Gerd Herold and colleagues

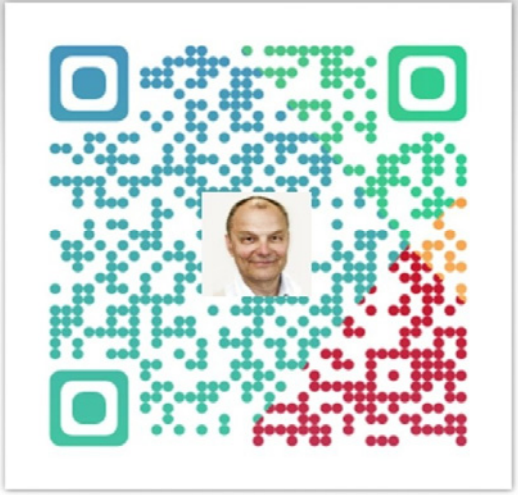
INTERNAL MEDICINE

second edition

Vol. I+II

A lecture oriented systematic and accurate representation of the complete topic catalogue for the medical examination for physicians

Systematically the complete topics of internal medicine · Accentuation of "pitfalls" which are important for exams · Taking account of the most important German and American textbooks · Therefore also recommended for the American ECFMG examination · Tables of biochemistry and haematology reference intervals with SI units · Taking account of "evidence based medicine" · ICD-10 codes within the text and the index



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Remark: ICD 10 code version 1.3 has been employed for the index. Since in the current edition ICD 10 code version 2.0 was used, different code numbers may have been assigned to indexed items!

Be careful about reading health books. You may die of a misprint. (Mark Twain)

Abbreviations

AAA	Abdominal aortic aneurism
AB	Antibodies
ACE	Angiotensin converting enzyme
ADB	Anti-Desoxyribonucleotidase B
ADH	Antidiuretic hormone
AET	Aetiology
AF	Atrial fibrillation
AG	Antigen
AIDS	Acquired Immunodeficiency Syndrome
AIHA	Autoimmune haemolytic anaemia
AN	Autonomic neuropathy
ANA	Anti nuclear antibodies
ANCA	Anti neutrophile cytoplasmatic antibodies
ANP	Atrial natriuretic peptide
A.O.	And others
APC	Activated Protein C
APS	Antiphospholipid syndrome
APPROX	Approximately
ARDS	Adult respiratory distress syndrome
ARF	Acute renal failure
ASAP	As soon as possible
ASD	Atrial septum defect
ASL	Antistreptolysin
AT	Antithrombin
ATP	Adenosine Triphosphate
AXR	Abdominal X-ray
BBB	Bundle Branch Block
BMI	Body Mass Index
BMT	Bone marrow transplant
BNP	brain natriuretic peptide
BP	Blood pressure
BU	Bread unit
BW	Body weight
C	Celsius
CA	Carcinoma
ca.	Circa
CDC	Centres for disease control
CH	Carbohydrate
CHD	Coronary heart disease
CI	Contraindications
CK	Creatine Kinase
CL	Clinical picture
CMV	Cytomegalovirus
CNP	Type C natriuretic peptide
CNS	Central Nervous System
CO	Complications
CON	Contagiousness
COPD	Chronic obstructive pulmonary disease
COX	Cyclooxygenase
CRF	Chronic Renal Failure
CRP	C-reactive protein
CSE	Cholesterol Synthesis Enzyme
CSF	Cerebrospinal Fluid
CT	Computer tomography
CU	Carbohydrate unit
CVI	Chronic venous insufficiency
CVP	Central venous pressure
CXR	Chest X-ray
DD	Differential diagnosis
DEF	Definition
DHD	Dengue haemorrhagic fever
DHS	Dengue haemorrhagic shock
DI	Diagnosis
DIC	Disseminated intravascular coagulation
DNA	Deoxyribonucleic acid
DSA	Digital subtraction angiography
DVT	Deep vein thrombosis
EBV	Epstein Barr Virus
ECF	Extracellular fluid
ECG	Electrocardiogram
EEG	Electroencephalogram
EF	Effects
EF	Ejection Fraction
EHEC	Enterohaemorrhagic E. coli
ELISA	Enzyme linked immunosorbent assay
EN	Enteral nutrition
ENT	Ear Nose & Throat
EP	Epidemiology
ESP	Especially
ESR	Erythrocyte Sedimentation Rate
ET	Etiology
EU	European Union
F	Female
FFP	Fresh Frozen Plasma
FH	Family History
FUO	Fever of unknown origin
GBM	Glomerular basement membrane
GFR	Glomerular filtration rate
GI	Gastrointestinal
GN	Glomerulonephritis
HBV	Hepatitis B Virus
HCT	Haematocrit
HI	Histology
HIT	Heparin induced thrombocytopenia
HIV	Human Immunodeficiency Virus
HLT	Half life time
HPV	Human Papilloma Virus
HSV	Herpes Simplex Virus
HUS	Haemolytic uraemic syndrome
HX	History
IA	Interaction
IBS	Irritable bowel syndrome
ICA	Internal carotid artery
ICD	Implantable Cardioverter - Defibrillator
ICF	Intracellular fluid
ICP	Intracranial pressure
ICU	Intensive care unit
IFAT	Indirect immunofluorescence antigen test
IG	Immunoglobulin
IHA	Indirect Haemagglutinin test
i.m.	Intramuscular
INC	Incidence
IND	Indication
INR	International normalised ratio
ISF	Interstitial fluid
ITP	Idiopathic thrombocytopenia
IU	International units
I.V.	Intravenous
IVF	Intravascular fluid
LAB	Laboratory tests
LAS	Lymphadenopathy syndrome
LBBB	Left Bundle Branch Block
LDH	Lactate Dehydrogenase
LDL	Low density lipoprotein
LDV	Lymphocyte doubling time
LMWH	Low molecular weight Heparin
LOC	Localisation
M	Male
MDS	Myelodysplastic syndrome
MI	Mentzer index
MI	Myomyocardiac infarction
MIO	Million
MM	Multiple myeloma
MOA	Mode of action
MRI	Magnet resonance imaging
MW	Molecular weight
NK (cells)	Natural killer (cells)
NSAID	Non steroidal anti-inflammatory drug
OAC	Oral anticoagulation
OAD	Occlusive atherosclerotic disease
OCC	Occasionally
OCC	Occurrence
OD	Overdose
PA	Pulmonary artery
PAT	Pathogen
PAT	Pathology
PCR	Polymerase chain reaction
PE	Pulmonary embolism
PEP	Post exposure prophylaxis
PET	Positron emission tomography
PFO	Persistent foramen ovale
PG	Pathogenesis
PI	Protease inhibitor
PID	Pelvic inflammatory disease
PM	Pacemaker
PMC	Pseudomembranous Enterocolitis
PMH	Past Medical History
PN	Parenteral nutrition
PNH	Paroxysmal nocturnal haemoglobinuria
P.O.	Per os
POSS	Possibly
PPC	Phenprocoumon
PPH	Pathophysiology

PPSB	Prothrombin proconvertin Stuart-Prower factor antihaemophilic factor B
PRG	Prognosis
PRO	Prophylaxis
PTCA	Percutaneous transluminal coronary angioplasty
PTH	Parathyroid hormone
PTS	Post Thrombotic Syndrome
PTT	Prothrombin time
RA	Rheumatoid arthritis
RBBB	Right Bundle Branch Block
RES	Reticular Endothelial Syncythium
RF	Rheumatoid factor
RNA	Ribonucleic acid
RS	Raynaud's Syndrome
RV	right ventricular
S.C.	Subcutaneous
SE	Side effects
SIADH	Syndrome of inadequate ADH secretion
SK	Streptokinase
S.L.	sublingual
SLE	Systemic lupus erythematosus
SOB	Shortness of breath
SPECT	Single Photon Emission Computed Tomography
SR	Slow release
SR	Sinus rhythm
ST	Stage
STD	Sexually transmitted disease
SU	Sulfonyl urea
SVT	Supraventricular Tachycardia
SYM	Symptoms
SYN	Synonym
TAA	Thoracic aortic aneurism
TCA	Tricyclic antidepressants
TEA	Thrombendarteriectomy
TEE	Transoesophageal echocardiography
TH	Therapy
THR	Total hip replacement
TIA	Transitory ischaemic attack
TOA	Thrombangiitis obliterans
TOS	Thoracic Outlet Syndrome
TPHA	Treponema Pallidum Haemagglutinin
TPN	Total parenteral nutrition
TSH	Thyroid stimulation hormone
TURP	Transurethral resection of the prostate
UFH	Unfractioned Heparin
URTI	Upper Respiratory Tract Infection
US	Ultrasound
UTI	Urinary tract infection
UV	Ultraviolet
VF	Ventricular Fibrillation
VT	Ventricular Tachycardia
VUR	Vesico-ureteric-renal reflux
VV	Varicose veins
VZV	Varicella Zoster Virus
WHO	World Health Organisation
Y	Year

Find more medical abbreviations at *www.medizinische-abkuerzungen.de*

Find more general abbreviations at *www.acronymdb.com*
www.chemie.fu-berlin.de/cgi-bin/acronym

II. C A R D I O L O G Y

Internet information: Deutsche Gesellschaft für Kardiologie [*German Cardiology Association*]: *www.dgkardio.de*

Course of a cardiological examination

I. Medical History

II. Clinical Examination

1. Inspection

2. Palpation of the precordial thoracic area and pulses

Five pulse states:

- Frequency: rapid - slow
- Regularity: regular - irregular: respiratory arrhythmia
  premature ventricular beats (extrasystoles)
  absolute arrhythmia
- Strength: hard (high systolic pressure)
  soft (low systolic pressure)
- Amplitude: large (high) - small (diminished)
- Celerity (speed of upstroke): rapid - slow

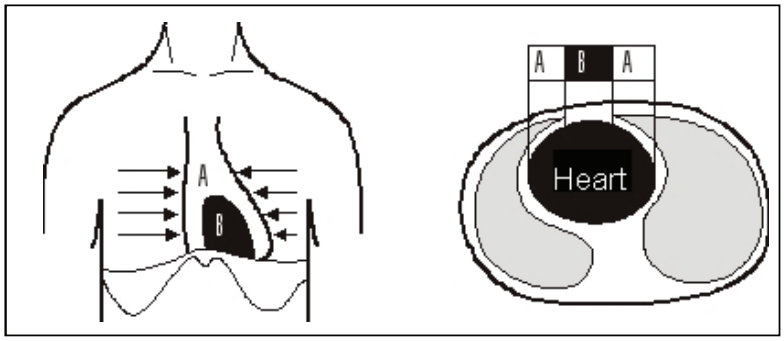
In cases of high pulse rate and normal blood pressure, the pulse upstroke will be rapid and the amplitude high; in cases of volume deficiency, however, the pulse upstroke will be rapid, but the amplitude will not be high. In aortic insufficiency with normal heart rate, the pulse upstroke is rapid and the amplitude high (due to the high blood pressure amplitude).

3. Cardiac percussion:

Determination of the pulmonary-liver border; this can also be used to some extent on the left side.

A) Determination of relative cardiac dullness by percussion from the outer cardiac border inwards.

B) Determination of absolute cardiac dullness by percussion from inside (at the sternum) and proceeding outwards.



Severe obesity and emphysema may make percussion impossible.

Cardiac percussion must be regarded as imprecise.

4. Cardiac auscultation with a stethoscope:

High-pitched frequencies are better heard with the membrane of the stethoscope while low-pitched frequencies are better heard with the bell and no membrane.

Disadvantage of auditory auscultation compared to phonocardiography:

· Auditory discrimination of low frequencies is poor (especially poor for low-pitched mitral murmurs).
· Precise auditory determination of the timing of heart sounds is difficult (e.g. no precise determination of mitral valve opening snap).

Advantage of auditory auscultation:

· Recognition of murmur configuration ("melody")
· Simultaneous registration of all frequencies

Except for pulmonary valve disorders, cardiac murmurs are best heard at the end of the patient's expiration.

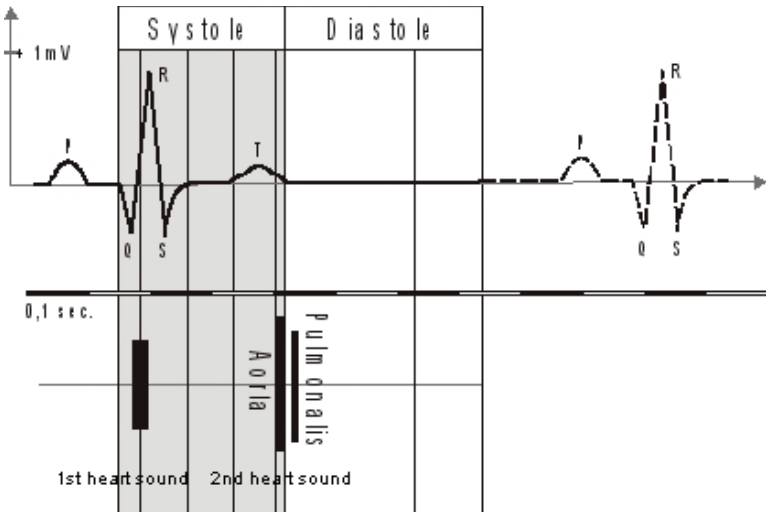
Classification of heart sounds (HS):

A) Valve closure sounds:

The 1st heart sound (S1) corresponds to the closure of the mitral and tricuspid valves and ventricular contraction (contraction sound) and appears 0.02 – 0.04 seconds after the beginning of the QRS complex.

The 2nd heart sound (S2), which is shorter and clearer than the 1st heart sound, is caused by the closure of the aortic and pulmonary valves (arterial valves). The 2nd heart sound occurs at the end of the T-wave; it is best heard in the 2nd intercostal space (ICS) parasternal right (aortic valve) and left (pulmonary valve).

Increased pressure in the pulmonary circulation results in a louder pulmonary valve component; an increase in pressure in the systemic circulation results in accentuation of the aortic component.



• Physiological splitting of the 2nd heart sound arises from the non-simultaneous closure of the aortic and pulmonary valves; the aortic sound normally occurs before the pulmonary sound. With deep inspiration, a physiological splitting of up to 0.08 seconds can be heard and is usually only audible under these conditions (due to negative thoracic filling pressures during inspiration and thus a temporary increased inflow into the right ventricle during diastole).

• Increased (pathological) splitting of the 2nd heart sound occurs with right bundle-branch block.

• Fixed (independent of respiration) splitting of the 2nd heart sound with
- Atrial-septal defect
- Pulmonary artery stenosis

• Paradoxical (reversed) splitting of the 2nd heart sound (first pulmonary, then aortic segment) with
- severe aortic and aortic isthmus stenosis
- left bundle-branch block, cardiac pacemaker with right ventricular stimulation

Di: Simultaneous recording of carotid pressure pulse + phonocardiogram: The aortic component of the S2 normally occurs 0.04 seconds before the incisure of the pulse curve.

B) Valve opening snap: Triggered by the sudden stop of the opening movement of an AV valve which has become stuck together:
- Opening snap of mitral stenosis (0.04 – 0.12 seconds after the aortic valve closing sound)
- Opening snap of tricuspid valve stenosis (very rare)
- Opening sound of mitral valve prosthesis

C) Ejection clicks ("ejection clicks") arise from the sudden stop of the opening movement of a stenosed semilunar valve.

D) Diastolic ventricular filling sounds are physiological in children and adolescents
- 3rd heart sound = different, quiet, low-frequency sound over the mitral valve area ~ 0.15 seconds after the 2nd HS as the result of "diastolic overloading" in cases of mitral regurgitation, heart failure and hyperthyroidism.
- 4th heart sound = soft, low-frequency atrial sound prior to the S1; occurs relatively rarely in cases of elevated ventricular pressure

E) Systolic click: e.g. in mitral valve prolapse

Classification of heart murmurs:

Murmurs arise from turbulence: a) forward (stenosis)
b) backwards (insufficiency)

Grading:

-Loudness of heart murmurs:
- 1/6: Can be heard only with special effort
- 2/6: Quiet, but immediately audible
- 3/6: Loud, no thrill
- 4/6: Murmur with thrill
- 5/6: Audible if only the edge of the stethoscope touches the skin
- 6/6: Audible from a distance without a stethoscope

- Punctum maximum, conduction
- Frequency
- Relationship of the heart sounds to each other (palpation of the carotid pulse)
- Type of murmur:

decrescendo / crescendo-decrescendo / pansystolic/holosystolic / crescendo type

A) Systolic murmurs

1. AV valve regurgitation (decrescendo or pansystolic/holosystolic, immediately following S1):
   a) Usually seen in organic mitral regurgitation
   b) More rarely observed in tricuspid regurgitation (relative tricuspid regurgitation as a result of overextension of valve ring associated with right ventricular dilatation).
2. Stenosis of the semilunar valves or ventricular outflow tract:
   (fusiform, distinct from S1)
   a) Aortic stenosis (with conduction of murmur into the carotids)
   b) Pulmonary valve stenosis
   c) Hypertrophic obstructive cardiomyopathy (HOCM)
3. Aortic isthmus stenosis (auscultation between the shoulder blades)
4. Septal defects (pansystolic/holosystolic or diamond-shaped)
5. Accidental and functional systolic heart murmurs (HM)
   Def.: Inorganic murmurs in a clinically healthy heart with no disease significance
   - Accidental HM: No structural or haemodynamic changes, usually observed in children and adolescents (prevalence > 50%).
   - Functional HM: Resulting from hypercirculation, elevated cardiac output or altered blood viscosity (e.g. in hyperkinetic heart syndrome, hyperthyroidism, fever, anaemia, bradycardia, pregnancy).

   Di: Low-frequency, crescendo-decrescendo murmur

   Notes: Diastolic murmurs are always organic.

   - Predominantly proto- to mesosystolic, always end before S2 (never holosystolic)
   - Quiet: Usually ≤ 2/6, i.e. no thrill
   - punctum maximum (p.m.) usually over the pulmonary valve, more rarely over the left ventricular outflow tract or over the apex
   - Lack of conduction ("they disappear where they arise")
   - Typically, reduction in loudness when sitting/standing or during inspiration and increase in loudness during strain.
   - Change in murmur:
     - when position is changed
     - during strain/exertion
     - at different times in the respiratory cycle
   - Normal echocardiogram

B) Diastolic murmurs

1. Stenosis of the AV valves (almost always mitral stenosis)
2. Functional AV valve murmur associated with augmented blood flow (e.g. during AV valve regurgitation)
3. Semilunar valve regurgitation
   a) Aortic regurgitation (due to organic valve defects)
   b) Relative pulmonary valve regurgitation (due to overextension of the valve ring in pulmonary hypertension)

C) Continuous systolic-diastolic ("machine gun") murmurs:

due to a shunt connection between a high and low pressure system:
- Patent ductus arteriosus
- Aortopulmonary window, ruptured aneurysm of the Valsalva sinus
- Arteriovenous fistulas (pulmonary angioma, post-traumatic)
- Coronary artery fistulas

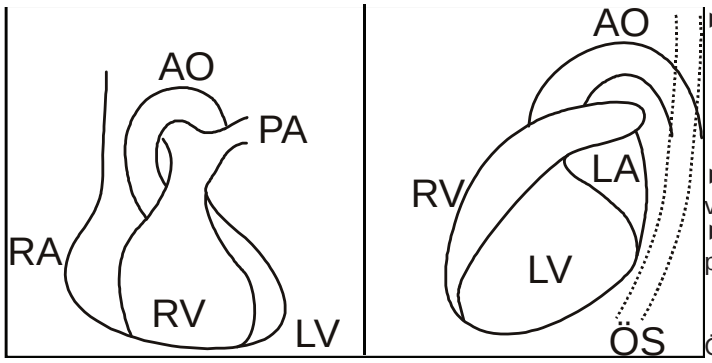
III. Non-Invasive Cardiac Tests

1. Blood pressure measurement, long-term blood pressure measurement
2. Electrocardiography
   a) Resting electrocardiogram (ECG)
   b) Exercise ECG (treadmill stress testing), main indications:
      · Coronary artery disease (diagnosis + determination of severity)
      · Cardiac arrhythmias (behaviour under stress)
      · Monitoring of blood pressure behaviour
      · Evaluation of capacity
   c) Long-term ECG: Continuous ECG monitoring and recording for at least 24 hours
      Main indications: detection of (intermittent) cardiac arrhythmias
   d) Event recorder → 2 recording methods:
      - Real Time Mode: When cardiac symptoms occur, the patient places the device on the chest and presses a recording button; the ECG recording begins after that.
      - Loop Mode: Continuous ECG recording with temporary storage for a certain time span. If the patient presses the recording button, the ECG taken before and after pressing the button is saved. When used with a cell phone, telemedical transmission of "events" (rhythmic disturbances) to a service centre is also possible. From there, it is forwarded to cardiologists.
   e) Impedance cardiography: Non-invasive measurement of stroke volume and cardiac output

3. Imaging diagnostics:

- Echocardiography
  - ▶ One-dimensional "time-motion" process } anatomy + function of the heart
  - ▶ Two-dimensional sector echocardiography }
  - ▶ Colour-coded duplex sonography:
    - Morphological assessment of heart and valves
    - Assessment of pressure gradients in stenoses (continuous wave (CW) Doppler)
    - Assessment of regurgitation across incompetent cardiac valves
    - Assessment of shunt flow across ventricular septal defects
  - ▶ Transoesophagel echocardiography (TEE): Optimal imaging of the heart (e.g. for the detection of thrombi or for assessing defects)
  - ▶ 3D echocardiography

- X-ray diagnostics



- ▶ Teleradiography of the heart (2 m) in 2 views: posterior - anterior + left lateral; for delimitation of the oesophagus from the left atrium, combination of the lateral image with oesophageal transit study.
- ▶ Cardio CT and dual-source CT: Assessment of valvular stenoses and regurgitation
- ▶ Cardio MRI: Coronary vessels (CT), myocardial perfusion (MRI)

ÖS = oesophagus

  - ▶ Electron beam tomography (EBT): Ultra-fast tomography method with an image refresh rate of up to 34 images/sec → visualization of anatomy + function of heart. Larger coronary arteries and bypasses can be imaged, especially calcifications in the coronary arteries; no assessment of the degree of stenosis or of the entire coronary system.

- Nuclear medicine examination procedures:
  - ▶ Myocardial perfusion scintigraphy with ^{201}thallium
    - · Enhanced activity in functional myocardium
    - · Reversible reduction in activity in ischaemic myocardium (e.g. in the context of ergometric strain)
    - · Irreversible loss of activity in necrotic and fibrotic myocardium
  - ▶ Internal cardiac scintigraphy (radionuclide ventriculography) mit ^{99m}technetium albumin: Diagnostic accuracy is similar to that of echocardiography.
  - ▶ Positron emission tomography (PET)
    Assessment of myocardial metabolism using suitable tracer substances → differentiation of normal, ischaemic and fibrotic tissue.

IV. Invasive Diagnostic Methods

The low risk of invasive diagnostics should always be weighed against the gain in information and the therapeutic consequences.

- ▶ Right-sided cardiac catheterization: As a result of the high diagnostic value of colour duplex sonography, right heart catheterization is still only used to answer specific questions. Pressure measurement in the right atrium/ventricle + pulmonary circulation + indirect measurement of pressure in the left atrium (pulmonary capillary wedge pressure = PCWP), wherein the tip of the catheter is washed into a small branch of the pulmonary artery and closes it.
  Pressure values: The pulmonary capillary closing pressure (PCP) usually correlates with the left ventricular end-diastolic pressure (LVEDP). 2 exceptions: Mitral stenosis (PCP > LVEDP) and acute aortic regurgitation (PCP < LVEDP). The central venous pressure (CVP) correlates with the right ventricular end-diastolic pressure (RVEDP).
  Normal values at rest:
  LVEDP: 5 - 12 mmHg - PCWP: < 15 mmHg
  RVEDP: 2 - 7 mmHg - CVP: 4 - 10 cm H20 (= 3 - 8 mmHg)
  Cardiac output (CO) - with respect to the body surface area = cardiac index (CI) - lower normal limit at rest > 2.5 l/min/m^2
- ▶ Left heart catheterization with probing of the heart and vessels close to the heart, intracardiac and extracardiac pressure measurement, recording of cardiac output and ejection fraction, shunt volumes, valve opening surfaces and other parameters, angiocardiography and coronary angiography. Main indication is the clarification of the question as to whether invasive therapeutic or surgical interventions are necessary (e.g. in coronary heart disease or defects)
- ▶ Electrophysiologic examinations with intracardiac mapping and programmed stimulation for cardiac arrhythmias.
- ▶ Myocardial biopsy for the clarification of cardiomyopathies
- ▶ Intracoronary artery angioscopy, Doppler and ultrasound examination for special diagnostic situations in patients with coronary artery disease

DISEASES OF THE ENDOCARDIUM

Def.: Chronic or acute inflammation of the endocardium; usually as endocarditis of the heart valves (valvular endocarditis), actually on the closing edge of a valve (and frequently as the cause of heart valve failure), but also in the area of the atrial and ventricular walls (parietal endocarditis), tendinous cords and papillary muscles.

Aet.: 1. Infectious endocarditis: Bacterial and mycotic endocarditis
2. Non-bacterial endocarditis: forms that can be attributed to antigen-antibody reactions and immune complexes; e.g. rheumatic endocarditis, Libman-Sacks endocarditis in systemic Lupus erythematodes, fibroplastic parietal endocarditis (Löffler's endocarditis); Endocardial fibrosis of the right heart in carcinoid heart disease (Hedinger syndrome)
3. Mixed form (e.g. bacterial endocarditis caused by non-bacterial endocarditis)
4. Endocardial-myocardial fibroses: Rarely occurring in the tropics; like constrictive pericarditis, these lead to the impediment of ventricular filling. AV valves often affected (tricuspid and mitral regurgitation).
5. Drug induced changes of the cardiac valves: Pergolid and cabergolin (Parkinson medication with dopaminergic effect) may cause fibrotic cardiac valve damage which might result in cardiac insufficiency. Ecstasy (MDMA) as well may cause heart valve changes.

INFECTIOUS (BACTERIAL) ENDOCARDITIS (IE) [I33.0]

Internet-infos: *www.endocarditis.org; www.dgk.org; www.p-e-g.de*

Def.: Septic disease caused by an infectious focus in the area of the endocardium or heart valves with the following cardinal symptoms: fever, heart murmur, bacteraemia, splenomegaly, embolisms. If untreated, the prognosis is usually bad.

Ep.: Incidence circa 3/ 100,000/ year in Western Europe

PPh.: With necrosis (ulcerative endocarditis) and fibrin deposits (polypoid endocarditis) involving bacterial (rarely mycotic) inflammation of the heart valves. Most frequently affected are the mitral and/or aortic valves. If very virulent pathogens are washed into the venous system (indwelling venous catheter, "intravenous drug abusers"), the right heart valves can also be affected. This usually results in valve regurgitation, so that a valve replacement is often necessary later on.

Aet.: 1. Staphylococci: about 45 - 65%
2. Streptococci: about 30%
3. Enterococci, gram-negative bacteria: about 10%
4. Rare pathogens: e.g. Coxiella burneti, Chlamydia, Mycoplasms, Legionellae and pathogens of the HACEK group (Haemophilus influenzae, Actinobacillus, Cardiobacterium, Eikenella and Kingella)
5. Fungi: about 1%
6. In 10% of patients, the pathogen cannot be isolated (blood culture negative).

While the frequency of streptococcal endocarditis is decreasing, cases of endocarditis caused by Staphylococci and rarer pathogens (including fungi) are increasing, especially due to the use of prosthetic materials in medicine (venous catheters, pacemakers, heart valves, endoprosthetics and others), also by the increase in the use of intensive medical measures. Drug addicts (intravenous drug abusers) are another risk group.

Especially methicillin sensitive staphylococcus aureus branches, various species of streptococci and enterococcus faecalis are to be expected in the native valve endocarditis and in the late endocarditis after balloon valvuloplasty. In the early endocarditis after valve replacement often staphylococcus aureus branches, coagulase negative staphylococci and gram-negative pathogens are found.

History: 60% of all patients with Streptococcus bovis endocarditis have colon tumours (polyps, carcinomas) ➔ perform colonoscopy in the latency period!

Prg.: Previous damage to the heart (endothelial damage), virulence of the pathogen and condition of the immune system determine the disease picture: Infectious endocarditis almost always attacks an already defective valve apparatus, regardless of whether it is a congenital or acquired defect. Mitral valve prolapse with regurgitation and atherosclerotic changes to the aortic valve (in older persons) play an increasing role.

Notes: A pre-existing defect of the heart always predisposes to endocarditis.

How do the bacteria colonize the heart valves?

Transitory bacteraemias are a frequent occurrence (in infectious diseases, after minor procedures such as tonsillectomies, even during teeth cleaning). The bacteria, which usually circulate in the blood for a few minutes only, are rapidly rendered harmless by the normal bactericidal effect of the serum. Fibrin deposits (platelets, fibrin, thrombi) occur around lesions on the endocardium (endothelial alteration) (non-bacterial thrombotic endocarditis) and present an ideal colonization site for pathogens (transition to infectious endocarditis).

In addition to general inflammatory symptoms (cytokines!), the clinical manifestation is triggered by:

1. Local destruction of the valves and myocardial damage.
2. Embolization of vegetations in the periphery (tissue infarction, septic colonizations)
3. Immune complex deposits and tissue destruction (glomerulonephritis, Osler's nodes)

CL.:

1. Fever (90%) and tachycardia, possibly chills
2. General symptoms: weakness, loss of appetite, weight loss, hyperhydrosis, arthralgias
3. Cardiac symptoms:
   - Cardiac murmurs: There is usually already a rheumatic valve defect with corresponding cardiac murmur, which can change its character (auscultate daily).
   - Increasing signs of heart failure
   -Possible valve perforation or tear (acute heart failure with pulmonary congestion or oedema!)
   -Myocardial abscess, danger of perforation.
   -ECG: non-specific, evidence of blocks: AV block, left bundle branch block (in myocardial abscesses), negative T-waves (concomitant myocarditis), infarct ECG (coronary embolism, perimyocarditis)
   - Echo (transoesophageal!): Detection of valvular vegetations and defects, myocardial abscess, pericardial effusion
4. Cutaneous symptoms:
   - Petechiae (30%), splinter bleeding under the nails
   - Osler's nodes: Lentil-sized, painful, reddish nodules, especially on the fingers and toes (= vasculitis caused by immune complex)
   - Clubbing of the fingers, hour-glass nails (rare and non-specific)
   - Janeway's lesions: Haemorrhagic lesions on the hand surfaces/ soles of the feet (not painful)
5. Bacterial microembolisms: Focal embolic encephalitis, possibly with transient hemiparesis and/or microembolization of retinal arteries
6. Renal manifestations with haematuria, proteinuria:
   - Almost regular focal glomerulonephritis (Löhlein)
   - Renal infarction in the context of embolic events
   - Rarely acute diffuse glomerulonephritis (immune complex deposits), proteinuria
7. Splenomegaly (caution: septic spleen rupture)
8. Eyes: Roth's spots: retinal bleeding

Lab.:

► Non-specific signs of inflammation:
ESR and CRP ↑ (a normal ESR speaks against endocarditis!)
Anaemia (80%), possibly leukocytosis, thrombocytopenia

► Concomitant immunological findings:
In the subacute course, anti-endothelial or anti-sarcolemmal antibodies and other immune phenomena have been regularly detected.

► Detection of pathogens by blood cultures: Essential findings for diagnosis and treatment

Rules for taking blood samples:
- Always perform blood culture diagnostics before beginning antimicrobial therapy
- 3-5 separately taken blood cultures; if an acute septic course, within 1-2 hours if at all possible; in case of prior antimicrobial treatment, possibly a larger number as well
- Perform collection regardless of course of body temperature (continuous bacteraemia)
- Take samples from cubital veins, not from indwelling venous catheters
- Adequate disinfection of skin and stoppers of the culture medium (disinfectant containing alcohol, observe dwell time, no subsequent palpation)
- Collect 5-10 ml blood each for the aerobic and anaerobic blood culture vials
- Store at room temperature or, even better, pre-warm the culture media to be inoculated to body temperature
- Before inoculating the culture medium: change the injection cannula; no ventilation of the aerobic vials (ventilate only if instructed by the manufacturer under sterile conditions in the laboratory)
- Inform the testing laboratory of the suspected diagnosis of "infectious endocarditis"
- Transport the blood culture vials to the testing laboratory within 2 hours

Course:

1. Acute sepsis:
   Highly virulent pathogens: Staphylococci and/or immune-deficient host.
   Rapidly progressing with fever, chills, tachycardia, arthralgia, deterioration of mental state and cardiac and renal failure. Multiple organ failure.
   Without immediate therapy, prognosis is poor.

2. Subacute sepsis = endocarditis lenta:
   Typical pathogen: Streptococcus viridans
   Insidious onset of disease!
   Subacute course of long duration
   Cardinal symptom: Undulating fever od unknown origin with or without chills, later increasing cardiac failure.

DD: Oligosymptomatic cases can easily be misjudged, especially if "routine blood cultures" are negative. Bacterial endocarditis is an important cause of "fever of unknown origin". The combined presence of cardiac murmur and fever should alert the physician to the possible presence of bacterial endocarditis!

Di:
- ▶ History (diagnostic or therapeutic interventions in patients with defects, i.v. drug use, etc.)
- ▶ Clinical picture (fever, cardiac murmur, ESR ↑, anaemia transoesophageal echocardiography (TEE): valvular vegetations of 2-3 mm detectable; possibly valve damage)
- ▶ Repeated blood cultures (at least 3 pairs of aerobic + anaerobic) before starting therapy

Notes: Since pathogen identification is often difficult, treatment must also be started in cases of a suspected clinical diagnosis that are culture-negative. The patient's life depends on the rapid initiation of treatment!

Duke criteria for diagnosing bacterial endocarditis:
Infectious endocarditis is probable/certain if 2 main criteria *or* 1 main criterion and 3 auxiliary criteria *or* 5 auxiliary criteria are present;

Main criteria:
a) Positive blood cultures with typical microorganisms for infectious endocarditis from two separate blood cultures
b) Determination of the involvement of the endocardium: Echocardiogram positive for infectious endocarditis (oscillating intracardial mass, abscess, new partial dehiscence of a valve prosthesis or new valve regurgitation)

Auxiliary criteria:
a) Predisposing heart disease or intravenous drug use
b) Fever >38.0°C
c) Vascular findings: arterial embolisms, septic pulmonary infarction, mycotic aneurysms, intracranial haemorrhagia, conjunctival haemorrhagia, Janeway's lesions
d) Immunological findings: glomerulonephritis, Osler's nodes, Roth's spots, rheumatoid factors
e) Echocardiography indicating infectious endocarditis, but not involving a main criterion (e.g. pericardial effusion)
f) Microbiology: Positive blood cultures that do not involve the main criteria or serological evidence of active infection with a pathogen that is consistent with infectious endocarditis.

Th.: Multidisciplinary coordination between cardiologists, cardiac surgeons and microbiologists
Calculated initial therapy with broad-spectrum antibiotics after taking repeated blood samples for aerobic and anaerobic culture (in commercially available culture media). Therapy also in cases of purely clinical diagnosis without positive results from a blood culture! Possible correction of therapy after the antibiogram is available. (Internet information: *www.p-e-g.de*)

Calculated initial therapy for unknown pathogen (Paul Ehrlich Society 2004)

Condition	Antibiotic for adults / dose	Duration of therapy
Native valves[2,3)]	ampicillin 12 - 24 g/day i.v. (3 - 6 SD)[1)] + gentamicin[4)] 3 mg/kg/day i.v. (3 SD) + cefotaxim 6 g/day i.v. (3 SD) or ceftriaxone 2 g/day i.v. (1 SD)	4 - 6 weeks
Valve prosthesis	vancomycin[5)] 2 g/day (2 – 3 SD) + gentamicin 3 mg/kg/day i.v. (3 SD) + rifampicin 900 mg/day i.v. (3 SD)	≥ 6 weeks 2 weeks ≥ 6 weeks

The concomitant care of a physician specializing in infections or a clinical microbiologist is always recommended. All doses are valid for adults with normal liver and renal function.

1) SD = single dose
2) If native valve endocarditis with an unknown pathogen responds insufficiently, combination therapy including a carbapenem or combination therapy with vancomycin and gentamicin can be tried.
3) In case of fulminant course and in intravenous drug addicts, an isoxazolyl penicillin should be tried instead of ampicillin.
4) If there is a good clinical response, the duration of treatment with gentamicin can be limited to 2 weeks.
5) As an alternative to vancomycin, teicoplanin can be used with an initial dose of 800 - 1200 mg over 4 - 5 days and a maintenance dose of 400 mg/day.

An early consultation with a cardiac surgeon, so that any possible necessary valve replacement for the elimination of the infection is not delayed. If there are vegetations > 10 mm, the risk of embolism rises significantly (up to 60%); therefore, rapid surgical elimination is necessary. Urgent indications for surgery are: Persistent infection, AV blocks, paravalvular abscess, heart failure, haemodynamically relevant valve defect, embolisms, vegetations > 10 mm

Follow-up check-ups: clinical examination, laboratory tests (ESR, CRP etc.), TEE (condition of valves, vegetations)

Prog: Untreated, poor prognosis; with antibiotic therapy, the prognosis depends on:
- previous damage to the heart
- condition of immune system, age of patient
- virulence and sensitivity of the pathogens to antibiotics

- Time of start of treatment

If optimal treatment is received, over 70% of patients survive. The prognosis is unfavorable in patients with cardiac valve prostheses, left heart endocarditis, infection with gram-negative pathogens and fungi, cyanotic congenital heart disease, acute disease course and additional heart failure. Cardiac decompensation is the most frequent cause of death (result of valve destruction and/or myocardial damage).

Prophylaxis: Patients should be issued endocarditis identity cards!

Recommendations for the prophylaxis of bacterial endocarditis

(Guidelines issued by the German Society for Cardiology and the Paul Ehrlich Society in 2007)

Ind: **Patients with the highest probability of a severe or lethal course of an infectious endocarditis:**

- Patients with valve replacement (mechanical or biological prostheses)
- Patients with reconstructed allo-prosthetic valves within the first 6 months after surgery
- Patients with history of endocarditis
- Patients with congenital cardiac defects have a higher risk of IE compared to acquired cardiac defects:
  - Cyanotic cardiac defects, which have not been or have only been palliatively treated with a systemic-pulmonal shunt.
  - Operated cardiac defects with implantation of conduits (artificial vascular-like connections) with or without valve or residual defects
- All operatively or interventionally with the use of prosthetic material treated cardiac defects within the first 6 months after surgery
- Patients with heart transplantation, who develop a cardiac valvulopathy.

Szenarios for endocarditis prophylaxis:

Patients without manifest infections

1. Dental procedures, e.g.
   - Extraction of teeth
   - Periodontal surgery
   - Removal of dental tartar
   - Curretage, probing, etc.
   - Implantation procedures and replantation of luxated teeth
   - Prophylactic cleaning of teeth/implants whenever bleeding cannot be excluded

   Note: Despite efficacy is not proven, prophylactic oral hygenic measures are recommended (hardly side effects).
2. Procedures on the respiratory tract
   - Adenoidectomy, tonsillectomy
   - Other types of surgery which include the mucosa.
   - Rigid bronchoscopy

   Prophylaxis for dental procedures according to guidelines mentioned below

An endocarditis prophylaxis in the context of gastrointestinal, respiratory or urogenital procedures (as well in cases of biopsy extraction) only still is recommended in case of existing infections.

Note: The background for the restriction of the indication for a medical endocarditis prophylaxis in the current guidelines is mainly the fact, that no prospective, randomized and placebo controlled trials exist, which prove the advantage of the former endocarditis prophylaxis up to now. These changes of the current recommendations/guidelines did NOT meet national and international consent. However it is up to the treating doctor, to continue the former existing prophylaxis pattern after consideration of the advantages and disadvantages and after discussion with the patient.

Patients with manifest infections

Should a procedure be performed in patients with risk conditions (see above), the antibiotic therapy should cover possible pathogens of an endocarditis.

1. Procedures of the repiratory tract:
   Efficacy against streptococci and s. aureus (e. g. aminopenicillin+betalactamase-inhibitor, cefazolin or clindamycin, in case of MRSA vancomycin)
2. Procedures of the gastrointestinal or urogenital tract:
   Efficacy against enterococci (e. g. ampicillin, piperacillin or vancomycin)
3. Procedures at the skin, skin appendages or musculoskeletal tissue
   Efficacy against staphylococci and ß-haemolysing streptococci (staphylococci senssitive penicillin or cephalosporin, in case of allergies clindamycin, in case of MRSA vancomycin)

Cardiac procedures

In cardiac valve prosthesis surgeries or procedures with implantations of foreign material (as well pace maker cable) prophylaxis is indicated directly before the operation, termination at latest after 48 h, in case of longer lasting surgeries poss. re-administration.

Recommended prophylaxis before dental procedures

Antibiotic prophylaxis usually 30 - 60 min. before procedure (single dose)

Adults:

Oral administration:	Amoxicillin 2 g p.o.
Oral administration not possible:	Ampicillin 2 g i.v.
Penicillin or ampicillin allergy	
- oral administration:	Clindamycin 600 mg p.o.
- oral administration not possible:	Clindamycin 600 mg i.v.

In children: 50 mg/kg BW amoxicillin p.o. or 50 mg/kg BW Ampicillin resp. 20 mg/kg BW clindamycin p.o./i.v.

Specific recommendations:

Penicillin G or V still represents an alternative to amoxicillin/ampicillin

Ampicillin alternative: Cefazolin, ceftriaxon 1g i. v. (adults; children 50 mg/kg BW)

Clindamycin alternative: Cefalexin 2 g p.o. (adults; children 50 mg/kg BW) or clarithromycin 500 mg p. o. (adults; children 15 mg/kg BW p.o.)

No cephalosporin administration after anaphylaxis/angioedema or urticaria following penicillin/ampicillin!

NON-INFECTIOUS (NON-BACTERIAL) ENDOCARDITIS

Rheumatic endocarditis (verrucous):

The most frequent form of endocarditis, in which wart-like deposits (fibrin, thrombocytes) appear, usually 1–3 weeks after an infection with β-haemolyzing A Streptococci, especially on the closing edges of the mitral and aortic valves; rheumatic endocarditis is one of the manifestations of pancarditis or rheumatic fever.

Libman-Sacks endocarditis in systemic lupus erythematodes:

Non-bacterial endocarditis with larger fibrin thrombi on the mitral valve, but also on the aortic and pulmonary valves, and with a strong tendency to local inflammatory infiltration; often accompanied by pericarditis and pleuritis. A manifestation of systemic lupus erythematodes (= SLE).

Löffler syndrome (eosinophilic endomyocarditis): Acute and subacute forms. Primarily affected is the endocardium of the right ventricle; this results in thickening and cellular infiltration (predominantly eosinophilic granulocytes) of the endocardial walls, with involvement of the myocardium. Occurs in different diseases in which the common feature is an increase in eosinophilic granulocytes; e.g. as an allergic hyperergic endocarditis (e.g. in bronchial asthma, periarteritis nodosa), as paraneoplastic endocarditis (e.g. in Hodgkin's and non-Hodgkin's lymphoma), bronchial carcinoma; also in eosinophilic leukaemia or idiopathic hypereosinophilia.

Th.: Treatment of the root disease. Glucocorticosteroids for SLE or hypereosinophilia. The tyrosine kinase inhibitor imatinib (Glivec®) for hypereosinophilia and myocardial involvement.

RHEUMATIC FEVER (RF) [I00]

Def.: Specific inflammatory reaction to toxins of Streptococci A; manifested in the joints (polyarthritis), heart (endocarditis, myocarditis, pericarditis), rarely in the (sub)cutis (erythema marginatum, rheumatoid nodules) and CNS (chorea minor). Begins about 2 weeks after an acute tonsillopharyngitis cause by β-haemolyzing streptococci A (GABS) with general reactions and high fever.

Ep.: Rare disease today in industrial countries (due to penicillin therapy of oropharyngeal Streptococci infections), frequently unchanged in poor developing countries. Peak occurrence of disease: 5-15 years of age

Aet.: Angina tonsillaris and pharyngitis due to Streptococci A cause RF. RF is not directly related to the infection, but rather the consequence of an infection-induced autoimmune reaction (secondary disease, allergic reaction to streptococcal antigen)

Classification of streptococci:

► According to haemolytic behaviour on blood agar (Schottmüller):

α-haemolyzing streptococci: Incomplete haemolysis with formation of green-coloured colonies via reduction of haemoglobin to biliverdin-type metabolites.
β-haemolyzing streptococci: haemolytic circles around colonies
γ-haemolyzing streptococci: no haemolysis

► Lancefield classification:

Due to different antigens of the C-polysaccharid β-haemolyzing streptococci are split into the sero-groups A -T (system according to Rebecca Lancefield).
Streptococci of the sero-group A = A-streptococci = streptococci pyogenes exist in > 80 types due to different antigens of the M-protein, with the help of the genes of the M-protein (emm-gene) > 150 different emm-types can be differentiated.

Diseases caused by Streptococci A (Streptococcus pyogenes):

- Tonsillitis/pharyngitis (complications: sinusitis, otitis media, pneumonia, peritonsillar abscess)
- Scarlet fever
- Skin and soft tissue infections: Erysipelas, contagious impetigo, necrotizing fascitis
- S. pyogenes sepsis, toxic shock syndrome (see section on this topic)
- Secondary diseases that are allergic reactions to Streptococci antigens:
  1. Rheumatic fever (only after streptococcal pharyngitis/tonsillitis)
  2. Acute post-streptococcal glomerulonephritis (after streptococcal infections of the pharynx, the tonsils and the skin)

  Note: In up to 20% of the population an asymptomatic colonization of the throat with s. pyogenes is found (esp. during the winter months)

Prg.: Streptococcus pyogenes binds to type IV collagen of the basal membrane and can therefore induce an autoimmune reaction. The type-specific M protein of the β-haemolyzing A Streptococci exhibits cross reactivity with the sarcolemmal antigens tropomyosin and myosin. This molecular mimicry explains the following findings in patients with rheumatic fever.

1. Evidence of cross-reacting antisarcolemmal antibodies in the serum
2. Evidence of antibodies bound to the myocardium and endocardium.
3. Damage to capillaries caused by immune complex (immune complex reaction type III) with evidence of immune complex in the myocardium (in the area of the Aschoff's nodules = rheumatic granulomas with fibrinoid necroses) and on the heart valves altered by inflammation (verrucous endocarditis).
4. In patients with chorea minor, cross-reacting antibodies against antigens of the nucleus caudatus and subthalamicus are observed.

CL.: RF occurs as a secondary disease after an interval of 10-20 days following an infection of the upper respiratory tract (pharyngitis, tonsillitis) with β-haemolyzing Streptococci A.

- General manifestations: Fever ("rheumatic" joint pain with no concomitant fever is of no diagnostic value), headache, sweating
- Acute "migrating" polyarthritis: Prefers the large joints and jumps from joint to joint. The affected joints are often overheated, swollen and very painful.
- Skin manifestations:
  - Subcutaneous rheumatic nodules (30%)
  - Erythema anulare rheumaticum (marginatum): pink-red, sometimes annular, polycyclic erythema on trunk (10%)
  - Erythema nodosum (details: see Boeck's disease)
- Cardiac manifestations: Rheumatic fever attacks the entire heart: endocarditis, myocarditis, pericarditis, thus pancarditis. Prognosis, however, is determined by the course of the rheumatic endocarditis [I09.1] (valve defects), while the myocarditis is relatively rarely accompanied by clinical symptoms.
  Hist.: Histiocytes with "owl eye" nucleoli (Anitschkow cells) + Aschoff nodules (= collection of round cells + giant cells around fibrinoid material).

Cardiac symptoms may be missing or unspecific in their manifestation:
- Quiet systolic and/or diastolic murmur
- Possible pericarditis with pericardial rub and precordial pain
- Possible myocarditis with extrasystoles; in more severe myocarditis, signs of heart failure
-ECG: Possible extrasystoles, prolonged PQ interval, ST-T prolongations (see also ECG signs in pericarditis)
-Echo: Evidence of possible valve changes, pericardial effusion, myogenic dilatation of the heart

- Rarely pleuritis, possibly with effusion in the intercostal space
- Chorea minor (Sydenham)[I02.9]: A late rheumatic manifestation that may occur after a longer latency period (up to months!) from the streptococcal infection. In this case, the presence of pancarditis must be ruled out. Typical are uncontrolled movements of the hands with clumsiness in children: They may spill their soup, break dishes, etc. The disease may recur, but recovery is possible with therapy.
- Laboratory tests:
  - Non-specific signs of inflammation: ESR/CRP ↑, possible infectious anaemia

Notes: A normal ESR largely excludes rheumatic fever and endocarditis.

-Detection of a streptococcal infection of group A:
1. Positive throat smear (gold standard is the culture; the rapid Streptococci antigen test has a specificity of > 90% and a sensitivity of about 85%)
2. Antibody detection:
   - Antistreptolysin 0 (ASO or ASL): Because Streptococci are endemic in the population, only titers above 300 IU and/or titer movements are valuable as evidence of an acute infection. In contrast to uncomplicated streptococcal angina, in rheumatic fever, the titer falls after the angina tonsillaris has disappeared.
   - Anti-deoxyribonucleotidase B (anti-DNAse B or ADB)

Notes: The ASL titer tends to increase in oropharyngeal streptococcal infections of the respiratory tract and is therefore useful for the diagnosis of rheumatic fever. - The ADB titer tends to rise in streptococcal infections of the skin; since this can induce acute glomerulonephritis, the ADB titer has a special meaning here.

Course of rheumatic fever:

<table>
<tr><td rowspan="2">Streptococcal infection</td><td>Latency</td><td>Rheumatic fever
* Exudative phase
↓
* Proliferative phase</td><td>Valve defects
scar
↑</td></tr>
<tr><td>1 - 3 weeks</td><td>6 - 12 weeks</td><td>1 - 3 years</td></tr>
</table>

Involvement of valves: Mitral valve (80%) and aortic valve (20%), can also affect both valves.

DD: See section on “Rheumatoid Arthritis”

Di: Jones criteria of the American Heart Association (1992):

Main criteria	Auxiliary criteria
1. Carditis	1. Fever
2. Migrating polyarthritis	2. Arthralgia
3. Chorea minor	3. ESR and/or CRP ↑
4. Subcutaneous nodules	4. Prolonged PQ or PR time
5. Erythema anulare rheumaticum	

The diagnosis of rheumatic fever is probable if the following findings are present:
1. Evidence of a prior streptococcal infection (positive throat culture or positive rapid antigen-test and/or evidence of streptococcal antigens)
2. Two main criteria or 1 main criterion and 2 auxiliary criteria

Th.: 1. Therapy of streptococcal infections:

Notes: Penicillin is the agent of choice in all streptococcal infections, for all Streptococci are sensitive to penicillin! - Resistances occur with all other antibiotics.

Dos: Penicillin V or propicillin: Children 100,000 IU/kg of body weight daily, adults 3-4 million IU daily; duration: 10 days

Side effects:Allergic reactions: Sensitization may occur due to earlier penicillin therapy, but also due to penicillin-containing foods. Paraallergic reactions with dermatomycoses have also been observed.

In case of penicillin allergy: change to macrolide (or clindamycin)

2. Anti-inflammatory treatment:
   - Acetylsalicylic acid: 2 g/d for adults
     Side effects + clinical: See “Antiphlogistics”
   - Corticosteroids:
     Ind: rheumatic carditis
     Dos: Initially 80 mg prednisolone/day; stepwise dose reduction

Side effects + clinical: See corticosteroids
Duration of anti-inflammatory treatment: about 4 - 6 weeks

3. Tonsillectomy during latency period with prophylactic penicillin, possibly eradication of focal dental abscesses
4. Repeat prophylaxis with penicillin for at least 10 years, up to the age of 25. After that, targeted penicillin prophylaxis only for diagnostic or surgical procedures (including dentistry). In cases of penicillin allergy, use macrolide.
   Dosage for permanent prophylaxis: e.g. benzyl penicillin 1.2 million IU i.m. every 4 weeks or penicillin V orally

Prog: Prognosis is determined by the course of the endocarditis: "Rheumatic fever licks the joints and bites the heart". With each relapse, the probability of later valve disease becomes greater. Therefore, it is of crucial importance that penicillin administration start early during the exudative stage of the disease. Fibrotic valve disease is not reversible!

AQUIRED VALVULAR HEART DISEASE (AQUIRED DEFECTS)

Internet information: *www.acc.org/clinical/guidelines/valvular*

In most cases, cardiac valve disease manifests as stenosis and/or regurgitation. If a valve is affected by both stenosis and regurgitation, it is a combined valve defect. One, several or all of the heart valves may be affected in one patient. In this case, we speak of a multivalvular defect.

Valve stenosis:
- Def.: Narrowing in the valve area that decreases the normal responsiveness of the valve, thus slowing the forward flow of blood. In adults, the normal opening surface of the mitral and aortic valves is > 2.5 cm^2.
- Cause: Degenerative processes or fibrous adhesions and contractions following inflammation, e.g. after rheumatic fever.
- A gradient over the stenosed region can be measured by echocardiography or manometry: The maximum gradient determined by Doppler echocardiography is higher than that of the peak-to-peak gradient measured by manometry, while the average gradients measured by both processes are largely equivalent.
- Stenoses are classified as mild, moderate or high-grade depending on the surface area of the valve opening and the gradients over the valve.

Valvular regurgitation:
- Def.: Inability of the valve to close completely, which can arise from both acute or chronic disease processes.
- Cause: Inflammatory or degenerative processes in the context of coronary heart disease, primary or secondary cardiomyopathy or congenital abnormalities.
- The reflux can be seen directly and quantified with colour duplex imaging. 3 degrees of severity can be distinguished in a levocardiogram depending on the amount of contrast medium reflux.

In the majority of cases, the valves of the left ventricle are affected due to the heavier mechanical demands on the valves of the left heart (absolute pressure and pressure gradient left > right).

Acquired organic valve defects of the right heart are relatively rare, e.g. as a result of bacterial endocarditis in intravenous drug addicts. In the majority of cases, valve defects of the right heart are cases of relative valve regurgitation:
- Relative pulmonary regurgitation due to overextension of the valve ring in severe pulmonary hypertension of differing genesis; auscultation: Graham Steell murmur: high frequency decrescendo murmur immediately following the pulmonary component of S2, punctum maximum over the pulmonary valve.
- Relative tricuspid regurgitation due to overextension of the valve ring with right ventricular dilatation (in the context of right heart failure of differing genesis). Auscultation: "Blowing" holosystolic murmur, punctum maximum over 4th intercostals space right parasternal.

Critical for the performance of the heart is the type of cardiac load resulting from the valve defect:
- Volume load in cases of where there is regurgitation of large volumes of blood across a valve: more favorable prognosis
- Pressure load in case of valve stenosis: Less favourable prognosis

According to the extent of the subjective discomfort, 4 degrees of severity can be distinguished (New York Heart Association - NYHA):
Class I: No discomfort
Class II: Discomfort with strenuous physical exertion
Class III: Discomfort with mild physical exertion
Class IV: Discomfort at rest (cardiac decompensation and confined to bed)

Prerequisite before deciding on therapy is knowledge of the following facts:
- Acute or chronic development of the disease?
- Aetiology?
- Symptom pattern in the patient?

- Findings of clinical and technical examination?
- Degree of severity of the valve changes?
- Degree of severity of the ventricular function disorder?
- What is the spontaneous course of the disease (without surgical therapy)?
- The spontaneous course, on the one hand, and the risk of the treatment in question, on the other hand, must be weighed against the expected benefit of a therapy.
- A treatment that addresses the cause of the disease should always be given preference over a symptomatic therapy if at all possible.

A) Internal therapy:
- treatment of heart failure (see section on this topic)
- Prophylaxis of endocarditis (see section on "infectious endocarditis")
- Prophylaxis of thromboembolisms with anticoagulants for all mechanical valve prostheses

B) Surgical therapy: see the section on "The patient who underwent valve surgery"
Remember: Exclude CHD (coronary angiography) before any scheduled cardiac surgery, so that a poss. CHD could be simultaneously treated.

THE PATIENT WHO UNDERWENT VALVE SURGERY

Indication for valve replacement:
- If the symptom pattern no longer permits conservative treatment or poses a danger of irreversible myocardial damage if surgery is delayed for a longer time.
- Primary objective is a valve-preserving correction. Only if this is not possible → prosthetic valve replacement.
- There are still no artificial valves available today that are comparable to natural valves in durability and function.

Requirements for artificial heart valves:
Life-long durability, optimal flow profile, good tissue tolerance, no haemolysis, no thrombogenicity, low space requirement, simple implantation technique, no burdensome sound phenomena, economic price.

Prosthetic valve replacement:

1. Mechanical valve prostheses:
   - Advantages: Long durability.
   - Disadvantages: High risk of thromboembolism → anticoagulation necessary; transvalvular gradient, haemolysis.
   - Ind: 1. Longer life expectancy (if repeat surgery probable in younger patients)
     2. Renal insufficiency
     3. Following previous malfunction of a bioprosthesis
     4. If anticoagulation is necessary for other reasons.
   - Ball valves: The first available valves worked according to this principles (e.g. Starr-Edwards) → relatively large, a lot of room required for the implantation.
   - Disk valves: "floating disk principle" → low space requirement, but hindrance of the central blood flow. Better haemodynamics with "tilting disk principle" (e.g. Björk-Shiley)
   - Butterfly valves: Currently preferred (e.g. St. Jude) → favorable haemodynamic properties and relatively low thrombogenicity with smaller size.

2. Biological valve prostheses:
   Made from animal or human tissues (including human dura mater or fascia lata, bovine pericardium or heart valves from pigs) over a metal or plastic framework. Pretreated for tissue sterilization and elimination of immune reactions.
   - Advantages: low thrombogenicity
   - Disadvantages: limited durability: Progressive calcification → Reduction of valve mobility and opening surface, tears in valve structures. Especially affected are patients with limited renal function, calcium metabolism disorders, patients after endocarditis, large prostheses, prostheses in the mitral position.
   - Ind: 1. Greater age (> 75 years), life expectancy < 10 years
     2. Contraindication for anticoagulants
     3. Repeat surgery for thromboembolic complications of a mechanical valve

3. Allograft/homograft valve prostheses:
   Human cadaveric valves. Fresh, antibiotic-treated, cryo-preserved or chemically preserved grafts are used. Availability limited.
   - Advantages: low thrombogenicity
   - Disadvantages: difficult to implant, degeneration
   - Ind: e.g. women who desire children, following subsided endocarditis, younger patients

4. Ross operation:
   Replacement of the aortic valve by the patient's own pulmonary valve (auto-graft), while the pulmonary valve is replaced by a pulmonary or aortic allograft.

Complication after valve replacement: (50% of all patients/10 years)

- Early complications: bleeding, infections, prosthesis endocarditis, arrhythmias, heart failure; perioperative renal, pulmonary, liver or multi-organ failure.
- Late complications: thromboembolisms, bleeding due to anticoagulants, prosthesis endocarditis
  Cardiac insufficiency in the late course → 3 causes:
  - Valve dysfunction
  - Concomitant hypertension and/or coronary heart disease
  - Preoperative heart muscle damage resulting in later indication for valve replacement!

Notes: The pre-operative functional state of the left ventricle essentially determines the long-term prognosis, especially in the case of valve regurgitation!

-Prosthesis complications: disproportion between valve and vessels or ventricle, tears in the sheath of valve cages, embolization of prosthesis leaflets or defects in old ball prostheses.

-Prosthesis malfunction: Disorders of the motion sequence → stenosis or regurgitation due to degenerative processes, material deficiencies or defective implantation techniques

Specific complications:

Valve thromboses:

- Incidence: rare with anticoagulation, more frequent with mitral valves than aortic valve prostheses, most frequently with tricuspid valve prostheses. Incidence influenced by valve type (rare at St. Jude Medical).
- CL.: Worsening of clinical condition, acute heart failure, embolisms (brain!) or rhythmic disorders
- Th.: Lysis treatment, possible repeat operation

Thromboembolisms:

- Incidence: Especially in mechanical valve prostheses, more frequently after mitral valve replacement than after aortic valve replacement, rarely in the case of homograft valves. Incidence about 2-3% per patient year.
- CL.: Ischaemia depends on the vascular area affected (brain, extremity and intestinal vessels).
- Th.: see the section on embolisms
- Prg.: Anticoagulation obligatory for all mechanical valves. Oral anticoagulants after implantation of a bioprosthesis are obligatory in the first 3 post-operative months, permanent anticoagulation in the case of chronic atrial fibrillation, after thromboembolisms, in the case of a large left ventricle or significantly reduced cardiac output. The target INR value depends on the type of valve and position (see section on the prophylaxis of thromboembolisms).

Prosthesis endocarditis:

- Incidence: With mechanical and bioprostheses, less with homograft valves.

Early endocarditis: Within the first two post-operative months; pathogens usually staphylococci and gram-negative pathogens, rarely fungi. The condition is very serious.

Late endocarditis: After the first two post-operative months; pathogens are identical with those that trigger endocarditis in native valves (Streptococcus viridans, Staphylococcus aureus, Staphylococcus epidermis, Enterococci, etc.).

- Di: Fever, newly occurring valve murmurs and/or altered opening/closing sounds, transoesophageal echocardiography, positive blood culture (double-check blood cultures before starting antibiotic therapy!).
- Th.: See the section on “Bacterial endocarditis”
- Prophylaxis: Life-long antibiotic endocarditis prophylaxis for all patients (see section on “Bacterial endocarditis”).

Paravalvular leaks:

- Incidence: Especially with prostheses that are sewn into highly calcified valve rings, but also triggered by endocarditis.
- Di: Regurgitation murmurs over the affected valve, haemolysis, echocardiography

Mechanical haemolysis:

Occurs especially in older valve models. In well-functioning, intact prosthetic valves, mechanical haemolysis is insignificant and manifests only as a slight increase in LDH. Haemolysis increases with valve function disorders.

Di: - LDH and HBDH ↑
- Haptoglobin ↓
- Possibly haemopexin ↓ (occurs in cases of severe haemolysis only, if haptoglobin can no longer be measured)
- Reticulocytes ↑
- Indirect bilirubin ↑
- Fragmentocytosis

Hb normal = compensated haemolysis
Hb reduced = decompensated haemolysis = haemolytic anaemia

Echocardiographic exclusion of prosthetic malfunction
Treatment depends on the underlying cause; in cases of severe haemolysis, surgical revision may be necessary.
The early mortality after surgery can be assessed e.g. according to the EuroSCORE-calculator (see internet)

Regular follow-up examinations:

- Medical history: Newly occurring fever, fatigue, lassitude, reduced physical activity, (night-time) dyspnoea, sweating, angina pectoris, oedema, palpitations, vertigo, syncope?
- Clinical examination: Pay attention to pleuropericardial rub (in the early post-operative stage with postpericardiotomy syndrome), tachycardia (e.g. during fever, with anaemia, endocarditis, hypovolemia, heart failure), atrial fibrillation, pulmonary congestion, jugular venous congestion, hepatomegaly, ascites, peripheral oedema, pleural or pericardial

effusion (in the early post-operative stage in postpericardiotomy syndrome; in the late post-operative stage in heart failure).

- Auscultation: Bioprostheses and homografts do not normally feature any specific murmur phenomena, while mechanical prostheses usually feature opening and closing clicks. The prosthesis closing click is louder than the opening click. If prosthesis sounds become quieter, this can be evidence of a thrombosis in an artificial valve! Newly occurring systolic or diastolic sounds may indicate malfunction.
- Echocardiography: Pattern of motion of the valve parts, flow profiles, gradients and opening surfaces, ventricular function and size, evidence of valvular or paravalvular leaks; vegetations in bacterial endocarditis
- X-ray, CT scan, MRI: Valve type, evidence of insufficiency or stenoses, ventricular function and morphology, lung perfusion
- ECG: Load on the atria and ventricles, repolarization disorders and bundle branch blocks or arrhythmias.
- Laboratory tests: Inflammation parameters (leukocyte count, ESR, CRP), blood cultures if bacterial endocarditis is suspected, evidence of anaemia (blood count, iron, ferritin) or haemolysis (LDH, HBDH, haptoglobin, bilirubin, fragmentocytes); coagulation tests in case of therapy with anticoagulants (INR)
- "Home monitoring" following alloprosthetic heart valve replacement:
  - Self-check of INR (CoaguCheck) → This contributes to a decrease in the frequency of severe bleeding complications
  - Self check of valve function by fully automated frequency analysis of valve sounds → early recognition of valve function disorders

MITRAL VALVE STENOSIS [I35.0]

Aet.: Except for rare congenital forms, mitral valve stenosis (MS) is usually the result of rheumatic fever. This cannot always be confirmed by the medical history, however.

PPh.: Stenosing of the mitral valve is stealthy (requires years to decades). Haemodynamics and clinical signs depend on:

- Severity of the obstruction
- Transmitral blood flow
- Cardiac rhythm and frequency
- Extent of secondary changes in the pulmonary circulation

► Narrowing of the mitral valve → impedance of diastolic left ventricular filling
The gradient between the left atrium (LA) and the end-diastolic pressure in the left ventricle (LV) depends on the severity of the stenosis and the current cardiac output. At first, enlargement of the LA prevents an elevation in pulmonary pressure and the patient is largely asymptomatic.

► Increasing obstruction of the mitral ostium → reduced filling of the LV. The increase in LA pressure causes the LV to be sufficiently filled, at first, and maintains cardiac output. As cardiac output decreases, fatigue and reduction of cardiac capacity occur. The elevated LA pressure is transmitted passively to the pulmonary veins (reactive and passive pulmonary venous hypertension) → pulmonary adjustment reactions (increase in lymph flow, reduction in permeability of alveolar capillary membranes). Reactive constriction of the pulmonary arteries → reduced blood flow to the pulmonary capillary system and lowering of hydrostatic pressure. These counter-regulatory processes prevent pulmonary oedema.

► If the capacity of the counter-regulatory processes is exceeded, symptoms of pulmonary congestion develop: dyspnoea, orthopnoea, (night-time) coughing.
With a left atrial or average pulmonary capillary pressure > 25 - 30 mmHg at rest, there is a risk of pulmonary oedema, especially with physical exertion, fever, anaemia, tachycardia, pregnancy.

► Secondary active pulmonary hypertension (as a result of reactive pulmonary arterial vasoconstriction, interstitial fibrosis and alteration of the pulmonary arterioles) develops during the phase of passive pulmonary venous hypertension. In this manner, the pulmonary pressure may increase to equal or exceed systemic pressure values.
Sequelae: pulmonary hypertension → right heart hypertrophy → dilatation of the right ventricle → right heart failure.

Degree of severity:

Degree of severity	Average pressure gradient (mmHg) *)	Mitral valve area = MVA(cm^2)	mPCP (mmHg) during exertion **)
Mild	≤ 7	> 1.5 - 2.5	≤ 20
Average	8 - 15	1.0 - 1.5	21 - 25
Severe	> 15	< 1.0	> 25

***)** At normal heart rate and average cardiac output (CO)

****)** mPCP= mean pulmonary capillary pressure

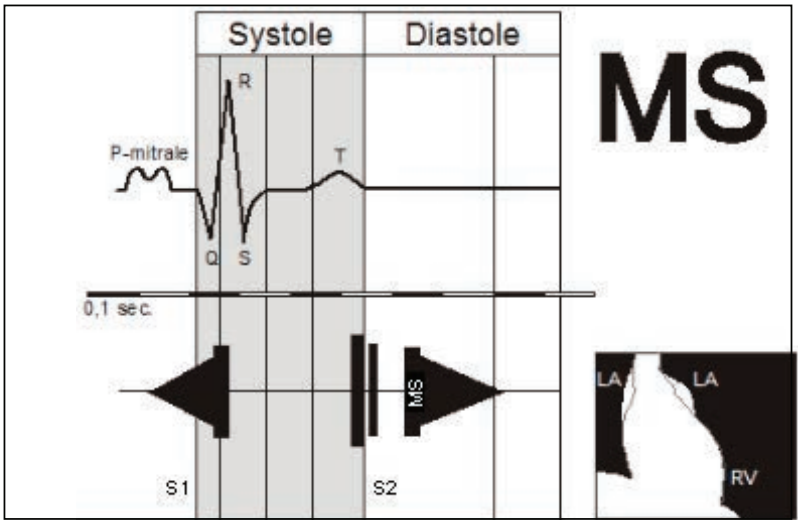
CL.: Symptoms depend on severity of disease:
1. Sequelae of the increase in pressure in the left atrium:

- Possible atrial fibrillation with absolute arrhythmia (cardiac output reduced by about 20%)
- Formation of thrombi in the left atrium (40%) with the risk of arterial embolisms (20% of cases) in the brain, extremities, kidneys, etc.

2. Sequelae of pulmonary congestion / pulmonary hypertension:
   - (exertion) dyspnoea
   - Night-time cough ("cardiac asthma")
   - Possible haemoptysis with "heart failure cells" in the sputum (= haemosiderin-containing lung macrophages)
3. Sequelae of right heart failure:
   - Elevated venous pressure with visible venous congestion in the neck and under the tongue
   - Congested liver, congested kidneys (possibly proteinuria), oedema of the dependent body parts
4. Sequelae of reduced cardiac output:
   - Loss of efficiency
   - Peripheral cyanosis with reddish-cyanotic cheeks (mitral facies)

Compl.: - Arterial embolisms (see above)
- Bacterial endocarditis
- Pulmonary oedema

Ausc.: (optimally in a left lateral position; punctum maximum over the apex of the heart) 4 sound phenomena:
- Accentuated 1st heart sound
- Mitral opening snap (MOS)
- Diastolic decrescendo sound (following the MOS), which passes over into a
- presystolic crescendo sound



- Accentuated 1st heart sound and MOS are caused by a loud turning up or down of the mitral leaflets whenever the ventricular pressure is greater or less than the pressure in the left atrium. Both sounds may disappear if the mitral leaflets become calcified. The presystolic crescendo occurs only with sinus rhythm!
- Combined mitral defect: Additional sound of mitral regurgitation.
- Severe MS with pulmonary hypertension: Immediately following the enhanced pulmonary component of the S2 diastolic Graham-Steell sound of a relative pulmonary valve regurgitation.

ECG: - Load on the left atrium: P-mitrale (double-peaked P-wave in lead II > 0.11 s), possibly atrial fibrillation with absolute arrhythmia
- Sign of right heart hypertrophy in pulmonary hypertension; development of right axis deviation, Sokolow-Lyons index for right heart hypertrophy: RV1 + SV5 or 6 ≥ 1.05 mV.

X-ray: 1. Left atrial enlargement:
   - In the p.a. image, possible double contour of the right border of the cardiac silhouette, left middle segment obscured by prominent left auricle, spreading of the tracheal bifurcation
   - In the left lateral image, the oesophagus appears curved (after swallowing contrast medium) because of the narrowing of the posterior of the heart at the level of the atria.
2. Mitral configuration of the heart ("standing egg") as a result of:
   - Enlargement of the left atrium (see above)
   - Prominence of the pulmonary artery in the presence of pulmonary hypertension
   - Right ventricular hypertrophy
3. Possible signs of pulmonary congestion:
   - Prominent pulmonary veins in the hilar area
   - Presence of Kerley B lines in the lower fields with interstitial pulmonary oedema
   - "Ground glass" opacity, etc., with alveolar pulmonary oedema
4. Possible signs of right ventricular hypertrophy with narrowing of the retrocardiac space in lateral views.
   History: With right ventricular hypertrophy, the right ventricle (p.a. view) can form the cardiac border; therefore, it is not advisable to consider the left cardiac border to be identical with the margins of the left ventricle when viewing a chest X-ray.
5. Possible presence of valve calcification

Echo: Transthoracic, optimally transoesophageal (TEE):

Evaluation of the valve anatomy / pathology; M-mode: EF slope flattened with multiple echoes due to valvular calcification; quantification of the degree of stenosis; measurement of the enlarged left atrium (> 40 mm); reduced left ventricle; evaluation of function of both ventricles; involvement of other valves; assessment of pressures in the pulmonary circulation and right ventricle; evidence of atrial thrombi (TEE).

Maximum and average gradient over the stenosed valve and the surface area of the valve opening can be quantified. Possible detection of concomitant valve regurgitation (colour duplex).

MRI: Pressure gradient over the valve stenosis, planimetry of the MVA

Invasive diagnostics (left heart catheterization):

Ind: Assessment of valve function, degree of stenosis and ventricular function. Measurement of pressures in the systemic and pulmonary circulation. Exclusion of coronary stenosis requiring therapy

Manometry:

Measurement of the pressure curve and pulmonary arterial pressure, gradients over the valve and calculation of the surface area of the valve opening.

With mitral stenosis, the average pressure in the LA increases significantly (> 20 mmHg). There is a gradient over the mitral valve (measured between the A-wave in the LA or pressure curve and the end-diastolic LV pressure), which is co-determined by the cardiac output.

Pulmonary hypertension:

- The diastolic PAP is greater than the average PCP (in persons with health hearts, these values are approximately the same).
- Calculation of pulmonary vascular resistance (normal 45 - 100 dsc), which can increase to up to > 1500 in mitral stenosis.

Levocardiogram:

LV not enlarged and well contrasted, possible segmental disorder in LV function

Natural course:

Symptoms of mitral stenosis usually do not appear until 10 – 20 years after rheumatic fever. Spontaneous course: 10-year survival rate for NYHA classes I and II is about 85%. For NYHA class III, it is about 40%. For NYHA IV, the 5-year survival rate is only 15%.

Causes of death: pulmonary oedema and right heart failure (65%), arterial embolisms (20%), pulmonary embolisms (10%), bacterial endocarditis

Regular control examinations: Clinical examination, echocardiogram, X-ray, stress testing. Control interval depends on degree of severity.

Th.: A) Conservative:

- The conservative therapy options for heart failure are limited to the use of diuretics (thiazide + spironolactone). ACE inhibitors ACE II inhibitors are contraindicated. Digitalis is only indicated in the case of atrial fibrillation.
- Patients with haemodynamically effective MS need a long diastole in order to achieve sufficient ventricular filling → maintain sinus rhythm of normal rate as long as possible. Reduce rate in cases of atrial fibrillation → digitalis glycoside in combination with verapamil or β-receptor blocker.
- Thromboembolism prophylaxis with anticoagulants in cases of atrial fibrillation or unstable sinus rhythm; beginning with moderately severe MS, in cases of sinus rhythm as well
- Prophylaxis of endocarditis (see section on “infectious endocarditis”)
- Long-term prophylaxis of rheumatic fever: up to about 25 years, longer in patients susceptible to infection (e.g. teachers)

B) Catheterization procedure: Mitral valvuloplasty (MVP): = percutaneous expansion of the mitral valve using a balloon catheter

In suitable patients, MVP shows results similar to those for surgical mitral valve commissurotomy.

Advantage: Large surgical procedure is avoided or postponed. The MVA is normally doubled by the procedure and the gradient approximately halved.

Decision regarding MVP after clinical data and echo score. Best results in young patients with low score values, sinus rhythm, minimal calcification and with no concomitant mitral regurgitation.

Compl.: Progression of mitral regurgitation, atrial septum defect due to transatrial puncture, perforation of the atrium or ventricle, thromboembolisms or AV blocks.

Contraindications: Higher-grade mitral regurgitation, atrial thrombi, history of thromboembolisms, thickened atrial septum

C) Surgical treatment options: (Internet infos: *www.dghg.de*)

A) Indications for mitral valvuloplasty in at least moderately severe mitral stenosis (mitral valve area < 1.5 cm^2)
1. Symptomatic patient: Suitable valve morphology, no left atrial thrombi, mild mitral regurgitation at the most, no additional indications for surgery (additional severe valve defects, CHD requiring revascularization)
2. Asymptomatic patient: To be considered in cases of pulmonary hypertension at rest (systolic pulmonary pressure > 50 mmHg) or during exertion (systolic pulmonary pressure > 60 mmHg) or average gradient at rest > 15 mmHg, suitable valve morphology, exclusion of left atrial thrombi, mild mitral regurgitation at the most and no additional indications for cardiac surgery (additional severe valve defects, CHD requiring revascularization)
B) Indications for surgical commissurotomy or, if necessary, for mitral valve replacement if a mitral valvuloplasty cannot be performed for the reasons listed above.
1. Patient with severe symptoms (NYHA III-IV) and a mitral valve area < 1.5 cm^2
2. Patient with mild or no symptoms (NYHA I-II) and a mitral valve area < 1 cm^2

Note: These indications have an evidence level of B I.

MITRAL VALVE REGURGITATION [I34.0]

Def.: Acute or chronic inability of the mitral valve to close between the left atrium and left ventricle due to changes in the valve annulus, both of the leaflets, the chordae tendineae or the papillary muscles.

Aet.:
- Relative mitral valve regurgitation: Dilatation of the mitral valve annulus due to dilated cardiomyopathy and left heart insufficiency of varying genesis
- Calcification of the mitral valve annulus in older patients
- After mitral valve dilatation (valvuloplasty)
- Rarer rheumatic and/or bacterial endocarditis
- In the context of degenerative, myxomatous changes in the valve leaflets (mitral valve prolapse syndrome, Ehlers-Danlos syndrome, Marfan syndrome)
- Elongation or rupture of the chordae tendineae: in mitral valve prolapse, acute myocardial infarction, after chest trauma or idiopathic
- Dysfunctions of a papillary muscle due to myocardial ischaemia (CHD)

Forms of progression:
- Acute mitral valve regurgitation due to bacterial endocarditis or after acute myocardial infarction
- Chronic mitral valve regurgitation

PPh.: Mitral valve leaflets close early in the systole when the pressure in the left ventricle (LV) becomes equal to the pressure in the left atrium (LA). The papillary muscles and chordae tendineae work in such a way that the leaflets are held closed and kept under tension when the ventricle becomes smaller during the systole.
Inability of the mitral valve to close → LV empties in two directions: One part of the cardiac output into the systemic circulation and the other part as regurgitation volume into the LA. Since the pulmonary veins do not have any valves and remain wide open, the blood regurgitated into the LA leaks into the pulmonary vessels → pulmonary congestion and reactive pulmonary hypertension → right heart strain → right heart failure. In order to maintain cardiac output, the stroke volume must be increased. Volume loading → hypertrophy and dilatation of the LV.

