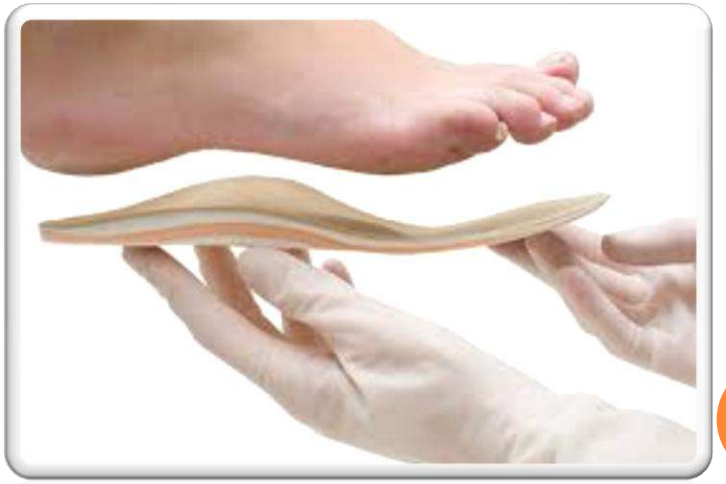
Answer 13

- Thermotherapy is commonly used in physical rehabilitation for OA patients.
- ACR recommended the use of thermal agents for hip & knee OA in combination with exercise supervised by a physiotherapist.
- Cold pack usage does not show a significant effect in pain reduction in knee OA.

Question 14

- Mrs. SH is keen to purchase special insoles or knee braces marketed for knee OA.

- Will orthoses help to reduce pain in knee OA?



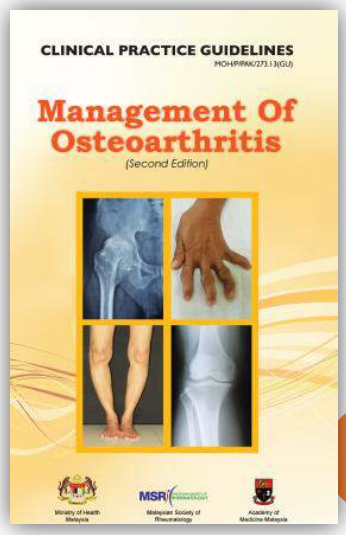
Answer 14

- Walking shoes with neutral, contoured orthoses reduce pain & stiffness, & improve function in knee OA at one year.

- Knee braces for medial, lateral or patella-femoral OA have not been shown to reduce pain, improve function or quality of life, even though they are widely used.

Recommendation 6

- Walking shoes with neutral, contoured orthoses may be offered in:-
  - knee osteoarthritis **(Grade A)**
  - hip osteoarthritis **(Grade C)**
- Knee braces should not be offered in knee osteoarthritis. **(Grade A)**



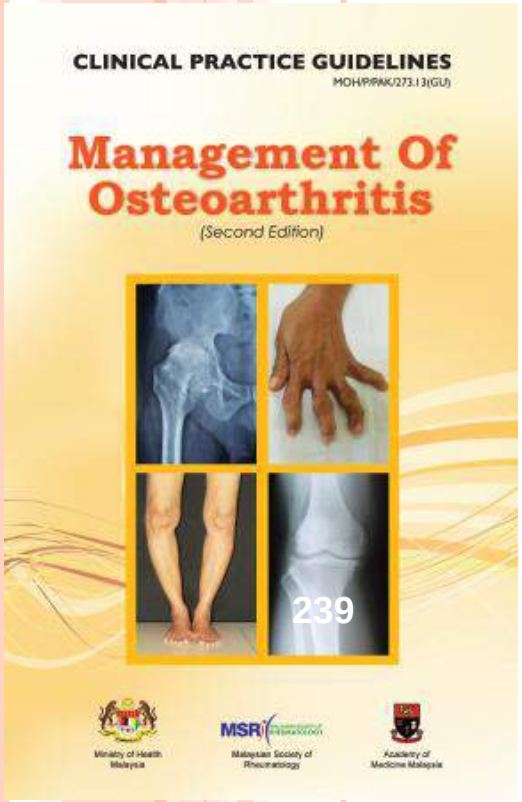
Take Home Messages

- Diagnosis of OA mainly involves evaluating clinical features (symptoms & signs) & supported by radiographic evidence & relevant laboratory results.

- Non-pharmacological approaches are important aspects of management in individuals with OA.

- Non-pharmacological approaches involve patient education, weight loss, exercise, physiotherapy, occupational therapy, orthoses & assistive device.

Thank You



TRAINING OF CORE TRAINERS – CASE STUDY 2

by
Dr. Lau Ing Soo
Consultant Rheumatologist, Hospital Selayang
Dr. Heselynn Hussein
Consultant Rheumatologist, Hospital Putrajaya

Case 1 - History

- A 55 year-old lady
- Presented with with bilateral knee pain
- Diagnosed mild OA of both knees
- Non-pharmacological therapy has been addressed

Question 1

- What oral pharmacological treatment would you consider?

Answer 1

- Paracetamol
  - A mild anaelgesic
  - Superior to placebo in pain relief
  - Less efficacious than NSAIDS for pain
  - Various formulation including sustained release
  - Well tolerated & safe

Recommendation 7

- Paracetamol can be used in patients with osteoarthritis. **(Grade A)**
  - It should be used as first-line analgesic in mild to moderate pain. **(Grade C)**

Question 2

- Patient comes back 2 months later
- Paracetamol only offers partial relief of the pain

- What is your next option?

