General considerations

Substance abuse has a high prevalence but is usually underreported. As a history and physical examination might not gain enough information from patients, obtaining a urine test is very useful. In certain cases, e.g., emergency or trauma cases, a toxicity screen, “tox screen,” as it is known colloquially, drawn preoperatively can be of great value. Even though the report may take several hours, the results can be of great help in the immediate postoperative period when a patient exhibits unusual physiological states that are otherwise difficult to diagnose.

Effects of behaviorally active substances not only alter patient physiologic status but also interact with a number of medications and anesthetic agents, which can complicate anesthesia even in young healthy people. Intoxicated patients cannot provide reliable information and often are not able to cooperate, which will limit some choices of anesthesia (regional anesthesia, awake intubation). Moreover, chronic drug abusers usually have psychological and physical comorbidities that make anesthesia more complicated. Specific concerns and anesthetic implications for individual substances will be discussed below.

Tobacco

Mechanism of action: tobacco contains more than 3,000 active substances, including nicotine and carbon monoxide. Nicotine stimulates nicotinic cholinergic receptors, causing sympathetic stimulation, increased HR, BP, and myocardial contractility. Carbon monoxide avidly binds to Hb (it has 210 times the binding capacity of oxygen) forming carboxyhemoglobin, which results in lower available stores of oxyhemoglobin, resulting in decreased tissue oxygenation. Hemoglobin, a tetramer, contains four oxygen-binding sites. The binding of carbon monoxide at one of these sites increases the oxygen affinity of the remaining three sites, which causes the hemoglobin molecule to retain oxygen that would otherwise be delivered to the tissue. This effect causes a shift to the left of the oxyhemoglobin dissociation curve. Heavy cigarette smokers, i.e., one to two packs per day, can have their oxyhemoglobin reduced by up to 8% to 9%. It is also thought that cigarette smoking may impair the viability of tissue flaps, perhaps from the effects of chronic elevated carbon monoxide levels on tissue oxygenation. Tobacco increases airway irritability and decreases mucociliary clearance. Long-term smoking also is associated with COPD, CAD, PVD, and stroke.

Smoking increases the risk of postoperative complications. Pulmonary complications (laryngospasm, pneumonia, respiratory failure, and ICU admission), potentially increase cardiovascular complications, impair tissue oxygenation, and lead to impaired wound healing.

Smoking cessation should be encouraged before elective surgery. Even only 12 to 24 hours of cessation will decrease carboxyhemoglobin levels and increase tissue oxygenation; 48 to 72 hours of cessation may lead to increased airway secretion and airway reactivity. One to two weeks may be enough to reduce sputum volume, but at least four to eight weeks of cessation is required to reduce pulmonary complications.
Alcohol

**Mechanism of action:** alcohol appears to act at GABA-A receptors at a specific ethanol-binding site and causes CNS depression starting from sedation and euphoria, but higher doses lead to disinhibition, impaired motor control, coma, impaired airway reflex, and aspiration. Benzodiazepines, such as oxazepam (Serax®), are useful in preventing delirium tremens (the DTs). It is thought that benzodiazepines, by binding to the benzodiazepine site at the GABA-A receptor, mimic the action of ethanol and induce a state of neuronal quiescence, thereby preventing the excitatory clinical manifestations of DTs.

**Acute intoxication** can delay gastric emptying time, leading to increased risks of aspiration; ethanol-induced hypoglycemia can worsen mental status; CNS depression induced by ethanol decreases anesthetic requirements during acute intoxication.

**Chronic alcohol abuse** is associated with gastritis, alcoholic cirrhosis, chronic pancreatitis, peripheral neuropathy, cardiac beriberi, Wernicke’s encephalopathy (vitamin B₃ should be administrated to prevent worsening cardiac beriberi or Wernicke’s encephalopathy). Withdrawal symptoms and delirium tremens can occur 6 to 48 hours following last alcohol consumption. Moreover, as alcohol is a liver enzyme inducer, chronic alcohol abuse tends to require higher concentrations/doses of anesthetic agents.

Opioids

**Mechanism of action:** opioids bind μ receptors, both μ₁ (analgesia) and μ₂ (respiratory depression), and cause euphoria, analgesia, and respiratory depression.

**Acute effects:** the most severe deleterious effect of strong μ agonists is opioid-induced respiratory depression, which consists of sedation, reduced respiratory rate, hypoxia, and pupillary constriction, progressing to coma and apnea in severe cases. Severe respiratory depression often results in unsuspecting clients who buy unusually potent lots of narcotic, such as heroin. Management consists of maintaining airway patency, supporting ventilation/oxygenation and, if necessary, an antidote (naloxone) can be carefully administered. It should be noted that a number of emergency facilities stock intranasal naloxone for use in suspected narcotic overdose. Opioids may delay gastric emptying time and place patients at increased risk of aspiration. Rapid sequence induction should be considered for intubation.

**Chronic effects:** chronic opioid users may develop tolerance and withdrawal symptoms (agitation, hypertension, tachycardia, lacrimation, and diarrhea). Naloxone and mixed agonist-antagonist agents are relatively contraindicated as they can precipitate withdrawal symptoms.

