Differences
spontaneous breathing / ventilation

- **according to pressure:**
  - **spontaneous breathing: negative pressure**
  - **mechanical ventilation: positive pressure**
- **according to breathing gas distribution (in the lungs):**
  - **spontaneous breathing: especially dorsal and basal (reason: active diaphragm)**
  - **mechanical ventilation: especially ventral and apical (reason: passive diaphragm)**

Expiration

- passive process (both during spontaneous breathing as well as during mechanical ventilation), only an active process in the case of forced expiration (contraction of muscles of expiration)
- elastic retraction forces of lung and chest
- outflow of air from the alveoli

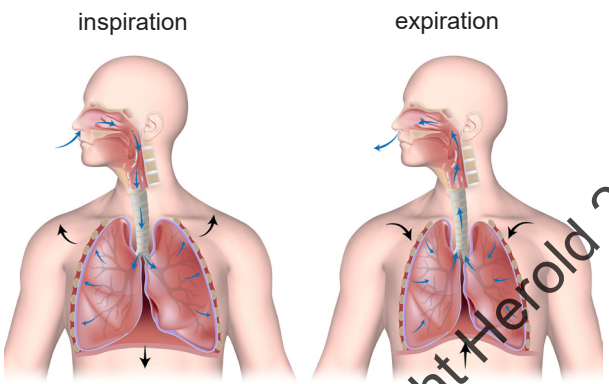


Fig. 172 spontaneous breathing: The inspiration is an active process (contraction of the diaphragm [main breathing muscle] and the intercostal musculature). The expiration, however, is a completely passive process.

Perfusion

- blood circulation in the alveoli
- transport of CO_2 with the blood to the alveoli and transport of O_2 out of the alveoli with the blood to the organs
- Perfusion is not homogeneous throughout the lung. It increases depending on gravity from apical to basal (in case of upright position) respectively from ventral to dorsal (in case of supine position). It is illustrated in the 3-zones-model (according to West).
- An extreme example of a perfusion disorder is the cardiac arrest: Here you have no more lung perfusion, i.e. no more transport of carbon dioxide to the alveoli and no oxygen transported out of the alveoli. In case of a cardiac arrest there is therefore also a disturbance of gas exchange (increase of pCO_2 and decrease of pO_2 in the blood).
- A good parameter for perfusion which is also easy to measure in ventilated patients (capnometry), is the end-tidal CO_2-concentration $ETCO_2$: The worse the perfusion, the less CO_2 is removed and the lower the end-tidal CO_2-concentration in the expired air.
- disorders (typical examples): pulmonary embolism, pulmonary arterial hypertension (PAH), heart failure, shock

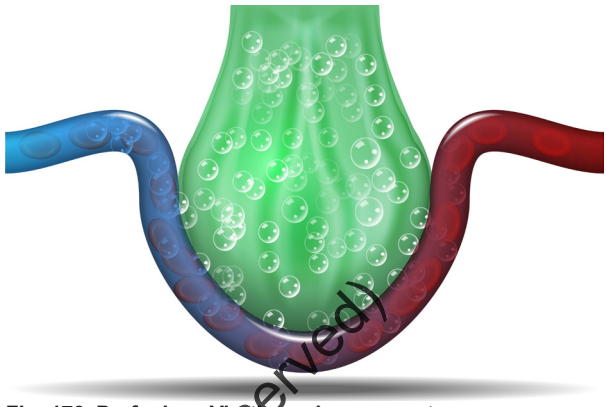


Fig. 173 Perfusion: Via the pulmonary artery oxygen-poor and carbon dioxide-rich blood gets to the lung capillary. There the gas exchange with the alveolus takes place. Then the oxygen-rich and carbon dioxide-poor blood is transported away via the pulmonary vein.

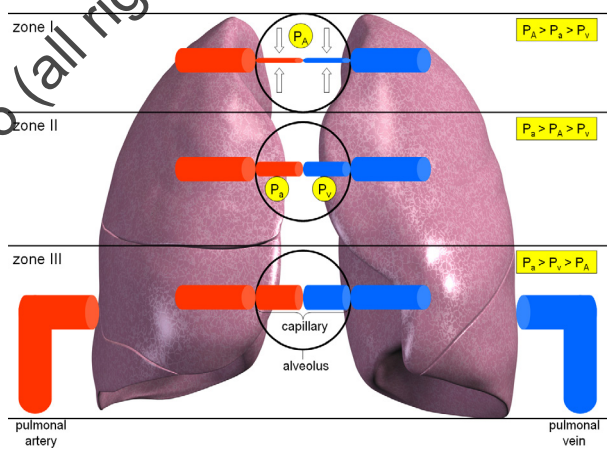


Fig. 174 3-zones-model of perfusion (lung perfusion; according to West [named after the Australian and US-American physiologist John West; born: 1928]): Perfusion is not homogeneous throughout lung. Due to gravity it increases from apical to basal. In zone I (apical zone) the pulmonary artery pressure (P_a) and the pulmonary venous pressure (P_v) are very low. Due to the alveolar pressure (P_A) the lung capillary gets compressed so that there is only a very low perfusion. In zone II (middle zone) the pulmonary artery pressure (P_a) and the pulmonary venous pressure (P_v) are significantly higher so that here significantly more perfusion occurs. In zone III (basal zone; the largest zone) due to gravity as well the pulmonary artery pressure (P_a) as the pulmonary venous pressure (P_v) are higher than the alveolar pressure (P_A) so that the lung capillary is no more compressed and stays open. The perfusion therefore is highest in this zone. This applies to the upright position. In supine position the same changes apply from ventral to dorsal instead of from apical to basal.

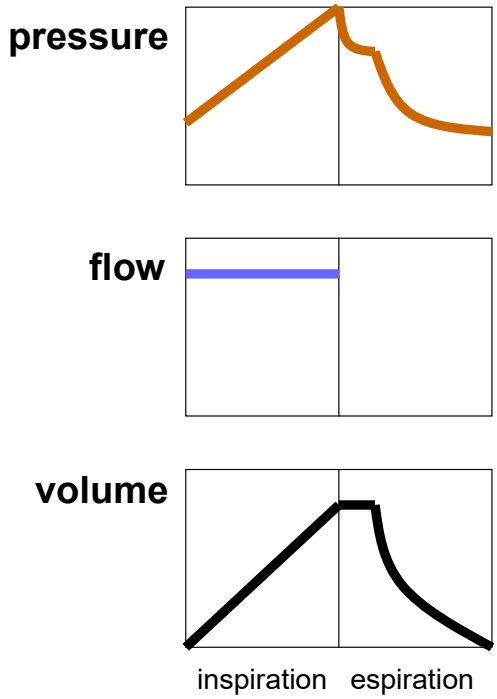
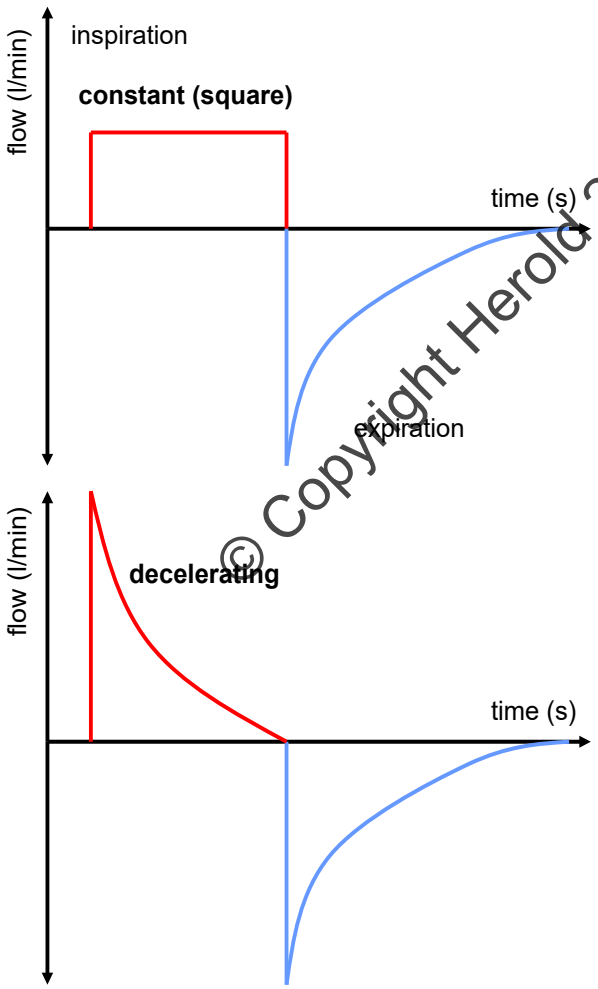


Fig. 204 volume-controlled ventilation (VCV)



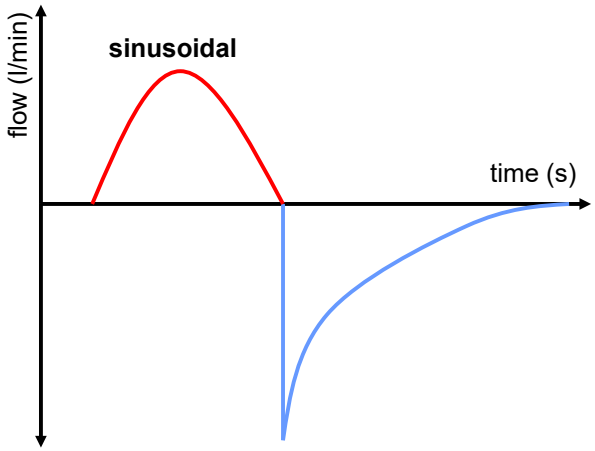


Fig. 205 the three different flow profiles (patterns of the inspiratory flow) in volume-controlled ventilation: The constant flow ("rectangle" flow) is standard today. The decelerating flow is mainly used in conscious patients, the sinusoidal flow is no longer used today.

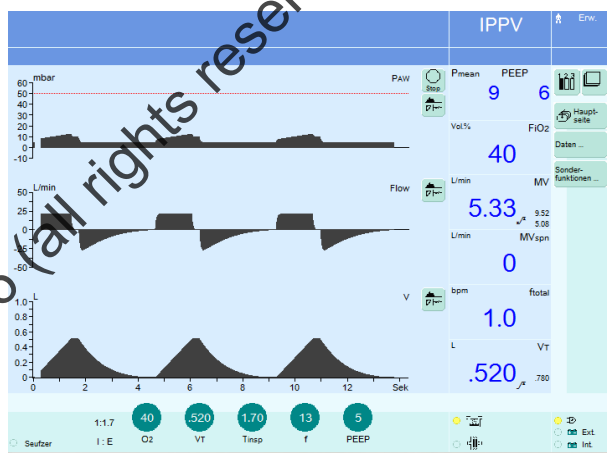


Fig. 206 IPPV (intermittent positive pressure ventilation): a typical volume-controlled ventilation (annotation: The correct term is continuous positive pressure ventilation [CPPV] because there is continuously a positive pressure in the airway and not only in the inspiration. Strictly speaking in IPPV there is no positive pressure during expiration (no PEEP).

Flow:
- *pressure-controlled ventilation: decelerating*
- *volume-controlled ventilation: constant*

Ventilation pressures

- inspiratory pressures:
  - peak pressure
  - plateau pressure
- expiratory pressure: The pressure at the end of the expiration is called PEEP.
- mean airway pressure (MAP): the average pressure generated during the respiratory cycle
- units:

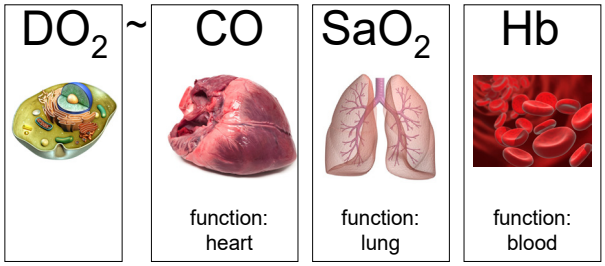


Fig. 346 The three determinants of oxygen delivery (DO_2) to the cell: the function of the heart (CO), the lung (arterial oxygen saturation [SaO_2]) and the blood (Hb).

The German physiologist Eduard Pflueger (1829-1910) stated already in 1872: "The cardio-respiratory system fulfills its physiological task in ensuring the cellular oxygen supply."

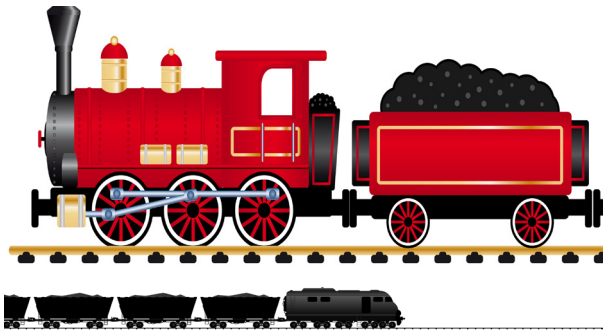


Fig. 347 The relationship should be illustrated by a comparison with a train: The oxygen delivery for the cell can be compared with the amount of coal supplied by a train (e.g. for heating). In this comparison, CO corresponds to the engine (power) of the locomotive (traction engine), the hemoglobin to the number of wagons and the SaO_2 to the proportion of the load volume of each wagon loaded with coal. The larger the individual parameters (i.e. stronger traction engine, more wagons, wagons loaded with coal up to the ceiling if possible), the more coal is ultimately delivered by the train and can then be burned for energy generation.

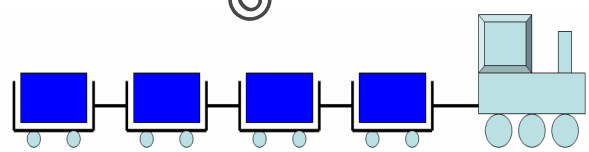


Fig. 348 normal oxygen delivery DO_2: strong traction engine (CO), enough (in the example here 4) number of wagons (hemoglobin), all of which are fully loaded (SaO_2 = 100%).

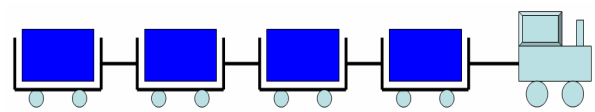


Fig. 349 reduced oxygen delivery DO_2: indeed a sufficient number (hemoglobin) of fully loaded (SaO_2) wagons, but a to small (too weak) traction engine (CO too low)

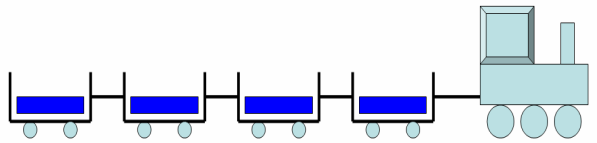


Fig. 350 reduced oxygen delivery DO_2: indeed a strong traction engine (CO) and a sufficient number (hemoglobin) of wagons, but which are underloaded (too little saturation SaO_2)

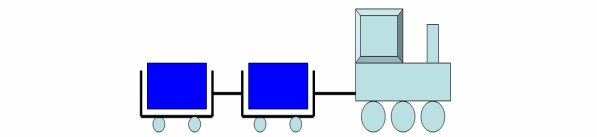


Fig. 351 reduced oxygen delivery DO_2: indeed a strong traction engine (CO) and fully loaded (SaO_2) wagons, but which are too few (only 2 instead of 4; too little hemoglobin)

In shock, by definition the oxygen delivery is smaller than the oxygen consumption.

shock: oxygen delivery DO_2 < oxygen consumption VO_2

So in order to optimize the oxygen supply to the cell, the following can be done:

- increase the oxygen delivery (DO_2):
  - cardiac output (CO; the main determinant of DO_2 [90%]):
    - CO = stroke volume (SV) x heart rate (HR)
    - stroke volume: optimization of preload, ejection fraction (EF) and afterload (e.g. volume administration, catecholamines)
  - hemoglobin (Hb): administration of red cell concentrates (RCC; the simplest and most effective measure); note: In the case of anemia, the body automatically increases the cardiac output (usually by increasing the heart rate) as a compensation mechanism to ensure a sufficient oxygen delivery.
  - arterial oxygen saturation: oxygen delivery (the most important emergency drug [is the fastest]!), starting respectively optimization of mechanical ventilation
- reduction of oxygen consumption (e.g. by deep analgosedation, hypothermia; usually therapeutically only little accessible)

oxygen: the most important emergency drug!

