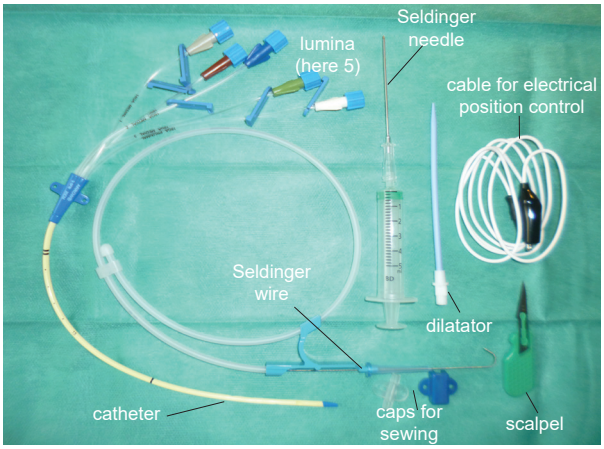


Fig. 015 components of a CVC set

Puncture of internal jugular vein

- lateral positioning of the head
- puncture site
  - based on landmark ("blind technique"):
    - lateral to the palpable carotid artery
      - Normally, the internal jugular vein is located lateral to the common carotid artery. There are, however, a number of abnormal positions so that this rule is not valid in 30% of the cases.
      - Moreover, this rule only applies if the head lies in a straight position. The head is often turned to the side during CVC insertion. In this position the vein is often directly anterior to the artery and therefore ventral instead of lateral to the artery.
      - lead structure: medial edge of the sternocleidomastoid muscle
  - based on sonography (ultrasound guided; at best!)
    - application of a sterile cover over probe (transducer) and cable (A sterile glove as cover is hygienically not sufficient!), use of sterile ultrasound gel or skin disinfectant
    - 7.5 MHz transducer (linear array probe)
    - compression ultrasonography (B-mode image): The vein can be compressed, but not the artery.
    - i.a. exclusion of thrombus
    - In our intensive care unit we almost exclusively perform insertions of CVC or Shaldon catheter into the internal jugular vein only under sonographic control (ultrasound guided): The puncture takes places under visual control and typically requires rarely more than one attempt (even in obese patients). Also, it is not uncommon to incidentally discover a thrombus in the internal jugular vein (especially in case of a previously inlying CVC) which would not be seen otherwise without ultrasonography and which would then be pushed further along by the guide wire or the dilator (risk of pulmonary embolism). One can certainly also drive at night without light: If you know the way, you probably also get to the intended destination. However if your car has headlights, you can also simply switch them on: So you can see exactly where you are going! The use of ultrasound for the insertion of a CVC is also highly recommended in the European Guideline for Interventional Ultrasound 2016 (EFSUMB: European Federation of Societies for Ultrasound in Medicine and Biology).

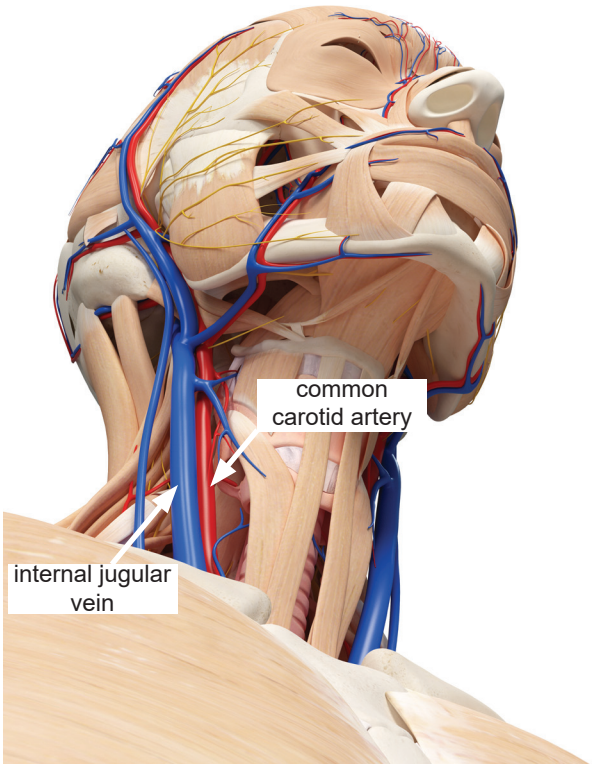
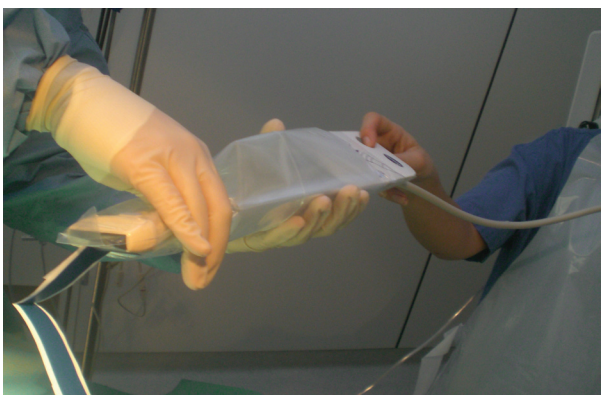
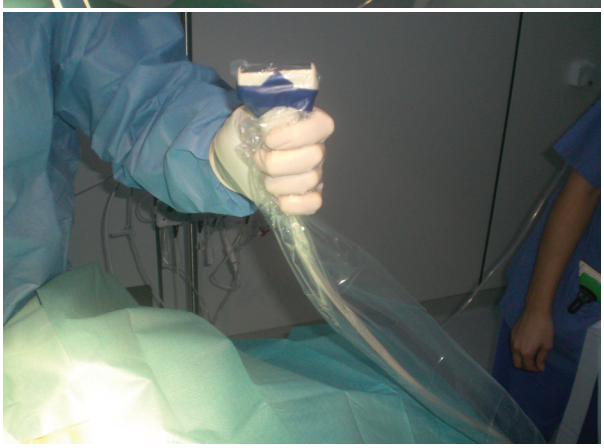


Fig. 016 Schematic representation of the anatomy





Blocking
Central venous catheters

- **Shaldon catheter: 5000 IU of UFH (1ml of 1 vial of UFH a 5ml a 25000IU)**
- **atrial catheter: 15000 IU of UFH (3ml of 1 vial of UFH a 5ml a 25000IU)**
- **port (port-a-cath system): 10ml of normal saline + 2000IU of UFH**
- **CVC: only flush with 20ml of normal saline (without heparin)**
- **CeVOX probe: 500ml of Ringer solution + 5000 IU of UFH (infusion rate 10 ml/h)**

Excursus: Intranasal drug application

Definition

- The drug is absorbed in the olfactory region by the mucous membrane.
- especially recommended if intravenous access is difficult or impossible:
  - seizures (especially in children)
  - pain (especially suitable for children, e.g. for pain treatment in case of burns / scalding [An out-of-hospital placement of an intravenous access is rarely necessary in these cases!)
  - aggressiveness (e.g. intoxicated patient who flails around and can only be held down by several persons [recommendation: ⚠ intranasal application of 15 mg midazolam])
  - heroin intoxication (intranasal application of the antidote naloxone)
- apply drugs with a 2 ml syringe (max. 1 ml per nostril [otherwise it runs back down the throat and would be swallowed]), always spread on both nostrils (larger absorption surface and therefore faster absorption)
- only use highly concentrated drug solutions (no dilutions), e.g. midazolam 5 mg/ml (not 1 mg/ml), ketamine 50 mg/ml or S-ketamine 25 mg/ml
- especially suitable for low-molecular and lipophilic drugs
- phases of absorption:
  - early phase: nasal absorption
  - late phase: gastrointestinal absorption (because a certain amount is always swallowed)
- not effective in sniff or nosebleed (epistaxis)
- The intranasal application of a drug, however, constitutes an off-label-use.

Intranasal drug application: first choice (especially out-of-hospital) in children (especially for treatment of seizures or pain; except for life-threatening cases: here intraosseous access!)

Applicators

- MAD (mucosal atomization device; the most common system): The applicator is inserted into the nose. The drug is then administered intranasally (Fine nozzles at the top cause the atomization).
- Carpuject
- OptiNose
- Accuspray Nasal Automizer

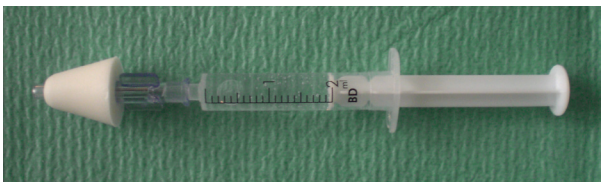


Fig. 033 MAD (mucosal atomization device): for the intranasal application of drugs

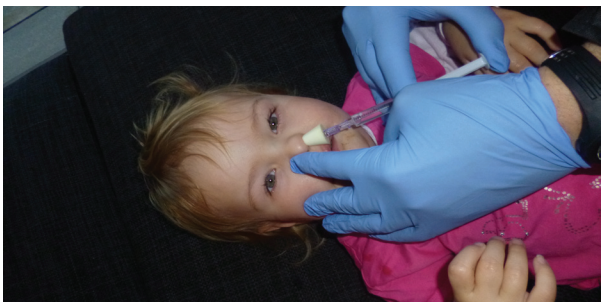


Fig. 034 Today, intranasal administration (here by MAD) is the first choice out-of-hospital drug application in children in emergency cases (exception: lifethreatening situations such as shock or resuscitation → here intraosseous access [no intravenous access] recommended); special thanks to my little daughter Lena

Dosage

- midazolam: 1 ml = 5 mg (always take the highly concentrated vial with 0.5 mg/kg; the solution is rather salty and acidic so that an unpleasant burning sensation in the nose might be felt; often second peak following gastrointestinal absorption)
  - < 50 kg: 2.5 mg (0.5 ml [vial 1ml = 5mg]; 0.2 mg/kg)
  - > 50 kg: 5 mg (1 ml)
- fentanyl: 1 ml = 0.05 mg, 2 µg/kg (0.04 ml/kg; titration)
- sufentanil: 1 ml = 0.05 mg, 2 µg/kg (0.04 ml/kg; titration)
- morphine: 1 ml = 10 mg, 0.1 mg/ml
- ketamine: 1 ml = 50 mg, 50 mg (apply 1 ml); 1-5 mg/kg (0.02-0.10 ml/kg)
- S-ketamine (Esketamin): 1 ml = 25 mg, 25 mg (apply 1ml); 2,5-5.5 mg/kg (0,1-0,2 ml/kg)
- naloxone: 1 ml = 0.4 mg, 0.4-0.8 mg (1-2 ml)
- flumazenil: 1 ml = 0.1 mg
- glucagon (e.g. in the case of hypoglycemia if no venous access is possible): can also be administered intranasally instead of i.v. (dosage: 2 mg dissolved in 1 ml of liquid)

our hospital sufentanil + propofol via perfusor)

- Three substances are required for anesthesia induction:
  - muscle relaxant (often necessary because the intubated emergency patients usually don´t have an empty stomach; ⚠ obligatory for RSI; caution: cannot intubate & cannot ventilate [CICV])
  - analgesic
  - hypnotic (sedative)

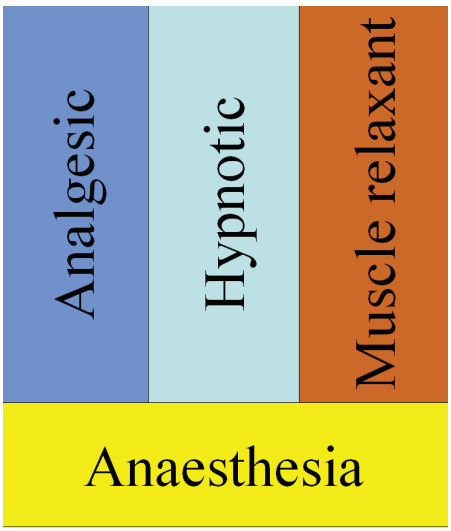


Fig. 069 components of anesthesia

Anesthesia is obligatory for intubation (except in cardiac arrest)!

Muscle relaxants

Definition

- syn.: neuromuscular blocking agents (NMBA)
- substances that are blocking the acetylcholine receptors (postsynaptic, nicotinic) at the neuromuscular junction
- indication: Muscle relaxants are mainly used for anesthesia induction (intubation) as well as perioperatively in the operating room. Muscle relaxants are rarely used in the intensive care unit (except for anesthesia induction for intubation):
  - to facilitate ventilation: You can use them when the patient cannot be sufficiently mechanically ventilated even though the mechanical ventilation has been adapted and the ventilation mode has already been changed. Sufficient analgesia and sedation is always the prerequisite. Muscle relaxants are never an alternative to analgosedation!
  - during invasive procedures (e.g. tracheotomy, exchange of the endotracheal tube)
  - early stage (< 48h) of severe ARDS (Horovitz index [paO_2/FiO_2] < 150 mmHg; but only optional)
- relaxometry: Whenever there is a long term medication with muscle relaxants, the effects should be monitored by relaxometry. Two transcutaneous electrodes are attached to the distal forearm above the ulnar nerve. Then, the muscle contractions of the hand are measured. There are various stimulation patterns. The most commonly used stimulation pattern is TOF ("train of four"), in which a series of 4 stimuli are given at a frequency of 2 Hertz.

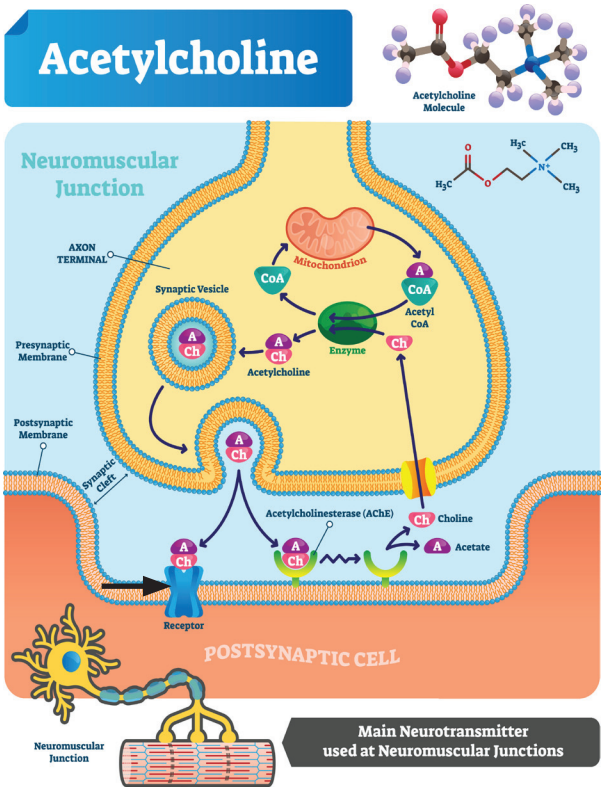


Fig. 070 Muscle relaxants block the acetylcholine receptors (see arrow) of the postsynaptic cell at the neuromuscular junction.

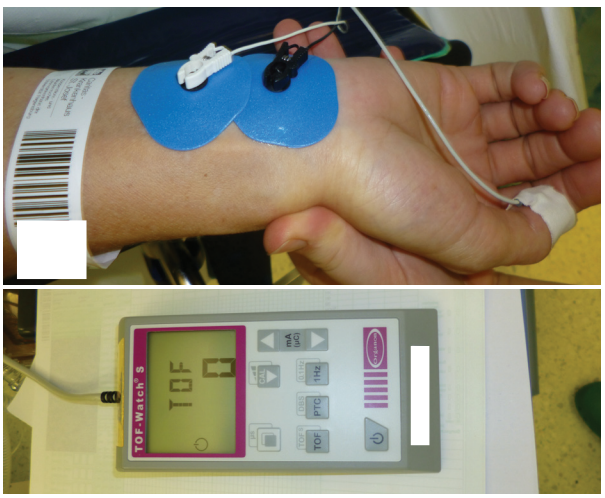


Fig. 071 TOF relaxometry

- expected
- unexpected (mostly in emergency and intensive care medicine)

- If the intubation was difficult, the patient should be handed out an anesthesia emergency card (e.g. at hospital discharge) with the corresponding grade of Cormack-Lehane classification.

study

The Out-of-Hospital Esophageal and Endobronchial Intubations Performed by Emergency Physicians
Timmermann et al, Anesthesia & Analgesia 2007

- prospective observational study
- 149 patients (out-of-hospital intubation by primary emergency physicians on site)
- subsequently evaluated by study physicians (laryngoscopy, esophageal detector device, capnometry)
- ⚠ incorrect intubation in 17%
  - one-sided in 10% (i.e. endobronchial instead of endotracheal)
  - esophageal in 7%
- approximately 3000 deaths in Germany due to incorrect intubation by emergency physicians (statistical projection)

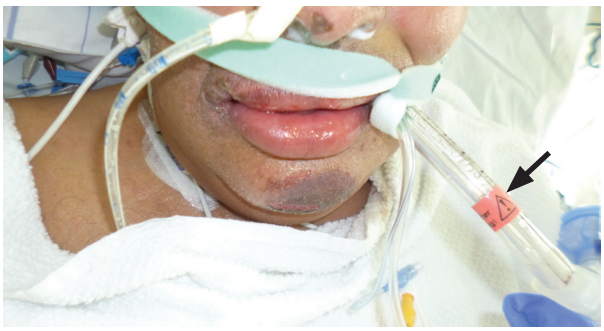
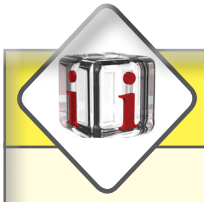


Fig. 102 If a patient was difficult to intubate, the tube is provided with a red warning tape ("difficult airway") in the intensive care unit.

Classifications

- difficulty levels of laryngoscopy
  - prediction by Mallampati classification (beforehand; see infobox)
  - classification by Cormack-Lehane (afterwards; see infobox)
- MACOCHA score: used to identify patients with an increased risk of difficult intubation (according to de Jong et al, AJRCC 2013; see infobox)



Mallampati classification

The patient is asked in a sitting posture to open the mouth and to protrude the tongue as much as possible (without phonation). The score depends on which structures then are visible (base of the uvula, fauces, pillars [the arches in front of and behind the tonsils] and soft palate)

class I	**all the structures (soft palate, uvula [completely], fauces, pillars [both arches]) are visible**
class II	**soft palate, uvula (incompletely, but the major part) and only the arch in front of the tonsils fauces are visible**
class III	**only the soft palate and the base of uvula are visible**
class IV	**only the hard palate is visible**

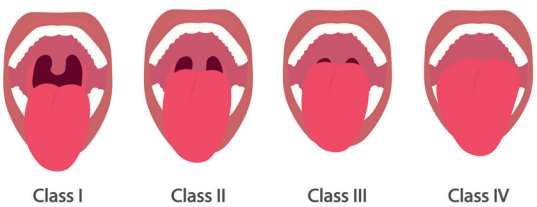
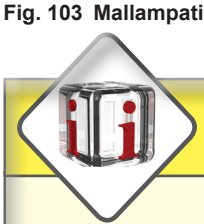


Fig. 103 Mallampati classification



Cormack & Lehane Classification

It classifies the views obtained by direct laryngoscopy based on the structures seen.

grade I	**full view of glottis**
grade II	**only posterior part of glottis or only arytenoid cartilages seen**
grade III	**only epiglottis seen**
grade IV	**neither epiglottis nor glottis seen (only soft palate)**

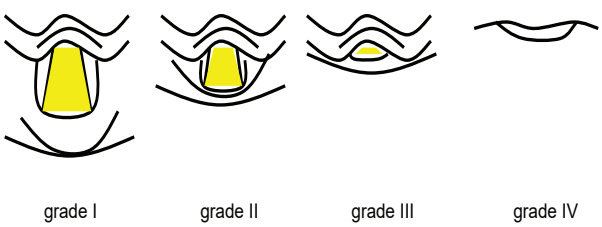


Fig. 104 Cormack-Lehane classification

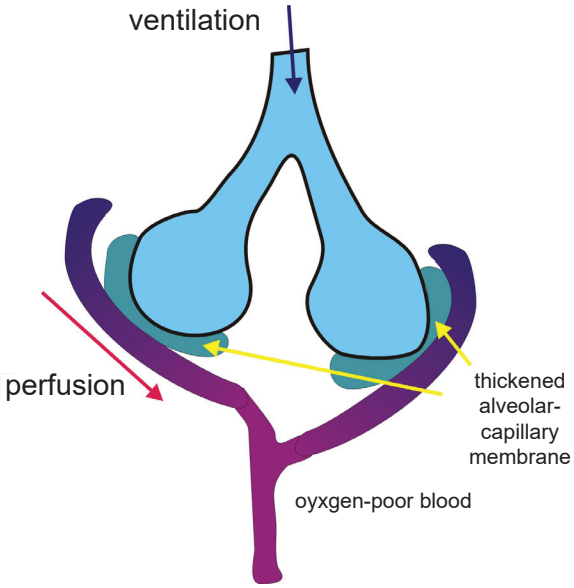


Fig. 171 impairment of diffusion in case of pulmonary edema (thickened alveolar-capillary membrane)

Typical example for a diffusion impairment: pulmonary edema!

Distribution

Definition

- ratio between ventilation (V) and perfusion (Q) in the lung
  - alveolar ventilation (V_A) in adults: 4-5 l/ min
  - lung perfusion (Q; = cardiac output): 5 l/min
- standard value (ventilation-perfusion ratio): V/Q = 0.8
- The ventilation-perfusion ratio determines the gas exchange in any lung area.
- gravity dependent changes:
  - Perfusion increases from apical to basal (see 3-zones-model of perfusion according to West [page 95].
  - Ventilation decreases from apical to basal (see page 90). That is because the pleural pressure increases due to gravity and the weight of the lung from apical to basal so that the alveoli get more and more compressed.
- 3 zones (annotation: This applies to the upright position. In supine position the same changes apply from ventral to dorsal instead of from apical to basal.):
  - zone I (apical zone): ventilation perfusion ratio V/Q ↑ (> 0.8) because
    - ventilation (V) ↑
    - perfusion (Q) ↓
  - zone II (middle zone): ventilation perfusion ratio V/Q normal (0.8) because
    - ventilation (V) normal
    - perfusion (Q) normal
  - zone III (basal zone): ventilation perfusion ratio V/Q ↓ (< 0.8) because
    - ventilation (V) ↓
    - perfusion (Q) ↑

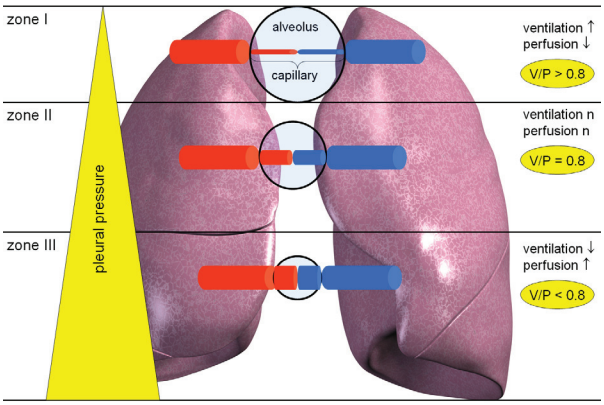


Fig. 172 3-zones-model of ventilation and perfusion in one figure projected on top of each other: Ventilation decreases from apical to basal, perfusion increases from apical to basal. Both is caused by gravity. In zone I (apical zone) the ventilation is increased, the perfusion is decreased. Therefore the ventilation perfusion ratio V/Q here is increased (> 0.8 [dead space]). In zone II (middle zone) both ventilation and perfusion and therefore the ventilation perfusion ratio V/Q are normal (0.8). In zone III (basal zone) the ventilation is decreased and perfusion increased. Accordingly the ventilation perfusion ratio V/Q here is decreased (< 0.8 [shunt]). This applies to the upright position. In supine position the same changes apply from ventral to dorsal instead of from apical to basal.

Euler-Liljestrand mechanism

- named after the Swedish physiologist Ulf von Euler (1905-1983) and the Swedish pharmacologist Goeran Liljestrand (1886-1968)
- syn.: hypoxic pulmonary vasoconstriction (HPV)
- Regional alveolar hypoventilation causes reflexive vasoconstriction in the affected area.
- significance: Blood from poorly ventilated lung areas is redistributed to better ventilated areas. The Euler-Liljestrand mechanism is a physiological mechanism to reduce shunt (which is the main pathomechanism of lung failure): Alveoli which are not ventilated any longer should not been perfused any longer.
- Hypocapnia (direct vasodilatation also in hypoxic areas) and hypercapnia (direct vasoconstriction in well-ventilated lung areas) inhibit the Euler-Liljestrand mechanism.
- The Euler-Liljestrand mechanism may reduce shunt a little, but not completely: Lack of perfusion in a non-ventilated area of the lung (e.g. pneumonia in the right upper lobe) would cause a massive increase of the right ventricular afterload (increase of pulmonary artery pressure; similar to pulmonary embolism) and lead to an acute right heart failure.

