# Patients with Substance Use Disorders and Addiction: Perioperative Issues

# 111

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## Contents



The list of references was limited to 70 citations. We acknowledge a multitude of additional contributions that are not mentioned here. This paper reflects also some of the work of many other colleagues in this understudied field.

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**Abstract**

Patients with substance use disorders are seen frequently in perioperative settings. It has been estimated that every third patient undergoing surgery is smoking; every fifth patient has alcohol use disorders such as hazardous use, abuse, harmful consumption, or dependence; every tenth patient is alcohol dependent; and every twelfth patient is consuming drugs regularly. Many patients use more than one substance regularly. Substance use disorders do vary in severity. Substance use is associated with significant somatic and psychiatric morbidity. Perioperative complications occur more often, even if underlying pathophysiological changes are subclinical. As an example, bleeding time can be prolonged, infection rate can be increased, cardiopulmonary complications can occur, or wound healing can be impaired even without clinical signs of, e.g., manifest liver cirrhosis and cardiovascular or lung disease. Patients with substance use disorders can safely undergo procedures under anesthesia. There are a variety of evidence-based treatment options to treat or prevent complications related to substance use. By secondary or tertiary preventive measures in a multimodal interdisciplinary concept, the increased risk can be significantly reduced. Elements are systematic screening, including the use of questionnaires and biomarkers, systematic diagnostic evaluation, brief interventions, tailored advice and information, patient-centered communication, tailored anesthesia, detoxification, abstinence, rehabilitation, psychosocial therapy, stepped care, monitoring of withdrawal symptoms, and prevention of withdrawal symptoms with pharmacological substitution therapy, monitoring and prevention of complications, goal-oriented therapy, symptom control, stress reduction, prevention of secondary injury, complex interdisciplinary treatment strategies, and teaching and training of the staff.

## 111.1 Introduction

Patients with substance use disorders (SUD) are seen frequently in perioperative settings. It has been estimated that every third patient undergoing surgery is smoking; every fifth patient has an alcohol use disorders such as hazardous use, abuse, harmful consumption, or dependence; every tenth patient is alcohol dependent; and every twelfth patient is consuming drugs regularly. These patients require medical care more often and more extensively. Substance use is associated with somatic and psychiatric morbidity. Perioperative complications occur more often, even if underlying pathophysiological changes are subclinical. As an example, bleeding time can be prolonged, infection rate can be increased, cardiopulmonary complication can occur, or wound healing can be impaired even without clinical signs of, e.g., manifest liver cirrhosis and cardiovascular or lung disease (Spies et al. 2001b; Tønnesen et al. 2009; Kork et al. 2010).

The term "substance use disorder" describes a continuum ranging from risky use over heavy use, hazardous use, abuse, harmful consumption to dependence. As we observe often similar morbidity among risky users as in dependent patients, it

seems to be more appropriate from the clinical point of view to describe relevant perioperative issues in all patients with substance use disorders without focusing on patients with physical dependence, with compulsive drug-seeking behavior, and with tolerance or with withdrawal. For didactic reasons alcohol, nicotine, and drug use disorders are described in distinct chapters as usual. However, many patients use more than one substance regularly.

In contrast to many other medical conditions, patients with SUD do often not get adequate treatment in the perioperative context. This has been related to underreporting and underasking. A variety of factors have been described: stigma or fear of stigma, lack of time and resources, lack of training, projections, and many (false) myths about the origin of these disorders. Early detection of SUD and their associated risk is essential to reduce complications, but an SUD is often suspected after complications occurred (Spies et al. 2001b; Runge et al. 2001; Tønnesen et al. 2009; Kork et al. 2010). Intoxication or acute delirium can interfere with the clinical presentation of other severe conditions (e.g., traumatic brain injury and alcohol intoxication, delirium, and thiamine deficiency). Therefore, the evaluation of all patients with SUD requires well-directed and proactive diagnostic approaches (Neumann and Spies 2003).

Many pathophysiological changes and organ dysfunctions in relation to substance use are potentially reversible by abstinence. The extent of recovery depends on the progression of the disease (Tønnesen et al. 2009).

The patient-doctor interaction is somehow different from what is seen in addiction centers. Patients undergoing surgery are usually expecting to receive the best surgery with a minimal risk, but are not actually seeking treatment for SUD. A comprehensive preoperative risk assessment is standard and substance use is a risk factor. Risks and risk-reducing options are discussed in order to reach informed consent. Most patients found alcohol intervention relevant in relation to surgery. Therefore, all steps should be explained to patients in their own language. Patient preferences should be explored. A working alliance should be established. The FRAMES concept (feedback, responsibility, advice, menu of behavioral changes, empathy, self-efficacy) summarizes useful elements of the communication. Patients with relevant psychiatric (co)morbidity should be seen by a psychiatrist (Spies et al. 2006b; Kork et al. 2010; Lau et al. 2011; Pedersen et al. 2011).

When a SUD is suspected, a brief intervention should be offered. Interventions like motivational interviewing are directive non-confronting and ambivalence accepting. Bridging into specific treatment can be appropriate. Open issues in this context are optimal strategies for communication, shared decision making, and psychoeducation including training and implementation of substance use medicine in the surgical facilities. The optimal architecture of a stepped care system is of great interest and might differ between health systems (VA/DoD 2009; NICE 24 2010; NICE 100 2010; NICE 115 2010; Spies et al. 2006b; Kork et al. 2010; Lange et al. 2011).

There is a risk of relapse ("drug reinstatement") in rehabilitated patients with a history of substance use and dependency after stressful events such as trauma or

surgery. Therefore, these patients should benefit from a careful and emphatic psychoeducation. They might need support also by addiction medicine professionals at some time after the event. This should be planned early.

As science and the health care develop rapidly, it is highly recommended to familiarize with today's guidelines ("systematically developed statements to assist physicians and, if necessary, other healthcare professionals and patients with decisions about appropriate health care in specific clinical circumstances") as only a systematic, formal, and group consensus approach is able to catch up with the developments in the field (Woolf et al. 1999).

## 111.2 Substance Use Disorders

### 111.2.1 Alcohol: Clinical Relevance

One of ten hospitalized surgical patients suffers from alcohol dependency; two might have an alcohol use disorder, and if they undergo surgery, they have more complications and length of stay is longer (Spies et al. 2001).

Among some patient groups, even higher rates of heavy drinking or alcohol dependency were reported: more than 25 % in patients with injury and 50 % of patients with aerodigestive system cancer. There is a variety in the clinical presentation of alcohol use-related morbidity in the different settings (e.g., younger trauma patient vs. older cancer patient vs. patients admitted for detoxification). Programs offered for the rehabilitation of addicted patients after detoxification might not attract other patient groups, e.g., young trauma patients. Even patients with addictions are rarely seen by addiction specialists, but frequently come in contact with health professionals in surgical or emergency units (Spies et al. 1996a, b, 2001b; Neumann et al. 2006; Neumann and Spies 2003).

AUD patients have a higher somatic and psychiatric morbidity: Postoperative or posttraumatic complications rate is two- to fivefolds higher. Chronic heavy drinking affects various systems as the nervous system, the cardiovascular system, the liver, the muscle, and the stress response and the immune system. The direct toxic effect of alcohol might be aggravated by malnutrition. Alcohol promotes carcinogenesis.

It has been consistently shown that patients who report heavy daily drinking (i.e., $>$60 g of alcohol) have an increased postoperative morbidity and more complications with increased postoperative healthcare use, including longer stays in the hospital and ICU and more second operations. Postoperative or posttraumatic morbidity is two- to fivefold increased: Infections and sepsis, cardiac complications (arrhythmia, congestive heart failure), bleeding and secondary hemorrhage, "acute respiratory distress syndrome" (ARDS), other surgical complications, alcohol withdrawal syndrome, and death occur more often. Therefore, length of stay is prolonged; requirement for critical care is increased. Also postoperative healthcare use is increased. Hospital and ICU stay is prolonged. Secondary operations are more often required. Already a consumption of more than two drinks a day has been associated in some reports with an increased risk. Interestingly, when diagnosing

dependency, information about consumption is not required (Tønnesen et al. 1992, 2009; Spies and Rommelspacher 1999; Spies et al. 1996a, b, 2001b; Moss and Burnham 2006; NICE 115 2011; Rubinsky et al. 2012).

