The cocaine abusing parturient: a review of anesthetic considerations

[L'abus de cocaïne chez les parturientes : une revue des aspects anesthésiques]

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Purpose: The prevalence of recreational drug abuse among young women, including in pregnancy, has increased markedly over the past two decades. Cocaine remains the drug commonly used for recreational purposes in pregnancy. However, there appears to be an absence of uniform guidelines for obstetric and anesthetic management of pregnant patients with a history of cocaine abuse.

Source: A Medline search for articles highlighting drug abuse in pregnancy, with particular emphasis on cocaine abuse in pregnancy, the drug's impact on the fetus and implications for administration of obstetrical anesthesia was performed.

Main findings: Because the pharmacological actions of cocaine are complex, the clinical picture can be very unpredictable, the diagnosis often difficult, and management at times controversial. The diverse clinical symptomatology of cocaine intake combined with physiologic changes of pregnancy, and pathophysiology of co-existing pregnancy specific disease may lead to life-threatening complications and significantly impact the management of obstetrical anesthesia.

Conclusions: In the absence of uniform anesthetic guidelines for pregnant patients with a history of cocaine abuse the decision regarding the administration of peripartum analgesia or anesthesia should be individualized and conducted on a case-by-case basis. This article will attempt to heighten the awareness of cocaine use and abuse in pregnancy and review the perioperative anesthetic management of these high-risk parturients.

Objectif: La prévalence d'abus occasionnel de drogues par les jeunes femmes, incluant les femmes enceintes, a beaucoup augmenté pendant les deux dernières décennies. La cocaïne est la drogue récréative la plus souvent utilisée pendant la grossesse. Il semble pourtant exister une absence d'uniformité dans les directives sur la prise en charge obstétricale et anesthésique des parturientes qui présentent une histoire d'abus de cocaïne.

Source : Nous avons cherché, dans Medline, des articles sur l'abus de drogues pendant la grossesse, surtout sur l'abus de cocaïne, sur les

conséquences des drogues sur le fœtus et les implications sur l'administration de l'anesthésie obstétricale.

Constatations principales : Face à la complexité des actions pharmacologiques de la cocaïne, le portrait clinique peut être très imprévisible, le diagnostic souvent difficile et le traitement parfois controversé. La symptomatologie clinique changeante de la consommation de cocaïne combinée aux modifications physiologiques de la grossesse et la physiopathologie des maladies concomitantes spécifiques à la grossesse peuvent entraîner de graves complications et influencer significativement la démarche anesthésique obstétricale.

Conclusion : En l'absence de directives anesthésiques uniformes pour les patientes enceintes qui ont abusé de drogues, la décision concernant l'analgesie ou l'anesthésie périnatale doit être individualisée et réalisée au cas par cas. Le présent article veut sensibiliser à l'usage et à l'abus de cocaïne pendant la grossesse et revoir la prise en charge anesthésique périopératoire de ces parturientes à haut risque.

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Summary

Introduction

Behavioural disorders from abuse of psychotropic substances may involve a socially acceptable drug (e.g., alcohol, tobacco), a medically prescribed drug (e.g., diazepam), or an illegal substance (e.g., cocaine).¹ In general substance abuse is defined as self-administra-

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tion of various drugs that deviates from medically or socially accepted use, which if prolonged can lead to the development of psychological and physical dependence.² Environmental, social, and perhaps genetic factors have all been implicated in the development of chemical dependency. Psychological personality characteristics seem to predispose to, rather than result from drug addiction.^{1,2}

Substance addiction is most often first suspected or diagnosed during medical management of another condition such as hepatitis B, hepatitis C, human immunodeficiency syndrome³ or pregnancy.^{2,4} Regardless of the drug(s) ingested and clinical manifestations it is always uniformly difficult to predict anesthetic implications in substance abusing patients.^{1,4,5} Knowledge of a parturient's substance abuse prior to administration of analgesia or anesthesia may prevent adverse drug interactions, predict tolerance to anesthetic agents, and/or facilitate the recognition of drug withdrawal. Concomitant use of several illicit substances is common.¹ Among patients with addiction to multiple substances, the combination of cocaine and ethanol is the most common.⁶ This article will review the epidemiology, pathophysiology, clinical symptomatology, interactions with pregnancy, and obstetric, anesthetic, and medicolegal implication of cocaine use, and abuse in pregnancy.

