Arthritis Research UK

Practical advice for GPs on management of rheumatic disease

Hands On

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The approach to the patient presenting with multiple joint pain

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Editorial

Patients present to their GP with symptoms rather than diseases, and often it takes time for musculoskeletal problems to evolve into a recognisable form. The challenge for the GP is to manage this uncertainty in a safe but balanced way with appropriate use of resources. One particular issue for GPs is ensuring that patients with inflammatory arthritis are identified at an early stage so that they can receive disease-modifying therapy with significant prognostic benefits.

Refreshingly in this era of data collection and quality targets musculoskeletal medicine still relies on good history-taking and clinical acumen.

The authors of this report have produced an excellent, very practical symptom-sorter approach to the patient who presents with multiple joint pain. They have provided not only a diagnostic framework but also sound advice as to how to manage the process leading to the diagnosis. I suspect this will prove to be a classic read for health professionals new or old.

Simon Somerville

Introduction

When assessing new presentations of multiple joint pain from the perspective of general practice, determining whether it is indicative of a significant underlying rheumatological condition is not always straightforward. This report aims to provide both a framework for the assessment of patients presenting with multiple joint pain and guidance for onward referral.

Why is this important?

Joint pain is a common reason for consultation in general practice. A typical practice of 10,000 patients would expect at least 12% of consultations to be for musculoskeletal problems. As shown in Figure 1, it might be anticipated that approximately 180 patients would be seen in a typical year with osteoarthritis (OA), compared to 25 with rheumatoid arthritis (RA), 4 with psoriatic arthritis, and 3 with ankylosing spondylitis.

Many causes of multiple joint pain, such as inflammatory arthritis, significantly impact not only on physical and psychological health but also on the wider population economy. RA alone is estimated as costing the UK £8 billion per year.