#### 111.2.1.1 The Scope of the Problem

Critically ill alcoholic patients are more likely to develop serious **infections** than nonalcoholic patients, especially nosocomial pneumonia, sepsis, wound, and urinary tract infections. Chronic alcohol abuse is also associated with an increase of ARDS (acute respiratory distress syndrome) and the severity of MODS (multiple organ dysfunction syndrome) in patients with septic shock.

Immune functions are altered by chronic heavy drinking. Stress response to surgical trauma induced by the hypothalamic-pituitary-adrenal axis (HPA axis) is augmented in AUD patients. A hypercorticolism was observed after surgical stress. Not only was hypercorticolism associated with complications, but a therapeutical suppression of the hypercorticolism at the level of the HPA axis reduced complications (Spies et al. 2006a). The skin response of the delayed-type hypersensitivity (DTH) is already reduced after surgical trauma due to associated stress. However, among alcoholic patients who undergo surgery, the DTH response was already reduced preoperatively compared with nondrinkers, and this impairment was exaggerated to a significantly larger extent postoperatively. This corresponds to other findings: Preoperatively, the T helper 1 to T helper 2 cells ratio is depressed in long-term alcoholic patients. This is predictive of later onset of infections. It remains suppressed after surgery. Postoperatively, the cytotoxic lymphocyte (Tc1/Tc2) ratio is also decreased in long-term alcoholic patients and remains depressed for 5 days. Correspondingly, the interleukin (IL)-6/IL-10 ratio and the lipopolysaccharide-stimulated interferon/IL-10 ratio in whole blood cells are decreased after surgery in long-term alcoholic patients. These anti-inflammatory changes in the postoperative period are predictive of subsequent postoperative infections.

Many other alterations of specific and nonspecific immune defense are reported that contribute next to other factors (e.g., smoking or aspiration) to the increased infection rate (Tønnesen et al. 1992, 1999; Spies et al. 2001b, 2004, 2006a; Sander et al. 2002; Moss and Burnham 2006; Lau et al. 2009).

**Wound healing** is impaired in heavy drinkers. Collagen and total protein accumulation in wound granulation tissue was impaired in treatment-seeking alcoholic patients, and proline and total protein increased significantly after 8 weeks of abstinence (Tønnesen et al. 1992, 1999, 2012; Spies et al. 1996a, b, 2001b).

The coagulation system can be affected even without clinical relevant alcoholic liver disease mainly by an altered thrombocyte function. Bleeding time can be prolonged. Beneficial effects of low-dose alcohol on cardiovascular disease have been related to these effects (Spies et al. 2001a; Tønnesen et al. 2009).

Heavy drinking can induce **cardiomyopathy**. A reduced ejection fraction can be found, which is often subclinical. However, heart rate can be increased and arrhythmias occur more often perioperatively. Cardiac morbidity is also increased due to arterial hypertension and the impact of smoking (Tønnesen et al. 1992, 1999; Spies et al. 1996a, b, 2001a, b, 2006a).

**Table 111.1** Differential diagnosis of delirium or alcohol withdrawal syndrome: "I WATCH DEATH" (Adapted from Spies and Rommelspacher 1999)

| | |
|---|---|
| I | Infections |
| W | Withdrawal |
| A | Acute metabolic |
| T | Trauma |
| C | CNS |
| H | Hypoxia |
| D | Deficiencies |
| E | Endocrinopathy |
| A | Acute vascular |
| T | Toxins/drugs |
| H | Heavy metals |

**Stress** due to surgery and trauma, infection, or withdrawal has a wide range of effects. Next to the abovementioned immune suppression changes in body fluid composition, electrolytes, catecholamines, and hormones are relevant (Tønnesen et al. 1992, 1999, 2009; Spies et al. 1996a, b, 2001a, b; Neumann and Spies 2003; Moss and Burnham 2006).

Alcohol is **neurotoxic**. In higher dosage/doses it affects the central and the peripheral including the autonomic nervous system. It alters neuronal transmission. It induces tolerance and withdrawal. Alcohol use is also associated with neurotrauma. There are many reasons for cognitive impairment or delirium or "acute brain dysfunction" in emergency or critically ill patients with alcohol use disorders. In acute situations, other reasons for delirium (e.g., infection, trauma, or others) are often misinterpreted as intoxication or alcohol withdrawal syndrome (Table 111.1). The clinical presentation of critically ill patients with a history of alcohol and/or drug misuse may differ from other patients. Delayed diagnosis of AUDs or related comorbidity (e.g., alcohol intoxication and head trauma, withdrawal state, vitamin deficiencies, drug use, significant psychiatric disorders, infections, etc.) may have severe consequences (Tønnesen et al. 1992, 1999, 2012; Spies et al. 1996a, b, 1999, 2001b; Neumann and Spies 2003; Moss and Burnham 2006; NICE 115 2011).

**Wernicke's encephalopathy** should be suspected in all clinical conditions which could lead to thiamine deficiency, and intravenous thiamine (before any carbohydrate, 200 mg thrice daily) is indicated in these patients. It is often undiagnosed during lifetime. For diagnosis, two of the following four signs are required (EFNS guidelines, Galvin et al. 2010): dietary deficiencies, eye signs, cerebellar dysfunction, and either altered mental state or mild memory impairment. Total thiamine in blood sample should be measured prior to thiamine administration, if possible. MRI should be used to support the diagnosis of acute WE.

**Re-trauma** rate was also higher compared to patients without AUD. Trauma has, therefore, been described as a recurrent disease (Neumann et al. 2004, 2006).

#### 111.2.1.2 Alcohol Intoxication

Alcohol is a central nervous system depressant. The clinical presentation of the alcohol intoxication ranges therefore from symptoms due to disinhibition like euphoria and agitation to a more global depression such as coma. Alcohol intoxication is potentially life threatening due to respiratory insufficiency, respiratory failure, aspiration, electrolyte disorders, rhabdomyolysis, hypoglycemia, temperature deregulation, and cardiovascular depression, with tachycardia and hypotension. The risk of trauma is high while intoxicated. A delayed diagnosis and treatment of other critical conditions such as trauma add to the high risk of alcohol intoxication (Neumann et al. 2003; Moss and Burnham 2006; NICE 100 2010; NICE 115 2011; NICE 24 2010).

#### 111.2.1.3 Alcohol Withdrawal Syndrome

AWS is still a potentially life-threatening state. About half of all alcoholic patients in intensive care undergo an untreated alcohol withdrawal syndrome. It occurs frequently in intensive care patients after reduction of the sedation. The range and severity of the symptoms of alcohol withdrawal varies: cognitive thought disorder, hallucinations, convulsions, and sympathetic hyperactivity resulting from the imbalance of various excitatory and inhibitory neurotransmitter systems. The alcohol withdrawal syndrome is typically a diagnosis of exclusion. First signs are autonomic symptoms such as sweating, tremor, nausea, anxiety, and restlessness. Grand mal seizures can occur. Delirium tremens is characterized by spatial and temporal disorientations, hallucinosis, ataxia, tremor, and autonomic dysfunction. Many conditions can mimic AWS or might occur concomitant. Other disorders associated with delirium should be quickly ruled out or treated, including hemorrhage, metabolic disorders, infection, intoxication, hypoxia, pain, or focal neurological lesions. Mortality is related to the quality of the treatment: 15 % mortality when untreated vs. 2 % mortality when treated (Spies et al. 1996a, b, 1999, 2001a, b, 2003; Moss and Burnham 2006; Bråthen et al. 2005; NICE 100 2010; NICE 115 2011; NICE 24 2010; Awissi et al. 2013; Ungur et al. 2013).

#### 111.2.1.4 Gastrointestinal/Metabolism

The **GI system** is impacted by alcohol in many ways: parenchymal liver injury (reduced synthesis, reduced enzyme activities, portal hypertension), hepatitis, gastritis, pancreatitis, enteral translocation, anorexia, malnutrition (substrates, vitamins, etc.), ulcers, gastrointestinal bleeding, autonomous dysregulation, and malnutrition.