1. Pharmacology

Cocaine is an alkaloid (benzoylecgonine, C₁₇H₂₁NO₄) derived from the leaves of *erythroxylon coca* plant, indigenous to Peru, Ecuador and Bolivia.⁷ Archeological evidence suggests that the Incas of the Andes region in South America have used cocaine (coca leaves) for perhaps as long as 5,000 years.⁸ Carl Koller, an Austrian ophthalmologist, first introduced cocaine to modern medicine as a local anesthetic for ophthalmologic procedures in 1884.^{9,10} However, as cocaine became widely used as a topical local anesthetic, concerns about addiction began to mount and over time the drug has been replaced in clinical practice by less toxic, synthetic local anesthetics.¹¹

Cocaine hydrochloride, the common pharmaceutical form, is prepared by dissolving the alkaloid in hydrochloric acid to form a water-soluble salt, which has the topical anesthetic properties.⁷ Cocaine is commercially available in a hydrochloride form as white powder, granules or crystals. The hydrochloride form of cocaine undergoes heat degradation and therefore, cannot be smoked for recreational purposes.⁷ In the mid-1980's, however, the use of "crack," a new form of cocaine, surged.¹¹ Crack is almost pure, highly concentrated cocaine obtained by converting the

hydrochloride form back into the alkalinized form. This can be accomplished easily by the addition of baking soda and water to the cocaine powder. Today, this alkalinized form of cocaine is widely smoked throughout the world.^{3,4,11,12} By the 1990's, the use of highly addictive crack cocaine became the most widely abused illicit substance in the United States.¹¹

Cocaine has a biological half-life of 0.5 to 1.5 hr, a volume of distribution of 2 L·kg⁻¹, and a systemic clearance of 2 L·min⁻¹. It is metabolized by the plasma and liver cholinesterases to water-soluble metabolites that are excreted in urine. Only a small percentage (1–5%) of the drug ingested is cleared unmetabolized in urine, where it may be detected for three to six hours after use.¹¹ However, its two major metabolites, ecgonine methyl ester and benzoylecgonine, can be detected in urine for 15 to 60 hr after cocaine intake.¹³

2. Epidemiology

The increasing use and abuse of cocaine in Western cultures is an issue of great national and international concern.¹⁴ Five million Americans are regular users of cocaine, 6,000 use the drug for the first time each day and more than 30 million have tried cocaine at least once.¹⁵ Cocaine abuse has crossed social, economic, geographic and international borders and today it remains a major problem (of global proportions) facing our society.¹⁶ The prevalence of cocaine abuse in young adults, particularly in young women, has increased markedly over the past three decades.^{17–19} Nearly 90% of cocaine-abusing women are of child-bearing age.¹⁷ Consequently it is no longer uncommon to find pregnant women who abuse this drug, and numerous reports of cocaine abuse in pregnancy have been published.^{4,15,20–23}

The typical cocaine abusing parturient does not fit into any specific socioeconomic, ethnic, or cultural profile.¹⁸ Associated risk factors, which may suggest cocaine use in pregnancy, include lack of prenatal care, history of premature labour, and cigarette smoking.^{1,17,24–26} Most patients with a history of cocaine abuse deny it when interviewed preoperatively by primary physicians, obstetricians and anesthesiologists.^{1,17,27} A high index of suspicion for cocaine use in pregnancy, combined with non-judgemental questioning of every parturient is therefore essential to determine the differential diagnosis of cocaine toxicity, avoid drug interactions and subsequent peripartum complications.^{1,17}

