Native and Prosthetic Valve Infective Endocarditis - Microbiology Full Clinical Guideline

Reference number: CG-ANTI/1346/24

Introduction

- Cardiac disease can affect blood flow. High pressures, turbulence, and regurgitant flows can induce endocardial lesions. Host inflammatory responses to the damaged endocardium include platelet lining and fibrin deposition, with the eventual formation of sterile vegetations.
- Microorganisms can colonise these sterile vegetations, and also invade the endocardial lesion.
- Microbial invasion, plus the localised host inflammatory response, is termed infective endocarditis.
- Shedding of microorganisms (i.e. bacteraemia, fungaemia) or fragments of the infected, platelet-fibrin vegetations (i.e. septic emboli) enables dissemination from the heart to multiple systems of the body.
- The commonest cause of infective endocarditis is the Gram positive *Staphylococcus aureus*.
- *Enterococcus* species, coagulase negative staphylococci, viridans streptococci, and *Streptococcus bovis* are other relatively common Gram positive causes.
- Less common causes include the nutritionally variant streptococci (*Abiotrophia defectiva* and *Granulicatella* species), HACEK group (*Haemophilus* species, *Aggregatibacter* species, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella* species), and fungi (*Candida* species ± *Aspergillus fumigatus*).

Investigation

- The provision of clinical details is the duty of the requesting physician and is integral to best practice.
- The microbiology department processes thousands of blood cultures annually. The provision of clinical details enable:
    - The biomedical scientists and medical laboratory assistants to process the blood cultures appropriately. For example, with regard to culture, extending the period of incubation - from the standard 5 days - to 10 days. For example, with regard to susceptibilities, performing minimum inhibitory concentration (MIC) testing immediately.
    - The consultant microbiologists to interpret the blood cultures appropriately. For example, communicating coagulase negative staphylococci bacteraemia to physicians re patients with past medical histories of prosthetic valves.
- The echocardiographers perform thousands of echocardiogram annually. The provision of clinical details enable:
    - The echocardiographers to vet and prioritise requests appropriately.
    - The echocardiographers and cardiologists to interpret the images appropriately.

Blood sciences

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

Microbiology

- Before starting antibiotics:
    - If the patient is clinically stable:

        - Blood cultures × 3; drawn approximately 12 hours apart; from 3 locations/venepunctures.
    - If the patient is clinically unstable (haemodynamic instability, sepsis, or septic shock):
        - Blood cultures × 3; drawn approximately 1-15 minutes apart; from 3 locations/venepunctures.
- NB1 Please provide relevant clinical details:
    - For example: “Fever. Intravenous drug user. Systemic phenomena. ?Infective endocarditis.”
- NB2 If the initial blood cultures are positive, repeats are also recommended 48-72 hourly thereafter for evidence of clearance. In general, the duration of antibiotics starts from the first blood culture repeat that is negative for the causative agent.

Echocardiogram, provided by cardiology and clinical measurements

- Clinical suspicions of infective endocarditis – emanating from physicians and/or pathologists – warrant investigation:
    - First line: transthoracic echocardiogram (TTE).
- Please provide relevant clinical details:
    - Symptoms and/or signs of infective endocarditis.
    - Past medical history of predisposing cardiac pathology, or social history of intravenous drug usage.
    - *Staphylococcus aureus* or *Candida* species bloodstream infection.
    - Persistent bloodstream infection with a microorganism typical (or atypical) for infective endocarditis.
    - For example: “New murmur. Mitral valve replacement. Bacteraemic with *Staphylococcus aureus*. ?Infective endocarditis.”
- Requests are triaged and can be rejected, e.g. a request received without symptoms or signs or differential diagnosis of infective endocarditis.
- Clinical suspicions of infective endocarditis and initial TTE findings may warrant further investigation:
    - Second line: transoesophageal echocardiogram (TOE).
        - Indications can include: past medical history of prosthetic valve or cardiac implantable electronic device; negative TTE and clinical suspicions remaining high; equivocal TTE and clinical suspicions persisting; positive TTE and clinical suspicions regarding complications.