Clinical signs of mitral valve regurgitation result from the small output in the systemic circulation and the reflux of blood back into the pulmonary circulation.

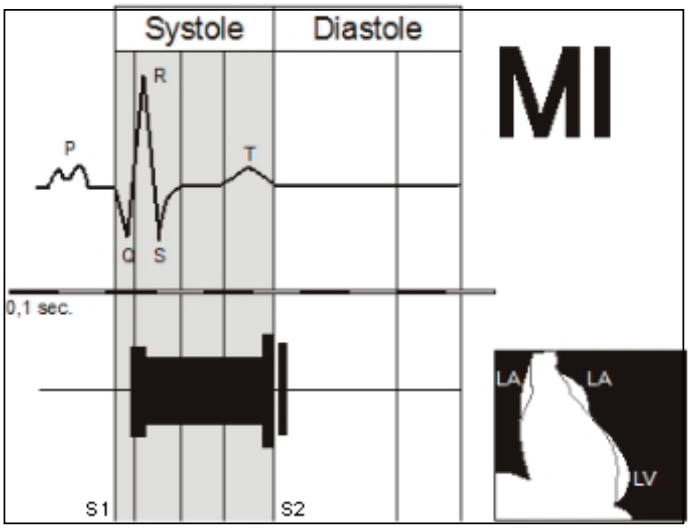
CL.:
- The body can tolerate chronic mitral valve regurgitation, which develops slowly, for a longer time because of adaptation mechanisms. Because of the more favorable volume load, life expectancy in cases of mild mitral valve regurgitation can be nearly normal. Symptoms may also be lacking or mild for a longer period of time, even in cases of significant mitral valve regurgitation. More severe symptoms such as dyspnoea, heart palpitations, nocturnal coughing attacks, etc., do not develop rapidly until the left ventricle fails. At that point, the clinical manifestations are similar to those of mitral stenosis (see section on that topic).
- In acute mitral valve regurgitation (e.g. as a result of papillary muscle necrosis due to infarction), there is no time for the heart to adjust → rapid left ventricular decompensation with pulmonary oedema and possible cardiogenic shock!

Compl.: Cardiac decompensation with pulmonary oedema; atrial fibrillation can trigger decompensation! Thromboembolisms due to atrial fibrillation, bacterial endocarditis

Inspection and palpation:
Rarely, peripheral cyanosis. Pulse normal or absolute arrhythmia due to atrial fibrillation. Systolic venous pulse due to tricuspid regurgitation. Apex impulse due to eccentric left hypertrophy, spread and displaced downwards/outwards. Accentuated pulsations over the right ventricle.

Auscultation (best in the left lateral position):

Immediately after S1, which is quite, there is a high-frequency, pansystolic (holo)systolic murmur, punctum maximum over the apex of the heart, conduction into the axilla. In higher-grade mitral regurgitation, there is a short interval diastolic murmur at the point of the rapid ventricular filling, possibly S3.



ECG: Left atrial P-wave = P-mitrale (P > 0.11 sec., double-peaked, with second part accentuated), P-pulmonale does not occur until later (right atrial); possibly atrial fibrillation. Left axis deviation; right axis deviation in pulmonary hypertension. In cases of severe mitral valve regurgitation: left hypertrophy (volume loading), later also right heart strain (in pulmonary hypertension). Left, possibly also right precordial repolarization disorders.

Echo: Semi-quantification of the degree of regurgitation (evidence of reflux in colour duplex), measurement of the size of the atrium, assessment of sizes and function of both ventricles, involvement of other valves and assessment of pressures in the pulmonary circulation and right ventricle. Evidence of thrombi in the left atrium (TEE). Evidence of cause: mitral valve prolapse, torn leaflet, calcifications, vegetations due to bacterial endocarditis.

MRI: Calculation of reflux (degree of regurgitation), anatomy + function of the heart

X-ray: - Enlargement of the left atrium and (in contrast to mitral stenosis) of the left ventricle as well. In the p.a. image: Cardiac enlargement with mitral configuration and middle segment of heart obscured. Lateral image: Narrowing of the retrocardial space at the levels of the atria and ventricles (after swallowing contrast medium).
- Prominent pulmonary veins in the hilar area due to pulmonary congestion
- Presence of Kerley B lines in the lower fields with interstitial pulmonary oedema
- "Ground glass" opacity, etc., with alveolar pulmonary oedema

Invasive diagnostics (left heart catheterization):

Ind: Assessment of the degree of regurgitation, determination of pressures in the systemic and pulmonary circulation, evaluation of ventricular function and exclusion of CHD requiring treatment.

Manometry: LA and PC pressures

Levocardiogram:

Extent of contrast medium reflux into the LA and regurgitation fraction permit classification of mitral regurgitation:

Classification	Contrast medium reflux	Regurgitation fraction
Grade I	• Minimal reflux • No complete dyeing	< 20%
Grade II	• Complete dyeing of the LA after several strokes • Density of contrast medium in LA < LV	20 - 39%
Grade III	• Complete, dense dyeing of the LA • Density of contrast medium in LA = LV	40 - 60%
Grade IV	• Immediate (after 1-2 strokes), complete dyeing of the LA • Density of contrast medium in LA > LV • Reflux of contrast medium into the pulmonary veins	> 60%

Determination of regurgitation fraction (RF):

Total stroke volume	=	End-diastolic volume minus end-systolic volume
Effective stroke volume	=	cardiac output / heart rate
Regurgitation volume	=	Total stroke volume minus effective stroke volume
Regurgitation fraction	=	Regurgitation volume / total stroke volume

Natural course:

Survival rate depends on the cause of the mitral regurgitation. In rheumatic mitral regurgitation, the 5-year survival rate is 80%; the 10-year survival rate is 60%.

The ejection fraction remains normal for a longer period of time. A reduction of contractility is evidence of advanced disease with the danger that surgery may no longer be able to normalize ventricular function.

Clinical monitoring:

Clinical examinations, ECG, echocardiography, chest X-ray. Monitoring intervals are determined by the degree of severity (e.g. every 6-12 months) so that surgery can be scheduled before there is irreversible ventricular dysfunction.

Th.: A) Conservative:

- In symptomatic patients a drug therapy should not delay the surgical therapy. Prognostic advantage of the drug therapy is not proven.
- Avoidance of physical strain
- Prophylaxis of thromboembolisms with anticoagulants for atrial fibrillation (see section on that topic)
- Prophylaxis of bacterial endocarditis (see section on that topic)
- Possible prophylaxis of rheumatic endocarditis (see section on that topic)

B) **Surgical treatment options for mitral valve defects:**

(Guidelines of the German Society for Thoracic and Cardiovascular Surgery, 2001)

- Mitral valve reconstruction with/without ring or partial ring
- Mitral valve replacement with mechanical prosthesis or with biological prosthesis

Ind: Indication for surgery in severe, chronic mitral valve regurgitation; reconstruction is always to be preferred over valve replacement if at all possible.

Symptomatic patients	EF ≥ 30%
	EF < 30%, if reconstruction is possible
Asymptomatic patients	EF < 60% and/or end-diastolic left ventricular diameter > 45 mm
	Paroxysmal or newly occurring, persistent atrial fibrillation
	Systolic pulmonary arterial pressure at rest > 50 mmHg
	EF > 60% and end-diastolic diameter > 45 mm, but no contractile reserve during exertion

Contraindications (relative): e.g. EF < 20%, risk of surgery < expected benefits

- Mortality in hospital: Mitral valve reconstruction 2,4 %; mitral valve replacement 8,4 %
- Life-long oral anticoagulation in mechanical heart valve prostheses; in biological prostheses at least for 3 months
- Endocarditis prophylaxis: See there

C) Intervention catheter therapy: Mitral leaflet clipping (MitraClip-system) in patients with contraindication for surgery.

MITRAL VALVE PROLAPSE (MVP) and MITRAL VALVE PROLAPSE SYNDROME [I34.1]

Synonyms: Barlow syndrome, click syndrome, click murmur syndrome, floppy valve syndrome

Def.: Mitral valve prolapse: Mitral valve dysfunction in which oversized parts of the mitral valve leaflet bulge into the left atrium during the ventricular systole and sometimes lead to mitral regurgitation.
Not referred to as MVP syndrome until symptoms occur, especially arrhythmias or neurocirculatory disorders.
In about 90% of cases, this is a harmless finding, but in a smaller group, it can lead to serious complications.

Ep.: Most frequent valve abnormality in the Western world. Occurs in about 3-4% of the adult population (depending on diagnostic criteria); familial clustering (autosomal dominant inheritance with incomplete penetrance is suspected). females > males

Aet.:

- Primary, idiopathic MVP: Myxomatous degeneration in the area of the mitral valve, possibly involving the mitral annulus and chordae tendineae as well. The chordae are often elongated and thin, but sometimes also clearly thickened. Disproportion between the size of the mitral valve apparatus and the left ventricle. The posterior, both, or rarely only the anterior mitral leaflets are affected.
- Secondary MVP: In cases of atrial septum defect, CHD, dilatative or hypertrophic cardiomyopathy, after myocarditis or in systemic diseases (such as Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta)

CL.: About 90% of patients with MVP are asymptomatic. Women are 5x more likely to be symptomatic than men.
Typical symptoms: arrhythmias (supraventricular and ventricular extrasystoles and tachycardia, WPW syndrome), palpitations, (pre)syncope, dyspnoea, reduced capacity, poor endurance, fatigue, states of anxiety, thoracic paresthesia, angina pectoris

Compl.:
- In about 10% of patients: progression of mitral valve regurgitation, rupture of chordae tendineae, endocarditis, higher-grade arrhythmias, arterial embolisms (source of embolisms: mitral valve or angle between the posterior mitral leaflet and the left atrial wall ("left atrial angle lesions")
- Sudden cardia death:
  - Incidence: not precisely known (about 1%)
  - Potential risk factors: higher-grade mitral regurgitation, severely deformed valve, increased heart weight, ventricular arrhythmia, severe autonomic dysfunctions with vagotonia, bradycardia; QT prolongation, possibly also obesity and hypertension

Clinical examination:

Frequently associated with asthenic body type, sometimes associated with skeletal abnormalities (e.g. scoliosis, straight back syndrome, pectus excavatum). Tendancy towards low body weight and low blood pressure

Ausc:
- Clicks: One or more high-frequency systolic clicks at the lower left sternal margin or over the apex of the heart resulting from the stretching of elongated chordae tendineae
- Mitral regurgitation systolic murmur

  Auscultation findings depend on the filling volume of the left ventricle and the position of the body. Loudness and characteristics may change within a short time in the same patient. In about 25% of cases, an MVP is "silent" during auscultation.

Dynamic auscultation (according to Devereux et al., 1989):

	Shift of click and murmur to the earlier systole	**Shift of click and murmur to the later systole**
Patho-physiology	• Measures that reduce left ventricular volume • Lowering of left ventricular afterload • Reduction of venous blood reflux to the heart • Increase in contractility	• Measures that increase left ventricular volume • Increasing of left ventricular afterload • Increase of venous blood reflux to the heart • Decrease in contractility
Maneuvre	• Standing up from a horizontal position • Administration of nitroglycerin • Straining phase of the Valsalva maneuver	• Autotransfusions (lifting the legs while lying down) • Taking a crouching position • Isometric exercises (e.g. pressing the hands together)

ECG: Usually normal. In 20% of cases (variable), flattening or inversion of the T-wave (especially in II, III, aVF). In patients with ST-T alterations, multiple episodes of supraventricular or ventricular arrhythmias. Also conduction disorders (AV blocks of every degree, left or right bundle branch blocks). QT-duration may be prolonged.

Exercise ECG:

Not infrequently, false positive findings in the sense of CHD (myocardial scintigraphy can also be falsely positive).

Echo:
- M-mode: In the vertical view during the mid- to late systole in the C-D segment, abrupt, at least 2 mm wide, movement in the posterior direction of the posterior and/or anterior mitral valve leaflet ("hammock" form) due to the prolapse of one or both mitral valve leaflets into the left atrium.

  Diagnosis of MVP using M-mode alone is not possible since a false positive diagnosis can result from incorrect positioning of the transducer.
- 2D Echo: Curved displacement of valve parts above the AV valve level in the left atrium (≥ 3 mm prolapse into the left atrium) in at least 2 views (parasternal and apical longitudinal section or apical 4-chamber view). Possible additional changes in the mitral valve annulus, thickened mitral valve leaflets, prolapse of tricuspid valve parts.
- Colour duplex: evidence of reflux due to mitral valve regurgitation

MRI: Quantification of any mitral regurgitation, anatomy + function of the heart

Invasive diagnostics:

If coronary heart disease must be excluded through differential diagnosis, possibly prior to surgery in cases of higher-grade mitral valve regurgitation.

Th.: Depends on the risk assessment:
- Low risk: Asymptomatic patients with no higher-grade arrhythmias or significant mitral regurgitation: Inform patients about the good prognosis of the cardiac findings, all athletic activities allowed. No drug therapy, no endocarditis prophylaxis. Progress monitoring at 5-year intervals.
- Moderate risk with mild mitral regurgitation, higher risk with higher-grade mitral regurgitation: Maintain normal weight; avoid caffeine, nicotine and alcohol; no athletics, no physical strain. Prophylaxis of bacterial endocarditis (see section on that topic). Treat arterial hypertension. Cardiological monitoring every 2-3 years, at least yearly in the high risk group.

Prophylaxis of complications:
- Arterial embolisms: If thrombus detection or embolisms in the patient's history: oral anticoagulants

- Supraventricular and ventricular arrhythmias:
  In symptomatic patients, administration of beta-receptor blockers; in malignant arrhythmias and in patients who have survived sudden cardiac arrest: implantation of an automatic cardioverter/defibrillator.
- Surgical treatment:
  In symptomatic patients with higher-grade mitral valve regurgitation: valve reconstruction or valve replacement.

AORTIC STENOSIS (AS) [I35.0]

Ep.: In Europe and Northern America nowadays the most common valve defect, prevalence in patients > 65 years ≥ 3 %.

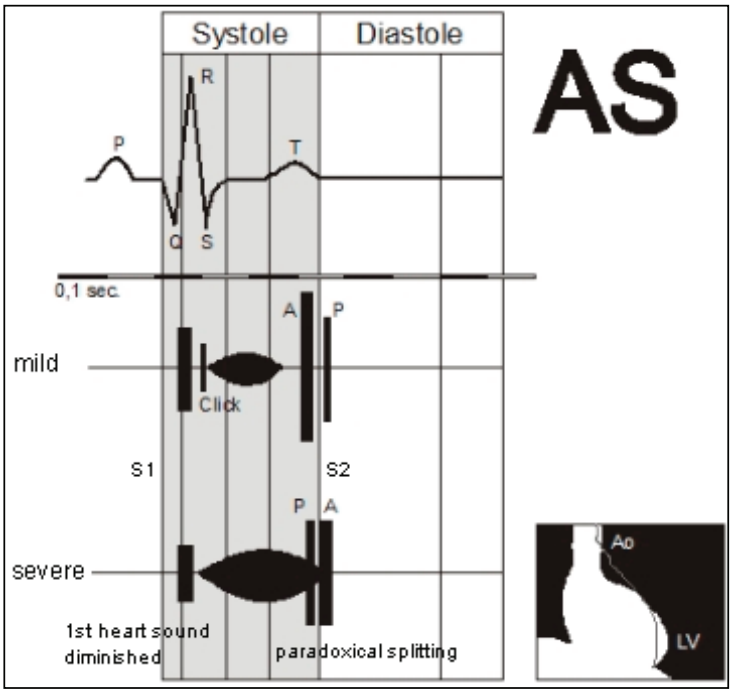
Aet.:
- Calcification of the valve is by far the most common underlying cause. Active process with similarities to atherosclerosis. Bicuspid valves develop AS earlier (require surgery in most cases between 50. and 70. year of age), tricuspid valves later (70. to 90. y.) .
- In younger adults in most cases it is a congenital AS, partially after palliative therapy with balloon valvuloplasty or surgical valvulotomy during childhood, in this case often combined with insufficiency.

  Special forms: Rarely subvalvular and supravalvular aortic stenosis (congenital)
- Rheumatic AS: In countries with modern health systems this has become rare thanks to consistent penicillin treatment of the underlying streptococcus infection. Semilunar valves are thickened, the commissures fused and later as well calcified. Combined with insufficiency of various degrees and usually additional post-rheumatic mitral valve changes.

PPh.: The aortic valve area (normal > 3 cm^2) must be severely narrowed (under 1,5 cm^2), before a haemodynamic effect occurs (very severe AS < 1 cm^2): Even severe AS can be asymptomatic.
- Pressure load on the left ventricle → concentric hypertrophy (not always present) → this enables the LV to override the gradients at the valve and maintain cardiac output. With maintained ventricular systolic function, which usually lasts long, primarily a diastolic dysfunction takes place and this finally leads to pulmonary congestion → increasing reduction in capacity and dyspnoea.
- Left hypertrophy → increased myocardial oxygen requirement, increased wall tension with subsequent impairment of coronary perfusion und subendocardial blood flow → angina pectoris (also with no coronary stenoses).
- Syncopes and vertigo during exercise due to decreased cerebral perfusion. Probably the reason is mainly an incorrect response of left-ventricular baroreceptors, which results in peripheral vasodilatation. Other causes: Arrhythmias, reduced cardiac output.
- Sudden cardiac death (during physical exercise) occurs almost exclusively in symptomatic patients

CL.: The spectrum of clinical manifestations and course range from the frequently occurring aortic valve sclerosis (prevalence of circa 30 % in patients > 65 years of age) to pronounced aortic valve calcification without haemodynamic effect to aortic stenosis with haemodynamic effect.
Patients are frequently not symptomatic until they have an aortic valve area < 1.0 cm^2, an average systolic gradient > 40 to 50 mmHg.
Mild AS: Many patients remain symptom-free for years (occasionally in cases of moderate stenosis as well!).
Higher-grade AS: Reduced capacity, rapid tiring, dyspnoea, angina pectoris, vertigo and syncope during exertion.

Inspection and palpation:
In the older patient a slow pulse with small amplitude is rare. Accentuated, broadened but not displaced apex impulse with concentric left hypertrophy. Thrill over the aorta and carotids.



Ausc.:

- ▶ Cardinal symptom: course, diamond-shaped systolic murmur:
  - punctum maximum: 2nd intercostal space right parasternal
  - offset from S1
  - conduction of murmur into the carotids
  - the greater the stenosis, the further into the late systole the maximum of the murmur is displaced
- ▶ Early systolic ejection click, which is lacking if the valve is immobile.
- ▶ In cases of high-grade stenosis, weakening of the aortic component of S2
- ▶ S2 splitting varies depending on respiration; in high-grade stenosis possible paradoxical splitting of S2
- ▶ In cases of concomitant aortic regurgitation: diastolic murmur

ECG: Changes are found in higher-grade stenosis: Left axis deviation, signs of left hypertrophy (Sokolow-Lyons index for left hypertrophy: SV1 + RV5 or 6 > 3.5 mV); left precordial T-wave negativity (V4-6) as indicative of pressure-induced cardiac hypertrophy.
Signs of hypertrophy can be absent even in severe AS!

Compl.: Arrhythmias and sudden cardiac death (20%), left heart failure

X-ray: In the compensated stage, normally sized heart (not until decompensation → left side enlargement), post-stenotic dilatation of the ascending aorta in aortic valve stenosis, possibly valvular calcification, pulmonary congestion with decompensation

Echo / Doppler (transthoracic / transoesophageal):

- Detection and quantification of the stenosis, measurement of the size of the atrium, assessment of sizes and function of both ventricles, involvement of other valves and assessment of pressures in the pulmonary circulation.
- Detection of calcifications or endocarditic vegetations.
- Thickening caused by fibrosis or calcified aortic cusps. Detection of leaflet abnormalities (unicuspid, bicuspid, tricuspid construction).
- Reduced valve opening with cupular "dome position" of the valves during systole
- Concentric left ventricular hypertrophy
- Maximum and average gradient over the stenosed valve and the surface area of the valve opening can be quantified (TEE).
- Detection of concomitant aortic regurgitation (reflux in the colour duplex)
- Possible post-stenotic dilatation of the ascending aorta

MRI: Calculation of the pressure gradient over the valvular stenosis, surface area of the valve opening, anatomy + function of the heart

Invasive diagnostics (left heart catheterization):

Ind: For quantification of the stenosis only if ECHO is not possible with sufficient quality or if a discrepancy of findings exist (rare). Pre-operative coronar angiography in male patients above 40 y. and female patients during menopause or in case of vascular risk factors.

Manometry:

Measurement of the systolic (peak to peak) and mean gradient over the valves (measured between LV and aorta) and calculation of surface area of valve opening

- Peak-to-peak gradient = Difference in pressure between maximum systolic LV pressure and maximum systolic aortic pressure (not measurable by Doppler ultrasound scan, because the peaks do not occur at the same time and thus the pressure difference cannot actually be measured at any time)
- Maximum instantaneous gradient = current maximum difference in pressure between the systolic LV pressure and the systolic aortic pressure, measured simultaneously (is not measured with heart catheter, but it would correlate with the Doppler ultrasound peak flow above the valve).
- Average gradient = area integral between the LV pressure curve and the aortic pressure curve, measured simultaneously (correlates with the mean instant Doppler gradient during the whole systole).

Gradient depends on degree of stenosis, blood flow over the valve and therefore cardiac output (with reduced ventricular function → lower gradient, in spite of relevant stenosis!) What is important is the aortic valve area (AVA), which can be calculated with the aid of the Gorlin formula.

Classification (gradation) of the severity of the AS:

	VA (cm^2)	VA/BSA cm^2/m^2)	Average Δp (mmHg)	Vmax (m/s)
Mild aortic stenosis	> 1. 5	> 1.0	< 25	< 3.0
Moderate aortic stenosis	1.0 – 1.5	0.6 – 1.0	25 – 50	3.0 – 4.0
Severe aortic stenosis	< 1.0	< 0.6	> 50	> 4.0

VA = surface area of valve opening; VA/BSA = surface area of valve opening/body surface area
Vmax = maximum transvalvular flow speed

History: Classification in the literature not uniform.

Natural course:

Patients with aortic valve stenosis may remain asymptomatic for many years in spite of higher-grade stenosis.

Memo: Patients with higher-grade stenosis are sometimes only ´asymptomatic´ because they avoid (sub-consciously) physical exertion, in order not to develop symptoms!

Asymptomatic patients: Good prognosis (sudden death clearly below 1% / year
Symptomatic patients: Prognosis very unfavourable with 2-year survival rate < 50%

In older studies, the average life expectancy in heart failure is 1-2 years, after syncope 2-3 years, with angina pectoris 4-5 years.

Follow-up examinations:

History (angina pectoris, vertigo, syncope, signs of heart failure?)
Echocardiography
Mild, asymptomatic stenosis: intervals of 3 years
Higher-grade, asymptomatic stenoses: 6 to 12 month intervals

Th.: A) Surgical valve replacement (Internet infos: *www.dgthg.de*)

Indication for surgery in aortic stenosis (level of evidence in brackets)

1) Symptomatic patients with severe aortic stenosis (IB)
2) Asymptomatic patients with severe aortic stenosis and
   - reduced left ventricular systolic function (EF < 50%) (IC)
   - Development of symptoms during exercise test (IC)
   - Medium to higher-grade calcified aortic valve and rapid haemodynamic progression (increase in AV Vmax > 0.3 m/s/year) (IIaC)
   - Pathological stress test with decrease of blood pressure below the initial BP (IIaC)
   - Pathological stress test with occurrence of complex ventricular arrhythmias (IIaC)
   - Severe left ventricular hypertrophy without existing hypertension (IIbC)

   (Indication and level of evidence according to ESC guidelines 2007)

B) Catheter intervention:
Balloon valvuloplasty only practical as a temporary measure in very young patients with a minimum calcified valve. In case of calcified stenosis only short lasting effect. At the moment a percutaneous valve replacement is developed, in which a biological valve is attached to a stent, which is applied via the arteria femoralis as an alternative for patients with a high risk of surgery (older patients with co-morbidity)

C) Pharmaceutical:
- Patients with AS, who develop symptoms must be considered for surgery (no place for pharmaceutical therapy, as long as patient is a potential candidate for surgery!)
- According to new guidelines AS no more indication for endocarditis prophylaxis.
- Statins are in discussion for avoidance resp. delay of the progression of the calcifying AS. Patients with hyperlipidaemia probably gain from it, in absent hyperlipidaemia so far no effect could be proven.
- In patients, who develop cardiac failure and who are no candidates for surgery (multimorbidity, short life expectation because of other factors, which cannot be influenced): Diuretics, ACE-inhibitors and ATII-inhibitors are contra-indicated.

AORTIC VALVE REGURGITATION (AR) [I35.1]

Def.: Acute or chronic inability of the semilunar valve to close between the aorta and left ventricle as a result of deformation of the semilunar valve, dilatation of the aortic root, prolapse of an aortic cusp or destruction of the valve.

Aet.: Acute AR: Frequently when the aortic valve is affected by bacterial endocarditis, more rarely after trauma or in aortic dissection type A.
Chronic AR: Often congenital (bicuspid aortic valve), dilatation of the aortic root and valve annulus: Dilatation caused by atherosclerosis (in patients > 60 years): Marfan syndrome, Ehlers-Danlos syndrome, syphilis
Prolapse of an aortic valve leaflet, fissures of the leaflets, rarely post-rheumatic.

PPh.: AR → diastolic reflux of blood through the aortic valve, which is incapable of closing, into the left ventricle (LV) → large stroke volume, which is increased by the regurgitant flow volume → volume loading of the LV, which in case of AR dilates and an eccentric left hypertrophy may develop. The end-diastolic pressure increases only slightly in the beginning due to the extensibility of the ventricle. Initially, the cardiac output can be maintained → patients are largely asymptomatic. A mildly to moderately chronic AR can sometimes be tolerated for decades.
Once the heart has attained a certain size, however, the stroke volume can no longer be maintained → ventricular compliance decreases → end-diastolic ventricular pressure and end-systolic ventricular volume increase.
Remember: If there is a higher-grade AR over a longer period of time, there is a danger of irreversible myocardial damage that persists even after successful valve replacement and can lead to progressive cardiac failure. The damage can even already be present in a stage, in which no serious symptoms yet have occured. Therefore the recognition for the right (early) time of surgery is important and apart from the development of symptoms is determined by the reaching of critical limits of ventricular size and function (see below).

CL.:
- Chronic AR:
  AR is clinically diagnosed and the findings of the physical examination allow a semi-quantitative assessment of the severity.
  In the beginning, physical capacity is maintained, but palpitations may occur. As the disease progresses, there is a decrease in capacity and left heart insufficiency develops.
  Syncope, arrhythmias, angina pectoris or sudden cardiac death are more rare in comparison to aortic stenosis.
- Acute AR:
  Rapidly leads to left cardiac decompensation and pulmonary oedema because there is no time of the heart to adjust.

Inspection and palpation:

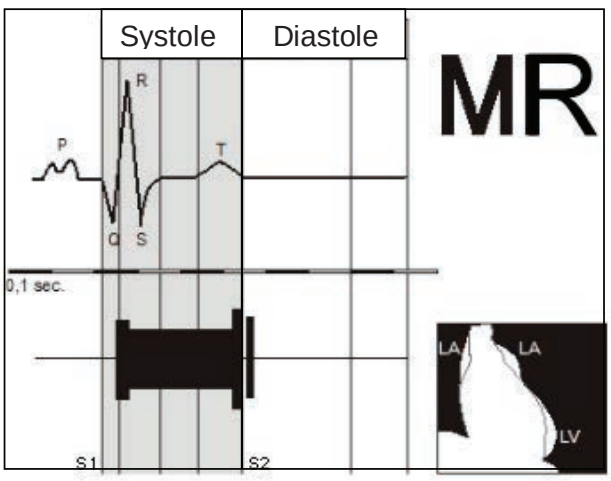
► Cardinal symptom: Large blood pressure amplitude with rapid pulse and high pulse pressure amplitude ("water hammer" pulse):
- Systolic blood pressure ↑ (large stroke volume)
- Diastolic blood pressure ↓ (air-chamber effect due to blood reflux)

This sign is fairly specific but not sensitive (despite severe AR it may be absent mainly in older patients in case of pathologic peripheral vascular resistance)

► Pulsatory phenomena as a result of the large blood pressure amplitude, e.g.
- pulse-synchronized hammering sensation in the head
- visible pulsation of the carotids (Corrigan)
- visible capillary pulse (Quincke) after light pressure on a fingernail
- pulse-synchronized head nodding (de Musset → pronounced: "moo-say")

► Pale skin

► Apex impulse with eccentric left hypertrophy, hyperdynamic, broad, displaced downwards and outwards.



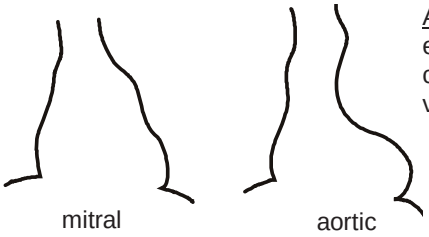
► Auscultation
1. Diastolic decrescendo murmur immediately following the 2nd heart sound.The murmur is a “blowing” sound of high frequency; it is best heard over the aorta or Erb’s point (3rd intercostal space left parasternal) while the patient is leaning forward.
2. Two additional murmur phenomena are of the functional type:
- A systolic crescendo-decrescendo murmur can regularly be heard as a result of relative aortic stenosis (volume murmur): The cause is a disproportion between the normally sized valve opening and abnormally large stroke volume.

- Austin-Flint murmur: Occasional rumbling late-diastolic murmur caused by impedance of the anterior mitral leaflet by the diastolic blood reflux.

► Over the femoral arteries: pistol shot phenomenon, Traube's double tone, Duroziez's double murmur

ECG: Signs of left heart hypertrophy (Sokolow-Lyon Index: SV1 + RV5 or 6 > 3.5 mV). Typical of volume hypertrophy are accentuated Q-spikes; in contrast to aortic stenosis (= pressure hypertrophy), negative T-waves do not occur until late.

X-ray:



cardiac configuration

Aortic configuration: Enlarged left ventricle discharges totheleft,dilatationand elongation of the ascending aorta, prominent aortic knob (in the pronounced condition, so-called "boat-shaped" heart). Pulsation of the aortia and left ventricle (fluoroscopy).

Echo (transthoracic / transoesophageal):

First indication often is a reflux through the valves (AR-jet) easily recognizable via colour Doppler; 2D-echo allows determination of the aetiology (bicuspid valve, endocarditis, secondary AR in case of aortic aneurysm etc), semi-quantification of proximal jet range (´vena contracta`, diastolic pressure gradient between aorta and ventricle imaging via CW-Doppler spectrum, retrograde flow within the aorta, volume load of the ventricle), assessment of left ventricular function and size, which is decisive for management (see below); involvement of other valves and estimation of pressure conditions in the pulmonary circulation.

MRI: Left ventricular volume and ejection fraction, aortic size, quantification of the reflux

Invasive diagnostics (left heart catheterization):

Ind: Assessment of the degree of regurgitation, if non-invasive methods not sufficiently possible; determination of pressures in the systemic and pulmonary circulation, evaluation of ventricular function, exclusion of CHD requiring treatment and determination of size of the ascending aorta.

Manometry:

- Aortic diastolic pressure ↓, high amplitude of blood pressure (in case of chronic AR)
- LVEDP: Increased in case of acute AR; in case of chronic AR the LVEDP initially is normal, later it is increased.

Levocardiogram and aortogram:

- Extent of contrast medium reflux (CM) into the LV
- Left ventricular size and function
- Relative mitral regurgitation

Classification of severity:

Classification	Contrast medium reflux	Regurgitation fraction
Grade I	• Low CM quantity reaches the LV outflow tract diastolically and is completely ejected again systolically.	< 20%
Grade II	• Entire cavity weakly filled with CM	20 - 39%
Grade III	• Entire cavity clearly filled with CM • Same CM density as in the ascending aorta	40 - 60%
Grade IV	• Entire cavity is already filled completely with CM during the first heart cycle • CM density in the LV exceeds that of the ascending aorta.	> 60%

Determination of regurgitation fraction (RF): See section on mitral regurgitation

Natural course:

Patients with AR may remain asymptomatic for a long time. The 10-year survival rate after diagnosis of mild to moderate AR is 90%; with a higher-grade AR, it is 50%. Symptomatic patients have an unfavorable prognosis.
The average survival time with angina pectoris is about 5 years; it is about 2 years with heart failure.

Follow-up examinations (with echocardiography and stress testing):

- Asymptomatic patients with maintained systolic ventricular function and end-systolic diameter of the left ventricle (LVESD) < 50 mm and repeated measuring of stable values: intervals of 12 months
- In cases of higher-grade changes resp. significant changes of findings: 3 to 6 month intervals

Th.: A) Conservative treatment:

- Asymptomatic patients with haemodynamically significant AR: Remain physically active, but avoid excessive exertion or competitive sports.
- Symptomatic patients: Surgery
- Treatment of left heart failure in patients, who are unsuitable for surgery: ACE inhibitors, digitalis, diuretics (avoid bradycardia)
- According to current guidelines endocarditis prophylaxis not recommended anymore
- More current data again suggest, that in the case of asymptomatic AR with an already dilated ventricle a therapy with nifedipine (poss. also ACE-inhibitors) does not put off the requirement for surgery

B) **Surgical treatment (level of evidence in brackets):**

Usually valve replacement, rarely valve reconstruction (e.g. if aortic ectasia/aneurysm is the cause for the AR)

Indication for surgery in severe aortic regurgitation

Ind:	1. Symptomatic patients	Dyspnoea during exertion from NYHA II on or angina pectoris (IB)
	2. Asymptomatic patients	EF < 50 % (IB)
	3. Asymptomatic patients	EF > 50 % but end-diastolic LV-diameter > 70 mm or end-systolic diameter > 50 mm (> 25 mm/m² of body surface area) (IIaC)

Indication for surgery independent of grade of severity in aortic dilatation:

- in Marfan syndrome with aorta ascendens ≥ 45 mm (IC)
- in bicuspid aortic valve and aorta ascendens ≥ 50 mm (IIaC)
- other patients and aorta ascendens ≥ 55 mm (IIaC)

(indication and grade of evidence according to ESC guidelines 2007)

ADULT PATIENTS WITH CONGENITAL HEART DEFECTS

Internet information: *http://leitlinien.dgk.org/ ; www.cachnet.org/downloads/AHA_ACC_2008-Guidelines.pdf*

Ep.: About 1% of live births suffer from a malformation of the heart or great vessels. Untreated, up to 25% die as neonates and an additional 60% die within the first 2 years. At best, a maximum of 15% reach adulthood untreated. The high primary mortality associated with congenital heart defects has declined to less than 15% over the last few decades, due to significant medical advances. Currently it is estimated in Germany, that more than 180 000 patients with a congenital heart valve defect have reached an adult age. This figure increases steadily

Aet.: Congenital heart defetcs in most cases develop in the early phase of the organ formation between the 5. to the 8. Weeh of pregnancy. Multifactorial causes are suspected (e.g. environmental influences, infections, genetic disposition).
Known causes include infections (e.g. rubella or other viral infections), exposition to irradiation, drugs, alcohol abuse and numerous drugs (➔ *www.embryotox.de*), furthermore some diseases (e.g. diabetes mellitus, lupus erythematosus).
Chromosomal defects of the child such as trisomie 21 (Down syndrome), trisomy 13, 18 or Turner-, Noonan- or Marfan-syndrome frequently are associated with congenital heart defects.

Introduction: Almost all patients with congenital heart defects require special cardiological care for their entire lives because of residual conditions and subsequent long-term clinical complications.
Residual condition: Anatomical or haemodynamic deviations from the norm that persist after surgery and existed before as part of the congenital malformation or that develop as a result of the heart defect, as well as abnormalities, which were unsuccessfully treated or in which treatment was not justified (due to an increased risk)
Long term complications: Anatomical or haemodynamic aftereffects of the operation that had been unavoidable at the time of the intervention.
Especially in the case of more complex heart defects, the follow-up of adults with congenital heart defects should be performed by cardiologists or child cardiologists, who underwent special training in this area.

In surgery on congenital defects, a differentiation is made between palliative and corrective procedures.
"Correction": A corrective operation establishes and maintains normal function, normalizes life expectancy and makes it so that no further medical or surgical measures are necessary at a later point in time (almost only achievable in case of ASD or PDA).
"Relative correction/partial correction": In this case, there is a risk that, sooner or later, additional medical or surgical measures are required (almost all heart defects: e.g. aortic isthmus stenosis, transposition of the great vessels,

tetralogy of Fallot, etc.).
Palliative operation: Installation of aortopulmonary shunts, implantation of conduits, interventions for pulmonary atresia with ventricular septal defect and aortopulmonary collaterals, as well as heart, heart-lung or lung transplantation.

Classification of congenital heart defects

ACYANOTIC DEFECTS		CYANOTIC DEFECTS
Obstruction of valves/ Vessels	**Primary left-to-right shunt**	**Right-to-left shunt**
• Pulmonary stenosis • Aortic valve stenosis • Aortic isthmus stenosis	• Atrial septal defect • Partial anomalous pulmonary venous connection • Ventricular septal defect • Atrioventricular septal defect • Aortal-pulmonal window • Persistent ductus Botalli	• Tetralogy of Fallot • Pulmonal atresia • Double outlet ventricle • Tricuspid atresia • Complete transposition • Truncus arteriosus • Univentricular heart • Total anomalous pulmonary connection

PULMONARY STENOSIS (PS) IN ADULS - OBSTRUCTIONS OF THE RIGHT VENTRICULAR OUTFLOW TRACT [I37.0]

Def.: Forms: Subvalvular, valvular, supravalvular, peripheral
- Valvular stenosis: The valve itself is affected. It is non-commissural, commissural, bicuspid, tricuspid or dysplastic (myxomatous thickened and restricted mobility).
- Subvalvular stenosis: Located in the area of the infundibulum or subinfundibulum. Subinfundibular stenoses (double-chambered-right-ventricle) through hypertrophic muscle bundles in the RV, frequently associated with SVD.
- Supravalvular stenoses: Stenoses of the PA-trunk, the pulmonalis bifurcation or of the PA side branches.
- Peripheral stenoses: Individual or multiple stenoses, also unilateral or bilateral, in the peripheral pulmonary arteries

Ep.:
- Valvular: About 10% of all congenital heart defects
- Subvalvular/supravalvular: About 3% of all congenital heart defects
- Gender ratio: m : f = 1 : 1
- Associated abnormalities: ASD, VSD, Noonan syndrome, supraclavicular stenosis frequently in case of tetralogy of Fallot, Williams syndrome
- Isolated or as components of more complex heart defects, e.g. in case of tetralogy of Fallot

PPh.: Stenosis of the right ventricular outflow tract → prestenotic (in the right ventricle) increase in pressure; poststenotic (pulmonary artery) fall in pressure. Pressure load on the right ventricle → concentric hypertrophy → right heart decompensation (in the longterm). Turbulent blood flow behind the stenosis → dilatation of the pulmonary artery (poststenotic dilatation).

Classification of degree of severity (based on pressure gradients between the right ventricle and pulmonary artery as determined by echocardiography):

Definition	Peak velocity	Peak-Gradient
Mild	< 3,0 m/sec	Δ p < 36 mm Hg
Average	3,0 - 4,0 m/sec	Δ p 36 - 64 mm Hg
High-grade	> 4,0 m/sec	Δ p > 64 mm Hg

Always measure the RV-pressure above a tricuspid insufficiency, since the determination of the gradient may be unreliable.

Natural course (spontaneous course without surgical treatment):
- Almost all reach adulthood (exception: children with critical pulmonary valve stenosis).
- Average age of death: 26 years (in older studies)
- Spontaneous courses up into the 8th decade of life
- Spontaneous course depends on
  - severity of the initial stenosis

- progress over time
- ability of the right ventricle to compensate for the additional strain

- With advancing age, the severity of previously diagnosed high-grade valvular stenosis as a result of progression of fibrosis; but all in all rare in adulthood; subvalvular/infundibular stenoses tend to progress.
- With the beginning of the 4th decade of life, valvular calcification
- With the increase in gradients, development of infundibular stenosis is possible, associated with increasing right ventricular hypertrophy.
- As a result of severe stenoses, development of right heart dilatation with consecutive right-sided heart failure
- Causes of death related to spontaneous progression: right heart failure, strain-induced sudden cardiac death
- Right-to-left shunt when volume overflow and shunt reversal occur at the level of a patent foramen ovale, leading to right atrial dilatation
- In rare instances, infectious endocarditis

CL.: Cardinal symptoms:
- Pattern of fixed, small cardiac output;
- Direct relationship between symptoms and severity of the stenosis

Symptoms:
Physical fatigability, (exertional) dyspnoea, heart failure, stenocardia, vertigo, syncope.

Inspection/palpation:
- Primarily acyanotic patient
- Peripheral cyanosis with at low minute volume
- Central cyanosis with right-to-left shunt at level of atria
- Rising pulsations at the left lower sternal edge
- Systolic thrill in the left parasternal area
- Possibly signs of right ventricular failure

Auscultation:

Stenosis	Valvular	Subvalvular	Supravalvular	Peripheral
Early systolic pulmonary valve ejection click	•With mild to moderate valvular stenosis •Not with dysplastic valve	Absent	Absent	Absent
2nd heart sound	Widely split with soft pulmonary valve component			
Murmur	• Systolic ejection murmur • Punctum maximum: In the $2^{nd}/3^{rd}$ intercostal space in the left parasternal region radiating into back	• Systolic ejection murmur • Punctum maximum: deeper	• Systolic ejection murmur • Punctum maximum: higher	•Systolic vascular murmur in the periphery of the lungs • sometimes, a continuous murmur

ECG: In cases of mild stenosis, the ECG may be normal.
In cases of higher-grade stenosis:
- P-dextroatrial and/or signs of right ventricular hypertrophy (right axis deviation, positive Sokolow-Lyon index), esp. if peak-gradient > 60 mmHg
- (In)complete right bundle branch block

X-ray:
- Transverse diameter of heart not enlarged as long as right ventricular function is intact.
- Cardiac apex raised in cases of right heart hypertrophy
- Narrowing of the retrosternal space
- Poststenotic enhancement of the pulmonary component (no association with the severity of the stenosis!)
- Left pulmonary artery sometimes disproportionately enlarged.
- Diminished visibility of peripheral pulmonary vasculature.
- Calcification of the pulmonary valve

Echo:
- 2-D echo: Evaluation of the pulmonary valve anatomy and function, size of the pulmonary valve ring and pulmonary artery, size and function of the right heart.
- Doppler: measurement of gradients; estimate of right ventricular and pulmonary artery pressure; classification of any concomitant pulmonary valve regurgitation

MRI: pressure gradient, planimetry of the pulmonary valves, localization of the stenosis well possible, estimation of the PA-dilatation, good quantification of the RV function and volume.

Pulmonal scintigram: For the assessment of lung perfusion and of the side resp. segmental distribution.

Cardiac catheterization → Indications:

- In cases of poor image quality
- If a catheterization procedure is planned at the same time
- In case of associated abnormalities
- In case of concomitant coronary heart disease

Th.: Indications for therapy:

- Symptomatic patients (dyspnoea at exertion, angina pectoris, pre-syncope or syncope)
- Maximum, invasively measured gradient above 50 mmHg
- Greater than half-systemic pressure in the right ventricle
  (***Caution***: Low RV pressure in case of heart failure!)
- Relevant arrhythmias (in most cases atrial flutter)
- Associated ASD or VSD, esp. with right-left shunt
- Possibly also if the patient wishes to participate in competitive sports or prior to planned pregnancy

1. Balloon valvuloplasty / stent implantation:
   - Meanwhile has become the therapy of choice in case of vascular, supraclavicular and peripheral stenoses
   - Excellent long-term results
   - Restenosis rate < 5%
   - Less favourable results for dysplastic or calcified valves
   - In cases of central or peripheral pulmonary artery stenoses, can be combined with stent implantation
2. Operation:
   Esp. in cases of infundibular/subvalvular stenosis, hypoplastic valve ring, dysplastic valves and in accompanied anomalies which require surgery

   Treatment indications:
   - All right obstructions – independent of symptoms – with a Doppler peak-gradient > 64 mm Hg (peak velocity > 4 m/s) should be treated if the RV function is normal and no valve replacement is required.
   - Asymptomatic patients, after ineffective balloon valvuloplasty, operative treatment if systolic RV pressure > 70 mm Hg (Vmax above the tricuspid valve > 4m/s).
   - Indication for intervention in symptomatic patients with peak-gradient < 64 mm Hg or if RV function is restricted, in case of relevant arrhythmias or of a right-left shunt above an ASD or VSD.
   - Peripheral pulmonal stenoses – independent of symptoms - with > 50 % restriction of the lumen, a systolic RV pressure > 50 mm Hg and/or relevant changes of the lung perfusion

Long-term results and clinical complications:

- In cases of early valvuloplasty or surgery, usually very good functional results
- Post-operative life expectancy nearly normal
- Gradual regression of right heart hypertrophy
- Residual stenosis (3 - 5%, both after valvuloplasty and after surgery)
- Pulmonary valve regurgitation, especially after dilatation of the right ventricular outflow tract
- Risk of endocarditis generally low, but also persistent after surgery
- Repeat operations: About 3% after 20 - 30 years

AORTIC ISTHMUS STENOSIS (COARCTATION OF AORTA) DURING ADOLESCENCE AND ADULTHOOD [Q25.1]

Syn: CoA = Coarctatio aortae

Def.:

- Organic stenosis of the physiological narrowing between the outlet of the left subclavian artery and the aortic opening of the ductus arteriosus. Basically it has to be differentiated between discrete resp. defined aortic isthmus stenosis and tubular hypoplasia of the distal aortic arc.
- Pathogenetic the CoA results from ductal tissue, which surround pincer-shaped the aortic wall and which causes a stenosis through postnatal atrophy. Thus every CoA is „juxta-ductal". The terminology „pre-" or „post-ductal" became outdated!
- Ectopic forms of the ascending (arcus stenosis) or descending aorta are rare.
- CoA presents a part of a generalized arteriopathy and not only a single localized atrophy of the aorta!

Associated anomalies:

- Bicuspid aortic valve (up to 85 %), ventricle septal defect, mitral valve anomaly
- Intracranial aneurysms around the area of the Circulus Willisii
- Turner-, Williams-Beuren-syndrome, neurofibromatosis
- „Cystic media necrosis" of the aorta ascendens and descendens with resulting wall stiffness of the aorta and of the cranial/cervical vessels.

Ep.: •About 8% of all congenital heart defects
- Gender ratio: m : f ~ 2 : 1

PPh.: • Perfusion of the lower half of the body through collateral vessels, the degree dependent on the degree of the stenosis.
Collaterals: Branches from the subclavian, internal thoracic, thyrocervical, subscapular or anterior spinal arteries → blood to the intercostal arteries → below the isthmus stenosis into the aorta → blood supply of the body parts located below the stenosis
- Stenosis → brachiocephalic hypertension and hypotension in the abdomen and lower extremities

Spontaneous course:
- Of the patients who survive the first 2 years, 25% die by the age of 20, 50% by the age of 32 and 75% by the age of 46.
- Few patients reach the 9. or 10. decade of life.
- Patients who reach adulthood untreated usually have a mild, postductal coarctation of the aorta and may be symptom-free.
- Complications in the spontaneous course: Left heart failure, intracranial bleeding following vessel rupture of preformed cerebral aneurysm, bacterial endocarditis, aortic rupture, premature coronary heart disease, complications caused by associated malformations of the heart.

CL.: 3 most prominent clinical symptoms:
- Higher blood pressure in the upper half of the body with large blood pressure amplitude, warm hands
- Symptoms of hypertension: headaches, nosebleeds, dizziness, tinnitus
- Low blood pressure in the lower half of the body (cold feet, gradient between upper and lower extremities > 20 mmHg)
- Femoral artery and foot pulses weak; possibly intermittent claudication
- Possibly palpable collateral circulation: intercostal, in the back or in the lateral chest wall
- Prominent apical cardiac beat: rising and broad, but not displaced (concentric left ventricular hypertrophy)

Ausc: • Second heart sound normally split, with loud A2
- Aortic ejection sound (click) in cases of bicuspid aortic valve, aortic ectasia or hypertension
- Vascular murmur in the back, interscapular
- Systolic interval crescendo-decrescendo murmur in the aortic region (in cases of bicuspid aortic valve or as a result of hypertension)
- Diastolic decrescendo murmur following aortic valve closure (in aortic regurgitation as a result of bicuspid aortic valve)
- Continuous murmur in the area of the collateral vessels

ECG: Left atrial and left ventricular load (Sokolow-Lyon index, Lewis index)

X-ray: • Normal heart size
- Widening of the ascending aorta
- Kinking or double contours in the area of the descending aorta ("triple" sign, epsilon sign during barium swallow)
- Dilatation of the left subclavian artery
- Notching of the inferior margin of the 3^{rd} - 4^{th} (- 8^{th}) ribs (usually not until after 5 years of age)

Echo: • The coarctation region is relatively easily recognized in children, but can usually only be visualized from the suprasternal notch in adults.
- Morphology, extent and location of the stenosis
- Left ventricular diameter (hypertrophy), ventricular function
- Associated cardiac abnormalities (bicuspid aortic valve!, ectasia of the aorta ascendens)
- Doppler examination: Turbulent flow pattern peripheral of the stenosis with increased flow speed and diastolic `run-off `(gradient assessment using the extended Bernoulli formula; ***caution***: Doppler gradient unreliable); with higher-grade stenosis, diastolic flow rate above the stenosis and also diastolic anterograde flow in the aorta abdominalis must be assessed as well!

MRI / CT: Imaging of the aorta in MRI and CT, determination of flow and gradients in MRI; assessment of the collateral circulation

Cardiac catheterization:
- Imaging of the anatomy in the area of the aorta and supraaortic vessels
- Determination of the pressure gradients through the isthmus region.
A CoA is regarded as significant in invasive peak-peak-gradient > 20 mmHg, if no larger collaterals exist. A direct comparison of the catheter gradient with the maximum and median flow rate, measured by Doppler-echocardiogram, is problematic. In strongly developed collateralization even stenoses of higher grades have no significant gradient.
- Detection of associated cardiac abnormalities
- Evaluation of left ventricular function
- Evaluation of coronary status (concomitant CHD!)
- Simultaneous balloon angioplasty and/or stent implantation

DD: Arterial hypertension of other genesis

Notes: Juvenile hypertension is not "essential" hypertension until the opposite is proven! (All forms of secondary hypertension must be excluded!)

Th.: Indications for therapy:

- All patients (independent of clinical symptoms) with non-invasive gradient > 20 mm Hg between upper and lower extremity and arterial hypertension (> 140/90 mm Hg in adults), pathologic blood pressure during exertion or significant left hypertrophy
- Independent of the pressure gradient: Patients with arterial hypertension and a stenosis diameter, which is < 50 % of the aortic width at the diaphragmatic level (in MRI, CT or aortography).
- Associated significant aortic valve stenosis or regurgitation
- Aneurysm of the aorta ascendens with a diameter > 50 mm (2,75 mm/m^2 BSA) or a rapid growth in size
- Aneurysms within the former isthmus area
- Symptomatic or large aneurysms of the Circulus Willisii
- Therapy should only be performed in centres who are experienced in the treatment of congenital heart defects.

Surgical intervention in adults:

- As soon as possible after diagnosis
- In case of surgery after pre-school age often an arterial hypertension persists.
- Interventions after the ages of 30 or 40 are associated with increased mortality related to increased degenerative changes in the aortic wall.
- In this age group, co-existing bicuspid aortic valves, mitral valve abnormalities, coronary heart disease and organ damage caused by arterial hypertension must be considered.

Surgical procedures:

- Resection and end-to-end anastomosis
- Resection and bridging by the interposition of a prosthesis
- Direct isthmoplasty as described by Vossschulte
- Indirect isthmoplasty as described by Vossschulte (patch plasty)
- Creation of a bypass using a prosthesis
- Subclavian plasty as described by Waldhausen.

Balloonangioplasty, possibly in combination with stent implantation → indications:

- In case of native coarctation of the aorta and suitable anatomic conditions the angioplasty – poss. with stent implantation - is the therapy of choice, esp. if surgery involves a high risk or is contraindicated for other reasons.
- Re-stenosis or residual stenosis following surgery.

Long-term results and clinical complications associated with surgery for CoA:

- Long-term course: Mortality due to hypertension and cardiovascular complications higher than for the normal population.
- Long-term survival rates after surgical correction: About 90% after 10 years, about 85% after 20 years, and about 70% after 30 years. The average age of death of those dying later is 38 years.
- Persistent or recurring arterial hypertension at rest and/or during exertion (!).
- Aneurysms of the ascending aorta and/or descending aorta (up to 30% after implantation of a synthetic patch)
- Restenosis/residual stenosis in the isthmus area
- Coronary heart disease
- Aortic sclerosis and stenosis / aortic regurgitation (with bicuspid aortic valve)
- Mitral valve abnormalities (mitral prolapse)
- Infectious endocarditis
- Rupture of aortic or cerebral aneurysms

CONGENITAL HEART DEFECTS WITH LEFT -> RIGHT SHUNT

ATRIAL SEPTAL DEFECT (ASD) IN ADULTS [A21.1]

Def.: Pathological/abnormal connection between the atria of the heart due to substance defect.

Main forms and location:

- Ostium secundum defect (ASD II): in the area of the oval fossa
- Ostium primum defect (ASD I; partial septal defect): directly cranial of the atrioventricular level. Portions of the atrioventricular septum are missing and there is an abnormal AV valve anatomy.
- Sinus venosus defect: Outside of the oval fossa, at the opening of either the superior or inferior vena cava into the atrium (in the superior type, cranial, in the inferior type, caudal).
- Rare defects: common atrium, defective coronary sinus
- Persisting foramen ovale (PFO) represents a norm variant, no septal defect in the narrower sense! Depending on examination conditions (echo, catheter, autopsy) different prevalences up to circa 30 % are described in the literature.

Ep.:
- In adults circa 25% of the congenital defects.
- ASD II about 80%, ASD I about 15%; remainder are rare defects
- Open foramen ovale (patent foramen ovale = PFO) prevalence up to circa 25% of total population.
- Gender ratio: m : f ~ 1 : 2

Associated abnormalities:
Nearly all congenital heart defects are possible (frequently: partial anomalous pulmonary venous connection, pulmonary stenoses, ventricular septal defect, mitral valve prolapsed, left upper portal vein a.o.).
Familial forms of ASD: e.g. in Marfan, Turner and Down syndrome

PPh.: Pulmonary and systemic circulation are connected to each other through an interatrial opening. In cases of simple ASD, the distensibility of the right ventricle is greater than that of the left → particularly left-to-right shunt with consecutive supply of oxygen-rich blood into the pulmonary circulation).
The actual shunt volume is dependent on the size of the defect (significant shunts in most cases < 10 mm in diameter), compliance of both ventricles, and pulmonary vascular and systemic vascular resistance.
Any reduction of the LV compliance or an increase of the LA pressure (hypertension, CHD, cardiomyopathy, aortic or mitral valve defects) cause an increase of the LR-shunt.
Consequence: Large minute volume in the pulmonary circulation, small minute volume in the systemic circulation!
Blood flow: Oxygenated pulmonary venous blood → left atrium → right atrium → tricuspid valve → right ventricle → pulmonary valve → pulmonary circulation.
Load: Volume load of right atrium, tricuspid valve, right ventricle, pulmonary valve and pulmonary circulation. The elevated flow volume on the right side causes relative stenosis of the tricuspid and pulmonary valves.
A moderate elevation in blood flow in the pulmonary circulation does not necessarily lead to a significant elevation in pulmonary arterial pressure.
There is usually not a secondary increase in resistance in the pulmonary circulation until late in the spontaneous course (after the 4. decade of life) → pressure load on the right heart with reduction of the left-to-right shunt and appearance of a right-to-left shunt (shunt reversal) = Eisenmenger syndrome (see special section).
Special form: `ASD Eisenmenger syndrome`. Rare! Hereby a pulmonary vascular defect develops already in the early ages of life. It is discussed, whether this represents a coincidence between an ASD and an idiopathic pulmonary arterial hypertension.

Spontaneous course:
- Spontaneous closure: In the case of a small ASD (< 5mm) in 80% within the first 4 years of life.
- Spontaneous life expectancy: In the presence of a small left-to-right shunt, patients may remain asymptomatic for more than 5 decades. Symptoms frequently do not appear until after the age of 40. Nearly all patients become symptomatic in the 6th decade of life.
- Atrial arrhythmias, especially atrial flutter and atrial fibrillation
- Elevated pulmonary arteriole resistance: Rarely in cases of isolated atrial septal defect, and then not until the patient is of advanced age.
- Causes of death: Cerebral embolisms with atrial fibrillation or the passage of thrombi through the ASD = paradoxic embolism, pulmonary embolisms; right heart failure in the late course; cerebral abscesses and endocarditis (with associated mitral valve prolapse).
- Danger of endocarditis: Low in cases of isolated ASD.

CL.:
- Findings variable and depending on the severity of the defect.
- Discomfort and symptoms: performance restriction, rapid fatigability, dyspnoea with minimal exertion, palpitations, recurring pulmonary infections, chest pain, cerebral insults; right heart failure
- Inspection/palpation: Delicate anatomy, pallor of the skin
- Prominent pulsations in the 3rd intercostal space on left (right ventricular outflow tract)

Auscultation:
- Fixed (= breathing-independent) splitting of the 2nd heart sound in the 2nd intercostal space on the left (delayed closure of the pulmonary valve caused by elevated right ventricular stroke volume and right bundle branch block).
- Continuous systolic murmur in the 2nd intercostal space on the left (relative pulmonary valve stenosis caused by increased blood flow)
- Protodiastolic murmur in the 4th intercostal space on the left (relative tricuspid stenosis)
- In the presence of pulmonary hypertension: early systolic pulmonary ejection click conducted to 2nd intercostal space on left, continuous systolic murmur, accentuated 2nd heart sound, protodiastolic decrescendo murmur (as a result of relative pulmonary regurgitation = Graham–Steell murmur)

ECG:
- Right axis deviation, vertical axis, rarely (marked) left axis deviation with associated mitral valve prolapsed or (typically) with ASD I
- Grade I AV block
- Right atrial P waves
- Incomplete or complete right bundle branch block
- Right heart hypertrophy (Sokolow-Lyon index)
- Ectopic atrial rhythm, atrial arrhythmia

X-ray:
- Enlarged right atrium and right ventricle
- Prominent pulmonary artery

- Increased central and peripheral pulmonary vascular pattern
- Narrow aorta

Notes: Typical radiologic sign of all congenital cardiac defects with left-to-right shunt is the associated increased perfusion of the pulmonary vasculature, with prominent pulmonary artery and pulmonary vessels.

Echo:
- Contour defect of interatrial septum (the defect can be seen especially well with transoesophageal echo!)
- Enlargement of the right atrium, the right ventricle and the pulmonary artery
- Paradoxical interventricular wall motion (right ventricular volume load)
- Detection of direction of shunt flow as well as assessment of right ventricular and pulmonary artery pressures using Doppler methods
- Where appropriate, contrast dye injection allows assessment of direction of shunt flow

MRI: ASD and shunt can be quantified

Cardiac catheterization → Indications:

When non-invasive methods are inadequate and in cases of suspected pulmonary hypertension, associated abnormalities or coronary heart disease

Allows defect assessment, determination of defect size (balloon sizing), estimation of shunt size, and severity of pulmonary vascular resistance

Th.: Patients of all ages benefit from the ASD closure in regards to their morbidity (exercise capacity, dyspnoea, RVF)

Ind:
- All symptomatic children and young adults
- Presence of right heart enlargement in echocardiogram
- Pulmonary/systemic volume in a given time (QP/QS) ≥ 1.5 – 2.0: 1
- Prophylaxis of cerebral insult (paradoxic embolism)
- Poss. women prior to pregnancy

Target: Prophylaxis of irreversible cardiac damage from chronic volume overload

CI:
- If the pulmonary resistance or PAP exceeds 2/3 of the systemic resistance resp. systemic pressure and if there is a QP/QS ratio of < 1,5 or if a vaso-reagibility does not exist anymore (Canadian Consensus Conference, 2001)
- Pulmonary hypertension with pulmonary vascular resistance (RP) >10 units of resistance x m^2 or RP > 7 units of resistance x m^2 after administration of a vasodilator
- In case of left ventricular systolic and/or diastolic functional defect, if a pulmonary oedema develops due increase of left atrial pressure during catheter test occlusion

1. Interventional catheter occlusion:
- Occlusive systems for the closure of an ASD have been available for several years (Amplatzer-Septal-Occluder®; Cardio-seal®, Helex-Occluder®).
- In cases of suitable indication, high primary closure rate and few serious complications.
- No long-term results are available!

Thrombocyte aggregation inhibitors and endocarditis prophylaxis for 6 months after interventional catheter occlusion.

2. Surgical therapy (if closure via catheter is not possible):
- Timing:
  - In cases of uncomplicated ASD II, in the 3^{rd} – 5^{th} year of life, before entering school
  - In older patients, elective according to diagnosis
- Technique: direct defect closure by suturing or patch closure
- In Eisenmenger syndrome: Lung transplantation + surgical closure of ASD or heart-lung transplantation
- Surgical mortality rate: In uncomplicated ASD II, < 1% in the first two decades

Long-term results and clinical complications associated with surgical ASD closure:
- If occlusion is performed before the age of 24 or in case of pre-operative pulmonalis pressure < 40 mmHg, the prognosis of an operated secundum defect is similar to that of the normal population.
- Early post-operatively: Postpericardiotomy syndrome
- Persistence of right heart dilatation and interventricular wall motion abnormalities frequently observed when surgery has not taken place before adulthood.
- Reduced right ventricular compliance and pump function
- Impairment of left ventricular function
- Dysrhythmias (especially atrial fibrillation or flutter, supraventricular tachycardias → ablation method!)
- Cerebral embolism
- Elevation of pulmonary artery pressure can remain, progress or recur
- Recurrence of atrial shunt or residual atrial shunt
- Occlusion of superior vena cava prior to occlusion of sinus venosus defect

Ventricular Septal Defect During Adulthood [Q21.0]

Def.: One or more interventricular connections of various sizes

Anatomy of the ventricular septum

1. Inlet septum, which separates the two AV valves from each other
2. Trabecular septum, begins at insertion site of chordae with continuation to the apex and cranially to the supraventricular crista
3. Outlet septum, from the supraventricular crista to the pulmonary valve
4. Membranous septum

Various methods of VSD classification:

(There are various methods of classification; unfortunately, this makes understanding difficult!)

1. According to defect localization:
   - (Peri)membranous VSD (infracristal), with extension into residual septal parts
   - Inlet-VSD (AVSD-type)
   - Muscular VSD
   - Outlet VSD (infundibular, supracristal)
2. According to haemodynamic effect
   - Restrictive VSD: RV pressure lower than LV pressure
   - Non-restrictive VSD: Pressure equalization at the ventricular level.

Ep.:
- VSD in its isolated form is the most common congenital heart defect (circa 35%)
- Gender ratio: m : f = 1 : 1

Associated abnormalities:
- Open ductus Botalli, ASD II, coarctation of the aorta
- Component of complex malformations (e.g. transposition of great arteries, tetralogy of Fallot, and others)
- Chromosomal anomalies (e.g. trisomy 13, 18 and 21)

PPh.: The actual shunt volume is dependent on the size of the defect and pulmonary vascular and systemic vascular resistance. Small to medium-sized VSDs maintain pressure separation, while large sized defects are associated with equalization of pressures. In these cases, the ratio between the pulmonary and systemic vascular resistance is decisive for the extent of shunt flow.

VSDs cause increased left atrial and left ventricular volume load. The right ventricle is not primarily affected by volume load or enlarged in the case of small or medium-sized VSDs.

QP/QS = Lung time volume/body time volume:
- Small VSD = Roger's disease (pronounced: roh-zhay) (Qp/Qs < 1.5 : 1):
  - The diameter is around > 25% of the aortic anulus diameter - no essential enlargement of the cardiac sinuses
  - At first normal pressure in right ventricle and pulmonary artery (PAP). Possible pressure increase of 1/4 - 1/3 of the systemic pressure (SP).
  - Left-to-right shunt during entire cardiac cycle
- Medium-sized VSD (Qp/Qs = 1.5 - 2 : 1):
  - The diameter is between 25 – 75% of the aortic anulus diameter
  - Significant pulmonal hyperperfusion
  - Significantly enlarged left atrium and left ventricle, whereas right ventricular size remains approximately normal.
  - The pressure in right ventricle rises to 1/3 - 1/2 of the systemic vascular pressure (PAP/SP $\leq$ 0.5).
- Large VSD (Qp/Qs = > 2 : 1):
  The diameter is > 75% of the aortic anulus diameter. The defect no longer has a restrictive effect and shunt blood is pushed into the right ventricle and into the pulmonary artery (PAP/SP > 0.5) → increased right cardiac pressure.

In the case of a large VSD, over the course of years → pulmonary vascular occlusive disease (Eisenmenger syndrome) with in most cases irreversible alterations to the pulmonary vessels and increase in pulmonary vascular resistance, pulmonary hypertension → shunt reversal (right-to-left shunt) → secondary cyanosis (see separate section on "Eisenmenger syndrome").

Spontaneous course:
- Spontaneous closure, esp. in case of muscular or perimembranous VSD, not in case of outlet VSD. Rate of closure high until the age of 7.
- Aortic insufficiency due to prolaps of the right or acoronary valve cusp occurs often in the case of outlet VSD but also in the case of perimembranous VSD. Frequently progression. Possible association with a sinus valsalva aneurysm → danger of rupture.
- Endocarditis: Up to 2 per 1000 patient years (6 times higher compared to the normal population)
- The size oft he shunt can increase over the years and it can become an indication for surgery according to the occurring clinical symptoms
- During its course development of a `double chambered right ventricle´, a discrete sub-aortic stenosis and (rare) a sub-pulmonary stenosis possible.
- Arrhythmias and heart blocks can occur.

CL.: Clinical findings dependent on defect size, defect localization, shunt volumes and the relationship between the pulmonary and systemic vascular resistances.

- Small VSD: Children and adolescents frequently are asymptomatic
- Medium / large VSD: Growth and developmental delay, limited endurance, dyspnoea with exertion, recurring bronchopulmonary infections, palpitations (supraventricular or ventricular arhythmias), heart failure
- Eisenmenger VSD: Cyanosis, limitation on performance, dyspnoea during exertion or even at rest, haemoptysis, right ventricular failure, dysrhythmias, syncopes, cerebral abscesses

Inspection:
- Acyanotic patient, normal jugular venous pulse; protrusion of cardiac region
- Eisenmenger VSD: cyanosis with hippocratic nails/clubbing of fingers

Palpation:
- Low blood pressure with small amplitude; systolic thrill along the lower left sternal border; accentuated murmur at the apex radiating downwards and outwards (eccentric left ventricular hypertrophy)
- Eisenmenger VSD: Absent or reduced left ventricular burst; palpable pulmonary valve closure, rising pulsations palpable in area of right ventricle and its outflow tract

Auscultation:
- Small VSD: Normally split 2nd heart sound in the 2nd intercostal space to the left; high-pitched early-systolic ejection murmur in the 3rd / 4th intercostal space parasternal to the left
- Medium / large VSD: 2nd heart sound frequently not audible due to loud murmur. Regular, variable splitting with respiration. Loud pulmonary valve component associated with pulmonary hypertension. 3rd heart sound. Systolic flow murmur in the 3rd / 4th intercostal space to the left parasternal (Intensity of flow murmur: No correlation to defect size). Protodiastolic murmur over the cardiac apex (relative mitral stenosis).
- Eisenmenger VSD: Single drumming 2nd heart sound in the 2nd intercostal space to the left. Pulmonary valve ejection sound. Right atrial 4th heart sound. No longer a typical VSD murmur. Short mesosystolic murmur in the 2nd / 3rd intercostal space to the left parasternal. Decrescendo-like diastolic murmur (pulmonary valve regurgitation = Graham-Steell murmur).

ECG:
- Small VSD: normal
- Medium - large VSD: Vertical position to left axis deviation, left atrial P wave, left ventricular hypertrophy or biventricular hypertrophy
- Eisenmenger VSD: Vertical position to right axis deviation, right ventricular hypertrophy

X-ray:
- Small VSD: normal
- Medium - large VSD: Enlarged transverse diameter. Dilatation of left atrium and left ventricle. Prominent pulmonary artery. Increased central and peripheral pulmonary vascular pattern. Narrow aorta.
- Eisenmenger VSD: Heart size usually normal. Prominent right ventricle. Prominent pulmonary artery and dilatation of central pulmonary vessels. Peripheral pulmonary vessel pattern reduced (sudden change in diameters at the periphery).

Echo:
- Diagnostic assessment of anatomic localization, size and extent of VSD
- Enlargement of the left atrium, left ventricle and pulmonary artery
- Doppler method: Assessment of right ventricular and pulmonary arterial pressure, interventricular pressure gradients and shunt direction. Assessment of QP/QS (lung time volume / body time volume).

MRI: Only rarely required. Localization of VSD can be seen. Qp/Qs and shunt can be quantified.

Cardiac catheterization:

Determination of the intraventricular pressure conditions, PAP, shunt size, pulmonary vascular resistance and of the pulmonary vessel morphology (***caution:*** Avoid pulmonalis angiogram in case of Eisenmenger reaction because of high complication rate!) ; determination of associated cardiac abnormalities; diagnostic assessment of status of coronary arteries (esp. in male patients > 40 y.)

Th.: 1. Surgical therapy – indications for surgery:
- VSD with symptoms caused by the shunt and without higher graded pulmonary vascular defects.
- Asymptomatic patients with increased left ventricular volume
- Patients who had an infectious endocarditis
- VSD with associated (!) aortic valve prolaps and progressive aortic valve insufficiency.
- VSD with PAH, if no left-right shunt yet is present and if the PAP resp. PVR is < 2/3 of the systemic resistance resp. pressure
- No closure in case of VSD with severe, irreversible PAH and in case of cyanosis, which is caused by exertion
- No closure in case of small VSD without increase of volume, without PAH and without infectious endocarditis

Technique:
- Transtricuspidal occlusion from the right atrium to avoid a ventriculotomy; rarely (depending on defect localization) from the right or left ventricle or through the pulmonary artery direct suture or patch occlusion
- Direct suture or patch occlusion
- Eisenmenger syndrome: Heart lung transplantation or lung transplantation with simultaneous occlusion of the VSD

2. Interventional therapy

Perimembranous or muscular VSDs increasingly are occluded via interventional catheter occlusion systems

Mortality rate: Depending on age, pulmonary artery pressure, pulmonary vascular resistance, number of defects

and associated abnormalities. With simple VSD < 2 %, with re-operations approx. 6 %.

Residual findings after surgical VSD-occlusion:

- Dysrhythmias (right bundle-branch block, bifascicular block of the anterior type, progressive conduction impairment up to complete atrioventricular block, ventricular arrhythmia)
- Sudden cardiac death
- Increasing pulmonary vascular occlusive disease
- Impairment of right and left-ventricular function
- Recurring / residual shunts
- Persistent risk of endocarditis

ATRIOVENTRICULAR SEPTAL DEFECT (AVSD) IN ADULTS

Syn: atrioventricular channel, endocardial cushion defect [Q21.2]

Def. Partial (incomplete) AVSD: Deep-seated atrial septal defect of the primum type (ASD I) and fissure formation in the mitral valve. Both AV valves are separated from each other. Common anterior and posterior leaflets (bridging leaflet) for both AV valves are connected to each other by connective tissue.

AVSD of the intermediary type: ASD I and an inlet ventricular septal defect. Separate valve rings for both AV valves.

Complete AVSD: Deep-seated ASD I, inlet ventricular septal defect and fissure formation in the anterior mitral and septal tricuspid valve leaflet.
All four chambers of the heart are connected to each other. Mitral and tricuspid valve are at the same level and form a common AV valve opening out of four to seven leaflets.
The complete AVSD is anatomically classified using the method developed by Rastelli (see special literature).

Unbalanced AVSD: "Left or right dominance", if the common valve is predominantly assigned to a ventricle, otherwise balanced type.

PPh.: Partial (incomplete) AVSD: Left-to-right shunt → volume load on the right atrium, the right ventricle and the pulmonary vessels. Fissure in the mitral valve leaflet → mitral valve regurgitation (usually of low haemodynamic significance)

Complete AVSD: ASD + VSD causes volume load on the right heart and pulmonary circulation. Volume load on the left heart results from VSD and mitral valve regurgitation.

Shunt size dependent on size of defect and ratio of the pulmonary / systemic vascular resistances.

Ep. About 3% of all congenital heart defects; 35% of patients have trisomy 21. Associated anomalies: Tetralogy of Fallot and other complex heart defects.

Spontaneous course: Untreated, most patients die by the age of 3.

CL.: Haemodynamics and clinical findings mainly are determined by the occurrence and significance/size of the ASD, the VSD and of the grade of the left-sided AV-valve insufficiency. Recurring bronchopulmonary infections; heart failure; growth and developmental delay; limited endurance

Inspection:

- Primarily acyanotic patient; with increasing pulmonary vascular resistance → cyanosis
- Arching (protrusion of cardiac region)
- Eisenmenger AVSD: Cyanosis with clubbed fingers and toes, hippocratic nails

Palpation:

Low blood pressure, small blood pressure amplitude; systolic thrill at the lower left margin of the sternum; Accentuated pulsations over the right ventricle and right ventricular outflow tract; palpable pulmonary valve closure; Accentuated murmur at the apex radiating downwards and outwards.

Auscultation:

- Heart sounds: Fixed split 2^{nd} heart sound with accentuated pulmonary valve component with pulmonary hypertension
- Cardiac murmurs:
  - Systolic ejection murmur in the $2^{nd}/3^{rd}$ intercostal space left parasternal (ASD with relative pulmonary stenosis)
  - Systolic murmur in the $4^{th}/5^{th}$ intercostal space left parasternal (VSD or tricuspid valve regurgitation)
  - Pansystolic murmur over the apex of the heart (mitral valve regurgitation)
  - Short, protodiastolic murmur at the lower left margin of the sternum or over the apex of the heart (mitral or tricuspid valve flow murmur)

ECG: Marked left axis deviation; grade 1 AV block; right bundle branch block; right, left or biventricular (volume) hypertrophy

X-ray: Enlarged transverse diameter. Enlargement of all four heart chambers. Prominent pulmonary artery. Increased central and peripheral pulmonary vascular pattern.

Echo:
- Localization and size of ASD and VSD
- AV valve anatomy and function: Mitral valve regurgitation
- Detection of the goose neck deformity of the narrowed and prolonged left-ventricular outflow tract
- Size of the atria, ventricles, pulmonary artery and aorta. Function of the ventricle
- Doppler method: Shunt direction, assessment of right ventricular and pulmonary arterial pressure and interventricular pressure gradients. Assessment of Qp/Qs.

MRI: Shunt quantification, anatomy + function of the heart

Cardiac catheterization and angiocardiography:

Determination of the intraventricular pressure conditions, shunt size, pulmonary vascular resistance; pulmonary vessel morphology; determination of associated cardiac abnormalities and of a stenosing CHD.

Indications for surgery:

In children, sometimes even in the first six months of life as an elective procedure in order to prevent irreversible pulmonary hypertension.

Complete AVSD:
- No surgical closure in case of Eisenmenger reaction
- Otherwise: see chapter on VSD

Partial AVSD:
- Surgical closure in case of significant increase of the right cardiac volume
- Otherwise see chapter on ASD

AV-valve insufficiency:
- Symptomatic patients with average or high-grade left-sided AV-valve insufficiency should be treated surgical, if possible valve-conserving
- Surgical treatment in asymptomatic patients with average or high grade AV-valve insufficiency and increased left ventricular volume, which probably will be valve-conserving.
- Asymptomatic patients with LVSED > 45 mm and/or reduced LV function (LVEF < 60%) should be surgically treated.

Sub-aortic stenosis:

Peak-to-peak catheter gradient or median echogradient > 50 mmHg plus leftventricular hypertrophy.

Persisting or newly occurring haemodynamically and/or clinically significant septal defects, insufficiencies or stenoses of the left-sided AV-valve, sub-aortic obstructions, atrial arrhythmias or deterioration of the ventricular function are important indications for treatment.

Th.: Palliative operation: Pulmonary artery banding (if concomitant abnormalities do not allow primary corrective surgery)

Correction in the case of balanced AVSD:

Correction using the single patch technique or double patch technique: First patch occlusion of the VSD, then reconstruction of the AV valve (possibly also a valve replacement), then patch occlusion of the ASD (pericardium)

Correction in the case of unbalanced AVSD:

Separation of the circulatory system in the sense of a partial cavo-pulmonary anastomosis (PCPC) with subsequent total cavo-pulmonary anastomosis (TCPC)

In the case of Eisenmenger reaction:

Heart-lung transplantation

Surgical mortality rate: Today, early post-operative mortality for primary correction during childhood is < 5% in experienced centres. In the very young age as well as in the older age the complication and mortality rate is high.