Answer 2

- Tramadol
  - A weak opioid anaelgesic
  - Effective in pain relief compared to placebo
  - Various formulation including sustained release & all are efficacious
  - Can be used in combination e.g tramadol/paracetamol
  - No major side-effects or significant adverse events
  - Common side effects include dizzines, nausea, vomiting, constipation & drowsiness
  - To be used with caution in the elderly

Recommendation 8

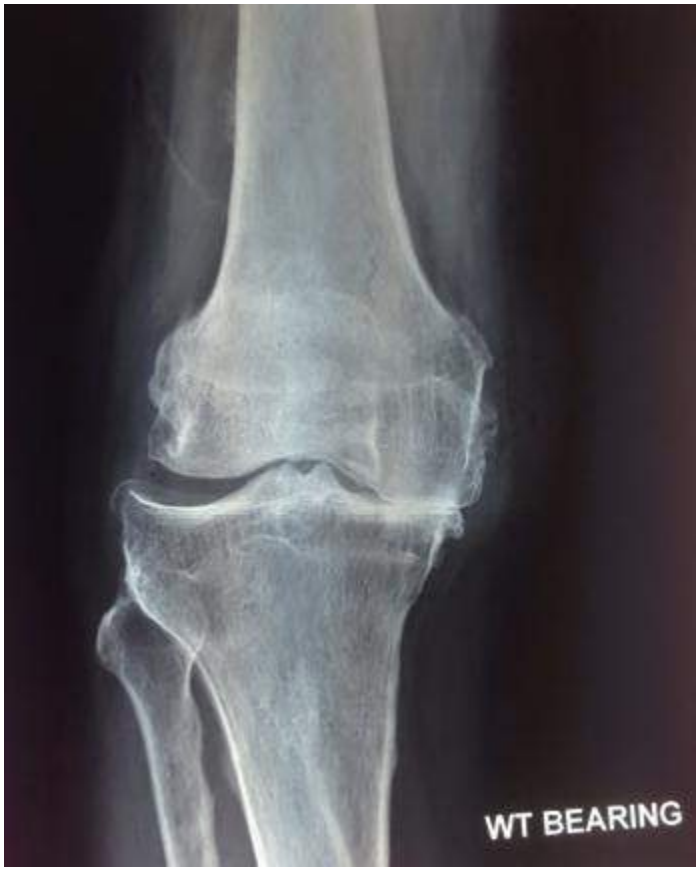
- Tramadol may be used alone or in combination with paracetamol in patients with osteoarthritis. **(Grade A)**

CASE 1 - HISTORY (CONT.)

- Tramadol is added to paracetamol for treatment of her knee pain.

- 10 years later, patient comes back for consultation, having been staying with her son in another town all these while.
  - Pain in both knees have worsen.
  - She has difficulty in climbing stairs & walking far.
  - Pain score 5
  - X-ray of knees KL Grade lll

X-ray Right Knee (AP View)



Question 3

- Your impression:
  1. Moderate OA both knees
  2. Knee pain not adequately controlled by tramadol/paracetamol

- Question: What other medications will you also consider ?

Answer 3

- NSAIDs
- COX-2 inhibitors

NSAIDs & COX-2 Inhibitors

- Provide analgesic & anti-pyretic effects, & in higher doses, anti-inflammatory effects

- COX-2 inhibitors selectively inhibit COX-2 & thus improve gastrointestinal tolerance

Gastrointestinal (GI) Safety

- Ulcer complications are seen significantly less frequent in COX-2 inhibitors compared to NSAIDs.
- Aspirin users experience more GI complications.
- Proton pump inhibitors are effective in the prevention of NSAID-induced peptic ulcers.
- Risk of GI events are more with NSAIDs with PPI then COX-2 inhibitor alone
  - Risk even less with COX-2 inhibitors plus PPI

Cardiovascular (CV) Safety

- Concerns among patients on long-term use of NSAIDs & COX-2 inhibitors is the increased risk of thrombotic CV events.
- Naproxen has lowest risk for CV events & stroke.
- Thrombotic CV events are low in both NSAIDs & CX-2 inhibitors.
- The CV events are comparable for both.

Renal Safety

- Conflicting evidence in the association between chronic NSAIDs usage & the development of chronic kidney disease.

- Renal function should be monitored regularly in patients on chronic NSAIDs or COX-2 inhibitors.

Recommendation 9

- Non-steroidal anti-inflammatory drugs (NSAIDs) or cyclo-oxygenase-2 (COX-2) inhibitors can be used in the treatment of osteoarthritis. **(Grade A)**
  - In patients with high risk of gastrointestinal (GI) complications, COX-2 inhibitors are preferred to non-selective NSAIDs with proton pump inhibitor (PPI) for primary ulcer prevention. **(Grade A)**
  - In patients with previous GI complications:-
    - NSAIDs or COX-2 inhibitors should be avoided. **(Grade C)**
    - combination of COX-2 inhibitors and PPI may be offered for GI protection if indicated. **(Grade A)**
  - In patients with renal impairment, NSAIDs and COX-2 inhibitors should be used with caution. **(Grade C)**

CAUTIONS ON NSAIDS/COX-2 INHIBITORS

- Combination therapy with more than one NSAID/COX-2 inhibitor should never be used. There is no benefit in combination therapy and the incidence of side effects may be additive.
- Caution is required when prescribing NSAIDs in the elderly and those with hypertension, cardiovascular disease, renal or hepatic impairment.
- Those who are allergic to one NSAID may also be allergic to others.

Case 1 - History (cont.)

- She is put on COX-2 inhibitor & her knee pain is adequately controlled.

Case 2 – History / Question 4

- Patient's younger sister aged 50 years comes with mild knee pain
- She is very health conscious & have read on the internet about the side-effects of the oral drugs & not keen to take them
- She wants to know other treatment options

- What are the other treatment options for her?

