# Prosthetic Joint Infection in Adults - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/2023/064

### Introduction

- Prosthetic joint replacements introduce foreign devices into sterile sites.
- The host response includes a macromolecule-coating of the prosthesis; microbial adherence to this protein-coat facilitates invasion. Biofilm formation enables persistence.
- The commonest causes of prosthetic joint infections (PJI) are *Staphylococcus* species:
  - Methicillin susceptible or resistant *Staphylococcus aureus* (MSSA or MRSA); and
  - Coagulase negative staphylococci (e.g. Staphylococcus epidermidis).
- Less common causes include *Streptococcus* species, *Enterococcus* species, *Enterobacterales* (e.g. *Escherichia coli*), and *Pseudomonas aeruginosa*.
- The pathogens of PJI can be inoculated through various mechanisms of transmission:
  - Haematogenous: another focus of infection culminates in bacteraemia; the microorganism disseminates via the blood and inoculates the prosthesis.
  - o latrogenic: direct inoculation via the surgical operation.
  - Contiguous: another focus of infection (e.g. soft tissue) disseminates locally and invades the prosthesis.
- Symptoms and signs of PJI include joint pain, fever, skin erythema, local heat, swelling, and a sinus tract.
- Temperatures > 38 ° C or < 36 ° 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.

### Suggestive and diagnostic criteria

The Infectious Diseases Society of America has provided both surgeons and pathologists with clinical and pathological means to suspect and diagnose PJI.

### Suggestive criteria

- "The presence of acute inflammation as seen on histopathologic examination of periprosthetic tissue at the time of surgical debridement or prosthesis removal as defined by the attending pathologist".
- "Growth of a virulent microorganism (e.g. *S. aureus*) in a single specimen of a tissue biopsy or synovial fluid may also represent PJI."

### **Diagnostic criteria**

- "The presence of a sinus tract that communicates with the prosthesis".
- "The presence of purulence without another known etiology surrounding the prosthesis".
- "Two or more intraoperative cultures or combination of preoperative aspiration and intraoperative cultures that yield the same organism (indistinguishable based on common laboratory tests including genus and species identification or common antibiogram)".

# **Classification**

PJIs can be classified into early, delayed, and late infections:

|         | Symptoms/Signs                                            | Symptoms/Signs<br>onset after<br>prosthesis<br>insertion | Mechanism of<br>transmission   | Virulence of pathogen |
|---------|-----------------------------------------------------------|----------------------------------------------------------|--------------------------------|-----------------------|
| Early   | Cellulitis<br>syndrome ±<br>systemic<br>stigmata          | < 3 months                                               | More commonly<br>iatrogenic    | Relatively<br>high    |
| Delayed | Chronic pain                                              | 3 to 12-24<br>months                                     | More commonly<br>iatrogenic    | Relatively<br>low     |
| Late    | Septic arthritis<br>syndrome with<br>systemic<br>stigmata | > 12-24 months                                           | More commonly<br>haematogenous | Relatively<br>high    |

### Pre-operative management

### Investigation<sup>1</sup>: radiology

• X-ray (XR).

## Investigation<sup>2</sup>: microbiology

- Aspirate:
  - With the potential repercussions of PJI including return to theatre for revision of the prosthesis, the range of bacterial pathogens, variations in bacterial resistance and susceptibility profiles, variable antimicrobial bone penetration, contraindications, side-effects, and with prolonged durations of months of antimicrobial chemotherapy, joint arthrocentesis in theatre is integral to best practice:
    - Fluid:
      - ≥ 1 ml of fluid in a universal container for microscopy (white cell count and differential), culture, and susceptibilities (MC&S); and
      - ≥ 1 ml of fluid in a blood culture aerobic bottle and ≥ 1 ml of fluid in a blood culture anaerobic bottle.
- MRSA screen.
- ± Blood cultures × 2:
  - E.g. if episode(s) of fever; or
  - E.g. if the differential diagnosis includes bloodstream infection, sepsis, or septic shock; or
  - E.g. if for initiation of treatment with intravenous antibiotics.
- NB Microbiology investigation is optimised through sampling off antibiotics for ≥ 2 weeks.

