

# Infectious endocarditis

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## **Why the Tenth Symphony of Gustav Mahler was Unfinished?**

*Gustav Mahler<sup>1,2</sup> was born on July 7, 1860, in Kalista (Bohemia) near Moravia. His first musical work was a polka composed at the age of 6 years. Mahler studied music at the Vienna Conservatory. He was a composer much criticized by the press. In 1902, Mahler married Alma Schindler, with whom he had 2 daughters, Anna and Maria. The latter died of scarlet fever at the age of only 5. The death of his younger daughter left him depressed; that same year, he discovered he had a heart disease. Forced by a largely anti-Semitic press, he accepted an offer to conduct the Metropolitan Opera in New York in 1907. In 1911, he fell seriously ill with endocarditis. He was attended by Dr. E. Libman who demonstrated the presence of Streptococcus viridans in a large volume (200 ml) of his blood. Mahler was taken to Paris and treated with "Metchnikoff's Bulgarian milk" (Lactobacillus bulgaricus), the probiotics of that era. However, septic abscesses began to appear in other parts of his body. He was taken back to Vienna, and died on May 18, 1911, leaving his Tenth Symphony incomplete.*

## INTRODUCTION

Infectious endocarditis is a major infection involving the endocardium, particularly the cardiac valves. For a long time, it was called bacterial endocarditis. Actually, in addition to bacteria, infectious endocarditis can be caused by other microbiological agents. Changes in the presentation of this disease are explained by modifications in susceptible populations, predisposing factors, and the evolution of microorganisms. Despite a great deal of progress made in recent decades, the diagnosis and treatment of endocarditis continue to be difficult.

## HISTORICAL ASPECTS

Fernel's *Medicini* in 1554 was the first book to introduce the term of endocarditis<sup>3</sup>. During the 17<sup>th</sup> and 18<sup>th</sup> centuries, anomalies of the cardiac valves were described during autopsies of these patients<sup>2</sup>. In 1669, Richard Low-

er in England was the first to diagnose endocarditis of the tricuspid valve. In 1806, Jean Nicolas Corvisart (1755-1821) was probably the first to use the term "vegetations"<sup>2</sup>. In 1816, Théophile Laënnec<sup>1</sup> invented the cylindrical stethoscope, improving cardiac auscultation. In 1835, Jean-Baptiste Bouillaud<sup>2</sup> defined the endocardium in his "*Traité clinique des maladies du coeur*". In France, routine blood cultures were introduced by Pasteur in the late 19<sup>th</sup> century<sup>1</sup>. Penicillin was discovered by Sir Alexander Fleming in 1929 and it has been administered for the treatment of this disease since 1940<sup>2</sup>.

## EPIDEMIOLOGY

Currently, the incidence of endocarditis is 1-4 cases/100,000 or 1/1,300 annual paediatric admissions<sup>4,5</sup>. The increased occurrence of endocarditis is related to improved survival of children with congenital heart disease, newborns or other very ill children. Vascular conduits, patches or valvuloplasty in children with congenital heart disease are risk factors for endocarditis<sup>6</sup>. Other risks are: catheter use in critically ill children, children with immunodeficiency, and the neonatology and the paediatric intensive care units<sup>7</sup>. Eight to 10 percent of paediatric infectious endocarditis cases occur in healthy hearts. Endocarditis caused by intravenous drug use is rare in paediatrics. In the past, rheumatic fever was a risk factor, but it has disappeared in the western world. The epidemiology of endocarditis also has changed, thanks to the development and evolution of paediatric cardiology.

## PATHOGENESIS

An injury in the endothelium is the first inducer of thrombogenesis<sup>4</sup>, allowing bacteria to adhere and form vegetation. In children with cardiac malformations and turbulent or abnormal blood flow, injuries to the endothelium can easily arise. Catheters traumatize the endocardium<sup>8</sup>. Cutaneous or mucosal injuries from tracheal suction, parenteral feeding and umbilical or peripheral

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catheters are at the origins of bacteraemia in newborns<sup>4</sup>. Neonatal endocarditis frequently affects the right heart of newborns. If there is a critical mass of bacteria in the blood during bacteraemia, they can propagate and adhere to the endocardium. During thrombogenesis, blood platelets, sanguinous fibrin and blood cells collect as deposits, and an aseptic thrombus is formed. Bacteria colonize the aseptic thrombus, and blood platelets, fibrin and blood cells are deposited over these organisms, creating vegetation. Microorganisms trapped in the vegetation are protected from phagocytes and other defence mechanisms<sup>4</sup>.

