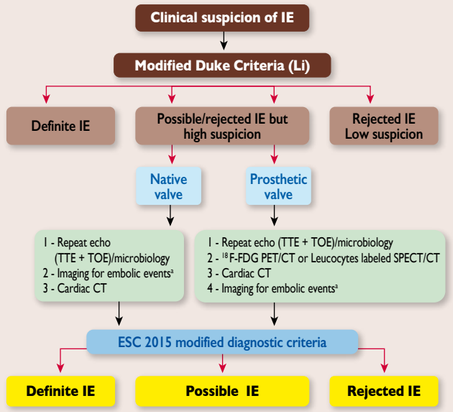
ESC 2015 algorithm for diagnosis of IE



IE = infective endocarditis; PET = positron emission tomography; SPECT = single photon emission computerized tomography; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.
[a]May include cerebral MRI, whole body CT, and/or PET/CT.

In summary, echocardiography, BC, and clinical features remain the cornerstone of diagnosis of IE. When BC are negative, further microbiological studies are needed. The sensitivity of Duke Criteria can be improved by new imaging modalities (MRI, CT, PET/CT) that allow the diagnosis of embolic events and of cardiac involvement when TTE/TOE are negative or doubtful. Those criteria are useful but they do not replace the clinical judgement of the 'Endocarditis Team'.

Antimicrobial therapy: principles and methods

The treatment of IE relies on the combination of prolonged antimicrobial therapy and - in about half patients - surgical eradication of the infected tissues.
Prolonged therapy with a combination of bactericidal drugs is the basis of IE treatment. Drug treatment of PVE should last longer (at least 6 weeks) than that of native valve endocarditis (NVE) (2–6 weeks).
In both NVE and PVE, the duration of treatment is based on the first day of effective antibiotic therapy, not on the day of surgery. A new full course of treatment should only start if valve cultures are positive, the choice of antibiotic being based on the susceptibility of the latest recovered bacterial isolate.
The indications and pattern of use of aminoglycosides have changed. They are no longer recommended in staphylococcal NVE because their clinical benefits have not been demonstrated but they can increase renal toxicity; and, when they are indicated in other conditions, aminoglycosides should be given in a single daily dose in order to reduce nephrotoxicity.

Antimicrobial therapy: principles and methods (cont.)

New antibiotic regimens have emerged in the treatment of staphylococcal IE, including Daptomycin and the combination of high-doses of cotrimoxazole plus clindamycin, but additional investingations are necessary in large series before they can be recommended in all patients.

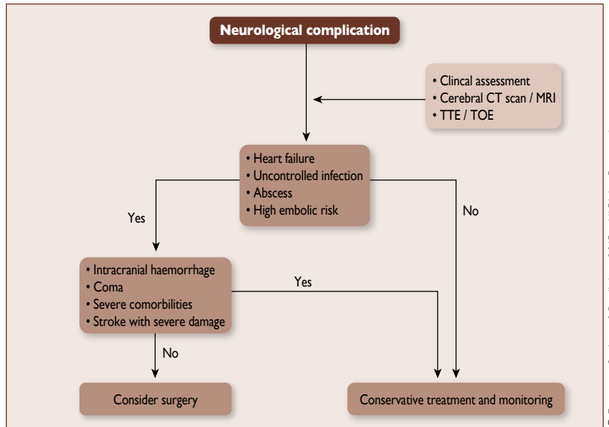
Main complications of left-sided valve IE and their management

Surgical treatment is used in approximately half of patients with IE because of severe complications.
Early consultation with a cardiac surgeon is recommended in order to determine the best therapeutic approach. Identification of patients requiring early surgery is frequently difficult and is an important scope of the 'Heart Team'.
In some cases, surgery needs to be performed on an emergency basis (within 24 h), urgent basis (within a few days, <7 days), irrespective of the duration of antibiotic treatment. In other cases, surgery can be postponed to allow 1 or 2 weeks of antibiotic treatment under careful clinical and echocardiographic observation before an elective surgical procedure is performed.
The three main indications for early surgery in IE are its 3 main complications, i.e. HF, uncontrolled infection, and prevention of embolic events.

Neurological complications

Symptomatic neurological events develop in 15–30% of all patients with IE and additional silent events are frequent. Stroke (ischaemic and haemorrhagic) is associated with excess mortality. Rapid diagnosis and initiation of appropriate antibiotics are of major importance to prevent a first or recurrent neurological complication.
After a first neurological event, if cerebral haemorrhage has been excluded by cranial CT and neurological damage is not severe (i.e. coma), surgery indicated for HF, uncontrolled infection, abscess, or persistent high embolic risk should not be delayed and can be performed with a low neurological risk (3–6%) and good probability of complete neurological recovery. Conversely, in cases with intracranial haemorrhage, neurological prognosis is worse and surgery should generally be postponed for at least 1 month.

Therapeutic strategy for patients with IE and neurological complications



CT = computed tomography; IE = infective endocarditis; MRI = magnetic resonance imaging; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

Adapted from the ESC Guidelines for the Management of Infective Endocarditis (European Heart Journal 2015;36:3075–3123 - doi/10.1093/eurheartj/ehv319).