Residual findings after surgical VSD occlusion:
- Inability of the reconstructed mitral valve to close, more rarely the tricuspid valve
- Mitral valve stenosis
- Progression of pulmonary vascular disease (Eisenmenger reaction)
- Complete AV block (especially after mitral valve replacement)
- Supraventricular arrhythmias (e.g. AV dissociations, atrial flutter, AV node tachycardias)
- Residual defects of the atrium or ventricle
- Second interventions result in higher mortality
- Persistent risk of endocarditis
- Development of subaortic stenosis
- Children of mothers with AVSD frequently have congenital heart defects.

PERSISTENT DUCTUS ARTERIOSUS (BOTALLI) (PDA) IN ADULTS [Q25.0]

Def.: Ductus arteriosus Botalli (PDA): Open vascular connection between the aorta and the confluence of the pulmonary arteries or left pulmonary artery.

Persistent ductus Botalli if, after birth, the connection between the pulmonary artery and aorta persists for longer than 3 months.

Ep.:
- Up to 10% of all congenital heart defects
- About 2% of all congenital heart defects in adulthood
- Gender ratio: m : f ~ 1 : 2 to 1 : 3

Associated abnormalities:
- Septal defects, tetralogy of Fallot, peripheral pulmonary stenoses
- Compensatory component of complex malformations (i.e: pulmonary valve atresia, tricuspid atresia)

PPh.: Ductus arteriosus Botalli is a fetal circuit between the pulmonary artery and the beginning part of the descending aorta bypassing the pulmonary circulation. Within hours to 3 days after birth a pO_2 increase in the blood induces a contraction-conditioned functional occlusion of the ductus which obliterates over the course of the following weeks. Obliteration of the ductus arteriosus can be delayed as a result of premature birth or rubella embryopathy.
In the presence of small PDA, the overall shunt volume depends on duct canal diameter, length and course; in the presence of a large PDA, shunt volume depends on the resistance ratio between the pulmonary and systemic circulation. Left-to-right shunt at the duct level → volume load in the pulmonary vessels, the left atrium, the left ventricle and the beginning portion of the aorta (up to the level of the duct).

- Small PDA (lung time volume / body time volume = QP/QS < 1.5 : 1): No significant enlargement of the left ventricle. The ratio of the pulmonary arterial pressure to the systemic pressure (PAP/SP) is normal. Left-to-right shunt during entire cardiac cycle.
- Medium-sized PDA (QP/QS = 1.5 - 2 : 1): Volume load on the left atrium, left ventricle and pulmonary vessels. Pressure separation between the two circulations (PAP/SP ≤ 0.5); pulmonary vascular resistance is not significantly elevated.
- Large PDA: Almost no pressure separation any longer → pulmonary vascular obstructive disease (= Eisenmenger syndrome) → with in most cases irreversible increase in pulmonary vascular resistance to that of the systemic vascular resistance and shunt reversal (right → left). Increase in right ventricular pressure load (see special section "Eisenmenger syndrome").

Spontaneous course:
- Spontaneous closures possible
- Especially in the presence of a small PDA, there is the danger of endarteritis (ductitis, aortitis) with possible septic embolisms and pulmonary abscess. The risk increases with age.
- With medium-sized PDA, discomfort usually does not appear until the beginning of the 3rd decade.
- With very large PDAs, heart failure occurs even in infancy. In many cases, the left ventricle can compensate for the volume load for decades, however.
- Eisenmenger syndrome usually appears in the presence of a large PDA after the age of 3, with a medium-sized shunt sometimes not until the second to fourth decade of life.
- Complications: Especially in older patients: calcification of the ductus and aneurysms
- Causes of death when PDA left untreated: complications of endarteritis, heart failure, pulmonary vascular occlusive disease (= Eisenmenger syndrome), death often does not occur until the third or fourth decade of life.

CL.: Symptoms: Dependent on size of shunt and pulmonary vascular resistance conditions
- Small PDA: frequently asymptomatic
- Medium-sized and large PDA: Frequently not until the 3rd decade → exertion dyspnoea, palpitations, bronchopulmonary infections, left heart insufficiency
- Eisenmenger PDA: Cyanosis (possibly only in the lower extremities), otherwise similar to VSD, but sometimes a lower degree of expression

Inspection/palpation:
- Medium-sized to large PDA:
  - Acyanotic patient
  - Protrusion of cardiac region
  - Large blood pressure amplitude, cannonball pulse and pulsatory phenomena as with aortic insufficiency (see section on this topic)
  - Prominent apical cardiac beat: hyperactive, broad, radiating downwards and outwards (eccentric left hypertrophy), palpably protodiastolic ventricular filling phase
  - Rising pulsations over the pulmonary artery
  - Systolic-diastolic thrill at the upper left margin of the sternum
- Eisenmenger PDA: Missing or reduced left ventricular burst; palpable pulmonary valve closure, rising pulsations over the right ventricle and the right ventricular outflow tract. Normal fingers and fingernails; clubbed toes and hippocratic nails on the toes. (Exception: In cases of distal branching off of the left subclavian artery distal of the opening of the ductus arteriosus, clubbing of the fingers and hippocratic nails also develop in the left upper arm).

Auscultation:
- Small PDA: Normal split 2nd heart sound in the 2nd intercostals space to the left; "silent duct"
- Medium-sized to large PDA: Paradoxically split 2nd heart sound in the 2nd intercostals space on the left; loud pulmonary valve component due to pulmonary hypertension. 2nd heart sound frequently not audible due to loud

murmur. Continuous systolic-diastolic machine-gun murmur in the 2nd intercostal space to the left, infraclavicular. Additional short, protodiastolic mitral valve flow murmur over the apex of the heart.
- Eisenmenger PDA: Auscultation findings similar to those for Eisenmenger VSD. The ductus cannot be heard any more.

ECG:
- Small PDA: Normal ECG
- Medium-sized/large PDA: Left or biventricular (volume) hypertrophy
- Eisenmenger PDA: Right hypertrophy

X-ray:
- Small PDA: Normal findings
- Medium-sized to large PDA: Enlarged transverse diameter. Enlargement of the left heart and ascending aorta (seldom detectable); prominent pulmonary artery; increased pattern of the central and peripheral lung arteries and veins.
- Eisenmenger PDA: Normal heart size. Prominent right ventricle. Enlarged pulmonary artery, enlarged central pulmonary vessels, reduced pattern of peripheral pulmonary vessels.

Echo:
- Echo projections: short axis suprasternal or parasternal
- Direct: Localization and size of the PDA (frequently flow phenomena can be seen better than the anatomical structure).
- Doppler: Retrograde diastolic flow from the bifurcation into the pulmonary artery trunk. Retrograde flow in the descending aorta during diastole. Assessment of right ventricular pressure and pulmonary arterial pressure as well as pressure gradients. Assessment of QP/QS.
- Indirect: Enlargement of the left heart and pulmonary artery

MRI: Shunt quantification, anatomy + function of the heart

Cardiac catheterization:
- In adulthood, if a catheterization procedure is planned at the same time.
- In case of associated abnormalities
- In case of concomitant coronary heart disease

DD: Other disorders with continuing systolic-diastolic:
- Aortopulmonary window
- Sinus Valsalva aneurysm with perforation into the right ventricle or atrium
- Coronary artery fistulas
- Arteriovenous fistula (traumatic or with pulmonary angioma)
- Aortic stenosis with aortic regurgitation

Th.: **Interventional catheter occlusion**

Procedure of choice: e.g. using various occluder systems (e.g. Amplatzer) or coils

Ind:
- PDA with increased LV volume
- Small PDAs with continuing systolic-diastolic murmur
- PDA, as long as the PAP is < 2/3 of the systemic pressure or PVR is < 2/3 of the systemic resistance
- Closure in case of PDA with PAP > 2/3 of the systemic pressure or PVR > 2/3 of the systemic resistance only if L-R shunt ≥ 1,5 or if pulmonary vaso-reagibility proven
- A ´silent duct´ does not present an indication for surgery
- In case of Eisenmenger reaction or cyanosis of the lower extremities induced by exertion
- Even small PDAs are occluded due to the risk of endarteritis, and since, with greater age, nearly all PDA patients become symptomatic (→ prevention or treatment of heart failure and avoidance of irreversible lung damage)

- Timing: In older patients, elective according to diagnosis

- Success rate after 1 year is up to 98%; the success rate with small ductus is the most favorable
- Compl.: Embolism due to the insertion, incomplete occlusion, infection, etc.

Surgical treatment:

Ind: PDAs that cannot be closed by surgery due to their size or for technical reasons.
- Mortality rate from surgery in cases of simple PDA in older patients < 0.5%
- Technique: Ligature, ligature and discission or suturing and discission (clamp and divide).
- Thoracoscopic procedures for ductus closure are in development
- Lung transplantation in Eisenmenger syndrome

Long-term results and clinical complications after PDA closure:

Persistent risk of endarteritis in the presence of residual shunt; recanalization of the ductus; persistent or progressive pulmonary vascular occlusive disease (= Eisenmenger syndrome); formation of false aneurysms (after ligature, after infections).

CONGENITAL HEART DEFECTS WITH RIGHT -> LEFT SHUNT

CL.: Cardinal symptom: Central cyanosis
Clinical consequences of hypoxemia:
- Erythrocytosis (= hyperglobulia)
- Reduced capacity, developmental delay
- Syncope
- Clubbed fingers and toes, hippocratic nails

DD: Cyanosis [R23.0]

Def.: Bluish colouration of the skin or mucus membranes

I. True cyanosis

A) Haemoglobin cyanosis

Haemoglobin cyanosis occurs if the concentration of deoxygenated Hb in the skin capillaries is > 5 g/dL. In erythrocytosis (=hyperglobulia), cyanosis appears earlier than with anaemia; in cases of severe anaemia with Hb values around 5 g/dL, cyanosis may no longer appear.
Chronic hypoxia leads to erythrocytosis (= hyperglobulia) and possibly hypertrophic osteoarthropathy (Pierre-Marie-Bamberger syndrome) with clubbing of the fingers and toes as well as hippocratic nails. (History: Rarely, Marie Bamberger syndrome can also occur as paraneoplastic syndrome with various tumours.)

Notes: The presence or absence of cyanosis does not permit any reliable conclusions regarding the O_2 supply to the tissues: In CO poisoning with formation of functionless HbCO, the skin becomes rose-coloured (normal O_2 saturation in pulse oximetry) and the patients die from lack of O_2. In cases of pronounced anaemia as well, there is no cyanosis in spite of a deficiency of O_2 in the tissues. On the other hand, cyanosis may occur in cases of pronounced erythrocytosis (=hyperglobulia) with sufficient arterial pO_2.

1. Central cyanosis:
   Reduced O_2 saturation of the arterial blood (pulse oximetry)
   Characteristics:
   - Skin + tongue/oral mucus membrane cyanotic (in peripheral cyanosis, the tongue/oral mucus membrane are not cyanotic)
   - Lewis test: After massaging the earlobes (until there is a capillary pulse), the earlobes remain cyanotic in central cyanosis (in peripheral cyanosis, the blue colouration disappears).
   - Pulmonary cyanosis: Insufficient oxygenation of the blood in the lungs due to pulmonary disease.
     Characteristics: After breathing in pure O_2 for several minutes, pulmonary cyanosis is reduced (but not, on the other hand, in cases of cardiac cyanosis due to right-to-left shunt).
   - Cardiac cyanosis: Mixing of venous with arterialized blood due to right-to-left shunt defects.
2. Peripheral cyanosis:
   The cause is an increased exhaustion of blood O_2 in the capillary periphery due to reduced blood flow and vasoconstriction (shock, heart failure, exposure to cold, local cyanosis due to venous or arterial circulatory disorders)
   Characteristics: Cyanosis of the acra (not of the tongue/oral mucus membrane)
3. Combination of central and peripheral cyanosis
   e.g. due to chronic pulmonary diseases + decompensated cor pulmonale

B) Haemoglobin cyanosis (= methaemoglobinaemia) [D74.9] with slate gray skin colour

MetHb contains trivalent iron (haemiglobin) and therefore cannot transmit O_2.
The physiologically normal met-Hb content of the blood is < 1.5% of the total haemoglobin. Haemoglobin cyanosis becomes clinically apparent with methaemoglobinemia > 10% of total Hb. Clinical symptoms usually do not occur until metHb values are > 35% of total Hb.

Causes:
- Rarely congenital: Hb-M; deficiency of metHb reductase; glucose-6-phosphate dehydrogenase deficiency. Newborns are not able to reduce methaemoglobin to normal haemoglobin due to reduced activity of metHb reductase. Drinking water with elevated nitrate content can cause metHb poisoning in infants.
- Usually acquired:
  - Medications, e.g. intoxication with sulfonamides, phenacetin
  - industrial toxins (nitro and amino compounds, nitrous gasses)

Di:
- Medication history (think about it!)
- Dark brown colouration of the blood that does not disappear when air is mixed in (agitation). (Rapid test: Place 1 drop of blood on a swab and compare colour with another drop of blood (that is metHb-free) after 1 minute: brown colouration means metHb content > 20%.)
- Heinz bodies inside erythrocytes
- Spectroscopic metHb determination

Antidote: methylene blue and ascorbic acid

C) Sulfhaemoglobinaemia

Very rare; irreversible oxidation of the Hb through intoxication with sulfonamides or phenacetin; the blood has a greenish colour; spectroscopic determination.

II. Pseudocyanosis

Due to pigmentation abnormalities or deposits of foreign substances, e.g. silver (argyrosis).

EBSTEIN ANOMALY [Q22.5]

Def: Malformation of one or more cusps of the tricuspid valve (TV). The downward displacement of the septal and mural TV cusp into the direction of the apex mainly determines the grade of severity. The apical displacement of the TV cusp divides the right heart into right atrium, an atrialized right ventricle and also into a residual ventricle. Often simultaneous TV- insufficiency, functional defect of the left ventricle, mitral valve anomalies, interatrial connection (open foramen ovale or atrial septal defect), accessory electrical conduction pathway (WPW-syndrome).

Ep.: < 1 % of all congenital heart defects. More common in mothers, who wrere treated with Lithium of benzodiazepines during pregnancy.

PPh: Volume increase of the right atrium resp. of the atrialized ventricle due to the systolic blood regurgitation from the right residual ventricle via the insufficient tricuspid valve into the atrialized ventricle resp. into the right atrium. In case of a small ventricle only small output volume ➔ reduced pulmonary blood circulation. Via interatrial connections left-right-shunt , but more often right-left-shunt..

CL.: Cardinal symptoms: From mild symptoms to the full picture of a high grade cyanotic heart defect. Frequent complaints: Dyspnoea, fatigue, activity restrictions, cardiac pains and palpitations.
Inspection/palpation: Cyanosis in case of right-left-shunt and/or low cardiac output. Pulsation of cervical veins often not detectable (despite right-atrial enlargement and TI!), only sometimes right-ventricular engorgement. Praecordium often normal ("silent thorax"). Hepatomegaly.
Auscultation: SI widely split, with loud 2. component (closure of tricuspid valve). SII widely split with delayed closure of PV, often silent. Serial clicks. Frequently SIII and SIV (triple or quadriple rhythm). Systolic instant murmur or TI above left lower sternal edge. Short mid-diastolic murmur.

Ecg: Right atrial hypertrophy. Prolonged PR interval. Right bundle branch block, sometimes containing 2. QRS complex. Deep Q in II, III, F, V1-V4. WPW-configuration possible. Increased supraventricular arrhythmias. Sometimes low-voltage.

X-ray.: Heart-transversal diameter variable (normal to extreme cardiomegaly - ´bocksbeutel-shape´). The enlargement of the right atrium is responsible for the typical silhouette of the Ebstein anomaly. Right ventricular outflow tract and left ventricle shifted to the left. Despite the enlargement of the right atrium the v. cava sup. in most cases is not enlarged. Pulmonary vessels normal or petite. Small caliber of aorta.

Echo (TTE and TEE): Answers all relevant questions: Anatomy and function of the tricuspid valve, distal displacement of the septal resp. posterolateral (mural) cusp (in adults at least 2,0 cm resp. 0,8 cm/m^2 body surface), size of the anterior segment, extent of the tethering of the septal or posterior tricuspid valve cusp onto the septum resp. ventricle wall, size and function of the right atrium, atrialized ventricle, right-sided residual ventricle, left ventricle, right-ventricular outflow tract obstruction, accompanied anomalies (e.g. ASD/PFO).

MRI: Poss. in addition to the echo for imaging of the cardiovascular structures free of overlaps.

Cardiac catheter: Catheter investigation in most cases dispensable. Important for the exclusion of an concomitant CHD.

Th.: **A) Conservative**

Treatment according symptoms. Rhythm defetcs are treated with drugs or by catheter ablation method. In case of thromboembolic risk and right-left-shunt an anti-coagulation therapy might be required.

B) Surgical

Therapeutic options: Operative correction preferably through tricusp valve reconstruction with creation of a „monocusp valve" or valve replacement. In the context of a primary intervention poss. ASD closure, resection of redundant atrial parts, poss. plication of the atrialized right ventricle or tricuspid valve anuloplasty.
Indication for surgery: Symptomatic patients with decreasing capacity of activity and function class > II, progressive increase of cardiac size and decreasing function of the right ventricle, more than moderate symptomatic tricuspid valve insufficiency, higher grade or progressive cyanosis (arterial basic saturation < 90 %), paradoxic embolies, significant right ventricular outflow tract obstruction.
Typical post-operative residual findings: Persisting or newly occuring tricuspid valve insufficiency, the usual complications after valve replacement, failure of the right or left ventricle, residual shunts on atrial level, supraventricular and ventricular arrhythmias, higher grade block formation.

TETRALOGY OF FALLOT IN ADULTS

Syn.: TOF

Def.: The tetralogy of Fallot is characterized by a displacement of the infundibular septum to the right and anterocephalic. This results in:
- Right ventricular outflow tract obstruction (RVOTO)
- Large so-called malalignment of the ventricular septal defect (VSD)
- Aorta overriding the VSD (> 50%)
- (Consecutive) right hypertrophy

Ep.:
- Most frequent cyanotic congenital heart defect: 10% of all congenital heart defects; 65% of all congenital cyanotic heart defects
- Gender ratio: m : f = 1.4 : 1
- A micro-deletion of chromosome 22q11 occurs in approx. 15% of the patients.

Associated abnormalities:
- e.g. right aortic arch, ASD, VSD, AVSD, coronary abnormalities (especially frequent: branching off of the RIVA from the RCA)
- Down's syndrome

PPh.: The predominant clinical sign is a large ventricular septal defect (VSD) in connection with a stenosis of the right ventricular outflow tract (RVOTO).
- VSD: Sub-aortic malalignment VSD with extension into the right ventricular outflow tract. The VSD is large enough for pressure equalization to develop between right ventricle, left ventricle and aorta.
- RVOTO: in the infundibulum (50%), in the valves (10%), in both places (30%). Pulmonary valve and pulmonary artery trunk usually hypoplastic; more frequently, peripheral pulmonary arterial stenoses. In 10% of cases, complete pulmonary atresia.

  Because of the RVOTO, the venous blood does not flow through the lungs, but rather through the large VSD directly into the systemic circulation → central cyanosis.

  Severity of the clinical picture dependent on the degree of RVOTO:
  - Mild RVOTO: Acyanotic form (pink Fallot)
  - High-grade RVOTO: cyanotic form
- Right hypertrophy: result of additional load on right heart.

Spontaneous course:
- Prognosis dependent on extent of pulmonary circulation
- Children with acyanotic form resulting from mild RVOTO: with large left-to-right shunt, heart failure possible. Often, cyanosis does not appear until the 2nd year of life.
- Children with cyanotic form: If the first years are spontaneously survived → increasing cyanosis and exertion dyspnoea
- Average life expectancy 12 years; 95% of patients die before 40 years of age.

CL.:
- Dyspnoea, even in the 1st year of life, especially with exertion.
- Squatting position: frequently in children → increase in systemic vascular resistance → increase in pulmonary perfusion and oxygen saturation
- Hypoxic spells: stenosis of the already hypertrophic infundibulum → blockade of blood flow to the pulmonary circulation. Occurs in infants and small children, not in adults.
- Capacity limitation
- Developmental delay usually small
- Usually no heart failure. Right heart insufficiency more likely in the spontaneous course of older patients.

Diagnostic targeting
- Non-operated patient: Detection and localization of the VSD and of the right-ventricular outflow tract obstruction; Estimation of the haemodynamic effects, especially on the pulmonary circulation and ventricular function; determination of the right-ventricular pressure; concomitant malformations.
- After palliative intervention: Anatomy of the pulmonary arteries, pulmonary arterial pressure; function of the left (volume load due to VSD) and right ventricle (pressure load due to pulmonary stenosis). Detection resp. exclusion of concomitant malformation.
- After surgical correction: Quantification of the pulmonary insufficiency, volume and function of the right ventricle; Detection of peripheral pulmonary arterial stenoses; residual shunts (ASD, VSD); residual right-ventricular outflow tract obstruction; diameter of the aortic root; aortic insufficiency.

Th.: Surgical treatment:
- Nowadays primary correction during the age of 6 – 18 months.
- In most cases, adult patients have already had corrective surgery to reduce the cyanosis and improve the patient's capacity.
- Today, the number of adults in whom only a palliative operation was performed is small.

1. Palliative operations: (Nowadays Waterston or Pott shunts are hardly performed anymore)
   Target: Improvement of pulmonary perfusion if primary correction is not possible (e.g. in the presence of hypoplastic pulmonary arteries, hypoplastic valve ring, coronary abnormalities, multiple VSDs).
   - Original Blalock-Taussig shunt: End-to-side anastomosis between the subclavian and pulmonary arteries.
   - Modified Blalock-Taussig shunt: Side-to-side interposition of a few millimeters thick tube of PTFE (polytetrafluoroethylene = Teflon®) between the subclavian and pulmonary arteries.
   - Central aortopulmonary shunt: Side-to-side interposition of a PTFE tube between the ascending aorta and trunk of the pulmonary artery
   - Waterston shunt or Waterston-Cooley shunt: Direct anastomosis between the ascending aorta and right pulmonary artery
   - Pott shunt: Direct anastomosis between the descending aorta and left pulmonary artery
2. Corrective operation:
   - Elimination of the right ventricular outflow tract obstruction: Pulmonary valve valvulotomy; resection of the infundibular musculature; frequently, patch extension using pericardium or PTFE strips
   - Transatrial or transventricular patch occlusion of the VSD
   - Surgical mortality rate: < 1%; in adulthood up to 9%
   - Long-term prognosis: survival rate after 30 years about 90%, after 40 years, about 75%

Long-term results and clinical complications after surgical correction:

1. After palliative operation:

   Complications after Blalock-Taussig shunt:
   - "Growing out" of the shunt
   - Occlusion of shunt
   - Stenosis / obstruction of the ipsilateral pulmonary artery
   - Subclavian steal (original BT shunt)
   - Seroma formation (modified BT shunt)
   - Risk of endocarditis
   - Cardiac insufficiency rare

   Residual complications after Waterston-Cooley or Pott shunt:
   - Large shunt volume → heart failure or pulmonary vascular occlusive disease
   - Aneurysms of the right pulmonary artery (Waterston-Cooley shunt)
   - Kinking or stenosing of the right (Waterston-Cooley shunt) or left pulmonary artery (Pott shunt)
   - Pulmonary vascular disease in case of excessive shunt flow
   - Difficult reversal of shunt at the time of the corrective operation
   - Risk of endocarditis
2. After corrective operation:
   - Pulmonary valve regurgitation:
     - In almost all post-operative Fallot patients, especially after transannular patch. In some cases the pulmonary valve regurgitation is well tolerated over the years. Results:
       · Enddiastolic enlargement of the right ventricle with subsequent right cardiac failure
       · Reduced capacity
       · Arrhythmias
     - Th.: Indication and optimum time for pulmonary valve replacement are controversial. Important parameters for indication: RV size and function., objective exercise capability, rhythm disorders and symptoms. Nowadays a pulmonary valve replacement is indicated earlier, that means before the RV functional defect becomes irreversible.
       Implantation of a homograft or of an artificial valve. In individual cases: Interventional implantation of a valve (`melody-valve´)
   - Obstructions of the right ventricular outflow tract (RVOTO):
     Possible at all places between the right ventricle and peripheral pulmonary arteries.
     Th.: In case of high pressure readings of the right ventricle (systolic right ventricular pressure > 2/3 of the systolic systemic pressure) → surgical revision.
   - Peripheral pulmonary arterial stenosis
     Angioplasty and/or stent implantation
   - Aneurysms in the RVOT:
     - Significance: possible substrate for ventricular arrhythmia
     - Rupture very rare.
     - Th.: Clinical monitoring. With increase in size → surgery.
   - Recurring / residual ventricular septal defect:
     - Significance: Volume load on the left ventricle.
     - Th.: Re-operation in case of LR shunt ≥ 1,5 : 1 or in case of surgery because of other indication.
   - Disorder of the left ventricular function
   - Aortic valve regurgitation:
     - Significance: volume load on the left ventricle.

- Th.: Poss. valve replacement.

- Aneurysms of the aorta ascendens: Occurrence in circa 15% of patients due to a defect of the aortic wall (so-called ´cystic media necrosis´) and due to the increased flow above the aortic valve before the correction, which is typical for the vitium. (In case of TOF the aorta ascendens is always dilated – and esp. in case of pulmonary atresia, which represents the extreme form of a tetralogy of Fallot!)
  -Significance: Unclear; the risk of rupture appears to be relatively small.
  - Th.: Ascendens replacement in case of a disproportional large aorta or in case of progression of the dilatation of the aorta (the measurements for the indication of an ascendens replacement in aortic aneurysms of other origins can not directly be transferred)
- Ventricular arrhythmias (50%) with danger of sudden cardiac death (up to 1-6 %)
  - Responsible for 30 – 50 % of all deaths
  - Problem: identification of patients at risk
  - Potential markers: QRS duration > 180 msec; inhomogeneous depolarization and repolarization, heart-rate-turbulence

  Th.: Consider possibly radio frequency ablation or ICD in cases of elevated risk for sudden cardiac death
- Supraventricular arrhythmias (atrial arrhythmias, sinus node dysfunction; atrial fibrillation / flutter)
- Post-operative grade III AV block
- Risk of endocarditis is relatively small after correction
- Pregnancy:
  - If no significant residual findings are present, pregnancy is usually well tolerated.
  - Risk of repetition for congenital heart defects: about 3%

Diagnostic after surgical treatment

ECG: Right axis deviation; right atrial and ventricular hypertrophy. QRS length correlates with the volume load of the right ventricle. QRS length > 180 msec is regarded as a risk marker for VT´s and sudden cardiac death, especially in case if it is progressive.

24h-ECG: For detection of malignant arrhythmias and/or clinical symptoms, which probably will lead to arrhythmias.

Ergospirometry: For objectivization of the exercise capability (important for monitoring of the course)

Echo:
- Quantification of the ventricular function (right and left), right heart hypertrophy
- Detection and rough quantification of a pulmonary and tricuspid insufficiency
- RVOT: Infundibular and/or valvular re-/residual stenosis, stenoses in the area of the pulmonary trunk and bifurcation
- Re-/residual VSD
- Large, overriding aorta (long parasternal axis), aortic valve insufficiency
- Detection of associated anomalies

MRI: Imaging of the post-operative anatomy and quantification of the right and left ventricular function. Detection of fibrosis in the ventricle area (late enhancement) ➙ risk stratification. The quantification of the ventricle volumes is especially important and also is the regurgitation fraction in PI. Aortic diameter.

CT: If MRI is contraindicated

Poss. cardiac catheterization:
- Imaging of the anatomy of the heart and of the pulmonary arteries
- Quantification of the pressure and flow conditions, esp. of an intracardial shunt and of the RVOTO
- In older adults or in cases of certain risk constellations in order to assess the coronary status. Especially in association with catheter interventions: Balloon angioplasty and/or stent implantations. Up to now only in individual cases: Interventional implantation of a valve („melody-valve“).

Indications for re-intervention following Fallot correction
- Pulmonary valve replacement in symptomatic patients with severe PI and/or pulmonary stenosis with peak-gradient ≥ 64 mm Hg or a Vmax above the tricuspid valve > 3,5 m/s
- Pulmonary valve replacement in asymptomatic patients with severe PI and/or pulmonary stenosis, in case of
  - Objective decrease o perfomance
  - Progressive RV dilatation
  - Progressive decrease of the systolic RV function
  - Progressive tricusp insufficiency
  - RVOTO with a systolic RV pressure > 70mmHg (TR velocity > 4 m/s)
  - Continuing atrial/ventricular arrhythmias
- Aortic valve replacement in case of higher graded AI with symptoms or indications for a LV function defect resp. decreasing LV function
- VSD closure in case of significant LV volume load

Indication for EPE (electrophysiolgic examination) **and ICD implantation:**

EPE in symptomatic patients with suspected or documented relevant atrial of ventricular arrhythmias

ICD indication for secondary prophylaxis of a sudden cardiac death. ICD for primary prophylaxis is discussed controversially.

COMPLETE TRANSPOSITION OF THE GREAT ARTERIES (TGA) IN ADULTS [Q 20.3]

Def.: In transposition of the great arteries (TGA), the aorta branches off from the morphologically right ventricle, the pulmonary artery from the morphologically left ventricle (ventriculo-arterial discordance). The ventral and/or right ascending aorta alongside the pulmonary artery. Both of the great vessels fun parallel without crossing ("D-TGA").

Ep.:
- About 5% of all congenital heart defects
- Gender ratio m : f ~ 2 : 1

PPh.:
- Pulmonary and systemic circulation are anatomically arranged in parallel.
- Unsaturated blood from the systemic circulation → right atrium → right ventricle → aorta (oxygen-poor blood)
- Oxygen-rich blood from the lungs left atrium → morphological left ventricle → pulmonary artery → lungs
- Survival only possible when mixing of both circulations via a short circuit on atrial, ventricular or vascular level occurs. Most frequently, there is a small defect on the atrial level.

Associated abnormalities: Frequently, atrial septal defect (ASD), ventricular septal defect (VSD), left ventricular outflow tract obstruction (LVOTO).

- Large ASD: Good mixing of both circulations and relatively high arterial oxygen saturation.
- Large VSD: Good oxygenation, therefore cyanosis may be absent. In cases of pulmonary hyperperfusion, there is an increased risk of heart failure. In non-restrictive VSD, high pressure in the pulmonary circulation → early pulmonary vasculature occlusive disease (Eisenmenger syndrome)

- VSD plus left ventricular outflow tract obstruction (LVOTO) → first, mixing of both circulatory systems at the ventricular level. Since the quantity of completely saturated blood that recirculates from the lung in the presence of a clinically significant LVOTO is inadequate, the systemic arterial oxygen saturation does not increase significantly. LVOTO does appear to protect against pulmonary hypertension, however.

Course in TGA:

Dependent on the type and severity of the concomitant heart malformations.

- If all forms of complete TGA are considered together, the overall mortality rate in the spontaneous course is around 95% within the first 2 years.
  Main causes of death in the spontaneous course:
  - TGA / intact ventricular septum: hypoxia, acidosis, pulmonary infections, cerebral insults or abscesses
  - TGA / VSD: heart failure or pulmonary infections
  - TGA / VSD and LVOTO: hypoxia
- 3 groups of patients with TGA reach adulthood:
  A) True spontaneous course without special treatment
  Most patients with a large VSD and moderate subpulmonary stenosis or a moderately elevated pulmonary vascular resistance. These patients may even survive into the 5th decade of life in rare cases.
  B) Status post palliative measures such as atrioseptostomy, pulmonary artery banding, creation of a shunt or other palliative surgical procedures.
  C) Status post corrective surgery such as atrial switch operations, arterial switch operation or Rastelli operation.

Th.:
- Atrial septostomy according to Rashkind and Miller:
  Balloon catheter through atrial septal defect into the left atrium → inflation → balloon pulled abruptly back into the right atrium → holes of 1.0 to 1.5 cm in diameter → oxygenated blood is fed into the systemic circulation.
  The intervention, which is carried out within the first days of life, leads to a better exchange between arterial and venous blood at atrial level and therefore to an increase of arterial oxygen saturation to > 70%.
- Atrial switch operation according to Mustard or Senning (as physiologic, but not as anatomic correction):
  Mustard-technique: Opening of the right atrium → excision of the atrial septum except for a thin band → fixation of a reversal patch (baffle) of pericardium, dacron or Gore-Tex. Also, frequently patch extension of the pulmonary vein atrium.

  Results: Systemic venous blood → newly created systemic venous atrium → mitral valve → morphological left ventricle → pulmonary artery. Pulmonary venous blood dorsal and lateral of the systemic venous tunnel → tricuspid valve → morphological right ventricle → aorta.

  In case of concomitant VSD: defect occlusion.

  In the presence of LVOTO: In the presence of valvular stenosis → commissurotomy; in the presence of subvalvular fibromuscular stenosis → resection or implantation of an extracardial valve-supporting conduit between the left ventricle and pulmonary artery

  Senning-technique: Similar to Mustard-operation, but with the use of autologous material (tissue of the septum and the atrial side walls)
- Arterial switch operation:
  This anatomic correction is performed within the first 3 weeks of life, since the left ventricle must be able to tolerate the pressure rise in the systemic circulation after the surgical switch has occurred.
  Technique: The ventrally positioned aorta is split peripherally of the coronary arterial ostia and the dorsally positioned pulmonary artery at the same level. The coronary arteries are then implanted with a small aortic tissue

fragment into the stump of the separated pulmonary artery. Then relocation of the ascending aorta behind the pulmonary artery and connection to the stump of the pulmonary artery carrying the coronary ostia. Reconstruction of the former aortic stump and connection to the pulmonary artery ventral of the “neo-aorta”.

- Rastelli operation:
  Pulmonary artery separated from the left ventricle. VSD patch occlusion, creating an intraventricular tunnel that connects the left ventricle with the aorta. The right ventricle is connected via a homograft or valve-containing conduit with the pulmonary artery.

Post-operative long-term results and clinical complications:

- Atrial switch operation:
  For this operation the most long-term results exist up to now: Total survival rate 25 years after surgery: All forms of the TGA 65 %, simple-TGA 80 %, complex TGA 45 %.
  - Main complications during the long-term course: The progressive insufficiency of the morphologic right systemic ventricle, cardiac rhythm disorders and sudden cardiac death (supraventricular rhythm disorders) determine mainly morbidity and mortality in the long-term course!
  - Dysfunction of the right ventricle acting as the systemic ventricle
  - Tricuspid valve regurgitation
  - Systemic venous obstructions at the transition of the superior or inferior vena cava to the systemic venous atrium
  - Pulmonary venous obstructions at the transition of the pulmonary veins to the pulmonary venous atrium
  - Baffle leaks
  - Subpulmonary stenoses (could actually be protective for the function of the systemic ventricle!)
  - Inadequate chronotropic response to exertion
  - Sudden cardiac death (probably rhythm related)

  Therapeutic options after atrial switch operation (in communication with experienced center):
  - Ventricle dysfunction/cardiac insufficiency: Managed controversially. Usual cardiac failure therapy with diuretics, digitoxin, ACE inhibitors/ATB/β-blocker are discussed controversially (amongst other reasons because of fixed pre-load, Baffle-obstruction!). Heart transplantation in case of severe cardiac insufficiency with severely impaired quality of life.
  - Tricuspid insufficiency: The cause of the tricuspid insufficiency is important: Expression of a failure of the systemic ventricle or morphologic changed tricuspid valve. A dosed pulmonary artery banding can positively influence geometry and function of both ventricles. Poss. tricuspid valve replacement. In severe tricuspid insufficiency due to failure of the right ventricle consider heart transplantation.
  - Stenosis within the systemic veins: In most cases balloon dilatation and stenting possible, otherwise operation
  - Stenosis within the pulmonary veins: In most cases re-operation required.
  - LVOTO: If symptomatic or in case of decreased function of the sub-pulmonary ventricle: Surgical correction via LV-PA-conduit
  - Baffle-leak: Closure interventional or surgical in case of substantial shunt volume or significant decreased oxygen saturation
  - Re-/residual VSD: Closure in case of substantial shunt volume
  - Symptomatic bradycardias, sinus node dysfunction, chronotropic insufficiency: Pace maker implantation (transvenous or epicardial)
  - Symptomatic tachyarrhythmias: Ablation techniques in case of intra-atrial re-entry-tachycardias/atrial flutter. Drug therapy preferably with β-blocker or amiodarones.

- Arterial switch operation:

  Main complications during the long-term course:
  - Disorders of the LV function
  - Stenoses of the re-implanted coronary arteries (ischaemia, infarctions)
  - Supravalvular pulmonary arterial stenoses
  - Supravalvular aortic stenoses
  - Ectasia of the aorta ascendens
  - Pulmonary valve regurgitation; aortic valve regurgitation
  - Cardiac arrhythmias

  Therapeutic options after arterial switch operation (in communication with experienced centre):
  - Dysfunction of the ventricles/cardiac insufficiency: After exclusion of structural causes pharmaceutical therapy for cardiac insufficiency
  - Stenosis of the re-implanted coronary arteries: Bypass operation; in case of suitable morphology percutaneous coronary intervention
  - RVOTO: Operative correction in symptomatic patients with peak gradient > 64 mm Hg (TR-velocity > 3.5 m/s); independent of symptoms – if a RV-dysfunction occurs.
  - Aortic ectasia (> 55 mm): reconstructive aortic surgery; in asymptomatic patients with peak gradient > 70 mm Hg (TR-velocity > 4,0 m/s).
  - Aortic valve insufficiency, higher graded: Aortic valve replacement
  - Periphere PS: Stenting or surgery in case of lumen stenosis > 50 % and a systolic RV pressure > 50 mm Hg or abnormal lung perfusion scan.

- Rastelli operation:

Main complications during the long-term course:
- Cardiac insufficiency
- Conduit degeneration
- Subaortic stenosis; aortic regurgitation
- AV valve function
- Recurring / residual VSD
- Cardiac arrhythmias: especially ventricular tachyarrhythmias
- Sudden cardiac death

Therapeutic options after Rastelli operation (in communication with experienced centre):
- Cardiac insufficiency: Established cardiac failure therapy after exclusion of structural causes
- In case of stenosis of the ´tunnel´ from the left ventricle to the aortaa: Revision of the ventriculo-arterial tunnel with a median gradient > 50 mm Hg.
- Conduit stenosis/insufficiency → Re-operation:
* In symptomatic patients with systolic RV-pressure > 60 mm Hg or a Vmax above the tricuspid valve > 3.5 m/s and/or at least average pulmonary insufficiency;
* In asymptomatic patients with systolic RV-pressure > 70 mm Hg or a Vmax above the tricuspid valve > 4,0 m/s and/or at least average pulmonary insufficiency and objective decrease of performance or progressive RV-dilatation or progressive decrease of the systolic RV-function or progressive tricuspid insufficiency or persistent atrial/ventricular arrhythmias
- New option in special centres: Percutaneous replacement of the pulmonary valve ("melody-valve")
- Re-/residual VSD: Closure in case of substantial shunt volume
- Symptomatic supraventricular or ventricular arrhythmias: Treatment according to the international guidelines

Congenital corrected transpositon of the great arteries [Q25.3]

Def: In a normal atrial site both ventricles are inverted: The right atrium is connected with a morphologic left ventricle, the left atrium is connected with a morphologic right ventricle (atrio-ventricular discordance). In addition transposition of the great vessels (ventriculo-arterial discordance), which means that the A. pulmonalis originates from the right sided, morphologic left ventricle , the aorta originates from the left sided, morphologic right ventricle. In addition the AV-valves, coronary arteries and the conduction system are inverted.
The coronary supply of the systemic ventricle is provided via the "right" coronary artery, which originates from the left sinus valsalvae. The morphologic left, sub-pulmonary ventricle is supplied by the "left" coronary artery, which originates from the right sinus valsalvae.
In the right atrium an accessoric superior/anterior AV-node exists in addition to a hypoplastic, posterior AV-node, which is connected to the His´band. The His´ band is very long and goes around in front of the pulmonary valve ring. The right Tawara bundle descends on the left side of the ventricle septum, the left bundle branch on the right side of the ventricle septum. In additional VSD the His´band descends antero-superior of the defect.

PPh: Blood circulation: Systemic venous blood from the right atrium ➞ morphologic mitral valve ➞ morphologic left, sub-pulmonary ventricle ➞ pulmonary circulation. Pulmonary venous blood ➞ left atrium ➞ morphologic tricuspid valve ➞ morphologic right, systemic arterial ventricle ➞ systemic circulation
Therefore functional correction of the circulation conditions, however the term ´corrected´ does not reflect the pathologic-anatomic conditions.
Natural course: Mainly determined through concomitant anomalies, higher graded AV-blocks, WPW-syndrome or infectious endocarditis. Many patients reach the adult age without any symptoms.

CL.: Complaints and clinical findings vary according to nature and extent of the concomitant anomalies!
Examination findings: Mainly correspond with those, which the relevant concomitant anomaly presents in patients without ventricle inversion:
- Insufficiency of the left sided, systemic AV-valves („tricuspid valve" insufficiency): Clinical picture of a "mitral valve" insufficiency. Manifestation often only between the 3. and 6. decade of life.
- Isolated pulmonary stenosis (PS) resp. obstruction of the sub-pulmonary outflow tract: Clinical picture of a pulmonary valve stenosis
- Isolated ventricle septum defect: Clinical picture of an isolated ventricle septum defect
- Ventricel septum defect plus pulmonary stenosis: Clinical picture of a tetralogy of Fallot

ECG: Initial depolarisation in the ventricle septum due to the inversion of the conductory system from right to left: Deep Q-wave in II, III, aVF and in the right precordial leads (V4r, V1, V2) and absent Q-waves lateral (V5, V6). Left hypertrophy in „TI", VSD. Right hypertrophy in VSD, VSD + PS. Biventricular hypertrophy in VSD with PHT. AV-blocks. 3° AV-blocks increase in later age. Often WPW syndrome.

X-ray: Cardiac outline, cardiac size and volume of the pulmonary vessels depend on nature and severity of the concomitant cardiac defect! Pulmonary phlebostasis and enlarged left atrium in case of left sided AV-valve insufficiency or insufficiency of the systemic ventricle. Increased volume of the pulmonary vessels in case of VSD,

decreased volume of the pulmonary vessels in case of PS. Shifting of the cardiac apex in case of dextroversio cordis.
AP-projection with `straight left cardiac margin" due to the aorta ascendens who forms the edge on the left side. The convex appearance of the aorta ascendens is absent, which usually is situated on the right cardiac edge. The central pulmonary segment does not form the edge, because the pulmonary artery trunk is situated centrally. In case of VSD increased lung perfusion. Enlargement, lifting and shifting of the right pulmonalis.

Echo: Essential for the diagnosis. All important anatomic changes can be assessed qualitatively and quantitatively.

	Morphologic left ventricle	**Morphologic right ventricle**
Trabecula	Discrete	Rough, moderator band
Form	Eliptical	Triangular
AV-valves	Situated near basis 2 cusps (fish mouth)	Situated near apex 3 cusps Reflux
Papillary muscle	Two	Multiple
Chordae	Towards the free wall of the LV	Towards the IVS
Relation AV/Semi-lunar cusp	Fibrous continuity mMV/PV	No continuity mTV/AoV
Great vessels	Parallel course of the great arteries; PA right-posterior originating and with bifurcation in its course	Ao left-anterior originating with no bifurcation in its course
Miscellaneous		
(Sub-)pulmonary-stenosis	Subvalvular fibromuscular pulmonary / pulmonary valve stenosis, Outflow obstruction due to ventricle septum aneurysm	
VSD	Malalignment type, rarely muscular or infundibular VSDs	

Note: IVS = interventricular septum
mMK/PV = morphologic mitral/pulmonary valve
mTV/AoV = morphologic tricuspid/aortic valve

MRI: In addition to the Echo for imaging of the cardiovascular structures and function without overlapping by other structures. Quantification of the volume and of the systolic ventricular function and imaging of the great vessels.

Heart catheterization: Assessment of pressure and flow conditions and as well of the underlying anatomy. In case of VSD assessment of the size of the shunt, the resistance of the pulmonary vessels and of the morphology of the pulmonary vessels; in case of PS assessment of the trans- resp. sub-valvular gradient. Assessment of the abnormal coronary status.

Th.: Indication for treatment individually depends on the severity of symptoms, the haemodynamics and on the spontaneous prognosis.
In symptomatic patients symptom-orientated pharmaceutica treatment according to the current guidelines.

Surgical therapeutic options: In principle the surgical intervention can be compared to the technique in case of similar defects without ventricular inversion. Morphologic pecularities, abnormal coronary supply, position of the conduction system and as well the position of the anterior papillary muscle of the right sided AV-valve are the reason for technical modifications.
In case of haemodynamic relevant VSD: VSD patch closure. The fixating sutures of the patch must be positioned on the left side of the septum to avoid a block, because of the position of the conducting system.
Valvular pulmonary stenoses: Commissurotomy. In most cases significant sub-pulmonary stenoses require the insertion of a conduit between morphologic left ventricle and of the pulmonary artery.
`Tricuspid valve´ insufficiency: Valve replacement. A re-construction of the tricuspid valve is only possible in exceptional cases.
`Double-switch operation´: Combination of a atrium switch operation with an arterial switch operation. Rarely performed in adult age.
Heart transplantation in case of systemic ventricular failure.

Typical post-operative residual findings: Tachycardic supraventricular and ventricular rhythm disorder, heart block, re-/residual shunts on ventricular level, persistent or newly occuring insufficiency of the tricusp and/or mitral valve, all known complications after valve replacement, stenosing and degeneration of conduits and as well deficient pace maker functions. Failure of the morphologic right ventricle.

The adult patient with Eisenmenger syndrome [Q21.0]

Def.: "Pulmonary hypertension at the systemic level due to a high pulmonary vascular resistance, with reversed or bidirectional shunting through a large ventricular septal defect." (Paul Wood)
Each large defect in which a free connection between the systemic and pulmonary circulation exists can lead to a fixed elevation of the pulmonary vascular resistance and then lead from a primary left-to-right shunt, via the stage of a balanced shunt, to a predominantly right-to-left shunt.
According to the WHO definition and the three world conferences about PHT (Evian 1998, Venice 2003, Dana Point 2008) the PHT in congenital heart defects (CHD) is classified as group 1, pulmonary arterial PHT.
Patients with Eisenmenger reaction have a complex multi-organ involvement.

Ep.: Prevalence: 8% of all untreated congenital heart defects and 11% of all untreated defects with left-to-right shunt.

Aet.: Cardiac defects that can cause Eisenmenger syndrome: Ventricular septal defect, atrioventricular septal defect, atrial septal defect, persistent ductus arteriosus, complex form of complete transposition of the great vessels, truncus arteriosus, surgically created aortopulmonary shunt, other atrium septum defects.
Depending on the location of the shunt, it can be classified as pre-tricuspid, i.e. proximal of the tricuspid valve (e.g. ASD, common atrium) or post-tricuspid, i.e. distal of the tricuspid valve (e.g. VSD, singular ventricle, aortopulmonary communications, large surgically created shunt).

PPh.: The patho-mechanism is not completely known. Endothelial dysfunction or platelet activation apparently play an important causal role.

Pat.: Lung biopsy with histology: Classification according to morphological changes (acc. to Heath and Edwards – see special literature):
Grade 1: media hypertrophy - Grade 2: additional intima proliferation - Grade 3: additional first vessel occlusions - Grade 4: additional angiomatous changes and dilatations - Grade 5: vessel wall atrophy - Grade 6: additional necrotizing arteritis.

Consequences of pulmonary vessel obstruction: pulmonary artery dilatation, concentric right ventricular hypertrophy, dilatation of the pulmonary/tricuspid valve ring, fibrosis of the right-side valves, calcification of the pulmonary arteries

CL.: Cyanosis and reactive erythrocytosis; exertion dyspnoea, fatigue, syncope (resulting from low cardiac output); heart failure; arrhythmia; haemoptysis (resulting from pulmonary infarctions, rupture of pulmonary vessels); headache, dizziness, visual disorders; cerebrovascular events (hyperviscosity, brain abscess, paradoxic embolisms).

Th.: **A) Conservative:**

- General recommendations: Mild exertion, limited by symptoms (capacity reduction). Avoid discotheques, alcohol, hot baths, saunas! Caution in case of: dehydration, fever, blood loss, vasodilation!
  It is important to exclude in all Eisenmenger patients a (relative) anaemia and an iron deficiency (always check the whole iron status!) and to replace if necessary (**Caution:** Disproportional increase of Hb and Hct with iron replacement)!
- Pharmaceutical treatment:
  - Avoid medications that lead to the reduction of resistance in the systemic circulation (Rs) (i.e. ACE inhibitors, calcium antagonists), that increase the risk of bleeding (aggregation inhibitors, anticoagulants) or that can lead to thromboembolisms (oestrogens, diuretics).
  - Pharmaceutical treatment of the pulmonary hypertension (see chapter on `pulmonary hypertension`) – treatment and monitoring only with involvement of an experienced centre!
  - Phlebotomy:
    Ind: Symptomatic hyperviscosity (headache, fatigue, dizziness, visual disorders, clouded consciousness)
    No (!) indications: Asymptomatic patient with elevated haematocrit (even with very high readings); higher but stable haematocrit that is not progressive.
    Technique: Max. 500 ml + isovolemic volume substitution – if at all possible, not > 4 x per year - danger: shock in the case of too much and/or too rapid withdrawal of volume. More frequent phlebotomy → iron deficiency → iron substitution → ***Caution:*** Exceeding increase of Hb and Hct
  - Possibly administration of oxygen in adults, who subjectively benefit (insufficient data)

B) Surgical:

Transplantation:
Options: Unilateral lung transplantation or bilateral lung transplantation plus intracardial correction; combined heart-lung transplantation
Ind: In the presence of unfavorable prognostic factors (recurring syncope, refractory right heart failure, bad tolerance of exertion, high-grade hypoxaemia)
Survival rates: Lung transplantation / heart-lung transplantation: 1 year about 80%, 5 years 70%, 10 years 50%

C) Special complications:

- Haemostatic complications: Dysfunctional thrombocytes; prothrombin, factor V, VII, IX deficiency; prolonged prothrombin time (PTT); abnormal fibrinolysis; acquired thrombocytopenia; disorder of the von Willebrand factor.
  Bleeding is usually mild and self-limiting; symptomatic treatment often sufficient; substitution of blood, coagulation factors; thrombocytes only rarely necessary; desmopressin may also be good. Avoid thrombocyte aggregation inhibitors and anticoagulants if at all possible!
  Exception: Replacement with mechanical valve, atrial fibrillation, thromboembolism.
  Caution: Coagulation parameters of the clotting status can only be used, if in case of an increased Hct the

amount of citrate in the test tube is adapted. (→ communication with the laboratory)

- Cerebrovascular events: Increased blood viscosity with danger of cerebrovascular thromboses with ischaemic insult. Concomitant risk factors: hypertension, atrial fibrillation, phlebotomy
  In the case of symptomatic hyperviscosity → phlebotomy
  In the case of paradoxic embolism: anticoagulants
- Endocarditis prophylaxis: In all cases necessary!
- Arthralgias (5%): → Causes
  - Hypertrophic osteoarthropathy Pierre-Marie-Bamberger due to hypoxaemia
  - Hyperuricemia

  Th.: Colchicine, oral corticosteroids. **Beware:** Non-steroidal antiphlogistics (Danger of renal failure!)
- Tendency of developing bile stones
- Defect of renal function
- Scoliosis
- Pregnancy:
  1. Maternal mortality rate up to > 30%. Deaths occur during delivery and in the first few weeks post-partum (thromboembolisms, hypovolemia, pre-eclampsia). Indication for termination of pregnancy.
  2. Risk for the child: Spontaneous abortions in about 30% of cases; premature births in 50% of cases; perinatal mortality up to > 20%; intrauterine growth retardation around 30%.

Prog: Survival rates (in older studies) after diagnosis: 10 years 80%; 25 years 40%, that means clearly better compared to idiopathic forms of PAH

Unfavorable prognosis factors: Advanced pulmonary vascular disease, severely reduced right ventricular function, low cardiac output, recurring syncope, high-grade hypoxaemia (SaO_2 < 85%).

Causes of death: Ventricular arrhythmia; cardiac failure, thromboembolisms, haemoptysis or intrapulmonary bleeding, cerebral abscess, pregnancy, non-cardiac surgical procedures.

Monitoring:

Follow-up check-ups only in cooperation with physicians who have experience in this field. Go to specialized centre if there are complications.

Fontan operation

Def.: The Fontan operation is a milestone in the surgical treatment of patients with univentricular hearts (1968 first Fontan operation), who are not suitable for a bi-ventricular correction. This operation causes the venous blood from the systemic circulation to be fed directly into the pulmonary circulation, i.e. without the interposition of a pumping ventricle

Basic concept: Increased venous pressure is sufficient as a driving force to attain sufficient pulmonary perfusion and filling of the systemic ventricle. A right ventricle as a “pump” is not absolutely necessary. A single ventricle works as a pressure-suction pump for the systemic circulation.
Benefit: Reduction or absence of cyanosis, reduction of volume load on systemic ventricle.
In the meantime, the Fontan operation is used in a modified form for a multitude of heart defects in which a separation of the two circulations (biventricular repair) is not possible. Surgical risk and morbidity are lowered while survival rates and quality of life increase for the patient undergoing surgery. Nevertheless, it is still a palliative operation.
At the moment the so-called complete cavo-pulmonary connection (TCPC) replaced the older atrio-pulmonary modifications (Fontan-Kreutzer, Fontan-Bjoerk etc). That represents an intra- or extra-cardiac connection between the lower vena cava and the pulmonary artery and as well the connection of the upper vena cava with the pulmonary artery (bi-directional Glenn-anastomosis)

Results of the operation:

Under ideal conditions, survival rates are about 90% after 10 years. About 80% of patients receiving this surgery experience improvement in capacity following the operation and feel well under everyday conditions.
Frequent causes of death are chronic heart failure and sudden death.
In case of newly occurring complications always look for disorders of the haemodynamics!

Long-term results and clinical complications after Fontan operation:

Main problem:

- ´Late-Fontan-Failure´ with progressive deterioration of the ventricular function, progressive V-valve insufficiency, increase of resistance of the pulmonary vascular system, atrial enlargement (esp. on the right side), PV-obstruction, and with the effects of a chronic increased venous pressure (venostasis of the liver). General recommendations can not be given. The therapy depends on the individual underlying cause, but in general is problematic and only should be performed in communication with an experienced centre.
- Stenoses in the area of the anastomosis, stenosis within the area of the pulmonary arteries or impairment of the pulmonary venous flow. Also minimal stenosis gradients have a high haemodynamic relevance! Often interventional treatment possible.

Further complications:

- Blood clot in the right atrium and in the arteria pulmonalis. Paradox arterial embolism (cerebral, coronary, peripheral) in case of persisting right-to-left shunt possible.
  Di.: Transoesophageal Echo
  Th.: Continuing anti-coagulation is recommended at least for adults (despite absent evidence) by many centres. Atrial blood clots, atrial arrhythmias or thromoembolic complications are definite indications.
- AV malformations, intrapulmonary fistulas and collateral vessel formation
- Cyanosis after Fontan operation:
  Cause: Pulmonary arterial stenoses, increased pulmonary vascular resistance or intra-pulmonary fistulas
  Th.: Depends on the cause (e.g. interventional closure of intra-pulmonary fistulas)
- PLE = protein losing enteropathy:
  PLE is a life-threatening complication following surgery, characterized by pleural effusion, ascites, generalized oedema and low serum protein.
  Cause: Elevated central venous pressure and unknown factors
  Incidence: About 10% of all patients after a Fontan operation, beginning an average of 4 years after surgery.
  Th.:
  A) Conservative: Various treatments: Salt restriction, protein rich diet, diuretics, ACE inhibitors (sometimes not well tolerated), steroids, albumin replacement, chronic administration of sub-cutaneous heparin. Interventional placement of an inter-atrial connection (baffle fenestration)
  B) Surgical: Conversion of the atrio-pulmonary Fontan operation into a extra-cardiac TCPC, heart transplantation (also here high recurrence rate)
  Prog: Unfavorable long-term prognosis; independent of the chosen therapy: 5 year survival rate after diagnosis about 45%
- Pregnancy after Fontan operation: High risk, supervision from a specialized centre
- Arrhythmias:
  Supraventricular arrhythmia – especially atrial flutter, atrial re-entry tachycardia. Occurrence in about 20% of all patients 10 years following Fontan operation. Maintenance of a sinus rhythm is very important for the haemodynamics. Arrhythmias are badly tolerated haemodynamically.
  Th.: In cooperation with experienced centres. Options are: Pharmaceutical therapy with beta-blocker or amiodarone. If possible: Catheter ablation. Poss. switch-operation to extra-cardiac Fontan, Maze operation.
  Bradycardic arrhythmias: Pace maker implantation, often epicardic.

Marfan syndrome [Q87.4]

Internet information: *www.marfan.de*

Def.:
- Marfan syndrome (MS) is one of the most frequently occurring connective tissue disorders. The clinical variability of the disorder is very large.
- Cardiovascular complications determine the course of the disease, prognosis and life expectancy.
- Classic MFS is triggered by a mutation in the fibrillin gene (FBN1) on chromosome 15q21.1 ; The Marfan syndrome type 2 is caused by mutation in gene TGFBR1 or 2.
- MS is an autosomal dominant inherited disorder. About 25% of patients have a new mutation with normal family history, however.

Incidence: Prevalence: About 1 : 10,000. There is no gender dominance.

CL.: At the moment the diagnosis is mainly based on clinical criterias, which are internationally defined by the so-called ´Ghenter nosology´.
Clinical symptoms vary. Many symptoms are not yet present in childhood and sometimes do not develop until later in life.

- Excessively long extremities and long body
- Short-sightedness
- Retinal detachment
- Aortic aneurysms (changes to the heart and vessels)
- Unexplained fatigue
- Loose joints, arachnodactyly
- Narrow jaw with crowded teeth
- Protruding or indented sternum
- Changes in the spine (e.g. scoliosis)

Selected cardiovascular aspects:

- The cardiovascular system is involved in 90% of patients with MS: Ectasia of the aortic root, aortic dissection or rupture, ectasia of the pulmonary artery, aortic and AV valve regurgitation.
- The entire aorta may be affected. A progressive degeneration of the media frequently develops, especially in the

ascending aorta, with the subsequent risk of an aortic aneurysm and aortic dissection or rupture (prevalence about 75%).
- The risk of aortic dissection increases with increasing lumen size, but can also occur in the presence of a normally sized aorta. Specific age and body surface adjusted normographs exist for the more detailed size assessment.
- Dissections typically occur after the 2. decade of life, rarely during childhood or adolescence
- Acute aortic dissection often have an atypical course in case of MFS without the typical ´killing pain´
- With increasing age, aortic valve regurgitation develops in up to 40% of patients.
- Mitral and tricuspid valves are often "floppy" and often show prolapse with regurgitation.
- A systolic and diastolic cardiac insufficiency possibly correlates amongst others with the extent of connective tissue changes within the myocardium and with the valve changes.
- Unexpected death cases in case of MFS are especially reported in connection with aortic ruptures or ventricular arrhythmias.

Di: According to Marfan diagnosis criteria (see internet information)

Th.:
- Explanation to the patient about his or her disorder and advice regarding physical strain. Life-long checkups.
- Medication: It is probably possible to reduce the occurrence or progression of aortic ectasia, decrease the risk of rupture or dissection and increase the survival rate with beta blockers and ACE inhibitors (losartan).
- All(!) patients with MFS should undergo endocarditis prophylaxis in the presence of the given indications. (Note: The American Marfan Society did not agree with the revisions of the endocarditis guidelines.
- Cardiovascular surgery:
  - The indication for aortic surgery depends, for instance, on aortic diameter, the dilatation tendencies of the aorta and family history of aortic dissection.
  - A prophylactic replacement of the ascending aorta is recommended if the diameter is about 45 mm, in a family history with aortic dissection often even earlier (> 40 mm).
  - A replacement of the descending aorta is recommended at diameters > 55 to 60 mm or – if discomfort, pain or signs of ischaemia occur – the aortic diameter increases by more than 0.5 - 1.0 mm per year or if the aortic diameter is more than twice as wide as the normal aorta. In small patients consider aorta ascendens replacement at a diameter of 2.75 cm/ m^2 of body surface.
- Marfan patients should receive not only cardiological, but also regular ophthalmological, orthopaedic and organ-specific follow-up care.
- Pregnancy represents an elevated risk, especially in the presence of a large aortic root, and requires special preconception genetic consultation.
- Relative (1^{st} degree) should be tested for the presence of MFS.

Prog:
- Aortic ectasia, aortic dissection and chronic aortic valve regurgitation are the main causes of mortality and morbidity in adults → regular monitoring.
- Surgical procedures on the aortic root and the aortic and mitral valves performed at the right time, the prophylactic use of beta-blockers and careful patient follow-up care have increased life expectancy to > 70 years.

CARDIAC INSUFFICIENCY (CI) [I50.9]

Def.: Inability of the heart to produce the cardiac output required by the body under normal ventricular end-diastolic pressure. - WHO: Reduced physical endurance due to a ventricular function disorder.
Cardiac insufficiency is a clinical syndrome of varying aetiology.

Ep.: Prevalence is age-dependent: 5th decade 1%, 6th decade 3%, 8th decade 10% (m : f = 1.5 : 1)
In 50% of cases, the primary cause is hypertension (Framingham Offspring Study). This frequently triggers the following pathogenetic sequence: hypertension → coronary heart disease → myocardiac infarction → heart failure! Hypertension and CHD are therefore the most frequent causes!
Various terms and classification systems have been developed in order to understand the cardiac insufficiency:

1. According to the cardiac output:
- Low output failure: Forward failure with reduction of cardiac volume. In this case the periphery is cold.
- High output failure: Deficient blood (O_2) supply to the periphery with elevated cardiac output: e.g. due to anaemia, hyperthyroidism, AV fistula. In this case the periphery is warm.

The arteriovenous O_2 difference (normal 3.5 – 5.0 ml/dl) is increased in the case of low output failure and normal or reduced in the case of high output failure.

2. According to the affected heart chamber:
- 1. Left, - 2. Right and - 3. Global heart failure

An isolated right ventricular failure is rather rare (cor pulmonale, right cardiac infarction, arrhythmogenic cardiomyopathy etc.). More often symptoms of a right ventricular failure develop during the course of a left ventricular insufficiency (due to a backflow of blood into the right heart).

3. According to the chronology of the development of heart failure:
3.1 Acute heart failure: Develops over hours/days.

a) Myocardial pump failure: e.g. acute coronary syndrome due to critical stenosis of the main trunk, myocardiac infarction, hypertensive crisis, myocarditis
b) Acutely occurring insufficiency or shunt defects:
e.g. ventricular septal defect with infarction, papillary muscle tear with mitral regurgitation and infarction; acute valve destruction due to bacterial endocarditis (aortic or mitral regurgitation)
c) Mechanical impairment of ventricular filling: e.g. pericardial tamponade
d) Tachycardic or bradycardic heart arrhythmias

3.2 Chronic heart failure: Develops over the course of months/years.
a) compensated - b) decompensated

4. According to the pathophysiology, whether in the first line the systole, diastole or both phases are affected:

- Systolic cardiac failure = HFREF (heart failure with reduced ejection fraction) is the consequence of a myocardial contraction disorder
- Diastolic cardiac failure = HFNEF (heart failure with normal ejection fraction) is the consequence of reduced diastolic distensibility (compliance) and relaxation of the left ventricle with maintained systolic pump function. This leads to a too rapid increase of pressure during the filling phase and to a decreased stroke volume. The proportional EF however is normal.
- Combined systolic and diastolic ventricular function disorders

5. According to the aetiology (assigned to the pathophysiology)

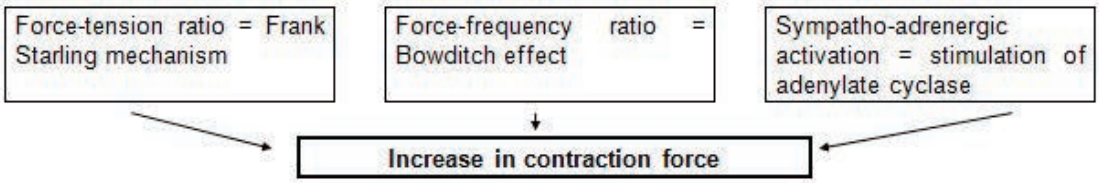
Pathophysiology	Aetiology
I. VENTRICULAR SYSTOLIC FUNCTION IMPAIRMENT 1. Due to weak contractions 2. Due to elevated ventricular wall tension: a) with volume load = increase in preload b) with pressure load = increase in afterload	Coronary heart disease (about 70%) Cardiomyopathies (15%) Myocarditis Defects High blood pressure Pulmonary hypertension
Pathophysiology	**Aetiology**
II. VENTRICULAR DIASTOLIC FUNCTION IMPAIRMENT 1. due to cardiac hypertrophy 2. due to impairment of ventricular filling	High blood pressure Constrictive pericarditis Restrictive cardiomyopathy Pericardial tamponade
III. CARDIAC RHYTHM DISORDERS	Bradycardia/tachycardia of various aetiologies

Increased preload Volume load	→	HEART: Weak contractions Arrhythmia Filling impairment	→	Increased afterload Pressure load

PPh.: Parameters of cardiac pump performance:

1. Contractility (inotropy):
Force and speed of muscle fibre shortening, measurable as the maximum speed of pressure increase (dp/dt) in the isovolumetric contraction phase.
Contractile force in the healthy heart can be increased through 3 mechanisms:

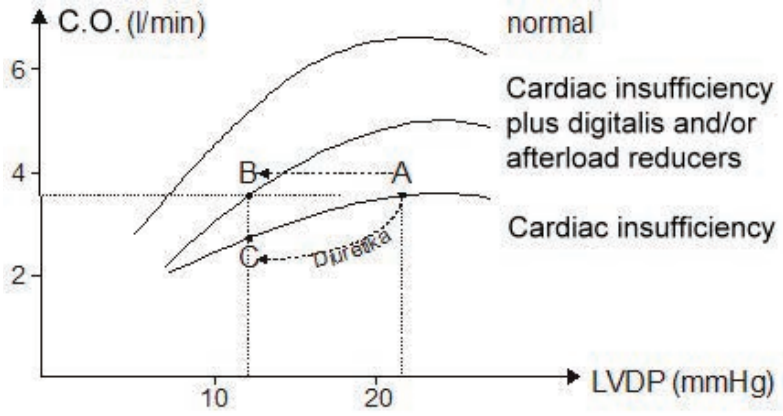
Sympatho-adrenergic activation:
Noradrenaline causes an increase in contractions by stimulating the beta-receptor adenylate cyclase system. - In heart failure, however, this effect falls off as a result of down regulation (= decrease in density) of the beta receptors.



2. Preload: Frank Starling mechanism (force-tension ratio):
With increasing preload (preload) = ventricular end-diastolic volume (measurable at ventricular end-diastolic pressure) increases ventricular contraction and diastolic prestretching of the heart muscle, causing the stroke volume to increase (within physiological limits). The cause of the Frank Starling mechanism is an increase in sensitivity of the contractile proteins for calcium. With increasing heart failure, the efficacy of the Frank Starling mechanism decreases!
3. Afterload:
Maximum ventricular end-diastolic wall contraction, dependent on the afterload, against which the ventricle works. The afterload of the left ventricle essentially represents the systolic blood pressure, which is dependent on

peripheral resistance. Increase in the afterload leads to a decrease in stroke volume.

4. Heart rate:
   Bowditch effect (force-frequency ratio)
   In a healthy heart, increasing heart rate also leads to an increase in contractile force. - In the insufficient heart, however, this effect is absent; with high heart rates, there is even a decrease in the contractility of the insufficient heart.



With the use of positive inotropic substances (e.g. cardiac glycosides) and afterload reducers (e.g. ACE inhibitors), the working diagram of the insufficient heart is improved, so that the same stroke volume can once again be achieved with decreased end-diastolic pressure (B).

Preload reducers (e.g. diuretics) do lower the end-diastolic pressure (C), but do not change the working diagram.

In heart failure, the working diagram of the heart flattens (Frank Starling curve), which means:

- The maximum achievable cardiac volume decreases, at first only under stress (exertion insufficiency), later even at rest (insufficiency at rest).
  Cardiac output (CO) – in relation to body surface area = cardiac index (CI) – normal lower limit at rest > 2.5 l/min/m^2
- In comparison to healthy heart muscle, insufficient heart muscle can only still achieve a certain stroke volume with increased left ventricular end-diastolic pressure = LVEDP (see A in the illustration) (normal LVEDP at rest: 5 - 12 mmHg).
- In ventricular systolic function impairment, the left ventricular ejection fraction is reduced while the end-diastolic volume is increased. In ventricular diastolic function impairment, the ejection fraction is not reduced by impairment of ventricular filling, however, stroke volume and cardiac output are reduced

$$\text{Ejection fraction (\%) = Ejection fraction (EF)} = \frac{\text{Stroke volume (SV)}}{\text{end-diastolic (ventricular) volume (EDV)}} \times 100$$

Severity grades of the systolic dysfunction (in % of EF)

Normal	> 50%
Mild	45 - 54%
Moderate	30 - 44%
Severe	< 30%

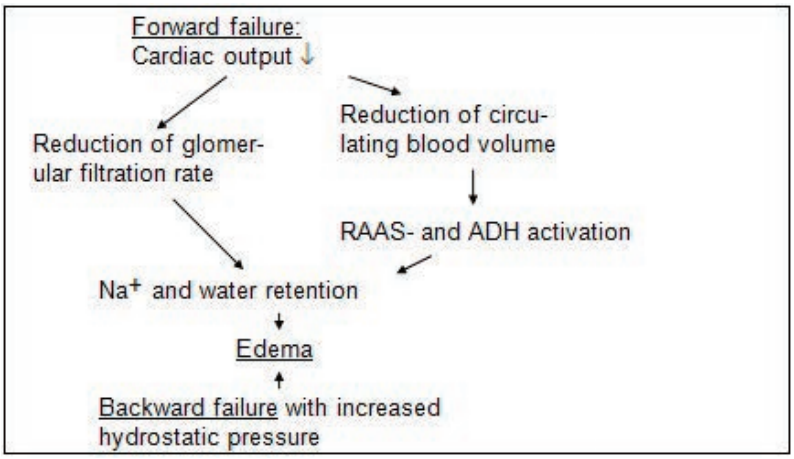
- A diagnosis of diastolic heart failure can be made if there are clinical signs of CI with a normal ejection fraction, but abnormal left ventricular relaxation, filling and/or distensibility (echo, cardiac catheter). This results in a too rapid increase of pressure in the diastole with reduced stroke volume. LVEDP (=left ventricular end-diastolic pressure) > 16 mm Hg in case of normal EF.

Consequences of the weak pumping action of the insufficient heart are:

a) Forward failure = reduction of cardiac output with inadequate blood pressure and peripheral perfusion deficit: muscle weakness, increased fatigability

b) Backward failure = congestion of the venous blood:
   - Before the left side of the heart: pulmonary congestion to pulmonary oedema
   - Before the right side of the heart: oedema, enlarged congested liver, possibly a small amount of ascites (ultrasound)

Pg.: cardiac oedema



Compensation mechanisms in heart failure:

1. Neuroendocrine activation:

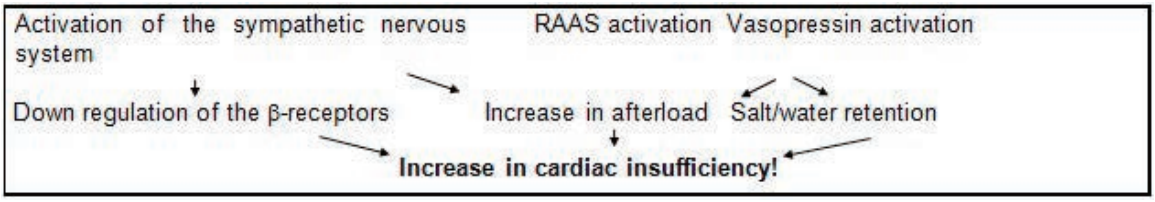
   1.1. Activation of the sympathetic nervous system + release of catecholamines lead, at first, to an increase in heart rate and contractile force. With increasing heart failure, the plasma noradrenalin level increases, correlating with a worsening of the prognosis. At the same time, the number of cardiac beta receptors decreases (down regulation). The catecholamines then have a less and less inotropic effect on the heart, but increase peripheral resistance, and therefore the afterload, through an increase in arteriolar tone!

   By increasing the venous tone with an increased supply of blood to the heart, the preload and contractile force are increased. The efficacy of this Frank Starling mechanism is reduced as heart failure increases

   1.2. Activation of the renin-angiotensin-aldosterone system (RAAS):
   Angiotensin II → vasoconstriction → afterload ↑
   Aldosterone → Na^+ and water retention → preload ↑

   1.3. Vasopressin (ADH) activation → water retention → preload ↑

   Notes: The neuroendocrine compensation mechanisms, which are helpful in the beginning, worsen the haemodynamic situation of heart failure in the long-term, leading to a vicious cycle that must be interrupted therapeutically!



   1.4. Release of natriuretic peptides: type A = ANP (= atrial natriuretic peptide), type B = BNP (brain natriuretic peptide) and type C = CNP. Trigger is straining of the atria (ANP) or ventricles (BNP). BNP and N-terminal pro brain natriuretic peptide (NT-pro BNP) are good parameters for confirming a diagnosis of heart failure and assessing the prognosis. BNP has a vasodilatory and natriuretic-diuretic effect (through its inhibitory action on the renin-angiotensin-aldosterone system). BNP levels increase as heart failure increases:
   Since BNP levels also increase slightly with age and are influenced by various factors (e.g. obesity with BMI > 30 kg/m^2: BNP ↓; renal insufficiency, COPD, myocarditis: BNP ↑), BNP values should only be interpreted in conjunction with the patient's medical history as well as clinical and echocardiogram findings.

   BNP/NT pro BNP in case of chronic cardiac insufficiency (CI):

BNP < 100 pg/ml NT-proBNP < 400 pg/ml	BNP 100 - 400 pg/ml NT-proBNP 400 - 2.000 pg/ml	BNP > 400 pg/ml NT-proBNP > 2.000 pg/ml
CI unlikely	CI probable, Diagnosis however not secure	CI very probable

   With acute left heart insufficiency, the BNP level may still be within normal range at first, but increase later.

   In heart failure with increasing BNP values, mortality rates are high (prognostic significance of BNP).

2. Remodeling, i.e. molecular, biochemical protein and cellular changes that manifest in the structure and function of the heart following damage.

3. Cardiac hypertrophy:
   Acute heart failure leads to dilatation of the heart.
   In chronic heart failure, the type of strain plays a role:

- Volume load (e.g. valve regurgitation) leads to eccentric hypertrophy (= hypertrophy with dilatation)
- Pressure load (e.g. valve stenosis, hypertension) leads to concentric hypertrophy (= hypertrophy without dilatation)

Notes: If compensatory myocardial hypertrophy exceeds a critical limit, heart failure worsens.
Once the critical heart weight of about 500 g is exceeded, a relative coronary insufficiency with reduction in the performance of the heart develops and structural dilatation occurs. Ventricular dilatation leads, through distension-induced programmed cell death (apoptosis), to further dilatation.

Failure of the physiological/therapeutic compensation possibilities for maintaining adequate pump performance of the heart is called decompensated heart failure.

Attention: Compensated heart failure can also become decompensated in the presence of non-cardiac disorders that have an unfavorable effect on heart function, e.g. pneumonia, anaemia, polycythemia, hyperhydration with renal insufficiency, etc.

CL.: A) Left heart failure [I50.1]

1. With backwards failure and pulmonary congestion:
   - Dyspnoea (first exertional dyspnoea, later dyspnoea at rest), tachypnoea
   - Orthopnoea (deployment of the respiratory musculature by sitting up helps the patient)
   - Cardiac asthma: Nighttime coughing + occasional orthopnoea ("heart failure cells" in the sputum = alveolar macrophages containing haemosiderin).
     Ausc: basal rales; pulse oxymetry: O_2 saturation ↓
   - Pulmonary oedema with orthopnoea, rales over the chest, foamy expectoration
   - Cyanosis (pulmonary function impairment + increased peripheral O_2-exhaustion)
2. With forward failure (low output):
   - Decline in performance, feeling of weakness
   - Cerebral function impairment, especially in older patients

B) Right heart failure [I50.0] with backflow into the systemic circulation:
- Visible venous congestion (neck veins, veins at the basis of the tongue)
- Weight gain and oedema of the dependent body parts: Pretibial foot and ankle region – presacral in bedridden patients; at first only in the evenings, later permanently; in severe cases anasarca = oedema of the trunk.
- Congested liver: Enlarged, possibly painful liver (especially in the presence of acute cardiac decompensation), possibly jaundice, increase in bilirubin and transaminase levels. Vena cava and hepatic veins enlarged in ultrasound images. In the presence of chronic right heart failure, possible development of cardiac “cirrhosis” (= indurated, atrophic congested liver), ascites (transudates from congestion)
- Congestive gastritis: Loss of appetite, meteorism, rarely malabsorption and cardiac cachexia
- Engorged kidneys with proteinuria

C) Common symptoms for left and right heart failure:
- Nocturia (due to nighttime reabsorption of oedema)
- Adrenergic hyperactivity: Tachycardia, possible arrhythmias, moist and clammy skin
- Possibly 3rd heart sound (bileop rhythm), possibly alternating pulse (due to varying large stroke volumes)
- heart enlargement, possibly with relative AV valve regurgitation
- Pleural effusion (congestive transsudates) occurs more frequently with right than with left insufficiency because the negative intrapleural pressure on the right is greater.