Extreme cases

- V/Q < 0.8: shunt (Lung areas are perfused, but not ventilated.), especially in West zone III
- V/Q > 0.8: dead space (Lung areas are ventilated, but not perfused.), especially in West zone I

on; VC-CMV: volume-controlled continuous mechanical ventilation)

Pressure-controlled ventilation (PCV)

- standard mode of ventilation in Europe
- There is no evidence that pressure-controlled ventilation is better than volume-controlled ventilation (i.a. Esteban et al, Chest 2000; Branson et al, Resp Care 2007; Chacko et al, Cochrane Database Syst Rev 2015).
- The ventilator delivers the breathing gas during the set inspiratory time with a constant, preset pressure (with a decelerating flow).
- pressure constant ventilation (constant pressure levels): The pressure is maintained during the whole inspiration.
- The resulting volume (tidal volume [V_T]) is determined by:
  - pressure difference ("driving pressure") between the inspiratory pressure (IPAP [inspiratory positive airway pressure]) and the expiratory pressure (PEEP [positive end-expiratory pressure])
  - resistance and compliance of the respiratory system (lung, chest)
  - inspiratory time
- The ventilation pressure determines the tidal volume.
- lower risk of barotrauma (e.g. pneumothorax) than with volume-controlled ventilation since pressures peaks are avoided
- In the beginning of the respiratory cycle the set pressure is tried to be achieved with a high flow. In the further course the flow is decreased by the internal control (decelerating flow) so that pressure peaks are avoided. In a pressure-controlled ventilation there is no distinction between peak pressure and plateau pressure, nor is there any plateau.
- ventilation parameters:
  - primary (independent): pressure (ventilation pressure)
  - secondary (dependent): volume (tidal volume [V_T])
- settings:
  - inspiratory pressure (IPAP [inspiratory positive airway pressure])
  - PEEP (positive end-expiratory pressure)
  - respiratory rate
  - I:E ratio
  - RMV monitoring
- pressure alarm for monitoring of patient-induced pressure increases (e.g. coughing, "pressing")
- A drop of the tidal volume can be caused by:
  - airway obstruction, kinking of tube, cuff hernia
  - increased airway resistance
  - decreased elasticity (compliance) of the lungs or chest
  - coughing / "pressing" of the patient

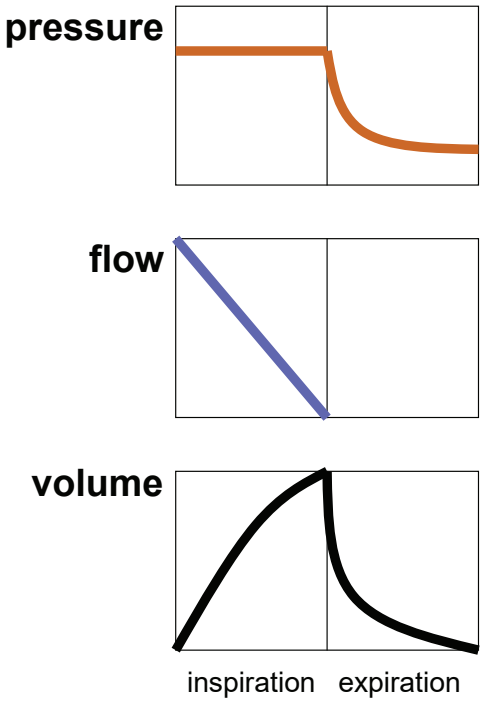


Fig. 196 pressure-controlled ventilation (PCV)

Volume-controlled ventilation (VCV)

- standard mode of ventilation in America (USA)
- The ventilator delivers a preset tidal volume (V_T) within the set inspiratory time (with a constant flow).
- syn.: IPPV (intermittent positive pressure ventilation)
- volume constant ventilation (constant volume level)
- The resulting pressure (ventilation pressure) is determined by:
  - tidal volume
  - resistance and compliance of the respiratory system (lung, chest)
  - inspiratory time
- The tidal volume determines the ventilation pressure.
- ventilation parameters:
  - primary (independent): volume (tidal volume [V_T])
  - secondary (dependent): pressure (ventilation pressure)
- settings:
  - tidal volume (V_T)
  - respiratory rate
  - I:E ratio
  - inspiratory flow
    - flow rate (common approximately 30 l/min)
      - velocity of the ventilator emitting the breathing gas during inspiration (syn.: peak flow; unit: l/min)
      - The higher the inspiratory flow, the higher is the ventilation pressure (peak pressure). High flow rates induce turbulences which heighten the airway resistance.
    - flow profiles (patterns)
      - constant ("rectangle" flow; standard today)

creasing diameter (note: Nowadays however, single-dilator systems [e.g. Ciaglia Blue Rhino] are the standard.)

- always under bronchoscopic control (alternative: ultrasound control [linear transducer; i.a. Alansari et al, Crit Care 2015; Gobatto et al, J Crit Care 2015] possible; in the TRACHUS study [Gobatto et al, Intensive Care Med 2016] it was shown that with exclusively ultrasound control there were not more complications than under exclusively bronchoscopic control.)
- insertion of the tracheal cannula

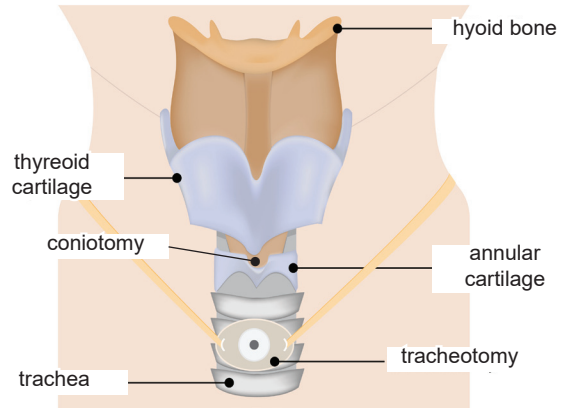


Fig. 290 Schematic representation of the anatomy: Tracheotomy is performed between the 2nd and 3rd tracheal ring. Coniotomy, on the other hand, is performed further cranially: between the thyroid and cricoid cartilage (cricothyreoid membrane).

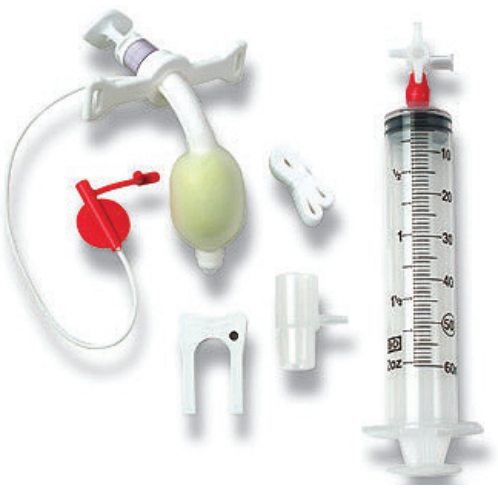
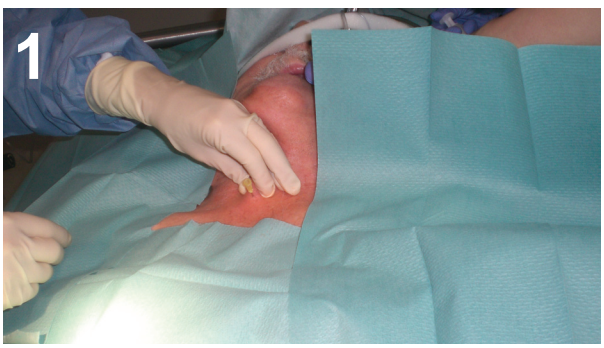
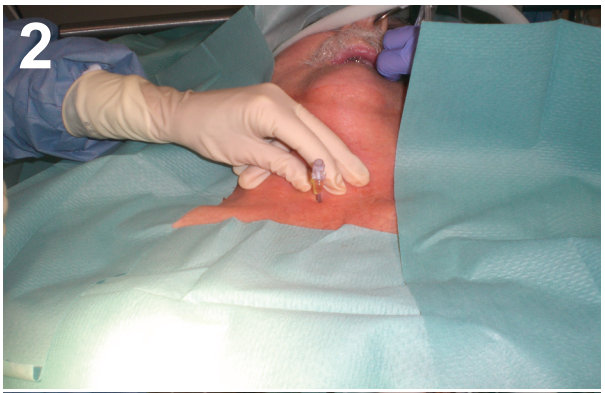
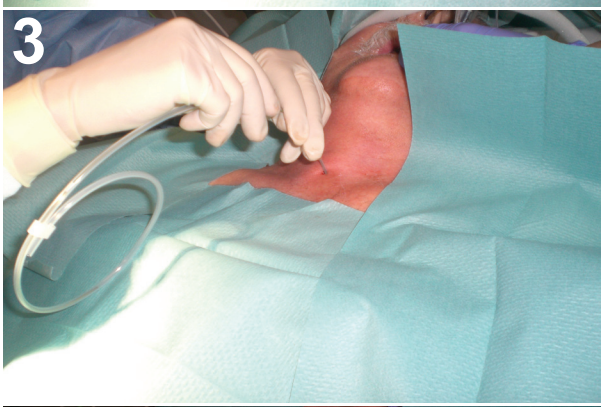
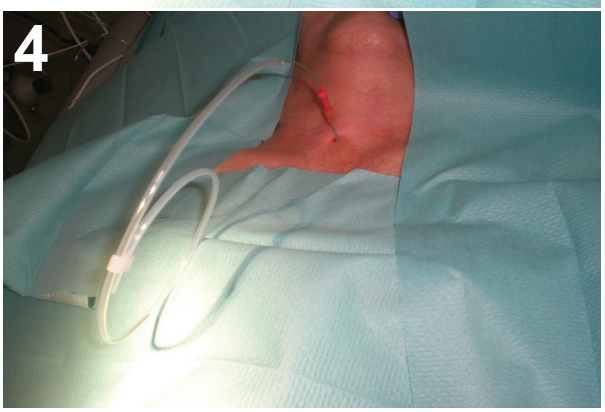


Fig. 291 tracheal cannula (tracheostomy tube) with accessories [32]









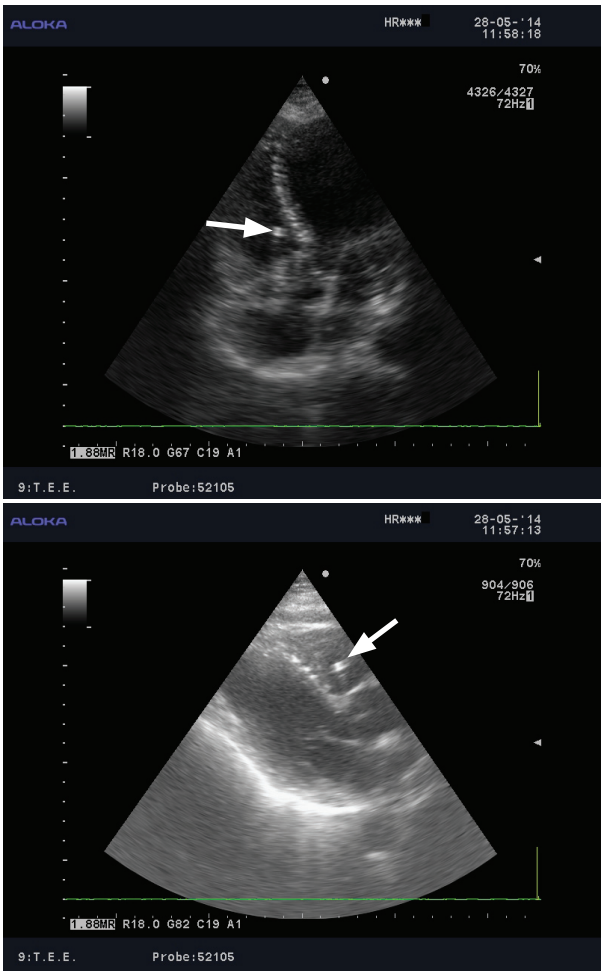


Fig. 380 As an option in difficult PAC insertion, echocardiography is helpful for orientation and control: Here, for example, the tip of the PAC is located in the right ventricle (arrow).

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.

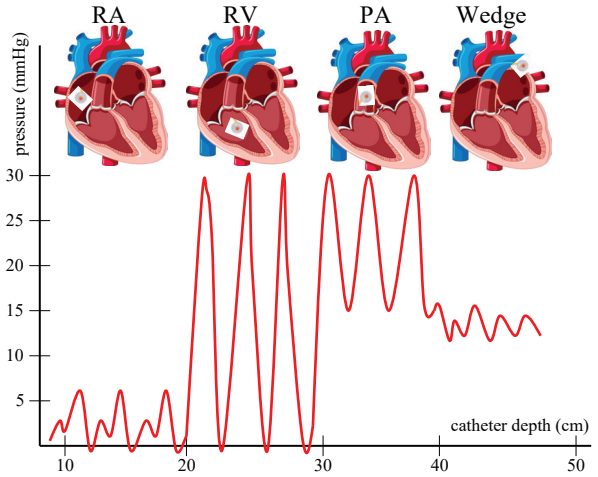


Fig. 381 the different pressure curves when the pulmonary artery catheter is inserted (RA: right atrium; RV: right ventricle; PA: pulmonary artery; Wedge: PCWP)

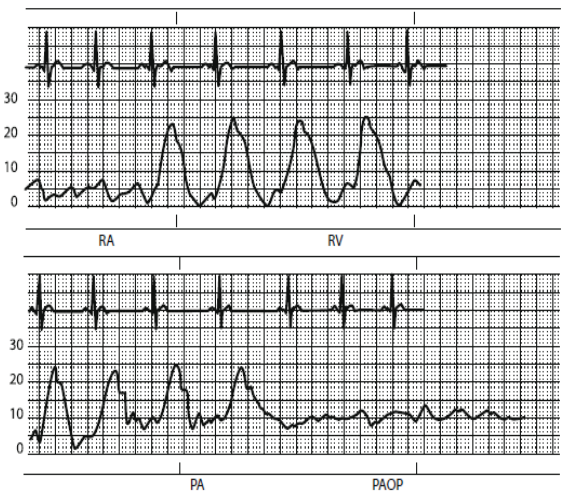


Fig. 382 pulmonary artery catheter: pressure curves (top RA, then RV; bottom PA, then wedge position [PAOP = PCWP]) [14]

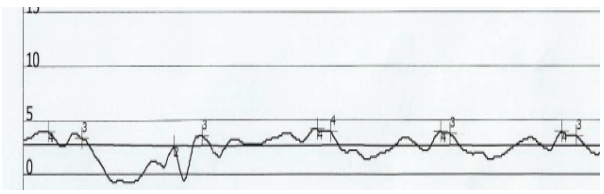


Fig. 383 pressure curve of the right atrium (RA): typical tripartite, low pressures (2-6 mmHg)

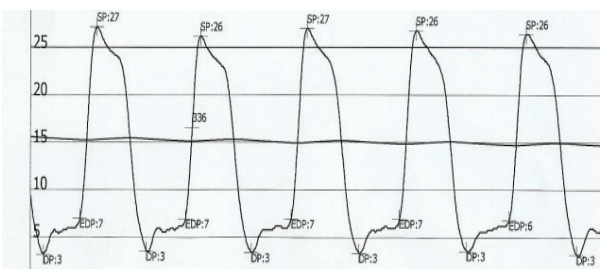


Fig. 384 pressure curve of the right ventricle (RV): systolic pressure 15-30 mmHg, diastolic towards 0 mmHg (typical for a ventricular pressure curve)

goes mainly into the cells [risk of cerebral edema]; therefore restrictive use [at best still in hypernatremia])

no infusion solutions containing glucose (e.g. glucose 5%) alone for volume therapy (increased risk of cerebral edema)!

Hypertonic crystalloids (hypertonic saline [NaCl 3%])

- indication: hyponatremia
- preparation:
  - 1000 ml saline 0.9% + 7 amp. saline 20% a 20 ml (9g [1000ml normal saline] + 7 x 4g [7 x saline 20% a 20ml] = 37g in 1140ml → 3g in 100ml [3%]) or
  - 500 ml saline 0.9% + 3 ½ amp. saline 20% (a 20ml)
- 1-2 ml/kg/h according to sodium deficit
- 1ml saline 3% = 0.5 mmol sodium

Colloids

- Greek: "kolla" (glue)
- syn.: plasma expander
- also contain macromolecules
- intravascular persistence (almost no migration into the interstitium [especially not in cases of intravascular hypovolemia; however, in patients with capillary leak, e.g. during sepsis, colloids also migrate into the interstitium to a considerable extent due to the disturbed vascular barrier])
- history: first use by James Hogan in patients with hemorrhagic shock in 1915 (The intravenous use of colloidal [gelatin] solutions in shock; JAMA 1915)
- representatives:
  - artificial colloids
  - natural colloids

Artificial colloids

- hydroxyethyl starch
- gelatin
- dextran

Hydroxyethyl starch (HES)

Definition

- a highly branched starch: amylopectin (polysaccharide consisting of linked glucose chains with of 1,4α-glycosidic bonds) with hydroxyl groups at C_2 and C_6 (The hydroxylation of the glucose molecules is used to modulate the pharmacological degradation rate.)
- production from corn or potato starch
- types:
  - isooncotic: HES 6%
  - hyperoncotic: HES 10%
- molecular weight between 70,000-450,000 Dalton
- substitution degree:
  - proportion of glucose units that are hydroxylated (e.g. 0.5: 50%)
  - between 0.4-0.7
  - The higher the degree of substitution, the lower the rate of degradation and thus the longer the half-life.
- substitution pattern:
  - ratio of glucose units substituted in C_2 and C_6 position
  - C_2/C_6-ratio: C_2 compounds are cleaved slower than C_6 compounds by the enzyme α-amylase. The more C_2 compounds, the lower the rate of degradation and the longer the half-life
- example HES 6% 130/0.4: solution with
  - HES concentration of 6%
  - molecular weight of 130000 D
  - substitution degree of 0.4
- maximum daily dose:
  - HES 10%: 20 ml/kg bw
  - HES 6%: 33 ml/kg bw
- contraindicated in creatinine > 2.0 mg/dl
- intravascular residence time: 4-5 hours (HES 6%)

Representatives

- isooncotic:
  - HES 6% 70/0.5 (Rheohes)
  - HES 6% 130/0.4 (Voluven, Volulyte, Tetraspan)
  - HES 6% 200/0.5 (Hemohes 6%, HES-Steril 6%)
  - HES 6% 450/0.7 (Plasmasteril)
- hyperoncotic: HES 10% 200/0.5 (Hemohes 10%, HES-Steril 10%): no longer used today; be aware: VISEP study (see page 1098): increased rate of acute kidney failure

Fig. 439 HES 6% [8]

Side effects

- disturbance of platelet function (inhibition of platelet aggregation ["coating"], acquired von Willebrand-Juergens syndrome), possibly bleeding
- α-amylase ↑ (5-fold)
- falsely high measurement of fibrinogen (= factor I)
- disturbance of renal function
  - pathomechanisms:
    - reabsorption of HES macromolecules in the tubular cells of the kidney with consecutive osmotic nephrosis
    - tubular damage by hyperviscous urine
  - contraindicated in creatinine > 2.0 mg/dl (Half-life increases from 36 to 88 hours!)
- allergic reaction (often difficult diagnosis; tryptase in serum ↑)
- pruritus (with prolonged use; HES is stored in the reticuloendothelial system [RES])

- suctioning for max. 5 seconds
- maximum suction: 0.2 mbar

- keep warm (wrap in a warmed towel; switch on the heating of the neonatal crash cart [37.5°C]; after successful resuscitation, however, switch off the heating in the post-resuscitation phase)
- no shaking (be aware of shaking trauma with rupture of the bridging veins and consecutive subdural hematoma [for picture of an autopsy specimen see page 1431])
- cutting the cord after 1 minute at the earliest (10 cm away from the child)
- in refractory cases consider extracorporeal life support (ECMO) at an early stage

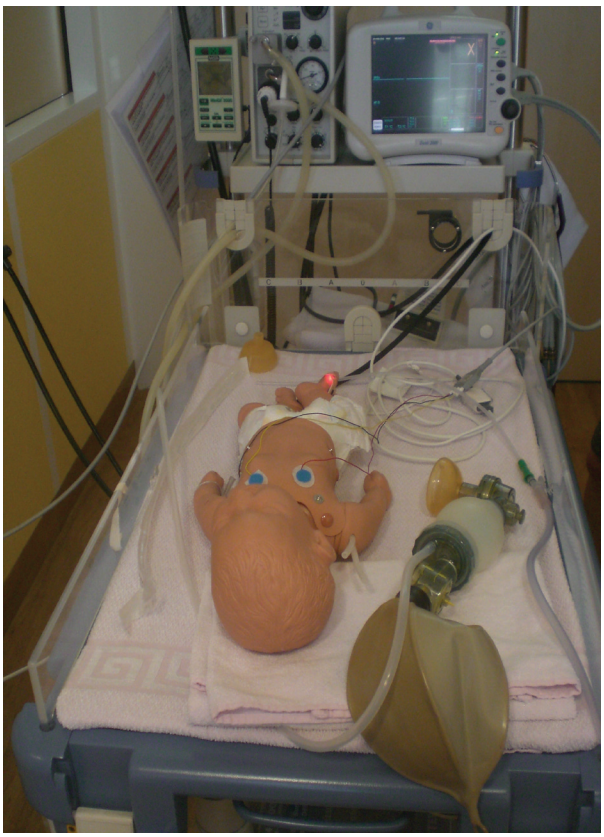


Fig. 503 neonatal crash cart

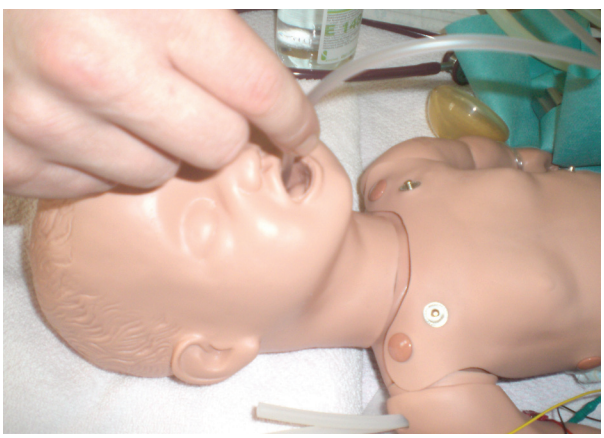


Fig. 504 suction: only if the airways are blocked, only orally (not nasally) and only in the anterior part of the mouth!

Chest compression

- ⚠ indication: heart rate < 60/min (despite adequate mask ventilation) and absence of vital signs (applies until puberty)
- techniques:
  - two-thumb technique (both thumbs; ⚠ more effective [Udassi et al, Resuscitation 2010]!)
  - two-finger technique
- pressure point: lower third of the sternum
- depth of pressure:
  - 1/3 of the diameter of the chest
  - depth 4-5 cm (< 12 months: 4 cm, > 12 months: 5 cm)
  - One must always press relatively deeply ("tennis ball" deep). Mostly, out of fear of hurting the child, unfortunately only much too shallow pressure is applied! The chest of newborns is very elastic.
- ratio chest compression to ventilation:
  - newborns (first 4 weeks): 3:1 (note: According to the recommendation of the GRC [German Resuscitation Council] 2018 and of the ERC [European Resuscitation Council] 2021, the ratio 3:1 should only be applied immediately postnatal, i.e. in the delivery room, in emergency medical service or in the case of a home birth. Otherwise, the ratio 15:2 should also be applied in the newborn age.)
  - children (from 4 weeks [or from leaving the delivery room] until puberty [12-14 years]; new ERC 2021: up to the age of 18): 15:2
  - from puberty signs (e.g. pubic hair, breast development) according to ERC 2015 or from the age of 18 according to ERC 2021: 30:2 (like adults [Adolescents who look like adults can also be treated according to the adult algorithm.])
- ⚠ even when intubated stop chest compressions during mechanical ventilation (no chest compressions during mechanical ventilation)
- frequency:
  - newborns: 120/min (2 times per second)
  - infants / children: 100-120/min (like adults)
- mechanical resuscitation alternatives (e.g. LUCAS): not recommended for children

The most important thing in resuscitation of newborns is ventilation and not chest compression! Therefore the ratio chest compression to ventilation with 3:1 instead of 15:2 is also shifted in favor of ventilation!

INCEPTION study

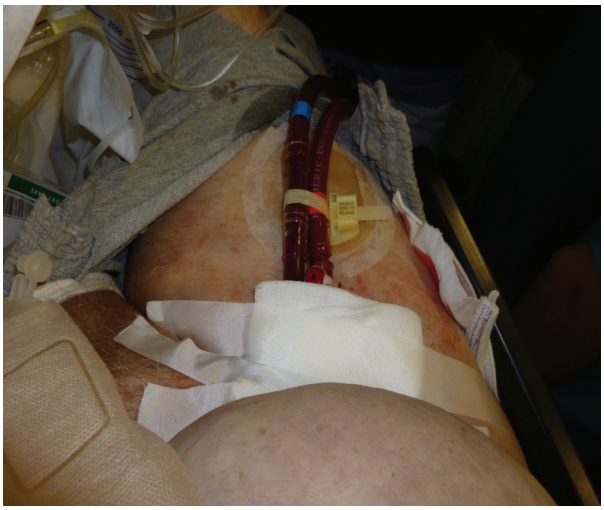
Early Extracorporeal CPR for Refractory Out-of-Hospital Cardiac Arrest
Suverein et al, N Engl J 2023

- multicenter randomized controlled study (Netherlands)
- 134 patients with witnessed (bystander CPR carried out) refractory (no ROSC within 15 minutes) out-of-hospital cardiac arrest (r-OHCA) with ventricular fibrillation
  - with va-ECMO (eCPR)
  - without va-ECMO (conventional resuscitation)
- ☹ result: no difference in the primary endpoint (survival with favorable neurological outcome [CPC score 1-2 P.] after 30 days)

ECMO is usually installed with ongoing resuscitation in the emergency room of the target hospital. It is also already possible to implant ECMO out-of-hospital. Corresponding projects are currently already being carried out, including the RECA study (Regensburg ECLS for Cardiac Arrest): Here, in the event of a cardiac arrest, the ECMO team (anesthesiologist and perfusionist) is already requested in the emergency medical service in parallel with the emergency physician. Indications for prehospital ECMO implantation here are:

- observed cardiac arrest including already performed bystander CPR
- still no ROSC after 5-10 minutes of CPR
- age < 70 years (relative; the biological age is decisive)

The duration of cannulation (veno-arterial; mostly bifemoral) and ECMO connection is approximately 10-15 minutes. At best, the cannulation is performed with ultrasound control. 5000 IU of unfractionated heparin is administered intravenously. From then on, circulation with a cardiac output of 4-6 l/min is available again and the patient is transported to the hospital. There, coronary angiography is usually performed (especially if CHD is suspected) immediately, unless another clear cause (such as pulmonary embolism) for cardiac arrest is found. Hypothermia can be started immediately after connection to the ECMO system. ECMO also increases coronary perfusion. However, in the case of hypoxemic resuscitation (e.g. non-observed cardiac arrest with a correspondingly unclear duration of hypoxia), the use of ECMO is certainly questionable: It can usually restore circulation, but ultimately the whole thing usually ends in a pronounced brain damage. In this context, attention should also be paid to harlequin syndrome (harlequin: stage character of the fool; syn.: watershed phenomenon, differential hypoxia phenomenon; "blue head & red legs", "north-south" syndrome): This syndrome occurs when a va-ECMO has been implemented in the context of cardiac arrest and suddenly ROSC (return of spontaneous circulation) occurs with the patient's own cardiac actions restarting: In this case there is a competing blood flow from the retrograde flow of va-ECMO and the antegrade flow of the patient´s own heart. A watershed then usually is formed in the area of the distal aortic arch. The result is that the legs are well perfused with blood ("red legs"), but the coronaries and the head ("blue head") are not. Myocardial ischemia and hypoxemic brain damage may occur.



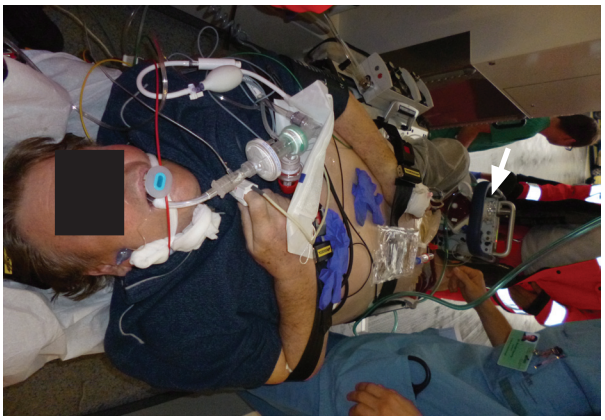


Fig. 551 out-of-hospital implantation (in the emergency vehicle) of a va-ECMO (here Cardiohelp [Maquet]; cannulation of the femoral artery and vein on the right) during resuscitation of a 42-year-old man. With ECMO a sufficient circulation could be established despite patient's cardiac arrest. Coronary 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.