### Investigation<sup>3</sup>: blood sciences

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

### **Treatment: surgical intervention**

- Collaborate with the orthopaedic consultant regarding:
  - Debridement, antibiotics, and implant retention (DAIR); synonym, debridement with prosthesis retention



• One stage exchange; synonyms, direct exchange procedure, 1-stage replacement



o Two stage exchange; synonyms, staged exchange, 2-stage replacement





### Intra-operative management

### Investigation<sup>1</sup>: microbiology

- Biopsy:
- With the range of bacterial pathogens, variations in bacterial resistance and susceptibility profiles, variable antimicrobial bone penetration, contraindications, side-effects, and with prolonged durations of months of antimicrobial chemotherapy, 6 surgical samples – obtained with 6 sets of instrumentation – are integral to best practice:
  - Fluid:
    - $\geq$  1 ml of fluid in a universal container for MC&S; and
    - ≥ 1 ml of fluid in a blood culture aerobic bottle and ≥ 1 ml of fluid in a blood culture anaerobic bottle.
  - Tissue(s):
    - Into a universal container, with Ballotini beads, for MC&S; ±
    - If the differential diagnosis includes fungal PJI (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.
- NB Microbiology investigation is optimised through sampling off antibiotics for ≥ 2 weeks.

### Investigation<sup>2</sup>: histology

- Biopsy:
  - $\circ \geq 2$  tissues for histopathology.

### ± Investigation<sup>3</sup>: biochemistry

- Analyses of synovial biomarkers are emerging investigations in the diagnosis of bone and joint infections.
- As an adjunct to the microbiology/histology gold standards, investigation of synovial fluid – e.g. leucocyte esterase, α defensin – can be considered by the orthopaedic consultant, case by case.

### **Treatment: surgical intervention**

- DAIR or one stage exchange or two stage exchange.
- Regarding local, intra-operative antibiotics with STIMULAN Rapid Cure®:

| STIMULAN Rapid Cure®<br>Powder | Vancomycin | Gentamicin                                                           |
|--------------------------------|------------|----------------------------------------------------------------------|
| 5 cc                           | 500 mg     | 120 mg; 3 ml of<br>gentamicin liquid (80 mg<br>in 2 ml per ampoule)  |
| 10 cc                          | 1 g        | 240 mg; 6 ml of<br>gentamicin liquid (80 mg<br>in 2 ml per ampoule)  |
| 20 cc                          | 2 g        | 480 mg; 12 ml of<br>gentamicin liquid (80 mg<br>in 2 ml per ampoule) |



- Add 500 mg, 1 g, or 2 g of vancomycin powder to 5 cc, 10 cc, or 20 cc of STIMULAN Rapid Cure® powder, respectively, and mix.
- Transfer 3 ml, 6 ml, or 12 ml of gentamicin liquid to syringe.
- Add 3 ml, 6 ml, or 12 ml of gentamicin liquid to 5 cc-500 mg, 10 cc-1 g, or 20 cc-2 g STIMLUAN Rapid Cure®-vancomycin powder mixes, respectively, and mix for 30 seconds.
- Apply to bead mat immediately.
- Sets in 3-5 minutes.
- CAUTION: when using liquid antibiotics, the mixing solution provided in the pack should not be used and should be discarded.
- https://www.youtube.com/watch?v=CrBee2Vhbn0v

