Heart inflammation

Infectious endocarditis

Infective endocarditis (IE) is a disease caused by an infectious agent that affects the endocardium, heart valves and related structures. Inflammation can be caused by bacteria, fungi, chlamydia, rickettsiae or viruses.

Risk factors

Risk factors - children:

- congenital heart defects;
- rheumatic heart defects (rare);
- iatrogenic - long-established central venous catheters;
- intravenous drug use;
- bicuspid aortic valve;
- mitral valve prolapse with regurgitation;
- stp. cardiac surgery using conduits and vascular prostheses, with artificial valves[1].

In congenital heart disease, IE occurs most commonly in:

- Tetralogy of Fallot,
- ventricular septal defect,
- aortic stenosis,
- patent ductus arteriosus

The risk is significantly lower in pulmonic stenosis and IE is virtually absent in atrial septal defects.

- The bicuspid aortic valve is a frequent site of IE, regardless of whether it causes stenosis or regurgitation.
- In mitral valve prolapse, patients are at risk of IE if the valve regurgitates.

IE is rare in newborns, infants, and young toddlers except for iatrogenic IE in critically ill children with catheter infections. The risk of IE increases with age in individuals with heart disease.

Etiology

In children, the most common cause of IE are:

- ***Streptococcus viridans***,
- staphylococci,
- more rarely enterococci.
- Coagulase-negative staphylococci (*Staphylococcus epidermidis*) are typical triggers of IE after cardiac surgery.

- Gram-negative microorganisms and fungi rarely cause IE. They usually affect immunosuppressed individuals, patients with artificial valves and drug addicts. Mycotic IE is also a serious complication of long-term central venous catheters usually after repeated administration of broad-spectrum antibiotics

Pathogenesis

An important factor in the development of IE is the presence of *turbulent blood flow* that disrupts the endothelium. However, vegetations can also form as a result of the Venturi effect at the site of slow blood flow. A cluster of platelets and fibrin forms in the damaged endothelium, which is subsequently colonized by infectious agents. Bacteremia occurs in association with various diagnostic or therapeutic procedures. Transient bacteraemia may also occur when brushing teeth or biting solid food. This mechanism explains the occurrence of IE in patients where a clear causative bacteraemia cannot be identified.

The main macroscopic findings are **vegetations** on the endocardium. They contain microbes and are covered by a layer composed of fibrin and leukocytes. Less virulent bacteria nestle in the thrombi, where fibrin protects them from phagocytosis and antibiotics.

The adjacent affected tissue is edematous, with cellular infiltration and is poorly vascularized, which impairs antibiotic penetration. Fragility of vegetations causes recurrent bacteremia and embolization to the lungs or systemic circulation, depending on the site of cardiac involvement and the presence of intracardiac shunts. Embolization into the lung mimics pneumonia; an unrecognized lung abscess may perforate into the vascular system with subsequent fatal hemorrhage. The skin, kidneys, spleen and brain are most commonly affected by systemic embolization. In prolonged disease, the heart valves are destroyed. Virulent bacteria (*Staphylococcus aureus*) cause rapid destruction of the valves or invasion of the myocardium leading to abscess formation. Septic embolization into the coronary arteries is also a frequent finding. IE significantly activates the humoral and cellular immune system. For example, circulating immune complexes are responsible for the development of glomerulonephritis[1].

Classification

- IE native valves,
- IE of drug addicts (predisposes to tricuspid valve involvement with risk of pulmonary embolization),
- IE of valve prostheses (early/late onset - threshold 2 months after surgery).

The division of IE into acute and subacute forms is obsolete and not used anymore. The division according to the causing agent is recommended. Microorganisms with low virulence (e.g. *α-haemolytic streptococcus*) usually induce the "subacute" form, whereas *Staphylococcus aureus* and other pyogenic bacteria induce the "acute" form.

Risks of infective endocarditis

High risk;

- Valve prostheses (lifelong),
- stp. cardiac surgery (up to 6 months after surgery),
- aortic defects,
- tetralogy of Fallot,
- mitral insufficiency,
- PDA,
- VSD,
- CoA,
- Marfan syndrome,
- history of IE.

Intermediate risk;

- Mitral stenosis,
- tricuspid defects,
- mitral prolapse,
- hypertrophic cardiomyopathy

Clinical picture

IE is always suspected in at-risk patients (see above) with a febrile state. Always bear in mind the mitigated forms of IE when p.o. antibiotic treatment has been given out of confusion, the febrile state may then even resolve. Endocarditis is most commonly manifested by **fever** and **non-specific complaints** such as myalgia, arthralgia, headache, fatigue. With a prolonged duration of the disease, splenomegaly is found, the skin is coloured with a hint of white coffee (caffé au lait). Other late symptoms are embolizing manifestations in the periphery: splinter-like subungual hemorrhages, petechiae on the skin or subconjunctivally, red spots on the palms (Janeway's spots), painful inductions on the bellies of the fingers (Osler's nodes). Embolization may reveal examination of the ocular background (hemorrhagic lesions on the retina = Roth spots) or hematuria. In up to 30% of patients, the first clinical sign of IE may be an acute embolic cause. Most commonly, the a. carotis interna basin is affected. Clinical signs are hemiplegia, aphasia, mental disorders, and rarely blindness when retinal arteries are affected. In general, IE of the left heart causes embolization to the periphery with subsequent ischemia, infarction in sterile emboli, abscesses in infective emboli, or mycotic aneurysms. Embolization from the right heart to the lungs is often asymptomatic because of good filtration properties of the lungs or presents with symptoms of pulmonary embolism followed by cough, auscultatory and radiographic findings on the lungs.