An increase in arterial oxygen saturation from 85% to 99% by optimizing mechanical ventilation (this must first be achieved) increases the oxygen delivery by (only) 14%. An increase in the cardiac output from 3.0 to 3.5 l/min increases the oxygen delivery by 16% and an increase in hemoglobin by administration of RCC from 7 to 10 g/dl (SI units: from 4.3 to 6.2 mmol/l) even by 43% (most effective and simplest [i.a. Langgartner et al, Intensiv- und Notfallbehandlung 2008]). The higher the hemo-

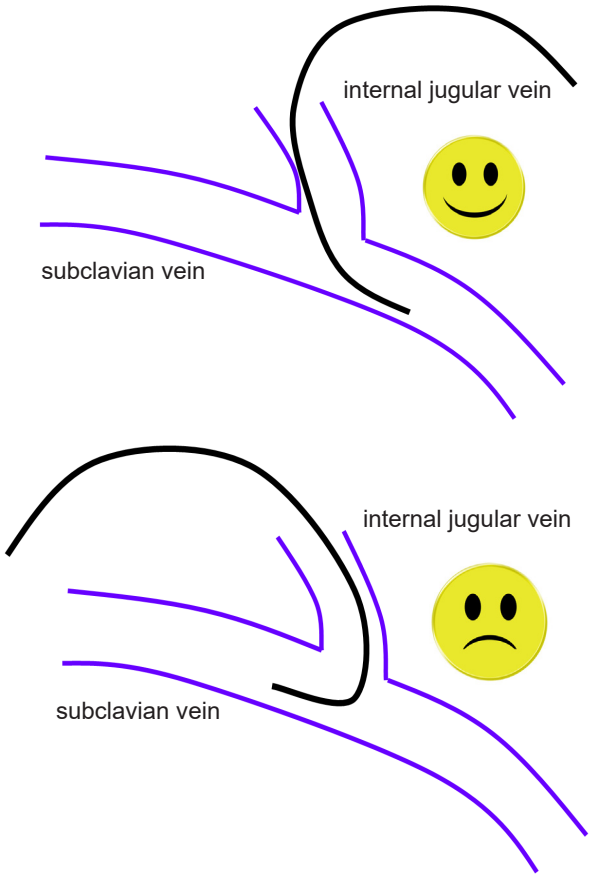
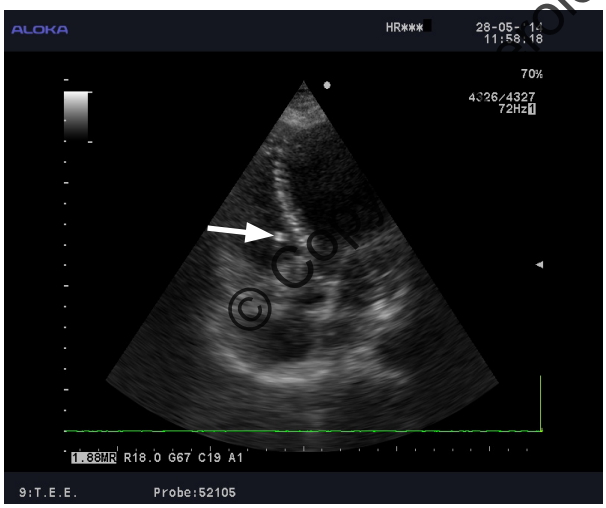


Fig. 389 The pulmonary artery catheter usually has a preformed bend. This should be observed when inserting it into the sheath according to the course of the vessel so that it does not slip into the brachial veins.



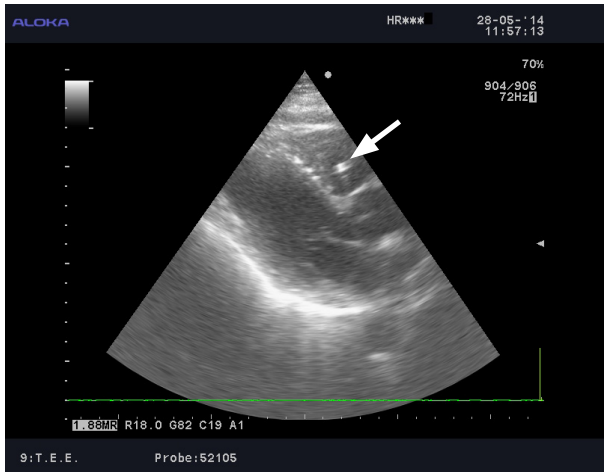


Fig. 390 As an option in difficult PAC insertion, echocardiography is helpful for orientation and control: Here, for example, the tip of the PAC is located in the right ventricle (arrow).

Pressure curves

- superior caval vein (SVC) / right atrium (RA): typically tripartite (three peaks), respiratory dependent, mean pressure 2–6 mmHg
- right ventricle (RV): systolic peaks 15-30 mmHg, diastolic values towards 0 mmHg
- pulmonary artery (PA): same systolic pressure as in the right ventricle, but increased diastolic pressure
- wedge position (PCWP): decrease of pressure level (usually slightly below the diastolic pressure of the pulmonary artery [PA_{dias}], flattening of the curve (disappearance of systolic pressure peaks; curve appears "damped")
  - flat
  - respiratory dependent
- After unblocking the balloon, the pressure of the pulmonary artery (PA) curve appears again.

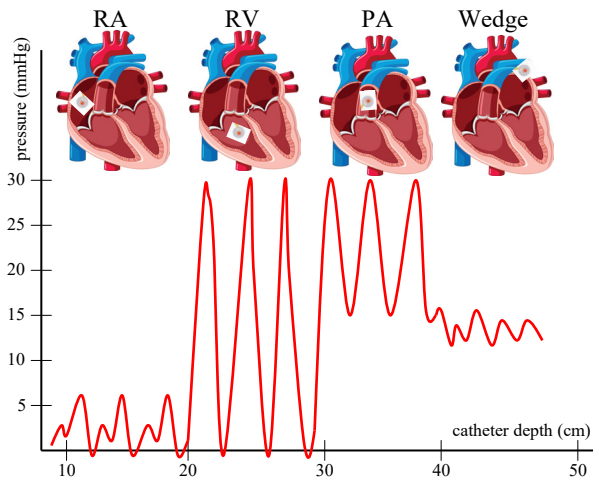


Fig. 391 the different pressure curves when the pulmonary artery catheter is inserted (RA: right atrium; RV: right ventricle; PA: pulmonary artery; Wedge: PCWP)

my or end ileostomy]; without remaining colon segments; worst prognosis)
- without stoma (with remaining colon segments [colon-in-continuity]):
  - type 2: jejunocolonic anastomosis (ileocecal valve no longer present)
  - type 3: jejunolileocolonic anastomosis (ileocecal valve still present; best prognosis)

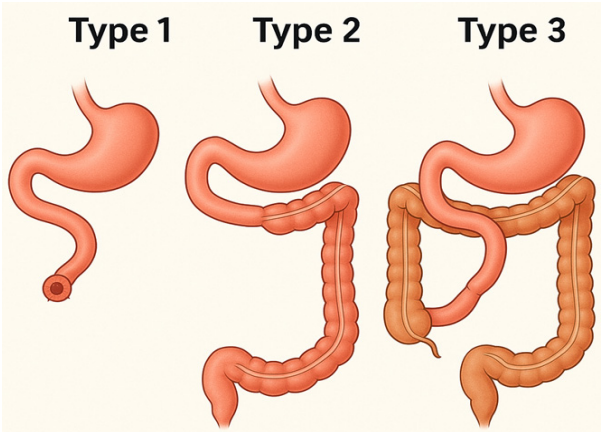


Fig. 518 Illustration of the different SBS types according to Messing

Phases

- hypersecretion (pronounced secretory diarrhea)
- adaptation (increased absorption due to villous hypertrophy and slowing of intestinal transit)
- stabilization

Symptoms and complications

- malabsorption
  - reduced absorption of fluid (Approximately 9 liters of fluid pass through the small intestine daily [20% exogenous through drinking and food, 80% endogenous through secretions formed locally in the intestine].) → diarrhea
  - reduced absorption of bile acids in the ileum → bile acid loss syndrome (note: Bile acids are subject to an enterohepatic circulation. Their main function is the absorption of fats via micelle formation.) →
    - reduced absorption of fats → steatorrhea
    - increased accumulation of bile acids in the colon: These are deconjugated there by the bacteria. Deconjugated bile acids inhibit water and sodium absorption resulting in osmotic (chologenic) diarrhea (usually watery). The chologenic origin of diarrhea can be confirmed using SeHCAT scintigraphy (seleno-homocholyl taurine; but only optional, not always necessary).
    - increased accumulation of bile acids in the colon → increased conjugation of unconjugated (fat-soluble) bilirubin in the colon (solubilization) → conjugated (water-soluble) bilirubin in the colon ↑ → absorption ↑ → hyperbilirubinemia
    - reduced absorption of fat-soluble vitamins (A, D, E, K; in case of resection of the terminal ileum also vitamin B12; for vitamin deficiency symptoms, see page 305)
  - reduced absorption of proteins → hypoproteinemia → edema
  - reduced absorption of iron, folic acid and vitamin B12 → anemia
- dehydration, electrolyte imbalance (especially loss of sodium, potassium, and calcium)
- weight loss
- meteorism, flatulence
- increased stone formation (increased lithogenicity)
  - urolithiasis (oxalate stones; due to reduced fat absorption, more fatty acids reach the colon and bind calcium there, so that less calcium is available to bind oxalic acid, which can no longer be excreted and is therefore increasingly reabsorbed.)
  - cholecystolithiasis: The cholesterol / bile acid ratio determines the lithogenicity. This ratio increases due to the loss of bile acids.
- gastroduodenal ulcers (reduced synthesis of inhibitory small intestinal hormones [GIP, VIP] → increased gastrin production [hypergastrinemia])
- exocrine pancreatic insufficiency: Cholecystokinin, which is produced in the jejunum, stimulates the exocrine secretion in the pancreas (digestive enzymes). In short bowel syndrome, cholecystokinin production is reduced. Cholecystokinin also causes contraction of the gallbladder and relaxation of the sphincter of Oddi, so that a deficiency of cholecystokinin leads to cholestasis.
- lactose intolerance (secondary; formation of the enzyme lactase in the enterocytes of the jejunum)
- high-output stoma (HOS)
  - in SBS type 1 (especially after jejunostomy)
  - especially in the early stages after stoma creation (in 16% [Baker et al, Colorectal Dis 2011])
  - stoma output > 2 liters per day
- D-lactic acidosis:
  - definition:
    - rare but life-threatening complication
    - Due to the insufficient small intestine, carbohydrate absorption is reduced, so that more carbohydrates accumulate in the colon and are broken down by the bacteria present there (primarily lactobacilli). This produces D-lactate (the dextrorotatory enantiomer), causing the colonic pH to drop. This is also due to the fact that the reduced absorption of fats leads to more fatty acids accumulating in the colon. The drop in colonic pH leads to an overgrowth of lactobacilli (primarily lactobacillus casei and delbrueckii), which predominantly produce D-lactate. The increased D-lactate produced in the colon is absorbed. Unlike L-lactate (the levorotatory enantiomer), D-lactate cannot be broken down in the human body because there is no enzyme (D-lactate dehydrogenase) to convert D-lactate to pyruvate. Metabolic acidosis (with an enlarged anion gap) occurs.
    - D-lactate has a direct neurotoxic effect on the brain.
    - D-lactic acidosis may also occur without short

Fig. 586 out-of-hospital implantation (in the emergency vehicle) of a va-ECMO (here Cardiohelp [Maquet]; cannulation of the femoral artery and vein on the right) during resuscitation of a 42-year-old man. With ECMO a sufficient circulation could be established despite patient's cardiac arrest. Coronary angiography showed proximal LAD occlusion. ROSC occurred a few minutes after recanalization. The patient survived without any neurological damage.

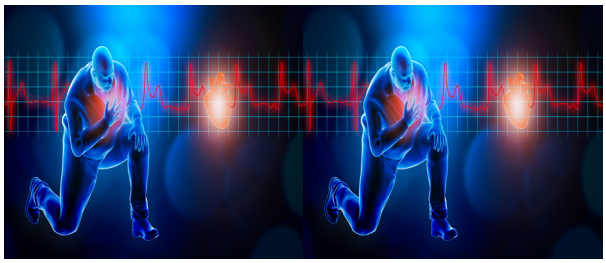
If asystole persists while va-ECMO is running, the blood in the left ventricle completely stops moving. This may lead to ballooning (possibly myocardial ischemia) and to a reversal flow into the pulmonary tract with consecutive pulmonary edema. Furthermore, thrombosis of the left ventricle and the ascending aorta can occur. Therefore, cardiocompression (press 5 times) should be performed every five minutes to relieve the left ventricle and to generate blood flow in the left ventricle and the ascending aorta to prevent thrombus formation. It is also suitable to insert a temporary pacemaker at an early stage if the asystole persists.

In the consensus paper 2018 "Recommendations for extracorporeal cardiopulmonary resuscitation (eCPR)" from various German societies (German Society for Internal Intensive Care Medicine and Emergency Medicine [DGIIN], German Society of Cardiology [DGK], German Society for Thoracic, Cardiac and Vascular Surgery [DGTHG], German Society for Cardiac Technique [DGfK], German Society of Anaesthesiology and Intensive Care Medicine [DGAI], German Interdisciplinary Association for Intensive Care and Emergency medicine [DIVI] and German Resuscitation Council [GRC]) pro and contra criteria were defined for the use of eCPR (va-ECMO implantation during resuscitation) that are shown (slightly modified) in the infobox. These criteria should help to decide whether va-ECMO should be installed or not in the emergency room (in-hospital) of a corresponding center if a patient with OHCA (out-of-hospital cardiac arrest) is delivered into the emergency room with ongoing CPR. The criteria can also be applied analogously for an IHCA (in-hospital cardiac arrest). If you decide to install va-ECMO (eCPR) during resuscitation, this should be performed within 60 minutes after the onset of cardiac arrest (collapse). The corresponding centers should offer eCPR standby completely (i.e. 24 hours / 7 days / 365 days).
There should also be the option of an advanced therapy (e.g. implantation of an LVAD system) in this hospital.

pro
eCPR in resuscitation

- **observed cardiac arrest**
- **suspected cardiac genesis (especially initially shockable rhythm [ventricular fibrillation])**
- **no-flow time < 5 minutes (At best bystander CPR was already performed.)**
- **low-flow time (duration of CPR) < 60 minutes**
- **presence of reversible causes (HITT / 4H & 4T)**

ACUTE CORONARY SYNDROME



Classification

According to a proposal by the European Society of Cardiology (ESC) and the American College of Cardiology (ACC), acute coronary syndrome has been divided into the following 3 groups since 2000:

- STEMI (ST elevation myocardial infarction): with ST elevations (exact: persistent, i.e. > 20 minutes)
- NSTEMI (Non-ST elevation myocardial infarction): without (persistent) ST elevation, but positive troponin
- unstable angina pectoris: by definition troponin negative (twice); definition unstable angina pectoris:
  - first event (de novo angina)
  - symptoms at rest
  - increase in duration, intensity or frequency

To simplify matters, the classification can also be made into STE-ACS and NSTE-ACS. By the way, this is also the terminology that should be used preclinically (out-of-hospital)! In the case of missing ST elevations, the term "NSTEMI" is often used here: For this, however, you need a positive troponin, which is usually not available out-of-hospital (except in the case of an alarm for transport from the medical practice where a rapid troponin test was carried out to the hospital):

- STE-ACS (acute coronary syndrome with ST elevation myocardial infarction)
- NSTE-ACS (acute coronary syndrome without ST elevation myocardial infarction)

The earlier division into Q wave and non-Q wave infarcts is obsolete since Q waves only develop after about 12 hours and can occur in both STEMI and NSTEMI.

As a counterpart to acute coronary syndrome, there is now also the term chronic coronary syndrome (i.a. ESC Guidelines for the diagnosis and management of chronic coronary syndromes 2019) instead of the term stable coronary heart disease (CHD).

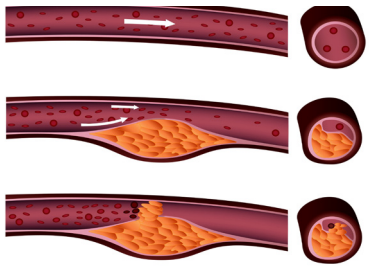


Fig. 604 Pathophysiology of acute myocardial infarction: Plaque rupture occurs with subsequent thrombotic occlusion of the coronary artery.