Pharmacodynamic or pharmacokinetic interactions, increased toxicity of medication, and altered metabolism are complex and beyond the scope of this chapter. Chronic alcohol use alters metabolism (e.g., cytochrome P450 2E1 induction resulting in increased toxicity of paracetamol) or neurotransmitter function (e.g., alcohol and narcotics interfere on GABA receptor function). Clinicians use the manufacturer's information.

## 111.2.2 Diagnosis

### 111.2.2.1 Diagnosis

An early diagnosis is essential. However, the prevalence of AUD is consistently underestimated, particularly in women and younger patients: One out of 14 patients was diagnosed with AUD by an anesthesiologist during the preoperative assessment, but with a computerized questionnaire, detection rate was one out of six patients (Kip et al. 2008).

The diagnosis of an AUD is based on the synopsis of medical and substance use-related history, physical examination, and on self-report (like structured interviews such as questionnaires), if available. More information is provided by paraclinical findings (laboratory, imaging) and collateral information. In intubated and analgosedated or in emergency situations, patients' self-report might not be available. Markers are helpful when self-report is not available or valid, e.g., after trauma. A complication might be the trigger for considering an AUD. The information from markers of acute and chronic alcohol consumption as well as indices of alcohol consumption-related changes in organ function (e.g., liver enzymes, metabolic indices, immune dysfunction) can add further information. Patients might have an extra benefit from anonymous and confidential programs parallel to the routine patient care (Neumann and Spies 2003).

### 111.2.2.2 Questionnaires

Systematic screening with questionnaires is recommended, e.g., with the ten-item Alcohol Use Disorders Identification Test (AUDIT). The AUDIT was designed to cover a range of AUD severity from risky use to dependence. The full AUDIT asks next to the three consumption questions (AUDIT-C) also for indicators of addiction (three questions) and about alcohol use-related negative consequences (four questions). The ten AUDIT questions sum up to a score between 0 and 40 points. The test is considered as positive once more than 8 points are counted; however, lower cutoffs for women (e.g., 5 points) have been recommended. Lower cutoffs can increase sensitivity. Every combination of answers resulting in at least 5 points reflects at least one alcohol use-related problem. It takes about 2 min to apply the AUDIT in paper-and-pencil or computerized versions. The use of a computerized version detected much more patients in a preanesthetic clinic compared to the clinical routine (Neumann et al. 2004, 2006; Kip et al. 2008; VA/DoD 2009; NICE 24 2010).

The three-item "AUDIT-Consumption" questions (AUDIT-C) can be a shorter alternative. It provides a rough quantity x frequency estimate plus one question addressing binging (five or more drinks/occasion). It was found to be clinically useful. An increased AUDIT-C (>8 points) up to a year before surgery has been clearly associated with postoperative complications. A cutoff of 4 points (men) and 3 points (women) of the AUDIT-C was recommended for screening; however, this corresponds also to patterns of low-risk alcohol use like small amounts of alcohol with a meal (VA/DoD 2009; Neumann et al. 2004; Kip et al. 2008; NICE 24 2010; Bradley et al. 2011; Rubinsky et al. 2012). The NIAAA (see Fig. 111.1)

General algorithm and clinical pathway for patients with substance use disorders
Structured AUD, NUD and DUD screening

- Do you drink alcohol? yes:
  - Alcohol Use Disorder Identification Test (AUDIT), or
  - abbreviated version, AUDIT-C or
  - NIAAA screen for risky drinking e.g. How many times in the past year have you had…
    -5 or more drinks in a day (men)
    -4 or more drinks in a day (women) (One standard drink = 12–14g in the (US)
  - Plus CAGE (if dependence is of interest)
- Do you consume drugs, yes:
  - DSM-IV criteria or ICD criteria
- Do you smoke? Yes
  - Fagerström

If questionnaire results are negative, history not available, questionnaire screening not applicable or reliable and patient undergoing major surgery, critical ill etc.

- Consider collateral information
- Consider the use of markers
  Laboratory testing:
  AUD: CDT, GGT, MCV, EtG, Peth
  NUD: CO-Hb, Cotinin
  DUD: substance or metabolite testing in urine, saliva or blood (depending on substance)
- Comprehensive assessment of comorbidity

If patient is positive

- Synopsis of clinical findings (Screening, history, physical examination, questionnaires, marker, collateral information) =>
- Diagnosis (ICD 10, DSM 4/5) =>
- Consider and discuss specific interventions, include the informed patient into the decision making process (shared decision making), psychoeducation, if appropriate
  Prophylactic, preventive Intervention =>
  - (Preventive) treatment
    - Pharmacological withdrawal prophylaxis,
    - Substitution,
    - Stress reduction…
    - Treatment (e.g. AWS, detoxification, rehab, self help groups…)
    - Abstinence
  - Risk communication,
    - brief Interventions, e.g. Motivational Interviewing
    - FRAMES
      - Feedback
      - Responsibility
      - Advice
      - Menu of behavioral change
      - Empathy
      - Self - efficacy
- Monitor for complications
- Monitor for continuous risky/unrisky use

If preventive treatment not necessary:

- Inform, endorse, confirm
- Maintenance or supportive therapy in former substance users,
- Reevaluation of substance use screening negative patients in special medical conditions

AUD, alcohol use disorder; DUD, drug use disorder; NUD, nicotine use disorder (adop. and modified from Kork et al. 2010).

**Fig. 111.1** General algorithm and clinical pathway for patients with substance use disorders

recommended the "Single-Item Alcohol Screening Questionnaire" as a screener (VA/DoD 2009).

CAGE ("cut down," "annoyance," "guilt," and "eye opener") is a four-item questionnaire. It is brief and easy to remember. The strength is detection of patients with dependence, but the sensitivity for risky, nondependent use has been considered as too low. Interestingly, the CAGE questionnaire can be used as a self-assessment tool (may be used in addition to an appropriate screening method to increase patient's awareness to unhealthy use or abuse of alcohol) (Neumann and Spies 2003; NICE 24 2010; VA/DoD 2009).

#### 111.2.2.3 Laboratory

Biomedical markers may provide additive, objective information about acute or recent consumption, intoxication, relapse, heavy drinking, hazardous or harmful alcohol use, or possible use-related organ dysfunctions. Biomarkers cannot differentiate between AUD with and without dependency. So far, no single laboratory test (e.g., for acute abuse, alcohol in blood or breath; for abstinence, metabolites such as ethyl glucuronide (EtG); for chronic heavy drinking, gamma-glutamyl transpeptidase (GGT), mean corpuscular volume of red blood cells (MCV), carbohydrate-deficient transferrin (CDT), phosphatidylethanol (PEth)) is reliable enough on its own to support the diagnosis of an AUD. In the clinical context, they can add important information, especially when questionnaires are not applicable or reliable. As laboratory parameters for alcohol abuse, MCV, γ-GT, and CDT are used. Sensitivity of the markers (e.g., MCV 34–89 %, γ-GT 34–85 %, CDT 12 or less -94 %) as well as specificity (MCV 26–91 %, γ-GT 11–95 %, CDT 82–100 %) can vary considerably according to gender, age, setting, drinking pattern and prevalence of more severe AUD, the prevalence of comorbidity, and the AUD criterion used. Markers of increased alcohol consumption can also be increased by nonalcoholic organ damage, e.g., non-alcoholic liver disease (Neumann and Spies 2003; Hannuksela et al. 2007; Neumann et al. 2009).

Phosphatidylethanol (Peth) is formed only in the presence of alcohol. It has reported sensitivities of 97–99 % and specificity of 100 % when differing heavy drinkers (60 g/day of alcohol and much more) from controls. However, the cutoff is not clear yet and Peth is not yet part of clinical routine. More research is needed to establish the role of this marker of chronic heavy drinking. Storage can be problematic, relevant in vitro formation and degradation has been described (Hannuksela et al. 2007; Niemela 2007 CCA).

