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Guidelines

BSR & BHPR, BOA, RCGP and BSAC Guidelines for the management of the hot swollen joint in adults

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Scope and purpose

Background to the disease

The clinical presentation of a hot swollen joint is common and has a wide differential diagnosis. The most serious is septic arthritis, which accounts for significant morbidity, and has a case fatality of 11% [1]. Delayed or inadequate treatment leads to irreversible joint damage [2]. Rapid diagnosis and treatment is vital to prevent permanent joint dysfunction. This guideline will focus on the diagnosis and management of septic arthritis. Hot swollen joints commonly have other underlying diagnoses, including crystal arthritis, reactive arthritis and a monoarticular presentation of polyarthritis.

The need for a guideline

The hot swollen joint presents to many different clinicians in primary or secondary care. Poor outcomes including permanent joint destruction and death can occur if the diagnosis of sepsis is not made rapidly and treatment instigated appropriately. Septic arthritis can be difficult to recognize even for experienced clinicians, yet such patients frequently present to doctors unfamiliar with the assessment and management of joint disease. We hope that this guideline will aid accurate diagnosis and appropriate treatment when a joint is hot because of sepsis, whilst also ensuring that other causes such as crystal arthritis are recognized and not over-treated.

Objectives of the guideline

This guideline sets out recommendations for the diagnosis and initial management of septic arthritis presenting clinically as a hot swollen joint. These recommendations are based on a systematic review of the literature and evaluation of the evidence using standardized criteria.

Target audience

The guidelines have been developed to assist all clinicians to whom patients with this clinical picture may present. This will include general practitioners (GPs) and emergency physicians, as well as rheumatologists, orthopaedic surgeons and general physicians, all of whom may provide in-patient care [3].

The areas the guideline does not cover

- children under the age of 16
- management of gout
- management of septic arthritis beyond 6 weeks
- management of reactive arthritis
- osteomyelitis
- infection of the axial skeleton
- management of septic prosthetic joints

Stakeholder involvement

The guidelines have been developed by a multi-disciplinary Working Party set up by the British Society for Rheumatology. The guidelines have been reviewed and agreed by the British Orthopaedic Association, the British Society for Antimicrobial Chemotherapy and the Royal College of General Practitioners.

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Rigour of development

Statement of the scope of the literature search and the strategy employed

Search strategy. We performed a systematic search of the literature. The following databases were searched: Cochrane Library, Medline (1951 to March 2005), Embase (1974 to March 2005) and the National Electronic Library for Health. The search strategies and terms used in the Medline and Embase searches are shown in Appendix Tables A1 and A2. The reference lists of retrieved articles, and of review articles from key authors and journals, were hand searched to confirm the sensitivity of the defined search strategy. Expert members of the group were invited to contribute additional references.

Study selection. Two members of the group independently reviewed the retrieved abstracts. The selection of papers for full text review depended on adherence to defined inclusion and exclusion criteria set out in Appendix Table A3. In all, 3291 citations were initially identified. Of these, 189 full text articles were identified for potential selection. Following review, 75 articles fulfilled the inclusion criteria and were in the final list (Evidence table).

Data interpretation. We evaluated the methodological quality of the selected papers using defined criteria set out by the Clinical Effectiveness and Evaluation Unit of the Royal College of Physicians (RCP) (Appendix Table A4).

Statement of the extent of Cochrane, National Institute for Clinical Excellence (NICE), RCP and Scottish Intercollegiate Guidelines Network (SIGN) guidelines

A joint working group established between the British Society for Rheumatology and the Research Unit of the RCP of London published 'Guidelines and a proposed audit protocol for the initial management of an acute hot joint' in 1992 [4]. There have been no recommendations from NICE or the Cochrane Collaboration on hot joints. The current guidelines have been developed in accordance with SIGN principles. A draft version of the current guideline was presented at the British Society for Rheumatology Annual General Meeting in Birmingham on 19 April 2005, and the guideline was revised in the light of verbal and written comments during and after the meeting.

Statement of the limitations of the search

As defined earlier.

Statement of when the guideline will be updated

The guideline will be updated within 5 yrs after the publication of this guideline.

Guideline for management of the hot swollen joint

Symptoms and signs suggestive of septic arthritis

Septic arthritis typically presents as a hot, swollen, tender joint with a reduced range of movement [1, 5, 6]. Though symptoms are usually present for <2 weeks at presentation [1, 7], a longer duration is sometimes seen. Any joint can be affected, but large joints such as the hip or knee are more commonly recognized and reported. In the context of pre-existing joint disease such as rheumatoid arthritis (RA) or osteoarthritis (OA), the symptoms in the affected joint (or joints) are out of proportion to the disease activity detected in other joints. In up to 22% of the cases, more than one joint is affected, and therefore, an oligo- or polyarticular presentation does not exclude the diagnosis of sepsis [8, 9]. The presence or absence of fever is not a reliable indicator of an infected joint [1, 2, 7].

Recommendations

(1) Patients with a short history of a hot, swollen, tender joint (or joints) with restriction of movement should be regarded as having septic arthritis until proven otherwise (B).
(2) If clinical suspicion is high, then it is imperative to treat as septic arthritis even in the absence of fever (B).

Who gets septic arthritis?

Risk factors for the development of joint sepsis include:

(1) pre-existing joint disease, usually RA or OA [1, 2, 5, 8–12];
(2) prosthetic joints [1, 8];
(3) low socio-economic status [1];
(4) intravenous drug abuse [1, 10, 12];
(5) alcoholism [10–12];
(6) diabetes [2, 10–12];
(7) previous intra-articular corticosteroid injection [13]; and
(8) ulcerated skin.

A number of factors constitute poor prognostic features in septic arthritis. These include older age, pre-existing joint disease and the presence of synthetic material within the joint [14].

Which organisms cause septic arthritis?

In the UK, the most common causative organisms of septic arthritis are either *Staphylococcus aureus* or streptococci, with an increasing incidence of meticillin-resistant *Staphylococcus aureus* (MRSA) [1, 2, 5, 6, 8–10, 15, 16]. In young adults, there is a significant incidence of gonococcal arthritis [17–20]. Gram-negative organisms are more common in the elderly and the immunocompromised than in the young. Anaerobic organisms are more likely when there is a history of penetrating trauma [21].

Investigation of synovial fluid

Recommendations. In cases of suspected joint sepsis:

(1) The synovial fluid must be aspirated, Gram stained and cultured prior to starting antibiotics [23, 24] (B). Anticoagulation with warfarin is not a contra-indication to needle aspiration (C).
(2) A possibly infected prosthetic joint should always be referred to an orthopaedic surgeon (C).
(3) Neither the absence of organisms on Gram stain, nor a negative subsequent synovial fluid culture, excludes the diagnosis of septic arthritis. If clinical suspicion is high, it is imperative to treat it as septic arthritis even in the absence of laboratory confirmation (B).
(4) Specimens must be sent fresh to the laboratory and obtained prior to starting antibiotics; there is currently no evidence to support routine bedside inoculation into blood culture bottles. The laboratory should process all specimens (C).
(5) Specimens should be cultured in either broth culture or with lysis centrifugation in addition to agar culture [25–27] (B).
(6) Routine polymerase chain reaction (PCR) is not currently indicated [28, 29] (B).
(7) Polarizing microscopy to evaluate crystals should be carried out on all synovial fluid samples. This should be performed on a fresh sample by a microscopist experienced in crystal identification and in a laboratory with adequate standardization and quality control [30, 31]. If samples cannot be processed immediately, they should be stored at room temperature overnight, since artefactual crystals can form on refrigeration (B).

Table 1. Summary of recommendations for initial empirical antibiotic choice in suspected septic arthritis

Patient group	Antibiotic choice
No risk factors for atypical organisms	Flucloxacillin 2 g qds i.v. Local policy may be to add gentamicin i.v. If penicillin allergic, clindamycin 450–600 mg qds i.v. or 2nd or 3rd generation cephalosporin i.v.
High risk of Gram-negative sepsis (elderly, frail, recurrent urinary tract infection, recent abdominal surgery)	2nd or 3rd generation cephalosporin e.g. cefuroxime 1.5 g tds i.v. Local policy may be to add flucloxacillin i.v. to 3rd generation cephalosporin. Discuss allergic patients with microbiology, Gram stain may influence antibiotic choice
MRSA risk (known MRSA, recent in-patient, nursing home resident, leg ulcers or catheters or other risk factors determined locally)	Vancomycin i.v. plus 2nd or 3rd generation cephalosporin i.v.
Suspected gonococcus or meningococcus	Ceftriaxone i.v. or similar dependent on local policy/resistance
Intravenous drug users	Discuss with microbiologist
Intensive care unit patients, known colonization of other organs (e.g. cystic fibrosis)	Discuss with microbiologist

Antibiotic choice will need to be modified in the light of results of Gram stain and culture. This table is based on expert opinion, and should be reviewed locally by microbiology departments.