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INFECTIVE ENDOCARDITIS

2015 GUIDELINES FOR THE MANAGEMENT OF INFECTIVE ENDOCARDITIS

Prevention

Main principles of prevention of infective endocarditis

1. The principle of antibiotic prophylaxis when performing procedures at risk of IE in patients with predisposing cardiac conditions is maintained.
2. Antibiotic prophylaxis must be limited to patients with the highest risk of IE undergoing the highest risk dental procedures. (dental procedures requiring manipulation of the gingival or periapical region of the teeth or perforation of the oral mucosa)
   a. Patients with a prosthetic valve, including transcatheter valve, or a prosthetic material used for cardiac valve repair.
   b. Patients with previous IE.
   c. Patients with congenital heart disease.
      a. any cyanotic congenital heart disease.
      b. congenital heart disease repaired with prosthetic material whether placed surgically or by percutaneous techniques, up to 6 months after the procedure or lifelong if there remains residual shunt or valvular regurgitation.
3. Good oral hygiene and regular dental review are more important than antibiotic prophylaxis to reduce the risk of IE.
4. Aseptic measures are mandatory during venous catheter manipulation and during any invasive procedures in order to reduce the rate of health care-associated IE.

Recommended prophylaxis for dental procedures at risk

Situation	Antibiotic	Single-dose 30–60 minutes before procedure	
		Adults	Children
No allergy to penicillin or ampicillin	Amoxicillin or ampicillin[a]	2 g orally or i.v.	50 mg/kg orally or i.v.[b]
Allergy to penicillin or ampicillin	Clindamycin	600 mg orally or i.v.	20 mg/kg orally or i.v.[b]

[a]Alternatively, cephalexin 2 g i.v. for adults or 50 mg/kg i.v. for children, cefazolin or ceftriaxone 1 g i.v. for adults or 50 mg/kg i.v. for children.
Cephalosporins should not be used in patients with anaphylaxis, angio-oedema, or urticaria after intake of penicillin or ampicillin due to cross-sensitivity.
[b]Paediatric doses should not exceed adult doses.

Non-specific prevention measures should be applied to the general population and particularly reinforced in high-risk patients

- Strict dental and cutaneous hygiene. Dental follow-up should be performed twice a year in high-risk patients and yearly in the others.
- Disinfection of wounds.
- Eradication or decrease of chronic bacterial carriage: skin, urine.
- Curative antibiotics for any focus of bacterial infection.
- No self-medication with antibiotics.
- Strict asepsis control measures for any at-risk procedure.
- Discourage piercing and tattooing.
- Limit the use of infusion catheters and invasive procedure when possible. Favour peripheral over central catheters, and systematic replacement of the peripheral catheter every 3–4 days. Strict adherence to care bundles for central and peripheral cannulae should be performed.

In summary, antibiotic prophylaxis should be limited to patients at high-risk of IE undergoing the highest risk dental procedures.
Hygiene measures, in particular oral and cutaneous hygiene, are of utmost importance. Epidemiological changes are marked by an increase in IE due to staphylococcus and of healthcare-associated IE, thereby highlighting the importance of non-specific aseptic measures.
This should not concern only high-risk patients, but should also be part of routine care in all patients since IE occurring in patients without previously known heart disease now accounts for a substantial and increasing incidence. This means that, although prophylaxis should be restricted to high-risk patients, preventive measures should be maintained or extended to all patients with cardiac disease.

The 'Endocarditis Team'

The presence of an 'Endocarditis Team' is crucial in IE. This multidisciplinary approach has been shown to significantly reduce the 1-year mortality in infective endocarditis. The management of patients with IE in reference centres by a specialized team ('Endocarditis Team') is strongly recommended.

When to refer a patient with IE to an 'Endocarditis Team' in a reference centre

1. Patients with complicated IE, i.e. endocarditis with HF, abscess, or embolic or neurological complication or CHD, should be referred early and managed in a reference centre with immediate surgical facilities.
2. Patients with non-complicated IE can be initially managed in a non-reference centre, but with regular communication with the reference centre, consultations with the multidisciplinary 'Endocarditis Team' and, when needed, with external visit to the reference centre.

Characteristics of the reference centre

1. Immediate access to diagnostic procedures should be possible, including TTE, TOE, multislice CT, MRI, and nuclear imaging.
2. Immediate access to cardiac surgery should be possible during the early stage of the disease, particularly in case of complicated IE (HF, abscess, large vegetation, neurological, and embolic complications).
3. Several specialists should be present on site (the 'Endocarditis Team'), including at least cardiac surgeons, cardiologists, anaesthesiologists, ID specialists, microbiologists and, when available, specialists in valve diseases, CHD, pacemaker extraction, echocardiography and other cardiac imaging techniques, neurologists, and facilities for neurosurgery and interventional neuroradiology.

