

Perioperative Management in the Patient with Substance Abuse

Sharon Moran, мD*, Jason Isa, мD, Susan Steinemann, мD

KEYWORDS

• Drug screening • Substance abuse • Perioperative management

KEY POINTS

- Chronic substance use and acute intoxication may affect all aspects of perioperative care, including starting an intravenous line, securing an airway, intraoperative management, and postoperative pain control.
- The clinician should screen for alcohol and drug use in all patients and obtain serum or urine tests on those who are likely by history, physical examination, or circumstances to be intoxicated.
- Operations on acutely intoxicated patients should be delayed, if possible, because of the potential for hemodynamic instability.
- Those caring for a substance user postoperatively should be wary of the potential for hemodynamic compromise, poor wound healing, altered consciousness, and difficulty with pain management.

INTRODUCTION

Alcohol and drug use and abuse have been an increasing problem in the United States. The major categories of drugs of abuse include alcohol, stimulants, opiates, cannabinoids, and hallucinogens. Both acute intoxication and chronic abuse of these substances present challenges for anesthetic management during and after an operation. Whereas some procedures may be delayed while the issue is addressed, others are urgent or emergent and the surgeon and anesthesiologist must be able to deal with the physiologic changes that may occur in these patients.

According to the 2012 National Survey on Drug Use and Health,¹ which interviews persons aged 12 or older, 23.9 million Americans, or 9.2% of the population, were current users of illicit drugs (Fig. 1). This was an increase compared with 2008. Current

0039-6109/15/\$ - see front matter © 2015 Elsevier Inc. All rights reserved.

Surg Clin N Am 95 (2015) 417–428 http://dx.doi.org/10.1016/j.suc.2014.11.001

surgical.theclinics.com

The authors have nothing to disclose.

Department of surgery, The Queen's Medical Center, University of Hawaii, 1356 Lusitana 6th floor, Honolulu, HI 96813, USA

^{*} Corresponding author.

E-mail address: sharonemoran@gmail.com

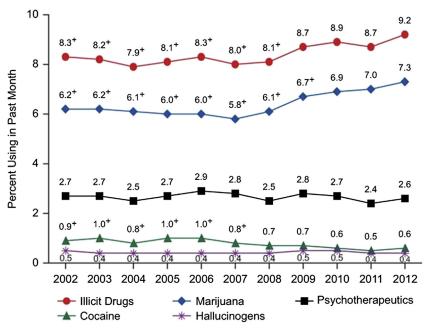


Fig. 1. Past month use of selected illicit drugs among persons aged 12 or older: 2002–2012. (*From* National Survey on Drug Use and Health (US), United States, Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Center for Behavioral Health Statistics and Quality (US). Results from the 2012 National Survey on Drug Use and Health: summary of national findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville (MD): Substance Abuse and Mental Health Services Administration; 2013.)

drinkers of alcohol represent 52.1% of the population, with 6.5% reporting heavy use (Fig. 2). Those rates are similar to 2008. A total of 8.5% were considered to have a substance dependence or abuse disorder.

SCREENING FOR SUBSTANCE USE

Questions regarding alcohol and drug use should be part of any history and physical. The surgeon and anesthesiologist should emphasize that the question allows them to better take care of the patient and is not meant to be judgmental or to be used for criminal charges. Most patients are honest with the provider, but testing should be considered in the unconscious patient and in certain populations.^{2,3} Substance abuse has been well studied in the trauma population because screening and intervention programs are required elements for a trauma center. Cost-benefit analysis supports testing those who arrive meeting trauma team activation criteria.⁴ Patients seeking liver transplants are often enrolled in routine testing, but other organ transplant patients can be at risk for substance use disorders.⁵ The bariatric surgery population has also been studied for increased substance use.⁶ Features of the physical examination, such as tachycardia, tremors, a smell of alcohol, and poor dentition, may lead the physician to suspect substance use.