Other laboratory investigations

Recommendations. In cases of suspected joint sepsis:

(1) Blood cultures should always be taken (B).
(2) The white cell count (WCC), erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should be measured (B). The absence of a raised WCC, ESR or CRP does not exclude the diagnosis of sepsis and if clinical suspicion is high then treatment for infection should always be instituted [1, 7, 9, 10, 32]. The inflammatory markers are often useful for monitoring response to treatment (B).
(3) The serum urate level is of no diagnostic value in acute gout or sepsis (B).
(4) Urea, electrolytes and liver function should be measured to detect end-organ damage, which is a poor prognostic feature in septic arthritis, and because renal function may influence the choice of antibiotic (B).
(5) If the history suggests the possibility of genitourinary, respiratory tract or other infection, then appropriate cultures and swabs should be taken prior to starting antibiotics [19] (B).

Imaging

Recommendations

(1) Plain radiographs of the affected joint are of no benefit in the diagnosis of septic arthritis, but may show chondrocalcinosis suggestive of pyrophosphate arthropathy. They should be performed as a baseline investigation for assessing any future joint damage (C).
(2) Scintigraphy and magnetic resonance imaging (MRI), both perform well for distinguishing sepsis from OA, but cannot distinguish between sepsis and inflammation and are, therefore, not indicated routinely in the investigation of the hot swollen joint [33, 34].
(3) The Working Party recommends that if advanced imaging is necessary then MRI would be most appropriate since it is sensitive in detecting osteomyelitis, which may require a surgical approach [35] (B).
(4) In suspected hip sepsis, diagnostic aspiration will usually require the use of ultrasound or an image intensifier (C).

Antibiotic treatment of septic arthritis

The Working Party acknowledges that there is very little high-quality evidence with regard to the choice or duration of antibiotic therapy in the treatment of septic arthritis [37–39].

The following recommendations are, therefore, guiding principles. The Working Party recommends that antibiotic policies be developed locally using the principles below in conjunction with local guidelines (Table 1). Antibiotic policies should be developed locally.

Recommendations

- Gram staining of synovial fluid is critical to early, targeted antibiotic therapy and must be performed as soon as possible in order to give immediate guidance on antibiotic choice (B).
- Likely pathogens are *S. aureus* and streptococci, and initial bactericidal antibiotic therapy prior to organism identification should reflect this (B).
- Gram-negative organisms are more common in the elderly and in those with sources of infection or immunosuppression. Antibiotic choice in these groups of patients should reflect this (B).
- MRSA should be considered especially in 'at risk' groups such as nursing home residents or recent hospital in-patients (B).
- Routine cover for *Neisseria gonorrhoeae* or *Haemophilus influenzae* type b is no longer required in the absence of specific clinical indicators (B).
- Shorter and less intensive courses of antibiotics for *N. gonorrhoeae* are normally sufficient [40] (A).
- Demographic and clinical risk data should also be used to make judgements on the likelihood of the involvement of atypical organisms (C).
- Antibiotic therapy must be amended as results on culture, sensitivity and specificity become available (C).
- There is no evidence on which to advise the optimal duration of i.v. or oral antibiotics. Conventionally, they are given intravenously for up to 2 weeks or until signs improve, then orally for around 4 weeks which should be able to achieve adequate joint and bone concentrations. Symptoms, signs and acute-phase responses are all helpful in guiding the decision to stop antibiotics. Expert review may be required if the expected resolution does not occur (C).

Joint drainage and surgical options

In addition to antimicrobial therapy, the successful treatment of acute septic arthritis requires the removal of pus. The Working Party notes that there is scant evidence on the mode of drainage that should be employed. The options include medical needle aspiration or surgical aspiration via arthroscopy. From the studies identified, no evidence was found to enable us to recommend one treatment strategy over another [41–45]. Both arthroscopy and needle aspiration, however, appear to have a favourable outcome.

Recommendation

(1) Septic joints should be aspirated to dryness as often as is required (C).

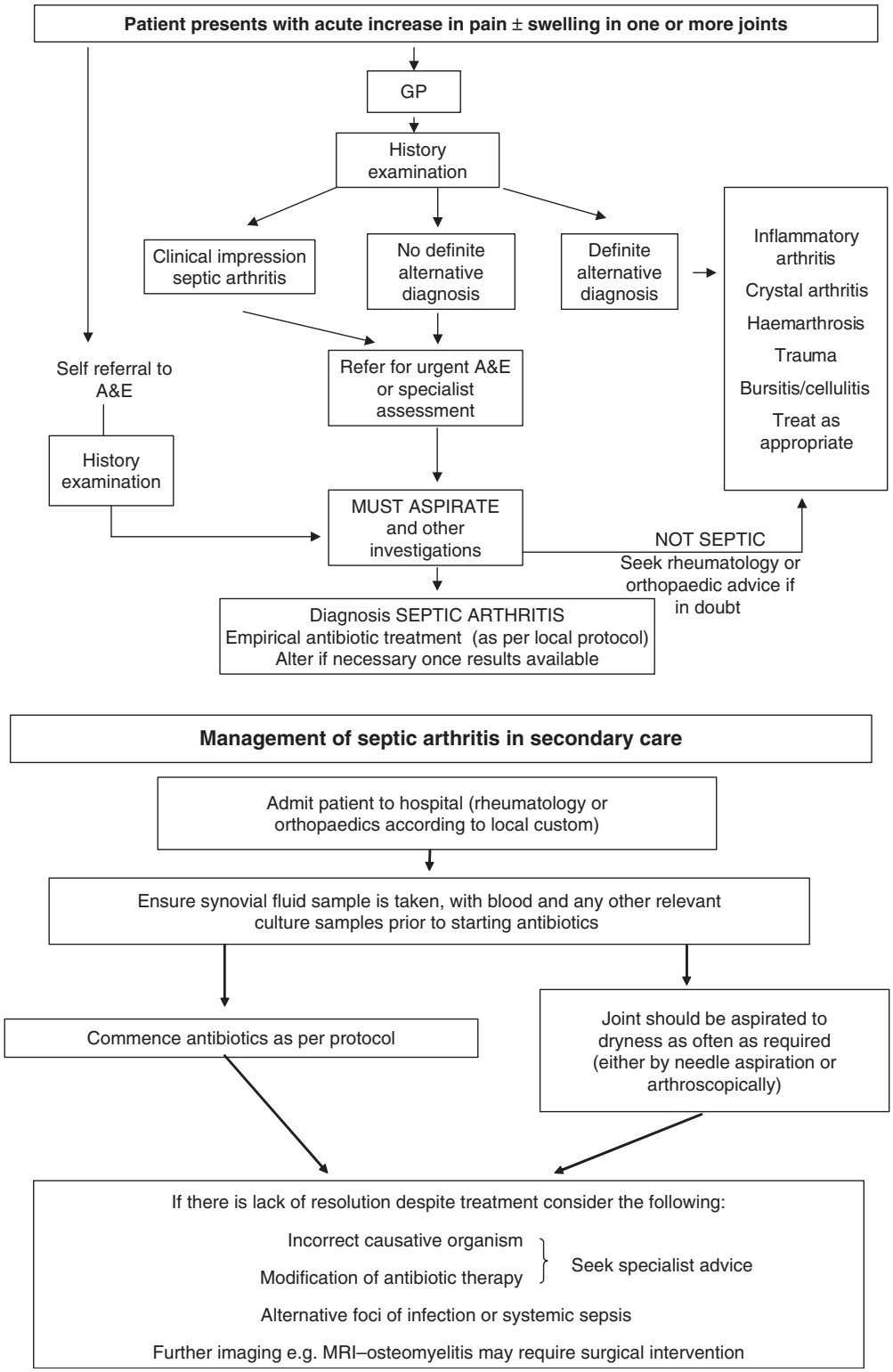

FIG. 1. Algorithm of guideline.

(2) This can be done either through a closed needle approach or arthroscopically according to local preferences (C).
(3) If the response is not satisfactory with a closed needle approach, or pus is thick and inspissated, arthroscopic aspiration should be used to allow biopsy and repeat culture, washout and perhaps debridement (C).
(4) There is no evidence to indicate whether septic joints should be splinted or mobilized, and local preferences should be followed (C).
(5) In suspected hip sepsis, there should be early referral for an orthopaedic opinion. The risks of avascular necrosis and chondrolysis are greatest in the hip and urgent open debridement is often necessary (C).

Recommendations specific to primary care and the emergency department

(1) The commonest hot joint to present in primary care is the great toe metatarsophalangeal joint. This is almost always due to gout and can be diagnosed on clinical grounds without requiring needle aspiration or referral to hospital. Referral should be made if there is an inadequate recovery (see also BSR guideline on gout) (B).
(2) Some GPs regularly aspirate and inject joints for patients with inflammatory arthritis or OA. However, if they aspirate unexpectedly cloudy fluid from a joint, they should send the sample with the patient to the local emergency department, and not inject corticosteroid (C).
(3) GPs and doctors in the emergency department should refer patients with suspected septic arthritis to a specialist within the hospital who has the expertise to aspirate the joint (C).
(4) Patients should be admitted to hospital if sepsis is suspected (C).
(5) If there is any doubt about whether sepsis might be present, intra-articular steroids should not be used (C).
(6) The skills necessary to aspirate a joint in hospitals will commonly be held by specialists and trainees in Emergency Medicine, Orthopaedics and Rheumatology (C).

