Management of patients with risk factors

Abstract

This review addresses concomitant diseases and risk factors in patients treated for diseases of the ears, nose and throat in outpatient and hospital services. Besides heart disease, lung disease, liver disease and kidney disease, this article also covers disorders of coagulation (including therapy with new oral anticoagulants) and electrolyte imbalance. Special attention is paid to the prophylaxis, diagnosis and treatment of perioperative delirium. It is also intended to help optimise the preparation for surgical procedures and pharmacotherapy during the hospital stay.

Keywords: heart disease, lung disease, liver disease, kidney disease, haemostasis

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Introduction

Clinical otorhinolaryngology is a speciality with a very broad patient spectrum, starting with neonates, progressing through infants and schoolchildren, and into adulthood and old age. As a rule, relevant pre-existing diseases (e.g. hypertension, atrial fibrillation, heart failure, diabetes mellitus with organ-specific sequelae, and dementia) also increase with advancing age. The associated risk factors are equally diverse. It also has to be remembered that many patients with head and neck cancer are already affected and prematurely aged by medical conditions related to alcohol and smoking (e.g. COPD, hepatic cirrhosis, atherosclerosis, encephalopathy).

The manifold risk factors are relevant not only to the anaesthetists but also to the ENT surgeons, who are ultimately responsible for the care and management of their patients during the entire hospital stay. Ideally, risk factors should be identified at the time the patient is given a date for admission to hospital.

Clear treatment strategies exist in the appropriate speciality for nearly all the relevant medical conditions (e.g. in the form of international or national clinical guidelines). But as it is practically impossible for doctors to keep up to date with all issues outside of their own specialities, this review addresses key aspects in managing patients with risk factors. It is intended especially for junior hospital doctors who are the ones primarily faced with patients (potentially) at risk.

Treatment and dosage recommendations given in the following sections relate to the typical case and not to any unusual situations which, of course, require individual assessment. Moreover, doctors have to decide for themselves the extent to which they feel comfortable with situations outside their own field and the point at which they should refer patients to the appropriate specialists. The overview of the medication refers to the current *Rote Liste* [German medicines compendium] (online version 2012) and the information for healthcare professionals.

1 Risk: age

"Children are not small adults" may sound obvious but certainly holds true in clinical practice. Before initiating any paediatric pharmacotherapy, check whether the designated medicinal product is actually licensed for use in children of that age. The Patient Information Leaflet (PIL) and Summary of Product Characteristics (SPC) will not contain specific dosage recommendations for the age group unless the particular indication has been approved. It is potentially dangerous to extrapolate the paediatric dose from that recommended for adults, even when the adult dose is related to body weight. In case of doubt, ask a paediatrician for advice and/or consult the specific professional literature [1]. It is not (advanced) age per se that represents an independent risk factor but rather the comorbidity that usually accompanies the aging process. Biological age is more relevant to treatment than the chronological age.

At first glance, it is gratifying when an (elderly) patient is not taking any long-term medication, but it may in fact cause problems if it means that relevant medical conditions have not yet been detected because the patient has a dislike of going to the doctor. This applies especially to diseases such as diabetes, atrial fibrillation and hypertension with few symptoms and which have (allegedly) little impact.

It sometimes happens that, although a disease basically requiring treatment has been diagnosed by the general practitioner, a benefit/risk assessment leaves the condition untreated or inadequately treated with respect to defined targets (e.g. HbA1c in diabetes controlled by diet or medication, or aspirin therapy for atrial fibrillation). Relevant risks may therefore develop when the patient is in hospital, especially around the time of surgery.

Make sure to ask elderly patients who do not report any relevant pre-existing disease or medication exactly when they last saw a doctor and which organ systems, if any,

Table1: NYHA classification of heart failure.

Class I	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitations, or dyspnoea.
Class II	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitations, angina or dyspnoea.
Class III	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes symptoms.
Class IV	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

were examined at the time. It is also helpful to ask questions directed specifically at warning symptoms such as palpitations, irregular heartbeat, urgency of micturition, lack of stamina, swollen ankles and shortness of breath. Well before elective surgery, request diagnostic investigations on an outpatient basis, referring the patient to other departments in the hospital as required. If, on the contrary, routine preoperative screening tests (lab tests, ECG, etc.) are not carried out until the day of admission, there is a danger that the operation has to be postponed while waiting for further necessary investigations (e.g. echocardiography, lung function tests, thyroid function tests, etc.). Depending on the person's normal environment, (mild) dementia may remain unnoticed or ignored for a long time, which carries an increased risk of developing postoperative delirium. The same applies to other neurodegenerative diseases (see section 8).

On the other hand, polypharmacy in elderly people may cause considerable problems during inpatient treatment. Geriatricians and pharmacologists have long warned of the dangers of interactions and adverse drug reactions in relation to many substances. The risk of interaction is 38% when taking four different substances [2]. Even if the patient's regular medication does not seem to cause any obvious adverse reactions in daily use, it is still possible that clinically relevant interactions with drugs prescribed in hospital (e.g. sedatives, anaesthetic agents, muscle relaxants, antibiotics, analgesics, contrast medium) occur for the first time. As ENT surgeons often do not know the value of this polypharmacy, and cannot evaluate it for themselves without knowing the reasons for its prescription in the first place, the patient's regular medication is usually continued in hospital, with the inherent risk of adverse events.

Remember that pharmacokinetics and pharmacodynamics may be different in elderly people, resulting in an inadequate dose or overdose despite the assumption that the dosage is correct [3].

2 Risk: cardiovascular system

2.1 Heart failure

"Heart failure" [4], [5] is not a disease in its own right but rather a **clinical syndrome**. Clinical signs of heart failure are tachycardia, tachypnoea, respiratory crackles, pleural effusion and peripheral oedema. The European Society of Cardiology (ESC) defines heart failure as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolising tissues, despite normal filling pressures.

The **New York Heart Association (NYHA) classification** defines the stages of heart failure, as shown in Table 1. Right heart failure is diagnosed when systemic venous congestion (ankle oedema) predominates, while left heart failure is predominantly pulmonary venous congestion (pulmonary oedema). Taking the chronology of events into consideration, a further distinction can be made between acute and chronic cardiac failure. Typical causes of heart failure are hypertension, coronary artery disease, cardiomyopathy, valve disease, heart defects with shunts, and cardiac arrhythmias.

Pre-existing chronic heart failure has to be taken into consideration for surgical procedures under both general and local anaesthetics. Refer the patient to the cardiologists before surgery if there is any indication that the current medication is insufficient and could be optimised, and to allow them to assess and possibly reduce the perioperative risk [6], [7]. Ideally this referral should be made well before the day of admission, at the time when the patient is given a date to come into hospital, so that there is enough time to implement any therapeutic suggestions and prevent the operation being postponed (e.g. treatment with beta-blockers should be administered for at least a month before surgery). After the ECG, **echocardiography** is a standard cardiological examination. Thanks to portable equipment, the examination can also be carried out at the bedside, if necessary. Ultrasound scanning can distinguish between systolic and diastolic heart failure.

Table 2: Cardiac glycosides (digitalis)

Active substance	Proprietary name(s)	Elimination	Plasma level measurement
Digoxin	Lanicor®	renal 70-80%	digoxin
β-acetyl digoxin	Novodigal®	renal 70-80%	digoxin
β-methyl digoxin	Lanitop®	renal 70-80%	digoxin
Digitoxin	Digimerck®	renal 60%	digitoxin

Preoperative invasive diagnostic investigation in the form of **coronary angiography** is worthwhile or even essential if there is any evidence of coronary heart disease (CHD). Remember, however, that a coronary intervention with stenting regularly requires anticoagulation afterwards (see sections 2.3 and 6), and this can introduce new difficulties when carrying out surgical procedures. Clear discussions between cardiologist and ENT surgeon are required to set treatment priorities.

BNP (brain type natriuretic peptide with 32 amino acids; NT-proBNP = N-terminal proBNP = prohormone with 108 amino acids and longer half-life) is a relatively new lab test to assess the degree of heart failure. It is determined in EDTA blood. The reference range depends on the individual laboratory [8], [9]. The BNP concentration is a measure of left ventricular stretch and volume (wall stress). It correlates well with the NYHA classification and the end-diastolic left ventricular pressure, and has an inverse correlation to the ejection fraction. BNP is not completely specific to heart disease, but may also be raised in diseases of the liver, kidneys, and lungs when the left ventricular volume is increased. There are no natural stores of BNP.

Raised BNP levels are associated with increased perioperative mortality, so that whenever possible cardiological treatment should be optimised before any elective surgical interventions.

In cases of acute decompensation, BNP determination also helps to distinguish between a cardiac and a non-cardiac cause. The probability of acute heart failure is more than 90% if the NT-proBNP is above 450 pg/ml (in a person <50 years old), above 900 pg/ml (aged 50–75) or above 1800 pg/ml (aged >75) [10].

Depending on the underlying cause and taking individual aspects into consideration, heart failure is treated with the following medications (as monodrug therapy or in combination):

- cardiac glycosides (digitalis)
- diuretics
- ACE inhibitors
- angiotensin II receptor antagonists (sartans, also called angiotensin receptor blockers (ARBs) or AT_1-receptor antagonists as they block the binding of angiotensin II to its AT_1 cell membrane receptors)
- possible combination of ACE inhibitors and angiotensin II receptor antagonists (without β-blockers)

- beta-blockers (β-blockers)
- aldosterone antagonists (Spironolactone)

The very narrow therapeutic range of cardiac glycosides means that their plasma levels should be monitored, especially if the patient has bradycardia, noting which glycoside in particular – digoxin or digitoxin – is being administered (Table 2). Measure both plasma levels if there is any evidence that both substances are being given (for whatever spurious reason).

If the result is too high, stop the medication until the concentration is back within the therapeutic range. Digitalis toxicity (symptoms and signs: cardiac arrhythmias = ventricular extrasystoles and AV-block, yellow/green vision, hallucinations, seizures, nausea, vomiting, diarrhoea; characteristic ECG changes) requires the patient to be transferred to cardiology intensive care, where it can be decided whether to give digitalis antitoxin.

Dyspnoea (shortness of breath in exertion, orthopnoea), new or increasing peripheral oedema, new pulmonary crackles, atrial fibrillation of recent onset, new elevation of the jugular venous pressure and/or pulmonary fluid overload all provide evidence of **acute congestive heart failure**. Widening of the cardiac shadow on the chest X-ray is also diagnostically relevant, as long as a previous film is available for comparison. Acute decompensated congestive cardiac failure is not uncommonly due to the overgenerous perioperative administration of fluids. Depending on the symptoms, carry out the following diagnostic investigations:

- ECG
- chest X-ray
- blood gas analysis
- BNP or NT-proBNP determination (see above)

At the same time as these measures, make sure that the patient has a sufficient supply of oxygen, given non-invasively or with invasive ventilation. Volume overload should initially be treated with a loop diuretic (furosemide 20–40 mg or torasemide 10–20 mg) and fluid restriction; if the response is not sufficient, add hydrochlorothiazide (25 mg). Further management (glyceryl trinitrate, sodium nitroprusside, nesiritide, catecholamines, or mechanical circulatory support) requires a referral to the cardiologists, who may take over the patient's treatment.

2.2 Atrial fibrillation

Atrial fibrillation [11], [12], [13], [14], [15] is the most common persistent cardiac arrhythmia, with an estimated prevalence of 1–2% in the general population, and of 9% in the over-85s. An even higher incidence is to be expected in hospital inpatients. Changes in the population age structure mean a future increase in the prevalence. Atrial fibrillation is a significant factor in morbidity and mortality, the main risks being **thromboembolic cerebrovascular events**.

Nevertheless, it is estimated that about half the patients with atrial fibrillation are treated either inadequately (e.g. with aspirin) or not at all [16].

The **CHADS$_2$ score** allows assessment of the stroke risk in patients with atrial fibrillation (Table 3). The annual risk of stroke is, for example, 20% with a score of 6. Symptoms of atrial fibrillation are palpitations, dyspnoea, "dizziness", and loss of physical stamina. In subjectively asymptomatic patients, however, an embolic event is not uncommonly the first thing that leads to the condition being diagnosed: 15% of cerebrovascular insults are the result of atrial fibrillation.

As a rule, the diagnosis is easy to make on the basis of electrocardiography or is already known. Distinctions can be made between paroxysmal and persistent/permanent atrial fibrillation and between slow atrial fibrillation (bradyarrhythmia) and rapid atrial fibrillation (tachyarrhythmia).

The two therapeutic goals in atrial fibrillation are to **control the rate** and **control the rhythm**: controlling the rate allows the arrhythmia to continue, so that anticoagulation still needed. Controlling the rhythm returns the heart to sinus rhythm. The therapeutic concept has to be determined in the individual case.

As a rule of thumb, the first-line treatment of bradyarrhythmias is a pacemaker (unless the bradycardia is reversible on discontinuing an inappropriate dose of medication, such as β-blockers or cardiac glycosides that slow the heart rate); tachyarrhythmias, on the other hand, respond well to medication (cardiac glycosides, β-blockers, diltiazem, and verapamil).

The main perioperative problem associated with **pre-existing atrial fibrillation** is the anticoagulation required and the implications of such therapy (see section 6).

The situation is different with atrial fibrillation that is newly discovered (on the routine preoperative ECG) or of new onset. There is regularly an acute need for treatment.

If there is **newly discovered atrial fibrillation**, postpone any elective surgery to allow time for cardiology workup and treatment.

The presence of atrial fibrillation has to be accepted if surgical intervention is urgent or in an emergency; as preoperative cardioversion is hardly possible, treatment has to focus on controlling the heart rate. Thanks to their rapid onset of action, β-blockers are the drugs of choice. It is particularly important to initiate adequate anticoagulation, with "full heparinisation" using unfractionated heparin, as anticoagulant therapy serves to reduce the stroke risk. Various studies have shown that aspirin is inferior to coumarin derivatives. Low-molecular weight (LMW) heparin is not approved for this indication. Regulatory approval of novel anticoagulants has brought a breath of fresh air to anticoagulant therapy (section 6).

It is not uncommon for **atrial fibrillation to occur postoperatively in patients previously in sinus rhythm**, and this has therapeutic implications as listed below.

- As long as the atrial fibrillation is of short duration (<7 days) with a clear date of onset, consider altering the rhythm back to normal. Cardioversion can be done with medication or other methods.

Possibilities for drug cardioversion include propafenone, flecainide and amiodarone (a class III antiarrhythmic agent, a potassium channel inhibitor). Although beta-blockers (reference drug = metoprolol) lower the heart rate (rate control) they are not particularly helpful in regaining and maintaining sinus rhythm. **Amiodarone** (Cordarex®) is considered the drug of choice for the acute management of ventricular and supraventricular tachycardia (with concomitant impairment of left ventricular function), so also for rapid atrial fibrillation. Give amiodarone at a dose of 150 mg to 300 mg as a short infusion (in glucose 5%) while monitoring the patient; the maximum effects are seen after about 15 minutes. Give amiodarone via a perfusor (10–20 mg/kg body weight/day or 900-–1800 mg/day in glucose 5%) or orally (300–600 mg/day) until a total loading dose of at least 10 g is reached. After that, the maintenance dose is 200 mg/day. As amiodarone has a high iodine content, there is a risk of interaction with **thyroid function**. Amiodarone inhibits the conversion of T4 to T3, so that high T4, low T3, and normal or slightly raised TSH levels are found in patients on amiodarone therapy. Problems may arise on amiodarone therapy particularly if there is pre-existing hyperthyroidism or thyroid gland autonomy. The appropriate thyroid function tests (at least TSH) have to be done close to the start of amiodarone therapy. Propafenone and flecainide are alternatives to amiodarone. Other methods of treatment involve electrical cardioversion (the gold standard, success rate >95%). In refractory cases, invasive procedures (catheter ablation, pulmonary vein isolation) are available.

- **Vernakalant** (Brinavess®) is a new multichannel blocker that is approved for the termination of short-lived atrial fibrillation.
- Adenosine (Adrekar®) is indicated for the termination of supraventricular arrhythmias including atrial flutter but not for atrial fibrillation.
- If the duration of atrial fibrillation is not known, check that there is no atrial thrombus before any cardioversion. Atrial fibrillation causes a reduction in flow rate through the atria; atrial thrombus can only be ruled out confidently by transoesophageal echocardiography.
- If the atrial fibrillation requiring cardioversion is of very recent onset (<48 hours), anticoagulation beyond the usual measures (unfractionated or LMW heparin) is not required. Otherwise oral anticoagulation should

Table 3: CHADS$_2$ score for assessing the risk of stroke in patients with atrial fibrillation

	Disease/symptom	Score
C	Cardiac failure	1
H	Hypertension	1
A	Age ≥ 75 years	1
D	Diabetes	1
S$_2$	Stroke (previous transient ischaemic attack or stroke)	2

be started at least three weeks before a planned cardioversion and it should be continued for up to four weeks afterwards. Electrical cardioversion is therefore quick and easy to perform only when the atrial fibrillation has definitely lasted less than 48 hours.

- If the atrial fibrillation persists, there is an indication for anticoagulant therapy. Heparin is used in the acute phase, switching to a coumarin derivative or new oral anticoagulant with time (section 6).

2.3 Coronary heart disease (CHD), heart attack, acute coronary syndrome

The prevalence of coronary heart disease (CHD) [16], [17], [18] in the over-65s is estimated to be 10–20%. Because of the high prevalence of CHD in smokers, ENT departments with a high proportion of cancer patients have to reckon with acute coronary events on a regular basis; ENT surgeons therefore have to be familiar with their management until the patient can be transferred to the care of the cardiologists.

Stable CHD is usually treated with one of the following medications: nitrates, molsidomine, beta-blockers (drugs of choice), calcium channel blockers, ivabradine (inhibits the pacemaker I$_f$ ion current in the sinus node), ranolazine (late sodium current inhibitor).

Non-ST-elevated myocardial infarction (NSTEMI) and **acute coronary syndrome** (ACS, unstable angina pectoris) are together designated NSTEMI-ACS, as they can only be distinguished by biomarkers some hours after the onset of symptoms (and the need to initiate treatment!). The acute management is the same, and also applies to **ST-elevated myocardial infarction** (STEMI).

Perioperative heart attacks are often asymptomatic or cause very little in the way of symptoms because the patients is being given analgesics. ECG monitoring is therefore particularly valuable, and troponin levels provide confirmation if there is any suspicion of an MI.

In the event of a suspected heart attack or acute coronary syndrome, initiate the following measures:

- give oxygen if oxygen saturation (SO$_2$) <90% on room air
- 12-lead ECG, ECG monitoring, non-invasive blood pressure measurement and SO$_2$; make sure there is a defibrillator handy

- basic lab tests: blood count, PT/INR, PTT, thrombin time, CRP, troponin I
- ensure adequate analgesia (usually morphine)
- GTN spray, 2 puffs
- anticoagulation: acetylsalicylic acid (>250 mg iv), clopidogrel (loading dose 300 mg orally. Possible use of prasugrel or ticagrelor after discussing treatment with the cardiologists. The Federal Joint Committee has recently established that the last-mentioned drug has considerable added benefit in NSTEMI and unstable angina), unfractionated heparin (bolus 60–70 IU/kg up to a maximum of 5000 IU, then 12–15 IU/kg/hour with a target PTT of 60-80 seconds). An increased risk of postoperative bleeding has to be taken into account.
- prompt contact with a cardiology unit to plan future management (coronary angiography, intervention, thrombolysis, etc.)