Intravenous drug users may exhibit difficult IV access, infective endocarditis, HIV, and hepatitis infection. However, chronic opioid users also include chronic pain patients and patients receiving opioid maintenance therapy for opioid dependence. It is very important in patients receiving high doses of opioids on a long-term basis for legitimate conditions (chronic pain, cancer, chronic pancreatitis) not to be judgmental and accuse them of drug-seeking behaviors when they present for emergent procedures. Although physicians are under great pressure to curb narcotic prescriptions in the case of abusers, the medical profession must be aware of legitimate narcotic use and take care not to embarrass or emotionally traumatize these patients.

**Opioid and elective surgery:** baseline opioids (morphine, methadone) should be maintained to control baseline pain levels and prevent withdrawal symptoms.

**Buprenorphine and elective surgery:** if patients who take mixed agonist–antagonist (buprenorphine or Subutex®, buprenorphine plus naloxone or suboxone) agents undergo major surgery (expecting considerable postoperative pain, as in joint replacement, laparotomy, thoracotomy), they should stop them one to three days before surgery (depending on the dose patients have been taking) to prevent their antagonist effect against postoperative opioids. Supplements of low-dose opioids may be needed at this time to prevent withdrawal symptoms. These mixed agents may be resumed postoperatively when acute pain is no longer an issue and large doses of potent narcotics are no longer needed.

For minor procedures (where severe pain is not expected, as in endoscopic procedures) patients should continue these medications until the morning of surgery to prevent withdrawal symptoms.

**Postoperative pain control:** as chronic opioid users usually develop opioid tolerance, postoperative pain control strategies also include the expectation of higher opioid requirements compared to opioid naïve patients, patient-controlled analgesia, and multimodal therapy (e.g., nonsteroid anti-inflammatory drugs, NMDA antagonist [ketamine, dextromethorphan], antiepileptic [Gabapentin], regional anesthesia [nerve block, neuraxial block].

Cocaine

**Mechanism of action:** cocaine blocks dopamine, serotonin, and norepinephrine reuptake, which results in CNS stimulation, manifested as euphoria and intoxication. Cocaine also stimulates the sympathetic nervous system (SNS), causing vasoconstriction, hypertension, tachycardia, arrhythmia, and can lead to myocardial infarction, cardiomyopathy, and aortic dissection.

**Acute effects:** with acute cocaine use, CNS stimulation results in increased anesthetic requirements. SNS stimulation results in hypertension, but beta-blockers are relatively contraindicated for treating the hypertensive effect from cocaine, as unopposed alpha activity could worsen hypertension (labetalol, which has some alpha blockage activity, may be less problematic). On the other hand, patients might have exaggerated hypertension with ephedrine and ketamine.
**Chronic effects:** as chronic cocaine use leads to depletion of the aforementioned neurotransmitters, patients will experience the opposite physiologic change of acute users. Patients require less anesthetic agents and have a lack of response to ephedrine. Cocaine-induced thrombocytopenia in chronic users might complicate regional anesthesia. Moreover, cocaine smokers are prone to respiratory complications, such as perforated nasal septum, pulmonary infiltrates, and pulmonary edema.

**Cocaine and elective surgery:** cocaine can last in the urine for two to three days. There is clinical evidence showing that if patients test positive for urine cocaine, but are clinically non-toxic and do not have an extensive cardiac history, they are at no greater risk, compared to drug-free patients, for proceeding to a surgical procedure.

**Amphetamine**

**Mechanism of action:** amphetamines release catecholamine, dopamine, and serotonin from presynaptic nerves, leading to euphoria, CNS stimulation, and SNS stimulation.

**Acute effects:** like cocaine, increased anesthetic requirements, hypertension, and tachycardia.

**Chronic effects:** chronic abuse causes neurotransmitter depletion (see above), resulting in decreased anesthetic requirements and downregulation of adrenergic receptors.

### Table 13.1 Common substances and clinical implications

<table>
<thead>
<tr>
<th>Substances</th>
<th>Mechanism of actions</th>
<th>Systemic effects</th>
<th>Clinical implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco (smoked)</td>
<td>Nicotine stimulates</td>
<td>Nicotine stimulates SNS (increases HR, BP)</td>
<td>Increased pulmonary complication (laryngospasm, bronchospasm, atelectasis, respiratory failure, mechanical ventilator) and impaired wound healing. Cessation of 24 hours will reduce CO–Hb level but needs more than four to eight weeks to decrease pulmonary complications. Concern for specific comorbid disease</td>
</tr>
<tr>
<td></td>
<td>nicotinic cholinergic</td>
<td>CO shift of oxygen dissociation to the left. Overall effects: increased airway irritability, increased mucous production, decreased mucociliary clearance. Associated with COPD, CAD, PVD, stroke, and many cancers.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>receptor</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Carbon monoxide</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other substance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Opioids (smoked, ingested, IV)</td>
<td>Mu receptor agonist</td>
<td>Acute: impair cognition, respiratory depression, delay gastric emptying time. Chronic: tolerance to opioids for pain control, withdrawal. IVDU associated with infective endocarditis.</td>
<td>Acute: at risk for aspiration, respiratory depression from sedating medication. Chronic: avoid mu agonist or agonist/antagonist, which can precipitate withdrawal symptoms. Pain control: maintain baseline opioids, multimodal therapy, anticipate increased opioid requirement.</td>
</tr>
</tbody>
</table>

resulting in attenuated responses to indirect sympathomimetics such as ephedrine. (A direct sympathomimetic such as phenylephrine is probably a better choice for hypotension.)

