Endocarditis (Inflammation of the Heart Valve) — Classification, Diagnosis, and Treatment

As an inflammatory disease of the interior heart lining, endocarditis mostly manifests in the area of the cardiac valves. In addition to that, an inflammation in the area of the atria or the ventricles is also possible. There can be both infectious and non-infectious causes. Mixed forms are possible as well. Rarely, endocardial-myocardial fibrosis or medication-induced cardiac valve changes occur.

Definition of Endocarditis

Endocarditis describes the inflammation of the inner membrane lining the heart (endocardium).

Epidemiology of Endocarditis
Frequency of endocarditis

In the United States, the incidence is approx. 12.7 cases/100,000 persons per year.

In Western Europe, endocarditis has an incidence of roughly 3 cases/100,000 persons per year. Men are affected twice as often as women.

**Table 1:** “Diagnosis data of hospitals in Germany, ICD10: B37.6 Candida-endocarditis,” bill of health report of the state (GBE).

<table>
<thead>
<tr>
<th>Year</th>
<th>2013</th>
<th>2012</th>
<th>2011</th>
<th>2010</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men</td>
<td>23</td>
<td>21</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Women</td>
<td>8</td>
<td>11</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>32</td>
<td>37</td>
<td>26</td>
</tr>
</tbody>
</table>

Etiology of Endocarditis

**Causes of endocarditis**

In 45–65 % of all cases, *Streptococci* are the cause of bacterial or infectious endocarditis. The 2nd most frequently observed pathogens are *Staphylococci*, accounting for roughly 30% of all cases, followed by *Enterococci* (10%). Also, other pathogens, including *Mycoplasma, Chlamydia*, and fungi can trigger endocarditis, though they occur rather rarely.

Non-infectious endocarditis can be explained by **antigen-antibody reactions or immune complexes**. Examples are endocarditis rheumatic, after infection with β-hemolyzing *A-Streptococci*, or endocarditis Libman-Sacks at systemic lupus erythematoses.

**Parkinson’s medications** or **ecstasy** can be the cause of medicament-induced cardiac valve changes.

**Overview of causes and presentation**

<table>
<thead>
<tr>
<th>Causes</th>
<th>Presentation</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staphylococcus aureus</em></td>
<td>Acutely very ill, abscess formation</td>
</tr>
<tr>
<td>Coagulase-negative <em>Staphylococcus</em></td>
<td>Subacute, chronic fevers</td>
</tr>
<tr>
<td>α-hemolytic <em>Streptococcus</em></td>
<td>Subacute, chronic fevers</td>
</tr>
<tr>
<td>Gram-negative rods</td>
<td>Subacute, chronic fevers, embolic disease</td>
</tr>
</tbody>
</table>
Classification of Endocarditis

Infectious endocarditis (IE)

Infectious endocarditis can be divided into bacterial, viral, and mycotic endocarditis.

With bacterial endocarditis, one has to further distinguish between:

- **Acute IE** that is rapidly progressive and destructive in nature. The disease affects normal valves and is fatal if not treated.
- **Sub-acute IE** (endocarditis lenta) that is indolent in nature, affects damaged valves, and fatality is seen after 1 year.

Infectious endocarditis can also be further classified into:

- Native valve endocarditis that is affected by *Staphylococcus* species, *Streptococcus* species, and the HACEK group of organisms.
- Prosthetic valve endocarditis, mostly affected by coagulase-negative *Staphylococci* and *S. aureus*
- Intravenous (IV) drug abuse endocarditis that is seen with more resistant bugs such as methicillin-resistant *S. aureus* (MRSA), *Pseudomonas*, *Lactobacillus*, and *Corynebacterium*.
- Nosocomial endocarditis that is seen with fastidious organisms such as *Coxiella burnetii* and *Brucella*.

Non-infectious endocarditis

Non-infectious endocarditis can be divided into 3 branches: antigen-antibody reactions (endocarditis rheumatic), residue of immune complexes (endocarditis Libman-Sacks) and cellular immune reaction (Löffler’s syndrome or endomyocarditis eosinophila).

Further classification

Another classification can be made on the basis of localization of the endocarditis. Hereby, **endocarditis valvularis** in the area of the cardiac valves has to be distinguished from **endocarditis parietalis** in the area of the walls of the atrium or the ventricles.

Pathophysiology of Endocarditis

Endocarditis at the cellular level

A pre-existing lesion of the heart, like a defective valvular apparatus, is always a risk factor for the settlement of bacteria in the endocardium. At defective locations of the endocardium, platelet-fibrin thrombi settle. E.g., after dental interventions or tonsillectomy, the blood is circulated by bacteria which can easily settle in damaged areas like these thrombotic plaques. This is called transitory bacteremia.