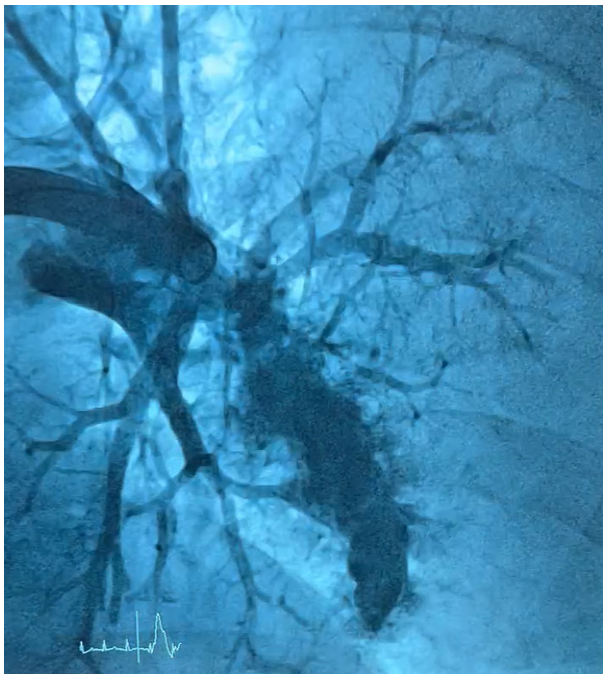
Epidemiology

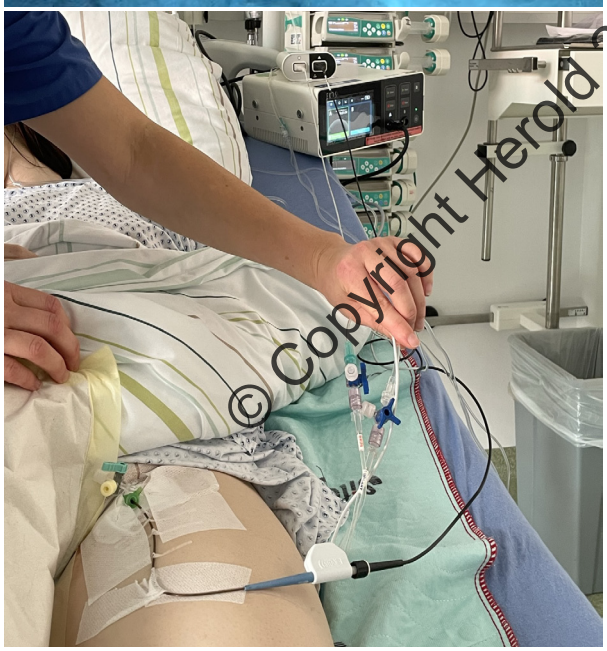
Coronary heart disease (CHD) is the leading cause of death in industrialized nations (like Germany) before malignancies (No.2) and stroke (No.3) and is responsible for 13% of all deaths. Approximately 300 infarcts / 100,000 inhabitants occur per year in Germany with about 140,000 deaths annually. Myocardial infarctions occur more frequently in the fifth to sixth decade of life. Myocardial infarction is the most frequent cause of cardiac arrest and thus the most frequent reason for resuscitation. The probability of suffering a myocardial infarction in the course of life (lifetime prevalence) is 30% for men and 15% for women. At an age below 75 years, men predominate, at an age above 75 years, women predominate (each in a ratio of 2:1). The mortality rate of myocardial infarction is still 16% despite all the progress made. If evaluations of death certificates with a suspected myocardial infarction are also included in the statistics, the mortality rate is even 50%. Most deaths occur prehospital. More women (52%) die of myocardial infarctions than men (48%). The mortality rate in women is almost twice as high as in men ("Eva infarction"), partly due to the frequently atypical symptoms (often only nausea, upper abdominal pain, dyspnea) and the associated delayed diagnosis. The early mortality in NSTEMI is ten times lower than in STEMI, but the cumulative mortality after one and two years is just as high as in STEMI. After four years, the mortality in NSTEMI is even twice as high as in STEMI (mainly due to the higher age and higher rate of comorbidities). In an observation study (Yeh et al, N Engl J Med 2010) on 46,086 North American patients, both the myocardial infarction rate and myocardial infarction mortality decreased by 24% during the observation period from 1999 to 2008. The incidences were 70/100,000 for STEMI and 132/100,000 for NSTEMI.

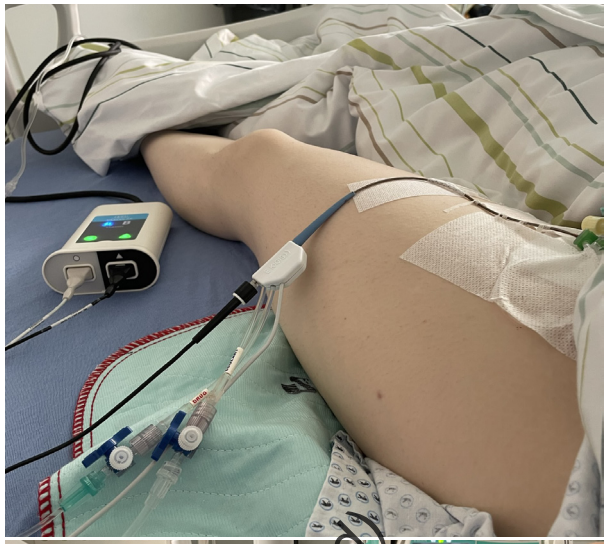
ACS is the second most frequent emergency for the EMS (emergency medical service) with a fraction of approximately 20% (after the seizure). 30% of all patients presenting with chest pain in the emergency room have an acute coronary syndrome.

The average prehospital time in Germany is 225 minutes (GOAL registry) and has even increased over the last 10 years (1995: 160 minutes) despite all efforts to educate and inform the people. The main loss of time is due to the extended time between the onset of symptoms and the patient's emergency call. 40% of all infarctions occur in the early morning hours (12 PM-6 o'clock AM; due to the sympathoadrenergic activation). In 30% an acute

catheter-directed interventions (CDI):
- catheter-directed thrombolysis (CDTL; most commonly used: EKOS
- catheter-directed thrombectomy (CDTE; most commonly used: FlowTriever)







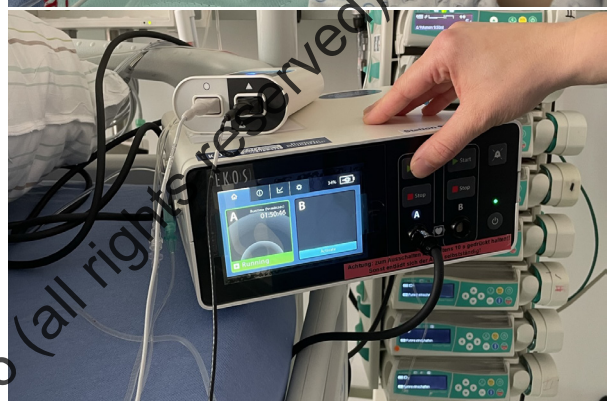
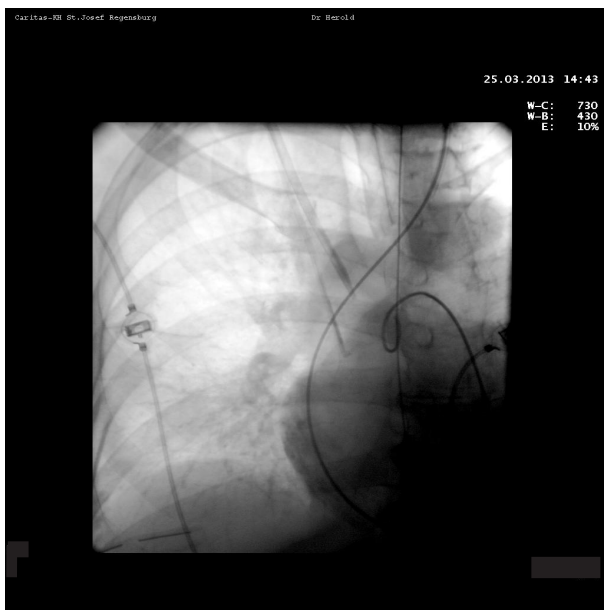


Fig. 965 catheter-directed thrombolysis (CDTL) using EKOS (Ekosonic Endovascular System; pharmacomechanical thrombolysis; courtesy of Dr. Maximilian Veddeler, Medical Director of Internal Intensive Care Medicine, Hospital Osnabrueck [Germany])



- if necessary intrapericardial lysis (e.g. alteplase 10 mg) in case of septation or purulent / tuberculous pericarditis
- unclear recurrent pericardial effusion → possibly pericardioscopy (possibly with biopsy)
- malignant pericardial effusion:
  - pericardiodesis (e.g. 30 mg bleomycin in 50 ml normal saline i.p. [intrapericardial]; note: The ESC guidelines 2015 + 2025 recommend cisplatin for lung cancer and thiotepa for breast cancer.)
  - oncological therapy (i.a. systemic chemotherapy, radiotherapy [especially for lymphomas and leukemias])
  - possibly pericardial fenestration (A window is created into the pericardium so that the pericardial effusion drains into the pleural space [mostly left], where there is considerably more space than in the pericardial sac.)
    - interventional (percutaneous balloon pericardiotomy: via wire under X-ray fluoroscopy expanding the puncture site in the pericardium using a balloon [e.g. valvuloplasty balloon])
    - surgical (cardiothoracic; via a left-sided mini-thoracotomy; ESC guidelines 2015 + 2025: class I recommendation for recurrent [especially malignant] pericardial effusion despite medical therapy)
  - possibly pericardectomy (ultima ratio; but usually no more operable)
- special cases:
  - autoimmune: triamcinolone 300-600 mg/m² i.p.
  - purulent: gentamicin 80 mg i.p. (via irrigation drainage); ⚠ generously surgical pericardial drainage!

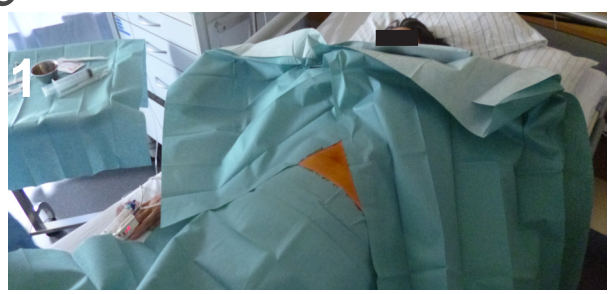
Pericardiocentesis (pericardial puncture)

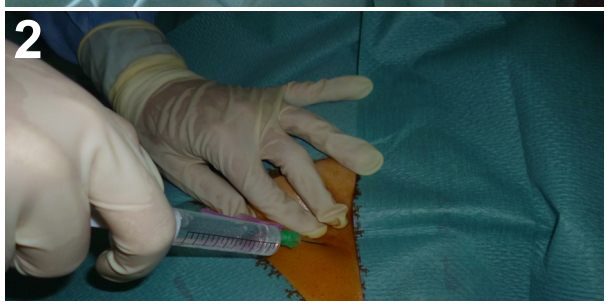
Puncture sites

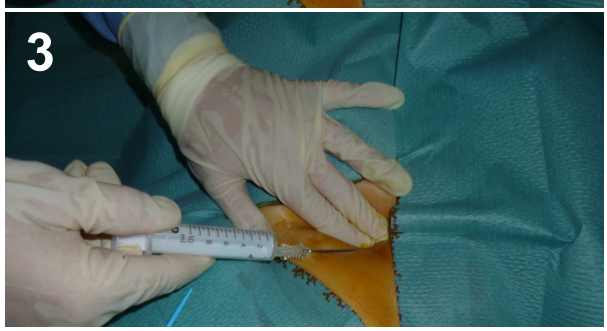
- subcostal:
  - 2-3 cm left and 2-3 cm below the xiphoid (Larrey point)
  - direction of puncture: left shoulder (tip: flat direction [almost parallel to the sternum!])
  - standard
- apical:
  - apex in MCL
  - direction of puncture: right shoulder
  - intercostal (upper edge of the rib)
  - very rarely necessary (e.g. in obesity, hepatomegaly, Chilaiditi syndrome)

Procedure

- flat position of the upper body
- analgosedation (e.g. fentanyl 0.05 mg, propofol 50-100 mg)
- best invasive blood pressure measurement (insert arterial line before if possible; but not absolutely necessary)
- sterile gown, sterile gloves, mouth protection, hood
- sterile covering, disinfection
- local anesthesia
- insertion of the wire via Seldinger technique, dilator, insertion of a 5 F-sheath
- via the sheath insertion of a pigtail up to the left apex of the heart
- control
  - fluoroscopy (only very rarely necessary)
  - echocardiography (with sterile cover)
- connection to drainage system (tip: Redon drainage with suction)
- If a turbid pericardial effusion appears, the pigtail drainage should not be removed for the time being. If further examination of the aspirate reveals signs (e.g. detection of neutrophilic granulocytes or bacteria) of a purulent pericardial effusion, then an antibiotic (e.g. gentamicin) can be applied locally via the drainage and the pericardial space can also be rinsed with sodium chloride. However, if the drainage has been removed beforehand, then the pericardial puncture and thus the re-insertion of the drainage is as good as impossible, since there is (almost) no pericardial effusion left.
- note: If you don't have all the material available (e.g. out-of-hospital as an emergency physician), you can quickly use a CVC (central venous catheter) set: After puncturing with the Seldinger needle and advancing the Seldinger wire. The needle is removed and the CVC is advanced over wire after dilatation. Then the wire is removed. All the lumina of the catheter are closed except for one (preferably one-lumen CVC), through which the effusion is then drawn off with a syringe.







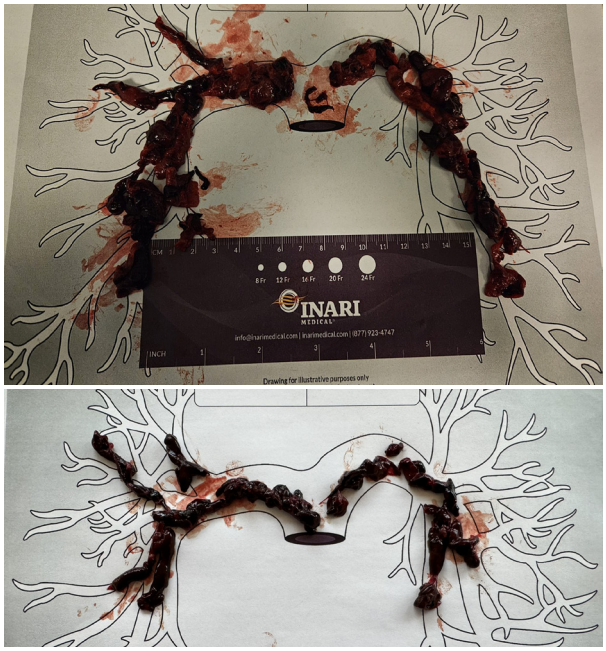


Fig. 967 catheter-directed thrombectomy (CDTE) using a thrombus aspiration catheter (here FlowTriever; courtesy of Dr. Maximilian Veddeler, Medical Director of Internal Intensive Care Medicine, Hospital Osnabrueck [Germany])

PEERLESS-I study

Large-bore Mechanical Thrombectomy Versus Catheter-directed Thrombolysis in the Management of Intermediate-risk Pulmonary Embolism
Jaber et al, Circulation 2024

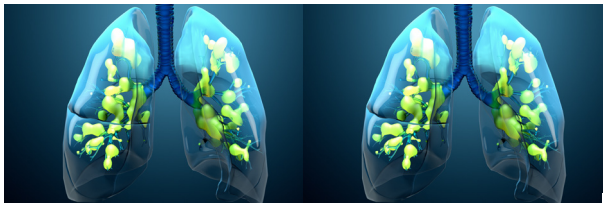
- multicenter randomized controlled study
- 550 patients with pulmonary embolism in the intermediate-high risk group
  - catheter-directed thrombolysis (any procedure)
  - catheter-directed thrombectomy (FlowTriever)
- result: catheter-directed thrombectomy (FlowTriever) → significant reduction in the primary endpoint (5-component win ratio [hierarchal]: mortality, intracranial hemorrhage [ICH], major bleeding, clinical deterioration, post-procedural need for admission to ICU and length of stay in ICU)
  - less clinical deterioration and less need for post-procedural ICU admission and length of stay in ICU (The latter is simply explained by the fact that the catheter for thrombolysis remains in the body longer.)
  - however, no reduction in mortality, ICH or major bleeding

Tip for everyday practice if there is a contraindication for systemic fibrinolysis in case of massive pulmonary embolism (high-risk group) or if you simply do not dare to go high with systemic fibrinolysis (e.g. because the patient only had major surgery the day before): A 7 French sheath is inserted into the internal jugular vein. Puncture is also possible if systemic fibrinolysis has already taken place shortly before and is usually very simple anyway in the case of a massive pulmonary embolism since the internal jugular vein is massively dilated here. Ultrasound guided puncture, however, is obligatory. Then a pulmonary artery catheter (PAC) is inserted at the patient's bed via the sheath under control of the pressure curve on the monitor and under echocardiography. Echocardiographically one can see the main stem of the pulmonary artery and possibly even the embolus in the parasternal short axis at the level of the aortic valve. For better visualization, echo contrast medium (easiest and cheapest: 20 ml agitated saline solution) can be applied intravenously. In case of poor ultrasound conditions in the transthoracic echocardiography (TTE), transesophageal echocardiography (TEE) which can also be performed at bedside is also very helpful. If the catheter is then located in the pulmonary artery (verified by the typical pressure curve and echocardiography), alteplase (10-20 mg; local fibrinolysis) is performed via the lying pulmonary artery catheter (via the lumen "PA distal") and if necessary, thrombus fragmentation is performed by pushing forward and pulling back the inflated balloon (tip: Block balloon with water instead of air). In the meantime there are also pulmonary artery catheters with a Y-shaped end for the bifurcation of the pulmonary artery so that local fibrinolysis can be applied selectively to the left oder right pulmonary artery. The great advantage of this procedure is that no fluoroscopy and thus no transport of the already massively unstable patient is necessary, but that all this can be carried out on the bedside in the intensive care unit or in the emergency room. Alternatively, the C-arm can be attached to the intensive care bed and right heart catheterization with appropriate thrombus fragmentation can be performed. In my opinion, the recommendation for surgical embolectomy in the case of a contraindication for fibrinolysis with massive pulmonary embolism is far away from clinical everyday life: Who has a cardiac surgery in the hospital? Usually the patient has to be transferred which is completely utopian for a massively unstable patient or during resuscitation: The patient usually does not even survive the transfer from the ICU bedroom to the corridor!