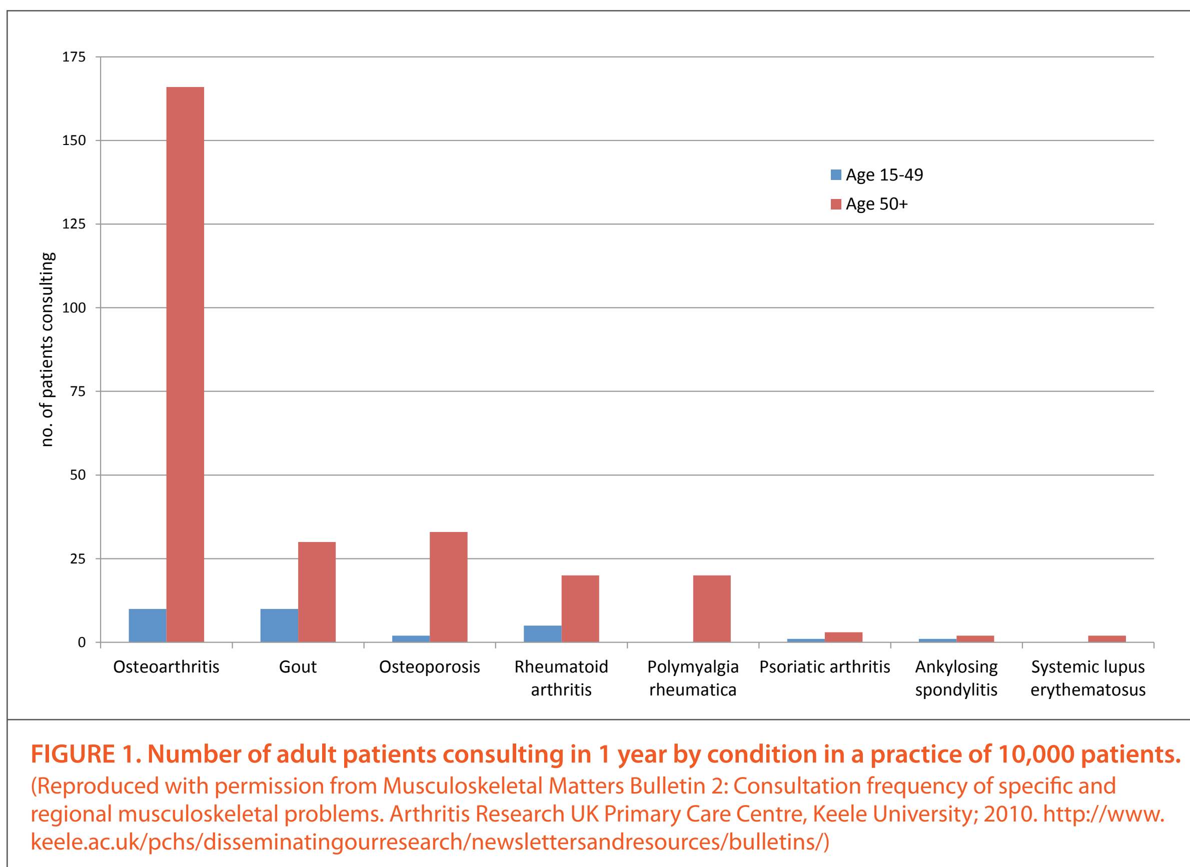

FIGURE 1. Number of adult patients consulting in 1 year by condition in a practice of 10,000 patients. (Reproduced with permission from Musculoskeletal Matters Bulletin 2: Consultation frequency of specific and regional musculoskeletal problems. Arthritis Research UK Primary Care Centre, Keele University; 2010. http://www.keele.ac.uk/pchs/disseminatingourresearch/newslettersandresources/bulletins/)

In recent years it has become apparent that early diagnosis and treatment in RA have a marked effect on improving disease outcomes, including disease progression and economic measures. A 'window of opportunity' is thought to exist in the first few months after symptom onset where early aggressive treatment may be more effective, not just in reducing disease severity, but actually in inducing disease remission. Research is currently under way to establish the importance of early diagnosis and treatment in other inflammatory arthritides, e.g. psoriatic arthritis.

As a result of new knowledge about the importance of early treatment, rheumatologists are encouraging early referral whenever inflammatory arthritis is suspected. Arthritis Research UK and the National Rheumatoid Arthritis Society have launched a media campaign to heighten

TABLE 1. Easily missed rheumatological conditions presenting with joint pain.

Easily missed conditions	Common reasons for delay or misdiagnosis
Early inflammatory arthritis: rheumatoid arthritis	May present initially with joint pain and/or fatigue with no examination findings
Early inflammatory arthritis: psoriatic arthritis	May have only one area affected with subtle findings, e.g. dactylitis (sausage toe or finger), or periarticular inflammation such as enthesitis, e.g. presenting with Achilles pain
Connective tissue disease	Symptoms may be non-specific, including fatigue and arthralgia
Gout: acute	Marked overlying joint erythema often confused with cellulitis
Gout: chronic	Gouty tophi on hands in the elderly easily confused with signs of osteoarthritis such as Heberden's nodes
Polymyalgia rheumatica	May present with shoulder **or** hip pain initially leading to other diagnoses such as soft tissue problems or frozen shoulder

BOX 1. Features of inflammatory cf. degenerative symptoms.

Inflammatory disease is

Less likely	**More likely**
Pain after use/at end of day	Pain worse after rest/in morning
Morning stiffness for <30 minutes	Morning stiffness for >30 minutes
No night-time pain	Night-time pain troublesome*
No systemic symptoms	Systemic symptoms present*
Chronic symptoms	Acute/subacute presentation

* Bear in mind that night pain and systemic symptoms can be indicative of other serious pathology including cancer, infections etc.

awareness of inflammatory arthritis among the general public (the 'S factor' campaign – see 'Further reading'), and GPs too need to know the warning signs that may be associated with inflammatory arthritis. However, signs and symptoms can be subtle and diagnosis can easily be confused by the presence of coexisting musculoskeletal problems, especially OA. As a result, a number of inflammatory conditions may easily be missed (Table 1).