  With regard to TOE, this specialist procedure requires collaboration with cardiology. Specifically, via switchboard, the physicians contact the cardiology registrar on call. This specialty trainee reviews the patient, and then contacts the cardiology consultant performing the next TOE list, regarding ± proceeding.
- NB1 TTE and TOE can periodically require repeating:
    - If the initial TTE and TOE are negative, and clinical suspicions remain high.
    - If the initial echocardiograms are positive, and clinical suspicions arise regarding cardiovascular complications.

Radiology and nuclear medicine

- If the echocardiogram(s) (TTE ± TOE) and repeat echocardiograms are negative:
    - The infective endocarditis team may recommend:
        - Cardiac computed tomography (CT); or
        - Fluorine-18 fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET) CT; or

        - Technetium metastable-99 hexamethylpropylene amine oxime (^{99m}Tc HMPAO) labelled white cell single photon emission computed tomography (SPECT) CT

    In collaboration with one of the consultant radiologists with a specialist interest in cardiac imaging for cardiac CT and nuclear medicine for PET CT or SPECT CT.

- With regard to nuclear medicine:
    - First line, in Nottingham, if the patient can be transferred:
        - ^{18}F-FDG PET CT.
        - Turnaround time approximately 7 days.
    - Second line, in Derby, if the patient cannot be transferred:
        - ^{99m}Tc SPECT CT.
        - Turnaround time approximately 10-14 days.
    - Third line, in Derby, if the patient cannot be transferred:
        - Gallium-67 SPECT CT.
        - Turnaround time approximately ≥ 14 days.
    - NB Ward doctor to liaise with one of the three radiologists supporting nuclear medicine regarding:
        - The request; and
        - The logistics of the procedure (for example, Atkin's diet for ≥ 72 hours before ^{18}F-FDG PET CT).

Criteria for diagnosis[1]: clinical

Modified Duke's criteria provide both physicians and pathologists with clinical and pathological means to diagnose infective endocarditis.

With regard to clinical diagnoses, combinations of major and minor criteria enable diagnoses of possible or proven infective endocarditis:

- Proven:
    - 2 major; or 1 major and 3 minor; or 5 minor.
- Possible:
    - 1 major and 1 minor; or 3 minor.

Major criteria: microbiology

- (a) Bloodstream infection with a microorganism consistent with infective endocarditis from 2 sets of blood cultures.
- (b) Persistent bloodstream infection with a microorganism consistent with infective endocarditis:
    - From blood cultures drawn > 12 hours apart; or
    - From 3 of 3 sets of blood cultures, with the first and last sets drawn > 1 hour apart; or
    - From the majority of ≥ 4 sets of blood cultures, with the first and last sets drawn > 1 hour apart.
- (c) Bloodstream infection with *Coxiella burnetii* from ≥ 1 set of blood cultures; or serological evidence of active Q fever with *Coxiella burnetii* anti-phase I IgG titre ≥ 1:800.

Major criteria: radiology

- Echocardiogram revealing:
    - (a) New valvular regurgitation; or
    - (b) Valvular perforation; or
    - (c) Valvular aneurysm; or
    - (d) Oscillating intracardiac mass on valve or supporting structures, in the absence of an alternative anatomic explanation; or
    - (e) Oscillating intracardiac mass in the path of regurgitant jets, in the absence of an alternative anatomic explanation; or

  - (f) New partial dehiscence of prosthetic valve; or
  - (g) Oscillating intracardiac mass on implanted material, in the absence of an alternative anatomic explanation; or
  - (h) Intracardiac fistula; or
  - (i) Abscess; or
  - (j) Pseudoaneurysm.
- Cardiac CT revealing:
  - (k) Paravalvular lesion.
- PET CT revealing:
  - (l) Accumulation of ^{18}F-FDG in leucocytes and other immune cells in cardiovascular sites of infection consistent with infective endocarditis.
- SPECT CT revealing:
  - (m) Accumulation of ^{99m}Tc HMPAO radiolabelled leucocytes in cardiovascular sites of infection consistent with infective endocarditis.