Summary

The recommendations outlined above are summarized in an algorithm (Fig. 1).

Applicability and utility

Statement of potential organizational barriers to introduction

In the absence of evidence, strong views have developed in the medical and surgical community as to the correct way to manage septic arthritis. These are often mutually contradictory, and have led to the current situation in which management is radically different depending on which professional group happens to be the predominant carer for these patients in different centres. It is likely that some of our recommendations will be controversial, and this may result in certain groups dismissing them.

Potential cost implications for introduction of the guideline

By applying the best available evidence to the diagnosis and management of septic arthritis, we expect that our guideline will be cost saving. This is because our guideline should reduce inappropriate treatment, leading to a shortened length of stay and the avoidance of inappropriate surgery.

Audit suggestions

Septic arthritis is a rare condition. It is likely that meaningful numbers of patients will only be identified for audit if collaborative audits are undertaken between several centres. In cases of proven septic arthritis:

(1) Was the joint aspirated at presentation prior to antibiotics, and if not, what was the reason?
(2) Was there any delay in treatment of septic arthritis, and if so why?
(3) Was ESR and CRP measured at diagnosis and serially?
(4) Were appropriate cultures taken?
(5) Was the initial antibiotic choice in keeping with the guideline?
(6) Was prosthetic joint sepsis managed by orthopaedic surgeons?

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Appendix

Search strategy and references

Table A1. Medline search strategy

1.	Arthritis-infectious.de
2.	Guidelines.pt
3.	Meta-analysis articles.pt
4.	Randomised controlled trials.pt
5.	Controlled clinical trials.pt
6.	Evaluation studies.pt
7.	1 and 2 or 3 or 4 or 5 or 6
8.	Drug therapy DT.de
9.	Therapy TH.de
10.	Diagnosis DI.de
11.	Epidemiology EP.de
12.	Microbiology MI.de
13.	Prevention and control PC.de
14.	Radiography RA.de
15.	Radionuclide imaging RI.de
16.	Surgery SU.de
17.	Etiology ET.de
18.	Staphylococcal-infections.de
19.	Streptococcal-infections.de
20.	Pneumococcal-infections.de
21.	Neisseria.gonorrhoeae.de
22.	Synovial-fluid.de
23.	Anti-bacterial-agents.de
24.	Joint-prosthesis.de
25.	Adrenal-cortex-hormones.de
26.	Glucocorticoids.de
27.	Arthroscopy.de

Table A2. EMBASE search strategy

1.	Infectious-arthritis.de
2.	Diagnosis DI.de
3.	Disease management DM.de
4.	Drug therapy DT.de
5.	Epidemiology EP.de
6.	Etiology ET.de
7.	Prevention PC.de
8.	Surgery SU.de
9.	Therapy TH.de
10.	Practice-Guideline.de.
11.	Antibiotic-agent.de
12.	Randomised controlled trials
13.	Meta analysis
14.	Staphylococcus-aureus.de.
15.	Streptococcus-infection.de.

Table A3. Inclusion and Exclusion Criteria

Inclusion criteria	Exclusion criteria
Randomized controlled trials	Paediatric studies (age <16)
Controlled clinical trials	Animal studies
Prospective observational studies	Case reports
Retrospective observational studies	Case series of less than 40 patients
Guidelines	Review articles
Meta-analyses	Studies on reactive arthritis
Case series including 40 or more cases	Studies on infection in other musculoskeletal sites e.g. osteomyelitis, tenosynovitis
	Chronic sepsis
	Infection of the axial skeleton
	Osteoarthritis
	Gout
	The management of septic arthritis beyond the first 6 weeks

Table A4. Example of graded evidence

Level of evidence*	Type of evidence	Grade of recommendation
Ia	Meta-analysis of randomised controlled trials (RCTs)	A
Ib	At least one RCT	A
IIa	At least one well-designed controlled study, but without randomization	B
IIb	At least one well-designed quasi-experimental design	B
III	At least one non-experimental descriptive study (e.g. comparative, correlation or case study)	B
IV	Expert committee reports, opinions and/or experience of respected authorities	C

*As used by the Royal College of Physician in the National Clinical Guidelines for Stroke.

Evidence Table

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
The value of synovial fluid assays in the diagnosis of joint disease: a literature survey. Swan A *et al*. Ann Rheum Dis 2002;61:493–8	Literature review	300 papers			Usefulness of synovial fluid analysis	Synovial fluid of benefit in acute arthritis (septic arthritis/crystal arthritis) but synovial fluid under-analysed and not standardized	A
Another look at synovial fluid leukocytosis and infection. Coutlakis *et al*. J Clin Rheumatol 2002;8:67–71	Retrospective study of records of patients with synovial fluid white cell counts over 2000 mm^3	202 cases, mixed arthropathies	1 yr	White cell count in acute arthritis	Value of white cell count (neutrophils) in cases of acute monoarthritis	Elevated synovial fluid white cell count is associated with infectious arthritis. But there is overlap between septis arthritis and other types of inflammatory arthritis, especially crystal arthritis. 18/27 cases of sepsis had counts $>50\,000\,mm^3$	B
Synovial fluid leukocyte count and differential for the diagnosis of prosthetic knee infection. Trampuz A *et al*. Am J Med 2004;117:556–62	Prospective study before total knee replacement revision	133 cases	5 yrs	White cell count in prosthetic joint synovial fluid	Value of neutrophil count in prosthetic joint synovial fluid	99 patients with aseptic joint failure, 34 with infection. Synovial fluid white cell count higher in infected prosthetic joints—median $189\,000\,mm^3$. Synovial fluid white cell count in aseptic failure median $300\,mm^3$. Upper limit of non-infected joint synovial fluid white cell counts $= 16\,000\,mm^3$. Neutrophil count 92 *vs* 7%. White cell count $>17\,000\,mm^3$ is 94% sensitive for sepsis and 88% specific Neutrophil count >65% is 97% sensitive for sepsis and 98% specific	B
Laboratory tests in adults with monoarticular arthritis: can they rule out a septic joint? Li SF *et al*. Academic Emergency Medicine 2004;11:276–80	Retrospective study of cases with septic arthritis	73 cases	5 yrs			61 cases with bacteria in aspirate (12 not so but five grew organisms post-surgery). *Staphylococcus* and *Streptococcus* are the commonest organisms. Older patients, diabetic patients and HIV-positive patients have higher relative risk of mortality. Low acute-phase response rare (3%), white cell count normal in 53%	III B
Acute monoarticular arthritis: a diagnostic approach. Freed JF *et al*. JAMA 1980;243:2314–6	Prospective, all cases of acute monoarthritis	59 cases	10 months		Efficiency of diagnosis	Paradigm suggested, 75% cases diagnosed within 2 days using history, examination, Gram stain and crystal examination	B
Infectious arthritis. Sharp JT *et al*. Arch Intern Med 1979;139:1125–30	Retrospective	120 episodes	14 yrs	Review of cases	Causes and bacteria involved	Predisposing causes: infection elsewhere 30/120, diabetes mellitus 11/120, sickle cell disease 7/120, underlying joint disease 6/20, i.v. drug abuse 5/120, alcoholism 5/120, intra-articular injection 3/120, *Neisseria* F > M, *Staphylococcus* F = M, *Streptococcus* F = M, 13/120 only blood culture positive	B
Clinical features and outcome of septic arthritis in a single UK health district 1982–1991. Weston VC *et al*. Ann Rheum Dis 1999;58:214–19	Retrospective	242 cases	10 yrs	Case notes study	Causes, poor outcome	*Staphylococcus* and *Streptococcus* 74% of cases, mainly large joints involved. *N. gonorrhoeae* incidence falling. Peaks of incidence in childhood and elderly. Poor prognostic features: confusion at presentation, closed drainage, over the age of 65 open drainage is better. Appropriate antibiotics not always used. Death predicted by: confusion, closed drainage, delay in diagnosis of >3 days, infection in childhood and prosthetic joint. Morbidity predicted by closed drainage, diabetes mellitus, childhood or elderly infection	

