

Septic Arthritis in Adults - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/2019/066

Introduction

- The infective and inflammatory processes mediated by microorganisms on the native joints of the musculoskeletal system coalesce in the term septic arthritis.
- The commonest cause of septic arthritis is *Staphylococcus aureus*.
- *Streptococcus* species - including beta-haemolytic streptococci and *Streptococcus pneumoniae* - are other relatively common bacterial causes.
- Less common causes include *Enterobacteriales* (e.g. *Escherichia coli*) and *Enterococcus* species.
- The pathogens of septic arthritis are most commonly inoculated through a haematogenous mechanism of transmission:
 - Another focus of infection culminates in bacteraemia; the microorganism disseminates via the blood and inoculates the joint.
- Less commonly, inoculation is via iatrogenic (procedures and surgery) or traumatic mechanisms of transmission.
- Symptoms and signs of septic arthritis include joint pain, skin erythema, local heat, tenderness, and swelling, with a reduced range of movement.
- Temperatures $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$, a respiratory rate > 20 breaths/minute, a heart rate > 90 beats/minute, and hypotension can denote progression of localised infectious disease into sepsis and septic shock.

Investigation

Microbiology: pre-operative

- Diagnoses of septic arthritis can be established by the culture of a microorganism consistent with native joint infection from ≥ 2 sterile site samples, e.g. aspirate and blood.
- Aspirate:
 - With the range of bacterial pathogens, variations in bacterial resistance and susceptibility profiles, contraindications, side-effects, and with prolonged durations of 4-6 weeks of antimicrobial chemotherapy, joint aspiration under aseptic technique is integral to best practice:
 - ≥ 1 ml of fluid in a universal container for microscopy, culture, and susceptibilities (MC&S), and crystal analysis; and
 - ≥ 1 ml of fluid in a blood culture aerobic bottle and ≥ 1 ml of fluid in a blood culture anaerobic bottle.
- Blood cultures $\times 2$.
- Methicillin resistant *Staphylococcus aureus* (MRSA) screen.

Microbiology: intra-operative

- If orthopaedics intervene:
 - Fluid:
 - ≥ 1 ml of fluid in a universal container for MC&S and crystal analysis; and
 - ≥ 1 ml of fluid in a blood culture aerobic bottle and ≥ 1 ml of fluid in a blood culture anaerobic bottle.

- And/or Pus:
 - ≥ 1 ml of pus in a universal container for MC&S.
- And/or Tissue(s):
 - Into a universal container, with Ballotini beads, for MC&S; \pm
 - If the differential diagnosis includes fungal septic arthritis (e.g. penetrating traumatic injury, with soil contact/potential inoculation of the joint), ≥ 1 extra tissue in a universal container, without Ballotini beads, for MC&S.

Blood sciences

- Full blood count (FBC), erythrocyte sedimentation rate (ESR), C reactive protein (CRP), lactate, urea and electrolytes (U&Es), and liver function tests (LFTs).

\pm Radiology

- Symptoms and signs of septic arthritis may prompt radiological investigation:
 - \pm X-ray (XR); and/or
 - \pm Ultrasound (US); and/or
 - \pm Magnetic resonance imaging (MRI).
- XR and US may reveal soft tissue swelling or abscess formation; however, no imaging modality is diagnostic of septic arthritis.

\pm Biochemistry

- Analyses of synovial biomarkers are emerging investigations in the diagnosis of bone and joint infections.
- As an adjunct to the microbiology gold standard, investigation of synovial fluid inflammatory markers – e.g. calprotectin – can be considered by the orthopaedic consultant, case by case.

Treatment

Surgical intervention

- With septic arthritis representing a closed abscess and the invasion-inflammation capable of causing extensive cartilage damage:
 - Collaborate with the orthopaedic consultant regarding joint washout.
- Surgical intervention could enable:
 - Reduction of the microbial inoculum; and
 - Identification of the causative agent; and
 - Restoration of host physiological function.
- With the pathogen and host responses capable of cartilage destruction and extension into bone:
 - In collaboration with the orthopaedic consultant, consider multiple joint washouts.
- NB If joint washout is contraindicated, consider arthrocentesis/serial needle aspirations.