Troponin I and troponin T are fairly specific biomarkers for the destruction of myocardial cells and are not found in skeletal muscle. A significant rise in troponin I levels can be seen even 1–2 hours after a heart attack. But it also may be some 8–12 hours before an increase occurs, so that repeat testing after this interval is essential. Chronic renal failure may give false positive results (more common with troponin T than troponin I). Troponin I is a much more rapid marker for myocardial infarction than the traditional blood tests with creatinine kinase (CK), creatinine kinase MB isoenzyme (CK-MB), lactate dehydrogenase (LDH) and alpha-hydroxybutyrate dehydrogenase (α-HBDH) [9].

Elective surgery should not be planned for at least 4–6 weeks after a confirmed myocardial infarction.

2.4 Cardiomyopathy

The current European Society of Cardiology (ESC) classification divides cardiomyopathies [19] into five types:

- dilated cardiomyopathy (DCM)
- hypertrophic cardiomyopathy (HCM)
- restrictive cardiomyopathy (RCM)
- arrhythmogenic right ventricular cardiomyopathy (ARVC)

- unclassified: Takotsubo cardiomyopathy, non-compaction cardiomyopathy

There are many reasons for cardiomyopathy: they can be roughly divided into genetic and non-genetic causes. The ENT surgeon is most often faced with cancer patients with alcohol-induced cardiomyopathy. Alcohol is the cause of non-ischaemic DCM in about 30% of cases.

In general, the treatment of cardiomyopathy consists of treating the associated functional disturbance (e.g. heart failure). Typically beta-blockers are indicated. Abstinence from alcohol improves cardiac function in only about 25% of cases. There may be an indication for inserting an implantable cardioverter-defibrillator (ICD).

Although it is a rare disease, **takotsubo cardiomyopathy** (broken heart syndrome) merits a brief mention here, as the author has recently come across two cases [20]. The disease was first described in Japan in 1991. Its name comes from the fact that the akinetic left ventricle gives the heart the appearance of an octopus pot = *takotsubo*. The condition may arise in completely healthy individuals (often young women) and is an abnormal reaction to catecholamine release; there is a dramatic deterioration of cardiac function. The typical trigger is emotional stress (usually negative, but can also be due to positive excitement), including an impending operation. In one of the author's cases a local anaesthetic with adrenaline was also used. The characteristic feature of the disease is a sudden loss of left ventricular pump function with arterial hypotension, tachy- or bradyarrhythmias and a fall in oxygen saturation. Destruction of myocardial cells gives rise to an increase in infarction markers (troponin, creatinine kinase, LDH), so that a heart attack obviously comes to mind in the differential diagnosis. The left ventricular apical akinesia (ballooning) seen on echocardiography is almost pathognomic for takotsubo cardiomyopathy but invasive diagnostic investigations cannot be avoided if there is any doubt. As takotsubo cardiomyopathy is triggered by catecholamines, the therapeutic administration of adrenaline or noradrenaline and other catecholamines to raise the blood pressure has to be considered critically. The condition usually resolves completely.

2.5 Hypertension

An acute hypertensive episode [18], [21], [22] is a frequent complication of inpatient treatment. It may affect patients with known treated hypertension and those with no previous history of the disease. Hypertension – especially associated with (sinus) tachycardia – may simply be the result of pain; check whether pain needs to be treated.

Otherwise the following therapeutic options are available:

- nitrendipine (Bayotensin® acute – 1 vial = 5 mg sublingual). NB: beware of reflex tachycardia
- urapidil (30 mg oral or 12.5–25 mg iv). Treatment of choice in pre-eclampsia, hardly any contraindications
- glyceryl trinitrate (nitroglycerin). Contraindicated in aortic stenosis (suspect aortic stenosis with large amplitude between systolic and diastolic blood pressure); adverse reaction = GTN headache
- magnesium sulfate 5 g/50 ml as short infusion
- metoprolol (oral or iv), esmolol (Brevibloc® iv, diluted to 10 mg/ml, has very short-lived effects, use as a test dose before giving metoprolol, only under close monitoring)

The following principles apply:

- administration of nifedipine is no longer recommended in acute hypertensive episodes
- ACE inhibitors and angiotensin II receptor antagonists do not have rapid effects
- in the acute case, beta-blockers tend to affect the heart rate rather than the blood pressure (esmolol test if necessary) and are therefore more suited to the symptomatic treatment of supraventricular tachycardia
- do not use clonidine to treat hypertension because of its CNS side effects (sedation) but keep in reserve for the treatment of delirium
- in the event of refractory hypertension: dihydralazine (Nepresol®), possibly in combination with clonidine (as perfusor); alternatively sodium nitroprusside.

2.6 Cardiac arrhythmias

Diagnosis and treatment of cardiac arrhythmias [23], [24] other than that of the commonly encountered atrial fibrillation belongs in the hands of the cardiologists. The topic is too complex to give more than a brief mention here.

Whenever a routine preoperative ECG shows a disorder of cardiac rhythm more than the isolated monotypic extrasystole, the patient should be referred to the cardiologists. A 24-hour ECG is often required.

Three points are particularly worth making in this respect.

- Sudden **bradycardia** and even asystole may occur because of vagal stimulation during manipulation of the base of the tongue, larynx, and neck. Even the pressure of the laryngoscope during intubation can trigger this complication. Bradycardia without manipulation is often caused by the overdose or accumulation of drugs that slow down the heart (e.g. cardiac glycosides, beta-blockers). Patients who are awake and asymptomatic (blood pressure?) do not require treatment in a hurry – although they should be monitored. If treatment is needed, use parasympatholytic agents (atropine 0.5 mg, or glycopyrronium 0.2 mg for preference in alert patients, because of the absence of adverse CNS effects). Sympathomimetics such as orciprenaline and adrenaline are second-line drugs. It may sometimes be necessary to insert an external pacemaker temporarily (many defibrillators contain this feature). If the bradyarrhythmia does not have a clear cause, the indication for a pacemaker always has to be reviewed.
- Numerous drugs may cause **prolongation of the QT interval**. With a QTc interval (Bazett formula: QTc = QT [ms]/$\sqrt{RR}$ interval [s]) of more than about 500 ms,

there is an increased risk of **torsade de pointes** tachy-cardia; a genetic predisposition represents an additional risk. Prolongation of the QT interval may be seen with many drugs, including: amiodarone, amitriptyline, astemizole, azithromycin, citalopram, clarithromycin, erythromycin, fingolimod, haloperidol, imipramine, mirtazapine, moxifloxacin, olanzapine, risperidone, sertraline, sotalol, terfenadine, venlafaxine, many tyrosine kinase inhibitors (see http://www.azcert.org).

- **Perioperative management of patients with pacemakers and implantable cardioverter-defibrillators (ICDs) [25].**

It may sound obvious but patients with pacemakers and ICDs have heart disease and therefore require appropriate perioperative management. As a rule, the devices should be checked close to the time of the planned surgery and the pacemaker identification card should be held in the medical records for the duration of the hospital stay. Even though one clinical study found that bipolar cautery caused no ICD malfunction [26], the device should be deactivated during the surgical procedure using a ring magnet (the constant magnetic field suspends tachyarrhythmia detection in a targeted fashion while bradycardia detection is unaffected). This also applies to lithotripsy. It should be remembered that the magnet deactivation mode can also be switched off at the device. Certain units react to the application of a magnetic field with a confirmatory tone and may also be reprogrammed with a magnet, if necessary. **Avoid the use of monopolar cautery systems! A ring magnet to deactivate ICDs should always be available in the (ENT) operating theatre.** It should also be noted that although an ICD "shock" can be felt by an assistant, e.g. during resuscitation, it is not dangerous.

2.7 Endocarditis prophylaxis

To all intents and purposes, clear rules exist for endocarditis prophylaxis but they are apparently not always observed. Operations in the nose, nasal sinuses, oral cavity, pharynx and larynx are all associated with an established high risk of bacteraemia. The German Society of Cardiology recommendations on endocarditis prophylaxis were therefore tightened up in 2007 [27], [28]. A new evaluation of the endocarditis risk compared with the risk of antibiotic prophylaxis was carried out beforehand. The fact that everyday dental hygiene regularly causes bacteraemia was taken into account. The resulting risk of endocarditis from routine dental hygiene in one year is 154,000 times higher than the risk from a tooth extraction. Endocarditis prophylaxis is therefore now recommended only in the following situations:

- the presence of a prosthetic heart valve
- a history of endocarditis
- congenital heart disease
- previous heart transplantation with subsequent valve defect

and

- surgical interventions on the gums
- perforation of the oral mucosa (including tonsillectomy)
- surgical interventions on infected skin, muscle or bones.

Standard antibiotics for endocarditis prophylaxis are the aminopenicillins (amoxicillin or ampicillin, 2 g), alternatively cefazolin (1 g), ceftriaxone (1 g) or clindamycin (600 mg). As neither amoxicillin nor ampicillin alone is available for intravenous injection there is a conflict with the fasting state required for surgery under a general anaesthetic. If no recourse is to be made to the intravenous preparation of cefazolin, ceftriaxone or clindamycin, oral administration may be permitted on the day of operation after discussion with the anaesthetist or alternatively a combination product, ampicillin/sulbactam or amoxicillin/clavulanic acid, may be given iv.

3 Risk: respiratory system

3.1 Bronchial asthma

It should be remembered that lay people often fail to distinguish between bronchial asthma [29], [30] and COPD (section 3.2). If a patient reports "asthma" during the history taking, it is important to view the diagnosis critically and ask more pertinent questions; earlier reports from reputable sources are helpful and clues can also be gained from the medication which the patient is taking. Bronchial asthma is a chronic inflammatory disease of the lower respiratory tract with bronchial hyperreactivity and variable obstruction. A distinction is made between extrinsic (allergic) asthma and intrinsic (non-allergic) asthma, such as aspirin-sensitive respiratory tract disease.

The division of asthma into four stages (stage 1: intermittent; stage 2: mild persistent; stage 3: moderate persistent; stage 4: severe persistent) has recently been replaced in the national clinical guidelines by a three-stage classification [29]. The three classes are nowadays based on disease control: controlled asthma, partially controlled asthma and uncontrolled asthma (Table 4).

A five-step treatment strategy is recommended for asthma; treatment can be stepped up or down depending on disease activity (Figure 1).

Anticholinergics (ipratropium, tiotropium) are not recommended as monodrug therapy for bronchial asthma.

In contrast, combination products with inhaled corticosteroids and long-acting beta-2 agents are commonly used. Treatment for asthma has, of course, to be continued perioperatively. When the asthma is not controlled, postpone elective surgical procedures until control is achieved, as otherwise there is an increased risk of perioperative respiratory complications. Refer the patient to a specialist in respiratory medicine if there is any doubt that therapy is following the guidelines.

Table 4: Degree of asthma control in adults (modified from [29])

Feature	Controlled (all of the following)	Partially controlled (1-2 features present in any week)	Uncontrolled
Daytime symptoms	≤ 2x per week	>2x per week	
Limitation of daily activity	no	yes	
Nocturnal symptoms/ waking up	no	yes	
Relief medication / emergency treatment	≤ 2x per week	>2x per week	3 or more features of partially controlled asthma present in any week
Lung function (PEF or FEV_1)	normal	< 80% of predicted (FEV_1) or of personal best (PEF)	
Exacerbation[1]	no	one or more per year	one per week

1: Any exacerbation within one week is by definition uncontrolled asthma. Definition of exacerbation: episode with increased breathlessness, cough, wheezing or tightness of the chest associated with a fall in PEF or FEV_1. FEV_1 = forced expiratory volume in one second, PEF = peak expiratory flow
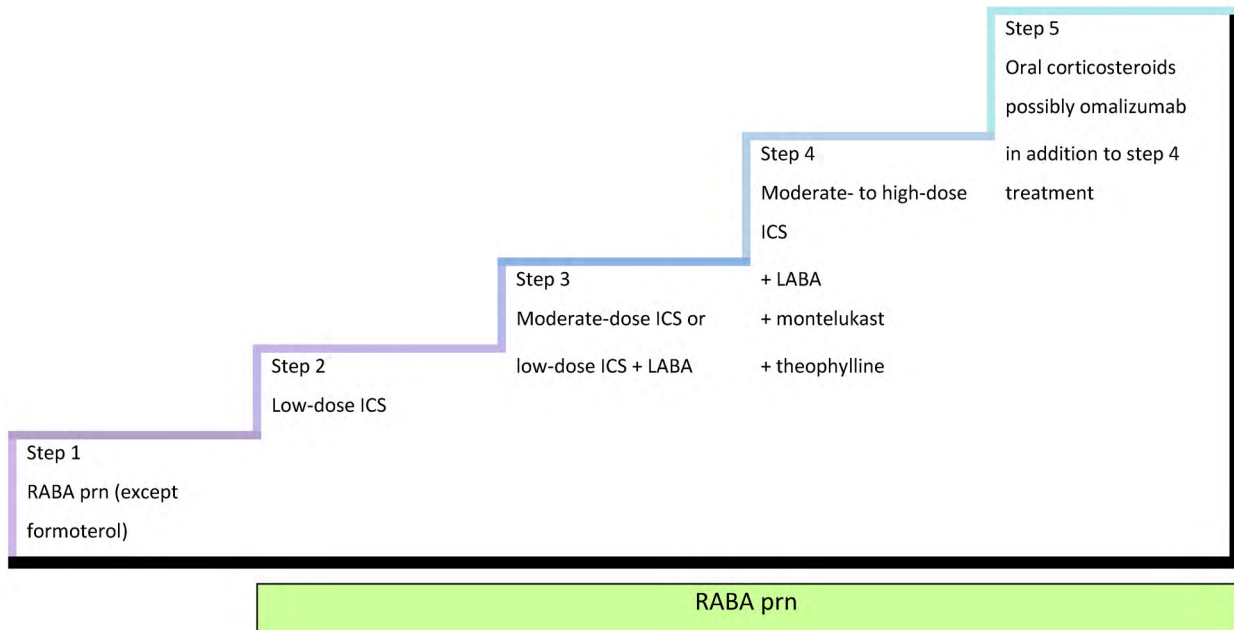

Figure 1: Figure showing the stepwise treatment of bronchial asthma in adults [29]. RABA = rapid-acting beta-2 agent: fenoterol, salbutamol, terbutaline (all three are also short-acting beta-2 agents (SABAs)). Formoterol has a rapid onset of action but long-lasting effects, so it also belongs to the LABA group. LABA = long-acting beta-2 agent: formoterol and salmeterol. ICS = inhaled corticosteroid: beclomethasone, budesonide, ciclesonide, fluticasone, mometasone. prn = as required (reliever).

If a patient with bronchial asthma has a tracheostomy, remember that the dose of the usual sprays makes allowance for loss in the upper airways. In other words, administering the same dose via a tracheostomy could lead to overdose. As a rule of thumb, halve the oral dose. Salbutamol (or ipratropium) is available in a ready-to-use form for tubes and tracheal cannulas and is the treatment of choice immediately after surgery.

The following principles apply to the treatment of an acute asthma attack:

- first determine whether it is a mild to moderate attack (normal speech, respiratory rate <25 min^{-1}), a severe episode (breathless speech, respiratory rate
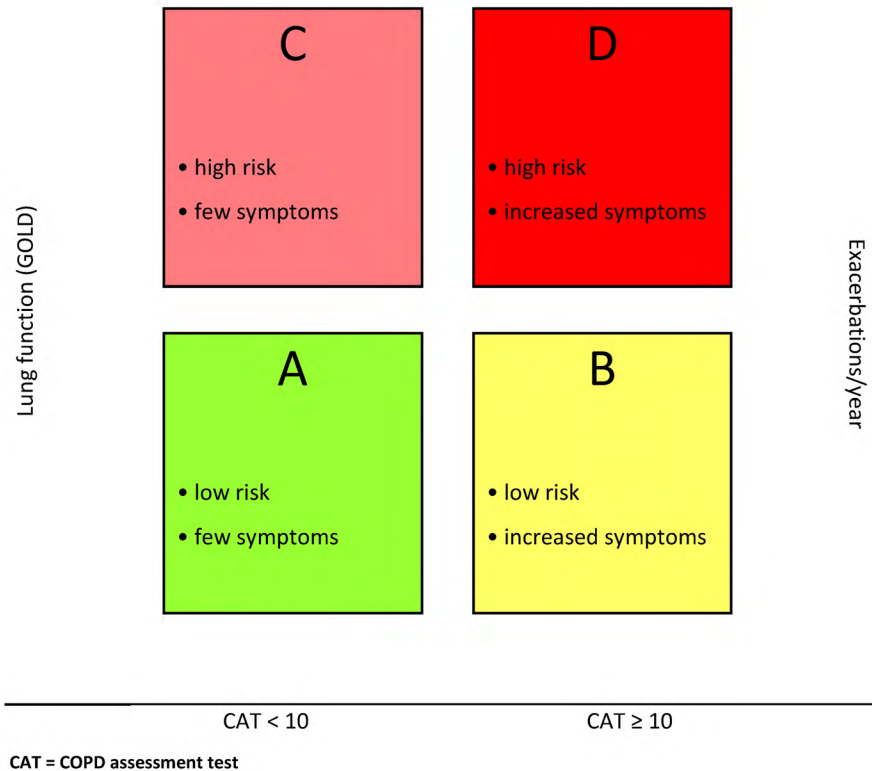
Figure 2: New classification of COPD [32]

>25 min^{-1}), or a life-threatening attack (silent lungs, hypotension, bradycardia)

- treat mild to moderate attacks with SABAs (2–4 puffs) and 25–50 mg prednisolone equivalent
- treat severe and life-threatening attacks with oxygen, SABAs (2–4 puffs), 50–100 mg prednisolone equivalent, and inhalation of ipratropium bromide 0.5 mg
- if there is no improvement, check the indication for intubation and ventilation
- after an asthma attack, check whether therapy needs to be stepped up.

3.2 COPD

Chronic obstructive pulmonary disease (CPOD) [31], [32] or chronic obstructive lung disease (COLD) is a typical disease of long-term smokers (the phenotypes of "blue bloaters" and "pink puffers" are well known). It can be assumed that most patients with head and neck cancer and a typical risk profile have COPD, even if the patient is not aware of the diagnosis. Affected patients often describe their lung disease in other ways, including as asthma. The necessary precise distinction between the two diseases is often not made outside professional healthcare circles (see above).

The Global Initiative for Chronic Obstructive Lung Disease (**GOLD**) defines COPD as a disease state characterised by airflow limitation that is not fully reversible.

The current national clinical guidelines define the disease as follows: "COPD is a chronic lung disease with progressive airway obstruction that is not fully reversible with the administration of bronchodilators and/or corticosteroids,

on the basis of chronic bronchitis and/or pulmonary emphysema. The cardinal symptoms are chronic cough, expectoration and shortness of breath, initially only on exertion."