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 division can also be made into:

- 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).

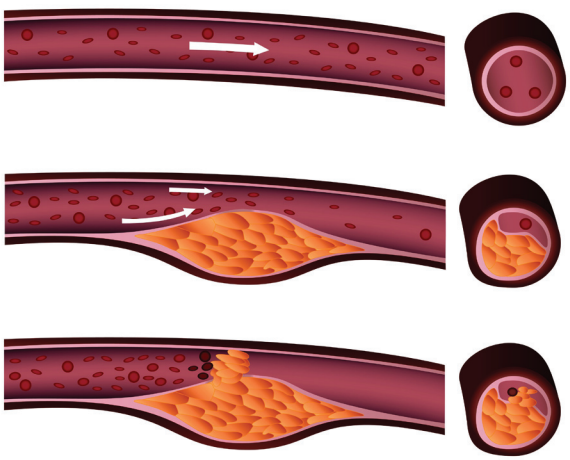


Fig. 570 Pathophysiology of acute myocardial infarction: Plaque rupture and consecutive thrombotic occlusion of the coronary vessel occur.

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 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 sympathicoadrenergic activation). In 30% an acute myocardial infarction occurs in previously asymptomatic patients (in the sense of a first manifestation of CHD). Unfortunately, it is still the case in Germany that despite all the discussion about the superiority of thrombolysis or PCI, 40% of all STEMI patients do not receive any reperfusion therapy at all. According to data from the German Myocardial infarction Registry 2013, however, the proportion has decreased to 10%

Epidemiology:
STEMI (1/3) ↓
NSTEMI (2/3) ↑

- causes:
  - ventricular filling too low (preload too low; Impella depends on preload) → fluid administration (⚠ The pump sucks relatively often on the wall, so that fluid should be administered generously, provided that the gas exchange allows it!)
  - incorrect position → repositioning (under echocardiographic control)
  - right ventricle failure
- consequences:
  - The Impella flow is less than expected. There is an average expected flow rate for the respective Impella version for each performance level which can be found in the corresponding tables of the company.
  - only insufficient circulatory support
  - hemolysis

• heparin perfusor (UFH) according to target-ACT 160-180 seconds or target-PTT 50-70 seconds (if HIT II: argatroban systemically [but not locally in the purge solution; here then only glucose without heparin])

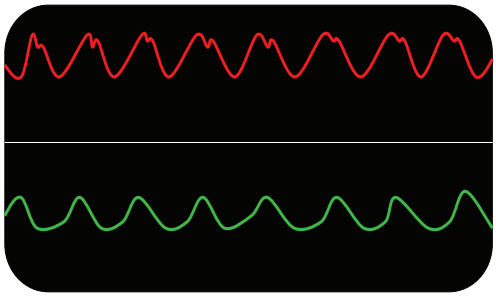


Fig. 645 curves on the display of the control console monitor: above (red) the placement signal, below (green) the motor current curve. The placement signal is configured correctly to be pulsatile and aortic, i.e. the diastolic pressure is significantly greater than zero. The position of the pump is correct. The motor current curve is also normally pulsatile.

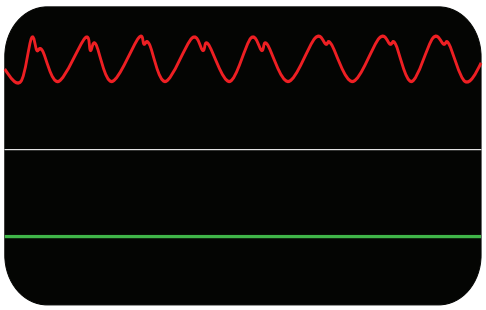


Fig. 646 The motor current curve (green) is flat, i.e. both openings (inlet and outlet) are in the same area. The placement signal (red) is configured aortically, i.e. both openings are in the aorta. The pump has slipped out of the left ventricle (most common cause: Valve was not screwed and shut.) and must be pushed forward. Procedure: reduction of performance level to p2, increase in catecholamines, then repositioning under echocardiographic control

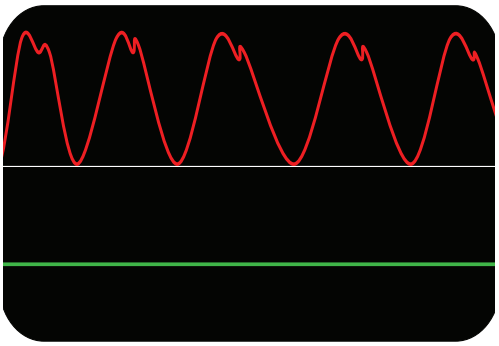


Fig. 647 The motor current curve (green) is flat, i.e. both openings (inlet and outlet) are in the same area. The placement signal (red) is configured ventricularly (diastolic blood pressure to zero), i.e. both openings are in the left ventricle. The pump has slipped too far into the left ventricle and must be withdrawn. Procedure: reduction of performance level to p2, increase in catecholamines, then repositioning under echocardiographic control

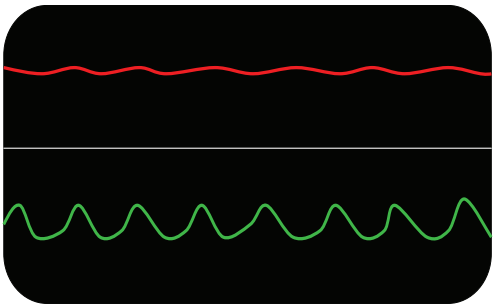
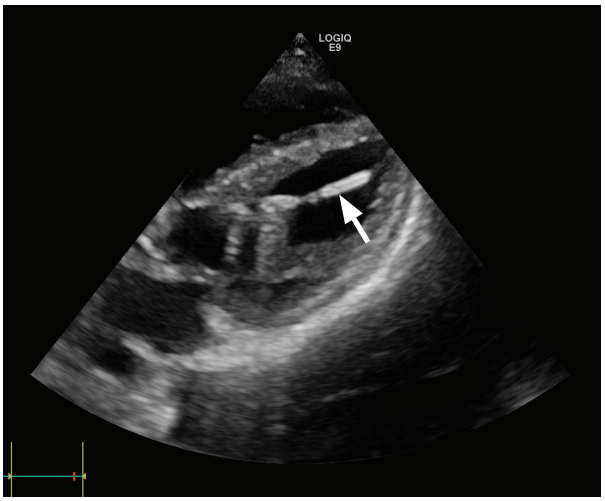


Fig. 648 The motor current curve (green) is normally pulsatile, but the placement signal (red) is flat. This is because the ejection fraction of the left ventricle is severely reduced. The lower the ejection fraction, the lower the pulsatility. Most of the work here is done by the pump which is also correct because the left ventricle should be relieved.



Efficacy
Flow rates (cardiac output [CO])

- IABP: 0.5 l/min
- Impella
  - Impella 2.5: 2.5 l/min
  - Impella CP: 4.0 l/min
  - Impella 5.0: 5.0 l/min
- Tandem Heart: 4 l/min
- HeartMate PHP: 4-5 l/min
- mini-va-ECMO systems (Lifebridge, Cardiohelp): 4-6l/min (almost complete circulatory replacement!)

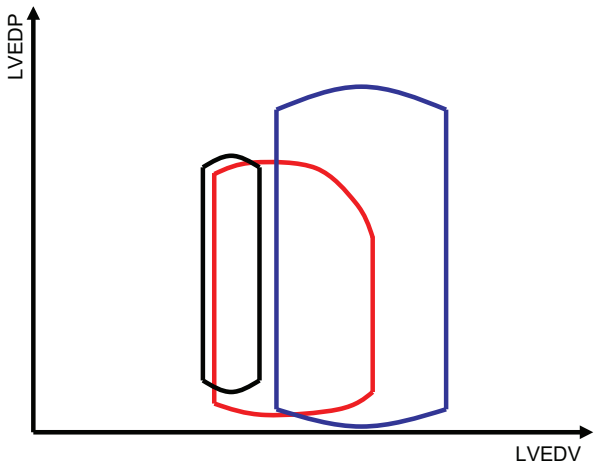


Fig. 657 Various working diagrams of the left ventricle (syn.: pressure-volume relationships; for basic principles see page 215) are shown. The area under the curve corresponds to the stroke work (syn.: pressure-volume work). The higher the stroke work, the higher the afterload and therefore the total oxygen turnover. It can be seen that the stroke work under Impella (black) is significantly lower than without any mechanical support (red). With ECMO (blue; veno-arterial: e.g. Lifebridge, Cardiohelp) the stroke work is even increased (due to the retrograde flow in the aorta)! The afterload for the left ventricle is reduced by Impella and increased by va-ECMO. For this reason, va-ECMO is often used in combination with the Impella (va-ECMO + Impella = ECmella).

va-ECMO increases the left ventricular afterload which is disadvantageous in cardiogenic shock!

meta-analysis

Percutaneous short-term active mechanical support devices in cardiogenic shock: a systematic review and collaborative meta-analysis of randomized trials
Thiele et al, European Heart Journal 2017

- 149 patients with cardiogenic shock
  - with use of devices for mechanical circulatory support (Impella, Tandem-Heart, va-ECMO)
  - without use of these devices (controll group)
- result: devices
  - improvement in hemodynamics (MAP ↑, PCWP ↓, lactate ↓)
  - 😕 no reduction in mortality

ECMO-CS study

Extracorporeal Membrane Oxygenation in the Therapy of Cardiogenic Shock
Ostadal et al, Circulation 2022

- multicenter randomized controlled study
- 117 patients with rapidly deteriorating or severe (SCAI classification D/E) cardiogenic shock (mean age: 67 years; in 74% men; in 51% STEMI as cause)
  - with va-ECMO
  - without va-ECMO (conservative; note: A later switch [crossover] to the va-ECMO group as bailout was allowed, which was also very common with 39%.)
- 😕 result: primary composite endpoint (death, resuscitated circulatory arrest, implementation of another mechanical device for circulatory support after 30 days) → no difference

mechanical circulatory support (in cardiogenic shock): no (positive) randomized controlled studies (still purely experimental!) ESC: also only IIB recommendation

Ventricular Assist-Devices (VAD)

Definition

- ventricular mechanical support systems
- surgical (cardiothoracic) implantation mostly via a combination of partial hemisternotomy (in the upper region) and an anterolateral mini-thoracotomy
- Due to the declining number of heart transplants, more and more VADs are being implanted (e.g. 350 in Germany in 2021). Gold standard, however, is the heart

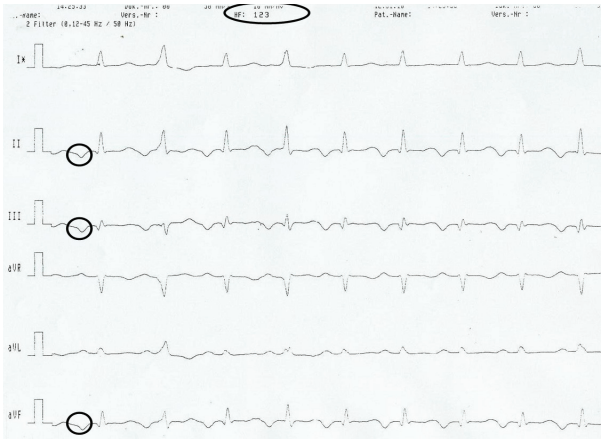


Fig. 697 PJRT (permanent junctional reciprocating tachycardia): The relatively (for a tachycardia) slow heart rate, the negative P waves in II, III and aVF as well as the retrograde P wave (behind the QRS complex) are conspicuous.

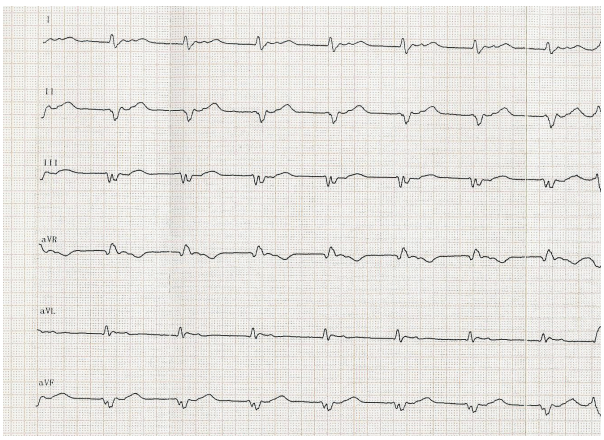
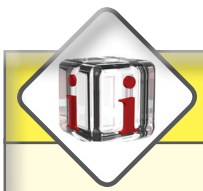


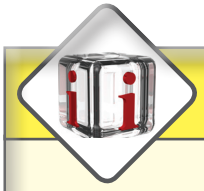
Fig. 698 PJRT (permanent junctional reciprocating tachycardia): retrograde P waves which are negative in II, III, aVF at (for tachycardia) relatively slow heart rate of only 112/min



DD regular narrow complex tachycardia based on the P wave

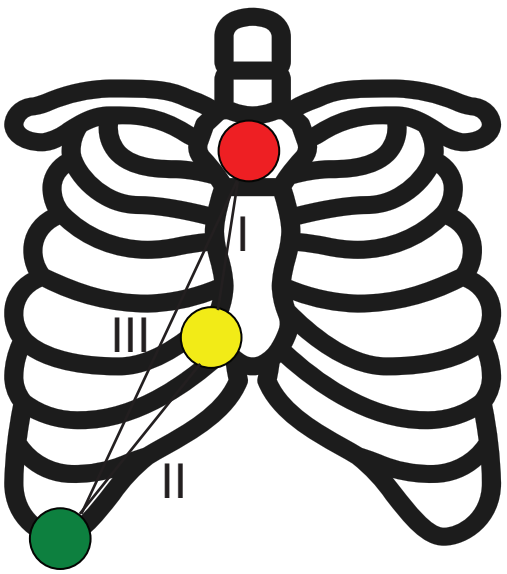
- P wave before the QRS complex → sinus tachycardia
- no P wave → AV node reentry tachycardia
- P wave after the QRS complex → orthodromic AV reentry tachycardia, PJRT

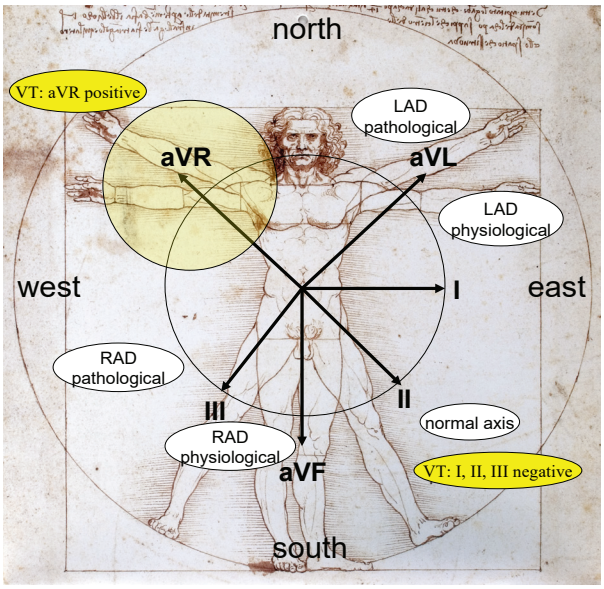
The best way to assess atrial actions is to use the Lewis lead!



Lewis lead

- definition:
  - a modified 12-lead ECG derivation with which one can better assess the atrial excitation (atrial actions; P wave discrimination)
  - named after the British cardiologist Thomas Lewis (1881-1945; originally developed to better detect atrial fibrillation waves)
- procedure (goes very quickly!): You apply a normal 12-lead ECG (note: also possible with the monitor ECG). The chest leads remain unchanged. The limb leads are changed at 3 of 4 positions:
  - electrode right arm (red) → to the manubrium of the sternum
  - electrode left arm (yellow) → to the right of the lower egde of the sternum (5th ICS parasternal right)
  - electrode left leg (green) → to the lower right costal arch
  - electrode right leg (black; "mass") → remains
- interpretation: The lead I is called Lewis lead. It runs exactly through the atrium. This is the best lead to identify and assess atrial actions because this lead is parallel to the atrial vector. However, it is perpendicular to the ventricular vector so that the atrial actions can be assessed better, the ventricular actions, however, can be assessed worse.
- indication:
  - unclear basic rhythm (possibly P waves recognizable in the Lewis lead?)
  - unclear regular tachycardia
    - unclear regular narrow complex tachycardia (possibly flutter waves recognizable in the Lewis lead?)
    - unclear regular wide complex tachycardia (differential diagnosis VT / SVT: possibly AV dissociation as evidence of VT recognizable in the Lewis lead?)





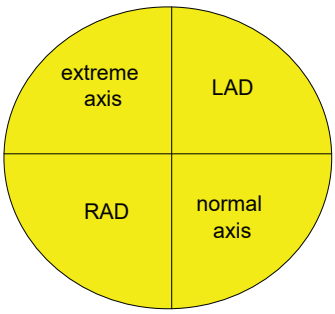


Fig. 709 Cabrera circle for determining the electrical axis (location type) using the limb leads (LAD: left axis deviation; RAD: right axis deviation): In ventricular tachycardia you often find an extreme axis and especially often a completely different axis as in the tachycardia-free ECG. The vector points to an area where the axis is normally never found ("no man´s land"; yellow circle). If you compare the Cabrera circle with a compass, the axis of a VT is often located in the north-west. In case of VT aVR is often positive and I, II and III negative. By the way, the distinction between indifference and steep type, which is often difficult in everyday clinical practice, should be noted: In indifference type there is I > III and aVL positive, in the steep type there is III > I and aVL negative. With an S in I and a Q in III you have a SIQIII type: Here the T wave must also be negative (inverted) in III by definition. If I, II and III show both an S and R, the heart axis cannot be determined in the frontal plane. Here it runs like an arrow (Latin: "sagitta") vertically through the frontal plane (through the Cabrera circle towards the eyes of the observer): Then it is a sagittal type.

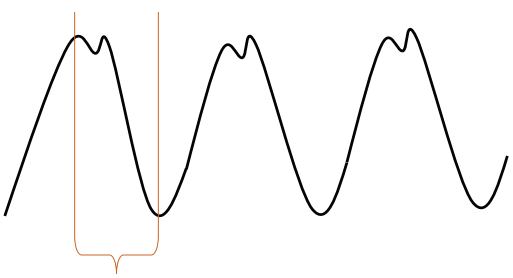


Fig. 710 Brugada's sign is defined as an RS distance of > 70 ms. It indicates ventricular tachycardia in the presence of a wide QRS complex tachycardia.

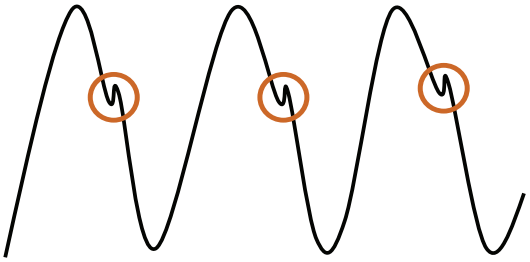
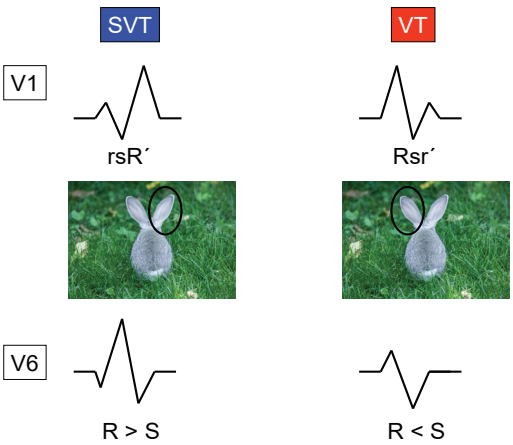
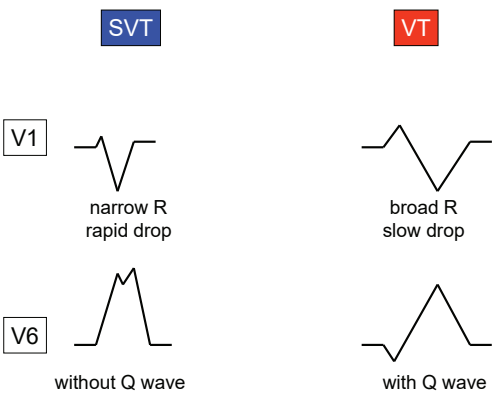


Fig. 711 Josephson's sign is defined as a notch in the descending part of the S wave of the QRS complex. It indicates ventricular tachycardia in the presence of a wide QRS complex tachycardia.



right bundle branch block

Fig. 712 Wide QRS complex tachycardia with right bundle branch block (RBBB): The chest wall leads V1 and V6 are considered. A rsR´ configuration in V1 (right rabbit ear, i.e. the second spike is higher than the first spike [typical RBBB]) indicates SVT, a Rsr´ configuration (left rabbit ear, i.e. the first spike is higher than the second spike [atypical RBBB]) indicates VT. If the R wave in V6 is higher than the S wave, it speaks of SVT. If the R wave is smaller than the S wave, this speaks of VT.



left bundle branch block

Fig. 713 Wide QRS complex tachycardia with left bundle branch block (LBBB): The chest wall leads V1 and V6 are considered. A narrow R wave with a rapid drop from RS in V1 indicates SVT, a wide R wave with a slow drop in RS indicates VT. If there is a Q wave in V6, this speaks of VT. If this is not the case, this speaks of SVT.

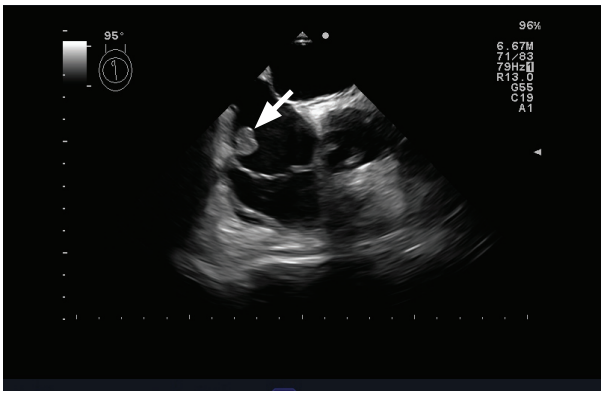


Fig. 817 pacemaker endocarditis: vegetation on the lead (various examples)

Therapy

- empirical antibiosis with vancomycin or daptomycin
- In case of vegetation on the pacemaker lead, the complete pacemaker system (i.e. lead and aggregate; analogous to an ICD) must be removed. This is also explicitly recommended (expert consensus Wilkoff et al, Heart Rhythm 2009; IB recommendation) in case of endocarditis (e.g. vegetation on the valve without vegetation on the lead) or also in case of a gram-positive (blood culture) sepsis, especially with staphylococcus aureus: Due to the pronounced tendency to biofilm formation, a sole antibiotic therapy is usually inefficient here. We do not immediately remove the entire system from every patient because he has a staphylococcus aureus bacteremia. This only takes place if the conservative therapy attempt (with antibiotics) has failed (e.g. persistent positive blood cultures).
- With small vegetations (< 15 mm) and an implantation period < 1 year, the lead removal can still be performed transvenously (so-called lead explantation; be aware of pericardial tamponade → pericardial puncture set within reach), with larger vegetations (> 15 mm) or implantation period > 1 year, this must be performed by cardiothoracic surgery (so-called lead extraction, using extraction set). Alternatively, interventional laser extraction is also performed in some specialised centres.
- The electrode in the coronary sinus (in a CRT system) can be removed by a simple pull.
- After 1-2 weeks (under monitor control) the implantation on the opposite side can then be performed if the inflammation parameters are normal. If the patient is completely pacemaker-dependent, a temporary pacemaker must transitionally be inserted.
- In the case of recurrent infections, the implantation of a leadless pacemaker (TPS: transcatheter pacing system; see info box) is also an option.

Excursus: Lead removal

- types:
  - lead explantation (< 1 year; screw leads are easier to remove than anchor leads): removal of the lead (transvenous) via the implantation route (cephalical / subclavial vein) without using special tools
  - lead extraction (> 1 year)
    - with using special tools (e.g. locking stylets, electrosurgical sheats, laser) or
    - removal of the lead by a route other than the implantation route
      - interventional: transvenous (femoral / jugular vein)
      - surgical: transthoracic (thoracoscopy, thoracotomy [mini thoracotomy or sternotomy])
    - Today, laser extraction is mostly carried out transvenously via the implantation route in a hybrid surgical room (cardiothoracic surgical room with option of coronary catheterization) with additional TEE monitoring.
- indications (Byrd criteria; updated according to Wilkoff et al, Heart Rhythm 2009 and Kusumoto et al, Heart Rhythm 2017):
  - infections (most common; the entire system, i.e. lead and aggregate, must be removed here)
    - pacemaker / ICD endocarditis (detection of vegetation on the lead)
    - valvular endocarditis (without evidence of vegetation on the lead [IB recommendation])
    - gram-positive blood culture (especially staphylococcus aureus [IB recommendation])
  - thromboembolism: detection of a thrombus on the lead and detection of a clinically relevant embolism (e.g. pulmonary embolism; here only the lead has to be removed and not the aggregate)
  - complications of a decommissioned lead:
    - life-threatening arrhythmias
    - acute danger from probe fragments (e.g. broken wire)
    - disturbance of treatment of a malignancy (e.g. radiation)
- complications:
  - main complication: pericardial tamponade (Therefore the possibility of an emergency sternotomy must be guaranteed within 10 minutes. Lead removal should actually only be carried out in hospitals where there is also cardiothoracic surgery.)
  - complication rate:
    - ELECTRA study (Bongiorni et al, Eur Heart J 2017): serious complications (especially pericardial tamponade, hemorrhage) in 1.7%, mortality 0.5%
    - Hosseini et al, JACC Clinical Electrophysiology 2019: serious complications in 10.4%, mortality 4.1%

treated surgically.