Results of urine testing are typically reported within a half hour of the sample being received. Serum alcohol results may take an hour to process. There are several different drug screen panels available, but most test for marijuana, amphetamines/methamphetamines, phencyclidine (PCP), cocaine, opioids, barbiturates, and benzodiazepines

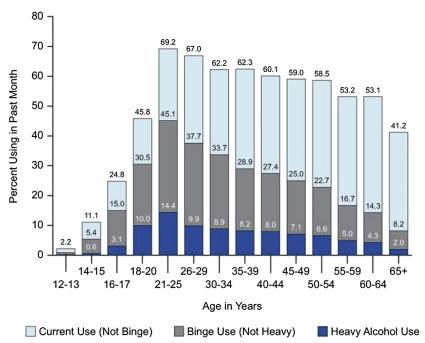


Fig. 2. Current, binge, and heavy alcohol use among persons aged 12 or older, by age: 2012. (*From* Substance Abuse and Mental Health Services Administration. Results from the 2012 National Survey on Drug Use and Health: summary of national findings, NSDUH Series H-46, HHS Publication No. (SMA) 13-4795. Rockville (MD): Substance Abuse and Mental Health Services Administration; 2013.)

(**Table 1**). If the patient screens positive for acute intoxication by history or laboratory testing and the operation is not urgent, the procedure should be delayed. The patient should be informed of the anesthetic risks particular to the substance used. If use is chronic, referral to treatment should be provided.

ALCOHOL

Depending on the screening tool used, up to 28.5% of patients presenting for an operation have an alcohol use disorder.⁷ Blood levels decrease by approximately 0.015 g/dL per hour.

Airway: Aspiration Risk and Lung Injury

The intoxicated patient with a full stomach presents an aspiration risk. In addition, alcohol decreases lower esophageal sphincter pressure.⁸ Chronic alcoholics have more airway colonization with pathologic bacteria, increasing the risk for pneumonia.⁹ Even without aspirating, an injured patient with elevated blood alcohol content has been shown to be at increased risk for acute respiratory distress syndrome.¹⁰ The chronic user is also at risk because of impaired cellular mechanisms and a decrease in antioxidants.^{11,12}

Intraoperative Management

Anesthetic requirements vary widely, depending on degree of intoxication and degree of liver and other organ damage. Care should be taken when titrating oxygen because acutely intoxicated patients have less tolerance for hypoxia.¹³ The patient with

Table 1 Approximate detection times for a urine drug screen and substances causing false-positives		
Drug	Detection Window	Substance Causing False-Positives
Alcohol	2–12 h	
Benzodiazepines	72 h Chronic use 4–6 wk	Sertraline
Cocaine	48–72 h	Amoxicillin, tonic water
Methamphetamine/amphetamines	48 h	Ephedrine, pseudoephedrine, amantadine, labetalol
Heroin	48 h	Poppy seeds, dextromethorphan
Methadone	72 h	Ibuprofen, quetiapine, verapamil
Prescription opioids	6–96 h	Poppy seed, dextromethorphan
Marijuana	7 d–2 mo with chronic use	Dronabinol, sulindac
3,4-methylenedioxymethamphetamine (ecstasy)	48 h	Pseudoephedrine, Vicks inhaler
Lysergic acid diethylamide (LSD)	36–96 h	Amitriptyline, sumatriptan
Phencyclidine (PCP)	8–14 d	Dextromethorphan, ibuprofen
Ketamine	7–14 d	
γ-Hydroxybutyric acid	12 h	Soaps

cirrhosis has special fluid and electrolyte needs, and is at risk for bleeding; blood products should be made available. Hypotension may result from dehydration, cardiomyopathy,¹⁴ or a diminished adrenocortical response to stress.¹⁵

Postoperative Management

Sensitivity to pain varies widely depending on degree of alcohol use and underdosing or overdosing of pain medicine is a possibility. In addition to pulmonary complications, alcoholics are at risk for wound infections caused by immunosuppression.¹⁶

The most serious postoperative complications are alcohol withdrawal and delirium tremens, because they are life-threatening conditions. Incidence varies depending on type of operation, age, and comorbidities. Symptoms of withdrawal can vary from mild tremors, confusion, and fever to severe electrolyte abnormalities (hyponatremia, hypokalemia, hypocalcemia, hypophosphatemia, and hypomagnesemia), hemodynamic instability, and seizures.