The hyperreactivity characteristic of bronchial asthma is usually absent in COPD. Patients with COPD are typically older than patients with asthma.

The classification of COPD has been modified recently. From now on, the three factors of lung function, early exacerbations, and the results of an assessment questionnaire direct the allocation into one of **four risk groups**, A–D (Figure 2).

- Lung function is divided into four stages according to the GOLD classification (Table 5): GOLD 1 and 2 carry a low risk (A or B), while GOLD 3 and 4 correspond to a high risk (C or D). Irrespective of the GOLD classification, more than two exacerbations within a year represent a high risk.
- The COPD assessment test (CAT) stratifies the symptoms into two classes (Table 6). The cut-off score is 10 points.

Current treatment recommendations are based on the new COPD stages (Table 7).

The table shows that anticholinergics are regarded as controller therapy for COPD.

The overview (Table 8 and Table 9) provides information on the medicinal products used in the treatment of COPD. If a patient with COPD has a tracheostomy, remember that the dose of the usual sprays could lead to overdose when given via a tracheostomy. It is recommended that

Table 5: GOLD classification of COPD [32].

GOLD	FEV_1/FVC	FEV_1
1	<70%	> 80%
2	<70%	50 < 80%
3	<70%	30 < 50%
4	<70%	< 30%

FEV1 = forced expiratory volume in one second; FVC = forced vital capacity; in each case measured after the administration of a bronchodilator

Table 6: COPD assessment test (www.catestonline.org)

I never cough	0 - 1 - 2 - 3 - 4 - 5	I cough all the time
I have no phlegm (mucus) in my chest at all	0 - 1 - 2 - 3 - 4 - 5	My chest is full of phlegm (mucus)
My chest does not feel tight at all	0 - 1 - 2 - 3 - 4 - 5	My chest feels very tight
When I walk up a hill or one flight of stairs I am not breathless	0 - 1 - 2 - 3 - 4 - 5	When I walk up a hill or one flight of stairs I am very breathless
I am not limited doing any activities at home	0 - 1 - 2 - 3 - 4 - 5	I am very limited doing activities at home.
I am confident leaving my home despite my lung condition	0 - 1 - 2 - 3 - 4 - 5	I am not at all confident leaving my home because of my lung condition
I sleep soundly	0 - 1 - 2 - 3 - 4 - 5	I don't sleep soundly because of my lung condition
I have lots of energy	0 - 1 - 2 - 3 - 4 - 5	I have no energy at all

the dose be halved or the patients switched to a nebuliser solution (e.g. sultanol, ipratropium).

The following considerations relate to COPD exacerbations within the hospital setting.

- All acute events causing deterioration of the respiratory symptoms beyond the usual variations and requiring a change in medication are regarded as COPD exacerbations
- Viral and bacterial infections are typical causes; the ventilation per se also comes into question after an operation.
- If the patient is on oxygen, saturation of 88–92% is sufficient (hypoxic drive). Consider non-invasive ventilation at an early stage (criteria: exhaustion, $paCO_2$, and pH).

- The use of SABAs and SAMAs is preferred in the acute situation; systemic corticosteroid therapy (40 mg prednisolone equivalent for 10–14 days) may shorten the course of the exacerbation.
- Bacterial infections (purulent sputum, infiltrates seen on chest X-ray) are often due to the following microorganisms: *Haemophilus influenzae*, pneumococci, *Moraxella catarrhalis*, and *Pseudomonas aeruginosa*. Take these pathogens into consideration when prescribing antibiotics (e.g. piperacillin+betalactamase inhibitor, alternatively fluoroquinolones) – microbiological investigation with determination of resistance is recommended.

Table 7: Recommended COPD therapy according to the stage [32]

	Stage			
	A	B	C	D
First choice	SAMA or SABA	LAMA or LABA	ICS and LABA or ICS+LAMA	ICS and LABA or ICS+LAMA
Second choice	LAMA or LABA or SABA and SAMA	LAMA and LABA	LAMA and LABA	ICS+LAMA or ICS+LAMA+LABA or ICS+LAMA+PDE4 inhibitors or LAMA and LABA or LAMA+PDE4 inhibitors
Alternative or combination	Theophylline	SABA and/ or SAMA	PDE4 inhibitors SABA and/ or SAMA theophylline	Carbocysteine SABA and/or SAMA Theophylline

SABA: short-acting beta-2 agent

SAMA: short-acting muscarinic antagonist

LABA: long-acting beta-2 agent

LAMA: long-acting muscarinic antagonist

ICS: inhaled corticosteroid

PDE4 inhibitor = phosphodiesterase-4 inhibitor (roflumilast = Daxas®)

Table 8: Medications used to treat COPD – monodrug therapy

Generic name	Proprietary name
SABA = short-acting beta-2 agent	
Fenoterol	Berotec®
Salbutamol	Sultanol®
Terbutaline	Aerodur®
LABA = long-acting beta-2 agent	
Formoterol	Foradil®
Indacaterol	Onbrez®
Salmeterol	Serevent®
SAMA = short-acting muscarinic antagonists	
Ipratropium bromide	Atrovent®
LAMA = long-acting muscarinic antagonist	
Aclidinium bromide	Eklira®, Bretaris®
Glycopyrronium bromide	Seebri®
Tiotroprium bromide	Spiriva®
ICS = inhaled corticosteroid	
Beclomethasone	Junik®, Ventolair®
Budesonide	Pulmicort®
Ciclesonide	Alvesco®
Fluticasone	Flutide®
Mometasone: has marketing authorisation only for asthma	Asmanex®

Table 9: Medications used to treat COPD – combination products

Proprietary name	SABA	LABA	SAMA	LABA	ICS
Atmadisc®	-	salmeterol	--		fluticasone
Berodual®	fenoterol	-	ipratropium	-	-
Foster®	-	formoterol	-	-	beclomethasone
Inuvair®	-	formoterol	-	-	beclomethasone
Rolenium®	-	salmeterol	-	-	fluticasone
Symbicort®	-	formoterol	-	-	budesonide
Viani®	-	salmeterol	-	-	fluticasone

Aarane®, Allergospasmin® = reproterol+sodium cromoglycate

3.3 Pulmonary embolism

It is well known that deep vein thrombosis (DVT) of the legs and pelvis is a common cause of pulmonary embolism (PE) [22], [33], [34] in patients confined to bed (the prevalence in hospital patients is about 0.4%). For this reason, adequate perioperative thrombosis prophylaxis is extremely important (see S3 guidelines [35]). Pulmonary embolism in patients anticoagulated according to the guidelines is rare but cannot be ruled out completely. Typical symptoms of a pulmonary embolus are: **dyspnoea, tachypnoea and chest pain**. Massive pulmonary embolism may cause syncope or shock. There are three different scoring systems for estimating the probability of pulmonary embolism (Table 10, Table 11, Table 12).

The following signs of acute right ventricular strain in the ECG may indicate a pulmonary embolus:

- $S_I Q_{III}$ pattern (McGinn and White pattern (Figure 3) or $S_I S_{II} S_{III}$ pattern or right ventricular type (compare with previous ECG)
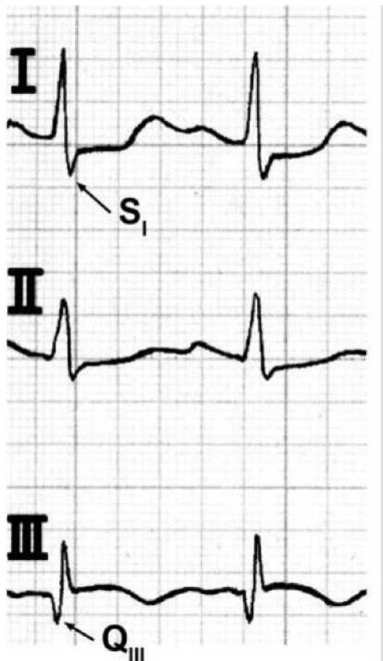

Figure 3: $S_I Q_{III}$ pattern in the ECG indicating acute right ventricular strain in pulmonary embolism (modified from So CD: *Praktische Elektrokardiographie*, Stuttgart, Georg Thieme Verlag 1993, 6th edition).

- new onset of (incomplete) right bundle branch block
- negative T wave in V_1–V_3
- delay in R/S transition (after V_5)
- QR in V_1 (the most sensitive marker)

Echocardiography is only recommended if there is haemodynamic instability.

Blood gas analysis typically shows hypoxaemia (paO_2 <100 mm Hg) and hypocapnia but does not have great diagnostic significance.

Although **D-dimers** (=cross-linked fibrin degradation products) are essentially a useful biomarker for excluding thrombosis and pulmonary embolism (cut-off 500 ng/ml), they are not very helpful postoperatively because surgical interventions with extensive soft tissue trauma per se cause an increase. Raised D-dimers after surgery do not, therefore, confirm a pulmonary embolus. Patients with extensive malignancy or pregnant women may already have raised D-dimers preoperatively [9], [36].

Spiral computed tomography (CT) is the diagnostic investigation of choice when pulmonary embolism is suspected clinically, and this procedure has widely superseded perfusion and ventilation scintigraphy. Scintigraphy, however, remains a good alternative in patients with renal failure or contrast medium allergy.

The first measures on suspicion of pulmonary embolism are to give oxygen and analgesia as required. Give fluids with caution, despite any hypotension. On confirmation of the diagnosis every effort should be made for further management by general (internal) medical specialists. If lytic therapy is considered, the risk of bleeding from the surgery carried out has to be weighed up against forgoing lysis. Bleeding after operations on the nose or nasal sinuses is relatively easy to control by packing; on the other hand, lysis is absolutely contraindicated after intracranial surgery. If thrombolysis is not carried out, anticoagulation with heparin is the treatment of choice. Low molecular weight heparins or fondaparinux are recommended today, except for patients with severe renal insufficiency (creatinine clearance <30 ml/min). Unfractionated heparin is used in renal failure. Surgical embolectomy or a catheter intervention has to be considered in the individual case (shock, contraindications to lysis or failed lysis).

Once pulmonary embolism has been confirmed, the following recommendations apply to anticoagulation:

- 3 months oral anticoagulation if this is the first event and risk factors are temporary (e.g. surgery)
- at least 3 months oral anticoagulation for a first event without a trigger
- treatment with low molecular weight heparin for at least 6 months, followed by oral anticoagulation, if the patient has cancer
- long-term oral anticoagulation for second or subsequent events, with regular reassessment
- long-term oral anticoagulation for patients with thrombophilia

3.4 Surgical emphysema

Surgical (subcutaneous) emphysema may occur after tracheostomy or surgical interventions in the larynx and trachea (characteristic crackling sensation on palpation). This condition is not a cause of great concern. It usually resolves spontaneously within a few days. It may be helpful to suppress the cough reflex, as coughing may renew or exacerbate the emphysema. The following drugs may be used for this purpose:

- levodropropizine (Quimbo®)
- noscapine (Capval®)

Table 10: Wells score to estimate the probability of a pulmonary embolus

Predictors	Score
Clinical Signs and Symptoms of DVT	3
Heart rate > 100/min	1.5
Immobilisation for at least 3 days or surgery in the previous 4 weeks	1.5
Previous PE or DVT	1.5
Haemoptysis	1
Malignancy	1
Pulmonary embolism is probable or more likely than other diagnoses after X-ray/lab tests/ECG etc.	3

Score	Probability of pulmonary embolism
<2	low
2-6	moderate
>6	high

Table 11: Revised Geneva score to estimate the probability of a pulmonary embolus

Predictors	Score
Age> 65 years	1
Previous DVT or PE	3
Surgery or fracture within 1 month	2
Active malignant condition	2
Unilateral lower limb pain	3
Haemoptysis	2
Heart rate 75 to 94 beats per minute	3
Heart rate 95 or more beats per minute	5
Pain on deep palpation of lower limb and unilateral oedema	4

Score	Probability of pulmonary embolism
0-3	low
4-10	moderate
>10	high

With the availability of these alternatives, do not use codeine preparations unless they are absolutely indicated. Surgical emphysema without a preceding surgical intervention is, however, a warning sign. Check immediately to see whether there is any previously unnoticed perforation of the oropharynx (epiglottic vallecula), hypopharynx (piriform fossa), trachea or oesophagus. A chest X-ray is essential to rule out a pneumothorax/tension pneumothorax.

Table 12: Wicki score to estimate the probability of a pulmonary embolus

Predictors	Score
Age 60-79 years	1
Age > 80 years	2
Previous venous thrombosis or pulmonary embolism	2
Recent surgery	2
Heart rate > 100 beats/min	1
$paCO_2$ < 4.8 kPa (36 mm Hg)	2
4.8 kPa (36mm Hg) $\leq paCO_2 \leq$ 5.19 kPa (38.9 mm Hg)	1
paO_2 kPa < 6.5 kPa (48.8 mm Hg)	4
6.5 kPa (48.8 mm Hg) $\leq paO_2 \leq$ 7.99 kPa (59.9 mm Hg)	3
8.0 kPa (60 mm Hg) $\leq paO_2 \leq$ 9.49 kPa (71.2 mm Hg)	2
9.5 kPa (71.3 mm Hg) $\leq paO_2 \leq$ 10.99 kPa (82.4 mm Hg)	1
Chest X-ray: discoid atelectasis	1
Chest X-ray: raised hemidiaphragm	1

Score	Probability of pulmonary embolism	PE prevalence
0-4	low	10%
5-8	moderate	38%
> 8	high	81%

3.5 Pulmonary hypertension

Pulmonary hypertension [37] is defined as a mean pulmonary artery pressure ≥25 mm Hg at rest. There are many causes (e.g. idiopathic pulmonary arterial hypertension, pulmonary venous occlusive disease, left heart disease, and chronic thromboembolic pulmonary hypertension). Pulmonary hypertension increases the perioperative risk, so that every effort should be made for the best possible treatment of the condition prior to elective surgery. Specialist centres may be needed to be involved to optimise treatment. The following drugs are used to treat pulmonary hypertension, usually in combination:

- iloprost (Ventavis®, Ilomedin®)
- treprostinil (Remodulin®)
- bosentan (Tracleer®), ambrisentan (Volibris®)
- sildenafil (Revatio®), tadalafil (Adcirca®)

Patients with known pulmonary hypertension usually require perioperative monitoring on intensive care.

3.6 Pneumothorax

Pneumothorax [18], [22], [34] may be caused by pleural lesions during surgery in the supraclavicular space or on the trachea, as well as during the insertion of a supraclavicular venous catheter. Nor can spontaneous pneumothorax be ruled out. The diagnosis is usually made on the

basis of the X-ray findings. It must not be forgotten that a pneumothorax may be masked in patients on mechanical ventilation. As a rule, a chest drain (Monaldi, Bülau) is indicated in all but the smallest pneumothoraces. Suction pressure of 20 cm H_2O is usually applied. The customary disposable systems have detectors to monitor the negative pressure. Lung expansion is usually checked by daily chest X-rays (taken in expiration). Once the lung has expanded completely, remove the drain, making sure that it does not trigger a new pneumothorax. The author has found a two-person procedure and the use of an ointment-covered occlusive dressing to be reliable. Take another chest X-ray after removing the drain.

3.7 Adult Respiratory Distress Syndrome

Adult Respiratory Distress Syndrome (ARDS) [22], [34] is a rare complication. The main causes are pneumonia, systemic inflammatory response syndrome (SIRS) or sepsis, and transfusion-related acute lung injury (TRALI). The **oxygenation ratio** (Horovitz quotient) is relevant to the diagnosis. ARDS is probable when paO_2/f_iO_2 <200 mm Hg (independent of the positive end-expiratory pressure (PEEP)). The chest X-ray shows the typical bilateral "white lungs". The differential diagnosis includes cardiac-induced pulmonary oedema in acute decompensated congestive heart failure, bilateral inflammatory infiltrates, and bilateral pleural effusion (on supine chest X-rays).

Stewart and Slutsky [38] summarised the therapeutic strategy for ARDS with the formula P^2R^2:

- **P**rotect the ventilated lung – **P**revent oxygen toxicity
- **R**ecruit the atelectatic lung – **R**educe the dead space

Mechanical ventilation for ARDS should follow a lung-protective protocol (reduced tidal volume, f_iO_2 <60% as much as possible, permissive hypercapnia, but SaO_2 >90% and paO_2 <60 mm Hg). A **lung recruitment manoeuvre** (Lachmann manoeuvre) – high PEEP for few breaths – brings about alveolar recruitment in non-ventilated areas of lung ("Open the lung and keep the lung open").

The value of kinetic therapy (Figure 4) also lies in recruiting additional areas for ventilation. In the supine patient, the posterior lung fields are usually cut off from ventilation due to atelectasis. Modern beds on intensive care also allow rotation of the patient but their limited rotational angle means they are suitable only for the prophylaxis of ARDS and not for its treatment. If there is no kinetic therapy system available, the patient can lie prone and be turned regularly, although the benefits of this are controversial. If the patient has an oro- or nasotracheal tube, there is a risk of accidental extubation, and corresponding precautions must be taken. Accidentally dislodging a tracheal cannula in a patient with a tracheostomy has less serious consequences.

Figure 4: Kinetic therapy for ARDS (copyright F. Waldfahrer, 2004)

Stepping up treatment involves ventilation with NO and extracorporeal membrane oxygenation (ECMO).

In the case of ARDS, there is an indication for more extensive haemodynamic monitoring (e.g. with the pulse contour cardiac output (PICCO) system) [39], [40], [41].

3.8 Obstructive sleep apnoea

Obstructive sleep apnoea syndrome (OSAS) [42] is a medical condition not uncommon in the general population; an even higher prevalence can be assumed in patients on ENT wards, as patients with OSA not infrequently require surgical interventions in the nose, nasal sinuses and pharynx. The question regularly arises as to how to monitor patients with OSA during and after surgery, especially as it is well known that patients with OSA have a higher cardiovascular risk and possibly also an increased perioperative risk.

At present, there are no pertinent guidelines but the German Society of Sleep Medicine working group on "Surgical procedures in sleep medicine" is planning a position paper on precisely this topic. Until their recommendations have been published, however, the following can be taken as a guide:

- ask patients with OSA on nasal continuous positive airway pressure (nCPAP) therapy to bring their machines into hospital with them

- as long as the surgical procedure does not require nasal packing, continue nCPAP therapy. Considered in isolation, additional postoperative observations are not then required.
- prolonged postoperative observations are necessary if nCPAP therapy is not possible because of a nasal pack. If there are no abnormalities (ECG, blood pressure, SO_2) after at least four hours on recovery, consider returning the patient to the ward as long as the SO_2 will still be monitored there. Otherwise monitor the patient on the intensive care unit until the following day or until the nasal pack is removed.
- monitor patients with OSA not on nCPAP therapy (if not, why not?) and no nasal pack on intensive care if the unit has sufficient capacity, even though there is no urgent reason for doing so if there have been no abnormalities during prolonged observation (4 hours) in recovery and subsequent SO_2 monitoring on the ENT ward can be guaranteed.

The planned position paper may provide authoritative recommendations in the near future.