Sometimes there may be up to a picture of Löhlein's nephritis with hematuria, proteinuria and a decrease in glomerular filtration rate. It is a manifestation of microembolization to the kidney or a consequence of focal or diffuse glomerulonephritis, which causes deposits of immunocomplexes in the glomeruli. Up to 20% of children have neurological symptoms: meningitis, brain abscesses, toxic encephalopathy.

Significant findings are new-onset or altered **heart murmurs** due to valve involvement; more rarely, the inflammatory process may affect the cardiac conduction system and cause AV block. Heart failure is the most common cause of death.

Always keep in mind the mitigated forms of IE when p.o. antibiotic treatment is given out of confusion, febrile episodes may then even subside!

Diagnostics

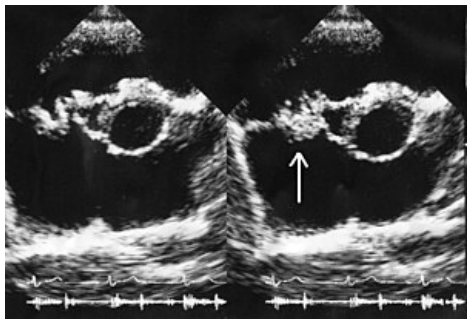
Laboratory examination

Common laboratory findings suggest high sedimentation rate, leukocytosis, microscopic hematuria, proteinuria, positive rheumatoid factor, and elevated CIK values for the diagnosis of IE. We often find anemia and hypergammaglobulinemia. Correct **hemoculture** is crucial for the diagnosis and treatment of IE. Three hemocultures are taken within 24 hours and in case of negative findings on the second day of incubation, two more hemocultures are taken. When IE is clinically suspected, we also take hemocultures in subfebrile or afebrile patients. Hemoculture negativity may be due to previous antibiotic treatment, IE caused by rickettsiae, chlamydiae, viruses, or slow-growing organisms. Molecular biological methods such as PCR provide further possible refinement of the diagnosis of IE. Negative hemocultures may also support the diagnosis of sterile thrombotic endocarditis, most commonly occurring in the context of the antiphospholipid syndrome.

False positivity of hemocultures is due to contamination during non-sterile collection. The most common are coagulase-negative staphylococci, corynebacteria, transiently colonizing enterobacteria, pseudomonads, etc. Repeated findings, isolation of the same strain from other biological samples and a corresponding clinical picture are indicative of the etiological agent.

Echocardiography

Echocardiography is a very valuable method for confirming IE. This examination reliably detects vegetations on the endocardium and valves and is also important in monitoring the development of any valvular regurgitation or other cardiac findings. We also use transesophageal echocardiography for unclear findings. Echocardiographic diagnosis of IE on an artificial valve is very difficult, in which vegetations are often hidden in the shadow of the strong signal caused by echodense material.



Vegetation on tricuspid valve by echocardiography. Arrow denotes the vegetation.

Neither a negative echocardiogram nor a negative hemoculture excludes the diagnosis of IE!

Special examination

When embolization into the pulmonary or systemic circulation is suspected, special imaging examinations such as CT scan and MRI are indicated to detect or exclude septic emboli or abscesses.

Always consult a dentist or ENT physician to rule out a focal infection. Remediation of the infectious lesion is performed while IE is still being treated.

Diagnostic criteria

The criteria currently recommended for the diagnosis of IE are those proposed by Durack of Duke University, USA (the Duke criteria), which are based on a combination of clinical, laboratory and echocardiographic findings. According to these criteria, patients with suspected IE are divided into 3 categories: proven IE, possible IE and excluded IE.

Definition of IE criteria (Duke criteria):

main criteria

- *positive hemoculture:* typical microorganism for IE detected from 2 different blood samples (*Streptococcus viridans* including nutritional variants or *Streptococcus bovis* or *HACEK* group organisms; *Staphylococcus aureus* or *Enterococcus spp*, if no other primary source of infection has been identified) / repeatedly positive hemocultures if there was: the same finding in 2 hemocultures taken 12 hours or more apart, or the same finding in 3, or 3 out of 4 hemocultures if the interval between the first and last collection was greater than 1 hour
- *signs of endocardial involvement*: echocardiographic findings consistent with IE (fluttering intracardiac structures on the valve or on surrounding structures at the site of accelerated blood flow or on foreign material for which there is no other anatomical explanation; abscess; new-onset paravalvular dehiscence at the site of the artificial valve)/new-onset valve regurgitation

secondary criteria

- *Predisposition*: structural heart disease, i.v. drug abuse,
- *temperatures* ≥ 38.0°C,
- *vascular symptoms*: embolization, septic pulmonary infarction, intracranial hemorrhage, conjunctival hemorrhage and skin petechiae,
- *immunological signs*: glomerulonephritis, Osler's nodules, Roth spots, rheumatoid factor,
- *microbiological findings*: positive hemoculture not meeting the above main criteria or serological evidence of active infection consistent with IE,
- *echocardiographic findings* consistent with IE but not meeting the above main criteria.

