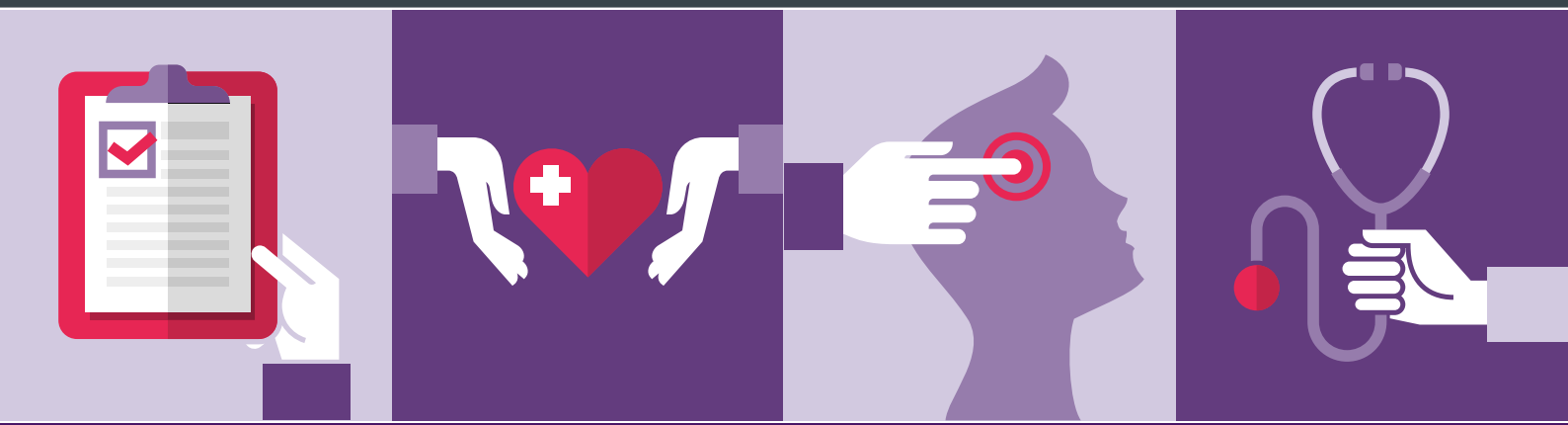
check

Independent learning program for GPs



Unit 519 August 2015

Bones and joints

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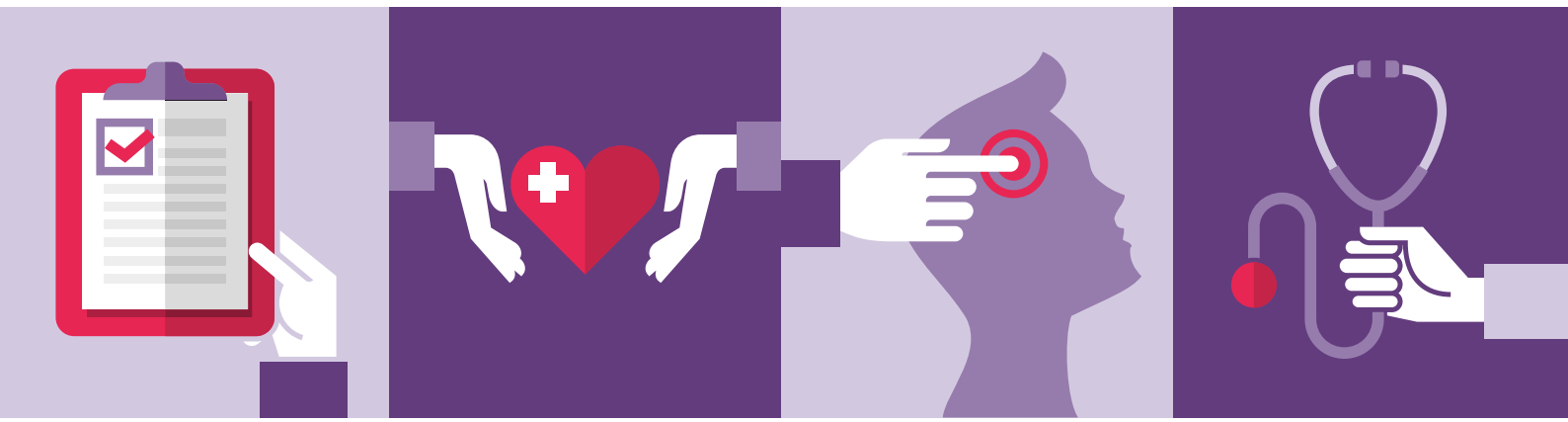

Bones and joints

Unit 519 August 2015

The five domains of general practice

- Communication skills and the patient–doctor relationship
- Applied professional knowledge and skills
- Population health and the context of general practice
- Professional and ethical role
- Organisational and legal dimensions

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ABOUT THIS ACTIVITY

Musculoskeletal conditions affect around 31% of the Australian population – more than 6 million Australians – and cost the country $5.7 billion in 2008–09.[1] These conditions, including arthritis and back complaints, are among the most common chronic conditions managed in primary healthcare settings and were the most common reasons for presentation to general practice, accounting for 18.4 per 100 encounters.[2] Musculoskeletal conditions cause severe long-term pain and physical disability, and are major causes of work limitation and early retirement.[1] Back pain, joint disorders (osteoarthritis and rheumatoid arthritis) and osteoporosis are listed together as one of the nine current National Health Priority Areas.[3,4]

This edition of *check* considers musculoskeletal conditions, such as back and joint pain, arthritis and fractures. The cases explore the management of patients who present to general practice with these conditions, and examine issues of treatments, medications and when referrals to specialists should be considered.

LEARNING OUTCOMES

At the end of this activity, participants will be able to:

- describe the diagnosis and management of osteoarthritis
- outline options for the management of ankylosing spondylitis
- explain approaches to assessment and treatment of rheumatoid arthritis
- discuss symptoms and management of gout
- identify and manage undisplaced fractures to the fifth metatarsal joint.

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ACRONYMS

AHS	allopurinol hypersensitivity syndrome
AMH	Australian Medicines Handbook
ANA	antinuclear antibodies
AP	anteroposterior
AS	ankylosing spondylitis
ASAS	Assessment of SpondyloArthritis international Society
BMI	body mass index
CCP	cyclic citrullinated peptide
CDAI	clinical disease activity index
CMC	carpometacarpal
COX-2	cyclooxygenase-2
CRP	C-reactive protein
DAS28	disease activity score derivative for 28 joints
DIP	distal interphalangeal
DMARDs	disease-modifying anti-rheumatic drugs
ESR	erythrocyte sedimentation rate
FBE	full blood evaluation
HLA-B27	human leukocyte antigen-B27
LFT	liver function test
MCH	mean corpuscular haemoglobin
MCP	metacarpophalangeal
MCV	mean corpuscular volume
MRI	magnetic resonance imaging
MTP	metatarsophalangeal
NSAIDs	non-steroidal anti-inflammatory drugs
PBS	Pharmaceutical Benefits Scheme
PIP	proximal interphalangeal
RA	rheumatoid arthritis
RhF	rheumatoid factor
SLE	systemic lupus erythematosus
SpA	spondyloarthritis
STIR	short T1 inversion recovery
SUA	serum uric acid
TNF-α	tumour necrosis factor-alpha
WCC	white cell count

CASE 1

JUNE HAS PAINFUL JOINTS

June, 55 years of age, comes to see you about her joint pain. She has noticed pain in multiple joints, which has been worsening over the past few years. She is worried because her mother had severe arthritis and she wants to know what she can do to avoid a similar outcome. She asks for your help.

QUESTION 1

What is your initial approach to this consultation?

FURTHER INFORMATION

June tells you she has had the pain for 5 years, but it has been worse since she went through menopause. She also noticed it worsened with recent weight gain as she has not been exercising because of the pain. The worst areas are her knees and the base of her thumbs, but her feet and some of the small joints of her hands are also sore. She noticed that her fingers are 'knobbly' and says her mother had the same problem. Her symptoms are exacerbated by housework and she has pain in her knees when climbing stairs. June tried paracetamol and ibuprofen, which helped a little. On examination, you find bony enlargement of her proximal interphalangeal (PIP) joint and distal interphalangeal (DIP) joint, and squaring of the thumbs. You also find crepitus over the kneecap but a good range of motion in the knees. The knees have a varus deformity and she is flat-footed. Her quadriceps muscles are wasted. June has a body mass index (BMI) of 30 kg/m^2.

QUESTION 2

What is your initial diagnostic impression?

QUESTION 3

What other diagnoses do you need to exclude before making a diagnosis of osteoarthritis?

QUESTION 4

How would you initially manage June?

QUESTION 5

June asks you about complementary and alternative therapies for osteoarthritis. What would you tell her?

FURTHER INFORMATION

June returns to see you 2 months later. She started doing some exercise with her physiotherapist and saw a dietitian. By exercising and adhering to the diet plan, June is losing weight. The occupational therapist has provided some hand splints and suggested some activity modification. June takes paracetamol regularly and finds non-steroidal anti-inflammatory drugs (NSAIDs) very helpful on bad days. She decided not to try any of the complementary therapies, as she does not want to take too many tablets. Recently, her aunt had knee surgery and is happy with it. She now wants to know if she should see a surgeon.

QUESTION 6

What advice should you give June about seeing a surgeon?

CASE 1 ANSWERS

ANSWER 1

A full medical history and physical examination should be performed to try to determine the sort of arthritis June has and her specific problem areas. It is important to exclude inflammatory arthritis and to identify possible contributing factors.[1]

Important questions to ask June include:

- How long have you had the symptoms and how have they changed? Is there anything that may have made things worse?
- Which joints are most painful?
- Do you find the symptoms are worse in the morning? Do you feel stiff first thing in the morning? If so, for how long?
- Do you have pain at night?
- Have you noticed any joint swelling? If so, is it constant or fluctuating?
- Are your symptoms aggravated by activities? If so, which activities?

It is also important to ask about:

- any diseases associated with arthritis, such as psoriasis, inflammatory bowel disease or other autoimmune diseases
- family history of arthritis
- exercise levels, diet and weight changes
- hormonal changes/menopause.