3.9 Assisted breathing: oxygen therapy, mechanical ventilation

Assisted breathing [43], [44], [45], [46] can be divided into six stages, as shown in Table 13. Oxygen delivered via a nasal cannula or sometimes an oxygen mask during spontaneous breathing is widely used, especially after surgery. The monitoring parameter measured almost exclusively in this case is the percutaneous oxygen saturation (pulse oximetry). Administering oxygen in this way rapidly reaches its limits, however, if large volumes of oxygen are required. While room air has an f_iO_2 of 0.21, oxygen insufflation at a rate of 2 l/min gives an f_iO_2 of 0.28, while a rate of 5 l/min achieves an f_iO_2 of 0.40.

It was thought previously that patients with COPD should not be given any extra oxygen, since they lack a hypercapnic drive and only the hypoxic drive is effective. In the past, this may have led to patients with COPD becoming dangerously hypoxic. Today oxygen therapy is also given in COPD if there are signs of clinically relevant hypoxia; it is given in the right dose and the patient's level of consciousness is monitored closely. Physical measures such as respiratory therapy and inhalation with bronchodilators are also important.

Many ENT operations are carried out on or in the immediate vicinity of the respiratory tract. There is, therefore, a corresponding risk of displacing the airways through bleeding and/or swelling. It is not always appropriate to perform a tracheotomy to protect the airways. In the individual case, it has to be decided whether there is an indication for mechanical ventilation via an endotracheal tube. Typical situations include extensive endolaryngeal surgery, tumour resections in the oro- and hypopharynx, when there is a risk of bleeding in patients on anticoagulants, and (transoral) treatment of large abscesses.

Without exception, mechanical assistance must be provided if the patient has an endotracheal tube in situ.

On no account should spontaneous breathing via an endotracheal tube be tolerated for more than a few minutes, as the high respiratory resistance leads to rapid respiratory exhaustion (you can see this for yourself by trying to breathe through a size 7 endotracheal tube for more than ten minutes at rest). Mechanical assistance requires at least **CPAP** mode with pressure support of spontaneous breathing, and, depending on the baseline situation, controlled ventilation under sedation/analgesia may be required. Pressure-controlled ventilation with bilevel positive airway pressure (**BIPAP**) is to be preferred over volume-controlled ventilation, such as intermittent positive pressure ventilation (IPPV) or synchronised intermittent mandatory ventilation (SIMV), as it comes closer to normal breathing and there is less risk of ventilator-induced lung injury (VILI). A combination of propofol and sufentanil is particularly well suited for sedation/analgesia [46]. Avoid drugs such as fentanyl and midazolam, which have a tendency to accumulate.

As an alternative to sedation analgesia with propofol/sufentanil, the anaesthetic gas enflurane can be used with the AnaConDa® system for volatile anaesthetics [47]. Enflurane in liquid form is administered through a perfusor and specially designed mask. Monitoring consists of measuring the anaesthetic gas and CO_2 concentrations in the expired air. It has its advantages especially in patients on propofol/sufentanil who experience hypotension requiring catecholamine therapy.

Another possibility for sedation is the intravenous administration of γ-hydroxybutyric acid (Somsanit®: initial dose 50 mg/kg body weight over 20 minutes, then 10–20 mg/kg body weight/hour). This substance induces sleep. This concept has proved its worth in patients with threatening alcohol withdrawal delirium. Remember that this product delivers a high sodium load.

Mechanical ventilation may also be indicated with an existing tracheostomy. The sedation concept described above can be used analogously in this situation. As spontaneous breathing via a tracheostomy is not a problem, the transition from controlled ventilation is not usually difficult.

Although rare, sedation with propofol carries a risk of **propofol infusion syndrome** (PRIS). Characteristic symptoms are lactic acidosis, rhabdomyolysis and circulatory failure [48].

As propofol is administered in a lipid solution, the supply of extra lipids has to be brought into the equation. Propofol may colour the urine green – but this does not indicate rhabdomyolysis.

Table 13: Stages of assisted breathing

Stage	Description
I	O_2 insufflation, breathing coach, Vibrax massage, physiotherapy/breathing exercises
II	Spontaneous breathing with pressure support (CPAP) – non-invasive or via tracheostomy
III	Spontaneous breathing with **triggered** pressure support (CPAP+ASB, BIPAP) – non-invasive or via endotracheal tube or via tracheostomy
IV	Controlled ventilation
V	Alteration of respiratory ratio (I >E)
VI	Additional measures: kinetic therapy (Rotorest®), inhaled NO, nebulised prostacyclin, liquid ventilation, extracorporeal CO_2 elimination (ECCO), extracorporeal membrane oxygenation (ECMO)

4 Risk: liver

4.1 Hepatic cirrhosis, ascites

It is well known that excessive alcohol consumption is a relevant risk factor for developing head and neck tumours. Drinking alcohol regularly also leads to structural and functional changes in the liver, which ultimately result in hepatic cirrhosis [18], [22], [49], [50]. Those affected are not always aware of the diagnosis or they are in denial. The traditional liver function tests (aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT)) contribute very little to the assessment of liver function (detoxification, protein synthesis) and this must be determined otherwise. Routine investigations are:

- serum albumin
- serum bilirubin
- serum cholinesterase
- clotting screen (basis = prothrombin time (PT)/Quick test)
- demonstration of ascites (ultrasound scan; seen in the abdomen included in the chest X-ray)

Hepatic cirrhosis is still divided according to the Child-Pugh classification (Table 14). The model for end-stage liver disease (MELD) score is only relevant for assessing the urgency of a liver transplant.
The Child-Pugh score correlates well with two-year survival and so may be used as a criterion for differential therapeutic decisions about head and neck tumours.
Plasma cholinesterase (= pseudocholinesterase; true cholinesterase is the acetylcholinesterase at cholinergic synapses) is an important biomarker for assessing the duration of effect of succinylcholine-type muscle relaxants and mivacurium. Cholinesterase deficiency or atypical cholinesterase variants may cause an accumulation of muscle relaxants and require the patient to be ventilated postoperatively [9], [51], [52].

Succinylcholine is not reversed by the known relaxant antagonists (neostigmine = Prostigmin®, pyridostigmine = Mestinon®). Steroidal muscle relaxant encapsulators (SMRE) such as Sugammadex® antagonise only steroidal relaxants (vecuronium, rocuronium, pancuronium).

Clotting factor deficiency obviously gives rise to a greater tendency to intraoperative bleeding and an increased risk of subsequent haemorrhage, especially because chronic liver disease is not infrequently associated with concomitant thrombocytopenia (see section 6). Even though albumin is a good marker to assess the synthesising capacity of the liver, this lab test has lost in importance to cholinesterase and clotting factors, as only in exceptional circumstances is human albumin administered to compensate for albumin deficiency these days. Remember that when liver function is impaired, adverse reactions are more likely to occur with drugs that are mostly or completely metabolised in the liver. As well as specific drug-induced effects, the possibility of hepatic encephalopathy has to be considered. In addition to the clinical and neurological picture (Table 16), determination of the serum ammonia levels (special sample tube [dipotassium EDTA plasma with added sodium borate, alternatively heparinised plasma or EDTA plasma] in an ice bath) is particularly important [9]. One trigger for hepatic encephalopathy is swallowing blood. Lactulose (20–50 ml tds) can be given orally to inhibit intestinal ammonia absorption, while the aminoglycoside antibiotic paromomycin (Humatin®, 1000–2000 mg/day in 3–4 divided doses) may reduce NH_3-producing intestinal bacteria.

4.2 Hepatotoxicity

Certain medicines and also reduced perfusion of the liver (e.g. during a cardiac arrest) may lead to an increase in transaminases and cholestasis markers.

Table 14: Child-Pugh score for hepatic cirrhosis

	1 point	2 points	3 points
Bilirubin (mg/dl)	<2.0	2.0-3.0	> 3.0
Albumin (g/dl)	>3.5	2.8-3.5	< 2.8
Ascites	none	mild	severe
Encephalopathy*	none	Grade I/II	Grade III/IV
PT as Quick (%) or INR	>70	40-70	< 40
	<1.7	1.8-2.3	> 2.3

	Score	2-year survival rate	
Child A	5-6 points	85%	
Child B	7-9 points	60%	
Child C	10-15 points	45%	

* see ➢ Table 16

Table 15: Hepatotoxic medicines [18]

Pattern of hepatocellular damage: AST raised	Pattern of mixed damage: AP and ALT raised	Pattern of cholestatic damage: AP and bilirubin raised
Allopurinol	Amitriptyline	Amoxicillin-Clavulanic acid
Amiodarone	Azathioprine	Anabolic steroids
Baclofen	Captopril, Enalapril	Clopidogrel
Fluoxetine	Carbamazepine	Erythromycin
Lisinopril	Clindamycin	Irbesartan
Losartan	Cotrimoxazole	Mirtazapine
Methotrexate	Phenobarbital	Oestrogens
NSAID	Sulfonamides	Oral contraceptives
Omeprazole	Verapamil	Phenothiazine
Paracetamol		Tricyclic antidepressants
Paroxetine		
Risperidone		
Sertraline		
Statins		
Tetracycline		
Valproic acid		

Table 15 presents a list – with no guarantee of completeness – of commonly used drugs that carry a risk of hepatotoxicity [18].
When the patient is known to have impaired liver function, the following aspects have to be taken into consideration:

- avoid giving medicines with predominantly or completely hepatic metabolism whenever there are suitable alternatives
- adjust the dose with respect to the liver function (see the SPC)

Table 16: Stages of hepatic encephalopathy

Stage	Feature
I	Apathy, increased need for sleep, slower movements
II	Somnolence, slurred speech, flapping tremor
III	Sopor (stupor: asleep but can be wakened), disorientation, confusion, ataxia
IV	Coma, no reaction to painful stimuli

- avoid giving medicines with known hepatotoxicity (e.g. paracetamol) whenever there are suitable alternatives
- protect the liver with N-acetylcysteine (controversial, effectiveness not proven except in fulminating hepatic failure)
- preoperative administration of (oral) vitamin K in an attempt to increase the synthesis of clotting factors
- think of hepatic encephalopathy if there are newly occurring neurological disorders (Table 16)
- prevent the patient from swallowing blood which might trigger hepatic encephalopathy
- the presence of ascites is at least a relative contraindication to the insertion of a PEG tube
- think of infected ascitic fluid (= peritonitis) if the patient has ascites and signs of an infection
- a special diet for liver disease (restriction of aromatic amino acids, branched chain amino acids supplements) is controversial
- the prophylactic administration of lactulose does not do any harm.

5 Risk: kidneys

5.1 Creatinine, creatinine clearance, glomerular filtration rate

The serum creatinine concentration is a primary screening parameter for assessing renal function [9]. As many medications prescribed during inpatient ENT treatment (e.g. antibiotics, heparin, cardiac glycosides, antidiabetic agents etc.) are excreted via the kidneys and may require dose adjustment according to the creatinine clearance, the serum creatinine should be determined promptly. If the patient is known to have kidney disease, measure the creatinine concentration repeatedly. Some point-of-care testing (POCT) appliances for blood gases and electrolyte analysis also allow measurement of the creatinine concentration [53]. This saves a great deal of time in comparison with the usual lab analysers and, for instance, is also helpful before planned procedures with contrast agents.

The glomerular filtration rate can be roughly calculated from the serum creatinine concentration, using the Cockroft-Gault formula, the (abbreviated) Modification of Diet in Renal Disease (MDRD) formula or the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation (Table 17). These calculated values are for orientation purposes only and must not be used as the basis for calculating the dose of drugs with critical effects on the kidneys. In this situation, at least determine the creatinine clearance in a 24-hour urine collection. Even this method does not determine the glomerular filtration rate (GFR) precisely but tends to overestimate it. Measurement of inulin clearance is still the gold standard but is reserved for specific problems.

The serum **cystatin C** (formerly γ-trace protein) is considered to be a "better", i.e. more sensitive, marker than creatinine for acute and chronic impairment of renal function and may be the renal function test of the future. Its disadvantage at the present time is the expensive and time-consuming assay method that involves anti-cystatin antibodies, which prevents its routine use. Cystatin C determination may be helpful in critical renal situations (e.g. treatment of transplant recipients with potentially nephrotoxic drugs). The GFR is calculated from the cystatin C concentration as follows:

$$GFR = 74835/[\text{cystatin C}]^{-1.333}$$

5.2 Raised creatinine during inpatient treatment

Should the serum creatinine concentration increase significantly during the hospital stay, consider the following:

- is the patient getting enough fluids? If no fluid balance chart has been kept so far, start one now.
- increase fluids if there are any signs of hypovolaemia. Do not forget the possibility of pre-existing heart failure.
- has the patients been given any nephrotoxic drugs? If so, are they absolutely indicated?
- is there any evidence of a post-renal disorder (men: prostate?)? Bladder filling can easily be assessed with an ultrasound scan. Insert a catheter (transurethral or possibly percutaneous) if necessary. Prompt urological referral may be required.
- the following lab tests are indicated in the work-up: serum creatinine, serum urea, serum potassium, serum osmolarity, urinalysis, and possibly creatinine clearance.
- with persistent impaired renal function, consider whether there is an indication for haemofiltration/haemodialysis. If necessary, insert a large-calibre catheter (Shaldon catheter) for this purpose.

Table 17: Estimation of creatinine clearance

Estimation of creatinine clearance from the serum creatinine concentration using the Cockroft-Gault formula

Men: creatinine clearance = [(140 - age in years) x body weight in kg]/ [72 x serum creatinine in mg/dl]

Women: creatinine clearance = [(140 - age in years) x body weight in kg]/ [72 x serum-creatinine in mg/dl x 0.85]

Estimation of creatinine clearance from the serum creatinine concentration using the abbreviated MDRD formula

Men: creatinine clearance = 186 x $\text{creatinine}_{\text{serum}}^{-1.154}$ x $\text{age}^{-2.03}$

Women: creatinine clearance = 186 x $\text{creatinine}_{\text{serum}}^{-1.154}$ x $\text{age}^{-2.03}$ x 0.724

The full version of the equation includes urea, albumin, age and sex, and is less often used.

The CKD-EPI equation for the estimation of GFR is thought to give the best calculated approximation at the present time:

Men, serum creatinine < 0.9 mg/dl: GFR = 141 x $(\text{serum creatinine}/0.9)^{-0.411}$ x 0.993^{age}

Men, serum creatinine > 0.9 mg/dl: GFR = 141 x $(\text{serum creatinine}/0.9)^{-1.209}$ x 0.993^{age}

Women, serum creatinine < 0.7 mg/dl: GFR = 144 x $(\text{serum creatinine}/0.7)^{-0.329}$ x 0.993^{age}

Women, serum creatinine > 0.7 mg/dl: GFR = 144 x $(\text{serum creatinine}/0.7)^{-1.209}$ x 0.993^{age}

5.3 Anticoagulation with impaired renal function

Low molecular weight (LMW) heparins, also called fractionated heparins, are without doubt the gold standard for perioperative thrombosis prophylaxis [35]. Remember, however, that there is at least a relative contraindication to the administration of LMW heparins in patients with impaired renal function (use with caution when the creatinine concentration is 1.5 mg/dl or more [18]). This becomes less important in patients with end-stage renal failure requiring dialysis so that LMW heparins are again commonly prescribed in this situation.
Table 18 shows the approved uses of LMW heparins.

5.4 Renal replacement therapy (RRT)

Should a patient on dialysis need an ENT operation, the following should be taken into consideration:

- it goes almost without saying that clear documentation should be available from the patient's dialysis centre
- for elective procedures, contact the hospital dialysis unit early to discuss management
- plan surgical interventions in such a way as to allow routine dialysis session the day before the operation. If this is not possible, an extra dialysis session may be needed the day before surgery.

- adjust perioperative fluids according to the situation. The decisive lab test is the serum potassium concentration. As a general rule, do not give any potassium-containing solutions; perioperative fluid consists of (scant) 0.9% NaCl solution.
- depending on the extent of soft tissue trauma, serum potassium, and the course followed by substances that are excreted in the urine, an extra dialysis session may be required the day after surgery
- if RRT is necessary following an ENT operation with a high tendency to bleed, citrate-based haemodialysis can be carried out instead of heparin-based haemodialysis
- the renal anaemia that typically develops is usually treated with erythropoietin. Patients on dialysis have usually adapted to low haemoglobin concentrations, and this should be taken into account when determining the indication for red blood cell transfusion
- continue any regular medication (erythropoietin, antihypertensives, phosphate binders etc.) perioperatively.

If acute renal failure develops in the course of treatment, or there is further deterioration of previously impaired kidney function, check whether there is an indication for renal replacement therapy (haemofiltration, haemodialysis). As consultation with the nephrologists is routinely required, categorical explanations can be dispensed with here.

Table 18: Overview of low molecular weight heparins. Note that the dose differs according to the indication

Proprietary name	Generic name	DVT prophylaxis[2]	Treatment of DVT/PE	HD	Angina, NSTEMI, STEMI
Clexane®	enoxaparin	l-m-h	+	+	+
Clivarin®	reviparin	l-m			
Fragmin® D	dalteparin	l-m-h		+	
Fragmin® P	dalteparin	l-m-h			
Fraxiparine®	nadroparin	l-m-h	+	+	
Innohep®	tinzaparin	l-m	+	+	
Mono-Embolex®	certoparin[1]	m-h	+		

[1] Additional primary prophylaxis with ischaemic stroke

[2] Refers to surgical interventions; enoxaparin, dalteparin and certoparin are also approved for non-surgical patients

DVT = deep vein thrombosis of the leg

PE = pulmonary embolus

HD = haemodialysis

l = low risk, m = medium risk, h = high risk

5.5 Contrast media and renal function

The serum creatinine concentration must be known before any X-ray contrast medium is given. POCT appliances with a creatinine option are extremely useful in this respect (see above).

Magnetic resonance imaging (MRI) contrast medium can also cause renal damage. In particular, the linear-structured, non-macrocyclic preparations containing gadolinium (Omniscan® = gadodiamide, Magnevist® = gadopentetate) have been associated with the development of contrast medium nephropathy (or **nephrogenic systemic fibrosis**) [54].

When the patient has impaired renal function, the first question to ask is whether CT without contrast medium would be sufficient in the circumstances or whether MRI (unenhanced or with a macrocyclic contrast medium) would be appropriate.

If the indication for the use of contrast medium still exists, take the following measures:

- measure the serum creatinine concentration promptly
- discontinue ACE inhibitors, angiotensin II receptor antagonists, diuretics, NSAIDs and metformin, for 24 hours before and after the investigation
- give sufficient (intravenous) fluids before and after the investigation (except with end-stage renal disease); ideally pre-examination hydration should be started at least 24 hours before the examination
- give N-acetylcysteine before and after the examination (e.g. 1200 mg starting immediately before the exam-

ination, and then every 12 hours afterwards until 36 hours after the examination)
- CT: warm iodine-containing contrast medium up to body temperature
- MRI: use macrocyclic contrast medium (ProHance®, Gadovist®, Dotarem®) – patients on dialysis need pre- and post-examination dialysis sessions
- monitor renal function after the examination.