### CLINICAL MANIFESTATIONS

The presentation can be insidious with prolonged fever and non-specific symptoms: fatigue, weakness, anorexia, weight loss, and sweating. At other times, it can be sudden, and these children are terribly ill. Endocarditis presents 4 phenomena:

1. Bacteraemia or fungemia.
2. Valvulitis: new heart murmur or cardiac insufficiency.
3. Immunological responses, much less frequent in children than in adults: petechias, haemorrhages, injuries of Roth or Janeway, Osler nodules or splenomegaly.
4. Embolic phenomena may involve the kidneys, abdominal viscera, brain or heart.

In newborns, the presentation is non-specific. Septic emboli are frequent, causing: osteomyelitis, meningitis or pneumonia<sup>4</sup>.

### ETIOLOGY AND LABORATORY DATA

Blood culture is indicated in all children with fever of unknown origin, pathological murmur, a history of cardiac malformation or antecedents of endocarditis. During endocarditis, bacteraemia is continuous; therefore, blood

cultures can be done at any time<sup>9</sup>. It is important to collect an adequate amount of blood; in small children, this can vary from 1 to 3 ml, and in older children, 5-7 ml. Three blood cultures<sup>4,5</sup> detect more than 95% of endocarditis in children not exposed to antibiotics, and 90% in children who have received antibiotics<sup>10-13</sup>.

Most agents which cause endocarditis are gram-positive cocci<sup>14</sup>: *Streptococci*, *Staphylococci*, *Enterococci*. The organisms most frequently detected in infectious endocarditis are the *S. viridans* and the *S. aureus*<sup>4</sup>. In endocarditis caused by catheters, the *S. aureus* and the *Staphylococci* coagulase-negative are frequent. In addition to those 2 agents, it is necessary in newborns to include the presence of *Candida*, *Klebsiella* and *Enterobacter*<sup>14</sup>. The organisms classified as the HACEK group are less frequently found at a paediatric age: *Haemophilus parainfluenzae*, *H. aphrophilus*, *H. paraphrophilus*, *H. influenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella Kingae* and *K. denitrificans*<sup>4</sup>. Fungi are represented by *Candida* and *Aspergillum*. Mylonakis et al<sup>15</sup> enumerated the percentage of microbiological agents detected according to patient age (table 1).

Endocarditis is diagnosed despite negative blood culture if clinical symptoms and heart ultrasound show evident signs of infection. The incidence of negative blood culture is approximately 5-7%, mostly occurring in patients taking antibiotics or in endocarditis produced by pathogens other than bacteria<sup>4,16</sup>. Vegetation culture can help in the diagnosis<sup>16</sup>. Other laboratory results are non-specific: anaemia, leucocytosis, abnormal sedimentation rate, protein C-reactivity, hyper-gammaglobulinaemia, haematuria, proteinuria.

### ECHOCARDIOGRAPHY

For more than 15 years, heart ultrasound has been revolutionizing the diagnosis of endocarditis. This technique visualizes the place of infection, the vegetation, the extent of injury to the valves, and cardiac function. It also evaluates disease severity and influences medical or surgical treatment decisions. Doppler ultrasound allows the diagnosis of stenosis and valve insufficiency. Transthoracic echocardiography, with a sensitivity of 81%, is very helpful in the diagnosis of paediatric endocarditis<sup>16</sup>. Transoesophageal echocardiography is employed less often in children, and frequently if transthoracic echocardiography is incapable of detecting vegetation<sup>17-19</sup>. However, the absence of vegetation does not exclude the diagnosis of endocarditis. Endocarditis affects the valves, but it can also be located in a defect of the septum, the tendinous cords or wall of the endocardium.