Sensitivity of markers can be lower, when patients reduce their alcohol consumption preoperatively. Another reason for false-negative findings are blood loss and volume replacement in critically ill patients (e.g., after severe trauma; therefore, sampling of the blood should be done as early as possible, e.g., at admission or in the resuscitation room) (Spies et al. 2001; Hannuksela et al. 2007; Neumann et al. 2003).

Sensitivities, specificities, and predictive values vary considerably between the studies according to patient and control group characteristics and differing alcoholism criteria (Neumann and Spies 2003). In patient groups with a high prevalence

of severe AUDs, in older patients, and in patients with a continuous daily consumption (in contrast to occasional binge drinking), the sensitivity is usually higher, whereas comorbidity might interfere with specificity (Neumann and Spies 2003).

Percent CDT (CDT/total transferrin ratio) levels were elevated in patients drinking 50–80 g/day or more. Elevated values were found also among patients with end-stage liver disease and genetic variants. Total CDT levels are additionally affected by factors that raise transferrin levels such as iron deficiency, chronic illnesses, and menopausal status. The roles of female gender, low body mass index, chronic inflammatory diseases, and medication on CDT levels require further study. Sensitivity can be lower in women and patients with episodic heavy drinking or cutting down for some time and acute blood loss. Therefore, CDT should be determined early after admission (Neumann and Spies 2003). Early sampling in the emergency room and before volume resuscitation increased the sensitivity from 65 % to 74 % for CDT. Complication rate was increased in trauma patients with increased CDT (increased CDTect, absolute CDT values, Spies et al. (1998), discussed in Neumann and Spies 2003; %CDT, McKinzie et al. 2010).

Furthermore, the determination of markers of acute consumption (alcohol in blood, urine, breath) or markers of recent use (e.g., ethyl glucuronide , ethyl sulfate, urinary 5-HTOL/HIAA) can add important information of recent consumption and hangover. Blood, breath, or urine alcohol is detectable for several hours; however, metabolites are detectable for longer (e.g., EtG up to 80 h) even after consuming smaller amounts. They can be used to monitor abstinence (e.g., in obstetrics or liver transplantation). Alcohol consumption in the evening before surgery is related to postoperative morbidity. These biomarkers are usually not available as a point-of-care application except breath alcohol. There are unsolved methodological issues concerning cutoffs and possible reasons for false positives. Therefore, markers cannot be used without the clinical context (Neumann and Spies 2003; Hanunksela et al. 2007).

The determination of the blood alcohol concentration (BAC) is considered as standard in trauma care: Between 16 % and 39 % of trauma victims were BAC positive on admission, and 55–75 % of injured patients who were BAC positive had an alcohol abuse or dependence diagnosis. However, a substantial number of trauma patients with AUDs (11–45 %) are BAC negative (Runge et al. 2001; Neumann et al. 2003). A high blood alcohol concentration indicates tolerance, which itself is linked to dependence. Alcohol metabolites such as ethyl glucuronide may be used for monitoring abstinence since they can be detected for a longer period than alcohol from blood or urine. So far some promising markers are not available as a point-of-care application (Neumann and Spies 2003).

Other indices of altered organ function (e.g., liver enzymes, metabolic indices, immune function parameters) might add valuable information. These surrogate markers give valuable insights into the impact of AU on organ function (e.g., immune response) and might guide therapeutical interventions, but are not considered as alcohol abuse markers per se (Neumann and Spies 2003; Spies et al. 2004, 2006; Lau et al. 2009).

#### 111.2.2.4 Screening and Diagnosis

All patients should be screened for AUD in a systematic approach in order to detect those patients who might benefit from evidence-based strategies to minimize the risk for a complicated perioperative clinical course. The use of an alcoholism-related questionnaire is recommended.

If self-report is not possible, not reliable, or negative, markers and collateral information should be used. All patients:

- Scoring positive (AUDIT: men $\geq$ 8/women $\geq$ 5).
- Scoring below the cutoff in a questionnaire or from those where a reliable history and/or questionnaire cannot be taken **and** with one or more positive biomarkers should undergo further assessment (Kip et al. 2008; Kork et al. 2010).

Confirmatory assessment includes a history of alcohol and substance use and consumption pattern, comorbidity, and the criteria for hazardous use or dependence (DSM/ICD); however, absence of earlier withdrawal symptoms does not exclude the possibility of an exaggerated stress response or withdrawal. Patients screened positive for AUD should further be evaluated in an interdisciplinary approach.

A clinically relevant alcohol abuse is defined in operative medicine as an intake of $\geq$ 60 g/day of alcohol; however, risky consumption has been defined as 30 g/day (men) or 20 g/day (women). High-risk patients with two or more positive biomarkers from different pathophysiological backgrounds are obvious candidates for preventive strategies (Neumann and Spies 2003; Tønnesen et al. 2009; Spies et al. 2001).

Consulting a specialist in substance abuse may be appropriate in order to provide advice on how to reduce long-term risk, e.g., to achieve abstinence. All patients being considered for high-risk surgery or having had a trauma should be offered counseling focusing on risk factors in relation to the operative treatment, diagnosis, and prognosis (e.g., in the preanesthetic evaluation). Alcohol is a risk factor. Especially in patients consuming 60 g of alcohol or more daily, options (e.g., remain abstinent for up to 4 weeks before elective surgery or receive preventive perioperative pharmacological prophylaxis targeting the stress response or withdrawal) should be discussed. Information and feedback on any pathological finding-associated alcohol consumption may contribute to the diagnosis. The patient-oriented communication style is ambivalence accepting, not confrontive, emphatic, but directive; one aim is a working alliance with the patient. It includes a feedback and advice about the risks and opportunities and it addresses patient's responsibility. Through these (brief) interventions longer-term changes in motivation might be achieved (Spies and Rommelspacher 1999; Neumann and Spies 2003; Neumann et al. 2004, 2006; Tønnesen et al. 1999, 2009).

One has to be aware that some patients are under triple stress during the evaluation: an operation, an AUD diagnosis, and the fear of stigma. Waiting patiently and reevaluating later can be an option. Approaching patients three times instead of one time before surgery doubled detection rate. The combination of laboratory markers and the CAGE questionnaire and up to three consultations can increase the detection rate from 16 % by clinical routine alone to 91 % in

surgical patients scheduled for upper digestive tract surgery (Martin et al. 2002). Markers might be used also as biofeedback. The patient might have a benefit to learn about the risk associated with a positive marker and the gain in health, when the marker normalizes (Neumann and Spies 2003). More research is needed to determine the value of biomarkers in the context of clinical decision-making algorithms.

## 111.2.3 Treatment and Prevention

### 111.2.3.1 Screening and BI

A brief intervention should be delivered at the point of care to all AUD patients, e.g., in the preanesthetic clinic. This approach is recommended by current guidelines. A consistent reduction of alcohol consumption by brief interventions was reported in primary health care, mainly in men. Also brief interventions were generally effective in hospital patients; however, some inconsistency was observed, especially in emergency settings (NICE 24 2010; NICE 115 2010; VA/DoD 2009). Effective screening and brief intervention strategy (feedback, advice, tailored information) can be provided by computer in many clinical settings (Neumann et al. 2006; Kip et al. 2008; Lange et al. 2011). A computerized questionnaire and brief report on lifestyle issues for surgical patients is available as a tool for quality management in Germany. It is applied by the German Anaesthesiological and Intensive Care Society (current access: http://www.dgai-lsa.de; username: HAI2008; password: dgai; Kork et al. 2010).

### 111.2.3.2 Choice of Anesthetics

Anesthetics should be given according to the clinical effect. As alcohol and inhalation agents as well as hypnotics work synergistically on the $GABA_A$ and on other receptors (NMDA, glycine) in intoxicated patients, a dose reduction is necessary as well as an increase in dosage in the withdrawal state. Muscle relaxants that are metabolized hepatically might have a prolonged effect in patients with a hepatic insufficiency; neuromuscular monitoring is recommended. Alternatives would be atracurium and cis-atracurium as relaxants. Alcohol consumption is not a contraindication for the use of inhalational anesthetics. Sevoflurane is normally metabolized to $<5$ % in the liver. However, also the induction of CYP2E1 could lead to an increased formation of plasma fluorides. Due to the small intrarenal metabolism of sevoflurane, nephrotoxic effects are not expected, but there are no studies on AUD patients at risk.