History

The history is, as ever, the critical part of the assessment. If the story is consistent with inflammatory joint pain, further action is advisable even if the signs on physical examination are few or even non-existent. While there are no clear-cut methods of assessment with which to produce a diagnostic algorithm, some of the features of inflammatory compared with other joint pain are set out in Box 1.

In RA, early morning stiffness is a common and important symptom; stiffness of >30 minutes is significant and frequently patients report stiffness that lasts several hours, or even most of the day. Systemic features such as fever, weight loss and malaise are also relatively common and help distinguish an inflammatory arthritis from OA.

Patients with OA may also commonly complain of stiffness, often related to inactivity; this stiffness or 'gelling' is typically worse as the day goes on and <30 minutes in duration. Pain is usually the dominant symptom in OA, and is usually aching in nature and eased with rest. Sometimes patients present because of altered joint shape and deformity, particularly in the hands where Heberden's nodes may be considered unsightly. Hand OA, often called nodal OA, can be difficult to distinguish from inflammatory arthritis symptomatically; however, involvement of the distal interphalangeal joints is more characteristic of OA. Other clues and tips to look for are shown in Table 2.

BOX 2. Red flags.

These red flags should always prompt consideration of serious pathology and can be indicative of any inflammatory, infective or neoplastic process.

- Weight loss
- Fever or other systemic manifestation
- Night pain
- Single joint involvement
- Neurological symptoms and signs

Examination

Is the problem with the joint or periarticular structures?

The first aim of examination should be to establish if the pain is coming from the joint or surrounding tissues. Articular problems are usually characterised by tenderness along the joint line and/or pain at the end of range of movement, with any restriction in range of movement tending to be equal in both passive and active movement.

Swelling: is joint inflammation or synovitis present?

Textbooks describe synovitis as a 'boggy' swelling. In practice the swelling may be better described as 'squidgy'. Synovitis may be felt along the joint line, but inflammation of the tendon lining (tenosynovitis) results in swelling often

TABLE 2. What to look for: diagnostic tips.

	Rheumatoid arthritis (RA)	Seronegative arthritides (e.g. reactive and psoriatic arthritis)	Gout	Connective tissue disease	Osteoarthritis (OA)	Fibromyalgia	Polymyalgia rheumatica
Onset	Usually acute or subacute	Acute/subacute/ chronic	Usually acute	Subacute	Chronic	Chronic	Usually within a few weeks
Typical age and gender	Female:male 3:1 Any age	Any age	Female:male 1:3 Very rare in pre-menopausal women	Female:male 10:1 Typical age 20–40	Hand OA more common in females Usually age ≥45	Female:male 7:1 Age 30–50	Female:male 2:1
Pattern of joint involvement	Usually symmetrical hands and feet	Can be monoarthritis or asymmetrical oligo/polyarthritis	Monoarthritis most commonly – MTP, ankle, knee	Often symmetrical	Any Hands, knees, hip and feet most common	Widespread	Usually shoulder and pelvic girdle
Other clues	Raynaud's syndrome Dry eyes and mouth Systemic upset as Table 1	May be associated with inflammatory back pain Psoriasis Inflammatory bowel disease Uveitis	Risk factors: obesity, alcohol, diuretic treatment	Raynaud's syndrome Rash (butterfly or vasculitic) Systemic features Pleuritic chest pain	Heberden's or Bouchard's nodes Crepitus	Poor quality of sleep Tender soft-tissue 'trigger points' on examination Multiple symptoms*	Overlap with temporal arteritis – ask about headache, visual symptoms, jaw claudication and scalp tenderness

* See Hands On: Fibromyalgia ('Further reading')

located away from the joint. A good example is the wrist joint, where synovitis may be felt over the bony prominence, the ulnar styloid, rather than over the joint line itself. Patients with chronic inflammatory arthritis may have chronic synovial thickening which is palpable on examination but not tender; the presence of tenderness (demonstrated by pain on palpation using just enough pressure to make the examiner's nail blanch) and boggy swelling indicates active inflammation: synovitis. Although erythema is a cardinal feature of inflammation, it is often not a striking feature in inflammatory arthritis; the exceptions to this are crystal arthritis (gout and acute calcium pyrophosphate deposition arthritis, formerly referred to as pseudogout) and psoriatic arthritis in which overlying erythema may be marked and lead to diagnostic confusion with cellulitis.