Minor Criteria

- (a) Fever (temperature ≥ 38.0 °C).
- (b) Immunological phenomena: Roth spots, Osler nodes, glomerulonephritis, or rheumatoid factor.
- (c) Vascular phenomena: intracranial haemorrhage, conjunctival haemorrhage, Janeway lesions, pulmonary infarcts, mycotic aneurysm, or major arterial emboli.
- (d) Past medical history of predisposing cardiac pathology, or social history of intravenous drug usage.
- (e) Bloodstream infection without major criteria (a), (b), or (c); or serological evidence of active infection with a microorganism consistent with infective endocarditis.

Criteria for diagnosis[2]: pathological

Modified Duke's criteria also provide both physicians and pathologists with pathological means to diagnose infective endocarditis:

- Histological evidence of active infective endocarditis from an intracardiac vegetation or intracardiac abscess; or
- Microorganisms demonstrated by histological examination or microbiology techniques from an intracardiac vegetation or embolised vegetation or intracardiac abscess

are diagnostic of infective endocarditis.

Treatment: medical

- Discussion with the microbiology consultant on clinical duty is recommended for empiric antibiotics. Liaise:
  - 1000-1730 with the duty microbiologist via hospital extension 88503.
  - 1730-2300 with the microbiologist on call via switchboard.
  - 2300-1000:
    - Medical/Surgical team to proceed with empiric antibiotic guidance and liaise with the duty microbiologist within the next working day via hospital extension 88503; or
    - If the medical/surgical consultant on call requests a microbiology consultant opinion, with the microbiologist on call via switchboard.
- Discussion with the microbiology consultant on clinical duty is also recommended for directed antibiotics. Please liaise with the microbiologist responsible for sterile site investigations and/or the infective endocarditis team.

Empiric antibiotics: native valve infective endocarditis

	After blood cultures × 3
If the patient is (i) clinically stable and (ii) without Duke's criteria for proven or possible native valve infective endocarditis	Withhold antimicrobial chemotherapy
If the patient is (i) clinically stable and (ii) symptom onset is subacute (weeks) in nature	First line, if no investigative history of MRSA: • Amoxicillin 2 g intravenously 4 hourly; **and** • Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l Second line, if drug history of penicillin allergy or investigative history of MRSA: • Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l; **and** ○ Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** ○ Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l
If the patient's symptom onset is acute (day[s]) in nature	Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l; **and** • Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** • Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l
If there is clinical concern regarding **sepsis** with the differential diagnosis including native valve infective endocarditis	Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l; **and** • Antibiotic(s) as per sepsis hospital guidelines. ○ For example, piperacillin tazobactam and teicoplanin

Empiric antibiotics: prosthetic valve infective endocarditis

	After blood cultures × 3
If the patient is (i) clinically stable and (ii) without Duke's criteria for proven or possible prosthetic valve infective endocarditis	Withhold antimicrobial chemotherapy

If the patient is (i) clinically stable and (ii) symptom onset is subacute (weeks) in nature
Or
If the patient's symptom onset is acute (day[s]) in nature
	First line:
	• Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min); **and**
	• Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l; **and**
	• Glycopeptide:
	  ○ Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or**
	  ○ Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l
	Second line, if vancomycin/teicoplanin is contraindicated:
	• Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min); **and**
	• Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l; **and**
	• Daptomycin 8-10 mg/kg intravenously 24 hourly

If there is clinical concern regarding **sepsis** with the differential diagnosis including prosthetic valve infective endocarditis	Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l; **and** • Antibiotic(s) as per sepsis hospital guidelines. ○ For example, piperacillin tazobactam and teicoplanin