Diagnosis of IE (Duke criteria):

Demonstrated IE

- Pathological criteria (at least 1 criterion): evidence of microorganism by culture or histology in vegetations or embolization of vegetations or intracardiac abscess, or histological evidence of active IE in vegetations or intracardiac abscess,
- Clinical criteria: 2 main criteria, or 1 main and 3 minor criteria, or 5 minor criteria.

Possible IE

- 1 major + 1 minor criterion / 3 minor criteria

excluded IE

- other diagnosis demonstrated to explain the symptoms / disappearance of IE symptoms within 4 days of antibiotic treatment / absence of IE findings at surgery or autopsy after antibiotic treatment within 4 days

Therapy

In **empirical treatment** or in case of negative hemoculture, we choose the combination of oxacillin 200 mg/kg/d á 4 h + gentamicin 3 mg/kg/d á 12 h i.v., in patients allergic to penicillins then vancomycin 40 mg/kg/d á 6 h + gentamicin 3 mg/kg/d á 12 h i.v.

In case of a **positive hemoculture**, we take into account the type of microbe detected, its sensitivity and MIC. As a rule, when penicillin-sensitive streptococci are detected, we administer Penicillin G 200 000-400 000 I.U./kg/d i.v. á 4 h, ev. + gentamicin. If enterococci and other resistant streptococci are detected, administer ampicillin 200-300 mg/kg/d i.v. + gentamicin for 6 hours. Gram-negative IE (HACEK) is treated with a combination of third-generation cephalosporins, e.g. ceftriaxone 100 mg/kg/d á 12 h i.v. or ampicillin 200-300 mg/kg/d á 6 h i.v. + gentamicin 3 mg/kg/d á 12 h i.v, Mycotic IE is treated with amphotericin B: the test initial dose is 0.1 mg/kg, if well tolerated, increase the dose to 0.5 mg/kg for 1 day and continue for at least 6-8 weeks with a maintenance dose of 1 mg/kg/d i.v. Surgery (replacement of infected valve, excision of infected tissue) is usually necessary. Aminoglycosides are administered for 14 days (longer administration is associated with a high risk of nephrotoxicity), other antibiotics for 4-6 weeks.

In general, we always choose bactericidal ATBs, taking care to achieve a synergistic effect when combining them. Periodic determination of the bactericidal activity of the serum and monitoring of the serum concentration is important, especially for potentially toxic antibiotics (gentamicin, vancomycin). We demonstrate the efficacy of ATB therapy by eradication of bacteraemia in hemoculture. Intermittent hemoculture monitoring is important for the first 8 weeks after the end of treatment, as this is the period when most relapses occur.

In the proposal of treatment, we can follow available guidelines in even more detail, e.g., from current recommendations by the American Heart Association ([www.americanheart.org]).

Prevention

Prevention of IE consists of the targeted administration of antibiotics to all at-risk individuals prior to surgical or diagnostic procedures known or suspected to cause transient bacteraemia. Typically, these are procedures in the oral cavity, nasopharynx, digestive or urogenital tract.1 Prevention of IE has significantly reduced the incidence of this devastating infection since its introduction. The most important thing is to prevent bacteraemia in children with structural heart disease. Particular care should be taken to ensure early treatment of all dental affections, including minor caries, even first dentition, increased oral hygiene, and vigorous treatment of purulent skin affections and respiratory bacterial infections. However, prevention of IE does not mean blanket treatment of all even non-bacterial infections with antibiotics or continuous administration of antibiotics. Cardiac patients are provided with a legitimate policy. In summary, the most effective prevention of IE is early and complete correction of the heart defect.

Patients requiring routine prevention of IE

- with congenital heart disease except atrial septal defect,
- rheumatic or other valvular defects,
- obstructive hypertrophic cardiomyopathy,
- mitral valve prolapse and concomitant regurgitation[1].

Patients requiring risk prevention of IE

- The first 6 months after cardiac surgery and after interventional catheterization procedures,
- lifetime in patients with artificial valves, including bioprostheses and allografts, after aortopulmonary switch operations.
- in complex cyanotic heart defects (functionally single ventricle, tetralogy of Fallot, transposition of large arteries)
- after IE.

Patients not requiring IE prophylaxis

- Isolated atrial septal defect,
- atrial septal defect and patent ductus arteriosus at 6 months postoperatively with no residual findings,
- mitral valve prolapse without regurgitation,
- febris rheumatica or Kawasaki disease without valvular involvement,
- functional murmurs,
- implanted pacemaker or defibrillator,
- coronary bypass surgery.