Squeeze test: subtle synovitis

It is well recognised that synovitis can be difficult to detect by examination alone, and new imaging techniques now pick up 'subclinical' synovitis in a number of patients with normal examination findings. The squeeze test is a useful clinical test to determine subtle synovitis that is not palpable and can be performed at the metacarpophalangeal (MCP) or metatarsophalangeal (MTP) joints as shown in Figure 2. Tenderness elicited with a gentle squeeze is suggestive of synovitis.

Systemic features

The presence of a high fever may suggest septic arthritis but pyrexia may occur in all the inflammatory conditions, particularly in RA and crystal arthritis.

Examination findings in osteoarthritis

In OA there is usually joint-line tenderness and there may be crepitus on movement. There may be bony enlargement of the joint, most noticeable at the knees and distal or proximal interphalangeal joints of the fingers (Heberden's and Bouchard's nodes respectively).

What if the examination is all normal?

A normal examination does not rule out the presence of an underlying inflammatory condition and if the history is very 'inflammatory'-sounding it is reasonable to refer on the basis of this alone. Similarly, examination can be normal in early OA. The diagnosis of fibromyalgia necessitates tender areas on examination so is not compatible with a completely normal examination.

It may also be worth considering common non-musculoskeletal causes of multiple joint pain such as viral myoarthralgia, endocrine causes such as hypo- or hyperthyroidism, and side-effects of medication such as statins. Other rarer causes of joint pain are listed in the 'small print' at the end of this report.

Use of tests

The decision about whether or not to seek a specialist opinion will generally already have been made on the basis of the history and examination. Investigations in multiple joint pain can be most useful either for maximising the benefit of the initial outpatient appointment or for trying to add certainty to a case which is already thought to be non-inflammatory or manageable in primary care (such as gout). Local clinical pathways may

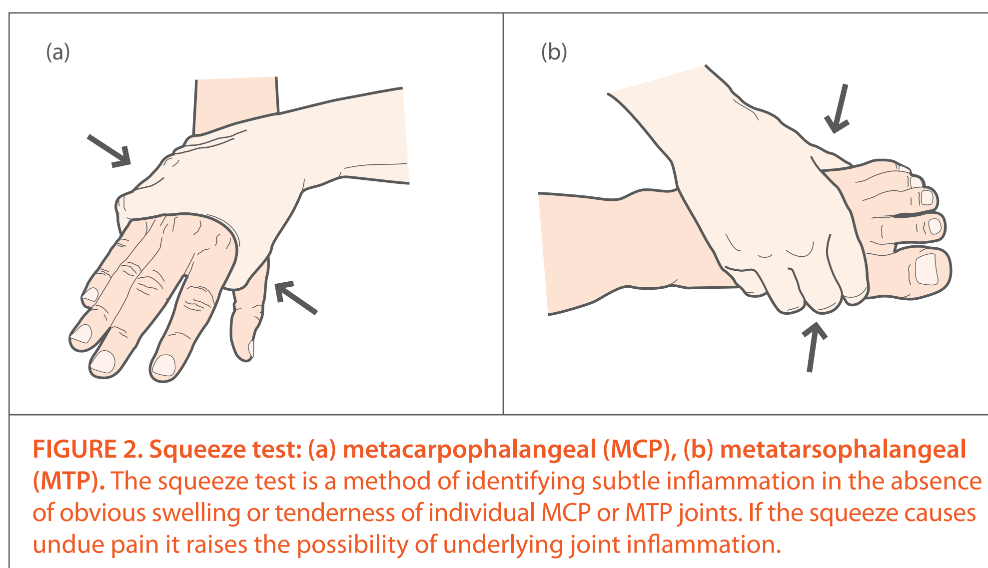

FIGURE 2. Squeeze test: (a) metacarpophalangeal (MCP), (b) metatarsophalangeal (MTP). The squeeze test is a method of identifying subtle inflammation in the absence of obvious swelling or tenderness of individual MCP or MTP joints. If the squeeze causes undue pain it raises the possibility of underlying joint inflammation.