6 Risk: coagulation and the haemopoietic system

Patients who are to undergo ENT surgery are often already being treated with anticoagulants [55], [56], [57]. The following risk factors are typical:

- oral anticoagulation with atrial fibrillation and after heart valve replacement
- oral anticoagulation after deep vein thrombosis and/or pulmonary embolism
- oral anticoagulation with thrombophilia
- subcutaneous anticoagulation after recent joint replacement or following limb fractures
- anticoagulation after stenting for coronary heart disease. The gold standard = dual therapy (aspirin+clopidogrel, alternatively prasugrel or ticagrelor)
- primary and secondary prophylactic administration of aspirin against cerebrovascular events.

The following substances are used for anticoagulation:

- **coumarin derivatives** (warfarin, phenprocoumon(Marcumar®)) are vitamin K antagonists that affect plasma coagulation by inhibiting the synthesis of vitamin K-dependent clotting factors (II, VII, IX and X) in the liver (main coagulation tests: prothrombin time (PT), often the Quick test given in % in Europe, or the international normalised ratio (INR))
- aspirin (acetylsalicylic acid (ASA)) affects platelet aggregation irreversibly
- clopidogrel (Iscover®, Plavix®), prasugrel (Efient®), ticagrelor (Brilique®) and ticlopidine (Tiklyd®) reversibly inhibit ADP-dependent platelet aggregation.
- new oral anticoagulants (**NOAC**s) include apixaban (Eliquis®), dabigatran (Pradaxa®) and rivaroxaban (Xarelto®).

In each case, the risk of perioperative bleeding has to be weighed up against the risk of a thromboembolic event.

6.1 Treatment with coumarin derivatives

Do not use **coumarin derivatives** perioperatively when there is more than a low risk of bleeding. The same applies to all operations under general anaesthetic, as even a gentle intubation technique may cause haematomas to form at the base of the tongue, in the supraglottic region or the glottis. Consider continuing this type of anticoagulant therapy only for surgical interventions with a low risk of bleeding and no danger of compromising the airways, such as the removal of skin lesions. Otherwise switch the oral anticoagulant to heparin perioperatively. **LMW heparin bridging therapy** is widely used, with self-management by the patient. Nevertheless, remember that none of the available products is licensed for this purpose – even if the manufacturer sometimes provides brochures on the subject. Bridging must consist of therapeutic doses (e.g. enoxaparin 1 mg/kg body weight every 12 hours) if there is a high thromboembolic risk (e.g. mechanical heart valve, atrial fibrillation with a CHADS2 score of 5 or above, stroke or TIA <3 months ago, venous thromboembolism <3 months ago, or thrombophilia). It is (only) possible to monitor therapy by determining anti-Xa activity (target value: 0.4–0.8 IU/ml) and not by measuring the conventional clotting parameters. Consequently, adverse events are not uncommon (Figure 5).

The author therefore prefers to anticoagulate by giving unfractionated heparin intravenously, monitoring the effects by determining the activated partial thromboplastin time (aPTT) (target: 1½ to 2 times the upper limit of normal, i.e. about 60–80 s). Therapy starts with a bolus injection (3000–5000 IU), as soon as the PT (Quick) or INR has left the therapeutic range. Heparin administration should be interrupted about four hours before surgery and re-started 4-8 hours afterwards (without any bolus injection). The patient is then re-warfarinised with overlapping administration. Once the Quick value is below 40%, heparin can be stopped.

Figure 5: Bleeding after bridging with LMW heparin in treatment with oral anticoagulants. The anti-Xa activity was way beyond the therapeutic range. Out-patient monitoring was not carried out. Copyright F. Waldfahrer.

Unfractionated heparin also has the advantage that it can be almost completely antagonised at any time by administering **protamine** as the antidote. Protamine only partially antagonises LMW heparins (see SPC for details). It should be diluted and administered slowly through a peripheral venous access.

Remember the risk of heparin-induced thrombocytopenia every time heparin is administered. Monitor the platelet count regularly. Request further diagnostic investigations (HIT II rapid test) if there is a significant fall in the platelet count.

Heparin-induced thrombocytopenia type I (HIT I) may occur at any time from the first day onwards and is a non-immune heparin-platelet interaction. As a rule, heparin therapy can be continued without reservation.

Heparin-induced thrombocytopenia type II (HIT II) is due to antibody formation; it occurs 5–20 days after the first administration of heparin, and just a few hours after re-exposure. Thromboembolic vascular occlusion is common. Stop heparin immediately, although anticoagulation can be continued with danaparoid (Orgaran®) or argatroban (Argatra®) if necessary.

Vitamin K antagonises the effects of coumarin derivatives, although the onset of action is usually delayed. If the PT (Quick) or INR is elevated (e.g. preoperatively or during bleeding), give vitamin K (Konakion® MM 10 mg) orally. Intravenous administration is reserved for severe or life-threatening haemorrhage.

Should it not be possible to wait for the delayed action of vitamin K, prothrombin complex (factor II – **p**rothrombin, VII – **p**roconvertin, X – **S**tuart Prower factor, IX – antihaemophilic factor **B**, protein C and protein S (**PPSB**)) is available for intravenous administration. One international unit of PPSB per kg body weight raises factors VII and IX by 1–2% and factors II and X by 2–4%. PPSB is therefore much more efficient than fresh frozen plasma. Do not forget, however, that PPSB is of human origin and, under the transfusion law, its administration has to be fully explained to the patient and documented.

Table 19: Perioperative risk stratification with platelet aggregation inhibitors (modified from [58])

		Low to medium	High	Very high
		Primary prevention	**Documented CAD considered stable in risk stratification**	**Documented CAD considered unstable in risk stratification**
		General atherosclerosis without documented CAD, CVD, PAOD	History of myocardial infarction > 1 month Coronary stenting: - bare metal stent > 1 month - drug-eluting stent > 12 months History of CABG > 6 weeks History of CVI/TIA > 1 month PAOD	History of myocardial infarction < 1 month Coronary stenting: - bare metal stent < 1 month - drug-eluting stent < 12 months History of CABG < 6 weeks History of CVI/TIA < 1 month
Risk of bleeding complications	low	Continue aspirin unchanged	Continue aspirin unchanged If clopidogrel still prescribed, clarify the indication and discuss in the individual case	Postpone surgery whenever possible Continue aspirin and clopidogrel unchanged
	medium	Discontinue aspirin 7 days preop., restart on day 2-3 postop.	Continue aspirin unchanged If clopidogrel still prescribed, clarify the indication and discuss in the individual case	Postpone surgery whenever possible Interdisciplinary discussion if surgery is inevitable
	high (spine and liver surgery)	Discontinue aspirin 7 days preop., restart on day 3-4 postop.	Discontinue aspirin 3 days preop., restart on day 1-2 postop. If clopidogrel still prescribed, clarify the indication and discuss in the individual case	Postpone surgery whenever possible Interdisciplinary discussion if surgery is inevitable
	very high (intra-cranial surgery)	Discontinue aspirin 7 days preop., restart on day 4-5 postop.	Discontinue aspirin 5 days preop., restart on day 2-3 postop. If clopidogrel still prescribed, clarify the indication and discuss in the individual case	Postpone surgery whenever possible Interdisciplinary discussion if surgery is inevitable

CABG = coronary aortic bypass grafting, CVD = cerebrovascular disease, CVI = cerebrovascular insult, PAOD = peripheral arterial occlusive disease, TIA = transient ischaemic attack

Each ml of fresh frozen plasma (FFP) contains one unit of the plasma clotting factors and their inhibitors. 1 ml plasma/kg body weight increases the Quick value by (about) 1%. If, for example, it is necessary to increase the Quick value from 20% to 60%, an 80 kg patient would require 40 × 1 ml/kg body weight × 80 kg = 3200 ml. This calculation emphasises the small benefit of fresh frozen plasma to improve coagulation in situations other than hypovolaemia.

6.2 Treatment with aspirin and clopidogrel

As a meta-analysis showed an increased risk of coronary and cerebrovascular events when aspirin had been discontinued perioperatively, Vogel Kahlmann et al. [58] recommend the approach shown in (Table 19).

In the article mentioned, the risks of bleeding in ENT interventions were generally considered "medium". Nevertheless, assume a higher risk for surgical procedures on the larynx and trachea, as well as for extensive tumour resections.

Elective surgical interventions should therefore be postponed; perform operations that cannot wait with continuation of the dual medication.

After the insertion of a coronary stent, dual platelet aggregation inhibitors are continued for at least four weeks with bare metal stents and for at least 6–12 months with drug-eluting stents [59].

In contrast to aspirin, **nonsteroidal anti-inflammatory** drugs (NSAIDs) inhibit platelet aggregation reversibly, i.e. platelet function can be expected to return to normal within 1–3 days. So it is sufficient to stop this medication 1–2 days before the planned operation. Remember that giving NSAIDs postoperatively carries an increased risk of bleeding.

6.3 Treatment with new anticoagulants

The therapeutic spectrum of anticoagulant therapy has recently been extended by the introduction of products designated as new oral anticoagulants (**NOAC**s).

Rivaroxaban (Xarelto®) and apixaban (Eliquis®) act as direct factor Xa inhibitors. Dabigatran (Pradaxa®) inhibits factor IIa. The indications for these new substances are still evolving; at the present time, all three products are approved for prophylaxis of DVTs after lower limb joint replacement, dabigatran and rivaroxaban also have marketing authorisation for stroke prophylaxis in atrial fibrillation. None of them can be administered by feeding tube. The dose may have to be adjusted in cases of renal insufficiency; details are given in the relevant SPCs.

Routine lab tests are not required (or possible) to monitor any of these three medications. The standard PT (Quick) and aPTT tests do not react to the presence of the active substances, so that problems arise in patients with acute bleeding (e.g. epistaxis). **While it was previously possible to determine an overdose of oral anticoagulant easily with the PT (Quick), a diagnostic tool is lacking for NOACs.** In addition, the effects of NOACs cannot be reversed at the present time (although antidotes are being developed). The situation is made even more difficult when patients cannot say which medication they are taking. The following statements apply:

- a relevant anticoagulant effect of dabigatran (factor IIa-inhibitor) can be ruled out if the thrombin time is normal
- a normal PT (Quick) value does not rule out the presence of any of the three NOACs
- when interpreting lab test results, it is important to know when the last dose was taken, as these products have a relatively short half-life

- the effects of dabigatran can be demonstrated with the Hemoclot® test
- the effects of rivaroxaban and apixaban can be demonstrated by means of a specific anti-Xa test in each case.

There is currently a diagnostic gap in the event of acute haemorrhage and unknown medication, as the presence of NOACs cannot be determined with absolute certainty by standard tests and each substance requires specific tests. Symptomatic therapy is therefore the most important.

- PPSB can be given in cases of severe and life-threatening haemorrhage. Otherwise it is sufficient to discontinue the therapy.
- depending on the risk of bleeding, stop dabigatran and rivaroxaban 24 or 48 hours before surgery. Start treatment again as soon as possible. Perioperative bridging with LMW heparins is not recommended at the present time (nor is it an approved indication).

6.4 Other clotting disorders (haemophilia, von Willebrand's disease)

Clotting factor concentrates are available for the treatment of haemophilia:

- haemophilia A – factor VIII: Advate®, Helixate®, Kogenate®, Recombinate®, ReFacto® (recombinant), Beriate®, Fanhdi®, Haemoctin®, Octanate® (human)
- haemophilia B – factor IX: BeneFIX® (recombinant), Alpha-Nine®, Berinin®, Betafact®, Haemonine®, Immunine®, Mononine®, Octanine® (human).
- factor VIIa is also available as a recombinant product (NovoSeven®)
- activated protein C (drotrecogin alfa, Xigris®) is used to treat severe sepsis in certain circumstances.

Postoperative coagulation management in the individual case should be discussed with a specialist in transfusion medicine. If products of human origin are used, they have to be documented correctly in accordance with the transfusion law.

With prevalence of 1–2%, von **Willebrand's disease** (vWD) is the most common inherited bleeding disorder. The disease causes a disorder of primary haemostasis, due to the abnormal synthesis or dysfunction of von Willebrand's factor (vWF). The three different types of vWD differ in their severity and treatment (Table 20). Diagnostically, prolongation of the aPTT may be one of the first indications of vWD. The following tests aid in diagnosis:

- vWF antigen – a quantitative test
- ristocetin cofactor (vWF:RCoF) – a qualitative factor
- factor VIII activity

Type II vWD can be subdivided by means of a special diagnostic test. **Desmopressin** (Minirin®) is a synthetic derivative of antidiuretic hormone (ADH; synonym=vasopressin) and also stimulates the release of vWF and factor VIII from endothelial cells. A dose of 0.3–0.4 µg/kg is

Table 20: Von Willebrand's disease [56,57]

Type	Heredity	Frequency	Severity	Treatment
I	Autosomal dominant	80%	tends to be mild	Desmopressin
II (A, B, M, N)	Autosomal dominant	20%	variable	Replacement therapy (Haemate® HS) Trial of desmopressin, except for type II B
III	Autosomal recessive	< 1%	severe	Replacement therapy (Haemate® HS)

given as a short infusion. One adverse effect of desmopressin is water retention. Take this into account in the perioperative fluid regimen (fluid balance chart).

6.5 Thrombocytopenia

Pseudothrombocytopenia may be mistakenly diagnosed due to the presence of EDTA in the sample, so that a check on citrated blood is recommended before introducing any further measures.

(True) thrombocytopenia has many possible causes. If thrombocytopenia is first discovered in the context of an elective surgical intervention, the patient should be referred to a haematologist for a full workup.

Depending on the cause of the thrombocytopenia, the preoperative administration of corticosteroids (e.g. 8 mg dexamethasone) or dapsone might boost the platelet count before any operation that cannot wait.

Heparin-induced thrombocytopenia may occur after the administration of heparin (see section 6.1).

Thrombocytopenia in severe infections may indicate the complication of progressive consumption coagulopathy (disseminated intravascular coagulation (DIC)). As long as the platelets show normal function, there is no significantly increased risk of bleeding above a concentration of 60×10^9/l.

With more pronounced thrombocytopenia, consider the option of platelet transfusion. Platelet concentrate should not be given until immediately before the operation because of its short half-life. If there is any question of allogeneic stem cell transplantation, make every effort to ensure that the platelet transfusion is HLA-compatible.

The ROTEM® system is a relatively new tool in platelet function diagnostics. Whole blood is subjected to thrombelastometry, a development of thrombelastography [60]. Coagulation is activated either extrinsically (EXTEM) or intrinsically (INTEM). HEPTEM reveals any possible heparin effects, APTEM measurements provide evidence of hyperfibrinolysis by the addition of aprotinin. FIBTEM measurements deactivate the platelets, so that the results correspond solely to fibrin-induced clotting. The method has proved its worth especially in major surgical procedures on patients with impaired liver function and septic conditions.

7 Risk: blood gases, fluid and electrolyte balance, and metabolism

7.1 Blood gases

Without doubt, every clinical and surgical facility must have access to a POCT system for blood gas analysis. These systems are used mainly for intraoperative diagnostic investigation, but also provide a good service for patients whose general condition deteriorates acutely and for preoperative risk assessment. Besides the routine tests for pH, pO_2, pCO_2 and HCO^{3-}, most systems can also measure the haemoglobin concentration and blood glucose levels. Ideally the POCT appliance should also be able to determine electrolyte concentrations (Na^+, K^+, Ca_2^+ and Cl^-) [53].

Although venous blood provides information useful for orientation purposes, arterial blood gas analysis is more reliable. If no catheter is in situ for arterial blood pressure measurement and it is not possible to insert one, blood samples can be obtained by radial artery puncture. Capillary blood gas analysis (e.g. from a drug-induced hyperaemic ear lobe) carries the risk of inaccurate interpretation due to crush artefacts (mixture of serum and lymphatic fluid). **The pO_2 in particular is not valid with capillary sampling.**

Treatment is needed in the acute case with non-compensated disorders, identified by an abnormal pH (normal range: 7.35–7.45). First ascertain whether the disorder is of a primary respiratory or metabolic origin. If there is respiratory acidosis, the pCO_2 is raised (CO_2 narcosis); if the condition is of metabolic origin, the HCO_3 concentration is lowered.

Primary respiratory disorders may require mechanical ventilation to blow off carbon dioxide. The first question to ask with a primary metabolic condition is that of its origin. Look into the possibility of medication with metformin if there is a concomitant increase in the serum lactate levels (see section 9.4). A similar combination of lab results can be seen with mesenteric infarction. Treatment depends on the assumed or confirmed cause. Respiratory alkalosis is the result of hyperventilation.

Table 21: Dehydration and hyperhydration

	Serum sodium	Haematocrit	Osmolarity	Treatment
Hypotonic dehydration	↓	↑	↓	NaCl solution
Isotone dehydration	n	↑	n	Isotonic solution
Hypertonic dehydration	↑	↑	↑	Electrolyte-free water (oral), Glucose 5% iv
Hypotonic hyperhydration	↓	↓	↓	Diuretics
Isotonic hyperhydration	n	↓	n	Diuretics
Hypertonic hyperhydration	↑	↓	↑	Diuretics, Glucose 5% iv

7.2 Fluid balance

The first distinction to be made is between hyperhydration and dehydration, which can be determined from the haematocrit. Secondly, distinguish between isotonic, hypertonic and hypotonic states, which can be done on the basis of the serum osmolarity [9]. Considerations are always based on the intravascular state, details of which can be seen in Table 21.

As long as the arterial blood pressure is being monitored, volume deficiency can easily be identified by an undulating curve (pulse pressure variation) with slow conduction (6.25 m/s), as shown in Figure 6. Moreover, the fluid balance can be estimated on the basis of the central venous pressure (CVP), as long as a central venous catheter lies in the superior vena cava; although it is possible to measure the CVP with a line in the inferior vena cava, it is of limited value. Whenever possible, take CVP measurements in patients lying flat without any mechanical pressure support (PEEP). Do not overestimate the value of a single CVP measurement [18], [39], [41]. As a rule of thumb, it can be said that there is a volume deficiency when the CVP <0 mm Hg (as measured by the monitor; conversion to cm water: 1 mm Hg = 1.36 cm water). No further volume replacement is required when the CVP >20–25 mm Hg.
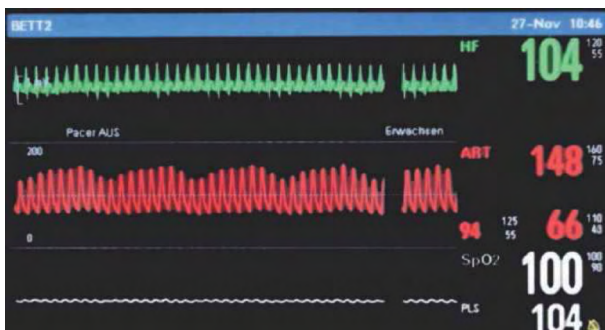

Figure 6: Undulating IBP curve indicating volume deficiency (prerequisite: sinus rhythm)

7.3 Electrolyte: sodium

Hyponatraemia [61] may have the following causes:

- medication: diuretics, antidepressants, aldosterone antagonists (spironolactone, potassium canreonate, eplerenone)
- syndrome of inappropriate antidiuretic hormone secretion (SIADH), also known as the Schwartz-Bartter syndrome – e.g. of paraneoplastic (small cell carcinoma) or inflammatory (pneumonia, encephalitis) origin, or drug-induced (antidepressants)
- hypovolaemia with gastroenteritis

Because sodium is located predominantly in the extracellular space, a low serum sodium is not necessarily an expression of sodium deficiency but much rather of hypotonic hyperhydration. In this situation, giving sodium would be wrong; on the contrary, the hyperhydration has to be dealt with by administering diuretics.