Surgical embolectomy

- Trendelenburg operation
  - named after the German surgeon Friedrich Trendelenburg (1844-1924) who first performed the surgery in 1872 (note: None of the operated patients survived the surgery at the time.)
  - with heart-lung machine
  - in patients with shock or resuscitation
- „no more room for surgery in acute pulmonary embolism“ (Oakley 1989)
- today modified Trendelenburg operation:
  - median sternotomy
  - access not from central, but from peripheral (with aspirators)
  - without cardioplegic cardiac arrest and without clamping of the aorta
  - technically relatively simple (at least according to the ESC guidelines 2014)
  - if necessary perioperative va-ECMO for stabilization

ARDS



Introduction

- "The fetal lung in the unborn child - pathology, therapy and forensic medication" (Eduard Joerg, 1835)
- first described by David Ashbaugh (pediatrician) and Thomas Petty (surgeon) 1967 in a case series of 12 patients (Lancet: "acute respiratory distress in adults")
- acute lung failure
- designations:
  - IRDS: infant respiratory distress syndrome
  - ARDS: adult (today better: acute) respiratory distress syndrome
- ARDS is the pulmonary manifestation of multiple organ failure (MOF).
- ARDS is a syndrome and not a disease!
- guideline:
  - Europe: ESICM (European Society of Intensive Care Medicine) guidelines 2023 on acute respiratory distress syndrome: definition, phenotyping and respiratory support strategies
  - America: ATS (American Thoracic Society) guidelines 2024 (An Update on Management of Adult Patients with Acute Respiratory Distress Syndrome)

Definition

(according to AECC [American European Consensus Conference]1994 [Bernard et al, Am J Respir Crit Care Med]; "old" definition)

- acute occurrence
- Horovitz quotient (paO_2/FiO_2; syn.: P/F ratio, oxygenation index; note: This parameter should be noted automatically on the BGA result [printout, PDMS] so that no one has to calculate it anymore! To do this, the FiO_2 must be entered into the BGA device by nursing staff.):
  - 200-300 mmHg: ALI (acute lung injury)
  - < 200 mmHg: ARDS
- bilateral infiltrates in the chest X-ray (a.p.); note: According to more recent radiological recommendations one no longer speaks of infiltrates but of consolidations.
- pulmonary capillary wedge pressure (PCWP) < 18 mmHg or missing signs of left heart failure, i.e. no cardiac pulmonary edema (by definition a non-cardiac pulmonary edema). PCWP is measured using pulmonary artery catheter (PAC) which is rarely used nowadays. Today one uses preferably:
  - echocardiography (Especially pulmonary edema due to a severe acute mitral valve regurgitation often looks very similar to ARDS!)
  - PiCCO: pulmonary vascular permeability index (PVPI):
    - PVPI < 3: cardiac (hydrostatic pulmonary edema)
    - PVPI > 3: ARDS (permeability pulmonary edema)
  - pro-BNP (The cut-off value of 100 pg/ml has a relatively high sensitivity of 95%, but only a relatively low specificity of 27% [i.a Levitt et al, Crit Care 2008].)
    - > 100 pg/ml: cardiac
    - < 100 pg/ml: ARDS

Criticism of the old definition

- no consideration of PEEP and mechanical ventilation ("blood gas" ARDS)
- increased PCWP also possible in septic cardiomyopathy (ARDS may also be present in sepsis!)

Due to these criticisms, an ARDS Task Force developed a new definition which was presented at the ESICM (European Society of Intensive Care Medicine) congress in Berlin 2011 as the ARDS "Berlin Definition" (published by Ranieri et al, JAMA 2012). The Berlin definition was supplemented in 2023 by the "new global definition of ARDS" (Matthay et al, Am J Respir Crit Care Med 2023; see infobox).

Berlin definition (ARDS)

	mild	moderate	severe
time	acute onset (< 1 week)		
Horovitz quotient (mmHg)	200-300	100-200	< 100
PEEP (cmH_2O)	5-10	5-10	> 10
origin of edema	respiratory insufficiency (not fully explained by heart failure or volume overload)		
radiological opacities (chest X-ray, CT)	bilateral	bilateral	3-4 quadrants
additional physiological disorder	-	-	$V_{E\ corr}$ > 10 l/min compliance < 40 ml/cmH_2O

$V_{E\ korr}$: corrected RMV (V_E x pCO_2 / 40); criticism: Patients with a Horovitz quotient < 100 mmHg and a PEEP between 5-10 cmH_2O are not considered.

Innovations (Berlin definition)

- The term "acute" was determined at less than 1 week.
- no more ALI (p.d. mild ARDS)
- consideration of PEEP (Therefore the diagnosis of ARDS is only possible with mechanical ventilation [invasive / non-invasive] and not with spontaneous breathing [e.g. HFNOT]!)

Types

- according to location (exactly: according to the type of vessel into which the blood is returned)
  - veno-venous (vv-ECMO)
  - veno-arterial (va-ECMO)
- according to invasiveness (technique)
  - interventional (percutaneous)
  - surgical (open)

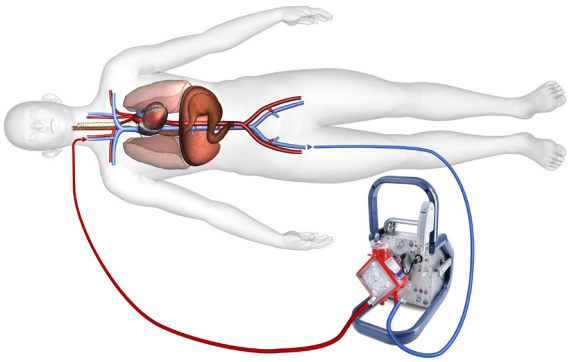


Fig. 1061 ECMO veno-venous (vv-ECMO [23])

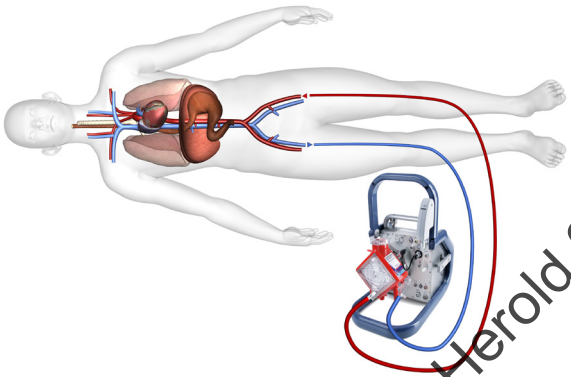
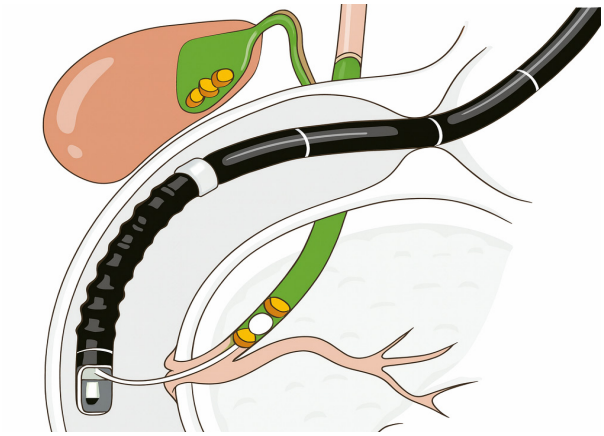


Fig. 1062 ECMO veno-arterial (va-ECMO [28])

vv-ECMO

- used more often than va-ECMO
- sites: The blood is usually withdrawn from the femoral vein (21-23 F) and returned to the internal jugular vein (15-19 F). The blood should always be withdrawn inferior and returned superior since the saturation in the inferior caval vein is lower (in critically ill patients) than in the superior caval vein and therefore the ECMO is much more effective!
- types:
  - femoro-jugular cannulation (standard): withdrawal of blood from the area of the inferior caval vein (mostly right femoral vein; long [38 cm] cannula [drainage cannula]) and return into the area of the superior caval vein (mostly right internal jugular vein; short [15-23 cm] cannula [reperfusion cannula])
  - femoro-femoral (bifemoral) cannulation (Here too, it is important to note that the cannulas are of different lengths to prevent recirculation.)
- technical: series connection
- ⚠ for lung replacement (pulmonary support ["pulmonary" ECMO]; in acute lung failure [ARDS]; mechanical ventilation is continued, but the invasiveness of mechanical ventilation can be significantly reduced then in the sense of [very] lung-protective ventilation; settings / goals: FiO_2 < 0.6, inspiratory pressure < 28 cmH_2O, PEEP mostly unchanged, tidal volume < 4 ml/kg, respiratory rate 10-12/min, I:E 2:1)
- classification according to blood flow:
  - < 2.5 l/min: low-flow vv-ECMO (especially for hypercapnic respiratory failure [e.g. AECOPD and NIV failure]; good for decarboxylation; for low-flow ECMO see also page 841)
  - > 2.5 l/min: high-flow vv-ECMO (especially for hypoxemic respiratory failure [especially ARDS])
- procedure:
  - low-low (blood flow < 2.5 l/min: If only decarboxylation (e.g. AECOPD) is required, lower blood flows are sufficient. A relevant decarboxylation is already possible from a blood flow of approximately 800 ml/min. Intubation can already be avoided from a blood flow of 1 l/min. This is because carbon dioxide is much more water-soluble than oxygen. A double lumen cannula (requiring only a venous puncture) is sufficient then. With a double lumen cannula a maximum blood flow of about 1.5 l/min is possible.
  - high-flow (blood flow > 2.5 l/min): If, on the other hand, oxygenation (e.g. severe ARDS) is required, higher blood flows are necessary. Sufficient oxygenation only begins at a blood flow of approximately 3 l/min. A double lumen cannula is no longer sufficient for this: Two cannulas have to be placed here (e.g. drainage via femoral vein and return via internal jugular vein).
- control:
  - oxygenation: It is controlled via the blood flow. This is set by means of the rotary wheel (rotational speed: number of revolutions of the centrifugal pump per minute [rpm]) on the control panel.
  - decarboxylation:
    - It is controlled both via the blood flow (however, the maximum of decarboxylation is reached at 2 l/min) and via the gas flow, i.e. via the oxygen supply (dry oxygen [100% and not just 21%; oxygen and not compressed air]) of the wall connection.
    - The oxygen hose is plugged into the oxygen connection of the membrane. This presses the carbon dioxide out of the capillaries of the membrane (sweep gas, purge gas).
    - By default, one starts with a gas flow of 1 l/min: Then after approximately 20 minutes, a BGA is taken and the respiratory minute volume at the respirator is accordingly reduced stepwise by 10% (respiratory rate and tidal volume [by reduction of the pressure difference between inspiratory pressure and PEEP). This is then repeated every 20 minutes. In small steps, the gas flow can be increased up to max. 10 l/min. The gas flow is increased until tidal volume is < 4 ml/kg and respiratory rate is 10-12/min (lung-protective ventilation). The gas flow should only be increased slowly so that no hypocapnia and possibly even cerebral ischemia

ERCP



- ERCP: endoscopic retrograde cholangiopancreatography
- significant reduction of mortality in severe (not mild [almost no significant mortality anyway]] biliary pancreatitis (Sharma et al, Am Journal Gastroenterol 1999)
- The sole (sonographic) detection of gallbladder stones is not a sufficient indication for ERCP. In everyday clinical practice, an endosonography is usually carried out beforehand: If a stone is detected in the common bile duct, ERCP is carried out immediately.
- If the cholestasis parameters are regredient or normal again the next day in biliary pancreatitis, the stone was spontaneously dislodged so that we often do not perform any ERCP at all and request the surgeon for an urgent (during the hospital stay) cholecystectomy. Since pancreatitis is mainly caused by small stones, spontaneous drainage of the stone is even relatively common!
- mostly with papillotomy (sphincterotomy) and stone extraction (e.g. basket catheter, balloon catheter, lithotrypter)
- in the case of cholangitis, additional insertion of a bile duct drainage (plastic stent or nasobiliary probe [mostly better; with rinsing 500 ml normal saline daily]) to secure bile flow
- timing:
  - urgent ERCP only in biliary pancreatitis with
    - cholangiogenic sepsis → immediately
    - cholangitis (Charcot´s triad: upper abdominal pain , fever, jaundice; also called Charcot's triad II [to distinguish it from Charcot's Triad I in disorders of the cerebellum; see page 1541]) → within 24 hours
  - ⚠ otherwise within 72 hours (or not at all!)
- recommendation according to the Neoptolemos and Nowak study: ERCP in severe biliary pancreatitis within 72 hours after onset of symptoms
- In severe biliary pancreatitis, in which the definitive cholecystectomy is only to be performed at an interval of 4-6 weeks, a stent (plastic stent) is usually inserted at the end of ERCP which is then electively removed again after surgery (e.g. at the end of the surgical hospital stay). This has two advantages: First, the patient is protected from recurrence until surgery, and second, the common bile duct is protected intraoperatively during laparoscopic cholecystectomy. The plastic stent is then removed after the cholecystectomy (at the latest 8 weeks after implantation). In case of mild biliary pancreatitis, no stent is inserted, but the patient should undergo cholecystectomy during the same hospital stay.
- A diagnostic ERCP in the free interval to clarify the etiology was previously recommended no earlier than 8-12 weeks after the acute event. However, performing an ERCP purely for diagnostic reasons is obsolete today. MRCP or endosonography are suitable here!
- Stapfer classification of ERCP related perforations (according to Stapfer et al, Ann Surg 2000):
  - type I: duodenum
  - type II: papilla (due to papillotomy)
  - type III: common bile duct

ERCP only in biliary pancreatitis and only with cholangitis (Charcot's triad) or proven choledocholithiasis (e.g. EUS)

biliary pancreatitis: not always an automatic indication for ERCP (mostly even not necessary; gall stones usually pass spontaneously through the papilla because they are usually small)! ERCP can no longer stop the pancreatitis that has already been triggered! mostly only EUS to rule out choledocholithiasis and then prompt cholecystectomy (during the initial admission)!

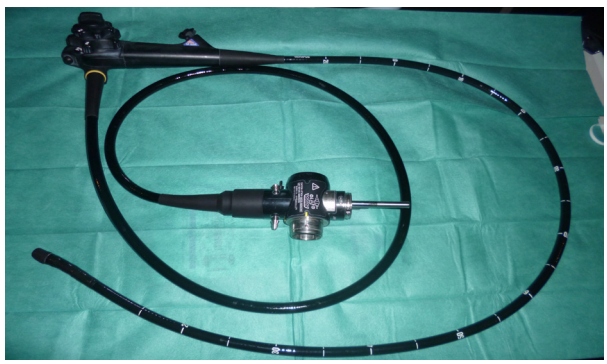
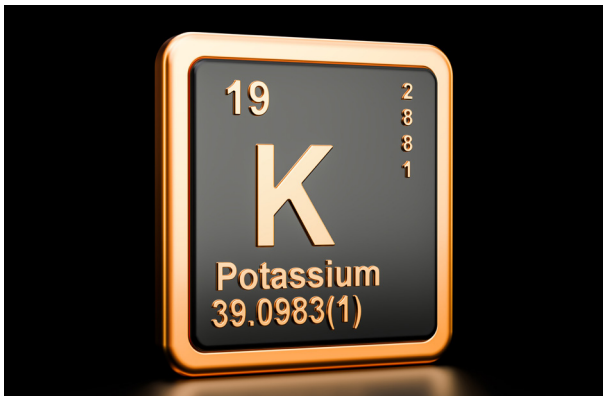


Fig. 1315 ERCP: duodenoscope (In contrast to the gastroscope, this does not have an orthograde, but a side-view optics and is longer.)

Disorders of potassium



- hyperkalemia (potassium > 5.5 mmol/l)
- hypokalemia (potassium < 3.5 mmol/l)

98% of potassium is intracellular and only 2% is extracellular. The intracellular potassium concentration (K_i) is 120-140 mmol/l, the extracellular potassium concentration (K_e) only 3.5-5.5 mmol/l. The measured concentration in the serum can therefore only be used with restrictions. ECG is therefore very valuable for diagnostic, especially in the case of acute changes in potassium! Potassium is the most important intracellular ion. The ratio of intracellular and extracellular potassium (K_i/K_e) determines the membrane potential and thus the neuromuscular excitability of the cell. The sodium-potassium-ATPase (syn.: sodium-potassium pump) maintains this ratio by actively transporting potassium into the cell and sodium out of the cell. The enzyme is magnesium-dependent. Insulin and stimulation of β-receptors (e.g. catecholamines) stimulate the sodium-potassium-ATPase and thus lead to a decrease in the extracellular potassium in the serum via an increased potassium uptake into the cells. Hyperkalemia lowers the membrane potential and increases excitability, hypokalemia increases the membrane potential and reduces excitability. The daily potassium intake with food is approximately 50-150 mmol/l. 90% of the potassium is excreted renally and 10% enterally. In case of renal insufficiency, enteral excretion is increased as compensation (up to 25%), but the mechanism is limited. Potassium is filtered in the glomerulus in the kidney and almost completely reabsorbed in the proximal tubule. A small part is secreted in the distal tubule and collecting tube. The excretion of potassium is stimulated by mineralocorticoids (especially aldosterone) via mineralocorticoid receptors in the distal tubule and collecting tube. The higher the distal urine flow rate (diuresis; e.g. polyuria in derailed diabetes mellitus), the more potassium is excreted in the urine.
Via the H^+/K^+ exchanger (Hamburger Shift [named after the Dutch physiologist Hartog Hamburger, 1859-1924]), potassium also has an influence on the acid-base balance: Hyperkalemia leads to acidosis (increase in potassium by 0.6 mmol/l → decrease in pH by 0.1) and hypokalemia to alkalosis (decrease in potassium by 0.6 mmol/l → increase in pH by 0.1). Similarly, acidosis leads to hyperkalemia and alkalosis to hypokalemia.