Case histories

1. Albert is a 57-year-old man who presents to his GP with a history of pain in both hands, right 'hip' and left knee. His body mass index (BMI) is elevated at 38.2 kg/m^2.

On assessment his GP finds that the symptoms tend to be worse toward the end of the day, though after a period of rest there may be a few moments of stiffness in the affected knee; this wears off after a few stretches. On examination she finds the presence of typical nodal OA changes in many of the interphalangeal joints in Albert's hands. There is tenderness over the right trochanter, and crepitus in the left knee with no effusion.

The hand pains have been gradually worsening over a couple of years, and are now interfering with his work as a carpenter. His knee has been slowly worsening over a similar period of time but the pain is variable, going through good times and not so good. The pain in the right 'hip' (actually over the greater trochanter) has been a feature for several months since a particularly troublesome flare in his knee symptoms.

Albert's GP diagnoses generalised (nodal) OA, predominantly affecting the hands and knee, and trochanteric bursitis. She recommends the core interventions for OA – weight loss, exercises and information provision, as well as topical non-steroidal anti-inflammatory drugs (NSAIDs) to apply to the affected joints.

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2. Brian is a 74-year-old man who presents with joint pains and swelling in his hands. It came on fairly quickly, over a period of some weeks. There is a lot of trouble with hand function early in the morning, though a hot bath helps.

Brian's GP thinks this might be new-onset RA, though the presence of swelling at both the proximal and the distal interphalangeal joints perplexes him. An x-ray shows no erosions – only OA changes throughout the hands. An ESR is a little raised at 34. Rheumatoid factor is weakly positive at 28 μ/l.

Brian's GP considers that the best approach is to seek advice from the early synovitis clinic. Brian is seen quickly and a diagnosis of inflammatory OA is made. He does well with short-term use of oral NSAIDs and proton-pump inhibitor (PPI) cover.

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3. Charlotte is a 67-year-old woman who has been feeling unwell for 6 weeks before seeing her GP. She complains of pain and stiffness in her hands which is especially bothersome in the early part of the day. She has been soaking her hands in a bowl of hot water for 15 minutes every morning before she can even wash herself or get dressed. It takes 2 hours before she is able to do her household chores.

She winces when her hand is shaken at the start of the consultation and again when the GP squeezes her MCP joints, though there is little else to find on examination. Given the strong history of inflammatory disease, her GP refers Charlotte to the early synovitis clinic and arranges for some baseline investigations. At the clinic appointment new-onset RA is strongly suspected and specialist tests are arranged with a view to commencing disease-modifying anti-rheumatic drugs (DMARDs).

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4. Denise is a 45-year old woman who presents to her GP with a history of rather non-specific aches and pains. She has an apparently incidental rash on her face. Her GP thinks that the joint pains are early OA and that the rash is likely to be rosacea. Treatment with topical agents is unsuccessful and a while later Denise returns for review.

At review there is a history of widespread joint pains, fatigue and low mood. The facial rash is examined again and a symmetrical rash over both cheeks is noted.

The GP now suspects that the original diagnoses were not correct and wonders if lupus might be the cause of the symptoms. He advises a referral to the local rheumatologists and arranges for an autoimmune profile test to be carried out.

The blood results show a strongly positive ANF (dilution 1:1280). The Rheumatology Department confirms systemic lupus erythematosus and commences treatment with hydroxychloroquine.

determine the use of tests in facilitating access to a specialist opinion.

It can be preferable to keep patients under active review, using time as an aid to diagnosis, rather than using special tests to rule out pathology – especially as it can take a while before the tests are positive.

- **Erythrocyte sedimentation rate (ESR)/C-reactive protein (CRP):** can be helpful in distinguishing inflammatory from other joint conditions but they are not very sensitive and are very non-specific. A normal ESR does not rule out the presence of inflammatory arthritis.