The physical examination should focus on:

- weight and BMI
- joint examination to confirm changes associated with osteoarthritis such as bony enlargement and deformity
- signs of inflammatory joint disease such as 'boggy' swelling of joints, fluid in joints, heat and erythema
- muscle condition (ie weakness, wasting)
- extra-articular signs of rheumatic disease, such as psoriasis.

ANSWER 2

June has typical features of primary generalised osteoarthritis. In routine practice, the diagnosis is made on clinical grounds and further investigations such as blood tests and X-rays may not be necessary unless there are symptoms to suggest an alternative diagnosis.[2] Typical clinical findings are bony enlargement, bony tenderness, crepitus, deformity and lack of inflammatory features such as boggy joint swelling or prolonged morning stiffness.[1] The disorder most commonly affects the hands with nodal changes at the DIP and PIP joints, base of thumbs as well as the hips and knees.[1] Primary osteoarthritis occurs in isolation and it is generalised when at least three joints are involved. Secondary osteoarthritis is due to another underlying condition such as inflammatory joint disease or trauma.

ANSWER 3

To make differential diagnoses, the problems to be considered are the number of joints involved, their distribution and the nature of the pain.

Non-articular or mononoarticular

- Non-articular soft-tissue problem (eg bursitis)
- Inflammatory monoarthritis (eg gout, pseudogout, septic joint)

Polyarticular

- Crystal arthritis (eg pseudogout or gout)
- Inflammatory arthritis (eg rheumatoid arthritis, psoriatic arthritis)

Widespread pain

- Fibromyalgia
- Myalgias (eg statin-induced, polymyalgia rheumatic)

It is essential to exclude inflammatory arthritis that can arise in addition to features of primary generalised osteoarthritis. Symptoms that will suggest inflammatory arthritis include pain at night or in the morning and prolonged early morning stiffness of more than 1 hour or intermittent joint swelling. Signs to look for include an unusual pattern of joint involvement (eg wrist, elbow or cervical spine involvement) and the presence of joint swelling.[3] If these are seen, consider further investigations including:

- blood tests for inflammation markers: erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)
- basic autoimmune serology: antinuclear antibodies (ANA), rheumatoid factor (RHF), anti-cyclic citrullinated peptide (anti-CCP) antibody
- X-rays or ultrasound.

Drainage of fluid from the joint can be done to see if there is inflammatory synovial fluid. Referral to a rheumatologist is recommended if there are any concerns.

ANSWER 4

Best practice medical care should involve the patient, the GP and other members of the multidisciplinary team as appropriate for June's care. The GP can have multiple roles, including advisor, patient advocate and initiator of therapeutic options. Initial treatment recommendations include:[4,5]

- **Education** – It is important to advise June of the diagnosis of osteoarthritis and that this is a chronic condition that can be managed. There are currently no treatments available to slow or reverse joint degeneration, but the symptoms can be managed with simple analgesia and physical therapies. It is important that June is central in managing her care.
- **Weight loss** – This is helpful for symptoms of osteoarthritis and may reduce the rate of joint degeneration. In particular, weight loss has been identified as a key measure for treating knee and hip osteoarthritis.[5,6] It is best achieved through a combination of diet and exercise. Referral to a dietitian is recommended for specific dietary advice. Specific exercises to target problem areas are important but general exercise is also essential.[7] Non-weight-bearing exercises, such as swimming or cycling, are helpful and can be done through group classes and government programs.
- **Physical therapies** – Although the underlying joint damage cannot be reversed, it is important to maintain muscle strength to support the joints. Studies suggest the pain-relieving benefits of exercise are similar to those of simple analgesics such as paracetamol or anti-inflammatory agents. June would particularly benefit from a quadriceps-strengthening program to assist with her knee pain.[7] A care plan could facilitate subsidised physiotherapy visits so that an individualised exercise program can be given.
- **Occupational therapy** – It is vital to maintain function through the use of aids and splints. Thumb splints and thermal gloves can be helpful for pain arising from OA of the first carpometacarpal (CMC) joint.[5] Patients with painful knee or hip osteoarthritis may require walking aids or home modifications.[6] The use of braces for knee osteoarthritis and orthotics to correct mal-alignment in the legs may be indicated, although guidelines vary. Rheumatologist advice on the use of braces and orthotics is appropriate if unsure.
- **Medications for pain relief**
  - Paracetamol: guidelines recommend paracetamol as a first-line agent for relief of OA pain as it is safe for long-term use.[1]
  - NSAIDs: recent literature suggests NSAIDs may be more effective than paracetamol, particularly in the management of hand osteoarthritis.[8] June should therefore be given the option of using non-selective or cyclooxygenase-2-selective NSAIDs if there are no contraindications such as uncontrolled hypertension or cardiovascular disease, significant renal impairment or history of peptic ulcer disease. Given their adverse effects, particularly cardiotoxicity, NSAIDs should always be used at the minimal effective dose and for the shortest possible time. However, it is important to allow an adequate therapeutic trial period of 2–4 weeks for a given NSAID, as its maximum beneficial effect may be delayed.[1] Care must be taken with long-term use of NSAIDs, because there is a risk of cardiovascular disease, and caution should be exercised when prescribing NSAIDs for patients with renal impairment.[1] Co-prescription with a proton-pump inhibitor will reduce the risk of gastrointestinal side effects, especially serious side effects such as bleeding peptic ulceration. Topical NSAIDs and capsaicin cream are recommended therapies for hand osteoarthritis.[8]
  - Opioid analgesics: these have not been shown to provide long-term benefits for patients with osteoarthritis but may be indicated in exceptional circumstances.[9]
  - Corticosteroids injections: the evidence suggests that corticosteroid injections into the joint are not particularly effective for pain associated with osteoarthritis. However, some patients benefit from them and they are used as an interim measure to alleviate pain and allow improved participation in physical therapies. Specialist referral is suggested to assess whether these may be appropriate.
  - Hyaluronic acid injections: these are no more effective than corticosteroids and are more expensive.[9] Referral to a rheumatologist for an opinion is appropriate if considering this treatment.

ANSWER 5

There are a number of complementary therapies that may be helpful for osteoarthritis.[10] Those most commonly used:

- Chondroitin sulphate: some studies have shown improvement of pain in patients with osteoarthritis, whereas other studies show no benefit over placebo.
- Glucosamine sulphate: some studies show benefit for pain in patients with knee OA, whereas other studies show no benefit. The hydrochloride form has not been found to be effective.

Some studies have suggested chondroitin and glucosamine may slow cartilage breakdown, but the evidence is very weak and no firm conclusions can be drawn at this stage.[10] A trial of these agents is reasonable, if the patient is keen to try them, to see if they improve pain.

Other agents that have been studied but have more limited evidence include:[11]

- acupuncture (knee and hip osteoarthritis)
- fish oil
- avocado-soybean unsaponifiables
- ginger
- green-lipped mussel
- Indian frankincense (Boswellia serrate)
- phytodolor
- pine bark extracts
- rosehip
- S-adenosyl methionine
- gamma-linoleic acid (found in evening primrose oil, borage/starflower seed oil and blackcurrant seed oil)
- Chinese herbal patches containing Fufang Nanxing Zhitong Gao and Shangshi Jietong Gao (SJG)
- devil's claw
- SKI 306X
- turmeric
- vitamins A, C, E, and B complex
- willow bark extract.

It is important to emphasise that there is no 'quick fix' for osteoarthritis and that the most important treatment is to maintain a healthy weight and good muscle strength.

ANSWER 6

Surgery is usually a last resort for osteoarthritis. There is no good evidence of benefit from arthroscopic surgeries for knee osteoarthritis.[12] Joint replacement is effective for relieving pain in the majority of patients but results in reduced range of movement and function.

June currently has a good range of movement and excellent function, and her pain is adequately managed. Thus, replacement surgery is not appropriate for her at this time. Her symptoms can be managed conservatively. She is also too young – a knee replacement is likely to last 10–15 years and she would need several repeat operations in her lifetime. Orthopaedic referral may be appropriate for patients with significant functional disability and pain despite conservative measures. The Royal Australian College of General Practitioners has guidelines to assist in making the decision of when and how to refer patients for surgery.[13]

RESOURCES FOR DOCTORS AND PATIENTS

- The Australian Rheumatology Association provides information and patient handouts on their website, www.rheumatology.org.au

RESOURCES FOR DOCTORS

- The Royal Australian College of General Practitioners clinical guidelines for musculoskeletal diseases has recommendations for the non-surgical management of hip and knee osteoarthritis, www.racgp.org.au/download/Documents/Guidelines/Musculoskeletal/oa_recommendations.pdf
- Therapeutic Guidelines. Nonsteroidal anti-inflammatory drugs: use in rheumatology, http://online.tg.org.au/complete/desktop/index.htm
- Australian Medicines Handbook (AMH) 2015, https://amhonline.amh.net.au/chapters/chap-15/musculoskeletal-conditions-other/osteoarthritis

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CASE 2

PAUL HAS A STIFF BACK

Paul, an office worker aged 35 years, presents with lower back pain and stiffness, which have worsened over the past 12 months. In addition, he has buttock pain that moves from one side to the other. The pain is worse in the early hours of the morning, occasionally forcing him out of bed at around 3.00 am. Each morning, there is prominent spinal stiffness of several hours' duration. The pain is relieved by activity, a hot shower and non-steroidal anti-inflammatory drugs (NSAIDs). When sitting at his desk for more than 30 minutes, the pain and stiffness recur. On examination, Paul's spinal mobility is normal and there are no inflamed joints.

QUESTION 1

What type of back pain does Paul have, given his symptoms and history?

QUESTION 2

What other clinical features need to be assessed?

QUESTION 3

What are the useful measures of spinal mobility? What is the significance of normal spinal mobility?

FURTHER INFORMATION

Paul has no non-spinal joint symptoms. Three years ago, he had an episode of plantar fasciitis, which improved with a corticosteroid injection, although he still has episodes of mild pain under the right heel when first stepping out of bed. He is tender to palpation over the plantar aspect of his right heel. He has no significant family medical history. He smokes 10–15 cigarettes per day.