Hyperkalemia

Etiology

- acute kidney failure, renal insufficiency (⚠ most frequent cause)
- drugs
  - potassium-sparing diuretics (mineralocorticoid receptor antagonist [MRA], syn .: aldosterone antagonists: spironolactone, eplerenone)
  - ⚠ RAAS inhibitors (ACE inhibitors, ARB [angiotensin receptor blockers], ARNI [angiotensin receptor neprilysin inhibitor]): from potassium > 5.0 mmol/l dose reduction by 50%, from potassium > 5.5 mmol/l contraindicated!
  - ⚠ NSAIDs
  - ⚠ digitalis (inhibition of the sodium-potassium-ATPase)
  - β-blockers (inhibition of the sodium-potassium-ATPase)
  - ⚠ heparin (inhibition of aldosterone synthesis → hypoaldosteronism, usually only in case of long-term therapy)
  - cotrimoxazole (inhibition of potassium secretion in the distal tubule and collecting tube)
  - succinylcholine
  - ciclosporin
- Addison´s disease
- acidosis (H^+/K^+ exchanger [Hamburger shift]):
  - A decrease of the pH value by 0.1 leads on average to an increase of potassium of 0.6 mmol/l.
  - not the case with lactic acidosis and ketoacidosis
- cytolysis with consecutive release of potassium:
  - myolysis (e.g. rhabdomyolysis)
  - hemolysis
  - tumor lysis
- transfusion of red cell concentrates (especially older concentrates, massive transfusion)
- pronounced constipation
- crush syndrome
- BRASH syndrome:
  - B: Bradycardia
  - R: Renal failure
  - A: AV block
  - S: Shock
  - H: Hyperkalemia
- diabetes mellitus (hyporeninemic hypoaldosteronism = Schambelan´s syndrome [i.a. bicarbonate loss via the kidney with consecutive metabolic acidosis]); therefore, potassium is often chronically elevated in long-term diabetics])
- pseudohyperkalemia: release of potassium from blood cells
  - iatrogenic (too long venous congestion [tourniquet] during blood collection, too long standing of the sample)
  - pronounced leukocytosis (e.g. in leukemia) or thrombocytosis (> 500,000/µl)

the Scottish botanist Robert Brown [1773-1858]), i.e. the random thermal movement of molecules in a liquid which results in the independent mixing of the different substances. The process is comparable to a tea bag, the contents of which are dissolved and distributed in hot water.

- In the filter, the blood and the dialysis solution always run in opposite directions (counter current principle). If blood and dialysis solution were to flow in the same direction (equal current principle), the difference in concentration would decrease in the course of the filter and dialysis would become increasingly ineffective. With the counter current principle, on the other hand, the difference in concentration is maintained over the entire length of the filter, so that the effectiveness of dialysis remains undiminished.
- separation limit: molecular weight 15-20 kD (D: Dalton)
  - lower than with hemofiltration, i.e. smaller molecules are removed with hemodialysis compared to hemofiltration
  - Dialysis is suitable for the removal of smaller molecules (e.g. potassium, protons [in metabolic acidosis], lactate, ammonia, lithium). ⚠ Therefore, hemodialysis and not hemofiltration should be performed in the case of life-threatening hyperkalemia!
  - In exceptional cases (e.g. tubular obstruction in multiple myeloma, rhabdomyolysis), dialysis can be carried out with a special HCO membrane (HCO: high cut-off; e.g. Septex filter from Gambro), with which molecules up to a size of 60 kD can be removed. In the HICOSS study (Honore et al, WFSICCM 2009) no benefit was shown in septic renal failure.
- standard at ICU in the USA
- responsibility: staff of the dialysis department
- cheaper than hemofiltration
- dialysis membrane: synthetic (made of polysulfone; biocompatible)
- HIV (human immunodeficiency virus) and hepatitis serology must always be determined prior to the start of hemodialysis in order to prevent transmission to patients who are subsequently treated with the same dialysis machine. In the event that a patient with HIV or hepatitis has actually been dialyzed, the dialysis machine must then be completely disinfected and some parts must be completely replaced. In some departments, extra machines for infectious dialysis are available.
- In intensive care patients, CVVH is usually the first RRT to be performed in clinical routine as those patients are usually hemodynamically unstable. Hemodialysis only takes place when the kidney failure still persists after stabilization of the circulation.
- In hemodialysis, unlike hemofiltration, water is removed within just a few hours which can lead to hemodynamic instability. For this reason, hemofiltration is usually the only option for hemodynamically unstable patients (e.g. requiring catecholamines), hemodialysis is usually not possible here. There are, however, some options to improve hemodialysis in case of hemodynamic instability:
  - often moderate blood pressure drop shortly after connection → short-circuiting of the system (simultaneous connection of the venous and arterial system with recirculation of the saline solution used to rinse the system)
  - prolonged hemodialysis (e.g. 6 hours instead of 3 hours)
  - reduction of blood flow (e.g. to 150 ml/min)
  - reduction of dialysate temperature to < 37°C

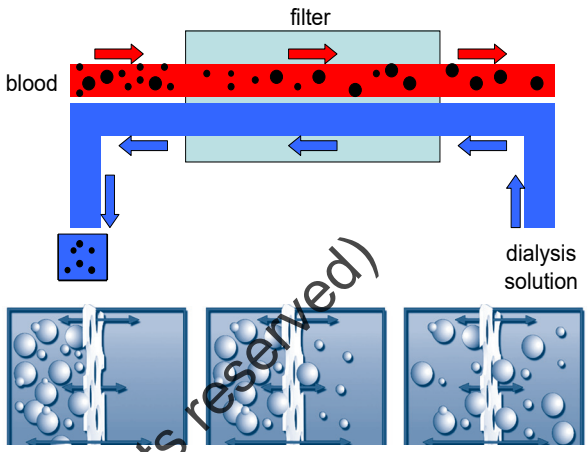


Fig. 1544 principle of diffusion [17]

Emergency therapy for hyperkalemia: hemodialysis and not hemofiltration (no CVVH)!

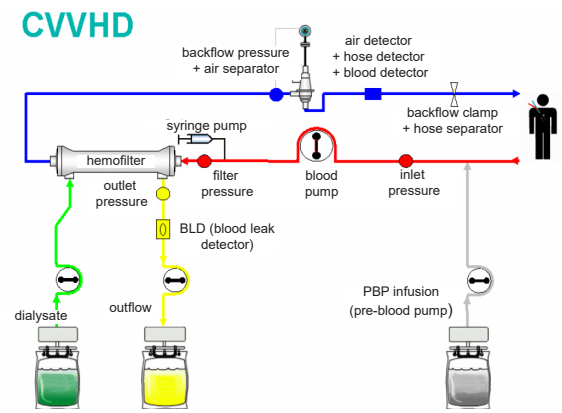


Fig. 1545 CVVHD [18]

Dose

- frequency:
  - 3-4 x / week (standard) or daily (Schiffl et al, N Engl J Med 2002 [see box]; but not established in clinical practice)
  - KDIGO recommendation: ⚠ 3 x / week for 5 hours each
- The dose in dialysis is described by the clearance of a dissolved substance (especially urea): Kt/V (K: urea clearance; t: duration of treatment; V: distribution volume of urea).
- The effectiveness of hemodialysis depends on:
  - blood flow

- synergistic combination effect
  - meropenem + fosfomycin (pneumonia)
  - vancomycin + fosfomycin (MRSA)
  - ceftriaxone + fosfomycin (meningitis)
- dosage
  - moderate infections: 2 x 5 g, 3 x 3 g
  - severe infections: 3 x 5 g, 2 x 8 g
- dose reduction in renal insufficiency
  - according to GFR:
    - 40-20 ml/min: 60-80% of the dose
    - 20-10 ml/min: 40-60% of the dose
    - < 10 ml/min: 20-40% of the dose
  - according to creatinine:
    - 0.8 mg/dl: 3 x 3 g
    - 2.0 mg/dl: 2 x 3 g
    - 3.5 mg/dl: 3 x 1.5 g
    - 6.0 mg/dl: 2 x 1.5 g
    - 15 mg/dl: 1 x 1.5 g
  - renal replacement therapy:
    - CVVH: 2 x 8 g
    - hemodialysis: 2 g after each hemodialysis
- side effects: especially
  - ⚠ hypernatremia: The i.v. applicable form is a sodium salt (very high sodium load [Be aware of acute heart and renal failure!]).
  - nausea, vomiting, diarrhea
  - headache
  - vulvovaginitis
- contraindicated in pregnancy
- EMA (European Medicines Agency) 3/2020: restriction of use for the i.v. form only to cases in which other antibiotics are not considered to be suitable (due to the side effects and the increasing resistance rate)

Ceftobiprole (Zevtera)

- cephalosporin of the 5th generation
- first cephalosporin with efficacy against MRSA (highly effective against MRSA)
- effect: bactericidal
- the only cephalosporin that is also effective against enterococci (usually "enterococcal gap" of cephalosporins)
- also effective against pseudomonas
- approvals:
  - pneumonia
    - community-acquired pneumonia (but not necessary for this purpose)
    - nosocomial pneumonia (but not approved for VAP [ventilator-associated pneumonia] since ceftobiprole was inferior to the compared substance [ceftazidime and linezolid] in the approval study [Awad et al, Clin Infect Dis 2014])
  - complicated skin and soft tissue infections (approved for this purpose by the FDA since 2024)
- dosage: 3 x 500 mg i.v. (better: 3 x 1,000 mg)
- dose reduction
  - renal insufficiency:
    - GFR 30-50 ml/min: 2 x 500 mg i.v.
    - GFR 10-30 ml/min: 2 x 250 mg i.v.
    - GFR < 10 ml/min or renal replacement therapy: 1 x 250 mg i.v.
  - hepatic insufficiency: no dose reduction necessary

Ceftaroline (Zinforo)

- cephalosporin of the 5th generation
- also effective against MRSA
- not effective against pseudomonas, ESBL and non-fermenters
- effect: bactericidal
- approvals:
  - complicated skin and soft tissue infections (cSSTI)
  - community-acquired pneumonia (i.a. Zhong et al, Lancet Infect Dis 2015)
  - note: The approval is relatively unfortunate. For the two diseases for which ceftaroline has been approved, we actually do not need it at all. Especially for therapy of community-acquired pneumonia no MRSA-effective antibiotic is necessary. It would have been particularly important for MRSA pneumonia (nosocomial) or for MRSA CNS infections.
- dosage: 2 x 600 mg i.v.
- dose reduction
  - renal insufficiency:
    - GFR 30-50 ml/min: 2 x 400 mg i.v.
    - GFR < 30 ml/min: not recommended
  - hepatic insufficiency: no dose reduction necessary

Prevention

- hygienic hand disinfection
- screening (smear of nose, if present of wounds) in case of risk factors (see infobox)
  - PCR (mecA gen; rapid test; faster [2-3 hours], but more expensive)
  - culture (slower [24-48 hours], but cheaper)
- isolation
- eradication
- rational use of antibiotics
- staff training
- limitation of intrahospital transports to the medically necessary minimum
- Since 2009, MRSA must be reported in Germany if it has been detected in the blood or CSF (cerebrospinal fluid).

If a patient is transferred from another hospital to the intensive care unit, protective isolation should be carried out until the result of MRSA smear is received!

Fever after staying in the tropics (malaria area): always test for malaria!

Pathogens

- plasmodium falciparum
- plasmodium malariae
- plasmodium vivax
- plasmodium ovale
- plasmodium knowlesi
  - initially discovered in macaques (Javanese monkeys) in Singapore; transferable to humans
  - named after British parasitologist and the malaria researcher Robert Knowles (1883-1936)
  - especially in Southeast Asia (especially in Malaysia: Plasmodium knowlesi is already the most common malaria pathogen there!)
  - ⚠ frequently severe courses (fulminant!)
  - difficult to differentiate microscopically from other plasmodia species (mostly only molecular biologically, i.e. by PCR)
  - therapy like tropical malaria (artesunate also the first choice for complicated form)

Types

- benign forms (1/3; mostly uncomplicated course):
  - quartan malaria (plasmodium malariae)
  - tertian malaria (plasmodium vivax / ovale)
- malignant form (2/3): tropical malaria (plasmodium falciparum)

Incubation periods

- tropical malaria: 12 days
- tertian malaria: 12-18 days
- quartan malaria: 3-6 weeks (very long; longest incubation period)
- notes:
  - ⚠ A feverish disease < 7 days after return (except after a stay of several weeks) is usually not malaria (minimum incubation period of malaria 1 week, mean incubation period 1 month).
  - but also incubation period longer than several months possible, so that stays abroad in malaria areas are still relevant up to 2 years back!

Pathogenesis

- Humans and anopheles mosquitoes are the only reservoir of pathogens.
  - mosquito: end host (here sexual phase [= gamogony])
  - human: intermediate host (here asexual phase [= schizogony])
- The anopheles mosquitoes (female form) use their saliva to transmit the sickle germs (sporozoites) into the blood of humans during bites.
- first infestation of the liver (short liver phase [5-8 days]; liver schizont), then infestation of the erythrocytes (erythrocytic phase)
- in erythrocytes multiplication and maturation (schizogony; blood schizont) → bursting of erythrocytes (hemolysis) and release (merozoites) → infestation of further erythrocytes and multiplication
- synchronization of intraerythrocytic parasitic growth → fever attacks every two (tertian malaria) or three days (quartan malaria)
- After some cycles, the sexual forms develop (sex form = gametocyte) → infection of the anopheles mosquito
- in synchronization (not the case with plasmodium falciparum) of parasite development: fever
- In tertian malaria (plasmodium vivax and plasmodium ovale), resting forms in the liver (hypnozoites) can remain asymptomatic for years and then lead to relapses. Therefore a final therapy (radical cure) with primaquine is necessary here!
- In tropical malaria there are no liver forms, therefore relapses are not possible in this type of malaria!
- special property of plasmodium falciparum: alteration of the erythrocyte surface (e.g. production of PfEMP1: plasmodium falciparum infected erythrocyte membrane protein 1) → "bonding" of erythrocytes (sequestration)

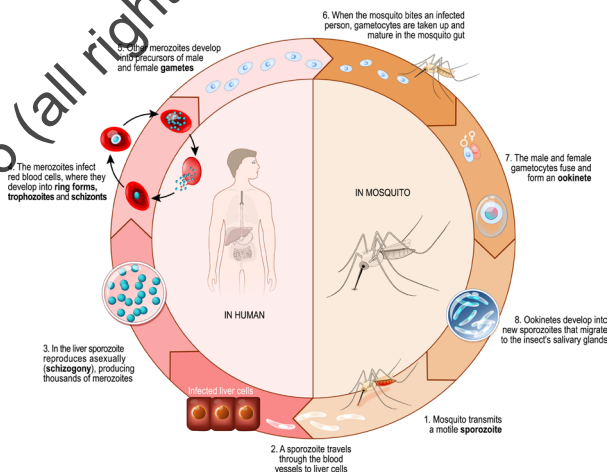


Fig. 1778 Life cycle of plasmodia (malaria cycle): Asexual reproduction (schizogony) takes place in human: First the hepatocytes (exoerythrocytic phase) and then the erythrocytes (erythrocytic phase) are infected. Sexual reproduction (gamogony) takes place in the anopheles mosquito. After the mosquito bite, the sporozoites (infectious forms of the pathogen) get from the saliva of the mosquito into the human blood. There they multiply in the liver (liver schizonts) and in the erythrocytes (blood schizonts). The liver schizonts disintegrate into numerous merozoites which then infect the erythrocytes. Finally, gametocytes (immature germ cells) develop which are ingested by the anopheles mosquito when it bites (blood meal). In the gut of the mosquito, these mature into gametes (mature germ cells). The female (macrogamete) and male (microgamete) gametes fuse to form the ookinet, from which the sporozoites then develop (sporogony).