- 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 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, 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)
  - possibly pericardectomy (ultima ratio; but usually no more operable)
- special cases:
  - autoimmune: triamcinolone 300-600 mg/m² i.p.
  - purulent: gentamycin 80 mg i.p. (via irrigation drainage)

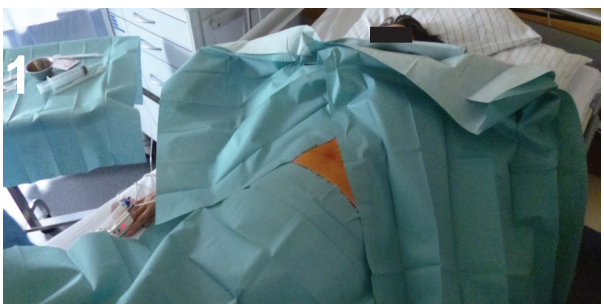
Pericardiocentesis (pericardial puncture)

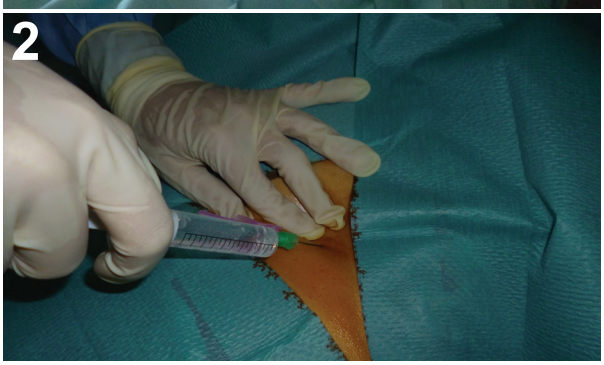
Puncture sites

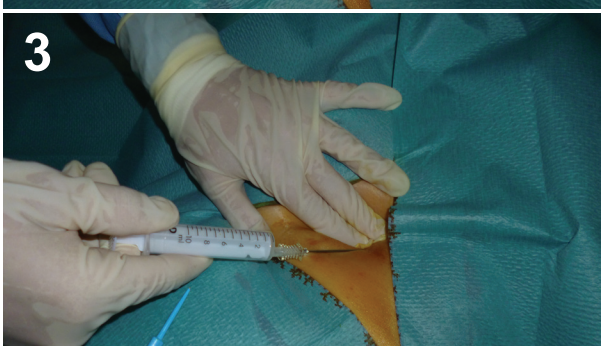
- subcostal:
  - 2-3 cm left and 2-3 cm below the xiphoid (Larrey point)
  - direction of puncture: left shoulder (tip: flat direction [almost parallel to the sternum!])
  - standard
- apical:
  - apex in MCL
  - direction of puncture: right shoulder
  - intercostal (upper edge of the rib)
  - especially in obese patients

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.







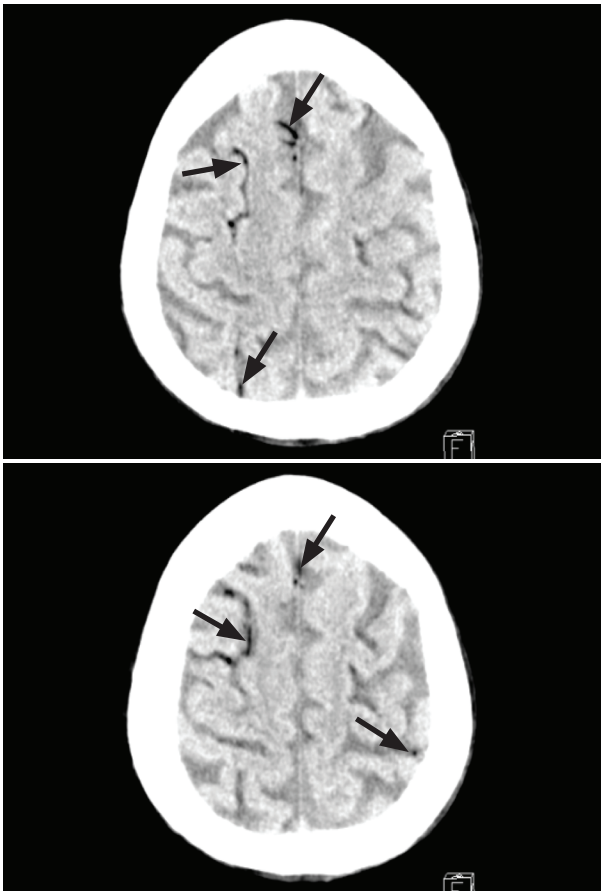


Fig. 903 CCT: pronounced air ubiquitous in the brain (see arrows; annotation: You can see the air best if you increase the brightness of the display.)

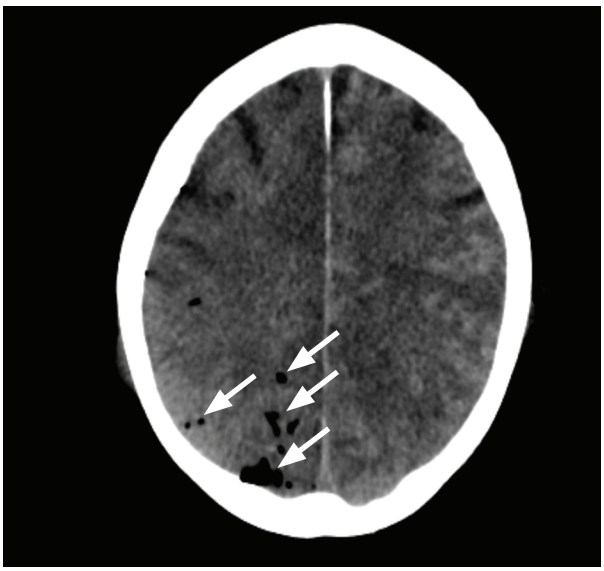


Fig. 904 CCT: air embolism (see arrows) with pronounced cerebral edema

Therapy

- positioning: In the past, lying on the left side with head-down position (Durant maneuver) was recommended. Today a flat supine position is recommended.
- aspiration of the air via right heart catheter or only via CVC (tip: If the patient has a CVC anyway [especially if air embolism occured as a complication of the CVC placement which is the most common cause], it is only necessary to advance the CVC as far as possible into the patient and then simply suck off the air. 50-100 ml per minute should be aspirated with a perfusor syringe until only blood and no more air appears.)
- ⚠ high-dose oxygen administration
- when occurring during surgery:
  - To prevent further air ingress, the surgeon should flood the surgical field with fluid if possible.
  - changing the table position so that the surgical field is below the level of the heart
  - in the case of air embolism during craniotomy: manual compression of both jugular veins on the neck
- possibly hyperbaric oxygenation (HBO, pressure chamber; preferably within 6 hours [but also up to 24 hours])
  - arterial gas embolism (AGE): ⚠ obligatory
  - venous gas embolism (VGE): facultative (especially if symptomatic [e.g. hemiparesis, seizure, visual impairment])
- lidocaine:
  - especially in arterial gas embolism (e.g. diving accident)
  - rationale: Lidocaine is said to have membrane-stabilizing effects and can thus prevent neurological (cerebral) damage.
  - Although there are only animal data, lidocaine is used by numerous HBO centers.
  - dosage: 1.5 mg/kg as bolus i.v., then continuous infusion over 24-48 hours in low doses (target level < 20 µmol/l)

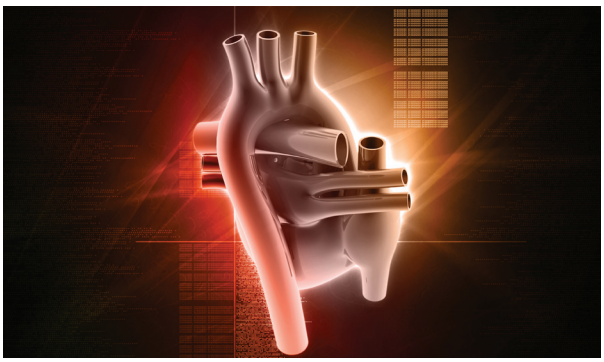
VGE (venous gas embolism): diagnosis by echocardiography (air in the right heart); therapy: place CVC, advance completely + aspirate!

Amniotic fluid embolism (AFE)

Definition

- syn.:
  - Steiner-Lushbaugh syndrome
  - amniotic infusion syndrome
- 4th most frequent maternal cause of death
- mortality:
  - ⚠ mother: 86% (catastrophic prognosis; of which 50% die in the first hour)
  - child: 21% (permanent neurological damage in 61%)
- incidence: 2/100,000 births
- always an diagnosis of exclusion (most important differential diagnosis: pulmonary embolism, myocardial infarction, peripartum cardiomyopathy, eclampsia, postpartum bleeding, aspiration, sepsis, anaphylaxis), ultimately only detectable post-mortem (autopsy)
- biphasic course: initial cardiorespiratory insufficiency, then DIC

ACUTE AORTIC SYNDROME



Definition

- acute chest pain (the 3 most important differential diagnoses):
  - acute coronary syndrome (ACS)
  - acute pulmonary embolism (APE)
  - ⚠ acute aortic syndrome (AAS)
- classification according to Svennson
- guidelines: ESC guidelines on the diagnosis and treatment of aortic diseases 2014

Svennson classification
acute aortic syndrome

- **Svennson type I: classic dissection**
- **Svennson type II: intramural hematoma (IMH)**
- **Svennson type III: local dissection**
- **Svennson type IV: penetrating aortic ulcer (PAU)**
- **Svennson type V: traumatic or iatrogenic dissection**

Acute aortic dissection (Svennson type I)

Definition

- rear of the intima layer of the aortic wall with dissection
- structure of the aortic wall:
  - intima (endothelium, basal membrane, connective tissue)
  - media (elastic fibres, musculature)
  - adventitia: connective tissue, vessels, nerves
- mostly hypertensive blood pressure (hypertensive emergency)
- Contrary to frequent opinion, the aorta in aortic dissection is not dilated previously (in 80%), i.e. there is no pre-existing aortic aneurysm.

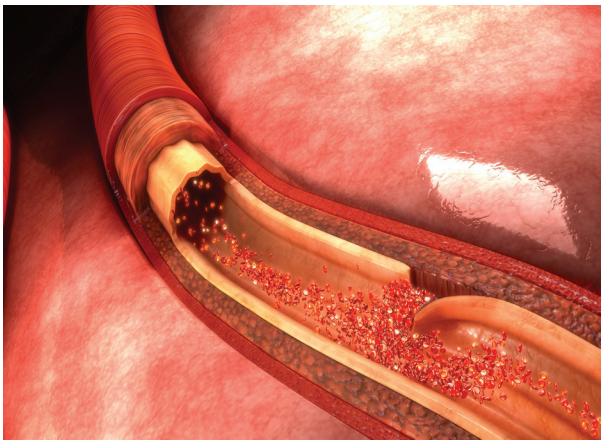


Fig. 909 aortic dissection: schematic illustration of the intimal tear

Pathophysiology

- tear (entry) in the intima layer of the aortic wall (in 90% ventral)
- Most dissections (65%) have their origin in the proximal ascending aorta immediately after the aortic valve (mostly in the area of the ostium of the RCA) because this is where the load on the aortic wall is greatest due to the flow properties.
- intramural bleeding into the aortic wall (bleeding inside the media)
- splitting into an inner and outer layer of the aortic wall (dissection)
- The blood flow opens up a new path, a false lumen develops.
- spread of the dissection:
  - antegrade (towards distal; mostly)
  - retrograde (towards proximal; rarely)
- mostly second tear (reentry)

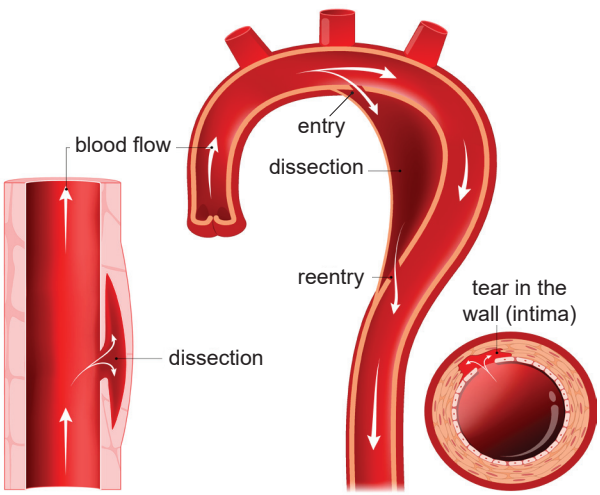


Fig. 910 aortic dissection: schematic illustration of the pathophysiology

in three weeks. If a patient in intensive care has a paO_2 of 49 mmHg in the BGA, it is not uncommon for panic to break out (not that code blue alarm is almost triggered) and mechanical ventilation is forced to such an extent that VALI is unfortunately often generated. The Italian anesthetist Antonio Pesenti described mechanical ventilation as "a life saving procedure that can kill the lung". Actually one should prohibit BGAs in the ARDS (exaggeratedly formulated)! The most important thing about mechanical ventilation in ARDS is the motto: "Keep cool man!"

Fig. 977 To ventilate a damaged lung is similar to running a 400 meter dash with a broken leg: You only have to go around the stadium round once here. So you have to do it slowly and don't want to set a world record with a super time, otherwise everything will break completely and you won't get 5 feet!

SpO_2 > 90%, paO_2 > 60 mmHg and $paCO_2$ < 70 mmHg completely sufficient! Most important: no damage to the lungs due to forced mechanical ventilation!

no BGA cosmetics in ARDS! no atmo-centric therapy (not the BGA values are in the foreground, paO_2 is not the target parameter)! improvement of oxygenation ≠ improvement of survival!

Patients in ARDS rarely die of hypoxemia, but unfortunately often of the consequences of VALI!

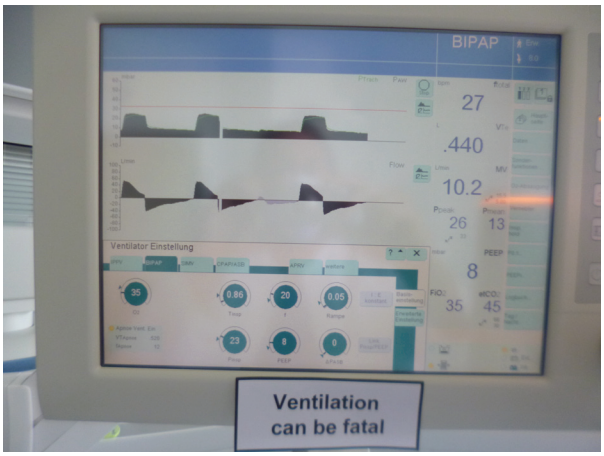


Fig. 978 The warning "Ventilation can be fatal" should be affixed to the ventilators in the intensive care unit (especially with ARDS) in analogy to to the inscription on the cigarette packs!

Mechanical ventilation
ARDS

- I:E 1:1
- set FiO_2 according to SpO_2 (target: SpO_2 > 90%)
- pressure controlled ventilation
- low tidal volume (V_T 6ml/kg PBW) → set low pressure difference Δp = IPAP - PEEP (target: pressure difference Δp < 15 mbar)
  - low inspiratory pressure (IPAP < 30-35 mbar; tip: set PEEP first, then inspiratory pressure [may be a maximum of 15 mbar higher than PEEP; orientate on the V_T])
  - high PEEP (10-20 mbar)
    - ARDS network table (orient on the set FiO_2)
    - but then reduction in case of improved oxygenation, no permanent lingering at high PEEP levels)
- high respiratory rate (RR 20-30/min)

Recruitment maneuver

Definition

- maneuver to re-open closed (atelectatic) lung areas that are no longer participating in the gas exchange
- The clinically most common recruitment maneuver is (better: was) the Lachmann maneuver.
- effective especially in the early phase of an extrapulmonary ARDS

Types

- intermittent sighs (type of mechanical ventilation in which several intermittent breaths with high inspiratory pressure and PEEP are applied at a set frequency per hour, resulting in hyperinflation of the lung and recruitment of atelectatic areas)
- airway pressure release ventilation (APRV):
  - spontaneous breathing with high CPAP level (20-30

*vv-ECMO: for **lung** replacement (respiratory failure [hypoxemic or hypercapnic])*
*va-ECMO: for **heart** replacement (circulatory failure [especially cardiogenic shock, cardiac arrest])*

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)

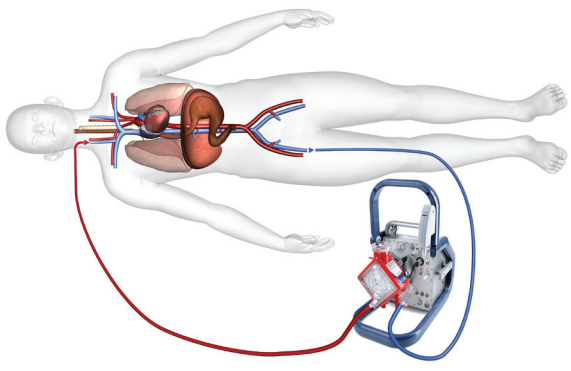


Fig. 985 ECMO veno-venous (vv-ECMO [23])

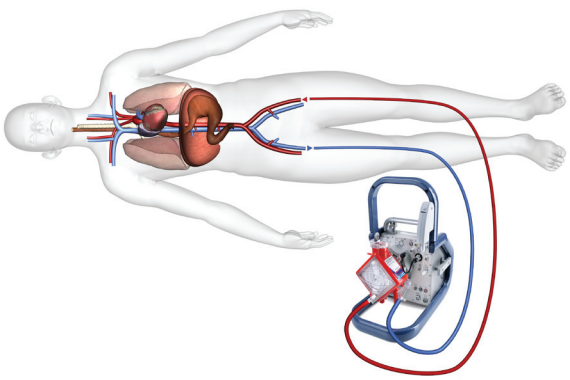


Fig. 986 ECMO veno-arterial (va-ECMO [23])

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!
- femoro-jugular cannulation: 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])
- 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 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 767)
  - > 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

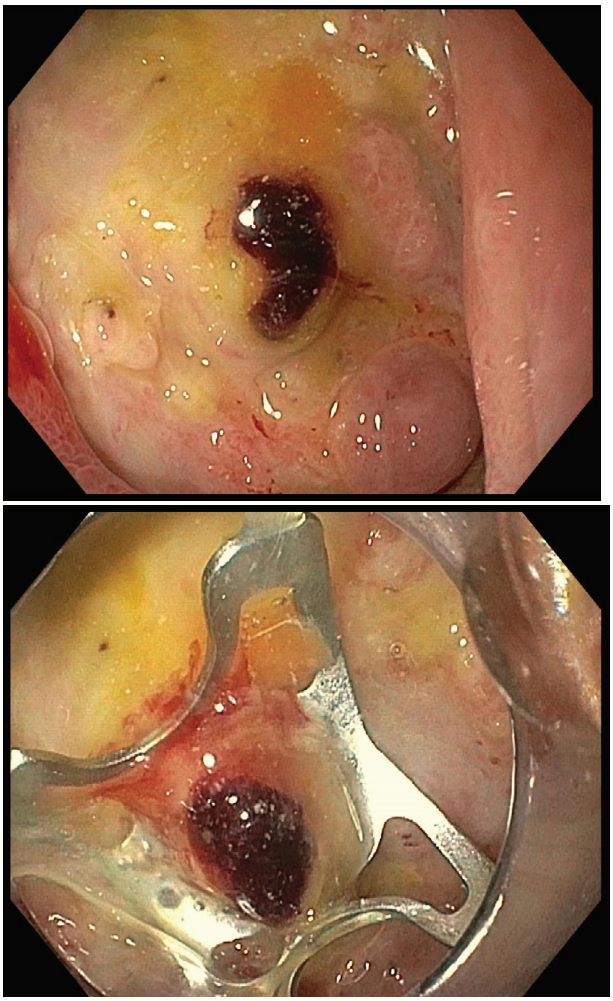


Fig. 1132 large callous duodenal ulcer with a vascular stump that was treated with an OTS clip

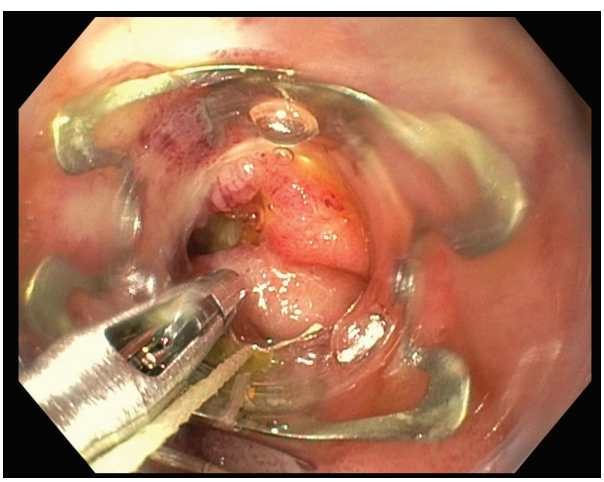


Fig. 1133 OTS clip for closing an anastomotic leak after excision of a gastric ulcer

Powder

- Hemospray (Cook Medical company)
- EndoClot PHS (Polysaccharide Hemostase System; MikroTech company)
- ABS (Ankaferd Blood Stopper; Turkish mixture of plant components with coagulating properties)
- PuraStat (a gel of synthetic peptides that is applied for hemostasis; Nicolai company)

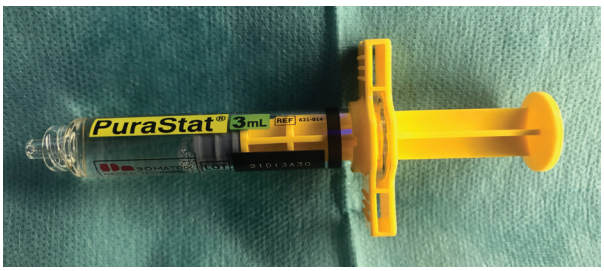


Fig. 1134 PuraStat: The gel is applied to the bleeding area using a special catheter (without a needle).

Hemospray (TC-325)

- definition: inorganic powder (nanopowder) with coagulating features
- set: a gun consisting of
  - powder (content: 20 g)
  - CO_2 cartridge
  - catheter:
    - sizes: 10 F (for the therapeutic device) or 7 F
    - The catheter is inserted via the working channel of the endoscope and the powder is then applied over a large area to the bleeding lesion.
- indications: especially
  - ⚠ tumor bleeding (main indication)
  - ulcer bleeding
  - bleeding after endoscopic interventions (e.g. biopsy, polypectomy, EMR [endoscopic mucosal resection], ESD [endoscopic submucosal dissection])
  - also suitable for arterial bleeding (i.e. Forrest Ia bleeding), but not for variceal bleeding
- costs (disposable set): 380 €
- studies:
  - meta-analysis Aziz et al, Ann Gastroenterolog 2020: equally effective as other primary hemostasis measures, but with a high rebleeding rate (35%)!
  - In a multicenter, randomized-controlled, non-inferiority study (Lau et al, Ann Intern Med 2022), it was found to be as effective as standard therapy in upper non-variceal gastrointestinal bleeding.
- S2k guideline of the DGVS (addendum 12/2021): can be used as an endoscopic first-line procedure for non-variceal upper gastrointestinal bleeding

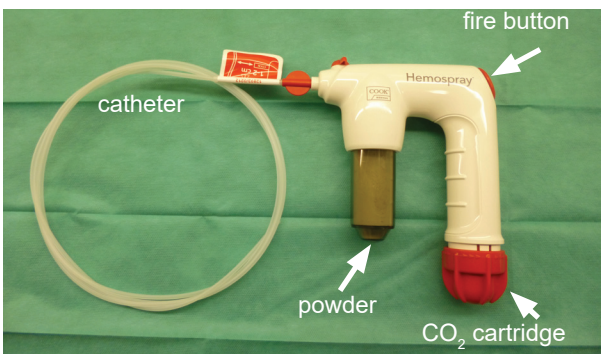


Fig. 1135 Hemospray (Cook Medical): a gun consisting of the powder, a CO_2 cartridge and the application catheter

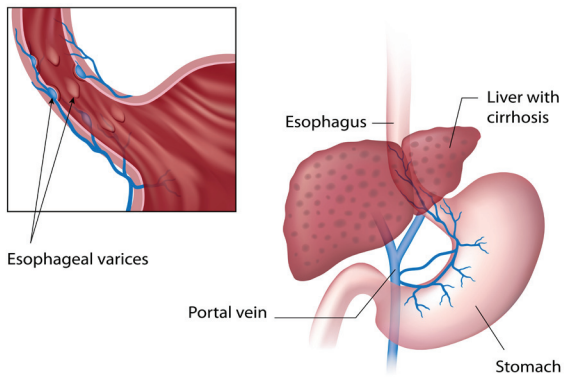


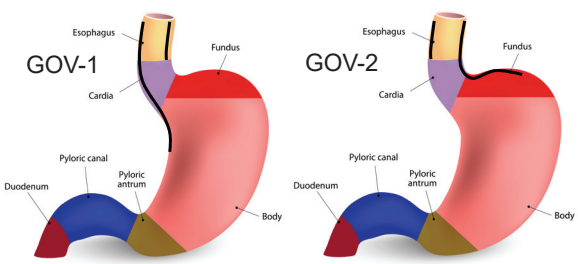
Fig. 1138 As a result of liver cirrhosis, the blood from the portal vein can no longer flow into the liver. The congestion leads to portal hypertension. Bypassing circuits (portocaval anastomoses) are formed (to the superior caval vein: especially via the gastric veins → esophageal veins; to the superior and inferior caval vein: i.a. via the umbilical veins; to the inferior caval vein: via the inferior mesenteric vein → rectal veins).

Types

- esophageal varices (90%)
- gastric varices (9%; especially fundal varices; classification according to Sarin → see infobox)
- duodenal varices (1%)

Classification according to Sarin

- **gastroesophageal varices (GOV)**
  - **GOV-1 (74%): esophageal varices that extend over the cardia into the corpus of the stomach (on the minor side, i.e. small curvature) → lower risk of bleeding**
  - **GOV-2 (16%): esophageal varices that extend over the cardia into the fundus of the stomach (possibly also into the corpus [on the major side, i.e. large curvature]) → higher risk of bleeding**
- **isolated gastric varices (IGV)**
  - **IGV-1 (8%): varices in the fundus (highest risk of bleeding among all gastric varices)**
  - **IGV-2 (2%): varices in all other parts of the stomach**



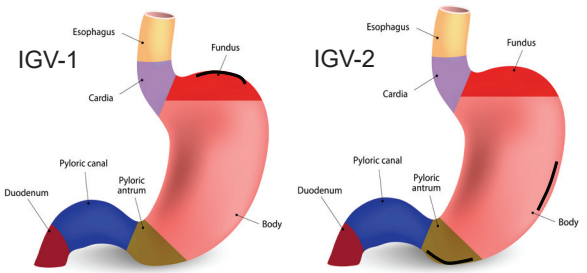


Fig. 1139 Sarin classification of gastric varices

Symptoms

- hematemesis
- tarry stool
- dizziness
- hypovolemic shock
- disturbance of consciousness; reasons:
  - reduced cerebral perfusion as a result of hypovolemic shock
  - hepatic encephalopathy (1000 ml blood contains 200 g protein → $NH_3\uparrow$)

Predictors (variceal GI bleeding)

- liver disease (previously known)
- thrombocytopenia (platelets < 88,000/µl)
- splenomegaly
- The lower the platelet count and the larger the spleen, the higher the probability of variceal bleeding: ⚠ ratio of platelet counts per µl to size of the spleen (longitudinal diameter) in mm < 909 → varicose bleeding (Colli et al, Cochrane Database Syst Rev 2017)!