The diagnosis of endocarditis is difficult<sup>20</sup> as its clinical manifestations are numerous and non-specific. This explains why the differential diagnosis of endocarditis is important. Considering the consequences of misdiagnosed

TABLE 1. Pathogens causing endocarditis according to age

Pathogen	Neonates (%)	2 months-15 years (%)
<i>Streptococci</i> spp	15-20	40-50
<i>Staphylococcus aureus</i>	40-50	22-27
Coagulase-negative <i>staphylococci</i>	8-12	4-7
<i>Enterococcus</i> spp	< 1	3-6
Gram-negative bacilli	8-12	4-6
Fungi	8-12	1-3
Culture negative and HACEK organisms*	2-6	0-15
Polymicrobial	3-5	< 1

\*HACEK: (*Haemophilus parainfluenzae*, *H. aphrophilus*, *H. paraphrophilus*, *H. influenzae*, *Actinobacillus actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella Kingae*, *K. denitrificans*)  
Adapted from Mylonakis et al<sup>15</sup>.

endocarditis, false-positives do occur. In countries with high immigration rates, it is necessary to remember that recurrence of rheumatic fever can present with the same clinics as endocarditis<sup>21,22</sup>. Echocardiography in conjunction with clinical suspicion is the best criterion for the diagnosis of endocarditis.

**CRITERIA FOR DIAGNOSIS**

In 1909, Sir Thomas Horder<sup>1</sup> from England described the first criteria for diagnosis: the signs and symptoms of endocarditis. Throughout the 20<sup>th</sup> century, these criteria have undergone various modifications. In 1981, Von Reyn et al<sup>23</sup> (table 2) proposed criteria to facilitate the diagnosis of the disease. These authors presented 123 adults treated at the Beth Israel Hospital in Boston and classified endocarditis as: definitive, probable, possible, or rejected. In 1994, at Duke University in North

Carolina, Durack et al<sup>24</sup> (tables 2 and 3) proposed new diagnostic criteria with the introduction of echocardiography: definitive, possible or rejected endocarditis. According to the criteria of Durack<sup>24</sup> et al, any case of endocarditis not rejected must be considered possible. These criteria seem to present good sensitivity, but are non-specific. In 2000, Li et al<sup>25</sup> (tables 2 and 3) tried to be stricter in endocarditis diagnosis and modified the earlier criteria of Durack<sup>24</sup> et al.

The above-mentioned diagnostic criteria have been validated for use in adult cardiology<sup>26</sup>. Some authors have tried to validate these criteria in paediatric cardiology<sup>27-29</sup>. However, infectious endocarditis is a disease with a very variable clinical presentation. Isolated criteria are not sufficient to make a diagnosis. The various criteria are clinical guides to help in the diagnosis, but they do not replace clinical judgement. Molecular diag-

TABLE 2. Criteria for diagnosis

The Von Reyn Criteria <sup>23</sup> (1981)	Duke Criteria <sup>24</sup> (1994)	Li Criteria <sup>25</sup> (2000)
<p><b>Definite Infective Endocarditis</b> Direct evidence of infective endocarditis based on histology from surgery or autopsy or on bacteriology of vegetation or embolus</p> <p><b>Probable Infective Endocarditis</b> Persistently positive blood cultures plus one of the following: – New regurgitant murmur – Predisposing heart disease and vascular phenomena Negative or intermittently positive blood cultures plus three of the following: – Fever – New regurgitant murmur – Vascular phenomena</p> <p><b>Possible Infective Endocarditis</b> Persistently positive blood cultures plus one of the following: – Predisposing heart disease or – Vascular phenomena Negative or intermittently positive blood cultures with all three of the following: – Fever – New regurgitant murmur – Vascular phenomena For <i>viridans streptococcal</i> cases only: at least two positive blood cultures without an extra-cardiac source and fever</p> <p><b>Rejected Infective Endocarditis</b> Alternative diagnosis Empiric antibiotic therapy warranted Culture negative endocarditis diagnosed clinically, but excluded by postmortem</p>	<p><b>Definite Infective Endocarditis</b> <i>Pathologic criteria</i> Microorganisms: demonstrated by culture or histology in a vegetation or in a vegetation that has embolized or in an intracardiac abscess or Pathologic lesions: vegetation or intracardiac abscess, confirmed by histology showing active endocarditis <i>Clinical Criteria</i> listed in table 3: – 2 major criteria, or – 1 major and 3 minor criteria, or – 5 minor criteria</p> <p><b>Possible Infective Endocarditis</b> Findings consistent with infective endocarditis that fall short of Definite but not rejected</p> <p><b>Rejected Infective Endocarditis</b> Firm alternate diagnosis, or Resolution of manifestations, with antibiotic therapy for 4 days or less, or No pathologic evidence of endocarditis at surgery or autopsy, after antibiotic therapy for 4 days or less</p>	<p><b>Definite Infective Endocarditis</b> <i>Pathologic Criteria</i> Microorganisms: demonstrated by culture or histologic examination of a vegetation, a vegetation that has embolized or an intracardiac abscess or Pathologic lesions: vegetation or intracardiac abscess confirmed by histologic examination <i>Clinical Criteria</i> listed in table 3: – 2 major criteria, or – 1 major and 3 minor criteria, or – 5 minor criteria</p> <p><b>Possible Infective Endocarditis</b> – 1 major criterion and 1 minor criterion, or – 3 minor criteria</p> <p><b>Rejected Infective Endocarditis</b> Firm alternate diagnosis, or Resolution of manifestations with antibiotic therapy for ≤ 4 days, or No pathologic evidence of endocarditis at surgery or autopsy with antibiotic therapy for ≤ 4 days, or Does not meet criteria for possible infective endocarditis</p>