- **Rheumatoid factor:** this too can be positive in the normal population (c.5% prevalence, higher in the elderly), especially at low titre (e.g. <23 units/ml). It will be positive in around 70% of patients with RA and >90% patients with primary Sjögren's syndrome. Just as a normal ESR may be seen in RA, a negative rheumatoid factor does not rule RA out.

- **Antinuclear factor (ANF):** low-titre ANF (titres of ≤1:80) may be clinically insignificant. Higher titres may be seen in various conditions, including RA and connective tissue diseases, and sometimes in viral and chronic infections.

- **X-rays:** OA may be diagnosed clinically without the requirement for x-ray (see National Institute for Health and Clinical Excellence (NICE) guidance in Hands On: Osteoarthritis – see 'Further reading'); however, x-rays may be useful when considering other pathologies or sometimes prior to referral for joint replacement. X-rays may take up to 2 years to show erosive changes in RA and are therefore not essential in decision-making around referral.

- **Joint aspiration** can also be of use diagnostically, notably if a crystal arthritis is suspected.

Other specialist investigations include other immunology tests such as anti-citrullinated protein antibodies (ACPA) – also known as anti-cyclic citrullinated peptide (anti-CCP) antibodies. ACPA-positivity is more specific than rheumatoid factor for RA; however it has relatively low sensitivity and so patients with RA may be ACPA-negative. ACPA testing is not currently recommended in primary care; however it may be of use in the future in predicting patients at risk of RA with non-specific prodromal symptoms such as pain and fatigue.

Referral

Referral to Rheumatology should be considered for:

1. **diagnosis and treatment** in patients who are suspected to have a rheumatological condition that requires secondary care input, such as most inflammatory arthritides (rheumatoid, psoriatic or reactive arthritis, ankylosing spondylitis, arthritis associated with inflammatory bowel disease etc) and connective tissue disease
2. **diagnosis** where there is diagnostic uncertainty
3. **treatment** of patients with conditions that are usually managed in primary care, such as OA, gout and polymyalgia rheumatica, but which are not responding to usual treatment measures.

Referral for diagnosis and treatment

Following the history-taking and examination, the presence of red flag features in the history and/or the finding of synovitis on examination in a patient not known to have inflammatory arthritis should prompt referral to Rheumatology. Acute synovitis in a single joint (except the first MTP joint) needs urgent aspiration to rule out septic arthritis, and these patients may be referred to Orthopaedics, A&E or Rheumatology depending on local pathways. The flowchart shown in Figure 3 illustrates the instances in which referral might be considered.

Referral for treatment – what's on offer in secondary care?

- **Osteoarthritis** In OA, patients are usually referred because of persistent pain and/or disability. The most common reason for referral is for consideration of joint replacement. There are some other treatments in the outer circle of the NICE guidelines 'target' (see 'Further reading' – Hands On: Osteoarthritis) that may be more readily available in secondary care, such as some corticosteroid injections and specialist therapy input. OA of the hand can give rise to inflammatory symptoms and referral can be useful to rule out the presence of an underlying inflammatory arthritis. DMARDs are sometimes used in nodal hand OA, although this is not currently supported by research evidence.