Implementation of a symptom-triggered withdrawal prophylaxis practice guideline using lorazepam, haloperidol, or clonidine can decrease the development of withdrawal syndromes.¹⁷ Dexmedetomidine has been investigated as an adjunct to benzodiazepine in the prevention of withdrawal.¹⁸

BENZODIAZEPINES

Benzodiazepines are available by prescriptions for the treatment of anxiety, posttraumatic stress disorder, and other psychiatric illnesses.

Airway

Because benzodiazepines are most often ingested, there are not usually airway concerns outside of overdose. If there has been an overdose, flumazenil can be used as a reversal agent. Although there have been concerns for using flumazenil in patients with concomitant tricyclic overdose or chronic benzodiazepine users, experimental studies have shown that with proper precautions, it can be used safely.¹⁹

Intraoperative Management

Intraoperative complications in benzodiazepine using patients are not widely reported.

Postoperative Management

Benzodiazepine withdrawal is manifested by anxiety, poor sleep, tremors, and in its most serious form, seizures. Patients who are preoperatively on benzodiazepine treatment should have their medication continued. Those who were abusing benzodiazepines may be started on a symptom-triggered or tapered dose withdrawal regimen using a long-acting benzodiazepine²⁰ or be treated with low-dose flumazenil.²¹

STIMULANTS

Stimulants include cocaine and amphetamines. Route of administration varies and influences the length of intoxication and the manifestations of chronic use.

Cocaine

Cocaine is still used as a topical anesthetic, especially in ear, nose, and throat surgery. It may be smoked, taken intranasally ("snorted"), or injected. Its effects last from 30 to 60 minutes. Toxicity is manifested by psychosis, dysphoria, paranoia, anxiety, and cerebral hemorrhage. Coronary vasoconstriction may occur because of inhibition of catecholamine reuptake and inhibition of nitric oxide synthesis.²²

Airway

Chronic nasal cocaine use can cause septal destruction and soft palate necrosis.²³ Caution should be taken while intubating or placing a nasogastric or orogastric tube. Smoked, or crack, cocaine can cause a wide variety of pulmonary complications including interstitial fibrosis, barotrauma, alveolar hemorrhage, and pulmonary hypertension that may make oxygenation or ventilation difficult.²⁴

Intraoperative management

If the patient has normal vital signs and the electrocardiogram is normal, anesthesia has been shown in one study to be used safely in chronic users²⁵; however, others argue for more caution. β -Blockers, such as propranolol, may result in unopposed α -adrenergic stimulation.²⁶ Nitroprusside, nitroglycerin, or demedetomidine may be used to control blood pressure. Hemodynamic instability may occur during acute intoxication when the patient can be hypertensive and hyperthermic, or hypotensive as a result of catecholamine depletion.²⁷ The hypotension may be ephedrine resistant, in which case phenylephrine may be effective.²⁷ Ketamine and halothane may potentiate negative cardiac effects and should be avoided.²⁷

Postoperative management

Withdrawal symptoms include anxiety, restlessness, and tremors. Animal studies have explored treatment with buspirone, ondansetron, and propranolol.²⁸

Methamphetamine and Amphetamines

Amphetamines may be used or abused during treatment for such conditions as narcolepsy and attention-deficit disorder. Methamphetamine can be ingested, snorted, smoked, or injected. Cardiac pathology includes arrhythmias, aortic dissection, acute

coronary syndrome, and cardiomyopathy.²⁹ An electrocardiogram should be obtained and, if time warrants, an echocardiogram in long-time users.

Airway

"Meth mouth" is caused by poor oral hygiene, xerostomia, and poor diet³⁰ and may lead to damaged and loose teeth that can be dislodged during intubation. Inhaled methamphetamine may lead to pulmonary toxicity including reduced number of alveolar sacs and arteriole remodeling³¹ and to pulmonary hypertension.³² Like cocaine, intranasal use can lead to septal necrosis and care should be taken with nasogastric tubes.

Intraoperative management

Like cocaine, the patient may become hypertensive or hypotensive, depending on the circulating catecholamines. Evidence supports continuing prescription amphetamines during the perioperative period³³ to prevent further instability. In addition, methamphetamine has been associated with cardiomyopathy^{34,35} and myocardial ischemia,³⁶ and the clinician should be aware of potential hemodynamic compromise in the patient who was unable to undergo preoperative work-up.

