
Article:
Sandler, R.D. and Dunkley, L. (2018) Osteoarthritis and the inflammatory arthritides. Surgery (United Kingdom), 36 (1). pp. 21-26. ISSN 0263-9319

https://doi.org/10.1016/j.mpsur.2017.10.004

<R/Heads>ORTHOPAEDICS I: GENERAL PRINCIPLES

Osteoarthritis and the inflammatory arthritides

Robert Sandler BMedSci (Hons) MB ChB MRCP is a Core Medical Trainee 2 within the South Yorkshire foundation school, UK. Conflicts of interest: none
Lisa Dunkley PGcertMedEd FHEA FRCP is a Consultant Rheumatologist at the Royal Hallamshire Hospital, Sheffield, UK. Conflicts of interest: none

ABSTRACT

This article aims to provide surgeons with a practical, clinical overview of different forms of ‘arthritis’ – a term encompassing most of the joint pathology causing joint symptoms or dysfunction. Conventionally, arthritis can be non-inflammatory (osteoarthritis) or inflammatory (crystal and autoimmune arthropathies). Septic arthritis is an important differential diagnosis when patients present with tender, swollen joints but is not covered in detail here. Common symptoms and signs in patients with different types of arthritis are reviewed, as well as aetiology and pathogenesis. Non-surgical treatment is described, with particular reference to the inflammatory arthropathies since the new, effective biologic treatments are particularly important where surgery is planned or patients present with suspected sepsis. Diagnosis of inflammatory arthritis (particularly in children) may be delayed and in an era of effective treatment it is important that all clinicians involved in musculoskeletal medicine and surgery are aware of potential differential diagnoses for joint pain and deformity. Good communication between rheumatologists and surgeons in managing different forms of arthritis is especially important.

Keywords

- Arthritis
- Osteoarthritis
- Gout
- Ankylosing spondylitis
- Rheumatoid arthritis
- Psoriatic arthritis
- Systemic lupus erythematosus
- Juvenile idiopathic arthritis
- Spondyloarthropathy

OSTEOARTHRITIS

Osteoarthritis (OA) is not a single disease or process; rather it is the outcome of the range of processes leading to pathological, structural and eventually symptomatic failure of one or more synovial joints. Recently a paradigm shift has moved the conception of OA from an exclusively degenerative condition of old or worn joints to an emphasis on OA as a dynamic, remodelling and regenerative condition. OA is the commonest type of arthritis and the leading cause of disability in those over the age of 65 years in developed countries. It may be classified as primary (idiopathic) or secondary to other processes such as trauma, congenital/developmental, mechanical or local factors (for example obesity or hypermobility) or as a sequelae of other inflammatory arthritides.

OA involves all tissues in the joint – initially there is loss of proteoglycan from the matrix of articular cartilage resulting in fibrillation, fissuring and degeneration. In more advanced disease, cartilage loss is such that the articulating surface is subchondral bone (eburnation). There is increased bone remodelling with subchondral osteosclerosis and cyst formation, articular surface deformity and osteophyte formation. Varying degrees of synovial inflammation and ligament

degeneration may also occur and OA is accompanied by peri-articular muscle wasting and biomechanical changes. These pathological processes lead to the characteristic x-ray (XR) features (FIGURE 1). There is often poor correlation between XR changes and symptoms. OA has multiple aetiological factors with gender, age and genetic factors increasing susceptibility and more local factors such as joint biomechanics, obesity, trauma and muscle weakness determining the site and severity of the disease.

OA can affect any synovial joint and typical presenting features are mechanical pain in joints (worse with activity or weight bearing), joint stiffness and deformity. Spinal OA may cause neurological symptoms such as radiculopathy and spinal stenosis.

Treatment is currently symptomatic – medical therapies aim to control pain and physiotherapy maintains mobility, muscle strength and biomechanical integrity of the joint. In advanced disease with joint failure (disabling joint pain - particularly nocturnal – and loss of joint function and deformity) management is surgical. Groups investigating the role of inflammation in the pathogenesis of OA have identified some potential therapeutic targets but current trial data show limited efficacy. There is increasing evidence that exercise has a crucial role to play in symptomatic management and explaining the importance of reducing obesity and promoting exercise to patients may help prevent OA progression.