**Amphetamine and elective surgery:** Some amphetamine derivatives (methyprylonidate, dextroamphetamine) are also indicated in certain medical conditions such as ADHD and narcolepsy. Even though there are case reports of safe continuations of these medications before elective surgery, this remains controversial.

**Marijuana**

**Mechanism of action:** Active substances in marijuana are tetrahydrocannabinol and cannabinoids, which stimulate cannabinoid receptors (CB1, CB2), produce euphoria, analgesia, anxiolysis, and sedation. Low doses can stimulate the SNS, causing hypertension and tachycardia, whereas high doses inhibit SNS, leading to bradycardia and hypotension.

**Effects:** Life-threatening cardiac arrhythmias in preexisting cardiac condition patients are potentially possible but rare. A fatal overdose is even more extremely rare, and withdrawal symptoms have been reported but mild. Marijuana smokers can have pulmonary effects similar to tobacco (airway irritation, increased CO–Hb level).

**Medical marijuana:** Marijuana is also beneficial and allowed in certain medical conditions such as chemotherapy-induced emesis, AIDS-related anorexia, glaucoma, certain psychiatric conditions, and chronic pain. There are relatively few reports discussing the risks and benefits of stopping medical marijuana before surgery; however, recreational use should be prohibited before elective procedure.

**Hallucinogens**

Hallucinogens include, but are not limited to, lysergic acid diethylamide or LSD, phencyclidine or PCP, psilocybin, and mescaline. **Mechanisms of action** include acting as partial agonist, agonist, or antagonist to serotonin, dopamine, adrenergic receptor, resulting in CNS stimulation and mild SNS stimulation.

**Effects:** As with cocaine and amphetamines, patients might exhibit hypertension, tachycardia, cardiac arrhythmia, and inadequate pressor response to ephedrine. Phenylephrine, a direct-acting adrenergic agent, may be a better choice for treating hypotension.

**Questions**

1. Which statement is true?
   a. Methadone and suboxone should be continued until the morning of the day of a major operation.
   b. In order to achieve the best postoperative outcome, smoking should be stopped at least two weeks before elective surgery.
   c. Buprenorphine is a drug of choice for pain control in opioid-dependent patients.
   d. Chronic amphetamine users may be resistant to the pressor effect of ephedrine.

2. Which statement is true?
   a. Labetalol is a better choice than metoprolol in cocaine-induced hypertension.
   b. Cocaine-abuse patients will always have an exaggerated response to ephedrine.
   c. Anesthetic requirements increase in acute cocaine, amphetamine, and alcohol abuse.
   d. All pulmonary effects from smoking will be reversed 24 to 48 hours after smoking cessation.

3. Which statement is true?
   a. Chronic alcohol abusers should receive vitamin B1 to prevent heart failure and encephalopathy.
   b. History and physical examination are reliable tools to detect substance abuse in patients.
   c. The primary action of cocaine is to enhance GABA and dopamine receptors.
   d. Marijuana is legal in some states in the United States; medical indications include chemotherapy-induced emesis, ADHD, and narcolepsy.

**Answers**

1. d. Methadone, but not suboxone, should be continued until the morning of an operation. Cigarette smokers need four to eight weeks of cessation to decrease pulmonary complications. Buprenorphine has a ceiling effect, and is not a good choice for pain control. Chronic amphetamine users may be resistant to the pressor effects of ephedrine.

2. a. Labetalol has alpha-antagonist activity, and is a better choice than metoprolol in cocaine-induced hypertension. Acute cocaine abuse, but not chronic, may have an exaggerated response to ephedrine. Anesthetic requirements increase in acute cocaine or amphetamine abuse, but decrease in acute alcoholic intoxication. After 24 to 48 hours of smoking cessation, only carboxy-Hb will be decreased, but for decreasing pulmonary complication, it needs four to eight weeks.

3. a. Chronic alcohol abuse is associated with vitamin B1 deficiency and patients should receive vitamin B1 to prevent cardiac beriberi and Wernicke’s encephalopathy. History and physical examination are not reliable in substance abuse patients; urine toxicology screen is very useful in this population. Mechanism of action of cocaine is interaction with dopamine, NE, and serotonin. Medical marijuana is legal in some states; indication includes chemotherapy-induced emesis, chronic disease-related anorexia, and glaucoma.
Further reading


Carbon Monoxide Poisoning, in En.wikipedia.org/wiki/carbon_monoxide_poisoning