Regional anesthesia should be used only in patients able to cooperate and with adequate vigilance. The coagulation should be monitored and a careful history of coagulation disorders and medication that interferes with the coagulation should be obtained. Limitation for regional method is agitation of the patient and the lack of protection of the respiratory tract. In the phase of intoxication, regional procedures are contraindicated (Klotz and Ammon 1998; Neumann et al. 2003).

#### 111.2.3.3 PACU

The patient can be transferred from the recovery room to the ward when sufficiently vigilant, cardiopulmonary stable, and pain-free. Monitoring for delirium is recommended (NuDesc, DDS, CIWAr). Regular monitoring includes the acid-base balance, electrolyte levels, and blood glucose levels. Hypokalemia and hypomagnesemia can occur during the early withdrawal. Inadequate drainage losses can be a sign of a coagulation dysfunction. In patients sobering up, acetaminophen should be used with caution (Martin et al. 2010; Spies et al. 1999, 2003; Otter et al. 2005; Riordan and Williams 2002; Moss and Burnham 2006).

#### 111.2.3.4 Postoperative Treatment

It is not possible to draw a clear line between prevention and treatment of alcohol withdrawal syndrome. Both prophylaxis and treatment should be carried out symptom-guided in time (Spies and Rommelspacher 1999; Spies et al. 2003). All patients are therefore closely monitored by means of the "Revised Clinical Institute Withdrawal Assessment for Alcohol Scale" to monitor or compare scores used in intensive care (e.g., CAM-ICU, DDS, Lütz et al. 2010; Martin et al. 2010; Otter et al. 2005).

#### 111.2.3.5 Therapy of Alcohol Withdrawal Syndrome

The diagnosis of an alcohol withdrawal syndrome can be made if other causes of delirium or complications such as bleeding, metabolic dysfunction, infections, ischemia/hypoxia, pain, or focal neurological symptoms are excluded (Table 111.1). Patient's history or laboratory tests should indicate an AUD. Alcohol withdrawal syndrome should be treated early. The severity of AWS in critically ill surgical or trauma patients as reflected by CIWA-Ar, however, is several times higher in ICU patients compared to psychiatric patients. The complex interactions between anesthesia, postoperative stress, trauma, infections, and other factors may enhance imbalances of transmitter systems and require a more effective therapy. The symptoms have to be closely monitored (Awissi et al. 2013; Moss and Burnham 2006; Martin et al. 2010; Spies and Rommelspacher 1999; Spies et al. 2003; Ungur et al. 2013).

If an alcohol withdrawal syndrome occurs, the use of more than one drug should be considered. Treatment should be symptom oriented: for agitation and seizures, benzodiazepines (first substance of choice, e.g., lorazepam, diazepam); for autonomic hyperactivity, alpha-2 agonists (clonidine or dexmedetomidine); and for hallucinations or productive-psychotic symptoms, neuroleptics according to the underlying transmitter imbalances: GABAergic (e.g., benzodiazepines, clomethiazole), dopaminergic (e.g., haloperidol), and noradrenergic system (e.g., clonidine). Dosage should be adjusted to the patient's clinical condition. Ethanol is obsolete in the manifest withdrawal state (Amato et al. 2011; Awissi et al. 2013; Spies and Rommelspacher 1999; Spies et al. 2003; Ungur et al. 2013).

Any delay or inadequacy of therapy may worsen symptoms. In contrast to a fixed-dose treatment, symptom-oriented treatment using a scoring system reduces time of treatment, can shorten the clinical course of AWS, and can reduce morbidity

use of medication, complication rates, time of ventilator support, and length of ICU stay when compared to a preassigned and fixed treatment plan. Different scores can be used in order to monitor delirium and to guide therapy. CIWA-Ar score was validated for normal wards, whereas the Delirium Detection Score (DDS) was validated for the ICU setting (Otter et al. 2005; Spies et al. 2003; Moss and Burnham 2006; Martin et al. 2010; Awissi et al. 2013; Ungur et al. 2013).

If simultaneously clonidine and haloperidol are used in the treatment of alcohol withdrawal syndrome, hypokalemia and hypomagnesemia should be avoided, as this can cause QT prolongation and arrhythmias. Clonidine can cause hypotension, bradycardia, AV block, and constipation. Electrolyte disorders should be treated, especially hypokalemia and hypomagnesemia (Moss and Burnham 2006; Spies and Rommmelspacher 1999).

#### 111.2.3.6 Prophylaxis

Drugs used to prevent withdrawal are benzodiazepines, clomethiazole (per os), clonidine, and haloperidol or risperidon, usually in dosages that are lower than used for treatment. If indicated, a long-acting benzodiazepine can be given the evening before surgery (e.g., lorazepam) for premedication and a short-acting benzodiazepine in the morning of surgery (e.g., midazolam). In patients not adequately premedicated before the induction of anesthesia, midazolam IV can be titrated to the desired effect; additionally clonidine, haloperidol, or ketamine can be given intravenously, if there are no contraindications. The prevention of alcohol withdrawal syndrome on a peripheral ward is usually done with a single substance. Monitoring on the ward is required. If the requirement for monitoring is not met by the ward's resources, the patient must be moved to a monitoring or intensive care unit. It is important to reduce prophylactic dosage after symptom control, as this – in unintended continued treatment – includes even a potential for addiction. Preventive treatment may avoid AWS or attenuate its severity; transition from prevention to treatment is continuous (Spies and Rommmelspacher 1999; Spies et al. 2006).

In alcoholic patients, hypercortisolism can occur postoperatively after surgical stress. Pharmacological intervention by inhibition of the HPA axis (stress prevention) with morphine, low-dose ketoconazole, and ethanol in alcoholic patients could prevent the prolonged cortisol response to surgical stress, compared with placebo, and thus reduce the incidence of infection Spies et al. (2006a). For blockade of the HPA axis and to reduce infectious complications, perioperative infusion of low doses of ethanol (0.5 g/kg/day IV) or low-dose morphine (15 μg/kg/h) has been shown to be effective in one study. As this is not a sufficient pain treatment, pain should be monitored by visual analog scale (VAS) or numerical rating scale (NRS) and treated according to evidence-based hospital standards (Spies et al. 2006; Martin et al. 2010).

Perioperative administration of prophylactic medication, especially alcohol, requires an assessment of the motivation regarding a change in alcohol consumption and informed consent after shared decision making. Risk and options are communicated. This communication should have a big overlap with motivational interviewing and change talk (Kork et al. 2010).

#### 111.2.3.7 Treatment of Wernicke's Encephalopathy

Intravenous thiamine (before any carbohydrate, 200 mg thrice daily) is indicated for the treatment of suspected or manifest WE. Oral substitution is initially inadequate. Hypoglycemic patients should receive thiamine latest when administering intravenous glucose (Galvin et al. 2010).

#### 111.2.3.8 Preoperative Abstinence

Pathophysiological dysfunctions due to heavy drinking are potentially reversible. Immune response, stress response, alcoholic cardiomyopathy, bleeding time, frequency of hypoxia, and wound healing improve during abstinence within a time frame of weeks or months (Tønnesen et al. 2009; Spies et al. 2001a).

Two studies from Denmark (one among nondependent alcohol consumers (60–420 g/day) undergoing radical colorectal resection patients and one that included elective hip arthroplasty patients) showed an effect of 4-week preoperative abstinence and psychosocial counseling combined with disulfiram substitution on the overall complication rates including infection rate. Postoperative morbidity was reduced from 74 % to 31 % after colorectal surgery. There was no significant reduction of in-hospital and 30-day mortality (Tønnesen et al. 2009; Oppedal et al. 2012).

