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Perioperative Considerations in Patients Using and Abusing Illicit Substances

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LESSON OBJECTIVES

Upon completion of this lesson the reader should be able to:

1. Define and discuss Dependence Syndrome.
2. Describe the various recreational drugs encountered in contemporary anesthetic clinical practice.
3. Describe the anesthetic management for patients using recreational drugs.
4. Compare and contrast the different presentations of drugs of abuse.
5. Criticize the interpretation of day-of-surgery random drug screens.
6. Distinguish several medications that may yield false-positive results on drug screens.
7. Formulate a reasonable discharge plan for patients with Dependence Syndrome.
8. Detail the anesthetic-related effects of illicit substances.
9. Review and apply applicable laws governing informed consent issues in substance-abuse patients.
10. Describe the societal implications and healthcare burden of substance abuse.

Current Reviews in Clinical Anesthesia® designates this lesson for 1½ CME contact hours in Pharmacology/Therapeutics.

Introduction

The use of illicit drugs has grown to epidemic proportions in the United States, with approximately 8-10% of people ages 12 years or older addicted to alcohol or other drugs (Volkow, et al., 2016). An increasing number of patients with addiction and drug dependence are presenting for perioperative evaluation in preparation for elective surgery. **Perioperative care presents challenging issues of pain management, treatment of anxiety and psychologic states, management of intraoperative hemodynamic lability, and postoperative withdrawal.**

Up to 40% of trauma patients are found to have a history of alcohol or illicit drug use, either acutely or chronically. **Pre-injury use of illicit substances is associated with increased odds of prolonged hospital and Intensive Care Unit (ICU) length-of-stay, mortality, need for operative intervention, and need for postoperative mechanical ventilation** (Cheng, et al., 2017). In the setting of acute trauma, the ingested substance is often unknown. The American College of Surgeons recommends drug of abuse (DOA) screening for all trauma patients presenting to Level 1 and 2 Trauma Centers.

Table of Abbreviations

ASA	American Society of Anesthesiologists
BIS	Bispectral Index
CINV	Chemotherapy-induced nausea and vomiting
DOA	Drugs of abuse
EKG	Electrocardiogram
GHB	Gamma-hydroxybutyrate
HIV	Human Immunodeficiency Virus
ICU	Intensive Care Unit
LSD	Lysergic acid diethylamide
MAC	Mean alveolar concentration
MACE	Major adverse cardiac event
MAO	Monoamine Oxidase
MDMA	3,4-methylenedioxy-methamphetamine
NMDA	N-methyl-D-aspartate
PCP	Phencyclidine
PDNV	Post-discharge nausea and vomiting
PONV	Post-operative nausea and vomiting
PPC	Postoperative pulmonary complications
THC	Delta-9-tetrahydrocannabinol
WHO	World Health Organization

As drug abuse continues to grow, anesthesia providers are increasingly involved in the care of patients under the acute and chronic influence of a variety of substances alone or in combination. Anesthesia providers encounter emergency cases where the use of “club drugs” and other substances is apparent, but also where abuse is present but unrecognized. Many illicit drugs have dangerous and lethal interactions with commonly used anesthetic medications, implicating the need for increased awareness of the anesthesia care team.

This lesson does not address issues related to opioid use and abuse unless pertinent to the discussion. This topic is thoroughly covered in another lesson.

Dependence Syndrome (Substance Use Disorder)

The nomenclature around illicit drug use is confusing, but in 2016 the World Health Organization (WHO) described dependence syndrome to encompass the older terms addiction, substance use disorder, and substance misuse. WHO defines

Dependence syndrome as: “A cluster of behavioral, cognitive, and physiological phenomena that develop after repeated substance use and that typically include a strong desire to take the drug, difficulties in controlling its use, persisting in its use despite harmful consequences, a higher priority given to drug use than to other activities and obligations, increased tolerance, and sometimes a physical withdrawal state” (WHO, 2016).

The American Society of Addiction Medicine expands the definition of dependence syndrome to a chronic disease of brain reward, motivation, memory, and related circuitry (ASAM, 2017). Patients presenting for surgery may be in any of the four stages of substance abuse (Figure 1).

Addiction is a chronic brain disease.

Preoperative Approach to Patients with Dependence Syndrome

Substance abuse takes a heavy toll on the body. **Patients with dependence syndrome are physiologically older than their chronologic age.** Numerous healthcare disparities exist for substance-abusing patients. Many do not have a primary care provider and have untreated chronic disease, such as hypertension, diabetes, and heart disease. Malnutrition is a common co-morbidity. In a study of hospitalized intravenous drug users, approximately 20% had evidence of severe protein-calorie malnutrition, and 30% met other criteria for malnutrition (Cohn, et al., 2006). Chronic infection with blood-borne viruses such as hepatitis B and C and human immunodeficiency virus (HIV) is prevalent in addicts, and universal precautions should be strictly observed.