Postoperative management

Methamphetamine withdrawal peaks at 24 hours after last use and is characterized by increased sleeping, eating, and depression symptoms.³⁷ There is no consensus on the treatment of methamphetamine withdrawal, although psychosocial support and medical treatments have been investigated.³⁸

OPIOIDS

Opioids have therapeutic and illicit uses. Prescription drug abuse has been increasing. As pharmaceutical companies produce drugs that are resistant to crushing, and therefore injecting, and as states are better at monitoring opiate prescribing, heroin use may increase. Local, regional, and epidural analgesia should be considered in the opioidtolerant patient. Opioids may be injected, inhaled, ingested, or snorted.

Heroin

Heroin is commonly injected or administered by "skin popping," either of which may make intravenous access difficult. Caution should be taken because intravenous drug abusers may have communicable diseases, such as HIV or hepatitis.

Airway

Several factors may compromise airway and oxygenation/ventilation. Pulmonary edema may occur in patients who have overdosed.³⁹ Chronic use may lead to pulmonary hemorrhage caused by hypoxia and to granulomatous infiltration.⁴⁰ Aspiration may occur because of delayed gastric emptying.

Intraoperative management

Like all opioids, anesthesia and analgesia may be difficult, especially in long-term users, who can have increased sensitivity to pain caused by opioid-induced hyperalgesia. The variability in purity makes it difficult to calculate an equianalgesic dose of a therapeutic opioid. Opioids need to be continued to prevent withdrawal, but other medications, such as acetaminophen, nonsteroidal anti-inflammatory drugs, gabapentin, and pregabaline, may be included in a multimodal therapy regimen. Ketamine has been used in the perioperative period to reduce the amount of narcotics needed and decrease hyperalgesia.⁴¹

Postoperative management

Withdrawal can begin within 6 to 18 hours. High doses of narcotics may be needed to prevent or alleviate symptoms. Opioid agonists-antagonists, such as nalbuphine, should not be given to chronic opioid users because they may precipitate with-drawal.⁴² Although a good adjunct for pain management, epidural anesthesia alone can lead to withdrawal if oral or intravenous opioids are not also given. Some centers are able to transition the patient to a methadone maintenance program.

Methadone

Methadone is prescribed by specialized physicians for opioid addiction or any physician for pain. It is a very effective analgesic because it has a fairly rapid onset, long half-life, and is a *N*-methyl-D-aspartate antagonist and a mu receptor agonist. It also has a potential for abuse.

Airway

Methadone is usually taken orally without physical effects on the airway. Naive users may exhibit impaired ventilator response to hypercapnea that resolves with chronic use.

Intraoperative management

The management is similar to that for heroin.

Postoperative management

Withdrawal can begin within 24 to 48 hours. Management of pain and withdrawal is similar to that for heroin. If methadone is used for pain control, caution should be taken because a small dose increase can result in a toxic level.

Prescription Opioids

Prescription opioid use and abuse has been an increasing problem. New formulations of pills have been designed to prevent the nonoral use of medications, such as grinding pills for inhalation or injection.

Airway

Inhalation of crushed pills can lead to septal and soft palate necrosis.⁴³ Pulmonary talcosis and resulting cor pulmonale may occur with injection of ground pills.⁴⁴

Intraoperative management

The management is similar to that for heroin. If the patient has been using a fentanyl patch, it should be removed because the distribution is altered by fluid shifts and temperature during the operation.⁴¹

Postoperative management

Time to withdrawal depends on the formulation of the drug used. There may be crosstolerance between systemic and epidural morphine. Epidural bupivacaine/sufentanyl has been shown to be effective in chronic morphine users.⁴⁵ Otherwise, management of pain and withdrawal is similar to that for heroin.