Upper GI bleeding in liver cirrhosis

- variceal (50%)
- non-variceal (50%)
  - erosive gastritis
  - ulcer
  - reflux esophagitis
  - Mallory-Weiss syndrome
  - PHG (portal hypertensive gastropathy)
    - PHG can also bleed (mostly chronic blood loss, less acute bleeding)! Detection of portal hypertensive gastropathy is an indication for a non-selective β-blocker!
    - frequent cause for inappetence and thus cachexia in cirrhotic patients
  - GAVE (gastric antral vasal ectasia)
    - "watermelon stomach"
    - ectasias of the vessels, especially in the antrum
    - frequent occurrence in:
      - liver cirrhosis
      - scleroderma (systemic sclerosis)
    - frequent cause of chronic blood loss (iron deficiency anemia)
    - therapy: APC (argon plasma coagulation; settings: mode pulsed-APC, power 20 Watt)

Hepatology 2003])
- ligation (especially in large varices)

study

Impact of statins and non-selective beta-blockers as primary prophylaxis of esophageal variceal bleeding and mortality in compensated cirrhotic patients
Chumbe et al, AASLD 2023

- retrospective analysis
- 6,523 patients with compensated liver cirrhosis; primary prophylaxis of variceal bleeding:
  - non-selective β-blocker
  - non-selective β-blocker + statin
- result: non-selective β-blocker + statin → significant reduction in the rate of variceal bleeding and mortality

Secondary prophylaxis

- Without secondary prophylaxis recurrent variceal bleeding occurs in 60% within 2 years.
- ligation and β-blocker (for secondary prevention both, for primary prevention only one of the two)
- The combination of ligation and β-blocker reduces the risk of recurrent bleeding from 70% to 15%.
- variceal eradication at the earliest 2 weeks after primary ligation therapy
- if necessary TIPS
- possibly statins (reduction of risk of variceal bleeding [Orman et al, AASLD 2013: Statins are associated with a decreased risk of variceal bleeding in compensated cirrhosis.])
- if necessary evaluation of liver transplantation (the only curative option!)

Primary prophylaxis: no combination therapy (β-blocker OR ligation)
Secondary prophylaxis: combination therapy (β-blocker AND ligation)

TIPS

Definition

- transjugular intrahepatic portosystemic shunt
- bypass connection between portal vein and hepatic veins (usually between the right portal branch and the right hepatic vein)
- goal: portal decompression (reduction of pressure in the portal vein circulation)
- first TIPS implantation 1988 by Roessle (University Hospital Freiburg [Germany])
- performance: approximately 2 liters/min

Types

- uncoated (high complication rate, occlusion rate by thrombosis after 1 year: 80%)
- coated: stents covered with PTFE (polytetrafluoroethylene [Teflon]; significantly higher rate of patency after 2 years [76% versus 36%; Bureau et al, Gastroenterology 2004])

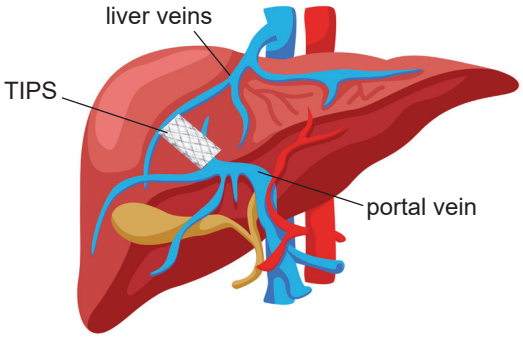
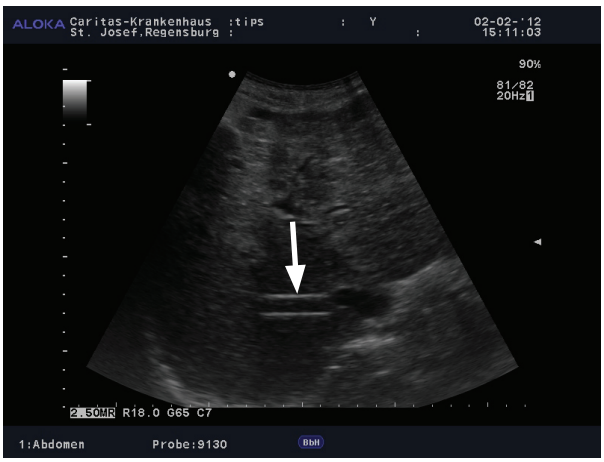


Fig. 1166 TIPS: bypass connection between the portal vein and hepatic veins



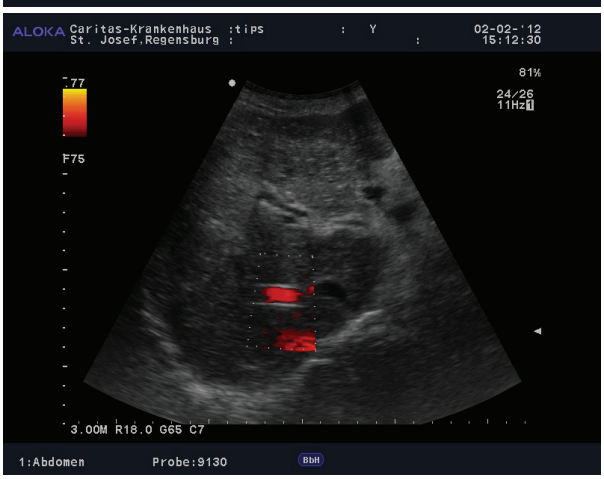


Fig. 1167 representation of the TIPS (see arrow) with regular flow in the color Doppler examination (sonographic check-up in the first year every 3 months, then every 6 months)

de, hydrochlorothiazide), steroids, aminosalycilates (e.g. mesalazine, sulfasalazine), metronidazole, cotrimoxazole, erythromycin, pentamidine, valproic acid (incidence 1: 40,000; mortality 20%), lamivudine, INH (isoniazid), ACE inhibitors, β-blockers, statins, diclofenac, acetaminophen (paracetamol), opiates, gliptins (e.g. saxagliptin), DPP-4 inhibitors, GLP-1 analogues, oral contraceptives, hormone replacement therapy (Oskarsson et al, CMAI 2014), thyreostatics (carbimazole, thiamazole), cimetidine, asparaginase, cisplatin

- postinterventional:
  - after ERCP: post-ERCP pancreatitis (PEP; in 5%)
  - after oral double balloon enteroscopy (in 0.34%)
  - after pancreatic puncture (EUS; in 1%)
- posttraumatic (e.g. horse kick, traffic accident, falling on a bicycle handlebar), postoperative (e.g. injury to the tail of the pancreas during a transperitoneal nephrectomy)
- pronounced hypertriglyceridemia (triglycerides > 1,000 mg/dl)
  - Pedersen et al, JAMA Intern Med 2016: The risk of pancreatitis is increased from triglyceride values > 2 mmol/l (178 mg/dl). For every 1 mmol/l (89 mg/dl) increase in triglycerides, the [relative] risk of pancreatitis increases by 17%.
  - Hansen et al, Clin Gastroenterol Hepatol 2020: triglyceride levels > 200 mg/dl → 3-fold increased risk of pancreatitis
  - Pothoulakis et al, Digestion 2021: 2.5 times more frequently severe course and 3 times higher mortality
- hypercalcemia (primary hyperparathyroidism [often no hypercalcemia due to released fatty acids with saponification!])
- pancreas divisum (see infobox), annular pancreas
- sphincter Oddi dysfunction (SOD; see infobox)
- duodenal diverticulum (juxtapapillary diverticulum)
- penetrating gastric ulcer / duodenal ulcer
- IPMN (intraductal papillary-mucinous neoplasia; obstruction of the pancreatic duct by mucin; typically cysts in the pancreas in the imaging)
  - main-duct type: MD-IPMN (75%)
  - branch-duct type: BD-IPMN (25%)
- viruses (mumps [often harmless accompanying pancreatitis; classically increased amylase here]; coxsackie, HIV, CMV, HSV, VZV, hepatitis viruses [especially hepatitis E virus])
- bacteria (especially mycoplasma [e.g. mycoplasma pneumoniae], mycobacteria [e.g. mycobacterium tuberculosis], leptospira, yersenia, campylobacter)
- ascariasis (roundworms) in the bile ducts
- tumor (e.g. first manifestation of pancreatic cancer [1.5%])
- autoimmune (autoimmune pancreatitis [AIP])
  - 5% of all chronic pancreatitis
  - m:w = 2:1; age mostly > 50 years
  - types:
    - AIP type I (LPSP: lymphoplasmacellular sclerosing pancreatitis)
    - AIP type II (IDCP: idiopathic ductocentric pancreatitis)
  - often associated with other autoimmune diseases (e.g. IgG4-associated cholangitis, Sjoegren's syndrome, SLE, vasculitis, Ormond's disease [retroperitoneal fibrosis], inflammatory bowel disease)
  - symptoms: painless jaundice, recurrent acute pancreatitis, weight loss, new onet of diabetes mellitus
  - often focal ("pseudotumor"; easily confused with pancreatic carcinoma in the imaging!)
  - IgG subtype 4 ↑ (only for type I)
  - very good response to steroids (drug of choice for maintenance therapy: azathioprine)
  - note: also possible with immune checkpoint inhibitors (especially CTLA-4 inhibitors)
- hereditary:
  - α1-antitrypsin deficiency (syn.: Laurell-Eriksson syndrome)
  - mutations (Genetic testing should be carried out primarily in younger patients with unexplained recurrent pancreatitis.):
    - PRSS1 gene (protease serine 1; syn.: cationic trypsinogen)
    - SPINK1 gene (serine protease inhibitor Kazal type 1)
    - CPA1 gene (carboxypeptidase A1)
- idiopathic (15%)

The most common causes of pancreatitis are gallstones and alcohol !

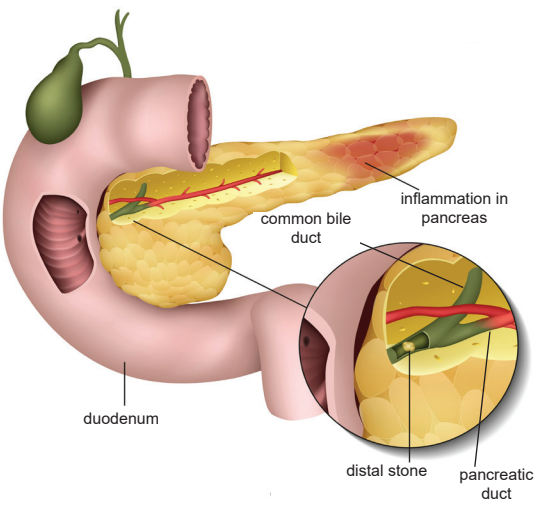
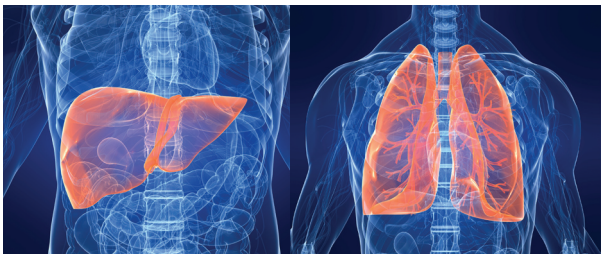


Fig. 1194 The most common cause of pancreatitis is a prepapillary impacted gall stone (biliary pancreatitis): This does not only result in a congestion of the common bile duct (CBD), but also of the pancreatic duct (syn.: duct of Wirsung): The increased pressure leads to a premature activation of the digestive enzymes.

Hepatopulmonary syndrome (HPS)



Definition

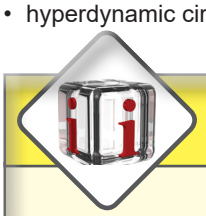
- occurrence of pulmonary dysfunction in liver cirrhosis
- arterial gas exchange disorder due to intrapulmonary vasodilation
- triad:
  - liver cirrhosis
  - reduced SpO_2 or paO_2
  - intrapulmonary vasodilatation or shunts (detection by contrast medium echocardiography)
- alveolar-arterial oxygen partial pressure difference $AaDO_2$ > 15 mmHg (for patients > 64 years: > 20 mmHg; for the calculation of the $AaDO_2$ see page 104)
- occuring in 10-15% in liver cirrhosis

Pathophysiology

- Due to the defective liver, too few vasoconstrictors can be produced and too few vasodilators (e.g. NO [nitrogen oxide]) can be degraded.
- The vasodilation of the pulmonary capillaries (especially basal) reduces the contact time and thus disrupts the oxygenation. Furthermore, the vasodilation of the pulmonary capillaries leads to a right-left shunt.
- increased formation of NO (vasodilator) due to an increased activity of NO synthase (NOS; note: Hepatopulmonary syndrome is less common in smokers because there are NO inhibitors in the tobacco.):
  - iNOS (inducible NO synthase)
  - eNOS (endothelial NO synthase)
- insufficient hypoxic pulmonary vasoconstriction (HPV; Euler-Liljestrand reflex) in the pulmonary vessels
- Due to the hyperdynamic circulation typical of liver cirrhosis, the red blood cell transit time at the alveolocapillary membrane is shortened and thus the diffusion is disturbed. Accordingly, the lung function shows a reduced DLCO (diffusion lung capacity for carbon monoxide).
- When standing upright, the vasodilation is increased by gravity with the following phenomenons:
  - platypnea (dyspnea is better when lying down; in contrast to orthopnea)
  - orthodeoxia (saturation is better when lying down than when standing; BGA is better when lying down than when standing [pO_2 > 5 mmHg])

Symptoms

- dyspnea
- ⚠ platypnea (in 25%)
  - definition: improvement of dyspnea while lying down (opposite of orthopnea)
  - occurrence: in shunts
    - intrapulmonary shunts (e.g. hepatopulmonary syndrome)
    - intracardiac shunts (shunt vitia)
- cyanosis
- drumstick fingers, watch glass nails (syn.: hippocratic nails [unguis hippocraticus])
- hyperdynamic circulation



DD Dyspnea
in patients with liver cirrhosis

- **ascites**
- **pleural effusion (typically right-sided), hepatic hydrothorax (possibly spontaneous bacterial empyema)**
- **congestive heart failure (often cirrhotic cardiomyopathy [CCMP] or ethyltoxic dilated cardiomyopathy [DCM])**
- **pneumonia**
- **interstitial lung disease (e.g. as part of PBC [primary biliary cirrhosis], e.g. as a result of interferon therapy for hepatitis C [note: therapy today usually without interferon])**
- **COPD ("Quis bibit, fumat")**
- **anemia**
- **hepatopulmonary syndrome**
- **portopulmonary syndrome (portopulmonary hypertension [POPH]; 3rd most common type of pulmonary artery hypertension [see page 728])**

Diagnosis (triad)

- liver cirrhosis
- SpO_2 < 90% or paO_2 < 70 mmHg under room air
- detection of intrapulmonary vasodilatation or shunts by contrast medium echocardiography (note: Quantification of the shunt is possible using ^{99m}technetium scintigraphy with macroaggregated albumin [MAA], but is rarely used in everyday clinical practice.)

Orthodeoxia test

- despite administration of 100% oxygen: paO_2 < 150 mmHg in BGA (cause: shunts [here: intrapulmonary])
- increase in saturation SpO_2 or paO_2 in the BGA (> 5 mmHg) when lying down compared to standing

Contrast echocardiography

- best with transthoracic echocardiography (be careful with transesophageal echocardiography [TEE] due to esophageal varices which are often present here)
- contrast agent: Both right and left heart contrast agent can be used for the question of intrapulmonary shunts. We mostly use both, although right heart contrast agent echocardiography alone would be sufficient. Left heart contrast agent, however, makes better pictures.

- mortality
  - paracetamol intoxication: 0.43%
  - paracetamol-induced acute liver failure: 32%
- If there is no acute liver failure in the course of paracetamol poisoning which is mostly the case, the liver recovers completely: There is no chronic permanent liver damage due to paracetamol intoxication.

Death cap poisoning

Definition

- syn.:
  - phalloides syndrome
  - amanita syndrome
- especially in late summer, autumn (July-October)
- death cap mushroom (amanita phalloides):
  - typically tuber on the stem, white lamella
  - types:
    - green (amanita phalloides; frequent; especially in deciduous forests)
    - white (amanita virosa; rare, especially in coniferous forests; mostly confused with the harmless forest or meadow mushroom [most important distinguishing feature: The lamellae of these mushrooms are always colored, those of death cap mushrooms are always white!])
- ⚠ by far the most frequent lethal mushroom poisoning (1 mushroom sufficient already [fly agaric: approximately 10 mushroom necessary])
- sweet taste ("non-toxic")
- toxin: amanitin (amatoxin)
  - a cyclic octapeptide
  - inhibition of RNA polymerase II so that the transcription of DNA into mRNA is inhibited and thus the biosynthesis of numerous proteins (both functional proteins [such as enzymes or hormones] and structural proteins [such as membrane receptors]) is blocked
  - heat-stable (not destroyed by cooking)
  - is subject to an enterohepatic circulation
  - The toxin is not only present in the death cap mushroom (90% of which is the cause of the phalloides syndrome), but also in some galerina species (skullcaps; especially deadly skullcap [syn.: funeral bell; galerina marginata] which can be confused with the sheathed woodtuft [an edible mushroom]) and in poisonous umbrella mushrooms (numerous lepiota species) with which the parasol (an edible umbrella mushroom; see page 1617) can be confused.
- frequent occurrence of amanita poisoning also in Syrian refugees (In its homeland, there is a edible mushroom that looks deceptively similar to death cap mushroom.)
- ⚠ mortality: 25%
- typically three-phasic course
- often a complete family affected
- history: Emperor Claudius (10 BC - 54 AD) was murdered by his wife Agrippina by death cap poisoning so that her son Nero came to power.

Fig. 1305 death cap mushroom (here green death cap mushroom [amanita phalloides]): Typical feature is the tuber at the bottom of the stem.

Fig. 1306 The most frequent cause of amanita poisoning is confusion with meadow mushroom. The most important distinguishing feature are the lamellae: In the case of meadow mushroom (first picture) the gills (lamellae) are colored, in the case of death cap mushroom (second picture) they are white!

Amanitin (Amatoxin) not only found in the mushroom species amanita, but also in the mushroom species galerina and lepiota!

Phases

- gastrointestinal phase (6-12 hours after ingestion; classically only after a latency period of > 6 hours after the mushroom meal! ⚠ The latency period is absolutely pathognomonic for death cap poisoning!):
  - nausea, vomiting (often bloody), diarrhea (massive

- bioartificial procedures (cell-based; not yet commercially available, also not yet approved)
  - hepatocyte cultures
  - HepatAssist (Alliqua Inc.)
    - with porcine hepatocytes
    - Demetriou et al, Ann Surg 2004: no survival benefit
  - ELAD (extracorporeal liver assist device; Thompson et al, Hepatology 2016: no survival benefit)
  - AMC-BAL (academisch medisch centrum bioartificial liver)
  - BELS (biological extracorporeal liver support)
  - MELS (modular extracorporeal liver support; with human hepatocytes)

MARS

Definition

- MARS: molecular adsorbent recycling system
- filtration procedure for detoxification ("liver dialysis")
- extracorporeal detoxification
- developed at the University of Rostock in Germany in 1993 by Stange
- Gambro Hospal company

Principle

- removal of water-soluble toxins (especially ammonia) via conventional dialysis membrane
- removal of albumin-bound toxins via special MARS membrane (dialysis against albumin [acts as "attractant protein"]; principle of albumin dialysis)
- subsequent recycling of albumin via carbon adsorbers and ion exchangers

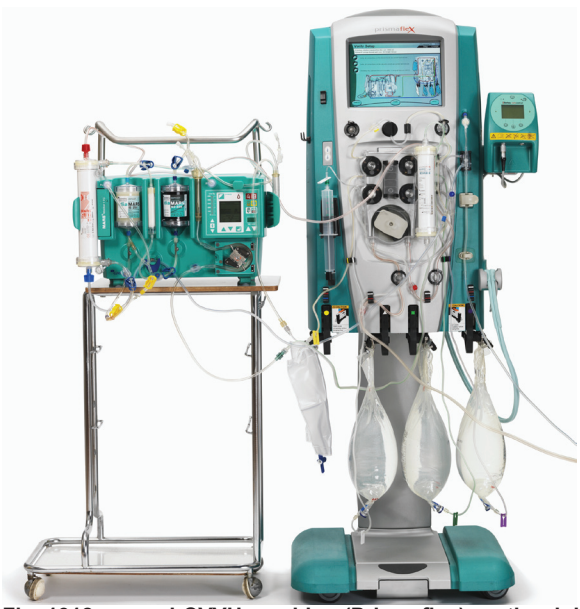


Fig. 1318 normal CVVH machine (Prismaflex) on the right, MARS as additional module on the left [18]

Fig. 1319 MARS

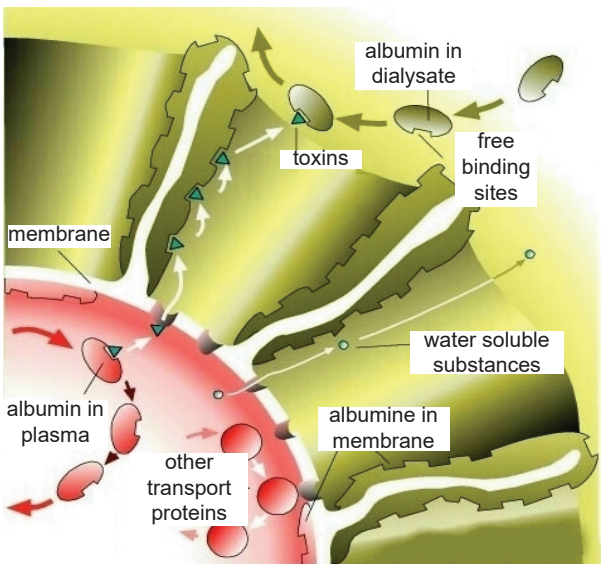


Fig. 1320 MARS membrane: Albumin is embedded in the membrane and acts as an attractant protein [18].

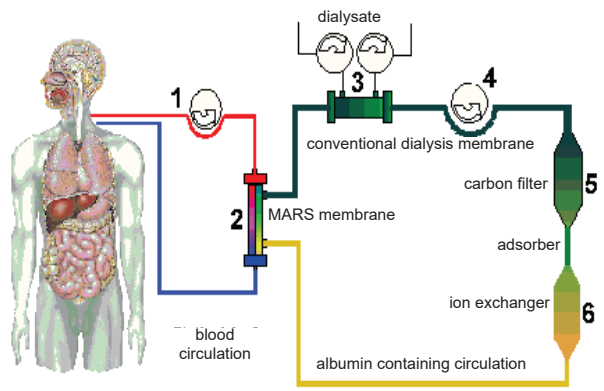


Fig. 1321 MARS flow circuit: Venous blood from the patient's Shaldon catheter is transported via a roller pump (1) to the MARS membrane (2): There detoxification of the albumin-bound toxins takes place. Then the blood flows to a conventional dialysis membrane (3): There detoxification of the water-soluble toxins takes place. Finally the "contaminated" albumin is recycled via carbon filters (5) and ion exchangers (6). [18]

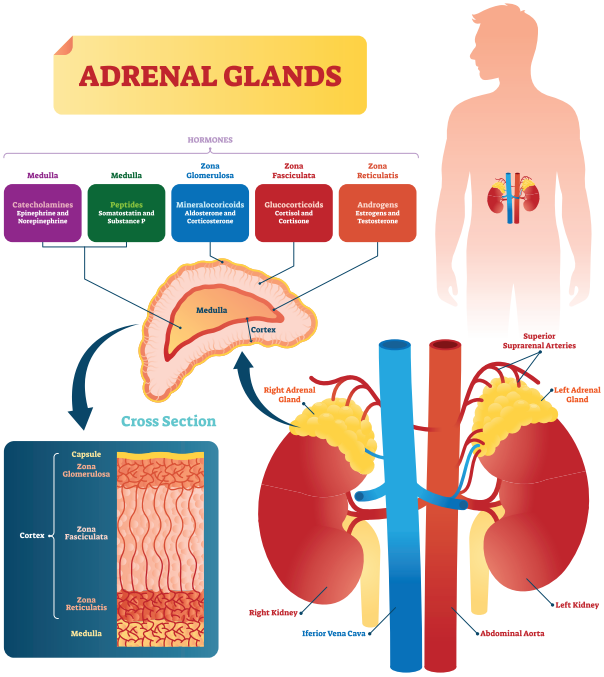


Fig. 1358 adrenal gland: structure and function

Adrenal gland
Hormones

- adrenal medulla (part of the autonomic nervous system [sympatheticus]): epinephrine (adrenaline; 80%), norepinephrine (noradrenaline; 20%)
- adrenal cortex:
  - zona glomerulosa (outer layer): mineralocorticoids (aldosterone, deoxycorticosterone [DOC]); no central control of the synthesis (only peripheral: via RAAS [renin-angiotensin-aldosterone system; especially via angiotensin II]; aldosterone causes an increased reabsorption of sodium and water and an increased excretion of potassium and protons [H^+] in the collecting ducts of the kidneys.)
  - zona fasciculata (middle layer): glucocorticoids: cortisol (syn.: hydrocortisone), cortisone (inactive); central control of the synthesis (hypothalamus: CRH [corticotropin-releasing hormone]; pituitary: ACTH [adrenocorticotropic hormone, adrenocorticotropin; ⚠ only the synthesis of the glucocorticoids in the adrenal cortex is ACTH-dependent!])
  - zona reticularis (inner layer): sex hormones (especially androgens [testosterone], but also estrogens); precursor for the sex hormones: DHEA (dehydroepiandrosterone); central control of the synthesis (hypothalamus: GNRH [gonadotropin-releasing hormone]; pituitary: gonadotropins [LH, FSH])

Etiology

- decompensation (by certain triggers) of a pre-existing chronic adrenocortical insufficiency; causes for chronic adrenocortical insufficiency:
  - inflammatory (adrenalitis)
    - autoimmune (most frequent cause [80%]); also possible with immune checkpoint inhibitors (e.g. ipilimumab, nivolumab); in 40% isolated, in 60% associated with other autoimmune diseases in the context of a polyglandular autoimmune syndrome (PAS; syn.: APS [autoimmune polyendocrine syndrome]):
      - type 1 (juvenile form; Blizzard syndrome; syn.: APECED [autoimmune polyendocrinopathy candidiasis ectodermal dystrophy syndrome]): Addison disease + hypoparathyroidism + mucocutaneous candidiasis
      - Type 2 (adult form): Addison disease + diabetes mellitus type 1 + autoimmune thyroiditis (either Hashimoto's thyroiditis [= Schmidt syndrome] or Graves disease)
    - infectious (tuberculosis, AIDS, CMV, mycoses)
  - neoplastic (especially metastases in the adrenal gland, e.g. bronchial carcinoma [especially small cell bronchial carcinoma], lymphoma)
- adrenocortical atrophy under prolonged steroid therapy (cause of a secondary adrenocortical insufficiency)
  - too rapid tapering
  - missing increase in stress situations: Long-term steroid therapy (e.g. polymyalgia rheumatica, Crohn's disease) leads to adrenocortical atrophy. If these patients, who have been on steroid therapy for a long time, suddenly experience an acute stress situation (e.g. surgery for perforated appendicitis with septic shock, traffic accident with polytrauma), hydrocortisone (100 mg i.v.) must always be administered!
- Waterhouse-Friderichsen syndrome
- bleeding
  - meningococcal sepsis
  - oral anticoagulants (VKA, NOAC)
- bilateral adrenal vein thrombosis (e.g. in HIT II, antiphospholipid syndrome)
- bilateral adrenalectomy
  - e.g. in renal cell carcinoma (RCC) with metastasis in the contralateral adrenal gland or with unresectable central Cushing syndrom
  - for the scheme of hormone substitution after bilateral adrenalectomy: see infobox
  - In 10% the reaction to the iatrogenic adrenal insufficiency is an aggressively and invasively growing pituitary tumor with (pronounced) ACTH production (Nelson tumor).
  - always issue an emergency card
- high-dose administration of thyroid hormones (e.g. L-thyroxine 500 µg as part of therapy of myxedema coma): The administration of thyroid hormones increases the glucocorticoid clearance and can thus trigger adrenocortical insufficiency up to Addison crisis!
- drugs: i.a.