Substance-abusing patients have numerous co-existing physiologic derangements.

Primary concerns for the anesthesia provider are the likelihood of the patient exhibiting acute abuse or possible withdrawal symptoms during the perioperative period. Table 1 details some of the signs and symptoms of acute intoxication and withdrawal and management strategies for commonly encountered substances in anesthesia practice.

Perioperative Screening for Dependence Syndrome

Preoperative screening for DOA is wide-spread and of limited value in acute clinical management. The sensitivity of drug tests is limited by drug me-

Experimental use	Regular use	Problem or risky use	Addiction
<ul style="list-style-type: none"> • Recreational use for pleasurable effects • Use voluntary, infrequent, and peer influenced • Brain reward systems positively reinforce effects • Positive effects lead to continued use 	<ul style="list-style-type: none"> • User begins to miss work and school • Social isolation begins • Worry about losing access to drug • Negative feelings and emotions present when abstinent • User frequently needs "fix" • Begins to experience withdrawal feelings 	<ul style="list-style-type: none"> • User loses motivation and care for work or school • Obvious behavior changes apparent • Drug use prioritized over other interests • Cravings lead to compulsive drug seeking • User may begin dealing drugs to support habit • Harder drug use increases • Legal problems increase 	<ul style="list-style-type: none"> • User cannot face daily life without drugs • Denies existence of problem • Loss of control over drug use • User may become suicidal • Financial and legal problems worsen • Problematic relationships with family and friends

Figure 1: Stage of Drug Use

Table 1: Withdrawal Signs & Symptoms and Management

	Signs & Symptoms of Acute Abuse	Withdrawal Signs & Symptoms	Withdrawal Management
Stimulants Cocaine, Amphetamines, Methamphetamine	<ul style="list-style-type: none"> • Tachycardia • Hypertension • Myocardial ischemia • Excitement • Delirium • Sweating and fever • Euphoria 	<ul style="list-style-type: none"> • Depression • Insomnia • Fatigue • Anxiety • Paranoia • Increased appetite 	Withdrawal usually does not involve medical danger and is managed based on symptoms
Marijuana	<ul style="list-style-type: none"> • Tachycardia • Labile blood pressure • Headache • Euphoria • Anxiety/panic reactions • Depression • Dysphoria 	<ul style="list-style-type: none"> • Irritability • Aggression • Depressed mood • Restlessness • Weight loss • Headaches • Sweating • Fever and chills 	Withdrawal usually does not involve medical danger and is managed based on symptoms <ul style="list-style-type: none"> • Benzodiazepines • Synthetic cannabinoids
Hallucinogens LSD, PCP, Ketamine	<ul style="list-style-type: none"> • Altered perception and judgment • Sympathomimetic and weak analgesic effects • Toxic psychosis • PCP-dissociative anesthesia 	<ul style="list-style-type: none"> • Anxiety • Shaking • Sweating • Palpitations • Paranoia • Depression • Emotional imbalance 	<ul style="list-style-type: none"> • Benzodiazepines • Beta-blockers
Ecstasy	<ul style="list-style-type: none"> • Increased energy • Visual hallucinations • Anxiety • Panic attacks • Hyperthermia • Dehydration 	<ul style="list-style-type: none"> • Fatigue • Anxiety • Irritability • Insomnia • Loss of appetite • Inability to concentrate • Paranoid • Depression 	<ul style="list-style-type: none"> • Benzodiazepines • Anti-depressants

Table 2: False-Positive DOA Test Results

False-Positive Result	Potential Causative Agent
False-positive amphetamine/methamphetamine result	Pseudoephedrine, ephedrine, phenylephrine, Dexedrine, Benzedrine, propranolol, atenolol, levodopa, carbidopa, desoxyn, methedrine, methylphenidate, promethazine, ranitidine, trazodone, fluoxetine
False-positive opioid results	Poppy seed ingestion, salad dressings, bagels, pastries; dextromethorphan, doxylamine, quinolone antibiotics
False-positive PCP results	Over-the-counter cold medications (doxylamine, dextromethorphan), tramadol, diphenhydramine, ibuprofen, lamotrigine, sertraline, venlafaxine
False-positive LSD results	Amitriptyline, bupropion, buspirone, diltiazem, fentanyl, fluoxetine, labetalol, methylphenidate, metoclopramide, prochlorperazine, risperidone, sertraline, trazodone, verapamil
False-positive cannabinoid or marijuana results	Hemp-containing food products, rare medication exposures (Marinol, Dronabinol), Cesamet, ibuprofen, naproxen

tabolism, last consumption, and the testing facility. **While it is unclear if the results directly affect clinical management, due to the length of time that test results are positive, such screening may identify the patient at risk for withdrawal.** Selective rather than routine testing is more cost-effective and beneficial.