MARIJUANA

Marijuana is the most commonly abused illicit drug. Marijuana has been legalized for medical use in many states and a few states have allowed sales for recreational use. Although traditionally smoked, marijuana dispensaries also dispense edible products with high concentrations of tetrahydrocannabinol that have been associated in the popular press with adverse events including psychosis and violent behavior.⁴⁶

Airway

Compared with nicotine cigarettes, the airway effects of smoking marijuana are mild. Bronchodilation can happen in the short term, but a chronic cough and mild airflow obstruction can develop over long-term use.⁴⁷ Upper airway edema has been described because of smoking.⁴⁸ Also, there are reports of pneumothorax from frequent Valsalva-like maneuvers.⁴⁹

Intraoperative Management

Marijuana may increase the stimulatory effects of amphetamines and cocaine and the depressant effects of alcohol and benzodiazepines. The cardiovascular effects are biphasic. Low doses result in sympathetic stimulation with tachycardia and slight hypertension.⁵⁰ High doses can inhibit sympathetic activity with unopposed parasympathetic activity leading to bradycardia and hypotension.⁵⁰

Postoperative Management

Withdrawal symptoms include anxiety, irritability, depressed mood, and lack of appetite.⁵¹ Patients with chronic cough are at risk for wound dehiscence. The patient should be observed for signs of stridor caused by upper airway edema.

CLUB DRUGS AND DESIGNER DRUGS

This is class that includes drugs that originally were used therapeutically and newer drugs that may not have consistent purity. Coingestion of multiple substances and use with alcohol are common. Some of the most popular drugs are ecstasy (methyl-enedioxymethamphetamine), lysergic acid diethylamide (LSD), PCP, ketamine, flunitrazepam (Rohypnol, "roofies") γ -hydroxybutyric acid, "bath salts," and "spice." There are few data on the effects of anesthesia on patients intoxicated with these substances, but physiologic and neurologic effects are well described.

Ecstasy/Methylenedioxymethamphetamine

The ecstasy high lasts about 6 hours and includes euphoria and relaxation. Toxicity is manifested by fever, hyponatremia, rhabdomyolysis, renal and liver failure, and death.⁵² Nondepolarizing muscle relaxers, benzodiazepines, propofol, nitroprusside, and nitroglycerin are safe.²² Atypical antipsychotics may lower the seizure threshold. Temperature should be controlled with cold fluid or a cooling blanket. Treatment with dantrolene is controversial, but has been used safely and effectively.⁵³ Hyponatremia should be corrected slowly to prevent central pontine myelinolysis. Creatine kinase or myoglobin levels can be used for suspected rhabdomyolysis. Ecstasy has also been associated with spontaneous pneumothorax and pneumomediastinum and should be suspected with any unexplained oxygenation or ventilation difficulty.⁵⁴

Lysergic Acid Diethylamide

LSD was legal until the 1960s and there is new interest in its use as an adjunct to psychotherapy. Toxic effects include hallucinations, dilated pupils, synesthesia, tachycardia, tachypnea, fever, hypertonia, and hyperglycemia. Effects last from 6 to 10 hours.⁵⁵

Phencyclidine

PCP ("angel dust") is typically inhaled, with effects lasting 4 to 8 hours. Toxic effects include nystagmus, violent behavior, tachycardia, hypertension, psychosis, coma, and cerebral hemorrhage. Supportive treatment includes benzodiazepines and

425

atypical antipsychotics.⁵⁶ Ketamine is a derivative of PCP and should not be used in these patients.⁵⁷

Ketamine

Ketamine, in its nontherapeutic use, is often snorted or ingested and called "Special K." It has a rapid onset, short duration, and induces a dissociative state. Adverse effects include confusion, apnea, nystagmus, cardiovascular dysfunction, and severe bladder toxicity.⁵⁸ Treatment is supportive. Benzodiazepines and haloperidol can be used.²² Contrary to classic teaching, ketamine does not increase intracranial pressure in either traumatic or nontraumatic brain injury.^{59,60}

Flunitrazepam

Flunitrazepam is a benzodiazepine used therapeutically in many countries. It has been used as a "date rape" drug for its sedative-hypnotic properties. Effects include slurred speech, bradycardia, respiratory depression, and coma. As with other benzodiazepines, there may be a withdrawal syndrome. Treatment may be started with a long-acting benzodiazepine, such as clonazepam. Flumazenil is used for overdoses.

γ-Hydroxybutyric Acid

 γ -Hydroxybutyric acid is an analogue of γ -aminobutyric acid and has a history of use as an anesthetic and body building supplement. More recently it has also become known as a "date rape" drug. Euphoria lasts around 4 hours, but the undesired effects of respiratory and central nervous system depression may linger and require intubation or cause death.⁶¹ A withdrawal syndrome is similar to that for alcohol, and should be treated accordingly.