Answer 4

- Neutraceutical
- Intra-articular injection
- Alternative therapy

NUTRACEUTICALS

- Glucosamine & Chondroitin
  - The glucosamine & chondroitin preparations available in Malaysia are in various combinations, strengths & purities which may affect their efficacy.

GLUCOSAMINE

- Not consistent in its effect as a structure modifier for OA
- Has pain reduction effect
- Glucosamine hydrochloride or its combination with chondroitin sulfate is not efficacious as a structure or symptom modifier.
- Glucosamine is well-tolerated & safe.

Recommendation 10

- Glucosamine sulfate 1500 mg per day may be used as pain relief for knee osteoarthritis. **(Grade C)**
  - Evaluation on pain reduction should be done at three months after initiation of treatment before deciding on its continuation. **(Grade C)**

CHONDROITIN

- The efficacy of chondroitin in the treatment of hip or knee OA is inconclusive.

- It may be beneficial for symptomatic relief in hand OA.

DIACEREIN

- Pain reduction in knee OA

- Adverse events such as diarrhoea, abdominal pain, nausea & vomiting mostly are mild to moderate

Recommendation 11

- Diacerein may be used in the treatment of knee osteoarthritis. **(Grade C)**

VISCOSUPPLEMENTATION

- Several different formulations of viscosupplements (hyaluronan & hylan) with widely differing molecular weights

Due to a lack of supporting evidence, the CPG is unable to recommend the use of viscosupplementation in the treatment of osteoarthritis.

Topical Treatment

- Topical NSAIDs
  - beneficial compared to LMS
- Topical capsaicin
  - ?available in local pharmacy

Recommendation 13

- Topical non-steroidal anti-inflammatory drugs may be offered in the treatment of osteoarthritis. **(Grade A)**
  - It may be used as adjunct therapy in mild to moderate pain. **(Grade C)**

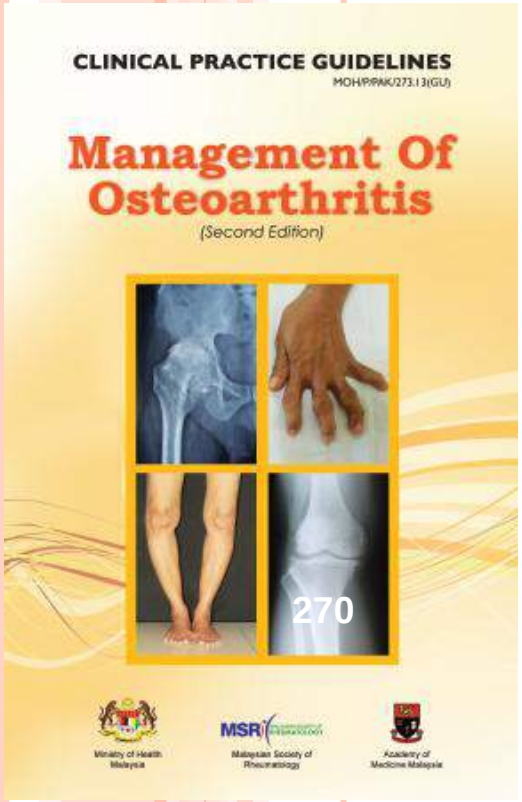
CASE 2 – HISTORY (CONT.)

- Patient asked “Is there a role for alternative therapy?”

- Acupuncture
- Avocado soybean unsaponifiables (ASO)
  - piascledine
- Ginger extract

- Acupuncture & avocado soybean unsaponifiables may be used as an adjunct short-term therapy in osteoarthritis. (Grade A)

Thank You



TRAINING OF CORE TRAINERS – CASE STUDY 3

by

Dr. Ong Swee Gaik

Consultant Rheumatologist

Hospital Kuala Lumpur

History

- 65 year-old woman
- Known case of hypertension x 5 years & IHD for 3 years
- c/o painful swelling over right knee for past 3 days

Question 1

- What further history would you like to elicit?

Answer 1

- Onset of pain – acute or insidious
- Intensity of pain
- Inflammatory or non-inflammatory joint pain – swelling, warmth, erythema, limited ROM
- Early morning stiffness
- Precipitating / relieving factors
- Associated fever, trauma, procedure
- Skin rash (psoriasis)
- Other joint involvement
- Similar attacks in the past

History – cont.

- Insidious onset
- Dull throbbing pain
- Similar intensity as 3 days ago
- Pain score 6/10
- Knee not red but warm
- Minimal stiffness of 5 mins
- Pain worse on movement & on weight-bearing
- Able to walk but with difficulty
- Has experienced pain over Lt knee joint
- No fever, recent trauma or intervention

History – cont.

- Has been having bilateral knee pain for past 5 years, especially on walking & on descending stairs
- Tried paracetamol & tramadol in the past but discontinued due to inadequate response
- Has been taking diclofenac or indomethacin on a regular basis for past 2 years - bought at local pharmacy
- Home-bound for past 1 year, manage to walk for short distance

Question 2

- What other history would you like to elicit?

Answer 2

- Medical history - hypertension, diabetes, IHD, kidney disease, peptic ulcer disease

- Drug history

HISTORY – CONT.

Past medical hx:

- 6 months ago, admitted to Medical Ward for melaena. Hb dropped to 5.6 g% & required 4 pints packed cell transfusion.
- OGDS - Forrest II ulcer at antrum
  - H. pylori negative
  - IVI pantoprazole x 72 hrs, then esomeprazole 40 mg od x 6/52
  - Repeat OGDS 8/52 later – healed ulcer
- Advised to stop NSAIDs

History – cont.