A prospective 2-year study of 75 patients with adult-onset septic arthritis. Gupta MN *et al*. Rheumatology 2001;40:24–30	Prospective multi-centre, hospital-based	75 cases	2 yrs	Prospective study	Causes, complications bacteria and treatment	Social deprivation a factor (78%). MRSA increasingly common. Underlying joint disease more common (61%) than previously recognized. White cell count and fever not universal at presentation (64% and 62%, respectively). Leg ulcers a problem in RA cases. Surgical intervention more common when patient on surgical wards. Mortality 11%. Incidence of diagnosis bacterially proven 1.5/100 000 (probably double if suspected cases included). Leg ulcers, raised white cell count at presentation and development of renal problems are poor prognostic signs. Usual antibiotic therapy 14 days i.v. followed by 3 weeks oral	B
Prospective comparative study of patients with culture proven and high suspicion of adult onset septic arthritis. Gupta *et al*. Ann Rheum Dis 2003;62:327–31	Prospective multi-centre hospital-based	82 cases (47 proven and 35 suspected)	1 yr	Prospective study	Comparison of clinical and biochemical features	All parameters identical or very similar. If antibiotics used early then may be more likely to show no bacterial growth. Outcomes very similar in presence or absence of bacterial growth. Long-term mortality also very similar	B
Septic Arthritis due to *Streptococcus pneumoniae* in Nottingham, United Kingdom, 1985–1998, Ispahani P *et al*. Clin Inf Dis 1999;29:1450–4	Retrospective analysis	32 cases	13 yrs	Description of cases		Comprises 8% of all septic arthritis cases with predisposing joint disease. Common (19/32). All penicillin sensitive. In the elderly there may be lack of febrile response, usually infection elsewhere. Similar distribution of joints to usual, and signs and results similar. High mortality (32%), elderly poor prognosis	B
Polyarticular septic arthritis. Dubost J-J *et al*. Medicine 1993;72:296–310	Retrospective and literature review	25 cases + literature review	12 yrs	Description of cases		Polyarticular arthritis usually *Staphylococcus aureus*. Concurrent disease (particularly longstanding RA) more common in polyartlicular than monoarticular sepsis. Predisposing factors: longstanding rheumatoid arthritis, with skin infections, steroids, SLE predisposing to Gram-negative bacteria, other diseases needing immunosuppression. White cell count and fever not universal. Poor prognosis in RA, aged >50, and staphylococcal infection.	B

Continued

Table 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
Guidelines and a proposed audit protocol for the initial management of an acute hot joint. Report of a Joint Working Group of the British Society for Rheumatology and the Research Unit of the Royal College of Physicians, Journal RCP 1992;26:83–5	Suggested guidelines					Septic arthritis needs rapid hospital admission with rheumatological and microbiological facilities. Gram stain, synovial fluid and blood culture, full blood count, acute phase response, X-rays to be done. Possible septic arthritis requires antibiotic therapy dependent on Gram stain. Flucloxacillin and B-penicillin required if treating blind and for 6 weeks. High dose NSAID required for septic arthritis. Gout and pseudogout need NSAID or colchicine. Allopurinol not to be started in acute attack. Audit projects suggested	C
The acute hot joint in medical practice, Walker DJ *et al* Journal RCP 1995; 29:101–4	Retrospective analysis	GP practice ($n=21$). Casualty attendance ($n=31$). Rheum in-patients ($n=36$)	6 months	Guideline protocol—is it adhered to?		GP all diagnosed as gout—no acute patients sent to A&E. No joint aspirations. All bar one on NSAIDs. Joint aspirate in one case. In A&E gout all discharge. Septic arthritis 2 cases. Not complete consensus. Joint aspiration not usual. In Rheumatology dept joint aspiration routine. Most light microscopy, All acute phase response, most blood cultured. All X-ray guidelines of no use to GPs. Partial use in A&E and fair value in rheumatology dept	B
The outcome of bacterial arthritis. A prospective community based study. Kaandorp CJE *et al*. Arth and Rheum 1997;40:884–92	Prospective community-based survey	Health district study, 154 cases, 121 adults, positive culture necessary.	2.5 yrs		Death, functional deterioration	Predisposing factors—pre-existing joint disease (50%), prosthetic joints. Adverse factors—old age, pre-existing joint disease, prosthetic joints	B
Incidence and sources of native and prosthetic joint infection: a community based prospective survey. Kaandorp CJE *et al*. Annals Rheum Dis. 1997;56:470–5	Prospective community-based study	188 cases	3 yrs		Incidence study	Pre-disposing factors in adults—skin infections (67%), pre-existing joint disease (59%), joint surgery (33%), incidence 5.9/100 000. 8% cases preventable	B
An 18 year clinical review of septic arthritis from tropical Australia. Morgan DS *et al*. Epidemiol Infect 1996;117:423–8	Retrospective study	191 cases with bacteria positive culture	18 yrs			Incidence 9.2/10 000 general, 29.1/100 000 in Aboriginals. Large joints. Occasional unusual organisms (local effect)	B
Synovial fluid lactic acid. A diagnostic aid in septic arthritis? Brook I *et al*. Arth and Rheum 1978;21:774–9	Prospective	84	8 months	Measurement of lactic acid in synovial fluid in bacteria proven cases compared with inflammatory arthritides		Synovial fluid lactic acid raised in septic arthritis. Not raised in gonococcal arthritis. Significant overlap between infectious and non-infectious arthritis. Glucose lower and white cell count higher in septic arthritis. Gas liquid chromatography not generally available	A

Abnormalities in synovial fluid in septic arthritis detected by gas-liquid chromatography. Brook *et al*. Annals of Rheum Dis 1980;39:168–72	Prospective	94	17 months	Gas-liquid chromatography analysis of synovial fluid from septic joints. Bacteria proven cases. Control group inflammatory arthritides		Synovial fluid lactic acid raised in non gonococcal septic arthritis. Synovial fluid—two other unidentified peaks but not specific for septic arthritis. Gas liquid chromatography not generally available	A
Salmonella septic arthritis in SLE and other systemic diseases. Chen JY *et al*. Clin Rheum 1998;17:282–7	Retrospective	41	6 yrs	Clinical features of patients selected. Detection of *Salmonella* in synovial fluid	Characterization of patients	Similar distribution of pre-existing diseases as with other organisms. Three patients died (7%). More common in SLE. Nephritis and high dose steroid use in SLE present in all cases. Avascular necrosis also more common in SLE. No idea how common *Salmonella* is in comparison to *Staphylococci* and other Gram-negative organisms. Possible local problem in China	B
Predictors of mortality in non-post-operative patients with septic arthritis. Yu LP *et al*. Scand J Rheum 1992;21:142–4	Not clear	50	Not clear	Selected cases excluding those within 6 months of joint replacement. Positive joint culture	Dead/not dead	Risk factors—diabetes mellitus, alcoholism, immunosuppression. The more joints affected the higher the mortality. Not clear how long follow-up was	B
Clinical study of culture-proven cases of non-gonococcal arthritis. Deesomchok U *et al*. J Med Assoc Thai 1990;73:615–23	Not clear	101	22 yrs	Clinical features of patients with septic arthritis. 73% synovial fluid culture positive, 27% blood culture positive	Characterization of patients. Comparison of populations from 1976–85 and 1986–88	Organisms: 85% Gram-positive, 14% Gram-negative (no *Gonococcus*). Lower limb >upper limb. No difference between organisms. Skin lesions common for Gram-positive (50% of cases), Urinary tract infection common for Gram-negative (57%). Raised white cell count only in 80%. Risk factors—diabetes, chronic liver disease, drug addiction, underlying joint disease or bone infection. 9% mortality. Higher in Gram-positive infections (aerobic *Streptococci* worst). Prognosis for infected joint 71%. 'Good' with no X-ray evidence of destruction. Gram-negative infections associated with more X-ray destruction (43%). (Not clear how long follow-up was for in this part of study)	B
Bacterial arthritis in the adult. Kelly PJ, Orthopaedic clinics of North America 1975;6:973–81	Retrospective	141	25 yrs	Clinical features in the adult cases of septic arthritis. Synovial fluid culture positive cases only. Excluded granulomatous disease	Literature review and commentary on 141 cases from Mayo Clinic	Lower>upper limb joints involved. Knee > hip > shoulder > elbow. *Staphylococcus aureus* most common, Gram-negatives increasing. *Gonococcus* needs special medium—Thayer Martin. White cell count may only be helpful in 25% cases. ESR most useful test. Most important is to identify cases and extract fluid early. Predisposing causes—pre-existing joint disease (RA), steroids (no evidence), joint injections, diabetes, alcoholism, cytotoxic drugs, radiotherapy for malignancy (no evidence). Poor prognosis if osteomyelitis present. Discussion on surgery, intervention with aspirate/wash out/replace (no data)	III