Bath Salts

Bath salts cause tachycardia, hypertension, delusions, dilated pupils, and can be fatal in severe cases. Treatment with benzodiazepines and antipsychotics has been explored.⁶²

Spice

Spice was originally marketed as legal marijuana and is a synthetic cannabinoid. Effects last 2 to 4 hours and can include hallucinations, tachycardia, and seizures.⁶³

SUMMARY

Drug and alcohol use is a pervasive problem in the general population and in those requiring anesthesia for an operation. History and screening can help delineate those who may be acutely intoxicated or chronic users. The clinician should be aware of problems that may be encountered during any part of anesthesia or postoperative care.

REFERENCES

 National Survey on Drug Use and Health (U.S.), United States, Substance Abuse and Mental Health Services Administration, Office of Applied Studies, Center for Behavioral Health Statistics and Quality (U.S.). Results from the 2012 National Survey on Drug Use and Health: summary of national findings. Rockville (MD): Substance Abuse and Mental Health Services Administration; 2013. p. 1 HHS publication no (SMA) 13-4795. Online resource.

- Brown J, Kranzler HR, Del Boca FK. Self-reports by alcohol and drug abuse inpatients: factors affecting reliability and validity. Br J Addict 1992;87(7):1013–24.
- 3. Rockett IR, Putnam SL, Jia H, et al. Declared and undeclared substance use among emergency department patients: a population-based study. Addiction 2006;101(5):706–12.
- Dunham CM, Chirichella TJ. Trauma activation patients: evidence for routine alcohol and illicit drug screening. PLoS One 2012;7(10):e47999.
- 5. Sirri L, Potena L, Masetti M, et al. Prevalence of substance-related disorders in heart transplantation candidates. Transplant Proc 2007;39(6):1970–2.
- 6. Kudsi OY, Huskey K, Grove S, et al. Prevalence of preoperative alcohol abuse among patients seeking weight-loss surgery. Surg Endosc 2013;27(4):1093–7.
- Agabio R, Gessa GL, Montisci A, et al. Use of the screening suggested by the National Institute on Alcohol Abuse and Alcoholism and of a newly derived tool for the detection of unhealthy alcohol drinkers among surgical patients. J Stud Alcohol Drugs 2012;73(1):126–33.
- 8. Castell DO. The lower esophageal sphincter. Physiologic and clinical aspects. Ann Intern Med 1975;83(3):390–401.
- Fernandez-Sola J, Junque A, Estruch R, et al. High alcohol intake as a risk and prognostic factor for community-acquired pneumonia. Arch Intern Med 1995; 155(15):1649–54.
- 10. Afshar M, Smith GS, Terrin ML, et al. Blood alcohol content, injury severity, and adult respiratory distress syndrome. J Trauma Acute Care Surg 2014;76(6):1447–55.
- Guidot DM, Roman J. Chronic ethanol ingestion increases susceptibility to acute lung injury: role of oxidative stress and tissue remodeling. Chest 2002;122(Suppl 6):309S–14S.
- 12. Kaphalia L, Calhoun WJ. Alcoholic lung injury: metabolic, biochemical and immunological aspects. Toxicol Lett 2013;222(2):171–9.
- 13. Nettles JL, Olson RN. Effects of alcohol on hypoxia. JAMA 1965;194(11):1193-4.
- 14. Biancofiore G, Mandell MS, Rocca GD. Perioperative considerations in patients with cirrhotic cardiomyopathy. Curr Opin Anaesthesiol 2010;23(2):128–32.
- 15. Haxholdt OS, Johansson G. The alcoholic patient and surgical stress. Anaesthesia 1982;37(8):797–801.
- **16.** Sander M, Irwin M, Sinha P, et al. Suppression of interleukin-6 to interleukin-10 ratio in chronic alcoholics: association with postoperative infections. Intensive Care Med 2002;28(3):285–92.
- Stanley KM, Amabile CM, Simpson KN, et al. Impact of an alcohol withdrawal syndrome practice guideline on surgical patient outcomes. Pharmacotherapy 2003;23(7):843–54.
- DeMuro JP, Botros DG, Wirkowski E, et al. Use of dexmedetomidine for the treatment of alcohol withdrawal syndrome in critically ill patients: a retrospective case series. J Anesth 2012;26(4):601–5.
- 19. Weinbroum A, Rudick V, Sorkine P, et al. Use of flumazenil in the treatment of drug overdose: a double-blind and open clinical study in 110 patients. Crit Care Med 1996;24(2):199–206.
- 20. McGregor C, Machin A, White JM. In-patient benzodiazepine withdrawal: comparison of fixed and symptom-triggered taper methods. Drug Alcohol Rev 2003;22(2):175–80.
- 21. Hood SD, Norman A, Hince DA, et al. Benzodiazepine dependence and its treatment with low dose flumazenil. Br J Clin Pharmacol 2014;77(2):285–94.
- 22. Demaria S Jr, Weinkauf JL. Cocaine and the club drugs. Int Anesthesiol Clin 2011;49(1):79–101.