What does a positive DOA test mean?

There are several modalities for DOA testing. **A positive result on a DOA screening means that the DOA of interest or its metabolite is present at or above the threshold concentration at the time of sample collection.** A positive DOA test neither implies acute intoxication nor that the DOA is present in clinically significant quantities since metabolites may be detected long after the acute phase has ended. The time after use for which a DOA test remains positive is highly variable, typically beginning within minutes of consumption and lasting for days to weeks. [Figure 2] Urine drug screen testing for cocaine is an unreliable indicator of acute intoxication since it only

The results of urine drug screening can be misleading and result in unwarranted case delays and cancellations.

tests for an inactive metabolite. This concept leads to considerable misunderstanding and results in unwarranted case delays and cancellations on the day of surgery. **DOA assays, particularly immunoassays, have poor sensitivity and specificity with a 5-10% rate of false-positive and a**

10-15% rate of false-negative results (Table 2) (Drugs.com, 2019).

When to cancel and when to proceed?

Surgical case cancellation leads to substantial financial losses for healthcare institutions and is wasteful of resources. The decision to cancel or proceed with scheduled surgery based on a positive DOA test is the responsibility of the anesthesia and surgical care teams at the time of evaluation. Elective surgery should be delayed or canceled in patients clinically suspected of being acutely under the influence of an illicit substance until further evaluation occurs. **A positive DOA screen result should not be the sole determinant of case cancellation.**

Acute drug intoxication should be diagnosed by clinical findings rather than laboratory values.

Physiologic and Perioperative Considerations of Substances of Abuse

Methamphetamine

Acute amphetamine intoxication can cause hyperthermia and increases the patient's anesthetic requirements. On presentation, methamphetamine-toxic patients are hypertensive with tachyarrhythmias and may be acutely psychotic.

Amphetamines	<ul style="list-style-type: none"> • Urine: 2-5 days • Blood: up to 12 hours • Saliva: 1-5 days; Hair: up to 90 days
Methamphetamine	<ul style="list-style-type: none"> • Urine: 1-4 days. Heavy use: up to a week • Blood: 1-3 days • Saliva: 1-4 days; Hair: up to 90 days
Cocaine	<ul style="list-style-type: none"> • Urine: 1-3 days • Blood: 1-3 days • Saliva: 1-2 days; Hair: up to 90 days
Marijuana	<ul style="list-style-type: none"> • Urine: 13-90 days, depending on regularity of use • Blood: a few hours • Saliva: a few hours; Hair: up to 90 days
PCP	<ul style="list-style-type: none"> • Urine: 1-7 days; Heavy use: 1-4 weeks • Blood: 24 hours • Saliva: 1-10 days; Hair: up to 90 days
LSD	<ul style="list-style-type: none"> • Urine: 8 hours • Blood: 6-12 hours • Hair: 3 months
Ketamine	<ul style="list-style-type: none"> • Urine: 14-30 days • Blood: 24 hours • Hair: several months
GHB	<ul style="list-style-type: none"> • Urine: 12 hours • Blood: 2.5-4 hours • Hair: not described

Figure 2: Positive Drugs of Abuse Test Results

Chronic methamphetamine users behave physiologically as a poorly-controlled hypertensive patient. While the patients are usually younger, their physiology is much older due to chronic methamphetamine exposure.

Preoperative considerations: Long-term amphetamine use depletes presynaptic catecholamine stores rendering chronic users vulnerable to hypotension. Direct-acting vasopressors should be used to augment blood pressure. Patients admitted following a stimulant binge present as irritable or acutely psychotic, only to become intensely somnolent once the drug wears off. This somnolence may be mistaken for hypoactive delirium, depression, or opioid overdose, but is benign and resolves spontaneously.

Intraoperative considerations: Heart rate control and maintenance of blood pressure are key

anesthetic considerations due to impaired cardiovascular function. An airway exam is vital since many users have severely decayed and fractured teeth due to the caustic substances involved in the manufacture of methamphetamine.