Compl.: - Arrhythmias:
Arrhythmias can be the cause as well as a complication of heart failure. The risk of sudden cardiac death correlates closely with the degree of severity of heart failure: 80% of patients with heart failure in NYHA stage III-IV die of tachycardic arrhythmias!
- Pulmonary oedema (backward failure)
- Cardiogenic shock (forward failure)
- Venous thromboses (flow deceleration, immobilization) with the danger of pulmonary embolisms; cardiac thrombus formation with the danger of arterial embolisms (especially cerebral embolisms)

ABCD stages of heart failure of the American Heart Association (AHA), 2001:

- Group A: Patients without symptoms of heart failure, but with risk factors for heart failure: Hypertension, CHD, intake of potentially cardiotoxic medications, alcohol abuse, rheumatic fever in the patient’s history, cardiomyopathy in the family history, etc.
- Group B: No symptoms of heart failure, but signs of structural heart damage: Left ventricular hypertrophy and/or dilatation, hypocontractility, infarction scars, etc.
- Group C: Structural heart damage in conjunction with symptoms of heart failure
- Group D: Terminal heart failure

Stage classification of heart failure (CI) according to subjective symptoms
(NYHA stages of the New York Heart Association):

NYHA Stage	Subjective symptoms of CI	ABCD groups
I	Freedom from symptoms, normal physical endurance	B
II	Discomfort with strenuous physical exertion	C
III	Discomfort even with mild physical exertion	C
IV	Symptoms at rest	D

NYHA stage classification of heart failure correlated with objective criteria:

NYHA Stage	Endurance	Cardiac output	Spiroergometry: Max. O_2 uptake (max. $\dot{V}O_2$ in ml/kg/min)
I	up to 150 W and more (> 1.5 - 2 W/kg)	Cardiac output normal at rest and during exertion	> 25
II	up to 100 W (> 1 – 1.5 W/kg)	Cardiac output adequate at rest and during exertion	15 - 25
III	up to 50 W (1 W/kg)	Cardiac output reduced during exertion	5 - 15
IV	Stress test not possible	Cardiac output reduced at rest	< 5

Diagnosis:

1. Clinical (NYHA stage)
2. BNP (normal BNP values exclude heart failure when clinical examinations are inconclusive)
3. Non-invasive diagnostic imaging procedures:

3.1 Echo:

- Evidence of systolic dysfunction
  -Percent fractional shortening = FS (normal ≥ 25 %) correlates approximately with the ejection fraction.

$$FS\ (\%) = \frac{(EDD - ESD) \times 100}{EDD}$$

EDD = end-diastolic diameter of the left ventricle
ESD = end-systolic diameter of the left ventricle

$$EF = \frac{(EDV - ESV)}{EDV}$$

EF = ejection fraction
EDV = end-diastolic volume
ESV = end-systolic volume

  - The planimetric determined ejection fraction is more accurate
- Detection of a diastolic dysfunction (Doppler technique) ➝ 4 stages: 1. Abnormal relaxation, 2. Pseudonormalization, 3. Reversible restriction, 4. Irreversible restriction
  Measurement of the transmitral flow via PW-Doppler (E- and A-wave) and as well measurement of the tissue velocity in the mitral annulus via tissue Doppler echocardiography) E´- and A`- wave). From this the quotient E/E´ can be calculated. Readings > 15 for E/E´ indicate a diastolic dysfunction, readings of < 8 practically exclude it.

Additionally:

- Detection of cardiac enlargement, myocardial hypertrophy
- Assessment of cardiac output and blood flow (colour duplex)
- Recording of causal factors for heart failure, e.g. defects, ventricular wall movement disorders following infarction, pericardial effusion, etc.

3.2 Chest X-ray in 2 views:

- In left heart failure, signs of pulmonary congestion:
  Signs of pulmonary congestion, e.g.
  - Kerley B lines: horizontal streaks up to 1 cm long in the lower lobes = congested lymph vessels in the presence of interstitial oedema
  - densely congested hilar vessels, enlarged congested pulmonary veins (in the hilar region)
  - ground-glass opacity in the presence of alveolar pulmonary oedema ▪ possibly pleural effusion
- In right heart failure:
  - enlargement of the azygos vein (earliest change)
  - enlargement of the superior vena cava and right atrium
- Detection of possible enlargement of the heart:
  Concentric hypertrophy of the ventricle as a result of the pressure load cannot be recognized at first in X-rays. On the other hand, eccentric hypertrophy can be seen early in the presence of volume load.
  a) Globally enlarged heart with cardiothoracic ratio (CTR) > 0.5: ratio of the maximum heart diameter (in the posterior-anterior image) and chest width at the same level is greater than 0.5.

b) Enlargement of the individual ventricle:

- Left ventricle:

  With enlargement of the left ventricle, the apex of the heart is displaced further to the left and projects at an obtuse angle (> 90°) diagonally into the left side of the diaphragm. In the lateral image, narrowing of the posterior cardiac space near the diaphragm.

- Right ventricle:

  Enlargement of the right ventricle displaces the heart by rotation to the left as well. However, this causes an accentuation of the apex of the heart, causing the angle between the left margin of the heart and diaphragm to become acute (< 90°). Narrowing of the retrosternal anterior cardiac space in the lateral image.

Remember: An enlargement of the right ventricle may form the left margin of the heart in the posterior-anterior image → therefore, it should not be automatically concluded that there is an enlargement of the left ventricle if there is an enlargement of the heart to the left → Refer to the lateral image as well! No conclusions can be made regarding the pump performance of the heart from its size! (e.g. the large heart of an athlete).

3.3 Cardio-MRI and -CT:

Determination of the cardiac volumes, wall thickness, ventricular muscle size, valve structures, pericardium, poss. signs of myocarditis or reduced perfusion of the myocardium (CHD), dysfunction of the ventricle wall mobility. (CHD and cardiac infarction)

3.4 Invasive diagnostics:

Due to the high level of diagnostic significance of the echocardiogram and other non-invasive diagnostics, cardiac catheterization is limited to special complications, e.g. assessment of the coronary arteries to exclude/detect CHD prior to surgery and for the diagnosis of defects

DD: e.g.
- Dyspnoea of non-cardiac genesis (→ DD dyspnoea)
- Cyanosis of non-cardiac genesis (→ DD cyanosis)
- Oedema of non-cardiac genesis (→ DD oedema)
- Nocturia of non-cardiac genesis (e.g. bladder/prostate disease)
- Neck vein congestion of non-cardiac genesis (e.g. upper inflow congestion caused by a tumour)
- Pleural effusions of non-cardiac genesis (→ DD pleural effusion)
- Ascites of non-cardiac genesis (→ DD ascites)
- Pulmonary oedema of non-cardiac genesis (→ section on pulmonary oedema)
- Circulatory shock of non-cardiac genesis (→ section on shock)

Di.:
1. Symptoms and clinical signs of heart failure and assignment to an NYHA stage
2. Detection of ventricular systolic (reduced EF) or diastolic (echo criteria) function impairment
3. Elevation of BNP or NT-pro BNP without other explanation as heart failure
4. Aetiologic clarification.

Th.: of chronic heart failure according to guidelines (e.g. *www.dgk.org*; *www.escardio.org*)

A) Causal: e.g.
- Treatment of high blood pressure, pulmonary hypertension
- Revascularization in the case of coronary heart disease and reduction of its risk factors
- Treatment of myocarditis or cardiomyopathy
- Treatment of a heart arrhythmia
- Surgical treatment of a defect or constrictive pericarditis, etc.

B) Symptomatic (compensatory):

1. General measures:
   - Reduction of cardiovascular risk factors (see chapter CHD)
   - Stable CI: Medically monitored therapeutic exercise training program for stable heart failure
   - Decompensated heart failure: Elimination of physical + mental stress, bed rest
   - Easily digested food, small meals, no meals late in the evening; high-potassium, low-salt diet (max. 3 g NaCl/day), monitoring and possible correction of electrolyte balance (especially K^+ and Mg^{++}), prevention of overweight
   - In case of risk of oedema limitation of fluid intake with monitoring of fluid losses (balance)
   - Avoidance of excessive volume replacement therapy
   - Avoidance of a hypokalaemia (which can increase the mortality of cardiac failure) (DIG study)
   - Avoidance of a hyponatraemia < 135 mmol/l, which as well can increase the mortality of cardiac failure (OPTIME-HF study)
   - Regulation of stools
   - Thrombosis prophylaxis, breathing exercises
   - In the presence of decompensation, temporary administration of O_2 by nasal cannula (monitoring via pulse oximetry)
   - Avoidance of medications that may worsen heart failure: e.g. NSAIDs, glucocorticosteroids,

glitazones, calcium antagonists with a negative inotropic effect (verapamil, diltiazem), α-blockers, interferon, some cytostatics (anthracyclines, carboplatin, cyclophosphamide, ifosfamide, trastuzumab), tricyclic antidepressants, lithium, clozapine (a neuroleptic), class I anti-arrhythmics, beta-sympathomimetics (also β2-agonists at higher doses), propofol (a short-acting hypnotic) and others

- Treatment of concomitant disorders that worsen heart failure: heart arrhythmias, heart valve defects, myocardial ischaemia (CHD), anaemia, thyroid function disorders, pneumonia, pulmonary embolism, sleep apnoea syndrome and others.
- Use of linked medical care programs poss. via tele-medicine to improve the therapy of cardiac failure (i.e. CORBENE → internet)

2. Medicinal therapy of chronic heart failure
   - Medications that improve prognosis: ACE inhibitors, AT1-receptor blockers, beta blockers (if these substances are approved for the treatment of heart failure) and aldosterone antagonists
   - Medications that relieve symptoms without improving prognosis: Diuretics and cardiac glycosides

NYHA stage	I	II	III	IV
ACE inhibitors[1]	x	x	x	x
Beta blockers[2]		x	x	x
Diuretics			x	x
Aldosterone antagonists[3]			x	x
Digitalis			x	x

[1] If intolerance of ACE inhibitors, change to AT1-blockers
[2] In case of hypertension and as well after MI administration of beta-blocker also in St.I
[3] Post MI administration of aldosterone antagonists also from ST II

Indication:

- ACE inhibitors are indicated from NYHA stage I or ABCD Group B.
- AT1-receptor blockers (ARBs, sartans) are indicated from stage I of CI against ACE inhibitors or side effects (e.g. coughing) (losartan, candesartan, valsartan).
- Beta blockers without ISAs (metoprolol, bisoprolol, carvedilol, nebivolol) are indicated from stage II, but only in stable patients, with a slow, gradual increase in dose under close medical monitoring. In patients with hypertension or status post myocardiac infarction, beta blockers are used regardless of the stage (i.e. even from stage I).
- Aldosterone antagonists (spironolactone/eplerenone) are indicated, in addition, from stage III (with monitoring of serum potassium levels) because of their favorable effect on prognosis. With status post myocardiac infarction, aldosterone antagonists are recommended even from stage I.
- Diuretics (thiazides, loop diuretics) are indicated in the presence of fluid retention and, in general, from stage III. In hypertension, thiazides are used regardless of the stage.
- Heart glycosides (digitalis) are used from stage III, and regardless of the stage in the presence of tachyarrhythmia with atrial fibrillation. Maintain low to normal glycoside levels. No influence on mortality has been proven for digitalis glycosides (DIG Study). The supplementary administration of digitalis has been proven effective, however (RADIANCE Study): Omitting digitalis increases the risk of decompensation and hospitalization!

Remember: Causes for a deterioration resp. Decompensation of a cardiac insufficiency often are, that guidelines fort he therapy are not followed or required drugs (i.e. diuretics) have been omitted.

3. Cardiac resynchronization therapy (CRT): By optimizing myocardial contraction processes via atrio-biventricular electrostimulation, pump function and prognosis can be improved (CARE-HF Study, among others). Possible combination with ICD (COMPANION Study).
   Ind.: Cardiac insufficiency NYHA Stage III - IV with EF ≤ 35%, preserved sinus rhythm and asynchronous action of both ventricles due to complete left bundle branch block. Only about 50% of CRT patients benefit from the therapy; therefore, correct patient selection is critical for success.
4. Implantable cardioverter defibrillator (ICD):
   a) Secondary prophylaxis with status post resuscitation due to ventricular flutter / fibrillation
   b) Primary prophylaxis:
   The prophylactic implantation of an ICD in patients with heart failure NYHA St. III-IV and EF ≤ 35%) can reduce overall mortality by up to 30% (MADIT II Study). - Devices with bioimpedance measurement can pre-warn of pulmonary oedema.

C) Heart transplantation (see further below)

Therapy of acute heart failure:

1. Causal therapy: e.g.
   - hypertensive crisis: lower blood pressure - myocardiac infarction: recanalization therapy (fibrinolysis, acute PTCA)
   - acute insufficiency or shunt defects: cardiac surgery
   - pericardial tamponade: pericardial drainage
   - bradycardic arrhythmia: possibly atropine, pacemaker therapy
   - tachycardic arrhythmia: possibly anti-arrhythmics, rate normalization, electrocardioversion

2. Symptomatic therapy of acute left heart failure:
- sitting position, sedation, O_2 administration - preload reduction: nitroglycerine + fast-acting loop diuretics (e.g. furosemide)
- possibly positive inotropic acting beta-receptor agonists: dobutamine and others (see section on myocardiac infarction)
- optimal control of blood pressure, central venous pressure, left ventricular filling pressure and cardiac output
- possibly mechanical support (haemofiltration, mechanical support systems, ventilation)

LOAD-REDUCTION THERAPY

1. ACE INHIBITORS

Ind.:Agents of choice from NYHA stage I
ACE inhibitors are the agents of choice since they improve the prognosis of chronic heart failure (e.g. CONSENSUS, SOLVD Study and others). Overall mortality reduced by about 25%. In post-infarction patients, they stop the unfavorable remodeling processes of the heart, thus preventing the progression of left heart failure in some patients (e.g. SOLVD, SAVE Study with ACE inhibitors).
At the start of therapy, severe drops in blood pressure may occur → start with the lowest dose and increase very slowly until the optimally tolerated + effective dose is achieved. The ATLAS Study with lisinopril showed that relatively high doses are most effective for reducing the load on the heart. On the other hand, the primary end-point of mortality is not more favorably influenced by a high dose than by a normal dose. Cardiac insufficiency improves slowly and often cannot be fully evaluated until after 1-2 months.

Note: The dose of the ACE inhibitors must not be increased further: 1. If hyperkalaemia occurs 2. If creatinine increases above the reference range (in a balanced water household) 3. In case of symptomatic hypotension!

ACE inhibitor dosing in mortality studies in chronic heart failure

Substance	First dose (mg/day)	Target dose (mg/day)	Study
Captopril	2 x 6.25	3 x 50	SAVE
Enalapril	1 x 2.5	2 x 10	SOLVD, CONSENSUS
Ramipril	1 x 1.25	1 x 10	AIREX
Trandolapril	1 x 1	1 x 4	TRACE
Lisinopril	1 x 2.5	1 x 20	ATLAS

(Additional details regarding effect, side effects and clinical: see section on hypertension)

2. ANGIOTENSIN II-RECEPTOR ANTAGONISTS= AT II BLOCKERS = SARTANS = AT1-ANTAGONISTS

Currently, losartan, candesartan and valsartan are approved for the therapy of heart failure. They reduce mortality in heart failure to a similar extent as ACE inhibitors (ELITE II Study for losartan, CHARM Study for candesartan, Val-HeFT Study for valsartan).

Ind.: Treatment alternatives in cases of contraindication or intolerance of ACE inhibitors

Doses of AT1-antagonists in chronic cardiac failure

AT1-antagonist	Initial dose (mg/d)	Target dose (mg/d)
Candesartan	1 x 4	32
Losartan	1 x 12,5	50 - 100
Valsartan	2 x 40	2 x 160

(For details on specific preparations, see the section on hypertension)

3. BETA-RECEPTOR BLOCKERS

Effect: Protection of the heart from toxic catecholamine effects, prevention of down regulation of beta-receptors, lowering of heart rate (optimal: 60-70/minute), anti-ischaemic effect, reduction of risk of sudden cardiac death, etc. In several studies, it was shown that patients with heart failure benefit from additional treatment with certain beta-blockers (without ISA): carvedilol, metoprolol, bisoprolol. In comparison to the basic triple therapy, mortality can be lowered by about 35% (e.g. COPERNICUS Study, MERIT- HF Study). In patients > 70y. Nebivolol also is licensed for therapy of cardiac failure (SENIORS Study)

Ind: Supplementary treatment of heart failure from stage II. In patients with hypertension or status post myocardiac infarction, beta blockers are used regardless of the stage.
Prerequisite: Stable chronic heart failure and complete basic therapy.

Side effects + clinical: See section on beta-blockers.

Dos: Beta-blockers (without ISA) must be used very carefully in cases of chronic heart failure since they may lead to decompensation! Always start with the lowest dose and monitor patients well, in-hospital if possible!

Dose of β-blocker in case of stable chronic systolic cardiac failure

β-blocker	Starting dose (mg/day)	Target dose (mg/day)
Bisoprolol	1 x 1,25	1 x 10
Carvedilol	1 x 3,125	2 x 25
Metoprolol(-succinate)	1 x 10	1 x 200
Nebivolol	1 x 1,25	1 x 10

Adjustment phase: double the dose about every 14 days, increase dose under medical monitoring only (weight checks!)

Complications:

- Deterioration of heart failure: slow down dose increases, optimize therapy with diuretics and cardiac glycosides, search for other causes
- Drop in blood pressure: slow down dose increases, search for other causes (too high a dose of diuretics, hyponatremia)
- Bradycardia: discontinue treatment only if haemodynamically significant bradycardia
- Deterioration of asthma bronchiale = contraindication for beta-blockers

4. NITRATES

Effect: Venous > arterial acting vasodilators (reduction of preload > reduction of afterload)

Nitroglycerin is the agent of choice for acute left insufficiency with pulmonary congestion (+ furosemide), especially in the presence of concomitant hypertension.
(For details regarding preparations, side effects + clinical: See section on CHD)

5. DIURETICS

Active principle: Thiazides and loop diuretics cause an increase in the excretion of NaCl and water ("saluretics"). Dietary NaCl restriction should be aimed for as an indispensable basic treatment.

Action in the presence of heart failure:

- Preferably reduction of preload with regression of pulmonary congestion and oedema
- Additional reduction of peripheral resistance and therefore after load

1. Thiazides and analogs:

Effect: Blocking of Na^+Cl^- co-transport in the near segment of the distal tubule, causing up to 15% of glomerular-filtered sodium to be excreted; potassium is also lost in this process. The individual substances are differentiated mainly by their duration of effect, which is 12-24 hours for hydrochlorothiazide and 48 hours or more for chlorothalidone. Thiazides also continue to work at a glomerular filtration rate < 30 ml/min, even if less effectively.

Generic name (examples)	Commercial preparation (e.g.)	Average oral daily dose in mg
a) Moderately long-acting saluretics (< 24 h)		
- Hydrochlorothiazide	Esidrix® HCT	12.5 - 25
- Xipamide	Aquaphor®	10 - 40
b) Long-acting saluretics (48 h or more)		
- Chlorothalidone	Hygroton®	25 - 50 (every other day)

2. Strong-acting "loop diuretics":

Effect: Blocking of the Na^+/K^+2Cl^+ carrier in the ascending limb of Henle's loop, causing up to 40% of the filtered sodium to be excreted.

The effect can be weakened in the course of treatment with loop diuretics due to a compensatory increase in reabsorption in the distal tubule. We then speak of diuretic resistance. Other causes of diuretic resistance are hyponatremia or treatment with NSARs.

Notes: In the presence of diuretic resistance while taking loop diuretics, do not continue to increase the dose; rather, combine loop diuretics with thiazide. This causes a sequential nephron blockade, thus causing diuresis to increase again. However, potassium and magnesium losses must be monitored and substituted as needed!

Furosemide is also diuretically effective at a glomerular filtration rate < 5 ml/min. After i.v. administration, diuresis starts after 10-20 minutes. All loop diuretics have a relatively short duration of effect (< 6 hours).

Generic name (examples)	Commercial preparation (e.g.)	Average oral daily dose in mg
Bumetanide	Burinex®	0.5 - 1.0
Etacrynic acid	Hydromedin®	50 - 150
Furosemide	Lasix®	20 - 80
Piretanide	Arelix®	3 - 6
Torasemide	Unat®	5 - 10

Furosemide, with which we have the most experience, has the widest therapeutic range. It also leads to direct venodilatation (reduction of preload), thus causing a reduction in pulmonary congestion even before the onset of the diuretic effect (single dose 20-40 mg i.v.).

3. Potassium-sparing diuretics:

Effect: Inhibition of Na^+ absorption and K^+ secretion in the collecting duct.

Because of a merely moderate diuretic effect, they have no role as monotherapeutic agents. Potassium-sparing diuretics are used in combination with thiazides and are contraindicated in the presence of renal insufficiency. If, in severe heart failure (NYHA III or IV), aldosterone antagonists must be combined with ACE-inhibitors or AT1-blockers, the creatinine clearance should be normal or only slightly reduced and potassium levels must be monitored.

► Aldosterone antagonists: spironolactone, eplerenone

Ind: Primary hyperaldosteronism (Conn syndrome), secondary hyperaldosteronism due to decompensated liver cirrhosis or hydropic heart failure (liver cirrhosis with ascites, heart failure with oedema)

As a supplement to the classic triple therapy (ACE-inhibitor, diuretic and digitalis), spironolactone can reduce mortality in patients with stage III - IV heart failure by about 30% (RALES Study). For this, a daily dose of 12.5 - 25 mg is often sufficient. Because of the danger of hyperkalemia, regular checks of serum potassium levels and creatinine should be performed.

The selective aldosterone antagonist eplerenone (Inspra®) (EPHESUS Study), which inhibits only the mineralocorticosteroid receptors but not the glucocorticoid receptors, acts in a similar manner. Hormonal side effects (such as gynaecomastia) are rarer than with spironolactone, but hyperkalemia is more common. Higher price! Dose: 25 mg/day

► (Aldosterone-independent) potassium-sparing diuretics:

amiloride, triamterene, which are too weak to be used as monotherapies, are used in combination with thiazides: e.g. hydrochlorothiazide + amiloride (or triamterene). When giving medications that can lead to hyperkalemia (ACE-inhibitors, aldosterone antagonists), potassium-sparing diuretics are contraindicated!

Dose: e.g. HCT 12.5 - 25 mg/day + 25 - 50 mg triamterene/day
or HCT 12.5 – 25 mg/day + 1.25 – 2.5 mg amiloride/day

Diuretics in heart failure:

In acute left heart failure with (threatening) pulmonary oedema, the quick i.v. administration of a loop diuretic (e.g. 40 mg furosemide) is indicated. In chronic heart failure with pulmonary congestion and/or oedema, diuretics are given orally in the lowest possible dose and combined with other agents against heart failure.

For long-term therapy, it is often enough to give thiazide intermittently every 2nd or 3rd day, in a single dose in the morning, so that rest at night is not disturbed by the onset of diuresis. Monotherapy with thiazides must be supplemented by K^+ substitution (high-potassium diet or oral administration of potassium). Potassium-sparing diuretics – which are contraindicated in renal insufficiency due to the danger of hyperkalemia – are well-suited for combination with thiazides for balancing their kaliuretic effect. If thiazides are not sufficiently effective, combination with loop diuretics is recommended.

Attention: Days of eating only apples and rice or drinking green leaf tea can also be used to induce mild diuresis through diet.

In the flushing out phase of oedema, strive for a slow loss of weight (maximum of 1 kg per day), weigh daily, perform regular tests of electrolytes + retention values and give concomitant thromboembolism prophylaxis (low-dose heparin) since the risk of thromboembolisms is great!

If salt intake is not restricted or non-steroidal anti-rheumatics (NSARs) are given, the effect of diuretics is reduced!

Recommendations in the case of therapy-refractory cardiac-related oedemas:

- Check the diagnosis (oedema of other genesis?)
- Check that the diuretics are being taken according to directions (compliance)
- Check concomitant medications (e.g. non-steroidal anti-inflammatories?)
- Check salt intake (determination of sodium in 24-hour urine sample)
- Adjust dose of distal-tubular diuretics or prescribe loop diuretics
- Increase dose of loop diuretics and/or try intravenous administration
- Combine diuretics (“sequential nephron blockade”)

SIDE EFFECTS	CONTRAINDICATIONS
▶ **Thiazides:**	
1. Serum electrolyte disorders: sodium, potassium (20%), magnesium ↓, possibly calcium ↑,	1. Severe renal / liver function disorder
2. Hypovolemia (possibly with increase in urea, creatinine), drop in blood pressure, increased tendancy for thrombosis, esp. in the flushing out phase of the oedema	2. Severe electrolyte disorders: - hypokalemia - hyponatremia - hypercalcemia
3. Metabolic disorders: glucose, uric acid, LDL-cholesterol and triglycerides ↑	3. Digitalis intoxication There is an increased risk in the presence of cardiac arrhythmias as well!
4. Activation of the renin-angiotensin-aldosterone system (result of hypovolemia) → increased action of ACE-inhibitors!	4. Sulfonamide allergy
	5. Pregnancy and lactation
5. Other side effects: Gastrointestinal discomfort, rarely allergic reaction and blood count changes (anaemia, leukocytopenia, thrombocytopenia), pancreatitis, etc.	History: Thiazides are not recommended for patients with diabetes mellitus and/or lipid metabolism disorders because these are metabolic disorders.
▶ **Loop diuretics:**	
Same as thiazides, except for hypocalcemia Furthermore: - nausea, vomiting (etacrynic acid) - reversible hearing loss (furosemide) - irreversible hearing loss (etacrynic acid) History: Hearing loss occurs esp. In cases of rapid i.v. administration at high doses.	Same as thiazides (except for hypercalcemia)
▶ **Aldosterone antagonists:**	
1. Hyperkalemia and hyponatremia	1. Renal insufficiency,
2. Gynaecomastia (10%), impotence, amenorrhea, bleeding between menstrual periods, breast tenderness, voice changes, hirsutism	2. Hyperkalemia, 3. Hyponatremia 4. Pregnancy and lactation
3. Gastrointestinal discomfort 4. Skin changes 5. Temporary confusion	5. Combination with ACE-inhibitors or AT1-blockers is relatively contraindicated if not combined with thiazides or loop diuretics (danger of hyperkalemia → potassium checks!)
History: Non-steroidal anti-inflammatory agents weaken the effect and increase the tendency towards hyperkalemia.	Caution with antikaliuretics in older patients with possibly reduced renal function (danger of hyperkalemia!)
▶ **Amiloride and triamterene:**	
1. Hyperkalemia and hyponatremia 2. Allergic reactions 3. Blood count changes (megaloblastic anaemia due to triamterene) 4. Gastrointestinal disorders	Same as aldosterone antagonists

Notes: Regular laboratory check-ups during diuretic therapy: sodium, potassium, calcium, creatinine, uric acid, cholesterol, glucose!

History: DD: hyponatraemia with heart failure:

Hyponatraemia with heart failure	Dilution hyponatremia	Loss hyponatremia
Serum sodium < 135 mmol/l	Sy.: oedema, haematocrit ↓ Th.: H_2O restriction, "water diuresis" (e.g. furosemide)	Sy.: No oedema. haematocrit ↑ Th.: Discontinuation of saluretics, NaCl (3-4 g/d)

CARDIAC GLYCOSIDES

Effect: Cardiac glycosides cause an increase in intracellular Na^+ concentration by an inhibition of Na^+/K^+-ATPase. The transmembrane Na^+ gradient reduced in this manner leads to an inhibition of the Na^+/Ca^{2+}-exchanger and then to an accumulation of Ca^{2+} inside the cell. This results in a more effective electromechanical coupling = positive inotropic effect. In the therapeutic effect range, the ion pumps (membrane Na-K-ATPase) are only partially inhibited (cardiac glycosides attached to 10 - 30% of the ATPase molecules), so that the intracellular K^+-/Na^+ ratio remains constant.

In the toxic range, the ion pumps are so strongly inhibited (cardiac glycosides attached to > 30% of ATPase molecules) that the intracellular Na^+ concentration rises and the K^+ concentration falls. This causes the membrane potential to fall and the frequency of spontaneous activities rises.

Cardiac glycosides have a narrow therapeutic range (= ratio of toxic range to therapeutic range) of 1.5 – 2.0.

The level of the toxic limit also depends on the electrolyte balance:

Ca^{2+} increases } digitalis effect (or sensitivity)
K^+ and Mg^{++} reduce }

Notes: 1. ***Never give calcium by i.v. to a patient taking digitalis!*** (danger of tachyarrhythmia, even ventricular fibrillation!).
2. By increasing serum levels of calcium and magnesium to high-normal levels, tolerance for digitalis is improved.

Four basic effects of cardiac glycosides:

1. Positive inotropic = increase in contractility of the heart
2. Positive bathmotropic = increase in excitability of the heart
3. Negative chronotropic = slowing of the heart rate (vagus effect)
4. Negative dromotropic = slowing of conduction speed

Note: Cardiac glycosides lower the heart rate at rest. However, the heart rate during exertion is not sufficiently reduced. This is best achieved with beta-blockers.

No influence on mortality has been proven so far for digitalis glycosides (DIG Study).

Pharmacokinetics:

- Resorption rate: See table
- Metabolism and excretion / selection of cardiac glycosides in the presence of renal insufficiency:
  - Digoxin is predominantly excreted through the kidneys; therefore, the dose must be reduced accordingly in cases of renal function limitation. This is a disadvantage in comparison to digitoxin.
  - Digitoxin, which is partially metabolized into digoxin, is excreted 60% renally and 40% through the liver and intestine. In this case, 25% is subject to enterohepatic circulation with recirculation between the intestine and liver. In the presence of renal insufficiency, the renal excretion of digitoxin is indeed reduced, but then more is excreted through the intestine by way of compensation. Therefore, digitoxin can be given in normal doses in the presence of renal insufficiency (0.07 mg/d; possibly with a pause one day per week).
- Half-life and decay rate: In persons with healthy livers and kidneys, the half-life for digoxin is about 40 hours, and for digitoxin 6-8 days. The glycoside is eliminated from the body after about 5 half-lives. Decay rate = daily loss of effect of the glycoside in %.
- Effective dose: The effective dose is that dose (in mg) of a cardiac glycoside contained in the body – either resorbed or given parenterally – that causes an optimal (maximum) inotropic effect.

Side effects: Symptoms of a digitalis intoxication (see section on that topic) may also occur in the presence of a "therapeutic" plasma level of the digitalis glycoside, if there is a reduced tolerance for glycosides caused by certain illnesses (see further below).

Interactions:

- Reduction of digoxin clearance (with possible necessity of dose reduction) caused by:
  Calcium antagonists, levodopa, amiodarone, tetracyclines, clarithromycin, etc.
- Increased risk of cardiac arrhythmias:
  - In the case of concomitant therapy with sympathomimetics, reserpine, theophylline, thyroid hormones, calcium
  - In the case of concomitant therapy with pharmaceuticals that can lead to hypokalemia (e.g. diuretics, laxatives, corticosteroids, etc.)
- Increased risk of bradycardia and AV (SA) blockades during concomitant therapy with beta-blockers

Conditions of reduced glycoside tolerance with increased risk of side effects or symptoms of intoxication:

- Hypokalemia and hypomagnesemia, alkalosis, hypercalcemia
- Hypoxemia
- Cor pulmonale
- Myocarditis
- Renal insufficiency (accumulation of digoxin)
- Mitral stenosis (danger of pulmonary oedema)
- Concomitant treatment with pharmaceuticals that exhibit adverse interactions with cardiac glycosides

- Advanced age (= reduced creatinine clearance and reduced muscle mass = reduced distribution volume for the glycoside)
- Hypothyroidism (delayed excretion of cardiac glycosides)

Ind: 1. Chronic systolic left heart failure from NYHA stage III
2. Tachyarrhythmia with atrial fibrillation

History: Cardiac glycosides are not indicated in the presence of cor pulmonale, ventricular diastolic dysfunction, cardiac failure caused by hyperthyroidism, amyloidosis

Dos:

Glycoside	PPB (%)	Enteral resorption	Decay rate	Daily oral maintenance dose	EHL
Digoxin	20 - 30	70%	average 20% (1/5)	0.25 mg	40 h
Digitoxin	> 95	90 - 100%	slow 7% (1/14)	0.07 mg*)	6 - 8 d

PPB = plasma protein binding
EHL = elimination half-life

*) Poss. 1 day break per week

	Effective dose	Therapeutic serum glycoside level (ng/ml)
Digoxin	0.8 – 1.2 mg	optimal 0.5 – 0.8 ng/ml *)
Digitoxin		10 - 20 ng/ml

*) Result from the "Digitalis Investigation Group"

- Moderately fast saturation: achievement of effective dose within 3-5 days
  e.g. Digitoxin: As long as there is no resorption disorder (e.g. cardiac decompensation or interaction with other drugs – see below), the dosage regimens for i.v. and oral therapy do not differ significantly:
  3 days long 0.3 mg/day, after that a maintenance dose of 0.07 mg/day

2. Slow saturation: In this case, the patient is treated with the maintenance dose from the beginning, meaning that the effective dose is not achieved until after about 5 half-lives:
   Digoxin with a t½ of about 1.6 days → Effective dose achieved in 8 days
   Digitoxin with a t½ of 6 days → Effective dose achieved in 1 month

Since the effective dose of cardiac glycosides shows individual fluctuations and the therapeutic range is narrow, the optimal dose must be determined through careful clinical observation with special attention paid to symptoms of intolerance and monitoring of serum glycoside concentration. In the case of advanced age and/or below-average body weight, the dose must be reduced (e.g. schedule a digitalis pause 1x/week).

CI:
- Digitalis intoxication
- Bradycardic heart arrhythmias, sick sinus syndrome, carotid sinus syndrome, SA/AV block > 1° (digitalis therapy not possible until after the implantation of a cardiac pacemaker)
- Ventricular tachycardia
- WPW syndrome
- Hypercalcemia
- Hypokalemia
- Recent myocardiac infarction
- Thoracic aortic aneurysm
- Hypertrophic obstructive cardiomyopathy
- Chronic constrictive pericarditis ("armored heart")
- Immediately before and after cardioversion
- Non-occlusive ischaemia of the mesenteric arteries

DIGITALIS SIDE EFFECTS AND INTOXICATION [T46.0]

Side effects and symptoms of intoxication may occur under conditions of decreased glycoside tolerance within the therapeutic range (or beforehand).

Causes: of digitalis intoxication:
1. Presence of contraindications for digitalis or conditions of decreased glycoside tolerance (usually limited renal function and/or drug interactions)
2. Dosage errors
3. Suicidal or criminal intent

Clinical:
1. Gastrointestinal disorders such as nausea (vagus effect), diarrhoea
2. Central nervous and visual disorders (colour vision, e.g. yellowness)
3. Disorders of the heart:

Arrhythmias: e.g.:

- Excitation disorders, e.g.:
  - sinus bradycardia
  - paroxysmal atrial tachycardia, often with 2 : 1 AV block
  - AV-node tachycardia
  - extrasystole, bigeminus
- Conduction disorders, e.g.: AV blocks (especially of the Wenckebach type)
- ECG changes may occur even within the therapeutic dose range: trough-like ST segment depression, T-wave flattening/negative T-waves, shortening of the QT interval (corrected for heart rate), PQ prolongation

Di.: ▶ History + clinical
▶ Serum glycoside level in digitalis intoxication:
Digoxin > 2.0 ng/ml
Digitoxin > 30.0 ng/ml

Th.: 1. Stop administration of digitalis
2. Promote elimination of digitalis:
   - In cases of suicidal or accidental poisoning, the usual detoxification measures (gastric lavage, defecation). In the case of digitoxin intoxication, additional administration of ion exchanger resins (colestyramine or colestipol). In case of a severe digitalis intoxication additionally haemoperfusion (not effective with digoxin)
   - Antidote treatment: Digitalis antitoxin (Fab antibody fragments), e.g. digitalis antidote BM®
     Dos: 80 mg digitalis antidote binds 1 mg digoxin or digitoxin in the body and lowers digoxin levels by 1 ng/ml (digitoxin levels by 10 ng/ml). The success of the therapy can be recognized by the regression of the cardiac arrhythmias and a QT normalization.
     Side effects: Since this is a preparation made from sheep serum, there is a danger of anaphylactic reaction with repeated use (→ conjunctival test).
3. Raise serum potassium levels to high-normal values (no more than 20 mmol K^+/h parenterally)
   The administration of potassium is contraindicated in the presence of AV block or renal insufficiency (worsening of AV block). No administration of potassium in cases of severe digitalis poisoning since this may cause complicating hyperkalemia!
4. Symptomatic treatment
   For bradycardic arrhythmias, trial with atropine, otherwise temporary pacemaker.

OTHER POSITIVE INOTROPIC SUBSTANCES

Ind: Only in intensive drug therapy of acute heart failure.

- Beta-receptor agonists (sympathomimetic agents): Dobutamine
  Effect: Activation of adenylate cyclase → Increase in intracellular concentration of c-AMP and calcium.
  In the early phase of heart failure, the increased activity of the sympathetic nervous system represents an important compensation mechanism. With increasing severity of heart failure, however, the elevated catecholamine levels lead to a progressive reduction in the density of myocardial beta-receptors (down regulation). The additional administration of exogenous catecholamines therefore leads to a temporary improvement in haemodynamics (for details, see the section on myocardiac infarction).
- Calcium sensitizers: Levosimendan (LIDO Study)

THERAPEUTIC MEASURES THAT CAN BRIDGE THE WAITING TIME UP TO TRANSPLANTATION

- Haemofiltration (e.g. venovenous): Effective reduction of preload (removal of fluid) if diuretics are insufficient.
- Mechanical support systems (assist devices):
  1. Completely implantable left ventricular pump: Left ventricular assist system (LVAS) or device (LVAD).
  2. Extracorporal blood pumps are only suitable for use in intensive care units.
  In the presence of reversible left heart failure (e.g. myocarditis), “assist devices” can be explanted following cardiac recompensation.
  Compl.: Infections, bleeding, haemolytic anaemia, thromboembolism
- Surgical elimination of a relative mitral insufficiency of the dilated left ventricle (anuloplasty) to improve pump function
- Passive cardiomyoplasty (in clinical trial): Reduction of left ventricular end-diastolic diameter via elastic netting stretched around the ventricle: cardiac support device (CorCap)
- Surgical reconstruction of the ventricle (in clinical trial)

HEART TRANSPLANTATION

Syn: HTX

Ind: Based on transplantation laws of the individual countries of the EC.
Terminal heart failure that can no longer be treated conservatively: Cardiac insufficiency in NYHA stage IV with an ejection fraction < 20%. Ergospirometry is helpful in assessing the urgency of a HTX: Patients with a maximum O_2 uptake < 10 ml/kg/min have a 1 year mortality rate of 77%.
Most transplant patients suffer from cardiomyopathies, CHD or heart valve diseases.

CL.:
- Severe pulmonary hypertension (pulmonary arterial resistance > 48 Pa · ml^{-1} · sec) → consider simultaneous heart-lung transplantation (HLTX)
- Active infectious diseases, malignancies, current ulcer disease
- Hepatic / renal failure → consider combined heart-kidney or heart-liver transplantation
- Significant peripheral / cerebrovascular arterial occlusive disease.
- Systemic diseases with unfavorable prognosis
- Alcohol or drug dependence, acute psychological diseases, lack of cooperation, age limit of about 70 years (maybe higher)

Process: Transplantation of the heart of a brain-dead person + triple immunosuppressive therapy (Cyclosporine A, Mycophenolate Mofetil, corticosteroids).Other immunosuppressive agents are also used long-term (e.g. Imurek, Tacrolimus). The most suitable donor is determined by taking compatibility criteria (see below) and priority into consideration.
- Orthotopic heart transplantation: standard method, removal of patient heart and implantation of donor heart
- Heterotopic heart transplantation: exceptional procedure; parallel connection of patient and donor heart

Prerequisites:

1. Documentation of brain death of the donor by 2 independent neurologists from the transplantation team or authorized physicians: coma, loss of cranial nerve reflexes and spontaneous respiration, flat-line in the EEG for more than 30 minutes, perfusion deficit in the brain (transcranial Doppler, cerebral angiogram), lack of acoustically evoked brain stem potentials.
2. Donor and recipient must have the same ABO blood group (see section on kidney transplantation). Cytotoxic antibodies to donor lymphocytes in the recipient's serum must be absent (negative lymphocyte crossmatch test).
3. Similar body size (± 10%) and weight (± 25%) between donor and recipient.
4. No contraindications: See above

Compl.:

A) Surgical complications

B) Non-surgical complications:

1. Rejection reactions:

a) Acute rejection

Non-invasive diagnostics:
- ECG:
  - 12-lead surface ECG: reduction of QRS-amplitude (voltage) ≥ 25%, change in QRS-axis, tachycardia, arrhythmia, occurrence of bundle branch blocks
  - Significantly amplified ECG signal: typical change in the frequency spectrum of the QRS complex
  - Intramyocardial ECG (= IMECG): With regular telemetric monitoring by telephone modem. A reduction in the voltage of the QRS complex and an increase in the heart rate are evidence of a rejection reaction.
- Echocardiography: Rapid increase in thickness of the posterior wall and septum of the left ventricle, reduced systolic and diastolic motility of the posterior wall (diastolic relaxation time ↓) and septum, possible AV valve regurgitation with reflux in the colour Doppler, reduction of fractional shortening, etc.
- MRI
- Immunoscintigraphy using marked antimyosin antibodies
- Laboratory tests:
  - Cytoimmunological screening: Rejection action: Appearance of activated lymphocytes and lymphoblasts in the blood
  - Gene expression profiling (GEP) test
  - Increase in CK-MB and troponin I/T

Invasive diagnostics:

Myocardial biopsy with histology: grading from 0 to 4
- Mild rejection reaction: lymphocytic cell infiltration without necrosis of the cardiac muscle cells
- Moderately severe rejection reaction: also beginning of necrosis of the cardiac muscle cells
- Severe rejection reaction: very high amount of lymphocytic cell infiltration, pronounced necrosis of the heart muscle cells, oedema

Th.: Glucocorticosteroid pulse therapy. If this is not sufficiently effective: antithymocyte globulin or monoclonal antibodies against T-lymphocytes

b) Chronic rejection

This manifests especially in the coronary vessels as transplant vasculopathy (TVP). This primarily affects the final coronary segment (while coronary arteriosclerosis primarily affects the main epicardial branches).

Frequency up to 10% per year and therefore the main cause of death over the long-term following HTX. As a result of surgical denervation, there is no angina pectoris pain! The most sensitive diagnostic: intravascular ultrasound!

2. Side effects from immunosuppressive therapy:
   - Infections: sepsis, pneumonia – most frequent pathogen: cytomegalovirus (Th.: Ganciclovir + CMV immunoglobulins); also HSV, VZV and fungi (aspergillus, candida)
   - Medication side effects: e.g. high blood pressure from cyclosporine A, osteoporosis from corticosteroids
   - Later appearance of malignancies (risk 5 - 10%) and post-transplantation lymphoproliferative diseases = PTLD (see section on that topic)

Prog: The prognosis of untreated manifest heart failure is poor: 1-year mortality rate by NYHA stage: I: < 10%; II about 15%, III: about 25%, IV: about 50%. The prognosis can be improved by about 50% under conservative, guideline-compliant treatment!
10-year survival rate following heart transplantation up to 70%, with a mortality rate of about 3%/year.
With chronic heart failure, about 50% of patients die from sudden cardiac death due to ventricular fibrillation.

CARDIOMYOPATHIES

Def.: WHO/ISFC-1995: Suggested revisions 2006-2008 are under discussion between American and European research groups, particularly regarding the significance of genetic investigations. We follow the European definition from 1995: Cardiomyopathies (CM) are defined as all diseases of the heart muscle involving a cardiac function disorder.

5 main forms:

Name	Abbreviation	Cardinal characteristic
1. Dilated cardiomyopathy	DCM	Systolic pump disorder of the dilated ventricle
2. Hypertrophic cardio-myopathy with and without obstruction	HCM	Diastolic distensibility disorder of the thickened heart muscle
3. Restrictive cardiomyopathy	RCM	Diastolic distensibility disorder, also with normal myocardial thickness, e.g. as a result of endomyocardial fibrosis
4. Arrhythmogenic right ventricular cardiomyopathy	ARVCM	Predominantly right ventricular combined pump failure with ventricular tachycardia
5. Non-classifiable cardiomyopathy	NCCM	Collection of different disorders, e.g. "isolated LV non-compaction" (see below)

Normal DCM HCM

In addition to the 5 main forms of CM, the WHO classification defines specific cardiomyopathies that are classified according to the underlying etiology:

1. Inflammatory CM [I42.0]:
   CM due to an autoimmune reaction (without pathogen persistence) or a "chronic myocarditis" with pathogen/virus persistence
   Immunohistological diagnosis criteria: > 14 lymphocytes or macrophages/mm^3 of myocardial tissue; possibly detection of virus DNA/RNA; possibly detection of autoimmune phenomena
   Aet.:- Microbial infection: Viruses (e.g. Coxsackie B), bacteria (e.g. Borrelia burgdorferi), protozoa (e.g. Trypanosoma cruzi = Chagas disease)
   - Autoimmune reactive (possibly induced by a viral infection)
   Additional details: See section on myocarditis
2. Ischaemic CM due to CHD / myocardiac infarction
3. Hypertensive CM due to many years of high blood pressure
4. Valvular CM due to defects
5. Metabolic CM
   -Diseases of the endocrine system, e.g. diabetes mellitus (diabetic CM), hyperthyroidism or hypothyroidism, phaeochromocytoma, acromegaly

- Storage diseases, e.g. glycogen storage disease, haemochromatosis, Fabry disease
- Deficiency diseases, e.g. selenium deficiency, kwashiorkor, beri-beri
- Cardiomyopathies due to systemic diseases (rheumatoid arthritis, collagenosis, etc.
- Cardiomyopathies due to muscular dystrophy
- Cardiomyopathies due to neuromuscular diseases

6. Toxic cardiomyopathies are caused primarily by alcohol and cardiotoxic medications, e.g. phenothiazines, tricyclic antidepressants, clozapine, lithium carbonate, doxorubicin and others, anthracyclines, cocaine consumption, etc. Toxic CM due to alcohol is relatively frequent. Occasionally, patients also suffer from toxic myopathies and arrhythmias (e.g. atrial fibrillation) due to alcohol after drinking excessive alcohol ("Holiday Heart Syndrome").
7. Pregnancy CM manifest in the peripartal phase from 1 month before to 5 months after birth (there is a danger of left heart failure with subsequent pregnancies → advise the patient to not become pregnant again!).
8. Stress cardiomyopathy [I42.8]
   - Syn.: Tako-Tsubo CM, transient left ventricular apical ballooning syndrome, "broken heart" syndrome
   - Def.: Acute, reversible left ventricular dysfunction with reduced EF and apical movement disorder (apical ballooning) in the presence of normal coronary arteries – triggered by emotional or physical stress.
   - Ep.: Relatively rare. About 2% of all acute coronary syndromes; 90% of all patients are female; the average age is > 60 years.
   - Aet.: Unknown; coronary spasms and catecholamine-associated microvascular dysfunction are discussed. There is usually a preceding psychological stress situation.
   - CL.: Chest pain, possible dyspnoea, reduction in capacity, syncope, possible third heart sound
   - ECG: ST segment elevation similar to infarction (without typical localization) and changes in the T-segments
   - Echo (MRI): Apical akinesis and basal normo- to hyperkinesis ("ballooning") without vascular correlation, reduced EF
   - Coronary angiography: Normal coronary arteries, "ballooning" in the levocardiogram, EF ↓
   - Laboratory tests: Usually, mildly increased troponin and CK (MB)
   - DD: Acute coronary syndrome as a result of CHD/critical coronary stenosis; pheochromocytoma, HOCM, and others
   - Di.: Medical history, ECG, echo (MRI), laboratory tests, normal coronary angiography
   - Th.: Symptomatic therapy of heart failure; watch catecholamines!
   - Prg.: Good – if the acute phase (~1 week) has been survived, normalization of the EF. Mortality 3%. Risk of recurrence about 10%.
9. Tachycardia-CM: Chronic tachycardia can lead to progredient left ventricular failure.

Dilated cardiomyopathies (DCM) [I42.0]

Syn.: Congestive Cardiomyopathy

Dilated cardiomyopathies (DCM) are hemodynamically defined as systolic pump failures with cardiomegaly and reduced ejection fraction; there is also impairment of the diastolic function (delayed, incomplete relaxation of the myocardium and increased rigidity). Pathological consequences are interstitial fibrosis and structural alterations of the extracellular matrix, subsequently resulting in relaxation disorders. In some cases, the cause is unknown (primary or idiopathic DCM); the remaining cases are the result / final state of various diseases or toxins (secondary or specific DCM).

Ep.: Most frequently idiopathic CM, incidence 6/100,000/year; prevalence about 36/100,000; m : f = 2 : 1

Genetics: Familial clustering in 20% of cases. Various hereditary transmissions and genetic defects are known:
- X-chromosome recessive inherited DCM due to mutations of the dystrophy gene (Duchenne's progressive muscular dystrophy)
- Autosomal dominant inherited DCM with conduction disorder and sick sinus syndrome (15 different gene loci are known, 6 genetic defects have been identified)
- Autosomal-recessive inherited DCM due to mutation of the genes for fatty acid oxidation
- DCM due to mutations of the mitochondrial DNA
- So-called "non-compaction CM" as a malformation of the LV myocardium with persistence of the embryonic network; phaenotype frequently appears as DCM in its later course.

Aet.:
1. Idiopathic (unknown causes): In about 40% of cases
2. Viral infections: In about 60% of cases (= Inflammatory cardiomyopathy = DCMi): Enteroviruses (e.g. Coxsackie virus B), adenoviruses, parvovirus B19, herpes viruses, EBV, CMV, HCV and others.
   In some cases, the virus-induced immune response may be directed, through molecular mimicry, against the body's own heart muscle proteins. With the formation of a post-viral autoimmunity, the disease becomes independent and persists.
3. Alcohol consumption / abuse and pregnancy can be trigger mechanisms of DCM (see definition of CM).

CL.:
- Progressive left heart failure with exertional dyspnoea, later global heart failure
- Arrhythmias (especially of the ventricular type)

Compl.: Arterial and pulmonary embolisms (resulting from cardiac thrombus formation), ventricular tachycardia, sudden cardiac death

Lab.: Specific findings are rare, sometimes auto-antibodies against beta1-adrenoreceptor can be found. Determination of BNP levels ("brain natriuretic peptide") as a meaningful heart failure parameter.

X-ray: Cardiomegaly, in advance disease: pulmonary congestion

Echo: Dilatation of both ventricles (with relative mitral regurgitation of the left atrium). Reduced movement amplitude (hypokinesis) of the ventricular wall due to reduction of the systolic inward movement (in ischaemic DCM, regional wall movement disorders). As an index for contractility, the systolic shortening fraction (expressed as a percent) is reduced < 25%; this correlates approximately with the angiographically measured reduction in ejection fraction.
Often, there are thrombi in the ventricle and/or atrium (the latter by TEE)

MRI: Anatomy + function of heart and valves, sometimes detection of intravital fibrosis (Gadolinium-enhanced MRI: late enhancement, located in the mid areas of the wall or subepicardial (unlike ischaemic scars which are usually subendocardial)

DD: Exclude any specific (secondary) CM (as above)

Invasive diagnostics: Exclusion of ischaemic CM is absolutely necessary, consider biopsy of myocardium + histology / immunohistology / viral diagnostics / auto-antibodies / PA and PC pressure, LVEDP

Di.: clinical – echocardiography – myocardial biopsy – exclusion of known causes

Th.: 1. General measures:
Elimination of cardiotoxic agents (alcohol, cardiotoxic medications) Physical rest
2. Treat any underlying disease, in the context of controlled studies, if at all possible:
- Attempt virus elimination with interferon in cases of proven viral genesis
- Immunosuppressive therapy or immune adsorption in cases of autoimmune genesis (see also the section on myocarditis)

3. Guideline-compliant therapy of heart failure (see section on that topic)
4. Thromboembolism prophylaxis with anticoagulants in cases of atrial fibrillation or enhanced risk of intraventricular thrombi
5. ICD implantation in cases of increased threat from ventricular fibrillation
6. In terminal heart failure, trial of load removal from the heart via a temporary mechanical heart replacement (left ventricular assist device = LVAD).
7. Last resort: heart transplantation

Prog: Depending on the degree of heart failure (NYHA class: ≥ III = bad), the ejection rate (Ejection fraction < 20% = bad) and the diastolic filling characteristic (restrictive = bad) of the left ventricle
10-year survival rate 10 – 20% with a mortality rate of up to 10%/year

Hypertrophic cardiomyopathy (HCM) [I42.2]

Def.: Idiopathic hypertrophy of the left ventricle or a left ventricular hypertrophy exceeding the magnitude of a possible concomitant increase in afterload, especially in the septal region (asymmetrical septum hypertrophy), with or without obstruction of the left ventricular outflow tract:
- Hypertrophic non-obstructive cardiomyopathy (HNCM) [I42.2]: ¾ of cases.
- Hypertrophic obstructive cardiomyopathy (HOCM [I42.1]): ¼ of cases.
  Syn: Idiopathic hypertrophic subaortic stenosis (IHSS)

Ep.: Incidence: 19/100,000/year; prevalence: 200/100,000. HCM (mostly non-obstructive, which cannot be detected in auscultation) is one of the most frequent causes of sudden cardiac death in young athletes! We used to think that HNCM was the most frequent form. But routine exercise tests have revealed, that in fact just 1/3 cases of HCM are 'non-obstructive'. Apart from the known 20-30% who already show obstruction at rest, there are another 30-40% showing exercise induced obstruction. Hence examinations under exercise are compulsory to make a decision regarding the subtype (HNCM vs. HOCM)!

Aet.: In HCM, 50% of cases are familial of autosomal-dominant inheritance with incomplete penetrance. More than 10 gene loci (see table) are currently known or are suspected of being responsible for HCM. Numerous mutations within the gene loci have been described, and the tendency is increasing. About 2/3 of analyzed disease cases, however, are distributed between the 3 most frequently occurring genes for MYH7, MYBPC3 and TNNT2 (see below). No conclusive genotype-phenotype correlation currently stands out.

Gene product	Symbol	Chromosome	Approximate % of cases
Beta-myosin heavy chain	MYH7	14q12	30 - 35%
Myosin-binding protein C	MYBPC3	11p11.2	20 - 30%
Troponin T	TNNT2	1q32	10 - 15%
Alpha-tropomyosin	TPM1	15q22.1	< 5%
Troponin I	TNNI3	19q13.4	< 5%
Myosin light chain (essential chain)	MYL3	3p21	< 1%
" " (regulatory chain)	MYL2	12q24.3	< 1%
Actin	ACTC	15q14	< 0.5%
Titin	TTN	2q24.3	< 0.5%
Alpha-myosin heavy chain	MYH6	14q12	< 0.5%

Prg. : 1. End-systolic narrowing of the left ventricular outflow tract (due to asymmetrical septal hypertrophy and mitral valve displaced in the anterior direction) with intraventricular pressure gradients and mitral regurgitation due to HOCM.
2. Impaired diastolic function with reduced diastolic distensibility of the ventricle (diastolic stiffness). In this case, intracellular calcium accumulation and interstitial fibrosis play a role.

The end-systolic (dynamic) obstruction of the left ventricular outflow tract is increased by:
- Increase in contractility (pharmacologically with positive inotropic substances such as digitalis or sympathomimetics)
- Reduction of preload and afterload (pharmacologically, e.g. with nitrates, ACE and angiotensin inhibitors, fluid restriction, Valsalva maneuver)

CL.: Patients are frequently symptom-free (especially in the case of HNCM, which cannot be heard on auscultation, diagnosis is often made by accidental finding).
Symptoms can be the following: dyspnoea, attacks of angina pectoris, higher-grade ventricular arrhythmias (even ventricular tachycardia with vertigo), syncope and cases of sudden death.

Ausc: In HOCM, late-systolic crescendo-decrescendo murmur (punctum maximum over left edge of sternum), increased by physical exercise or Valsalva maneuvre, often 4th heart sound (due to atrial overload).

ECG: Signs of left hypertrophy, pattern of pseudoinfarction with deep Q-spikes and negative T-waves left precordial (result of septal hypertrophy), possibly left anterior hemiblock (25%), ventricular arrhythmia, prolongation of QT interval (40%).

Echocardiography: Asymmetrical septal hypertrophy or hypertrophy of the entire myocardium of the left ventricle with hourglass-shaped narrowing of the left ventricular outflow tract (LVOT); ratio between septum thickness and left ventricular posterior wall > 1.6 : 1. Thickness of the septum > 13 mm. In HOCM, the anterior mitral leaflet bulges against the septum during systole (SAM = systolic anterior motion), systolically increased narrowing of the left ventricular outflow tract with mesosystolic, premature aortic valve closure. Late systolic flow profile like a "sabre sheath" (Doppler) with narrowing of the LVOT. Determination of the late systolic pressure gradient (also increased after an extrasystole).

MRI: Pressure gradient, anatomy + function of the heart, lately also detection of fibrosis (contrast)

Invasive diagnostics (left cardiac catheterization), indicated when echo findings are not sufficient, for diagnosis (gradient measurement). In HOCM: Septal branch anatomy suitable for possible ablation? Co-existent CHD? LVEDP as marker of diastolic function impairment.

Myocardial biopsy: Hypertrophy and structural loss ("disarray") of myocytes and myofibrils, interstitial fibrosis, increase in number of mitochondria + widening of Z-lines, thickening of intima in intramural coronary arteries. As a rule, can be dispensed with in HOCM, but widely indicated in HNCM since 2-5% of patients have infiltrative CM / storage disease (see below).

DD: 1. Secondary hypertrophy of the left ventricle as a result of pressure load (e.g. high blood pressure, aortic stenosis)
2. Membranous or fibromuscular subvalvular aortic stenosis (often with concomitant aortic valve regurgitation)
3. Storage diseases (e.g. cardiac Fabry disease, amyloidosis). Suspect findings constellation for this: wall hypertrophy in the echo + low voltage in the ECG!

Di.: (Family) history, clinical, ECG, echocardiography, invasive diagnostics – family diagnostics

Th.: • Conservative:
- Examination of family for possible additional cases of the disease
- Avoid heavy physical loads (danger of sudden cardiac death!)
- Positive inotropic substances (digitalis, sympathomimetics), strong afterload reducers and nitrates are contraindicated in HOCM, which lead to an increase in the systolic stenosis.

- Administration of calcium antagonists of the verapamil type or beta blockers (but not both!)
- If atrial fibrillation occurs: anticoagulant therapy
- In HOCM, endocarditis prophylaxis
- ICD: Risk factors indicating primary prophylaxis:
    - LV wall thickness > 30 mm,
    - VT in the 24h-ECG,
    - recurring syncope,
    - insufficient increase in blood pressure during stress test and
    - cases of sudden cardiac death in the family

• Interventional therapy:
Percutaneous transluminal septal myocardial ablation (PTSMA) = transcoronary ablation of the septal hypertrophy (TASH): Occlusion of a septal branch of the LCA and triggering of a localized necrosis of the septal myocardium via an alcohol injection that is as precise as possible; side effects: Trifascicular block in approximately < 10 (-25)% with the necessity of pacemaker therapy; success rate > 90%; mortality < 2%.

History: DDD pacemaker therapy has not proven especially good.

• Transaortic subvalvular myectomy (TSM) when all other therapy fails: Success rate > 90%; mortality < 2%.

• Heart transplantation in patients with a dilatative course (NYHA stage III and IV)

Prg: Annual mortality rate without therapy in adults averages 1%, in severely symptomatic patients about 2.5%, children/adolescents up to 6%. Most cases of death result from ventricular arrhythmias. The risk of sudden death does not correlate with the severity of the symptoms or severity of a pressure gradient. Especially at risk are young male patients with a family history of sudden cardiac death as well as troponin T-mutation.

RESTRICTIVE CARDIOMYOPATHY (RCM) [I42.5]

Def.: Very rare disease of unknown aetiology with reduction of diastolic distensibility, usually of the left ventricle. However, the right ventricle can also be affected. Familial clustering also occurs. In early stages, often "unexplained" heart failure symptoms with large atria and (largely) maintained ventricular systolic function (differentiated from DCM) and normal or only slightly thickened walls (differentiated from HCM). The endocardium is thickened and covered with thrombi in the advanced stage (→ embolisms), increasing ventricular diastolic function impairment and development of therapy-resistant right heart failure with inflow congestion before the right heart.

1. Myocardial forms of RCM
    • Non-infiltrative RCM:
        - Idiopathic RCM
        - Familial RCM
        - RCM due to scleroderma
    • Infiltrative RCM: e.g. amyloidosis, sarcoidosis
    • RCM due to storage diseases: e.g. haemochromatosis, Fabry disease
2. Endomyocardial forms of RCM: e.g.
    • Endomyocardial fibrosis (Africa)
    • Hypereosinophilia (Löffler's endocarditis)
    • Carcinoid (endocardial fibrosis, especially of the right heart (Hedinger syndrome)

DD: • Constrictive pericarditis (CP): In both diseases, the x-ray often reveals a normal heart size. Analysis of the transmitral inflow profile (E/A-wave, deceleration time) and tissue Doppler analysis for assessing diastolic function are the two most important parts of the ECHO.
RCM: Protodiastolic speed of the mitral ring's E' (pronounced "E prime"): < 8 cm/s
CP: Protodiastolic speed of the mitral ring's E' > 8 cm/s:
Pericardial effusion, apical thrombi and increased echogenicity ("granular sparkling") indicate RCM. Pericardial calcifications and abnormal septal movement ("septal notch") indicate CP.
In CP, there are often calcifications and pericardial thickening (MRI, CT) as well as a typical diastolic pressure equalization in all chambers of the heart and normal respiratory variance in the pressure values; both signs are absent in RCM.
• Storage diseases (amyloidosis, haemochromatosis)

Di.: Echo with Doppler (enlarged atria with ventricles of normal size and nearly normal systolic contraction) - X-ray/CT/MRI - Invasive diagnostics with simultaneous RV/LV pressure measurement and endomyocardial biopsy

Th.: • Treatment of any underlying disease
• Early treatment of the heart failure with diuretics (no digitalis)
Heart rate monitoring with the objective of the longest possible duration of the diastole
• Thromboembolism prophylaxis
• In terminal heart failure: heart transplantation

Prg: Without heart transplantation: poor

ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY [I42.8]

Syn: Arrhythmogenic right ventricular dysplasia cardiomyopathy (ARVD, ARVCM or ARVC); right ventricular dysplasia

Def.: Cardiomyopathy with fibrolipomatous degeneration of the right ventricular myocardium and right ventricular dilatation

Ep.: 10-20% of all cases of sudden cardiac death in young men (including athletes) are the result of ARVCM. The disease is relatively rare (1: 5,000); m : f = 2 : 1

Aet.: Unknown; in 40% there is a positive family history with cases of sudden cardiac death; 9 gene mutations have been found, e.g. for plakophilin-2, desmoplakin, plakoglobin (Naxos disease), ryanodine receptor 2

Cl.: Usually the disease becomes symptomatic around the age of 30. Syncope, ventricular tachycardia (LBBB morphology in the ECG) or sudden cardiac death, often triggered by physical exertion (athletes!); less frequent: heart failure

ECG: In about 10% of cases, there is evidence of an epsilon wave at the end of the broadened QRS complex (V1-3); this corresponds to a late potential in the signal-averaged ECG. Ratio of the QRS spreads in V1-3/V4-6 ≥ 1.2, possibly negative T-waves, possibly right bundle branch block

Echo: Targeted search for local movement disorders and hypokinesis of the RV, RV dilatation (diameter of the right ventricular outflow tract (RVOT) > 30 mm. Normal findings do not exclude the disease!

MRI: Right ventricular fatty deposits and similar findings as in the echo; detection of aneurysms in the heart

Consider right ventricular angiography: Look for local movement disorders and hypokinesis of the RV, RV dilatation due to the complex RV geometry

Consider myocardial biopsy: Accumulation of intramyocardial fat cells = fibrolipomatosis

Proliferation of intramyocardial fat cells = fibrolipomatosis → 2 histological variations:

- Fibrolipomatosis 1 with mainly intramyocardial lipomatosis
- Fibrolipomatosis 2 with mainly intramyocardial fibrosis. In type 2 can the left ventricle can be affected.

DD:
- Uhl's disease [Q24.8]: Aplasia of the right ventricular myocardium (poor prognosis) (variants of ARVD?)
- Brugada syndrome, long QT syndrome and other "primary electrical heart diseases" with malignant arrhythmias (see section on this topic)
- Myocarditis

Di.: History / clinical symptoms (syncope, ventricular tachycardia in young patients, cases of sudden cardiac death in the family), ECG + imaging diagnostics

Th.: Symptomatic only: avoidance of physical strain (no sports), treatment and prophylaxis of arrhythmia: Beta-blockers, implantation of an ICD; in right heart failure: consider heart transplantation.

Prg.: Without therapy, the 10-year mortality rate is 30%.

Isolated ventricular non-compaction cardiomyopathy (NCCM)

Def: An inherited disease of the left ventricular myocardium. There are single cases ore those with a family history. Other heart abnormalities can be associated. We know various gene mutations, e.g. of the Tafazzin-Gene (Xq28). There is a typical prominent trabecularization of the apical part of the left ventricle with deep intertrabecular recessuses. This is thought to be a persistent embryonic matrix.

Ep: In children 9% of all primary CM

Sym: heart failure, ventricular arrhythmias and the risk of thromboembolism

DD: In the later stages the disease resembles DCM; in earlier stages it can be misdiagnosed as HCM, when the apical matrix is misinterpreted as compact myocardium.

Di:
- Echo criteria (Jenni and Stöllberg):
  - -detection of at least four prominent trabecules and recessuses
  - -detection of blood flow between the ventricular cavity and the recessus
  - -typical double-layered structure of the affected left ventricular myocardium
  - -ratio non-compact subendocardial layer/compact subepicardial layer during systole >2
- MRI: Alternative investigation in equivocal echocardiogram

Th: Treat the heart failure, provide thrombosis prophylaxis with anticoagulant drugs; consider ICD, consider heart transplantation

MYOCARDITIS [I51.4]

Def.: Myocarditis is an inflammatory heart muscle disease that can affect the heart muscle cells, interstitium and cardiac vessels.

Ep.: It is estimated that 1% of cardiotropic viruses affect the heart (up to 4% for Coxsackie B viral infection). The estimated number of unreported cases is fairly high since the majority of cases are mild or asymptomatic.

Aet.: 1. Infectious myocarditis
- Viruses (50% of cases), especially enteroviruses: Coxsackie B1 - B5 (frequent and dangerous!); also parvovirus B 19, Coxsackie A, herpes viruses, influenza viruses, adenoviruses, echoviruses, HIV, etc. There are numerous other viruses that can trigger myocarditis in isolated cases.
- Bacteria:
  - In septic diseases, especially bacterial endocarditis (staphylococci, enterococci, etc.)
  - Beta-haemolyzing streptococci A (tonsillitis, scarlet fever, erysipelas)
  - Borrelia burgdorferi (Lyme's disease)
  - Diphtheria
  - Rarer causes: typhus, tuberculosis, syphilis, etc.
- Fungi in immunodeficient parents
- Protozoa: Toxoplasmosis, Chagas disease (Trypanosoma cruzi/South America)
- Parasites: Trichina, Echinococci, etc.

2. Non-infectious myocarditis:
- Rheumatoid arthritis, collagenosis, vasculitis
- Myocarditis following radiation therapy to the mediastinum
- Hypersensitivity myocarditis due to medication (e.g. Clozapine)
- Idiopathic Fiedler's myocarditis

Prg.: Viral myocarditis can lead to immune phenomena as a result of cross-antigenicity of viral and myocardial structures: In acute myocarditis, the following findings (which usually disappear after clinical improvement) are present in 70-80% of cases:
- Antimyolemmal antibodies (AMLA) of the IgM type
- Antisarcolemmal antibodies (ASA) of the IgM type
- IgM antibodies and complement factor C3 in the myocardial biopsy

Hist.: Histological and immunohistological classification of myocarditis and inflammatory dilated cardiomyopathy (DCMi):

Diagnosis	Conventional histology (Dallas criteria 1987)	Histological and immunohistological criteria (ISFC classification 1998)
1. Active/acute myocarditis	Infiltrate, myocytolysis, oedema	The same in 1, 2 and 3: infiltrate characterized by monoclonal antibodies, immunoglobulin and complement fixation. Noncompulsory: new onset of class I + II HLA antigen and adhesion molecules *)
2. Lingering myocarditis	Like 1., but in follow-up biopsy during observation	
3. Healing myocarditis	Abating infiltrate, facultative myocytolysis, reparative fibrosis	
4. Borderline myocarditis	Small number of dispersed lymphocytes without myocytolysis	Equivocal findings for myocarditis with 1-13 lymphocytes/mm^3
5. Chronic myocarditis, dilated cardiomyopathy with inflammation	Not defined	≥14 lymphocytes (+ macrophages)/mm^3, facultative immunohistological evidence of viral RNA or DNA

*) Leukocytes can be differentiated precisely through the use of monoclonal antibodies. An increased expression of class I and II HLA antigens to myocytes and vascular endothelium as well as the detection of endothelial CAMs (Cellular Adhesion Molecules) indicate inflammation even if there is no cellular infiltration.

Special histological forms:
Rheumatoid myocarditis: Aschoff nodules, Anitschkow cells (= histiocytic cells), Aschoff giant cells
Idiopathic Fiedler myocarditis: lymphocellular/plasma cell infiltrates + giant cells

Cl.: The clinical course of myocarditis is very variable and ranges from asymptomatic or mild courses (majority of cases) to severe courses with fatal outcome (rare). Chronic courses with transition into dilated cardiomyopathy are possible.

The signs and symptoms of infectious myocarditis are those associated with an infection (medical history!):
- Fatigue, feeling of weakness (decline in performance), palpitations
- Tachycardia
- Arryhythmia, especially extrasystole (patient feels irregular heart beat), ventricular tachyarrhythmia, AV blockades
- Clinical signs of heart failure

Ausc: Unspecific, sometimes transient systolic murmurs, in heart failure there is sometimes a 3rd heart sound; in perimyocarditis a pericardial rub is possible

Lab.:
- CK/CK-MB, possibly troponin T/I ↑
- Possible signs of inflammation (erythrocyte sedimentation rate (ESR), blood count)
- Special bacteriological/virological diagnostics (stool analysis for enteroviruses, antibody titer, etc.)
- In the presence of viral myocarditis, possibly circulating antibodies (AMLA, ASA)
- BNP: Rises in early heart failure, but can also rise as a result of inflammation of the heart muscle (also true for inflammatory cardiomyopathy).

(24h) ECG: ECG changes are relatively frequent and usually transient:
- Sinus tachycardia
- Arrhythmia, especially extrasystoles
- In diphtheria and Lyme carditis, frequently conduction disorders (e.g. AV block)
- Pattern of inner heart muscle damage: ST-segment depression (DD: digitalis effect, coronary insufficiency), T-wave flattening, negative T-waves (DD: regression stage after infarction or pericarditis)
- With concomitant pericarditis ("myopericarditis") possibility of monophasic change in the ST-segment in the sense of outer layer damage (DD: myocardiac infarction – in myocarditis, no R loss and no Q spikes)
- Possibly low voltage → DD: myocardial damage or pericardial effusion (echocardiography!)

Imaging procedures:

Echo: Frequently normal findings; sometimes regional kinetic disorders, possible pericardial effusion with myocarditis/pericarditis; the development of heart failure sometimes goes with reduced ejection fraction and heart dilatation

CXR: Heart failure, enlarged heart, possibly signs of pulmonary congestion

MRI: Anatomy + function of the heart

Possible invasive diagnostics: Left cardiac catheterization with endomyocardial biopsies (in DD myomyocardiac infarction: coronary arteries are normal)

DD of inflammatory heart muscle diseases:

Histology	**Myocarditis / inflammatory dilated cardiomyopathy (DCM)**			
Immunohistology	No inflammation	No inflammation	Active inflammation	Active immunological process in the myocardium
Molecular biology	No evidence of viral persistence	Viral persistence in the myocardium	Viral persistence in the myocardium	No detection of virus
Diagnosis	Post-myocarditis heart muscle disease	Viral heart muscle disease	Virus-positive myocarditis	Autoimmune reactive myocarditis / DCM

Di.: History + clinical symptoms, consider myocardial biopsies with histology/immunohistology/viral diagnostics

Th.: A) Causal: e.g. Penicillin treatment of rheumatic carditis, treatment of diphtheria, Lyme carditis, Chagas disease (see section on those topics)
- In progressive viral myocarditis with evidence of viral DNA/RNA in the myocardial biopsy. Consider a trial of antiviral therapy in the context of controlled studies (e.g. with interferon).
- If auto-antibodies against the beta1-adrenoreceptor are detected: extracorporeal immune adsorption, corticosteroids and maybe immunosuppressives (e.g. Azathioprine)

B) Symptomatic:
1. Avoid any physical exertion: as long as there are signs of heart failure (inability to work).
2. Thromboembolism prophylaxis with anticoagulants in dilated cardiomyopathy
3. Treatment of complications (heart failure, cardiac arrhythmia → see section on that topic)
4. In terminal heart failure, try to reduce cardiac pre- and afterload using a temporary mechanical heart replacement

C) Last resort for terminal heart failure: heart transplantation

Prg: 1. The majority of viral myocarditis cases come to a full recovery } > 80%
2. Persistence of harmless arrhythmia (e.g. extrasystole) }
3. Relatively rare death from acute complications (rhythm/conduction disorders, heart failure). High rates of complications are found with Coxsackie B infection (especially in infants), diphtheria and Chagas disease, among others
4. Chronic course (about 15%) with the development of dilated cardiomyopathy and heart failure (especially viral myocarditis)

APPENDIX:

CHAGAS DISEASE

Pathogen: Trypanosoma cruzi; transmission through the faeces of “kissing bugs”

Incubation: 1 - 4 weeks

Cl.: Acute:
- Local (painless) swelling/ulcer at the entrance site, often periorbital (chagoma)
- Acute inflammatory disease pattern with fever, fatigue, enlargement of lymph nodes/liver/spleen, occasionally myocarditis

Chronic: Onset after 20 years
- Cardiac manifestation as DCM, cardiac arrhythmia, possible sudden cardiac death
- Gastrointestinal manifestation with oesophageal or colon dilatation

Di.: Clinical (triad: cardiomegaly, megaoesophagus and megacolon), country of origin, detection of pathogen, antibody detection

Th.: In the acute stage: Nifurtimox, Benznidazole
In the chronic stage: Only symptomatic therapy is possible (see section on DCM)

PERICARDITIS AND PERIMYOCARDITIS [I31.9]

The clinical differentiation of myocarditis (sinus tachycardia, arrhythmia, enlarged heart, etc.) and pericarditis (retrosternal pain, pericardial rub, etc.) is not always possible or meaningful; the simultaneous involvement of subepicardial myocardial layers (which is responsible for the ECG changes!) in the context of pericarditis has led, in these cases, to the description as perimyocarditis.

ACUTE PERICARDITIS [I30.9]

Aet.: 1. Infectious pericarditis:
- most often viruses: Same pathogen spectrum as for myocarditis: Coxsackie A and B, adenoviruses, echoviruses, HIV, etc.
  The majority of cases of "idiopathic" pericarditis are caused by viruses!
- More rarely, bacteria: mycobacteria (Tbc), pericarditis in the presence of septic diseases, etc.

2. Immunological-related pericarditis:
- Systemic lupus erythematosus
- Rheumatic fever! (in the context of rheumatic pancarditis, pathological-anatomical involvement of 100% of the pericardium, however only 10% are symptomatic).
- Allergic pericarditis (serum disease, medications)
- Post-myocardial infarction syndrome (= Dressler syndrome)[I24.1], laboratory: anti-SMA
  Post-cardiotomy syndrome [I97.0]:
  1 - 6 weeks after myocardiac infarction or cardiac surgical procedures, a feverish pericarditis/pleuritis may occur (increase in ESR, leucocytosis, temporary detection of circulating antibodies against heart muscle).

3. Epistenocardiac pericarditis over large areas of infarction near the epicardium [I30.8.] occurs within the 1st week after infarction.
4. Pericarditis with uraemia
5. Posttraumatic pericarditis
6. Tumor pericarditis (infiltrative growth or metastatic disease): bronchial, breast, oesophageal carcinoma; leukaemia, malignant lymphoma, etc.)
7. Pericarditis following radiotherapy

Cl.: a) Dry pericarditis (fibrinous pericarditis): occurs at the beginning or end of acute percarditis; most often with uraemia, also with myocardiac infarction (no anticoagulants → risk to develop a hemopericardium)
Sy.: Sharp pain behind the sternum (DD: myocardial infarction), increases in horizontal position, with deep inspiration and when coughing
Ausc.: Systolic or systolic-diastolic high-pitched "rasping" crepitation, best heard over the area of the lingula near the sternum and after expiration.