- 23. Birchenough SA, Borowitz K, Lin KY. Complete soft palate necrosis and velopharyngeal insufficiency resulting from intranasal inhalation of prescription narcotics and cocaine. J Craniofac Surg 2007;18(6):1482–5.
- 24. Restrepo CS, Carrillo JA, Martinez S, et al. Pulmonary complications from cocaine and cocaine-based substances: imaging manifestations. Radiographics 2007; 27(4):941–56.
- 25. Hill GE, Ogunnaike BO, Johnson ER. General anaesthesia for the cocaine abusing patient. Is it safe? Br J Anaesth 2006;97(5):654–7.
- 26. Wong GT, Irwin MG. Poisoning with illicit substances: toxicology for the anaesthetist. Anaesthesia 2013;68(Suppl 1):117–24.
- 27. Hernandez M, Birnbach DJ, Van Zundert AA. Anesthetic management of the illicit-substance-using patient. Curr Opin Anaesthesiol 2005;18(3):315–24.
- 28. de Oliveira Cito Mdo C, da Silva FC, Silva MI, et al. Reversal of cocaine withdrawal-induced anxiety by ondansetron, buspirone and propranolol. Behav Brain Res 2012;231(1):116–23.
- 29. Kaye S, McKetin R, Duflou J, et al. Methamphetamine and cardiovascular pathology: a review of the evidence. Addiction 2007;102(8):1204–11.
- 30. Hamamoto DT, Rhodus NL. Methamphetamine abuse and dentistry. Oral Dis 2009;15(1):27–37.
- **31.** Wang Y, Liu M, Wang HM, et al. Involvement of serotonin mechanism in methamphetamine-induced chronic pulmonary toxicity in rats. Hum Exp Toxicol 2013;32(7):736–46.
- 32. Chin KM, Channick RN, Rubin LJ. Is methamphetamine use associated with idiopathic pulmonary arterial hypertension? Chest 2006;130(6):1657–63.
- **33.** Fischer SP, Schmiesing CA, Guta CG, et al. General anesthesia and chronic amphetamine use: should the drug be stopped preoperatively? Anesth Analg 2006;103(1):203–6. Table of contents.
- 34. Won S, Hong RA, Shohet RV, et al. Methamphetamine-associated cardiomyopathy. Clin Cardiol 2013;36(12):737–42.
- **35.** Yeo KK, Wijetunga M, Ito H, et al. The association of methamphetamine use and cardiomyopathy in young patients. Am J Med 2007;120(2):165–71.
- **36.** Hawley LA, Auten JD, Matteucci MJ, et al. Cardiac complications of adult methamphetamine exposures. J Emerg Med 2013;45(6):821–7.
- **37.** McGregor C, Srisurapanont M, Jittiwutikarn J, et al. The nature, time course and severity of methamphetamine withdrawal. Addiction 2005;100(9):1320–9.
- **38.** Pennay AE, Lee NK. Putting the call out for more research: the poor evidence base for treating methamphetamine withdrawal. Drug Alcohol Rev 2011;30(2):216–22.
- 39. Lynch K, Greenbaum E, O'Loughlin BJ. Pulmonary edema in heroin overdose. Radiology 1970;94(2):377–8.
- **40.** Kringsholm B, Christoffersen P. Lung and heart pathology in fatal drug addiction. A consecutive autopsy study. Forensic Sci Int 1987;34(1–2):39–51.
- Richebe P, Beaulieu P. Perioperative pain management in the patient treated with opioids: continuing professional development. Can J Anaesth 2009;56(12): 969–81.
- 42. Preston KL, Bigelow GE, Liebson IA. Antagonist effects of nalbuphine in opioiddependent human volunteers. J Pharmacol Exp Ther 1989;248(3):929–37.
- **43.** Greene D. Total necrosis of the intranasal structures and soft palate as a result of nasal inhalation of crushed OxyContin. Ear Nose Throat J 2005;84(8):512, 514, 516.
- 44. Griffith CC, Raval JS, Nichols L. Intravascular talcosis due to intravenous drug use is an underrecognized cause of pulmonary hypertension. Pulm Med 2012; 2012:617531.