CRYSTAL ARTHROPATHIES

Arthritis, both acute and chronic, can be caused by crystal deposition in joints. Gout is characterised by hyperuricaemia and monosodium urate crystal deposition; typically this is in peripheral joints, where the crystals can precipitate at cooler temperatures. Classically this will manifest in the great toe, but commonly also in the knee and ankle, wrist, hand and any joints affected by OA.

The crystals trigger acute episodes of cytokine release and consequent neutrophilic inflammation. The patient experiences excruciating joint pain, which typically starts in the early hours of the morning. The affected joints are often swollen and erythematous with patients unable to weight bear on them. Where hyperuricaemia and gout are chronic, urate may be present as macroscopic deposits (tophi) around joints or in cartilaginous structures such as the ear. Urate may also accumulate in the kidney causing at micro-level, urate nephropathy and at macro level, urate calculi.

Urate is a by-product of purine metabolism and normally excreted through the kidneys. A minority of people with gout produce excess urate but much more commonly gout results from the under-excretion of urate. This may be due to renal failure, concurrent drug therapy, particularly aspirin and thiazide diuretics and alcohol intake. Hyperuricaemia is probably under-recognised and not everyone with hyperuricaemia has gout. Diagnosis of acute gout is on typical history and presentation, high serum urate (although this may paradoxically lower in acute attacks, as urate crystals precipitate in the extravascular space) and by demonstration of the typical negatively birefringent needle-shaped urate crystals in joint aspirate under polarised light microscopy. A key differential for an acute monoarthritis is septic arthritis, which would be diagnosed on synovial fluid microscopy and culture, highlighting the importance of joint aspiration.

Treatment of gout involves lifestyle factor modification - to avoid high purine foods e.g. meat and shellfish, reduce alcohol & fructose intake (fructose increases serum uric acid by increased purine breakdown and increased purine synthesis) and avoid obesity. Precipitating medicines such as aspirin and diuretics should be avoided but this is often not possible. Acute gout is treated symptomatically by aspiration and injection of affected joints with corticosteroids and systemic administration of non-steroidal anti-inflammatory drugs (NSAID), low-dose colchicine or low-dose oral prednisolone (particularly where patients have comorbidity and NSAID or colchicine are contraindicated). Long-term

treatment of hyperuricaemia is with xanthine oxidase inhibitors such as allopurinol or febuxostat, which act to reduce serum urate levels. Lesinurad, a uric acid transport inhibitor, has just been licensed as an add-on therapy for patients whose urate levels are unsatisfactory despite first-line therapy, though it is not yet recommended by NICE. Recent work has demonstrated involvement of interleukin-1 (IL-1) pathways in gout and treatment with Anakinra (IL-1 receptor antagonist) shows promising results. It is worth noting that, on initiation, these treatments may paradoxically trigger a flare of gout and must always be started alongside prophylactic treatment such as NSAID or low-dose colchicine for around 3 months.

Pseudogout or calcium pyrophosphate dehydrogenase (CPPD) arthropathy is the result of calcium pyrophosphate deposition in joint tissues, which triggers inflammation in a similar way to gout. This acute arthritis is commoner in older people and often poly-arthritic. It is associated with chondrocalcinosis on XR particularly in the knee and the wrist (FIGURE 2). Diagnosis is based on clinical presentation, typical XR appearances and the demonstration of positively birefringent, rhomboid crystals under polarised light. Aetiology is unknown but CPPD can be associated with haemochromatosis and acromegaly and in younger patients these conditions should be actively excluded. Hydroxyapatite is the third type of crystal arthropathy, commonest in older women and recognised as a cause of destructive shoulder arthritis, classically described as the ‘Milwaukee shoulder syndrome’. In this syndrome there often is significant humeral head destruction, CPPD deposits and rotator cuff tears. Treatment of both is symptomatic with NSAIDs, intra-articular steroid injections, physiotherapy and surgery where joint failure supervenes.

RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a destructive, autoimmune arthritis that affects 1% of the adult population; women three times more commonly than men. It can occur at any age, but most often between the ages of 40 – 50. Risk factors include presence of the “shared epitope” (a sequence of 5 amino acids on the HLA-DRB1 chain - chromosome 6), a personal or family history of autoimmune disease, and smoking.

RA principally affects synovial joints, but is a systemic inflammatory disorder affecting structures beyond the joints including for example, skin (rheumatoid nodules, pyoderma gangrenosum), lungs (fibrosis), mucous membranes (dryness “sicca syndrome”), eyes (episcleritis, scleritis) and blood vessels (vasculitis). Classically the arthritis involves the small joints of hands and feet, but large joints are also involved, either in addition, or alone. Pathologically, the affected joints develop a chronically inflamed, overgrown “tumour-like” synovium (pannus) that destroys cartilage and bone.

RA remains a clinical diagnosis but the most recent international diagnostic criteria (2010) include synovitis of at least one joint, high acute phase markers, positive Rheumatoid Factor and/or positive anti-cyclic citrullinated peptide (CCP) antibodies and symptoms persisting beyond 6 weeks, not better explained by an alternative diagnosis.

The radiological hallmark is of peri-articular erosions (FIGURE 3) but modern management of RA is predicated on early treatment, well before radiological erosions are apparent. Treatment in this pre-erosion “window of opportunity” is now known to be associated with significant reductions in morbidity and long-term disability, and in some patients can even lead to “switching off” the systemic inflammation altogether.

Treatment begins as soon as possible after the onset of symptoms. A zero-tolerance approach to inflammation is adopted – the so-called 'treat to target' approach where the target is disease remission. Disease modifying anti-rheumatic drugs (DMARDs) such as Methotrexate, Hydroxycholorquine, Sulfasalazine and Leflunomide are commenced early, and in combination. If inflammation continues, biologic drugs – typically anti-TNF drugs (multiple examples now commonly used), B-cell depletion therapy (Rituximab), anti-IL6 drugs (Tocilizumab) or inhibitors to co-stimulatory molecules (Abatacept) – are commenced within 3-6 months of onset. Biologic drugs are usually prescribed concurrently with at least one DMARD. The major adverse effect of the biologic anti-rheumatic drugs is the increased risk of infection and patients presenting unwell on such therapy must be carefully evaluated.

The clinical multi-disciplinary team remains key to management of patients with RA. Physiotherapy, podiatry and occupational therapy are important adjuncts to pharmacological treatment. Patients are at increased risk of osteoporosis and cardiovascular disease and should be actively screened for both. Despite modern therapy, patients still require surgical intervention and close liaison between rheumatologist and orthopaedic surgeon is crucial. Management of drug therapy peri-operatively should be discussed in each case, but the basic principle is that DMARDs continue throughout. Guidance from the British Society for Rheuamtology (2010) suggests suspending biologic therapy 3-5x the half-life of that agent prior to surgery. The American College of Rheumatology, in association with the American College of Hip & Knee Surgeons (2017) have released specific guidance for patients undergoing elective total hip or total knee arthroplasty, suggesting withholding the biolofic agent prior to surgery and scheduling the procedure at the end of the dosing cycle for that specific agent. The agent should then be restart edonce the wound shows evidence of healing, the staples are out, there is no significant swelling, erythema, or drainage, and there is no clinical evidence of non-surgical site infections. This would typically be around 14 days post-operative. This guidance also suggesting continuing the

pre-operative dose of glucocorticoids rather than administering peri-operative supra-physiological doses.

Biologic therapy should cease at a time three to five times the half-life for the relevant drug prior to surgery and be recommenced 2 weeks later, or when wounds are healed.