Hallucinogens (LSD, PCP, Ketamine)

LSD, PCP, peyote (mescaline), psilocybin, and ketamine are the most commonly used hallucinogens. The substances have similar effects, but the mechanisms of action are different. **Ketamine and PCP are nonspecific N-methyl-D-aspartate (NMDA) receptor antagonists, while the remainder act primarily on serotonin receptors (5-HT_{2A}).** Short-term effects include hallucinations, tachycardia, nausea, and altered perception of time. Persistent psychosis and flashbacks occur mainly with long-term use. **Ketamine (the**

Table 3: Perioperative Cardiovascular Complications of Cocaine Use

- **Stroke**
- **Myocardial infarction**
- **Dysrhythmia**
- **Angina**
- **Hypertension**
- **Tachycardia**
- **Prolonged QT-interval**
- **Coronary vasospasm**
- **Aortic dissection**

most widely used drug of this class), and PCP cause nystagmus, a feature that distinguishes these substances from the other hallucinogens and substances (Beaulieu, 2017). Withdrawal symptoms include anxiety, shaking, sweating, and palpitations, and may persist for up to two weeks. Benzodiazepines and beta-blockers are useful for managing these withdrawal symptoms.

PCP is similar to ketamine and thought to have several central nervous system sites of action, all synergistically acting to produce varying degrees of anesthesia and analgesia. In addition to its NMDA receptor affinity, PCP also acts at serotonin, norepinephrine, dopamine, and opioid receptors. Patients with PCP intoxication present with violent behavior with perceptions of superhuman strength, acute schizophrenia, nystagmus, blank staring, tachycardia, hypertension, and anesthesia and analgesia. Higher doses are associated with coma with open eyes.

Preoperative considerations: PCP and LSD have anticholinergic properties and cause inhibition of monoamine oxidase (MAO), which potentiates the effects of endogenous serotonin and histamine. Effects include hypo- or hyperthermia, tachycardia, and salivation (Haldar, et al., 2015).

Intraoperative considerations: Anesthetic management entails managing hyperdynamic drug effects, such as tachycardia and hypertension. Anesthesia providers should anticipate an exaggerated response to vasopressors, particularly indirect-acting agents such as ephedrine. Hypotension should be managed with direct-acting agents, such as phenylephrine. Hallucinogens prolong the analgesic and respiratory suppressant effects of opioids. **LSD and PCP inhibit plasma cholinesterase and prolong the effects of succinylcholine. The anticholinergic properties of these agents likely also potentiates the non-depolarizing neuromuscular blocking drugs.** Desflurane should be used cautiously to avoid worsening tachycardia.

Cocaine

Cocaine use is a known risk factor for perioperative cardiovascular complications, as noted in Table 3. This association prompts many anesthesia providers to cancel or delay elective surgery in the presence of a positive DOA screen despite cocaine having a half-life of 60-90 minutes (with inactive metabolites detected in urine up to 10 days following usage). Most cocaine-related perioperative deaths result from pathophysiology developed from long-term use and not from acute overdose. MACE risk is not reduced by delaying for a negative test (Saggese, et al., 2019).

Preoperative considerations: Patients who are acutely intoxicated on cocaine display a hyperdynamic state characterized by a significant increase in cardiac output coinciding with intense vasoconstriction and direct sympathetic cardiac stimulation. Isolated treatment with beta-blockers intensifies the alpha-agonist effect and worsens hypertension, which may lead to myocardial ischemia or infarction, malignant arrhythmias (such as ventricular tachycardia or fibrillation) or death.

Laboratory testing for drugs-of-abuse is complex and requires careful attention to the timing of specimen collection and interpretation of results.

Current evidence indicates that elective general anesthesia in cocaine-positive patients with preoperative cardiovascular stability (normal blood pressure, heart rate, temperature, and electrocardiogram), imparts no higher MACE risk than drug-free patients of comparable age and ASA physical status. Chronic cocaine users have higher analgesic requirements.

Intraoperative considerations: Emergent anesthetic management in the acutely-intoxicated cocaine user centers around minimizing hemodynamic extremes and avoiding precipitating coronary vasospasm. Induction, laryngoscopy, and intubation may worsen hypertension in acutely-intoxicated patients. As noted above, treatment of hypertension with pure beta-blockers exacerbates the alpha-agonist effect of cocaine leading to cardiovascular complications.

Marijuana

About 35 million (some surveys quote 55 million) US adults are classified as regular users of marijuana, defined as at least once or twice a month usage (Ingraham, 2017). This number will likely increase as more states legalize marijuana consumption (Table 4). **Chronic marijuana use is associated with many of the same long-term effects seen with cigarette use, such as**

Table 4: States where Marijuana Use is Legal

Recreational & Medical Use	Medical Use Only
Washington Oregon California Nevada Colorado Alaska Illinois Vermont Massachusetts Maine	New Hampshire Rhode Island Connecticut New York Pennsylvania New Jersey Delaware Maryland West Virginia Ohio Michigan Minnesota Arkansas Louisiana Florida Oklahoma North Dakota Montana New Mexico Arizona Hawaii

lung cancer and other respiratory illnesses.

