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 fibroses or medicament-induced cardiac valve changes occur.

Definition of Endocarditis

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

Epidemiology of Endocarditis
Frequency of endocarditis

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

In Western Europe, endocarditis has an incidence of roughly three cases out of 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” of the 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>Male</td>
<td>23</td>
<td>21</td>
<td>26</td>
<td>18</td>
</tr>
<tr>
<td>Female</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 second most frequently observed pathogens are *staphylococci*, with 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 an infection with β-hemolyzing A-streptococci, or endocarditis Libmann-Sacks at systemic lupus erythematoses.

*Parkinson medications* or *ecstasy* can be the cause for 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

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

With bacterial endocarditis, one has to further distinguish between:

- **Acute I.E** that is rapidly progressive and destructive in nature. The disease affects normal valves and is fatal if not treated.
- **Sub-acute I.E** (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 that is mostly affected by coagulase negative staphylococci and staphylococcus aureus.
- IV drug abuse endocarditis that is seen with more resistant bugs such as MRSA, pseudomonas, lactobacillus and cornebacterium.
- Nosocomial endocarditis that is seen with fastidious organisms such as coxiella burnetti and brucella.

Non-infectious endocarditis

Non-infectious endocarditis can be divided into three branches: **antigen-antibody reactions (endocarditis rheumatic)**, **residue of immune complexes (endocarditis Libmann-Sacks)** and **cellular immune reaction (Löffler's syndrome or endomyocarditis eosinophilica)**.

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. For example, after dental interventions or tonsillectomy, the **blood** is circulated by bacteria which can easily settle at damaged areas like these thrombotic plaques. This is called **transitory bacteraemia**.

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 extra cardiac 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 micro abscesses.
- In roughly one-third 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** (see right image) 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 first 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 with increasing cardiac insufficiency.

Diagnostic of Endocarditis

Options for diagnosing endocarditis

Besides anamnesis, where the physician has to inquire for previous interventions on the patients with cardiac defects as well as for intravenous 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 present valvular defects, can be detected.

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

Diagnosis of bacterial endocarditis

For diagnostic of bacterial endocarditis, the Duke criteria are suitable. If two primary criteria, or one primary criterion and three secondary criteria, or five secondary criteria, are present, infectious endocarditis is probable.

The primary criteria include:
- At least two 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 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.
Review Questions

The answers can be found below the references.

1. Which pathogens most frequently cause bacterial endocarditis?
   A. Streptococci
   B. Staphylococci
   C. Enterococci
   D. Chlamydia
   E. Clostridia

2. Which of the following symptoms is least typical for endocarditis?
   A. Fever
   B. Tachycardia
   C. Petechiae
   D. Osler’s nodules
   E. Pulsus paradoxus

3. Which of the following antibiotic combinations is most suitable for treating artificial valve endocarditis?
   A. Vancomycin, Gentamicin, Rifampicin
   B. Ampicillin, Sulbactam, Gentamicin
   C. Amoxicillin, clavulanic acid, Gentamicin
   D. Ampicillin, Sulbactam, Rifampicin
   E. Amoxicillin, clavulanic acid, Rifampicin

References

Le T, Bhushan V, Bagga HS. First Aid for the USMLE Step 2 CK. McGraw-Hill Medical; 2009.


Correct answers: 1B, 2E, 3A

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