Directed (with susceptibilities): *Staphylococcus* species

	Native valve infective endocarditis	Prosthetic valve infective endocarditis
First line, if methicillin susceptible	Flucloxacillin 2 g intravenously 4-6 hourly (6 hourly if ≤ 85 kg; 4 hourly if > 85 kg) 4 weeks	Flucloxacillin 2 g intravenously 4-6 hourly (6 hourly if ≤ 85 kg; 4 hourly if > 85 kg) 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 2-6 weeks; **and** Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min) 6 weeks
Second line, if methicillin susceptible and if non-immediate without systemic involvement penicillin allergy	Cefuroxime 1.5 g intravenously 8 hourly 4 weeks	Cefuroxime 1.5 g intravenously 8 hourly 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 2-6 weeks; **and** Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min) 6 weeks
Third line, if methicillin resistant or if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy	Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min) 4 weeks; **and** Glycopeptide 4 weeks: • Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** • Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l	Rifampicin 300-600 mg per oral 12 hourly (300 mg if creatinine clearance < 30 ml/min; 600 mg if ≥ 30 ml/min) 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 2-6 weeks; **and** Glycopeptide 6 weeks: • Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** • Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l

Directed (with susceptibilities): *Streptococcus* species, penicillin minimum inhibitory concentration (MIC) ≤ 0.125 mg/l

	Native valve infective endocarditis	Prosthetic valve infective endocarditis
First line	Benzylpenicillin 1.2 g intravenously 4 hourly 4 weeks	Benzylpenicillin 1.2 g intravenously 4 hourly 6 weeks
Second line, if non-immediate without systemic involvement penicillin allergy	Ceftriaxone 2 g intravenously 24 hourly 4 weeks	Ceftriaxone 2 g intravenously 24 hourly 6 weeks
Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy	Vancomycin intravenously, target pre dose level 15-20 mg/l 4 weeks	Vancomycin intravenously, target pre dose level 15-20 mg/l 6 weeks

Directed (with susceptibilities): *Streptococcus* species, penicillin MIC > 0.125 to 2 mg/l

	Native valve infective endocarditis	Prosthetic valve infective endocarditis
First line	Benzylpenicillin 2.4 g intravenously 4 hourly 4-6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks	Benzylpenicillin 2.4 g intravenously 4 hourly 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks
Second line, if non-immediate without systemic involvement penicillin allergy	Ceftriaxone 2 g intravenously 24 hourly 4-6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks	Ceftriaxone 2 g intravenously 24 hourly 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks
Third line, if immediate rapidly evolving or non-immediate with systemic involvement penicillin allergy	Vancomycin intravenously, target pre dose level 15-20 mg/l 4-6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks	Vancomycin intravenously, target pre dose level 15-20 mg/l 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, ≥ 2 weeks

Directed (with susceptibilities): *Enterococcus faecalis*

	Native valve infective endocarditis	Prosthetic valve infective endocarditis
First line	Amoxicillin 2 g intravenously 4 hourly 4-6 weeks (4 weeks if symptoms < 3 months; 6 weeks if symptoms > 3 months); **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 4-6 weeks (4 weeks if symptoms < 3 months; 6 weeks if symptoms > 3 months)	Amoxicillin 2 g intravenously 4 hourly 6 weeks; **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 6 weeks
Second line, if drug history of penicillin allergy	Glycopeptide 4-6 weeks: • Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** • Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 4-6 weeks	Glycopeptide 6 weeks: • Vancomycin intravenously, dose as per hospital guidelines, target pre dose level 15-20 mg/l; **or** • Teicoplanin intravenously, dose as per hospital guidelines, target pre dose level 30-40 mg/l **and** Gentamicin 3 mg/kg intravenously 24 hourly (NB maximum of 240 mg), target pre dose trough < 1 mg/l, 6 weeks

- NB *Enterococcus faecium* infective endocarditis treatment to be discussed with the microbiology consultant responsible for blood cultures and within the infective endocarditis team meetings.