Adapted from<sup>23-25</sup>.

TABLE 3. Criteria for diagnosis

Duke Criteria <sup>24</sup> (1994)	Li Criteria <sup>25</sup> (2000)
<p><b>Major Criteria</b></p> <p><i>Positive blood culture</i></p> <p>Typical microorganism for endocarditis from two separate blood cultures:</p> <ul style="list-style-type: none"> <li>– <i>Viridans streptococci</i>, <i>Streptococcus bovis</i>, HACEK group*, or</li> <li>– <i>Staphylococcus aureus</i> or <i>enterococci</i>, in the absence of a primary focus, or</li> </ul> <p>Persistently positive blood culture, defined as recovery of a microorganism from:</p> <ul style="list-style-type: none"> <li>– Blood cultures drawn more than 12 hours apart, or</li> <li>– All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart</li> </ul> <p><i>Evidence of endocardial involvement</i></p> <p>Positive echocardiogram:</p> <ul style="list-style-type: none"> <li>– Oscillating intracardiac mass, on valve or structures, or in the path of regurgitant jets, or on implanted material, or</li> <li>– Abscess, or</li> <li>– New partial dehiscence of prosthetic valve, or</li> </ul> <p>New valvular regurgitation</p> <p><b>Minor Criteria</b></p> <p>Predisposing heart condition or intravenous drug use</p> <p>Fever <math>\geq 38</math> °C</p> <p>Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway's lesions</p> <p>Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor</p> <p>Positive blood culture but not meeting major criterion</p> <p>Echocardiogram consistent with endocarditis but not meeting major criterion</p>	<p><b>Major Criteria</b></p> <p><i>Positive Blood Culture</i></p> <p>Typical microorganisms from two separate blood cultures</p> <ul style="list-style-type: none"> <li>– <i>Viridans streptococci</i>, <i>Streptococcus bovis</i>, HACEK group*, <i>Staphylococcus aureus</i>, or</li> <li>– <i>Enterococci</i> in the absence of a primary focus, or</li> </ul> <p>Microorganisms from persistently positive blood cultures:</p> <ul style="list-style-type: none"> <li>– At least two positive cultures of blood samples drawn &gt; 12 hour apart, or</li> <li>– All of three or a majority of <math>\geq 4</math> separate cultures of blood with first and last sample drawn at least 1 hour apart</li> <li>– Single positive blood culture for <i>Coxiella burnetii</i> or antiphase I Ig G antibody titer &gt; 1:800</li> </ul> <p><i>Evidence of endocardial involvement</i></p> <p>Positive Echocardiogram. Transesophageal echocardiography recommended in patients with prosthetic valves, rated at least possible endocarditis by clinical criteria, or complicated endocarditis; transthoracic echocardiography as first test in other patients, defined as follows:</p> <ul style="list-style-type: none"> <li>– Oscillating intracardiac mass on valve or structures, in the path of regurgitant jets, or on implanted material, or</li> <li>– Abscess, or</li> <li>– New partial dehiscence of prosthetic valve</li> </ul> <p>New valvular regurgitation</p> <p><b>Minor Criteria</b></p> <p>Predisposing heart condition or injection drug use</p> <p>Fever <math>\geq 38</math> °C</p> <p>Vascular phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages, Janeway's lesions</p> <p>Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factor</p> <p>Positive blood culture but not meeting major criterion</p> <p>Echocardiographic minor criteria eliminated</p>

\*HACEK: *Haemophilus species*, *Actinobacillus (Haemophilis) actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella species* and *Kingella kingae*. Adapted from <sup>24,25</sup>.