Continued

TABLE 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
Pyogenic arthritis and rheumatoid disease: the importance of the infected foot. Morris IM *et al.* Rheum and Rehab 1978;17:222–6	Retrospective	75	9 yrs	Bacteria proven cases. Compared with RA controls	Retrospective study of 75 cases with septic arthritis of whom 22 (30%) had RA	20/22 had infection elsewhere—*Staphylococcus aureus* most common. 9 infected foot ulcers, 9 infected skin. Upper > lower limbs but knee predominantly. 36% on steroids or ACTH. Controls: in 205 rheumatoid arthritis patients, 52 had callosities, 21 had foot ulcers. Steroid use equal in callosity group (53%) and ulcerated callosity group (61%), but lower in non-callosity group (35%)	III
Synovial leucocytosis in infectious arthritis. McCutchan HJ *et al.* Arthritis and Rheum 1990;257:226–30	Retrospective	41	Not given	Bacteria proven cases, very selected. No control group for analysis	Synovial fluid white cell count	Cases: malignant disease 10, i.v. drug abusers 9, RA 6, alcohol 5, diabetes mellitus 5. Lower limb > upper limb. White cell count high in synovial fluid when infection present. Synovial fluid white cell count lower in i.v. drug abusers but no statistics	B
Septic arthritis in a general hospital 1966–1977. Manshady BM *et al.* J Rheumatol 1980;7:523–30	Retrospective	85	11 yrs	33 *Gonococcus* positive in synovial fluid or other site. 54 *Gonococcus* negative	Gonococcal *vs* non-gonococcal arthritis. Clinical features. Outcome at discharge	*Gonococcus* mostly age 10–29 and females aged 31/32/33 more than one joint. Culture often from cervix too. Wrist/finger joints as common as knee/ankle. Mean hospital stay 9.5 days. Milder outcome + no deaths. Non-gonococcal septic arthritis 74% male. Mean age 38. Increased incidence with i.v. drug abuse. Knee and ankle predominantly, only 11/54 polyarticular. i.v. drug abuse 19 > trauma 12 > diabetes mellitus 8 > RA 4. *Staphylococcus aureus* + others. Surgery in 23, hospital stay 35 days. 5 deaths. X-ray not much help. Suggests surgery for patients non responsive after 5–7 days	B
Changing pattern of bone and joint infections due to *Staphylococcus aureus*: study of cases of bacteremia in Denmark, 1959–1988. Esperson F *et al.* Revs Infect Dis 1991;13:347–58	Retrospective	185	30 yrs	Selected by presence of *Staphylococcus aureus* bacteraemia	Analysis of cases of osteomyelitis and septic arthritis derived from and compared with results from all bacteraemia cases	*Staphylococcus aureus* bone/joint infections account for 6% of all staphylococcal bacteraemias. Septic arthritis increasingly more common (2.5% in early 1980s of all bacteraemias, 0.5% in 1960s). Over the decades older people more affected, but case numbers in 0–20 group the same. Phage types changing, group I type infections common pre-1980 but not later. Antibiotic sensitivities changed over this time (penicillin resistance). Chronic osteomyelitis less in long leg bones now, more in vertebrae. Chronic osteomyelitis less common over age 30. Mortality staphylococcus infections 36%. Mortality from staphylococcus arthritis 9%, acute osteomyelitis 5%, chronic osteomyelitis 15%, acute septic arthritis 9%	B

Comparative study of gonococcal arthritis and Reiter's syndrome. Hurd ER *et al*. Ann Rheum Dis 1979; (38 Supp):55–8	Retrospective	123 gonococcal arthritis, 12 Reiter's syndrome	5 yrs	Cases admitted to hospital. No comparison group	Only 12 Reiter's Syndrome and 58% of gonococcal arthritis cases negative culture. One case of Reiter's syndrome presented 18 yrs before admission. Case selection very suspect	55% gonococcal arthritis cases had skin lesions. Younger than Reiter's Syndrome. Short presentation. Migratory polyarthralgia more common. Synovial fluid analysis no difference. Mild differences in clinical features. Always culture all potential sites of infection	B
Bacterial arthritis: are rigors, leucocytosis and blood cultures of diagnostic value? Schlapbach P *et al*. Clinical Rheumatology 1990;9:69–72	Retrospective	43 cases	10 yrs	Clinical features at presentation. No comparison group. Culture media at the bedside		Knee > shoulder > wrist > hip > elbow. Rigours in 22%. Normal temperatures in 35%. ESR <20 mm/h in 14%. Normal white cell count in 58%. Synovial fluid culture postive in 72%, blood culture positive in 24%. Synovial fluid or blood culture positive in 7/13 afebrile patients	B
Bacterial arthritis in a district hospital. Peters RHJ *et al*. Clinical Rheumatology 1992; 11:351–55	Retrospective	72	11 yrs	Clinical features at presentation. No comparison group. Assessment post infection, time not characterized	Synovial fluid positive culture only. Gonococcal cases symptoms only	Knee > hip > ankle > upper limb. *Staphylococcus aureus* 52%, *Streptococcus* 11%, *Gonococcus* 3%. Portal of entry common, usually skin, urogenital tract, respiratory, gastro-intestinal tract, joint replacement. Predisposing causes RA, OA, diabetes mellitus, malignancy. Usual treatment antibiotics with aspiration and/or drainage. Mortality 11% (not gonococcal cases). Joint function recovered to normal in 52% (no characterization of follow up duration). RA patients 52% deteriorated *vs* 45 in non-RA patients. Early treatment (1 day) 8% serious impairment of joint function. Late treatment (2/52) 27% serious impairment of joint function. Prosthetic joints—not all removed. Long-term antibiotics an option	B

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TABLE 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
Non-gonococcal infectious arthritis: a retrospective study. Meijers KAE *et al.* Journal of Infection 1986;14:13–20	Retrospective	76	14 yrs	Clinical features and outcome of acute infection	Synovitis in the presence of bacterial growth from synovial fluid	Knee > hip > shoulder > elbow. *Staphylococcus aureus* 62%, *Streptococcus* 14%, *Mycobacterium* 8%. Admission time <25 days or >25 days. Predisposing causes RA (45%), diabetes mellitus, skin entry 42%, respiratory, genitourinary, gastrointestinal (13%), intra-articular injections (8%). 23 patients (30%) on steroids and/or cytostatic drugs. 12 prosthetic joints. Number of joints—60 monoarticular, eleven 2 joints, four 3, one 6. Gram-positive in 65%, helped early antibiotic choice. Blood culture positive in 31%. 12% mortality. Predisposing factors RA and older age at diagnosis. Late admission no effect on mortality but better joint outcome. Treatment antibiotics and aspiration, splinting + traction, joint washout if no improvement. 7/9 prostheses removed. Outcome 61% had impaired joint function, not clear at which time point. Worse in RA patients only 4/35 getting complete recovery. 16 developed moderate limitation and 15 severe	B
Streptococcal septic arthritis in adults:a study of 55 cases with a literature review. Dubost J-J *et al.* Joint Bone and Spine 2004;71:303–11	Retrospective	55 *Streptococcus*, 168 *Staphylococcus*	20 yrs	Clinical features and outcome of acute infection. Literature review of streptococcal arthritis	Synovial fluid or blood culture positive cases	Knee > shoulder > hip = ankle. Similar distribution for *Staphylococcus* and *Stretococcus*. Possible increasing incidence of Streptococci. Streptococcal infection less likely in males, RA and diabetes mellitus patients, but more in crystal disease. Subtyping of little help (small numbers) but Group A/B female preponderance. Group A, G and *Pneumoniae* most likely to have systemic features. Group B less likely to have systemic features. Common in diabetes and malignancy. Group G RA and alcohol risk. 2 antibiotics given in most cases. i.v. for 2–3 weeks, oral for about 3 months. Beta-lactams in 52 (allergy in 3), with aminoglycoside in 37. rifampicin, vancomycin, macrolides fosfomycin/quinolones rarer. Resistance to lactams increasing. All aspirated. Surgery in 35%, joint lavage, drainage and prosthesis removal. Mortality about 20% in group A, B and *Pneumoniae*, group G only 3%. Residual abnormalities in about 50% of cases (no subtype worse.)	B

Bacterial arthritis in an English Health District: a 10 year review. Cooper C *et al*. Ann Rheum Dis 1986;45:458–63	Retrospective	74	10 yrs	Typical features and synovial fluid or blood culture positive (81%). Typical features, culture negative but with previous antibiotic treatment and synovial fluid white cell count over 105 (19%). Excluded prostheses and tuberculosis	Clinical features and outcome of acute infection. Included children	Peak age 2–30 and over 60. Blood culture positive when negative in synovial fluid (14%). *Staphylococcus* 44%, *Streptococcus* 14%, *Gonococcus* (all synovial fluid positive) in 11%. Knee > Hip > upper limb. Predisposition OA > RA > gout > psoriatic arthritis. Trauma (32%), immunosupression 16%, insulin-dependent diabetes 7%. Immobilization, aspiration, systemic antibiotics in all (multiple aspirations in 26%). Intra-articular antibiotics in 15 cases, surgical drainage in 25%. Early diagnosis less morbidity and shorter hospital stay. Complications: osteomyelitis, permanent immobility, recurrent effusions, OA, avascular necrosis, *Gonococcus* notably more favourable outcome. *Streptococcus* benign, *Staphylococcus* and Gram-positives poor prognosis. Hip worse outcome than knee, and elderly worse than young (*Gonococcus*). No difference between surgical or medical treatment	B
Suppurative arthritis. Argen *et al*. Ann Int Med 1966;117:661–6	Not clear	42	4 yrs	Clinical features and outcome of acute infection in veterans. Hospital *Gonococcus*, tuberculosis and synovial fluid/blood culture negative excluded	Synovial fluid positive (38), synovial fluid negative, blood culture positive (4). No control group	Knee most common. All other large joints roughly equal. High incidence in elderly, not in children. *Staphylococcus* 25 cases, with infection elsewhere in 13. Predisposing systemic features—RA (+steroids), type one diabetes, alcohol. Local factors—joint disease (including RA + steroids), local trauma, neuromuscular disease. Blood investigations—white cell count normal in 11 and synovial fluid Gram-positive in 10/17, but 14 grew organisms. White cell count raised but number variable. Glucose lower than blood. X-ray no help. Treatment bed rest, splinting, traction, physical therapy. Antibiotics with aspiration (repeated as required) ± surgery initially or subsequent repeated aspirations. 3 died (8%). Joint function related to underlying diagnosis and delay in treatment. Repeated antibiotics into the joint lead to subsequent synovitis	B

