Infective Endocarditis

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1 Summary

a Infective endocarditis (IE) often presents non-specifically, most commonly with fever and symptoms/signs of embolism.

b Consider historical sources of bacteraemia, such as indwelling vascular catheters, recent dental work, and intravenous drug use.

c Symptoms are often subtle and examination is often non-specific, but may demonstrate cardiac murmur, peripheral emboli, Osler nodes, Roth spots, or Janeway lesions.

d If you suspect IE, evaluate the patient urgently and seek early input from a cardiologist and an infectious disease or microbiology specialist. A multidisciplinary approach (e.g., with an 'endocarditis team') is crucial for diagnosis and management.

e Prioritise obtaining **three sets of blood cultures** taken at 30-minute intervals prior to initiation of antibiotic therapy and echocardiography. However, if the patient is unwell (e.g., with sepsis) do not delay empirical antibiotic therapy.

f Treatment is guided by presentation, clinical findings, and organism virulence.

2 Definition

IE is an infection involving the endocardial surface of the heart, including the valvular structures, the chordae tendineae, sites of septal defects, or the mural endocardium.

3 Epidemiology

Infective endocarditis (IE) is becoming more frequent. The online NHS for England Hospital Episode Statistics (HES) reported 10,097 finished consultant episodes for acute and subacute endocarditis during 2019-20 compared with 3969 during 2009-10. In the US, one study found that between 2000 and 2011, the incidence of IE increased from 11 per 100,000 to 15 per 100,000. Another study looking at the incidence of drug use-related IE between 2002 to 2016 found the overall incidence of IE increased from 18 per 10,000 to 29 per 10,000, and the incidence in those with drug use-related IE increased from 48 per 10,000 to 79 per 10,000.

In developed countries, IE is more common in the setting of previous valve surgery or as a consequence of iatrogenic or nosocomial infection, whereas chronic rheumatic disease is an uncommon antecedent. IE in pregnancy is rare and is associated with intravenous drug use and pre-existing cardiac disease and, in particular, mechanical prosthetic valves, where the incidence is higher than in the general population. Maternal mortality reaches 33% and is usually due to embolic events or heart failure.

The overall causative agents in IE are well documented and have been relatively stable, based on population-based studies over time. The most common pathogens are listed below; these together with any underlying risk factors indicate the most likely causative organism:

- Viridans group streptococci
- *Staphylococcus aureus*
- Enterococci
- Coagulase-negative staphylococci
- *Haemophilus parainfluenzae*
- *Streptococcus bovis*
- Fungi
- *Coxiella burnetii*
- Brucella species
- Culture-negative Haemophilus species, Aggregatibacter, Cardiobacterium hominis, Eikenella corrodens, and Kingella species (HACEK).

Patients who develop native valve endocarditis in the absence of intravenous drug use commonly present with viridans group streptococci, enterococci, or staphylococci, with other pathogens being less frequent. Patients who use intravenous drugs often present with right-sided valvular involvement and are more likely to have *S aureus*, streptococci, gram-negative bacilli, or polymicrobial infections. Prosthetic valve endocarditis is most commonly caused by coagulase-negative staphylococci, *S aureus*, enterococci, or gram-negative bacilli. It should be noted that early prosthetic valve endocarditis is often caused by *Staphylococcus epidermidis*.

4 Pathophysiology

IE typically develops on the valvular surfaces of the heart, which have sustained endothelial damage secondary to turbulent blood flow. As a result, platelets and fibrin adhere to the underlying collagen surface and create a prothrombotic milieu. Bacteraemia leads to colonisation of the thrombus and perpetuates further fibrin deposition and platelet aggregation, which develops into a mature infected vegetation.

Acute IE is usually associated with more virulent organisms, classically Staphylococcus aureus. Thrombus is formed by the offending organism and S aureus may invade endothelial cells and increase the expression of adhesion molecules as well as prothrombotic factors.

5 Classification

Clinical classification

a Acute symptoms typically develop over a period of days and for up to 6 weeks; include spiking fevers, tachycardia, fatigue, and progressive damage to cardiac structures.

b Subacute: symptoms occur over the course of weeks to months. Patients will often describe vague constitutional symptoms.

c Chronic: symptoms continue for more than 3 months.

Classification by nidus or location of infection

Native valve endocarditis (NVE)

Patients who develop NVE in the absence of intravenous drug use commonly present with viridans group streptococci, enterococci, or staphylococci, with other pathogens being less frequent. Patients who use intravenous drugs often present with right-sided valvular involvement and are more likely to have Staphylococcus aureus, streptococci, gram-negative bacilli, or polymicrobial infections.