Regular use of marijuana leads to many of the same perioperative adverse outcomes as smoking traditional cigarettes, such as an increased incidence of postoperative pulmonary complications and surgical site infections (Whitlock, 2019). Several case studies describe airway hypereactivity and hemodynamic lability in patients who smoked marijuana 4-hours before surgery. Regular use of marijuana is also associated with the need for increased anesthetic drug dosing.

Marijuana is often cut (combined) with hallucinogens such as PCP or other dangerous drugs. In this situation, the side effects of the other drugs, such as acute hypertension, chest pain with heart rhythm disturbances, seizures, strokes, cardiac arrest, may manifest.

Marijuana use is common and has several anesthetic-related effects.

Marijuana use is a known risk factor for myocardial infarction and stroke. The cardiovascular effects of marijuana range from benign to problematic in a time and dose-dependent manner. Acute usage at low or moderate doses is associated with sympathetic stimulation, with tachycardia beginning with inhalation and persisting for about 90 minutes. Systolic and diastolic hypertension result

along with premature ventricular contractions, a Brugada-like pattern on EKG, atrial fibrillation, and advanced degrees of atrioventricular block. Higher doses result in parasympathetic stimulation leading to bradycardia and hypotension. It is postulated that higher doses result in THC blockade of CB-1 receptors. Table 5 details some of the signs of acute marijuana use in adolescents and adults.

Synthetic Cannabinoids: Synthetic cannabinoids are various synthetic chemicals used as an alternative to marijuana. They are increasingly popular in the US and Europe and sold under various names, such as synthetic marijuana, Spice, and K2, via the internet or in paraphernalia shops. These substances have serious side effects relative to natural marijuana, including an increased incidence of tachycardia, vomiting, agitation, confusion, and hallucinations.

Perioperative considerations: There is relatively little data investigating perioperative marijuana use and its effect on surgical outcomes. The general consensus is that its effect on outcomes mirrors that of traditional cigarette smoking (increased risk of surgical site infections, reintubation, and postoperative pulmonary complications). **Preoperative marijuana abstinence, similar to that seen with smoking cessation, reduces the risk of adverse outcomes.** When conducting the Preanesthetic Assessment, patients should be advised to abstain from marijuana use for 12-hours before surgery. This period allows for the elimination of carboxyhemoglobin. Carboxyhemoglobin levels of 15% decrease

The health effects of synthetic cannabinoids are unpredictable, harmful, and life-threatening.

the oxygen availability by up to 25% and increase the risk for patients with coronary artery disease. With long-term use, THC is stored in adipose tissue for up to 30-days, maintaining steady levels of THC in the circulation, rendering the utility of an abstinence period debatable in chronic users. The use of cannabinoids and marijuana has demonstrated efficacy in the reduction of chemotherapy-induced nausea and vomiting (CINV), leading some patients to advocate use for post-operative (PONV) or post-discharge nausea and vomiting (PDNV) prophylaxis. The use of marijuana or cannabinoids for PONV or PDNV prophylaxis is not efficacious and results in a hyperemesis syndrome.

Intraoperative considerations: Significantly higher induction doses of propofol to achieve a Bispectral Index (BIS) less than 60 are required in marijuana users compared to nonusers (Alexander, et al., 2019). While less information is available about the effects of marijuana use on anesthetic

Table 5: Signs of Marijuana Intoxication in Adolescents and Adults

- **Hemodynamic lability**
 - Tachycardia
 - Hypertension
 - Orthostatic hypotension, especially in the elderly
- **Airway hyperreactivity**
- **Tachypnea**
- **Red eye**
- **Dry mouth**
- **Increased appetite**
- **Nystagmus**
- **Ataxia**
- **Slurred speech**
- **Panic**
- **Paranoia**
- **Acute psychosis**

maintenance, anecdotal data suggests that acute intoxication decreases the mean alveolar concentration (MAC) of volatile anesthetic agents while chronic use increases MAC. In addition to altered propofol dosing requirements, **THC is associated with potentiation of non-depolarizing neuromuscular blocking agents due to depletion of acetylcholine stores**, potentiation of norepinephrine, augmentation of cardiopulmonary depressant effects of opioids and sedatives, and sensitization of the myocardium to catecholamines. Chronic marijuana smoking causes airway hyperreactivity and is a significant cause of intraoperative complications.