- QRS widening
- bradycardia, AV block, possibly asystole

Therapy

- causal (therapy of the underlying disease)
- symptomatic: ⚠ therapy like hyperkalemia (preferably calcium gluconate)

Disorders of phosphate

- hypophosphatemia (phosphate < 0.8 mmol/l)
- hyperphosphatemia (phosphate > 1.5 mmol/l)

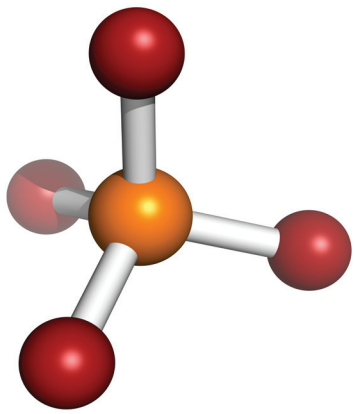


Fig. 1397 Phosphate (PO_4) is the salt of phosphonic acid and consists of 1 atom of phosphorus (central) and 4 atoms of oxygen (peripheral).

Hypophosphatemia

Definition

- phosphate < 0.8 mmol/l
- Phosphate is essential for the formation of ATP (adenosine triphosphate; "energy currency") and thus an important energy supplier.
- phosphate mostly located intracellular (99%)
- ⚠ 30% of all ICU patients (in sepsis even in 80% [due to increased consumption]!)
- shift of the oxygen binding curve of hemoglobin to the left → reduced release of oxygen

Severity (degress)

- 0.6-0.8 mmol/l: mild hypophosphatemia
- 0.3-0.6 mmol/l: moderate hypophosphatemia
- < 0.3 mmol/l: severe hypophosphatemia

Etiology

- sepsis (most frequent cause)
- ⚠ renal replacement therapy (relatively frequent [in 50%!]; the substitution solutions are phosphate-free)
- long-term parenteral nutrition
- malnutrition
- ⚠ refeeding syndrome (Hypophosphatemia is the most important marker here!)
- chronic alcohol abuse
- acute liver failure
- diabetic ketoacidosis
- COPD
- drugs:
  - ⚠ catecholamines
  - antacids (containing aluminum; e.g. sucralfate)
  - diuretics
  - insulin
- vitamin D deficiency (reduced absorption; therefore in case of unclear hypophosphatemia determination of 25-OH vitamin D and in case of proven vitamin D deficiency [< 20 µg/l] substitution with Dekristol oil 20,000 IU p.o. or via gastric tube once a week)
- hyperparathyroidism
- hypothermia (e.g. after resuscitation)

Symptoms

- neurological:
  - muscle weakness, i.a. respiratory muscles (CIP, CIM) → respiratory insufficiency, weaning problems
  - paresthesia
  - confusion, delirium, coma
  - seizures (up to status epilepticus)
  - central pontine myelinolysis
- cardiac: myocardial weakness → heart failure
- hematological: hemolysis (Due to the lack of ATP, the erythrocytes are destroyed.)
- muscular: rhabdomyolysis (Due to the lack of ATP, the muscle cells are destroyed.)

Hypophosphatemia: frequent in ICU → determine phosphate regularly (e.g. twice a week)! Think of hypophosphatemia especially in case of unclear circulatory insufficiency / weaning problems!

Therapy

- p.o.: 3 x 20 mval / day (1-3 g)
- i.v.: sodium phosphate 0.02 mmol/kg/h (in hypernatremia alternatively potassium phosphate); perfusor: 2 amp. sodium phosphate a 20 ml a 40 mval (pure) = 40 ml = 40 mval → 1 mval/ml
  - for the substitution of 40 mval (mostly sufficient): infusion rate 10 ml/h for 4 hours
  - for the substitution of 80 mval (necessary in case of severe hypophosphatemia, i.e. phosphate < 0.50 mmol/l): infusion rate 20 ml/h for 4 hours
- with proven vitamin D deficiency (< 20 µg/l) substitution with Dekristol oil 20,000 IU p.o. or via gastric tube once a week

creatine formed in the liver takes place in the muscles.) can be produced which can simulate a normal renal function. Evaluation of the renal function with cystatin C would be better here.

- If the renal function does not recover (rarely the case), although the patient is hemodynamically stable, it can be switched to intermittent hemodialysis.

Special form: SCUF (slow continuous ultrafiltration)

- only ultrafiltration (= filtration of water due to a difference in pressure) of plasma water (only drainage), no detoxification
- only indicated in individual cases (e.g. in cardiac decompensation and simultaneous anuria [cardiorenal syndrome in the context of cardiogenic shock]: Here, only the water should be removed.)

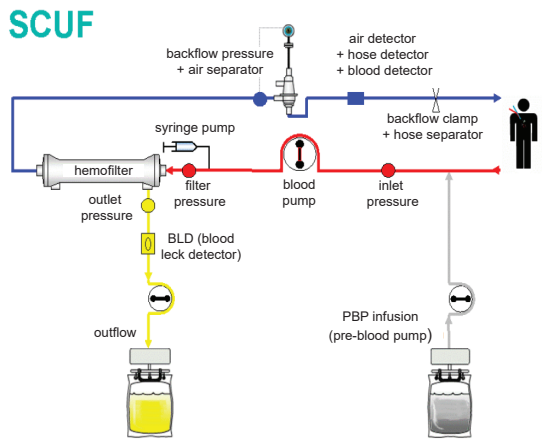


Fig. 1432 SCUF: slow continuous ultrafiltration [18]

The combination of hemodialysis and hemofiltration (CVVHDF) is most frequently used in the intensive care unit!

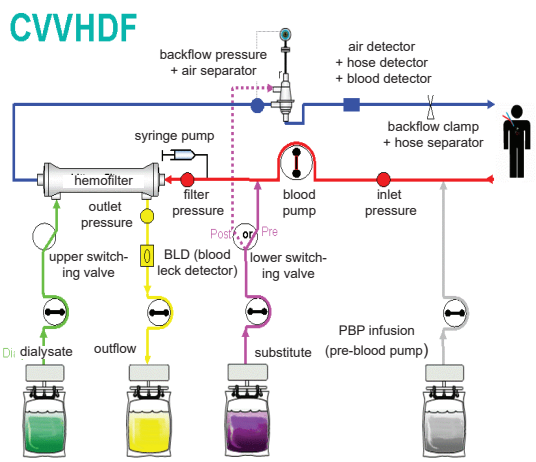


Fig. 1433 CVVHDF (hemodiafiltration) [18]

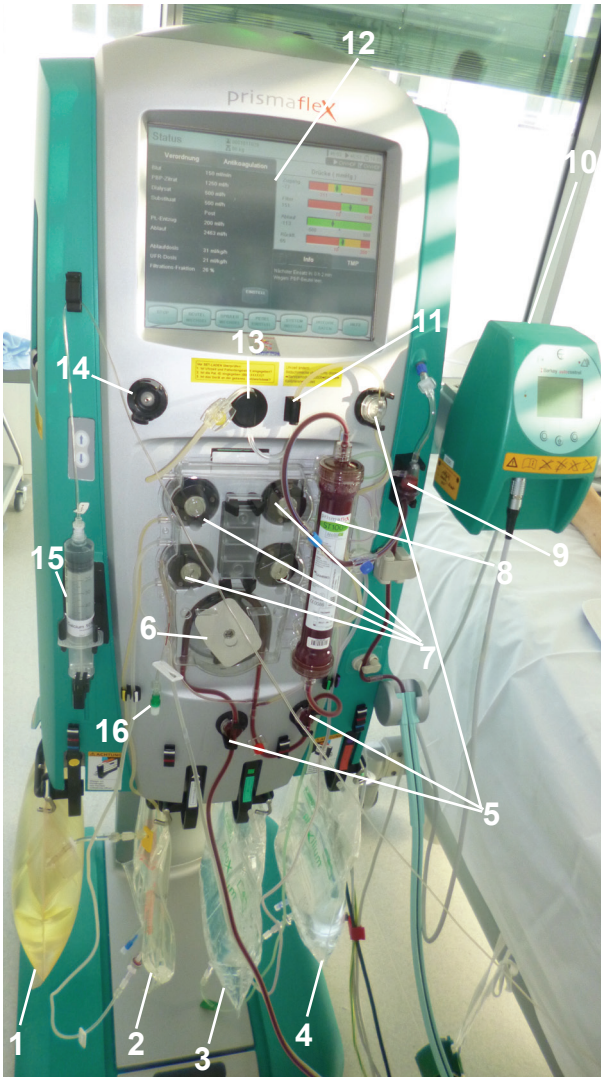


Fig. 1434 Construction: 1: drain bag, 2: citrate bag, 3 and 4: substitute bag, 5: pressure sensor, 6: pump for the blood, 7: pumps for the substitute and citrate, 8: hemofilter, 9: air bubble detector ("air trap"), 10: heating, 11: equipotential bonding, 12: operating window (touchscreen), display (prescription, anticoagulation, pressures), 13: blood leak detector (BLD; indicates leakage of erythrocytes; can be caused by filter rupture [e.g. due to too high TMP]), 14: connection for MARS system (as additional module in acute liver failure), 15: syringe with calcium, 16: connection for heparin (if anticoagulation is performed with it [In our clinic it is performed with citrate.])

Settings

(example for Prismaflex Gambro Hospal)

- substitute: Kalilactasol (electrolyte solution with lactate and potassium)
- filter: Prismaflex M 100 (Pre)
- dilution method: predilution
- blood flow rate: start with 80 ml/h and increase to at least 150 ml/h
- anticoagulation:
  - unfractionated heparin (UFH)
  - 10,000 IU of UFH in 20 ml normal saline syringe → 500 IU/ml

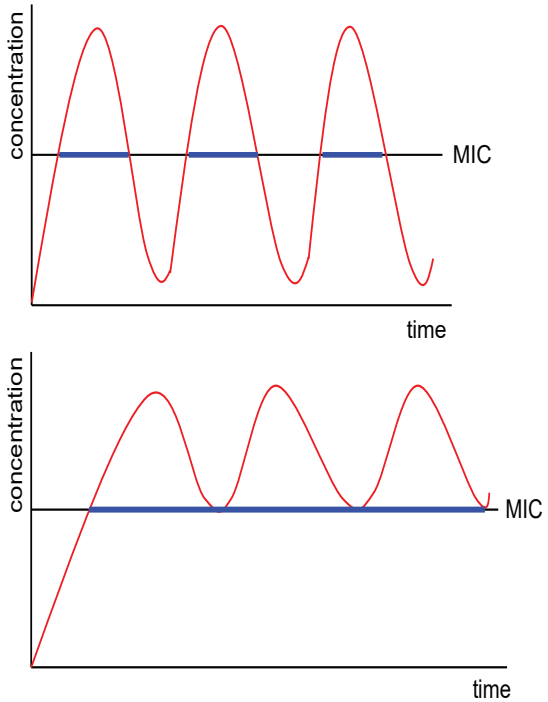


Fig. 1467 The pharmacodynamics of time-dependent antibiotics are shown here. The time in which the concentration is above the MIC (minimum inhibitory concentration) is decisive for their effectiveness. This time (in the graphic shown in blue) is significantly shorter with only three bolus doses (top) than with prolonged infusions (bottom) or even continuous administration.

Antibiotics
Types II

- according to plasma protein binding
  - antibiotics with high protein binding (i.e. > 90%; e.g. cefazoline, ceftriaxone, sulfonamides, tetracyclines, isoazylpenicillins, ertapenem, teicoplanin): If the protein level in the plasma is low (albumin < 25 g/dl), these antibiotics are increasingly eliminated. Here the dose has to be increased! ⚠ For example, the dose of ceftriaxone must be doubled if serum albumin is low, that means 2 x 2 g instead of just 1 x 2 g have to be administered!).
  - antibiotics with low protein binding
- according to elimination
  - renal (60%): In critically ill patients, they should not be underdosed because of false regard to the kidneys. You should also be careful if the GFR is increased (> 130 ml/min; frequently hyperdynamic circulation in the initial phase of sepsis): Here the renal clearance is increased (augmented renal clearance [ARC]) so that the dose has to be increased! This applies especially to β-lactams. If GFR > 130 ml/min, e.g. piperacillin / tazobactam has to be administered 4-5 times a day.
  - hepatic (40%)

Antibiotics
Classes

- β-lactams
  - penicillins
  - cephalosporins (not effective against "LAME": Listeria, Atypical [legionella, chlamydia, mycoplasma] pathogens, MRSA [exception: 5th generation] and Enterococci)
    - oral (note: almost no oral bioavailability and therefore almost no importance)
    - parenteral
  - carbapenems
  - monobactams: aztreonam (Azactam)
- fluorchinolones (gyrase inhibitors)
- macrolides
- aminoglycoside
- oxazolidinones
  - linezolid (Zyvoxid)
  - tedizolid (Sivextro)
  - radezolid
- glycopeptides
  - vancomycin
  - teicoplanin (Targocid)
- lipoglycopeptides
  - telavancin (Vibativ)
  - dalbavancin (Xydalba)
  - oritavancin (Orbactiv)
- tetracyclines
  - tetracyclin
  - minocyclin (Minocin)
  - doxycyclin (Vibravenoes)
- glycylcyclines: tigecycline (Tygacil)
- polymyxines
  - polymyxin B
  - polymyxin E (= colistin)
- other:
  - sulfonamides (folic acid antagonists): cotrimoxazole (trimethoprim sulfonamide [Bactrim, Cotrim])
  - lipopeptides: daptomycin (Cubicin)
  - lincosamides: clindamycin (Sobelin)
  - nitroimidazoles: metronidazole (Clont)
  - nitrofuranes: nitrofurantoin
  - epoxides: fosfomycin (Infectofos)
  - ansamycines: rifampicin (Eremfat)
  - streptogramines: quinupristin-dalsopristin (Synercid)

Differential diagnoses

- primary sclerosing cholangitis (PSC)
  - most common in patients with ulcerative colitis
  - laboratory: pANCA ↑
- IgG4 associated sclerosing cholangitis (can immitate exactly the same picture and can be treated with steroids very effectively; therefore always determine IgG4 level in the serum)

Therapy

- ursodesoxycholic acid
  - a naturally occurring tertiary bile acid that is found in low concentrations in humans, but in very high concentrations in bears (Latin "ursus": bear).
  - dosage: 10-15 mg/kg p.o.
- antibiosis in case of infection (if necessary also antimycosis)
- if necessary liver transplantation
  - the only curative option (therefore early contact with a corresponding transplant center!)
  - However, liver transplantation is only carried out very rarely (in 0.6%) in SSC.

Prognosis

- main cause of death: recurrent cholangitis with cholangiosepsis (The only way to eliminate this smoldering focus of infection is liver transplantation!)
- ⚠ mortalitity: 50% (Voigtlaender et al, Endoscopy 2012)
- median survival time: 13 months (Ruemmele; Nat Rev Gastroenterol Hepatol 2009)

Diagnostics

- sonography: i.a. resistance index (RI; syn.: Pourcelot index) in the hepatic artery $(v_{sys} - v_{dias}) / v_{sys} > 0.8$ indicates reduced liver perfusion
- laboratory

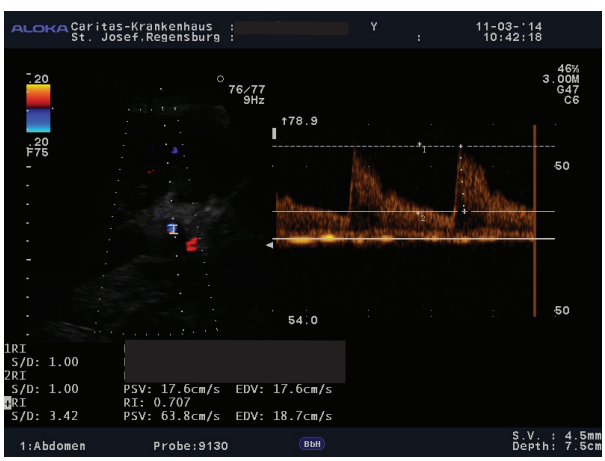


Fig. 1483 determination of the resistance index RI (syn.: Pourcelot index) in the hepatic artery by determination of the maximum systolic velocity and the end-diastolic velocity; RI = $(v_{sys} - v_{dias}) / v_{sys}$; RI > 0.8 indicates a reduced liver perfusion

Laboratory

- static tests:
  - bilirubin
    - ⚠ pragmatic p.d. liver dysfunction from bilirubin > 4 mg/dl (septic cholestasis; note: An increase in liver function tests [transaminases, µGT] can be found relatively frequent in ICU. This is usually due to drug-toxicity [mainly due to antibiotics]. As rule of thumb for the clinical everyday life with an increase of liver function tests one can remember: If bilirubin is not elevated, it is usually harmless [Hy's law]).
    - ⚠ Typically the direct (conjugated) bilirubin is increased. The conjugation still works, but energy-dependent excretion and transport processes do not work any longer (typically intrahepatic cholestasis!).
  - GOT (= AST), GPT (= ALT)
  - parameters of liver synthesis
    - Quick < 50% resp. INR > 1.5
    - albumin ↓ (half-life 19 days → reacts only very slowly → subordinated significance in acute liver failure)
    - cholinesterase ↓ (half-life 14 days → reacts only very slowly → subordinated significance in acute liver failure)
    - factor V (activity) ↓
- dynamic tests:
  - ICG clearance
  - LiMAx test
  - MEGX test

ICG clearance

- indocyanine green:
  - a phosphatidylcholine
  - anionic dye
  - strict hepatic clearance
  - no enterohepatic recirculation
- norm: ICG clearance > 16%
- an early marker of liver dysfunction
- correlation with mortality in sepsis (i.a. Malbrain et al, Intensive Care Med 2006)
- The lower the ICG clearance, the higher the mortality (e.g. ICG clearance 8% → mortality 80%).
- Kortgen et al, Shock 2009: significantly higher sensitivity and specificity for septic liver failure than bilirubin
- systems
  - LiMON system (Pulsion company)
  - PiCCO 2 monitor (from software version 3.x, available since 2009; the ICG module is inserted instead of the module for central venous oxygen saturation)

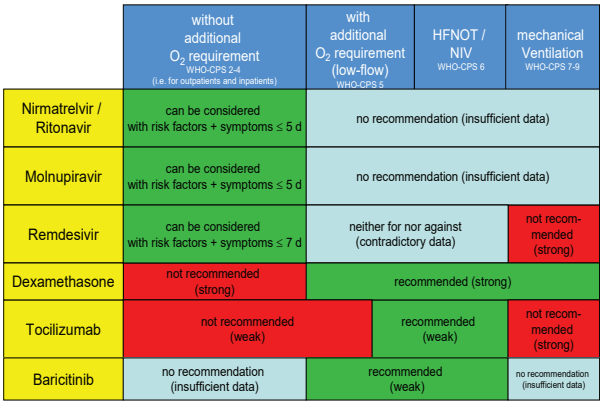


Fig. 1588 Overview of drug therapy for COVID in outpatients and inpatients analogous to the S3 guideline of the DGIIN of 12.09.2022 (It is new that sotrovimab has been completely deleted. Furthermore, the presence of vaccination protection no longer plays any role. For the antiviral drugs, there is now more than only one risk factor necessary.)

Supportive therapy

- if necessary admission to ICU
  - 5% of all patients require intensive care.
  - 20% of all patients admitted to hospital require intensive care in the further course.
  - admission to ICU: ⚠ typically on average 10 days after the onset of symptoms
  - indication (according to the S1 guideline):
    - dyspnea + tachypnea (respiratory rate > 25-30/min) + SpO_2 < 90% despite administration of oxygen (up to 4 liters / minute); note: According to the S2k (23.11.2020) and S3 guideline (since 23.02.2021) of the DGIIN this is the only criterion.
    - SBP < 100 mmHg
    - increased lactate
  - invasive ventilation: in 50% of all patients admitted to ICU necessary (i.a. Grasseli et al, JAMA 2020; Richardson et al, JAMA 2020)
  - length of ICU stay: on average 9 days (in case of invasive ventilation: 18 days)
  - mortality:
    - if requiring intensive care: ⚠ 50% (Meng et al, Anesthesiology 2020; analogue ICNARC report 2020 [UK]); according to a meta-analysis (Armstrong et al, Anesthesia 2021): 35,5%; according to RKI (Robert Koch Institute) and DIVI registry in Germany: 33% (as of November 2020: 22%; as of February 2021: 29%); according to the largest study from Western Europe (COVID-ICU study; Intensive Care Med 2021): 31%
    - if requiring intubation and invasive ventilation: ⚠ 66% (ICNARC report 2020 [Intensive Care National Audit and Research Center; UK]); according to Namendys-Silva et al, Lancet Resp Med 2020 even 86%, according to Zhou et al, Lancet 2020 even 97%!); according to an observation study in Germany (Karagiannidis et al, Lancet Resp Med 2020): ⚠ 53% (first wave), according to an analysis of the Scientific Institute of the AOK in Germany 2021: 50% (second wave)
- hygienic measures
- respiratory insufficieny:
  - oxygen administration (usually sufficient in mild to moderate cases; close control of saturation [target SpO_2 > 90%]; patient should wear mouth-nose mask!)
  - if necessary mechanically ventilation
  - in obstruction (e.g. by SARS-CoV-2 exacerbated COPD): nebulization (e.g. Berodual [fenoterol + ipratropium bromide] 10 drops + 5 ml normal saline 4 x daily)
    - The staff should wear the appropriate protective equipment (especially FFP-2 masks) due to the increased risk of aerosol formation.
    - However, there was no evidence of a significantly increased delivery of infectious aerosols under nebulization (jet nebulizer) compared to spontaneously breathing patients (neither in vitro nor in vivo). Under nebulization with sodium chloride, the excretion of aerosols was even reduced (due to a reduced surface tension)!
    - One should therefore not withhold this therapy from the patient out of fear of infection!
- antibiotic therapy only in case of bacterial superinfection (e.g. ampicillin / sulbactam, piperacillin / tazobactam)
  - no prophylactic administration recommended (national S1 + S2k + S3 guideline); note: In the international COVID guideline of the SSC 2020, antibiosis was initially recommended as soon as the patient is mechanically ventilated (but only a weak recommendation! In the first update (28.01.2021) this topic was unfortunately not addressed at all.
  - In contrast to influenza, in which a bacterial co-infection is present in 50% and therefore prophylactic antibiosis is always recommended for critically ill patients, bacterial co-infection is overall rare in COVID (only in 6.9% of all COVID patients [of which already at admission in 3.5% and later in the further course in 14.3%], especially in the intensive care unit in 8.1% [meta-analysis Langford et al, Clinical Microbiology and Infection 2020). However, a Europe-wide retrospective observational study (coVAPid study [Rouze et al, Intensive Care Med 2021]) in > 48 hours mechanically ventilated patients showed a higher rate of bacterially caused ventilator-associated pneumonia (VAP) with COVID (36%) than with influenza (22%). The most common bacteria were pseudomonas (22%), enterobacter (19%; was considered relevant here) and klebsiella (12%).
  - procalcitonin > 1.5 ng/ml → in 80% bacterial superinfection and thus (possibly) an indication for antibiosis (Berkel et al, Crit Care 2020)
  - As part of the fifth wave (Omicron) in Germany, however, we generously carried out antibiotic treatment in case of pulmonary infiltrates since these were almost always caused by bacteria and the patients were only incidentally COVID positive (by the way). Infiltrates in the chest x-ray due to Omicron are a rarity!