Directed (with susceptibilities): nutritionally variant streptococci, HACEK group, and other bacteria

- Collaborate with the microbiologist responsible for sterile site investigations and/or the infective endocarditis team.

Directed: *Candida* species

- **Native and prosthetic valve infective endocarditis**:
    - Awaiting speciation and susceptibilities:

        - First line: caspofungin 150 mg* intravenously 24 hourly.
        - Second line: Ambisome® 3 mg/kg intravenously 24 hourly ± flucytosine 25 mg/kg intravenously 6 hourly.
    - Options, with speciation and susceptibilities, in collaboration with the infective endocarditis team:
        - Caspofungin 150 mg* intravenously 24 hourly.
        - Ambisome® 3 mg/kg intravenously 24 hourly ± flucytosine 25 mg/kg intravenously 6 hourly.
        - Fluconazole:
            - *Candida albicans*, 800 mg for the first 24 hours, 400 mg 24 hourly thereafter.
            - *Candida glabrata*, 800 mg 24 hourly.
            - Other *Candida* species, collaborate with the infective endocarditis team.
    - ≥ 6 weeks from valvular replacement; collaborate with the infective endocarditis team.

***** Caspofungin 150 mg is unlicensed for infective endocarditis.

Directed: *Aspergillus fumigatus* and other fungi

- Collaborate with the microbiologist responsible for sterile site investigations and/or the infective endocarditis team.

Outpatient parenteral antimicrobial therapy

- Complications of infective endocarditis occur, in general, within the first 2 weeks of antimicrobial chemotherapy. Therefore, patients routinely receive the first half or third of their antibiotic courses as an inpatient.
- Case by case, the infective endocarditis team may recommend outpatient parenteral antimicrobial therapy (OPAT) for patients with:
    - Cultured bacteria with MICs amenable to OPAT regimens; and
    - Antibiotics administered intravenously as an inpatient for ≥ 2 weeks.
- If feasible, the infective endocarditis team may recommend flucloxacillin, ceftriaxone, teicoplanin, etc. therapies in the community.
- If for OPAT, management requires:
    - Monitoring of bloods (FBC, CRP, U&Es, and LFTs) weekly; and
    - Cardiology consultant review once-twice weekly.

Per oral

- In general, the medical literature is relatively uniform in its recommendation that, for infective endocarditis, intravenous therapy represents best practice.
- However, peer reviewed publications are beginning to emerge that could indicate a possible role for per oral antibiotics.
- Case by case, the infective endocarditis team may periodically recommend per oral step down for patients with:
    - Diagnoses of native valve infective endocarditis; and
    - Cultured bacteria amenable to per oral regimens; and
    - Antibiotics administered intravenously as an inpatient for ≥ 2 weeks.

Non-compliance with intravenous or per oral

- Minor criteria for clinical diagnoses of infective endocarditis include a social history of intravenous drug usage.
- The management of infective endocarditis sub-populations can prove challenging.
- If intravenous, OPAT, and/or per oral antimicrobial chemotherapy options have been exhausted, the infective endocarditis team may consider dalbavancin therapy.

- Dalbavancin indications are limited, presently, to superficial, soft tissue infections. Medical literature is only beginning to emerge regarding dalbavancin usage beyond the skin. Reflecting this, recommendations and prescriptions of this antimicrobial – in the context of infective endocarditis – require the input of the infective endocarditis team.

Treatment: surgical

- Infective endocarditis guidance from the British Society for Antimicrobial Chemotherapy (BSAC; Gould, *et al*.) provides recommendations including:
    - "A surgical opinion should be sought for every patient with endocarditis".
    - "A surgical opinion should be sought at the earliest opportunity for every patient with endocarditis affecting intracardiac prosthetic material".
- BSAC guidelines also provide indications for cardiac surgery, and sub-divide timeframes into emergency, urgent, and elective categories: (https://academic.oup.com/view-large/figure/12336261/dkr45005.gif).