QUESTION 4

What investigations are indicated at this stage?

FURTHER INFORMATION

Paul had blood tests for human leukocyte antigen B27 (HLA-B27), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). He also had anteroposterior (AP) X-ray of his pelvis and lumbar spine. His CRP (12 mg/L) and ESR (8 mm/hour) were within the normal ranges but HLA-B27 was detected. The sacroiliac joints appeared normal on an AP radiograph of the pelvis.

Paul was referred to a rheumatologist who ordered magnetic resonance imaging (MRI) of the sacroiliac joints with fat-suppressed short T1 inversion recovery (STIR) sequences. This showed bilateral bone marrow oedema at the sacroiliac joints, indicating acute inflammation. Paul was diagnosed with non-radiographic axial spondyloarthritis (SpA).

QUESTION 5

What is non-radiographic axial SpA?

QUESTION 6

How should Paul be managed?

FURTHER INFORMATION

Paul was started on regular NSAIDs and commenced an exercise program. He agreed to quit smoking.

One year later, Paul returned with right knee pain and swelling, which had recurred despite a radiologically guided corticosteroid injection organised by another doctor. He has not been performing regular exercise because of the knee pain, and his back pain and stiffness have worsened.

He is referred again to his rheumatologist. Repeat pelvic X-ray shows unilateral grade 1 (suspicious) sacroiliitis. His rheumatologist commences sulfasalazine and switches Paul to an alternative NSAID. A corticosteroid injection to the right knee is readministered by the rheumatologist to good effect. Paul resumes his exercise regimen.

QUESTION 7

What is the rationale for using sulfasalazine? What are the common side effects and recommendations for monitoring of this medication?

FURTHER INFORMATION

Paul sees you for a follow-up visit to have his blood counts and liver function checked. His ESR and CRP levels remain normal. He heard about a new medication, a tumour necrosis factor-alpha (TNF-α) inhibitor, which his friend Jim says is effective in treating rheumatoid arthritis (RA). Paul asks if a TNF-α inhibitor could be considered for his condition.

QUESTION 8

What is a TNF-α inhibitor? Is it an appropriate medication for Paul?

CASE 2 ANSWERS

ANSWER 1

Paul's symptoms suggest inflammatory back pain, which invokes consideration of an SpA as the underlying cause. Although chronic back pain is a common complaint in primary care, inflammatory back pain is uncommon (5%) and can be distinguished from other causes of spinal pain on the basis of targeted history taking.[1]

In a patient with chronic back pain (>3 months' duration) with onset before 50 years of age, inflammatory back pain is present with a sensitivity of 70.3% and specificity of 81.2%, if two or more of the following criteria are fulfilled:[1]

- morning stiffness lasting >30 minutes
- improvement in back pain with exercise but not with rest
- awakening during the second half of the night
- alternating buttock pain.

ANSWER 2

The spondyloarthritides are a group of inflammatory disorders characterised by inflammation of the axial skeleton, entheses and peripheral joints.[2] They include ankylosing spondylitis (AS), psoriatic arthritis, reactive arthritis, arthritis of inflammatory bowel disease and juvenile SpA. These disorders may also target extraskeletal structures such as the eyes, skin, gut and genitourinary tract. As such, it would be important to assess Paul for other features of SpA such as psoriasis, peripheral arthritis, anterior uveitis, inflammatory bowel disease, dactylitis, enthesitis or genitourinary disease. The presence of these additional features may guide treatment decisions and should prompt referral for specialist assessment (eg ophthalmological assessment if uveitis is present). Comorbidities and a family history should also be obtained.

ANSWER 3

The most useful measures of spinal mobility that can be readily performed in general practice include:[3–5]

Modified Schober's test

The patient stands upright and the midpoint of an imaginary line connecting the posterior superior iliac spines is marked. A mark is also made 10 cm above this point. The patient is asked to bend forward maximally. The distance between the two marks should reach ≥15 cm. The best of two attempts is recorded. A restricted Schober's test is non-specific and may also occur in mechanical spinal disease. However, documenting serial measurements in SpA is useful to assess progression and/or response to treatment.

Occiput-to-wall distance

The distance between the occiput and the wall when the patient stands with their heels and shoulders against the wall is zero in the normal population. Increasing occiput-to-wall distance is associated with loss of cervical lordosis and increasing thoracic kyphosis.

Lateral lumbar flexion

The distance between the fingertips and the floor is measured with the patient standing erect, then in full lateral flexion and the difference between these values is documented. This is best indicator of active SpA.

Chest expansion

The difference between full expiration and full inspiration is measured at the fourth intercostal space. Normal values are influenced by age and gender, but expansion <2.5 cm is abnormal.

In early disease, spinal mobility is often preserved and the examination may be entirely normal.[6]

ANSWER 4

Patients with inflammatory back pain should undergo an anteroposterior (AP) pelvis and lumbar spine X-ray. Relevant investigations include blood tests for HLA-B27, ESR and CRP levels. Renal function and liver function tests (LFTs) should also be obtained as these patients often require NSAIDs.

ESR and CRP are elevated in 50–70% of patients and the level of elevation may be modest.[7,8] Raised inflammatory markers occur more commonly in patients with concurrent peripheral arthritis than among those with only axial disease.[8] The association between HLA-B27 and AS is well established and occurs in 85–95% patients. However, it also occurs in 5–15% of the general population, with some variability according to ethnicity.[9] Only 5% of these HLA-B27-positive people will go on to develop AS.[10] As such, this test is useful to perform in a patient with inflammatory back pain, but should not be performed as a general screening test in all patients with back pain.

ANSWER 5

The diagnosis of AS still requires the presence of sacroiliitis on conventional X-ray, in addition to symptoms of inflammatory back pain. Such radiographic changes tend to occur late in the disease course, contributing to a mean delay in diagnosis of 5–8 years. More recently, the importance of early diagnosis has been recognised.[7]

The Assessment of SpondyloArthritis international Society (ASAS) has classified axial SpA into two groups:[11,12]

- axial SpA with radiographic (plain X-ray) sacroiliitis (identical to ankylosing spondylitis)
- axial SpA lacking these radiographic changes, which is termed 'non-radiographic axial SpA'.

MRI with STIR sequences can be a useful tool to identify patients who are in the non-radiographic axial SpA category, as it allows visualisation of early inflammation in the sacroiliac joints and spine. It should be noted that a nuclear bone scan is not helpful in this setting because of the normal high radiolabelled tracer uptake by the sacroiliac joints.[4] In general, the burden of symptoms and disease activity tend to be similar in patients with radiographic and non-radiographic axial SpA, and treatment approaches are similar.[13] Approximately 10% of patients with non-radiographic axial SpA will progress to radiographic ankylosing spondylitis over 2 years and 20% progress if MRI findings of active sacroiliitis are present.[14]

ANSWER 6

The mainstay of treatment for axial SpA is an appropriate exercise and spinal stretching program, together with NSAIDs. In addition to relieving symptoms, daily NSAID use has been shown to delay radiographic progression.[10,15] The potential complications of long-term NSAID therapy need to be taken into consideration for each individual patient. Patients may benefit from physiotherapy advice regarding appropriate home exercises to improve spinal

mobility.[16] Smoking cessation is important, as it is an independent modifiable risk factor for poor outcome in axial SpA.[17]

ANSWER 7

Traditional disease-modifying anti-rheumatic drugs (DMARDs) can be used to treat peripheral arthritis, which can occur in association with axial SpA.[2] Sulfasalazine is particularly helpful, although methotrexate is also often used. These medications are not used to treat the axial component of the disease, as their effect on spinal stiffness is minimal.[2]

Sulfasalazine can cause rash, gastrointestinal upset, headaches, dizziness, tinnitus, photosensitivity and an orange discolouration of bodily secretions. Less common side effects include oligospermia, blood dyscrasias and hepatitis. Patients on this medication require regular monitoring of their blood counts and liver function.[18] These blood tests should generally be performed every 2–4 weeks for the first 3 months then every 3 months.[19]

ANSWER 8

TNF-α is a pro-inflammatory cytokine that has a major role in the pathogenesis of SpA. TNF-α inhibitors are biologic agents that directly target this molecule. These agents lead to rapid and major improvement in both the axial disease and peripheral manifestations. TNF-α inhibitors are more effective in younger patients and those with shorter disease duration.[13] Recent evidence suggests that, in addition to symptomatic relief, TNF-α inhibitors may reduce radiographic progression of disease, particularly with early initiation.[20] Paul would almost certainly benefit from one of these agents. In Australia, these agents are listed on the Pharmaceutical Benefits Scheme (PBS), and can only be prescribed by a rheumatologist, for those with:[21]

- inflammatory back pain for more than 3 months
- reduced spinal mobility
- at least bilateral grade 2 or unilateral grade 3 sacroiliitis on X-ray
- active inflammatory symptoms despite 3 months of exercise and regular NSAIDs
- raised ESR and/or CRP.

Paul does not meet these criteria, as his ESR and CRP levels are normal and his X-rays demonstrate unilateral grade 1 sacroilitis only, so he would not be eligible for PBS-subsided TNF-α inhibitors on current PBS criteria.

CONCLUSION

In SpA, first-line therapy consists of a spinal stretching program and on-demand NSAIDs. Many patients will respond to this regimen and not require escalation of therapy. Traditional DMARDs can be used to treat peripheral arthritis, but have minimal effect on spinal disease. TNF-α inhibitors are highly effective and can be used in patients who do not respond to first-line therapies. However, these agents can only be prescribed by a rheumatologist, and the availability of these medications on the PBS is restricted in Australia for patients with early presentations of SpA.[2]

RESOURCES FOR DOCTORS

- The National Ankylosing Spondylitis Society (NASS) provides examples of exercises on their website, http://nass.co.uk/exercise
- The Australian Rheumatology Association has recommendations for the use of biological agents for the treatment of rheumatic disease, www.rheumatology.org.au/downloads/FINAL-BiologicalRecommendations060111.pdf

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CASE 3

JULIE HAS JOINT PAINS

Julie, an accountant aged 32 years, comes to see you about pain and stiffness in her hands, wrists and feet. These symptoms have been present for the past 8 weeks and the pain has been gradually worsening despite taking paracetamol. Julie has noticed increasing difficulty with opening jars and typing at work. Her health has otherwise been good. She does not take any other regular medications and has no known drug allergies.