Procedures requiring prevention of IE in patients at risk

- Dental procedures accompanied by gingival or mucosal bleeding, including professional scaling,
- tonsillectomies and adenoidectomy
- operations affecting the lining of the bowel or respiratory tract,
- bronchoscopy with a rigid bronchoscope,
- dilatation of the oesophagus and sclerotisation of esophageal varices,
- gall bladder surgery,

- cystoscopy and urethral dilatation,
- catheterisation of the bladder if infection is present*,
- urological surgery if infection is present*,
- prostate surgery,
- incision and drainage of infected tissue*,
- vaginal delivery, if infection is present*,
- vaginal hysterectomy.

asterisk - for these procedures, antibiotics are given in addition to the recommended prophylaxis according to sensitivity

Procedures that do not require IE prophylaxis

- Dental procedures that do not involve bleeding from the gums or mucous membranes, e.g. treatment of caries above the level of the gums,
- loss of the first dentition,
- diagnostic cardiac catheterisation,
- endotracheal intubation,
- bronchoscopy with a flexible bronchoscope including biopsy*,
- endoscopic examination of the GIT including biopsy*,
- transesophageal echocardiography,
- cesarean section,
- in the absence of infection: uncomplicated labour, cervical dilatation and curettage, IUD insertion and removal*.

asterisk - except for patients at risk

Myocarditis

Myocarditis is a disease characterized by an inflammatory infiltrate of the cardiac muscle with necrosis or degeneration of adjacent myocytes. It is a clinically highly variable group, ranging from the most severe forms manifesting as severe heart failure or sudden death to a mild or asymptomatic course of the disease. Inflammatory diseases of the heart rarely affect the pericardium, myocardium or endocardium alone; more often, inflammation affects the whole heart, i.e. we speak of **pancarditis**.

Etiology

Infection

- Enteroviruses: (Coxsackie B viruses are the most common causative agent, the most severe course is described for serotypes B3 and B4), echoviruses are less common,
- influenza,
- adenoviruses,
- parvovirus B19,
- parotitis,
- EBV, CMV,
- hepatitis C virus,
- mycoplasmas,
- chlamydia,
- Borrelia,
- neisseria,
- leptospira,
- streptococci,

Autoimmunity

- SLE,
- JIA,
- Kawasaki disease,

Allergies

Idiopathic form.

Pathogenesis

Viral myocarditis is now considered to be a three-phase disease: a phase of viral infection, an autoimmune phase and, in genetically predisposed individuals, a phase with transition to dilated cardiomyopathy. These 3 phases may transition smoothly into each other with a difficult to distinguish transition. However, each phase differs in pathogenesis, diagnosis and, to some extent, therapeutic approach.

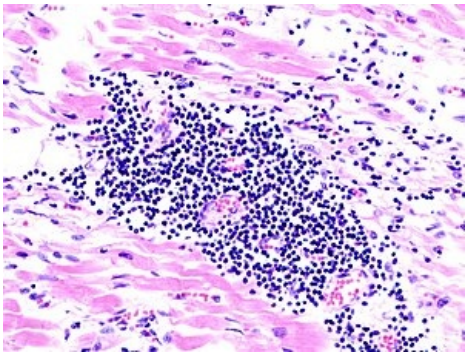
Phase 1 = viral phase.

Viruses enter the body via the gastrointestinal (enteroviruses) or respiratory tract (adenoviruses). The critical phase of viral infection is the entry of the viral genome into the myocytes. This is mainly facilitated by binding to the immunoglobulin receptor on the surface of the myocytes (CAR = coxsackie-adenovirus receptor). The virus

proliferates and the immune system is subsequently activated. Viral titres gradually decrease and antibody levels rise. However, the activation of the immune system can continue despite the elimination of the virus.

Stage 2 = autoimmune.

Fragments of viral proteins on the surface of myocytes are bound to newly synthesized HLA class I molecules. Monocytes release cytokines (IL-1, IL-6, IL-12 and TNF-alpha) that, among other things, activate T-lymphocytes and stimulate B-lymphocyte proliferation and differentiation and antibody production. The formation of the antigen-antibody complex activates the complement system. IL-2 has an activating effect on cytotoxic T-lymphocytes, which preferentially destroy myocardial cells with fragments of viral proteins. Naturally cytotoxic NK cells are activated by interferon and specifically destroy only virus-infected myocytes. Both T-lymphocytes and NK cells thus reduce the number of contractile cells.


Microscopic picture of viral myocarditis

Stage 3 = dilated cardiomyopathy.

Cytokines activate enzymes such as gelatinase, collagenase or elastase, simultaneously stimulating fibroblast activity and leading to fibrosis associated with dilated cardiomyopathy.

Clinical picture

Diagnosis is often difficult.

- Suspicion of myocarditis is always aroused by unexplained heart failure, especially with a history of ongoing or previous viral illness with fever.
- The course of the disease can vary widely, from subtle tachycardia in febrile illness to a severe fulminant course with circulatory collapse and shock.
- In children and adolescents with a fulminant course, we often find an indication of previous physical exertion at the onset of the infection.