Empiric, intravenous antibiotics

- If there is no history of (i) penetrating traumatic injury to the joint, (ii) immunocompromise, or (iii) intravenous drug usage:

	No history of MRSA	History of MRSA
First line	Flucloxacillin 2 g 6 hourly	Vancomycin or teicoplanin, dose as per hospital guidelines , vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l
Second line	If non-immediate without systemic involvement penicillin allergy , cefuroxime 1.5 g 8 hourly	Daptomycin 6 mg/kg 24 hourly
Third line	If immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy , vancomycin or teicoplanin, dose as per hospital guidelines , vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l	Linezolid 600 mg 12 hourly (or per oral [absorption 100%])

- If there is history of (i) penetrating traumatic injury to the joint, (ii) immunocompromise, or (iii) intravenous drug usage:

First line	Piperacillin tazobactam 4.5 g 6 hourly and Vancomycin or teicoplanin, dose as per hospital guidelines , vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l
Second line, if non-immediate without systemic involvement penicillin allergy	Ceftazidime 2 g 8 hourly and Vancomycin or teicoplanin, dose as per hospital guidelines , vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l
Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy	Ciprofloxacin 400 mg 8 hourly and Vancomycin or teicoplanin, dose as per hospital guidelines , vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l

Directed, intravenous antibiotics (**with susceptibilities**)

- Methicillin susceptible *Staphylococcus aureus* (MSSA), **according to susceptibilities**:
 - First line:
 - Flucloxacillin 2 g 6 hourly.
 - Second line, [if non-immediate without systemic involvement penicillin allergy](#):
 - Cefuroxime 1.5 g 8 hourly.
 - Third line, [if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy](#):
 - Vancomycin or teicoplanin, [dose as per hospital guidelines](#), vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
- MRSA, **according to susceptibilities**:
 - First line:

- Vancomycin or teicoplanin, [dose as per hospital guidelines](#), vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
 - Second line:
 - Daptomycin 6 mg/kg 24 hourly.
 - Third line:
 - Linezolid 600 mg 12 hourly (or per oral [absorption 100%]).
- *Streptococcus* species, **according to susceptibilities**:
 - First line:
 - Benzylpenicillin 2.4 g 6 hourly.
 - Second line, [if non-immediate without systemic involvement penicillin allergy](#):
 - Ceftriaxone 2 g 24 hourly.
 - Third line, [if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy](#):
 - Vancomycin or teicoplanin, [dose as per hospital guidelines](#), vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
- *Enterobacterales* (e.g. *Escherichia coli*) **according to susceptibilities**:
 - First line:
 - Penicillin; narrowest spectrum of amoxicillin or co-amoxiclav or piperacillin tazobactam [standard dosage](#).
 - Second line, [if non-immediate without systemic involvement penicillin allergy](#):
 - Cephalosporin; narrowest spectrum of cefuroxime or ceftriaxone [standard dosage](#).
 - Third line, [if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy](#):
 - Ciprofloxacin 400 mg 12 hourly (consider per oral [absorption 60-80%]).
- *Enterococcus* species, **according to susceptibilities**:
 - First line:
 - Amoxicillin 1 g 6 hourly.
 - Second line:
 - Vancomycin or teicoplanin, [dose as per hospital guidelines](#), vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
 - Third line:
 - Daptomycin 6 mg/kg 24 hourly.

Multi-disciplinary meeting, intravenous to per oral step down, and outpatient parenteral antimicrobial therapy

- After 7-14 days of intravenous antimicrobial chemotherapy, if the patient is afebrile, observations stable, and inflammatory markers downward trending, collaborate with the orthopaedic consultant regarding their preference for:
 - Referral to the University Hospitals of Derby and Burton (UHDB) orthopaedic multi-disciplinary meeting (1200-1300 Fridays); or
 - Per oral step down; or
 - Outpatient parenteral antimicrobial therapy (OPAT).