Three types of crepitation are differentiated:
- Pleural rub: This disappears when the patient holds his/her breath
- Pleuro-pericardial rub (in combination of pericarditis with left-side pleuritis): In addition to the pericardial rub, there is a respiratory rub.
- Pericardial rub: The crepitation doesn't change when the patient holds his breath

b) Moist (exsudative) pericarditis
Most frequently due to Tbc, viral infections, rheumatic fever, uraemia
In the transition from dry to moist pericarditis, the heart sounds become quieter and the pain and crepitation frequently also disappear.

Compl.: PERICARDIAL TAMPONADE [I31.9]

Large quantities of exudates may cause inflow congestion via hindrance of diastolic ventricular filling, with the risk of cardiogenic shock (critical quantities of exudates with the rapid formation of effusion: 300 - 400 ml → risk of cardiogenic shock).

PPh.: 1. Accumulation of blood before the right side of the heart:

Cl.:
- Increased venous pressure with tightly filled veins (veins at basis of tongue / jugular veins)
  DD for volume deficiency shock: collapsed veins.
- Kussmaul's sign: paradoxical increase in inspiratory pressure in the jugular veins
- Liver capsule tension with upper abdominal pain
- Sometimes small amount of ascites (ultrasound!)

2. Low cardiac output syndrome
- Weakness, exertion dyspnoea
- Drop in blood pressure, which increases during inspiration
- Paradoxic pulse: Drop in blood pressure amplitude with inspiration > 10 mmHg
  History: A paradoxic pulse can also be found in the presence of calcified constrictive pericarditis, tension pneumothorax and in severe asthma attacks.
- Tachycardia

3. Soft heart sounds (auscultation)

Lab.: In cases of infectious genesis: CRP, ESR ↑, virus serology, culture for bacteria and mycobacteria

ECG: The ECG is not altered per se by the pericarditis, but rather by the fact that the bordering myocardial layer is affected by the inflammation: Therefore, there are signs of outer layer (subepicardial) damage in all leads: In contrast to an infarction (which only affects regionally assigned leads), the ST-segment elevation runs concavely curved from the rising leg of the S-spike. In the 2nd week, a terminal negative T-wave develops (but never with a loss of R-wave height as in myomyocardiac infarction). In cases of severe pericardial effusion, there is often a low voltage in the ECG, occasionally also an electrical alternation (this is explained echocardiographically by a beat-to-beat change in the anatomical position of the heart).

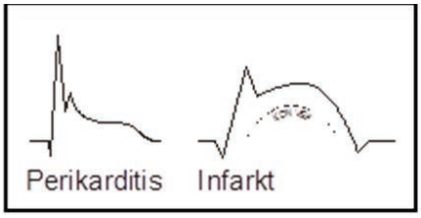
Echo: This is a more rapid and more sensitive way to detect an effusion (from 50 ml): Echo-free space behind the heart; with a large quantity of effusion, also in front of the heart. Small amount of effusion is defined as < 100 ml, moderate amount of effusion 100-400 ml, large amount of effusion > 400 ml ("swinging heart"). In the presence of pericardial tamponade, compression of the right ventricle and collapse of the right atrium.
In order to be able to precisely evaluate the development of pericardial effusion, close monitoring of the blood pressure (falling), central venous pressure (increasing) + echocardiography is recommended.

X-ray: Enlargement of the cardiac shadow (without signs of pulmonary congestion); in typical cases, flaccid triangular shape (broad, generous middle parts like a bottle of Franconian wine). The DD for myogenic cardiac dilatation is clarified via echocardiography.

MRI/CT: Anatomical and functional diagnosis

DD: 1. Myogenic cardiac dilatation (no low voltage in the ECG, no evidence of effusion in ultrasound, frequently signs of pulmonary congestion)
2. Myomyocardiac infarction:
In perimyocarditis, there are no Q spikes or
Loss of R-wave height. With infarction, there is reciprocal

ST-segment depression in other leads (but not in pericarditis). CK levels may also increase slightly with perimyocarditis.



Di.: Clinical, auscultation, ECG, echocardiography, possible pericardial puncture and biopsy (with bacteriology, cytology, histology)

Th.: a) Treat any underlying disease: e.g.
- In the case of bacterial genesis: antibiotics
- If tubercular genesis is suspected, attempt to detect the pathogen by pericardial aspiration. A negative result does not exclude tubercular genesis. Therefore anti-tuberculous therapy should be started if Tbc is suspected (see section on pulmonary tuberculosis).
- In cases of rheumatic fever, Penicillin + ASA or possibly corticosteroids
- In cases of allergic pericarditis, post-myocardial infarction syndrome and post-cardiotomy syndrome: NSAID, possibly corticosteroids
- In cases of uraemic pericarditis: dialysis, etc.

b) Symptomatic treatment:
anti-inflammatory therapy (NSAID, possibly steroids)
In cases of recurring idiopathic pericarditis: therapeutic trial with colchicines (1 g/d).
In cases of threatening pericardial tamponade: aspiration (intensive care unit): Starting from the xiphoid process, carefully insert the needle in the direction of the pericardial effusion under ultrasound monitoring. Make sure you hold the syringe in aspiration mode all the time. Introduction of a drainage catheter. Severe complications are to be expected in 5% of cases (e.g. bleeding, missed punctures, etc.).
In cases of recurring effusion, consider pericardial drainage via catheter. In cases of chronic recurring effusion (e.g. in uraemia) pericardial fenestration to the pleura or peritoneum.

CHRONIC CONSTRICTIVE PERICARDITIS [I31.1]

Def.: Scarring caused by acute pericarditis.
Narrowing of the heart due to the scarred, shrunken pericardium which is partially permeated with circular calcified plaques. This in turn leads to the impaired diastolic ventricular filling with signs of inflow congestion and, in cases of prolonged existence, heart muscler atrophy.

Nomenclature:
- Accretion: adhesions of the pericardium to neighbouring organs
- Concretion: adhesion of both pericardial sheats
- Constriction: The heart is effectively enceased in a rigid box of callous, shrivelled pericardium, often with calcium deposits

Aet.: Same as for acute pericarditis, with tubercular genesis supposedly the most frequent

Cl.: 1. Symptoms caused by accumulation of blood before the right side of the heart:
- Increased venous pressure (> 12 cm H_2O)
- Kussmaul's sign: paradoxical increase in pressure of the jugular vein pulse during deep inspiration
- Enlarged liver, sometimes with ascites (false diagnosis: liver cirrhosis)
- Oedema, congestion proteinuria, hyponatraemia (false diagnosis: nephrotic syndrome), possibly congestive hypersplenism

2. Low cardiac output syndrome with weakness, exertional dyspnoea
possibly paradoxic pulse: Drop in blood pressure amplitude with inspiration > 10 mmHg

Auscultation: Possibly soft heart sounds, possibly 3rd heart sound (false diagnosis: mitral valve defect)

ECG: Negative T-waves, low voltage, possibly AF

Echo: Increased echo from calcified pericardial callosities, reduced movement amplitude of the posterior wall of the left ventricle with sudden stop of ventricular filling in mid-diastole (dip-plateau phenomena with invasive pressure monitoring)

CXR, MRI, CT: Usually normal heart size, frequently calcifications

***Note**:* The incongruity between clinical signs of right heart failure and a normal sized heart would lead one to think of constrictive pericarditis, especially heart failure averse to treatment!

DD: Restrictive cardiomyopathy (RCM): See the section on that topic

Di.: Clinical symptoms + echocardiography + CT or MRI

Th.: Surgical removal of callosities (decortication) of the heart, pericardectomy
Do not decide to operate too late; otherwise, acute cardiac dilatation may occur postoperatively as a result of myocardial atrophy.

CORONARY HEART DISEASE (CHD) [I25.9]

Internet references: *www.athero.org; www.bcs.com; www.khk.versorgungsleitlinien.de/en; www.ajconline.org*

Syn: ischaemic heart disease = IHD, coronary artery disease = CAD, coronary heart disease = CHD

Def.: CHD is atherosclerosis ***in*** the coronary arteries. Coronary insufficiency results from coronary stenosis that limits flow causing lack of oxygen in the heart muscle. Myocardial ischaemia may present in many ways:

- Asymptomatic CHD (silent ischaemia)
- Symptomatic CHD:
  1. Angina pectoris: pain in the chest as a result of reversible myocardial ischaemia
  2. Myomyocardiac infarction: ischaemic myocardial necrosis
  3. Ischaemic cardiac muscle damage with left heart failure
  4. Cardiac arrhythmias (particularly ventricular fibrillation)
  5. Sudden cardiac death

Latent CHD	:	silent ischemia
Manifest CHD	:	stable angina pectoris / acute coronary syndrome (ACS)
Complic.: rhythm disorders		myocardial infarction → left cardiac insufficiency ↘ ↓ ↙ (sudden) cardiac death

Ep.: CHD is the most frequent cause of death in the industrialised countries. In Germany, 20% of deaths are attributable to CHD. Life time prevalence in Germany for men is 30%, and for women, 15% (m : f = 2 : 1). Incidence increases with age.

Frequency of various forms of CHD as initial presentation:
- Angina pectoris: 40 %
- ACS and myocardial infarction: 40 %
- Sudden cardiac death: 20 %

Aet.: Risk factors for premature arteriosclerosis = atherosclerosis
(According to the guidelines of the International Atherosclerosis Society; *www.athero.org*):

A) High risk conditions:
- Known CHD
- Other manifestations of arteriosclerosis (PAVK, abdominal aortic aneurysms, stenosis of the A. carotid > 50 %, ischaemic stroke)
- Diabetes mellitus in assosiation with other risk factors

B) Risk factors:

1. Major risk factors:
   - 1.1 Smoking (Risk increases with concomitant use of ovulation inhibitors containing oestrogen)
   - 1.2 Arterial hypertension
   - 1.3 LDL ↑
   - 1.4 HDL ↓
   - 1.5 Age (m ≥ 45 yr. ; f ≥ 55 yr.)
   - 1.6 CHD/myocardial infarction in first degree relatives prior to the age of 55 yr. (m) or 65 yr. (f)
   - 1.7 Diabetes mellitus is listed under A and B: A) with other risk factors; B) as the sole risk factor

   Note.: > 50 % of all CHD patients have impaired glucose tolerance or diabetes mellitus (Euro-Heart survey)
2. Other risk factors:
   - 2.1 Atherogenic diet (The Mediterranean diet is protective)
   - 2.2 Obesity
   - 2.3 Physical inactivity
   - 2.4 Lipid metabolism disorders: different than under 1.3/1.4: e.g., hypertriglyceridaemia, Lp(a) increase, etc.
   - 2.5 Glucose tolerance disorder
   - 2.6 Inflammatory states in CHD patients (CRP as a possible indicator)
   - 2.7 Thrombosis tendency (see thrombophilia)
   - 2.8 Hyperhomocysteinaemia (> 12 µmol/l) is only a risk indicator (not an independent risk factor)
   - 2.9 Hyperfibrinogenaemia
   - 2.10 Genetics: There are 11 identified gene locations in 8 differnet chromosomes, that are associated with increased risk of MI (e.g. 9p21.3). Very few genes revealed an association with the classical risk factors. Risk alleles are common, but they only increase the risk of MI moderately (10-30% per allel).

The 10-year risk can be calculated using risk calculators:

- PROCAM risk calculator for Germany (*www.chd-taskforce.com*)
- ESC risk calculator for Europe (*www.escardio.org)*
- Framingham risk calculator for the USA (*www.nhlbi.nih.gov*)

Since the risk calculators do not take into account all known risk factors, myocardial infarctions are also observed in patients who, according to the risk calculation, do not fall into the high risk group. The p21 mutation on chromosome 9 is a genetic risk factor.

Definition of high risk (moderately elevated risk in brackets):

- IAS (International Atherosclerosis Society): risk of a cardiovascular event, e.g., infarction (morbidity + mortality) > 20 %/10 yr. (10 – 20 %/10 yr.)
- ESC (European Society of Cardiology): risk of cardiovascular death (mortality only in brackets) ≥ 5 %/10 yr. (2 – 4 %/10 yr.) or indicator diseases:
  Established CHD/infarction or stroke or abdominal aortic aneurysm or carotid stenosis ≥ 50 % or PAD or diabetes mellitus

In people with infarcts under 30 years of age, one should search for:

- Familial lipid metabolism disorders
- Antiphospholipid syndrome or other causes of thrombophilia
- Hypothyreodism (with hypercholesterolemia)
- Vasculitis (e.g., polyarteritis nodosa, Kawasaki syndrome, Takayasu arteritis)
- Coronary anomalies
- History of drug abuse (e.g., cocaine)

Pg.: Coronary insufficiency:

I. Increased coronary resistance

1. Major vascular factors:

- Macroangiopathy (> 90 %): stenosing arteriosclerosis of the large epicardial coronary arteries. An infarction usually results from a detached arteriosclerotic atheroma (plaque rupture) and the formation of a thrombus occluding a vessel.
- Microangiopathy (small vessel disease) [I77.9] of the intramural small coronary vessels (< 10 %): angina pectoris without stenoses of the large epicardial coronary arteries.
  Aet.: Arterial hypertension (hypertensive microangiopathy), diabetes mellitus, vasculitis
- Coronary spasms can occur as an isolated event or in association with macroangiopathy.
- Coronary anomalies: e.g., primary malformations with origin of a coronary artery from the pulmonary artery (Bland-White-Garland syndrome) or of the LCA from the right sinus and course between the aorta and pulmonary artery
- Arterio-venous coronary fistula
- Congenital myocardial bridges (muscle bridges) can cause exercise induced angina pectoris in rare cases (→ the extend of a stenosis can be measured by quantitative coronary angiography, intracoronary ultrasound and Doppler).

2. Additional myocardial factors:

- Cardiac hypertrophy
- Contractile insufficiency (with increased end diastolic ventricular pressure)
- Hypertension and tachycardia/tachyarrhythmia in the presence of atrial fibrillation: If hypertension and tachycardia exceed a critical limit (increase in cardiac activity), this may result in an angina attack.

II. Additional extra coronary factors:

1. Cardiac: e.g., aortic valve defect, hypertrophic cardiomyopathy, arrhythmias, etc.
2. Extracardiac:
   - Elevated O_2 requirement (e.g., fever, hyperthyroidism, physical activity, cocaine, etc.)
   - Lowered O_2 supply (anaemia, pulmonary disease, sleep apnoea syndrome, staying at high altitude, CO poisoning; cocaine can cause coronary spasms)
   - Elevated blood viscosity (polyglobuly, polycythemia vera, hyperfibrinogenaemia)

Pat: **Coronary artery distribution:**

The most frequent type is the balanced (normal) type (60 - 80 %), in which the left coronary artery (LCA) supplies the anterior wall of the left ventricle and the major part of the septum. The right coronary artery (RCA) supplies the right ventricle and the posterior septum.
There are also a right dominant or a left dominant type, each comprising in 10 - 20 % of cases.
The main stem of the LCA branches into the Ramus interventricularis anterior (RIVA) and the Ramus circumflexus (RCX). Depending on the number of stenosed vessels, we talk of 1, 2, or 3 vessel disease.

PPh: Corresponding to the reduction in diameter (in %), 4 degrees of severity of coronary stenosis are defined:
Grade I: 25 - 49 %
Grade II: 50 - 74 % (significant stenosis)
Grade III: 75 - 99 % (critical stenosis)

Perfusion of the coronary arteries depends on the perfusion pressure during diastole, the duration of diastole and the coronary resistance.

The coronary resistance is comprised of 3 components:

1. Proximal components (depends on the lumen diameter of the epicardial coronary artery)
2. Distal components (resistence of the intramyocardial arterioles)
3. Extravascular components (systolic vascular compression as a result of intramyocardial increase in pressure)

As a result of the compression load, O_2 requirement in the inner layers of the myocardium is higher than in the outer layers. For this reason, the subendothelial myocardium is the first to be affected by myocardial ischaemia.

Regional perfusion disorders of the myocardium are only expected, once the coronary stenosis exeeds 50 % of the vessel lumen. However, the extent of collateral vessels plays a role as well. Once > 75 % of the vessel volume is restricted (critical stenosis), and when there is a lack of compensating collaterals, the coronary reserve is exhausted. This results in exercise induced angina pectoris.
Coronary reserve: Difference between coronary perfusion (O_2 supply) at rest and maximum possible coronary perfusion. Distally from a coronary stenosis that exceeds 40 % of the diameter, the coronary reserve is permamently reduced.

Cl.: Angina pectoris usually becomes symptomatic in critical coronary stenosis (=75%). The leading symptom of coronary insufficiency is angina pectoris (stenocardia): Primarily retrosternal localized pain, triggered by physical or mental stress and usually ceases within 5 – 15 minutes at rest or subsides within 1 -2 min. after taking nitro.
The pain can radiate to the neck, lower jaw, shoulder, left (right) arm into the ulnar fingertips or into the upper abdomen.
Cold temperatures and a full or distended stomach (Roemheld syndrome) can intensify the pain. Many patients complain only of retrosternal pressure or a sensation of tightness or burning in the ribcage.
Note.: In an angina attack, the perfusion pressure in the poststenotic region of the coronary artery decreases, while the end diastolic ventricular pressure increases. This leads to a critical perfusion disorder in the inner layer of the myocardium, and deterioration in ventricular pump function.

Types of angina pectoris (AP):

1. Stable AP:

   AP regularly triggered by certain mechanisms (e.g., physical activity) which responds well to nitrates.

   CCS classification of AP (Canadian Cardiovascular Society):

   0: Silent ischaemia
   I: No AP under normal physical stress, AP under heavy physical labour
   II: Slight effect on normal physical activity by AP
   III: Considerable effect on normal physical activity due to AP
   IV: AP at the slightest physical stress or pain at rest

2. Unstable AP = pre-infarct syndrome [I20.0]:
   - Primary unstable AP: every first instance of angina
   - Secondary unstable AP: increasing severity, duration, frequency of pain attacks (crescendo angina), angina at rest, increasing need for anti-angina medications

   Braunwald classification:

   I. Newly occurring, severe or increasing AP, no symptoms at rest
   II. Rest AP within the last month, but not within the last 48 hr.
   III. Rest AP within the last 48 hr.

   A. Extracardiac causes
   B. Primary unstable without extra-cardiac origin
   C. Post-infarct angina within 14 days

   For unstable AP always check troponin T or I (if results are negative, check again after 6 hr.). There is a risk of acute infarction (20 %). The transition to infarction is usually introduced by a tear in atheromatous plaque with subsequent coronary thrombosis. In the case of critical coronary stenosis of a larger vessel, this can result in left ventricular heart failure, complex arrhythmia and even VF.

   Acute coronary syndrome can present in 3 ways:
   - Unstable AP without an increase in troponin I or T
   - NSTEMI = non-ST segment elevation MI: unstable AP/myocardial infarction with increase in troponin I or T, but without ST segment elevation
   - STEMI = ST segment elevation myocardial infarction: MI with troponin T/I and enzyme changes and ECG changes typical of infarct (initial ST elevation)

3. Special forms:
   - Prinzmetal angina [I20.1] = variant angina: AP with reversible ST elevation (!) without enzyme derailment. Patients often have coronary stenoses on coronary angiography. In that area transient coronary spasms may occur. There is an increased risk of acute coronary syndrome and myocardial infarction!
   - "Transitory angina": AP at the start of stress which disappears after further stress (release of vasodilating metabolites)
   - "Angina nocturna": AP at night, causing insomnia and/or dyspnoea

DD: Chest pain:

A) Cardiac chest pain:

- Angina pectoris and myocardial infarction as a result of CHD
- Postmyocardial infarct syndrome (= Dressler syndrome)
- Rapid tachycardia
- Hypertensive crisis
- Aortal defects (auscultation/echocardiography)
- Mitral valve prolapse (Echocardiography)
- Hypertrophic cardiomyopathy (ECG, echocardiography), deterioration of angina by glyceryl nitrate in HOCM (auscultation during Valsalva)!
- Perimyocarditis (auscultation, ECG, echocardiography)
- Takotsubo (stress) cardiomyopathy (see there)
- Coronary anomalies

B) Non-cardiac chest pain:

1. Pleural/pulmonary origin
   - pulmonary embolism; chronic cor pulmonale
   - Pleurisy (respiration dependent pain, auscultation), pneumothorax
   - Bronchial carcinoma, Pancoast tumour
   - Pleurodynia(Coxsackie B virus infection, Bornholm disease)
   - (Spontaneous) pneumothorax (auscultation, CXR)
2. Diseases of the mediastinum and the aorta:
   - Mediastinitis, mediastinal tumour
   - Aortal dissection and/or intramural hematoma of the aorta (CT, MRT, transesophageal echocardiography)
3. Diseases of the oesophagus:
   - Reflux disease (retrosternal burning, heartburn → endoscopy of the oesophagus)
   - Motility disorders: diffuse oesophageal spasms, nutcracker oesophagus, achalasia
   - Mallory-Weiss syndrome
   - Boerhaave syndrome = spontaneous oesophagus rupture due to vomiting (excruciating thoracic pain, x-ray thorax + oesophagus with water soluble contrast medium)
4. Diseases of the ribs, vertebrae, nerves:
   - Vertebrogenic thoracic pain: cervical/thoracic spine osteochondrosis, ankylosing spondylitis
   - Tietze syndrome [M94.0] (painful swelling on the cartilage/bone junction of the upper ribs)
   - Thorax trauma, rib fracture
   - Herpes zoster
5. Abdominal diseases with thoracic pain radiation:
   - Acute pancreatitis (amylase, lipase)
   - Biliary colic (ultrasound)
   - Roemheld syndrome (a full or distended stomach can cause genuine angina pectoris or non-CHD thoracic pain)
6. Functional thoracic pain (Da Costa syndrome [F45.3])
   History + exclusion of any other causes!

Note: There are 5 serious causes of chest pain ("The big five"):
-Acute coronary syndrome
-Pulmonary embolism
-Dissecting aorta
-Tension pneumothorax
-Oesophagus rupture

To find out if the patient does suffer from angina, in 2006 the European society of cardiology suggested the following:

Typical angina pectoris - all criteria have to be fulfilled:
1.Typical retrosternal symptoms
2.Symptoms caused by physical or psychogenic stress
3.Resting and/or application of nitrate leads to quick cease of symptoms

Atypical angina pectoris - only two of the above criteria are fulfilled

Non-cardiac pain - only one or none of the criteria is fulfilled

Di: of coronary insufficiency

1. **Calculate the cardiovascular risk (e.g. PROCAM- or ESC-score)**
2. **History:** The presence of typical angina pectoris attacks makes the diagnosis of CHD likely. The absense of typical angina pectoris attacks however, does not exclude CHD (particularly in diabetes mellitus). > 50 % of all ischaemic attacks are not accompanied by pain (= silent ischaemia) and women frequently complain of different symptoms!

3. ECG

▶ Resting ECG

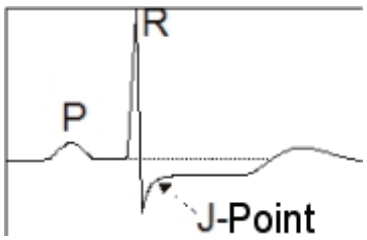
As long as no infarction has occurred, the resting ECG is unremarkable in 50% of cases, even in the presence of severe CHD. In chronic CHD, the smallest disseminated infarctions can occur with non-specific ECG changes (e.g., T wave flattening, negative T wave). Compare with prior ECG!

▶ Exercise ECG (ergometry)

An increase in the minute heart volume (stroke volume x heart rate) and O_2 requirement is induced by dynamic stress under controlled conditions. If there is significant CHD, ischaemia is triggered due to the reduced O_2 supply, which presents in the form of ST-changes.

The following ST changes are typical of myocardial ischaemia:

- Horizontal or descending reversible ST depression of at least 0.1 mV in the limb leads or at least 0.2 mV in the precordial leads
- A slowly ascending ST segment, which still runs 0.1 mV below the baseline 80 msec after the J point (junction point = transition point between S wave and ST segment), is less specific for an ischaemic reaction. Rapidly ascending ST gradations are harmless findings due to tachycardia.
- ST elevation > 0.1 mV (regional distribution pattern) from coronary spasm (Prinzmetal angina)



***Note**:* Diverse medications (digitalis, Chinidine, antidepressants) can cause ST depression and should be discontinued prior to the exercise ECG, if clinically justifiable (1 week pause for Digoxin, 3 week pause for Digitoxin). The higher the ergometric stress and the achieved heart rate, and the more pronounced and numerous the coronary stenoses, the higher the sensitivity of an exercise ECG (= proportion of CHD patients in percent with positive test result). Maximum heart rate = 220 minus age; submaximal heart rate = 200 minus age. An unremarkable exercise ECG therefore is not of high diagnostic value if the submaximal heart rate has not been attained at least. In cases of submaximal stress, one can expect approx. 20 % false negative test results (= unremarkable exercise ECG in spite of critical coronary stenosis → sensitivity in one-vessel disease is 60 %, in two-vessel disease 70 % and in three-vessel disease 80 %.

The informative value of ergometry is extremely limited under the following conditions:
- Under anti-angina and/or bradycardia therapy or under digitalis therapy
- In the presence of pre-existing ST changes (e.g., LBBB and pacemaker stimulations)
- If stressing is not possible due to orthopaedic complications.

The specificity of the exercise ECG is approx. 80 %. False positive findings (suspicious ST depression under stress without the presence of a critical coronary stenosis) are present in approx. 50 % of women and 25 % of men) and are most frequently caused by hypertensive heart disease.

If the coronary angiogram is normal in patients with angina pectoris and pathological ergometry findings, this is also called syndrome X (an aetiologically heterogeneous group of patients).

Sensitivity + specificity are lower for women than for men.

The risk of ergometric stress is 1 - 2 severe incidents out of 10,000 tests (risk of ventricular fibrillation approx. 1 : 15,000, death 1 : 42,000). For this reason resuscitation equipment must be present as well as a defibrillator for treating ventricular fibrillation!

Ind:
1. Confirmed evidence of myocardial ischaemia as a result of CHD
2. Detection of exercise induces arrhythmia
3. Analysis of blood pressure and heart rate behaviour under exertion
4. Evaluation of performance capacity

If there is an accumulation of vascular risk factors, an exercise ECG is recommended even in symptom-free patients in their early 40ies (detection of silent myocardial ischaemia!).

Absolute contraindications:

- High grade main stem stenosis of the left coronary artery
- Unstable angina pectoris with increase in troponin I or T as well as recent myocardiac infarct (within the first 2 weeks)
- Acute endo-/myo-/pericarditis
- Severe heart failure (NYHA III and IV)
- Clinically manifest cardiac defect (in particular severe aortal stenosis and severe hypetrophic obstructive cardiomyopathy (HOCM)
- Significant aneurysms of the heart or the aorta
- Acute aortal dissection
- Severe pulmonary hypertension
- Severe uncontrolled cardiac arrhythmias
- Severe general diseases, febrile infections, phlebothrombosis, pulmonary embolism, etc.
- Caution in the presence of QT prolongation! (increased risk of ventricular fibrillation)

Relative contraindications:
- Non-high grade main stem stenosis of the left coronary artery
- Arterial hypertension (syst. > 200 mm Hg, diast. > 110 mm Hg)
- Known electrolyte disorders
- Tachy- or bradyarrhythmia
- Higher grade AV blockades

Absolute termination criteria:
- Subjective symptoms: angina pectoris (→ nitroglycerine administration), dyspnoea, dizziness, muscular exhaustion
- ST depression ≥ 3 mm
- ST elevation ≥ 1 mm
- Persistent ventricular tachycardia (> 30 sec.)
- Drop in blood pressure > 10 mm Hg with signs of myocardial ischaemia (angina pectoris, ST depression) or lack of systolic increase in blood pressure (indication of left ventricular insufficiency)
- Lack of increase in frequency (possible indication of "sick sinus")
- Achieving a maximum cardiac frequency (220 – age). However, at least the submaximal cardiac frequency (200 minus age) should be strived for.
- Under consideration of medication that induces bradycardia (e.g., beta blockers), lower the target rate by 10 - 15 %.

Relative termination criteria:
- Hypertensive dysregulation (syst. > 230 mm Hg, diastolic ≥ 115 mm Hg)
- Polymorphic extrasystoles, pairs, salvos
- Supraventricular tachycardia
- Bradyarrhythmia
- Conductance disorders (high grade AV block, bundle branch block)

▶ **24h-ECG:**
Detection of ischaemic induced ST depressions (and arrhythmia) under conditions of daily stressors (work – leisure time – nocturnal rest): also important for the diagnosis of nocturnal angina pectoris attacks (angina nocturna) and silent ischaemia.

3. Stress tests in combination with imaging techniques:
Advantages: higher sensitivity, quantification + localization of ischaemic areas

▶ **Stress echocardiography:**
a) Stress using ergometry
b) Stress using pharmaceuticals: e.g.,
- Infusion of a vasodilator Dipyridamol, which triggers ischaemia in stenosis areas via steal phenomena (antidote: Theophyllin).
- Infusion of a short acting sympathomimetic (Dobutamine or Arbutamine), which elevates the myocardial O_2 usage (antidote: beta blockers).

Detection of systolic wall movement disorders as a result of stress induced myocardial ischaemia. Sensitivity and specificity up to 90 % (dependent on the echogenicity (anatomy) and the experience of the examiner). For wall movement disorders that already occur under resting conditions (e.g., following infarction), the value of stress echocardiography is limited.

▶ **Nuclear medicine diagnostics:**
- Myocardial perfusion scintigraphy (MPS) and single photon emission computed tomography (SPECT) with the potassium analogues ^{201}thallium or Tc-99m-marked perfusion markers Sestamibi or Tetrofosmin. Sensitivity 90 % and specificity approx. 75 %.
  - Irreversible activity loss in scarred myocardial regions
  - Reversible activity reduction in ischaemic myocardial areas under ergometry stress. CHD patients with unremarkable findings should have a relatively good prognosis.
- Positron emission tomography (PET):
  PET is a non-invasive method for evaluation of myocardial perfusion and vitality. It requires the use of positron emitting isotopes. The absorption of ^{18}Fluorodeoxyglucose (FDG) in myocytes is evidence of metabolic activity and thereby vitality in dysfunctional myocardium. Regional perfusion can be determined by ^{13}N-ammonia. Consequently, through the use of PET, it is possible to differentiate between normal, hibernating, stunned and necrotic myocardium. The hibernating myocardium (myocardium in “hibernation”) is defined by the increased absorption of FDG in regions with reduced blood flow (PET mismatch). A regional dysfunction in the presence of normal blood flow characterizes a stunned myocardium. A uniform reduction in blood flow and metabolism characterizes a necrosis.

▶ **Stress MRT with pharmacological stress:** Information analogous to stress echocardiography

▶ **MRT spectroscopy:** analysis of the myocardial metabolism without radioactive substances; Information similar as for PET

4. Imaging diagnostics for the evaluation of the coronary arteries:

- **Electron beam CT (EBCT), multilayer spiral CT (MSCT), dual source CT (DSCT):** Sensitive detection of calcifications in the coronary arteries ("calcification screening"). The detection of coronary calcification does not correlate with the degree of stenosis and is not an indication for coronary angiography. The lack of calcifications argues against the presence of CHD. No detailed representation of the entire coronary system. If calcifications and stenoses are detected, further clarification through coronary angiography is advised. It is difficult to assess thrombi within a stent. If calcifications and stenoses are detected, further clarification through coronary angiography is advised. CT carries a high dose of radiation.
- **MR angiography with contrast medium gadomer-17:** detection of coronary (sensitivity 80%, specificity 90%)
- **Coronary angiography including levocardiography (gold standard) - indication:**

  High degree of evidence in patients:
  - with stable AP of CCS class III and IV or with acute coronary syndrome
  - with high risk characteristics* and AP, regardless of the severity of the AP
  - with high risk characteristics* and typical symptoms in spite of anti-angina therapy
  - with high risk characteristics* and positive evidence of ischaemia in spite of anti-angina therapy (CCS II), even in the absense of symptoms
  - Following survival of circulatory arrest or a heart attack with malignant ventricular cardiac arrhythmia
  - with unexplained heart failure
  - with high risk characteristics*, for which non-invasive diagnostics did not yield reliable conclusions

  Moderate degree of evidence in patients:
  - with high risk characteristics*, for whom a non-invasive test is not possible due to disability or disease
  - for whom certain exclusion of coronary heart disease in cases of suspected disease is indispensable due to occupational constraints (e.g., pilots, firemen)

  Single occurrence indication:
  Patients with stable angina (CCS class I or II) with good response to medication and lack of ischaemic evidence

  No indication:
  - if the patient is unwilling to undergo revascularization therapy
  - if there is no therapeutic consequence
  - in patients with a high comorbidity for whom the risk of coronary angiography is higher than the benefit achieved through a sure diagnosis

  Beware: * Patients with high risk characteristics have a risk of cardiovascular events (death, myocardial infarction) of > 20 %/10 years [calculated according to PROCAM]

  Access:
  - Femoral arteria (Judkins technique)
  - Brachial arteria or radial arteria (modified Sones technique)

  Conclusion: Definitive proof + localization of stenoses of the coronary arteries, functional diagnostics of the left ventricle

  Compl.: myocardial infarction, ventricular fibrillation, cerebral embolism, aneurysma spurium and AV fistulas at the puncture site; acute renal failure in the presence of pre-existing renal failure (existing elevated risk in the presence of concomitant diabetes mellitus) → prevention by prior sufficient hydration
  Mortality rate: < 0.1 % (higher in emergency indications than for elective indications)

  Possibly supplemental diagnostics in the context of coronary angiography:
  - Coronary angioscopy } Evaluation of vascular morphology, plaques
  - Intravascular ultrasound (IVUS) }
  - Intracoronary Doppler flow measurement:
    Evaluation of functional value of a coronary stenosis

Limits of detection of diagnostic techniques for the recognition of CHD:

Method	Degree of stenosis
1. Non-invasive:	
– Ergometry	75 %
– Scintigraphy	70 %
– Stress echo	70 %
– Stress MRT	70 %
– PET	60 %
– EBCT, MSCT	40 %
2. Invasive:	
– Angiography	40 %
– IVUS	20 %

Th.: **I. Causal:**

- Eliminating risk factors for arteriosclerosis:
  - Primary prevention (prior to the occurrence of vascular disease)
  - Secondary prevention (prevention of vascular disease)

  Prevention based on risk stratification → approach:
  - Identification of cardiovascular risk factors: LDL cholesterol, HDL cholesterol, triglycerides, blood pressure, diabetes mellitus, smoking, myocardial infarction or stroke in the family history (particularly at < 60 yrs); age: men > 45 yr., women > 55 yr.
  - Adaption of the intensity of the therapeutic measure to the overall risk:

    > High risk:
    - Vascular disease: coronary heart disease (CHD), peripheral arterial occlusive disease, arteriosclerosis of the aorta, cerebrovascular disease (stroke, TIA, carotid stenosis)
    - Diabetes mellitus
    - Multiple risk factors: 10-year risk > 20 % after PROCAM (see above)

    > Intermediate risk:
    - 2 risk factors and 10-year risk 10 – 20 % after PROCAM
    - Metabolic syndrome (see related section):
      - Abdominal obesity
      - Fasting triglycerides ≥ 150 mg/dl (1.7 mmol/l)
      - HDL cholesterol < 40 mg/dl (1.0 mmol/l) for men, < 50 mg/dl (1.3 mmol/l) for women
      - Blood pressure ≥ 130/85 mm Hg
      - Fasting blood sugar ≥ 100 mg/dl (≥ 5.5 mmol/l)

  Treatment of risk factors:
  - Life-style change: reduce weight, give up smoking: offer smoking cessation courses – nicotine abstinence reduces the cardiovascular 10-year risk by up to 50%!
  - Low fat, fibre-rich diet + addition of polyunsaturated omega-3 fatty acids (e.g., from cold water fish and fish oil)
  - A "Mediterranean" diet (with regular consumption of fruit, salad, vegetables, olive oil, fish, moderate wine consumption) reduces the cardiovascular 10-year risk by 50 % (Lyon Study)
  - Controlled physical training in coronary sport groups (3 to 7 x/week for 15 to 60 min. at 40 - 60 % of the maximum performance capacity). In primary prevention, the cardiovascular 10-year risk was reduced by up to 50 %.
  - Avoidance of stress, over stimulation, acute excessive physical exertion

  Learning to cope with stress and relaxation training
  - Target values for blood pressure: Patients at high risk < 130/80 mm Hg, other risk categories < 140/90 mm Hg
  - Target values for LDL cholesterol:
    - Patients at very high cardiovascular risk: < 70 mg/dl (1.8 mmol/l)
    - Patients at high risk: < 100 mg/dl (2.6 mmol/l)
    - Patients at moderate risk: < 130 mg/dl (3.4 mmol/l)
    - Patients with no elevated risk: < 160 mg/dl (4.1 mmol/l)
  - At low HDL cholesterol levels, optimize triglycerides and LDL cholesterol.
  - Fasting triglycerides ≤ 150 mg/dl (1.7 mmol/l)
  - Optimal adjustment for diabetes mellitus: HbA1c < 6.5 %

  Note.: folic acid, vitamin B6 and B12 can certainly lower the homocysteine level but not the cardiovascular mortality (NORVIT, HOPE2, WAFACS studies).

- In cases of microangiopathy, optimal adjustment of arterial hypertension, diabetes mellitus, exclusion of vasculitis etc.

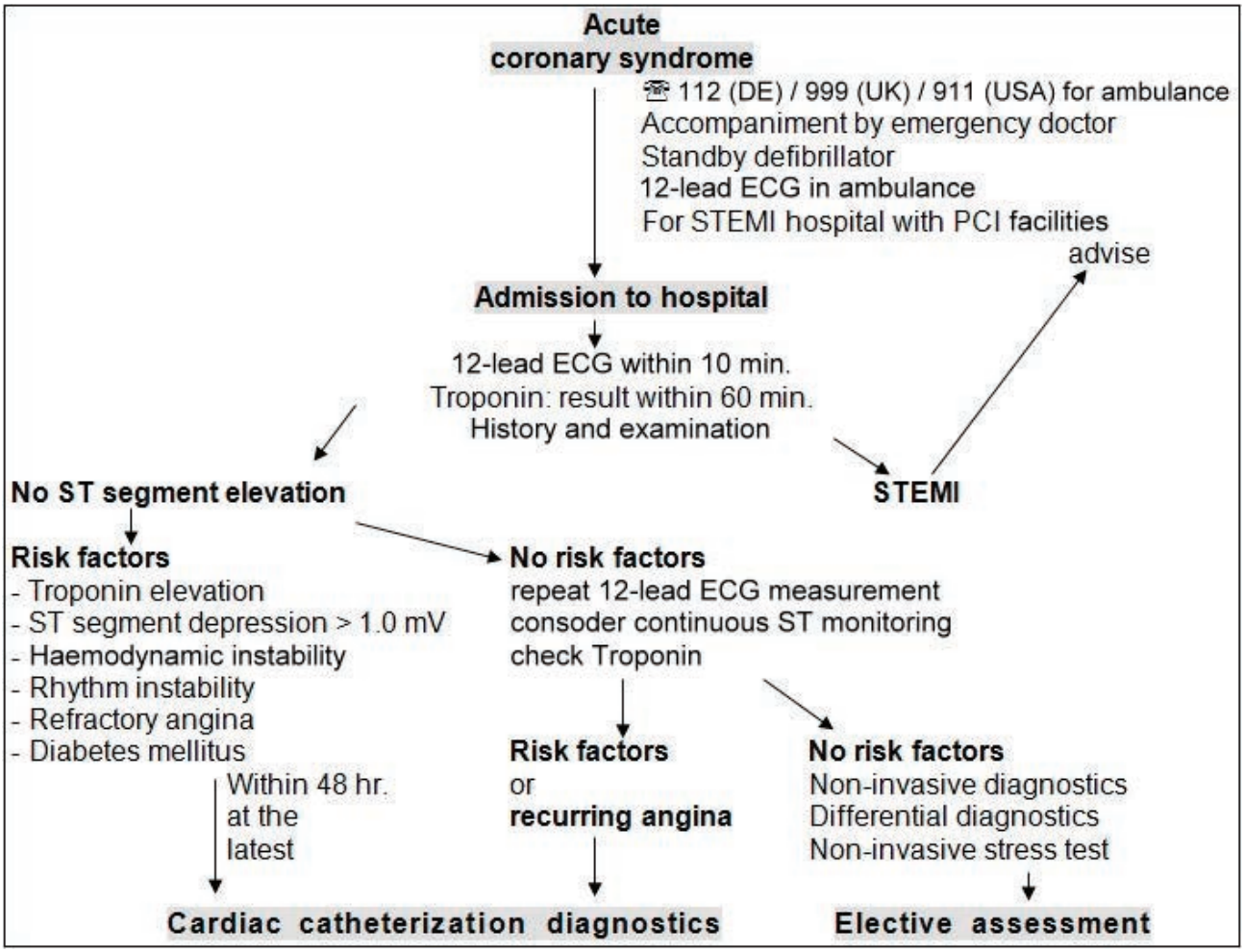
  Note.: ASA is not recommended as primary prevention at this time. Although when taken for primary prevention, the rate of cardiovascular events seems to be reduced.

II: Symptomatics:

Stable angina pectoris is treated on an outpatient basis; unstable angina pectoris is an absolute indication for referral to the hospital via ambulance, since there is an increased risk of MI with possible arrhythmia and/or haemodynamic complications.

***Note**:* Explain the difference between stable and unstable angina pectoris to patients. It is imperative to advise them that an emergency physician should be called at once if there are signs of unstable angina pectoris. Admission to hospital in an ambulance is required.

■ **Treatment of acute coronary syndrome:**



See also *leitlinien.dgk.org*

Initial treatment:

- Oxygen inhalation via nasal tube (4-8 l/min), pulse oximetry check
- Unfractionated heparin (70 IU/kg body wt., max.5000 IU as bolus) or low molecular weight heparin, e.g., Enoxaparin (dose: see manufacturer's specifications)
- ASA (initially 250 - 500 mg, later 100 mg/d) and Clopidogrel (loading dose: 600 mg for intervention within 2 hr. or 300 mg for interventions after 12 hr), maintenance dose: 75 mg/day). clopidogrel in addition to ASA lowers the risk by 20 % (CURE trial).
- Nitroglycerine (1 - 5 mg/hr. IV via perfusor (caution with blood pressure < 90 mm Hg and/or higher grade AV-Block)
- Beta blockers, taking into account side effects and contraindications; optimal heart rate < 60/min
- ACE inhibitors if there is insufficient blood pressure lowering from nitroglycerin and beta blockers
- For severe pain, optionally Morphine 5 mg IV
- For vagal reactions, Atropine 0.5 mg IV, can be repeated
- For nausea / vomiting, antiemetics (e.g., Metoclopramide)

■ **Further treatment depends on ECG and laboratory parameters** (CK, CKMB, troponin I or T)

1. Acute myocardial infarction with initial ST segment elevation (STEMI): for treatment see Ch. Myocardial infarction
2. NSTEMI = Unstable AP/myocardial infarction without ST segment elevation, but increase in cardiac muscle specific laboratory parameters. Rapid performance of a cardiac catheterization with the option for revascularization therapy within 24 to 48 hours.
3. Unstable AP without increase in cardiac muscle specific laboratory parameters (on admission and 6 - 12 hours later). Stabilize the patient and perform an ischaemia test (exercise ECG, myocardial scintigraphy or stress echocardiography) – if the result is positive: indication for cardiac catheter examination with the option for revascularization treatment

■ **Treatment for stable angina pectoris:**

A) Medication:

- Basis therapy (for prevention of a myocardial infarction and lowering the mortality risk):

- Acetylsalicylic acid (ASA) 75 or 100 mg/d
  (side effects + contraindications: see chapter on Thrombosis therapy)
  Alternative for ASA intolerance; e.g. Clopidogrel (75 mg/day)
- Beta blockers (see below)
- Statins

• Anti-angina therapy

1. Beta receptor blockers
   Eff.: lowers the myocardial O_2 requirements by reducing heart rate and blood pressure under stress. Prognostic benefit (lowers mortality) for cases of acute myocardial infarction as well as in post-infarct patients.
   SE: Dose dependent negative inotropic effect, bradycardia, AV block
   Contra: bronchial asthma, AV block ∅ II°, etc.
   (further details and preparations: see chapter on Antiarrhythmics)

2. Nitrates
   Eff.: - Vasodilatation with lowering of the peripheral resistance, blood pressure drop and increase in capacity of the venous vessels: lowering of preload and afterload of the heart → lowering of end diastolic ventricular pressure → better perfusion of the inner layer of the heart (reduced myocardial wall tension)
   - Lowering of the myocardial O_2 demand
   - No effect on prognoses/mortality (purely symptomatic effect)
   SE: headache, drop in blood pressure, reflectoric tachycardia
   Contra: Hypotension, shock, hypertrophic obstructive cardiomyopathy (HOCM) and aortal stenosis; no concomitant prescription of PDE-5 inhibitors (e.g., Sildenafil, Vardenafil, Tadalafil) → risk of myocardial infarction

   ► Glycerol trinitrate (nitroglycerine), e.g., Nitrolingual®:
   Ind: therapy of choice for treating angina pectoris attacks
   Dos: 1 - 2 - (3) 0.8 mg capsules sublingually for treatment of an attack (1 spray = 0.4 mg), onset of efficacy within a few minutes, wears off after 20 – 30 minutes; intravenously for unstable angina pectoris (Intensive Care Unit) 1 - 5 mg/he with blood pressure monitoring!

   ► Isosorbide dinitrate (ISDN):
   To prevent development of tolerance – as is observed with regular administration of long acting nitrates – an interval therapy is recommended (with severely fluctuating nitrate levels). Furthermore, vitamin C should reduce nitrate tolerance.
   Dose: for attacks 5 - 10 mg sublingual, for prophylaxis 1 x daily 1 extended release preparation at 20 - 120 mg orally.

   ► Isosorbide-5 mononitrate (ISMN):
   Is not subject to a first-pass effect in the liver, has a relatively long biological half life of 4 – 5 hr.
   Dose: for prophylaxis 1 x daily 1 extended release preparation at 40 - 60 mg orally

   ► Pentaerithrityl tetranitrate (PETN):
   Dose: for prophylaxis 2 x 50 mg/d orally

3. Molsidomine: effect, side effects + contraindications similar to nitrates, however less development of tolerance
   Dose: 2 - 3 x 2 mg/day orally or 8 mg/day as an extended release preparation

4. Calcium antagonists (CA):
   The L-channel antagonists found on the market block the L- (long-lasting) calcium channels → reduction in peripheral vessel resistance (afterload)
   • Benzothiazepine (Diltiazem) type
   • Phenylalkylamine (Verapamil) type
   Both groups belong to the class IV antiarrhythmic agents (see that section) and may not be combined with beta blockers (danger of AV block and/or bradycardia)
   • Dihydropyridine (Nifedipine) type: for preparations see chapter on hypertension

***Note**:* long acting CAs are considered reserve measures if beta blockers alone are insufficiently effective or contraindicated. Dihydropyridine CAs are contraindicated in the time period of 4 weeks following a myocardial infarction and in acute coronary syndrome.

Effect	Nitrates	Calcium antagonists	Beta blockers
Oxygen consumption	↓	↓	↓
	Preload reduction > afterload reduction	primarily afterload reduction (peripheral resistance ↓)	Reduces afterload and heart rate

5. Ivabradine (Procoralan®):
Eff.: f-ion channel blocker of the pacemaker cells. The anti-ischaemic effect, as with beta blockers, is based on lowering heart rate. No effect on intraatrial, atrioventricular or intraventricular conduction times. Effect is purely symptomatic without prognostic benefit.
Ind: Symptomatic treatment of CHD if beta blockers are contraindicated or not tolerated.
Side effects: visual disorders, bradycardia, etc.
Note interactions and contraindications (manufacturer information)

B) Revascularization

Goals: - Myocardial perfusion improvement
- Improvement of angina pectoris symptoms
- Lowering the risk of (re-)infarct
- Improvement of load and prognosis in CHD

► **Percutaneous transluminal coronary angioplasty = PTCA or percutaneous coronary intervention = PCI:**

1. Standard method: balloon catheter dilatation, usually in combination with:
2. Stent implantation (often following prior balloon dilatation) → 3 objectives:
   - Elimination of (threatening) acute occlusions following PTCA
   - Improvement in vessel patency after inadequate PTCA results
   - Reduction in the relapse rate in comparison to PTCA

   The restenosis rate can be reduced by temporary use of strongly effective thrombocyte aggregation inhibitors (ASA + clopidogrel, GP IIb/IIIa antagonists). Drug eluting Stents (DES) which are coated with immunosuppressives, should prevent excessive intima hyperplasia with the danger of restenosis and reduce the rate of re-interventions. However, due to delayed endothelialization, they also increase the risk of a stent thrombosis. In meta-analyses of studies, a trend towards slightly elevated mortality of the DES patients was exhibited in comparison to uncoated stents (bare metal stents). For this reason, 12 months after DES implantation, dual platelet inhibition with ASA and clopidogrel should be administered (see also the position of the German Society for Cardiology (DGK) on the internet).

   Current clinic trials:
   -Bio-resorbable stents (Polylactic acid, degradable magnesium alloy) give support for a few weeks, and then dissolve and provide free physiological movements of the treated wall
   -healing stents are coated with antibodies; they attract cells to grow into the vascular wall providing fast healing
3. Other catheter methods only have limited significance in special indications:
   - Rotation angioplasty (Rotablation): severely calcified stenoses, outlet stenoses
   - Direct coronary atherectomy (DCA) for ostial stenoses
   - Ultrasound angioplasty/ultrasound thrombolysis
   - Intracoronary aspiration thrombectomy (ICAT): suction of a thrombus in a recent myocardial infarction
   - Cutting balloon: treatment of complex stenoses

Ind: vascular disease with significant stenoses (> 70 %); selected patients with 2-vessel disease
Acute and chronic closure of native coronary and bypass vessels
Therapeutic target: Partial or complete coronary perfusion (corresponding to TIMI classification II or III)

CI: Bifurcation stenosis of the unprotected main stem of the left coronary artery (→ bypass operation)

Success rate of PTCA: immediate success rate (remaining degree of stenosis: < 50 % = grade 1): 90 - 95 %

Mortality of PTCA: in stable angina pectoris < 0.5 %, in unstable angina pectoris up to 1 %

Complications:

- Dissection of the coronary artery by rupture formation in atheromatous plaque that is too severe with acute coronary occlusion (7 % for PTCA) and possible infarction (2 %) → 3 treatment possibilities:
  1. Insertion of a stent = method of choice (success rate 85 %)
  2. Emergency bypass operation after stent insertion is rare
  3. Conservative intensive medical infarct therapy.
- Subacute stent thrombosis (depending on the risk situation 0.5 - 5 %, particularly after discontinuing clopidogrel!)
- Reformation of stenosis: After balloon dilatation up to 40 %, after stent implantation < 30 %, after DES < 10 %, whereby 95 % of al restenoses appear within 6 months. Most patients with restenosis can undergo another PTCA/stent implantation without increased risk.
- Intravasal embolization (use of protection systems, particularly in bypasses)
- Brain embolisms in elderly patients with generalized arteriosclerosis (0.4 %)

▶ **Operative coronary revascularization (CABG = coronary artery bypass graft)**

Ind: • Significant main stem stenosis of the left coronary artery
• Symptomatic 3-vessel disease with complex stenoses
• Symptomatic 2-vessel disease with so-called main stem equivalent (= stenoses near the stem of RIVA and RCX)
• 3-vessel disease and 2-vessel disease with involvement of the proximal RIVA

Prerequisites:
• Significant (> 50 %) proximal coronary stenosis
• Evidence of viable myocardium in the revascularization region
• Peripheral coronary artery that can be anastomized

CI (relative): • Generalized (proximally + distally localized) coronary sclerosis
• Considerably limited pumping function of the heart (ejection fraction of the left ventricle < 20 - 30 %)
• Other general medical contraindications

A) Classic operative procedure

Sternotomy access, stopping the heartbeat with the use of a heart-lung machine (or without heart-lung machine = off-pump technique)
– Bypass of the coronary stenosis via the right or left A. thoracica (mammaria) interna (RIMA or LIMA bypass)
– A. radialis bypass
– Aorto-coronary venous bypass (ACVB)

B) Minimally invasive procedures (forgoing sternotomy):
• MIDCAB (minimally invasive direct coronary artery bypass): revascularization of the Ramus interventricularis anterior (RIVA) with left sided Arteria-mammaria-interna-bypass (LIMA bypass) on the beating heart via an anterior mini thoracotomy
• OPCAB ("off-pump coronary artery bypass"): operative revascularization of multivessel disease on the beating heart (without heart-lung machine)
• Hybrid procedure (combination of operative revascularization +PCI, e.g., no bypass material is inserted)

Results:
– Hospital mortality in stable angina pectoris, normal left ventricular function and elective operation: approx. 1 % (higher in unstable angina pectoris and/or heart failure). In approx. 5 % of patients, myocardial infarctions (usually small) occur.
– 80 % of patients are symptom free postoperatively
– The mortality rate within the first 5 years for three-vessel disease and left main stem stenosis is 30 % lower than with conservative treatment. Annual death rate approx. 2 % → 10-year survival rate approx. 80 % (in patients with limited left ventricular function, the results are less favourable).
– Restenosis rate:
Venous bypass: up to 50 % after 10 years
IMA bypass: only 10 % after 10 years! After IMA bypass, 27 % fewer patients die within 15 years than after venous bypass!
A. radialis bypass: Restenosis rate approx. 10 % after 35 months

Post-treatment after PTCA or bypass op.:
Thrombocyte aggregation inhibitors (ASA 100 mg/day) are used as long-term therapy. Switch to thienopyridine (clopidogrel 75 mg/day) in case of intolerance to ASA.
After stent implantation, dual platelet inhibition with ASA / clopidogrel for a limited time: uncoated stents at least 4 weeks, coated stents (DES) at least 12 months.
Side effects and contraindications: Refer to respective sections

C) Pain treatment for angina pectoris refractory to treatment:
Spinal cord stimulation (SCS): Using a probe in the peridural space, the patient can trigger an electrostimulation when he perceives pain which has a pain-relieving effect.

D) Heart transplantation:
Ind: CHD with terminal heart failure (NYHA IV)

E) Autologous stem cell transplantation:
Intracoronary injection of autologous myoblasts or stem cells for cases of recent myocardial infarction; long-term data are still outstanding.

Prg: The following factors determine the course of CHD:

1. Localization of stenoses and number of affected coronary arteries:

Annual mortality rates (without revascularization):

1- vessel disease:	3 - 4 %
2- vessel disease:	6 - 8 %
3- vessel disease:	10 - 13 %
Main stem stenosis of the LCA:	> 30 %

2. Extent of myocardial ischaemia: The risk of infarct rises with the frequency and severity of the angina pectoris attacks

3. Functional status of the left ventricle: The prognosis worsens with increasing left heart insufficiency and the occurrence of higher grade ventricular arrhythmias (see heart failure). A resting EF < 35 % is associated with an annual mortality rate > 3 %.

4. Progression of coronary sclerosis, dependent on the extent of vascular risk factors: see Risk stratification!

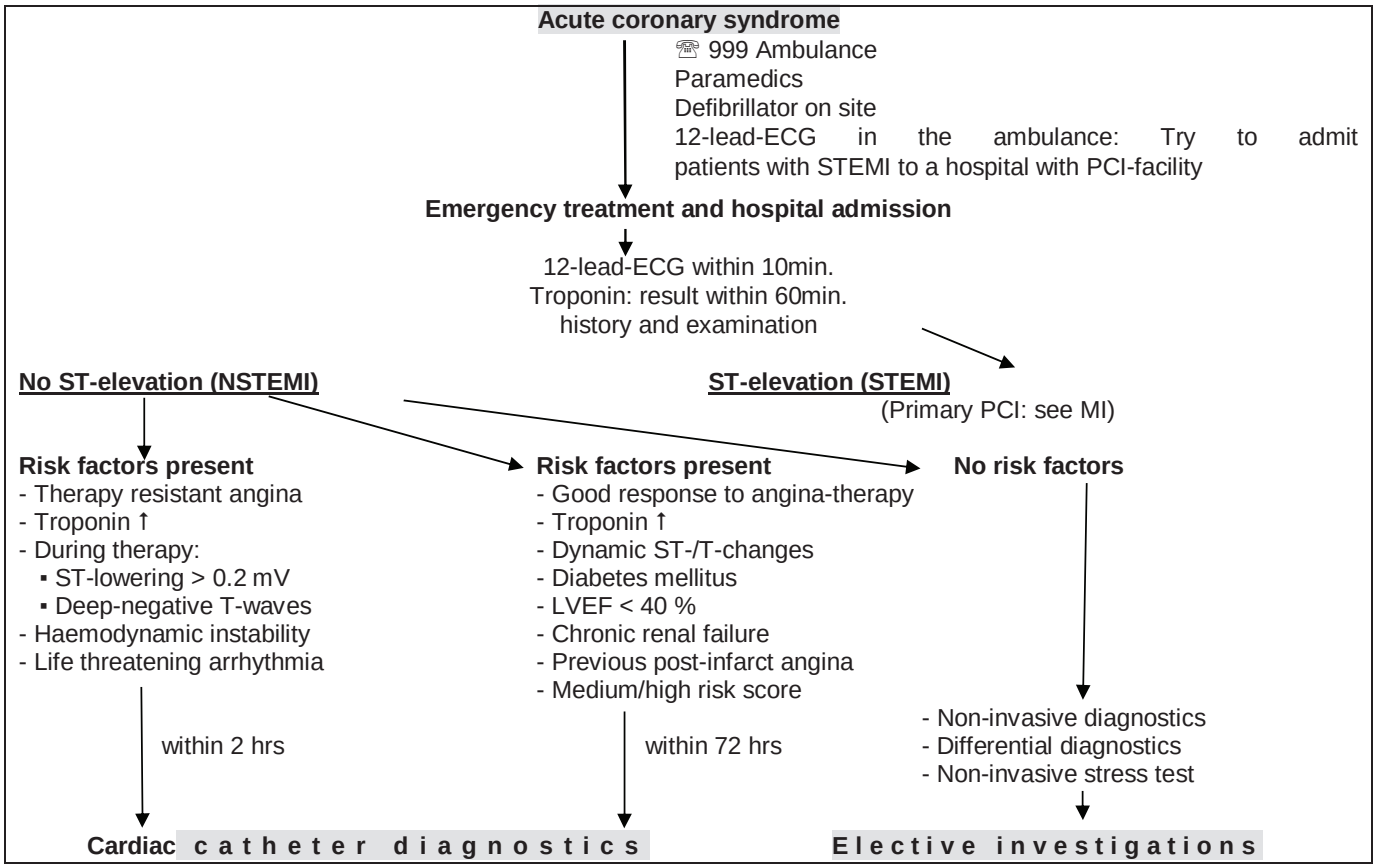
Note.: According to the results of the Courage trial, PCI therapy does not significantly improve the prognosis in stable CHD which is optimally treated with medication (observation period 4.6 years).

ACUTE CORONARY SYNDROME **Fehler! Textmarke nicht definiert.**

Def: The acute coronary syndrome consists of unstable angina pectoris, acute myocardiac infarction and sudden cardiac death. According to ECG-changes we divide into those with ST-elevation (STEMI) and without ST-elevation (NSTEMI/unstable angina).

The first assessment aims to allocate the patient to one of the following 3 groups (taking in consideration the type of pain, age, risk factors, history of CHD and ECG:

1. CHD / ACS unlikely
2. ACS without ST-elevation (NSTEMI)
3. ST-elevation MI (STEMI)



Initial treatment:

- O_2-inhalation via nasal tube (4-8 l/min), pulse oximetry when O_2-Sat is <90%
- Unfractionated Heparin (70IU/kg BW, max.5000IU as bolus) or low molecular weight Heparin, e.g. Enoxaparin (1mg/kg s.c.), Fondaxaparinux (2.5mg/day); always follow manufacturer's guidelines)
- Aspirin (initially 250-500mg, later 100mg/day p.o.) and Clopidogrel (loading dose: 300mg, maintenance dose: 75mg/day). Clopidogrel in addition to Aspirin lowers the risk of cardiovascular death by 20% (CURE trial).
- Nitroglycerol 1 capsule (=0.8mg) or 2 puffs (=0.8mg) s/l; in hospital 1-5mg/hr i.v. via perfusor (caution when BP is <90mmHg and/or in higher grade AV-block)
- β-blockers, taking into account side effects and contraindications; optimal heart rate <60/min
- For severe pain consider Morphine 3-5mg i.v.; this may be repeated until the patient is pain free
- For vagal reactions: Give Atropine 0.5mg i.v. (can be repeated)
- For nausea/vomiting: Give antiemetics (e.g. Metoclopramide)

- **Further treatment depends diagnosis confirmation and risk assessment**
  1. Acute MI with initial ST-elevation (STEMI): for treatment see chapter 'Myocardial infarction'
  2. NSTEMI = Unstable angina/MI without ST-elevation, but increased cardiac muscle specific laboratory tests. Cardiac catheterization with the facility for re-vascularisation therapy. Priority depends on the individual patient's risk (see graphic)
  3. Unstable angina without abnormal cardiac muscle specific laboratory tests (on admission and 6-12hrs later). Stabilize the patient and perform an ischaemia test (exercise-ECG, myocardial scintigraphy or stress-echocardiography) – if the result is positive: indication for cardiac catheter examination with the possibility for re-vascularization treatment.

MYOCARDIAC INFARCTION (MI) [I21.9]

Syn: heart attack

Def.: Ischaemic myocardial necrosis, usually on the basis of coronary heart disease (CHD) with high-grade stenosis or occlusion of the coronary artery. According to the WHO definition, a MI is present when markers of myocardial damage are detectable (troponin T or I, CK-MB) in the presence of unstable angina if additional ischaemic symptoms are present (exception: silent infarcts), ECG changes occur, or a corresponding angiographic finding is made.
The myocardial infarction is a form of acute coronary syndrome (see corresponding section)

Definition of myocardial infarction:
Type1: MI due to ischaemia, caused by a primary coronary event like plaque rupture, tear or dissection.
Type2: Ischaemic MI, caused by coronary spasm, coronary embolism, arrhythmia, anaemia, hyper-/hypotension
Type3: Sudden cardiac death, sometimes after herald symptoms indicating myocardial ischaemia
Type 4a: MI associated with percutaneous cardiac intervention
Type 4b: MI caused by stent-thrombosis, diagnosed by angiography or post mortem
Type 5: MI associated with bypass operation (CABG)

Ep.: Incidence (infarcts/100,000/yr.) exhibits major geographical differences: < 100: Japan; 100 - 200: Mediterranean countries, Switzerland, France; approx. 300: Germany, North America, Austria, The Netherlands, Poland; 300 - 400: Denmark, Scandinavia; 400 - 500: Ireland, England, Hungary; > 500: North Ireland, Scotland, Finland. The lifetime prevalence in Germany is approx. 30 % for men and 15 % for women (m : f = 2 : 1).

Aet.: Arteriosclerosis with risk factors (see Chap. CHD); rarely coronary embolisms

Pg.: Arteriosclerosis → stable → unstable = vulnerable plaque → plaque rupture → thrombotic occlusion → unstable angina pectoris or myocardial infarction

Triggering factors:
- Sudden physical exertion, stress situations with marked fluctuations in blood pressure
- There is an acute risk of infarction in cases of unstable angina pectoris (20 %)!
- 40 % of all infarctions occur during the morning hours (6 am – 12 noon). Circadian rhythm of the clustering of infarcts is due to the increase in clotting activity during this time period.

Cl.:
- ▶ Intensive, angina pectoris pain of long duration (precordial pain), which shows little improvement by rest or nitroglycerin. Pain radiation: See Clinical manifestations of angina pectoris. There may be only retrosternal feeling of pressure.

  However: 15 - 20 % of myocardial infarctions occur without pain ("silent" infarctions), in particular in diabetes mellitus (as a result of autonomic diabetic neuropathy) and in elderly patients. 40 % of all infarction patients have no angina pectoris history (infarction = first manifestation of CHD!).

  Diagnostic difficulties are encountered in atypical pain symptomatology, in particular in diabetics, women and elderly patients: there may be no thoracic pain, only upper abdominal pain, in particular in posterior wall infarcts.
- ▶ Feeling of weakness, anxiety and accompanying vegetative symptomatology (sweating, nausea, vomiting, etc.), possibly also subfebrile temperatures
- ▶ Cardiac arrhythmia (95 % of cases): Ventricular arrhythmias (ventricular tachycardia, ventricular fibrillation), AV blocks
- ▶ Often drop in blood pressure, possibly with cerebral functional disorders

  However: In the presence of elevated sympathetic tone, the blood pressure can also be normal or slightly elevated.
- ▶ Symptoms of left heart insufficiency (1/3 of patients): Dyspnoea etc. – see chapter on Cardiac insufficiency
- ▶ Right ventricular infarction: absence of lung congestion but congestion in the thoracic veins; often bradycardia

Ausc.: In the presence of cardiac complications, characteristic sound findings may result, e.g.,
- Pericardial rub in pericarditis epistenocardica

- Systolic sound in ventricular septal perforation due to necrosis or in cases of mitral insufficiency as a result of papillary muscle dysfunction or dilatation of the heart with relative AV valve insufficiency ➔ daily auscultation!
- Moist rales in pulmonary congestion/pulmonary oedema

Lab.:

- Non-specific accompanying parameters: Leukocytes, glucose, BSG ↑, CRP ↑
- Biomarkers:
  - Myoglobin: A recent infarct will already exhibit an increase in myoglobin in serum after 2 hours. However, the positive myoglobin evidence is not proof of the infarct because skeletal muscle damage can also lead to elevations in myoglobin.

  - Troponin I and T: Cardiac troponin I and T are cardiac muscle specific and very sensitive. They are the earliest evidence of myocardial necroses. Elevation begins 3 hr after the start of the infarct, maximum after approx. 20 hr, normalization after 1 - 2 weeks. If troponin I or T increase in the presence of unstable angina pectoris without ST segment elevation/ECG changes, this is referred to as NSTEMI = "non ST segment elevation myocardial infarction".
    Positive troponin values are also present after severe pulmonary embolism, heart op, PTCA, anthracyclines therapy, and renal insufficiency, etc.
  - Enzyme diagnostics:
    - Creatine Kinase (total CK): Signal enzyme for the diagnosis of damage to the heart and skeletal musculature. The degree of CK elevation correlates with the size of the infarct.
      The total CK is the total of 4 isoenzymes:
      - CK-MM (skeletal muscle type) - CK-MB (myocardial type)
      - CK-BB (brain type) - CK-MiMi (mitochondrial type)

      Causes for elevation in total CK, e.g.,
      - Myocardiac infarction and myocarditis
      - IM injections, operations, trauma, physical exertion, epileptic seizure, arterial embolisms/occlusions, resuscitation, childbirth
      - Muscle diseases (muscular dystrophy, polymyositis, rhabdomyolysis, muscle injury)
      - Intoxications, alcoholism and delirium tremens
      - Necrotizing pancreatitis, acute liver cell necrosis, malignancies
      - Endocrine myopathies: hypothyreosm, hypoparathyroidism, M. Addison
      - Trichinosis, Coxsackie B virus infection
      - Medications: CSE-inhibitors, lipid lowering medications, tricyclic antidepressants
      - Alcohol abuse, heroin abuse

      CK-MB proportion between 6 - 20 % of the total CK – measured within a time period of 6 - 36 hr. after a infarct-suspect event – indicate enzyme release from the cardiac musculature (DD: infarction, myocarditis, cardiac operation, cardiac contusion).
      CK-MB proportion < 6 % of the total CK indicate enzyme release from the skeletal muscle.
      CK-MB proportion > 20 % of the total CK are present in disorders due to the isoenzyme CK-BB or the presence of a macro CK.

      CK-MB elevations can rarely be feigned by increases in activity of:
      - CK-BB (e.g., by tumours, neurological diseases)
      - Macro-CK: 2 variants:
        - Macro-CK-1 = Immunocomplex of CK-BB and IgG: Occurs in 1 % of the elderly (in particular, women); it does not indicate any disease
        - Macro-CK-2 = Association of several CK-MiMi molecules; Occurs, e.g., in malignant tumours, necrotizing liver diseases

      Mass CK-MB (CK-MB protein concentration)
      Is determined using enzyme immunoassay technique (ELISA) and is more sensitive than the CK-MB activity determination. The specificity of the mass CK-MB determination has been significantly improved by the discontinuation of the analytical interference with CK-MM, CK-BB, macro-CK type 1 and type 2. Furthermore, a relative increase in CK-MB protein concentration of > 4-fold in 90 min. after thrombolysis therapy is a sign of successful reperfusion.

Diagnostic sensitivity (%) of the parameters in the early phase of acute myocardial infarction:

Parameter	Hours after onset of pain		
	0 - 2	3 - 4	5 - 6
Troponin I or T	25	60	80
Mass CK-MB	30	70	90
CK-MB activity	10	25	55
Myoglobin	35	80	95

- AST = GOT:
  Since liver, heart and skeletal muscle have relatively high GOT (AST) activities, this is a non-specific parameter. Elevation approx. 4 h after the start of infarction, normalization after 3 - 6 days.
  Simultaneous elevation in GPT indicates liver disease or hepatic congestion in the presence of decompensated (right) heart insufficiency.
- LDH:
  As a cytoplasmatic enzyme of all tissues, it is a non-specific parameter. However, it is important for the delayed diagnosis of a myocardial infarction since the LDH only normalizes after 1 -2 weeks.

■ Evidence of h-FABP (heart fatty acid binding protein) in the rapid test: should already be positive approx. 30 minutes after the start of the infarction.

E C G

The ECG finding can be negative within the first 24 hours; therefore, an infarct can only be ruled out after two ECGs have been conducted at an interval of 24 hours after an infarction, as long as troponin I/T and CK-MB remain normal. If available, compare with an older ECG.

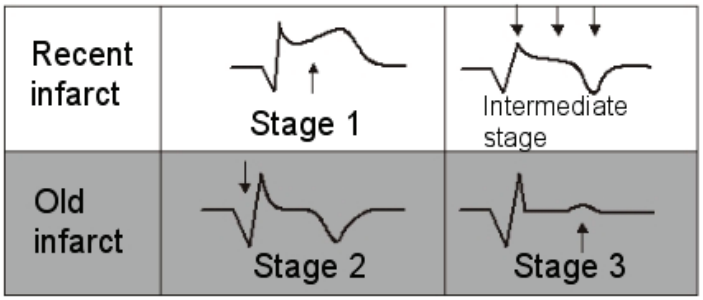
The informative value of the ECG:
1. Extent and localization of the infarction (extent of loss of R-wave height, which branches are primarily affected)
2. Age of the infarction (see below)

The actively contracting heart muscle represents a kind of Faraday's cage. In a transmural infarction, a 'hole in this cage' results from the breakdown of potentials belonging to the infarct region and a distortion of the vector loop opposite of the infarct region.

ECG signs that arise directly over the infarct region by a tap, are called direct signs of infarction, mirror-opposite changes in the opposite conductor are known as indirect infarct signs.

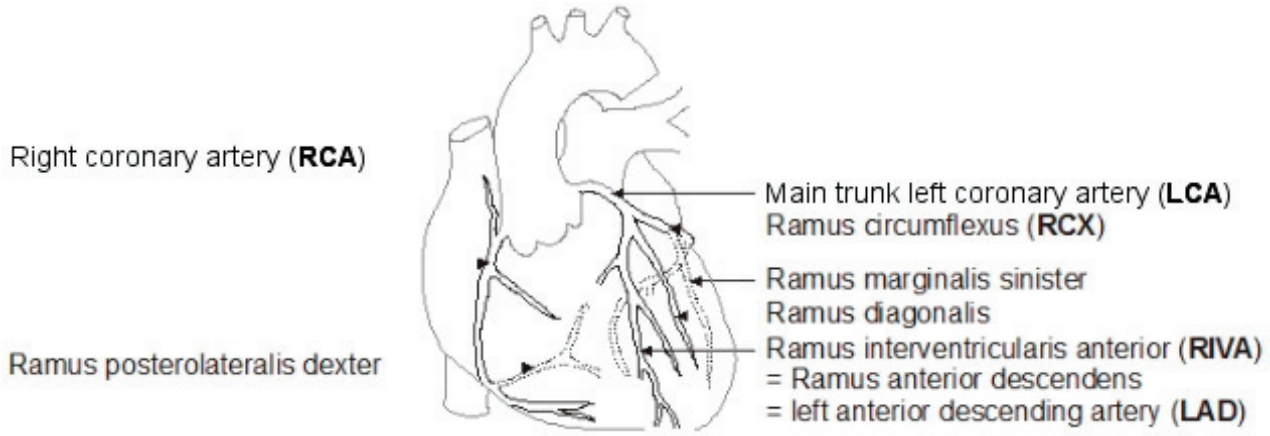
► ST segment elevation infarct (STEMI) **with direct infarction signs in the ECG → 3 stages:**

- St. 1: recent infarct (acute stage):
  The earliest ECG change in the form of briefly increased T wave amplitude (referred to as "hyperacute T wave") usually goes undetected. At the border between healthy and damaged myocardium, there is the formation of an injury potential with excessive ST segment elevation (monophasic deformation of the chamber complex). The ST segment runs immediately from the decreasing R and joins into the T spike forming a plateau or cupular formation ("T-en-dôme").
- St. 2: intermediate stage:
  With a decrease in the excessive ST elevation, the R loss becomes visible as well as a QS complex or a broad deep Q spike = pathological Q or Pardee-Q (width ≥ 0.04 sec; depth > ¼ R).
  Formation of a terminal negative T spike = same branch, peak negative T inversion
  DD ST elevation: 1) heart wall aneurysm, 2) pericarditis, 3) Prinzmetal angina
  DD deep Q wave: 1) hypertrophic cardiomyopathy, 2) pulmonary embolism (SI/QIII type), 3) WPW-syndrome (sterna positive type)
  DD terminal negative T:
  1. Transmural infarct, St. 2 or 3
  2. Non-ST elevation infarct (NSTEMI)
  3. Pericarditis (secondary condition)
  4. Myocarditis
  5. HOCM
- St. 3: Old infarct (chronic stage):
  Persistent terminal negative T or T normalization. Although a small R-spike can reform, the deep Q usually remains life-long.



Direct Infarct signs

***Note**:* In LBBB (pre-existing or as a complication of infarction), the signs of infarction can be less obvious such that the ECG does not allow a certain diagnosis under these circumstances.



▶ **Non-ST segment elevation infarction (NSTEMI):** Do not exhibit pathological Q spikes, possibly slight R spike reduction, ST segment depression and same-branch negative terminal T.
In these cases, only positive serology (enzyme increase, troponin T or I) provides evidence of recent myocardial infarct.

Infarction localization:

In most cases, infarcts involve the musculature of the left ventricle. The location corresponds to the supply region of the occluded coronary arteries (see diagram). Depending on the localization of the infarct, the typical ECG changes occur in certain conduction lines.
The variability of the coronary arteries makes it almost impossible to localize the occlusion of the coronary vessel with certainty from a typical ECG. This is only possible using angiography. However, the following classification can be considered an aid for infarct localization:

Coronary artery	Infarct localization	Direct signs of infarct	Indirect signs
RIVA proximal	Large anterior wall infarct	V1-V6, aVL, I	(II), III, aVF
RIVA after exit of the diagonal branches	Anteroseptal infarct	V1-V4, aVL, I	(II), III, aVF
Diagonal branch	Lateral infarct	aVL, I, V5-V7	
Posterolateral branch	Posterolateral infarct	II, III, aVF, V5-6	I, aVL, V1-3
RCX	Strict posterior posterior wall infarct	V7-V9, aVF, III	V1-2
RCA	Inferior posterior wall infarct Right ventricular infarct	II, III, aVF V3r-V6r, V1	V1-3

Isolated right ventricular infarcts are rare. Within the context of inferior posterior wall infarcts, an infarct expansion to the right ventricle can occur → write an ECG if right thoracic involvement is also suspected (V3r - V6r).

Imaging Techniques

1. (Colour duplex) echocardiography:
   a) Morphological cardiac diagnostics (heart enlargement, valve status, evidence of thrombi (highest sensitivity using TEE) and complications: pericardial effusion, papillary muscle dysfunction or tear with acute mitral insufficiency, ventricular septal rupture)
   b) Functional diagnostics: Evaluation of ventricular wall motility, pump performance, atrial and ventricular filling and valve function
   - Regional wall motion disorders:
     - Hypokinesia (reduced wall motion)
     - Akinesia (absense of wall motion)
     - Dyskinesia (systolic external movement)
     - Aneurysms (see below for definition)
   - Reduced/lack of increase in thickness of the infarct zone

   ***Note**:* In recent cardiac infarcts, the localized wall motion disorders occur very early in the course of time (even before enzyme and ECG changes). Absense of localized wall motion disorders indicates with 95 % predictive value, that there is no myocardial infarction. The age of the infarct cannot be determined from the echo.