- Hypertension x 5 years
- IHD x 3 years

Current medications:

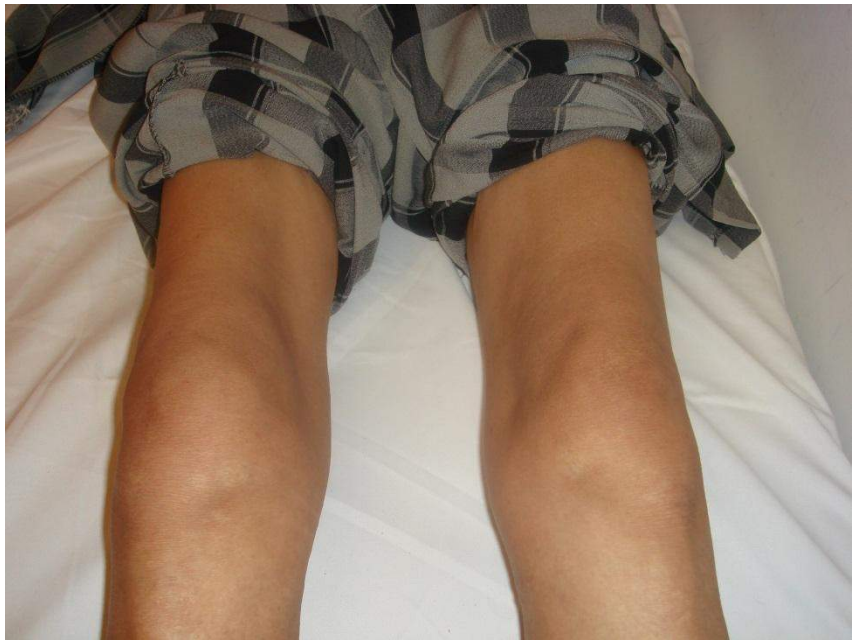
- Cardiprin 100mg od
- Isosorbide mononitrate 50 mg od
- Metoprolol 50 mg bd
- Simvastatin 20 mg on
- Perindopril stopped 6/12 ago due to renal insufficiency
- Pantoprazole 40 mg od (long-term)

Physical Examination

- BMI 30kg/m^2
- Afebrile, BP 145/95mm Hg, PR 92/min
- No pallor, jaundice or pedal oedema
- No rash
- CVS, respiratory system & abdomen – normal

Physical Examination - 2

- Right knee
  - quadriceps wasting
  - knee swelling, overlying skin not erythematous
  - warm, tender, positive patellar tap
  - ROM limited: 20^{o} to 45^{o}



- Left knee
  - quadriceps wasting
  - knee not warm or tender
  - crepitus ++
  - ROM limited: 0^{o} to 90^{o}

Question 3

- What are your differential diagnoses?
- What is your next line of action?

Answer 3 - Differential diagnoses

- Infection - septic arthritis
- Crystal arthropathy - gout, pseudogout
- Acute exacerbation of osteoarthritis

Answer 3 - Investigations

- FBC, RP, LFT, Uric acid, ESR/CRP
- FBS, FSL, ECG
- X-ray knees (AP & lateral, standing)
- Rt knee arthrocentesis – synovial fluid analysis i.e. appearance
  microscopy
  Gram stain
  culture & sensitivity
  crystal identification under polarised light microscope (if available)

Investigation Results

FBC	WCC 6.8x10^9/L, Hb 10.3 g%, Plt 265x10^9/L
RP	BU 10.8 mmol/L, Na 145 mmol/L, K 4.2 mmol/L, Crea 158 µmol/L
Uric acid	415 µmol/L
LFT	Total protein 70 g/L, Albumin 38 g/L, Bilirubin 15 mmol/L, ALP 140 mmol/L, ALT 32mmol/L

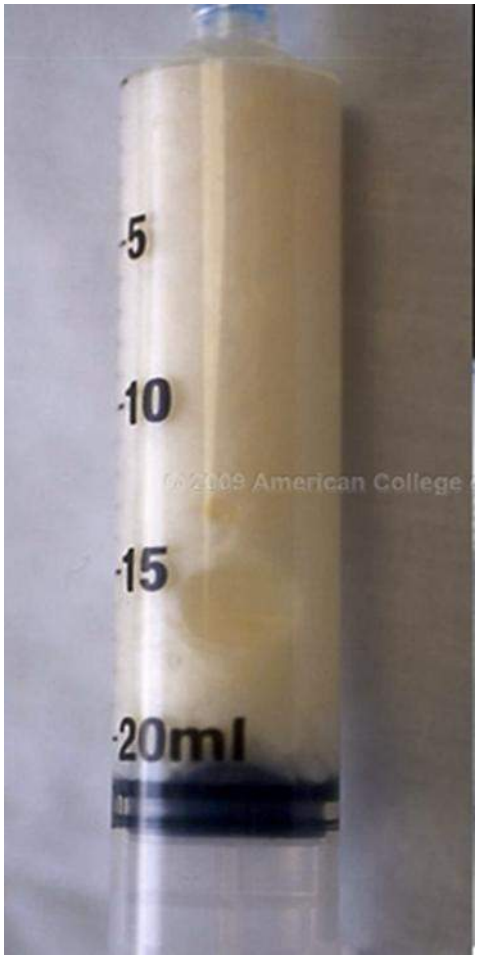
SYNOVIAL FLUID-1

SYNOVIAL FLUID-2

Appearance	Transparent & yellow
Leucocytes	500/mm^3
Gram stain	No Gram positive or negative organism
Culture & sensitivity	Results pending
Crystal analysis	No monosodium urate (MSU) crystals or calcium pyrophosphate dihydrate (CPPD) crystals identified