QUESTION 1

What further information do you need to assist in your assessment and management of Julie?

FURTHER INFORMATION

Julie says her pain and stiffness are worse in the morning but improve after 2 hours of activity. The pain returns at the end of the day, especially if she has been busy at work. She has noticed some swelling in her fingers and her rings now feel tight. Julie has not had any preceding infective symptoms or skin rashes, dry eyes or mouth, Raynaud's phenomenon or mouth ulcers. She admits to feeling very tired lately but has not had any fevers, night sweats or weight loss. Julie has no previous history of joint pain. Her sister has rheumatoid arthritis (RA) but Julie is not aware of any family history of psoriasis. Julie has never smoked.

On examination Julie has 'boggy' swelling and tenderness of the metacarpohalangeal (MCP), proximal interphalangeal (PIP), metatarsophalangeal (MTP) joints and wrist bilaterally. There is restricted range of movement at the MCP and PIP joints and wrists. Grip strength is decreased. There are no skin rashes or nodules. Her spine and other joints are normal. Respiratory, cardiac and neurological examinations are unremarkable.

QUESTION 2

What is your provisional diagnosis? Are there any other diagnoses to consider?

QUESTION 3

What specific investigations could you perform to confirm your initial diagnosis?

FURTHER INFORMATION

Julie's test results are shown in *Table 1*.

Table 1. Julie's results

Test	Julie's result	Reference ranges
FBE:		
Haemoglobin	102 g/L	119–160
MCV	89 fL	80–100
MCH	30 pg	27–32
WCC	5.6 x 109/L	4–11
Platelets	320 x 109/L	150–450
Electrolytes, urea and creatinine	Normal	
LFTs	Normal	
ESR	52 mm/hour	1–21
CRP	3.6 mg/L	0.0–5.0
RhF	42 IU/mL	<16
Anti-CCP	133 U/mL	<5
X-rays of hands, wrists and feet	Periarticular osteopaenia affecting the MCP and PIP joints, carpal bones and MTP joints	

MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; WCC, white cell count FBE, full blood evaluation; LFT, Liver function tests; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; RhF, rheumatoid factor; anti-CCP, anti-cyclic citrullinated peptide

QUESTION 4

What is the diagnosis? How would you manage Julie?

FURTHER INFORMATION

You refer Julie to a rheumatologist, who confirms that she has very active seropositive RA. Given that Julie has poor prognostic factors, the rheumatologist commences her on methotrexate, an oral disease-modifying anti-rheumatic drug (DMARD) 20 mg weekly, folic acid 5 mg weekly (to reduce gastrointestinal/hepatic adverse events) and meloxicam 15 mg daily.[1] Screening tests for hepatitis B and C, and a baseline chest X-ray taken before starting methotrexate were normal.

QUESTION 5

What is the GP's role in monitoring Julie's disease activity?

QUESTION 6

How will you monitor and manage Julie's treatment?

QUESTION 7

As the GP, what additional considerations should you take in Julie's case?

FURTHER INFORMATION

Six weeks after starting methotrexate treatment, Julie notices only slight improvement in joint pain, swelling and stiffness. Although it may take 2–3 months before the effects of methotrexate are seen, given that Julie has very active disease with a number of poor prognostic features, the rheumatologist adds sulfasalazine 1 g twice daily and hydroxychloroquine 200 mg daily. Meloxicam is replaced with a weaning course of low-dose prednisone.

Julie has a good response to combination therapy and achieves disease remission, which is defined by symptomatic relief, absence of joint swelling and normal inflammatory markers.

QUESTION 8

Why are sulfasalazine and hydroxychloroquine given in addition to methotrexate? What other treatments could be considered if Julie's RA becomes active again?

CASE 3 ANSWERS

ANSWER 1

It is necessary to determine whether Julie's pain is mechanical or inflammatory in nature.

Mechanical pain is classically exacerbated by activity and relieved by rest, whereas inflammatory pain is present at rest and often eased by activity.[1,2]

Features that may be associated with inflammatory pain include:[1,2]

- joint swelling and warmth
- stiffness after inactivity
- early morning stiffness lasting longer than 1 hour
- pain worse at either end of the day
- improvement with non-steroidal anti-inflammatory drugs (NSAIDs).

The pattern of joint involvement is important. Typically, RA presents as a symmetrical polyarthritis that most commonly affects the MCP and PIP joints of the fingers, interphalangeal joints of the thumbs and wrists, and MTP joints of the toes.[3] Osteoarthritis may also affect the small joints of the hands but typically involves the distal interphalangeal (DIP), PIP and carpometacarpal joints.[4] An asymmetrical arthritis with spinal involvement suggests the presence of spondyloarthritis such as psoriatic arthritis.

It will also be important to obtain the following information:[3]

- Are there any precipitating factors such as a recent viral illness, or other infections (eg enteric or genitourinary infections)?
- Does Julie have any extra-articular features such as sicca symptoms, rash, mouth ulcers or Raynaud's phenomenon?
- Has Julie had any systemic symptoms such as weight loss, fatigue, fever or night sweats?
- Does Julie have a family history of psoriasis, RA or other autoimmune disease?
- Is there any functional impairment?
- What is Julie's smoking status (smoking is strong risk factor for RA)?

ANSWER 2

Julie has a recent-onset, symmetrical inflammatory polyarthritis affecting the peripheral joints. The pattern of joint involvement and family history support a diagnosis of RA.

The Royal Australian College of General Practitioners (RACGP) *Clinical guidelines for the diagnosis and management of early rheumatoid arthritis* recommends that RA should be suspected in patients with one or more of the following:[4]

- persistent joint pain and swelling affecting at least three joint areas
- symmetrical involvement of the MCP or MTP joints
- morning stiffness lasting more than 30 minutes.

Other possible causes of inflammatory polyarthritis affecting the hands and feet include:

- Viral polyarthritis: parvovirus B19, hepatitis B, hepatitis C and mosquito-borne viruses (eg Ross River and Barmah Forest) can cause symmetrical polyarthritis that can mimic RA.[5] These symptoms are usually self-limiting.
- Connective tissue disease: systemic lupus erythematosus (SLE), Sjögren's syndrome, dermatomyositis and overlap syndromes. These conditions tend to have additional features such as skin rash, dry mouth and eyes, and alopecia.[6]
- Psoriatic arthritis: personal or family history of psoriatic skin or nail changes suggests this diagnosis.[6]
- Reactive arthritis and inflammatory bowel disease associated arthritis: although typically associated with large joint monoarthritis or oligoarthritis, it can also affect the hands. It tends to be asymmetrical and may be associated with rash, enthesitis, spinal involvement, gastrointestinal symptoms and a history of recent urethritis or enteric infection.[6]
- Crystal arthropathy: occasionally gout and pseudogout can cause a polyarthritis. They are distinguished by the presence of urate and calcium pyrophosphate crystals in synovial fluid respectively. A prior history of acute gout, and the presence of tophi on examination, would also support a diagnosis of gout.[6]
- Paraneoplastic disease: rarely, polyarthritis can be associated with malignancies.[7]
- Sarcoid arthropathy: sarcoidosis may cause an inflammatory polyarthritis with a similar pattern of joint involvement as RA. It is, however, associated with parenchymal lung disease, bilateral hilar lymphadenopathy, skin lesions and eye involvement.[6]

ANSWER 3

Appropriate initial investigations that the GP can order include:

- Full blood evaluation (FBE),[1,3,4,6] electrolytes, renal function and liver function tests (LFTs):[1,3,6]
  - Active disease may be associated with anaemia of chronic disease, thrombocytosis and mild leukocytosis.[3]
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels:[1,3,4,6,7]
  - Acute-phase reactants may be elevated but are normal in 40% of patients with recent-onset disease.[8]
  - Alternative diagnoses such as infection, vasculitis or crystal arthritis should be considered if these markers are substantially elevated.[7]
  - High levels are predictive of long-term radiographic progression.[4]
- Rheumatoid factor (RhF) and anti-cyclic citrullinated peptide antibody (anti-CCP) levels[1,3,4,6–8]
  - RhF is present in 60–70% of patients with RA and up to 4% of healthy, young individuals[7]

  - RhF positivity is associated with more aggressive joint disease[7] and extra-articular manifestations[4,7]
  - RhF specificity is poor and false positives may occur in other conditions (eg SLE, Sjögren's syndrome, chronic infections, cryoglobulinaemia, lymphoproliferative disorders)[7,8]
  - anti-CCP sensitivity is similar to that of RhF but specificity is higher[5]
  - anti-CCP is a strong predictor of erosive disease.[4,7]
- Plain X-rays of the hands and feet:[1,3,4,6,7,9]
  - Radiographic changes include periarticular osteopaenia, soft tissue swelling, uniform joint space narrowing and marginal bone erosions. Joint deformities may occur with advanced disease.[3]
  - Plain films are often normal in early disease but can serve as a baseline for monitoring disease progression.[3,6]

Additional investigations that may be useful include:

- serum uric acid levels[6]
- antinuclear antibody (ANA): if there are additional features, such as sicca symptoms, rash, alopecia, photosensitivity or Raynaud's phenomenon[6,7]
- serological studies: for viral infection in patients with symptoms for <6 weeks (eg Parvovirus B19, hepatitis B and C)[5–7]
- angiotensin converting enzyme: if there is suspicion for sarcoidosis[6]
- ultrasound or MRI may confirm the presence of joint inflammation,[4,6,10] show changes such as synovitis, bone oedema, erosions, and tenosynovitis[10] and detect bone erosions earlier compared with plain films[3]
- chest X-ray: to exclude alternative diagnoses such as sarcoidosis[1,6] or malignancy
- synovial fluid analysis: may reveal an inflammatory joint fluid and exclude gout, pseudogout or infectious arthritis.[7]

These investigations, however, should not delay further management.