In addition to the inflammation, destruction of the valves and the myocardium, as well as immune complex settlements and tissue destruction occur.
Symptoms and Clinical Manifestations of Endocarditis

The features could be acute or sub-acute. They could also be classified as cardiac and extracardiac manifestations. For the exam, extra-cardiac manifestations are especially important.

General acute and sub-acute signs and symptoms include:
- Fever
- Tachycardia
- Fatigue
- Abdominal pain
- Chest pains
- Difficulty in breathing
- Loss of appetite and weight loss
- Finger clubbing

Cardiac features include:
- Cardiac murmur
- Signs of cardiac insufficiency can occur on the cardiac level on auscultation.
- Perivalvular abscess
- Heart blocks

Extra-cardiac manifestations include:
- Septic emboli i.e. subungal hemorrhages
- Brain microabscesses
- In roughly 1/3rd of the cases, petechiae can be found.

Also, splinter-bleedings under the nails, painful, reddish nodules on the fingers and the toes (Osler's nodules, see left image) and, occasionally, clubbed fingers and Hippocratic nails, as well as Janeway-lesions, can be symptoms. In the eyes, retinal bleedings (Roth spots) can appear.

The kidney can also be affected. Hematuria and proteinuria can be present. Kidney infarction in the context of embolic events, diffuse glomerulonephritis, or glomerular focal nephritis can occur.

Course of Endocarditis

Different courses of endocarditis

With bacterial endocarditis, one can distinguish between an acute and a subacute (endocarditis lenta) form. Usually, the 1st form is due to a Staphylococci infection.
with a quickly progressive course, fever and shivers, tachycardia and clouded awareness, quick cardiac and renal insufficiency and multi-organ failure. If this form is not treated immediately, its course is usually lethal.

Typical pathogen of endocarditis lenta is *Streptococcus viridans*. The beginning of this form is insidious with unspecific fever. The course is slow and is accompanied by increasing cardiac insufficiency.

Diagnosis of Endocarditis

Options for diagnosing endocarditis

Besides anamnesis, where the physician has to inquire about previous interventions on the patients with cardiac defects as well as for IV drug abuse and the overall clinical picture, transesophageal echocardiography (TEE) is also a part of the diagnostic procedure. With this method, valvular vegetations from 2-3 mm, and eventually valvular defects, can be detected.

**Note:** Gold standard is the preparation of at least 3 pairs of aerobic and anaerobic blood cultures before the start of therapy!

Diagnosis of bacterial endocarditis

For diagnosis of bacterial endocarditis, the Duke criteria are suitable. If 2 primary criteria, or 1 primary criterion and 3 secondary criteria, or 5 secondary criteria, are present, infectious endocarditis is probable.

**The primary criteria include:**

- At least 2 positive blood cultures with typical pathogens before the start of antibiotic therapy
- Positive echocardiography finding

**The secondary criteria include:**

- Fever over 38°C
- Predisposing factors
Immunological phenomena like Osler’s nodules or glomerulonephritis
Serological detection of a germ, which does not meet the requirements for a primary criterion
Echocardiography finding, which suggests endocarditis, but does not meet the requirements for a primary criterion

Therapy of Endocarditis

Treatment of endocarditis

Mainly, therapy depends on the pathogen. If it is unknown, one should follow the calculated initial therapy and adjust it if an antibiogram is available.

For the treatment of native-valve endocarditis or a valve prosthesis surgery, which has been performed more than 12 months in the past, the application of ampicillin with sulbactam and gentamicin or amoxicillin with clavulanic acid and gentamicin and ciprofloxacin is recommended.

If the valve prosthesis surgery has been performed less than 12 months ago, the combination of vancomycin, gentamicin, and rifampicin is obligatory. For patients that are allergic to β-lactam-antibiotics, the combination of vancomycin, gentamicin, and ciprofloxacin is recommended.

Prophylaxis of Endocarditis

For prophylaxis of endocarditis, there are several indications. Those include patients with valve replacement or reconstructed valves, patients who have already overcome endocarditis and patients with inherent cardiac defects.

Indications for endocarditis

Situations in which endocarditis is indicated are dental interventions like tooth extractions, periodontal interventions, and interventions in the respiratory tract like adenotomies and tonsillectomies, even if the patients do not exhibit a manifested infection.

If the patients already have manifested infections, interventions in the gastrointestinal and urogenital tract or on the skin and dermal appendage tissues represent indications for endocarditis prophylaxis, which should correspond to the pathogen if possible. Also, prophylaxis is always indicated just before surgery in the context of cardiac surgical interventions.

References


Agabegi SS, Agabegi ED. *Step-Up To Medicine*. Baltimore, MD, USA: Lippincott Williams & Wilkins; 2013.


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