SYNOVIAL FLUID-3

Normal synovial fluid

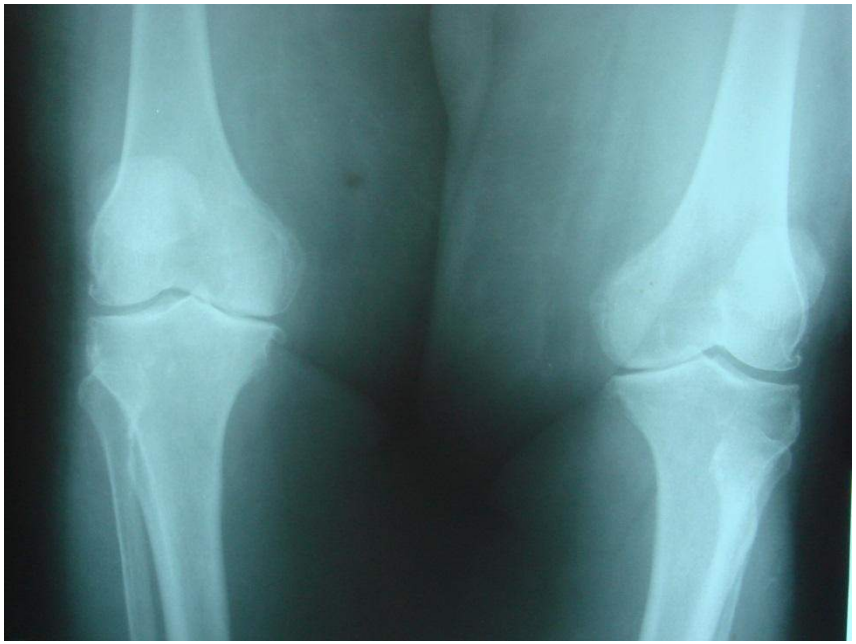


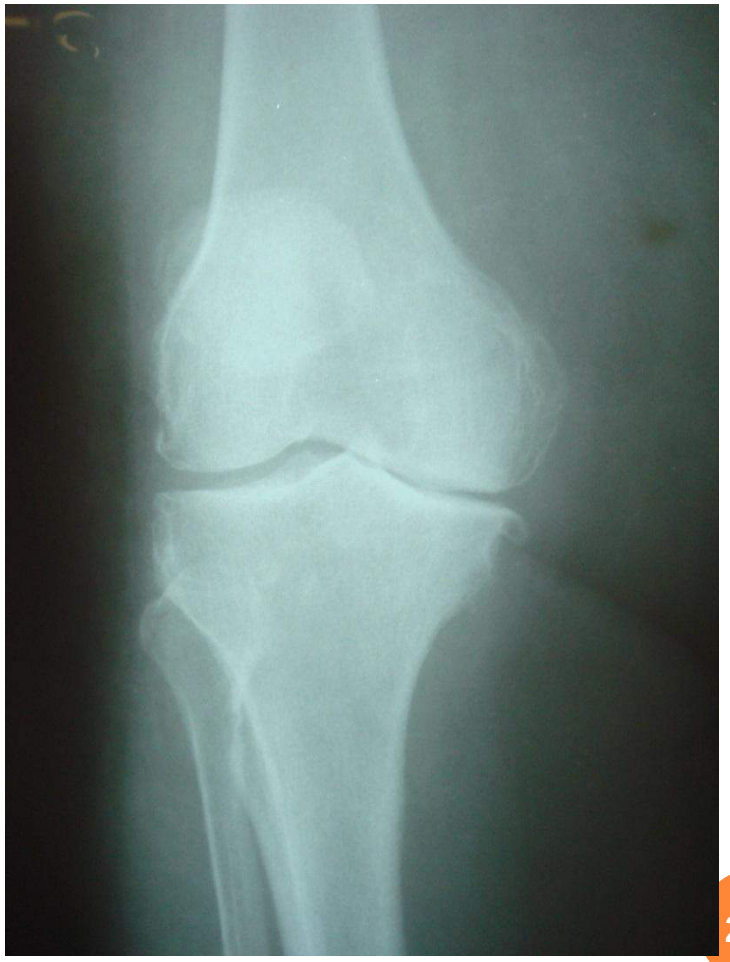
Turbid

Categories of Synovial Fluid Based Upon Clinical & Laboratory Findings (Adapted from 2013 UpToDate, Graphic 76506, version 2069.0