Consideration of joint replacement in inflammatory arthritis is the same as osteoarthritis (OA), being based on pain and loss-of-function, rather than inflammation. Ideally, inflammation would be controlled prior to surgery, however this is not an absolute necessity. It is not anticipated that inflammatory arthritis would recur in a replaced joint, as the synovium is removed. Compared to patients with OA, RA patients are at increased risk of dislocation following total his arthroplasty (THA) and increased risk of infection following total knee arthroplasty (TKA). RA itself is an independent risk factor for infection, in addition to the use of immunosuppressive therapy, such as corticosteroids or DMARDs.

SPONDYLOARTHRITIS

The spondyloarthritides include Ankylosing Spondylitis, Psoriatic Arthritis, Inflammatory Bowel Disease-associated (formerly enteropathic) arthritis and Reactive Arthritis. All can be associated with the HLA B27 tissue-type, although this association is strongest in Ankylosing Spondylitis (AS) where up to 95% patients are HLA B27 positive. In AS, symptoms typically first occur in the early twenties, although average diagnosis lags 10 years behind the onset of symptoms. Men are affected three times more commonly than women, and may have a more severe phenotype.

There is much clinical overlap amongst the spondyloarthritides - peripheral inflammatory arthritis, enthesitis, spinal inflammation (often sacroiliitis) and the extra-articular manifestations of inflammatory eye disease (anterior uveitis), skin

psoriasis and inflammatory bowel disease (Crohn's, Ulcerative colitis) can occur across all sub-types. Treatment however is targeted according to the clinical features present in an individual patient.

Recent diagnostic criteria have acknowledged this overlap between the conditions and allowed for a generic diagnosis of "spondyloarthritis with axial (spinal) involvement" or "spondyloarthritis with peripheral involvement" (Table 1). The key shift in emphasis is that radiological evidence of sacroiliitis on plain film does not have to be present for diagnosis of axial disease; this is now recognised as a late sequelae. Synovitis/ bone oedema of the sacroiliac joint on MRI is now taken as the diagnostic standard, with or without inflammatory lesions e.g. Romanus lesions (fatty change at anterior vertebral corners) higher up the spine (FIGURE 4).

Clinically, axial spondyloarthritis presents with inflammatory back pain (Box 1) and peripheral spondyloarthritis presents with arthritis, enthesitis (eg plantar fasciitis, achilles tendonitis), or dactylitis (sausage digit). Symptoms tend to respond to non-steroidal anti-inflammatory drugs [NSAIDs] and there may be a family history of one of the related conditions. Inflammatory markers can be elevated but, unlike rheumatoid arthritis, it is not unusual for them to remain normal throughout.

Peripheral spondyloarthritis is treated with DMARDs, escalating to biologic therapy in much the same way as RA. Axial spondyloarthritis does not respond to DMARDs; patients with axial disease move from regular NSAIDs straight to biologic treatment. Even in patients with long-standing disease, biologic drugs have demonstrated that disease we previously labelled as "burnt-out" can in fact still be active. Care has to be taken to elicit complications of long-standing disease, such as cardiorespiratory problems (aortic regurgitation, apical lung fibrosis) and neurological sequelae of spinal disease (usually compressive). Patients are at increased risk of osteoporosis and cardiovascular disease just like

their counterparts with RA. Established biologic drugs for spondyloarthritis remain the anti-TNF group. Recent work has demonstrated the importance of the IL12/23 and IL17 axis, leading to the development of newer biologic drugs such as anti IL-17 (Secukinumab), which is now recommended by NICE for axial disease and anti IL-12/23 (Ustekinumab) which is effective for peripheral disease and shows promise for axial involvement..

The rheumatological multi-disciplinary team is again very important. These patients tend to be young and have a whole working and family life ahead of them. Continued physiotherapy review and occupational therapy input with an emphasis on workplace advice are key.