NB If for orthopaedic multi-disciplinary meeting discussion, please liaise with the clinical audit team of the orthopaedic department, of the Royal Derby Hospital, regarding the pro forma and the Microsoft Teams meeting hyperlink.
- After 7-14 days of intravenous antimicrobial chemotherapy, if the patient is febrile, observations unstable, and/or inflammatory markers upward trending, collaborate

with the orthopaedic consultant regarding further washouts, update the microbiologist, and continue intravenous therapy.

Directed, per oral antibiotics (**with susceptibilities**)

- *Staphylococcus aureus* (MSSA and MRSA), **according to susceptibilities**:
 - First line:
 - Ciprofloxacin 500-750* mg 12 hourly **and**
 - Rifampicin 300-450* mg 12 hourly or fusidic acid 500 mg 8 hourly.
 - Second line:
 - Clindamycin 300-450* mg 6 hourly.
 - Third line:
 - Doxycycline 100 mg 12 hourly.
- *Streptococcus* species, **according to susceptibilities**:
 - First line:
 - Amoxicillin 500 mg-1* g 8 hourly.
 - Second line:
 - Clindamycin 300-450* mg 6 hourly.
 - Third line:
 - Doxycycline 100 mg 12 hourly.
- *Enterobacteriales* (e.g. *Escherichia coli*), **according to susceptibilities**:
 - First line:
 - Ciprofloxacin 500 mg 12 hourly.
 - Second line:
 - Co-trimoxazole 960 mg 12 hourly.
 - Third line:
 - Penicillin; narrowest spectrum of:
 - Amoxicillin 1 g 8 hourly **or**
 - Co-amoxiclav 625 mg 8 hourly plus amoxicillin 500 mg 8 hourly.
- *Enterococcus* species, **according to susceptibilities**:
 - First line:
 - Amoxicillin 1 g 8 hourly.
 - Second line:
 - Linezolid 600 mg 12 hourly**.
 - Third line:
 - Co-trimoxazole 960 mg 12 hourly.
- * Final dosage to be tailored to specific parameters of the patient (e.g. weight) and the pathogen (e.g. minimum inhibitory concentration) in collaboration with the microbiology consultant responsible for sterile site investigation or within the orthopaedic multi-disciplinary meeting.
- ** In general, maximum duration of treatment 28 days.

Directed, outpatient parenteral antibiotic treatment

- Collaborate with the OPAT consultant.

Empiric, per oral or outpatient parenteral antibiotic treatment

- If a clinical diagnosis of septic arthritis, and if the microbiology is negative, collaborate with a microbiologist regarding empiric options.

Duration of antibiotics

- If for per oral step down or OPAT, monitor bloods (FBC, CRP, U&Es, and LFTs) weekly.
- *Staphylococcus aureus*: 4-6 weeks total (e.g. 2 weeks of intravenous therapy and 2-4 weeks of per oral treatment).
- *Streptococcus* species, *Enterobacterales* (e.g. *Escherichia coli*), and *Enterococcus* species: 4 weeks total.
- Follow up with the orthopaedic team, on intravenous or per oral therapy.

Management

Clinical concerns re septic arthritis



Consultation with the orthopaedic registrar/consultant on call



Investigation: pre-operative

- Microbiology:
 - Aspirate for MC&S
 - Blood cultures x 2
 - MRSA screen
- Blood sciences:
 - FBC, ESR, CRP, lactate, U&Es, and LFTs
- ± Radiology:
 - Symptoms and signs of septic arthritis may prompt XR, US, or MRI; however, no imaging modality is diagnostic of septic arthritis



Treatment

- Collaborate with the orthopaedic consultant regarding joint washout:
 - If joint washout is contraindicated, consider arthrocentesis/serial needle aspirations
- Empiric, intravenous antibiotics (please note, page 2)



Investigation: intra-operative

- Microbiology:
 - Fluid and/or pus and or tissue for MC&S
- ± Biochemistry:
 - Investigation of synovial fluid inflammatory markers can be considered by the orthopaedic consultant, case by case



Treatment

- Collaborate with the orthopaedic consultant regarding ± joint washout repeat
- Directed, intravenous antibiotics (please note, pages 3-5)
- ± Referral to the UHDB orthopaedic multi-disciplinary meeting (1200-1300 Fridays)

References

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