If there is an indication for sodium, it must be given slowly, as too-rapid adjustment carries a risk of **osmotic demyelinating diseases** (central pontine myelinolysis, extrapontine myelinolysis) [62]. Diurnal increase in the sodium level by up to 8 mmol/l is considered harmless (this value has been gradually reduced from an initial 20 mmol/l in the last few years). Isotonic NaCl solution is preferred to adjust the electrolyte balance as long as there is an associated hypochloridaemia; use hypertonic solutions with caution. Patients with nasogastric tubes or PEG tubes can also be given NaCl supplements with the tube feeds.

Aldosterone antagonists (spironolactone = Aldactone®, potassium canreonate = Aldactone® for injection = active metabolite of spironolactone; eplerenone = Inspra®) are used particularly for diuretic therapy in hepatic cirrhosis with ascites. These substances inhibit sodium resorption and potassium secretion, which may lead to hyponatraemia and hyperkalaemia.

Hypernatraemia is rare except in cases of excessive intake, Conn's syndrome (primary hyperaldosteronism), and diabetes insipidus.

7.4 Electrolyte: chloride

Serum chloride [9] concentration is often less closely observed in routine clinical practice than the levels of the cations. Deviations from the norm are relatively frequent.

Hypochloridaemia, usually in association with hyponatraemia, is sometimes seen in cachectic cancer patients who have an inadequate food and fluid intake. It may lead to confusional states.

Combined sodium and chloride deficiency can be balanced out by the administration of physiological/normal saline solution (see below) or additional salt in the diet (also by adding salt to tube feeds). Take the same precautions as described for sodium above.

On the other hand, draining gastric juices via a nasogastric tube or a PEG tube can lead to isolated hypochloridaemia. The same may occur with chronic hypercapnia and on treatment with mineralocorticoids.

Hyperchloridaemia is often the result of inappropriate, uncritical intravenous fluid administration: with respect to the normal serum chloride concentration, "normal" saline solution is by no means physiological, as it contains about 145 mmol/l chloride ions. In the case of hyperchloridaemia, therefore, prefer to use an electrolyte solution with a more physiological chloride content (e.g. Jonosteril®, Sterofundin®, Ringer's acetate, Ringer's lactate).

Routinely used infusion solutions have therapeutically relevant differences in composition of which you should be aware.

7.5 Electrolyte: potassium

As a rule, most attention is paid to the potassium [9] concentration. Hypokalaemia can affect cardiac function just as much as hyperkalaemia. From the anaesthetist's point of view, knowing the potassium level is important for the use of muscle relaxants. As taking (loop) diuretics is often a part of the treatment of arterial hypertension, hypokalaemia occurs frequently in everyday practice.

Interpretation of the potassium concentration requires knowledge of the pH and glucose levels, as these three parameters interact.

- An increase in the blood pH by 0.1 reduces the serum potassium by about 0.5 mmol/l (acidosis – hyperkalaemia; alkalosis – hypokalaemia).
- Hyperglycaemia causes a fall in potassium levels. Insulin drives potassium into the cells.

Implausible or unexpected lab test results always have to be looked at critically, and may indicate preanalytical error (tourniquet applied for too long, haemolysis because of a narrow cannula, sample taken from infusion arm or distal CVP access, etc.).

The following rules apply to treating (true) hypokalaemia:

- the potassium requirement (in mmol/l) can be calculated with the following formula:
  K^+ (target) = K^+ (measured) × kg body weight × 0.2
- the safest means of potassium replacement is orally or via a feeding tube (1 effervescent tablet of Kalinor® = 40 mmol). Overdose is practically impossible when kidney function is intact.

- the role of bananas in overcoming clinically relevant hypokalaemia is overestimated. One banana contains about 14 mmol potassium per 100 g.
- The usual 1 millimolar KCl solution (7.46%) consequently contains 1 mmol/l of the ions.
- KCl solution must be diluted before administration: max. 40 mmol/l, i.e. a maximum of one 20 ml ampoule KCl per 500 ml infusion solution for peripheral venous infusion. Infusion time ≥3 hours. It follows, therefore, that the treatment of severe hypokalaemia (replacement requirements >80 mmol) requires a central venous line. Potassium replacement in hypokalaemia with typical ECG changes needs monitoring on intensive care.

Hyperkalaemia can be treated as follows:

- loop diuretics (e.g. furosemide 20–40 mg iv, torasemide 6–12 mg iv)
- calcium gluconate 10%, 10 ml iv
- if there are circulatory complications: 200 ml glucose 20%+20 IU rapid-acting insulin iv/30 minutes (CVL)
- resonium, given orally or per rectum
- haemofiltration, haemodialysis.

7.6 Electrolyte: calcium

When assessing the serum calcium [9] levels, check whether the total calcium or the ionised calcium (commonly measured by many POCT systems) has been determined. The normal ranges differ:

- total calcium: 2.2–2.6 mmol/l
- ionised calcium: 1.12–1.32 mmol/l

As a rule of thumb: ionised calcium = ½ total calcium

There is obviously room for error in assessment if the method used and the normal range are unknown.

As a general rule, hypocalcaemia in asymptomatic patients (e.g. after thyroid gland surgery) is less relevant than hypercalcaemia.

In the event that it is necessary to treat hypocalcaemia, oral replacement is preferable, whenever possible.

Calcium levels in the body are strictly regulated by a hormone feedback loop (parathormone, calcitonin), so hypercalcaemia is always pathological (unless it is due to preanalytical error) and needs to be investigated for cause.

The following therapeutic options are open for symptomatic treatment of hypercalcaemia:

- fluids, rehydration,
- forced diuresis, possibly with potassium replacement
- calcitonin 5–10 IU/kg body weight/day sc
- in the case of tumour-associated hypercalcaemia: bisphosphonates iv (e.g. pamidronate).

7.7 Diabetes mellitus

Without doubt, diabetes mellitus is one of the most commonly encountered pre-existing diseases in routine clinical practice. Stop metformin-containing medicines at least 48 hours before elective surgery, because of the risk of lactic acidosis (see section 9.4). Do not give any oral antidiabetic agents or intermediate- or long-acting insulins on the day of operation, but control the blood glucose by giving rapid-acting insulin – with repeated doses if necessary – on the basis of the blood glucose levels.

In acute conditions such as pneumonia and sepsis, a correlation between glucose levels and outcome has been described, so it is always important to keep the blood glucose within the normal range as much as possible. In particular, avoid hyperglycaemia of more than 180 mg/dl (renal threshold).

7.8 Thyroid gland

Preoperative lab tests can be dispensed with if there is no evidence of thyroid disease. TSH measurement is sufficient before elective surgery if the patient is known to have thyroid disease. When the TSH concentration is in the normal range, there is no contraindication to surgical intervention. Elevated TSH levels (indicating hypothyroidism) and reduced TSH levels (indicating hyperthyroidism or thyroid autonomy) require preoperative workup and appropriate treatment. Postpone elective surgery until the patient is euthyroid. In the case of urgent surgical intervention, initiate hormone replacement for hypothyroidism and thyrostatic therapy for hyperthyroidism.

Hypothyroidism is to be expected after radiotherapy in the region of the thyroid gland.

Administration of iodine-containing contrast medium for computed tomography means that subsequent thyroid gland scintigraphy cannot be evaluated. If there is any suspicion of a thyroid carcinoma, the use of contrast medium during a CT scan should be challenged.

7.9 Steroid therapy

Patients requiring ENT surgery are not infrequently on **long-term steroid therapy**. Typical indications are:

- pulmonary disease: bronchial asthma, COPD
- rheumatic disease, autoimmune disease

As exogenous therapy with corticosteroids impairs or may impair the endogenous function of the adrenal cortex, determine before surgery whether there is an indication for supplemental perioperative steroids to prevent postoperative adrenal cortical insufficiency. Supplementation ("stress dose") is indicated especially when the patient has been on steroid therapy for more than three months preoperatively. As a rule, 50 mg hydrocortisone is given as a short infusion, followed by a further 50 mg via per-fusor over 12 hours. Then continue with the patient's usual oral dose.

Table 22 shows the comparative dose effects of commonly used corticosteroids [63], [64].

Glucocorticoid dose equivalence is therefore:

- 1 mg prednisone/prednisolone is equivalent to 0.8 mg methylprednisolone equivalent to 0.15 mg dexamethasone equivalent to 5 mg hydrocortisone

It is now a generally accepted standard that patients with healthy stomachs, who are prescribed monodrug therapy with corticosteroids (i.e. no concomitant NSAIDs) do not require gastric protection (e.g. proton pump inhibitor (PPI), H₂-blocker, sucralfate, etc.), as corticosteroids per se are not ulcerogenic.

8 Risk: central nervous system (CNS)

8.1 Dementia

Increasing life expectancy increases the prevalence of dementia syndromes. The ENT surgeon therefore often faces patients with dementia [65] in both the outpatient and inpatient settings (e.g. epistaxis, marantic parotitis, skin tumours). Patients admitted to hospital have particular problems with orientation in the unaccustomed environment. Surgical procedures associated with general anaesthesia as well as new medication can also lead to an acute deterioration in cognitive function. Causative treatment is not possible but contact with the usual carers often helps. Symptomatic treatment may require sedation (e.g. melperone, pipamperone) and even restraint to prevent self-injury or harm to others. Antidementia drugs do not work in the short-term, if at all. Make every effort to discharge patients promptly back to their usual surroundings. The differential diagnosis includes delirium (see section 8.4 for differentiating features).

8.2 Parkinson's disease

It is important to distinguish between idiopathic Parkinson's disease [66], [67] and Parkinsonism. The cardinal symptoms are bradyhypokinesia, rigor, tremor and impaired postural reflexes. Further symptoms include dementia, disturbances of smell, and disorders of the autonomic nervous system. The pathophysiology consists of a dopamine deficiency in the substantia nigra with the formation of intracellular inclusion bodies (Lewy bodies). Parkinson's disease can be treated with the following drugs:

- L-dopa+decarboxylase inhibitors: L-dopa+benserazide (Madopar®), L-dopa+carbidopa (Nacom®)
- catechol-O-methyltransferase (COMT) inhibitors: entacapone (Comtess®), tolcapone (Tasmar®)
- monoamine oxidase B (MAO-B) inhibitors: selegiline (Movergan®, Xilopar®), rasagiline

Table 22: Overview of commonly used corticosteroids

	Generic name	Proprietary name	Relative gluco-corticoid potency	Relative mineralo-corticoid potency
Glucocorticoids	Hydrocortisone	Hydrocortison®	1	1
	Cortisone	Cortison®	0.8	0.8
	Prednisone	Decortin®	4	0.6
	Prednisolone	Decortin® H	4	0.6
	Methylprednisolone	Urbason®	5	0
	Fluocortolone	Ultralan®	5	0
	Triamcinolone	Volon®	5	0
	Paramethasone	Monocortin®	10	0
	Betamethasone	Celestan®	30	0
	Dexamethasone	Fortecortin®	30-40	0
Mineralocorticoids	Fludrocortisone	Astonin®	0	3000

- (Azilect®)
- dopamine agonists: apomorphine (APO-go®), bromocriptine (Pravidel®), cabergoline (Cabaseril®), (-dihydroergocriptine (Almirid®), lisuride (Dopergin®), pergolide (Parkotil®), piribedil (Clarium®), pramipexole (Sifrol®), ropinirole (Requip®), rotigotine (Neupro®)
- N-methyl-D-aspartate (NMDA) antagonists: amantadine (PK-Merz®)
- anticholinergics: biperiden (Akineton®), methixene (Tremarit®), trihexyphenidyl (Artane®)

Patients with known Parkinson's disease may have perioperative complications, especially when their usual medication is interrupted.

If oral medication is not possible in the perioperative phase, an infusion of amantadine (200 mg/500 ml/3 hours) may be used, especially in akinetic crises (take care if the patient has renal failure). Amantadine is, in fact, a virostatic agent but also has antagonistic effects on the NMDA receptors. Its advantage lies in its rapid onset of action.

8.3 Wernicke's encephalopathy, Korsakoff's psychosis

Both these clinical pictures are the expression of thiamine (vitamin B) deficiency and are seen particularly with alcohol abuse [67]. Wernicke's encephalopathy (polioencephalitis haemorrhagica superior) is an acute condition with predominantly neurological symptoms (Wernicke's triad: mental confusion, ophthalmoplegia and ataxia, affecting the lower limbs in particular; other symptoms include clouding of consciousness, agitation, and cerebellar speech disorders). Korsakoff's psychosis represents chronic progressive disease with predominantly psychiatric symptoms (Korsakoff's triad: disorientation, anterograde amnesia (inability to assimilate new information although older memories are maintained), and confabulation). In up to 80% of cases, acute Wernicke's encephalopathy progresses to chronic Korsakoff's psychosis. Administration of **thiamine** (50–100 mg/day) is the first-line treatment.

In patients with a history of alcohol abuse and neuropsychiatric features, there is nothing to argue against a trial of thiamine.

8.4 Delirium

This term delirium [68], [69], [70] is derived from the Latin *delirare*: to deviate from the straight track, to be deranged. It describes CNS changes characterised by an acute onset and fluctuating disturbances of mental and psychomotor function, affect, and level of consciousness [71]. "Acute confusional state", "acute brain failure" and the previously used term "acute organic brain syndrome" do not describe a specific medical condition but are synonyms for delirium. A distinction is made between delirium with pre-existing dementia and that without. Delirium requires prolonged hospital stay and is associated with a higher mortality. Only 50% of cases of delirium are completely reversible. The aetiology and pathogenesis of delirium are currently explained by a multifactorial model. Factors enhancing delirium are: advanced age, pre-existing CNS diseases (dementia, stroke, Parkinson's disease), multimorbidity, sensory deficits, medication, dehydration, fever, infection, pain, constraint, alcohol or drug withdraw-

Table 23: Distinguishing features of delirium and dementia

Feature	Delirium	Dementia
Consciousness	clouded	clear
Hallucinations	visual	rare
Delusions	frequent	rare
Physical symptoms	usually present	usually absent
Onset of symptoms	acute	gradual
Course of symptoms over the day	fluctuating	constant

al, and more than three new medicines (opiates, antibiotics, benzodiazepines, corticosteroids).
Typical symptoms of delirium are:

- clouding of consciousness and attention
- global disorder of cognition
- psychomotor dysfunction: hyporeactivity, hyperreactivity, mixed type
- disturbance of sleep/wake rhythm
- sudden onset and fluctuation during the course of the day
- evidence of a physical cause (admission to hospital, operation, alcohol or drug withdrawal).

If the symptoms indicate delirium, perform the following diagnostic investigations:

- lab tests: full blood count, electrolytes, creatinine, CRP, blood glucose, TSH, ammonia, blood gas analysis, and if appropriate, levels of any drugs being administered
- diagnostic imaging of the CNS (CT, MRI), if necessary
- lumbar puncture and examination of the cerebrospinal fluid (CSF), if necessary

(Acute) delirium has to be differentiated from (chronic) dementia; Table 23 lists the criteria used to distinguish the two.
The following basic rules apply to the treatment of delirium:

- provide adequate supervision
- deal with identifiable causes
- optimise bodily functions, e.g. mobilisation, occupation
- take measures to improve orientation (e.g. radio, TV, daily newspapers)
- avoid complications (e.g. falls) – but wherever possible, avoid constraint, such as the use of patient restraints. Should restraints be absolutely necessary, keep the patient under constant supervision.

The following pharmacotherapeutic options are available:

- antipsychotic drugs (also known as neuroleptics)
  - classic antipsychotic drugs affect only positive symptoms
  - atypical antipsychotic drugs affect both positive and negative symptoms of psychosis; adverse extrapyra-

midal effects are rarer than with classic antipsychotic drugs
  - quetiapine (Seroquel®, 6.25–25 mg) or risperidone (Risperidal®, 0.5–2 mg) can be given when there are thought disorders, delusions or hallucinations – although an increase in mortality has been reported in dementia-induced psychosis
  - haloperidol 0.3–2.5 mg orally or benperidol (Glianimon®) 1–2 mg iv can be given for productive psychotic symptoms.

NB: patients given intravenous haloperidol must always be under continuous ECG monitoring because of the risk of prolonged QT interval (Drug Safety Mail from the Drug Commission of the German Medical Association, dated 05/05/2010)

- benzodiazepines (e.g. lorazepam 0.5–1 mg) are used particularly in anxiety states; venlofaxine (Trevilor®) is an alternative
- sleep disorders can be treated with low potency neuroleptics: melperone (Eunerpan®) 12.5–50 mg or pipamperone (Dipiperon®) 10–40 mg
- give thiamine (vitamin B1) to all patients with a history of alcohol abuse who show an acute disturbance of consciousness. Dose: 100 mg/day
- SSRIs are indicated if there is any evidence of a depressive episode – however, the onset of action is not seen for several days.

The following aspects need to be considered in the prevention of delirium tremens (due to alcohol withdrawal):

- take perioperative measures to prevent delirium tremens if there is known alcohol abuse. The usual drinking can possibly even be tolerated for minor interventions (e.g. diagnostic panendoscopy) as long as the patient is fasting before intubation. As a rule, however, patients who have to come into hospital for a short stay – urgent diagnosis of cancer – will not be motivated to long-term abstinence. Continued alcohol consumption is therefore a justifiable option, as long as the patients organise their own supplies. Intravenous ethanol administration is not an option.
- for patients undergoing long-term stays and/or who want to give up drinking, the following treatment regi-

mens have proved useful under appropriate supervision:

- **clonidine** (peripheral and central α-agonists, α2>α1) suppresses psychophysiological functions. Dosage: loading dose 75–150 µg, then 30–120 µg/hour via perfusor. Monitor arterial blood pressure continuously as hypotension and bradycardia may be dose-limiting factors. Clonidine therapy has to be tapered off gradually. Classic signs of pain (hypertension + tachycardia) are masked by clonidine therapy.
- **physostigmine** (Anticholium®, initially 0.03–0.04 mg/kg body weight as a short infusion, then 1 mg/hour via perfusor)
- **γ-hydroxybutyric acid** (Somsanit®, initially 50 mg/kg body weight over 20 minutes, then 10–20 mg/kg body weight/hour via perfusor). Ventilation equipment has to be on hand because of the risk of respiratory depression, use is therefore preferred in patients with tracheostomies
- clomethiazole (Distraneurin®), although popular previously, should no longer be used because of its poor safety profile
- it is essential to treat postoperative pain adequately.