Anamnestic findings include fatigue, pallor, crankiness or apathy.

- Some children may complain of abdominal pain, decreased appetite, vomiting.
- Dyspnea and tachypnea are present even with little physical exertion.
- Muscle pain or reduced muscle tone is an important symptom.
- Children often have fevers and tachycardia, which does not correspond to the level of body temperature and is also present during sleep.
- At the heart, muffled echoes and galloping are heard in severe forms of myocarditis.
- A systolic murmur at the tip is heard in significant mitral regurgitation.
- At the bases of the lungs, wheezes are heard, congestion with hepatomegaly, leaky eyelids and sometimes perimaleolar edema are found.
- The skin in the periphery is cool, the peripheral pulsations less palpable (threadlike).

The fulminant course is manifested by a shock state accompanied by signs of heart failure, cardiac rhythm disturbances (SVT, ventricular extrasystoles, atrial fibrillation, AV blocks), impaired consciousness and vomiting.

- The most severe course is in neonates and infants.
  - Here there is often a fulminant onset with pulmonary edema and cardiogenic shock.
- A sudden onset of severe heart failure to cardiogenic shock is typical, with the appearance of pulmonary oedema, large cardiomegaly, and left ventricular dysfunction.
- Symptomatology develops after a "common" virosis.
- "Large-cell" myocarditis has a poor prognosis with progression and death within 18 months unless cardiac transplantation is performed.

Diagnostics

Laboratory examination

Myolysis of the heart muscle in the acute stages of the disease is confirmed by the detection of elevated levels of cardiac creatine kinase MB = CK-MB mass and troponin. LDH and transaminase levels are also elevated.

Finding the viral agent is usually difficult. Serological examination or analysis of endomyocardial biopsy material by PCR (a variant of rt-PCR to detect enteroviruses) is an option.

Immunological testing assesses signs of activation of the body's cellular response or T-lymphocyte subpopulations. The humoral immune response is assessed by determining total IgG, IgA and IgM levels and by testing for specific autoantibodies such as anti-alpha-myosin. These autoantibodies are usually secondary.

ECG

Myocarditis is characterised by **low ECG waveform voltages** in all leads and **T-wave opacification or inversion**. There is a strikingly small to absent Q oscillation in the left precordium. Depression of ST segments and enlargement of the QRS complex are sometimes evident. Characteristic of myocarditis are **cardiac rhythm**

disturbances = atrial or ventricular extrasystoles, ventricular tachycardia, AV blockade (AV blockade of grade III has been described in borreliosis, rubella, coxsackie and RS viruses). The ECG changes during the course of the disease and therefore its dynamics should be monitored.

A changing ECG curve over time is typical of acute myocarditis!

Echocardiography

Echocardiographic examination will demonstrate a disturbance in cardiac function, which may be only regional. The thickness of the left ventricular wall may change on repeated examinations depending on when the disease was detected. The acute phase is characterised by tissue oedema, which is manifested by an increase in **left ventricular wall** thickness. In the later stages, dilatation of the left ventricle occurs. Secondary mitral regurgitation is a relatively common finding. Rarely, mural thrombi may be seen in the left ventricle.

Cardiac biopsy

Cardiac biopsy **is not routinely used** for the diagnosis of myocarditis. This is because of the risk of the procedure and the relatively low yield of the test. Cardiac biopsy is indicated in patients with a subacute or chronic form of the disease to differentiate it from dilated cardiomyopathy before deciding whether to initiate immunosuppressive therapy.

An endomyocardial biopsy is performed for which the so-called Dallas criteria, which represent a uniform histological grading, have been developed. According to the histology, active myocarditis is defined by the presence of an inflammatory infiltrate as well as necrosis. Recently, immunocytochemical methods using monoclonal antibodies have been used to detect different types of lymphocytes in the myocardium.

Other methods

X-ray demonstrates nonspecific cardiomegaly, and there may be normal findings at baseline. Myocardial scintigraphy using gallium radioisotope can also be used.

Differential diagnosis

Various causes of circulatory failure can mimic acute myocarditis. Heart failure in the newborn can be caused by hypoxia, hypoglycemia, metabolic defects, and severe sepsis. Myocarditis may accompany febris rheumatica, systemic connective tissue diseases, and other autoimmune diseases. Anomalous left coronary artery spacing from the pulmonary artery is associated with severe circulatory failure in myocardial ischemia. Patients with endocardial fibroelastosis, morbus Pompe or medionecrosis of the coronary arteries may also have similar symptoms to acute myocarditis. Many other cardiac VVVs, such as aortic coarctation or aortic stenosis, present with severe heart failure. The diagnosis is reliably determined by echocardiography.

Therapy

Therapy is mainly **symptomatic**, its extent and intensity depends on the severity of the patient's condition and complications accompanying the disease.

The aim of treatment of **acute heart failure** is to maintain sufficient cardiac output, i.e. sufficient tissue perfusion. In acute conditions with significant left ventricular dysfunction, we choose inotropic therapy, usually dopamine or a combination of dopamine + dobutamine. Vasodilator therapy is important to reduce left ventricular work. In severe heart failure that does not respond to conventional resuscitation therapy, ECMO is indicated.

