

# The infective endocarditis team: recommendations from an international working group

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## INTRODUCTION

Infective endocarditis (IE) is uncommon but important because it is difficult to manage and universally fatal unless appropriately treated. The estimated incidence is 3–10 episodes each year per 100 000 population.<sup>1</sup> In industrially developed countries, IE increasingly occurs in older adults with intracardiac devices (pacemakers and implantable defibrillators), replacement heart valves and medical interventions such as haemodialysis.<sup>2–4</sup> Younger age groups are also affected, particularly intravenous drug users and those with adult congenital heart disease.<sup>5</sup> Staphylococci are now the most common causative organisms in international series and streptococci the second most common.<sup>6</sup> Resistance to antimicrobial agents, particularly vancomycin, is increasing.<sup>1 7</sup>

Patients with IE remain in hospital for a median of 4–6 weeks<sup>8 9</sup> and approximately a half require inpatient cardiac surgery.<sup>1 10 11</sup> The in-hospital mortality rate is about 20%<sup>8 12</sup> but varies widely according to age, comorbidity, heart failure, the presence of prosthetic material and the organism.<sup>13</sup> For example, in prosthetic valve IE with associated renal failure, the reported mortality may be 40%–50%<sup>14 15</sup> and with severe heart failure as high as 64%.<sup>15</sup> The outcome can be improved by prompt diagnosis and antibiotic therapy and by early surgery when indicated.<sup>8 10 16 17</sup> Despite

this, the diagnosis may be delayed, mistakes may be made in the type, duration or dose of antibiotic<sup>18</sup> or the antibiotic may be started before blood cultures are obtained.<sup>11</sup> Patients are still frequently referred to a specialist only at an advanced stage with heart failure<sup>6 11 18–20</sup> or may not receive surgery even when indicated.<sup>8</sup> As expected, non-compliance with guidelines is associated with a worse outcome.<sup>20</sup>

A multidisciplinary team (MDT) approach is increasingly seen as best practice where decision making may be complex.<sup>21 22</sup> Such teams are widely accepted for heart failure, transcatheter procedures, mitral valve repair and complex revascularisation, but are not yet common for IE despite being specifically recommended.<sup>7 11 23</sup> A team approach has been shown to decrease 1-year mortality in IE from 18.5% to 8.2%.<sup>23</sup> The British Heart Valve Society formed a working group including an invited international panel to discuss ways of improving the clinical care of patients with valve disease. This article describes recommendations for organising multidisciplinary IE teams which we believe should be applicable internationally.

## ORGANISATION AT CARDIOTHORACIC CENTRES

Because IE is uncommon, a dedicated MDT with appropriate experience is best placed to provide or advise on high quality care. At surgical centres, the team should include consultants in: cardiology with specialist competencies in valve disease, echocardiography (often doubling as the specialist in valve disease), surgery with expertise in complex valve surgery, infectious diseases and/or medical microbiology (depending on the local model of service delivery).

A fully accredited, expert echocardiography department is fundamental. In addition, there must be ready access to CT and MRI (for differentiating discitis and osteomyelitis, identifying splenic and cerebral emboli) and ideally for CT coronary

angiography and PET.<sup>24</sup> Other experts must be available: a specialist in spinal conditions (orthopaedic surgeon or rheumatologist depending on national practice); an electrophysiologist specialising in device extraction;<sup>25</sup> a neurologist and neurosurgeon to advise on the management of cerebral complications; a renal physician since renal dysfunction is an important complication of IE; and a haematologist to advise on the management of anticoagulation in prosthetic valve endocarditis. Outpatient parenteral antibiotic treatment should be feasible for selected cases.<sup>26–28</sup>

All cases of possible IE identified on clinical grounds, including cardiac implantable electronic device (CIED) infections, should be referred to the specialist team. A significant number of patients, probably more than identified clinically, will also be detected from the results of blood cultures and echocardiography.<sup>29</sup> Management of patients with confirmed IE should then be assumed or closely directed by the specialist team. The patient should be nursed in a specialist area by staff with the competencies required to recognise deteriorating valve function and other complications.

All cases should be discussed immediately on transfer or admission by the specialist cardiologist, the infection specialist and cardiac surgeon. If surgery appears likely, the cardiac surgeon should be actively involved immediately to discuss timing and to plan preparations, for example, booking operating time. The team should hold MDT meetings regularly to follow the progress of inpatients and referrals, make decisions about their management, and discuss and develop general management protocols and policies.

## ORGANISATION AT REFERRING HOSPITALS

A large non-surgical centre should consider designating a team consisting of a specialist in infection and a cardiologist with recognised competencies in valve disease. However, it may be difficult or impractical to set up comprehensive specialist IE care in small hospitals since the incidence of IE is low. Therefore, there must be strong links between referring hospitals and the specialist IE team at the cardiothoracic centre. There must be an established means of communicating with the IE team during working hours whether by email or telephone. Echocardiograms can be reviewed via cloud-archiving. Out-of-hours advice should be possible at a minimum via the established on-call services and informed by departmental protocols.