#### 111.2.3.9 Addiction and Psychosocial Treatment

The alcohol-dependent patient should be seen early by an addiction specialist. The indication of ambulatory or inpatient detoxification before or after surgery should be evaluated. Alcohol-dependent patients may profit from anti-craving medication such as acamprosate, naltrexone, or alcohol deterrent medication such as disulfiram. Naltrexone can interfere with postsurgical pain therapy, if opioids are indicated. One large multicentre study by Anton et al. (2006) underlined the importance of medical management (Spies and Rommelspacher 1999; Anton et al. 2006; Tønnesen et al. 2009; Kork et al. 2010).

## 111.3 Tobacco Dependency, Nicotine Use Disorder (NUD)

As tobacco use is associated with cancer and cardiovascular or pulmonary diseases, smokers are overrepresented among these patients. Accordingly, the incidence of perioperative pulmonary complications, cardiovascular complications, impaired wound healing, and wound infection is increased. Smokers, who continue to smoke until surgery, have a higher two- to sixfold pulmonary morbidity compared to nonsmokers (Bluman et al. 1998; Møller et al. 2002; Tønnesen et al. 2009).

Smoking is usually reported spontaneously. Standardized questionnaires such as the Fagerström Test evaluate degrees of dependency and were used to guide therapy, e.g., nicotine replacement therapy. Different from the construct of the ICD or DSM dependence definition, the number of cigarettes is needed for a positive score (Heatherton et al. 1991).

An established point-of-care biomarker of acute smoking is carbon monoxide-hemoglobin (COHb). It is routinely determined in anesthesiology workplaces. CO binds to the hemoglobin and reduces the oxygen binding capacity of the hemoglobin significantly (up to 15 %). This might cause hypoxia even in patients without coronary heart disease and is associated also with wound complications. COHb predisposes for ST-segment depressions in stress situations. In addition, increased nicotine levels are associated with an increased sympathetic activity: There is an increased heart rate, increased blood pressure, and a reduced peripheral blood flow through vasoconstriction. Increased oxygen consumption meets a lowered oxygen supply. The net effect might result in a relative hypoxia. In patients with coronary heart disease, the incidence of myocardial ischemia increases significantly. Patients smoking immediately prior to surgery with elevated expiratory CO concentration (>35 ppm) showed more ST depressions. The half-life of COHb and nicotine is about 12 h, e.g., after abstaining overnight. In cardiac risk patients, an abstinence of 12–48 h reduces perioperative cardiac morbidity. A perioperative smoking cessation of 12–48 h is required (Zwissler and Reither 2005; Neumann et al. 2008; Tønnesen et al. 2009; Kork et al. 2010). COHb in blood was an excellent marker to detect current smoking in trauma patients. The cutoff of COHb should be lowered to 1.6 % in women and to 1.8 % in men (Neumann et al. 2008).

The pulmonary morbidity is two- to sixfold higher in patients smoking until the surgery. In smokers, the lung capacity and ciliary function are reduced; closing capacity is increased. The production of mucus is increased, but the secretion of pulmonary clearance reduced. This can also affect otherwise asymptomatic younger smokers. This is associated with an elevated pulmonary postoperative morbidity. In smoking patients undergoing elective surgery, pulmonary complications were 22 % vs. 5 %. In abdominal surgery, the rate may be even higher. Smokers are more frequently admitted to ICUs than nonsmokers (Zwissler and Reither 2005; Møller et al. 2002; Tønnesen et al. 2009).

Smoking lowers the pressure in the lower esophageal sphincter; however, this effect is fully reversible after 5 min. The emptying of solid but not liquid food particles from the stomach is delayed after smoking. In respect to acute smoking, there is no increased risk of aspiration neither to gastric volume nor to the acidity of the gastric juice. However, smokers experience less postoperative nausea and vomiting (PONV) (Zwissler and Reither 2005).

Smoking impacts on the immune function. This leads to an increased risk of infections. The immune system recovers after 2–6 weeks of abstinence from smoking, wound healing after 3–4 weeks, and the lung function after 6–8 weeks (Tønnesen et al. 2009).

More intensive smoking cessation programs are more effective than briefer interventions; however, briefer interventions might bridge the patient into more intensive programs that include nicotine replacement therapy (NRT), CO monitoring, and psychoeducation and counseling about the expected advantages and disadvantages of abstinence, side effects, withdrawal symptoms, diet and exercise, weight gain, and other issues. Six randomized trials have been published that evaluated preoperative smoking cessation with abstinence rates between 40 %

and 89 %. Three studies suggest that preoperative smoking cessation programs of 3–4 and 6–8 weeks duration are beneficial in respect to complications. Shorter periods of abstinence are not disadvantageous. A potential negative effect of a preoperative smoke stop had been reported in retrospective studies with considerable methodological weaknesses. Also postoperatively nicotine replacement is recommended, adapted to the degree of nicotine dependence (Fagerström test) (Bluman et al. 1998; Møller et al. 2002; Lindström et al. 2008; Sørensen and Jørgensen 2003; Tønnesen et al. 2009).

Wound healing is affected by smoking. Collagen production is impaired. The wound infection rate of sacral incisions in 78 volunteers was lower at 4–12 weeks after randomization, compared with smokers without cessation, but not after a week examined. No difference was observed between placebo and patch therapy (Sørensen and Jørgensen 2003; Møller et al. 2002; Tønnesen et al. 2009).

Nicotine represents a cholinergic agent. Therefore, in case of surgery without preoperative abstinence, nicotine replacement therapy (NRT) and other cholinergic agents like physostigmine are an option in these patients as adjunctive for treatment of pain and the potential of saving postoperative opioids. Perioperative NRT initiated before induction of anesthesia and maintained after surgery should be considered. Physostigmine 1.5 mg IV at the end of surgery then 1 mg/h for 24 h can be given as an cholinergic agent and for pain reduction, if no NRT was started. Cholinergic agents are basically emetogenic; PONV prophylaxis might be necessary (Møller et al. 2002; Beilin et al. 2005; Kork et al. 2010).

## 111.4 Opioids

### 111.4.1 Clinical Relevance

Patients with opioid dependency undergoing surgery might be polysubstance users with significant comorbidity or chronic pain patients treated with opioids. They are at risk for withdrawal. Complex individualized treatment strategies are required. Many patients were seen in emergency facilities. The effects of opioids are enhanced by CNS depressant drugs, e.g., ethanol and GABEergic medication. Respiratory depression (with aspiration (pneumonia), cyanosis, and/or pulmonary edema) and consecutive hypoxia are the most common causes of morbidity and death after acute opioid intoxication. This is associated with ST-segment changes, tachycardic arrhythmias, hypotension and congestive heart failure, and cerebral and spinal ischemia or nerve compression syndromes and muscle damage with consecutive crush syndrome or rhabdomyolysis after immobilization when intoxicated. Patients might suffer from acute and chronic infections including HIV and hepatitis, intravenous and polysubstance drug use-associated bacteriemia, heart valve pathologies, atherosclerosis from smoking, trauma, and psychiatric comorbidity. Peripheral and central venous access is often difficult (Hernandez et al. 2005; Kork et al. 2010). Relevant withdrawal symptoms are tachycardia, diarrhea, hyperhidrosis with dehydration next to mydriasis, and goose bumps.

### 111.4.2 Perioperative

Opioid-dependent hospital patients should receive a basal substitution ("baseline") with methadone or racemate plus opioids as clinically required for analgesia under the control of the vital signs and withdrawal parameters. Regional anesthesia alone or in combination with general anesthesia, NSAIDs, alpha-2 agonists (clonidine, lofexidine), and ketamine can be considered. Postoperatively, the need for analgesia can be increased in drug-dependent patients. Partial agonists (e.g., buprenorphin) should be avoided. Treatment should be symptomatic, e.g., NSAIDs, alpha2-agonists (clonidine, lofexidine) (APA 2006; Kork et al. 2010).

Clinical signs of over- and underdosage should be observed. Vital signs and symptoms of withdrawal (e.g., Objective and Subjective Opiate Withdrawal Scale, OOWS, SOWS) should be documented regularly. Written bedside standard operating procedures should clearly describe:

- In case of overdose: command breathing; administer oxygen and ventilation, eventually titration of naloxone.
- In underdosing: rescue medication (give opioids).