ANSWER 4

Julie's results support a diagnosis of seropositive RA. She has several factors associated with a poor prognosis. These include:

- RhF positivity[1,7,11,12]
- anti-CCP positivity[1,7,11,12]
- large number of swollen joints at disease presentation (>20)[1,7,12]
- high disease activity at onset[12]
- elevated ESR[1,12]

Other indicators of poor prognosis, not applicable in Julie's case, include:

- smoking[12,13]
- early functional impairment[1,11,12]
- early radiological bone erosions[1,7,11,12]
- extra-articular disease manifestations (eg nodules, vasculitis)[11]
- long disease duration at presentation (>3–6 months)[8]

The RACGP guidelines recommend referral to a rheumatologist if there is persistent joint swelling beyond 6 weeks. Immediate referral is recommended when there are multiple swollen joints, particularly if tests for RhF and/or anti-CCP antibodies are positive.[3] This is consistent with a number of international guidelines.[9,13,14] It is not necessary to confirm the diagnosis prior to referral, nor should referral be delayed by the above investigations as normal results do not necessarily rule out RA.

Joint destruction can begin within a few weeks of symptom onset and studies suggest that an early window of opportunity exists where the disease is much more susceptible to treatment.[3,15–17] It is thought that initiation of treatment within this window may change the rate of disease progression and alter long-term outcomes.[4,16] Early referral to a rheumatologist allows for early aggressive disease-modifying therapy, which may in turn reduce long-term joint damage and disability.[4]

ANSWER 5

The rheumatologist commonly performs the formal assessment of disease activity but it is important for the GP to also recognise when the patient's RA is active. The RACGP guidelines suggest that ongoing monitoring should be 'shared care' between the GP, patient and rheumatologist. The GP should be involved in monitoring disease progression, response to treatment, medication toxicities and comorbidities in conjunction with a rheumatologist.[4]

The goal of treatment is to suppress disease activity as quickly as possible in order to reduce symptoms and prevent joint damage.[14,15,17] There is good evidence that frequent assessment of disease activity, and adjusting DMARD therapy to meet targets of disease remission or minimal inflammatory disease activity (ie 'treat-to-target') is associated with improved long-term outcomes.[15,16,18]

Measures of disease activity include:

- number of tender and swollen joints[1,4,13,15]
- duration of early morning stiffness[1,4,15]
- visual analogue scale for patient-reported global assessment[1,16]
- ESR and CRP[1,4,9,15]
- functional assessment.[1,4,15]

A number of composite scores such as the Disease Activity Score derivative for 28 joints (DAS28) and the Clinical Disease Activity Index (CDAI) have also been developed for use in clinical research and practice.[15]

ANSWER 6

Methotrexate has a number of significant adverse effects, which are outlined in *Table 2*. Management of these adverse effects requires collaboration with the treating rheumatologist.

Table 2. Adverse effects of methotrexate

Adverse effects	Possible management
Nausea, vomiting and diarrhoea	• Administration with food or evening dosing[19,20] • Anti-emetics[21] • Increase folic acid supplementation[1,21] • Calcium folinate supplementation[22] • Dose reduction[1] • Parenteral administration[1] • Split the once-a-week dose into 2 or 3 divided doses given over 24 hours (ie instead of 15 mg all at once, take 5 mg at 0, 12 and 24 hours)[22]
Mouth ulcers	• Folic acid or calcium folinate supplementation[1,22] • Dose reduction[1]
Headaches, fatigue, difficulties concentrating	• Dose reduction[20] • Discontinuation may be necessary[22]
Alopecia	• Hair normally grows back on methotrexate cessation
Photosensitivity	• Avoid excessive sun exposure[19–22] • Sunscreen and protective clothes[20,21]
Hepatotoxicity • LFT abnormalities (transaminases) • Steatosis • Fibrosis • Cirrhosis	• LFT abnormalities are more common in patients with diabetes, obesity, renal impairment, viral hepatitis or excessive alcohol[1] • Regular monitoring of LFTs and renal function is required: – The Australian Medicines Handbook (AMH) suggests every 2–4 weeks for first 3 months, then every 3 months (or more frequently if clinically indicated)[19,20] – Methotrexate should be ceased if LFTs are greater than 3 times the upper limit of normal[1] – Less marked elevations may require dose reduction • Liver biopsy may be required if persistently elevated transaminases and/or low albumin[1]
Haematological abnormalities • Macrocytosis • Leucopenia, thrombocytopenia, anaemia	• More common in older patients and with renal impairment[1] • AMH suggests every 2–4 weeks for the first 3 months, then every 3 months (or more frequently if indicated)[20] • Depending on severity, may necessitate dose reduction or discontinuation[22]
Pulmonary toxicity: • Pneumonitis	• May present with cough, dypsnoea or fever[2] • A baseline chest X-ray is important[1,22]
Increased susceptibility to infection	• Usually does not cause opportunistic infections unless taken with other immunosuppressants (eg glucocorticoids and other DMARDs)[22] • Withhold in patients with severe infection[2]

ANSWER 7

In collaboration with the rheumatologist, the GP's role is to:

- Confirm compliance with the dosing regimen of methotrexate. Given its toxicity and dosage regime, errors in methotrexate dosing are common and potentially serious. The importance of weekly dosing and risk of serious toxicity if the recommended dose is exceeded should be reinforced.[1]
- Advise safe alcohol consumption. Alcohol is known to increase the risk of hepatotoxicity of methotrexate. However, the amount that can be safely consumed is not known and is likely to vary between individuals. Abstinence from alcohol is frequently recommended, but low levels (eg 1–2 standard drinks taken once or twice a week) are unlikely to be harmful in the absence of other risk factors for hepatotoxicity.[21,23]
- Provide information about teratogenicity and contraindications. Methotrexate is a teratogen and is contraindicated for breastfeeding.[1,2] Julie therefore needs to be counselled about reliable contraception and advised that methotrexate will need to be ceased for 3 months prior to conception.[1,2,20,21]
- Provide information about drug interactions. Care needs to be taken when new medications are prescribed; use with other folate antagonists such as trimethoprim is contraindicated.[1,20]
- Discuss vaccinations. Pneumococcal and influenza vaccinations are safe and recommended, but live vaccinations require special consideration and should be discussed with the treating rheumatologist.[21] There is a risk of live vaccines causing infection in an immunosuppressed host.
- Discuss cardiovascular risk. Active RA is associated with an increased risk of cardiovascular disease.[17] Guidelines recommend managing risk factors such as smoking, obesity, physical inactivity, hypercholesterolaemia, hypertension and diabetes.[4]

ANSWER 8

A number of international guidelines recommend combination DMARD therapy as first-line treatment, especially if there are unfavourable prognostic features, as in Julie's case.[9,11,14]

If Julie's RA becomes active again, although other conventional DMARDs could be considered, she will probably require a biological DMARD. These include tumour necrosis factor-alpha (TNF-α) inhibitors (etanercept, adalimumab, infliximab, golimumab, certolizumab) and/or other monoclonal antibodies such as rituximab, abatacept and tocilizumab. These medications would need to be prescribed by a rheumatologist or clinical immunologist, and strict eligibility criteria need to be met before they can be accessed through the Pharmaceutical Benefits Scheme (PBS). Current PBS criteria restrict the use of biological DMARDs to patients with severe, active disease (as defined by swollen and tender joint count and inflammatory markers), despite 6 months of intensive treatment with conventional DMARDs.

Recently, tofacitinib has become available in Australia and, at the time of writing, is awaiting PBS listing. It is an oral Janus kinase inhibitor that has been approved for moderate to severe RA refractory to other

disease-modifying treatments.[23] European guidelines recommend its consideration following failure of biological DMARD therapy.[14]

RESOURCES FOR PATIENTS

- Arthritis Australia provides information sheets on their website, www.arthritisaustralia.com.au
- The Australian Rheumatology Association provides information sheets on their website, www.rheumatology.org.au/community/PatientMedicineInformation.asp
- The American College of Rheumatology, www.rheumatology.org/Practice/Clinical/Patients/Diseases_And_Conditions/Rheumatoid_Arthritis

RESOURCES FOR DOCTORS

- The Royal Australian College of General Practitioners. Clinical guidelines for the diagnosis and management of early rheumatoid arthritis, www.racgp.org.au/your-practice/guidelines/musculoskeletal/rheumatoidarthritis/
- Chakravarty K, McDonald H, Pullar T, et al. BSR/BHPR guidelines for disease modifying anti-rheumatic drug (DMARD) therapy in consultation with the British Association of Dermatologists. Rheumatology (Oxford). 2008;47:924–25.
- PBS Prescribing for TNF Inhibitors, http://pbs.gov.au/medicine/item/1964J-3447K-3450N-5735W-9455P-9456Q-9457R-9458T-9459W-9460X-9461Y-9462B-9641K [Accessed 6 July 2015].

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CASE 4

TIMOTHY PRESENTS WITH AN ACUTELY SWOLLEN KNEE

Timothy is a mechanic aged 42 years. He presents to your clinic with an extremely painful and swollen right knee, which developed over the past 2 days. He has limited mobility and has just started taking an over-the-counter non-steroidal anti-inflammatory drug (NSAID) but has had little improvement. He has not had any preceding injury. He tells you he was at a friend's party over the weekend and may have had a few more beers than is usual for him.

QUESTION 1

What relevant questions should you ask Timothy?

QUESTION 2

What are the key aspects of examination to focus on?

FURTHER INFORMATION

Timothy tells you that, apart from the pain and swelling in his knee, he is well. He has not had any fevers and there are no obvious infective foci. He has had recurrent pain in his right big toe (first metatarsophalyngeal [MTP] joint) in the past 5 years. He has never sought medical attention for this pain as it generally settles in a few days. He has no personal or family history of psoriasis. There was no family history of any autoimmune conditions.

Timothy has been married for 12 years. He and his wife have a stable and happy relationship. When prompted, Timothy tells you that he has a sedentary lifestyle and has been steadily gaining weight over the past few years. He also reveals that he drinks excessively; he admits to having 12 standard drinks per week and often binge drinking at the weekends.

On examination, he is well and afebrile. His body mass index (BMI) is 31 kg/m^2. He has a moderate–large right knee effusion with restricted range of motion due to the pain. There is no evidence of tophi elsewhere.