Excursus: Carbapenem-resistant organisms (CRO)

CRO

- **carbapenem-resistant organisms**
- **p.d. always 4-MRGN**
- **mechanisms (of carbapenem resistance):**
  - **formation of carbapenemases (most common)**
  - **loss of porins (loss of specific channel proteins, especially in case of pseudomonas)**
  - **efflux pumps that actively pump the antibiotic out of the bacterium**
- **types:**
  - **carbapenem-resistant enterobacteriaceae (CRE; 25%; most common carbapenemase: OXA-48)**
  - **carbapenem-resistant non-fermenters (75%)**
    - **pseudomonas aeruginosa (60%; most common carbapenemase: VIM-2)**
    - **acinetobacter baumanii (15%; most common carbapenemase: OXA-23)**

CRE

- Carbapenem-resistant enterobacteriaceae (especially klebsiella pneumoniae [most common CRE], escherichia coli)
- syn.: carbapenemase-producing enterobacteriaceae (CPE)
- proportion only 2-3% in Germany (more often in Greece, Italy, Turkey, Malta, Israel, USA, India, Iran, Iraq, Egypt, China, Thailand, Japan), but significant increase in Germany
- They will be the largest problem in the future!
- obligation to report according to §7 Infection Protection Act (IfSG) in Germany
- ⚠ mortality: 50% (Correa et al, BMC Inf Dis 2013), 4-fold increased mortality
- carbapenemases (Ambler classification [according to the British molecular biologist Richard Penry Ambler [1933-2013]):
  - class A: e.g. klebsiella pneumoniae-carbapenemase (KPC)
  - class B (most dangerous; only effective here: tigecycline [but only an option for uncomplicated intraabdominal infections], combination aztreonam + avibactam [contained in Zavicefta: ceftazidime + avibactam] or cefiderocol)
    - VIM (Verona integron encoded metallo-betalactamase; most common)
    - NDM (New-Delhi-carbapenemase)
    - IMP (imipenemase)
  - class C (e.g. AmpC)
  - class D (e.g. OXA-48 [oxacillinase])
- Carbapenemasen are β-lactamases:
  - class A, C and D: serin-β-lactamases (SBL)
  - class B: metallo-β-lactamases (MBL)
- the most common carbapenemases in Germany: OXA-48 (No.1), VIM (No.2), KPC (No.3), NDM (No.4)

Therapy

- polymyxins
  - colistin (⚠ the "backbone" [basis] of CRE therapy! renaissance! see page 1266)
  - polymyxin B
- tigecycline
  - for CRO in double dosage (loading dose 200 mg, then 100 mg 2 x daily i.v.; not officially approved for this dosage)
  - also effective against metallo-β-lactamases (Ambler class B)
  - but not for sepsis or urinary tract infection since insufficient levels are achieved, furthermore off-label in pneumonia; therefore only recommended for uncomplicated intraabdominal infections (Gales et al, Clin Infect Dis 2021)
- ceftazidime + avibactam (Zavicefta): The β-latamase inhibitor avibactam is very effective against CRE (especially against KPC [i.a. CRACKLE study: van Duin et al, Clin Infect Dis 2018] and OXA-48; however, not effective against metallo-β-lactamases [Ambler class B]: As an option, however, you can combine ceftazidime / avibactam with the monobactam aztreonam [not available in Germany] here [Marshall et al, Antibiol Agents Chemo 2017]).
- carbapenem as combination partner to colistin or fosfomycin (actually absurd; also recommended only for MIC < 8 mg/l; for CRO in double dosage [e.g. meropenem 3 x 2 g])
- meropenem + vaborbactam (Vabomere)
  - vaborbactam:
    - a new β-latamase inhibitor with effectiveness against carbapenemases (especially KPC)
    - boric acid derivative
  - approved by the FDA (USA) 2017 and by the EMA (EU) 2018 as a reserve antibiotic for complicated urinary tract infections (including pyelonephritis) caused by klebsiella pneumoniae, escherichia coli or enterobacter cloacae
  - dosage: 2g/2g 3 x daily. as short infusion over 3 hours
  - dose reduction:
    - renal insufficiency:
      - GFR 30-50 ml/min: 1g/1g 3 x daily
      - GFR 15-30 ml/min: 1g/1g 2 x daily
      - GFR < 15 ml/min: 0.5g/0.5g 2 x daily
    - hepatic insufficiency: no dose reduction necessary
  - approval study: TANGO I/II
- Recarbrio = imipenem + cilastatin + relebactam
  - cilastatin: an inhibitor of dehydropeptidase in the kidney that prevents the renal inactivation of imipenem
  - relebactam: a new β-latamase inhibitor with activity against carbapenemases of classes A and C (not active against classes B and D)

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):
  - 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 (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])
- 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 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)

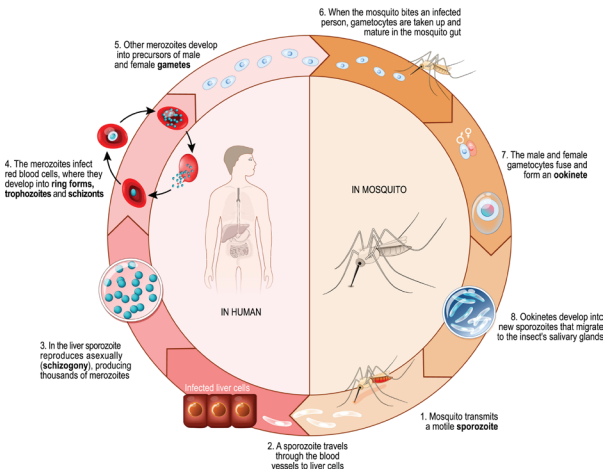


Fig. 1634 Life cycle of plasmodia (malaria cycle): Asexual reproduction (schizogony) takes place in human: First the hepatocytes (exoerythrocytic phase) and then the erythrocytes (erythrocytic phase) are infected. Sexual reproduction (gamogony) takes place in the anopheles mosquito. After the mosquito bite, the sporocytes (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 sporocytes then develop (sporogony).

Symptoms

- fever (This should be kept in mind even up to 2 years after a stay in the tropics!)
  - quartan malaria: 1 day fever, 2 days no fever
  - tertian malaria: 1 day fever, 1 day no fever
  - tropical malaria: fever irregular
- chills
- headache (typically severe!)
- back pain

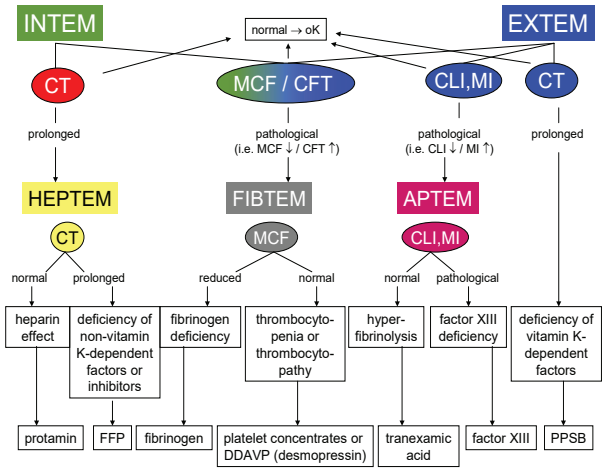
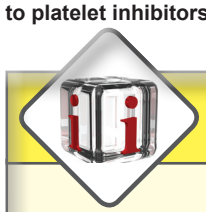


Fig. 1671 Interpretation of ROTEM (procedure for acute diffuse bleeding); as an alternative to fibrinogen deficiency, it can also be a fibrinogen polymerisation disorder (i.e. factor XIII deficiency); note: In the case of active bleeding despite normal CT and MCF in EXTEM and INTEM, the following should be considered or checked: co-factors (general conditions such as hypothermia, metabolic acidosis, hypocalcemia), presence of bleeding that can be stopped surgically, von Willebrand disease, thrombocytopathy due to platelet inhibitors (e.g. ASA)



Therapy algorithm ROTEM

- **EXTEM-ML > 15%**
  - **APTEM-ML < 15% → hyperfibrinolysis → administration of tranexamic acid**
  - **APTEM-ML > 15% → factor XIII deficiency → administration of factor XIII (fibrogammin; e.g. 1250 IU)**
- **FIBTEM-A10 < 7 mm: fibrinogen deficiency → administration of fibrinogen (Haemocomplettan)**
  - **FIBTEM-A10 0-3 mm: 6 g**
  - **FIBTEM-A10 3-6 mm: 3 g**
- **EXTEM-CT > 80 s (with normal FIBTEM) → deficiency of vitamin K-dependent coagulation factors → administration of PPSB:**
  - **EXTEM-CT 80-100 s: 500 IU Beriplex or 600 IU Baxalta**
  - **EXTEM-CT 100-120 s: 1000 IU Beriplex or 1200 IU Baxalta**
  - **EXTEM-CT > 120 s: 1500 IU Beriplex or 1800 IU Baxalta**
- **INTEM-CT > 240 s:**
  - **HEPTEM-CT normal → heparin effect → administration of protamin**
  - **HEPTEM-CT prolonged → deficiency of non-vitamin K-dependent coagulation factors or inhibitors → administration of FFP**
- **EXTEM-A10 < 40 mm (FIBTEM-A10 > 7 mm, platelets < 50,000/µl) → lack of platelets → administration of platelet concentrates**

Limitations

- thrombocytopathies (e.g. thrombasthenia Glanzmann [absence of GIIb/IIIa receptors])
- platelet inhibitors (ASA, clopidogrel, prasugrel, ticagrelor)
- von Willebrand disease
- factor XIII deficiency
- GpIIb-IIIa receptor antagonists (especially abciximab)
- only relatively low sensitivity for oral anticoagulants (e.g. VKA [coumarins]; NOAC, however, have no influence on the measured values), LMWH, danaparoid (Orgaran) and fondaparinux (Arixtra)
- no standard validation (yet) using round robin tests

Multiplate

Definition

- multiple platelet function analyzer (Roche company)
- measurement of platelet function (for overview of possible methods: see infobox)
- method: impedance aggregometry
  - Platelets are activated and aggregated at the surface of a sensor wire leading to an increase in electrical resistance (impedance). This resistance is measured.
  - measurement of the increase of the impedance as area under the curve after activation of the platelets
- can be performed on the bedside (e.g. in the emergency room, intensive care unit or operation room) as POCT (point of care testing; results within 10 minutes)
- material: whole blood
- 4 channels for different activators:
  - TRAP (thrombin receptor activating peptide; basic stimulability of platelets)
  - collagen (physiological stimulability of platelets)
  - arachidonic acid (measured value < 250 AUC: good ASA effect)
  - ADP (adenosine diphosphate; measured value < 200 AUC: good clopidogrel effect [responder])
- only valide with a normal account of platelets and erythrocytes (applies to all methods of measuring platelet function)

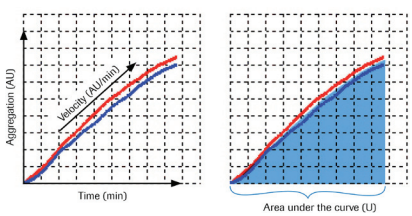


Fig. 1672 In the Multiplate system, the impedance increase is measured as an area under the curve (AUC) of aggregation time after activation of the platelets [41].

ONCOLOGICAL EMERGENCIES

Introduction

The decision whether to transfer a critically ill patient with an underlying hemato-oncological disease (especially AML, autologous / allogeneic stem cell transplantation, non-Hodgkin´s lymphoma) to an intensive care unit or not is often not easy in clinical practice. In chronically bedridden patients (> 3 months), lack of a life-prolonging therapy option, uncontrolled or refractory GvHD or an overall prognosis of less than one year, the intensive care admission must certainly be considered very critically. Life and not suffering should be prolonged. 20% of all intensive care patients have cancer. In a sample prevalence study (Kochanek et al, Med Klin Intensivmed Emergency Med 2020), every fourth patient in ICU or IMC in Germany had cancer. The most common cause for admitting a hematological-oncological patient to ICU is acute respiratory insufficiency (mostly due to pneumonia; No. 2: sepsis; especially neutropenia). Early non-invasive ventilation is particularly important here: It leads to a significant reduction in mortality (Hilbert et al, N Engl J 2001; Molina et al, Crit Care 2012) and should be used early to avoid intubation. However, another study (Lemiale et al, JAMA 2015) could not show any mortality reduction in cancer patients with acute respiratory insufficiency (mostly due to pneumonia) by using NIV compared to pure oxygen therapy. In the EFRAIM study (Azoulay et al, Intensive Care Med 2017), NIV was also unable to reduce the intubation rate or mortality. HFNOT (high-flow nasal oxygen therapy) was also unable to reduce the intubation rate or mortality in immunosuppressed patients (HIGH study [Azoulay et al, JAMA 2018]).
Intensive-care mortality is determined by organ dysfunction and not by malignancy. Malignancy determines the long-term mortality. If the acute problem leading to ICU admission is being survived, the prognosis is exactly the same as before ICU admission. They practically return to their initial prognosis before the intensive care stay.
In the German iCHOP registry (intensive care medicine in hematologic and oncologic patients; mean age 62 years; 2/3 hematologic and 1/3 oncologic disease), acute respiratory failure was the most common reason for admission to the intensive care unit. The ICU mortality was 58% and the hospital mortality was 45%.
The prognosis of critically ill cancer patients has improved considerably in recent years (i.a. Darmon et al, Intensive Care Med 2019): Mortality has been reduced by 30% (absolute risk reduction) over the last thirty years (i.a. Gristina et al, Crit Care Med 2011). Long-term survival is possible with some tumors even in the metastatic stage (e.g. in metastatic malignant melanoma: 20% still live 10 years). Therefore, a generally restrictive ICU admission policy for cancer patients should be abandoned.
In addition, the emergency and intensive care physician is often unable to make an adequate assessment of the prognosis due to the time pressure of the emergency situation, incomplete informations and possibly also a lack of knowledge of the underlying disease. Patients with advanced solid tumors should also be treated with full code management both according to the recommendations of an international team of experts (Azoulay et al, Ann Intensiv Care 2011) and according to the consensus recommendations of German-speaking intensive care and hematological-oncological societies (Kiehl et al, Ann Hematol 2018) if a life-prolonging oncological therapy option still exists. This includes, for example, patients with colorectal cancer with liver metastases, who have currently a survival time of approximately 30 months with modern chemotherapy. In principle, full code management is indicated in sace of remission, existing curative therapy approach or newly diagnosed cancer (prognosis > 1 year). On the other hand, patients with "common diseases" are often admitted to ICU ("without batting an eyelid"), although the prognosis which is unfortunately often unknown to many, is sometimes considerably worse than for many cancers: e.g. heart failure (5-year-survival rate 50%), COPD (GOLD IV: 5-year survival rate 30%) or liver cirrhosis (Child C: 1-year survival rate 50%). Furthermore, the fact that a palliative patient is still young is also not a sufficient reason alone for ICU admission ("Oh, he's still so young!"). Children also die of cancer!

Intensive mortality is determined by organ dysfunction and not by malignancy!

no generally restrictive ICU admission policy towards cancer patients!

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
  - 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
  - meningitis, encephalitis
  - myelitis
- musculoskeletal:
  - myositis (possibly rhabdomyolysis)
  - fasciitis
  - arthritis (therapy: possibly MTX, 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%]!)

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 Rechovot (Israel) in the late 1980s ("T-body", "immune receptor")
- 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) 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. The production 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. The second relapse occurred at the age of 6 so that all conventional therapy options were exhausted. The parents agreed to an experimental CAR-T-cell therapy which was carried out for the first time in 2012. The girl is now (2023) 15 years old and completely tumor-free.
- indications (if refractory or relapsed):
  - lymphomas (B-cell non-Hodgkin lymphomas; adults)
    - diffuse large B-cell lymphoma (DLBCL)
    - primary mediastinal large B-cell lymphoma (PMBCL)
    - transformed follicular lymphoma (tFL)
  - acute lymphoblastic leukemia of the B-cells (B-ALL; exactly: BCP-ALL [B-cell precursor]; children)
- very effective ("revolutionary"): response rates
  - diffuse large B-cell lymphoma: 82%
  - B-cell ALL: 90%
- procedure: The tumor cells are often not recognized by the normal T-cells. Here, the patient's T-cells (autologous) are removed by leukapheresis and sent to a special laboratory. There they are genetically modified via gene transfer so that they can now recognize the malignant B-cells better. The gene transfer (transduction) takes place with the help of a virus (viral vector; mostly lentivirus or retrovirus) which smuggles in the genetic information for an antigen receptor that has the ability to recognize the target protein (e.g. CD19) on the surface of the malignant B-cells. In order to have a sufficient number of T-cells available for therapy, amplification takes place which usually lasts 2-3 weeks. After the patient has been appropriately prepared by lymphocyte-depleting chemotherapy, the modified T-cells are finally returned to the patient (re-transfused). Since the T-cell receptors are built partly from their own and partly from foreign (synthetic) genetic material, they are referred to as "chimeric" (chimera: a hybrid

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%)

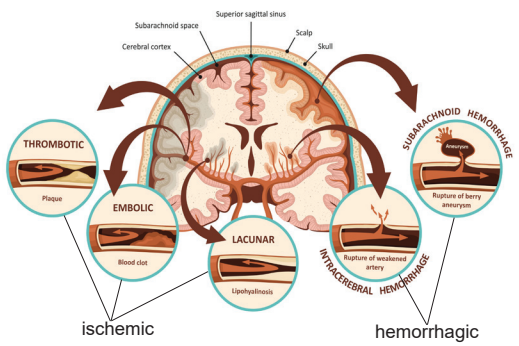


Fig. 1710 the different types of stroke

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)!

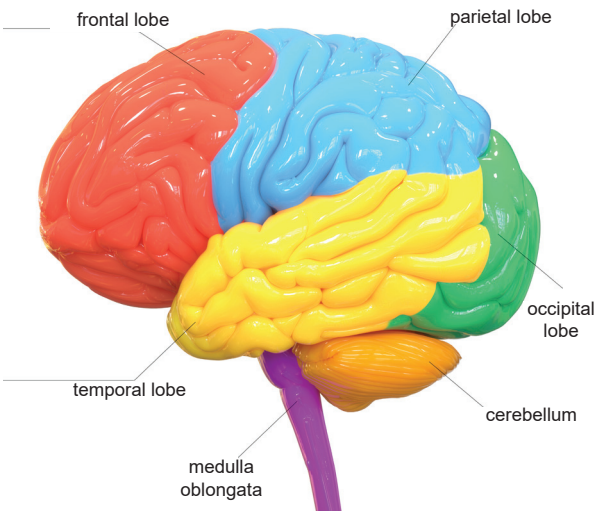


Fig. 1711 Brain: anatomy

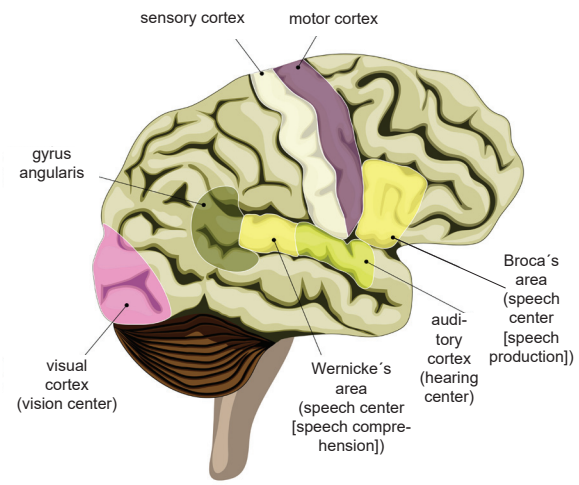


Fig. 1712 Brain: function

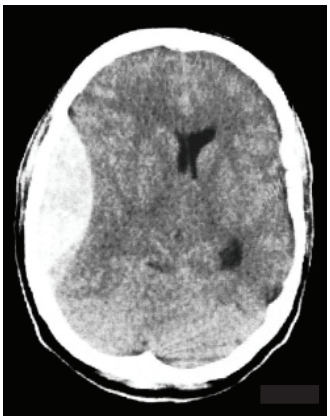


Fig. 1772 CCT: right-sided epidural hematoma - typically temporal and lenticular (courtesy of PD Dr. K.-M. Schebesch, Senior Physician of the Department of Neurosurgery, University Hospital Regensburg [Germany])

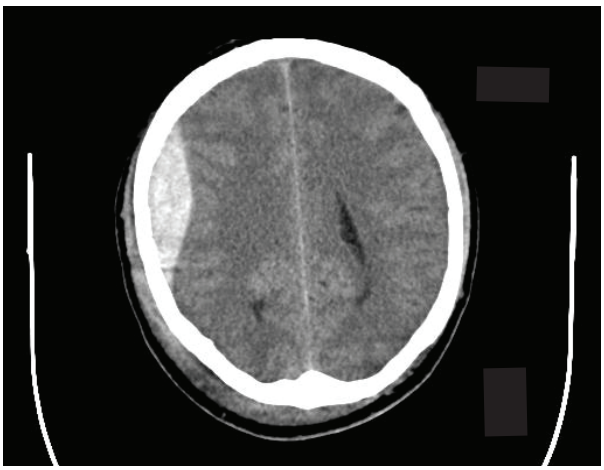


Fig. 1773 CCT: right-sided temporal epidural hematoma

Symptoms

- after traumatic brain injury (TBI) with disturbance of consciousness (commotio cerebri) typically free interval, then renewed disturbance of consciousness
- hemiparesis (contralateral)
- headache
- vomiting
- psychomotor restlessness
- seizure
- anisocoria (ipsilateral)
- often rapid neurological deterioration ("talk and die")

Complications

- increase in intracranial pressure (ICP) with herniation and decerebration
- hemorrhagic shock due to bleeding into the galea (especially in children)

Therapy

- emergency surgery (trepanation and haematoma evacuation)
- indication for surgery i.a. if the hematoma is larger than the width of the calotte
- if no neurosurgery is available in the hospital:
  - relocation (transfer to a hospital with neurosurgery; best)
  - if necessary Kroenlein burr hole trepanation (two relief holes in the temporal region at eyebrow level anterior and posterior to the ear; named after the Swiss surgeon Rudolf Ulrich Kroenlein [1847-1910])

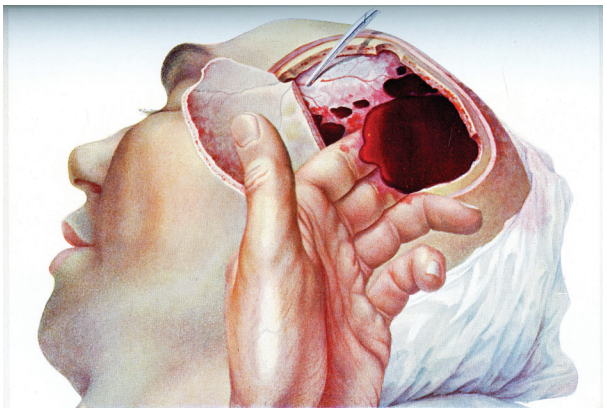


Fig. 1774 hematoma evacuation

Subdural hemorrhage (SDH)

Definition

- bleeding in the subdural space (= space between hard meninx [dura mater] and arachnoid mater)
- a venous bleeding (slowly expanding; tear of bridging veins)
- frequent in elderly people
  - incidence at age > 65 years: 60/100,000
  - reason: Due to the increasing brain atrophy with age, the traction on the bridging veins and thus the risk of rupture also increases.

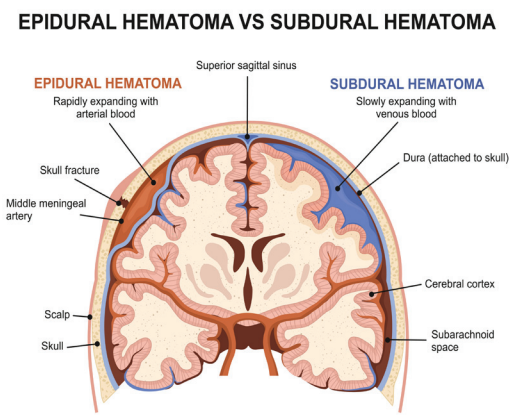


Fig. 1775 Difference between epidural and subdural hematoma: While the epidural hematoma (red; bleeding between the skull bone and dura mater) is an arterial bleeding (from the middle meningeal artery; almost always result of a trauma with skull fracture) which therefore expands rapidly and increases in size with a space-occupying effect, the subdural hematoma (bleeding between the dura mater and arachnoid mater) is only a venous bleeding with correspondingly slow expansion.

In the case of infratentorial brain damage, irreversibility must always be proven by an additional ancillary tests!

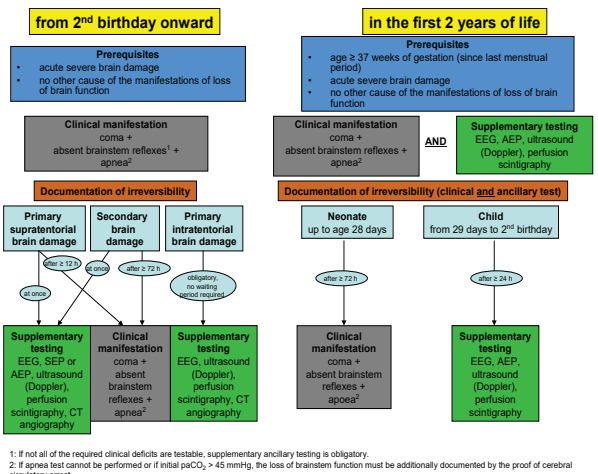
Annotations

- In the case of combined brain damage, the most conservative procedure is always indicated: In a combination of primary supratentorial and infratentorial brain damage, the same procedure is used as for primary infratentorial brain damage, i.e. the proof of irreversibility by the observation period is not permissible and therefore an ancillary test is always indicated. A combination of primary supratentorial and secondary brain damage is treated in the same way as isolated secondary brain damage (i.e. observation period 72 hours).
- For children up to the age of 2 years, both the clinical and the instrument-based diagnostics (ancillary test) must always be repeated.

in children up to the age of 2 years, proof of irreversibility always clinical AND instrumental (ancillar)!

Ancillary tests (instrument-based diagnostics; supplementary testing)

- EEG (most common)
  - at least 8 channels, sensitivity of 2 µV/mm
  - detection of a zero line ("brain-electric silence") for at least 30 minutes
  - In practice, it is often difficult to obtain a continuous zero line (without artifacts) with the newer (very sensitive) EEG devices. Therefore one should consider to use a rather older EEG device for brain death diagnostics.
  - Artifacts (e.g. from devices, infusions, muscle activity, spinal automatisms) should be taken into account, if necessary a muscle relaxant must be administered (but only after the clinical examination).
- evoked potentials (only possible with supratentorial brain damage, not with infratentorial brain damage)
  - auditory (AEP; standard)
  - somatosensory (SSEP; median nerve)
    - not possible with diseases in which the conductivity of the peripheral nerves is disturbed (e.g. polyneuropathies, damage of cervical medulla)
    - only permitted from the age of 2 years
- proof of cerebral circulatory arrest (independent of drug effects; prerequisite: MAP > 60 mmHg; all 3 methods are also possible with vv-ECMO, but not with va-ECMO.)
  - Doppler sonography (transcranial)
    - ⚠ mostly fastest available (means of choice)
    - at least 2 examinations at interval of 30 minutes
    - if necessary with contrast agent (e.g. SonoVue)
    - lack of flow signal or detection of oscillating flow (biphasic)
    - However, residual perfusion (e.g. in open traumatic brain injury or osteoclastic trepanation) does not contradict the diagnosis of brain death.
  - perfusion scintigraphy
    - tracer: Tc-HMPAO (hexamethylpropyleneamine-oxime)
    - diagnosis and evaluation by a specialist in nuclear medicine
  - angiography:
    - conventional angiography (only by a specialist in radiology): obsolete today
    - CT angiography:
      - now approved in the guidelines since 2015 (but only for adults [age > 18 years], not for children)
      - A missing contrast of the cerebral arteries of the brain base (anterior cerebral artery, middle cerebral artery, posterior cerebral artery as well as basilar artery on both sides) is required with detectable extracranial perfusion.
      - diagnosis and evaluation by a specialist in radiology with several years of experience in neuroradiological diagnostics (preferably neuroradiologists)



1: If not all of the required clinical deficits are testable, supplementary ancillary testing is obligatory.
2: If apnea test cannot be performed or if initial $paCO_2$ > 45 mmHg, the loss of brainstem function must be additionally documented by the proof of cerebral circulatory arrest.