Role of the 'Endocarditis Team'

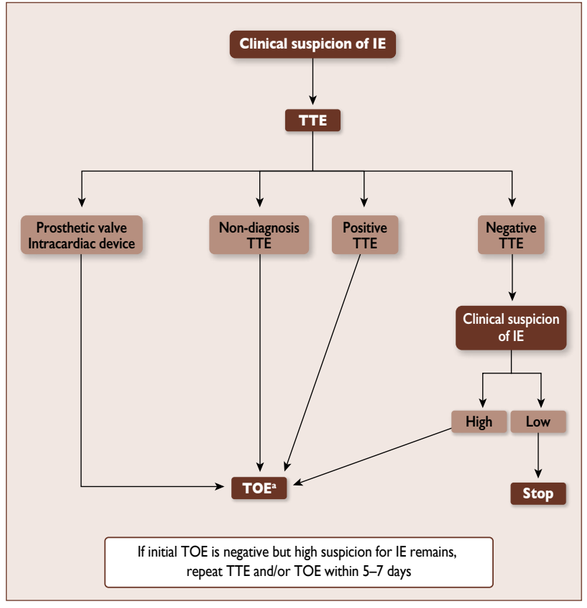
1. The 'Endocarditis Team' should have meetings on a regular basis in order to discuss cases, take surgical decisions, and define the type of follow-up.
2. The 'Endocarditis Team' chooses the type, duration, and mode of follow-up of antibiotic therapy, according to a standardized protocol, following the current guidelines.
3. The 'Endocarditis Team' should participate in national or international registries, publicly report the mortality and morbidity of their centre, and be involved in a quality improvement programme, as well as in a patient education programme.
4. The follow-up should be organized on an outpatient visit basis at a frequency depending on the patient's clinical status (ideally at 1, 3, 6, and 12 months after hospital discharge, since the majority of events occur during this period).

CHD = congenital heart disease; CT = computed tomography; HF = heart failure; ID = infectious disease; IE = infective endocarditis; MRI = magnetic resonance imaging; TOE = transoesophageal echocardiography; TTE = transthoracic echocardiography.

Diagnosis

The clinical history of IE is highly variable according to the causative microorganism, the presence or absence of pre-existing cardiac disease and the mode of presentation. Atypical presentation is common in elderly or immunocompromised patients. Diagnosis may be also more difficult in patients with a prosthetic valve or an intracardiac device and in BCNIE. The Duke criteria are useful for the classification of IE, but they are of limited value in some subgroups (CDRIE, PVE, BCNIE) and do not replace clinical judgement.
Echocardiography and blood cultures are the cornerstone of diagnosis of IE. Addition of results of cardiac/whole body CT scan, cerebral MRI, ^{18}F-FDG PET/CT and leukocytes SPECT/CT might improve the detection of silent vascular phenomena as well as endocardial lesions and may improve the sensitivity of the modified Duke criteria.
The ESC 2015 modified diagnostic criteria include these new imaging techniques as new criteria for IE.

Indications for echocardiography in suspected infective endocarditis



TTE = transthoracic echocardiography; TOE = transoesophageal echocardiography.
[a]TOE is not mandatory in isolated right-sided native valve IE with good quality TTE examination and unequivocal echocardiographic findings.

Definition of the terms used in the ESC 2015 modified criteria for diagnosis of IE, with modifications in boldface

Major criteria

1. Blood cultures positive for IE
   a. Typical microorganisms consistent with IE from 2 separate blood cultures:
      - Viridans streptococci, *Streptococcus gallolyticus (Streptococcus bovis), HACEK group, Staphylococcus aureus*; or
      - Community-acquired enterococci, in the absence of a primary focus; or
   b. Microorganisms consistent with IE from persistently positive blood cultures:
      - ≥2 positive blood cultures of blood samples drawn >12 h apart; or
      - All of 3 or a majority of ≥4 separate cultures of blood (with first and last samples drawn ≥1 h apart); or
   c. Single positive blood culture for *Coxiella burnetii* or phase I IgG antibody titre >1:800

2. Imaging positive for IE
   a. Echocardiogram positive for IE:
      - Vegetation
      - Abscess, pseudoaneurysm, intracardiac fistula
      - Valvular perforation or aneurysm
      - New partial dehiscence of prosthetic valve
   b. **Abnormal activity around the site of prosthetic valve implantation detected by ^{18}F-FDG PET/CT (only if the prosthesis was implanted for >3 months) or radiolabelled leukocytes SPECT/CT.**
   c. **Definite paravalvular lesions by cardiac CT.**

Minor criteria

1. Predisposition such as predisposing heart condition, or injection drug use.
2. Fever defined as temperature >38°C.
3. Vascular phenomena **(including those detected only by imaging)**: major arterial emboli, septic pulmonary infarcts, infectious (mycotic) aneurysm, intracranial haemorrhage, conjunctival haemorrhages, and Janeway's lesions.
4. Immunological phenomena: glomerulonephritis, Osler's nodes, Roth's spots, and rheumatoid factor.
5. Microbiological evidence: positive blood culture but does not meet a major criterion as noted above or serological evidence of active infection with organism consistent with IE.

Adapted from Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Jr., Ryan T, Bashore T, Corey GR. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30:633-638.