QUESTION 3

What are the differential diagnoses for Timothy's symptoms? What is the most likely cause of Timothy's symptoms?

QUESTION 4

How would you investigate Timothy's symptoms?

FURTHER INFORMATION

You arrange for Timothy to have initial blood tests, which reveal leukocytosis with neutrophilia. Kidney and liver function tests are within range and blood cultures are negative. The other results are shown in *Table 1*.

Table 1. Timothy's blood test results

Test	Timothy's result	Normal range
Erythrocyte sedimentation rate (ESR)	26 mm/hour	0–15 mm/hour
C-reactive protein (CRP)	17 mg/L	<5.0 mg/L
Serum uric acid (SUA)	0.56 mmol/L	0.24–0.48 mmol/L (men)

You also arrange for Timothy to have an X-ray of his right knee, which shows the presence of a large effusion with early degenerative change. An X-ray of his right foot shows erosion at his first MTP joint.

You then refer Timothy to a rheumatologist for further management of suspected gout. The rheumatologist performs a joint aspirate; 35 mL of cloudy fluid is aspirated and sent for analysis.

The synovial fluid is found to have a white cell count (WCC) of 51,000 x 10^6/L; 70% of this represents polymorphs. Needle-shaped intracellular and extracellular crystals that exhibit negative birefringence are seen. Testing for microbial cultures remains negative (*Table 2*).

Timothy returned to you to refill his script for his antihypertensive medication just prior to his follow-up appointment with his rheumatologists and asks you about the results of his joint aspirate.

QUESTION 5

What can you tell Timothy about the results of his synovial fluid analysis?

QUESTION 6

Timothy asks you for your opinion as to how he should be managed in an acute setting. What would you tell him?

QUESTION 7

Timothy asks you whether anything needs to be done to prevent his gout from recurring. How would you advise him?

QUESTION 8

Are there any safety concerns for use of allopurinol? Are there alternative treatment options?

FURTHER INFORMATION

Timothy returned to his rheumatologist for his follow-up appointment. The rheumatologist gave Timothy an intra-articular steroid injection. He was started on allopurinol 100 mg daily in conjunction with low-dose colchicine 500 µg daily to reduce the risk of a gout flare triggered by introduction of allopurinol. The increased risk of gout flares associated with introduction of allopurinol is due to monosodium urate shedding into the joint synovial fluid as the serum urate level decreases.

Timothy asks if his gout can be managed by you, so the rheumatologist provides recommendations to increase his allopurinol dose in increments of 100 mg per month until the SUA target is reached. The rheumatologist also advises that colchicine be continued until Timothy has been free of gout for 1–3 months on the therapeutic dose of allopurinol (ie the dose at which the SUA target has been achieved).

QUESTION 9

How would you manage Timothy at his follow-up visits?

CASE 4 ANSWERS

ANSWER 1

Relevant questions to ask Timothy include:[1,2]

- What are the characteristics of the joint pain?
  - onset and quality
  - any diurnal variation
  - factors that exacerbate or relieve the pain (inflammatory arthritis is, in general, worse with immobility, whereas pain from non-inflammatory arthritis, such as from osteoarthritis is exacerbated by weight bearing and movement and improve with rest)
  - a history of prior joint pain or swelling
  - a history of preceding trauma.
- Does he have any associated constitutional symptoms (high-grade temperatures, fatigue and anorexia) that would raise the suspicion of infection or sepsis?
- Has he had any gastrointestinal or genitourinary symptoms, or any recent sexual exposures that may be a clue to a seronegative spondyloarthropathy such as reactive arthritis or an inflammatory arthropathy associated with Crohn's disease or ulcerative colitis?
- Has he had a history of conjunctivitis, new rash or urethritis?
- Does he have a history of psoriasis, which might raise the suspicion of psoriatic arthritis?
- Is Timothy immunosuppressed? If so, he would be more vulnerable to opportunistic infections.
- Has he had any recent surgery/procedures?
- Are there any other risk factors such as travel, alcohol and intravenous drug use?
- Does he have a family history of any rheumatic disease or psoriasis?

ANSWER 2

A full physical examination should be conducted, focusing on:[1,2]

- joint examination to evaluate for the presence of synovitis or effusion:
  - warmth and tenderness over the joint
  - palpation for soft tissue swelling
  - establish the presence of an effusion (eg with the 'bulge sign' or 'patella tap' for knee effusions)
  - joint assessment for range of motion
  - mechanical or degenerative pathology may result in restricted active and passive range of motion with maximum pain at the limit of joint motion
- Evaluating for the presence of other musculoskeletal/extra-articular signs:
  - enthesitis/dactylitis suggestive of a seronegative spondyloarthropathy
  - conjunctivitis, anterior uveitis, episcleritis and corneal ulcers can be seen in reactive arthritis
  - skin lesions such as keratoderma blennorrhagica and erythema nodosum are associated with reactive arthritis
  - psoriatic nail changes: nail pits, onycholysis, nail bed hyperkeratosis points to the possibility of psoriatic arthritis
- Identification of any septic foci including the presence of stigmata of endocarditis
  - this would point to an infective cause
- The presence of gouty tophi.

ANSWER 3

The differential diagnoses for an acute monoarthritis include:[3,4]

Crystal arthropathy

- Monosodium urate deposition disease, or gout, is one of the most common cause of an acute monoarthritis.
- Calcium pyrophosphate deposition disease, or psuedogout, can also present in such a manner.
- Less commonly, calcium oxalate and apatite crystals can also present as a monoarthritis.

Septic arthritis

This can result in significant morbidity if treatment is delayed.

- Gonococcal infection: *Neisseria gonorrhoea* is an important cause of septic arthritis in sexually active adults. Other clinical findings may include tenosynovitis, a new rash and a history of urethral discharge.
- Non-gonococcal bacterial infection: *Staphylococcus aureus* infection is the most common causes of non-gonococcal septic arthritis. This can occur in the context of recent skin infection, prosthetic joint, intravenous drug use, joint surgery and immunosuppression.

Osteoarthritis

- Acute exacerbations with swelling can occur. Symptoms are generally mild, typically with non-inflammatory synovial fluid.

Monoarthritis as an initial presentation of a systemic rheumatic condition

- Rheumatoid arthritis rarely presents as a monoarthritis.
- Psoriatic arthritis, reactive arthritis and inflammatory arthropathy associated with inflammatory bowel disease are also known to cause monoarthritis, especially involving the lower extremity.

In Timothy's case, gout is high on the list of differentials given his history of probable podagra, excess alcohol intake and weight gain. Septic arthritis and reactive arthritis are less likely given the absence of risk factors, but need to be considered.

ANSWER 4

The key investigation required to confirm the diagnosis of gout and to exclude septic arthritis is joint aspiration for microscopy/culture and sensitivity, cell count and differential and crystal analysis. This can be done by GPs who have been trained and are able to perform joint aspirates. Alternatively, the procedure can be done by a rheumatologist or by a radiologist under ultrasound guidance.

Other investigations include:

- full blood evaluation (FBE), electrolytes, liver function tests (LFTs)
- erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels: elevation of these inflammatory markers signifies an underlying inflammatory process
- serum uric acid levels: these may be normal in up to 50% of patients during an acute episode of gout
- blood cultures: these are particularly warranted if an infective cause is suspected
- radiographs to assess for the presence of gouty erosions

It should be noted that crystal arthropathy can present in an identical manner to septic arthritis and cannot be reliably distinguished clinically or by WCC counts, raised ESR and CRP, or synovial WCC counts. Differentiating between the two conditions is imperative as management is very different and failure to identify septic arthritis can result in rapid, irreversible joint damage. If there is a high clinical suspicion for septic arthritis the patient should have their joint aspirated and then be given intravenous antibiotics until septic arthritis is excluded or confirmed through microbiological testing for cultures.

ANSWER 5

A WCC count of >2000 x 10^6/L with >50% polymorphs in Timothy's synovial fluid confirms the presence of inflammation. His aspirate is negative for culture, which rules out sepsis. This is important to establish as crystals can be present in a septic joint.[5] Monosodium urate crystals are needle-shaped crystals with negative birefringence and their presence confirms the diagnosis of gout.

ANSWER 6

Reducing inflammation and pain is the focus of gout management in the acute setting. Drugs used to treat an episode of acute gout include NSAIDs, glucocorticoids and colchicine.

NSAIDs are very effective and, in the absence of contraindications, they reduce symptoms rapidly, particularly when given in the upper dosing range and initiated early. All NSAIDs, including cyclooxygenase-2 (COX-2) inhibitors are effective in acute gout. Timothy can continue to use NSAIDs until the attack has settled.[11]

Drainage of his knee effusion followed by intra-articular steroid injection is an effective option for relieving his symptoms. This can be done by a skilled GP or by a rheumatologist or under image guidance by a radiologist.

If Timothy were to present with polyarticular gout, oral corticosteroids can be considered. The current Australian *Therapeutic Guidelines*[12] recommend prednisolone at doses of 15–20 mg daily, typically for 3–5 days. Prednisolone can then be weaned to cessation over 2 weeks.

Table 2. Synovial fluid analysis[6–10]

	Normal	Non-inflammatory	Inflammatory (crystalline)	Inflammatory (non-crystalline	Septic (gonococcal)	Septic (non-gonococcal)
Transparency	Transparent	Transparent	Translucent – opaque	Translucent – opaque	Opaque	Opaque
Colour	Clear	Straw	Yellow	Yellow	Yellow–green	Yellow–green
Viscosity	High	High	Low	Low	Variable	Variable
White cell count	<200 x 10^6/L	200–2000 x 10^6/L	2000–100,000 x 10^6/L	2000–100,000 x 10^6/L	34,000–68,000 x 10^6/L	>50,000 x 10^6/L (>100,000 x 10^6/L is more specific)
Polymorph cell count (%)	<25	<25	≥50	≥50	≥75	≥75
Gram stain	Negative	Negative	Negative	Negative	Variable (<50%)	Positive (60–80%)
Culture	Negative	Negative	Negative	Negative	Positive (25–70%)	Positive (>90%)
Crystals	Negative	Negative	Positive	Negative	Negative	Negative

Colchicine can also be effective in the acute setting. Guidelines recommend that patients be commenced on 1 mg of colchicine, followed by 500 µg 1 hour later. No further colchicine is to be taken for 72 hours.[13] There is no benefit in administering higher doses. Colchicine must be used cautiously in people with renal impairment. Increasingly, colchicine is used for prophylaxis against flares of gout as urate-lowering therapy is introduced.[14]

ANSWER 7

Preventive interventions should include non-pharmacological and pharmacological strategies.