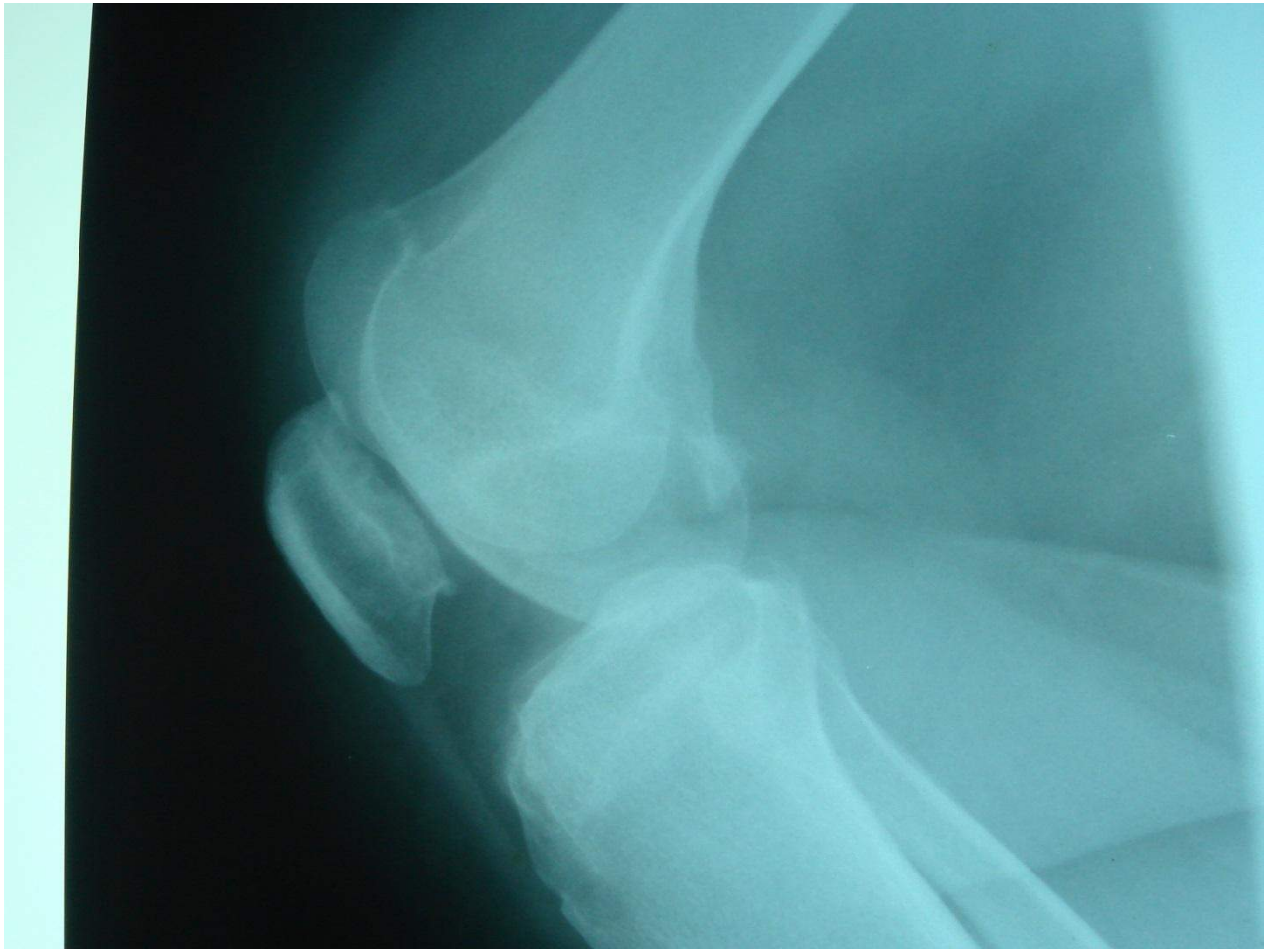
Measure	Normal	Non-inflammatory	Inflammatory	Septic	Hemorrhagic
Volume, mL (knee)	<3.5	Often >3.5	Often >3.5	Often >3.5	Usually >3.5
Clarity	Transparent	Transparent	Translucent-opaque	Opaque	Bloody
Color	Clear	Yellow	Yellow to opalescent	Yellow to green	Red
Viscosity	High	High	Low	Variable	Variable
WBC, per mm3	<200	0-1,000	1,000-100,000	15,000->100,000*	200-2,000
PMNs, percent	<25	<25	≥50	≥75	50-75
Culture	Negative	Negative	Negative	Often positive	Negative
Total protein, g/dL	1-2	1-3	3-5	3-5	4-6
Glucose, mg/dL	Nearly equal to blood	Nearly equal to blood	>25, lower than blood	<25, much lower than blood	Nearly equal to blood

X-RAY OF KNEES-1





X-RAY OF KNEES-2



Answer to Differential Diagnoses

- Septic arthritis

Points against
- no fever
- no surrounding cellulitis or puncture wounds
- WCC not elevated
- synovial fluid: appearance is clear, WCC in non-inflammatory range

Answers to Differential Diagnoses

- Crystal arthropathy

Points against

- insidious onset of pain
- synovial fluid - appearance is clear,
  - low WCC
  - no crystals (MSU or CPPD identified

Diagnosis

- Acute exacerbation of OA knee

Question 4

- How would you manage the patient now?

Answer 4

- Management:
  - Intra-articular triamcinolone acetonide injection – 40 to 80 mg + 1 ml lignocaine 2%
  - Ice pack
  - Simple analgesics – paracetamol, tramadol
  - Refer physiotherapy – quadriceps strengthening exercise
  - Weight reduction

Recommendation 12

- Intra-articular corticosteroid may be used for short-term pain relief in an acute exacerbation of knee osteoarthritis. **(Grade A)**

Oral corticosteroid have no role in the treatment of osteoarthritis.

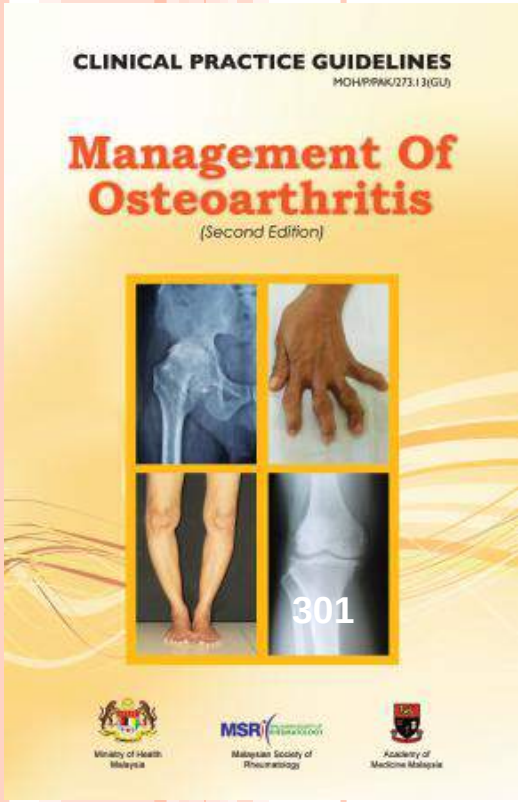
Answer 4

- Management:
  - Refer to orthopaedic surgeon

Recommendation 16

- Referral of osteoarthritis cases to either rheumatology or orthopaedic clinic should provide the following information:-
  - Diagnosis
  - Severity and its impact on activity of daily living
  - Co-morbidities that might require further medical assessment
  - Relevant investigation results and current medications **(Grade C)**