TABLE 4. Therapy of Infectious Endocarditis<sup>4,6</sup>

<i>Streptococci, Enterococci</i>			
– Penicilin G plus	200.000 U IV	q 4-6 h	4-6 weeks
– Gentamicin*	3 mg IM or IV	q 8 h	2-6 weeks
Allergic to penicillin:			
– Vancomycin	40 mg IV	q 6-12 h	4-6 weeks
– $\pm$ gentamicin*	3 mg IM or IV	q 8 h	2-6 weeks
<i>Staphylococci</i>			
– beta-lactamase resistant penicillin	200 mg IV	q 4-6 h	6 weeks
– $\pm$ gentamicin*	3 mg IM or IV	q 8 h	3-5 days
Allergic to penicillin			
– Vancomycin	40 mg IV	q 6-12 h	6 weeks
– $\pm$ gentamicin*	3 mg IM or IV	q 8 h	2 weeks

\*Dose of gentamicin should be adjusted to achieve peak and trough concentration in serum of approximately 3.0 and < 1.0  $\mu$ g of gentamicin/ml. Adapted from Ferrieri<sup>4</sup> and Danilowicz<sup>6</sup>.

nosis can be helpful in cases with negative blood culture<sup>30</sup>. Echocardiography also has been very useful. In the paediatric population, transthoracic echocardiography gives considerable information; transoesophageal echocardiography is rarely necessary<sup>17-19</sup>. Echocardiography is not indicated if there is no clinical evidence to support the diagnosis of endocarditis. Each patient with suspicion of endocarditis deserves critical evaluation, to improve the clinical-microbiological diagnosis and treatment<sup>31</sup>.

**TREATMENT**

In general, treatment is given for 4 weeks, but is extended up to 6 weeks if the symptoms of presentation have lasted more than 3 months (table 4)<sup>4,6,15,32</sup>. Treatment is initiated in the hospital, but in some cases, it is complemented with antibiotic therapy at home.

TABLE 5. Risk for complications

<p><i>Complications of Infectious Endocarditis</i><sup>4</sup></p> <p>Congestive heart failure</p> <p>Emboli: cerebral, pulmonary, renal, coronary</p> <p>Periannular abscess</p> <p>Arrhythmia or new heart block</p> <p>Valvular dehiscence or graft or shunt occlusion</p> <p>Persistent bacteremia or fungemia</p> <p>Metastatic infection</p> <p>Mycotic aneurysms</p> <p>Glomerulonephritis or renal failure</p> <p><i>High risk for complications for infective endocarditis</i><sup>31</sup></p> <p>Prosthetic cardiac valves</p> <p>Left side infective endocarditis</p> <p><i>Staphylococcus aureus</i> endocarditis</p> <p>Fungal endocarditis</p> <p>Previous infective endocarditis</p> <p>Prolonged clinical symptoms &gt; 3 months</p> <p>Cyanotic congenital heart disease</p> <p>Patients with systemic to pulmonary shunts</p> <p>Poor clinical response to antimicrobial therapy</p> <p><i>Echocardiographic features suggesting potential surgical intervention</i><sup>4</sup></p> <p>Vegetation:</p> <ul style="list-style-type: none"> <li>- &gt; 10 mm</li> <li>- ≥ 1 embolic event during first 2 weeks of therapy</li> <li>- ≥ 2 emboli during or after therapy</li> <li>- Increase in vegetation size after 4 weeks of therapy</li> </ul> <p>Valvular dysfunction:</p> <ul style="list-style-type: none"> <li>- Aortic or mitral insufficiency</li> <li>- Heart failure</li> <li>- Valve perforation or rupture</li> </ul> <p>Perivalvular extension:</p> <ul style="list-style-type: none"> <li>- Valvular dehiscence, rupture or fistula</li> <li>- New heart block</li> <li>- Large abscess or extension of abscess</li> </ul>
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Adapted from<sup>4,31</sup>.