2. Left heart catheter examination (gold standard):
- Coronary angiography: Identification of stenoses or occlusions of the coronary arteries
- Prerequisite for PTCA/bypass operations
- Levocardiogram: Identification of hypo-/akinetic ventricular wall areas (infarction size)
- Pressure measurement (aortal pressure, LV pressure) and determination of cardiac time volumes and ejection fraction

3. MRT: Early infarct localization (late enhancement)! Evaluation of myocardial perfusion and contractility

Complications after myocardial infarction:

▶ Early complications: **Most dangerous period: The first 48 hours! 40 % of patients do not survive the first post-infarct day!**

1. Cardiac arrhythmias (95 - 100 %) e.g.,
   - Ventricular extrasystoles (95 - 100 %): Frequent polymorphic VES, R-on-T phenomenon and couplets are regarded as warning arrhythmias with increased risk of ventricular fibrillation. However, ventricular fibrillation can also occur without warning arrhythmias!
   - Ventricular tachycardia and ventricular fibrillation:
     Ventricular fibrillation occurs most frequently within the first 4 hours after an infarction; in 80 % of all cases, within the first 24 hours. 80 % of patients who die during the infarction succumb to a ventricular fibrillation.
   - Atrial fibrillation with absolute tachyarrhythmia (poor prognosis)
   - Bradycardic cardiac arrhythmias: Sinus bradycardia, AV-blocking (particularly in inferior infarction)

   ***Note**:* Ventricular fibrillation is the most frequent cause of death following infarction and pump failure is the second most common!

3. Complications from extensive necrosis:
   - Rupture of the heart wall with pericardial tamponade (perforation is often hidden)
   - Ventricular septum rupture (→ newly occurring systolic murmur! Colour Doppler)
   - Papillary muscle rupture can occur and is associated with acute mitral regurgitation (→ new onset systolic murmur!, colour duplex sonography)

▶ Late complications:
- Cardiac wall aneurysms [I25.3]: up to 20 % of all infarct patients
  Di.: Echo: Systolic + diastolic bulging of the thinned left ventricular wall with systolic paradoxical outward wall movement; usually in the region of the anterior wall apex, less often in the basal posterior wall; thrombus formation in approx. 50 %.
  ECG: possibly persistent ST elevation
  Complications of aneurysms: embolisms, left heart failure, arrhythmias, rupture with pericardial tamponade
- Arterial embolisms; risk of thromboembolism with the detection of mural LV thrombus 5 %
- Early pericarditis (Pericarditis epistenocardica) some days after infarct
- Postmyocardial infarction syndrome = "Dressler syndrome" [I24.1]: 1 - 6 weeks after infarct in approx. 3 % late pericarditis/pleuritis occurs - Th.: NSAID, possibly corticosteroids
- Arrhythmias
- Cardiac insufficiency
- Persistent or recurrent angina pectoris and recurrent infarct

DD:
- Angina pectoris: Pain lasts only for minutes, responds to nitro, patient is restless – infarct patients are often restless with cold sweat (pre-collaptic)
- Particularly in case of posterior myocardial infarction the infarction pain can project itself infradiaphragmally → DD of the acute abdomen (biliary colic, acute hepatomegaly, perforated ulcer, acute pancreatitis, etc.
- Pulmonary embolism with pleural pain (D-dimer elevation) (possibly also accompanied by infradiaphragmal projection), collapse and ECG images similar to infarction.
  Di.: Typical enzyme constellation with myocardial infarction.
- Dissecting aneurysm or aortal dissection: severe, sometimes wandering chest pain; in the proximal type, Stanford A dissection there may be a weakened or missing pulse and blood pressure difference between both arms, in aortal valve insufficiency, there is a diastolic murmur.
  Di.: MRT or CT chest, CXR (doubled aortal contour), transesophageal colour duplex echocardiography! (details: see Chap. Hypertension)
- Takotsubo cardiomyopathy: cardiac ischaemic syndrome with balloon-like reversible akinesia of the cardiac apex in the presence of unremarkable coronary angiogram (see Cardiomyopathy) apparently triggered by microvascular spasms
- Further DD: see chap. CHD!

Di.:
1. History / hospital
2. ECG
3. Biomarkers: Enzymes, troponin T and I
   Do not delay the therapeutic decision by waiting for any biomarkers!
4. Imaging techniques (Echo, etc.)

Th.: 1. General measures
2. Reperfusion therapy
3. Prophylaxis of a coronary re-thrombosis
4. Treatment of complications

A) **Pre-hospital:**

- Call Emergency (Germany tel. 112, UK tel. 999, USA tel. 911)
- While still in the ambulance make a decision about possible referral to a centre with PCI option, taking into consideration the time passed since the onset of pain and the 12-lead ECG (STEMI).
- If left heart insufficiency: position the patient sitting upright!
- Venous access, no IM injections, surveillance via monitor + availability of defibrillator
- O_2 supply via nasal tube (3 ℓ O_2/min, pulse oximetry monitoring)
- Administration of nitrates: e.g., nitroglycerin (1 capsule = 0.8 mg) sublingual or 2 puffs (= 0.8 mg) with blood pressure monitoring (contraindication: BPsyst < 100 mm Hg), nitro infusion via metering pump, if needed
- Sedation and analgesia as needed (see below)
- Unfractionated heparin (60 IU/kg body weight, max. 5000 IU IV) or low molecular weight heparin (dosage according to manufacturer's instructions) **and** acetylsalicylic acid (250 - 500 mg ASA IV)
- Beta blockers: If there are no contraindications, cautious administration of beta blockers which reduce the risk of ventricular fibrillation and favorably affect overall mortality.
- Initial treatment of complications (as described below)

***Note**:* Immediate administration of ASA (even if myocardial infarction is just suspected) has been shown to reduce the mortality rate by over 20 % in the ISIS-2 trial!

B) **In hospital:**

1. General measures
   - Intensive care station during the initial days with circulatory system monitoring (rhythmologic and haemodynamic monitoring) and equipment for resuscitation
   - Bed rest, the patient sitting upright if there are signs of left heart insufficiency
   - Protect the patient from any stress, medication for sedation, e.g., Diazepam, initially 5 mg slow i.v.
   - O_2 administration vial nasal tube (3 l/min, pulse oximetry monitoring)
   - Light diet, make sure that the patient can open his bowels regularly
   - Treatment of pain:
     - Nitrates relieve the heart and also have a positive effect on infarct pain
       Side effects: headaches, drop in blood pressure, reflectory tachycardia
       Contraindications: systolic blood pressure < 100 mm Hg
       Dose: glycerol trinitrate (nitroglycerin): 1 - 2 0.8 mg capsules sublingually, subsequently 1 - 5 mg/hr. via infusion under BP monitoring
       or: Isosorbide dinitrate (ISDN): 2 - 10 mg/hr. via infusion with BP monitoring
     - Administration of analgesics: for severe pain, opiates, e.g., morphine: 2 - 5 mg slow IV
       Side effects: respiratory depression, hypotension, nausea
   - ASA, clopidogrel, beta blockers and ACE inhibitors lower early mortality associated with myocardial infarction:
     - ASA: continuation of ASA therapy started in the pre-hospital phase (100 mg/day)
     - By additional administration of clopidogrel (75 mg), cardiovascular events and death can be lowered by 20 % (CURE trial); be aware of side effects (higher risk of hemorrhage) + contraindications
     - Beta blockers: immediate administration if there are no contraindications (see above), regardless of any concomitant fibrinolysis or PCI. In case of contraindications within the first 24 hr., re-evaluation of a possible later beta blocker therapy.
     - ACE inhibitors: start within 24 hr. for anterior wall infarction, pulmonary congestion, LVEF < 40 % if there are no contraindications.
     - AT1 receptor antagonists (Valsartan): if the patient doesn't tolerate ACE inhibitors
     - CSE inhibitors should have a positive effect on plaque stabilization in acute myocardial infarction (e.g., MIRACL trial).

Caution Don't give any IM injections, as they cause non-specific CK elevation and because of a possible planned fibrinolysis/anticoagulant therapy.

2. Reperfusion therapy:

   A) Acute PTCA with or without stent implantation:

   Results: The combined rate point of death and reinfarction within the first 30 days was 8 % after PCTA in the DANAMI-2 trial and 13.7 % after lysis. The rate of restenosis can be reduced by temporary use of clopidogrel, GPIIb/ IIIa antagonists as well as DES (drug eluting stents).

   B) Conservative therapy with activators of fibrinolysis (fibrinolytic agents, thrombolytic agents):

   This should be implemented as rapidly as possible ("time is muscle") → success criterion: patency (reperfusion) rate within 90 minutes after the start of thrombolysis.

   Prerequisites:

   - No contraindications (see chap. Deep vein thrombosis)
   - Recent infarct with ST elevation (STEMI) up to 6 hr. after the onset of pain without the possibility of an acute PTCA (a benefit is also possible up to 12 hr.)

- Don't perform any fibrinolysis therapy prior to planned PTCA

Drugs (Details: see Chap. Deep vein thrombosis):

- Streptokinase (SK) has an indirect fibrinolytic effect (all other fibrinolytic agents have a direct effect)
- tPA = tissue-type plasminogen activator = Alteplase

- Genetically engineered tPA preparations with longer half life:
  - rPA = reteplase (T50 = 15 min.)
  - TNK-tPA = tenecteplase (T50 = 20 min.)
  - nPA = lanoteplase (T50 = 25 min.)

	SK	TNK-tPA tenecteplase
Antigenicity	+	-
Plasma half life	26 min.	20 min.
Pre-injection of corticosteroids	+	-

	rPA = reteplase	tPA = alteplase
Antigenicity	-	-
Plasma half life	15 min.	6 min.
Pre-injection of corticosteroids	-	-

Concomitant heparin therapy improves the lysis results with tPA/rPA use.

Success rates: Recanalisation is observed in 70 - 80 % of cases (patency rate after 90 minutes). Early thrombolysis can reduce mortality after 35 days by 50 %.

	Dosage	**Concomitant heparin therapy**
Streptokinase (SK) Anistreplase	1.5 Mio IU over 30 - 60 min. 30 U in 5 min. IV	No initial administration Heparin after 12 to 24 h
Alteplase (tPA)	15 mg IV bolus 0.75 mg/kg over 30 min., followed by 0.5 mg/kg over 60 min. IV Total dose ≤ 100 mg	IV bolus: 60 U/kg, max. 4000 IU IV infusion: 12 IU/kg/hr. over 48 hr. max. 1000 IU/hr. target PTT: 50 - 75 sec.
Reteplase (r-PA)	10 IU and 10 IU IV bolus at an interval of 30 min.	IV bolus: 60 IU/kg, max. 5000 IU IV infusion: 12 IU/kg/hr. over 48 hr. max. 1000 IU/hr. target PTT: 50 - 75 sec.
Tenecteplase (TNK-tPA)	IV bolus 30 mg at body wt. < 60 kg 35 mg at body wt. 60 to < 70 kg 40 mg at body wt. 70 to< 80 kg 45 mg at body wt. 80 to < 90 kg 50 mg at body wt. > 90 kg	IV bolus: 60 IU/kg, max. 5000 IU IV Infusion: 12 IU/kg/hr. over 48 hr. max. 1000 IU/hr. target PTT: 50 - 75 sec.

Indirect criteria of successful reperfusion therapy following lysis:

- Infarction pain disappears
- ST elevation disappears

Note.: development of reperfusion arrhythmia is possible

Direct proof of recanalization with coronary angiography.

***Note**: Since re-occlusion after successful thrombolysis occurs in 20-25 % of cases, all patients should undergo coronary angiography after completion of the acute treatment for determining further possible reperfusion measures (PTCA, bypass surgery).*

3. Long-term thrombocyte aggregation inhibitors lower the mortality within the first year following infarction by 15%; the reinfarction risk drops by 30%.
   Dose: ASA 75 or 100 mg/day lifelong; side effects + CI: see chap. Thrombosis
   After DES implantation dual thrombocyte inhibition with ASA (see above) + clopidogrel (75 mg/day) for 12 months.

4. Indication for temporary anticoagulant therapy with Coumarin: echocardiographic evidence of left ventricular thrombi
   Up to 50% of larger anterior wall infarcts with apical involvement lead to parietal left ventricular thrombi (in contrast, in only 5% of posterior wall infarcts). To reduce the risk of cerebro-embolism, temporary anticoagulant therapy is therefore recommended for at least 3 months (INR target range: 2.0 - 3.0).

5. Treatment of complications:
   Arrhythmias and left heart insufficiency are the most frequent complications following myocardial infarction.

a) Arrhythmias

The administration of beta blockers at an early stage can reduce the risk of ventricular fibrillation and the overall mortality.

- ▶ Tachycardic ventricular arrhythmias:
  - Ventricular tachycardia: if circulation is stable, e.g., amiodarone 150 mg IV
    If this is unsuccessful or if there is imminent left heart failure, ECG-controlled electrocardioversion (starting at 100 J) under short anaesthesia
  - Ventricular flutter/fibrillation: defibrillation (200 - 300 Joule)
  - Prophylaxis of tachycardic ventricular rhythmia relapse: monitoring and if needed, correction of electrolyte imbalance; administration of beta blockers, possibly Amiodarone (in consideration of SE + CI)
- ▶ Tachycardic supraventricular arrhythmias:
  - Administration of beta blockers or Verapamil (never both together!)
  - For hemodynamically threatening supraventricular tachycardia, electrocardioversion

  (For further details see chap. Arrhythmias)
- ▶ Bradycardic arrhythmias and conduction defects:
  - Sinus bradycardia, possibly with VES due to bradycardia: Atropine 0.5 - 1.0 mg IV; in cases of threatening bradycardia, temporary pacemaker
  - AV block > I°: In posterior wall infarction, AV blocks can occur due to release of adenosine caused by ischaemia.
  - Bifascicular block: If a bifascicular block occurs in the acute phase → implantation of a temporary pacemaker if the patient has symptoms (haemodynamic instability, syncope)

  Note.: AV conduction disorders in posterior wall infarction (ischaemia of the AV node) have a better prognosis than in anterior wall infarction with involvement of the septum (Tawara branch blocked).

***Note**:* Prior to any antiarrhythmic treatment, the serum potassium level should be checked and if necessary, raised to high normal values (approx. 5.0 mmol/l)!

b) Left heart insufficiency [I.50.1] **and cardiogenic shock** [R57.0]**:**

Cause:
1. Myocardial function failure: If the infarction involves 20% of the left ventricle, regular signs of left heart insufficiency are detectable: if more than 40% of the left ventricle is infracted, this usually results in cardiogenic shock with a mortality rate of over 90%.
2. Cardiac arrhythmias
3. Therapy with negative inotropic agents, e.g.,
   Antiarrhythmic agents, beta blockers, etc.
4. Volume deficiency
5. Rare causes of cardiogenic shock:
   - Perforation of the ventricular septum (newly occurring systolic murmur!)
   - Papillary muscle tear with acute mitral insufficiency (newly occurring systolic murmur)
   - Rupture of the ventricle wall with pericardial tamponade
   - Pericardial effusion (anticoagulants relatively contraindicated!)

Diagnosis of left heart failure:
- Cl. signs: moist rale over the basal lung segments, 3rd heart sound, dyspnoea
- CXR: signs of lung congestion
- (Colour duplex) echocardiography: Evidence of hypo-/akinetic infarction areas, perforation of the ventricular septum, papillary muscle dysfunction or tear, pericardial effusion, estimation of the ejection fraction, etc.

Definition of cardiogenic shock:
- Arterial hypotension (BP systolic < 80 - 90 mm Hg)
- Cardiac index < 1.8 l/min/m^2 (normal: > 2.5 l/min/m^2)
- Left ventricular end diastolic pressure (LVEDP) > 20 mm Hg,
  PCW pressure > 20 mm Hg

Note.: Normal LVEDP at rest = 5 - 12 mm Hg
normal PCW pressure (PCWP) 8 - 12 mm Hg

Treatment of left heart failure and cardiogenic shock

1 Causal therapy: Reperfusion therapy and treatment of correctible causes (arrhythmias, discontinuation of negative inotropic drugs, etc.)

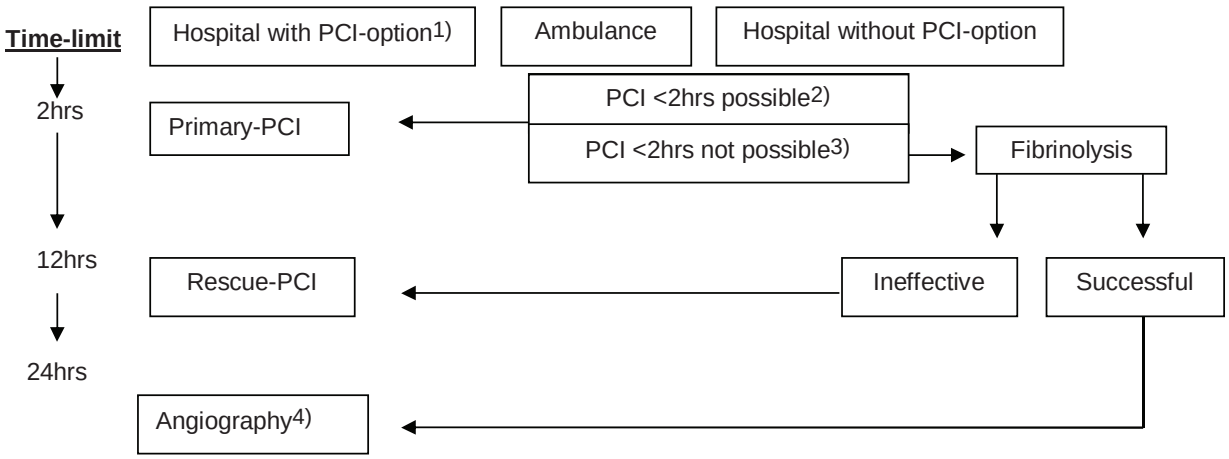
***Note**:* For patients in cardiogenic shock, the prognosis can be decisively improved by rapid reperfusion therapy (emergency PTCA or emergency bypass surgery).

2. Symptomatic treatment:

- Placement into a sitting position + O_2 administration through a nasal tube
- Optimal regulation of the preload while monitoring BP, CVP, left ventricular filling pressure and cardiac output
  - ▶ In case of pulmonary congestion:
    - Preload reduction with nitrates: e.g., nitroglycerin
      Dose.: 1 - 4 mg/hr by infusion under BP monitoring
      CI: cardiogenic shock, systolic blood pressure < 90 - 100 mm Hg
    - In addition, consider Furosemide (Lasix®): initially 20 - 40 mg IV, repeat in 1-4 hr
      In cases of pulmonary oedema additional respiration with positive end-expiratory pressure (PEEP), preferred non-invasively with CPAP mask (if the patient tolerates it)
    - Hemofiltration (e.g., venovenous)
  - ▶ In patients with low circulatory volume: controlled volume administration; the cardiac output per minute can usually be increased up to a critical value of left ventricular filling pressure (e.g., pulmonary capillary pressure) of 18 mm Hg, after which the cardiac output drops again and pulmonary oedema is imminent. In right myocardial infarction, a higher preload is often necessary.
- Afterload lowering: Normalization of any elevated blood pressure (e.g., nitroglycerin, ACE inhibitor). In acute mitral valve insufficiency or acute ventricular septum defect, Nitroprusside Sodium (Nipruss®) with invasive arterial and venous pressure monitoring (details: see chap. Hypertensive crisis)
- Positive inotropic agents:
  - ▶ Beta receptor agonists:
    In the initial stages of congestive heart failure, the increased sympathetic nerve activity represents an important compensatory mechanism. With progression of the severity of heart failure, the elevated catecholamine levels, however, lead to a progressive decrease in myocardial beta receptors (down regulation). Additional administration of exogenous catecholamines only leads to a temporary improvement in hemodynamics; a prognostic benefit has not been proven.
    - Dobutamine: Only a slight vasoconstrictive effect and also has only a slight positive chronotropic effect.
      Dose: 5 - 10 µg/kg/min IV
      SE: Tachycardia, proarrhythmic effects, increase in myocardial O_2 consumption, among others.

    ***Note**:* Due to the vasopressoric effect, the blood pressure can be raised during cardiogenic shock. However, the afterload increases at the same time → therefore do not increase systolic blood pressure > 100 mm Hg.
    Metabolic acidosis reduces the effect of sympathomimetic agents and should therefore be adjusted.
  - ▶ Noradrenalin:
    It is indicated in cardiac shock when the blood pressure cannot be stabilized through the use of Dobutamine alone.
- Mechanical circulation support systems:
  - Intra-aortal balloon counter pulsation (IABP):
    In cases of imminent pump failure and cardiogenic shock, placement of an IABP may be indicated (contraindication: significant aortal insufficiency and aneurysms of the thoracic and abdominal aorta.
    Principle: Intraaortal balloon pump, which is blown up during diastole under ECG control, collapses during systole → better coronary perfusion during diastole
  - Left or biventricular support systems (Assist devices)

Therapy synopsis (ESC Guidelines / 2010):



1) 24hrs-availability
2) Period of first contact with the patient to dilation should be <90min.
3) If PCI is not possible: opt for fibrinolysis ASAP
4) Not sooner than 3hrs post start of fibrinolysis

Memo: 20 % of all successfully thrombolysed infarct patients without more extensive invasive diagnostics/therapeutics suffer from a reinfarction within 4 – 8 weeks.

Rehabilitation after myocardial infarction in 3 phases:

1. Acute hospital
   - ICU with permanent monitoring, (transfer to) coronary angiography
   - Early mobilization

   In uncomplicated cases: hospital stay approx. 7 days
2. Post-hospital rehabilitation: Rehabilitation clinic or ambulatory therapy centre:
   Sport therapy, reassurance and reducing fears, health education, preparation for job re-entry, stress challenges
3. Return to occupational and everyday life
   Participation in an outpatient heart group

Medications that improve the prognosis of post-infarction patients:

Note*:* All post-infarction patients should receive the following medications taking into account the CI and SE:

1. Beta blockers without intrinsic activity (ISA):
   Lower the frequency of sudden death due to arrhythmia and the reinfarction risk in post-infarction patients.
2. Thrombocyte aggregation inhibitors: acetylsalicylic acid (ASA) 100 mg/day. If intolerant to ASA, administer e.g., clopidogrel (75 mg/day). The additional administration of clopidogrel for at least 9 months is associated with a prognostic gain (CURE trial).
3. Cholesterol lowering medications (cholesterol synthesis inhibitors, Statins):

   Note*:*
   - The GRIPS trial (Göttinger Risk, Incidence and Prevalence Study) showed that persistent hypercholesterolemia is associated with a high re-infarction risk:
     - At LDL cholesterol levels > 160 mg/dl (4.1 mmol/l): reinfarction rate 50 % in 5 years
     - At LDL-cholesterol levels > 190 mg/dl (4.9 mmol/l): reinfarction rate almost 100 % in 5 years
   - The survival rate is poorer for diabetics than for non-diabetics.

   Several studies showed the high significance of intensive cholesterol lowering in post-infarction patients: e.g., 4S Study, CARE Study, LIPID Study, LCAS Study. In these studies, infarction incidence and mortality could be reduced by approx. 30%. The LDL cholesterol level should be reduced to values below 100 mg/dl, for high risk patients, < 70 mg/dl. Patients with normal LDL values also benefit from Statins (Heart Protection Study)!
4. ACE inhibitors:
   After a myocardial infarction, structural design and adaptation processes of the heart ("remodeling") take place. In unfavourable circumstances this can lead to an expansion of the infarct scar, hypertrophy and dilatation of the left ventricle. This in turn worsens the prognosis. ACE inhibitors can slow down this negative process and reduce the overall mortality in patients with reduced ejection fraction (SAVE, AIRE, TRACE studies, among others).
   When ACE inhibitors are contraindicated or not tolerated (e.g., coughing), AT1 blockers (Sartans) may be an alternative.

Prg: 40 % of patients die on the first post-infarction day; of these, over half of these die during the first hour after the onset of symptoms (VF being the most common cause of death). Without revascularization therapy, approx. 15% die in hospital (= hospital mortality). The use of systemic thrombolysis reduces hospital mortality to almost 10%, the use of primary PCI, to approx. 5%. Within the first 4 weeks post MI, 50% die, thus approximately 50 % of all patients die after an MI = results of the MONICA project (monitoring trends and determinants in cardiovascular disease). The risk of developing lethal arrhythmias is highest immediately after an infarction. The chance of survival also depends on the time period between the MI and availability of effective therapy.

Mortality rises with increasing left heart failure in acute MI

➜ Killip Classification of heart failure:

I	No left heart failure:	mortality < 5 %
II	Moderate left heart failure with basal rale:	mortality up to 20 %
III	Severe left heart failure/pulmonary oedema:	mortality up to 40 %
IV	Cardiogenic shock:	mortality up to 90 %

Within two years following hospital discharge, an additional 5 - 10 % die due to sudden cardiac death.

Long-term prognosis for coronary disease patients depends on

1. Degree of the left ventricular functional limitation: size of the akinetic/dyskinetic myocardial area. An ejection fraction < 30 % is considered to be prognostically poor.
2. Signs of ischaemia (angina pectoris or signs of ischaemia in the exercise ECG or in the myocardial perfusion scintigraphy)

3. Higher grade ventricular arrhythmias, proof of late potentials in highly amplified ECG, reduced heart rate variability and reduced baroreflex sensitivity are considered to be risk factors for sudden cardiac death, in particular in the presence of reduced ejection fraction.
4. Number of affected vessels: The annual mortality rate is proportional to the number of diseased coronary arteries, and is highest in untreated trunk stenosis.
5. Duration of risk factors = progression of coronary heart disease
   Although stopping smoking can reduce the 10-year mortality by approx. 50%, 30% of all patients are smokers at the time of their first infarction and 20% are still smokers at the time of their second infarct.

Primary cardiac neoplasms

(I would like to thank Dr. Stephan Wüsten from Düsseldorf for completing this chapter.)

Ep.: The frequency of cardiac neoplasm in various autopsy series is up to 0.3%: f : m = 3 : 1; peak age 40 to 60 years

Aet.: - Familial: In approx. 5% so-called "myxoma syndrome": heart myxoma, pigmented naevi, subcutaneous myxoma
- Unknown

Loc: Left atrium: 85% (usually an appendage with a peduncle on the septum)
Other sites: 15%

Hi.: 90% benign: usually myxoma (70 %); more rarely fibromas, lipomas; in 20 % rhabdomyomas (especially in children), MICE tumours (mesothelial incidental cardiac excrescences), apparently caused by cardiac catheter examinations
10% malignant: sarcomas, etc.

Clin: Palpitations, possibly tachycardia, rapidly progressive dyspnoea, possibly position dependent chest pain
Other symptoms: dizziness, syncope, nausea, fever, weight loss

Ausc: Unspecific cardiac murmur

Lab.: - In almost all cases, raised ESR
- More rarely, leucocytosis, Hb drop, thrombocyte count changes

Co.: Frequent initial symptoms:
- Cardiac arrhythmias (> 50%)
- Thromboembolic events (25%): cerebral embolism, arterial embolism
- Acute pulmonary oedema as a result of left heart failure
- Sudden cardiac death
- Metastatic spread of malignant heart tumours

DD: - Defects
- Chest pain of other origin
- Stroke of other origin
- Intracardial thrombi (in the left atrium due to mitral defects, atrial fibrillation: in the left ventricle usually due to infarct); endocarditis valve vegetations
- Secondary cardiac tumours (metastases, malignant lymphoma) are significantly more frequent than myxoma

Di.: - Transesophageal echocardiography, CT, MRT, possibly cardiac catheter

Th.: - Physical rest, anticoagulation
- Due to the high complication rate and the very good prognosis of the mostly benign cardiac tumours, surgery should be performed as soon as possible after the diagnosis has been made: total extirpation; if appropriate, patch implantation on the septum.
- Malignant cardiac tumours: usually only palliative therapy is possible

Prg: Good for benign cardiac tumours: Relapse rate 0 - 3%, higher for myxoma syndrome
Poor for malignant cardiac tumours: mean survival time 9 months

Functional cardiac pain [F45.3]

Syn: Cardiac neurosis, cardiac phobia, cardiac anxiety syndrome, Da Costa syndrome

Def.: Chronic recurring thoracic symptoms without evidence of any somatic cardiac condition. The patients feel that something is wrong with their heart, however there is no objective organic finding that explains the symptoms.

Ep.: Common, approx. 15 % of patients, who see a doctor for suspected heart symptoms; the majority of patients are < 40 yr old.

Aet.: Psychogenic/psychosomatic: Increased tendency for anxiety and disordered processing of fear, over-cautious personality type, vegetative lability.

Cl.:
- Thoracic pain unrelated to stress, which occasionally can radiate into the arms
- Sometimes hyperventilation
- "Heart attacks" with tachycardia, feeling of panic, anxiety attacks, fear of dying, globus sensation, feeling faint, sweating, shivering
- Continuous preoccupation with the possibility of having a cardiac disease; protective tendency, exaggerated need for control with fear that something is overlooked. Close doctor-patient relationship, pedantic following of doctor's instructions.

DD: Organic diseases (cardiac arrhythmia, CHD, MI, recurrent PE, hyperthyroidism, cervical and thoracic spine syndrome, etc.); see also DD of angina pectoris

Di:
- History (younger patients with similar symptoms persisting for years and repeated cardiological examination without any pathological findings)
- Exclusion of organic disease (physical examination, BP, ECG, ergometry, CXR, laboratory screening including basal TSH), possibly additional cardiological examination with echo and 24h-ECG, etc.

Th.:
- Reassure the patient about the innocuousness of the symptoms (mini psychotherapy in the context of the office consultation).
- Relaxation techniques, physical training
- If tachycardia or extrasystoles are present: consider beta blockers
- Psychosomatic therapy
- If symptoms are severe: consider the temporary use of tranquilizers (no long-term therapy! Caution: drug dependency!)

Prg: In general good; in > 50 % of cases, the problem becomes chronic with frequent physician consultations, unnecessary consumption of various medications, unnecessary hospitalizations

Cardiac arrhythmias (CA) [I49.9]

Cardiac arrhythmias occur in organically healthy people prior to a cardiac or extracardiac disease, or they can be the result of these. The ECG provides the basis for recognition of the causes, along with the history of RD and the detection of cardiac and extracardiac diseases. In turn, this is the prerequisite for symptomatic and causal treatment, as well as an estimation of the individual prognosis.

Aet.:
1. Myocardial causes:
   - Coronary heart disease and myocardiac infarction
   - Myocarditis and cardiomyopathies
2. Hemodynamic causes:
   - Cardiac volume load: defects with valve insufficiency or shunt
   - Cardiac pressure load, arterial or pulmonary hypertension, valve stenosis, outflow tract stenosis, HOCM
3. Extracardiac causes, e.g.,
   - Psychovegetative factors
   - Electrolyte disorders (potassium, calcium; in particular hypokalaemia)
   - Hyperthyreoidism
   - Hypoxia
   - Medications (e.g., cardiac glycosides, antiarrhythmic agents, tricyclic antidepressants, etc.)
   - Alcohol, caffeine, drugs, toxins
   - Hyperreactive carotid sinus
   - Flatulence with diaphragmatic elevation (Roemheld syndrome)

Cl.:
1. Subjective symptoms:
   Slight and/or occasional CAs are not perceived at all by many patients; other patients complain of:
   - Palpitations, skipping a beat (e.g., with extrasystoles)
   - Racing heartbeat with tachycardia/tachyarrhythmia
2. Objective symptoms due to reduction in the cardiac output:
   While healthy individuals tolerate fluctuation of heart rate between 40/min and 160/min (and more) without complications, patients with pre-existing cardiac disease and/or stenoses of the coronary and cerebral arteries will experience discomfort already at frequencies > 130/min.:
   - Cerebral: lightheadedness, dizziness, syncope, confusion, epileptic-type attacks, temporary visual or speech disturbances, cerebral infarction
   - Cardiac: Angina pectoris, deterioration of existing heart failure, MI
   - Generalized: cardiogenic shock, sudden cardiac death (> 60 % of all cardiac deaths)

3. Arterial embolisms during ablation of cardiac thrombi, in particular in the presence of atrial fibrillation: approx. 20 % or all strokes are caused by AF!

Di.:
- History and clinical examination (count pulse and heart rate for at least 1 minute → compare with simultaneously palpated pulse and the heart rate in the ECG for determination of a pulse deficit)
- Resting ECG (25 mm/sec) with long strips (10 mm/sec)
- Long-term ECG (detection of intermittent CA, quantification of CA)
- Event recorder: detection of sporadic CA; classification of subjective symptoms of the patient (racing heart, palpitations, dizziness, etc.) as possible arrhythmia. Telemedical transmission possible.
- Ergometry (detection of stress dependent CA, testing the frequency behaviour under stress: insufficient increase in frequency in sick sinus nodes)
- Pharmacologic tests (e.g., Ajmaline test for suspected Brugada syndrome)
- Invasive diagnostics (electrophysiology):
  - Programmed stimulation (with various baseline cycle lengths and premature individually simulated extrasystoles)
    a) Atrial stimulation:
       - Detection of any accessory conduction pathway (WPW syndrome, Mahaim fibres)
       - To determine the refractory time of the atrium, AV nodes and any accessory bundles
       - Diagnostic supraventricular tachycardia
    b) Ventricular stimulation:
       - Detection of any hidden accessory conduction pathway
       - To determine the refractory time of the ventricle AV nodes and any accessory bundles
       - Induction of ventricular re-entry tachycardia
       - Test/inducibility of hemodynamically intolerable VT/VF (risk assessment for selected patient groups to determinw the probability of suffering from sudden cardiac death)
       - Passive intracardial conduction: bundle-of-His-ECG: determination of the A-H time (AV nodes) and the H-V time (distal specific stimulus conduction system)

Th.: Antiarrhythmic therapy:
1. Causal treatment
2. Symptomatic treatment:
   a) General measures (reassurance, sedation, if necessary, possibly vagal stimulation, bed rest and oxygen, etc.)
   b) Antiarrhythmic treatment:
      - Antiarrhythmics - electrotherapy – catheter ablation
      - Antiarrhythmic cardiac surgery

Some rules:
- Objectify symptoms indicative of arrhythmia through the use of long-term ECG.
- Cardiac arrhythmias in otherwise healthy persons usually have a good prognosis; symptoms set the indication for treatment for most of the part. However, they can become subjectively stressful/unpleasant if they are of long duration (hours, days) and in the presence of concomitant diseases, can lead to severe symptoms.
- Don't practice "ECG cosmetics"!

Indications for treatment:
1. Pronounced symptomatology, impaired circulation (tachycardia and bradycardia with decreasing cardiac output)
2. Threatened/existing tachycardia-induced cardiomyopathy
3. Elevated risk of sudden cardiac death in the presence of
   - Status post resuscitation in cases of VF; rapid VT
   - Ventricular cardiac arrhythmia in patients with severe myocardial underlying diseas and restricted left ventricular pump function

- Causal therapy is the most important measure in patients with cardiac arrhythmia, e.g., coronary heart disease, myocarditis, heart failure.
- If cardiac arrhythmia is the result of an extracardiac disorder, this must be treated as well (e.g., electrolyte disorders, hyperthyroidism, and digitalis intoxication).
- Weigh side effects of anti-arrhythmics against benefit! The CAST Study (Cardiac Arrhythmia Suppression Trial) showed that anti-arrhythmics of class I C (for example, Flecainide) worsen the prognosis of patients after MI, because anti-arrhythmics themselves can cause cardiac arrhythmia = proarrhythmic effects. Other anti-arrhythmics of class I can also induce proarrhythmic effects, particularly in patients with structural cardiac diseases. Proarrhythmic side effects can also occur with class III anti-arrhythmics in cases of advanced heart failure (NYHA III, IV). For this reason, these medications (Sotalol, Amiodarone) also provide no prognostic advantage. In advanced heart failure, deterioration in the prognosis has even been observed.
  No benefit derives from antiarrhythmic therapy with regard to the mortality rate. The CAST and SWORD studies even demonstrated a worsening of the prognosis in post-infarct patients. From a prognostic view, there is no indication for long-term therapy with anti-arrhythmics, with the exception of beta blockers. With an elevated risk of VF, non-drug therapeutic alternatives should be employed (implantable cardioverter/defibrillator = ICD, catheter ablation, rhythm surgery).
- Watch out for any side effects of anti-arrhythmics! Older patients are especially sensitive to side effects. In the presence of

heart failure, beware of the negative inotropic effect of anti-arrhythmics! Sick sinus syndrome and AV block > I° are usually contraindications for anti-arrhythmics without prophylactic pacemaker placement. Anti-arrhythmics must be discontinued or replaced if the arrhythmia deteriorates during treatment, or if the QT interval (> 120 %) or the QRS duration (> 125 %) increase.

- Readjustment with anti-arrhythmics should only be as an inpatient under monitoring surveillance: K^+, Mg^{++} and QTc-time (= frequency corrected QT time) must be normal!
  Hypokalaemia / hypomagnesaemia as a well as prolonged QTc time are contraindications (high risk of proarrhythmia including VF).
- In general, only one antiarrhythmic should be given; the combination of two anti-arrhythmics can be even more dangerous! If the decision is made to use a combination of two anti-arrhythmics, only well tested, recommended combinations should be chosen.
- IV administration of anti-arrhythmics must be very slow (5 - 10 minutes) under ECG monitoring.

ANTIARRHYTHMICS

The following three groups of drugs belong to the medications that are effective anti-arrhythmics:

Digitalis

Ind: Reduction of ventricular frequency, AF or atrial tachycardia (usually only effective in association with β blockers) by slowing AV node conduction

***Note**:* Cardiac arrhythmia can be triggered by digitalis overdose or intolerance!

(Details: see chapter on Cardiac insufficiency)

Parasympatholytics (vagolytics)

Atropine, ipratropium bromide

Ind: Temporary treatment of severe bradycardia

SE: Dry mouth, impaired accommodation, increased intraocular pressure, stool and urinary retention, confusion

CI: Angle closure glaucoma, urinary retention (e.g., in prostate adenoma) etc.

Dose: 0.5 mg IV, repeat after 10 minutes if necessary

Sympathomimetics

Ind: Temporary treatment of severe bradycardia, when vagolytics are contraindicated or do not work sufficiently. In these cases, the use of Orciprenaline should only be understood as a bridging measure until implantation of a pacemaker is possible.

AE: Ventricular ES with the risk of VT and VF

CI: Hyperthyroidism, hypertrophic obstructive cardiomyopathy (HOCM), recent MI

Dose: e.g., Orciprenaline (Alupent®) 0.25 - 0.5 mg i.v. slowly over 5 minutes under ECG monitoring

Antiarrhythmics in a narrower sense

Classification of anti-arrhythmics according to Vaughan Williams:

Classes with examples	Mechanism of action	Indication
I. Sodium channel blocker A Quinidine, ajmaline, disopyramide B Lidocaine C Propafenone, flecainide	Inhibition of rapid Na^+ inflow → membrane stabilization IA: duration of the action potential ↑ IB: duration of the action potential ↓ IC: duration of the action potential ↔	Acute ventricular arrythmias Drugs of group IC also for AF Tachycardia, post MI ventricular arrhythmias, AF

II.	Beta receptor blockers	Sympathicolysis	SVT
III.	Potassium channel blockers Amiodarone, sotalol	Inhibition of K^+ outflow Repolarization inhibition	
IV.	Calcium antagonists	Inhibition of the slow Ca^{++} inflow	

Remark: The class I anti-arrhythmics are distinguished according to their binding behaviour to Na^+ channels:
- "Fast drugs", which are quickly released again from the Na^+ channels (Lidocaine, Mexiletin, Tocainide) and
- "Slow drugs", which are slowly released from the Na^+ channels (all other class I anti-arrhythmics)

Class I-anti-arrhythmics: Sodium channel blockers

The CAST Study (Cardiac Arrhythmia Suppression Trial) showed that class Ic anti-arrhythmics (e.g., Flecainide) worsen the prognosis of patients following MI due to proarrhythmic effects. The other class I anti-arrhythmics can also exhibit proarrhythmic effects, in particular in patients with heart failure. Ventricular fibrillation can result from the interaction of Disopyramide with other medications (e.g., Macrolides). For this reason, a careful risk/benefit assessment is recommended! From a prognostic point of view, there is no therapeutic indication. Class I anti-arrhythmics are contraindicated in heart failure as well as after MI.

Class IA anti-arrhythmics of the quinidine type: e.g.,

▶ **Quinidine:** Resorption rate approx. 80 %; half life: approx. 6 - 7 hr. (in liver cirrhosis up to 50 hr.!);
Excretion: primarily hepatic
Ind: Regularization of AF in patients without organic heart disease (see chap. Atrial fibrillation)
CI: Post MI, heart failure, sick sinus syndrome, AV block > I°, QT(U) prolongation (risk of VF under quinidine therapy), digitalis intoxication, quinidine allergy etc.
SE: - Gastrointestinal: diarrhoea, nausea, vomiting, liver damage
- Allergic skin reactions with fever, thrombocytopenia, agranulocytosis, haemolytic anaemia. An initial test dose is recommended to detect any allergic reactions.
- Cardiac: heart failure, AV block, bundle block, ventricular tachyarrhythmia including VF (particularly with QT(U) prolongation!); cardiotoxic SE present as QRS widening and QT prolongation. When the relative prolongation of the QT interval exceeds > 120 %, the anti-arrhythmic must be discontinued!
- Central nervous: double vision, tinnitus, headaches
Interact: Quinidine reduces the renal clearance of digoxin → cut Digoxin dose in half and check digoxin level, if necessary!

▶ **Ajmaline and prajmalium bitartrate**
Resorption rate of Prajmalium is high (80 %), for Ajmaline low (therefore only parenteral usage)
HL: Ajmaline 12 minutes, Prajmalium 5 hr.; excretion: primarily hepatic
Ind: Drug of choice for acute treatment of tachycardia with narrow and wide QRS complex (supraventricular and ventricular tachycardias).
CI: myocardial infarction, heart failure; no combination with other anti-arrhythmics
SE: headaches, visual disturbances, gastrointestinal SEs, intrahepatic cholestasis (discontinue medication!), cardiac SEs are similar to that of quinidine
Dose: Ajmaline (Gilurytmal®) 25 - 50 mg over 1 minute IV (ECG monitoring)
Note: rapid administration – otherwise, no effect!

Class IB anti-arrhythmics of the Lidocaine type:

▶ **Lidocaine**
Lidocaine is rapidly metabolized in the liver. For this reason it is only used parenterally.
Ind: In the past it was used for ventricular tachycardia in acute MI. However, the success rate is lower (~ 15 %) than with Ajmaline (> 60 %) and Amiodarone.
CI: heart failure, sick sinus syndrome and AV block > I°, lidocaine allergy
SE: Proarrhythmic SEs, dizziness, somnolence, cramps, drop in blood pressure, negative inotropic effect

Class IC anti-arrhythmics

▶ **Propafenone**
Resorption rate: 50 %; HL: 3.6 hr. At high doses, also beta receptor blocking effect.
Excretion: primarily hepatic → cumulative risk in impaired liver function
Ind: e.g., WPW syndrome, supraventricular tachycardia, focal atrial tachycardia, regularization of AF in patients without organic cardiac disease
CI: heart failure, post MI, in particular in the case of restricted cardiac output, sinus node syndrome, AV block > I°, bifascicular block, obstructive ventilation disorder, propafenone allergy, pregnancy, etc.
SE: cardiac: As with all class I anti-arrhythmics, proarrhythmic SEs.
Discontinue treatment if there is widening of the QRS complex.
Gastrointestinal: nausea, vomiting, rarely intrahepatic cholestasis
CNS: headaches, dizziness, visual disorders, taste disorders, paraesthesias, impairment of the reaction potential
Rarely allergic dermatological reactions, erectile dysfunction, intensification of obstructive respiratory disorders by beta blocking property

Interact: effect is intensified by local anaesthesias.
Dose: 2 - 3 x 150 mg orally

▶ **Flecainide**
Ind: same as propafenone, however it has no β-blocker effect
Numerous side effects, interactions and CI should be observed.

Class II anti-arrhythmics: Beta receptor blockers

Ef.: Beta blockers suppress catecholamines at their receptors and consequently reduce the sympathetic-adrenergic stimulation of the heart:
- Negative bathmotropic = reduction in the excitability of the heart
- Negative chronotropic = slowing of the heart rate
- Negative dromotropic = slowing of the conduction speed
- Negative inotropic = initial reduction in cardiac contractility (however: improvement of heart failure under long-term therapy with beta blockers!)
- Improved prognosis in the presence of hypertension, CHD, heart failure
- Lowering of blood pressure
- Anti-ischaemic effect in CHD (lowering of O_2 consumption)

Cardioselective beta blockers show a relative preference for cardiac beta1 receptors. Some beta blockers show an intrinsic sympathomimetic activity (ISA) = sympathomimetic intrinsic effect. Beta blockers with additional α1-receptor - blockade also have a vasodilatatory effect.
The duration of efficacy of propranolol is only 10 hr., for most of the other preparations, 12-24 hr., for Bisoprolol, 24 hr. Lipophilic beta blockers (e.g., Metoprolol, Carvedilol) are primarily excreted via the liver. Hydrophilic beta blockers (e.g., Atenolol) are excreted renally. Bisoprolol is dually excreted via the liver and kidneys. For the treatment cardiovascular diseases, beta1-selective beta blockers without ISA are recommended.

Ind:
1. Supraventricular extrasystoles and tachycardia, sinus tachycardia in hyperthyroidism, hyperkinetic cardiac syndrome.
2. In patients with acute myocardial infarction, post-infarct patients and CHD, beta blockers without ISA can reduce the risk of sudden cardiac death and improve the prognosis.
3. Arterial hypertension (Commentary: see Chap. arterial hypertension)
4. Angina pectoris
5. Treatment of heart failure in combination with ACE inhibitors and other medication (for Carvedilol, Metoprolol and Bisoprolol the improvement of prognosis has been proven in several studies → see chap. Heart failure)
6. Migraine prophylaxis (see that section)

CI: Decompensated heart failure (only commence beta blockers under careful monitoring after cardiac recompensation), severe hypotension, severe bradycardia, sick sinus nodes, AV block > I° (without pacemaker protection), bronchial asthma; COPD is no CI (→ careful use of β1-selective beta blockers under monitoring, e.g., peak flow meter), advanced PAOD

SE: Frequent (up to 20 %): Especially at the beginning of treatment: tiredness, hypotension, reduced performance; occasional (< 10 %): feeling of coldness in the extremities, dizziness, headache, gastrointestinal symptoms, erectile dysfunction; rare (< 1 %): bradycardia, worsening of heart failure when the starting dose is too high; sleep disorders, depression, nightmares; bronchospastics in pre-existing bronchial asthma; reduced tear production; allergic skin reactions; increased risk of hypoglycaemia in diabetes mellitus; masking of hypoglycaemia symptoms (through reduced opposing adrenergic regulation), worsening of advanced PAOD, sometimes activation of psoriasis, etc.

Interact: Use caution in combination with other anti-arrhythmics: increased inhibition of sinus node function and the conduction system. Therefore, do not combine beta blockers and calcium antagonists of the Verapamil type (risk of AV block)! Beware of the rebound effect on the sympathetic system: Do not suddenly discontinue beta blockers! Continue perioperative dose.

Increase the dose slowly, beware of any CI, particular in elderly patients and at the beginning of therapy for heart failure!

Up to 10 % of all people (they have the gene polymorphism CYP2D6) metabolize metoprolol and carvedilol in a delayed mode, which can lead to elevated plasma concentrations.

Dose: There are over 20 beta blockers on the market. For this reason, only several examples are named in the following.

Substance	Trade name	Mean oral daily dose (mg)
1. Generation: non-cardioselective beta blockers		
1.1. without ISA:		
Nadolol	Solgol®	1 x 60 - 240
Propranolol	generic	2-3 x 40 - 80
1.2. with ISA:		
Carteolol	Endak®	1 x 5 - 20
Mepindolol	Corindolan®	2 x 2,5 - 5
Oxprenolol	Trasicor®	2-3 x 40 - 80
Penbutolol	Betapressin®	1 x 20 - 80
Pindolol	Visken®	1-3 x 5

2. Generation: Beta1-selective beta blockers		
2.1. without ISA:		
Atenolol	generic	1 x 50 - 100
Betaxolol	Kerlone®	1 x 10 - 20
Bisoprolol	generic	1 x 5 - 10
Metoprolol	generic	2 x 50 - 100
2.2. with ISA:		
Acebutolol	Prent®	1 x 400 - 800
Celiprolol	Selectol®	1-2 x 200
3. Generation: Beta blockers with vasodilating effect		
3.1. without ISA:		
Nebivolol (highest β1-selectivity)	Nebilet®	1 x 5
Carvedilol (α and β blockade)	generic	1 x 12,5 – 25
3.2. with ISA:		
Celiprolol (β1-selective)	Celipro® Selectol®	1 x 200

Class III anti-arrhythmics: potassium channel blockers

▶ **Amiodarone**

Resorption rate: 50 %; T1/2 = 50 to 100 days! → cumulative risk! Class I – IV mechanism of action

Ind: severe symptomatic AF with the target of permanent rhythm normaliization. If this cannot be achieved in cases of permanent AF even with the use of electrical cardioversion, amiodarone may not be used simply for frequency deceleration (rate of side effects too high).

Acute supraventricular and ventricular Tachycardia in urgent need of treatment in patients with heart failure.

In patients who are at risk of VF (sudden cardiac death), treatment with Amiodarone cannot guarantee a decrease in the overall mortality; in one study, the mortality was even elevated.

CI: allergy to iodine, thyroid diseases, etc.

SE: corneal microdeposits sometimes associated with visual deterioration, photosensitivity, hepatitis, pneumonia, pulmonary fibrosis, peripheral neuropathy, proarrhythmic effects (e.g., Torsades de pointes tachycardia), iodine allergy, functional thyroid disorders, etc. Due to its iodine content, Amiodarone is contraindicated in thyroid autonomous nodules or hyperthyrodism (triggering/intensification of hyperthyroidism). Beware of any other CIs! Approx. 25 % of patients discontinue therapy because of SEs. Check thyroid function prior to use of amiodarone!

Dose: e.g., Cordarex®: see manufacturer's instructions

▶ **Sotalol**

Ind: Regularization of AF in patients without organic cardiac disease

SE + CI: See beta blockers; in approx. 5 % of cases, proarrhythmic SEs will be encountered (e.g., Torsades de pointes ventricular fibrillation); watch out for QT-prolongation (= CI !).

In the SWORD Study, an increased mortality rate was observed for D-sotalol in comparison to placebo in post-infarct patients. Also D/L-sotalol did not exhibit any advantages in prognosis and led to Torsade de pointes tachycardia in up to 4% of cases.

Class IV anti-arrhythmics:

1. Calcium antagonists of the phenylalkylamine type: verapamil, Bileopamil
2. Calcium antagonists of the benzothiazepine type: Diltiazem

Ind: To slow down AV conduction in chronic AF; therapy for episodes of AV node re-entry tachycardia

CI: Pre-excitation syndrome, decompensated heart failure (NYHA III and IV), sick sinus node, AV block > I°, severe hypotension, etc.

SE: Cardiac: conduction delay, bradycardia, blood pressure drop, negative inotropy
Gastrointestinal: constipation, nausea
Central nervous: dizziness, headache
Further: Allergic rash, increased enzymes, flush, joint oedema

Interact: Do not combine with beta blockers → risk of higher grade conduction block!

Calcium antagonists of the verapamil type can raise the plasma level of some medications: e.g., Digoxin, Cyclosporin A, Theophyllin, Carbamazepine → reduce dose of these medications and check plasma level, if necessary.

Bioavailability of Verapamil < 20 % (due to first-pass effect in the liver)

Substance	Trade name	Mean oral daily dose (mg)
Verapamil	As non-proprietary name e.g., Procorum®	3 x 80 - 120
Bileopamil		3 x 25 - 50
Diltiazem	As non-proprietary name	3 x 60 - 90

Parenteral administration of Verapamil: 5 mg slowly (over 5 minutes) IV, ideally under ECG monitoring; if necessary repeat the dose after 30 minutes.

Other anti-arrhythmics

Adenosine (e.g., Adrekar®)

Ind: Tachycardia with narrow QRS complex

Ef.: Short-term blockade of AV node conduction

SE: Flush, dyspnoea, feeling of pressure in the chest, bronchospasm, drop in blood pressure

CI: Pre-excitation syndrome with AF (irregular tachycardia with QRS complex widening of varying degrees); there is the risk of accelerating antegrade conduction of AF along the accessory conduction pathway with induction of VF! Bronchial asthma, AV block > 1°, sick sinus syndrome, QT prolongation, prior treatment with verapamil, etc.

Dose: Due to the very rapid half-life (few seconds only) 3 – 6 mg i.v. rapidly as a bolus; if this is unsuccessful, repeat the injection after 3 min. using twice dose (6 -12 mg) (antidote: Theophylline)

***Note**:* Only administer adenosine while the patient is on ECG monitor (late analysis of termination often leads to diagnosis), treatment for a possible asthma attack must be available.

ELECTROTHERAPY OF CARDIAC ARRHYTHMIAS

I. Pacemaker therapy

A) Antibradycardia pacemaker (NASPE/BPEG coding):

1st letter: Stimulation site: A = atrium, V = ventricle, D = dual = A + V

2ndt letter: Site of perception (detection site): as under 1.

3rd letter: Operation type (reaction type): I = Inhibition, T = Triggering, D = doubled = I + T

4th letter: Frequency adaptation: R = rate modulation

5th letter: Multifocal stimulation: as under 1.

- Operation type:

  Demand pacemakers are activated, whenever the frequency drops below a set minimum; two types are in use:

  I = Inhibition: Impulse release is inhibited in cases of spontaneous excitation of the heart

  T = Triggering: Impulse release does not occur in cases of spontaneous excitation of the heart in the refractory phase of the R spike

  D = dual = triggered + inhibited (most frequent mode of operation)

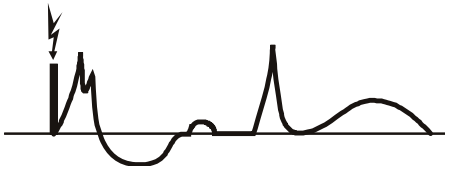
- Programmability:

  What is important is the possibility for variation of the stimulation frequency and the impulse energy (amplitude and duration of the stimulation impulse). After determination of the stimulus threshold (which can rise during the first three months after probe placement), an energy-saving setting is selected. If there are any detection complications, the amplification sensitivity can be increased.

  Hysteresis = programmed delay up to 1st appearance of the PM impulse, in order to avoid interference with its own action (e.g., 60 to 70 hysteresis means that a PM set to 70/min comes into action when the sinus rhythm drops < 60/min and that the sinus rhythm blocks the PM impulse when it returns to > 70/min).

a) Single chamber pacemaker:

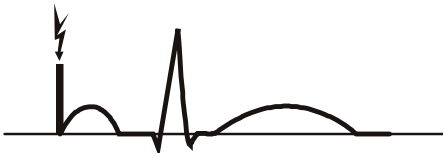
1. Ventricular demand pacemaker (VVI):



Ind: Bradyarrhythmia in atrial fibrillation.

Disadvantage: Non-physiological type of stimulation:
When sinus rhythm is maintained, the ventricle stimulation leads to retrograde atrial excitation and atrial contraction against the closed AV valve → loss of atrial systole and sudden pressure increase in the atrium → this can lead to reflectoric drop in blood pressure with dizziness episodes = so-called pacemaker syndrome in 20 % of all VVI pacemaker patients. The loss of atrial systole has an unfavourable effect in pre-existing heart failure.

2. Atrial demand pacemaker (AAI):

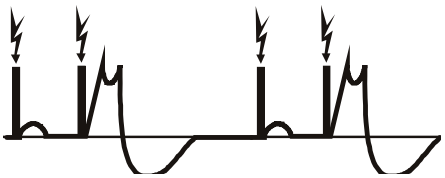


AAI stimulation is useful in isolated intermittent sinus node functional disorders (sinus bradycardia, sinus node arrest) in the presence of intact AV conduction. The patients should not have any intermittent atrial fibrillation. In AAI stimulation, the atrium is stimulated when the rate drops below the intervention frequency. Intrinsic actions of the atrium inhibit the pacemaker.

Advantage: maintained atrial/ventricular contraction sequence → improvement in the heart output volume by approx. 20 % in comparison to the VVI system.

b) Two-chamber pacemaker:

AV-sequential pacemaker (DDD):



In patients with AV block a two chamber pacemaker is used. It stimulates the atrium and ventricle in physiological sequence as needed when a minimum set frequency has been reached. The DDD-pacemaker therefore substitutes the AV conduction and stimulus formation in the sinus node as needed. The atrial/ventricle synchronization improves the ejection performance of the heart (as it does with the AAI system).

c) Frequency adaptive pacemaker:

- Frequency adaptive single chamber system (VVI-R) → Ind.: e.g., bradyarrhythmia in AF
- Frequency adaptive dual chamber system (DDD-R) → Ind.: binodal disease of the stimulus formation and conduction

Frequency adaptive pacemakers can increase the stimulation frequency depending on the load. A biosignal is detected via a sensor that indicates whether and with what intensity the patient is physically active. The sensor controls the stimulation frequency of the pacemaker in proportion to the electric charging.

The most frequently used types of sensors are the "activity sensors" and the "respiratory minute volume sensors". The activity sensor uses the forces of acceleration occurring during physical activity. These are transferred to a Piezo crystal. The main disadvantage is the insufficient correlation of the sensor signal with the actual metabolic requirement.

In contrast to the activity sensor, the minute respiratory volume sensor is based on a physiological sensor principal. With the minute respiratory volume, it uses a control unit, which correlates linearly with the metabolic requirement up to an anaerobic threshold. A disadvantage of the minute respiratory volume sensor is the delayed response at the beginning of the charhing. This, however, can be corrected by using a combination with an activity sensor. Physically active pacemaker patients with chronotropic incompetence (= insufficient increase in frequency under physical stress) should receive a frequency adaptive pacemaker if possible.

The following general rule applies to the clinical evaluation of chronotropic incompetence: A relevant limitation of physical performance capacity is to be expected when the cardiac rate is at the anaerobic threshold of less than 90 to 95 beats per minute (which corresponds to approximately half maximum ergometric performance).

d) Further PM functions that are optionally available for suitable patients:

- Frequency smoothing (rate-smoothing, e.g., during sinus pauses during charging)
- Mode-switching (automatic change of the stimulation type e.g., from **DDD®** to DDI(R)) or the automatic limiting of maximum frequency (during atrial tachyarrhythmias)

Ind:
- ► Symptomatic bradycardia: dizziness, syncope or Adams-Stokes attacks as a result of intermittent or permanent bradycardic arrythmia or asystole > 3 sec (sinus node syndrome, carotid sinus syndrome, bradyarrhythmia absoluta).
- ► Higher grade SA or AV blocks: AV block 2nd°/type II (Mobitz), SA or AV block 3rd°, trifascicular block
- ► Bradycardia due to heart failure and output reduction
- ► Critical bradycardia during treatment with medications which can intensify bradycardia (e.g., beta blockers, digitalis, anti-arrhythmics)

B) Antitachycardic systems

For VT and VF:

- Implantable cardioverter defibrillator (ICD): When ventricular tachycardia is detected, usually a pre-programmed cascade of overstimulations is attempted. If this is not successful, automatic internal defibrillations follow until the tachycardia has been terminated. Defibrillation is first used for ventricular flutter and fibrillation.
- Mobile cardioverter defibrillator (WCD):

  Ind: Bridging a limited period of time at high risk of sudden cardiac death, whenever ICD is not available temporarily (e.g., catheter infections), in post-infarct patients during the first 3 months following infarction when the ICD indication is not yet clear.

Ind: a) Secondary prevention: known risk of sudden cardiac death after survival of VF or rapid haemodynamically intolerable VT

b) Primary prevention: identified elevated risk of sudden cardiac death: e.g. VT in the presence of significantly reduced ventricular function (EF < 30 %); positive family history in symptomatic persons; a genetically fixed repolarization disorder with cases of mortality in the family (Brugada syndrome, QT syndrome)

C) Antitachycardic/Antibradycardic pacemaker:

PCD = Pacer Cardioverter Defibrillator with

1) Cardioversion/defibrillation function
2) Over-stimulation function and
3) Antibradycardic stimulation function

Ind: As for ICD with additional bradycardic cardiac arrhythmias

Co.: 1. Surgical complications:

- Probe dysfunction (dislocation, insulation defect, probe breakage, etc.)
- Haematoma, (pocket) infection, thrombosis, pneumothorax, ventricular perforation with pericardial

tamponade, etc.
- Pectoralis/diaphragmatic flutter

2. Non-surgical complications:
   - Increase in the stimulation stimulus threshold
   - Detection disorders
   - Misinterpretation of atrial arrhythmias or supraventricular tachycardia
   - Misinterpretation of muscle potentials
   - Technical complications (pacemaker/battery defect)
   - Phantom programming by external interfering frequencies, e.g., electrosurgical instruments

D) CRT= Cardiac resynchronization therapy

In association with antibradycardic stimulation (atrial and ventricular), optionally also with cardioversion/defibrillation function. Principle: A transvenous atrial and two ventricular probes are each placed right ventricularly, septally and via coronary venous vascular system left ventricularly, epicardial laterally. (In the realm of complex congenital heart defects, also epicardial approximation of the probe in the context of cardiac surgery)

Ind: left heart failure (NYHA III or IV), left bundle branch block (QRS widening > 150 msec), AV interval > 120 msec. Ideally, echocardiographically proven desynchronization of the LV contraction (old myocardial infarction).

Follow-up: Regular monitoring of pacemaker function by authorized physicians/cardiologists: 1st check within the first 3 months (determination of the chronic stimulus threshold and programming re-adjustmend if required). Afterwards, check-ups every 6 – 12 months (depending on the PM type and individual situation). PM identification card

The fundamental tasks of every check-up are the testing of the stimulus response and perception function as well as evaluation of the battery status. It must be tested whether the programmed pacemaker's mode of operation is still adapted to the current requirements of the patient.

Supplemental examinations: stimulus threshold measurements, telemetric querying of saved recordings, etc.

II. External electrocardioversion and defibrillation

Ind: - Absolute: supraventricular and ventricular tachycardia with impending cardiogenic shock, VF, ventricular fibrillation
- Relative: Failure to normalize AF with medications, AF

CI: Non-life-threatening tachycardia in digitalis intoxications

Principle: All cardiac cells capable of stimulus formation and conduction are temporarily depolarized simultaneously by a massive direct current shock applied to the heart via the thorax. This sends all cells synchronously into their refractory phase. This "electrical silence" in the myocardium is followed by the first spontaneous depolarization in those cells that exhibit the lowest resting membrane stability. These are typically cells of the sinus node region. However, potentially arrhythmia inducing ectopic foci (autonomic automatic centres) can still continue to dominate the rhythmic action.

In tachycardia the current release is synchronized, i.e., it is controlled by the cardiac phases, so that the shock is not administered in the vulnerable T phase (increasing T bundle): Triggering of the current release by the QRS complex: current release 0.02 sec after the R spike. In VF, the defibrillation is not R spike triggered.

Which energy dose to choose in monophasic operating devices:

- Ventricular flutter/fibrillation, polymorphic ventricular tachycardia: 1st shock at 200 J = Ws. If unsuccessful, deliver further shocks at 360 J.
- Monomorphic ventricular tachycardia, atrial fibrillation/flutter: 200 J

Biphasically operating instruments require lower energy release.

If the patient is conscious, an intravenous short-term anaesthesia is administered beforehand (e.g., with Etomidate = Hypnomidate®). It is important that paramedics and other helpers do not come into contact with the patient or the bed during the defibrillation process! For cardioversion of AF lasting longer than 48 hr. with the risk of thrombus formation in the atria, the patient must receive pre-treatment and follow-up with anticoagulants for at least 4 weeks (risk of embolism) + transesophageal echocardiography!

Automated external defibrillators (AED) are suitable for early defibrillation by lay helpers. Only through comprehensive use of these instruments will it be possible to increase the survival rate for ventricular fibrillation outside the hospital!

III. High frequency ablation (HF ablation)

High frequency ablation of arrhythmogenic tissue using electrode catheters after prior identification by intracardial mapping.

- **AV node ablation:**

  Ind: Is only rarely used today as a last resort in therapy refractory atrial tachycardia/atrial fibrillation with haemodynamically dangerous tachyarrhythmia. After AV ablation, the patients require permanent placement of a pacemaker (VVI with frequency adaptation).

- **AV node modulation:**

  Ind: AV node re-entry tachycardia

  The "slow-fast form" of AV node re-entry tachycardia is based on a functional longitudinal dissociation of the AV

node, typically with a slow AV node conduction pathway for antegrade conduction, and a fast path for retrograde conduction.
Procedure: Selective modulation/ablation of the slow conduction pathway
Success rate: > 95 %
Complication risk: rarely total AV block (up to 1 %)

- **Ablation of accessory conduction pathways:**
  Ind: Atrioventricular re-entry tachycardia in WPW syndrome (bi-directional conducting accessory conduction pathway), hidden accessory conduction pathways, Mahaim fibres
  Procedure: Selective ablation
  Success rate: > 95 %.
- **Ablation in atrial tachycardia of focal origin (focal atrial tachycardia = FAT)**
  Ind: frequent to permanent FAT (unifocal or definable number), symptomatic or with limited LV function (possibly tachycardia induced cardiomyopathy)
  Procedure: focus ablation
  Success rate: > 90 % (the more foci, the lower the success rate)
- **Ablation in atrial re-entry tachycardia (ART):** rotary stimulation around myocardial scars
  Ind: frequent or permanent ART, symptomatic or with limitation of LV function
  Success rate: > 80 % (significantly higher with 3-D electro-anatomic reconstruction)
- **Ablation in AF of normal type (A. Flutt):** rotary stimulation around the tricuspid valve through the so-called cavo-tricuspid isthmus
  Ind: recurrent events (danger of rapid AV conduction with consecutive acute heart failure)
  Procedure: linear HF ablation for electrical dissection of the cavo-tricuspid isthmus
  Success rate: > 95 %
- **Ablation in paroxysmal atrial fibrillation:** Triggered by focal automatic centres, typically in the pulmonary vein ostia
  Procedure: electrical insulation of the pulmonary venous outlets from the rest of the left atrium using linear high frequency current lesions
  Ind.: selected younger patients with paroxysmal AF
  Success rate: approx. 80 %
  Complication risk: pulmonary venous stenosis, damage with possible perforation of surrounding organs (oesophagus, bronchial tubes)
- **Ablation in ventricular re-entry tachycardia:** rotary stimulation of the myocardial scars
  Ind: reduction in the number of tachycardial events in patients who have been fitted with an ICD
  Procedure: usually linear ablation concept
  Success rate: approx. 60 %
- **Ablation in idiopathic left ventricular tachycardia (ILVT):** rotary stimulation taking into consideration the left ventricular, usually posterior Purkinje fibres
  Ind: recurrent symptomatic events
  Success rate: > 80 %
- **Ablation in focal outflow tract tachycardia:** focal automatic centres, usually in the right ventricular outflow tract, rarely also left ventricular and epicardial origin
  Procedure: Focal ablation (in left ventricular epicardial focus localization, sometimes this can be done transaortal)
  Success rate: > 75 %

Surgical therapy

Rhythm surgery has retreated somewhat into the background due to the development of catheter ablation.
Procedures:
- Pulmonary vein isolation in focally triggered paroxysmal AF
- Pulmonary vein isolation: in additional atrial macro-re-entry tachycardia with the setting of additional linear lesions (modified Maze operation)
- Operative excision of VT focus in therapy resistant monomorphic VT, of which the origin can be determined by intra-operative or catheter mapping

CLASSIFICATION OF CARDIAC ARRHYTHMIAS [I49.9]

I. Stimulus formation disorders (SFD)

1. Nomo topic SFD (originating from the sinus node)
   - Sinus arrhythmia
   - Sinus bradycardia (< 60/min)
   - Sinus tachycardia (> 100/min)

2. Heterotopic SFD (arise outside the sinus node)
   Localization:
   – Supraventricular (atrium, AV node)
   – Ventricular (ventricle)
   ▶ Passive heterotopia:
   Substituted takeover of a secondary or tertiary cardiac stimulus formation centre, which come into action in the event of failure or slowing of the sinus node activity and in conduction blocks
   – Escape beats
   – Escape rhythms: secondary automation (atrium, AV node), tertiary automation (ventricle)
   – Wandering pacemaker
   ▶ Active heterotopia:
   – Extrasystoles
   – Extra rhythms (heterotopic rhythm is faster than the sinus rhythm):
   – Accelerated junctional rhythm
   – Accelerated idioventricular rhythm

II. Stimulus conduction disorders
- Sinoatrial block (SA block)
- Atrioventricular block (AV block)
  · infranodal block (A-H time)
  · infrahissary block (H-V time)
- Intraventricular stimulus propagation delay/bundle branch block

III. Special types
- Sick sinus syndrome
- Hypersensitive carotid sinus

IV. Tachycardia
▶ General mechanisms:
- Triggered activity
- Increased autonomy
- Rotary stimulation (re-entry)

▶ Tachycardia types:
1. AV node re-entry tachycardia
2. Atrioventricular re-entry tachycardia
   - WPW syndrome
   - Mahaim tachycardia
   - Hidden accessory conduction pathway
   - Chronic junctional re-entry tachycardia
3. Focal atrial tachycardia (FAT)
4. Junctional ectopic tachycardia (JET)
5. Atrial fibrillation
6. Atrial re-entry tachycardia (ART)
7. Atrial fibrillation
   - Paroxysmal
   - Permanent
8. Ventricular tachycardia
9. Ventricular flutter / ventricular fibrillation

V. Sudden cardiac death (cardiac arrest)

I. STIMULUS FORMATION DISORDERS

Nomotopic stimulus formation disorders

Sinus arrhythmia [I49.8]
- Respiratory sinus arrhythmia:
  Physiological increase in heart rate during inspiration (Bainbridge reflex due to increased venous reflux) and decrease during expiration (vagus involvement); most pronounced in children and adolescents
- Non-respiratory sinus arrhythmia: rare; it is a sign of sinus node damage

Sinus bradycardia [R00.1] (heart rate < 60/min)
- Physiological: Adolescents and elderly, athletes, increased vagus tonus
- Pathological:
  - Extracardiac origin: e.g., hypothyroidism, hypothermia, vomiting, increasing intracranial increase, typhoid and hyper-reactive carotid sinus
  - Cardiac origin: sick sinus node (sick sinus syndrome)

• Pharmacological: beta blockers, anti-arrhythmics, digitalis, etc.
The critical limit of bradycardia depends on the output capacity of the heart; athletes have isolated nocturnal bradycardia down to < 40/min without any complaints, while those with cardiac disease and the elderly can easily experience symptoms of impaired cerebral perfusion (dizziness, syncope). In pathological sinus bradycardia, the heart rate does not sufficiently increase under stress.

Sinus tachycardia [R00.0] (heart rate > 100/min)
• Physiologic: infants, young children, physical and psychological stress, emotional reactions, increased sympathetic tonus
• Pathologic:
- Extracardiac origin: e.g., fever (per 1 °C rate increase by approx. 10 beats/min), hyperthyroidism, anaemia, hypoxia, hypotension, haemorrhage, shock
- Cardiac origin: heart failure, coronary ischaemia, MI, hyperkinetic cardiac syndrome = inappropriate sinus tachycardia without known organic or medication associated cause: vegetative regulation disorder in the form of increased adrenergic stimulation of the beta receptors with slight resting tachycardia, excessive (inappropriate) sinus tachycardia under stress and systolic hypertension)
• Pharmacologic: stimulants (alcohol, nicotine, caffeine), adrenalin derivatives, atropine, etc.
The critical limit of tachycardia depends on the output capacity of the heart and the age (maximum heart rate in ergometry = 220 - age). With increasing tachycardia, the diastole becomes so short that the cardiac output drops (whereby the ECG shows an ST segment drop due to tachycardia as a sign of disordered stimulus degeneration/repolarization)

Th.: • Treat the underlying cause ! (most important measure)
• Symptomatic treatment:
- For vagal mediated sinus bradycardia: temporary administration of parasympatholytic drugs (e.g., Atropine - see Anti-arrhythmics); in sick sinus node and hyperreactive carotid sinus pacemaker therapy if needed.
- For sinus tachycardia: only for hyperkinetic cardiac syndrome and for hyperthyroidism (as a supplement to thyreostatic treatment) beta receptor blockers may be used (see Anti-arrhythmics).

Heterotopic stimulus formation disorders

▶ **Passive heterotopia**
Whenever the impulse frequency of the sinus node falls below a critical limit (due to sinus bradycardia or sinus arrest) or if conduction is impaired (SA block, AV block), slower (than sinus node) heterotopic stimulus centres are capable of taking over as a substitute. If a missing sinus impulse is replaced, this is called an escape beat; if sinus impulses fail for a longer time, heterotopic stimulus centres form escape rhythms [I49.8]:
- Secondary pacemaker centres in the lower region of the atria and AV node: Junctional (node) rhythm with an escape frequency of approx. 30 - 50/min.
***Note**:* The AV node itself does not possess any pacemaker cells, only the bordering atrial region including the coronary sinus do.
Escape rhythms from secondary pacemaker centres are the most frequent since their frequency is higher than those of the tertiary centres.
- Tertiary pacemaker centres of the ventricles with a critical bradycardia of 20 - 30/min come into action whenever the node rhythm fails or the AV conduction is blocked.

Wandering pacemaker [I49.8]:
Short term switch between sinus rhythm and ≥ 1 ectopic secondary site of stimulus formation (corresponding to atrial or junctional escape rhythm).
ECG: alternating change of the P wave morphology, PQ time and frequency
Cause: temporary lowering of the sinus node frequency below the innate frequency of secondary pacemaker centres.
Incid.: healthy people (vagotonus), occasionally seen under digitalis therapy and cardiac diseases.
Th.: none

▶ **Active heterotopias**
These occur when an ectopic stimulus formation leads to premature cardiac stimulation, either in the form of individual heterotopic stimulations (extrasystoles) or in the form of a heterotopic rhythm, that has a faster rate that the sinus rhythm (accelerated AV node rhythm and accelerated idioventricular rhythm).

Accelerated junctional (AV node) rhythm [I49.8] and accelerated idioventricular rhythm [I44.3]

Normally the secondary (AV node region) and tertiary pacemaker centres (ventricle) only passively come into action at their lower innate frequency, whenever the sinus rhythm fails or a conduction block occurs.
In isolated cases, however, they can intermittently take over the pacemaker function as active heterotrophic centres with pathologically increased frequencies > 100/min.

Incid.: Organic cardiac diseases (e.g., recent infarction), digitalis intoxication, rarely also in children/adolescents with healthy hearts

DD:
- In accelerated idioventricular rhythm: VT (rate > 100/min)
- Intraventricular blockages (often permanent → pre-ECG; idioventricular rhythm is transient)

Th.: treat any underlying disease, ask if the patient takes digitalis medication!

EXTRASYSTOLES (ES) [49.4]

Incid.: Very frequent, even in healthy people. The majority of people experience extrasystoles sometime during their lives, 30% notice the extrasystoles as "irregular or missed beats" and only some of those affected feel unwell because of it. Supraventricular (SVES) and ventricular extrasystoles (VES) are distinguished according to their site of origin.

Aet.:
1. Physiologic: Simple VES often occur even in healthy individuals. There is a variety of causative factors: vegetative lability, emotional excitement, increased vagal tone (with bradycardia-conditioned VES), fatigue, stimulant intake (alcohol, caffeine, and nicotine)
2. Organic cardiac diseases, e.g., coronary heart disease, cardiomyopathy, myocarditis, etc.
3. Extracardiac causes: potassium deficiency (e.g., due to diuretic therapy), medications (digitalis, sympathomimetics, anti-arrhythmics, tricyclic antidepressants, etc.); Roemheld syndrome (distended abdomen with pressure on the diaphragm can cause of cardiac symptoms), hyperthyroidism

Supraventricular extrasystoles (SVES) [I49.4]

1. Atrial extrasystoles [I49.1]: deformed P wave, shortened PQ, ventricular complex (QRS) normal
2. Junctional (AV node) extrasystoles [I49.2]: negative P waves before, during or after the QRS complex. The terminology consequently derived as upper, middle, and lower AV node ES is not relevant (although still in use) because the morphological basis is missing! It is better to call it AV node ES with or without delayed retrograde atrial excitation.

Aet.:
1. Often seen in healthy individuals; triggering factors: emotional excitement, fatigue, stimulants (alcohol, caffeine, nicotine)
2. Occasionally in cardiac diseases, hypokalaemia

ECG: SVES usually show a non-deformed QRS complex of normal width → exception: in premature incidence of a SVES, aberrant ventricular conduction can occur with deformation of the ventricular complex as with a ventricular extrasystole; in such cases the SVES can be identified by the preceding P wave.
If an SVES occurs still earlier, the conduction system can still be refractory; in antegrade conduction disorder of an atrial extrasystole, the QRS complex is missing. In retrograde conduction disorder of an AV node ES, the P wave can be missing which is known as blocked SVES [I49.9]. As a rule, the SVES depolarizes the sinus stimulation with displacement of the basic rhythm. The interval between pre- and postextrasystolic cardiac action is smaller than a doubled normal interval (non-compensatory pause).
If with AV-node extrasystole, atrium and ventricle contract simultaneously against a closed AV valve, a stop wave occurs as part of the venous pulse (usually perceived as very unpleasant by patients).

Di.: Resting ECG, 24h-ECG, ergometry, echo
The most frequently affected sites for increased autonomy at atrium level are known from studies in interventional electrophysiology: Crista terminalis, ostial region of the superior and inferior vena cava, coronary vein sinus ostium and the ostia of the pulmonary veins. This is important to know for interventional as well as for surgical treatment of focally triggered paroxysmal AF.

Th.:
- SVES in healthy individuals does not require treatment.
- If cardiac disease is present, it is treated.
- Check potassium levels and ask if the patient takes digitalis
- If SVES triggers paroxysmal supraventricular tachycardia or intermittent AF (24h-ECG), treatment is required (e.g., with Verapamil or beta blockers).