QTc time (ECG) has to be monitored. Under methadone medication, the QTc time can be prolonged, which is a risk factor for arrhythmias (APA 2006; Kork et al. 2010).

Laxatives (e.g., lactulose) are administered as adjuvant until the stool consistency has normalized. Adequate hydration replaces volume loss in hyperhidrosis (e.g., during withdrawal). Diverse drug interactions must be considered in patients with methadone substitution therapy. Methadone interaction with other medications should be anticipated. Manufacturer's information should be consulted, as enzyme induction (cytochromes) or inhibition concerns a variety of substance, (e.g., antiviral medication, carbamazepine, phenytoin, cimetidine, and rifampicin). Medication with sedating properties (e.g., benzodiazepines) can act synergistically and can cause respiratory depression. Partial antagonists (e.g., buprenorphine) can trigger withdrawal symptoms and are contraindicated in this case. Clonidine and lofexidine attenuate heroin or methadone withdrawal symptoms more effectively than placebo and can be perioperatively or intraoperatively applied once hemodynamic monitoring is available (Hernandez et al. 2005; APA 2006; Gowing et al. 2009; Kork et al. 2010). The pain treatment **in former opioid-dependent patients** is an understudied issue. There are concerns that this may trigger a relapse ("drug reinstatement") when mu agonists (or other psychoactive drugs) are potentially indicated in the perioperative period. Regional anesthesia or general anesthesia combining inhalation anesthetics with N2O, ketamine, and nonsteroidal anti-inflammatory drugs is not always possible. If indicated, titration of adequate amounts of a short-acting μ-agonist can be necessary; alpha-2 agonists can relieve withdrawal symptoms. Patients should be carefully informed (e.g., about craving) and educated about the small but relevant risk of relapse. This should be documented, and written informed consent should be obtained. Possible treatment options should be discussed, including post-hospital psychosocial and medical care. Any relapse is a potentially life-threatening situation. Opioid-related death occurs

often in former users. Some patients seem to be unaware of the decreased tolerance and use opioids in usual doses. Patients should be educated about these phenomena (Kork et al. 2010).

In the first days of the postoperative period, opioid substitution therapy is continued. In addition, opioids are administered for analgesia. Increased demand in comparison to "opioid-naive" patients can be expected (Kork et al. 2010).

In the emergency situation, preoperative switching to methadone is not possible in opioid-dependent patients. Symptomatic patients are treated if necessary and the presence of withdrawal symptoms with a μ-agonists. A regional anesthesia should be considered (Kork et al. 2010).

The consequences of drug-induced respiratory depression with consequent hypoxia or atelectasis, aspiration, cardiovascular symptoms, neurological symptoms, nerve compression and damage, and polysubstance comorbidity have to be evaluated. Next to the ABCDE (airway, breathing, circulation, disability, evaluation) approach, an ECG, cardiac enzymes, echocardiography, chest X-ray, imaging, lab and drug screening, and neurological and psychiatric evaluation are helpful (Hernandez et al. 2005; Kork et al. 2010).

Naloxone carefully titrated is one option to treat overdose. This is also helpful to establish the diagnosis. The effect of naloxone lasts only about 30–60 min. In emergency situations, naloxone administration can be potentially harmful. The initiation of (immediate) withdrawal stress in patients with impaired organ function is potentially dangerous. Craving-associated drug-seeking behavior in the emergency situation after antagonist administration can cause difficult situations. Trauma or impaired organ function, severe prolonged hypoxia, suicide intention, or intake of other CNS depressants that are non-mu agonists cannot be ruled out. Cases of pulmonary edema have been reported after naloxone treatment. Intubation and ventilation by skilled personal might be of lesser risk (Osterwalder 1996; Kork et al. 2010).

Complex psychiatric and somatic morbidity requires individualized psychosocial and medical care. Brief intervention might bridge into more intensive treatment. Detoxification should be carefully planned, (e.g., cold, agonist assisted, symptomatic treatment, or opioid antagonist induction therapy (naltrexone), e.g., under anesthesia (APA 2006).

The opiate antagonist-induced withdrawal under anesthesia is indicated only in special cases and is not associated with a better outcome. This method must be performed under ICU conditions. Opiate antagonist application induces a pronounced withdrawal syndrome with an increase in catecholamine and a strong cardiovascular stimulation in opioid-dependent patients. Severe hypokalemia may occur. In published protocols, multiple doses of naltrexone were administered intragastral during several hours under general anesthesia. Relevant other side effects are severe electrolyte disorders, nausea, gastric reflux, diarrhea, and muscle and stomach pain. The procedure continues until the withdrawal symptoms have subsided or a negative challenge test (intravenous administration of naloxone). The naltrexone maintenance treatment should be carried out for several months in an interdisciplinary psychosocial treatment approach (APA 2006; Brewer et al. 1998; Hensel and Kox 2000; Kork et al. 2010; Schmidt et al. 1998).

## 111.5 Cocaine

### 111.5.1 Clinic

The central and peripheral reuptake inhibition of norepinephrine, dopamine, and serotonin is responsible for the stimulatory effects of cocaine resulting in a stimulation of the CNS and the sympathetic system with pronounced cardiovascular and cerebrovascular effects and related complications. It has also a local anesthetic effect. The pathogenesis of ischemic complications is multifactorial: increased oxygen demand with a fixed or limited myocardial oxygen supply, myocardial vasoconstriction, and increased platelet aggregation tendency. By the chronic use of cocaine, there is a depletion of dopamine and other neurotransmitters and a decrease in dopamine receptors D2. This is associated with depression and the so-called crash. Therefore, all patients with a history of cocaine as well as stimulant use should be carefully evaluated, especially for cardiovascular and neurological morbidity (Egred and Davis 2005; Hernandez et al. 2005; Hollander and Henry 2006).

### 111.5.2 Therapy

Treatment of patients with chest pain and ECG changes includes oxygen, benzodiazepines, nitrates, and acetylsalicylate. Benzodiazepines can reduce the elevated blood pressure, tachycardia, and anxiety. Calcium channel blockers and alpha-blockers may be given in addition. Beta-blockers without alpha-blockade are contraindicated for the treatment of cocaine-induced hypertension and tachycardia. They increase the cocaine-related mortality, possibly due to increased α-adrenergic stimulation, e.g., coronary spasm. The 1-selective blocker esmolol along with an infusion of sodium nitroprusside or the administration of calcium antagonists can be used. The indications for thrombolytic therapy should be made cautiously in the context of cocaine use. If symptoms persist, catheter revascularization seems to be safer (Egred and Davis 2005; Hernandez et al. 2005; Hollander and Henry 2006).

### 111.5.3 Urgent and Emergency Intervention

Cocaine is rapidly metabolized and is therefore difficult to detect in the blood, but it can be detected in the urine up to 6 days after ingestion. The sympathomimetic effect may persist beyond the actual phase of intoxication. A cardiopulmonary and neurological evaluation should be performed. A drug screening reveals drug use. In addition to injuries, often associated with violence, chest pain is common among cocaine-induced symptoms in the ED patients. Cardiac troponin I or T is more specific compared to the CK-MB or even myoglobin for acute myocardial infarction after cocaine use. There is a high rate of false-positive myoglobin and creatine kinase values, especially in rhabdomyolysis. Acute cocaine ingestion can have cardiotoxic effects and is related to sudden death. ECG findings are abnormal in

56–84 % of patients with cocaine-associated chest pain. It should be noted that the sensitivity of the ECG is only 36 % and specificity is 90 %. Regional anesthesia during cocaine intoxication is not recommended because local anesthetics have similar pharmacological effects as cocaine and might potentiate toxicity. If general anesthesia is required in an urgent situation, avoid the potentiating substances, e.g., adrenergic stimulants, ketamine, etomidate, aminophylline, MAO inhibitors, tricyclic antidepressants, acetylcholinesterase inhibitors, muscle relaxants with autonomic side effects, local anesthetics, and volatile anesthetics with stimulating properties. The sympathomimetic effect of cocaine can make the assessment of the intravascular volume or blood loss difficult, so more extended monitoring next to arterial (and central venous) pressure measurement and monitoring of urine and hemodynamic stabilization before induction of anesthesia is important. As part of the intensive inpatient treatment, possible withdrawal symptoms are observed. Cerebral blood flow is reduced. First signs are lower blood pressure, hypothermia, and miosis. Benzodiazepines and clonidine can be considered (Egred and Davis 2005; Hernandez et al. 2005; Hollander and Henry 2006).