Continued

TABLE 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
Bacterial or crystal arthritis? Discriminating ability of serum inflammatory markers. Soderquist B *et al.* B Scand J Infect Dis 1998;30:591–6	Retrospective	88	3 yrs	Comparison of clinical and laboratory features in septic arthritis and crystal arthritis. White cell count, cytokines. Acute-phase proteins	Proven bacterial (54). Crystal verified (34)	In septic arthritis *Staphylococcus* and *Streptococcus* predominate. RA more common in septic arthritis, and OA more common in crystal arthritis. Septic arthritis after joint replacement and other joint surgery. Gram-positive in 13/31 cases. All culture positive later. Antibiotics started in all septic arthritis cases (only 50% of crystal arthritis). i.v. antibiotics for mean of 11 days in septic arthritis (1–2 days in crystal arthritis) 11% septic arthritis cases died during admission, 0% of crystal arthritis. Blood white cell count/lactoferrin, not discrimatory. ESR, CRP both higher in septic arthritis than crystal arthritis but range large with overlap so no real help. Glucose discrepancy in blood/synovial fluid over 2.5 more in septic arthritis than in crystal arthritis (64% *vs* 15%.) Very high procalcitonin levels in septic arthritis but generally non-discriminatory. Cytokines-TNF, IL-8, GM-CSF higher in septic arthritis than crystal arthritis but non-discriminatory	B
Acute non-gonococcal infectious arthritis. Evaluation of risk factors, therapy and outcome. Rosenthal J *et al.* Arthritis Rheum 1980;23:889–97	Retrospective	71	5 yrs	Patient clinical features. Non-gonococcal septic arthritis. Outcome defined by medical or surgical therapy	All cases with proven septic arthritis including children	Peaks 0–20 and 50 yrs and above. Children—hip 60%, knee 35%. In adults—knee 50%, hip 22%. Gram-positive cocci 56 cases (*Staphylococcus* 40/56). Large number of Gram-negatives (23/63). Steroids >10 mg/day in 14 cases. RA in 9 cases. Debility in 4 cases (diabetes mellitus, alcohol, malignancy). Multiple joint involvement in 11 cases—3 RA, 1 SLE. Primary source in 34/63 cases. Genitourinary 6, bone 6, skin 4, i.v. drug abuse 4, intra-articular injection 4, sinuses 2. Medical therapy 17 hips and knees. Surgical therapy 33 hips and knees—all with parenteral antibiotics. 4 adults died, all aged over 60, all with underlying disease. Longer time to diagnosis worse prognosis. Surgery worse outcome, 22/33 cases poor outcome, only 5/17 medical poor outcome. Single organisms no difference in outcome. Mixed organisms worse prognosis. At risk patients (debility, RA, steroids, immunocompromised) 7/11 of medically treated had good outcome, 0/10 surgical	B

Acute infectious agent arthritis (IAA): a detailed comparison of proved gonococcal and other blood-borne bacterial arthritis, Garcia-Kutzbach A *et al.* J Rheumatol 1974;1:93–101	Retrospective	66	5 yrs	29 *Gonococcus* cases (all proven). 37 bacterial arthritis cases (all proven) some with chronic bacterial arthritis removed for odd reasons, bias of study	Including children	*Gonococcus* ages 14–30, female preponderance, polyarticular with tenosynovitis too. Bacterial arthritis all ages (young and old peak), *Staphylococcus*, *Streptococcus*, monoarticular. Clinical and laboratory features similar but bacterial arthritis more likely to have previous joint damage. *Gonococcus* response good (young) and hospital stay shorter	B
Peripheral pyogenic arthritis. A study of one hundred seventy-nine cases. Le Dantec L *et al*. Rheum Rev 1996;63:103–10	Retrospective	179	27 yrs	6–9 cases per year. Age 13 onwards. 65% bacteria proven	Patient clinical features	78% over 50 yrs, 22% polyarticular. Causes alcohol > diabetes mellitus > OA > malignancy, steroid therapy for RA (4 of only 5 RA cases). Gram-negative organisms more common with underlying chronic lung disease. Lower limb 68% knee > hip > shoulder > foot. Raised ESR in 67%, CRP 85%, white cell count 35%. *Staphylococcus* > *Streptococcus* > Gram-negatives. X-rays suggestive in 82% not much specific help. Bone Scan (Tcn or Gallium) 97.5% were abnormal (in 5% polyarticular). CT helpful in unusual joints, e.g. axial. Oral therapy in majority. One antibiotic in 18%, two in 80%. Duration of therapy 4 months, antibiotics changed in 23% of patients. Only three patients died	B
Review of septic arthritis throughout the antibiotic era. Newman JH. Ann Rheum Dis 1976;35:198–205	Retrospective	134	30 yrs	Includes children. Cases divided by bacteria proven, bacteria in blood. Suggestive diagnosis	Clinical features	Change in age distribution (more elderly later). Young hip > knee, older knee > hip. *Staphylococcus* increasing frequency of resistance to penicillin. Only one death but 40 toxic on presentation. Blood culture positive in 8 cases where synovial was negative. Outcome good—70% assessed by no pain + 75% of movement *vs* other side. Osteomyelitis in 25%—bad outcome in 48% of these cases. 13 recurrent infections. Hip worse prognosis than knees, delay in diagnosis longer stays and worse prognosis. No case for intra-artcular antibiotics	B
Rheumatological audit – a hospital perspective – the acute hot joint. Walker DJ *et al*. Eur Journal Rheum 1994;14(Supp 3):5–6	Audit	GP 21, Casualty 31, Inpatient Rheum 36			Audit of treatment of the acute hot joint against standards agreed by the RCP	GPs failed to comply with guidelines. In casulaty over-reliance on X-rays and reluctance to aspirate joints. In rheumatology department not all joints aspirated either, but this especially with 1st MTP gout	

Continued

TABLE 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)
Streptococcal arthritis in Thai adults: case series and review. Osiri M *et al.* J Med Assoc Thai Dec 1996;755–61	Descriptive	286	17 yrs	Review of clinical records	Microbiological identification of organism, clinical and laboratory features, therapy and outcome	Incidence similar to Western reports. most Group A, elderly, often associated disease (DM, malignancy, alcohol) or joint disease. Leg soft tissue infection common source. Knee most common joint, then shoulder and elbow. Synovial fluid culture most reliable investigation. All penicillin sensitive	B
An epidemiological study of septic arthritis in Kuala Lumpur hospital. Razak M *et al.* Med J Malaysia 1998;53(Suppl A):86–94	Retrospective	41 patients, 42 episodes	5 yrs		Outcomes divided onto 4 grades Excellent, good, fair and poor	Earliy diagnosis and treatment are crucial. Knee joint commonest. Hip leads to significant morbidity. Aspiration essential. Take samples before antibiotic therapy	B
116 cases of gonococcal arthritis treated with acupuncture. Kan W. Journal Trad Chinese Med 1996;16:108–111	Descriptive	116		Gonococcal arthritis—acupuncture, garlic, blood pricking, cupping and drawing hydrarthus		Poor detail and questionable	B
Gonococcal arthritis. A survey of 54 Cooke CL *et al.* JAMA 1971;217:204–5	Characterization study	54 cases	10 yrs		*Gonococcus*-positive culture from a site in the context of acute arthritis	*Gonococcus* difficult to culture. 11/21 Gram-positive. 7/26 synovial fluid culture positive. Young females > young males. Only 6/54 were over 30. 17/54 previous genitourinary infections as well. Large joints. Blood cultures positive in 6/43. 14 cases white cell count normal. 10 apyrexial. Gonococcal infection often not in differential diagnosis. Delay in getting Gram stains. Failure to study 13 cases. Preceding trauma not regarded as a factor	B
The acute arthritis-dermatitis syndrome. The changing importance of *Neisseria gonorrhoeae and Neisseria meningitidis*. Rompalo AM *et al.* Arch Intern Med 1987;147:281–3	*Neisseria gonorrhoea* and *meningitides* cases, comparison between presentations in the 1970s and 1980s	Study 1: 32 cases, 30 gonococcus, 2 menigitidis. Study 2 26 gonococcus, 5 menigitidis				*N. gonorrhoeae* incidence decreasing. *N. meningitidis* increasing. Systemic meningococcal infection needs increasingly to be in differential diagnosis	B
Gonococcal arthritis in an era of increasing penicillin resistance. Presentations and outcomes in 41 recent cases (1985–1991). Wise CM *et al.* Arch Intern Med 1994;154:2690–5	Characterization study	41 cases				Urogenital symptoms common. 26 cases arthralgias beforehand. Skin lesions. Fever but not universal (20 apyrexial). Large joints main site. Common sites for bacteria: urogenital tract (34%), synovial fluid (44%), rectal (39%), blood (12%), throat (7%)	B
Evaluation of infections of the locomotor system with indium-111-labeled human IgG scintigraphy. Nijhof MW *et al.* J Nuc Med 1997;38:1300–5	Retrospective	243 cases various infections: joint, bone, soft tissue, prosthetic joints	4 yrs	Labelled IgG in various arthritides	Sensitivity and specificity examined	Very sensitive for infectious bone and joint disease. Does not discriminate between infected and inflammatory causes unless the pattern of uptake is different from non infectious causes. 2/16 false positives in septic arthritis. Useful for infected prostheses but only after 14 months	B