Non-pharmacological interventions

Weight and alcohol reduction are important for Timothy's management. Referral to a dietitian should be considered. Timothy should be counselled to reduce caloric intake, replace refined sugars with complex carbohydrates and reduce intake of saturated fats. Intake of foods that are high in purines, such as liver, kidney and shellfish, should be restricted.

Timothy should be advised to refrain from sugar-sweetened drinks and foods that contain fructose as these increase the risk of gout. Regular or low-fat milk or yoghurt, soybeans and vegetable sources of protein, and cherries may have a mild effect on reducing SUA.[15]

Timothy's baseline SUA, 0.56 mmol/L, is well above the normal range of for men (0.24–0.48 mmol/L). Lifestyle changes alone are unlikely to be sufficient in achieving the target SUA.[15] It is well documented that lifestyle changes alone rarely lead to more than 10–18% reduction in serum urate.[16] Note that serum urate can drop by 0.1–0.2 mmol/L in an acute flare, reducing the utility of testing in an acute flare and also of using that reading as a true baseline in established gout.

Pharmacological interventions

Urate-lowering intervention is required given Timothy's history of recurrent gout attacks and radiographic changes. The aim is to achieve a sustained level of serum urate below the threshold for saturation of urate, which will promote spontaneous dissolution of monosodium urate crystals to prevent further attacks, joint/bone damage and deposition of tophi in other tissues and organs. The current Australian *Therapeutic Guidelines*[12] recommend lowering SUA levels to ≤0.3 mmol/L.

Allopurinol, a hypouricaemic drug, remains the first-line treatment for lowering serum urate.[15] In Timothy's case, allopurinol should be prescribed at a starting dose of 100 mg daily (in patients with renal impairment, the initial dose should be 50 mg daily or less). The dose can be tritated up every 4 weeks in increments of 100 mg (or 50 mg for patients with renal impairment) until the target SUA level is reached.[17]

Failure to titrate the dose of allopurinol to achieve the target SUA level results in the poor management of a treatable condition. Most prescriptions are for 300 mg daily or less. However, it has been shown that only 21% of patients achieved an SUA <0.36 mmol/L on a dose of 300 mg/day.[18]

ANSWER 8

The incidence of major allopurinol hypersensitivity syndrome (AHS) is rare and estimated to be 0.1–0.4%. However, AHS is associated with a high mortality rate (up to 27%).[19] It is characterised by severe cutaneous reactions (eg with Stevens-Johnson syndrome or toxic epidermal necrolysis), eosinophilia/leukocytosis, fever and multi-organ failure.

Risk factors for AHS include pre-existing renal impairment, concomitant diuretic use, recent initiation of allopurinol (especially when doses of >200 mg/day are used) and *HLA-B*5801*, an allele that occurs in high frequency in patients of Han-Chinese ancestry, Thai and Korean populations.[20,21]

Other adverse reactions of allopurinol include induced rash, which occurs in about 2% of patients and is commonly preceded by pruritis. About 50% of these patients are able to successfully restart allopurinol after desensitisation.

Alternatives to allopurinol, for patients who are allergic to, or intolerant of, allopurinol, include probenecid. This can be used in patients with adequate renal function. Febuxostat has just been approved by the Therapeutic Goods Administration and can now be accessed commercially. It can be considered in allopurinol intolerant patients with poor renal function. There is currently an application for febuxostat to be listed on the Pharmaceutical Benefits Scheme (PBS) and this may occur in late 2015.

ANSWER 9

During follow-up visits, you should:

- assess and reinforce compliance to allopurinol
- provide advice for lifestyle changes
- monitor SUA levels and adjust the dose of allopurinol if required (see Answer 7)
- arrange monthly FBE, kidney function tests and LFTs to monitor for adverse effects until stable, after which the frequency of monitoring can be decreased. Using allopurinol above the dose based on creatinine clearance is effective and safe in patients with chronic gout, including those with renal impairment.[22]

Discontinue allopurinol at the first appearance of skin rash or other signs that may indicate an allergic reaction. Stevens-Johnson syndrome or toxic epidermal necrolysis reactions typically occur 5 days to 3 weeks after starting allopurinol.[20]

Managing concurrent comorbidities is important because gout is a risk factor for hypertension, cardiac and all-cause mortality, metabolic syndrome, diabetes mellitus and obesity.[23]

If Timothy develops adverse reactions to his gout medications or has refractory joint symptoms, you should refer him back to the rheumatologist.

RESOURCES FOR PATIENTS

- The Gout and Uric Acid Education Society has an interactive quiz on gout, patient education kit and a video library, www.gouteducation.org
- Arthritis Australia provides general disease and treatment information, and support services, www.arthritisaustralia.com.au/images/stories/

documents/info_sheets/2015/Condition%20specific/Gout.pdf; www.arthritisaustralia.com.au/images/stories/documents/info_sheets/2015/General%20management/Goutanddiet.pdf

- The American College of Rheumatology, www.rheumatology.org/practice/clinical/patients/diseases_and_conditions/gout.asp
- National Institute of Arthritis and Musculoskeletal and Skin Diseases, www.niams.nih.gov

RESOURCES FOR DOCTORS

- Rheumatology Expert Group. Crystal deposition disease. Gout. In Therapeutic guidelines: rheumatology. Melbourne: Therapeutic Guidelines Limited; 2010, www.tg.org.au/?sectionid=117
- The Royal Australian College of General Practitioners. Clinical guidelines for the diagnosis and management of early rheumatoid arthritis, www.racgp.org.au/your-practice/guidelines/musculoskeletal/rheumatoidarthritis/
- Australian Rheumatology Association, www.rheumatology.org.au
- Arthritis Australia is recommended for general disease and treatment information, as well as support services, www.arthritisaustralia.com.au

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CASE 5

LILY HAS HURT HER FOOT

Lily, 16 years of age, is fit and healthy, and enjoys dancing and running. Two days ago she landed awkwardly at ballet and thought she had 'rolled her ankle'. She had immediate pain in the lateral foot and was unable to bear weight. She put ice on her foot, but by that night it was moderately swollen and bruised.

QUESTION 1

What examinations are needed for Lily's foot and ankle?

FURTHER INFORMATION

Lily's parents gave her some paracetamol at the appropriate dosage for her weight, and she managed to get around on crutches. Lily had no previous ankle or foot injuries.

On physical examination you find that Lily is tender at the base of her fifth metatarsal. Resisted eversion of the foot is painful and a little weak. Her ankle is stable and there is no increase in anterior draw or talar tilt, and no tenderness in the fibula. Neurovascular examination of the foot is intact.

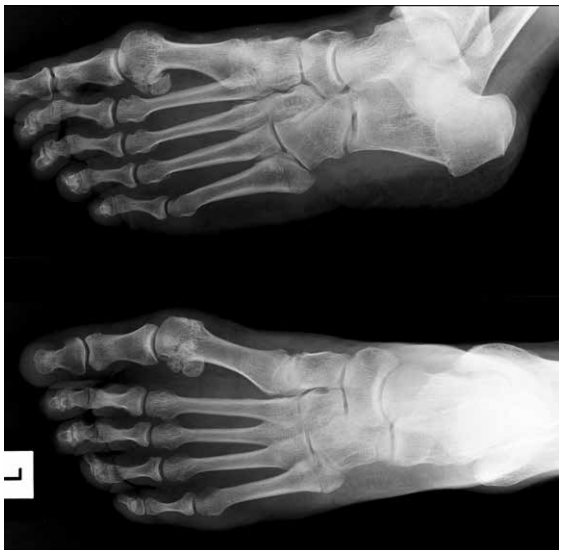
QUESTION 2

On the basis of your examination findings, what are the differential diagnoses for Lily's foot injury?

FURTHER INFORMATION

You arrange for Lily to have plain X-rays taken of her foot. Lily returns later that day with her X-rays (*Figure 1*) and the radiologist's report.

Figure 1. Plain X-rays of Lily's foot



QUESTION 3

What does the X-ray (*Figure 1*) show?

QUESTION 4

Is any other imaging required for Lily's foot?

QUESTION 5

How should Lily's fracture be managed?

QUESTION 6

When would surgical referral be indicated for fifth metatarsal fractures?

FURTHER INFORMATION

Lily's parents ask, 'How soon can Lily return to dancing?'

QUESTION 7

How would you respond to Lily's parents?

CASE 5 ANSWERS

ANSWER 1

The Ottawa Ankle Rules[1] recommend the following investigations:

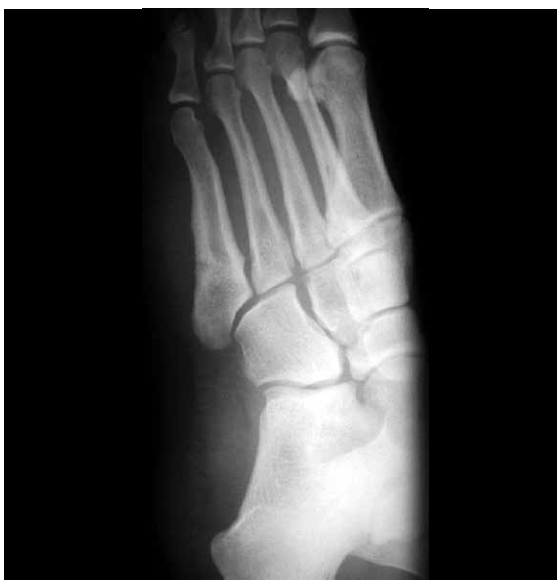
- Plain radiographs of the ankle are indicated if there is pain in the malleolar zone of the ankle AND any one of the following:
  - bony tenderness along the distal 6 cm of the posterior edge or tip of the fibula
  - bony tenderness along the distal 6 cm of the posterior edge or tip of the tibia
  - an immediate inability to bear weight and, on later examination, an inability to take more than four steps.
- Plain radiographs of the foot are indicated if there is pain in the midfoot AND any of:
  - bony tenderness at the base of the fifth metatarsal
  - bony tenderness at the navicular
  - an immediate inability to bear weight and, on later examination an inability to take more than four steps.