Fig. 1847 Diagnostics of brain death (irreversible brain function loss)

Confusions

- Lazarus sign
  - Lazarus: in the biblical story (Gospel of John) the human being who was brought back to life by Jesus four days after his death
  - Lazarus sign: movement of a person declared dead
  - occurrence in brain-dead patients: in 50% (frequently!)
  - Brain-dead patient often show sudden movements, especially of the upper extremities which often unsettle physicians, nurses and especially relatives completely. These are only spinal reflex automatisms and are no sign that the patient is still alive. If they occur frequently, the patient may have to be treated with a muscle relaxant (after brain death has

- laser ablation (laser hair removal): Toxic substances such as carbon monoxide and cyanide might be released with potential risk for physicians and patients (Chuang et al, JAMA Dermatol 2016). Smoke outlet and airing must therefore be ensured.

Etiology

- smoke gas from burning plastic, textiles (most common cause; especially at low combustion temperature [smoldering])
- accident in electroplating plants
- suicide / homicide (murder) with potassium cyanide

most common cause of cyanide intoxication: smoke inhalation in a fire! most common cause of death from smoke inhalation: cyanide intoxication!

Symptoms

- bitter almond odour (cannot be smelled by everyone [only approximately 40%; determined genetically])
- headache
- ⚠ rosy skin color (as in case of CO intoxication; despite hypoxia; pulse oximeter also shows high saturation!)
- nausea, vomiting
- abdominal pain (colics)
- dizziness
- dyspnea (agonizing breathlessness without cyanosis!)
- angina pectoris (due to the lack of oxygen; often also ST elevations in the ECG)
- mydriasis
- ⚠ bradycardia (typical sign)
- tachypnea
- impaired consciousness, coma
- seizures (due to hypoxia; tonic-clonic)
- ⚠ attention: death within a few seconds (in contrast to CO [takes longer!])

Laboratory

- metabolic acidosis
  - severe lactic acidosis due to blockage of the enzymes of the respiratory chain
  - Carbon monoxide intoxication usually does not lead to an (pronounced) increase in lactate (but it can also occur here as a result of hypoxemia). If lactate is also increased during smoke inhalation (e.g. during a fire), it is very likely that there is also cyanide intoxication in addition to carbon monoxide intoxication! A lactate > 90 mg/dl (> 10 mmol/l) in the context of smoke gas intoxication is a very sensitive and specific sign of cyanide intoxication.
  - degrees of severity according to pH value and lactate (are available immediately; Baud criteria [according to Baud et al, Crit Care Med 2002; see infobox])
- determination of the cyanide level in the serum
  - due to the short half-life immediately and before the administration of the antidote
  - mostly not available immediately
  - only retrospectively to confirm the diagnosis, no influence on acute therapy
  - ⚠ If (in the context of a domestic fire) the CO-Hb (carboxyhemoglobin) value is high (> 25%), the cyanide level is also always high (good correlation), i.e. the antidote should be administered generously here.
  - degrees of severity according to the cyanide level:
    - < 1 mg/l: mild intoxication
    - 1-3 mg/l: moderate intoxication
    - > 3 mg/l: severe intoxication (mostly lethal)

Degrees of severity
Baud criteria

- **mild intoxication:**
  - **pH > 7.35**
  - **lactate < 8 mmol/l or < 70 mg/dl**
- **moderate intoxication:**
  - **pH 7.20-7.35**
  - **lactate 8-10 mmol/l or 70-90 mg/dl**
- **severe intoxication:**
  - **pH < 7.20**
  - **lactate > 10 mmol/l or > 90 mg/dl**

smoke gas intoxication with increased lactate: cyanide poisoning!

Therapy

- administration of highly dosed oxygen, if necessary endotracheal intubation and mechanical ventilation with FiO_2 of 1.0
- in case of oral uptake (ingestion; very rarely; let patient drink or insert a gastric tube):
  - 300 ml potassium permanganate solution (1:5,000; pink colour) to oxidize the cyanide or (if not available)
  - activated charcoal, laxatives
- lactic acidosis → sodium bicarbonate 8.4%, if necessary hemodialysis
- antidotes:
  - 4-DMAP (dimethylaminophenol)
  - hydroxycobalamin (Cyanokit)
  - sodium thiosulfate 10% (S-Hydril)

4-DMAP

- dimethylaminophenol
- mechanism of action:
  - a methemoglobin producer
  - oxidizes Fe^{2+} to Fe^{3+} in the hemoglobin (intentional

ularly at risk. For this reason, the rescue service staff has already been equipped with portable gas warning devices for their own protection in the most rescue service districts.

- mortality: 30-40%
- S2k guideline "Diagnostics and therapy of carbon monoxide poisoning" of the German Interdisciplinary Association for Intensive Care and Emergency Medicine (DIVI) 2021

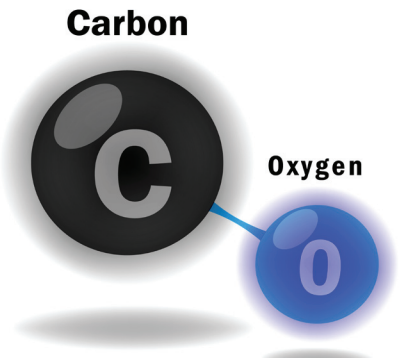


Fig. 1929 carbon monoxide (CO)

Pathophysiology

- blockage of the oxygen transport: Carbon monoxide has a 200 times higher affinity for divalent iron in hemoglobin than oxygen resultimg in competitive displacement.
- blockage of oxygen utilization in the cell by inhibiting the cytochrome oxidases in the mitochondrial respiratory chain
- shift of the oxygen binding curve to the left with consecutive reduced oxygen release to the tissue
- blockage of the oxygen binding not only in hemoglobin, but also on myoglobin (40 times higher affinity; heart / skeletal muscles)
- Due to the low ischemia tolerance, the brain and heart are particularly affected.

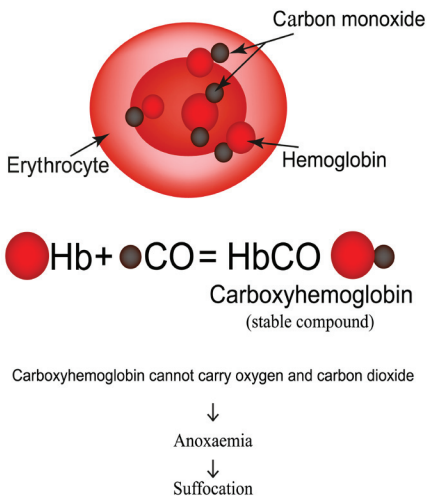


Fig. 1930 Carbon monoxide has an affinity for hemoglobin that is 200 times greater than oxygen, so hat CO displaces it. Carboxyhemoglobin is formed instead of oxyhemoglobin.

carbon monoxide: not only blockade of oxygen transport, but also of oxygen utilization

Occurrence

- smoke gas in case of fire
  - ⚠ most frequent cause
  - especially in closed rooms (typical domestic fires: 10% of carbon monoxide in the smoke gase → after 1 minutes already carbocyhemoglobin of 75 % [lethal!])
- suicide attempts:
  - inhalation of car exhaust fumes (since the introduction of regulated catalytic converters only rarely today)
  - a suicide method widespread in the Asiatic area and now also in Germany: The suicidal person goes into the bathroom, closes the windows and seals the door from the inside with adhesive tapes. Then he lights a charcoal grill. A carbon monoxide concentration of up to 50 % then develops in the room which is usually lethal. However, this also poses a considerable risk to the arriving emergency service staff as neither smoke nor gas odour can be detected beforehand!
  - self-production (mixture of formic acid with sulphuric acid: Formic acid is degraded to carbon monoxide [Instructions for use can be found in the internet].)
- exhaust gases in poorly aired garages (i.a. suicidal; declining due to the increasing use of regulated catalysts)
- instantaneous water heater in non-aired bathrooms (typical: "found unconscious in the shower"!)
- defective gas ovens (e.g. old cokery ovens, poor room airing), defective gas boilers
- mobile radiant heaters
- closed room with open fire (open fireplaces + defective smoke outlet!)
- poorly maintained heating systems
- illuminating gas (still partly used as "cokery gas" in factories)
- smoking with water pipes ("shishas"): 10 times higher carbon monoxide inhalation (by burning the charcoal) than when smoking cigarettes
- wood pellets / wood chips stored improperly (especially insufficiently aired cellars): Chemical processes were initiated by shredding and drying the wood so that carbon monoxide is constantly evaporated from it. The storage rooms must therefore be well aired (i.e. cellar windows always open or installed electrical airing) and equipped with a carbon monoxide warning system.
- Also in case of intoxication with the organic solvent dichloromethane (see page 1577), carbon monoxide intoxication may occur because dichloromethane is degraded to carbon monoxide.
- laser ablation (laser hair removal): Toxic substances such as carbon monoxide and cyanide might be released with potential risk for physicians and patients (Chuang et al, JAMA Dermatol 2016). Smoke outlet and airing must therefore be ensured.

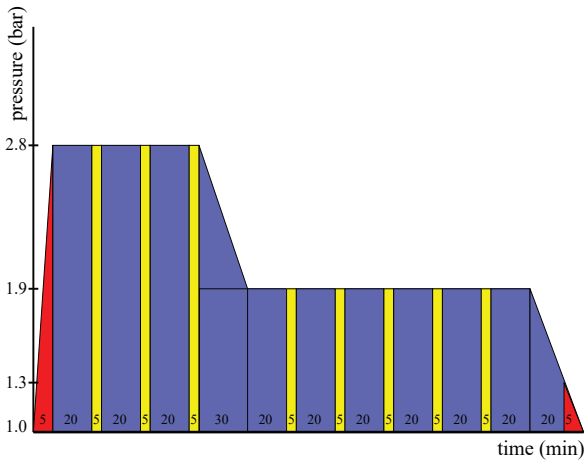


Fig. 1939 therapy scheme for diving accident and arterial gas embolism: TS 280-60 (syn.: US Navy Table 6). The time of pure oxygen breathing is shown in blue, the oxygen breaks (air breathing) in yellow and the time of breathing without a mask in red. Total duration of the session: 285 minutes

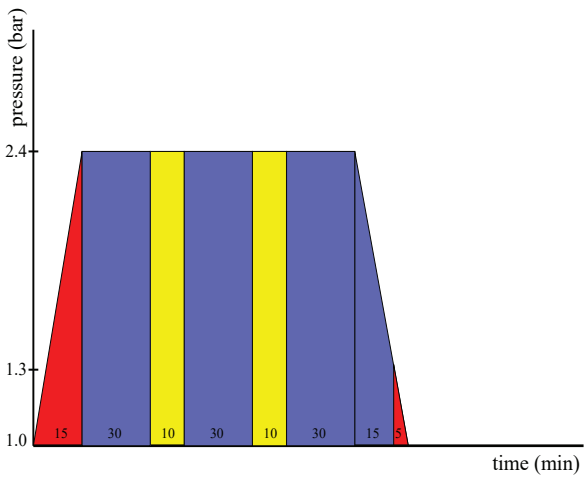


Fig. 1940 therapy scheme for problematic wounds: TS 240-90. The time of pure oxygen breathing is shown in blue, the oxygen breaks (air breathing) in yellow and the time of breathing without a mask in red. Total duration of the session: 140 minutes

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 chamber increases (just think of the air pump when you put your finger on the opening; in case of rapid compression, a temperatur of up to 50°C in the chamber may be possible).
  - During decompression, the temperature in the chamber decreases again.
- hypoglycemia

Contraindications

- An untreated pneumothorax is a contraindication for HBO. If a thoracic trauma is possible (e.g. patient fell down the stairs), an X-ray of the thorax should be performed beforehand to exclude pneumothorax. In case of pneumothorax, thoracic drainage (chest tube) should be performed prior to HBO.
- HBO is relatively contraindicated in patients with a pacemaker / AICD since the overpressure can lead to a deformation of the aggregate with consecutive loss of function. However, most of the aggregates today are also suitable for pressure chambers.
- severe obstructive pulmonary disease: Air trapping often occurs here. Trapped air might expand during decompression and cause pulmonary rupture.
- inability to equalize ear pressure (In order to assess this condition, an otoscopy is performed and the patient is asked to perform a Valsalva maneuver; if necessary, the patient is given nasal drops into the chamber)
- after intracranial surgery with inclusions of air, acute traumatic brain injury

The only contraindication for HBO in an emergency is an undrained pneumothorax!

Fig. 1967 plants containing digitalis: lily of the valley

Fig. 1968 plants containing digitalis: oleander

Monkshood

Definition

- syn.: wolfsbane, Devil's helmet (aconitum napellus)
- ⚠ most dangerous plant in Europe
- occurrence:
  - ornamental plant in gardens (unfortunately frequent)
  - damp meadows, brook banks, around alpine huts (Only a few plants grow there which are not eaten by cattle!)
  - use of the plant for homeopathy and TCM (traditional Chinese medicine): Cooking causes hydrolysis of the toxin aconitine. However, incorrect preparation 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 or lovage
- suicidal (e.g. mixing the blossoms in tea, Chinese herbal teas, ingestion of topical substances from TCM [traditional Chinese medicine])

Fig. 1969 monkshood: most toxic plant in Europe (should not be planted in gardens, in which children play)

TRAUMATOLOGY

Overview
Traumatology

- **mechanical: polytrauma**
- **electric: electrical accident (electric shock)**
- **aquatic (hydraulic):**
  - **drowning accident**
  - **diving accident**
- **thermal:**
  - **affection of the core temperature of the body:**
    - **decrease: hypothermia**
    - **increase: hyperthermia (heat emergencies)**
  - **affection of the skin of the body: burns (thermal)**
- **toxic: chemical burns (see chapter toxicology page 1568)**
  - **acid chemical burns**
  - **caustic chemical burns**

POLYTRAUMA

Definition

- syn.: major trauma, multiple trauma, multisystem trauma
- Greek "poly": many, "trauma": injury
- According to the Austrian trauma surgeon Harald Tscherne: simultaneous injuries to several body regions or organ systems, of which one injury or the combination is life-threatening (in short: a life-threatening multiple injury)
- according to AIS (Abbreviated Injury Scale): combination of injuries with an Injury Severity Score (ISS; see infobox; according to Baker et al, J Trauma 1974) ≥ 16 P.
- according to the Berlin definition (note: There is also a Berlin definition for the ARDS!): at least 2 injuries of severity degree 3 (according to AIS) and one of the following criteria:
  - hypotension (SBP ≤ 90 mmHg)
  - GCS ≤ 8
  - metabolic acidosis (BE ≤ -6)
  - coagulopathy (INR ≥ 1.4)
  - age ≥ 70 years
- main cause: traffic accidents
- mostly (90%) blunt injuries
- anamnestic hints for polytrauma (accident constellation):
  - fall from a height > 3 meters
  - high-speed trauma
  - rollover trauma
  - thrown out of car (ejection)
  - stuck in the car
  - heavily deformed car (especially passenger cell ["B pillar])
  - pedestrians or cyclists hit by a car
  - occupant fatally injured (dead)
  - spill
  - explosion
- procedure according to the ABCDE scheme (see infobox) according to ATLS (Advanced Trauma Life Support)

    - consequences: hypervolemia (hypotonic hyperhydration), hyponatremia, hemolysis with potassium release (severe hyperkalemia) and kidney failure (due to free hemoglobin)
  - drowning in salt water (hypertonic liquid [saline 2%]):
    - draws water into the lung (wet lung)
    - consequences: hypovolemia (hypertonic dehydration), pulmonary edema, hemoconcentration, hypernatremia

Epidemiology

- especially toddlers (1-4 years) and young adults (especially under the influence of alcohol and drugs)
- even possible with the shallowest water depths (e.g. water puddles, rain or water barrel, water-filled bucket)
- incidence:
  - 1-2/100,000
  - declining
- drowning sites (according to frequency):
  - rivers (No.1)
  - lakes (e.g. fall through the ice, stand-up-paddling [SUP])
  - sea
  - garden pond
  - swimming pool
    - private
    - public (outdoor, indoor)
  - other:
    - bath tub (especially for infants)
    - rain or water barrel
    - wells, water ditches
    - building excavation
    - canals, harbour basins
- especially in the summer months and on weekends
- m > w (2:1)
- frequent accident-related cause of permanent disability and death
- third most frequent cause of death in children (among toddlers, i.e. children < 5 years, even the second most frequent cause of death [after traffic accidents, i.e. polytrauma])
- annual deaths:
  - national (in Germany): approximately 500
  - international (worldwide): approximately 450,000

drowning: the second most frequent cause of death among toddlers!

Etiology

- unattended toddlers (most common cause; e.g. child falls into insufficiently secured garden pond; e.g. toddler unattended in bathtub)
- non-swimmers
- exhaustion
- alcohol intoxication
- epilepsy (e.g. seizure), disability (physical / mental)
- injury when jumping into the water
- boat accident, ship accident
- swimming pool blackout: Before diving (e.g. as a "competition" with friends in the public swimming pool), hyperventilating is done consciously so that the pCO_2 drops. By venting down the pCO_2, the respiratory drive is reduced and you can dive longer. The point in time from which the rising pCO_2 exceeds the critical value, from which the respiratory drive and thus the ascent is forced, is delayed. Hypoxemia causes almost no respiratory drive, only hypercapnia. However, hypoxemia can cause the diver to become unconscious.
- suction pumps in swimming pools: If they are insufficiently secured (e.g. in hotel pools on vacation, wave pool), children in particular can be sucked in over the grids under water (especially through their hair) and drown while diving.

Pathophysiology

- initial panic reaction with frantic automatic swimming movements (fighting for survival)
- after submersion, deliberate cessation of breathing (apnea) for 1-2 minutes
- then forced breathing due to the no longer deliberately suppressible stimulation of the respiratory center due to the pCO_2 increase (maximum breathing stimulus) with aspiration
- diving reflex:
  - reflexive laryngospasm
  - In this phase, large amounts of water are often swallowed.
  - increased hypoxemia and hypercapnia
  - usually only present in small children
- unconsciousness
- release of the laryngospasm (persists in 10% which then leads to dry drowning) → aspiration of water
- The amount of inhaled (aspirated) water is usually low (< 22 ml/kg; the average is usually only about 10 ml/kg). Most of it is swallowed!
- The aspiration of water leads to inactivation and washout of surfactant which causes atelectasis with intrapulmonary shunts, reduced compliance of the lung and ARDS.
- seizures (caused by hypoxia; hypoxic convulsions; asphyxiation cramps)

- ROSC (return of spontaneous circulation) within 10 minutes
- pH > 7.1
- potassium < 7.5 mmol/l

meta-analysis

Predicting outcome of drowning at the scene: A systematic review and metaanalysis
Quan et al, Resuscitation 2016

- meta-analysis of 24 cohort studies with approximately 4,000 drowning accidents
- prognostic factors (for survival and good neurological outcome):
  - submersion time
    - the most important prognostic factor
    - < 5 minutes → good prognosis (3 times higher probability of survival); > 25 minutes → very poor prognosis
  - salt content of the water: The prognosis was better for drowning accidents in salt water (sea) than in fresh water.
  - Surprisingly, age (no advantage for children) and water temperature (no advantage of low water temperatures) had no influence on the outcome in this study.

50% of all resuscitated patients after a drowning accident leave the hospital alive without neurological damage!

Prophylaxis

- 86% of all fatal drowning accidents in children are preventable!
- Always provide garden ponds with a child-proof fence (minimum height: 1.5 m)!
- Never leave small children unattended near water (e.g. open-air swimming pool, bathtub; not even if they wear inflatable armbands [water wings])!
- Provide bathtubs with non-slip surfaces and handles!
- obligatory use of life jackets when practicing water sports
- early swim training (30% of all eleven-year-old children cannot swim!)
- providing an adequate number of well-trained lifeguards in public swimming pools

DIVING ACCIDENT

Definition

- potentially life-threatening event that can occur while diving with (SCUBA: self-contained underwater breathing apparatus) or without diving equipment by a rapid reduction of the ambient pressure during the ascent phase (decompression phase)
- Pressure increases by 1 bar per 10 meters diving depth. On the water surface, an atmospheric pressure of 1 bar prevails, i.e. at 30 meters diving depth an ambient pressure of 4 bar prevails.
- The most dangerous phase during diving is the ascent phase (decompression phase): The ambient pressure decreases and thus also the solubility of the gases according to the gas laws (see page 1602; when diving with breathing air, the nitrogen [78% nitrogen contained in breathing air]) decreases continuously. Nitrogen bubbles appear which usually get into the exhaled air via the alveoli. However if the ascent occurs too quickly (failure to observe the decompression regulations ["holding times", "panic ascent"]), critical oversaturation with nitrogen bubbles in the vessels and in the tissue occurs. Free gas bubbles are formed in the blood and tissue.
- also possible when working under overpressure (e.g. civil engineering, tunnel construction [e.g. Brenner base tunnel], underground railway construction)
- The symptoms of decompression sickness usually only occur with a latency period of up to several hours

- > 60 years: 25%
- occurrence:
  - home (65%)
  - accidents at work (25%)
  - suicidal (5%)
  - other (5%; e.g. traffic accidents, abuse)

Symptoms

- pain
  - Burn pain is one of the worst pains at all!
  - The less pain, the more severe the burn!
- redness
- swelling
- blisters (burn blisters)

Extent

- according to the percentage of the burned area (TBSA: total burned surface area) of the body surface area (BSA); is initially often overestimated]; ⚠ life-threatening [risk of shock] from > 15% [in children from > 10%]; > 50%: mostly lethal; note: ⚠ First-degree burns are not counted [only from second-degree]!):
  - rule of nines according to Wallace (each 9%; not applicable to children due to the relatively large head [The following applies to children: head 18%, trunk each front and back 18%, arms each 9%, legs each 14%, genitals 1%]):
    - head: 9%
    - trunk
      - front: 18% (2 x 9%)
      - back: 18% (2 x 9%)
    - arms: 9% each
    - legs: 18% each (2 x 9%)
    - genitals: 1%
  - palmer rule: patient's palm = 1% of BSA (also applicable to children [remember: child's palm and not the physician´s palm])
- according to the depth (is initially often underestimated as it usually increases over time [phenomenon of deepening] and only develops fully after 4 days [therefore less important for the emergency physician; important especially for the subsequent surgical treatment]):
  - first-degree burn (epidermis; like sunburn): redness (erythema), pain, spontaneous healing (healing without scars)
  - second-degree burn (dermis [syn.: corium]): additional blisters
    - second-degree superficial (2a; superficial dermis): rosy wound base (still vital; hyperemic; capillarization still present [glass spatula test positive]), severe pain, spontaneous healing (healing without scars)
    - second-degree deep (2b; deep dermis): pale wound base (already dead [avital], capillarization no longer present [glass spatula test negative]), slight pain, no longer spontaneous healing (healing with scars; ⚠ therefore surgery necessary from here)
  - third-degree burn (hypodermis, subcutaneous tissue]): necrosis, scab (= eschar), white (leather-like) skin, ⚠ no more pain (e.g. when pricking with the needle)
  - note: Frequently, a fouth-degree burn (subdermis) is mentioned: This occurs mainly in high-voltage accidents that cause charring. Subcutaneous fatty tissue, bones, muscles, fascia and tendons are also affected here.

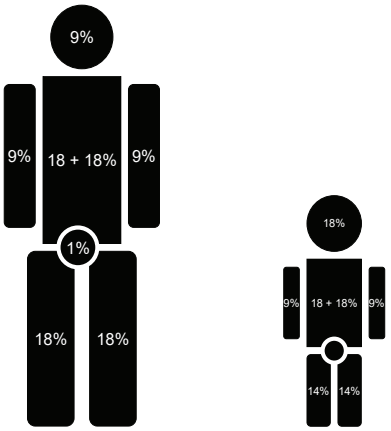
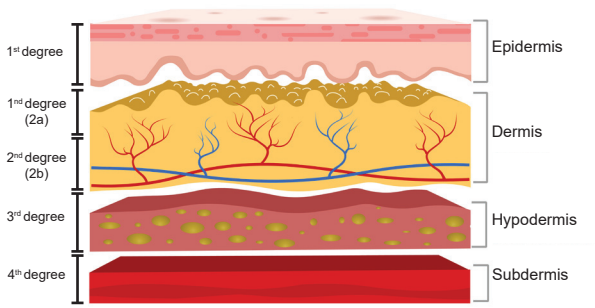


Fig. 1996 estimation of the percentage of total burned surface area (TBSA) according to the rule of nine according to Wallace: The body is divided here into sections by multiples of 9%. On the left it is shown for an adult and on the right for a child (infant: Here there are different values for the head [higher value] and the legs [lower values] compared to adults.)



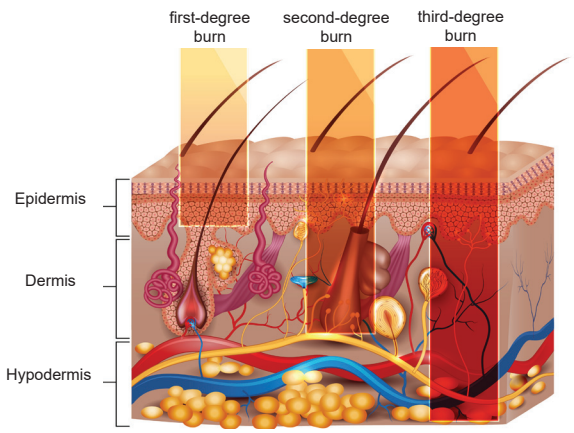


Fig. 1997 presentation of the different degrees of burns (according to the depth; based on the different skin layers)

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. 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. 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. 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 1680) and finally represents a burden for the resources of the health system. In a meta-analysis (Cardona-Morrell et al, Int J Qhal 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. This 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, DNI: do not intubate, AND: allow natural death) 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

- **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**
- **team meeting or (if necessary) ethic council has taken place**
- **informed consent has taken place (with patient, relatives, caregiver)**
- **The following measures will no longer be carried out (The corresponding should be issued.):**
  - **resuscitation**
    - **mechanical**
    - **electrical (defibrillation)**
  - **ventilation**
    - **invasive**
    - **non-invasive**
    - **increase of invasiveness of ventilation**
  - **extracorporeal support procedures**
  - **catecholamine therapy (start or increase)**
  - **renal replacement therapy**
  - **therapy with blood products**
  - **antibiotic therapy**

The decision should and must be made by the treating physician himself and must not be left to the relatives alone which unfortunately happens very often in prac-