Gamma Hydroxybutyrate (GHB) and Flunitrazepam (Rohypnol®)

Gamma-hydroxybutyrate (GHB) is a central nervous system depressant used recreationally for its intoxicating effects. It is ingested orally and metabolized by the liver. All traces of GHB typically vanish from the body within 3 to 10 hours, leading to its clandestine use for the facilitation of sexual assault. GHB intoxication causes respiratory depression, seizures, and coma.

Flunitrazepam is a benzodiazepine with an onset of about 15 minutes lasting up to 12-hours. Like GHB, it is used in the perpetration of sexual assault. Urine drug testing detects the presence of a pharmacologically-active metabolite to confirm consumption. As with other benzodiazepines, the sedative effect is compounded by concurrent use of alcohol, opioids, or other substances, increasing the risk of respiratory depression or coma.

Perioperative considerations: Patients acutely intoxicated with GHB require supportive

care and definitive airway establishment. They usually present with drowsiness, loss of consciousness, visual disturbances, confusion, seizures, respiratory arrest, hypothermia, and coma with higher doses. Sudden awakening and rebound agitation occur as effects dissipate. Management of flunitrazepam-intoxicated patients is similar to those who have ingested other benzodiazepines, GHB, or alcohol. Reversal with flumazenil risks precipitating seizures or acute withdrawal.

Intraoperative considerations: GHB-intoxicated patients are usually simultaneously intoxicated on alcohol, resulting in reduced MAC requirements. Those patients who chronically use GHB may develop intra- or postoperative withdrawal signs such as sudden unexpected cardiovascular stimulation, and should be managed aggressively with drugs that increase the seizure threshold, such as midazolam. Intraoperative hemodynamic instability may indicate the onset of withdrawal from flunitrazepam and requires appropriate management such as a long-acting benzodiazepine taper with clonazepam (Klonopin®).

Ecstasy (MDMA)

Ecstasy or MDMA (3,4-methylenedioxymethamphetamine) is a synthetic drug with properties of both hallucinogens and methamphetamine. Ecstasy is a standard “rave drug” usually consumed in party settings associated with overnight dancing. Consumption produces feelings of increased energy, pleasure, emotional warmth, and distorted sensory and time perception. Cortisol levels increase, and most users report pleasant visual hallucinations, while others experience anxiety and panic attacks. Intense physical activity and overexertion with little fluid intake results in hyperthermia, rhabdomyolysis, or heat stroke. Other reported adverse effects include metabolic acidosis, hypertension, arrhythmias, and disseminated intravascular coagulopathy.

Withdrawal symptoms, such as fatigue, anxiety, insomnia and irritability usually begin about three days after the last usage and last about one week. Benzodiazepines and beta-blockers are useful for symptom management.

Preoperative considerations: Hyperthermia and dehydration are anesthetic concerns in ecstasy-toxic patients, and are significant causes of ecstasy-related mortality (Bryson, et al., 2012). The clinical presentation is often confused with neuroleptic malignant syndrome or serotonin syndrome (in presentation and severity). Sympathetic stimulation produces tachycardia, hypertension, and in rare cases, acute myocardial infarction and dilated cardiomyopathy. Significant hypotension follows this hyperdynamic phase due to catecholamine depletion. Hyponatremia results from excessive thirst and triggers seizures and altered

mental status. The aftermath of ecstasy use results in depression, anxiety, myalgias, and fatigue, and usually resolve without requiring treatment.

Intraoperative considerations: Induction with propofol or etomidate is appropriate. Induction with ketamine may worsen the sympathetic stimulation or result in myocardial depression due to catecholamine depletion. Volatile anesthetic agents and non-depolarizing neuromuscular blocking agents are safe. Intraoperative hypertension and tachycardia should be treated with labetalol, as pure beta-blockers may worsen hypertension. Hypotension responds to fluid administration or direct-acting vasopressors such as phenylephrine. Indirect-acting agents such as ephedrine should be avoided to prevent an intense endogenous catecholamine release. Hyperthermia management entails cold fluids and active cooling.