Thank You



Training of Core Trainers – Case Study 4

by

Dr. Asyraf Wong Abdullah

Consultant Orthopedic

Hospital Tuanku Ampuan Najihah

History

- 65 year-old lady
- No medical illness
- Complaint of pain & deformity on right knee
- Inability to perform activities of daily living (ADL) for duration of 1 year

HISTORY - CONT.

- Her pain scale score (VAS) is at 7 - 8 on ambulation.
- She did not respond to tramadol & paracetamol.
- She had gastric discomfort on NSAIDs & been given intra-articular corticosteroid; however she did not respond to it.
- Her ADL is markedly affected & is house-bound for the past 1 year.

Question 1

- What would you do next?

Answer 1

- Counsel patient that she might require surgery
- Refer to orthopedic surgeon

REFERRAL

Recommendation 16

- Referral of osteoarthritis cases to either rheumatology or orthopaedic clinic should provide the following information:-
  - Diagnosis
  - Severity and its impact on activity of daily living
  - Co-morbidities that might require further medical assessment
  - Relevant investigation results and current medications **(Grade C)**

History - cont.

- She is referred to orthopedic surgeon for further management.

Clinical Examination

- General examination is unremarkable.

- Local examination of right knee:
  - Varus deformity of 10 degrees
  - ROM - flexion 10 - 100 degress
  - Crepitus present on ROM
  - Varus/valgus stress test - LCL showed grade 1 laxity
  - ACL/PCL no laxity

Clinical Examination - cont.

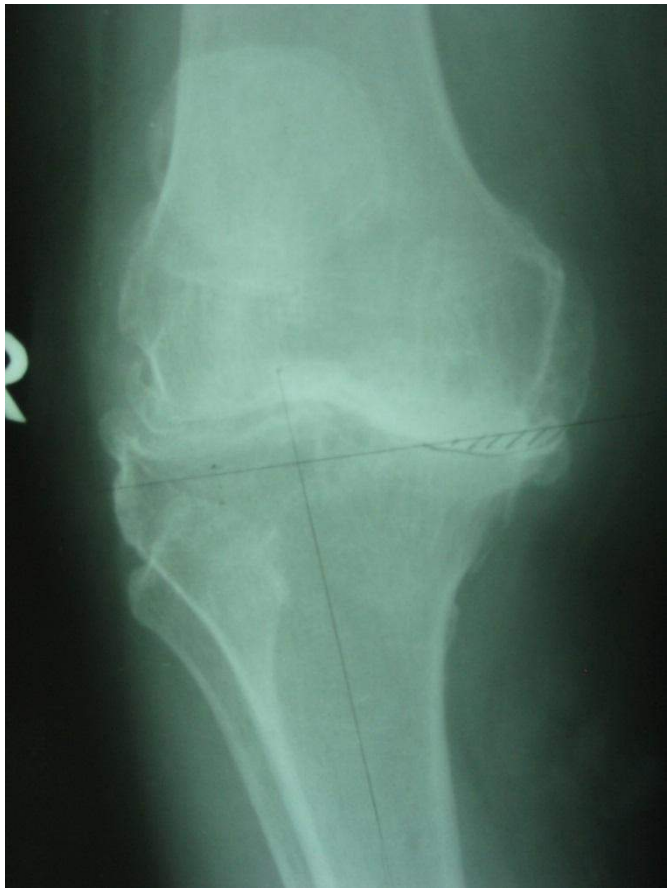
- Local examination of right knee (cont.):
  - No retropatellar pain on patellar grinding test
  - Mild warmth & fullness on suprapatellar pouch
- Distal pulses are intact.
- Hip & ankle joints are normal.

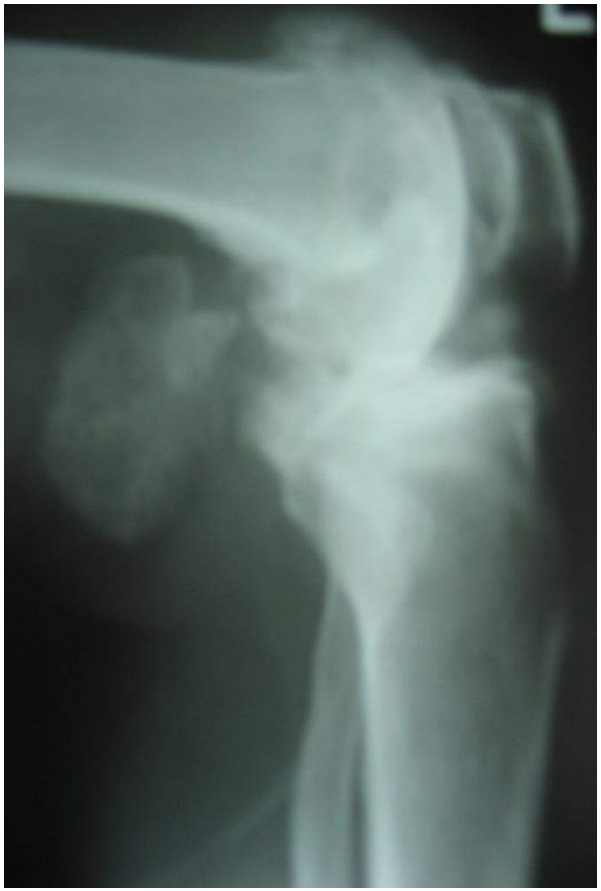
INVESTIGATIONS

- Routine blood investigation
- CXR/ECG
- X-ray of knee - AP/Lat. (standing view)
- X-ray of hip - AP/Lat.