8.5 Central anticholinergic syndrome (CAS)

Central anticholinergic syndrome may occur as a complication of a general anaesthetic. The central action may be excitatory (agitation) or depressant (stupor, respiratory depression) [51]. Peripheral effects include tachyarrhythmias, flushing of the skin and urinary retention. General anaesthetics, hypnotics, opioids and centrally acting parasympatholytics such as atropine may trigger CAS. Treatment consists of physostigmine (Anticholium®, at a dose of 0.03–0.04 mg/kg body weight as a short infusion). Unlike other "stigmines", physostigmine crosses the blood-brain barrier.

8.6 Stroke

ENT inpatients are also at risk of stroke [67], [72], particularly patients with cancer and a corresponding risk profile. Remember that anticoagulation with heparins lowers only the risk of venous thromboembolism and not the risk of cerebrovascular events (emboli mainly affect the lungs; the exception is paradoxical embolus with a patent foramen ovale). This is particularly relevant when anticoagulant therapy for atrial fibrillation is discontinued perioperatively. As a rule of thumb, pulmonary emboli rarely occur in an adequately anticoagulated patient but the same does not apply to strokes. Emergency diagnostic investigation is indicated as soon as an acute neurological deficit is noticed (except when a decision for palliative care has already been taken). Investigation consists, on the one hand, of determining the clinical neurological status and, on the other, of diagnostic imaging (CT with perfusion measurement). CT allows bleeding to be ruled out at once and with certainty, but ischaemia cannot always be detected or excluded immediately. Further management is based on neurological measures. If lytic therapy is indicated, remember that there will be an increased risk of bleeding at the operation site. The indication for mechanical ventilation (e.g. after surgical interventions on the larynx and hypopharynx) needs to be made relatively generously but interacts with the ability to record neurological findings. Emergency l**igation of the internal carotid artery** or common carotid artery cannot be avoided in some cases of acute tumour haemorrhage (a temporary balloon occlusion test prior to elective surgery allows the risk of cerebral ischaemia to be estimated). If the internal carotid artery is acutely occluded, the following measures may reduce the chances of ischaemic infarction:

- treatment on intensive care is indicated
- postoperative ventilation (aim to obtain a high normal paO_2 with mild hyperventilation, i.e. $paCO_2$ that is just subnormal).
- terminate sedation analgesia as soon as possible, to allow assessment of the neurological status. It is a good idea to perform a tracheostomy if the patient does not already have one, as it makes weaning easier and less stressful
- the patient should lie flat (but not with a head-down tilt)
- consider giving corticosteroids (dexamethasone – typical dosage 8 mg tds) for the prophylaxis of cerebral oedema
- also consider inserting a probe to measure intracranial pressure in the individual case
- if there are no neurological deficits (main finding is hemiparesis on the contralateral side) continue a generous supply of oxygen and slowly elevate the upper body step by step (about 10°/day). Return immediately to the 0° position if the patient experiences any paraesthesia etc. Provided no neurological symptoms arise, the patient can start to be mobilised into a sitting position after about 7–10 days.
- if neurological deficits occur immediately, further management follows the usual lines for ischaemic stroke, although malignant infarction and pronounced swelling have to be reckoned with. Curative treatment may require hemicraniectomy (Figure 7).

8.7 Post-hypoxic state

Displacement of the respiratory tract by tumours, swelling or bleeding is a typical complication in ENT surgery; it may cause hypoxic brain injury in isolated cases. CNS tolerance of hypoxia depends on many influencing factors. **The most important thing to do in the acute case is to cool the previously hypoxic patient for neuroprotection [72], [73].**

In patients who do not regain consciousness spontaneously, the prognosis can be estimated by measuring neurone-specific enolase (NSE) and/or S-100B protein (both in serum); the S-100B is the more reliable marker
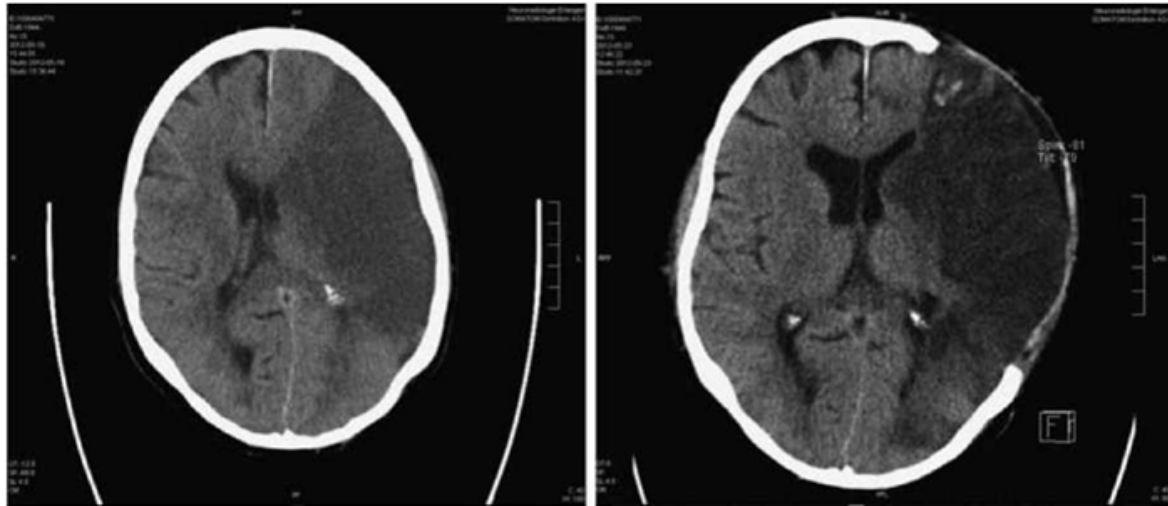
Figure 7: a. Patient with right-sided malignant MCA infarction after emergency internal carotid artery ligation for erosion haemorrhage. b. After hemicraniectomy one week later – clearly showing increased cerebral swelling.

within the first 24 hours of the event. These biomarkers can also be measured in the CSF, although it is doubtful that the results are more significant. The cut-off for a poor prognosis determined in earlier studies varies considerably, however, so the reader is strongly recommended not to base therapeutic decisions on these results at the present time [74]. For this reason, no cut-off value is given here. For the latest information see [75].

Computed tomography (CT) with perfusion measurements and **magnetic resonance imaging (MRI)** (diffusion weighted imaging (DWI); apparent diffusion coefficient (ADC) maps; perfusion weighted imaging (PWI)) allow further prognostic considerations.

Myoclonus occurring after a hypoxic event (Lance-Adams syndrome) is also seen as an unfavourable prognostic sign. Effective symptomatic treatment consists of:

- midazolam (give via perfusor, titrate dose according to effect)
- piracetam (Nootrop®) 12 g/day
- levetiracetam (Keppra®) initially 250 mg every 12 hours as a short (15 min) infusion, it is possible to increase the dose up to 1000 mg.

8.8 Critical illness polyneuropathy (CIP)

Patients who have been on intensive care for a long time may develop symptoms and signs of critical illness polyneuropathy [67], [72]. The clinical picture covers multiple neurological symptoms – disorders of sensation, motor function (critical illness myopathy (CIM)) and the autonomic nervous system. Predisposing factors include sepsis, multiorgan failure, and long-term ventilation. Characteristically, there is difficulty in weaning the patient from the ventilator, without there being any pulmonary reason, and limb weakness due to atrophic paralysis (denervation atrophy and even assumed tetraparesis). The diagnosis is based on electrophysiological findings (electromyography (EMG), nerve conduction velocity (NCV)); the condition is one of axonal neuropathy. CIP obviously delays mobilisation and rehabilitation. There is some

evidence that aggressive management of blood glucose levels (especially the prevention of hyperglycaemia) can reduce the incidence of CIP. Signs of CIP may resolve completely but there may also be residual defects. Although CIP and CIM are regarded as separate conditions, they occur in the same circumstances and have considerable overlap.

8.9 Guardianship, enduring power of attorney for health care

Patients who are under legal guardianship at the time of hospital admission or surgery are not usually a problem. Obviously both guardian and patient have to be fully informed. This means that a personal briefing session has to be held with the guardian in the same way as for a patient who is legally competent. In its ruling of 15/06/2010 (VI ZR 204/09), the Federal Court of Justice has made it abundantly clear in a headnote that briefing over the phone is appropriate only in specific circumstances: "In straightforward cases, the doctor can in principle also inform the patient of the risks of a pending intervention by telephone, if the patient is in agreement with this." The ruling was made on the basis of the briefing about anaesthesia in the case of a child prior to a hernia operation.

On this basis, information solely by fax is viewed as inadequate, as this obviously confirms that there was no personal contact between doctor and patient or guardian. The situation is different when the need for guardianship does not arise until during the hospital stay. Typical situations are prolonged postoperative ventilation and postoperative delirious states. The responsible guardianship court must be contacted promptly in such circumstances. In principle, the guardianship court responsible is the one with jurisdiction over the place where the patient is at the present time. An application for adult guardianship has to be made (pursuant to § 1896 of the German Civil Code (BGB)). It is helpful to designate a guardian by name, as long as that person has agreed to act in this capacity. If

there is no suitable guardian close to the patient, the court will appoint a professional guardian. Ensure that the guardianship decision states explicitly the scope of responsibility for healthcare and the associated right to determine the patient's place of residence.

In the event of medical measures "when there is a justified danger that the person under guardianship will die or will suffer serious injury to his or her health that lasts for a long period" (§1904 (1) BGB) guardians cannot give their consent independently but have to have the court's approval.

If the patient has already signed an advance directive in the form of an **enduring power of attorney for health care** (not to be confused with a living will), then guardianship is not necessarily required. The National Association of Notaries maintains a central register where enduring powers of attorney for health care can be lodged. Only the guardianship courts have access to this information, so the responsible court should be contacted if there is any uncertainty whether such an enduring power of attorney for health care exists.

8.10 Restraint

Restraint [76] has to be considered if a patient is at risk of self-harm or a danger to other people, when other means such as talking to them or sedation are not sufficient. Rule out any possible treatable causes for psychomotor excitability promptly. There are clear rules for using restraints, intended to prevent future legal problems. In each individual case, the patient's welfare has to be weighed up against his or her autonomy. Restraining a patient is legally a deprivation of personal freedom under § 239 of the German Penal Code (StGB) but it may not be considered illegal with necessity as the justification (§ 34 StGB). An acute danger to others (e.g. physical attack on members of staff) may be assumed to be a justifiable necessity. The same applies to behaviour with an acute risk of self-harm (e.g. pulling out an arterial line). If conditions are foreseeable and likely to be prolonged (rule of thumb: next working day) the restraints should be approved by the responsible guardianship court. The court is also a good source of information on any open questions. The reason and duration of restraint has to be documented (preferably in both the medical and nursing records, with photos). Restrained patients require uninterrupted observation. Staff should be trained in the use of the commonly employed patient restraints (e.g. Segufix®). Magnets to release such restraints are very popular on the black market with those in the know, so they should be stored securely and not left lying on the patient's bedside table.

Forced administration of medication (e.g. to treat psychosis) is a controversial subject in Germany at the moment, both in legal circles and amongst the general public. The event prompting this discussion was the ruling by the Federal Court of Justice on 12/06/2012 (XII ZB 99/12), according to which there is no legal basis for forced treatment under guardianship law. An amendment of § 1906 BGB on this subject has recently been enacted. That said, such cases are the exception in the ENT department.

9 Risk: medication

9.1 The patient's regular medication in hospital

The correct administration of prescribed medicines (the right indication, the right substance, the right dose and the right patient) is ultimately the responsibility of the doctor in charge of the patient's care in hospital. As ENT surgeons cannot regularly enquire closely about a patient's medication from other specialties, they have to presume that the drugs prescribed elsewhere are correct on a basis of mutual professional trust. This clearly does not apply when there is an obvious error (e.g. concomitant administration of an active pharmaceutical ingredient in the form of two different generic products, concomitant administration of two different cardiac glycosides, concomitant administration of agonist and antagonist drugs). The best way of managing things is to obtain a current treatment schedule or list of medications from the patient's general practitioner or specialist, if one is not already available. Information from patients and relatives is not always accurate or sufficiently precise (every doctor is familiar with the problem of "you know, doctor, the little white tablets" or "the long red ones" and the patient's absolute incomprehension when the doctor doesn't immediately know which tablets are meant). If the treating physician is not available, it may be helpful to contact the patient's usual pharmacy.

Medication errors may sometimes occur when one generic is exchanged for another (discount agreements) or more than one doctor is involved in prescribing: another problem lies in the deplorable habit, when a drug is available in various strengths, of not prescribing the right strength but rather allowing the patient to break higher-strength tablets to give the desired dose.

It has been reported repeatedly that medicines supposed to be taken once a week have been mistakenly ingested every day (e.g. methotrexate in the treatment of rheumatoid arthritis).

Pill organisers or dosettes can also pose problems, especially when they are filled by lay persons and the medicines can no longer be identified clearly. A **pill identification guide** (like the *German Gelbe Liste Identa*), in book form or as a smartphone app, may be useful. If the identity of the medicinal product cannot be determined with certainty or there is any discrepancy between the patient's list of medicines and what is actually written on the dosette, new drugs should be supplied from a clearly identified source.

Figure 8 shows an example of the meaningless use of a pill organiser.

On the other hand, blister packs put together by a pharmacist (Figure 9) present no difficulties, as the medicines
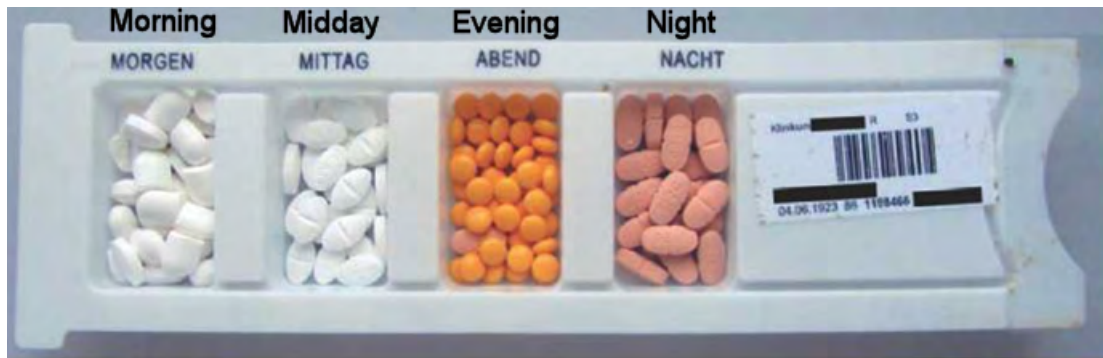
Figure 8: Meaningless pill organiser issued by a hospital

Figure 9: Blister pack professionally prepared for a patient (reproduced with the kind permission of AvidiaMed GmbH, Hamburg)

they contain are clearly labelled and the work of the pharmacist or contracted blister packer is to be trusted. When entering the medication into a treatment chart, take particular care with look alike, sound alike (LASA) drugs [77]:

- cotrim forte vs calcium forte
- Dipidolor® (piritramide, an opiate) vs. Dipiperon® (pipamperone, a low-potency antipsychotic drug)
- Esmeron® (rocuronium, a muscle relaxant) vs. esmolol (a beta-blocker)
- HAES vs. hyper-HAES (the strongly hypertonic hyper-HAES solution is indicated only for use in acute hypovolaemia for small volume resuscitation)
- insulin vs. Inzolen® (an injection solution supplying electrolytes and trace elements)
- metamizole vs. metronidazole
- methotrexate vs. Meto Hexal (metoprolol)

- Lisino® (H$_1$ antihistamine, recently renamed Lorano®) vs. lisinopril
- propranolol (a beta-blocker, generic name "propra...") vs. propafenone (a class 1c antiarrhythmic agent)
- Topamax® (topiramate, an anticonvulsant) vs. Fosamax® (alendronic acid, a bisphosphonate)

A detailed list of reported (near-miss) mistaken identities can be found in reference [78].

Hospital pharmacies stock a cross-section of the most commonly used drugs. It is therefore not always possible to provide exactly the same medication as the patient usually takes from the hospital formulary, but it is not necessary to do so on a regular basis. Conversion tables exist for many drug classes (e.g. ACE inhibitors, angiotensin II receptor antagonists, beta-blockers, calcium antagonists, diuretics, insulins, statins, PPIs, etc.); other medications (e.g. anticonvulsants, cardiac glycosides,

psychotropic drugs) cannot always be replaced so easily. Switching products inevitably opens up new sources of error but, for economic reasons, they often cannot be eliminated completely. If in doubt, discuss the matter with the hospital pharmacist.

Another source of error arises when inpatients continue to be responsible for taking their own medication. In this case, control over the accuracy and reliability of administration is lost. Some control should be established (e.g. nursing staff should assemble the medication on medical prescription) if there is any doubt that the patient is taking the medication reliably. The instruction to "continue regular medication" is at best problematic with respect to the extensive responsibility of the hospital doctor, so this instruction should be replaced by a precise prescription (drug names, doses, and timing).

On the day of operation, all medication and not just the premed should be prepared and administered under supervision.

This recommendation results from the fact that most patients are given a sedative the evening before elective surgery, and this may affect their alertness the following morning. Subject to the regulations in the premedication protocol, the following recommendations apply to the administration of the patient's regular medication at the time of surgery [58]:

- continue medication with beta-blockers, calcium antagonists, cardiac glycosides, and anticonvulsants. The cardioprotective effect of perioperative beta-blocker medication for primary prevention is disputed, but the benefits of beta-blockers in overt heart failure have been demonstrated. If beta-blocker therapy has to be introduced preoperatively, it should be given for at least one month before the planned operation.
- interrupt administration of ACE inhibitors and angiotensin II receptor antagonists on the day of operation, as otherwise they frequently cause hypotension during the induction of anaesthesia
- stop all oral antidiabetic agents (metformin: 48 hours preop., see below) and intermediate/long-acting insulins; regulate blood glucose levels with glucose iv (max. 5% glucose via a peripheral venous line) or rapid-acting insulin (**rule of thumb: 1 IU insulin lowers the blood glucose concentration by 20–25 mg/dl**).
- patients on long-term steroid therapy usually require a perioperative "stress dose" of corticosteroid (see section 7.9).
- stop transdermal opiates on the day of operation, so that there is no interaction with opiates administered during surgery. Any exceptions must be communicated clearly before the operation, to prevent the postoperative administration of inappropriate analgesics.

9.2 Medication administered via feeding tubes

If it becomes necessary to give medicine previously administered by mouth via a feeding tube (nasogastric tube, PEG tube), first check whether this is possible. Not only is the physical solubility of the drug relevant, but also the fact whether the active substance is intended for direct gastric administration at all. For example, gastro-resistant, modified release, and sublingual products cannot usually be crushed. Reference [79] gives further recommendations. In addition, the tube manufacturers usually provide very helpful brochures on administering drugs via feeding tubes.

9.3 Medication in emergencies

It is easy to understand why no written instructions are possible in emergency situations. When giving verbal instructions, use the read-back procedure, which has been employed in aviation for many years: instructions are not acknowledged merely by "yes" or a nod of the head (or even carried out wordlessly) but with verbatim repetition of the instruction. To a large extent, this practice prevents hearing and comprehension errors.

Do not use nicknames such as Mariacron (a type of brandy) instead of Mivacron® (mivacurium, a muscle relaxant) or Al Capone (an historic gangster from Chicago) instead of Aldactone® (an aldosterone antagonist) in critical situations.