ANSWER 2

The differential diagnoses for Lily's fifth metatarsal injury are:

- an avulsion fracture of the tuberosity, proximal to the joint between the bases of the fourth and fifth metatarsals
- a stress fracture of the diaphysis, either at the joint (Jones fracture; *Figure 2*) or distal to the joint
- a spiral fracture of the metatarsal shaft
- a midfoot joint sprain
- a peroneal tendon tear.

Figure 2. Plain radiographs of a Jones fracture



ANSWER 3

Lily's X-ray shows an avulsion fracture of the fifth metatarsal. This is the insertion of the peroneus brevis tendon. These fractures always have a transverse orientation, which distinguishes them from the normal apophysis of the fifth metatarsal, usually apparent at the age of 9–12 years in girls and 11–15 years in boys.[2] This apophysis is aligned longitudinally at the base of the metatarsal. Apophysitis can occur in children in these age groups; it resolves with rest.[3]

ANSWER 4

No other imaging is necessary in this situation. If Lily's plain radiographs were normal and her pain and inability to bear weight were unchanged after 7 days, further imaging may be considered. In the latter situation, repeating the plain X-rays would be appropriate. If these were still inconclusive, magnetic resonance imaging (MRI) or a technetium-99 nuclear bone scan would be indicated to assess for an occult fracture, such as at the lateral talar process, or joint injury, such as subtalar or mid-tarsal joint sprain, or peroneal tendon injury. Rarer causes of ongoing pain could include systemic arthropathy (eg juvenile rheumatoid arthritis/Still's disease), joint sepsis or osteomyelitis, or bony tumour.[4]

ANSWER 5

Lily's fracture can be managed conservatively with non-weight bearing as necessary, progressing to partial and then full weight-bearing as tolerated. This usually takes 3–4 weeks. Immobilisation or bracing may provide support and comfort but is not essential.[5,6] Simple analgesics, such as paracetamol, may be used unless there are contraindications. Non-steroidal anti-inflammatory drugs (NSAIDs) may inhibit fracture healing, depending on the choice of medication and duration of use.[7,8]

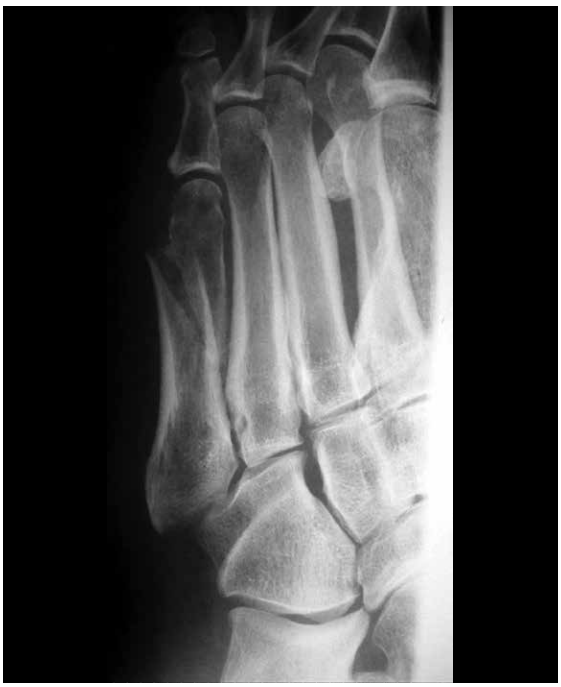
ANSWER 6

Surgical assessment of an avulsion fracture is indicated if the fracture is displaced by more than 2 mm, involves greater than 30% of the articulation with the cuboid, or in non-union.[4]

Stress fractures of the fifth metatarsal diaphysis frequently proceed to non-union. Conservative management with non-weight bearing immobilisation for 6 weeks may be considered, although the re-fracture rate is as high as 15–20%. These fractures are best managed in consultation with an orthopaedic surgeon, as internal fixation may be required.[9]

An undisplaced, spiral fracture of the fifth metatarsal (*Figure 3*) can be managed with immobilisation in a plaster or fibreglass slab for 6 weeks, followed by progressive weight-bearing and rehabilitation.[10] Medial or lateral displacement is generally well tolerated, but dorsal or plantar displacement by more than 3–4 mm, or dorsal or plantar angulation of more than 10° may warrant reduction. This should be discussed with an orthopaedic surgeon to determine the optimal timing of referral.[10]

Figure 3. Plain radiographs of a spiral fracture of the fifth metatarsal



ANSWER 7

Before returning to dancing, Lily will need to progress through a structured rehabilitation program including:[11]

- partial then full weight-bearing
- regaining a normal range of ankle dorsiflexion (knee-to-wall lunge)
- regaining calf strength and regaining pain-free, normal eversion strength
- regaining normal balance and proprioception
- initially returning to dance drills that do not require jumping and landing.

Up to 25% of patients with an avulsion fracture at the fifth metatarsal base may report ongoing pain at 1 year, although <10% report any limitation in activities.[12]

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ACTIVITY ID: 29495

BONES AND JOINTS

This unit of *check* is approved for 6 Category 2 points in the RACGP QI&CPD program. The expected time to complete this activity is 3 hours and consists of:

- reading and completing the questions for each case study
- you can do this on hard copy or by logging on to the *gplearning* website, http://gplearning.racgp.org.au
- answering the following multiple choice questions (MCQs) by logging on to the *gplearning* website, http://gplearning.racgp.org.au
- you must score ≥80% before you can mark the activity as 'Complete'
- completing the online evaluation form.

You can only qualify for QI&CPD points by completing the MCQs online; we cannot process hard copy answers.

If you have any technical issues accessing this activity online, please contact the *gplearning* helpdesk on 1800 284 789.

If you are not an RACGP member and would like to access the *check* program, please contact the *gplearning* helpdesk on 1800 284 789 to purchase access to the program.

QUESTION 1

What clinical features support a diagnosis of primary generalised osteoarthritis in a patient who presents with joint pain?

A. Boggy joint swelling

B. Prolonged morning stiffness

C. Bony enlargement and tenderness in at least two joints

D. Nodal changes and tenderness in the hands, hips and knees

QUESTION 2

Which of the following options would you recommend for a patient with painful osteoarthritis of the hips and knees?

A. Physical therapy

B. Opioid analgesics

C. Corticosteroid injections

D. Chondroitin sulphate

QUESTION 3

Which of the following warrants consideration of inflammatory back pain in a patient under the age of 50 years who presents with chronic lower back pain (>3 months' duration)?

A. Awakening throughout the night

B. Improvement of pain with rest

C. Morning stiffness lasting >30 minutes

D. Worsening of pain with exercise

QUESTION 4

A diagnosis of axial spondyloarthritis (SpA) in a patient with symptoms of inflammatory back pain requires:

A. presence of HLA-B27

B. the presence of sacroilitis on a plain X-ray

C. reduced spinal mobility

D. none of the above.

CASE – MARTHA

Martha is 45 years of age and comes to see you with a 2-month history of pain and swelling affecting the wrists and metacarpal joints of both hands. She has morning stiffness lasting 1 hour.

QUESTION 5

What specific investigations would you perform for a suspected diagnosis of rheumatoid arthritis?

A. Antinuclear antibodies (ANA), double-stranded DNA (dsDNA), extractable nuclear antigens (ENA)

B. Whole body bone scan

C. Erythrocyte sedimentation rate (ESR), rheumatoid factor (RhF), anti-citrullinated peptide (CCP) antibody and X-rays of the hands

D. Cytomegalovirus and Epstein-Barr virus serology

E. Joint aspiration and measurement of serum urate levels

FURTHER INFORMATION

Martha is diagnosed by her rheumatologist has having rheumatoid arthritis and is commenced on oral methotrexate 20 mg weekly. She comes and sees you 6 weeks later and complains of mild nausea and vomiting for 1–2 days after taking the weekly methotrexate dose.

QUESTION 6

Which of the following would be most appropriate initial management?

A. Folic acid 10 mg weekly and metoclopramide 10 mg PO weekly with the methotrexate dose

B. Order an upper abdominal ultrasound

C. Cease methotrexate and prescribe daily oral calcium folinate 15 mg

D. Prescribe pantoprazole 40 mg daily

QUESTION 7

What primary investigations should be performed to differentiate gout from other inflammatory conditions?

A. Full blood count, inflammatory markers, rheumatoid factor

B. Full blood count, rheumatoid factor and serum uric acid

C. Blood cultures, rheumatoid factor and serum uric acid

D. Joint aspirate for culture, cell differential and crystal analysis

QUESTION 8

What are the recommendations for pharmacological intervention in patients with normal renal function, a serum uric acid (SUA) concentration >0.52 mmol/L and recurrent gout attacks?

A. Allopurinol, 50 mg/day and a non-steroidal anti-inflammatory drug (NSAID) as required

B. Allopurinol, starting at 100 mg/day and titrating up in increments of 100 mg every 4 weeks to achieve the target SUA level of ≤0.3 mmol/L

C. Allopurinol starting at 100 mg/day and titrating up in increments of 50 mg every 3 weeks to achieve the target SUA level of ≤0.4 mmol/L

D. Allopurinol 300 mg/day and an NSAID as required

QUESTION 9

What is the most useful imaging procedure to diagnose an injury to the fifth metatarsal joint?

A. Ultrasonography

B. Magnetic resonance imaging (MRI)

C. Plain X-ray

D. Computed tomography (CT) scan

QUESTION 10

How should simple fractures to the fifth metatarsal be managed?

A. Surgery and immobilisation as required

B. Non-weight-bearing and NSAIDs as required

C. Paracetamol and physiotherapy as required

D. No weight bearing and paracetamol as required

check

Independent learning program for GPs