In the treatment of **chronic heart failure**, digoxin is still the drug of choice in children. However, especially in the acute phase of the disease, there is an increased sensitivity of the myocardium to digoxin, which can manifest itself in severe cardiac rhythm disturbances. Therefore, offensive digoxin therapy is inappropriate. Treatment of heart failure includes ACE inhibitors (captopril 0.1 to 1 mg/kg for doses up to 8 h p.o.) and diuretics. Captopril reduces afterload and simultaneously serves as a free oxygen radical scavenger, thereby reducing the extent of myocardial necrosis. In chronic phases of the disease after the transition to dilated cardiomyopathy, gradually increasing doses of β-blockers (carvedilol) have recently been used.

Heart rhythm disturbances are a serious complication of myocarditis, worsening the prognosis, and must therefore be treated intensively. In addition to its antiarrhythmic effects, amiodarone inhibits TNF-α and IL-6 production.

Antiviral therapy for viral myocarditis (ribavirin) in the acute phase of viremia reduces viral replication in the myocardium and reduces myocardial damage. Treatment with interferon γ in patients with myocarditis and proven adenoviral or enteroviral aetiology leads to improved left ventricular function. However, the limiting factor in this treatment is its effect only in the early phase of the disease; later administration is no longer of any significance. Some authors even warn against interferon, as it may promote an autoimmune response of the organism. In the acute phase of the disease, a beneficial effect on improving left ventricular function has been observed after administration of high doses of gamma globulins. Gamma globulin is administered at 2 g/kg in an infusion over 24 hours.

The effect of **immunosuppressive therapy** is equivocal. It was found that the treatment had a positive effect in patients with proven circulating cardiac autoantibodies and in the absence of the viral genome in the myocardium. Immunosuppressive therapy (prednisone, azathioprine, cyclosporine A) is usually initiated only in the subacute or

chronic phase of the disease and should be reserved for the autoimmune phase of myocarditis. Administration of immunosuppression early in the course of viral infection may worsen the course of the disease.

Prognosis

The prognosis of myocarditis is generally **uncertain**. Mortality is high in newborns with acute myocarditis, older children have a better prognosis. Prognosis is worsened by cardiac arrhythmias. It also depends on the improvement of myocardial function and the duration of its significant dysfunction. The longer the duration of dysfunction after the acute phase, the worse the long-term prognosis. Patients with fulminant myocarditis have a good long-term prognosis if they overcome the period of transient cardiac dysfunction.

Pericarditis

Pericarditis is an inflammatory disease:

- pericarditis,
- of the pericardial space and
- adjacent tissues of the heart and large vessels.

In childhood, acute viral pericarditis (Coxsackie group viruses, adenoviruses, influenza virus, herpes viruses, ECHO viruses and EB virus) are the most common; and purulent pericarditis secondary to bacterial sepsis is rarer. Pericarditis may also accompany general diseases such as rheumatic fever, autoimmune diseases, malignancies, renal failure, tuberculosis or mycotic diseases.

The disease typically has a sudden onset with high fever. The characteristic auditory finding is a pericardial friction murmur audible in systole and diastole and increasing with greater pressure of the phonendoscope on the chest. As the pericardial effusion progresses, it disappears and the heart sounds are remarkably quiet. The effusion may result in cardiac tamponade and sudden circulatory collapse. The picture of cardiac tamponade includes severe dyspnea, tachycardia and hepatomegaly, faint palpable pulsations in the periphery, weakening on inspiration (paradoxical pulse), hypotension with little systolic-diastolic differential. Pericarditis may result in adhesions of both pericardial sheets and constrictive pericarditis, but this is very rare in children.

Etiology

Etiology of pericarditis in children

Infection	Autoimmunity	Malignancy	Other
▪ mycoplasmas, ▪ chlamydia, ▪ borrelia, ▪ TB, ▪ Haemophilus influenzae, ▪ Staphylococcus aureus, ▪ enteroviruses, ▪ adenoviruses, ▪ influenza, ▪ parotitis, ▪ varicella, ▪ HIV, ▪ Candida, ▪ Aspergillus, ▪ Toxoplasma gondii.	▪ SLE, ▪ JIA, ▪ M. Kawasaki, ▪ Sarcoidosis, ▪ non-specific intestinal inflammation, ▪ rheumatic fever.	▪ leukemia, ▪ lymphomas.	▪ hypothyroidism, ▪ uremia, ▪ postpericardiotomy syndrome, ▪ trauma, ▪ circulatory failure.

Fibrous (dry) pericarditis is characterized by more or less large fibrin deposits on the pericardium.

- Usually, it is the initial stage of the development of exudative inflammation, in which effusion accumulates between the pericardial leaves.
- The fluid in the pericardium may be transudate, exudate, blood or pus.
- As a consequence of pericarditis, adhesions of both leaves may form in the pericardium, sometimes resulting in *constrictive pericarditis.*

Within the viral etiology, coxsackies, adenoviruses, influenza, herpes and echoviruses are the most common.