Question 2

- What are the findings in these knee x-ray?





Answer 2

- Narrowing of joint space
- Osteophytes
- Subchondral sclerosis
- Subchondral bone cyst
- Varus deformity

Question 3

- What are the indications for surgery?

Answer 3

- Pain (sleep interruption & while resting)
- Limitations to ADL (walking & self- care)
- Psychosocial health (psychological well-being)
- Economic impact
- Recent deterioration

History – cont.

- Patient is advised for total knee replacement surgery.

- However, she is undecided regarding surgery. She would like to get more information on other available options.

Question 4

- What are the other available options?

Answer 4

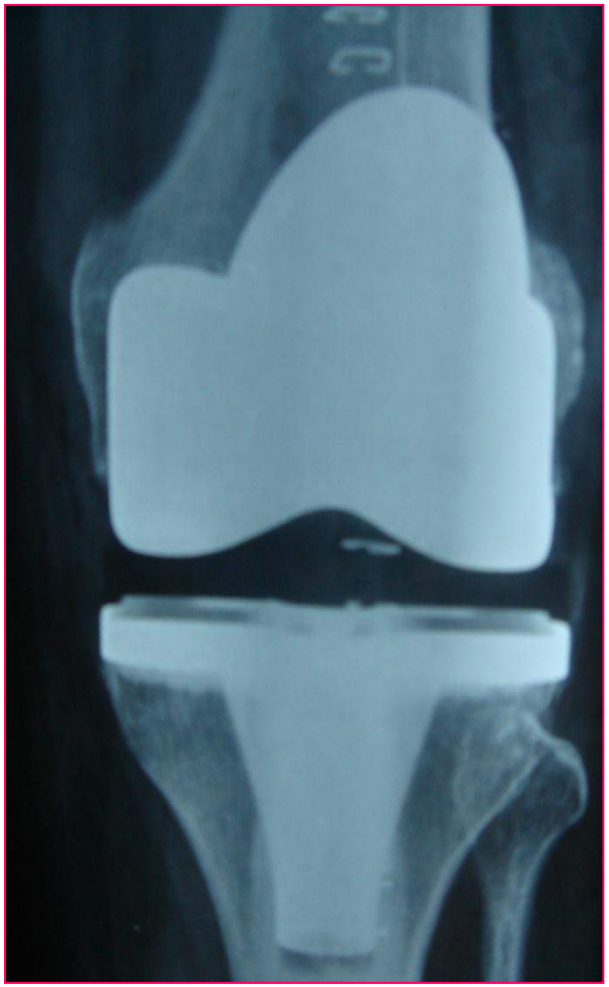
- Intra-articular Stem Cells Therapy
- Autologous Chondrocyte Implantation
- Platelet Rich Plasma
- Intra-articular steroid injection

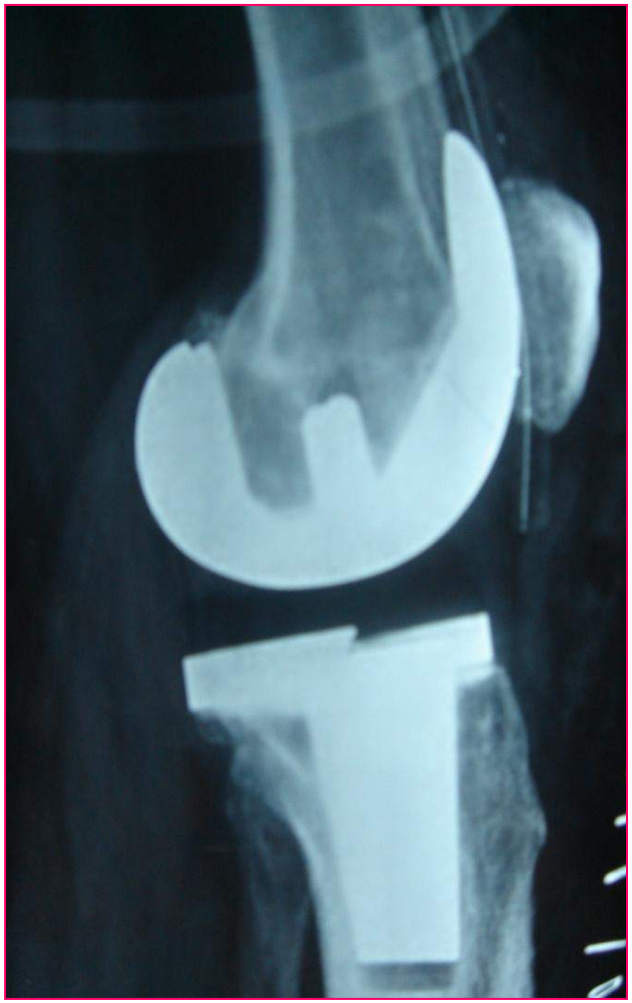
Due to a lack of available evidence, the CPG is unable to recommend the use of intra-articular stem cells, autologous chondrocyte implantation or platelet-rich plasma in the treatment of osteoarthritis.

History – cont.

- She finally agrees for TKR.
- She in operated in view of pain & limitation of function.
  - TKR done and patient recovers fully
- She undergoes physiotherapy post-operatively

Surgical Treatment - TKA





Thank You