### 111.5.4 Elective Procedure

Patients with cocaine abuse have a higher risk of cardiovascular disease, also after the intoxication phase. The sympathomimetic effect can be prolonged and withdrawal also can be a risk for a cardiovascular event. Benzodiazepines in an adequate dosage can be given for premedication. Any stimulating medication should be used with caution, including those inhalation anesthetics or muscle relaxants such as pancuronium with autonomic side effects that sensitize the myocardium to catecholamines. The total intravenous anesthesia is preferred (Egred and Davis 2005; Hernandez et al. 2005; Hollander and Henry 2006).

## 111.6 Other Drugs

It is beyond the scope of this chapter to describe all specific features of abused drugs with an addictive potential relevant for anesthesia. Synthetic drugs are increasingly used. Clinically important is a heterogeneous group of stimulatory, entactogenic ("touching the inside"), hallucinogenic, or hypnotic drugs with overlapping properties. As a general rule, symptomatic treatment, screening for drug use, and consulting expert help (e.g., poison control center) can be recommended for critically ill patients with suspected drug use. A systematic diagnostic approach might reveal unexpected morbidity, as acute and chronic use has been related to a wide spectrum of neurological, cardiovascular and pulmonary, metabolic, and infectious/immunological complications even in younger undergoing smaller procedures: Diagnostic strategies that include, e.g., a full lab, drug screen, echocardiography, or imaging, should be considered early. Patients with suspected intoxication should be monitored

continuously. Street drugs may be mixed with many other relevant substances (Steadman and Birnbach 2003; Hernandez et al. 2005). Many patients use more than one drug, e.g., many self-medicate in order to overcome withdrawal symptoms, such as "the crash" that comes after taking stimulants or sedatives. A distinction between intoxication, withdrawal, and neurological insult is often difficult, and important other causes for delirium should be ruled out (Table 111.1, Kork et al. 2010; Spies and Rommelspacher 1999).

### 111.6.1 Stimulants, Entactogens, and Hallucinogens

Ecstasy (e.g., MDMA), amphetamines, and LSD act more or less stimulating. Tachycardia, hypertension, dizziness, panic attacks, or visual illusions can occur. Clinical important complications are cardiac arrhythmias, hyperthermia, renal failure, hepatotoxicity, multiorgan failure, rhabdomyolysis, hyponatremia and cerebral edema, seizures and intracranial hemorrhage, altered consciousness, or sudden death (Hernandez et al. 2005; Hall and Henry 2006). When used in dance marathons, extreme dehydration and hyperthermia up to 42 °C might occur or hyponatremia due to excessive water intake. Cerebrovascular accidents and complications due to acute anxiety and panic disorders may also occur (Hernandez et al. 2005; Hall and Henry 2006).

### 111.6.2 Treatment of Acute Intoxications

The treatment of acute stimulant intoxication is symptomatic. Dehydration and hyperthermia is treated with external and internal cooling, rehydration, antipyretics, correction of electrolyte imbalance and (metabolic) acidosis, and sedative and anticonvulsant therapy. Intubation and ventilation can be required. A sedative, antianxiety, and anticonvulsant treatment with benzodiazepines is usually indicated. Seizures can be treated with benzodiazepines or barbiturates. Arterial hypertension can be treated with urapidil, clonidine, nitroprusside, nitrates, or labetalol; beta-blockers alone without alpha-blockade should be avoided. The spectrum of cardiovascular complications and side effects is similar to cocaine stimulants (myocardial vasoconstriction, increased oxygen demand with a fixed or limited myocardial oxygen supply, and increased platelet aggregation propensity). Dantrolene is also recommended for hyperthermia, if temperature is $>39$ °C after initial treatment. It was considered probably safe and effective. The association with malignant hyperthermia is controversial. Clomethiazole or diazepam was effective in animal experiments for hyperthermia. Antipsychotic drugs are contraindicated as they might lower the seizure threshold, and it is difficult to differentiate the clinical presentation from the neuroleptic malignant syndrome. Hyponatremia should be carefully corrected. Metabolic acidosis should be corrected (especially when the QT interval is prolonged). In case of organ failure, conventional supportive ICU therapy is provided. Especially dangerous is the concomitant use of tricyclic antidepressants and monoamine oxidase inhibitors with MDMA.

Excessive release of serotonin leads to cerebral seizures, tremors, loss of consciousness, ventricular fibrillation, and death (Steadman and Birnbach 2003; Hernandez et al. 2005; Hall and Henry 2006; Grunau et al. 2010).

### 111.6.3 Elective Procedure

If patients undergo procedures in the drug-free interval, a careful evaluation is necessary as outlined above. A history of seizures, a decreased hepatic and renal function, and coagulation disorder infections are of interest in all patients. All anesthetics should be titrated according to the effect (Kork et al. 2010). PCP and LSD might prolong succinylcholine via inhibition of plasma cholinesterase (Hernandez et al. 2005). Patients with MDMA-induced hyperthermia in the history should undergo a trigger-free anesthesia (Hernandez et al. 2005; Hall and Henry 2006; Steadman and Birnbach 2003). A brief intervention addressing risky use should be delivered. An interdisciplinary psychosocial counseling and treatment plan should be initiated early (Kork et al. 2010).

## 111.7 Cannabis

The risk profile of cannabis, also used in a dependent way, is predominantly characterized by an increased pulmonary morbidity due to smoking. During intoxication it has some dose-dependent effect on the sympathetic activity; an increase is followed by a decrease, thus tachycardia or hypotension and bradycardia. Components of cannabis might have relevant antiemetic, analgesic, anticonvulsant, and appetite increasing effects (Hernandez et al. 2005).

## 111.8 GABAergic Substances

Gamma-hydroxybutyrate is abused increasingly. The effect is dose dependent, may be influenced by consuming other drugs, and ranges from euphoric-relaxing effect to drowsiness and deep sleep with subsequent coma and possible respiratory depression. Side effects – nausea, vomiting, hypotension, respiratory distress, confusion, myocloni, and convulsions – were observed. It is used as K.O. drops or as a growth hormone releaser among bodybuilders. After intake it can cause a pronounced amnesia. It is not detected by routine drug screening (Steadman and Birnbach 2003; Hernandez et al. 2005). Many patients are dependent from benzodiazepines or are using them to cope with symptoms of withdrawal or comorbidity. Relevant interactions on the pharmacodynamic and pharmacokinetic level have to be considered. In these patients, an altered GABA receptor function can be assumed. All anesthetics should be titrated to the desired effect. Neuromonitoring is recommended to avoid intraoperative awareness. Abrupt withdrawal causes anxiety and may cause seizures and should be avoided. Also hypnotics are misused

and have been linked to dependency. Not only healthcare providers have misused propofol in a risky or dependent way. In short-acting hypnotics, the range between the desired effect and relevant respiratory depression is narrow, especially in combination with other substances (Steadman and Birnbach 2003; Hernandez et al. 2005; Tan et al. 2011; Lader 2011).

## 111.9 Conclusion

Dependent patients with SUD can safely undergo procedures under anesthesia. In general, SUD and related complications can be successfully treated. By secondary or tertiary preventive measures in a multimodal interdisciplinary concept, the increased risk can be significantly reduced.

Elements are:

- Systematic screening, using questionnaires/markers
- Systematic diagnostic evaluation
- Brief interventions, tailored advice, and information
- Patient-centered communication style
- Individually tailored anesthesia
- Detoxification
- Abstinence
- Rehabilitation
- Psychosocial therapy
- Stepped care
- Harm reduction
- Monitoring and prevention of withdrawal symptoms, substitution therapy
- Monitoring and prevention of complications, goal-oriented therapy, symptom control, prevention of secondary injury, and stress reduction
- Complex interdisciplinary treatment strategies
- Teaching and training

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