Pain Management in Patients with Dependence Syndrome

A well-developed, multimodal plan involving regional analgesia for postoperative pain management is particularly crucial for chronic marijuana smokers and users of cocaine and methamphetamine. Studies in trauma patients suggest that postoperative opioid analgesic requirements are 40% higher in users of these substances compared to non-users (Salottolo, et al., 2019). Chronic marijuana smokers depend entirely on coughing to clear respiratory secretions, and abdominal splinting increases the likelihood of atelectasis, worsening shunt, hypoxia, and the development of PPCs. Withdrawal from marijuana

Postoperative pain management in patients with dependence syndrome is challenging.

is not life-threatening and usually manifests as anxiety and agitation. **In addition to increasing PONV, rebound hyperalgesia increases the need for postoperative pain medication.**

A common perception among perioperative patients is that marijuana and synthetic cannabinoids help decrease postoperative pain. Marijuana and cannabinoids are used for the management of certain chronic pain conditions, but efficacy is not established for acute pain management. Studies show higher postoperative pain scores and greater analgesic use among marijuana users (Alexander, et al., 2019). Even though evidence supports the analgesic effects of marijuana in chronic pain conditions, long-term users experience increased acute postoperative pain. **Enhanced Recovery and Multimodal Pain Management protocols**

are effective in improving postoperative pain management.

Discharge Considerations and Relapse Prevention

Discharge planning begins at hospital admission and should ensure that patients are discharged into a safe and supportive environment. Early consultation with hospital social workers allows sufficient time to formulate a discharge plan to minimize relapse. Communication with primary care providers, pharmacists, and drug treatment services helps ensure that patients re-engage with community support services. When opioids are required for pain control on discharge, immediate-release formulations are recommended, even though these medications carry a higher diversion and overdose risk (Quinlan, et al., 2017). Naloxone should also be included in the discharge prescriptions. Patients should be given small quantities of opioids and have frequent follow-up appointments to ensure adequate pain management and diversion prevention.

Issues of Informed Consent in Substance Abusing Patients

When DOA screening is felt clinically indicated, the anesthesia provider should have a careful discussion with the patient or patient and parents in the case of children and adolescents. State laws differ in terms of ages at which adolescents can consent to medical treatment. In Alabama, it is 14 years of age. Moreover, whether the adolescent's parents must be notified when the adolescent consents to treatment or testing also varies by state. **If emergent clinical and surgical care for a patient, adolescents included, is required following events such as attempted suicide, motor vehicle collision or other scenarios where drug intoxication is suspected, consent is implied, and written permission for treatment or testing is not required** (Hadland, et al., 2016).

Laws pertaining to informed consent vary from state-to-state.

A point of debate centers around whether or not patients who chronically use illicit substances or even chronic legal use of marijuana in individual states can sign a surgical consent form. The American Surgical Association states that if a patient appears acutely intoxicated from substance use, then he or she is not able to consent to surgery. If the patient is cognitively normal and competent,

then they are capable of giving informed consent (Spader, 2018). This issue makes it necessary to document the patient's mental status on the Pre-anesthetic Evaluation before obtaining procedural consent.

Societal and Health Care Burden of Substance Abuse

Substance abuse is a costly problem. The US spends nearly \$1 trillion annually on drug-related crime, decreased productivity, and healthcare, an amount equal to 5% of the US gross domestic product (Cidambi, 2017). The societal costs of drug abuse go beyond just the financial aspect. Indirect costs include the spread of infectious diseases such as HIV and hepatitis C, death from overdose, effects on unborn children, as well as increased crime, unemployment, domestic abuse, divorce, and homelessness. Loss of workplace productivity costs more than \$120 billion per year and includes reduced labor participation, incarceration, hospitalization, and participation in drug treatment programs.

The National Drug Intelligence Center (NDIC) estimates the annual healthcare costs in the US related to substance abuse of greater than \$11 billion. This figure includes both direct and indirect costs attributable to medical intervention, emergency services, inpatient drug treatment, and prevention and treatment research (NDIC, 2019).

Summary

The use of illicit drugs is a significant healthcare and public health problem in the United States. Acute and chronic perioperative substance abuse presents many challenges to anesthesia providers. **In addition to alterations in MAC and analgesic requirements, these patients often have unaddressed physiologic derangements such as uncontrolled hypertension, unrecognized coronary artery disease, and malnutrition.** A team-oriented, multidisciplinary, and multimodal approach is the best means of providing postoperative analgesia to minimize issues of drug relapse and diversion. An accurate history of illegal substance use is often difficult to obtain due to fears of legal repercussions or refusal to acknowledge that a problem exists. Consequently, numerous healthcare disparities exist with regard to this patient population. Obtaining an accurate history of substance abuse either from the patient or friends and family will allow for safer anesthetic planning and disparity reduction.