Symptoms

- fever (even possible up to 2 years after a stay in the tropics!)
  - quartan malaria: 1 day fever, 2 days no fever

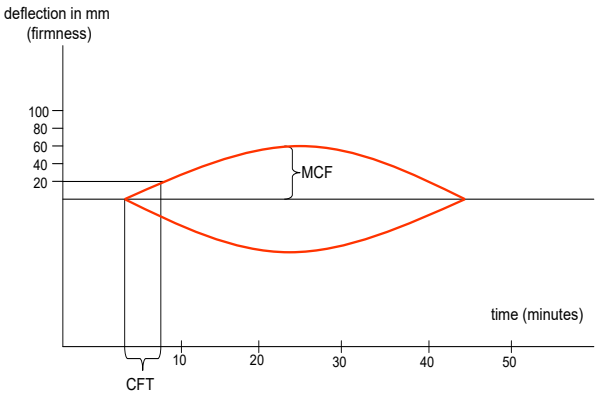
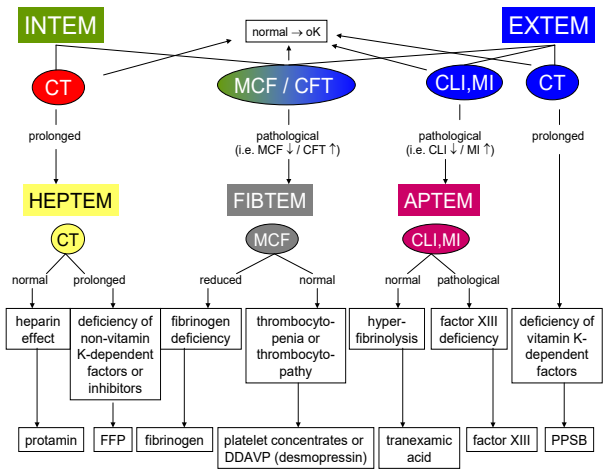


Fig. 1813 curve in case of a disturbance of the platelet function (thrombocytopathy [e.g. platelet inhibitor] or thrombocytopenia): prolonged CFT (clot formation time) and reduced MCF (maximum clot firmness) which leads to a flat curve

Tests

- without inhibitors
  - EXTEM:
    - measurement of the extrinsic system
    - activator: recombinant tissue factor
    - EXTEM also contains hexadimethrine bromide (Polybrene) to neutralize heparin.
    - The clotting time (CT) measured in EXTEM corresponds to the prothrombin time (Quick value): EXTEM-CT = prothrombin time (Quick).
  - INTEM:
    - measurement of the intrinsic system
    - activator: ellagic acid
    - The clotting time (CT) measured in INTEM corresponds to the PTT (partial thromboplastin time): INTEM-CT = PTT.
- with inhibitors
  - APTEM:
    - for the detection of hyperfibrinolysis
    - activation: like EXTEM + blockade of fibrinolysis (previously with aprotinin, today with tranexamic acid)
    - Whereas EXTEM already shows dissolution of the clot early (including pathological lysis indices [CLI, ML]), this is not the case with APTEM (here normal finding). EXTEM-ML is pathological (> 15%), APTEM-ML is normal (<15%). Tranexamic acid should be administered for therapy. If, in addition to EXTEM-ML, APTEM-ML is also pathological, the instability is not due to hyperfibrinolysis, but (most often) due to factor XIII deficiency in the sense of a fibrinogen polymerization disorder. Then factor XIII should be administered for therapy.
  - FIBTEM:
    - to differentiate the plasmatic from the cellular (platelets) part of the clot formation (Only the part of the fibrinogen, i.e. without platelets, of the coagulation is measured here.)
    - activation: like EXTEM + blockade of platelets (cytochalasin D)
    - FIBTEM-A10 < 7 mm: fibrinogen deficiency → administration of fibrinogen for therapy (target FIBTEM-A10: 10-12 mm)
  - HEPTEM:
    - for the detection of heparin effect: It is examined here whether a heparin effect (i.e. too much heparin; e.g. after intraoperative re-transfusion of blood from an auto-transfusion system [CellSaver]) may be the cause of a bleeding. If this is the case, protamine should be administered for therapy to antagonize heparin.
    - for ROTEM analysis in fully heparinized patients
    - activation: like INTEM + blockade of heparin (heparinase)
    - Heparin effect is present if CT and CFT are prolonged in INTEM, but normal in HEPTEM.
  - note: NATEM (without activator and inhibitor; NA: not activated; only addition of calcium chloride for recalcification)

Fig. 1814 ROTEM with severe fibrinogen deficiency: In FIBTEM (see arrow), in which the platelets are deactivated, there is no spindle formation at all (courtesy of Dr. Helmut Meyringer, Deputy Director of the Department of Anesthesiology, Caritas Hospital St. Josef Regensburg [Germany]).



        - endomyocardial biopsy (not absolutely necessary [only rarely performed]): lymphocytic infiltration, giant cells
      - often fulminant course with high mortality (17%); i.a. Mahmood et al, J Am Coll Cardiol 2018: in 46% MACE (major adverse cardiac event): AV block III (in 9%), cardiogenic shock (in 9%), cardiac arrest (in 11%), death (in 17%); also acute left heart failure (in 42%) and atrial arrhythmias (in 26%)
      - therapy:
        - discontinuation of the immune checkpoint inhibitor
        - methylprednisolone (first choice; preferably in a high dose, i.e. 2 mg/kg), possibly immunoglobulins (0.4 g/kg daily for 5 days), mycophenolate mofetil, ATG (anti-thymocyte globulin), infliximab (but attention: deterioration possible), abatacept, alemtuzumab
  - pericarditis (therapy: methylprednisolone)
- pulmonary (in 5%):
  - pneumonitis
    - hypersensitivity pneumonia, possibly ARDS
    - especially under PD-1 and PD-L1 inhibitors
    - therapy (always broad-spectrum antibiotics [e.g. piperacillin / sulbactam] in addition to immunosuppressive therapy):
      - methylprednisolone (after exclusion of an infectious cause; here for 8 and not just for 4 weeks)
      - if refractory: infliximab (very good option here!), mycophenolate mofetil, cyclophosphamide, IVIG
  - pleuritis
- renal (in 3%; possibly acute kidney failure):
  - interstitial nephritis
  - glomerulonephritis
- neurological (in 2%):
  - tremor
  - ataxia
  - seizures
  - PNP (peripheral polyneuropathy)
  - Guillain-Barré syndrome (GBS)
  - myasthenia gravis (especially with PD-1 and PD-L1 inhibitors)
  - meningitis, encephalitis (especially with CTLA-4 inhibitors)
  - myelitis
- musculoskeletal:
  - myositis (possibly rhabdomyolysis)
  - fasciitis
  - arthritis (if steroid refractory: MTX, leflunomide, hydroxychloroquine, sulfasalazine, TNFα blockers)
- ophthalmological: especially uveitis (most common), conjunctivitis, episcleritis, keratitis, retinitis (up to blindness), optic neuritis, inflammation of the orbit, endocrine orbitopathy
- hematological:
  - hemolysis
  - anemia, leukopenia, thrombopenia (pancytopenia)
  - thrombotic microangiopathy (TMA)
  - hemophilia
  - arteritis
- psychical: fatigue (very often [in 25%]!)

unclear hyponatremia under ICI:
always determine ACTH + cortisol
- ACTH ↑ + cortisol ↓: primary adrenal insufficiency (adrenalitis)
- ACTH ↓ + cortisol ↓: secondary adrenal insufficiency (hypophysitis)

CAR-T-cell therapy

Definition

- syn.: adaptive T-cell transfer
- new form (ATMP [advanced therapy medicinal products]) of cancer therapy (immunological, gene therapy; only offered by corresponding specialized centers)
- CAR: chimeric antigen receptor (synthetic hybrids of receptor and signal units to target T-cells against target proteins of tumor cells [especially malignant B-cells])
- discovery and development by the Israeli immunologist Zelig Eshhar at the Weizmann Institute in Rehovot (Israel) in the late 1980s ("T-body", "immune receptor")
- approved in Germany since 2018
- The patient's own T-cells are modified ex vivo in such a way that they express chimeric antigen receptors on their surface that are directed against a cancer-specific antigen (most commonly CD 19 and BCMA [B-cell maturation antigen]) of malignant cells (mostly B-cells) and then destroy them.
- detection independent of the MHC (major histocompatibility complex; HLA [human leukocyte antigen] system)
- The CAR-T-cells are produced individually for each patient. This is relatively complex and takes about 4 weeks.
- This therapy was first carried out in a 6 year old girl (Emily Whitehead from Pennsylvania, USA). At the age of 5, she developed acute lymphoblastic leukemia (ALL) and received intensive chemotherapy.

flutter (significantly lower cardioembolic risk than atrial fibrillation)
    - anterior wall aneurysm (e.g. after a large anterior wall myocardial infarction)
    - paradoxical embolism in patent foramen ovale (PFO)
    - endocarditis
  - aorto-arterial (plaques / atheromas of the ascending aorta or aortic arch; especially from size > 4 mm)
  - vasculitis (very rare; CNS vasculitis; should be kept in mind especially in younger patients without cerebrovascular risk factors)
    - primary CNS vasculitis (PACNS: primary angiitis of the CNS)
    - secondary CNS vasculitis (infect-associated or non-infect-associated, e.g. Horton´s disease, Takayasu´s disease)
  - antiphospholipid syndrome (20% of all patients < 45 years [Every 5th stroke patient who is younger than 45 years has an antiphospholipid syndrome!])
  - Moyamoya disease (progressive, genetically determined fibrosis with severe stenosis or occlusion of the distal internal carotid artery and middle cerebral artery with formation of pronounced collaterals that look like "fog" or "smoke" [Japanese: moyamoya] in the angiogram; especially children and young people; especially in Asia)
  - unknown (40%)
- thrombotic; especially microangiopathic:
  - ⚠ frequent (about 1/3 of all ischemic strokes!)
  - typical in older patients with arterial hypertension and diabetes mellitus
  - lacunar infarctions (p.d. subcortical infarction in the territory of the small cerebral arteries with a maximum extension of 1.5 cm in the CT or 2.0 cm in the MRI)
  - in CCT mostly not visible, in MRT tiny, mostly subcortical located lesions
- hemorrhagic (intracranial bleeding; 20%)

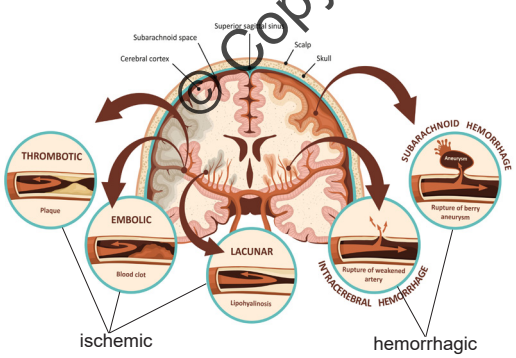


Fig. 1858 the different types of stroke

Symptoms

- hemiparesis (predominantly arm weakness; facial palsy [central])
- hemihypesthesia, hemiparesthesia
- visual disturbances
  - amaurosis fugax (ipsilateral)
  - homonymous hemianopsia (contralateral visual field)
- conjugate eye deviation (CED) to the ipsilesional (non-paretic) side
- dysarthria (speaking disorder)
- aphasia (speech disorder)
  - motor aphasia (syn.: Broca aphasia, expressive aphasia, non-fluent aphasia): disorder of speech production
  - sensory aphasia (syn.: Wernicke aphasia, receptive aphasia, fluent aphasia): disorder of speech comprehension
- somnolence, coma
  - ⚠ absolutely untypical for ischemic stroke of the anterior circulation (only in malignant media infarction)
  - Think of other differential diagnoses (hemorrhagic stroke [intracranial bleeding], basilar thrombosis, postictal after epileptic seizure)!

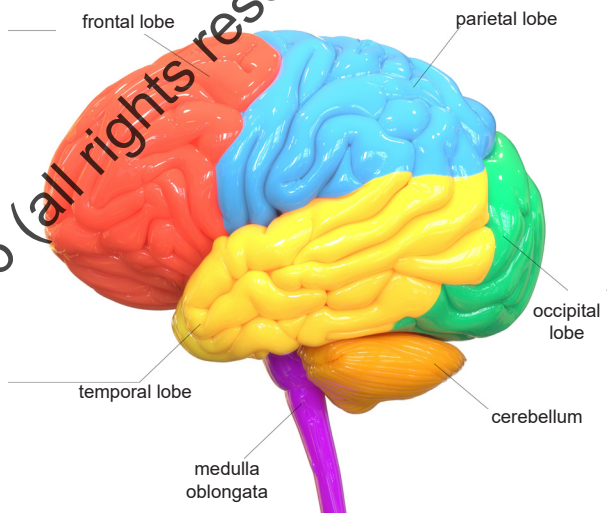


Fig. 1859 Brain: anatomy

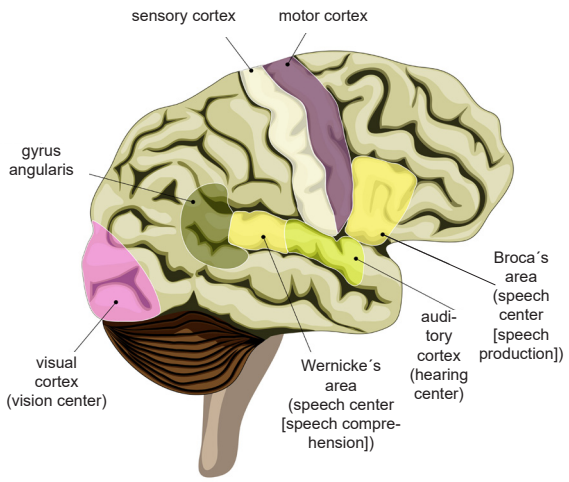


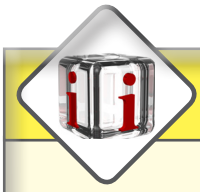
Fig. 1860 Brain: function

Step 4
super-refractory status epilepticus

- definition: status epilepticus that could not be broken even with narcotics (anesthesia and intubation; duration mostly > 24 hours)
- mortality: 25% (In 75% of the survivors, severe neurological impairments remain [Cornwall et al, JAMA Neurol 2023].)
- options:
  - inhalative anesthetics (if not already used in step 3; e.g. isoflurane, sevoflurane; e.g. via AnaConDa system)
  - combination of barbiturate + propofol (recommended dosage: 10 mg/kg/h [70 kg → propofol 1% infusion rate 70 ml/h; relatively high dosage → be aware of propofol infusion syndrome])
  - ketamine
  - clomethiazole (Distraneurin; 5-12 mg/kg as bolus, maintenance dose 0.6-4 mg/kg/h)
  - lidocaine (Xylocaine; 1.5-3 mg/kg as bolus, maintenance dose 2-4 mg/kg/h)
  - steroid pulse therapy (e.g. methylprednisolone 1 g i.v. daily for 5 days; with the idea of a possibly present autoimmune encephalitis that may have been overlooked)
  - verapamil (Isoptin; total dose 3 mg)
  - chloral hydrate (2 g as a bolus, maintenance dose 1.5 g every 4-6 hours)
  - ketogenic diet (KD)
    - A low-carbohydrate diet is performed. To ensure sufficient calorie intake, fat intake is increased (e.g. with a 20% lipid solution) as a compensatory measure. The low-carbohydrate diet leads to increased production of ketone bodies: These inhibit the production of glutamate (the most important excitatory neurotransmitter in the CNS) and increase the production of GABA (the most important excitatory neurotransmitter in the CNS).
    - termination rate: 50-60%
  - electroconvulsive therapy (ECT; ultima ratio)

Diagnostics (after seizure)

- laboratory (i.a. blood glucose, creatine kinase; if necessary level determination of antiepileptic drugs)
- BGA (metabolic acidosis)
- ⚠ CCT
- ECG
- if necessary lumbar puncture for cerebrospinal fluid (to exclude meningitis [only if there is urgent suspicion])



STESS
Status Epilepticus Severity Score

- definition
  - score for estimating prognosis in status epilepticus
  - according to Rossetti et al, J Neurol 2018
- parameters
  - consciousness:
    - awake, somnolent or confused: 0 P.
    - comatose or stuporous: 1 P.
  - initial seizure type:
    - convulsive - focal: 0 P.
    - convulsive - generalized: 1 P.
    - non-convulsive: 2 P.
  - age:
    - < 65 years: 0 P.
    - ≥ 65 years: 2 P.
  - previous seizures:
    - known: 0 P.
    - unknown: 1 P.
- interpretation
  - 0-2 P.: favorable prognosis (probability of survival: 97% [very high negative predictive value!])
  - 3-6 P.: unfavorable prognosis (probability of survival: 61%; at 6 P. withdrawal of treatment may be considered)

Forensics (driving regulations)

- after a seizure driving ban for 3 months (after brain surgery or injuries 6 months)
- with diagnosed epilepsy: lifelong driving ban (In case of a seizure-free period of at least 12 months under regular medical control, the driving license can be regained.)
- must be communicated to the patient and documented in writing in the file (liability risk for the physician!)