Ventricular extrasystoles (VES) [I49.3] Ventricular extrasystoles

Originate below the bifurcation of the budle of His. The sinoatrial node is normally not activated retrogradely. Hence the patient's regular sinus rhythm remains intact (RR interval between pre- and post-extrasystolic cardiac action corresponds to the doubled RR interval of two normal actions); the compensatory post-extrasystolic pause is the result of this (which the patient perceives as palpitations or "skipping a beat"), because the due sinus impulse falls on a refractory ventricular myocardium. Only in sinus bradycardia the ventricle can be ready for stimulation again. Therefore normal action is not possible (interpolated or interponated ES).

Classification:

1. Right ventricular ES: picture of complete LBBB (QRS > 0.11 s)
2. Left ventricular ES: picture of complete RBBB (QRS > 0.11 s)
3. Bundle branch ES: no QRS widening like the other VES, but otherwise they fulfil the characteristics of VES: They do not disturb the sinus rhythm; a compensatory pause follows.

- Monomorphic (monotopic) ES: similarly deformed ventricular complexes, partly in healthy individuals, partly of organic origin
- Polymorphic ES: variously deformed ventricular complexes as a result of various stimulus origins: always of organic origin (cardiac muscle damage).

Polymorphic VES are usually also polytopic (of various origins). However, sometimes premature ES of the same origin can exhibit a polymorphic image. This is the result of different stimulus conduction. Supraventricular ES can show an expanded ventricular complex like VES as a result of such an "abnormal conduction". This can then be recognized by the preceding P wave.

Repetitive ES possibly have a regular relationship to normal rhythm: If every normal action is followed by two ES, e.g., this is called bigeminus or trigeminus (frequent in digitalis intoxication). If ES occur regularly after 2 (or 3) normal beats, this is a 2 : 1- (3 : 1-) extrasystole. If 3 or more VES follow one another without a normal beat in-between, this is called salves.

N	N	N	N	Normal action (N)
NE		N	N	VES (E) with compensatory post-extrasystolic pause
N E	N	N	N	Interponated (= interpolated) ES
NE		NE		Bigeminus
NEE		NEE		Trigeminus (couplets = 2 sequential extrasystoles)
N	NE	N	NE	2 : 1 extrasystoles
NEEE		N	N	Salvo (3 sequential extrasystoles)

Remark: The definition of trigeminus varies: Germany: NEE - NEE; USA: NNE - NNE.

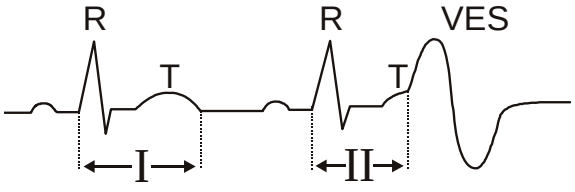
With premature occurring extrasystoles, the stroke volume of the extrasystole is reduced due to the short diastole. Therefore a bigeminus can lead to a pulse deficit and can mimic bradycardia on pulse palpation. The stroke volume of the post-extrasystolic cardiac action is increased due to the longer diastole.

In organic cardiac diseases (in particular MI) and left ventricular failure, the occurrence of complex VES can be precursors of dangerous ventricular tachyarrhythmias including ventricular fibrillation. Such warning arrhythmias are:

- Frequent polytopic (polymorphic) VES
- Bigeminus
- Couplets and salvoes
- R-on-T phenomenon: with the very premature occurrence of a VES, there is the risk that the VES falls in the vulnerable phase of T (increasing bundle of T) ("R-on-T phenomenon") and thereby triggers VT. In order to recognize such a risk, the so-called prematurity index (PI) is calculated:

$$PI = \frac{Q_N \text{ to } Q_{ES}}{Q_N \text{ to } T_{End}} \quad \frac{II}{= I}$$

PI < 1.0 = R-on-T phenomenon



Classification of VES according to LOWN in 24h-ECG

	Degree	
Simple VES	0	No VES
	I	Monomorphic VES (< 30/h)
	II	Monomorphic VES (> 30/h)
Complex VES	IIIa	Polymorphic VES
	IIIb	Ventricular bigeminus
	IVa	Couplets (2 VES one after the other)
	IVb	Salvoes (≥ 3 VES one after the other)
	V	Premature occurring R/T VES (R-on-T phenomenon)

The Lown classification is not of great prognostic value. The differentiation between absence and presence of non-sustained ventricular tachycardia (nsVT) is more important. These are defined as a sequence of ventricular extrasystoles (VES) with a frequency of more than 120/min and a minimum number of three consecutive VES.

Di.: Resting ECG, 24h-ECG, ergometry, echocardiography

Th.:
- VES in healthy individuals, in particular those which disappear under stress ("overdrive suppression") require no treatment; Exceptions: increasing limitation of cardiac function (rare tachycardia induced cardiomyopathy) or in cases with subjective symptoms.
- VES in organic cardiac diseases:
  1. Causal therapy: most important and decisive for the prognosis e.g., revascularization measures in CHD, etc.!
  2. Symptomatic therapy:
     - Check K^+ and Mg^{++} balance and check for any digitalis therapy: Treatment of digitalis intoxication (see that section), consider reducing the digitalis dose (the more damaged a heart is, the less it tolerates digitalis!), adjust K^+ and Mg^{++} to high-normal serum levels.
     - Antiarrhythmic therapy:

       Indicated in elevated risk of sudden cardiac death as a result of VF: Complex VES in patients with severe myocardial underlying diseases and limitation of left ventricular pump function.

       Class I anti-arrhythmics are contraindicated for patients with structural cardiac diseases (in particular, CHD and heart failure) because they worsen the prognosis. Sotalol and amiodarone also have no advantage with regard to the prognosis; in advanced heart failure (NYHA III), they even worsen the prognosis. For this reason, in the presence of increased risk of VF or sudden cardiac death, an ICD should be employed.

       Beta blockers without intrinsic activity reduce the risk of VES triggering VF and are therefore anti-arrhythmics of choice for patients post MI as well as in patients with limited pump performance.

Prg: VES in healthy individuals: harmless, good prognosis (independent of the Lown classification)

VES in individuals with heart disease:
Frequent occurrence of VES after a recent infarction is a warning sign of increased risk of VF. However, VF can occur without prior warning signs.
Risk factors for sudden cardiac death: see that section

II. STIMULUS CONDUCTION DISORDERS

Sinuatrial (SA) block [J45.5]

3 Degrees of severity:

- SA block 1st degree: delayed conduction of the stimulus from the sinus node to the atrial musculature. Not detectable in the ECG.
- SA block 2nd degree: intermittent conduction interruption:
  Type 1 (Wenckebach periodicity):
  ECG: The PP intervals become shorter with PQ time remaining the same until a longer pause occurs. This however, is shorter than the doubled preceding PP interval (DD: sinus arrhythmia).
  Type 2 (Mobitz):
  ECG: Conduction interruptions with a length of duration that is at least double or longer than the normal P-P interval.
- SA block 3rd degree: Total conduction interruption with absent impulse transmission to the atrial myocardium.
  When the latency until initiation of an AV or ventricular rhythm is too long, Adams-Stokes attacks occur (as with total AV block). In the usual ECG, 3rd degree SA block cannot be distinguished from sinus arrest.

Aet.: Sick sinus syndrome, overdose of digitalis or anti-arrhythmics, myocarditis, coronary heart disease and MI

Cl.: Symptoms of dizziness including loss of consciousness/syncope (Morgagni-Adams-Stokes attack) in higher grade blocks with longer asystolic pauses or severe bradycardia.

Di.: (24h-)ECG

Th.: If there are any toxic effects of digitalis or anti-arrhythmics, discontinue these medications. Give Atropine in an emergency. In cases of dizziness/syncope (Adams-Stokes attack): pacemaker therapy.

Atrioventricular (AV) block [I44.3]

3 Degree of severity:

- AV block 1st degree: delayed stimulus conduction
  No symptoms, only recognizable in the ECG: PQ interval > 0.20 sec. In the bundle of His-ECG (HBE), the AH interval is prolonged. With severely prolonged PQ interval, the P wave can fall into the repolarization phase of the previous beat.
- AV block 2nd degree: Intermittent conduction interruption:

- Type 1 Wenckebach periodicity (Syn.: Mobitz I):
  Localization of the block above the bundle of His
  ECG: The PQ intervals become longer while the PP interval remains the same until conduction (cardiac action) is missing; the pause that arises is shorter than a doubled PP interval.
  In the bundle of His ECG (HBE) a supra-His conduction delay or block is exhibited with increasing prolongation of the AH interval until a His potential is missing; this course of events can repeat periodically.
- Type 2 Mobitz (Syn.: Mobitz II):
  Localization of the block below or within the bundle of His.
  ECG: Sudden missing QRS complex after a preceding P wave with normal or continuously prolonged PQ interval. The pause corresponds to a doubled PP interval.
  · Isolated AV blocking or
  · Regular AV blocking:
  If 1 of 2 sinus node stimuli is transmitted, this is called a 2 : 1 block. If only 1 out of 3 stimuli is transmitted, this is called a 3 : 1 block.
  Organic cardiac disease is always the cause. There is the risk of progression to AV block IIIrd degree with Adams-Stokes attacks. Consequently this is an absolute indication for a pacemaker.
  In the HBE, an infra-His conduction delay or blocking with prolongation of the HV interval or the periodic absence of individual ventricular potentials (with of normal AH interval) is exhibited.

  DD: From a superficial ECG, AV block 2nd degree/type 2 with 2 : 1 transmission cannot be distinguished with certainty from AV block 2nd degree/type 1 with dropping of every 2nd conduction → Atropine test (0.5 – 1.0 mg Atropine IV) or exercise ECG: In AV block 2°/type 1 the AV conduction with prolongation of the Wenckebach periodicity (or transition to AV block 1.°) improves. In AV block 2°/type 2 there is worsening of the AV conduction: A 2 : 1 block proceeds to a 3 : 1 or 4 : 1 block.

- AV block 3rd degree: total conduction interruption with complete dissociation of atrial and ventricular action: normal frequent P spikes unrelated to the slower QRS complexes.
  The pacemaker function is taken over either by secondary stimulus formation centres in the AV node or in the bundle of His (with narrow ventricular complexes and a frequency > 40/min) or by tertiary stimulus formation centres in the ventricular myocardium (with bundle branch-like deformed ventricular complexes and frequency < 40/min). The latency time until the replacement centre springs into action is called the pre-automatic break.

Aet.:
- Increased vagotonus, e.g., athletes: AV block 1° (disappears under stress)
- Coronary heart disease and MI, cardiomyopathies, congenital heart defects (e.g., L-transposition of the great arteries), myocarditis (including borreliosis)
- Complication during/after cardiac surgical intervention
- Post-traumatic
- Drug-induced (digitalis, anti-arrhythmics), hyperkalaemia
- Idiopathic degeneration of the stimulus conduction system (Lenègre's disease) and idiopathic sclerosis/calcinosis of the connective tissue of the heart structure (Lev's disease)

Remark: AV conduction disorders in posterior wall infarction (transient ischaemia of the AV node) have a better prognosis than in anterior wall infarction with septum involvement (Tawara branch blocked).

Cl.: There are two major risks associated with total AV block:

1. Asystole of longer duration between the beginning of the total block and the establishment of a ventricular escape rhythm (= pre-automatic break) leads to a hypodynamic form of Morgagni-Adams-Stokes (MAS) attacks [I45.9]:

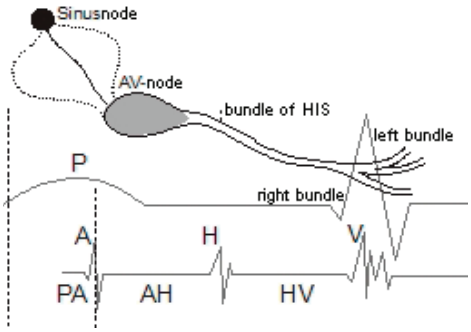
Asystole duration:	3 - 5 sec.:	pallor, dizziness
	10 - 15 sec.:	loss of consciousness
	20 - 30 sec.:	convulsions (misdiagnosis: epilepsy)
	30 - 60 sec.:	respiratory arrest
	> 3 min. :	irreversible brain damage or death

During the attack pupils are wide, and reflex activity is decreased or absent.
Every attack can be lethal!

2. Bradycardia (< 40/min) can lead to HF.

DD: 1. Tachycardic cardiac arrhythmias including ventricular flutter/fibrillation
2. Other causes of syncope (see that section)

Di.: - History + clinical picture (dizziness, syncope?)
- (24h-)ECG
- Bundle of His ECG (HBE):



A = atrial stimulation
H = bundle of His stimulation
V = ventricular stimulation

Conventional ECG

Bundle of His ECG

Normal times:
PA = 25 - 50 msec.
AH = 60 - 125 msec.
HV = 35 - 55 msec.

With the aid of the intracardially derived bundle of His ECG, the global conduction recorded in the PQ interval of the conventional ECG can be determined as to before and after the bundle of His. According to this, the following can be distinguished:

- ▶ Supra-His block (intranodal block):
  - ➞ Prolonged AH-interval or lack of H potential
- ▶ Intra- and infra-His block (= infranodal block):
  - ➞ Prolonged HV-interval or lack of V potential

The proximally localized junctional blocks have a better prognosis than the distally localized subjunctional blocks: Supra-His blocks are often reversible. They seldom lead to Adams-Stokes attacks and often exhibit an escape rhythm from the bundle of His with still tolerable frequencies around 40/min. With an infra-His block, the very slow ventricular escape rhythm (with a frequency between 20 – 30/min.) is initiated only after a lengthy pre-automatic break ➞ high risk of Adams-Stokes attacks!

Th.: a) Causal treatment: In case of drug induced AV-block: Stop digitalis or anti-arrhythmics. Treatment of myocarditis or a myocardial infarction.

b) Symptomatic treatment:

- AV block 1st and 2nd degree (Wenckebach): Besides causal measures (e.g., check or discontinue digitalis therapy), usually no symptomatic therapy is required. If there is severe bradycardia, consider Atropine. Orciprenaline can provoke VES and is therefore contraindicated in digitalis induced bradycardia!
- AV block 2nd degree (Mobitz): Since it usually involves an infra-His block with the risk of total block, conduction delaying medication (digitalis, anti-arrhythmics) must be discontinued. Relative pacemaker indication. Atropine should not be administered because it leads to deterioration with the risk of a total AV block.
  Pacemaker therapy is indicated if there is a history of symptoms (dizziness, syncope) or threatening total AV block.
- AV block 3rd degree: In Adams-Stokes attack, resuscitation as with cardiovascular arrest (➞ see below) and pacemaker therapy

Intraventricular blocks [I45.4]

Synonyms: bundle branch blocks, fascicular blocks

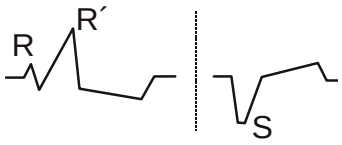
Loc: Below the bundle of His (infra-His blocks)
Taking into consideration the trifascicular structure of the ventricular stimulus conduction system, the following are distinguished:
1. unifascicular - 2. bifascicular - 3. trifascicular blocks
As with the other stimulus conduction disorders, there are 3 degrees of severity:
Ist.: incomplete - IInd: intermittent - IIIrd: permanent block
With the exception of the trifascicular block (which in the ECG resembles a total AV block) no clinically detectable arrhythmia (diagnosis only by ECG) results from bundle branch blocks.

1. Complete right bundle branch block (RBBB) (blockage in the right Tawara bundle):
   ECG: QRS time ≥ 0.12 sec., delayed start of the final negative movement, discordance of the final ventricular portion (ST/T) to the ventricular complex (QRS), S wave in I, R in V1, M-shaped split ventricular complex
   Incomplete RBBB: QRS time 0.10 – 0.11 sec., rSr' or RSr' in V1-2, S wave in I
2. Left anterior hemiblock (LAHB): the most frequent form of intraventricular block; ECG: marked left axis deviation = RI/SII/SIII-type; R/S transition displaced to V6, deep S in V5/6.
3. Left posterior hemiblock (LPHB): ECG: right axis deviation or marked right axis deviation with normal QRS time. The diagnosis can only be made provided that the right axis deviation cannot be explained by right ventricular volume load.
4. Complete left bundle branch block (LBBB): This can arise from a unifascicular block (left Tawara branch blocked

before the branch) or by a bifascicular block (2 + 3).

ECG: QRS time ≥ 0.12 sec., delayed start of the final negative movement, wide and deep S wave in V1,2, split ventricular complex ("broken spike") in V5/6, discordance of the final ventricular portion (ST/T) to ventricular complex (QRS). No Q precedes the coarse split R wave in I/aVL.

5. Incomplete LBBB: QRS time 0.10 – 0.11 sec



RBBB / LBBB

Bifascicular blocks arise from the combination of unifascicular blocks; these can be early signs of a trifascicular bundle branch block (with the risk of Adams-Stokes attacks as with total AV block).

Conduction V1

Aet.: Coronary heart disease and MI, myocarditis and cardiomyopathies, left hypertrophy (most frequent cause of LBBB), right heart overload (e.g., due to congenital defects or pulmonary embolism → incomplete or complete RBBB), idiopathic (Lenègre's disease and Lev's disease)

Th.:
- treat the underlying disease
- In bifascicular block (e.g., right bundle branch block + left anterior hemiblock) a pacemaker might be indicated for those patients with a history of dizziness or syncope or when a first degree AV block is present (PQ prolongation) → if a prolonged HV interval is seen in the bundle of His ECG, prophylactic pacemaker therapy is indicated.
- Treatment of trifascicular block as in total AV block (see below)

III. SPECIAL TYPES

Sick sinus syndrome (SSS) [I49.5]

The following arrhythmias fall into this category:
1. Persistent sinus bradycardia with symptomatic complaints
2. Intermittent sinus arrest or SA block
3. Tachycardia-bradycardia syndrome: Paroxysmal supraventricular tachycardia or atrial flutter/atrial fibrillation. At the end of a tachycardic episode, a prolonged asystolic pause follows before the (possibly) bradycardic rhythm begins again. This can lead to cerebral ischaemia with dizziness and syncope.
   Comment: Occasionally, a carotid sinus syndrome can indicate a sick sinus node (see below).

Aet.:
1. Coronary heart disease
2. Cardiomyopathies and myocarditis (possibly with autoantibodies against the sinus node)
3. Idiopathic degeneration of the conduction system (M. Lenègre and M. Lev)
4. Congenital: mutations of sodium (SCN5A) and funny-(HCN4) ion channels

Cl.: During tachycardia: palpitations, dyspnoea, angina pectoris.
During bradycardia: dizziness and syncopes (Adams-Stokes attacks), heart failure

Di.:
1. Long-term ECG: recording and quantification of the bradycardic arrhythmias
2. Exercise ECG: Inability to achieve at least 70 % of the max. age dependent increase in heart rate under ergometric stress (chronotropic incompetence)
3. Atropine test: There is an insufficient increase in heart rate after injection of 1 mg Atropine IV: heart rate remains < 80/min
   CI: glaucoma, prostate adenoma
4. Sinus node recovery time is prolonged (> 1.500 msec.) = time until sinus rhythm restarts after previous rapid atrial stimulation (via pacemaker).

Th.:
- for symptomatic bradycardia (dizziness, heart failure or syncopes): pacemaker therapy
- for tachycardia-bradycardia with clinical symptoms: pacemaker + antiarrhythmic treatment

Carotid sinus syndrome [G90.0]

Def.: Oversensitivity of the baroreceptors in the region of the carotid bifurcation with clinical symptoms after carotid stimulation → 3 types:
- Cardio-inhibitory type (90 % of cases): Vagal stimulation leads to asystole or bradycardia
- Vasodepressor type (10 % of cases): BP drop > 50 mm Hg without essential bradycardia
- Mixed type

Ep.: frequent seen in older people (up to 25 %), 90 % of patients are symptom-free.

Aet.: Usually arteriosclerotic (in older men)

Cl.: dizziness or syncopes caused by spontaneous head rotations, tight collars, or after massage of the carotid bifurcation

Di.: History + trial of carotid massage : asystole > 3 seconds and/or blood pressure drop > 50 mm Hg after single-sided carotid sinus massage (Caution in patients with stenosis of the carotid artery!)
The carotid massage trial is positive in 25 % of patients > 65 years. Therefore it should only be evaluated in conjunction with the history/clinical picture.

Th.: Only when there are clinical symptoms in the history (dizziness, syncopes), which occur with spontaneous movements in the head/neck region, pacemaker therapy is indicated.

IV. TACHYCARDIA

AV NODE RE-ENTRY TACHYCARDIA

Def.: The common term for AV node re-entry tachycardia and atrioventricular re-entry tachycardia used to be "paroxysmal supraventricular tachycardia" (PSVT).

Ep.: It is the most frequent form of PSVT, usually seen in younger patients, f > m

Aet.: Congenital disorder in the region of the AV node: functionally dual conduction capacity of the antegrade as well as partially of the retrograde AV node conduction. Presence of a relatively slow and a more rapidly conducting AV node conduction pathway ("slow and fast pathway").

Pg.: AV node re-entry tachycardia is typically precipitated by atrial extrasystole. The functionally separated conduction pathways with different conduction speeds and refractory behaviour enable a persistent rotary stimulation (re-entry) lasting one minute to several hours. In 90 % of cases, this is a matter of tachycardia of the "slow-fast" type, which uses the slower pathway in the antegrade direction, and the fast path in a retrograde direction. The atypical form with use of a fast path in the antegrade direction and a slow path in the retrograde direction (fast-slow type) occurs or a slow path in the antegrade direction and the retrograde direction (slow-slow type) are less frequent.

ECG: During normofrequent sinus rhythm there are no anomalies in the ECG
During tachycardia, normally configured and narrower QRS complex, usually without visible P wave. If there is a visible wave, it appears shortly before or after the QRS complex depending on the conduction speed. Tachycardia rate is between 150 to 220/min.
In case of an abnormal transmission, there are broad QRS complexes resembling a bundle branch block; in which case differentiation from ventricular tachycardia is difficult (see below).

Cl.: Sudden episodes of tachycardia. Duration: Minutes, hours or longer, often sudden return to normal sinus rhythm. In otherwise healthy people, except for the fast heart beat, there are often no symptoms. In patients with heart failure and/or coronary heart disease, there is critical reduction of cardiac output with hypotension, angina, dizziness, syncope and rarely cardiogenic shock. During and after tachycardia, polyuria can develop (caused by atrial natriuretic peptide – ANP). If there is simultaneous contraction of atria and ventricles, so-called pulsations can be seen in the neck veins ("frog sign").

DD:
- Atrioventricular re-entry tachycardia (in latent accessory conduction pathway)
- Atrial or sinus tachycardia with constant 1-1 AV transmission and relative long PQ interval, such that the P wave is buried within the previous QRS complex.
- When the QRS complex is broad: ventricular tachycardia, antidrome atrioventricular re-entry tachycardia.

***Note**:* Every tachycardia with wide QRS complex is treated as a ventricular tachycardia ("treat the worst case") until proven otherwise.

Di.: Clinical picture: abruptly occurring regular tachycardia (sinus tachycardia not abrupt) + ECG (regular tachycardia with narrow QRS complexes)
Often otherwise healthy individuals.

Th.: A) Symptomatic treatment:
- ▶ in hemodynamically stable patients (majority):
  1. Vagal stimulation: Valsalva maneuvre (after deep inspiration, try to exhale against closed mouth and nostrils as long as possible), massage a carotid sinus (not longer than 5 sec.; after auscultation of the carotid arteries), rapidly drink a large glass of cold carbonated water, dip the face into cold water, ice collar, etc.
  2. Medication:
     - Adenosine (e.g., Adrekar®): drug of choice
       Act.: short-term blockage of the AV conduction in the AV node (lasting maximal 8 sec.). It is the drug of choice for all regular tachycardia with narrow ventricular complex.

SE: possibly short-term asystole, drop in blood pressure, flush, dyspnoea, chest tightness, bronchospasm
CI: Atrial tachycardia / atrial fibrillation in WPW syndrome (significantly broadened QRS complex, often with irregular sequence), bronchial asthma, AV block > 1°, sick sinus syndrome, QT prolongation, atrial fibrillation or flutter
Dose: Due to the very short half-life (20 sec.), 6 mg i.v. as a rapid bolus; if unsuccessful, repeat with 12 mg after 3 minutes. (Due to the short duration of action, Theophyllin as an antidote is usually not required.)

- Verapamil:
  Ind: therapeutic alternative to Adenosine
  SE: negative inotropic effect, drop in blood pressure, asystole, etc.
  CI: Atrial tachycardia / atrial fibrillation in WPW syndrome (significantly broadened QRS complex, often with irregular sequence), ventricular tachycardia, hypotension, decompensated heart failure (due to negative inotropic effect), sick sinus syndrome with bradycardic episodes in the history, prior treatment with beta blockers
  Dose: 5 mg i.v.. slowly over 10 min. under ECG control (can be repeated after 15 - 30 min.)
- Ajmaline: drug of choice for tachycardia with broad ventricular complex (see WPW syndrome)

***Note**:* ajmaline is also the drug of choice, when an exact differentiation between supraventricular and ventricular tachycardia is not possible. It is effective in both instances. (tachycardia with broad ventricular complex).

3. Electrotherapy:
   Ind: failure of drug therapy
   - Overdrive pacing for termination of rotary stimulation
   - Electrocardioversion
   Ind: patients with unstable circulation with imminent cardiogenic shock:
   In alert patients without hypotension → short intravenous anaesthesia (e.g., with Etomidate = Hypnomidate®)
   First dose of energy: 100 J, if unsuccessful, repeat with higher dose
   CI: Digitalis intoxication, recurrent PSVT after prior cardioversion

B) Interval treatment:

- For refractory AV node re-entry tachycardia high frequency (HF) catheter ablation: slow pathway ablation.
  Success rate > 95 % - rate of recurrence up to 5 % - AV block III° up to 1 %

ATRIOVENTRICULAR RE-ENTRY TACHYCARDIA (AVRT) [I47.1]

Ep.: It is the second most frequent type of paroxysmal supraventricular tachycardia (PSVT). The majority of patients have a healthy heart.

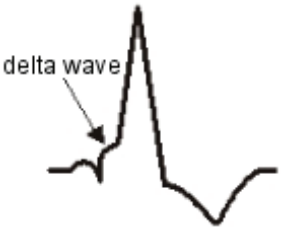
Def.: The underlying pathology is always an accessory atrioventricular conduction structure, which connects the atrial and ventricular muscle tissue with various conduction properties. These conduction pathways can lead to recurrent tachycardia by activating the retrograde branch. The conduction pathway of the AV-node is used as a branch of the re-entry loop, and the myocardium is included into the re-entry loop as well.
If antegrade (atrium-ventricle) conduction is performed via the specific stimulus conduction system and the retrograde (ventricle-atrium) via the accessory pathway, a normally configured narrow QRS complex typically results during tachycardia – orthodromic AVRT.
In reversed looping stimulation, i.e., in the antegrade direction via the accessory pathway, a maximally broad QRS complex results – antidromic AVRT.

4 Variants:

- **WPW syndrome (Wolff-Parkinson-White) [I45.6]:** (most frequent)
  The cause is an accessory conduction pathway (ACP) = conduction path between atrium and ventricle. During sinus rhythm, the atrial activation is conducted over the AV node as well as in the auxiliary connection via the accessory atrioventricular conduction pathway (Kent bundle) in the direction of the ventricle. Due to the lower conduction delay over the ACP in comparison to the AV node, a relatively premature ventricular activity in the area of the ventricular insertion of the ACP occurs (pre-excitation syndrome). This is seen as premature start of the QRS complex (Δ wave). The polarity and configuration of the Δ wave depends on the ventricular insertion site:
  - Right-sided ACP: negative Δ wave in V1 and positive in I, aVL
  - Left-sided ACP: positive Δ wave in V1 and negative in I, aVL
  The extent of the Δ-wave depends on the relative proportion of simulated ventricular musculature (position of the AL, conduction speed of the AV node).

Typically the ACP also exhibits retrograde conduction properties which then transmit the orthodromic atrioventricular re-entry tachycardia (narrow QRS complex!).

If the accessory conduction pathway conducts exclusively in the retrograde direction (ventricle → atrium), there is a normal superficial ECG without Δ wave and this is referred to as a hidden accessory conduction pathway (see below).



ECG: PQ interval < 0.12 sec. + Δ wave (broadening of the QRS complex through pre-excitation with slow R increase)
The pre-excitation can occur permanently or intermittently.

Cl.: 3 groups of patients:
1. Asymptomatic ECG finding without occurrence of paroxysmal tachycardia (PSVT)
2. Occasional occurrence of PSVT
   - Orthodromic type of AVRT (most frequent): rotary stimulation antegrade over the AV node, retrograde over the accessory pathway. During tachycardia the QRS complexes are narrow without Δ wave. The PSVT begins and ends abruptly (frequency 150 - 220/min).
   - Antidrome type of AVRT (rarer): antegrade over accessory path, retrograde over the AV node: broad QRS complexes
3. Patients with potentially life-threatening tachyarrhythmias. This group has a short refractory time of the accessory path. In these cases AF can lead to ventricular tachycardia including VF (sudden cardiac death).

Di:
- History, clinical picture, ECG, long-term ECG, event recorder
- Intracardial ECG with localization of the accessory pathway:
  It is important to identify patients with short refractory time of the accessory pathway (shortest R-R interval in AF), because these patients are at risk of sudden cardiac death.
  Patients who exhibit a loss of Δ wave in the (24h-)ECG or under ergometric stress have a long refractory time of the accessory pathway and are usually not endangered.

Th.:
- In AVRT in the context of a pre-excitation syndrome, Ajmaline has proven to be effective: 50 mg Gilurytmal® slow IV under ECG control.
  Reserve drug: Propafenone

  ***Note**:* Verapamil, digitalis and adenosine are contraindicated in pre-excitation syndrome with atrial fibrillation because it leads to a shortening of the refractory time of the accessory bundle → danger of ventricular fibrillation!
- For threatening cardiogenic shock resulting from tachycardia: electrocardioversion.
- For refractory AVRT: selective high frequency (HF) catheter ablation of the accessory conduction pathway. Success rate: > 95 %.

- **Mahaim fibre (rare)**
  The arrhythmogenic tissue is a structure similar to an AV node. It consists of dispersed embryonic tissue of the specific conduction pathway system and is always found along the tricuspid valve anulus. Typically it has only antegrade, slow and delayed conduction properties – the resulting tachycardia is antidromic - (maximum pre-excitation!).
  ECG in sinus rhythm: normal PQ interval, sometimes small Δ waves.

- **Concealed accessory conduction pathway**
  In approx. 50 % of cases, accessory conduction pathways only conduct the electrical stimulation from the cardiac ventricle back to the atrium (exclusively retrograde conducting accessory pathway). Clinically, the typical paroxysmal orthodromic atrioventricular re-entry tachycardia occurs. It is always clearly recognizable in the ECG as regularly occurring tachycardia (rate: 180-200/min.) with a narrow QRS-complex but without visible P wave (fast retrograde conduction). If antegrade conduction over the accessory conduction pathway is missing, there is not an increased risk of ventricular fibrillation or sudden cardiac death.

- **Permanent junctional re-entry tachycardia (PJRT) - rare**
  Accessory conduction pathway with exclusively retrograde, slow and hesitant conduction properties. The tachycardia rate is lower than with the normal concealed conduction pathway and is often not perceived by the patient because it is permanent. It can lead to tachycardia induced cardiomyopathy.
  ECG: Narrow QRS complex with long R-P interval (typically R-P > P-R), P wave polarity in II, III, aVF is usually negative, since these conduction pathways usually lie inferoseptally on the tricuspid or mitral valve anulus.
  Comment: The Lown-Ganong-Levine syndrome (LGL syndrome: PQ time < 0.12 sec. without Δ wave) is an ECG variant without pathological significance.

FOCAL ATRIAL TACHYCARDIA (FAT)

- Unifocal atrial tachycardia
  Prev.: often in healthy people, also following heart operations
  ECG: Regular tachycardia at atrium level with monomorphic and altered P wave configuration. Depending on the frequency of the atrial tachycardia and the antegrade conduction capacity of the AV node, a stable 1: 1 or a stable (Mobitz type) or alternating (Wenckebach type) AV conduction is possible. The QRS complexes are typically narrow; however at higher frequency or in cases of inappropriate cardiac stress they can be deformed as in bundle branch block.
  The beginning and termination of focal atrial tachycardia are often gradual (warming-up / cooling-down).
- Multifocal atrial tachycardia
  Prev.: inappropriate cardiac stress (following heart operations, congenital heart defects) Cor pulmonale, severe heart failure, Theophyllin intoxication etc.
  ECG: At least 3 different P configurations, frequently with alternating PP and PQ intervals

Ther: 1. Causal: e.g., therapy of a digitalis intoxication (see corresponding section)
2. Symptomatic (e.g., β-blockers)

Comment: Atrial tachycardia with AV block suggests a digitalis intoxication until proven otherwise → check glycoside level, administration of digitalis contraindicated!

3. HF ablation is the therapy of choice when the patient has to be on permanent drug treatment or if there is risk of tachycardia induced cardiomyopathy, (success rate > 80 %).

Caution: Even with mild clinical symptoms or absence thereof, a frequently occurring focal atrial tachycardia can lead to tachycardia induced cardiomyopathy, independent of their frequency and the presence of a structural heart defect, even in young patients. This is usually reversible after appropriate treatment of the cardiac arrhythmia.

JUNCTIONAL ECTOPIC TACHYCARDIA (JET)

Aet.: Often organic cardiac disease or immediately following cardiac surgery (often seen in small children)

Pg.: increased autonomy with focus localization in the area of the AV node

ECG: Normal QRS configuration

Either: with dissociated P waves. The p-waves have a normal configuration as in sinus rhythm, when the tachycardia finds no way out of the AV node into the atrium in a retrograde direction.

Or: with not clearly visible P waves in the chronological course of the QRS complex (in retrograde junction to the atrium).
The tachycardia is often very rapid with rates up to 250/min.

Ther: 1. Causal (if possible)
2. Symptomatic:
   - class I C anti-arrhythmics, amiodarone
   - reduce the body temperature (this is only temporarily possible in the postoperative phase in anaesthetized patients).
   - HF ablation (Ultima ratio) with the risk of accidental complete blockage of the AV node (→ pacemaker indication)

ATRIAL FLUTTER

Aet.: The most frequent causes are organic cardiac diseases, in particular CHD, occasionally, however it occurs in healthy older individuals.

Pg.: Macro-re-entry with rotary intra-atrial stimulation, propagation in the right atrium along the circumference of the tricuspid valve. The anatomical structures responsible for maintaining the macro-re-entry are the cavo-tricuspid isthmus and the Crista terminalis.

ECG: Flutter waves ("sawtooth pattern"); there is no visible isoelectric line between the individual flutter waves;

2 types:

Type I (common type): flutter waves in leads II, III, aVF are negative at a flutter rate of 250 - 350/min. Macro-re-entry runs counter clockwise around the tricuspid valve anulus (ventricular view on the anulus)

Type II (reverse common type): flutter waves in leads II, III, aVF are positive at a flutter rate of 250 - 450/min. Macro-re-entry runs the opposite of common type flutter

Usually the ventricular frequency is reduced by a protective II° AV block (often 2:1 or 3:1) corresponding to the blocking conditions. However, there is the risk of a 1:1 transmission with impending ventricular tachycardia. In the

presence of the frequent 2:1 block, the ventricles usually beat at approx. 150/min. (DD: paroxysmal supraventricular tachycardia: 160 - 200/min.). In the presence of constant AV conduction: regular tachycardia. In cases of inconstant AV conduction: irregular tachycardia. The ventricular complexes are narrow (exception in conduction abnormality → here the individual ventricular complexes are spread out).

Transesophageal echocardiography (TEE): to exclude left atrial thrombi

Ther: 1. Causal (as far as possible)

2. Symptomatic:
   - Thromboembolism prophylaxis with heparin
   - Atrial overstimulation (overdrive stimulation) is usually successful.
   - Electrocardioversion: Initially with 200 J (Ws)
     If electrotherapy is not available, treatment e.g., with Amiodarone, can be attempted (Dose/SE/CI: see chap. Atrial fibrillation).
   - HF ablation: Curative treatment is possible through electrical dissection of the cavo-tricuspid isthmus using high frequency(HF) ablation. It is the treatment of choice for refractory events (success rate: > 95 %).

ATRIAL RE-ENTRY TACHYCARDIA (ART)

Aet.: Often organic cardiac diseases; in particular it can be a late complication after cardio surgical intervention

Pg.: Macro-re-entry with rotary intra-atrial stimulation propagation in the right or left atrium along surgically or degeneratively acquired myocardial scars and natural barriers (e.g., AV valve ring, vein outlets).

ECG: Monomorphic P waves, an isoelectric line is typically seen between the individual flutter waves, atrioventricular conduction conditions as with AF.

Ther: Basically as with AF, HF ablation provides an individualized linear ablation concept, today generally derived from 3-D reconstruction of the electro-anatomical situation (success rate: approx. 80 %).

ATRIAL FIBRILLATION (AF) [I48]

Incid: It is the most common type of supraventricular tachyarrhythmia
The incidence is age-dependent:
5th decade up to 1 %;
6th decade approx. 5 %;
7th decade and older up to 10 %

Aet.: 1. Primary or idiopathic in those with healthy hearts ("lone atrial fibrillation" - approx. 15 % of cases), occasionally familial disposition

2. Secondary:
   a) Cardiac: mitral valve defects (most frequent cause in younger patients), coronary heart disease/ myocardial infarction, heart failure (in NYHA I in 5 %, in NYHA IV in > 50 %), cardiomyopathies, myo-/pericarditis, heart operations, sick sinus syndrome, pre-excitation syndrome
   b) Extracardiac: arterial hypertension, PE, hyperthyroidism, heart trauma, alcohol toxicity ("holiday heart syndrome"), medication toxicity (e.g., thyroxine, beta sympathomimetics, Sumatriptan, Theophyllin, Fluoxetine, Clozapine, Sildenafil, Gemcitabine, Cisplatin, etc.)

Pg.: The abnormality is not located primarily in the sinus node, but in the atrium and the orifices of the pulmonary veins: An uncoordinated stimulation rotates so slowly in the atrium that it always encounters excitable tissue. Due to the high AF rate of 350 - 600/min., a haemodynamically effective atrial contraction is no longer possible. The lapse of atrial pump function reduces the cardiac output in healthy people by 15%, in patients with left cardiac failure up to 40%! Thanks to the filter function of the AV node, only a small portion of the atrial stimulations are transferred to the ventricles. Due to the irregular sequence of ventricular contractions with varied diastolic filling time, pump volumes vary greatly. This results in variations of the systolic blood pressure and pulse deficit.. Cardiac output drops with increasing tachyarrhythmia.

ECG: Irregular conduction in the AV-node results in absolute ventricular arrhythmia. A rate between 100-150/min is called tachyarrhythmia absoluta. A rate < 60/min (as in e.g., sick-sinus-syndrome) is called bradyarrhythmia absoluta.

The ECG typically shows absence of P waves, irregular R-R intervals, fibrillation waves (cilium-shaped tremor line of the isoelectric line, mainly visible in lead V1). The ventricular complexes are usually narrow. Individual or (less often) salvo-shaped broadened ventricular complexes can be the result of abnormal ventricular conduction, typically in the sequence of a long beat interval followed by a short beat interval (Ashman phenomenon). DD: ventricular extrasystoles/salvoes.

Course:
- First (possibly single) episode
- Paroxysmal: spontaneous termination usually after < 48 hr. (self-limiting)
- Persistent: does not convert spontaneously, but converts after therapeutic intervention
- Permanent: therapeutically non-converting permanent AF (cardioversion was not successful)

Paroxysmal AF that can evolve into chronic AF over the years is often differentiated into two types:
- Vagotonic type: Before the occurrence of the paroxysmal activity, the heart rate drops; onset is usually at night or at rest
- Sympathetic type: Before occurrence of paroxysmal activity, the heart rate increases; the onset is often in the morning or on a day after stress or stressful physical activity

Cl.: Symptoms occur particularly with the paroxysmal form: palpitations, possible feeling of dizziness, syncopes and dyspnoea in tachyarrhythmia with decreasing cardiac minute volume, anxiety, polyuria (ANP effect), irregular pulse with pulse deficit (= difference between pulse determined by auscultation and radial pulse in tachyarrhythmia). Refractory AF may not be noticed by the patient in some cases!

Co.: 1. Acute left ventricular failure with tachyarrhythmia or bradyarrhythmia (critical drop in cardiac minute volume)

2. Formation of atrial thrombi with the risk of arterial embolisms, primarily in the systemic circulation (cerebral embolisms!). 20 % of all strokes are caused by AF!
Low risk of embolism in idiopathic paroxysmal AF in individuals with healthy hearts, as long as the AF lasts < 24 hr.
Great risk of embolism in permanent AF, in particular in the presence of additional risk factors

Thromboembolism risk factors are:
- Age > 75 years
- Prior stroke or TIA
- History of thromboembolism
- Cardiac insufficiency with poor ejection fraction
- Cardiac valve replacement
- Mitral valve stenosis
- Arterial hypertension, diabetes mellitus
- In TEE: enlarged atrium, atrial thrombi, spontaneous echo contrast (SEC), auricular flow rate < 20 cm/s

CHADS risk classification for cerebral embolisms and haemorrhage risk under anticoagulants taking into consideration 5 risk factors:
Recently occurring deterioration of heart failure = congestive heart failure (C) / hypertension (H) / age (A) ≥ 75 yr. / diabetes mellitus (D) / TIA or stroke (S)

Every risk factor has been assigned a point, TIA or stroke in the history has been assigned 2 points:

CHADS points	Annual rate of cerebral embolisms to be expected according to the literature (%)
0	2
1	3
2	4
3	6
4	8.5
5	12.5
6	18

Oral anticoagulation (Marcumar/Warfarin) at INR 2.0 – 3.0 carries a risk of intracranial haemorrhage of ca. 0.3/year.

The benefit (stroke prevention) is much higher.

Di: History, clinical symptoms (irregular rapid pulse with pulse deficit) + ECG, possibly long-term ECG

Ther:
- Causal (as far as possible)
- Symptomatic: 2 therapy strategies that are prognostically identical:

1. Frequency control (FC):

1.1. Tachyarrhythmia absoluta: normalize the ventricular rate with medications
- Digitalis: Ind: heart failure (in combination with beta blockers)
  Digitalis lowers the ventricular rate (negative dromotropic effect).
  SE, CI, dosage: see appropriate sections!
- Antiarrhythmics:
  - Verapamil (Isoptin®): In patients with no heart failure, it is a very effective drug for normalization of the ventricular rate in tachyarrhythmia

SE, CI, dosage: see keyword Verapamil

- Beta receptor blockers: Ind.: Particularly tachyarrhythmia caused by hyperthyroidism as well as tachyarrhythmia in heart failure. Do not combine beta receptor blockers and verapamil (risk of total AV block).
  SE, CI, dosage: see keyword "Beta blocker"

- If in rare cases, a sufficient reduction in heart rate cannot be achieved, there is the option of AV node ablation + VVI pacemaker implantation.

1.2. Bradyarrhythmia absoluta is usually caused by AV conduction disorder. Symptomatic bradycardia is an indication for pacemaker implantation: Use the VVI(R) pacemaker type with frequency adaptive stimulation; there is often chronotropic incompetence under stress.

2. Rhythm control (RC) = regularization of AF = transition into sinus rhythm:
In spite of improved cardiac minute volume (of up to 20 %), heart failure occurred more frequently in the RACE trial under RC. Since in the PAFAC trial, 70 % of VF-refractory patients were asymptomatic (were unnoticed), anticoagulation is also recommended with RC.
Disadvantage: high rate or recurrence, proarrhythmias due to the anti-arrhythmics used; other SE due to anti-arrhythmics, more frequent necessity for pacemaker therapy

Prerequisites for a regularization attempt:

- AF had not been existing longer than approx. 12 months
- No advanced underlying cardiac disease
- Left atrium < 50 mm ∅
- Treatable causes have been addressed (e.g., hyperthyroidism)
- No sick sinus syndrome (place pacemaker prior to this!)
- Mitral valve defect only in stage I or II.
- Patients with underlying cardiac diseases, in particular heart failure, should be regularized on an inpatient basis under monitoring control (risk of proarrhythmic side effects with regularization employing drugs!) Serum potassium and QT time must be normal.
- Concomitant administration of potassium/magnesium preparations can possibly reduce proarrhythmic SE of anti-arrhythmics.
  The prospects for success of a regularization attempt decline:
  - when the diameter of the left atrium is > 4.5 cm
  - when the cardiac pump function is reduced
  - in chronic AF
- If AF lasts longer than 48 hr., thromboembolism prophylaxis with anticoagulants is necessary at least 4 weeks prior to regularization + exclusion of thrombi in the left atrium (TEE). Continuation of anticoagulant therapy after successful regularization for at least 4 weeks, since there is an elevated risk of thromboembolism after cardioversion (atrial stunning) due to atrial dysfunction. Continuous anticoagulation in the presence of risk factors (see above).

  Remark: If thrombi in the heart could be ruled out with certainty by TEE, the 4-week anticoagulation prior to cardioversion can be omitted. In any case, anticoagulation is performed after cardioversion.

2 Alternatives to regularization (cardioversion):

A) Drug cardioversion:

- patients ***without*** underlying cardiac disease: administration of a class I anti-arrhythmic drug (e.g., Flecainide or Propafenone)
- patients ***with*** underlying cardiac disease: administration of amiodarone which is the most effective drug for regularization. Rhythmization attempt of these patients as an inpatient control (due to the risk of sudden death).
- patients with paroxysmal AF can possibly be regularized with a single dose of one of the named anti-arrhythmics. For individuals with healthy hearts, this can be performed on an outpatient basis (possibly also by educated patients: "pill in the pocket" concept).

B) ECG triggered electrocardioversion (electrode position anterior-posterior) with an initial external energy dose of 200 J for AF (for intraatrial electrocardioversion, lower energy doses)
If the patient is conscious, a brief intravenous anaesthesia is introduced (e.g., with 10 mg diazepam followed by 20 mg Etomidate = Hypnomidate® slow IV).
Absolute indication: threatening cardiogenic shock
Relative indication: failure of pharmacologic regularization
Serum potassium level must be normal! Previous digitalis therapy is not a contraindication, as long as the digitalis level is not toxically elevated.

Refractory prophylaxis:
The rate of recurrence after electric cardioversion of AF is 30 % after one week and up to 75 % after 1 year. Consequently, anti-arrhythmics are used as prophylaxis for recurrence, the selection of which is outlined above. Amiodarone is the most effective but its use is limited by SE and clinical effects. ACE inhibitors and AT1 blockers (for treatment of hypertension and/or heart failure) can also lower the risk of recurrence.

Curative procedure: in selected cases of AF:

- Catheter ablation procedure: Pulmonary vein ablation has a success rate up to 80 %; however, serious SE can also result.
  Ind: selected younger patients with paroxysmal AF
- Maze operation to stabilize sinus rhythm (possibly in the context of other planned cardiac operations)

Thromboembolism prophylaxis in atrial fibrillation (ACC / AHA / ESC Guidelines 2006)

Risk category	Therapy recommendation
No risk factors	ASA 100 - 300 mg/day
1 moderate risk factor	ASA 100 - 300 mg/day or Marcumar/Warfarin (INR 2 - 3, optimally 2.5)
≥ 1 high risk factor or ≥ 2 moderate risk factors	Marcumar/Warfarin (INR 2 - 3, ideally 2.5)

Slight risk factors	Moderate risk factors	High risk factors
Women	Age ≥ 75 years	Stroke, TIA or history of cerebral embolism
Age 65 – 74 years	Hypertension	Mitral valve stenosis
CHD	heart failure	Mechanical cardiac valve replacement
hyperthyroidism	Left ventricular EF ≤ 35 %	(adjust INR > 2.5)
	Diabetes mellitus	

AF plus CHD: if coumarins are administered, additional ASA is not necessary!

Secondary prevention after stroke: Marcumar/Warfarin (INR: 2 - 3)

Prg: Depends on the underlying cardiac or extracardiac disease, the embolism risk associated with it and a good thromboembolism prophylaxis. There is no difference in the prognosis between patients who receive sinus-preserving therapy and patients whose heart rate is controlled with medication (AF-FIRM trial). Exception: In patients suffering from heart failure and AF, the mortality rate is twice as high as for those with preserved sinus rhythm.
Anticoagulants reduce the risk of stroke due to cerebral embolisms by almost 70 %.

Ventricular tachycardia (VT)

Aet.:
- Usually severe organic cardiac diseases, in particular coronary heart disease and myocardial infarction
- Overdose/intoxication with digitalis or anti-arrhythmics
- Primary electrical diseases of the heart (younger patients!): LQTS, SQTS, Brugada syndrome, CPVT (see Chap. Ventricular flutter/fibrillation)
- Arrhythmogenic right ventricular dysplasia (ARVD)
- Idiopathic: ventricular tachycardia in young healthy patients
  - Idiopathic left ventricular tachycardia (ILVT)
  - Idiopathic right ventricular tachycardia (IRVT) as outflow tract tachycardia

Pg.: Mechanisms:
- Increased automatism
- Re-entry

In the case of increased automatism following myocardial infarction, the focus is typically found in the transition zone between infarction scar and viable myocardium.
In a re-entry, the stimulation rotates around the myocardial scars (also using natural electrical barriers) frequently also through borderline viable myocardial channels within the scarred myocardial tissue (re-entry mechanism).

Cl.: Depending on the severity and duration of VT as well as functional status of the heart, the symptoms can vary from racing heartbeat, dyspnoea and angina pectoris to pulmonary oedema and cardiogenic shock.

ECG:
- Regular tachycardia (100 - 200/min.) with bundle branch block-like deformed broad ventricular complexes (QRS ≥ 0.12 sec.):
  - Monomorphic VT with uniform ventricular complexes
  - Polymorphic VT with polymorphic ventricular complexes
  - Salvo: 3 - 5 ventricular complexes following one after the after
  - Non-persistent VT: > 5 consecutive ventricular complexes, duration up to 29 Sec.
  - Persistent VT: duration ≥ 30 sec.
- AV dissociation = uncoordinated action of atria and ventricles: P spikes beat at a slow frequency independent of the QRS complexes.

Special form: Torsade-de-Pointes (TdP) tachycardia in long QT-syndrome = LQTS:

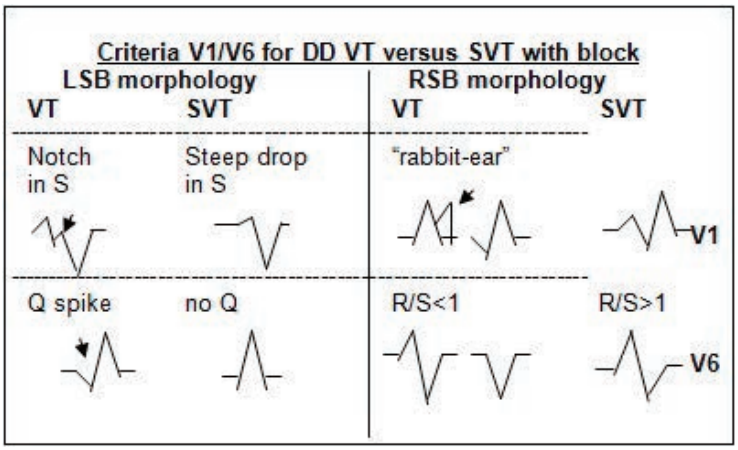
- Paroxysmal ventricular flutter of alternate amplitude direction whereby the ventricular complexes “dance” around the baseline with alternating amplitude.

24h-ECG (Holter monitor), event recorder

DD: In tachycardia with broad bundle branch block-like configured QRS complexes:

1. SVT with pre-existing branch block
2. SVT with aberrant conduction (functional)
3. SVT with pre-excitation syndrome (rare)
   - Antidrome WPW tachycardia
   - AF with rapid conduction

AV dissociation is indicative of VT, i.e., atria and ventricles do not beat in a synchronized fashion. This is only present in 50 % of the cases and is not always clearly visible in the ECG. In incomplete dissociation, a sinus node impulse can be transferred to the ventricle, triggering a capture-beat with normal QRS morphology or a mixed representation between normal QRS and bundle branch block (fusion systole).



In haemodynamically stable patients, a long ECG strip should be used for the detection of capture beats or fusion beats as well as a 12-lead ECG for the application of the algorithm represented below (modification according to Brugada/Wellens). With the use of these, a correct diagnosis is often possible!

Flow chart for DD of tachycardia with broad QRS complexes:

Missing RS complex in V1-V6?	*No* →	RS duration ≥ 120 ms in a chest wall lead?	*No* →	AV disso-ciation?	*No* →	Fusion beats, capture beats?	*No* →	Criteria V1, V6 positive? (see above)	*No* →	**SVT with block**
Yes ↓		*Yes* ↓		*Yes* ↓		*Yes* ↓		*Yes* ↓		
V E N T R I C U L A R T A C H Y C A R D I A										

***Note**:* For tachycardia with the appearance of bundle branch block, always look for capture beats and fusion systoles (longer ECG strips) because these indicate ventricular tachycardia! Vagal stimulation can arrest supraventricular tachycardia but has no effect on VT. Until proven otherwise, every instance of tachycardia with wide QRS complex is treated as ventricular (treat the worst case).

Ther: VT is a life-threatening arrhythmia; immediate action is required! (risk of VF, cardiogenic shock)

1. Acute therapy:
   - Check for possible digitalis therapy and check electrolytes, in particular, the potassium level in serum; O_2 administration via nasal tube
   - Anti-arrhythmics:
     - Ajmaline: drug of choice in patients without heart failure. In contrast to lidocaine, it is effect for both ventricular as well as supraventricular tachycardia. The success rate is > 60 %, substantially higher than that of Lidocaine.
       Dose: Adults receive 50 mg i.v. slowly over a 5 min. period (under ECG control)
     - Amiodarone (Cordarex®): first choice for patients with heart failure
       Dose: 300 mg slow IV over a 5 min. period (SE + CI: see anti-arrhythmics)
   - Electrocardioversion under short anaesthesia; initial energy dose: 200 J (start high, since otherwise many administrations are necessary)
     Ind: imminent cardiogenic shock, imminent pulmonary oedema, failure of drug therapy. To ensure the success of cardioversion, administration of Amiodarone is recommended afterwards.
   - For torsade-de-pointes tachycardia or polymorphic ventricular tachycardia with prolonged QT time: Magnesium infusion is the drug of choice. Dose: 2 g i.v. slowly over 5 min. period.
2. Treatment of the underlying disease: most important e.g., revascularization measures in CHD, etc.
3. Prophylaxis for recurrence: In post-infarction patients and in patients with limited cardiac output, beta blockers (without intrinsic activity) can reduce the incidence of sudden cardiac death by approx. 40 %. A long-term treatment with class IC anti-arrhythmics (CAST trial) showed a worse prognosis in post-infarction patients.

Amiodarone and Sotalol also cannot reduce the mortality in risk groups. Patients at risk of VF can only be protected by an ICD = implantable cardioverter defibrillator. If patients provided with ICD have frequent VT, catheter ablation can be attempted to reduce the intervention rate of the ICD; possibly also with adjuvant administration of amiodarone and beta blockers.
In idiopathic VT in individuals with healthy hearts, recurrence prophylaxis is performed with beta blockers or catheter ablation. The prognosis is good.

Prg: Depends on underlying cardiac disease and the prophylaxis for recurrence.

VENTRICULAR FLUTTER / VENTRICULAR FIBRILLATION [I49.0]

Def.: - Ventricular flutter: ECG: high amplitude hairpin curves with a frequency of 250 - 320/min. Fluid transition from ventricular tachycardia to ventricular flutter and fibrillation.
- Ventricular fibrillation: Hyperdynamic (hypersystolic) form of cardiac arrest due to uncoordinated ineffective twitches of the ventricular myocardium and lack of cardiac time volume.
ECG: Arrhythmic high frequency fibrillation waves (initially rough, later fine) at a frequency of > 320/min.

Special form: Torsade-de-Pointes (TdP) tachycardia in long QT syndrome = LQTS:
Paroxysmal ventricular flutter of alternate amplitude direction whereby the ventricular complexes “dance” around the 0 line with alternating amplitude.

Pg.: Microre-entry mechanism

Aet.: Lowering of the fibrillation threshold by:
1. Cardiac diseases: Myocardial ischaemia (coronary cardiac disease, myocardial infarction), cardiomyopathies, myocarditis, severe heart failure
2. Electrolyte disorder (hypokalaemia, hypomagnesemia)
3. Electrical accident, cardiac trauma
4. Rare in stroke and encephalitis
5. Congenital sympathetic dysinnervation of the myocardium (autosomal dominant hereditary)
6. **Primary electrical diseases of the heart:**

Def.: Ion channel diseases of the heart with increased risk of syncopes and sudden cardiac death (responsible for approx. 5 - 10 % of the yearly sudden cardiac death cases). Often increased familial occurrence and detection of specific ion channel mutations.

6.1 Long QT syndrome (long QT syndrome) = LQTS [R94.3]:

Pathologically prolonged frequency corrected QT time (QTc). The QTc is calculated from the nomograms (ECG scale) or according to the Bazett formula: $QTc = QT(sec)/\sqrt{RR sec}$. Increased risk for ventricular flutter/ventricular fibrillation for QTc > 440 ms.

A) Acquired:

- Drugs that inhibit the transmembranous potassium flow:
  - Antiarrhythmics (class I and III)
  - antidepressants, neuroleptics
  - Adrenalin derivatives, antihistamines
  - Antimycotics: ketoconazole, itraconazole, fluconazole
  - Antibiotics: macrolides, fluorquinolone, cotrimoxazole, antimalaria agents, etc.
  - Other drugs: see *www.torsades.org; www.qtdrugs.org*

  ***Note**:* When prescribing drugs that can prolong the QT interval, check ECG + serum potassium! If there is QTc prolongation, discontinue drugs! Do not use these drugs in the presence of known LQTS!
- Additional risk factors: Interactions with other drugs, overdose, excretion disorder; other risk factors (see Etiology).

B) Hereditary:

Genetically heterogeneous group of diseases:

- Romano-Ward syndrome: Autosomal dominant inheritance
- Jervell-Lange-Nielsen syndrome: LQTS1 or 5 + deafness; autosomal recessive inheritance
- Sporadic LQTS (in the presence of unremarkable family history)

LTQ syndrome	Gene	Chromosome	Gene product	Mutation frequency
LQTS1	KCNQ1	11p15.5	KvLQT1 (IKs-α)	approx. 45 %
LQTS2	KCNH2	7q35-36	HERG (IKr-α)	approx. 45 %
LQTS3	SCN5A	3p21-23	Nav1.5(INa)	approx. 6 %
LQTS4	ANK2	4q25-27	Ankyrin B	rare
LQTS5	KCNE1	21q22.1	MinK (IKs-β)	approx. 2 %
LQTS6	KCNE2	21q22.1	MiRP1 (IKr-β)	< 1 %
LQTS7	KCNJ2	17q23.1	Kir2.1 (IK1)	rare
LQTS8	CACNA1C	12p13.3	Cav1.2 (ICaL)	rare

Remarks:

- The ion channel for slow potassium influx IKs (slow) consists of two proteins, the product of the KvLQT1 gene (α subunit) and the product of the minK gene (β subunit).
- The ion channel for the rapid potassium influx IKr consists of two proteins, the product of the HERG gene (α subunit) and the product of the MiRP1 gene (βsubunit).
- LQTS7: with KCNJ2 mutation in combination with periodic paralysis as well as skeletal deformities, this is referred to as Andersen syndrome.
- LQTS8: The mutation of the CACN1C gene (L-type Ca2+ion channel) is associated with syndactyly of the fingers and toes, facial morphea, tooth anomalies, intermittent hypoglycaemia, immune defects and autism (Timothy syndrome).

Cl.: signs of congenital LQTS: syncopes already during childhood due to paroxysmal ventricular flutter of the peak reverse type = Torsades de pointes (TdP) ventricular flutter
Cardiac arrest, sudden cardiac death

Ther: 1. Symptomatic:
For cardiac arrest (see corresponding section), resuscitation
For torsade de pointes, the agent of choice is Magnesium sulfate: 2 g IV (e.g., Cormagnesin®), then 2 - 20 mg/min (If injection is too rapid, danger of AV block!). Cardioversion is usually followed by a recurrence of the arrhythmia.
2. All drugs that prolong the QT interval or could lead to hypokalaemia are forbidden (observe information on side effects!)
3. Prophylactic therapy with ICD, additionally, administration of beta blockers (without intrinsic activity) + oral magnesium.

Prg: The five-year mortality of congenital LQTS is 50 % without ICD.

6.2 Short QT syndrome (short QT syndrome) = SQTS

Incid.: Incidence unclear, however less frequently than LQTS

Aet.: Potassium channel mutations with accelerated repolarization, autosomal dominant inheritance

Cl.: Primary electrical disease of the heart with the risk of atrial fibrillation, syncopes and sudden cardiac death, also sudden infant death. Family history! In young patients with atrial fibrillation and syncopes, a QT interval shortening must be excluded.

ECG: Shortening of the QTc interval < 320 ms, often high T waves, no ST intervals, significantly limited frequency adaption of the QT time under stress, very short refractory times

SQTS	Gene	Gene products	Function
SQTS1	KCNH2 (HERG)	Potassium channel α subunit	Repolarization (I_{kr})
SQTS2	KCNQ1 (K_vLQT1)	Potassium channel α subunit	Repolarization (I_{ks})
SQTS3	KCNJ2	Potassium channel	Maintenance resting potential (I_{k1})

Di: ECG, exclusion of other causes of a QT time shortening (hyperkalaemia, hypercalcemia, digitalis overdose), family history, electrophysiological examination.

Ther: ICD implantation.

6.3 Brugada syndrome

Incid.: Incidence unclear, increased incidence in southeast Asia; M : f = 8 : 1; manifestation usually before age 40.

Aet.: In approx. 25 % of cases, mutations of the SCN5a gene of the sodium channel. Family clusters, autosomal dominant inheritance

Cl.: - Tachycardic ventricular arrhythmias (dizziness, syncopes)
- sudden cardiac death (due to family clusters, even among relatives!)

coved type *saddleback-type*

ECG: instant diagnosis!!

Leads V1-3

- Atypical "roof shaped" elevation of the ST interval ≥ 0.2 mV in more than one precordial lead V1-3 with transition into negative T wave (so-called "coved-type") (left ECG example)
- The course of ECG changes can be very variable from the so-called saddle-back type over the course (right ECG example) up to fully unremarkable ECG → make multiple ECG traces and compare!
- Diagnosis only with detection of a coved-type ECG (spontaneously visible or demasked by the ajmaline test)
- For unexplained syncopes, positive family history, detection of a saddleback type ECG or unremarkable ECG, conduct an ajmaline test (1 mg ajmaline/kg body weight under continuous ECG control) for demasking a coved type ECG.

DD: Other causes of a right precordial ST elevation (myocardial ischaemia, myocardial infarction, acute myocarditis, bundle branch block appearance, arrhythmogenic right ventricular cardiomyopathy, etc.)

Di: History, ECG, ajmaline test
Exclusion of other cardiac diseases (CHD, cardiomyopathies) and other causes of syncopes

Ther: ICD implantation

6.4 Catecholaminergic polymorphic ventricular tachycardia (CPVT)

Polymorphic ventricular tachycardia under physical or emotional stress in children and young adults. Syncopes and sudden cardiac death. Mutations of the Ryanodine receptor gene (RyR2) and calsequestrins (CASQ2) with disordered electromechanical coupling on the sarcoplasmatic reticulum.

Ther:
- Treatment for ventricular flutter/fibrillation as in cardiac arrest (see corresponding section)
- Treatment of the underlying disease (e.g., CHD)

Pro: Depends on the underlying disease and an effective prophylaxis (ICD); idiopathic ventricular tachycardia has a good prognosis.

V. CARDIAC ARREST and CARDIOPULMONARY RESUSCITATION

Def.: Two forms:
1. Tachysystolic (hyperdynamic) cardiac arrest (80 %): ventricular fibrillation or flutter (VF) and pulseless ventricular tachycardia (VT)
2. Asystolic (hypodynamic) cardiac arrest (20 %): Non-VF/VT: asystole and pulseless electromechanical dissociation (EMD = "weak action" = hyposystole) = pulseless electrical activity (PEA) = cardiac actions in ECG without pump output

Aet.:
1. Cardiac (> 90 % of all cases): CHD/myocardial infarction (80 %), cardiomyopathies (10 %); myocarditis, hypertensive cardiac disease, defects, primary electrical disorders of the heart = ion channel diseases (younger patients!), electrical shock accidents, hypo- or hyperkalaemia, severe acidosis, medication-toxic, pericardial tamponade, hypothermia
2. Circulatory: circulatory shock of various origins, pulmonary embolism
3. Respiratory (hypoxia): displacement of the respiratory tract, aspiration, central respiratory disorder, poisonings, neuromuscular causes, O_2 deficit of dyspnoea (drowning, suffocation), tension pneumothorax
4. Terminal stage of various diseases

Pg.:
- Ventricular tachycardia (with degeneration in ventricular fibrillation): 60 %
- Primary ventricular fibrillation: 10 %
- Bradycardia, including asystole: 20 %
- Torsade de pointes: 10 %

Di:

Loss of consciousness:	No response when addressed
(after 10-15 sec.)	No reaction to shaking the shoulders
• Respiratory arrest:	No visible respiratory movement
(after 30-60 sec.)	No audible respiratory sounds
	No palpable respiration
• Circulatory arrest:	No palpable carotid pulsation

- Wide reactionless pupils (after 2 minutes): observe signs of disorder (e.g., wide pupils after administration of adrenaline or atropine).

Asystole Ventricular fibrillation Ventricular flutter Ventricular tachycardia

Th.: Cardiopulmonary resuscitation (CPR):
ERC Guidelines for Adults, 2005

***Note**:* Notify emergency services immediately (Tel. 112 D; 144 A/CH)! Do not lose time with auscultation, taking pulse, measuring blood pressure, recording ECG, etc., but instead begin immediately with the following measures, eye on the clock! (A circulatory arrest of 3 minutes can result in irreversible brain damage.)

A) Basic measures (Basic Life Support = BLS)

- Patient lifeless (see Diagnosis)
- Open/clear airways
- CPR: cardiac massage/respiration = 30 : 2 (independent of the number of helpers)

B) Expanded measures according to ECG analysis (Advanced Life Support = ALS)

B1) Ventricular flutter, ventricular fibrillation, pulseless ventricular tachycardia

- If ventricular fibrillation occurs in the presence of medical personnel, immediate defibrillation is usually successful. In all other cases, CPR is performed first for 2 minutes.
- 1 defibrillation (D): 360 J in monophasic defibrillation / 150 - 360 J (instrument dependent) in biphasic defibrillation. Immediately afterwards, 2 minutes of CPR followed by monitoring.
- If unsuccessful, always repeat the cycle: CPR 2 minutes – 1 defibrillation (highest energy level)
- Placement of venous access
- Adrenaline (= epinephrine): 1 mg + 9 ml NaCl 0.9 % every 3 - 5 minutes IV
  If the third electroshock is unsuccessful, amiodarone (Cordarex®) is recommended (300 mg IV). If the next defibrillation is unsuccessful, 150 mg amiodarone may be injected subsequently (only once).
- Intubation and ventilation: After intubation cardiac massage (100/min.) is performed and ventilation, independently of one another. If possible, with O_2: 10 - 15 l/min., corresponding to an FiO_2 up to 0.8 or 80 % O_2 concentration of the inspired air.

B2) Asystole and electromechanical dissociation:

- CPR (2 min.) – 1 mg adrenaline every 3 - 5 min. (as for ventricular fibrillation)
- Possibly single dose of 3 mg atropine IV
- If unsuccessful, pacemaker therapy (transthoracic electrostimulation)
- Sodium bicarbonate is usually not used preclinically.
- If there is a strong suspicion of pulmonary embolism as a cause of the cardiac arrest and unsuccessful resuscitation, consider use of thrombolytics and continue CPR afterwards.

Monitoring of success in the postresuscitation phase (ROSC): pupils become smaller, palpable carotid pulse, improved skin colour, spontaneous respiration, pulse oximetry. If resuscitation is unsuccessful, continue for at least 30 minutes (for hypothermia accidents > 1 hr.).

- On the intensive care station after resuscitation and loss of consciousness, hypothermia treatment, if necessary (32 - 34°C for 12 - 24 hr.)
- Monitor blood glucose and maintain it in the normal range.

Complications due to resuscitation measures:

- Rib/sternum fractures with possible injuries to the heart/lungs (e.g., pneumothorax)
- Liver/spleen injury, overinflation of the stomach, aortal/cardiac rupture, pericardial effusion, etc.

⇒ Immediate examination after successful resuscitation! (hospital, chest x-ray, ultrasound of the abdomen, etc.). Also important is a check and possible correction of the electrolyte levels!

Complications due to cardiac arrest:
Cerebral damage, including brain death, acute renal failure, etc.

Prg: Depending on the cause of the cardiac arrest, promptly initiated resuscitation as well as possible complications. The success rate of defibrillation is time dependent: Defibrillation immediately after the start of ventricular fibrillation (e.g., Intensive Care station) is successful in 95 % of cases. Every minute of delay reduces the chance of survival by approx. 10%. The long-term prognosis after cardiac circulatory arrest is determined by the underlying disease, e.g., CHD.

***Note**:*

1. The implantable cardioverter/defibrillator is the most effective prophylaxis measure for recurrent ventricular fibrillation and for the prevention of sudden cardiac death (CASH trial, AVID trial)!
2. Only through the comprehensive use of automated external defibrillators (AED), which can be operated by trained lay persons, can the success rate of resuscitation be increased by early defibrillation! (MADIT trial etc.)

Risk factors for sudden cardiac death (SCD):

- Severe underlying myocardial disease (see Etiology)
- Recent myocardial infarction during the first 72 hr.
- Persisting coronary risk factors in CHD
- Primary electrical diseases of the heart (younger patients)
- Left ventricular function limitation (Ejection fraction < 30 %)
- Condition after resuscitation due to ventricular fibrillation/flutter
- Higher grade ventricular arrhythmias in the 24 hr. long-term ECG/event recorder
- Ventricular late potentials in highly amplified ECG
- Reduced baroreflex sensitivity
- Pathologically prolonged QTc time
- Reduced heart rate variability
- Pathological heart rate turbulence (analysis of the RR intervals after VES)
- T wave alternans (analysis of the T waves in the microvolt range under stress)

Ventricular late potentials are observed in pathological conduction disorder in the border region of myocardial infarctions and can be an indication of an elevated risk of ventricular tachyarrhythmias as a result of re-entry mechanism. The lack of ventricular late potentials is a good prognostic indicator (low risk of ventricular tachyarrhythmias). The risk of tachyarrhythmic complications in postinfarct patients with late potentials is approx. 25 %.

Pro: 1. Treatment of the causal disease
2. Prophylaxis of an SCD in risk patients by ICD

Pararhythmias (Double rhythms)

Def.: Occurrence of 2 (or more) independent pacemakers, that either occur next to one another (parasystole) or alternate in their pacemaker function (frequency dependent AV dissociation).
DD: In AV block III degree, the atrium and ventricular rhythms beat fully independent of one another.

1. Frequency dependent AV dissociation: [I45.8]
   a) Without rhythm association: simple AV dissociation:
   Atria and ventricles temporarily beat independently of one another, whereby the ventricular frequency is determined by a heterotopic autonomous centre in the AV node or the ventricles.
   ECG: P-waves and QRS complexes exhibit similar frequency but no relation to one another; the P-waves pass through the QRS complex.
   Cause: Transient, often harmless appearance in vegetative dystonia, occasionally in myocardial infarction or toxic digitalis effect
   b) With rhythm association: interference dissociation:
   Atria and ventricles beat independently of one another as in simple AV dissociation, although the frequency of the AV node rhythm is more rapid than that of the sinus rhythm (retrograde protective block of the sinus node).
   Cause: Vegetative lability, toxic causes (digitalis, quinidine, etc.), myocardial infarction, etc. cardiac diseases
2. Parasystole [I49.8] (rare)
   The ventricular contractions are controlled by 2 pacemakers which operate independently of one another. In addition to the sinus rhythm, a slower ventricular rhythm is also seen (which is not deleted by faster sinus rhythm due to a protective block).

ARTERIAL HYPERTENSION [I10]

Internet information: *www.hochdruck-liga.de*

Def.: (JNC/NIH, USA 1997)

Blood pressure (mmHg)	Systolic	Diastolic
Optimal	< 120	< 80
Normal	< 130	< 85
High-normal	130 - 139	85 - 89
High blood pressure:		
St. 1	140 - 159	90 - 99
St. 2	160 - 179	100 - 109
St. 3	≥ 180	≥ 110
Isolated systolic hypertension	≥ 140	< 90

The individually recommended upper threshold is dependent on the cardiovascular risk profile and any concomitant disorders (e.g. diabetes, renal disorders).

Assignment to one of these categories is only possible after repeated measurements at different times. In the USA (JNC 7 Report), the blood pressure range of 120 – 139 mmHg systolic and 80 – 89 mmHg diastolic is defined as prehypertensive. In this range, lifestyle changes are advised. This applies to the majority of the population, however.

Cardiovascular risk correlates with systolic and diastolic blood pressure and blood pressure amplitude (= pulse pressure = systolic minus diastolic blood pressure). Systolic blood pressure correlates the most with the risk of stroke.

Ep.: The frequency of high blood pressure increases with age and overweight. Prevalences in the Western industrial nations: On average: 25%; for persons > 60 years: up to 50%; in cases of obesity: up to 75%
Hypertension occurs most frequently in northern Japan, most rarely among the Inuit.
About 50% of persons with hypertension do not know that they have high blood pressure; of those known to have hypertension, about 50% are not treated at all and about 50% are inadequately treated!

Forms of high blood pressure:

- Labile hypertension and stress-dependent hypertension: hypertension occurs intermittently or as a result of physical or mental stress
- Stable hypertension = full-time hypertension (blood pressure values continuously elevated)
- Hypertensive crisis: Critical rise in blood pressure (> 230/130 mmHg systolic/diastolic) without organ damage
- Hypertensive emergency: blood pressure > 230/130 mmHg + endangerment of life due to organ damage
  2 main causes: - Advanced renal failure (80% of cases)
  - Pheochromocytoma

PPh.: Hypertension is the result of elevated cardiac output, elevated peripheral resistance or both factors.
Blood pressure = cardiac output x vascular resistance

In the early stage of essential hypertension, cardiac output is mildly elevated. Later on, there is an increase in peripheral resistance, mediated by both a functional vasoconstriction with increased sympathetic nervous system activity and structural changes in the vessel walls (vascular remodeling). The accelerated phase of arterial hypertension (hypertensive crises) is characterized morphologically by a fibrinoid necrosis of the aterioles, which leads to the occlusion of the arteries and arterioles with consecutive tissue ischaemia in the downstream vascular region.

1. Essential Hypertension

(> 90% of all cases of hypertension)

Cause unknown.
Essential hypertension – usually not appearing until after the 30th year of life – is a multifactorial, polygenic disorder (e. g. gene mutation GNB 3-825T). In about 60% of cases, essential hypertension is inherited. Constitution (endomorphic body type), nutritional factors (consumption of sodium, coffee and alcohol; overweight), stress, smoking and endocrine factors can all favor hypertension (more frequent onset of hypertension in menopausal women).

Essential hypertension frequently is accompained by other disorders of the so-called metabolic syndrome = "affluence" syndrome (see there).

History: 1) Genetic research on hypertension has identified individual monogenic inherited forms of hypertension with increased sodium reabsorption, which are very rare (glucocorticoid-suppressible aldosteronism, apparent mineralocorticoid excess and Liddle syndrome).

2) The MRIs of some patients with essential hypertension show an aberrant course of the posterior inferior cerebellar artery, anterior inferior cerebellar artery or vertebral artery, causing pulse-synchronous pressure on the control centre for arterial blood pressure in the medulla oblongata (neurovascular compression of the brain stem). Decompression surgery has (partially) normalized blood pressure in small case groups.

DD: Exclusion of all secondary forms

2. Secondary Hypertensions

(< 10% of all cases of hypertension; numbers vary in the literature)

Cause known:

1. Renal hypertension
   - Renoparenchymatous hypertension, e.g. due to glomerulonephritis, chronic pyelonephritis, cystic kidneys, etc.
   - Hypertension due to renal tumours
   - Stenosis of the renal arteries
2. Endocrine hypertension
   - Primary hyperaldosteronism (Conn's syndrome): Most frequent type of secondary hypertension
     - As the classic hypokalaemic form
     - As the normokalaemic form
   - Pheochromocytoma, Cushing's syndrome, AGS (Alagille syndrome), acromegaly

3. Sleep apnoea syndrome with nocturnal hypertension

4. Aortic isthmus stenosis

Temporary increases in blood pressure:

- Temporary increases in blood pressure due to disorders of the central nervous system (encephalitis, intracranial pressure, poliomyelitis) and acute poisoning (e.g. carbon monoxide)
- Temporary increases in blood pressure due to pharmaceuticals (ovulation inhibitors, corticosteroids, erythropoietin, carbenoxolone, non-steroidal antirheumatics, Ciclosporin A, liquorice) and drug abuse (cocaine, amphetamines). Blood pressure normalized again after discontinuing these drugs.
- Pregnancy-induced hypertension (PIH) = normal blood pressure prior to pregnancy, hypertension during pregnancy [O13]

  Incidence: 10% of all pregnancies, especially younger primigravidae. 1% of all pregnant women develop preeclampsia, but only 0.1% develop eclampsia.