Post-operative management: DAIR and one stage exchange

### Empiric/Directed antibiotics (intra-operative investigations pending)

- If the pre-operative microbiology (aspirate/fluid) was negative:
  - First line:
    - Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l, **and**
    - Rifampicin 300 mg per oral 12 hourly.
    - Second line, if vancomycin/teicoplanin is contraindicated:
      - Daptomycin 6 mg/kg intravenously 24 hourly and
        - Rifampicin 300 mg per oral 12 hourly.
- If the pre-operative microbiology (aspirate/fluid) was positive with a microorganism consistent with PJI (e.g. *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Enterobacterales* [e.g. *Escherichia coli*], or *Pseudomonas aeruginosa*):
  - o Directed antibiotics.
- NB If clinical concerns re sepsis (life threatening organ dysfunction caused by a dysregulated host immune response to infection) secondary to PJI:

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

### Directed antibiotics<sup>1</sup> (with susceptibilities)

- Methicillin susceptible Staphylococcus species, according to susceptibilities:
  - First line:
    - Flucloxacillin 2 g intravenously 6 hourly and
    - Rifampicin 300-450\* mg per oral 12 hourly.

- Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
  - Cefuroxime 1.5 g intravenously 8 hourly and
  - Rifampicin 300-450\* mg per oral 12 hourly.
- Third line, <u>if immediate rapidly evolving or non-immediate with</u> <u>systemic involvement penicillin allergy</u>:
  - Vancomycin or teicoplanin intravenously, <u>dose as per hospital</u> <u>guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l, **and**
  - Rifampicin 300-450\* mg per oral 12 hourly.
- Methicillin resistant *Staphylococcus* species, according to susceptibilities:
  - First line:
    - Vancomycin or teicoplanin intravenously, <u>dose as per hospital</u> <u>guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l, **and**
    - Rifampicin 300-450\* mg per oral 12 hourly.
    - Second line:
      - Daptomycin 6 mg/kg 24 hourly and
      - Rifampicin 300-450\* mg per oral 12 hourly.
- Streptococcus species, according to susceptibilities:
  - First line:
    - Benzylpenicillin 2.4 g intravenously 6 hourly.
  - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
    - Ceftriaxone 2 g intravenously 24 hourly.
  - Third line, <u>if immediate rapidly evolving or non-immediate with</u> systemic involvement penicillin allergy:
    - Vancomycin or teicoplanin intravenously, <u>dose as per hospital</u> <u>guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
- Enterococcus species, according to susceptibilities:
  - First line:
    - Amoxicillin 1 g intravenously 6 hourly.
  - o Second line:
    - Vancomycin or teicoplanin intravenously, <u>dose as per hospital</u> <u>guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
  - Third line:
    - Daptomycin 6 mg/kg intravenously 24 hourly.
- Enterobacterales (e.g. Escherichia coli), according to susceptibilities:
  - First line:
    - Penicillin; narrowest spectrum of amoxicillin or co-amoxiclav or piperacillin tazobactam intravenously <u>standard dosage</u>.
    - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
      - Cephalosporin; narrowest spectrum of cefuroxime or ceftriaxone intravenously <u>standard dosage</u>.
    - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:
      - Ciprofloxacin 400 mg intravenously 12 hourly (consider per oral [absorption 60-80%]).
- Pseudomonas aeruginosa, according to susceptibilities:
  - First line:
    - Piperacillin tazobactam 4.5 g intravenously 6 hourly.

- Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
  - Ceftazidime 2 g intravenously 8 hourly.
- Third line, <u>if immediate rapidly evolving or non-immediate with</u> <u>systemic involvement penicillin allergy</u>:
  - Ciprofloxacin 400 mg intravenously 8 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 investigations or within the orthopaedic multi-disciplinary meeting.

# 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 surgeon 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 surgeons regarding surgical intervention or return to theatre, update the microbiologist, and continue intravenous therapy.