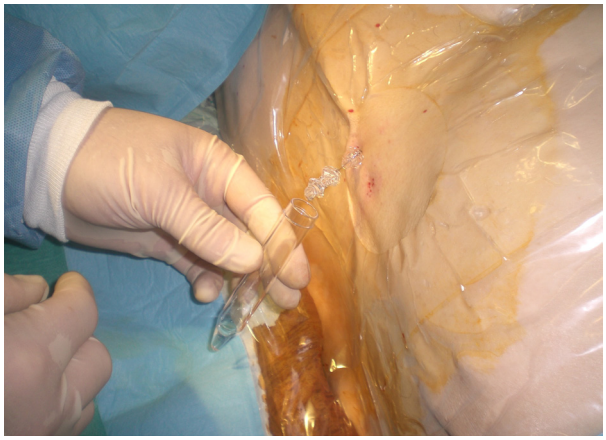


Fig. 1982 lumbar puncture

Cerebrospinal fluid (CSF)
Findings

- normal finding
  - aspect: clear
  - protein: 15-45 mg/dl
  - glucose:
    - > 50 mg/dl
    - ratio CSF / serum > 0.55
  - lactate: < 2 mmol/l (< 18 mg/dl)
  - cell count: < 12/3 cells or < 5/µl
- finding in case of bacterial meningitis
  - aspect: turbid
  - protein: increased (mostly > 100 mg/dl)
  - glucose: decreased
    - < 30 mg/dl
    - ratio CSF / serum < 0.30
  - lactate: increased (> 3.5 mmol/l or > 32 mg/dl [Huy et al, Crit Care 2010: sensitivity 93%, specificity: 96%])
  - cell count: increased (pleocytosis) mostly > 1,000/µl [Bijlsma et al, Lancet Infect Dis 2016: however, in 34% < 1,000/µl despite bacterial meningitis!]; especially granulocytes)

	aspect	cell count (per µl)	cell type	glucose CSF / serum	lactate (mmol/l)	protein (mg/dl)
bacterial	turbid	> 1,000	granulocytes (polynuclear)	< 0.30	> 3.5	> 100
viral	clear	< 1,000	lymphocytes (mononuclear)	> 0.30	< 3.5	< 100
tuberculous	variable	< 1,000	mixed	< 0.30	> 3.5	> 100

Differential diagnosis of the different types of meningitis: bacterial meningitis, viral meningitis and, as a special form of bacterial meningitis, tuberculous meningitis (Meningitis due to listeria is an exception: Although it is a bacterial meningitis, protein is not or only slightly increased, glucose is usually not reduced and lymphocytes instead of granulocytes are predominantly found.)

generously perform CCT before lumbar puncture to exclude increased intracranial pressure! otherwise danger of herniation!

As a rule, however, no CCT is necessary before lumbar puncture (if there is no disturbance of consciousness, focal neurological deficit or seizure) and no laboratory (if no petechiae are present; only loss of time)!

Mortality increases by 12.5% for every hour of delay in starting antibiotic therapy!

Therapy

- antibiosis
  - only after lumbar puncture (Exception: In case of disturbance of consciousness, focal-neurological deficit or after a seizure, the antibiosis should already be administered prior to the lumbar puncture and also prior to the CCT).
  - initially calculated (⚠ standard: ceftriaxone 4 g, then 2 g 1 x daily + ampicillin 4 g 4 x daily [to close the listeria gap of the cephalosporins]); ⚠ immediately after sampling for microbiology (reduces mortality by the factor of 30!)
  - In patients from south-eastern Europe, France, Australia and South Africa vancomycin 2 x 1 g i.v. should be added initially due to the increased penicillin resistance of the pneumococci.
  - In nosocomial meningitis or in patients with immunosuppression, the combination of meropenem (3 x 2 g i.v.) and vancomycin (2 x 1 g, then according to level) is the means of choice for calculated antibiosis.
  - then according to antibiogram, for example:
    - meningococci (duration of therapy: 7 days):
      - MIC < 0.1 µg/ml: penicillin G 6 x 5 million IU i.v.
      - MIC > 0,1 µg/ml: ceftriaxone 2 x 2 g i.v.
    - pneumococci (duration of therapy: 14 days): penicillin G 6 x 5 million IU i.v.
    - listeria monocytogenes (duration of therapy: 3 weeks [with immunosuppression: 4-6 weeks]): ampicillin 6 x 2 g + gentamicin 5 mg/kg (single dose)
    - haemophilus influenzae: ceftriaxone 2 x 2 g i.v.
    - staphylococcus aureus:
      - MSSA: flucloxacillin 6 x 2 g i.v. or cefazolin 3 x 2 g i.v.

fluid, saliva, tear fluid or corneal swab; postmortem from the brain)

Therapy

- no causal (antiviral) therapy available
- Once the disease begins, i.e. symptoms appear, it is no longer curable and almost inevitably leads to death! There are only reports of 15 survivors, all of whom suffered severe sequelae (Jackson et al, Curr Infect Dis Rep 2017).
- supportive care (including circulatory therapy, sedation and mechanical ventilation); possibly use of the Milwaukee regimen: a combination of deep analgosedation (with phenobarbital, midazolam and ketamine) and antiviral therapy (ribavirin + amantadine)
- isolation (The patient's saliva, tears and urine are contagious, but not the blood!)

Prophylaxis

- post-exposure prophylaxis (PEP):
  - ⚠ the most important measure to prevent disease after exposure (especially after a bite from an animal suspected of having rabies), which should be initiated immediately (It is very effective and prevents the disease in almost 100% [Wilde et al, Vaccine 2007]!)
  - wound care: primarily cleaning the wound with soap and water ("washing out the pathogen"), extensive surgical debridement, disinfection (e.g., povidone-iodine, 70% ethanol [Because the viruses have an envelope, they are easy to kill!]), no suturing (open wound treatment), tetanus protection
  - both active (either according to the Essen or Zagreb scheme) and passive immunization (HRIG [human rabies immunoglobulin; Berirab or Merieux P]; useful up to a maximum of 7 days after the bite; dose: 20 IU/kg i.m. [1 ml = 150 IU])
  - In vaccinated patients, only active immunization (2 doses immediately and then after 3 days) is indicated, not passive immunization.
  - not necessary in:
    - touching or feeding animals, licking intact skin
    - bites from rodents (e.g. mice, rats): They cannot transmit rabies.
- pre-exposure prophylaxis: vaccination (active immunization)
  - vaccines:
    - Rabipur (PCEC [purified chick embryo cells]; Bavarian Nordic; one dose = 1 ml = 2.5 IU [also applies to children])
    - Verorab (HDC [human diploid cell strain]; Sanofi Pasteur; one dose = 0.5 ml = 2.5 IU [also applies to children])
  - application: i.m. (deltoid muscle)
  - schemes:
    - Essen regimen: one vaccine dose immediately, followed by one on days 3, 7, 14, and 28
    - Zagreb regimen: two vaccine doses immediately (into the right and left deltoid muscle), followed by one on days 7 and 21
  - recommended for:
    - people with occupational contact with wild animals and bats (e.g., hunters, foresters, veterinarians, animal caretakers)
    - people working in laboratories with rabies viruses
    - travels to risk areas (especially India, Indonesia, Sri Lanka, Bali, Thailand, China, Vietnam, Egypt, Turkey, Cuba, Dominican Republic) with likely close contact with animals (especially for backpacking and adventure trips with predominantly outdoor activities; especially for trips over a longer period of time; especially if no post-exposure prophylaxis is available locally [relatively expensive])
  - no booster vaccination recommended (WHO)

Fig. 1991 Louis Pasteur (1822-1895): The French chemist and biologist developed the first vaccine against rabies in 1885: He saved the life of the 9-year-old boy Joseph Meister, who was bitten by a rabid hunting dog.

Rabies: the infectious disease with the highest mortality rate! Bite from a stray dog in a risk area abroad (Asia, Africa) → immediate PEP! Key symptoms: delayed wound pain, hydrophobia, aerophobia

BRAIN DEATH

Definition

- For many centuries, the only sure signs of death were rigor mortis, livor mortis, putrefaction and injuries incompatible with life (e.g. decapitation). However, with the beginning of intensive care medicine in 1952 with the possibility of artificial mechanical ventilation and maintaining cardiovascular function, these were no longer sufficient, so the term "brain death" was defined for the first time in 1968 by a committee of the Harvard Medical School (USA; definition of irreversible coma; published in JAMA) and was introduced as a new sure sign of death.
- Brain death is defined as an irreversible loss of overall function of the cerebrum, cerebellum and brainstem when mechanical ventilation and circulation are maintained in intensive care unit.
- determination only possible in the intensive care unit in mechanically ventilated patients
- Critical voices claim that brain death was made up as a construct only to enable organ transplantations (brain death as the "invention of transplant medicine").
- new term (according to the current guidelines in Germany 2015): irreversible loss of brain function (ILBF; The term "brain death" is avoided in the current guidelines. Instead, the term irreversible loss of brain function, which can also be proven scientifically and medically, should be used. This should avoid the discussion whether the brain is dead even according to a philosophical-ethical understanding. In the following, however, the term "brain death" will continue to be used for reasons of practicality.
- It is often difficult to convey to relatives as a sure sign of death because it is very vague.
- guidelines (directives) of the Scientific Advisory Board of the German Medical Association:
  - 1997 (3rd update): state of irreversible extinction of the entire function of the cerebrum, cerebellum and brain stem during controlled mechanical ventilation in the event of cardiovascular function still being maintained
  - 2015 (4th update): With the determination of the final, irreversible loss of the overall function of the cerebrum, the cerebellum and the brain stem (irreversible loss of brain function), the death of man is determined scientifically and medically.
  - 2022 (5th update)
- every 1,000th deceased patient (rare in total; 8% of all resuscitated patients)
- Brain death is the death of the human being.

Causes

- intracranial bleeding (most frequent cause)
- traumatic brain injury (TBI)
- resuscitation (hypoxic brain damage, hypoxic ischemic encephalopathy [most frequent cause in internal intensive care medicine])
- pronounced ischemic stroke (e.g. malignant MCA infarction)
- drowning
- meningoencephalitis

Symptoms

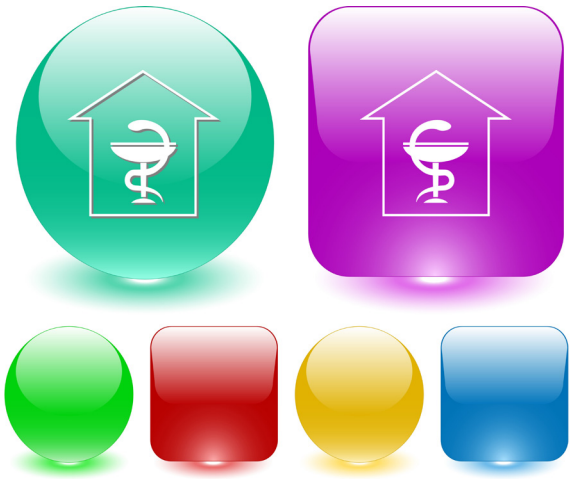
- coma
- brain stem areflexia (missing brain stem reflexes)
- apnea

Legal foundations

- Brain death is a prerequisite (dead donor rule) for the removal of organs for transplantation (§ 3 part 2 Transplantation Act; DBD: donation after brain death). In some countries (e.g. in Austria; not in Germany) cardiac death (cardiac arrest) is also sufficient for organ removal (DCD: donation after cardiac death).
- time of death: time at which the brain death diagnosis and documentation was completed
- The legal supervisor no longer has the authority to insist on continuation of "life-sustaining" therapy if brain death has already been diagnosed. The legal care ends with the brain death of the patient. The ventilator may then be switched off.
- ⚠ obligation of the hospitals in Germany to report potential organ donors to the responsible transplant centre (§ 11 part 4 Transplantation Act); you should know who is the transplantation officer in your hospital!
- remuneration:
  - no DRG reimbursement (only up to the time of brain death)
  - Organ donation is only paid once brain death has been determined (according to a module). In the case of an uncompleted organ donation (e.g. rejection by the relatives), an expense allowance will also be made. Mostly, however, this is not covering the costs. This topic should deliberately not be subject to financial incentives.

Every physician working in intensive care unit is obliged to ensure that potential organ donors are reported!

INTOXICATION WITH CHEMICALS



Intoxication with alkylphosphates

Definition

- syn.: organophosphates, phosphonic acid esters, acetylcholinesterase inhibitors
- occurrence
  - plant protection agents (pesticides, insecticide [The most frequently used pesticides are organophosphates!]); representatives:
    - Parathion (E 605; taken from the market in Germany [also officially banned in the EU since 2002], but relatively easily available abroad, e.g. from the Czech Republic; furthermore, many farmers still have remainders)
    - Methydemeton (demeton S-methyl sulfoxide; Metasystox)
    - Dimethoate (Roxion, Bi 58)
    - Sulfotep (an acaricide [agent for combating mites and ticks]; no longer approved in the EU since 2007)
  - warfare agents (neurotoxins; poison gases)
    - sarin (e.g. Tokyo subway sarin attack in 1995 committed by the Aum cult with 12 dead and 5,500 injured persons; poison gas use in Syria 2013)
    - VX nerve agent (i.a. murder of the half-brother of the North Korean ruler Kim Jong Un in February 2017)
    - Nowitschok
      - Russian: "newbie" (developed in Russia)
      - a nerve warfare agent
      - i.a. assassination of the former Russian spy and defector to England Sergej Skripal and his daughter on 08.03.2018, assassination of the Kremlin critic Alexej Navalny on 20.08.2020
    - tabun (i.a. produced during the final phase of WWII, but no longer used; tons of it were dumped in the Baltic Sea after the end of WWII])
    - soman
- blue warning colour
- irreversible inhibition of the enzyme acetylcholinesterase
- almost exclusively with suicidal intent
- typical cholinergic syndrome
- ⚠ mortality: 50%

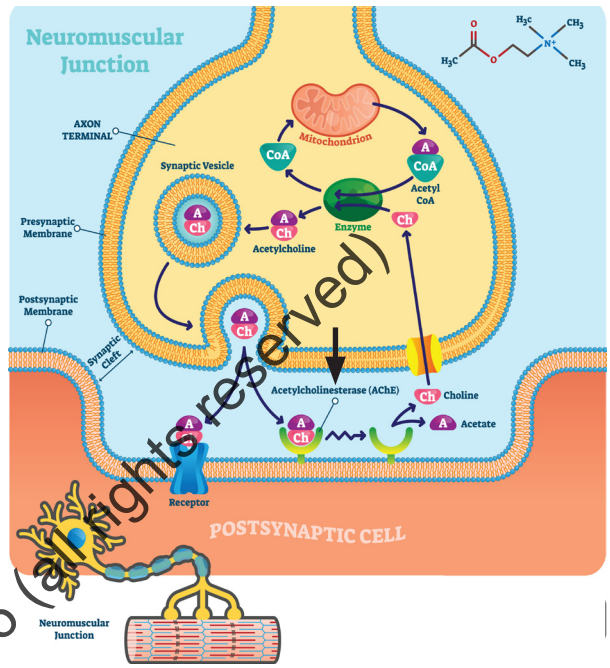


Fig. 2057 The enzyme acetylcholine esterase (AChE; see arrow) splits the neurotransmitter acetylcholine (ACh) which has bound to the acetylcholine receptor of the postsynaptic membrane, into acetic acid and inactivates it. Alkylphosphates inhibit the acetylcholine esterase so that there is a permanent depolarization of the postsynaptic membrane so that the cell is ultimately no longer excitable.

Etiology

- intentional:
  - suicidal (almost ever)
  - homocidal
- accidental (almost never)

Uptake

- peroral (No.1)
- percutaneous (No.2; contact poison; don't forget to protect yourself!)
- inhalative (No.3)

Symptoms

- blue-coloured oral mucosa (due to the warning colour)
- excessive sweating (hyperhidrosis)
- secretion of saliva (blue foam), epiphora, rhinorrhoea, bronchorrhea (Patients “drown” in their own secretions!)
- urination, stooling
- nausea, vomiting (possibly blue coloured vomit), di-

- currently ongoing study of the NKSG (national clinical study group) in Germany under the leadership of the Charité in Berlin (interim analysis [presented at the DIVI congress on 05.12.2024]: significant improvement in quality of life [SF-36], fatigue and physical functioning)

- note: The 4 GBA compliant (GBA: Gemeinsamer Bundesausschuß [Federal Joint Committee]) and thus officially recognized indications in Germany are: carbon monoxide intoxication, diving accident, gas gangrene, arterial gas embolism.