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Tips for Your Clinical Practice: Key Points

- An increasing number of patients with addiction and drug dependence are presenting for surgery. They present **challenging issues** of pain management, anxiety, hemodynamic lability and postoperative withdrawal.
- **Drug screening tests**, although wide-spread, are of little value in clinical management. The length of time that drugs of abuse (and/or their metabolites) can test positive are variable. Selective drug tests are more beneficial.
- **Surgery cancellation** should not be based on a positive drug screening test. Delay or cancellation of surgery should be based on the decision of whether the patient is acutely under the influence of a DOA.
- As many states are legalizing the use of marijuana, anesthesia providers will be encountering an increasing number of marijuana using patients. **Chronic marijuana use** is associated with the same long-term effects seen in smokers (i.e., lung cancer and respiratory illnesses).
- **Acute marijuana intoxication** is associated with hemodynamic lability and airway hyper-reactivity, both of which are of particular importance to anesthesia providers.
- The drug abusing patient may respond aberrantly to the analgesics administered to treat **postoperative pain**. A multimodal approach to pain management is important. It can minimize the issues of drug relapse and diversion.
- **Drug withdrawal** may present in the postoperative period in patients with Dependence Syndrome.

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1. **According to the American Society of Addiction Medicine, dependence syndrome is defined as:**
 - ☐ A. A chronic mental health condition characterized by schizophrenia and mood disorder.
 - ☐ B. A chronic disease of brain reward, motivation, memory, and circuitry.
 - ☐ C. A chronic condition including persistent problems of sustaining attention accompanied by hyperactivity and impulsive behavior.
 - ☐ D. A chronic mental health disorder with persistent feelings of sadness or loss of interest leading to a range of behavioral and physical symptoms.
2. **The stage of substance use/abuse where the user begins to miss school or work and worries about losing access to a drug is:**
 - ☐ A. Experimental use.
 - ☐ B. Regular use.
 - ☐ C. Problem or risky use.
 - ☐ D. Addiction.
3. **A positive result on a drug-of-abuse screening test means that:**
 - ☐ A. A patient recently used an illegal substance and the surgery should be canceled.
 - ☐ B. The DOA of interest or its metabolite is present at or above the threshold concentration at the time the sample was obtained.
 - ☐ C. The patient is at higher risk for intraoperative major adverse cardiac events.
 - ☐ D. Surgery should be delayed for 8 hours to allow for more extensive testing.
4. **A 35-year old female presents for an out-patient arthroscopic anterior cruciate ligament reconstruction. A urine drug test is performed which is positive for LSD. Despite emphatic denial of drug use by the patient, the surgery is cancelled. What prescription medication could explain a false-positive result:**
 - ☐ A. Sertraline (Zoloft®).
 - ☐ B. Quinolone antibiotics (Cipro®).
 - ☐ C. Promethazine (Phenergan®).
 - ☐ D. Atenolol (Tenormin®).
5. **The effects of ketamine are mediated by antagonism of which receptor:**
 - ☐ A. NMDA receptors.
 - ☐ B. Serotonin receptors.
 - ☐ C. Beta adrenergic receptors.
 - ☐ D. Muscarinic receptors.
6. **Which of the following medications prolongs the effects of succinylcholine by inhibiting plasma cholinesterase:**
 - ☐ A. PCP.
 - ☐ B. GHB.
 - ☐ C. Marijuana.
 - ☐ D. Cocaine.
7. **Which of the following is an anesthetic-related effect of marijuana use:**
 - ☐ A. Reduces respiratory depressant effects of opioids.
 - ☐ B. Prolongs the duration of action of rocuronium.
 - ☐ C. Induction dose of propofol are reduced.
 - ☐ D. Lower carboxyhemoglobin levels.
8. **An 18-year-old female patient presents following a motor vehicle collision and requires emergency fracture stabilization. She is tachycardiac, hypertensive, and acutely psychotic. Her accompanying friend states that they were at a dance party and using hallucinogenic substances. Examination of the eyes reveals the presence of nystagmus. What class of substances was the most likely ingested:**
 - ☐ A. Methamphetamine.
 - ☐ B. Cocaine.
 - ☐ C. Hallucinogens.
 - ☐ D. Ecstasy.
9. **For the patient described above, it is determined that a drug screening test is indicated to further guide clinical management. How should the patient be consented for the drug screening test:**
 - ☐ A. Consent should be obtained from her parents.
 - ☐ B. Consent should be obtained from her friend.
 - ☐ C. Consent should be obtained from the courts.
 - ☐ D. Consent is implied and written permission is not required.
10. **Hospital discharge planning begins at:**
 - ☐ A. Discharge.
 - ☐ B. Admission.
 - ☐ C. Time of surgery.
 - ☐ D. Diagnosis.

CORRECT ANSWERS TO LESSON 21 VOLUME 40 (NELSON)

1. D 2. C 3. C 4. A 5. D 6. B 7. A 8. C 9. B 10. A