## Directed antibiotics<sup>2</sup> (with susceptibilities): per oral

- Staphylococcus species (methicillin susceptible and resistant), according to susceptibilities:
  - First line:
    - Ciprofloxacin 500-750\* mg 12 hourly and
    - Rifampicin 300-450\* mg 12 hourly.
  - Second line:
    - Clindamycin 300-450\* mg 6 hourly and
    - Rifampicin 300-450\* mg 12 hourly.
  - Third line:
    - Doxycycline 100 mg 12 hourly and
    - Rifampicin 300-450\* mg 12 hourly.
- Streptococcus species, according to susceptibilities:
  - First line:
    - Amoxicillin 500 mg-1\* g 8 hourly.
  - Second line:
    Clind:
    - Clindamycin 300-450\* mg 6 hourly.
  - Third line:
    - Doxycycline 100 mg 12 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.
- Enterobacterales (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.
- Pseudomonas aeruginosa, according to susceptibilities:
  - First line:
    - Ciprofloxacin 750 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 investigations or within the orthopaedic multi-disciplinary meeting.
- \*\* In general, maximum duration of treatment 28 days.

# Directed antibiotics<sup>3</sup> (with susceptibilities): outpatient parenteral antimicrobial therapy

• Collaborate with the OPAT consultant.

### Empiric, per oral or outpatient parenteral antimicrobial therapy

• If a clinical diagnosis of PJI, 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 with OPAT or fortnightly with the general practitioner.
- DAIR or one stage exchange:
  - Shoulder: 3\* months.
  - Elbow: 3\* months.
  - Wrist: 3\* months.
  - Hip: 3\* months.
  - Knee: 6\* months.
  - Ankle: 3\* months.
- \* Final duration to be tailored to specific parameters of the patient and the pathogen in collaboration with the microbiology consultant responsible for sterile site investigations or within the orthopaedic multi-disciplinary meeting.
- Follow up with the surgical team, on intravenous or per oral therapy.

### Post-operative management: two stage exchange

### Empiric/Directed antibiotics (intra-operative investigations pending)

- If the pre-operative microbiology (aspirate/fluid) was negative:
  - First line:
    - Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.



- Second line, if vancomycin/teicoplanin is contraindicated:
  - Daptomycin 6 mg/kg intravenously 24 hourly.
- If the pre-operative microbiology (aspirate/fluid) was positive with a microorganism consistent with PJI (e.g. *Staphylococcus* species, *Streptococcus* species, *Enterococcus* species, *Enterobacterales* [e.g. *Escherichia coli*], or *Pseudomonas aeruginosa*):
  - Directed antibiotics.
- NB If clinical concerns re sepsis (life threatening organ dysfunction caused by a dysregulated host immune response to infection) secondary to PJI:

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

## Directed antibiotics<sup>1</sup> (with susceptibilities): intravenous

- Methicillin susceptible Staphylococcus species, according to susceptibilities:
  - o First line:
    - Flucloxacillin 2 g 6 hourly.
  - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
    - Cefuroxime 1.5 g 8 hourly.
  - Third line, <u>if immediate rapidly evolving or non-immediate with</u> systemic involvement penicillin allergy:
    - Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
- Methicillin resistant *Staphylococcus* species, according to susceptibilities:
  - First line:
    - Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, 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.
- Streptococcus species, according to susceptibilities:
  - First line:
    - Benzylpenicillin 2.4 g 6 hourly.
  - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
    - Ceftriaxone 2 g 24 hourly.
  - Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy:



- Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
- Enterococcus species, according to susceptibilities:
  - First line:
    - Amoxicillin 1 g 6 hourly.
  - Second line:
    - Vancomycin or teicoplanin, <u>dose as per hospital guidelines</u>, vancomycin target pre dose level 15-20 mg/l, teicoplanin target pre dose level 20-40 mg/l.
    - Third line:

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- Daptomycin 6 mg/kg 24 hourly.
- Enterobacterales (e.g. Escherichia coli), according to susceptibilities:
  - First line:
    - Penicillin; narrowest spectrum of amoxicillin or co-amoxiclav or piperacillin tazobactam <u>standard dosage</u>.
  - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
    - 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%]).
- Pseudomonas aeruginosa, according to susceptibilities:
  - First line:
    - Piperacillin tazobactam 4.5 g intravenously 6 hourly.
  - Second line, <u>if non-immediate without systemic involvement penicillin</u> <u>allergy</u>:
    - Ceftazidime 2 g intravenously 8 hourly.
  - Third line, <u>if immediate rapidly evolving or non-immediate with</u> systemic involvement penicillin allergy:
    - Ciprofloxacin 400 mg intravenously 8 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 surgeon 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 surgeons regarding surgical intervention or return to theatre, update the microbiologist, and continue intravenous therapy.