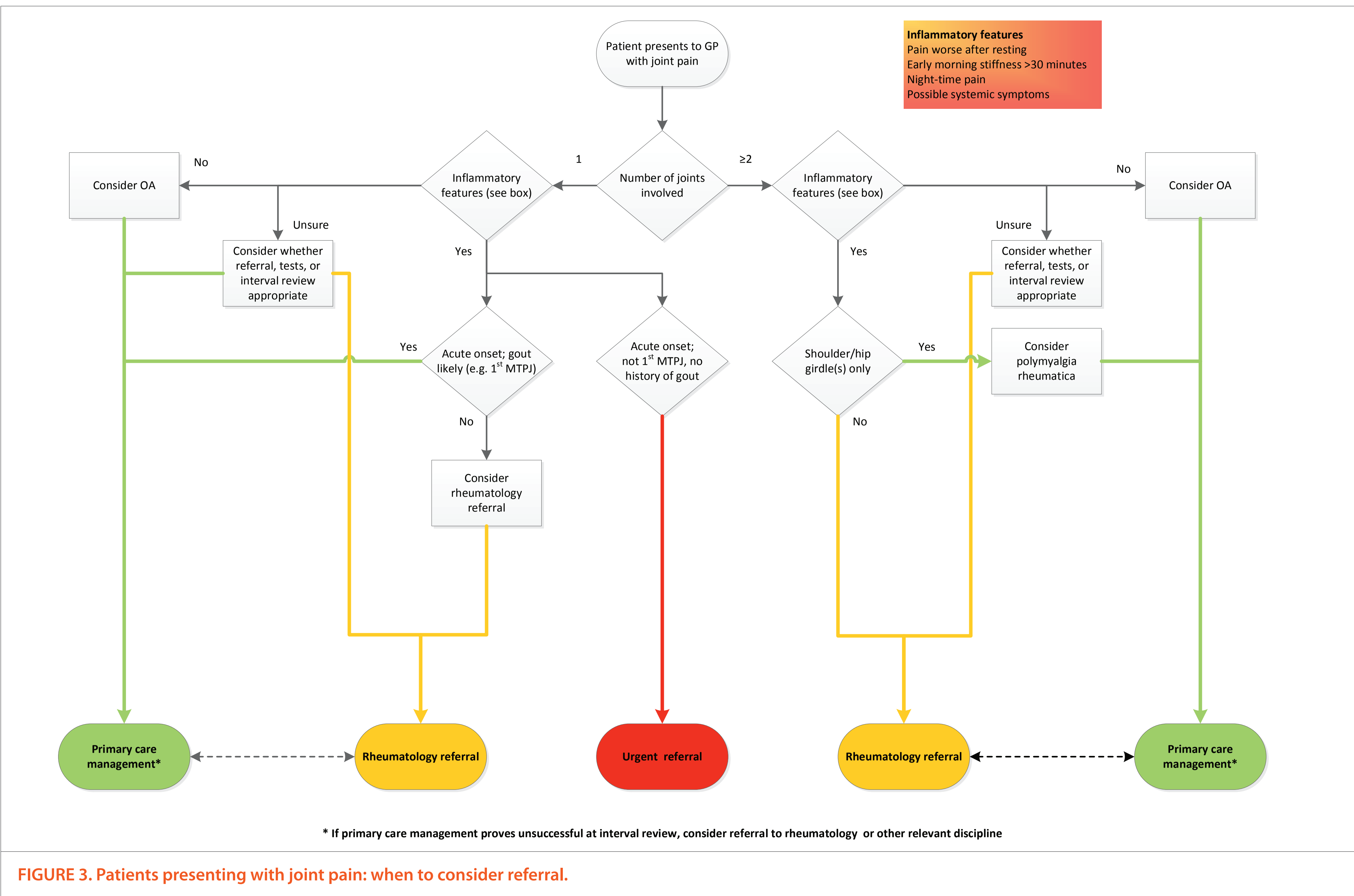

FIGURE 3. Patients presenting with joint pain: when to consider referral.

• **Polymyalgia rheumatica** In polymyalgia rheumatica, referral would be indicated if steroid withdrawal or dose reduction was proving difficult; again the diagnosis could be confirmed, but also the use of a steroid-sparing agent considered.

• **Gout** Acute gout may sometimes necessitate urgent referral if not settling with conservative measures; specialist advice is also advisable in patients intolerant of allopurinol (see 'Further reading' – Hands On: Gout).

• **Fibromyalgia** For most patients with fibromyalgia, treatment is aimed at coping with the condition and controlling symptoms and consequently secondary care does not really have a great deal to offer for management of the condition; however, referral can be useful if there is diagnostic uncertainty and perhaps if there is patient request for a specialist opinion (see 'Further reading' – Hands On: Fibromyalgia).