- 45. de Leon-Casasola OA, Lema MJ. Epidural bupivacaine/sufentanil therapy for postoperative pain control in patients tolerant to opioid and unresponsive to epidural bupivacaine/morphine. Anesthesiology 1994;80(2):303–9.
- 46. Colorado to revisit edible marijuana rules after deaths. USA Today 2014.
- 47. Tashkin DP. Airway effects of marijuana, cocaine, and other inhaled illicit agents. Curr Opin Pulm Med 2001;7(2):43–61.
- 48. Mallat A, Roberson J, Brock-Utne JG. Preoperative marijuana inhalation-an airway concern. Can J Anaesth 1996;43(7):691–3.
- Feldman AL, Sullivan JT, Passero MA, et al. Pneumothorax in polysubstanceabusing marijuana and tobacco smokers: three cases. J Subst Abuse 1993; 5(2):183–6.
- 50. Ghuran A, Nolan J. Recreational drug misuse: issues for the cardiologist. Heart 2000;83(6):627–33.
- 51. Kouri EM, Pope HG Jr. Abstinence symptoms during withdrawal from chronic marijuana use. Exp Clin Psychopharmacol 2000;8(4):483–92.
- Ben-Abraham R, Szold O, Rudick V, et al. "Ecstasy" intoxication: life-threatening manifestations and resuscitative measures in the intensive care setting. Eur J Emerg Med 2003;10(4):309–13.
- 53. Grunau BE, Wiens MO, Brubacher JR. Dantrolene in the treatment of MDMArelated hyperpyrexia: a systematic review. CJEM 2010;12(5):435–42.
- 54. Mazur S, Hitchcock T. Spontaneous pneumomediastinum, pneumothorax and ecstasy abuse. Emerg Med 2001;13(1):121–3.
- 55. Passie T, Halpern JH, Stichtenoth DO, et al. The pharmacology of lysergic acid diethylamide: a review. CNS Neurosci Ther 2008;14(4):295–314.
- **56.** Bey T, Patel A. Phencyclidine intoxication and adverse effects: a clinical and pharmacological review of an illicit drug. Cal J Emerg Med 2007;8(1):9–14.
- 57. Vadivelu N, Mitra S, Kaye AD, et al. Perioperative analgesia and challenges in the drug-addicted and drug-dependent patient. Best practice research. Best Pract Res Clin Anaesthesiol 2014;28(1):91–101.
- Corazza O, Assi S, Schifano F. From "Special K" to "Special M": the evolution of the recreational use of ketamine and methoxetamine. CNS Neurosci Ther 2013; 19(6):454–60.
- 59. Zeiler FA, Teitelbaum J, West M, et al. The ketamine effect on intracranial pressure in nontraumatic neurological illness. J Crit Care 2014;29(6):1096–106.
- 60. Zeiler FA, Teitelbaum J, West M, et al. The ketamine effect on ICP in traumatic brain injury. Neurocrit Care 2014;21(1):163–73.
- 61. Mason PE, Kerns WP 2nd. Gamma hydroxybutyric acid (GHB) intoxication. Acad Emerg Med 2002;9(7):730–9.
- Centers for Disease Control and Prevention (CDC). Emergency department visits after use of a drug sold as "bath salts"—Michigan, November 13, 2010-March 31, 2011. MMWR Morb Mortal Wkly Rep 2011;60(19):624–7.
- **63.** Harris CR, Brown A. Synthetic cannabinoid intoxication: a case series and review. J Emerg Med 2013;44(2):360–6.