Diagnosis of bone, joint, and joint prosthesis infections with In-111-labeled nonspecific human immunoglobulin G scintigraphy. Oyen W *et al*. Radiology 1992;182:195–9	Prospective study of possible infections analysed retrospectively for infection	113 cases (120 suspected infections) various sites including prosthetic joints	6 months post-presentation	Indium-labelled IgG injected up to 14 days post-presentation	Comparison between Indium IgG and Tc MDP	Very rarely negative in absence of inflammation or infection but not specific for either. 2/13 were false positive in absence of septic arthritis	B	
Indium-granulocyte scanning in the painful prosthetic joint. Pring DJ *et al*. AJR 1986;146:167–72	Prospective study of 40 cases of painful joints with the possibility of infection/loosening	50 prosthetic joints in 40 patients. 9 asymptomatic joints in patients with other painful prostheses		Scan 8 weeks post-implantation		9 asymptomatic prostheses all normal on WCC scanning. 11 infected prostheses all positive. 10 cases not infected. 8 scans negative. 2 weakly positive. 100% sensitivity 89% specificity. 93% accurate. Remainder of cases 6 strong suspicion of sepsis all scans positive. 9 not infected. None positive. 5 unclear diagnosis. 3 scans positive, 2 negative		
MRI Findings of septic arthritis and associated osteomyelitis in adults. Karchevsky M *et al*. AJR 2004;82:119–22	Prospective study of MRI (T1, T2 weighted or STIR or contrast enhanced) scanning in septic arthritis	50 cases in 38 patients, 46 bacteria postive and 4 suspected. 22 in control group normal joints. Osteomyelitis confirmed by bone biopsy	Septic arthritis within 3 days of admission	MRI scan appearances		Odd sites infected (metatarsophalangeal joint most common). *Staphylococcus Aureus* > *Streptococcus* Group A > Gram-negative most common organisms. MRI shows synovial enhancement (98%), joint effusions not invariable (70%) more common in large joints. synovial thickening on 22%. 33 cases of biopsy proven osteomyelitis marrow changes diffuse in 86% and focal in 14% but all positive. One third of all cases with oedema had no infection on biopsy. No control group of inflammatory joint disease	B	
Bacterial joint infections in England and Wales: analysis of bacterial isolates over a 4 year period. Ryan MJ *et al*. Br J Rheumatol 1997;36:370–3	Retrospective case series based on voluntary reporting of bacterial isolates to the PHLS	1158	4 yrs	Epidemiology of bacterial arthritis	Bacterial isolates	Staphylococci and streptococci majority of isolates. Haemophilus isolates occurred frequently including adults as well as children. Haemophilus not seen. Disease of the young and elderly	B	Significant ascertainment bias due to reporting bias inherent in study design
No changes in the distribution of organisms responsible for septic arthritis over a 20 year period. Dubost JJ *et al*. Ann Rheum Dis 2002;61:267–9	Retrospective case series based on hospital records of patients admitted	303	20 yrs	Epidemiology of bacterial arthritis	Characteristics of patients admitted with culture proven septic arthritis	Staphylococci and streptococci majority of isolates. Haemophilus isolates occurred frequently including adults as well as children. Decreasing prevalence of gonococcus and *M. tuberculosis*. Haemophilus not seen. Disease of the young and elderly	B	Based on hospital admissions and required proven infection
Treatment of the gonococcal arthritis-dermatitis syndrome. Handsfield HH *et al*. Ann Intern Med 1976;84:661–7	Prospective non-randomized comparative case series	98 patients out of 123 patients with suspected Gonococcus	3 yrs recruitment, 1 yr follow-up	Non-randomized, unblinded case series comparison of different treatment regimens for disseminated gonococcus	Resolution of symptoms and outcome	Similar outcome regardless of treatment used so oral or lower doses of parenteral penicillins equally effective for disseminated gonococcal infection	B	In era of penicillin sensitivity and results no longer necessarily applicable
Treatment of skin, skin structure, bone, and joint infections with ceftazidime Gentry LD. Am J Med 1985:79S–2A:67–74	Case series including some data from comparative studies	600 patients of whom 104 had bone and joint infections of which only 13 had septic arthritis	Data collected over an undefined period	Ceftazidime compared with multiple other regimens	Clinical resolution of signs and symptoms of infection and clearance of organism	Too few patients with septic arthritis to draw valid conclusions as there were no comparative group		Too few patients, no control group

Continued

Table 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)	
Anaerobic osteomyelitis and arthritis in a military hospital: a 10 year experience. Brook I *et al.* Am J Med 1993:94;21–8	Case series	65 patients with septic arthritis	11 yrs	Description of anaerobic isolates	Organisms identified, description of eradication rates and clinical management	Anaerobes important organisms particularly in the setting of trauma but no comparator group		Military hospital with likely higher prevalence/ incidence of penetrating trauma
Acute infectious arthritis: a review of patients with nongonoccal joint infections (with emphasis on therapy and prognosis) Goldenberg DL *et al.* Am J Med 1996;60:369–77	Case series	59 patients of which 12 children	7 yrs	Epidemiological study and description of interventions/ therapies	Organisms identified, risk factors and outcome according to therapy. Positivity of Gram stain compared to organism	*Staphyloccous aureus* is the commonest organism followed by streptococci. Gram-negative organisms important (13) Polymicrobial infection in 3 patients. Synovial fluid analysis suggested Gram stain more likely to be positive with Gram-positive organism. Gram stain positive in 65%. Delay in treatment associated with poorer outcome. Needle aspiration provided better outcome than open drainage (80% recovery *vs* 47%)	B	Small series. Gonococcal infection excluded. Comparator group not present
The efficacy and safety of Linezolid as treatment for *Staphylococcus aureus* infections in compassionate use patients who are intolerant, or who have failed to respond to, vancomycin. Moise PA *et al.* J Antimicrob Chemother 2002; 50:1017–26	Open label case series	52 patients with bone and joint infections	Unclear	Linezolid therapy for patients with staphylococcal infections who were intolerant or non-responsive to vancomycin	Clinical resolution and mortality	Linezolid is a possible third line agent in infection but with a low success rate		Small series with limited detail and limited breakdown of cases
Low-dose penicillin for gonococcal arthritis: a comparative therapy trial. Trentham DE *et al.* JAMA 1976;236:2410–2	Prospective double-blind. randomized, controlled	63	10 day treatment, 2 week follow-up	Procaine penicillin 600000U bd for 10 days *vs* im procaine penicillin 600000U bd for 10 d + i.v. aqueous penicillin G 10 million units od for 3 days	Clinical resolution	Lower-dose regimen equivalent to high-dose regimen	A	Penicillin resistance has subsequently emerged
Use of BACTEC 9240 blood culture system for detection of Brucella mellitensis in synovial fluid, Yagupsky P *et al.* J Clin Micro 2001;39:738–9	Laboratory comparison of culture methods	1072 synovial fluids	3.5 yrs	Broth culture method with BACTEC 9240 Ped plus bottle *vs* Isolator 1.5 microbial tube (lysis centrifugation system for blood culture designed to increase yield for intracellular organisms) *vs* direct plate inoculation in some	Bacterial isolates	Increased yield of Brucella mellienis with BACTEC culture system with more rapid isolation of the organism	A	Small numbers. NB laboratory handling of fresh specimen. In UK a rare pathogen
Bacterial PCR in the diagnosis of joint infection. Jalava J *et al.* Ann Rheum Dis 2001;60:287–9	Retrospective comparison of PCR with direct culture methods	94 swabs, 64 fluids from 133 patients	n/a	Usual culture *vs* PCR using 16S ribosomal RNA (common bacterial species primer) with subsequent sequencing	Positivity	19/154 samples had PCR inhibitors and were not used. Yield from PCR not superior to culture methods	B	Included swabs including charcoal swabs that are known inhibitors of PCR, also age of samples unclear