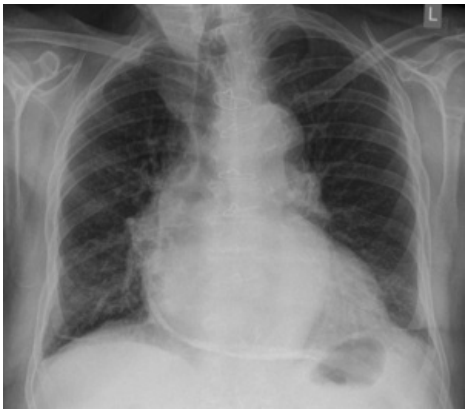
- Viral pericarditis is usually preceded by an upper respiratory tract infection or other viruses.
- The prognosis is usually good, but recurrences are common (up to 30% of patients).
- The course is usually shorter and milder.

Purulent pericarditis is a rare but life-threatening disease.

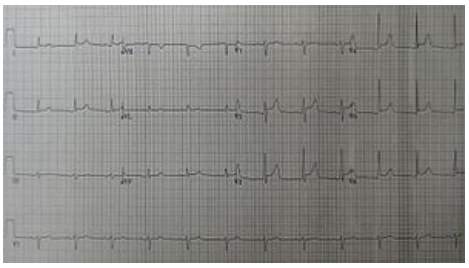
- The most common cause is secondary hematogenous dissemination in common bacterial diseases (pneumonia, meningitis, septic arthritis).
- The most common causative agents are *Staphylococcus aureus* and *Haemophilus influenzae* type b.
- Later, constrictive pericarditis may develop.

Pathogenesis

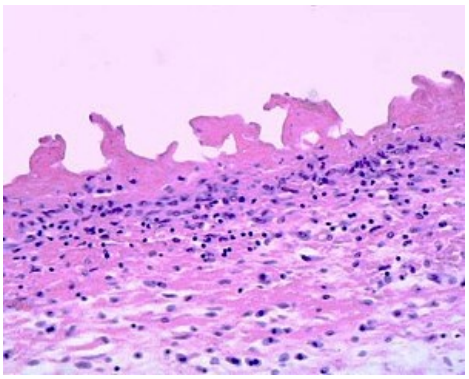
The pericardium is the thin covering of the heart and the proximal parts of the great vessels. There is a space between the visceral and parietal pericardium, which normally in an adult contains about 30 ml of lymph (facilitating movement of the heart in the pericardial sac). The effect of pericarditis on hemodynamics is the result of excessive fluid accumulation in the pericardial space or anatomical changes of the pericardium (it turns into a rigid unyielding shell - constrictive pericarditis). The accumulation of fluid in the pericardial space causes a rise in intrapericardial pressure, which decreases diastolic filling of the heart => decrease in cardiac output and CO/CI and decrease in coronary perfusion. Rapid accumulation of pericardial fluid can cause **cardiac tamponade** which is life threatening, even with a large volume of fluid may not lead to severe circulatory disturbances.


Skiagram showing pericarditis calcarea

In pericardial tamponade, several compensatory mechanisms are involved in pericardial tamponade, the most effective being an increase in heart rate (tachycardia compensates for the decrease in diastolic filling of the heart). *Pulsus paradoxus* is a common symptom of acute tamponade. It is characterized by a greater fall in systolic BP during inspiration than under physiological conditions, i.e. > 10 mmHg, at the same time we find a weakly filled peripheral pulse that weakens in inspiration and disappears. During inspiration, venous return to the right atrium and ventricle increases, but at the same time more blood accumulates in the lungs => paradoxical decrease in left ventricular output. Pulsus paradoxus is also found in constrictive pericarditis and status asthmaticus.


Pericarditis on ECG

Pulsus paradoxus is a common symptom of acute tamponade. It is characterized by a greater decrease in systolic BP during inspiration than under physiological conditions, i.e. > 10 mmHg, and at the same time we find a weakly filled peripheral pulse that weakens in inspiration and disappears.


Microscopic findings in fibrinous pericarditis

Clinical picture

- The onset of the disease is usually sudden with **high fever**.
- Cough and pain on breathing indicate concurrent pleural involvement.
- Fibrous pericarditis causes **pain behind the sternum** that shoots into the shoulder and behind the neck.
- Dyspnea is accompanied by an irritating cough.
- Auditory manifestation is a **pericardial friction murmur** audible in systole and diastole. The murmur is produced by displacement and friction of the inflammatory pericardial sheets during cardiac movements, and is loudest when standing and bending over. It resembles the crunching of frozen snow under a shoe. It intensifies with greater pressure of the phonendoscope on the chest. It fades as the fluid in the pericardium increases.
- Exudative pericarditis is manifested by **increasing dyspnea**. Auditory heart sounds are remarkably quiet and the flutter disappears.
- The liver is enlarged and swelling is often found.
- Cardiomegaly may compress the left lung lobe, which manifests as weakness and altered respiratory phenomena (Ewart's sign).

Cardiac tamponade

Rapidly arising effusion in the pericardium can cause so-called **cardiac tamponade**.