JUVENILE IDIOPATHIC ARTHRITIS

Inflammatory arthritis affects around 1 in every 1000 children and in contemporary terminology is juvenile idiopathic arthritis (JIA) rather than the historical descriptions of juvenile rheumatoid arthritis or juvenile chronic arthritis. The diagnosis of JIA is essentially clinical and made when a child under 16 presents with joint inflammation persisting for at least 6 weeks where other conditions, such as infection and malignancy, have been excluded.

JIA is a heterogeneous group of disorders with seven subtypes classified according to the number of joints involved and the pattern of symptoms (Table 2). It can be a serious and disabling condition complicated by joint destruction, impaired joint function, limitation of growth and osteoporosis. There are also significant effects on the emotional and social well being of a child with JIA - school attendance may be adversely affected with the attendant loss of educational or vocational opportunities and peer relationships. In common with other chronic illnesses, a diagnosis of JIA can also have effects on family dynamics and impact on all members of the family. Delayed diagnosis is common, not least because young children rarely complain of pain and are often

presented with non-specific complaints such as limps or because they are not walking or moving properly. It is only if and when they are examined that synovitis becomes apparent. JIA is significantly associated with chronic anterior uveitis and all children and young people with JIA should have regular ophthalmic screening. Delaying a diagnosis of JIA may mean missing a potentially reversible cause of blindness.

Treatment of JIA is symptomatic with intra-articular steroid injections alone in oligoarthritis, escalating to systemic treatment with methotrexate and biologic drugs in more aggressive forms. It is important to recognise that 40-60% of children with JIA have continued arthritis into adulthood. Good coordination and transitional planning between paediatric rheumatology and orthopaedic services is critical in the care of these young people.

SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)

This immune complex mediated, multisystem disease often presents with arthralgia rather than frank inflammatory arthritis, although the latter can be a clinical feature. There is a recognised deforming arthritis – Jaccoud's arthritis – that can occur. Phenotypically, it resembles rheumatoid arthritis but typical erosive RA changes on XR are absent. The pathology is thought to be fascial and tendon fibrosis rather than synovitis and patients tend to maintain function with relatively few symptoms.

CONCLUSION

Arthritis is common and potentially disabling. In an era of new, effective treatments, prompt recognition and referral to rheumatologists of inflammatory arthritis in both children and adults is key. Equally important is the prompt and

appropriate referral of patients with joint failure by rheumatologists and general practitioners for surgical management. Both the medical and surgical management of arthritis should be within part of a multidisciplinary team involving physiotherapists, occupational therapists and nurses. Clear channels of communication and joint working between medical and surgical musculoskeletal disciplines is in patients' best interests.

Table 1. ASAS (Assessment of Spondyloarthritis International Society) Classification Criteria for axial spondlyloarthritis (SpA) in patients with back pain for more than 3 months and age at onset of less than 45 years (Rudwaleit M et al. Ann Rheum dis 2009;68:*777-83*)

*Sacroiliitis on imaging	^SpA Features
MRI Active inflammation highly suggestive of sacroiliitis associated with SpA	Inflammatory Back Pain Arthritis Enthesitis (heel) Dactylitis Uveitis Psoriasis Crohn's/ colitis Good response to NSAIDs Family history of SpA HLA B27 Elevated CRP
Plain Xray Definite sacroiliitis as defined by modified NY criteria	

Sacroiliitis on imaging* AND ≥1 SpA feature^ OR HLA B27 AND ≥2 other SpA features^

Box 1. ASAS (Assessment of Spondyloarthritis International Society) Criteria for Inflammatory Back Pain (Sieper J et al. Ann Rheum Dis 2009;68:*784-8*)

Back pain of more than 3 months duration is inflammatory if:

- Age at onset less than 40 years
- Insidious onset
- Improvement with exercise
- No improvement with rest
- Pain at night (with improvement on getting up)

The criteria are fulfilled if at least 4 out of 5 parameters are present

Further reading

Lithman OA, et al **2013** Exercise for lower limb oseteoarthritis: a systematic review incorporating trial sequential analysis and network meta-analysis BMJ 347:f5555 doi.10.1136/bmj.f5555

Loeser R, et al **2012** Osteoarthritis; A Disease of the Joint as an Organ Arthritis Rheum 64(6): 1697-1707. doi:10.1002/art.34453.