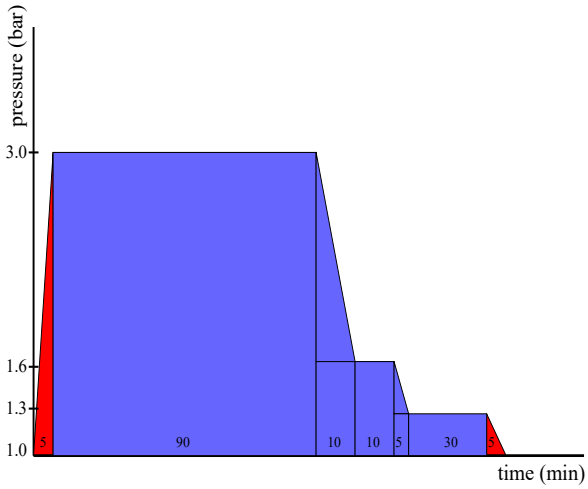


Fig. 2087 therapy scheme for carbon monoxide intoxication and gas gangrene: TS 300-90 (syn.: Boerema scheme). The time of pure oxygen breathing is shown in blue and the time of breathing without a mask in red. Total duration of the session: 155 minutes

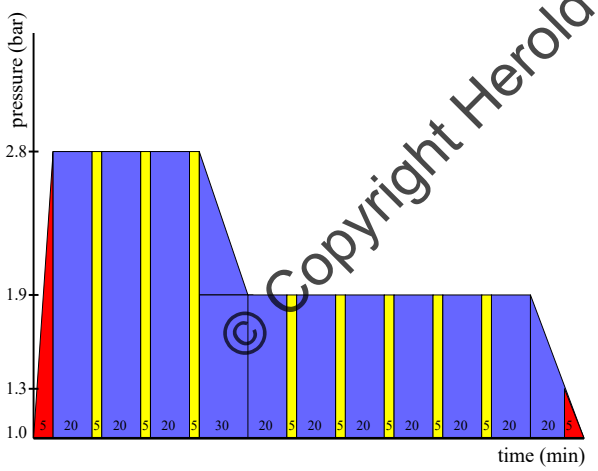


Fig. 2088 therapy scheme for diving accident and arterial gas embolism: TS 280-60 (syn.: US Navy Table 6). The time of pure oxygen breathing is shown in blue, the oxygen breaks (air breathing) in yellow and the time of breathing without a mask in red. Total duration of the session: 285 minutes

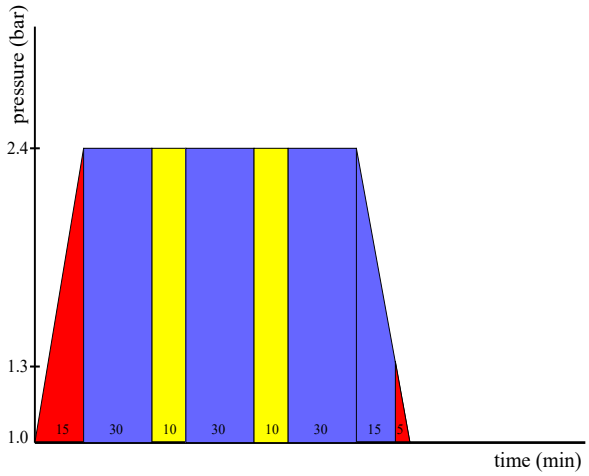


Fig. 2089 therapy scheme for problematic wounds: TS 240-90. The time of pure oxygen breathing is shown in blue, the oxygen breaks (air breathing) in yellow and the time of breathing without a mask in red. Total duration of the session: 140 minutes

Side effects

- barotrauma
  - middle ear (tympanic membrane); in intubated and mechanically ventilated patients bilateral paracentesis (incision) necessary beforehand to equalize the pressure in the middle ear
  - lung (e.g. pneumothorax)
- oxygen toxicity (In order to reduce oxygen toxicity, most therapies include repeated short phases [so-called oxygen breaks] in which the patient only breathes air and not pure oxygen. The therapy scheme for carbon monoxide intoxication [Boerema scheme] has no oxygen breaks so that the risk of oxygen toxicity is increased here.)
  - CNS (central nervous system)
    - Paul Bert effect: toxic effect of oxygen on the CNS
    - signs: dizziness, nausea, vomiting, double vision, restlessness, anxiety, paresthesia or facial spasms
    - main danger: seizures (so-called oxygen seizures); therapy: Here, the breathing gas should be switched from pure oxygen to air immediately. If the seizure persists, a benzodiazepine should be administrated.
  - lung
    - Lorraine-Smith effect: toxic effect of oxygen on the lungs
    - consequences:
      - ARDS (increased capillary permeability → permeability pulmonary edema)
      - decrease of functional residual capacity (FRC)
      - increase of resistance in the small airways
      - fibrosis (but only after a very long exposure time)
  - eye (e.g. temporary myopia [short-sightedness] by deformation and thus change of the refractive power of the lens, deterioration of a cataract)
- psychological (i.a. claustrophobia)
- temperature changes:
  - During compression, the temperature in the cham-

can lead to intoxication.
- poisonous plant of the year 2005 (highly toxic!)
- toxin: aconitine
  - lipophilic
  - acts especially as a neurotoxin → central respiratory paralysis
  - It causes a persistent activation of voltage-dependent sodium channels of the cell membrane (especially of the nervous system, myocardium and peripheral muscles).
- lethal dose: 5-10 mg (About 4 blossoms are enough!)
- serum level of aconitine measurable in toxicological laboratory (from > 2.6 µg/l mostly lethal)
- history: i.a. used by Pope Clement VII for executions
- etymology (Greek mythology): The first monkshood grew on the hill aconitos (today Turkey) where Herakles dragged the hellhound Kerberos up from Hades (underworld). It was said that Kerberos had a poisonous bite and his poison dropped onto the ground and sprung up as monkshood.

Etiology

- accidental
  - ingestion of the blossoms by small children (These plants should not be planted in gardens, in which children play!)
  - confusion of the leaves of monkshood with those of parsley, lovage or horseradish
- suicidal (e.g. mixing the blossoms in tea, Chinese herbal teas, ingestion of topical substances from TCM [traditional Chinese medicine])

Fig. 2119 monkshood: most toxic plant in Europe (should not be planted in gardens, in which children play)

Symptoms

- ⚠ relatively typical toxidrome (burning paresthesia on the acra and face)
- dry mouth
- nausea, vomiting, diarrhea, abdominal pain (convulsive; usually very strong)
- ear noises, impaired vision
- chills, strong sensation of cold, typical icy cold ("anesthesia dolorosa")
- numbness all over the body ("I can no longer feel my body.")
- muscle weakness, respiratory paralysis
- seizures
- cardiotoxicity
  - bradycardia (i.a. AV block III)
  - tachycardia (i.a. multidirectional ventricular tachycardia [several autonomous focal centres])
- dyspnea, tachypnea (later bradypnoea and apnoea)
- hypersalivation, hyperhidrosis
- mydriasis
- consciousness: mostly preserved for a long time

Therapy

- symptomatic
- possibly primary toxin elimination (gastric lavage in case of ingestion < 1 hour, activated charcoal)
- possibly ERCP with insertion of a nasobiliary probe (Wurbs probe) to drain the bile to interrupt the enterohepatic circulation to which the toxin is subject (rinsing the probe with 500 ml normal saline / 24 hours)
- cardiac arrhythmia
  - bradycardic: if necessary temporary pacemaker
  - tachycardic: amiodarone (Amiodarone is a sodium channel blocker. Aconitine activates the sodium channels).
- in case of prolongation of the QT interval or torsade de pointes: magnesium (initially 2 g as bolus i.v., then continuously 120-140 mg/h until a serum concentration of 1.2-2.0 mmol/l is reached)
- sodium bicarbonate 8.4%
- 20% lipid emulsion (e.g. Intralipid, Clinoleic)
  - Aconitine is highly lipophilic.
  - dosage: 100 ml as bolus, then administration of the remaining 400 ml over 20 minutes
- if necessary va-ECMO (often helpful for bridging [especially in refractory ventricular tachycardia]!)

White hellebore

- veratrum album
- The intoxication (i.a. pathoyphysiology, symptoms, therapy) is very similar to that of the monkshood. Typically here is mainly a strong urge to sneeze!
- Here, too, the alkaloids (especially protoveratin and germerine) which are mainly contained in the root, lead to a persistent activation of voltage-dependent sodium channels in the cell membrane.
- Intoxication is typically caused by confusion with the yellow gentian (gentiana lutea; especially when it is not in bloom; typically with home-made schnapps [distilled spirit]).

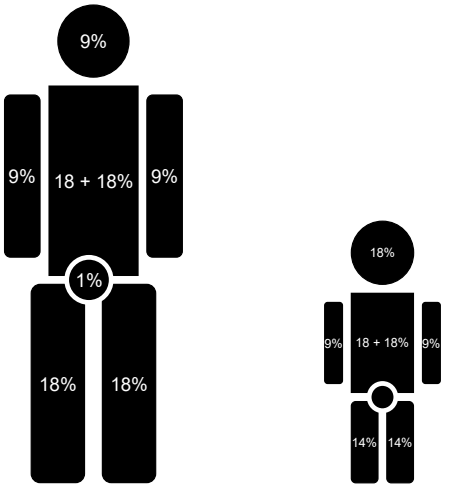
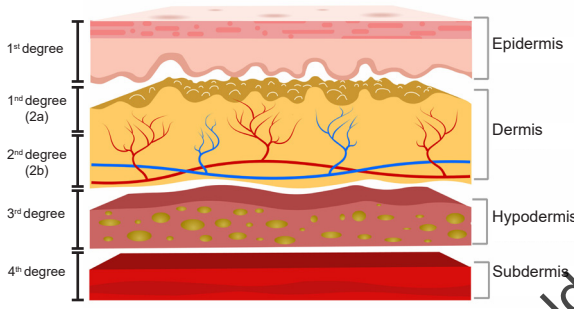


Fig. 2158 estimation of the percentage of total burned surface area (TBSA) according to the rule of nine according to Wallace: The body is divided here into sections by multiples of 9%. On the left it is shown for an adult and on the right for a child (infant: Here there are different values for the head [higher value] and the legs [lower values] compared to adults.)



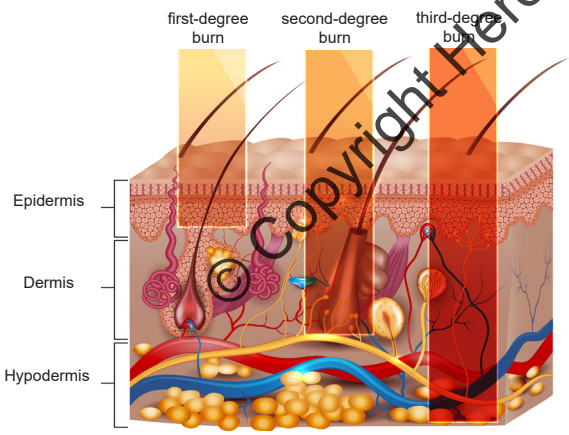


Fig. 2159 presentation of the different degrees of burns (according to the depth; based on the different skin layers)

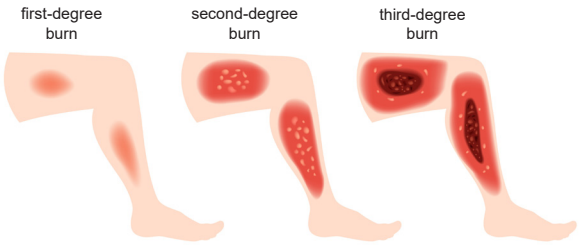


Fig. 2160 presentation of the different degrees of burns (according to the clinical findings)

Fig. 2161 Blisters (burn blisters) are the typical finding of a second-degree burn.

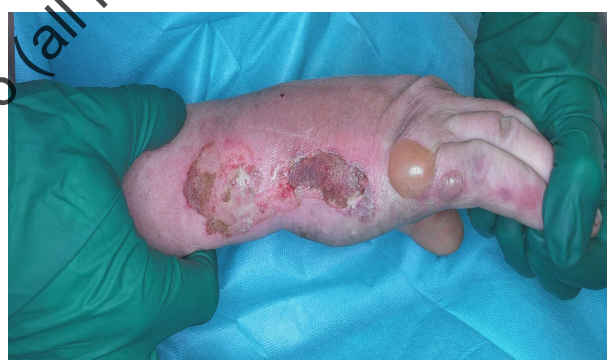


Fig. 2162 second-degree burn of the hand mit with predominantly still rosy (2a), but also pale (2b) wound base

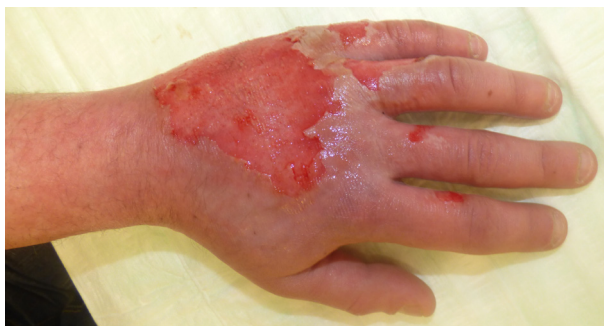


Fig. 2163 third-degree burn

ETHICS & LAW

Intensive care medicine has the primary goal of treating potentially reversible damage that has caused acute danger to the patient. It is intended to bridge life-threatening phases and create time for the causal therapy of the underlying disease. The patients should then be able to lead an independent and self-determined life again with an adequate quality of life. Interdisciplinary (between the different departments [e.g. anesthesiology and internal medicine]) and interprofessional (between the different professional groups [e.g. physicians and nurses]) collaboration is essential. However, intensive care medicine also has its limits which should be accepted. The death of an intensive care patient must not be understood as an accident or even as a defeat. Life has a mortality of 100% ("Mors certa, hora incerta." [Death is certain, its hour uncertain.])! Dying should be accepted as an inevitable process. Especially at the end of life, dying with dignity and with peace must be made possible for the patient, preferably in the presence of his relatives. The natural limits of life are artificially pushed further and further by intensive care medicine. It does not make sense to do everything that can be done. The maxim "to live at any price" (rule of rescue) or "to prevent death at any price" must not apply which would only prolong an irreversible dying process. "The progress in medicine is tremendous - one is no longer sure of one's own death" (Hermann Kesten, German writer, 1900-1996). In case of hopelessness, intensive therapy is pointless ("futility"; Latin: futilis [useless, in vain]). Intensive care medicine should not be too intensive ("less is more"). It should always be questioned whether the often extremely high burden of intensive care treatment is justified at all for the patient with regard to the realistically achievable quality of life for the patient. A major problem that is common especially in the intensive care unit at the end of life, is overtherapy (oversupply), i.e. overuse of medical services. It plays a major role, especially in industrialized nations such as Germany. With 34 intensive care beds per 100,000 inhabitants (a total of approximately 28,000 intensive care beds), Germany has the highest density of intensive care beds worldwide at all. 50% of all people in Germany die in a hospital, 25% of them in ICU. In Germany, approximately 1.5 million patients receive intensive care treatment each year. 11% of all people who died in Germany (between 2019 and 2022) died with mechanical ventilation (Karagiannidis et al, Lancet Reg Health Eur 2024)! Overtherapy means the excessive use of medical services (diagnostics, therapy) which no longer lead to any relevant improvement in duration (prognosis) or quality of life, and ultimately does more harm than good ("senseless" therapy) or which is anyway not wanted or even rejected by the patient (after appropriate information). Overtherapy disregards all four basic medical ethical principles (see page 1834) and finally represents a burden for the resources of the health system. In a meta-analysis (Cardona-Morrell et al, Int J Qual Health Care 2016) it could be shown that every third patient at the end of his life is still receiving an unjustified therapy in the sense of overtherapy. The problem of overtherapy is also taken into account in a corresponding position paper of the section for ethics of the German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI) and German Society for Medical Intensive Care Medicine and Emergency Medicine (DGIIN) 2021 in Germany.

In palliative situations, decisions must be made about limitation or discontinuation of therapy (so-called "controlled" intensive medicine; WLST: withdrawal of life-sustaining therapy). In this case, the goal of therapy is changed. The goal of therapy is then no longer curative, but palliative (Latin "pallium": the cloak, "palliare": to cover with a cloak [to protect the patient from suffering]; comfort terminal care [CTC]). The term “therapy discontinuation” should be avoided, especially when communicating with relatives, as this could suggest that the patient will no longer be cared for at all from now on. The therapy will continue, just with a different goal! The change of the therapy goal should and must also be documented clearly and unambiguously (e.g. no resuscitation, no intubation) and not only masked with acronyms (DNE: do not escalate, DNR: do not resuscitate, DNACPR: do not attempt cardiopulmonary resuscitation, DNI: do not intubate, AND: allow natural death, CMO: comfort measures only) or any drawings (e.g. "flowers") in the patient´s record for unfounded fear of any legal consequences. For this we use a document (see infobox for content), on which the individual therapy limitations for the patient are clearly documented and signed by the physicians and then filed in the patient´s record. Proper documentation should always be ensured. The documentation sheet on therapy limitation of the section for ethics of the DIVI (available on the homepage of the German Interdisciplinary Association for Intensive Care and Emergency Medicine [www.divi.de]) is analogous and can be recommended.

Therapy limitation
Checklist - part I

- **reasons:**
  - **no more medical indication (e.g. further maximum therapy pointless, dying process has already begun)**
  - **will of the patient (rejects intensive care therapy)**
  - **pronounced frailty (Clinical Frailty Scale [CFS] ≥ 7; see infobox)**
  - **other**
- **advance directive / health care proxy present**