## COMPLICATIONS AND OUTCOME

The clinical situations that favour complications<sup>4,31,32</sup> and surgical indications according to the anomalies found at echocardiography are listed in table 5. Coward et al<sup>33</sup> reported a 49% incidence of complications. Mylonakis et al<sup>15</sup> found 20-25% adult mortality secondary to endocarditis. Danilowicz<sup>6</sup> recorded a 20-30% incidence of mortality in paediatric age patients, but recently some authors<sup>33</sup> have determined the incidence to be 12%.

## PREVENTION

The indications and doses of antibiotics to prevent infectious endocarditis are listed in table 6<sup>4-6,34-38</sup>.

## CONCLUSION

1. Paediatric infectious endocarditis is rare, but its incidence has risen owing to the survival of children with operated congenital heart disease.

2. In recent decades, the paediatric population at risk of endocarditis has changed, given the increase of chil-

TABLE 6. Prophylaxis of endocarditis

<p><i>Cardiac conditions associated with infectious endocarditis and prophylaxis recommendations</i><sup>4-6,34-38</sup></p> <p>High risk:</p> <ul style="list-style-type: none"> <li>- Complex cyanotic heart diseases (single-ventricle, transposition of great arteries, tetralogy of Fallot)</li> <li>- Aortic valve lesion or coarctation of the aorta, mitral stenosis or regurgitation, ventricular septal defect</li> <li>- Prostheses or homograft</li> <li>- Shunts or conduits</li> <li>- Previous endocarditis</li> <li>- Previous rheumatic heart disease with valvular dysfunction</li> </ul> <p>Moderate risk:</p> <ul style="list-style-type: none"> <li>- Other congenital cardiac malformations, other than above (except ASD)</li> <li>- Acquired valvular dysfunction (rheumatic heart disease)</li> <li>- Hypertrophic cardiomyopathy</li> <li>- Mitral valve prolapse with valvular regurgitation</li> </ul> <p><i>Endocarditis prophylaxis not recommended</i><sup>4-6,34-38</sup></p> <p>Atrial septal defect</p> <p>Surgical repair of atrial septal defect, ventricular septal defect or patent ductus arteriosus</p> <p>Mitral valve prolapse without valvular regurgitation</p> <p>Innocent heart murmur</p> <p>Previous Kawasaki disease without valvular dysfunction</p> <p>Previous rheumatic heart disease without valvular dysfunction</p> <p>Pacemakers, defibrillators or stents</p> <p><i>Infective Endocarditis Prophylaxis recommended</i><sup>5,34,36</sup></p> <p>Dental procedure: tooth extraction, periodontal surgery, brushing teeth, dental implant, root canal, gingival placement of bands, orthodontic treatment, intraligamentary injections, professional cleaning and scaling</p> <p>Respiratory procedure: tonsillectomy or adenoidectomy, surgery that involve respiratory mucosa, rigid bronchoscopy</p> <p>Gastrointestinal procedure: endoscopy, sclerotherapy for oesophageal varices, oesophageal dilatation, endoscopic retrograde cholangiography, gallbladder surgery, surgery that involve intestinal mucosa</p> <p>Genitourinary procedure: prostatic surgery, cystoscopy, urethral dilatation</p> <p><i>Prophylaxis regimens</i><sup>5,37</sup></p> <p>General profilaxis:</p> <ul style="list-style-type: none"> <li>- Amoxicillin: 50 mg/kg orally 1 h before procedure</li> <li>- Ampicillin: 50 mg/kg IM or IV 30 min before procedure</li> </ul> <p>Allergic to penicillin:</p> <ul style="list-style-type: none"> <li>- Clindamycin: 20 mg/kg orally 1 h before procedure</li> <li>- Cephalexin or cefadroxil: 50 mg/kg orally 1 h before procedure</li> <li>- Azithromycin or clarithromycin: 15 mg/kg orally 1 h before procedure</li> <li>- Clindamycin: 20 mg/kg IV 30 min before procedure</li> <li>- Cefazolin: 25 mg/kg IM or IV 30 min before procedure</li> </ul>
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Adapted from<sup>4-6,34-38</sup>.

dren with immunodeficiency disease and children under neonatal and paediatric intensive care.

3. Infectious endocarditis in healthy children is rare but not exceptional.

4. Complications continue to be frequent.

5. Diagnostic criteria are guidelines that do not replace clinical judgement.

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