Prosthetic valve endocarditis (PVE)

Between 10% and 30% of all patients with IE have prosthetic heart valves. PVE is defined as being early or late depending on whether it arises within 1 year after valve replacement (early) or after 1 year (late). The focus is placed on the likely causative organisms involved at different time points in the disease process. Early PVE is often caused by S aureus or coagulase-negative staphylococci. Late PVE tends to be caused by the same organisms as NVE, and non-surgical treatment in this group may be effective.

Device-related endocarditis

The increasingly widespread use of implanted devices has contributed to the rising incidence of this complication, though it remains relatively rare overall. Estimates of incidence vary but it is a serious complication that is often difficult to diagnose and carries with it significant mortality.

Although clinically challenging, distinction should be made between local device infection and device-related IE. Risk factors for device-related IE include renal failure, haematoma at the site of implantation, diabetes mellitus, and anticoagulation.

Right-sided endocarditis

Infections of right-sided heart valves make up 5% to 10% of the total number of patients with IE, and are most commonly associated with patients who use intravenous drugs. S aureus is the most common causative organism and accounts for 60% to 90% of patients with IE. The tricuspid valve is the most commonly affected, although the pulmonary valve is also susceptible to infection.

6 Presentation

Case history: example of a typical presentation

A 31-year-old woman presents with a 1-week history of fever, chills, fatigue, and unilateral ankle pain. Her past medical history includes mitral valve prolapse and hypothyroidism. She admits to infrequent intravenous heroin use and has a 10-pack-year history of smoking. Physical examination reveals temperature of 39°C, regular heart rate 110 beats per minute, blood pressure 110/70 mmHg, and respiration rate of 16 breaths per minute. Her cardiovascular examination reveals a grade 2/4 holosystolic murmur that is loudest at the right upper sternal border. Her right ankle appears red and warm, and is very painful on dorsiflexion.

Other presentations

There is a wide spectrum of presentations, which are often dependent on the organism responsible as well as any underlying risk factors. Acute IE can present with septic embolic phenomenon such as stroke, septic joint, or splenic infarct accompanied by fever and cardiac murmur. Subacute IE may be associated primarily with constitutional symptoms such as fever, malaise, weakness, and peripheral stigmata such as embolic phenomenon, Osler nodes, Janeway lesions, or splinter haemorrhages.

7 Diagnosis

a Blood cultures, since we are looking for bacteraemia nad/or fungaemia

b Echocardiography, since we are looking for vegetations and valve mobility. Echocardiography is important not only for confirming or ruling out the diagnosis but also for evaluation of complications and prognosis.

c Full blood count

d C-reactive protein

e Serum urea, electrolytes, and glucose. Lliver function tests

f ECG

8 Management: recommendations

The management of IE is guided by identification of the causative organism and whether the infected valve is native or prosthetic. Refer any patient with suspected or confirmed IE for multidisciplinary evaluation. Ideally this will be within a specific endocarditis team, if available, including a cardiologist who is an accredited specialist in echocardiography (or a cardiologist and an additional accredited specialist in echocardiography who can be

a cardiologist or clinical physiologist/scientist), a cardiac surgeon, an infectious disease or microbiology specialist, a neurologist, and a neurosurgeon.

Patients with "red flags" should be urgently transferred to the endocarditis team in a reference centre with rapid access to cardiac surgery facilities. This transfer should ideally be: immediate if the threat is high (e.g., heart failure); within 2 days if the threat is moderate (e.g., Staphylococcus aureus infection on a mechanical valve with no cardiac dysfunction). Red flags include:

- Prosthetic valve dehiscence
- Valve regurgitation (moderate or severe) and heart failure or haemodynamic instability
- Large/highly mobile vegetations
- Cardiac abscess, fistula, and pseudoaneurysm
- Neurological complications
- Infectious endocarditis in a patient with congenital heart disease.

Start empirical antibiotic treatment once you have taken three sets of blood cultures at 30-minute intervals. However, if the patient is unwell (e.g., with sepsis), **do not delay empirical antibiotic therapy** while waiting to take three sets of blood cultures. Adjust antibiotic therapy accordingly when blood culture results are known (usually within 48 hours). Many patients require **surgery**; urgently refer any patient with acute heart failure for emergency surgery if they have persistent pulmonary oedema or cardiogenic shock despite medical treatment.