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**Box 1 Indications for transfer to a surgical centre**

- ▶ Prosthetic valve or implantable cardiac electronic device infection
- ▶ Severe regurgitation even if currently stable haemodynamically
- ▶ Abscess
- ▶ Invasive organism, for example, *Staphylococcus aureus*\*
- ▶ Organisms that are hard to manage medically, for example, fungi
- ▶ Failure to respond to antibiotics
- ▶ Stroke (or other embolism) and large residual vegetation
- ▶ Recurrent emboli
- ▶ Renal failure†

\*Cases of *S aureus* infective endocarditis (IE) may be respond to antibiotics therapy alone, but should trigger a discussion.

†Renal failure in IE has many and sometimes multiple origins including glomerulonephritis, renal emboli, aminoglycoside therapy and low cardiac output. It can contribute to the decision for early surgery when associated with severe valve destruction or failure to control sepsis and should therefore trigger a discussion with the surgical centre.

There should be a low threshold for transferring a case for assessment at a specialist centre (box 1) particularly for IE on prosthetic valves, CIEDs and congenital disease. If immediate surgery is not required, the patient may be sent back to complete antibiotic therapy and monitoring.

**POLICIES AND GUIDELINES**

Local policies at the cardiac centre and referring hospitals should be informed by national and international guidelines and recommendations<sup>1 30–32</sup> in order to promote standardised high-quality diagnosis and management. There should be guidance available, for example, on the hospital intranet, on when to suspect and how to diagnose and manage IE including

indications for echocardiography, and the number and timing of blood cultures.<sup>7</sup>

In the UK, it should be agreed locally whether to adopt National Institute for Health and Clinical Excellence (NICE) IE prophylaxis guidelines<sup>33</sup> in place of international prophylaxis guidelines.<sup>1 31</sup> In some hospitals, this will require the completion of processes for non-compliance with NICE guidelines.

IE may be the first medical presentation of intravenous drug abuse. After operation for a first episode, a referral should be made to a rehabilitation team. There should be an understanding within the department of the principles for treating a second episode of IE in an individual who continues intravenous injections despite

involvement in a rehabilitation programme.<sup>34</sup> This is a difficult area of practice which requires an individualised approach based on discussions within the IE team, with the patient and family, and with case-workers and hospital ethics teams if these exist.

Coexistence of infection with the HIV cannot be taken as an exclusion criterion for surgical treatment since this is a chronic illness and clinical results in IE are comparable in HIV-infected and non-infected patients.<sup>35</sup>

**ROUTINE CARE**

General principles of care are given in box 2. Inpatients with IE should be reviewed and examined at least daily and should be under the direct supervision of the specialist team. Triggers should be in place for urgent discussion with the cardiac centre, for example, changing murmur or new signs of heart failure. Every effort must be made to reduce the risks of complications of therapy, such as avoiding or minimising the use of nephrotoxic and ototoxic medication and optimising monitoring of renal function and antibiotic levels. Intravascular catheter-related bloodstream infection increases mortality in IE patients and can be influenced by selecting appropriate vascular access.<sup>37</sup>

**EDUCATION AND TRAINING**

Patients with IE should be informed and educated about their condition and their questions and concerns should be discussed. Education of patients is also important for the prevention of IE. Some countries, for example, Germany and Spain, publish information leaflets about the need for dental surveillance and how to suspect IE.

IE should be in the syllabus of undergraduate medical courses. Physicians in training (junior doctors) should have access to educational material about IE and the difficulties of diagnosis and management. Local hospital-based valve specialists or the general or community cardiologist with valve competencies should ensure that there is sufficient training and available material to educate general practitioners (community physicians), general hospital physicians and cardiologists about IE.

**SURGERY**

Surgery is required in 40%–50% of cases.<sup>12–14</sup> The mortality is worse if this is delayed, but may be approximately halved<sup>10</sup> when performed as soon as indicated clinically.<sup>10 18 19</sup> Surgery is indicated according to international guidelines<sup>1 31</sup> for heart failure, failure to control

**Box 2 Checklist for optimal care**

- ▶ Blood cultures taken before antibiotics started
- ▶ Echocardiography including transoesophageal echocardiography reviewed
- ▶ Diagnosis and management discussed with lead infective endocarditis cardiologist and microbiologist
- ▶ Case discussed with the regional centre including need for transfer
- ▶ Confirmation of sensitivities and antibiotic doses and duration
- ▶ Appropriate route of antimicrobial delivery (eg, peripherally inserted central catheter (PICC) line) considered