Any drugs administered during the emergency management have to be documented straight afterwards. It helps if empty ampoules are not thrown away immediately but kept, for example, in a kidney dish.

9.4 Diabetes mellitus

Metformin, commonly used in the treatment of diabetes, is renowned for its adverse effect of lactic acidosis. The drug should therefore be stopped 48 hours before any elective surgery and re-introduced on the first postoperative day (unless any further surgical procedures are planned). A transient increase in blood glucose within defined limits (up to 180 mg/dl = renal threshold) can either be tolerated or treated with rapid-acting insulin. In critical illness, make every effort to keep the patient normoglycaemic.

Case report

A 56-year-old woman with known diabetes mellitus required surgery for tonsillar carcinoma. When she was given the date for surgery, she was also given an information sheet with the instruction to stop all medication containing metformin two days before the operation. On admission, the patient said that she had followed this instruction. Postoperatively the patient developed mild lactic acidosis, which resolved without problem on appropriate treatment. When investigating the reason for the

Table 24: Metformin-containing medicinal products

Metformin, monodrug preparations	Diabesin®, Glucophage®, Metfogamma®, Siofor®
Combination metformin/pioglitazone	Competact®
Combination metformin/vildagliptin	Eucreas®, Icandra®
Combination metformin/sitagliptin	Janumet®, Velmetia®

lactic acidosis, the patient admitted that she had stopped her single metformin product but not the combination product Janumet® (sitagliptin+metformin). The ward physicians had not realised this, possibly because "Janumed" was erroneously written in the patient's list of medicines and no-one made the connection with metformin from the syllable "med".

Without doubt, not every doctor can be familiar with about 2300 medicinal products and some 7000 associated proprietary names. The case report above shows, however, that it is essential to obtain more information about any unknown medicine. The *Rote Liste* (German Medicines Compendium) is the standard reference, to which every doctor has free online access. Many relevant SPCs/Information for healthcare professionals can also be accessed from that site.
The disadvantage, however, is that some manufacturers have ceased working with the publishing company so that their products no longer appear in the *Rote Liste*.
Table 24 lists all the proprietary products containing metformin.
If the diabetes is being treated with insulin, do not give any intermediate/long-acting insulin on the day of operation. Control the blood glucose solely with rapid-acting insulin, to prevent symptomatic hypoglycaemic episodes. Hyperglycaemia (up to 180 mg/dl) can be tolerated better than hypoglycaemia. Treat hypoglycaemic episodes by giving glucose (e.g. infusion of a 5% glucose solution).

9.5 Anticoagulants

See section 6.

9.6 Psychotropic drugs

Treatment with psychotropic drugs is frequently encountered. During a hospital stay, it is usually necessary to continue therapy initiated elsewhere, even when this has to be considered critically (e.g. long-term administration of benzodiazepines).
The commonest indications for psychotropic drugs are depressive disorders. Manic and schizophrenic disorders are less common.
Table 25, Table 26, Table 27 and Table 28 present the most commonly used psychotropic drugs.
Detail about each individual drug is beyond the scope of this article, but the following points are important:

- benzodiazepines and benzodiazepine-like substances can be antagonised with flumazenil if there is any respiratory depression
- benzodiazepines do not have antipsychotic effects
- a short hospital stay is not appropriate to treat benzodiazepine dependency adequately, so weigh up whether to continue the regular medication (and motivate the patient for withdrawal therapy at a later date).
- low-potency antipsychotics (neuroleptics) are mainly sedative with little antipsychotic effect; high potency antipsychotics (neuroleptics) have mainly antipsychotic effects and are only mildly sedative
- the more potent an antipsychotic drug, the more likely it is to cause extrapyramidal disorders (acute dyskinesia, Parkinsonism, akathisia, tardive dyskinesia).
- low-potency antipsychotics carry a risk of cardiotoxicity
- lorazepam and venlafaxine have proved their worth, particularly in conditions where anxiety predominates
- consider the use of SSNRIs in depressive disorders with physical symptoms.

9.7 Medication in elderly people

Pharmacotherapy in elderly people has been subject to considerable criticism in recent years. As a result, a list of potentially inappropriate medications (PIM) in elderly patients, called the **PRISCUS list**, has been compiled in Germany [80], [81]. The following recommendations have been taken from it:

- view the use of pethidine (Dolantin®) critically, as it appears to increase the risk of delirium
- view the use of digoxin critically, because of the risk of accumulation and increased risk of falling
- view the use of amitriptyline (Saroten®) and imipramine (Tofranil®) critically, as they appear to increase the risk of delirium – alternative = SSRIs
- view the use of clomipramine (Anafranil®) critically, because of the risk of orthostatic dysregulation – alternative = SSRIs
- regarding selective serotonin reuptake inhibitors (SSRIs), sertraline (Zoloft®) and citalopram/escitalopram are preferable to fluoxetine (Fluctin®)
  NB: reduced dosage of citalopram/escitalopram in elderly people.
- clonidine is not recommended for hypertension because of its negative effects on cognition

Table 25: Benzodiazepines

Generic name	Proprietary name
Short-acting:	
Midazolam	Dormicum®
Medium-acting:	
Oxazepam	Adumbran®
Lormetazepam	Noctamid®
Long acting:	
Bromazepam	Lexotanil®
Chlordiazepoxide	Multum®, Librium®
Clobazam	Frisium®
Clonazepam	Rivotril®
Clorazepate	Tranxilium®
Diazepam	Valium®
Flunitrazepam	Rohypnol®
Flurazepam	Dalmadorm®
Lorazepam	Tavor®
Tetrazepam	Musaril® (withdrawn since 01.08.2013)

Table 26: Benzodiazepine-like substances: act on GABAA receptors like benzodiazepines, clinical use as sleeping tablets

Generic name	Proprietary name
Zaleplon	Sonata®
Zolpidem	Stilnox®
Zopiclon	Ximovan®

- non-modified release nifedipine is not recommended for hypertension because increased mortality has been reported
- haloperidol is not recommended at a dose greater than 2 mg, as adverse extrapyramidal and anticholinergic effects have been reported – alternatives risperidone, melperone, pipamperone
- olanzapine is not recommended for use in persons over the age of 75 because of the increased risk of cerebrovascular events – alternatives risperidone, melperone, pipamperone
- liquid paraffin is not recommended as a laxative because of the danger of lipid pneumonia in patients at risk of aspiration
- short-acting benzodiazepines (e.g. lorazepam, lormetazepam, and brotizolam) are preferable to long-acting drugs in this class (chlordiazepoxide, diazepam, flurazepam, bromazepam, flunitrazepam etc.) – other alternatives are the Z- drugs (zolpidem, zopiclone, and zaleplon) or low-potency antipsychotic drugs (melperone, pipamperone). Nevertheless, use of these alternatives has also to be viewed critically because of the increased risk of falls
- on the basis of study data, the use of pentoxifylline, naftidrofuryl, nicergoline or piracetam is not recommended to treat dementia.

Table 27: Antidepressants

Generic name	Proprietary name
Tricyclic antidepressants: imipramine type	
Imipramine	Tofranil®
Clomipramine	Anafranil®
Tricyclic antidepressants: amitriptyline type	
Amitriptyline	Saroten®
Amitriptyline oxide	Equilibrin®
Doxepin	Aponal®
Opipramol	Insidon®
Trimipramine	Stangyl®
Tricyclic antidepressants: desipramine type	
Desipramine	Pertofran®
Nortriptyline	Nortrilen®
Tetracyclic antidepressants	
Maprotiline	Ludiomil®
Mianserin	Tolvin®
Selective serotonin reuptake inhibitors (SSRIs)	
Citalopram	Cipramil®
Escitalopram	Cipralex®
Fluoxetine	Fluctin®
Fluvoxamine	Fevarin®
Paroxetine	Tagonis®
Sertraline	Zoloft®
MAO inhibitors (MAOIs)	
Moclobemide	Aurorix®
Tranylcypromine	Jatrosom®
Serotonin and noradrenaline reuptake inhibitors (SSNRI)	
Duloxetine	Cymbalta®
Venlafaxine	Trevilor®
Atypical antidepressants	
Mirtazapine	Remergil®
Reboxetine	Edronax®, Solvex®
Trazodone	Thromban®
Herbal antidepressants	
St John's wort	Yarsin®

Table 28: Antipsychotic drugs (neuroleptics or major tranquillisers)

Generic name	Proprietary name
Classic antipsychotic drugs, low potency	
Chlorprothixene	Truxal®
Levomepromazine	Neurocil®
Melperone	Eunerpan®
Perazine	Taxilan®
Pipamperone	Dipiperon®
Promethazine	Atosil®
Sulpiride	Dogmatil®
Classic antipsychotic drugs, high potency	
Benperidol	Glianimon®
Droperidol	Xomolix®
Haloperidol	Haldol®
Atypical antipsychotic drugs	
Amisulpride	Solian®
Aripiprazole	Abilify®
Clozapine	Leponex®
Olanzapine	Zyprexa®
Quetiapine	Seroquel®
Risperidone	Risperdal®
Ziprasidone	Zeldox®
Zotepine	Nipolept®

9.8 Medication in pregnancy and lactation

This aspect can be dealt with only briefly here. There is information on prescribing in pregnancy and lactation in the Rote Liste and the SPCs of each medicinal product. Schaefer and Weber-Schoendorfer have recently written a review on the subject [82]. Reference books are also available and ideally these should be to hand in routine clinical practice [83]. If in doubt, consult an obstetrician and gynaecologist.

9.9 Outpatients

More than a few patients are unable to name their medication correctly and accurately at an outpatient visit. For medicolegal reasons as well, it is worth getting new patients to fill out a form on their medical history, including previous illnesses and regular medication, while they are in the waiting room. A completed form can quickly counter any possible future accusation that "the doctor didn't ask me what medicines I was taking".

A potential risk in the outpatient setting is the **attenuation of oral contraceptives** by antibiotics. Give the patient an appropriate warning and make sure it is well documented, as being sued for child support looms in the worst case scenario.

Corticosteroids are frequently prescribed in the ENT clinic. One example can be found in the current guidelines for the treatment of acute hearing loss with 250 mg prednisolone on three consecutive days, if necessary [84]. These doses have the potential to cause **avascular necrosis in the bone** [63], [85]. In a ruling that caused a sensation (VI ZR 108/06), given certain requirements (in

that case: trial of a licensed medicine in a specific treatment situation = heart disease), the Federal Court of Justice demanded that the patient be fully informed of the risks, so that it is well worth documenting a corresponding full explanation. Telling the patient to read the package leaflet is not considered sufficient.

As **intratympanic corticosteroid therapy** for acute hearing loss and intratympanic gentamicin therapy in Menière's disease are off-label uses, more detailed explanation is also required in these cases.

When treating children, check the marketing authorisation in that particular age group before prescribing any medication (antiallergics, antibiotics, topical nasal corticosteroids), as it may be mandatory to provide more detailed information to the patient or parents.

9.10 Other risks related to medication

This section outlines a few individual risks that have not been covered under previous headings:

- ACE inhibitors (generic names ending in "-pril") may cause **ACE inhibitor-induced angioedema** – even after long-term use. Angioedema may give rise to a life-threatening situation if the base of the tongue or larynx is involved. As a rule, the patient requires monitoring and treatment on intensive care. The underlying pathophysiology is a bradykinin excess, as ACE inhibitors also inhibit the enzyme kininase II, which catalyses the breakdown of bradykinin. Corticosteroids are therefore hardly effective, although there is nothing against a trial of steroids in the acute situation when considering the differential diagnosis. The same applies to H_1-antihistamines. The bradykinin B2-receptor antagonist icatibant (Firazyr®), the C_1-INH products, Berinert® and Cinryze®, and the recombinant conestat alfa (Ruconest®) have specific actions. At the present time, these four types of product are licensed only for the treatment of hereditary angioedema (HAE). Angiotensin II receptor antagonists (generic names ending in "-sartan") may also trigger angioedema, although less commonly. Following an episode of angioedema related to taking ACE inhibitors or sartans, switch the antihypertensive medication to an alternative drug.
- **5-fluorouracil** is a standard drug in the treatment of head and neck cancer. As the result of a DPD exon 14-skipping mutation, about 1% of the population has a deficiency of the enzyme **dihydropyrimidine dehydrogenase** (DPD), which is responsible for the metabolism of 5-FU. This enzyme deficiency considerably increases 5-FU toxicity on the skin, gastrointestinal tract and haematopoietic system. Clinical chemistry and genetic testing demonstrate the enzyme defect. Treatment is symptomatic.
- opiate analgesics usually cause constipation, so give adequate laxatives
- diarrhoea is a relatively common adverse reaction to antibiotic therapy. Brewer's yeast (*Saccharomyces cerevisiae*) has proved useful if treatment is necessary.

Consider the possibility of **pseudomembranous colitis** (PMC), also called *Clostridium difficile*-associated diarrhoea (CDAD), if the diarrhoea is severe. PMC is to be expected more often after second- and third-generation cephalosporins, aminopenicillins, clindamycin and fluoroquinolones. The diagnosis depends on demonstrating toxin in the stools. Stop the antibiotic agent responsible. Oral (!) vancomycin (125–250 mg qds, either as Enterocaps® or by oral administration of an infusion solution) was the drug of choice for a long time. Recently, though, fidaxomicin (Dificlir® 200 mg bd) has taken its place. Metronidazole is considered the next best but can also be given intravenously if necessary. Rifaximin (Xifaxan®) is currently licensed in Germany only for treatment of traveller's diarrhoea and is reserved for recurrences [86].

- headaches due to loss of CSG (e.g. after lumbar puncture or with a CSF drain in situ) are often helped by caffeine (200 mg tablets or as a hot drink).

10 Risk: infection

10.1 C-reactive protein and procalcitonin

C-reactive protein (CRP) [9] is a marker of bacterial infection. CRP is excreted mainly from the liver when interleukin 6 is released. Apart from bacterial infection, general anaesthetics and surgical interventions lead to the release of interleukin 6, so that CRP levels increase postoperatively almost as a matter of course and do not necessarily indicate bacterial infection.

Although a raised CRP after surgery is not proof of an acute bacterial infection, neither does it rule one out.

Procalcitonin (PCT) is a specific biomarker of acute bacterial infection and no non-specific perioperative elevation of this parameter is to be expected. A significant increase in the procalcitonin level therefore confirms bacterial infection (cut-off: 0.5 ng/ml). One exception is the presence of medullary thyroid carcinoma.

10.2 Systemic inflammatory response syndrome and sepsis

Differential therapeutic aspects of sepsis are beyond the scope of this article; monographs and guidelines on the subject already exist [87].

Recognition of sepsis depends on knowledge of the definition (Table 29).

A procalcitonin level below 0.5 ng/ml more or less excludes (severe) sepsis.

When the criteria for sepsis are met, initial measures are to:

Table 29: Definitions of SIRS, sepsis, and septic shock

I	Evidence of infection (microbiological or clinical)
II	Systemic inflammatory response syndrome (SIRS), at least two criteria:

- fever ≥38°C or hypothermia ≤ 36°C

- tachycardia ≥90 beats/min

- tachypnoea ≥ 20/min or hyperventilation ($paCO_2 \leq$ 33 mm Hg)

- leucocytosis (WBC ≥ 12 x 10^9/l) or leucopenia (WBC ≤4 x 10^9/l) or ≥ 10% bands (immature neutrophils)

III	Acute organ dysfunction, at least one criterion:

- acute encephalopathy: impaired vigilance, restlessness, delirium

- thrombocytopenia (platelets ≤ 100 x 10^9/l) or fall in platelet count >30% in 24 hours

- arterial hypoxaemia: $pO_2 \leq$ 75 mm Hg on room air

- renal dysfunction: diuresis ≤ 0.5 ml/kg/hour for at least two hours despite adequate volume or increase in serum creatinine to > twice normal

- metabolic acidosis: base excess ≤-5 mmol/l or lactate > 1.5 times normal

Sepsis	Criteria I+II
Severe sepsis	Criteria I+II+III
Septic shock	Criteria I+II+ $BP_{systolic} \leq$ 90 mm Hg for at least one hour or MAD ≤ 65 mm Hg or vasopressor administration to maintain these values. Hypotension despite adequate volume of fluids

- send samples for microbiology (take blood cultures from peripheral veins, not from CVL; bronchial lavage; tracheal secretions)
- give generous fluids
- give prompt antibiotic therapy ("hit hard and early") – the choice of antibiotic depends on circumstances
- plan further interdisciplinary management.

11 Risk: surgical interventions

11.1. Monitoring

Standard procedure after surgical interventions under general anaesthesia is for the patient to be monitored postoperatively and there are dedicated guidelines in anaesthetics [39], [88], [89]. Observation is the responsibility of the anaesthetist, who also decides when the patient may leave the recovery room. As many ENT operations may compromise the respiratory tract, close cooperation between the ENT surgeon and the anaesthetist is particularly necessary and helpful.

If the monitoring facilities in recovery (ECG, non-invasive blood pressure measurement, pulse oximetry) are not sufficient, then the patient should be transferred to the intensive care unit for monitoring and treatment. Monitoring respiration is the most important thing after ENT operations. Other problems may relate to the lungs in cases of pre-existing COPD (cancer patients who smoke) or bronchial asthma (patients with chronic rhinosinusitis, aspirin-sensitive airways disease), the cardiovascular system (arterial hypertension, atrial fibrillation, cardiomyopathy, coronary artery disease) and the central nervous system (delirium in alcohol-dependent cancer patients and elderly people). Acute impairment of renal function requiring treatment may also occur.

The extent of monitoring in these situations depends greatly on the clinical setting. Some ENT departments have the possibility of their own observation unit, in other hospitals they work together with a central or specialty-specific intensive care ward.

Should patients have to be transferred to another department or hospital, make sure that sufficient relevant information accompanies them (medical history, lab test results, operation reports, anaesthetic records).

In cases of hyper- or hypotension and respiratory disorders, **invasive blood pressure measurement** (via the radial or femoral artery) is extremely valuable. Arterial access must be clearly labelled as such (colour code: red; with "artery" written on the dressing tape in red letters)

to prevent unintentional intra-arterial injections. Differently coloured (e.g. blue = venous) stoppers are unacceptable for arterial lines. Remove the arterial catheter once the arterial blood pressure is no longer being measured (compression dressing!) to prevent any possible disconnection.

Extended haemodynamic monitoring (e.g. with the PICCO system) has been shown to be useful in ARDS, SIRS, sepsis and other conditions with circulatory instability. It allows measurement of cardiac output, extracellular lung water, stroke volume variation and other parameters in order to optimise volume replacement and catecholamine therapy.

Conclusions

For obvious reasons, this overview is not complete. Rare diseases, even more seldom encountered combinations of findings, and the resultant diagnostic and therapeutic dilemmas are all part of routine clinical practice. The aim of the review is to present typical common situations and address their therapeutic implications. Special cases require interdisciplinary management. It is self-evident that appropriate sources of information have to be consulted in individual cases to ensure the optimal treatment of the patient concerned.

Notes

Competing interests

The author declares that he has no competing interests.

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