- The underlying haemodynamic disturbance is limited filling of the heart in diastole and increased central venous pressure.
- In advanced cases, cardiac output is reduced and circulatory collapse occurs rapidly.
- The main subjective symptom is pronounced **dyspnea**.
- On physical examination, we find dilatation of the jugular veins (in children, always limitedly visible), tachycardia, hepatomegaly.
- **Pulsus paradoxus and a decrease in systemic arterial pressure** with a small systolic-diastolic differential are late signs of cardiac tamponade, which can result in sudden cardiac arrest.

Clinical triad of critical cardiac tamponade: cyanosis, tachycardia and hypotension.

You can find more detailed information on the Cardiac Tamponade page .

Diagnostics

ECG and X-ray examination

ECG changes depend on the stage of the disease. Initially, we find **ST segment elevation** and a positive T wave, later the T wave becomes isoelectric and in the further course it inverts symmetrically. QRS complex voltages are low. In the recovery period, the described changes gradually normalize.

On X-ray, with pericardial effusion, the cardiac shadow is enlarged in both directions with a flattened left contour and a shortened and wide cardiac pedicle (the heart is "tent-shaped"). If there is no large pericardial effusion, the heart may be normal in shape and size.

Echocardiography

Fluid accumulation in the pericardium is demonstrated elegantly on echocardiography. Invasion (inherniation) of the free wall of the right atrium or even the right ventricle in massive pericardial effusion is a warning indirect sign of cardiac tamponade. In high-protein exudate, there are often distinct fluttering denser bands in the fluid corresponding to fibrinoid fibers.

We examine every child with cardiomegaly by echocardiography!

Laboratory examination

In pericarditis of unclear etiology, laboratory examination are aimed at demonstrating a viral or bacterial etiology. In addition to standard examination, we collect hemocultures and serum for virological investigations (PCR, serology). At the same time, we have to exclude an autoimmune origin of pericarditis by autoimmune markers. Fluid accumulation in the pericardium may also occur secondary to malignant disease in the mediastinum. In this case, a CT scan of the mediastinum is indicated.

We always think of pericarditis when a febrile child has chest pain!

Therapy

- Treatment of viral pericarditis is **symptomatic**, bed rest and NSAIDs (e.g. ibuprofen 10 mg/kg for doses 3 times a day) are recommended. Corticosteroids are added if treatment fails after 48 hours. With significant effusion, pericardial drainage is indicated.
- Treatment of purulent pericarditis usually requires surgical drainage of the pericardium and intravenous antibiotic therapy. Potentiated aminopenicillins or III generation cephalosporins for 3 to 4 weeks are most commonly chosen.
- Pericardiocentesis is indicated in urgent cases with signs of cardiac tamponade with severe alteration of circulation, but is usually ineffective to definitively eliminate the effusion, due to its considerable viscosity because of its high protein content.

Pericardial drainage

In large pericardial effusions, especially when cardiac tamponade is imminent, therapeutic pericardial drainage is indicated. Pericardiocentesis is performed in children under general anaesthesia with echocardiographic control and continuous ECG monitoring. In the elevated position, a pig tail catheter is inserted from the subxiphoid approach using a puncture technique. The second option is to introduce a chest drain from the subxiphoid incision. After the initial evacuation of fluid to release the cardiac tamponade, the remaining effusion is drained slowly while replenishing the blood volume. In this way, severe hypotension from relative hypovolemia can be avoided during redistribution of circulating blood volume after tamponade release. The obtained punctate is sent for microbiological and virological examination and for biochemical analysis. Total protein is determined and lipid electrophoresis is performed to demonstrate the presence of chylomicrons when chylopericardium is suspected.

See the Pericardial Punctures (Pediatrics) page for more information

Constrictive pericarditis

Constrictive pericarditis is very rare in children, most often coming in association with TB. Clinically it presents with exertional dyspnea, general weakness and fatigue, edema, chest pain and sometimes syncope. Critical to the diagnosis is the disparity between marked circulatory failure, poor physical findings on the heart and a small heart on chest X-ray. On ECG, there may be P wave changes, decreased voltages of QRS complexes, and T wave that are flattened to inverted. Echocardiography can sometimes show thickening of the pericardium, indirect signs are atypical septal movement in diastole, inferior vena cava dilatation and enlarged atria. Therapy is pericardiectomy.

Postpericardiotomy syndrome

Postpericardiotomy syndrome is a nonspecific reaction of the pericardium, epicardium, and pleura, manifested by generalized inflammatory manifestations and increased pericardial and pleural effusions. It comes days but also weeks after cardiac surgery. Clinically, it presents with subfebrile chest pain, abdominal pain and sometimes vomiting. Lab shows elevation of both erythrocyte sedimentation rate and CRP. Treatment is NSAIDs, corticosteroids in case of failure. Prognosis is good.

Links

Sources

- HAVRÁNEK, Jiří: *Srdeční záněty*. (managed)
- LEBL, J, J JANDA and P POHUNEK, et al. *Clinical pediatrics.* 1st edition. Galén, 2012. 698 pp. 510-512. ISBN 978-80-7262-772-1

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