Rees, F. Hui M, Doherty M. Optimizing current treatment of gout Nat. Rev. Rheumatol. 10, 271–283 (2014); published online 11 March 2014; doi:10.1038/nrrheum.2014.32

Prakken B, Albani S, Martini A. Juvenile idiopathic arthritis Lancet. 2011 Jun 18;377(9783):2138-49. doi: 10.1016/S0140-6736(11)60244-4.

Beausang E, Barnett V, Goldstein, S **1967** *Jaccoud's Arthritis; A Case report* Annals of the Rheumatic Diseases 26 239-245

Petty R. et al **2004** International League of Associations for Rheumatology Classification of Juvenile Idiopathic Arthritis: Second Revision, Edmonton 2001. J Rheum **31**(2): p. 390-392.

Dougadas M, Baeten D **2011** Spondyloarthritis Lancet; 377: 2127-37

Gottlieb A et al **2009** Ustekinumab, a human interleukin 12/23 mononuclear antibody, for psoriatic arthritis: randomised, double-blind, placebo-controlled, crossover trial. Lancet; 373: 633-640

Baeten et al **2013** Anti-interleukin 17A monoclonal antibody secukinumab in treatment of Ankylosing Spondylitis: a randomised, double-blind, placebo-controlled trial. Lancet; 382: 1705-1713

Sieper J et al **2009** ASAS Criteria for Inflammatory Back Pain Ann Rheum Dis 68:784-8.

Rudwaleit M et al **2009** ASAS Classification for axial spondyloarthritis. Ann Rheum Dis 2009;68:777-83.

ACR/ EULAR Collaborative **2010** Rheumatoid Arthritis Classification Criteria, Arthritis & Rheumatism 62:2569-2581.

Van Vollenhoven RF **2009** Treatment of rheumatoid arthritis: state of the art Nat Rev Rheumatol 5:531-41.

Adebajo A (Ed) **2010** ABC of Rheumatology 4th edition Blackwell Books

Watts RA, Conaghan PG, Denton C, Foster H, Isaacs J, Muller-Ladner U (Eds) **2013** Oxford Textbook of Rheumatology 4th edition Oxford University Press

Philip AM et al **2017** Developing anti-inflammatory therapeutics for patients with osteoarthritis. Rheumatology 1;56(6):869-881

Bardin T et al **2017** Lesinurad in combination with allopurinol:
a randomised, double-blind, placebo-
controlled study in patients with gout with inadequate response to standard of car e (the multinationalCLEAR 2 study). Ann Rheum Dis; 76(5):811-820

Goodman SM et al **2014** Outcomes in Rheumatoid Arthritis Patients Undergoing Total Joint Arthroplasty. Int J Clin Rheumatol. 2014;9(6):585-593.

Goodman SM et al **2017** 2017 American College of Rheumatology/American Association of Hip and Knee Surgeons Guideline for the Perioperative Management of Antirheumatic Medication in Patients With Rheumatic Diseases Undergoing Elective Total Hip or Total Knee Arthoplasty. J Arthroplasty. 2017; 32(9):2628-2638.

Ding T et al **2010** BSR and BHPR rheumatoid arthritis guidelines on safety of anti-TNF therapies. Rheumatology. 2010; 49(11):2217-2219

CAPTIONS

Figure 1. X-ray of right knee showing severe joint space narrowing with osteophytes and subchondral cysts

Figure 2. X-ray of both knees with typical chondrocalcinosis in menisci, spiking of tibial spines and preservation of joint spaces

Figure 3. X-ray of both hands showing severe symmetrical erosive arthropathy with involvement of wrist, metacarpophalangeal and proximal interphalangeal (PIP) joints. Fused intercarpal joints and secondary OA in several PIP joints

Figure 4. Magnetic resonance image of sacroiliac joints showing florid marrow oedema on both sides of the joints.