PCR rapidly detects methicillin resistant Staphylococci periprosthetic infection. Tarkin IS *et al*. Clin Orthop Rel Res 2003;414:89–94	Laboratory comparison of a septic arthritis model plus analysis of clinical samples obtained at revision arthroplasty	35 clinical samples from 18 patients at revision arthroplasty		PCR for mecA (methicillin resistance gene) *vs* routine direct broth culture and sensitivity testing	Identification of organism and sensitivity. Time to identification of organism	PCR detected organism with concordance of 34/35. Time to detection probably 1–2 days quicker provided samples run	B	Putative organism directly searched for. Gold standard was still culture, information obtained limited regarding organism identification and other senitivities
Culture with BACTEC Peds Plus/F bottle compared with conventional methods for detection of bacteria in synovial fluid. Hughes JG *et al*. Clin Micro 2001;39:4468–71	Laboratory comparison of culture methods	805 synovial fluid samples (74 positive in 60 patients of which 62 deemed pathogens)		BACTEC culture system *vs* direct inocculation onto agar + broth culture	Identification of organism	Yield greater with BACTEC system 62 *vs* 51 pathogens and contamination rate higher with the conventional methods	B	Institution may have a high intralaboratory contamination rate. Inoculation done in laboratory
Use of the Isolator 1.5 microbial tube for culture of synovial fluid from patients with septic arthritis. Yagupsky P *et al*. Clin Micro 1997;35:2410–2	Laboratory comparison of culture methods	144 samples from 137 patients (29 positive)		Isolator tube (lysis centrifugation system—inhibits complement and lyses RBC and WBC) *vs* direct inoculation into agar only	Identification of organism	Isolator tube superior to agar plate. Gram stain positive in 56% of situations where performed	B	No broth culture
Synovial fluid and blood culture in acute arthritis. Kortekangas P *et al*. Scand J Rheumatol 1995;24:44–7	Case series with comparison of three different culture methods for the synovial fluid	90 of which 29 considered to have septic arthritis	3 yrs	Epidemiology of patients with acute effusion and the positivity of blood and synovial fluid cultures. Culture methods agar only *vs* Isolator tubes *vs* broth enrichment with BACTEC bottles	Bacterial isolates	No difference in culture methods. Blood cultures added additional information in two patients who had a more severe course	B	Small numbers. NB laboratory handling of fresh specimen
Systematic review and meta-analysis of antibiotic therapy for bone and joint infections. Stengel D *et al*. Lancet Infect Dis 2001;1:175–88	Systematic review	n/a	papers from 1966–2000	Antibiotic therapy		Lack of evidence from RCT and quasi-RCTs of antibiotic therapy of bone and joint infections with the exception of tuberculosis	A	
Culture of joint specimens in bacterial arthritis. Impact of blood culture bottle utilization. von Essen R. Scand J Rheumatol 1997; 26:293–300	Retrospective case series of synovial fluid aspirates where both blood culture inoculation and solid phase culture compared	89	20 yrs	Blood culture inoculation *vs* solid phase culture on agar	Bacterial isolates and relevance judged by clinician	Higher yield with blood culture inoculation	B	Lab inoculation
Improved method of isolating bacteria from joint fluids by the use of blood culture bottles. von Essen R *et al*. ARD 1986;45:454–7	Retrospective case series of synovial fluid aspirates where both blood culture inoculation and solid phase culture compared	47	10	Blood culture inoculation *vs* solid phase culture on agar	Bacterial isolates and relevance judged by clinician	Higher yield with blood culutre inoculation	B	Same data as later study in that this is the first 10 yrs of data
Arthroscopic treatment of septic joints: prognostic factors. Vispo-seara *et al*. Arch Orthop Trauma Surg 2002;122:204–11	Retrospective	88	6 yr collection period, mean follow up 2.5 yrs	All patients had arthroscopy, but depending on grade, also had shaving, limited synovectomy, resection of adhesions, and even debridement of loose bone and cartilage. Divided into 4 groups (Gachter score)	Number of procedures, Lysholm functional score, extension, flexion and pain	Correlated outcome to presence of premorbid degenerative change, age of patient, and delay from onset to first surgery. Number of procedures was related to organism, but final result was not related to organism	B	Outcome may be related to several factors. Study power not great enough to control for them all. Surgery not same for all groups—outcome may be determined by surgery rather than severity

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TABLE 4. Continued

Study name	Study type	No. of patients	Duration of study	Treatment/ intervention	Outcome measures	Conclusions from study	Level of evidence provided (as per RCP table)	
Septic arthritis of the knee in adults: treated by arthroscopy or arthrotomy. Wirtz *et al*. International Orthopaedics (SICOT) 2001;25:239–41	Retrospective	51	12 yr collection period, mean follow up 2.2 yrs	24 in arthrotomy and synovectomy group, 27 in arthroscopy group. Both groups drained	Larson score, range of motion (total). Correlated with time to treatment	Arthroscopic treatment was better than arthrotomy and synovectomy on all measures overall, but stats significant only for patients treated within 5 days when analysed relative to time from onset	B	Statistics poor: not certain if differences are statistically significant
Arthroscopic management of septic arthritis: stages of infection and results. Stutz *et al*. Knee Surg Sports Traumatol Arthrosc 2000;8:270–74	Retrospective	76	10 yrs collection period, mean follow up not stated	Arthroscopy, irrigation and debridement where necessary, all groups. Divided into 3 groups	Number of procedures, presence of infection at 1 yr	The number of procedures required to eradicate infection is related to the stage of the infection at presentation	B	Staging may have led to different (more interventional) operations for higher grades, so more than one variable. No other outcome measures mentioned
Acute septic arthritis of the fingers: a clinical study of 87 cases. Richard JC *et al*. Ann Chir Main 1982; 1:214–20	Retrospective, large case series, heterogeneous group, descriptive paper	87	5 yrs collection, mean follow-up not stated	Mixed: 'conservative' (open lavage/ synovectomy, debridement/splintage/ oral antibiotics) or 'joint sacrifice'—arthrodesis, joint excision or amputation	Presence or absence of infection. Description of functional results. 50% cure of infection with 'conservative' therapy. 31/87 amputated. Articular resection remained painful and stiff. There were 8 arthrodeses	Results better if inoculation was direct and punctiform. Regional infection led to poor results	B	Conclusions specific to finger surgery. No generalizations can be made. No detailed statistical analysis could be made of this series
Arthroscopic drainage in septic arthritides of the knee: a multicenter study. Thiery JA. J Arth and Rel Surg 1989;5:65–9	Multicentre, retrospective, questionnaire	46	average follow-up 7.1 months	All cases had arthroscopic drainage	Results according to aetology, pathological agent, delay prior to arthroscopy, analysis of 'failures of treatment'	80% cure rate, 10% failure, 10% relapse. Better if done early. No cure if >3 months. As good as other methods, so safe	B	
Treatment of septic arthritis: comparison of needle aspiration and surgery as initial modes of joint drainage. Goldenberg DL *et al*. Arth and Rheum 1975; 18:83–9	Retrospective review	59	8 yrs	42 needle aspirations, 17 open lavage	Complete recovery, poor result indicated by reduction of movement, ankylosis, secondary osteomyelitis, persistent effusion, death	Better function in needle aspiration group (67% *vs* 42% good result). 12% *vs* 5% death rate for aspiration group *vs* surgical	B	Heterogeneous groups, hips mostly surgical, wrists mostly aspirated etc. Not strong evidence
Risk factors for prosthetic joint infection: case-control study. Berbari EF *et al*. Clin Infect Dis 1998;27:1247–54	Retrospective review	462 cases, 462 controls	5 yearly patient follow-up (1969–1991)	Case controls with no infection compared with infected cases. Risk factors expressed as odds ratios	Risk factors divided into host risk factors (drugs, comorbidity), index arthroplasty risk factors, post-operative risk factors	Risk factors are: wound infection after op, malignancy, other joint replacement, diabetes, RA, steroids, prior septic arthritis, lymphocytopaenia, high NNIS score, haematoma, wound drainage	B	Strong evidence, large numbers, good stats
Aspiration as a guide to sepsis in revision total hip arthroplasty. Fehring TK J Arthropl 1986;5:543–47	Prospective	165		Aspiration prior to revision of Total Hip Arthroplasty to identify organisms	Analysis of aspirate obtained—cell count, gran stain, and culture	Not useful. 171 aspirations. 166 revealed fluid: 140 true −ve, only five true +ve, 18 false +ve, three false −ve. Not recommended	B	
Factors influencing the incidence and outcome of infection following total joint arthroplasty. Poss R *et al*. Clin Orthop Relat Res 1984;182:117–26	Retrospective review	4240	10 yrs	Heterogeneous group. All arthroplasties. Factors pre-disposing post-operative infection analysed	Incidence of infection correlated with proposed risk factors	Overall infection rate 1.25%. Risk of infection increased with RA over OA and in revision surgery. Organism most often *S. aureus*. Organism did not determine outcome. High rate of failure to eradicate infection: only 25 out of 53 retained	B	