University Hospitals of Derby and Burton NHS Foundation Trust

Management summary

Clinical concerns re infective endocarditis

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Investigation: blood sciences and microbiology

- FBC, CRP, lactate, U&E, and LFT
- If the patient is clinically stable:
  - Blood cultures × 3; drawn approximately 12 hours apart
- If the patient is clinically unstable (haemodynamic instability, sepsis, or septic shock):
  - Blood cultures × 3; drawn approximately 1-15 minutes apart
- Please provide relevant clinical details:
  - For example: “Fever. Intravenous drug user. Systemic phenomena. ?Infective endocarditis”

Investigation: echocardiogram

- First line, TTE
- Please provide relevant clinical details:
  - Symptoms and/or signs of infective endocarditis; past medical history of predisposing cardiac pathology, or social history of intravenous drug usage; *Staphylococcus aureus* or *Candida* species bloodstream infection; persistent bloodstream infection with microorganism typical (or atypical) for infective endocarditis
  - For example: “New murmur. Mitral valve replacement. Bacteraemic with *Staphylococcus aureus*. ?Infective endocarditis”
- Requests are triaged and can be rejected, e.g. requests received without symptoms or signs or differential diagnoses of infective endocarditis

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Treatment[1]

- Empiric, intravenous antibiotics:
  - Native valve infective endocarditis, please note page 5
  - Prosthetic valve infective endocarditis, please note page 6

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Modified Duke’s criteria review (please note pages 3 and 4):

- Proven infective endocarditis: 2 major; or 1 major and 3 minor; or 5 minor
- Possible infective endocarditis: 1 major and 1 minor; or 3 minor

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Treatment[2]

- Directed, intravenous antibiotics (please note pages 7-9)
- UHDB infective endocarditis meetings (1200- Thursdays)

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Continuity of care pro forma (to be completed/updated, within the infective endocarditis multi-disciplinary team meeting, every week until discharge)

Name:

Date of birth:

Hospital number:

NHS number:

Consultant:

Insert Addressograph

Diagnosis

- Infective endocarditis: possible □ proven □ date (if proven) / /
- Diagnostic criteria, if possible: 1 major and 1 minor □ 3 minor □
- Diagnostic criteria, if proven: 2 major □ 1 major and 3 minor □ 5 minor □
- Valve: native □ prosthetic □
- Valve: mitral □ aortic □ tricuspid □ pulmonary □
- Past medical history of infective endocarditis: yes □ no □

Investigation

- TTE: yes □ no □ date(s) / / / /
- TOE: yes □ no □ date(s) / / / /
- Echocardiogram findings: _____
- Blood culture date(s): / / / / / /
- Blood culture positive date(s): / / / / / /
- Causative agent: _____
- Evidence of clearance: yes □ no □ date(s) / / / /

Treatment

Empiric/Directed Therapy	Start Date	Duration (weeks)	Planned Stop Date
	/ /		/ /
	/ /		/ /
	/ /		/ /
	/ /		/ /

- Maxillofacial review requested: yes □ no □
- Surgical opinion requested: yes □ no □

Multi-disciplinary team (MDT) meeting: week 1 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional completing the pro forma:

MDT meeting: week 2 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional updating the pro forma:

MDT meeting: week 3 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional updating the pro forma:

MDT meeting: week 4 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional updating the pro forma:

MDT meeting: week 5 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional updating the pro forma:

MDT meeting: week 6 date / / /

MDT participants	Management
Cardiology senior:	
Microbiology senior:	
Pharmacy senior:	

Name and signature of healthcare professional updating the pro forma:

Discharge

Name of discharging consultant:
Date of discharge:
Management on discharge:
Outpatient review date:

Appendix 1: infective endocarditis team

- The University Hospitals of Derby and Burton (UHDB) NHS Foundation Trust infective endocarditis team is comprised of:
    - The cardiology registrar and ≥ 1 consultant; and
    - ≥ 1 of the cardiology ward team; and
    - ≥ 1 of the microbiology/OPAT consultants; and
    - ≥ 1 of the antimicrobial/OPAT pharmacists.
- The UHDB team convenes - via Microsoft Teams, 1200- , every Thursday - to review the inpatients (± outpatients) with infective endocarditis.