Early arthritis clinics

Many centres around the country now operate early arthritis clinics in which patients with suspected inflammatory arthritis are seen. These clinics typically have easy access so that delay from referral to being seen can be minimised. They may operate as a 'one-stop' clinic where patients can be seen, investigated with x-rays, ultrasound and further blood tests, and even counselled about their diagnosis and implications of disease-modifying treatment, all in a single visit. If diagnosed with inflammatory arthritis, the patient can then be referred to the multidisciplinary team (including specialist nurse, physiotherapist, occupational therapist and podiatrist) for further treatment and patient education. Patients with inflammatory arthritis, particularly RA, can be followed up at frequent intervals after diagnosis for repeated measures of disease activity and adjustment of treatment; the term 'treat to target' is being used to describe this aggressive treatment approach with the aim of inducing disease remission.

Ultrasound findings are not currently part of the diagnostic criteria for any inflammatory arthritis, and many questions exist about the extent to which ultrasound findings should inform treatment decisions; increasingly, however, musculoskeletal ultrasound is being used by rheumatologists as an adjunct to clinical examination to aid in decision-making regarding diagnosis and treatment (see 'Further reading' – Topical Reviews: Ultrasound).

Conclusion

Rheumatology remains the specialty par excellence in which a careful clinical history and examination provide the most useful information in assessing a patient. In the case of patients presenting with multiple joint pain, such assessment is invaluable in moving forward with a management plan. Finally, there will always be patients in whom there remains significant doubt. If inflammation or a red flag diagnosis are a significant possibility, our steer would be to get a rheumatologist's opinion.

The small print!

In this report we have tried to concentrate on the more common causes of joint pain. There are many other rarer causes that we are unable to cover within the scope of the report, including (but not restricted to):

Congenital
- benign hypermobility

Neoplastic
- malignant deposits
- arthritis associated with malignancy
- hypertrophic pulmonary osteopathy

Metabolic bone disease
- Paget's disease
- osteomalacia

Other metabolic causes
- haemochromatosis

Neurological conditions
- Parkinson's disease

Infections
- rheumatic fever
- Lyme disease

(continued)

Further reading

Arthritis Research UK reports *(see the Reports on the Rheumatic Diseases archive pages accessible via http://www.arthritisresearchuk.org/health-professionals-and-students/reports.aspx)*:

- Glennon P. Fibromyalgia syndrome: management in primary care. Hands On (Series 6) No 7; 2010 Autumn.
- Roddy E. Gout: presentation and management in primary care. Hands On (Series 6) No 9; 2011 Summer.
- Porcheret M, Healey E, Dziedzic K et al. Osteoarthritis: a modern approach to diagnosis and management. Hands On (Series 6) No 10; 2011 Autumn (plus Information and Exercise Sheet : Osteoarthritis).
- Taggart A, Benson C, Kane D. Ultrasound in rheumatology. Topical Reviews (Series 6) No 9; 2011 Summer (plus ultrasound videos).

Health talk online *[examples of patients describing early symptoms of RA]*. http://www.healthtalkonline.org/Bones_joints/Rheumatoid_Arthritis.

The S factor campaign *[public awareness campaign about symptoms of RA]*. http://www.arthritisresearchuk.org/arthritis-information/inflammatory-arthritis-pathway.aspx.

Continuing professional development (CPD) task

The details of the RCGP credit scheme for CPD can be found at http://www.rcgp.org.uk/revalidation-and-cpd/cpd-credits-and-appraisal.aspx.

On-line learning modules for examination and disease management:

- BMJ Learning. http://learning.bmj.com/learning/info/GP-CME-CPD-for-general-practice.html
- Doctors.net.uk. http://www.doctors.net.uk
- JointZone. www.jointzone.org.uk.

- Review personal use of Rheumatology investigations (e.g. ANF, rheumatoid factor). In patients not referred to Rheumatology, how much information did the tests add to the clinical picture?
- Review the outcomes of referrals. What, if any, was the source of the delay in accessing definitive treatment for diagnosed inflammatory arthritis?

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