**Inpatient monitoring**

- ▶ Clinical monitoring daily, more frequently if there is a change
- ▶ Multidisciplinary team review weekly or more frequently if clinically unstable
- ▶ Baseline echo with a repeat study if the clinical state changes and routinely predischarge
- ▶ Monitor C reactive protein (CRP) twice weekly<sup>36</sup> (in European, not US practice)
- ▶ Monitor renal function initially daily but twice weekly as condition improves
- ▶ Monitor full blood count twice weekly or more frequently if changing rapidly
- ▶ Monitor antibiotic levels as indicated
- ▶ 12-Lead ECG at baseline, and sequentially when aortic valve is involved or with persistent bacteraemia

infection (usually after 1–2 weeks of appropriate antibiotic therapy), significant valve destruction or periannular extension, or for recurrent emboli. Indicators of a high likelihood of surgery may already be obvious at or soon after admission (box 3). For these patients, surgery may be necessary as an emergency, for example, severe valve destruction and haemodynamic compromise. Some intermediate groups may require surgery within 48 h and should be discussed individually, for example, severe valve destruction with large residual vegetations.<sup>17</sup> The presence of cerebral emboli should not deter early surgery if otherwise indicated<sup>38</sup> although intracerebral bleeding is a contraindication.

Much aortic and mitral valve endocarditis surgery should be within the remit of an appropriately trained consultant surgeon. However, certain situations might call for additional expertise such as aortic root abscess and where there is a realistic chance of mitral valve repair. The relative merit of immediate surgery with a lower chance of repair as against elective surgery with a higher chance of repair<sup>39</sup> but also of heart failure and irreversible myocardial damage may require fine judgement. Team working and clear communication among surgeons in an individual unit are essential and centres should consider joint consultant operating for challenging cases.

Patients must be discussed with an expert cardiac surgeon at admission and at regular MDT meetings to agree triggers for and timing of surgery, but the need for a formal MDT discussion should never delay urgent surgery. Operating lists must be organised flexibly with the capacity to work out of hours or in designated emergency slots within hours or to allow cases with IE to displace cases on a routine waiting list.

### OUTPATIENT SURVEILLANCE AFTER THE ACUTE EVENT

The episode of IE should not be seen as ending once the patient has been discharged. The left ventricle may

decompensate if residual severe regurgitation is not addressed and the valve may deteriorate despite bacteriological cure. The likelihood of surgery in the first 2 years after discharge is about 10%,<sup>12</sup> but may be higher if inpatient surgery is not performed when indicated. The presentation then tends to be with acute heart failure which is associated with a far higher surgical risk than for elective surgery.

There should therefore be follow-up with a cardiologist usually within a specialist valve clinic<sup>40</sup> at 1, 3, 6 and 12 months after discharge<sup>23</sup> and thereafter at a frequency appropriate for the residual valve disease. This is to detect deterioration in valve or left ventricular function, and relapse or recurrence of IE. The rate of relapse is about 8%<sup>12</sup> and of recurrence about 15% within 2 years.<sup>41–44</sup> Infective markers and blood cultures should be taken at the initial visit routinely and otherwise if clinical suspicion occurs.

The clinic should check maintenance of good oral health and preventative dentistry and give advice about skin hygiene including tattoos and skin piercing. Current deficiencies in dental surveillance<sup>13 45</sup> may be one reason for the continuing gradual increase in incidence of IE.<sup>46</sup>

### COMMUNITY

Community physicians (general practitioners) need to be aware that IE is exceptionally rare but should be suspected in patients with intracardiac devices, replacement heart valves and acquired or congenital valve disease. In these patient groups, it is prudent to obtain blood cultures before antibiotics are started. In those on antibiotic therapy, further evaluation is indicated if fever does not settle or there are other suggestive features, for example, vasculitic rash, anaemia or a transient ischaemic attack. There should be channels of communication with the IE team at the local hospital or cardiothoracic centre for advice. There must also be good communication between the outpatient valve clinic and the community

physician (general practitioner) and information supplied must include alerts for early referral.

Community physicians (general practitioners) should be informed of local policies including those on antibiotic prophylaxis.

### CONCLUSIONS

IE has an unacceptably high morbidity and mortality, which can be reduced substantially by a standardised team approach to early diagnosis, appropriate management including antimicrobial therapy and early surgery when indicated.

IE is uncommon and sufficient experience in its management is difficult to obtain by general cardiologists or physicians. All cases should be discussed with the specialist team and there should be a low threshold for transfer from a non-surgical hospital to the cardiothoracic centre.

The acute episode cannot be seen as ending at discharge since there is a substantial likelihood of surgery for residual valve disease or a further episode of endocarditis within 1 or 2 years.

Sustained programmes of education for non-specialist cardiologists, cardiac surgeons, trainees, general physicians, general infection specialists, community physicians and patients are essential.

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### Box 3 Early indicators of a high-likelihood of surgery\*

- ▶ Severe valve destruction with or without clinical heart failure<sup>12 15 23</sup>
- ▶ Cerebral embolism<sup>18</sup> with severe valve destruction or large residual vegetations
- ▶ Abscess<sup>12</sup>
- ▶ Early infective endocarditis after valve replacement (within one year)
- ▶ Infection with *Staphylococcus aureus*<sup>12 18</sup> or fungus
- ▶ Severe valve disease and large residual vegetation<sup>19</sup>

\*The exact timing is decided individually on clinical grounds and varies between immediate and 1–2 weeks.

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