  PIH is usually a temporary hypertension that first manifests after the 22nd week of pregnancy and disappears again once the pregnancy has ended.

  Classification of PIH:

  I. Isolated PIH = gestational hypertension: Usually occurs in the 3rd trimester of pregnancy and disappears within 6 weeks postpartum.

  II. PIH with proteinuria and possible oedema = preeclampsia (formerly EPH gestosis, pregnancy toxicosis)

  Compl.: • HELLP syndrome (haemolysis, elevated liver enzymes, low platelet count)
  • Eclampsia with neurological symptoms (flickering before the eyes, hyperreflexia, seizures)

  Notes: The degree of hypertension determines the perinatal mortality of mother + child!

  DD: Pregnancy hypertension: 3 forms:

  1. Pregnancy-induced hypertension (PIH)
  2. Pre-existing hypertension, already present prior to the pregnancy.
  3. Superimposed PIH (superimposed gestosis), developing on the basis of a pre-existing chronic hypertension in 30% of cases.

Cl.: Symptoms may be absent for a longer period of time. A typical symptom is early morning headache (especially in the back of the head) that often improves if the head of the bed is raised. With nocturnal hypertension, sleep complications.

Dizziness, tinnitus, nervousness, precordial pain, heart palpitations, vasomotor lability, nose bleeds, exertion dyspnoea.

Compl.: ► Hypertensive crisis and hypertensive emergency (see below)

► Vascular system: The majority of all hypertensive patients develop premature arteriosclerosis.

- Hypertension-induced vascular changes to the fundus of the eye:

  4 stages of hypertensive retinopathy (Hypertensive retinopathy):

  St. I: Functional vascular changes: arteriolar vasoconstriction
  St. II: Additional structurally changed vessels: Copper wire arteries with irregularities in caliber, Salus-Gunn crossing sign (at the arteriovenous crossing).
  St. III: Additional damage to the retina: Spot haemorrhages, soft exudates ("cotton-wool" spots), macular star (tiny calcium-like spots around the macula).
  St. IV: Additional bilateral papillary oedema

- Sonographic evidence of thickening of the carotid artery wall (thickness of intima/media > 0.9) or evidence of arteriosclerotic plaques

► Heart: Left heart insufficiency and coronary heart disease are the cause of death in 2/3 of all hypertension patients. Hypertensive heart disease includes all cardiac disorders resulting from hypertension:

• Stress-induced hypertrophy of the left ventricle: Initial concentric hypertrophy, then conversion to eccentric hypertrophy with enlargement of the cardiac muscle fibres (hyperplasia) once the critical heart weight of 500 g is surpassed.

Hypertensive cardiomyopathy (I11.9]: Diastolic relaxation disorder (early symptom) and later also systolic function disorder of the hypertensive heart and development of left ventricular insufficiency.

Remark: If the blood pressure falls due to decompensated left heart insufficiency, we speak of “decapitated” hypertension.

Echocardiography: Direct evidence of left heart hypertrophy: End diastolic septum thickness > 11 mm (point of measurement at the level of the opened mitral valve).

X-ray: In cases of mild left hypertrophy, no radiographical changes in the p.a. image, later lengthening of the heart towards the lower left and elongation of the aorta. In cases of decompensated insufficiency of the left ventricle, widening of the heart towards the left.

ECG: Signs of left heart hypertrophy (Sokolow-Lyon Index: SV1 + RV5 or V6 > 3.5 mV), later left precordial repolarization abnormalities as a sign of left heart damage due to eccentric hypertrophy or subsequent to coronary heart disease.

- Coronary heart disease (macroangiopathy) with its 5 forms of manifestation: Angina pectoris, myocardiac infarction, left heart insufficiency, cardiac arrhythmias, sudden cardiac death
- Coronary microangiopathy
- Endothelial dysfunction with reduced formation of vasodilating NO (nitrogen oxide) and increased formation of vasoconstricting angiotensin II and endothelin.

▶ Brain: Cause of death in about 15% of hypertensive patients
- Cerebral ischaemia and brain infarction usually occurs due to arteriosclerosis of the extracranial and intracranial vessels.
- Massive hypertensive bleeding: Frequency relation of ischaemic infarction to massive bleeding 85 : 15
- Acute high pressure encephalopathy [I67.4]: See above

▶ Hypertensive nephropathy [I12.9]- 3 stages:
- Mikroalbuminuria (30 - 300 mg/d oder 20 - 200 mg/l)
- Benign hypertensive nephrosklerosis with albuminuria > 300 mg/d
- Arterio-arteriolosclerotic contracted kidney with renal insufficiency

Through the mechanism of reduced renal circulation with activation of the renin-angiotensin-aldosterone-(RAA-) system, every case of hypertension (both essential and secondary renal hypertension) can lead to a renal fixation of high blood pressure (so that, for example, blood pressure remains elevated even after eliminating renal artery stenosis).

▶ Abdominal aortic aneurysm: 10% of male hypertensive patients > 65 years (see section on this topic)

▶ Aortic dissection: Approximately 80% of these patients have hypertension (see section on this topic)

▶ Malignant hypertension:
- Diastolic blood pressure > 120 - 130 mmHg
- There is no day-night rhythm of blood pressure during long-term measurement any more
- Changes in the fundus of the eye St. III - IV
- Development of renal insufficiency

Malignant hypertension can develop from any form of high blood pressure.
Malignant hypertension then develops into secondary malignant nephrosclerosis.

Hist.: Fibrinoid necrosis of the arterioles develop in the area of the vasa efferentia. A proliferative endarteritis with an onion-skin-like arrangement of thickened intima cells around the vessel lumen ("onion-skin" lesion) and vessel occlusions with ischaemic obliteration of the glomeruli can be found in the interlobular arteries.

Clinical stages / WHO classification of hypertension

▶ Hypertension without end organ damage (WHO Grade I)

▶ Hypertension with end organ damage (WHO Grade II):
- Hypertensive heart disease
- Hypertensive nephropathy (creatinine < 2 mg/dl)
- Hypertensive retinopathy I and II
- Plaque formation in the large vessels (carotid artery, femoral artery, and others)

▶ Hypertension with cardiovascular sequelae/concomitant disorders (WHO Grade III)
- Heart: Angina pectoris, myocardial infarction, heart failure
- Kidneys: Hypertensive nephropathy, renal insufficiency (creatinine < 2 mg/dl)
- Eyes: Hypertensive retinopathy III and IV
- CNS: TIA, ischaemic cerebral infarction, cerebral haemorrhage
- Vessels: Peripheral arterial occlusive disease, aortic dissection

Risk stratification for estimating overall cardiovascular risk: See section on coronary heart disease!

Notes: The risk of cardiovascular disease doubles with each increase by 20/10 mmHg in comparison to the optimal value of < 120/80 mmHg.

Blood pressure measurement:

Measurement methods:

■ Direct (invasive) method with pressure transducer
Indicated in exceptional cases in intensive care only

■ Indirect method according to Riva Rocci (RR):
2 measurement variants:
· Oscillometry: Measurement of the fluctuations in arterial blood flow (not suitable in cases of atrial fibrillation/arrhythmia)
· Auscultation of Korotkov sounds

Rules for measuring blood pressure:

- Blood pressure measurement in horizontal or sitting position (after 3-5 minutes of rest, if at all possible): Position the arm used for measuring at the level of the heart with a slight bend at the elbow (with a stretched out arm, the measured values are about 10% higher). Pump the cuff up to about 30 mmHg above the point at which the radial pulse disappears and then allow the pressure to release slowly (about 3 mmHg/second). Once the pulse can be heard again, release the air

immediately and pump up to higher pressure values again after 1-2 minutes (do not pump the pressure up again immediately!). The systolic pressure is read with the first audible Korotkov sound, the diastolic pressure with the disappearance of the sound. Blood pressure measurements at the wrist are less precise than upper arm measurements. Blood pressure measurement devices for the finger are not suitable.

- Measure at least once on both arms; repeat the measurement at least 1x.
- At elevated blood pressure values, always check the femoral pulse as well, and with weakened pulses, measure the blood pressure at the thigh where the values must be higher than at the arm (30-40 mmHg difference). Hypotension in the legs with hypertension in the arms occurs in cases of aortic isthmus stenosis.
- To ascertain orthostatic hypotension, e.g. in the context of autonomic neuropathy or drug therapy, measure the blood pressure after the patient stands up from a horizontal position (immediately and after two minutes).
- When measuring with the customary blood pressure cuff, the measured value is only correct if the upper arm circumference is normal (about 25-35 cm). If the upper arm is significantly thicker, the value is about 10 mmHg too high, and if the upper arm is very thin, the value is too low (up to 30 mmHg) if an adjusted cuff is not used.
- Korotkov sounds can be heard down to 0 mmHg if the cardiac output is elevated or in cases of hypercirculation (e.g. pregnancy, fever, anaemia). In these cases, the diastolic value is read at the point at which the Korotkov sounds become quieter.

Attention: With hypertension, there is a danger of erroneous measurement due to so-called auscultatory gaps: Disappearance of Korotkov sounds below the systolic blood pressure value: Cause of RR values read too low in error! Therefore, always pump blood pressure cuffs up high enough and check the auscultation findings with simultaneous palpation of the radial pulse!

False elevated values are measured in Mönckeberg's media sclerosis = Mönckeberg's disease:
Deposits of hydroxyapatite crystals in the media of arteries of the muscular type; sequela: reduced compressibility of the arteries, especially the legs → ankle-arm index cannot be evaluated when diagnosing PAOD.
1. Primary - 2. Secondary with diabetes mellitus
Diag: X-ray: Skeletal, finely granulated vascular shadows, bridge-like calcifications in the CT scan, echogenic levels in duplex sonography

Interpretation of the measured values:
Since blood pressure is affected by the time of day and psychological and physical stresses, hypertension can only be diagnosed by **repeated** measurements. Long-term measurements show a biphasic course over 24 hours with peaks in the early morning and late afternoon and the lowest values during sleep at night. No fall in blood pressure at night or a small drop in night blood pressure < 10 mmHg ("Non-dipper") occurs in 75% of all patients with secondary forms of hypertension, in preeclampsia, if there has been renal damage due to high blood pressure, in sleep apnoea syndrome, and also in insomniacs! (If there is no nightly drop in blood pressure, ask about sleep complications!)

Notes: In non-dippers, always exclude secondary forms of hypertension first. Look especially for renovascular hypertension!

Blood pressure differences between the two arms > 20/15 mmHg (syst./diast.) lie outside the reference range. Incidence:
1. Aortic arch syndrome due to arteriosclerosis, rarely vasculitis (Takayasu arteritis, see section on this topic)
2. Stenosis/occlusion of the subclavian artery (e.g. due to cervical rib or exostosis of the clavicle)
3. Aortic isthmus stenosis with branching off of the left subclavian artery distal of the stenosis
4. Aortic dissection
5. In the majority of cases, however, no cause can be found.

Diag: hypertension through repeated RR measurements:

Measurement in doctor's office ≥ 140 / 90 mmHg	Self-measurement ≥ 135/85 mmHg	24 hour measurement Day profile ≥ 135/85 mmHg	Ergometry ≥ 200/100 mgHg at 100 Watts

1. Casual blood pressure measurement in the doctor's office: Normal values < 140/90 mmHg
2. Normal values with self-measurement: < 135/85 mmHg
3. 24-hour blood pressure measurement (ABPM = ambulatory blood pressure measurement)

The 24-hour measurement is the most accurate assessment of the actual blood pressure situation (day/night - at work/at home). Self-measurement eliminates elevated values caused by the "white coat" effect in the doctor's office. About 20% of patients with elevated values measured in the doctor's office have normal blood pressure values outside the doctor's office!

Normal values with ABPM:

- Average daytime value: < 135/85 mmHg
- Average night-time value: < 120/75 mmHg
- 24-hour average < 130/80 mmHg
- Frequency of values > 140/90 mmHg: during the day < 25%; during the night < 20%
- Normal night-time drop in pressure ("Normal dipper")
  Nighttime drop in blood pressure > 10% and < 20% of the average daytime value of the ABPM
- Reduced night-time drop in blood pressure ("non-dipper"):
  Night-time drop in blood pressure > 0% and < 10% of the average daytime value of the ABPM

- Inversion of the day/night rhythm ("inverted dipper" or "reversed dipper"):
  Night-time drop in blood pressure < 0% of the average daytime value or night-time rise in blood pressure with an inversion of the day/night rhythm.

  In "non-dippers" with normal daytime blood pressure, the dosing of an antihypertensive in the evening only may be sufficient. If the circadian blood pressure rhythm is inverted, i.e. values are higher during the night than during the day, this is usually due to advanced hypertensive disease requiring combination therapy with multiple antihypertensive drugs.

Basic program for diagnosing hypertension:

1. Medical history:
   - Duration and maximum of known elevated blood pressure values, previous diagnoses
   - Symptoms/complications of hypertension: Headache, tinnitus, palpitations, exertion dyspnoea, among other symptoms
   - Drug history: Antihypertensives (side effects?), blood pressure increasing drugs (e.g. NSARs, corticosteroids, ovulation inhibitors, erythropoietin, etc.)
   - Nicotine consumption, alcohol consumption, coffee consumption, illegal drugs
   - Earlier diseases, concomitant diseases
   - Family history: Hypertension, myocardial infarction, stroke, renal diseases
2. Examination and diagnostics:
   - Blood pressure in both arms(!), pulse status (in arms + legs → aortic isthmus stenosis?), abdominal auscultation (any paraumbilical sounds with renal artery stenosis), fundus of the eye
   - Have patient record values from self-measurement of blood pressure
   - ABPM (24 hour measurement)
   - Lab.: Urinary status with test for microalbuminuria, creatinine in serum, serum electrolytes (potassium?) Screening for additional risk factors for premature arteriosclerosis (blood pressure, cholesterol, HDL/LDL cholesterol, triglycerides, etc., see section on CHD)
3. Diagnosis of secondary hypertension:
   Ind: Young patients, severe hypertension that cannot be normalized with a 3-drug combination, non-dipper/reversed dipper, etc.
   - If pheochromocytoma suspected: catecholamine in 24-hour urine sample
   - If Cushing's syndrome is suspected, dexamethasone suppression test (see section on this topic)
   - If hypokalaemia (not caused by treatment), exclude Conn syndrome (see section on this topic)
   - Technical diagnostic procedures:
     - ECG
     - If left heart hypertrophy is suspected: Echocardiography
     - If renal artery stenosis is suspected: Colour duplex sonography
4. Calculate 10-year cardiovascular risk (see section on CHD)

Th.: Three (3) aspects play a role in determining the indication for treatment of high blood pressure:
- The level of blood pressure (systolic, diastolic, blood pressure amplitude, night-time blood pressure behaviour)
- Individual CHD risk, e.g. calculated according to PROCAM-Score (see section on this topic)
- Hypertensive organ damage

The most important objective is to reduce cardiovascular risk!

Target blood pressure values to strive for:	
< 140/90 mmHg	General therapy objective
< 130/80 mmHg	In high-risk patients: Renal insufficiency, CHD, diabetes mellitus
< 125/75 mmHg	With proteinuria > 1 g/d

A. Causal therapy of the cause of secondary hypertension (e.g. elimination of an aortic isthmus or renal artery stenosis, treatment of endocrine hypertension).

B. Symptomatic therapy

▶ **General measures = basic treatment for all hypertension!**
- Normalization of weight (10 kg loss in weight lowers systolic blood pressure by 10-15 mmHg)
- Low-salt diet (max. 6 g NaCl/day): No high-salt food, no salt added to food; 1/3 of all hypertensive patients are sensitive to salt and profit from a low-salt diet. Low-salt diet also reduces the danger of hypokalaemia caused by diuretics. Use of low-sodium salt substitute based on KCl.: potassium has a blood pressure lowering effect.
- Mediterranean diet (a lot of fruit, vegetables, salad; little animal fat, a lot of fish, use of olive oil) reduces the risk of myocardial infarction by 50% and lowers blood pressure.
- Discontinuation of medications favoring hypertension (see above)
- Regulation of lifestyle: Stop smoking, no coffee, reduce alcohol consumption (< 30 g alcohol/day), anti-stress training and relaxation exercises
- Dynamic endurance training, e.g. regular brisk walking (at least 1 hour/week) reduces the risk of myocardial infarction by 50% and lowers blood pressure (DASH Study).
- Warm baths, mild sauna use (without subsequent use of cold water or ice, which increase blood pressure).

- Elimination or treatment of other cardiovascular risk factors (e.g. hypercholesterolemia, diabetes mellitus).

Notes: By simply exhausting the general measures named above, 25% of mild hypertension cases (severity degree 1) are normalized!

▶ **Drug therapy:**

The following therapy strategies can be used as primary therapy depending on the situation of the patient:

- Step therapy: Start with monotherapy and give an additional antihypertensive if effect is insufficient
- Primary combination therapy in low doses:
  Diuretic + ACE-inhibitor (or AT1-blocker) or diuretic + beta-blocker: Primary combination therapy is indicated by blood pressure far above the target values as well as concomitant diseases that make a combination therapy necessary anyway (e.g. CHD, heart failure).
- Sequential monotherapy, i.e. one antihypertensive is exchanged for another in monotherapy, as necessary, until an effective lowering of the blood pressure is achieved.

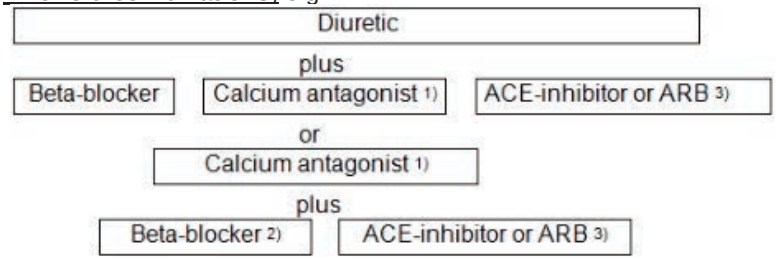
Notes: The 5 medications of choice are thiazide, ACE-inhibitors, angiotensin receptor blockers (ARB), long-acting calcium antagonists and beta-blockers. A prognostic advantage (lowering of mortality rate in hypertensive patients) has been demonstrated for the medication of choice.
With regard to beta-blockers, there are guidelines (e.g. England, Austria) that no longer recommend these agents as antihypertensives of first choice since study analyses have shown a lower decrease in cardiovascular sequelae. This data applies predominantly to one substance, however: atenolol. In post-infarction patients or heart failure, beta-blockers are indispensable from a prognostic viewpoint.
ACE-inhibitors and angiotensin receptor blockers can delay the progression of diabetic nephropathy and non-diabetic renal disorders.

Drug therapy is usually given for more than a year, frequently for the entire lifetime of the patient. Good cooperation between doctor and patient is necessary for success. Before starting treatment, patients should be informed that there are often significant side effects (fatigue, lassitude, lethargy, etc.), regardless of the preparation, but that these usually disappear once blood pressure is normalized. Self-checking of blood pressure and ABPM are suitable for ongoing check-ups.
Blood pressure should not be lowered too quickly or too far (→ danger of falling due to orthostasis). Antihypertensives should not be discontinued suddenly (danger of rebound with rise in blood pressure).

Notes: The objective is to normalize blood pressure with the agent having the mildest side effects.
Medication is selected based on individual tolerance, concomitant disorders and possible interactions with other drugs that the patient is taking. Because of circadian blood pressure behaviour, with the highest values in the morning and lowest values during sleep, antihypertensives should be taken in the mornings after waking; any additional doses depending on the day and night blood pressure profile.

ABPM measurements show that an evening dose of the antihypertensive is not indicated when there is a normal drop in pressure at night with normal blood pressure values during the night. Night-time hypotension must be avoided, especially in elderly patients! (Danger of cerebral ischaemia and orthostatic collapse when getting up, with possible fracture as a result!)

▪ **Two-fold combinations;** e.g.



1) Only long-acting calcium antagonists
2) Do not combine beta-blockers with calcium antagonists of the diltiazem or verapamil type
3) ARB = angiotensin receptor blocker = angiotensin II antagonist = AT1-blocker

▪ **Three-fold combinations:**

If blood pressure is not normalized after testing different double combinations, a suitable 3rd antihypertensive is added, e.g. diuretic + ACE-inhibitor (or ARB) + beta-blocker (or calcium antagonist).

Resistance to therapy:

If, in case of established hypertension (ABPM) and assurance that the patient is adhering to the drug regimen (compliance), a 3-fold combination also does not result in normalization of blood pressure, the following causes of resistance to therapy must be excluded:

- True resistance:
  - Unrecognized secondary hypertension (exclude pheochromocytoma and renal artery stenosis!)
  - Unrecognized sleep apnoea syndrome (begin diagnostics)
  - Malignant hypertension (see above)
  - Increasing renal insufficiency

- Pseudo-resistance:
  - Lack of compliance (prescription intervals too long!)
  - White-coat hypertension (→ self-measurements + ABPM)
  - Erroneous blood pressure measurement
  - Disregard for general measures (see above)
  - Drug interactions: Intake of drugs that favor hypertension (oestrogens, glucocorticosteroids, non-steroidal anti-inflammatories, etc.)
  - Cocaine abuse

Selection of antihypertensives according to concomitant disorders:

Concomitant disorder (examples)	appropriate (+) / inappropriate (-) antihypertensives	Explanation
Heart failure	(+) ACE inhibitor, ARB (+) metoprolol, bisoprolol, carvedilol (+) diuretics (–) verapamil	Pre- and afterload decrease, improvement of prognosis Preload decrease Negative inotropic effect
Bradycardia	(–) beta-blocker (–) verapamil (–) clonidine	Negative chronotropic effect
Coronary heart disease	(+) cardioselective beta-blocker	Anti-angina effect Improvement of prognosis
Status post myocardial infarction	(+) beta-blocker (+) ACE inhibitor	Improvement of prognosis
Arterial occlusive disease	(–) beta-blocker	Worsening of AOD (contraindication!)
Metabolic syndrome, diabetes mellitus	(+) ACE inhibitor, ARB (-) beta-blocker, diuretics	Nephroprotective; metabolically neutral Increased risk of diabetes
Gout	(–) diuretics	Increase in uric acid
Bronchial asthma	(–) beta-blocker	Bronchospastic side effects
Renal insufficiency	(–) potassium-sparing diuretics (+) loop diuretics	Danger of hyperkalaemia (contraindication!)

Antihypertensives:

- **Diuretics** are given in low doses as antihypertensives (e.g. chlorthalidone 12.5 – 25 mg/day). No further lowering of blood pressure is achieved by increasing the dose. Diuretics are often used in combination with other antihypertensives. Diuretics have a rather unfavorable effect in diabetes mellitus. (details: see the section on heart failure)
- **Beta-blockers:** The ESC guidelines continue to include beta-blockers among the 5 antihypertensives of first choice, even if there are differing opinions regarding this. For post-infarction patients or those with heart failure, beta-blockers are indispensable from a prognostic viewpoint.
  Beta1-selective beta-blockers without an intrinsic sympathomimetic effect are preferred for antihypertensive therapy (details: see the section on antiarrhythmic agents).
- **ACE inhibitors (prilats):**
  Effect: Blocking of the angiotensin-converting-enzyme, which converts angiotensin I into the vasoconstricting angiotensin II → Results:
  -Decrease in peripheral vascular resistance due to reduced angiotensin II production
  -Reduction of angiotensin II-induced stimulation of the sympathetic-adrenergic system and catecholamine release
  - Restriction of aldosterone and ADH secretion and therefore reduction of sodium and water retention with subsequent decrease in volume
  - Inhibition of the breakdown of the vasodilator bradykinin (→ synergistic effect)
  - Regression of left ventricular hypertrophy
  - Improvement of prognosis in patients with heart failure (e.g. CONSENSUS-, SOLVD Study)
  - Reduction of cardiovascular mortality rate in cardiovascular risk patients (e.g. HOPE Study)

  The cardioprotective effect is explained by the tissue effects of ACE inhibitors, which include the heart and blood vessels (tissue renin-angiotensin system). The majority of ACE inhibitors are prodrugs which are then hydrolyzed in the liver into active "prilats". Captopril and lisinopril are active ingredients. ACE inhibitors do not cause any negative changes in the lipid and glucose metabolism. In patients treated with ACE inhibitors, the risk of cancer is supposed to be lowered.

  Interactions: Hyperkalaemia if ACE inhibitors are combined with potassium-sparing diuretics and/or potassium preparations or cyclosporine. Possible reduction in the effect of ACE inhibitors by NSARs. Serum lithium levels may rise if lithium is given concomitantly. The risk of leucopenia rises with the concomitant administration of allopurinol. Hypoglycaemia has been observed in diabetics when given concomitantly with insulin or oral antidiabetic agents (→ possible dose reduction).

  Side effects: Dry cough is relatively frequent (5 -10%) and is mediated by bradykinin; headache, dizziness,

gastrointestinal disorders; hyperkalaemia (do not combine with potassium-retaining diuretics). Other side effects are rare: Disorders of the sense of taste, proteinuria, renal/liver function disorders, cholestasis, exanthem, leucopenia, agranulocytosis, angioneurotic oedema, vasculitis, allergic pulmonary changes, myalgias, increased risk of hypoglycaemia in diabetics, etc.
In patients with a stimulated renin-angiotensin system (e.g. heart failure, renal artery stenosis, treatment with diuretics), an alarming drop in blood pressure may occur at the start of therapy → therefore, start with the smallest dose! The dosage must be reduced in case of renal insufficiency. Urine, creatinine and blood count check-ups are indicated.
Ind: arterial hypertension, condition after myocardial infarction, heart failure

Contraindications: pregnancy, lactation, bilateral renal artery stenosis or renal artery stenosis when the patient has only one kidney, transplanted kidneys, concomitant therapy with potassium-sparing diuretics, hyperkalaemia, concomitant immunosuppressive therapy, intolerance reactions (coughing, angioneurotic oedema), hepatic insufficiency, severe renal insufficiency (creatinine clearance < 30 ml/min), aortic and mitral stenosis, obstructive hypertrophic cardiomyopathy, hyposensitization therapy, among others

Generic name	Trade name e.g.	Duration of effect with one dose (hours)	Average daily dose (mg)
captopril	**generics**	up to 12	12.5 - 50
cilazapril	Dynorm®	up to 18	2.5 - 5
enalapril	**generics**	up to 18	5 - 20
benazepril	**generics**	up to 24	5 - 20
fosinopril	Dynacil®	up to 24	5 - 20
imidapril	Tanatril®	up to 24	2.5 - 10
lisinopril	**generics**	up to 24	5 - 20
moexipril	Fempress®	up to 24	3.75 – 15.0
perindopril	Coversum®	up to 24	4 – 8
quinapril	Accupro®	up to 24	5 – 20
spirapril	Quadropril®	up to 24	3 – 6
trandolapril	Udrik®, Gopten®	up to 24	1 – 2
ramipril	Delix®, Vesdil®	up to 48	2.5 - 5

- **Angiotensin II antagonists = angiotensin receptor blockers (ARBs) = AT1-(receptor) antagonists = AT1-receptor blockers = AT1-blockers = sartans:**

Effect: AT1-receptor blockers inhibit the effect of angiotensin II on the AT1-receptor → decrease in blood pressure.

Side effects: Rarely headache, fatigue, gastrointestinal side effects, hyperkalaemia, creatinine elevation, hepatic function disorders. Cough and angiooedema are only very rarely observed with ACE inhibitors overall (due to the lack of effect on the breakdown of bradykinin); isolated cases of stomatitis, loss of sense of taste, paresthesia, and others.

Contraindications: pregnancy, lactation, bilateral renal artery stenosis, primary hyperaldosteronism, aortic and mitral valve stenosis, hyperkalaemia, hepatic insufficiency, cholestasis, and others

Ind: 1. Arterial hypertension
2. Heart failure (losartan, valsartan, candesartan) in cases of intolerance or contraindication of ACE inhibitors
3. After myocardial infarction (valsartan)

Generic name	Trade name e.g.	Average daily dose (mg)
candesartan	Blopress®, Atacand®	4 - 32
eprosartan	Teveten®, Emestar®	600
irbesartan	Karvea®, Aprovel®	75 - 300
losartan	Lorzaar®	50 - 100
olmesartan	Votum®; Olmetec®	10 - 40
telmisartan	Micardis®	40 - 80
valsartan	Diovan®, Provas®	80 - 320

When treating heart failure, or after myocardial infarction, treatment is initiated with the smallest dose, and then the dose is slowly increased depending on tolerance; this also applies to ACE inhibitors and beta-blockers.

- **Calcium antagonists:**

Effect: The L-channel antagonists on the market block the L(long lasting)-calcium channels → decrease in peripheral vascular resistance (afterload)

1. Benzothiazepine (diltiazem) type
2. Phenylalkylamine (verapamil) type

Both groups are class IV antiarrhythmic agents (see section on this topic) and may not be combined with beta-blockers (danger of AV block and/or bradycardia)

3. Dihydropyridine (DHP) = nifedipine type:

Generic name	Trade name e. g.	Average daily dose (mg)
amlodipine	**generics**	1 x 5
felodipine	**generics**	1 x 5
isradipine	Vascal®	1 x 5
lacidipine	Motens®	1 x 2
lercanidipine	Corifeo®, Carmen®	1 x 10
manidipine	Manyper®	1 x 10
nicardipine	Antagonil®	3 x 20
nifedipine	**generics**	2 x 20
nilvadipine	Nivadil®	1 x 8
nisoldipine	Baymycard®	1 x 10
nitrendipine	**generics**	1 x 20

Attention: Short-acting calcium antagonists show an unfavorable prognostic effect in some studies and are therefore not indicated for the treatment of CHD and hypertension; in cases of unstable angina pectoris and acute myocardial infarction, they are even contraindicated. Indications for short-acting calcium antagonists are supraventricular tachycardia (verapamil) and Prinzmetal's angina (coronary spasm). - Only long-acting calcium antagonists should be used for antihypertensive therapy.

Side effects: flushing, headache, dizziness, fatigue, allergic reactions, paresthesia, ankle oedema, rarely blood count changes, and others

Contraindications: heart failure (NYHA III and IV), unstable angina pectoris and acute myocardial infarction, pregnancy, lactation, and others

Additional contraindications for calcium antagonists of the verapamil and diltiazem type: Sinus node disease, AV block > grade I, bradycardia; concomitant therapy with beta-blockers, atrial fibrillation with Wolff-Parkinson-White syndrome, and others

Interactions: Elevation of digoxin plasma levels → possible dose reduction of digoxin and determination of concentration in the plasma.
A combination of beta-blockers and verapamil/diltiazem is relatively contraindicated due to summation of the negative chronotropic and dromotropic effects (danger of AV block, especially in the case of a damaged conduction system and bradycardia).
Grapefruit juice increases the bioavailability of nifedipine.

Reserve antihypertensives:

1. Alpha1-(receptor) blockers: doxazosin, bunazosin, terazosin, urapidil

   Since the doxazosin arm of the ALLHAT Study was stopped early due to an unfavorable result with regard to heart failure in comparison to the diuretic chlorthalidone, alpha1-blockers should not be used as monotherapy in hypertension.

2. Sympatholytics affecting the central nervous system (antisympathotonics):
   - Alpha2-(receptor) agonists: clonidine
     Effect: Stimulation of the alpha2-adrenoreceptors and imidazol-receptors of the brain stem → reduction of adrenergic tone in the periphery. Combination with beta-blockers is not recommended!
     Side effects: sedation, dry mouth, orthostatic reaction, constipation, bradycardia, sleep disorders, possible nightmares, erectile dysfunction, depressive mood.

     Notes: Sudden discontinuation may trigger hypertensive crises!

     Ind: Clonidine in hypertensive crisis/emergency

     Contraindications: sick sinus syndrome, bradycardia, AV block > grade I, depression, hepatic or renal insufficiency, pregnancy and others
     Dos: 0.15 – 0.9 mg/day
   - Methyldopa
     Effect: α-methyldopa is metabolized into α-methylnoradrenalin; this "false neurotransmitter" stimulates central α2-receptors centrally in the CNS, thus increasing the sensitivity of the baroreceptor reflexes → reactive sympatholysis.
     Side effects: allergies, Coombs-positive autoimmune haemolytic anaemia, drug-induced lupus, sedation, dry mouth, sodium and water retention, orthostatic reaction, liver damage, erectile dysfunction, gynaecomastia, psychical disorders and others
     False positive values for catecholamines in the urine occur when taking methyldopa!
     Ind: For pregnancy hypertension only
     Contraindications: hepatic disorders, renal insufficiency, depression
     Dos: Average dose 1-3 x 125 mg/day orally; do not discontinue methyldopa abruptly (danger of hypertensive crisis); dose reduction with renal insufficiency, monitoring of blood count, Coombs test, possibly antihistone antibodies

■ **Arteriolar vasodilators:**

Effect: Arteriolar vasodilation by direct action on the smooth vessel musculature.

Ind: Therapy-refractory hypertension, dihydralazine in pregnancy hypertension as well

- Dihydralazine (e.g. Nepresol®)
  Side effects: Reactive tachycardia with possible triggering of angina pectoris → combine with beta-blockers; orthostasis, headache, gastrointestinal side effects. The frequency of drug-induced lupus is dose-dependent (no daily doses > 100 mg!). Slow acetylators are especially in danger.
  Contraindications: e.g. coronary heart disease, and others
- Minoxidil (e.g. Lonolox®): strongest peripheral vasodilator
  Side effects: Reactive tachycardia, sodium and water retention → therefore always combine with diuretics and beta-blockers, commonly hypertrichosis (troublesome side effects in women) and others
  Contraindications: e.g. coronary heart disease, heart failure, relatively contraindicated in women because of hypertrichosis

Rules for antihypertensive therapy in older patients:

- Careful, slow reduction in blood pressure within weeks.
- Reject normalization of blood pressure if the patient's general well-being deteriorates or side effects of drug therapy, especially orthostasis, occur at blood pressure values < 160/90 mmHg (as long as no additional predisposing conditions are present).
- Choice of antihypertensive by considering the concomitant diseases.
- Start of treatment with low doses and simple therapy regimen (compliance!)
- Isolated systolic hypertension with enlarged blood pressure amplitude also involves elevated cardiovascular risk and should be treated with medication starting at values of 160 mmHg.
- Regular blood pressure monitoring, also while standing. An orthostatic drop in blood pressure with symptoms must be avoided (danger of orthostatic collapse, fall and fracture).
- Regular follow-up examinations with questions on subjective side effects and monitoring of important laboratory parameters (e.g. potassium, creatinine, blood sugar, etc.)
- Use of blood pressure self-measurements (with protocols) and ABPM

Treatment of pregnancy hypertension:

- Cooperation between gynaecologists and internists
- In mild gestational hypertension, ambulatory therapy, physical rest, abstinence from alcohol and nicotine
- In preeclampsia, in-hospital therapy
- Daily self-measurement of blood pressure in the morning + in the evening (night-time hypertension frequently as well!) + monitoring of body weight, urine findings, renal function, liver enzymes, thrombocytes
- Blood pressure values > 160/100 mmHg are considered an indication for drug therapy in asymptomatic pregnant women.
- Suitable oral antihypertensives:
  Agent of choice: methyldopa; agents of 2nd choice: Beta1-selective beta-blockers (metoprolol), dihydralazine
- Emergency treatment of eclampsia with generalized seizures:
  - magnesium sulfate: 2 - 5 g by slow i.v. or diazepam: 5 - 10 mg by slow i.v.
  - Dihydralazine: 6.25 mg or urapidil (Ebrantil®): 12.5 mg i.v.

Notes: The only possible causal therapy for preeclampsia is the earliest possible termination of the pregnancy; with HELLP syndrome, immediate interruption of the pregnancy! Conservative in-hospital treatment up through delivery consists of parenteral antihypertensive + anticonvulsive therapy (see above).

Salt restriction is not indicated in pregnancy hypertension since it decreases plasma volume and uterine circulation is impaired (diuretics do this also). - The prophylactic treatment of pregnancy-induced hypertension with low-dose ASA + ketanserine (a serotonin-2 receptor blocker) appears to reduce the risk of preeclampsia and perinatal death of the fetus.

Hypertensive Crisis und Hypertensive Emergency [I10]

Def.: Hypertensive crisis (= hypertensive urgency): Critical rise in blood pressure (> 230/130 mmHg) with no symptoms of acute organ damage
Hypertensive emergency: Critical rise in blood pressure with endangerment of life due to organ damage: High pressure encephalopathy, intracranial bleeding, retinal bleeding, papillary oedema, acute left heart insufficiency, pulmonary oedema, unstable angina pectoris, myocardial infarction, aortic dissection.

Th.:
- During a hypertensive crisis, it is sufficient to check the blood pressure after 30 minutes of rest and to bring the pressure down within 24 hours through the oral administration of antihypertensives (e.g. an additional dose of the antihypertensive used by the patient). The blood pressure must not be lowered a great deal and suddenly, especially in patients with cerebrovascular diseases (danger of collapse!). In acute stroke, the blood pressure is reactively elevated in 50% of cases and normalized in 2/3 of patients within 24-48 hours. The only indications for the careful lowering of blood pressure are repeated blood pressure values > 200/110 mmHg or hypertensive emergency with threat to life due to hypertensive encephalopathy, angina pectoris or pulmonary oedema. Always lower blood pressure values carefully, no more than about 20% in relation to the initial value!

- In a hypertensive emergency, therapy must be started while the patient is still outside the clinic. Immediate admission to the clinic accompanied by an emergency physician!
  Decrease of average arterial blood pressure by a maximum of 25% in the first 2 hours.
  Supreme commandment: Primum nihil nocere (First do no harm)!

1. First outpatient treatment (treatment alternatives with onset of action after about 10 minutes):
   - Nitroglycerin (Glycerol trinitrate): Agent of choice in angina pectoris, left heart insufficiency, pulmonary oedema
     Break a 0.8 – 1.2 mg capsule with the teeth
   - Short-acting calcium antagonists (e.g. 5 mg nifedipine or nitrendipine in a rapidly absorbable form) are contraindicated in cases of angina pectoris and myocardial infarction.
   - Urapidil (e.g. Ebrantil®):
     25 mg by slow i.v.
   - Clonidine
     0.075 mg by slow i.v. or s.c.
     If there are signs of hyperhydration, additional administration of furosemide (20 - 40 mg i.v.).
     Contraindications: hypovolemia, dehydration

   All the medications named here can be repeated.

2. In-hospital therapy in the intensive care unit:
   - Continuation of the therapy started outside the hospital by infusion (nitroglycerin, urapidil, clonidine or dihydralazine) with close monitoring of the blood pressure; in doing so, the infusion speed is titrated for high-normal to slightly elevated blood pressure values. Dos: e.g. Nitroglycerin 1 - 5 mg/hour and more.
   - Additional administration of 20 - 40 mg furosemide i.v., as long as there are no contraindications (e.g. dehydration)
   - Nitroprusside sodium (e.g. Nipruss®):
     Ind: Therapy-refractory hypertensive crisis.
     To prevent cyanide poisoning when taking higher doses, sodium thiosulfate must be given additionally.
     Dos: See manufacturer's information
   - In case of a hypertensive crisis resulting from terminal renal insufficiency: higher doses of furosemide, haemodialysis

Prognosis of hypertension:

By permanently lowering blood pressure to normal levels, cardiovascular complications can be reduced: left heart insufficiency (-50%), strokes (-40%), myocardial infarction (-25%), deaths from myocardial infarction + stroke (-20%).

RENOVASCULAR HYPERTENSION AND ISCHAEMIC NEPHROPATHY [I70.1]

- Renovascular hypertension: Hypertension caused by significant renal artery stenosis
- Ischaemic nephropathy: Bilateral renal artery stenosis or renal artery stenosis of a single functioning kidney with a significant reduction in the glomerular filtration rate (serum creatinine > 1.5 mg/dL)

Incidence: 1% of all cases of hypertension

Aet.: 1. Arteriosclerotic stenosis (80%): males > females; higher age
2. Fibromuscular stenosis (20%): women > men; younger age; bilateral in 60%
Rarely other causes (e.g. aneurysm of the renal artery)

Prg.: Renal artery stenosis with a narrowing of the lumen by 60% or more leads to the Goldblatt effect (= activation of the renin-angiotensin-aldosterone system) with renovascular hypertension. In bilateral renal artery stenosis, bilateral ischaemic nephropathy develops.

Cl.: Renal artery stenosis may occur isolated, either asymptomatically or in combination with hypertension (renovascular hypertension) or in connection with renal insufficiency (ischaemic nephropathy) or in combination with both.

Diag:
- Take into consideration, especially with diastolic hypertension (> 110 mmHg) in younger patients, with difficult to control (more than 2 antihypertensives necessary) or rapidly progressing hypertension, if blood pressure does not drop during the night, hypertensive emergencies in the medical history
- Stethoscope: possible stenotic murmur, paraumbilical or in the sides (30% of cases)
- Laboratory values: Possible hypokalaemia (hypokalaemic hypertension)

Notes: All screening procedures give false negative and false positive results. If there is a clinical suspicion of renal artery stenosis, conducting an imaging diagnostic of the renal arteries immediately is recommended:

- Imaging diagnostics for detecting renal artery stenosis:
  - Colour-coded duplex sonography of the renal artery: With a renal artery resistance index = RI ≥ 80, most patients will no longer profit from an elimination of the stenosis.
  - MRI or spiral CT angiography
  - Arteriography of the kidneys: This should only be conducted if it is also possible to conduct a balloon catheter dilatation at the same time and if the patient agrees to a possible dilatation!

Th.:
- Percutaneous transluminal angioplasty (PTA) of the stenosed renal artery with or without a stent

Ind: Fibromuscular stenosis; possibly with arteriosclerotic stenosis if RI < 80
Compl.: intima dissection, embolization with renal infarction, restenosis (> 30% of cases with arteriosclerotic stenosis)

- In the remaining cases with unfavorable RI values, conservative therapy with several antihypertensives

Results following angioplasty or surgery: blood pressure normalization in the majority of cases with fibromuscular stenosis, but only in about 20% with arteriosclerotic stenosis (often fixated nephrogenic hypertension).

PHAEOCHROMOCYTOMA [D35.0]

Incidence: About 0.2% of all hypertensive patients; incidence: 1/100,000/year. Average age for the sporadic forms: 40-50 years; for the hereditary forms: < 40 years

Def.: Pheochromocytomas are catecholamine-producing neuroendocrine tumours of the chromaffin tissue of the renal cortex or extra-adrenal paraganglia. 85% are benign, 15% are malignant (with extra-adrenal tumours, about 30%) – 90% are on one side only, 10% are bilateral. 2/3 of pheochromocytomas secrete adrenalin + noradrenalin. Extra-adrenal tumours located above the diaphragm form noradrenalin only. Malignant pheochromocytomas also form dopamine.
85% of pheochromocytomas are located in the renal cortex; the remainder are extra-adrenal in the area of the abdominal or thoracic sympathetic trunk (paraganglioma). In children, 1/3 of the tumours are extra-adrenal.
Pheochromocytomas are hereditary in up to 25% of cases:
1. Multiple endocrine neoplasia (MEN), type 2
2. von-Hippel-Lindau syndrome, type 2 (mutation in the VHL gene)
3. Neurofibromatosis type 1 (Recklinghausen's disease; mutation of the neurofibromatosis type 1 gene)
4. Familial paraganglioma (mutation of the genes for the mitochondrial enzyme SDHB and SDHD)

Cl.:
- Paroxysmal hypertension with blood pressure crises (50% in adults)
- Persistent hypertension (50% in adults – but 90% in children)

Especially during a blood pressure crisis, which can sometimes be triggered by palpation of the abdomen, the patient often (75%) complains of headache, sweating, heart palpitations, tremor, internal unrest, possible pain in the abdomen or sides. Possible paradoxical rise in blood pressure following the administration of beta-blockers.

Additional findings:
- Pale skin!
- Hyperglycaemia and glucosuria (1/3 of cases)
- Leukocytosis
- Loss of weight (hypermetabolism)

Attention: Weight gain and skin rash speak against pheochromocytoma. Diagnosis is more difficult in the non-paroxysmal cases involving permanent hypertension.

DD:
- Blood pressure crises of other genesis, especially in advanced renal insufficiency
- In hyperglycaemia, diabetes mellitus
- Hyperthyroidism
- Cocaine or amphetamine abuse

Diag: ▶ Suspicious clinical symptoms: Hypertension (crises) with heart palpitations, headache, sweating, facial pallor, 24-hour blood pressure measurement (lack of drop in pressure at night)

▶ Detection of the autonomic overproduction of catecholamine:
A biochemical diagnostic should be conducted in the following patients:
- Patients with newly occurring treatment-resistant hypertension
- Patients with paradoxical blood pressure reaction during anaesthesia or surgical procedures
- Patients with a hereditary predisposition to pheochromocytomas
- Asymptomatic patients with an incidental tumour of the adrenals
- Patients with sudden panic attacks

Because of the low prevalence of pheochromocytomas, a biochemical screening of asymptomatic patients with hypertension is not normally conducted.

Attention: Interfering medications (e.g. tetracycline, clonidine, theophylline) must be discontinued, if at all possible, 2 weeks before laboratory diagnostics. Diuretics, calcium antagonists, ACE inhibitors and sartans do not need to be discontinued.

1. Screening test: double determination of catecholamines (adrenalin, noradrenalin) or catecholamine metabolites (metanephrine, normetanephrine) in acidulated 24-hour urine. Most reliable diagnostic procedure!
   Values > 200 ng/L for total catecholamines are pathological, values < 50 ng/L are considered normal.
2. Determination of catecholamines in plasma: Only valuable in the context of a hypertensive crisis! Otherwise, increased false-positive results are obtained with this test if strict sampling conditions are not observed (use of a venule, 30-60 minutes with the patient in a horizontal position before withdrawing the blood sample).

Values > 2000 ng/L are pathological, values < 500 ng/L are considered normal.

3. If a malignant pheochromocytoma is suspected, additional determination of dopamine and homovanillic acid.
4. Confirmation test:
   Ind: If a pheochromocytoma is clinically suspected and catecholamine values are borderline
   Clonidine inhibition test (prerequisite: systolic blood pressure values > 120 mmHg): After administering clonidine, plasma catecholamine concentrations decrease due to central inhibition of the sympathetic nervous system in healthy test subjects, in contrast to the autonomic catecholamine secretion resulting from a pheochromocytoma.

   In one variation of the clonidine inhibition test, catecholamines in daytime urine are compared to those in nighttime urine (after administering clonidine in the evening): In healthy persons and in patients with primary hypertension, there is a steep drop in nighttime catecholamines, in contrast to the case of a pheochromocytoma.
5. Localization diagnostics:
   - (Endo)sonography
   - CT or MRI of the abdomen (sensitivity about 95% and specificity about 75%)
   - Scintigraphy or SPECT (Single Photon Emission CT) with ^{123}iodine-MIBG (metaiodobenzylguanidine) to exclude or detect extra-adrenal pheochromocytomas
   - PET can be used as an alternative to ^{123}MIBG or as a supplementary procedure if the ^{123}MIBG-scintigraphy is negative. The PET provides better diagnostic sensitivity than the ^{123}MIBG-scintigraphy for metastasizing pheochromocytomas.
6. Diagnostics for MEN 2 syndrome in cases of proven pheochromocytoma (see section on that topic)

Th.: Laparoscopic tumour removal (if this does not work: surgical).

In cases of unilateral pheochromocytoma, unilateral total adrenalectomy. In MEN 2 syndrome and bilateral tumours, bilateral subtotal adrenalectomy (to prevent the life-long substitution of glucocorticoids).

The following points must be kept in mind:
- "No touch" technique (to prevent the release of catecholamines)
- Preoperative alpha blockade (phenoxybenzamine); in tachyarrhythmia, in combination with beta-blockers (but only after sufficient alpha blockade)
- Preoperative volume filling (to prevent a post-operative blood pressure drop).
- Watch for hypoglycaemia following surgery!
- Follow-up examinations in the first 5 years

Conservative:
- Treatment of a hypertensive crisis: See the section on that topic
- In cases of inoperability: Therapy with alpha blockers (phenoxybenzamine, prazosin) or α-methyl-p-tyrosine = MPT (Demser®), which inhibits tyrosine hydroxylase and therefore the synthesis of catecholamines.
- In cases of metastasizing pheochromocytoma: For ^{123}MIBG-positive metastases, ^{131}MIBG-therapy (response rate about 25%); otherwise, there are the following treatment options: chemoembolization of liver metastases, palliative chemotherapy

Prog: > 50% of patients with benign pheochromocytoma are normotensive following the operation; in the remaining cases, there is also an essential hypertension. Over the long-term course, about 15% of patients experience a recurrence; therefore, follow-up examinations are indicated.

CHRONIC ARTERIAL HYPOTENSION [I95.9] AND ORTHOSTATIC HYPOTENSION [I95.1]

Def.:
- Arterial hypotension: RR < 100 mmHg systolic.

  Regulatory hypotension can be found in people who are physically well trained: The circulatory system is in a parasympathicotonic state when they are at rest.
- Orthostatic hypotension (OH):
  Blood pressure regulation disorder: drop in systolic blood pressure by at least 20 mmHg or the diastolic blood pressure by at least 10 mmHg when getting up, within 3 minutes after getting up, in comparison to the resting values after 4 minutes of lying down. The cause is a collection of the venous blood in the legs and the area of the splanchnic nerve. This can lead to symptoms of a cerebral perfusion deficit: dizziness, lightheadedness, visual disorders, headache, possibly syncope. If the autonomic nervous system is intact, the sympathetic nervous system may react with tachycardia, pallor, cold extremities, sweating, possibly nausea. These reactive symptoms are lacking in diseases involving a disorder of the autonomic nervous system. Resting blood pressure values may therefore be hypotensive, normotensive or even hypertensive; therefore, the resting blood pressure is not critical for the diagnosis! Up to 50% of patients have hypertensive values while lying down.

Remark: The autoregulation of cerebral circulation, which keeps cerebral circulation constant within a range of 70-180 mmHg through the tonus changes of the small cerebral vessels (Bayliss effect), no longer fully functions in arteriosclerotically altered cerebral vessels; in this case, a sudden drop in systolic pressure to < 120 mmHg may

lead to neurological deficits with danger of falling.

Ep.: Orthostatic hypotensive episodes are observed in 25% of older people > 65 years.

Classification and aetiology:

A) Hypotension

1. Primary (essential) hypotension (most frequent form):
   Familial clustering is especially observed among young women of small body build. Harmless findings, no disease.

2. Secondary hypotension:
   - Drug-induced: e.g. psychopharmaceuticals, antiarrhythmic agents, antihypertensives, diuretics, coronary agents, vasodilators, etc.
   - Endocrine-related: hypothyroidism, adrenal cortex insufficiency, adenohypophysis, hypoaldosteronism
   - Cardiovascular-related: e.g. aortic stenosis, heart failure, arrhythmias, pulmonary hypertension, constrictive pericarditis, etc.
   - Immobilization, long periods of bed rest, after infectious illnesses
   - Hypovolemia and hyponatremia of varying genesis

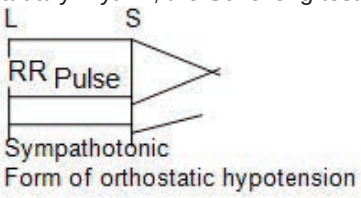
B) Orthostatic hypotension

- In the context of hypotension, especially secondary hypertension
- Varicosis and post-thrombotic syndrome
- Disorders of the autonomic nervous system with asympathotonic orthostatic hypotension (lack of reactive activation of the sympathetic nervous system): e.g.
  - Diabetic autonomic neuropathy (frequent!)
  - Polyneuropathies of varying genesis, Parkinson's disease
  - Isolated autonomic insufficiency (Bradbury-Egglestone syndrome) } rarely
  - Multisystem atrophy (Shy-Drager syndrome and others) } rarely
  - Baroreflex failure } rarely
  - Dopamine-β-hydroxylase deficiency, and others } rarely

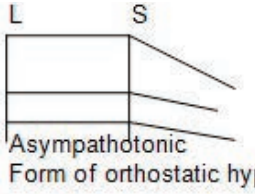
3 reaction types according to the behaviour of the pulse and blood pressure in the Schellong test:

- Sympathotonic orthostatic hypotension = most frequent type (2/3 of all cases)
  In the Schellong test, decrease in the systolic blood pressure > 20 mmHg with varying behaviour of the diastolic blood pressure, rise in pulse rate by more than 16/minute.
- Asympathotonic orthostatic hypotension:
  Drop in the systolic (> 20 mmHg) and diastolic blood pressure (> 10 mmHg), pulse rate remains the same or falls
- Orthostatic intolerance (syn.: postural orthostatic tachycardia syndrome = POTS):
  Increase in pulse > 30/minute or increase in heart rate > 130/minute without Hypotension

Schellong test:
10 minutes lying down (L) + 10 minutes standing (S), measurement of blood pressure + pulse at intervals of 1 minute (or as a quick test after 1, 3 and 5 minutes)
Normal reaction:
Fall in systolic blood pressure < 20 mmHg/diastolic < 10 mmHg. Since the behaviour of the circulatory system exhibits a daily rhythm, the Schellong test should be repeated at different times of the day.



Sympathotonic
Form of orthostatic hypotension



Asympathotonic
Form of orthostatic hypotension

Cl.:

1. Arterial hypotension: Arterial hypotension usually has no significance as a disease. Exception: symptoms of reduced cerebral blood flow and reduced performance occur.
   - Decrease in performance, rapid fatigability, long morning "start-up time", complications concentrating
   - Depressive mood, internal unrest, sleep complications
   - Cold hands and feet (DD: autonomic dystonia)
2. Orthostatic hypotension and orthostatic intolerance:
   Feeling of dizziness, blacking out or flickering before the eyes when standing up from bed or when stooping, possible orthostatic collapse (syncope): Sudden drop in blood pressure as a result of acute reduction in venous return current to the heart with clouding of consciousness or short-term loss of consciousness. Compl.: fractures!
   - Headaches, tinnitus
   - Cardiac sensations: palpitations of the heart, pain around the heart, feelings of anxiety

Diagnosis of hypotension: medical history, Schellong test, ABPM, causal diagnostics

Th.: a) Causal: In symptomatic hypotension: e.g. discontinuation of drugs that cause hypotension or orthostatic reaction (e.g. diuretics, psychotropic drugs, and others)

b) Symptomatic: Lower blood pressure per se is not an indication for treatment. General measures are usually sufficient for symptoms resulting from hypotension (hypotensive symptom complex).

1. General measures:
   - Increased salt intake (e.g. Salted bread and butter for breakfast) + increased fluid intake (2-3 L/day); more frequent, small meals – contraindication: heart failure
   - Cycle training (athletics)
   - Massages, hydrotherapy (Kneipp)
   - Sleeping with the upper body raised by 20 degrees reduces any hypertension when lying down, night-time diuresis and orthostatic reactions in the morning
   - Stand up slowly after bed rest
   - Compression hose
   - If there is a tendency towards orthostatic hypotension, crossing the legs when standing up or stooping over

2. Medications:
   - Sympathomimetic (alpha-adrenoreceptor agonists):
     Side effects: tachycardia, ventricular arrhythmias; bladder emptying disorders due to prostatic adenoma, angina pectoris due to CHD
     Contraindications: cardiac arrhythmias, CHD, prostatic adenoma with urinary disorders, narrow-angle glaucoma, hyperthyroidism, 1st trimester of pregnancy, competitive sports (positive doping test)
     Midodrine (e.g. Gutron®) or norfenefrine (e.g. Novadral®): Direct-acting α-sympathomimetics
     Side effects: Itching of the scalp, hair standing on end (piloerection) and others
     Ind.: hypo- and asympathicotonic orthostatic hypotension
   - Mineralocorticosteroids: Fludrocortisone
     Effect: sodium retention with increase in the circulating blood volume
     Side effects: hypokalaemia, sodium/water retention, possibly with oedema and weight gain, hypertension, depression, acne
     Contraindications: heart failure and others
     Ind: asympathicotonic orthostatic hypotension (in combination with sympathomimetics)
     Dos: 0.1 mg/day (initially possibly more)
   - Erythropoietin
     Ind: Patients with orthostatic hypotension who do not respond to other drugs. A haematocrit of 50% should not be exceeded (side effects, contraindications, dosage – see section on "renal anaemia")

SYNCOPE [R55]

Def.: Suddenly occurring, spontaneous, reversible loss of consciousness and tonus result from a decrease in cerebral circulation with or without falling. Injuries occur in 20% of cases.

Ep.: About 40% of all people suffer at least one episode of syncope in their lifetime.

Classification (European Society of Cardiology – ESC):

1. Reflex-mediated syncopes:
   - Neurocardiogenic syncope (NCS): = vasovagal syncope: most frequent form of syncope in healthy persons.
     Prodromes of NCS: dizziness, blacking out of vision, heart palpitations, sweating, pallor, nausea and others
     Prg.: Anxiety, pain and stress trigger a reflex cascade with reduction of the activity of the sympathetic nervous system and an increase in the activity of the parasympathetic nervous system → drop in blood pressure and bradycardia → NCS (emotional syncope).
     Diag: Tilt table test.: The patient fastened to a tilt table is passively propped up by 60-80° after 15 minutes of lying horizontal and positioned thus for up to 45 minutes. If syncope occurs, the test is positive and proves vasovagal syncope.
   - Carotid sinus syndrome with syncope
   - Coughing syncope }
   - Micturition syncope } pressor syncope
2. Orthostatic syncope: triggering factors are sudden standing up from a horizontal position or standing for a long period of time
   Prg.: failure of the vasoconstrictive reflex in the area of the capacity vessels (veins) of the legs.
3. Arrhythmic syncope due to bradyarrhythmia, Adams-Stokes attack, tachyarrhythmia
4. Syncope due to heart/lung diseases: e.g. syncope due to aortic stenosis, pulmonary embolism, etc.
5. Cerebrovascular syncope (rare): e.g. in Steal syndromes (subclavian steal syndrome)

DD: Syncope due to other causes of loss of consciousness, e.g. hypoxia, hyperventilation/hypocapnia, epilepsy, etc. must be differentiated.

Di: - (Hetero)history (most important!)
- Clinical / laboratory results
- Technical diagnostic procedures:

Medical history / findings	Diagnosis
Pain or other emotional stress situations, standing for long periods of time with premonitory symptoms such as "weak knees" or "dull feeling in the stomach"	Vasovagal syncope (NCS)
Syncope immediately after standing up. Drop in systolic blood pressure when standing by > 20 mmHg or to < 90 mmHg	Orthostatic syncope
Pathological ECG: • Sinus bradycardia < 40/min • Sinus node arrest > 3 seconds • AV block, grade II/III (Mobitz type) • Alternating left and right bundle branch block	Arrhythmogenic syncope (Adam-Stokes attack)

Test	Suspected diagnosis
Tilt table test	Vasovagal syncope
Schellong test	Orthostatic syncope
Echocardiography Ergometry Long-term ECG Loop recorder (external or implantable)	Rhythmogenic syncope (Adam-Stokes attack)

- Supplementary diagnostics: Possible neurological consult, electrophysiological examination in cases of suspected arrhythmogenic syncope

Th.: • of orthostatic syncope:
Lying flat with raised legs
• Options for preventing NCS:
- Learn to recognize prodromes and avoid NCS by sitting/lying down in time. The Jendrassik maneuver is also helpful (Hook fingers together and pull outwards strongly with both arms). Intake of salt and fluids; discontinuation of drugs with blood pressure lowering side effects. Avoidance of dehydration, stress, alcohol consumption, hot rooms, and other triggers
- Prescription of compression hose
- Tilt table training in specialized clinics or stand training
• Arrhythmogenic syncope: Check indication for pacemaker therapy.

Prog: Reflex-mediated syncope and orthostatic syncope have a good prognosis (as long as there are no accidents). Arrhythmogenic syncopes due to structural heart diseases involve an elevated risk of death, depending on the root disease.

SHOCK

Def.: Critical reduction in microcirculation with tissue hypoxia and metabolic disorders.

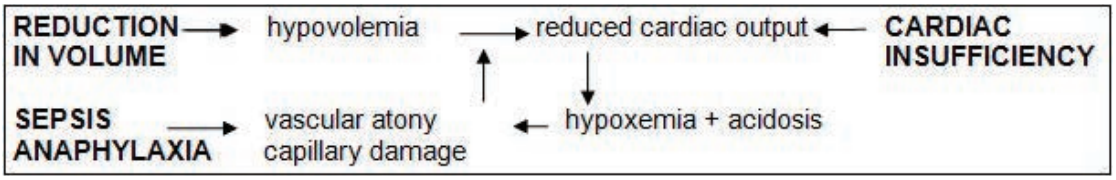
Aet.: 1. Reduction in the quantity of circulating blood = hypovolemic shock [R57.1]: loss of blood, plasma, vomiting, diarrhoea, etc.

2. Pumping failure of the heart: cardiogenic shock [R57.0]
Cause: ▪ Weak contractions: myocardial infarction, myocarditis, cardiomyopathies
▪ Volume loading with increase in preload: valvular insufficiency, shunt defects
▪ Pressure load with increase in afterload: valve stenoses, pulmonary embolism
▪ Deterioration of filling of the heart: Pericardial tamponade, constrictive pericarditis
▪ Cardiac arrhythmias

3. Failure of the regulation processes of the peripheral circulation:
- Septic shock [A41.9](usually in sepsis with gram-negative bacteria, often with consumptive coagulopathy)
- Anaphylactic shock [T78.2] – Two pathophysiological mechanisms:
1. IgE-mediated type I reaction according to Coombs and Gell. Occurs after sensitization with renewed contact with the allergen.
2. Non-immunological, so-called pseudoallergic reaction through the direct release of the mediator. No prior exposure necessary.

Prg.: The fall in blood pressure during shock causes the release of catecholamines with an increase in heart rate and constriction of arterioles and venous capacity vessels. Initially, the arterial blood pressure may still be normal due to this regulation mechanism. According to the different distribution of α- and ß-receptors, the remaining quantity of circulating blood is redistributed (centralization) in order to guarantee the blood supply to the heart and brain. - While

initially there is a compensatory influx of interstitial fluids into the vessels, there is increasing tissue hypoxia and the accumulation of acid metabolites (see below) lead to transcapillary losses and intravasal fluid and thus to the worsening of the volume deficit. The pre-capillary sections of the vessels react to the acidosis more sensitively than the post-capillary vessels; this results in an atony of the pre-capillary sections of the vessels along with the still existing constriction of the post-capillary sections; this leads to local cut-off of blood and worsening of the erythrocyte sludge phenomenon and the formation of microthrombi (in extreme cases, the formation of multiple microthrombi leads to consumption coagulopathy).



The "shock spiral" can start at different places; once the vicious cycle has set in, the event continues to progress independently of the triggering cause.

Metabolism during shock:
Because of the lack of O_2, the aerobic breakdown of carbohydrates is impeded and end products of the anaerobic breakdown of carbohydrates accumulate (lactate). This leads to metabolic acidosis.

Effect of shock on some organs:
- Kidneys: oliguria/anuria
- Heart: reduced coronary perfusion with heart failure
- Lungs: Adult (Acute) Respiratory Distress Syndrome = ARDS (shock lung): thrombocyte aggregation, microembolisms, interstitial oedema, reduction of surfactant factors with microatelectases, formation of hyaline membranes.
  ARDS involves intrapulmonary shunts, reduced compliance and O_2 diffusion complications: Danger of respiratory insufficiency (high rate of mortality!). See ARDS for additional details.
- RHS (right heart syndrome): highly impaired function with susceptibility to infection
- Coagulation system: possible disseminated intravasal coagulation (DIC)

Cl.: **A) Hypovolemic shock:** [R57.1]

3 stages of hypovolemic shock:

I. Moist, cool, pale skin, blood pressure (almost) normal
II. Pulse > 100/min., RR < 100 mmHg, neck veins collapsed (when lying down), thirst, oliguria
III. RR < 60 mmHg, pulse barely palpable, shallow, rapid breathing, impaired consciousness with wide, barely reactive pupils, anuria

$$\text{"Shock Index} = \frac{\text{Pulse}}{RR_{syst.}} \quad \text{(Index > 1 = danger of shock!)}$$

But: In Stage I, an index < 1 in spite of hypovolemia! In younger patients, the shock index often fails.
Acute blood losses of < 1,000 mL are usually well compensated; there is a danger of shock with higher losses!

History: While arterial pressure usually does not drop to pathological levels until after volume losses of 20% (1,000 mL) or more, central venous pressure (CVP) is already reduced with a loss in blood volume of around 10% (normal CVP: 4-10 cm H_2O). - Furthermore, at systolic blood pressure values of < 70 mmHg, indirect blood pressure measurement using the Riva-Rocci method is not accurate, so that the direct (invasive) method of measuring arterial blood pressure is to be preferred in shock. A good laboratory parameter for shock is the arterial lactate level.

B) Cardiogenic shock resulting from left heart failure: [R57.0]

Def.: • Arterial hypotension with systolic blood pressure of < 80-90 mmHg
• Cardiac index < 1.8 L/min/m^2
• Left ventricular end-diastolic pressure > 20 mmHg

Diagnosis of left heart failure:

- Cl.: Wet rales over the basal sections of the lungs, dyspnoea
- Chest X-ray:signs of pulmonary congestion
- Echo: Evidence of a possible pericardial tamponade, evaluation of valvular and pumping function, ventricular kinetics and others
- Invasive diagnostics (pulmonary catheter)

The degree of heart failure is measured by the end-diastolic ventricular filling pressure. Here, the left ventricular end-diastolic pressure corresponds to the pulmonary capillary pressure and end-diastolic pulmonary pressure, the right ventricular end-diastolic pressure to the central venous pressure. The level of the central venous pressure does not allow any conclusions regarding the function of the left ventricle!

C) Anaphylactic shock: [T78.2]

4 Degree of severity of the anaphylactic reaction:

O: locally limited cutaneous reaction with no clinical significance

I: General symptoms (dizziness, headache, anxiety, etc.) + skin reactions (flushing, itching, urticaria, etc.)

II: Additionally: Drop in blood pressure + tachycardia and gastrointestinal symptoms (nausea, vomiting, etc.), mild dyspnoea

III: Additionally: Bronchospasms (asthma attach) and shock, rarely also laryngeal oedema with inspiratory stridor

IV: Respiratory, circulatory arrest

D) Septic shock: [A41.9]

Def.: • Bacteraemia: Detection of bacteria in the blood (blood culture)

• Systemic Inflammatory Response Syndrome (SIRS):
Generalized inflammatory reaction of varying genesis (e.g. infection, burns, trauma)
≥ 2 criteria present:
1. Temperature: > 38°C or < 36°C
2. Tachycardia > 90/min.
3. Tachypnea: > 20/min (essential cardinal symptom)
4. pCO_2 < 32 mmHg
5. Leukocytes > 12,000/µL or < 3,800/µL; unsegmented/immature neutrophils > 10%

History: The definition of SIRS does not require proof of an infectious cause (as required for sepsis). An increase in procalcitonins is considered a sensitive parameter in sepsis, but is not a routine parameter.

• Sepsis: SIRS caused by an infection.
Most frequent cause: nosocomial infections (intensive care unit, ventilation, central venous catheters, urinary catheters), pancreatitis, shock, polytrauma, burns over a large surface of the body, etc.

Notes: If sepsis is suspected, always look for a focus/route of entry + perform repeated blood cultures (aerobic + anaerobic)!

• Severe sepsis: Sepsis with organ dysfunction

• Septic shock: 3 Diagnostic criteria:
1. SIRS
2. Evidence of an infectious genesis (blood cultures!)
3. Arterial hypotension (RRsyst. < 90 mmHg or average arterial blood pressure < 70 mmHg) in spite of sufficiency volume substitution

Additional symptoms:
- Fever (not obligatory!), unrest, confusion, hyperventilation
- Possible septic skin manifestations (pustules, necroses, blisters), bleeding of the skin with meningococcal sepsis
- Evidence of bacteraemia from a positive blood culture

2 haemodynamic forms of septic shock:

• Hyperdynamic form (early phase):
- Peripheral resistance ↓
- Arteriovenous difference in O_2 content ↓
- Warm, dry skin, rosy appearance
- Blood pressure and CVP normal or slightly low

• Hypodynamic form:
- Peripheral vascular resistance ↑
- Arteriovenous difference in O_2 content ↑
- Blood pressure, CVP, diuresis ↓, tachycardia
- Pale, moist, cool skin as in hypovolemic shock

Fulminant course of sepsis:

• Meningococcal sepsis or Waterhouse-Friderichsen syndrome (often with bilateral haemorrhage of the adrenals, petechial skin haemorrhage and consumption coagulopathy)

• Sepsis following splenectomy (see OPSI syndrome)

• Toxic shock syndrome (TSS)
- Staphyloccocus-associated TSS caused by TSS toxin 1 from vaginal infections, e.g. from tampons: "tampon-associated shock syndrome" (formation of exotoxin C and enterotoxin F); gynaecological consultation
- Streptococcal-associated TSS from enterotoxins from group A streptococci (GAS) bacteria in necrotizing fascitis or myositis; surgical consultation

Compl.: Multiple organ failure syndrome (MOFS) = Multiple organ dysfunction syndrome (MODS)

DD: Hypovolemic and cardiogenic shock: While the CVP is decreased in hypovolemic shock, it is usually elevated in heart failure! One of the most important criteria is venous filling: collapsed veins in case of decreased volume, congested veins in cardiogenic shock. The veins at the root of the tongue and in the neck are good for evaluation.

Di: Medical history + clinical (pulse/blood pressure) + additional diagnostics

Th.: A) Causal therapy: elimination/treatment of the cause of the shock

B) Symptomatic therapy:

- Basic monitoring:
  - · pulse, blood pressure, CVP, skin colour/temperature
  - · ECG (monitor), respiration rate, diuresis
  - · blood count, haemoglobin, haematocrit, coagulation analysis, urea, creatinine, electrolytes, etc.
  - · arterial blood gas analysis and pulse oxymetry (= transcutaneous O_2 measurement)
  - · possible pulmonary catheter (determination of pulmonary pressure and cardiac output)
- General measures: keep airways clear, protect from loss of heat, administration of O_2 by nasal cannula
- Positioning: horizontal position, possibly with raised legs in hypovolemic shock
  Sitting position in cardiogenic shock

▶ **Treatment of hypovolemic shock:**

A) Volume substitution through 2 large-lumen veins, if at all possible

Volume substitution is indicated in all forms of shock – except in cardiogenic shock. In hypovolemic shock, this is the only life-saving measure. Initially, 500 – 1,000 mL of a plasma expander is given, and the additional volume requirement is covered with isotonic, isoionic saline solutions in order to balance the interstitial and cellular fluid deficit. In cases of larger amounts of blood loss, a more rapid administration of erythrocyte concentrates is necessary following initial volume substitution. With massive transfusion of erythrocytes, also administer fresh frozen plasma (FFP) and thrombocyte concentrates.
Central venous pressure (CVP) should not exceed 14 cm H_2O. Vein filling (veins under the tongue, external jugular veins) are observed as a guide.

Remarks: Drugs having a vasoconstrictive effect are contraindicated during hypovolemic shock; normal CVP 4 - 10 cm H2O (3 - 8 mmHg)

1. Colloidal plasma substitute

Plasma expanders are colloidal plasma substitutes with a higher oncotic pressure than that of plasma → initial volume effect > 100% by the influx of extravasal fluid into the intravasal space. The oncotic pressure depends on the concentration of the solution. The intravasal dwell time is determined by the molecular weight and breakdown/excretion.

Substance	Example of preparation	Volume effect (%)	Intravasal dwell time (h)
HES 200/0.5 = average molecular weight 200,000 and degree of substitution 0.5	HES-steril 10% HES-steril 6%	about 130 about 100	3 - 4 3 - 4

▶ Hydroxyethyl starch (HES) is a good volume substitute and works by "coating" thrombocytes and erythrocytes in such a way as to inhibit aggregation. HES is broken down into smaller molecules by α-amylase and then excreted through the kidneys. Larger molecules are taken up by the reticulohistiocytic system. Serum amylase levels may increase. The infusion of high-molecular HES solutions may increase the risk of bleeding by reducing factor VIII/von Willebrand factor complexes. This is not true for rapidly cleavable HES 200/0.5 or low-molecular HES 70/0.5

Side effects: Common: sometimes long-lasting pruritis (deposits of HES in the skin), allergic reactions. Severe anaphylactic reactions are very rare (1 in 1 million), possible worsening of renal function, possible risk of bleeding (see above).

Contraindications: Renal insufficiency (creatinine > 2 mg/dL)

▶ Colloidal solutions made from substances manufactured in the body (plasma preparations)

-Human albumin (not indicated due to lack of prognostic benefit)
- Pasteurised plasma protein solution (PPS)
- Coagulation-promoting preparations: fresh frozen plasma (FFP).
  Disadvantage: risk of infection (see below)

2. Isotonic crystalline saline solutions (e.g. Ringer's solution) have a short intravasal dwell time of 30 - 40 minutes. Crystalline solutions and plasma expanders are used in pronounced volume deficits. No Ringer's lactate solution if lactate acidosis!

3. Erythrocyte concentrates:

Disadvantages:
- Risk of infection (The following numbers apply to NAT testing for virus RNA/DNA only): HBV: ~ 1 in 260,000; HCV and HIV: about 1 in 4.5 million; additional risk of infection from Herpes viruses, parvovirus B 19, HTLV-1/2, bacteria and protozoa. Risk of bacterial sepsis 1 in 500,000.
-Loss of time through blood group determination/cross-matching
-Limited storage time and availability
- Hypersensitivity reactions
- Transfusion-related acute lung injury (TRALI) with acute dyspnoea, bilateral pulmonary infiltrates
  Cause: leukocytic antibodies in the plasma of the blood donor; occurs within 6 hours after blood transfusion.

Also to be taken into consideration is the fact that older preserved erythrocytes contain an increased amount of potassium . The risk of infection is significantly reduced by screening blood donors for virus antibodies. Use leukocyte-depleted preserved erythrocytes only (BSE prevention).
Transfusion indication in patients with normal cardiopulmonary function: Hb < 7 g/dL

B) Correction of metabolic acidosis with bicarbonate buffer
- Lactate buffers are contraindicated! -

C) Recognition (urinary catheter) and prophylaxis of a threatening shock kidney (see under Renal Failure).
D) Treatment of ARDS: See the section on that topic
E) Treatment of DIC (see section on that topic)
F) Stress ulcer prophylaxis; early enteral nutrition

▶ **Therapy for anaphylactic shock**
(Severity grade III of anaphylactic reaction):

- Flat, horizontal position, legs possibly raised, O_2 administration
- Stop any further administration of antigen, discard i.v. needle after giving contrast medium! Large-lumen venous access.
- Adrenaline (Suprarenin®): 1 mL = 1 mg ➜ dilute with 9 mL NaCl 0.9%: Dose in 1 mL steps according to effect.
- Rapid volume substitution in sufficient quantity (in adults with cardiac sufficiency: 2,000 – 3,000 mL in 30 minutes)
- Prednisolone: 500 mg i.v.
- Histamine antagonists:
  - H1 antagonists: e.g. Clemastine (Tavegil®) 2 mg i.v.
  - H2 antagonists: e.g. Ranitidine (Zantic®) 50 mg i.v.

Additional measures:

- In case of bronchospasms: Fast-acting beta$_2$ sympathomimetics as a spray (see chapter on asthma)
- If there is swelling in the upper airways, intubation, if necessary. If there is airway displacement due to oedema of the larynx, emergency airway puncture as the last resort
- If circulatory arrest (grade IV of anaphylactic reaction): cardiopulmonary resuscitation
- Monitor patients in the hospital for at least 24 hours.

▶ **Treatment of septic shock:**

- Treatment of the underlying disease: Search for focus/access route and eliminate infection!
- Broad-band antibiotics for unknown pathogens (take several blood samples for aerobic + anaerobic blood cultures beforehand!). For details, see the section on "bacterial endocarditis".
- Goal-oriented cardiovascular therapy with volume substitution, O_2 administration, etc. ➜ Targets: CVP 8 – 12 mmHg; MAP 65 – 90 mmHg; Hct ≥ 30%; central venous O_2 saturation ≥ 70%
  If the blood pressure cannot be normalised in spite of volume substitution, possible administration of noradrenalin.
- Maintenance of normal blood glucose levels
- If adrenal cortex insufficiency is detected, administration of hydrocortisone, which also improves the response of the vessels to catecholamine.
- Possible supplementary administration of the activated protein C analog drotrecogin alpha (Xigris®), which should reduce mortality in cases of severe sepsis.
- Prophylaxis and treatment of complications: e.g.
  Prophylaxis of consumption coagulopathy by giving heparin in low doses. Monitor antithrombin and substitute as needed.
  Lung-protective ventilation in case of ARDS

Prog: - "Sepsis": low mortality
- "Severe sepsis" with MODS: mortality up to 40%
- "Septic shock": Mortality up to 70%

▶**Treatment of cardiogenic shock:**

a) Causal treatment, e.g.
- Myocardial infarction: reperfusion therapy: fibrinolysis, acute PTCA
- Ventricular septum perforation, papillary muscle tear: surgical correction
- Pericardial tamponade: relief puncture
- Pulmonary embolism: fibrinolysis, possibly embolectomy
- Cardiac arrhythmia: antiarrhythmic therapy

b) Symptomatic (compensatory) treatment:
- Raised position of upper body
- Administration of O_2 with pulse oxymetry monitoring
- Sedation, analgesics for pain
- Dobutamine and others

Additional details: See the respective sections!

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