### Directed antibiotics<sup>2</sup> (with susceptibilities): per oral

- Staphylococcus species (methicillin susceptible and resistant), 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 **and**
    - Rifampicin 300-450\* mg 12 hourly or fusidic acid 500 mg 8 hourly.
  - Third line:
    - Doxycycline 100 mg 12 hourly and
    - Rifampicin 300-450\* mg 12 hourly or fusidic acid 500 mg 8 hourly.
- Streptococcus species, according to susceptibilities:
  - First line:
    - Amoxicillin 500 mg-1\* g 8 hourly.
  - $\circ$   $\,$  Second line:
    - Clindamycin 300-450\* mg 6 hourly.
  - Third line:
    - Doxycycline 100 mg 12 hourly.
- Enterococcus species, according to susceptibilities:
  - First line:
    - Amoxicillin 1 g 8 hourly.
    - $\circ$   $\,$  Second line:
      - Linezolid 600 mg 12 hourly\*\*.
    - $\circ$   $\,$  Third line:
      - Co-trimoxazole 960 mg 12 hourly.
- Enterobacterales (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.
- Pseudomonas aeruginosa, according to susceptibilities:
  - First line:
    - Ciprofloxacin 750 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 investigations or within the orthopaedic multi-disciplinary meeting.
- \*\* In general, maximum duration of treatment 28 days.

# Directed antibiotics<sup>3</sup> (with susceptibilities): outpatient parenteral antimicrobial therapy

• Collaborate with the OPAT consultant.

### Empiric, per oral or outpatient parenteral antimicrobial therapy



• If a clinical diagnosis of PJI, 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 with OPAT or fortnightly with the general practitioner.
- After operation 1 of 2 (i.e. after removal of the old prosthesis and placement of the antibiotic loaded spacer): 6 weeks and then stop antibiotics.
- Before operation 2 of 2 (i.e. before removal of the antibiotic loaded spacer and placement of the new prosthesis), no antibiotics for ≥ 2 weeks. Consider repeating pre-operative investigations, including repeat joint aspirate in theatre.
- After operation 2 of 2, re-start antibiotics. If the patient is afebrile, observations stable, and repeat surgical samples yield no growth on direct and enrichment cultures, collaborate with the surgeon and/or microbiology consultant regarding stopping antibiotics.

**Management summary** 



### **References**

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Mr Simon Cockshott, Kayleigh Lehal, Dr Peter **Development of guidelines:** Slovak Lead Antimicrobial Pharmacist, Microbiology Consultation with: Consultant, Orthopaedic Consultant Version: 2 Antimicrobial Stewardship Group on 31/01/2023 Approval date: and by Surgical division 24/01/2023 Introduction: reworded (minor) and reformatted (minor). Suggestive and diagnostic criteria. Classification. Pre-operative management: reworded (minor) and reformatted (major). Intra-Changes from previous operative management: reworded (minor) and reformatted (minor). Post-operative management: version: reworded (minor) and reformatted (major). Management summary: reworded (minor) and reformatted (minor). References: updated (minor). 01/03/2023 Date uploaded: Next review date: 01/03/2026 Dr Peter Slovak, Microbiology Consultant p.slovak@nhs.net Key contacts: Kayleigh Lehal, Lead Antimicrobial Pharmacist kayleigh.lehal@nhs.net

# Document control