Appendix 2: gentamicin

Please note the bespoke gentamicin infective endocarditis prescription chart.

Treatment dose	Infective endocarditis: 3 mg/kg IV 24 hourly (NB maximum of 240 mg)
Contraindications	BNF: "myasthenia gravis"
Interactions	Please review the BNF for up-to-date interactions
Common or very common side-effects (please review BNF for uncommon and rare or very rare)	Skin reactions, tinnitus
Important side-effects of note	Vestibular toxicity, ototoxicity, nephrotoxicity
Renal impairment	BNF: "If there is impairment of renal function, the interval between doses must be increased; if the renal impairment is severe, the dose itself should be reduced as well. Excretion of aminoglycosides is principally via the kidney and accumulation occurs in renal impairment. Ototoxicity and nephrotoxicity occur commonly in patients with renal failure"
Therapeutic drug monitoring • Recommended • Pre dose • Therapeutic level, trough • Repeat	 Yes 1-2 ml serum, pre dose < 1 mg/l Daily, until pre/trough level is within range. Weekly, thereafter
Dose and frequency advice	Within the working day, discuss with the ward pharmacist or antimicrobial pharmacist Out-of-hours, discuss with the on call pharmacist

In native and prosthetic valve infective endocarditis:

- **Please inform the patient of gentamicin's known side effects, especially vestibular toxicity, ototoxicity, and nephrotoxicity**.
- Please refer the patient to the audiology department for baseline assessment of hearing, and re-refer if the patient or the physician notes side-effects, for example impaired balance, dizziness, and/or hearing impairment.
- Please monitor the patient's kidney function ≥ twice weekly.
- **If side-effects of vestibular toxicity, ototoxicity, or kidney dysfunction-failure manifest, stopping/withholding gentamicin is recommended.** Please notify the infective endocarditis team if gentamicin is stopped/withheld.

Appendix 3: culture negative endocarditis

- Patients can:
    - Present with symptoms and signs of infective endocarditis
    - Satisfy major, radiological criteria for infective endocarditis
    - Satisfy minor, clinical criteria for infective endocarditis

  and cultures may be negative.
- Common causes of culture negative infective endocarditis include early administration of antibiotics with spectrums of activity covering the commonest (*Staphylococcus*, *Streptococcus*, and *Enterococcus* species) bacterial causes.
- Bacteraemia and fungaemia, specifically persistent bloodstream infections, can be one of the hallmarks of infective endocarditis. Therefore, if the patient is clinically stable, stopping/withholding antimicrobial chemotherapy, and investigating for bacteraemia and fungaemia, can be considered in collaboration with the infective endocarditis team.
- Uncommon causes of infective, culture negative endocarditis include bacterial and fungal pathogens:
    - Bacteria: *Bartonella*, *Brucella*, *Coxiella*, *Legionella*, and *Mycoplasma* species.
    - Fungi: *Aspergillus fumigatus*.
- The infective endocarditis team may periodically recommend investigation of culture negative endocarditis with bacterial serology and also with fungal cell wall (beta glucan and galactomannan) markers.
- Uncommon causes of culture negative endocarditis also include medical phenomenon.
- The infective endocarditis team may also periodically recommend antinuclear antibodies and anti-phospholipid syndrome screening (anticardiolipin antibody, anti-glycoprotein antibody) to gain insights into the medical differential diagnosis that includes autoimmune (e.g. systemic lupus erythematosus), neoplastic (e.g. atrial myxoma), iatrogenic (e.g. stitch), and traumatic (e.g. ruptured mitral chordae) aetiologies.

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Document control

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