In addition to cocaine, other substances abused in pregnancy include caffeine, tobacco, ethanol, marijuana, amphetamines, toluene-based solvents and hallu-

cinogens.^{1,5,17,26} Concomitant abuse of several substances is very common.^{1,4-6,17,26,28} Among those with abuse of multiple substances; the combination of cocaine and ethanol is the most common.^{4,6} The combined use of cocaine and ethanol appears to be associated with higher rates of complications, including death, than either drug used alone.⁶

3. Pathophysiology

Cocaine produces prolonged adrenergic stimulation by blocking the presynaptic uptake of sympathomimetic neurotransmitters including norepinephrine, serotonin and dopamine.^{29,30} The euphoric effects of cocaine also result from prolongation of dopaminergic activity in the limbic system and the cerebral cortex.^{31,32} Other mechanisms by which cocaine produces prolonged adrenergic stimulation include blockade of catecholamine-binding mechanisms, allowing free catecholamine to continue to stimulate the sympathoadrenal axis.³³ Smoking crack cocaine results in very effective transmucosal absorption and high concentrations of plasma cocaine.⁶ Cocaine has a low molecular weight and high lipid solubility, which allows easy diffusion through lipid membranes.

The cardiovascular effects of cocaine occur predominantly secondary to increased levels of plasma catecholamines.³² Hypertension, tachycardia, malignant arrhythmias, myocardial ischemia and infarction are all life-threatening cardiovascular complications of catecholamine accumulation following acute cocaine intake.³⁴⁻³⁹ Mechanisms of cocaine induced myocardial ischemia and/or infarction include thrombosis, vasospasm, or both, and direct myocardial depression.^{34,37,40} Cocaine-induced cardiovascular complications do not seem to be dose-dependent and even small recreational doses can lead to significant mortality and morbidity in an otherwise healthy parturient. It is important to note that cocaine-abusing patients are at risk of cocaine-related complications, even if the last drug intake occurred more than 24 hr earlier.⁴¹ Pregnancy is associated with increased sensitivity of the cardiovascular system to cocaine (see 5. Impact on pregnancy).³⁵

The use of cocaine rapidly leads to physical dependence. Sudden discontinuation of cocaine intake results in fatigue, mental depression and craving for the drug.

4. Clinical symptomatology and diagnosis

Identification of cocaine abuse in the pregnant patient presents a significant diagnostic challenge. Women with chronic uncontrolled substance abuse often do not present until they go into labour, whereas women who use drugs only occasionally are more likely to

TABLE I Maternal complications of cocaine intake

<i>System involved</i>	<i>Clinical manifestations</i>
<i>Central nervous system</i>	Emotional instability Dilated pupils Hyperreflexia Seizures Intracranial hemorrhage Cerebrovascular accident
<i>Cardiovascular system</i>	Tachycardia Hypertension Arrhythmias Myocardial ischemia Myocardial infarction Asystole Aortic rupture
<i>Respiratory system</i>	Aspiration of gastric contents Bronchospasm Pneumothorax
<i>Renal system</i>	Proteinuria Renal failure
<i>Gastrointestinal system</i>	Nausea Vomiting Bowel ischemia
<i>Hepatobiliary system</i>	Hepatic failure Hepatic rupture
<i>Hematological system</i>	Disseminated intravascular coagulation Altered platelet function Intravascular thrombosis

receive prenatal care.¹⁹ Lack of prenatal care may suggest the possibility of cocaine or other drug abuse. The patient's denial is a common response to direct questioning regarding drug abuse in pregnancy.⁴² It has been estimated that only 20% of physicians inquire about substance abuse when interviewing their patients.⁴³ In addition to cardiovascular symptoms (hypertension, tachycardia, arrhythmias), other symptoms of cocaine abuse include seizures, hyperreflexia, fever, dilated pupils, emotional instability, proteinuria and edema (Table I).^{1,4,6} The combination of hypertension, proteinuria and convulsions resulting from acute cocaine intake may be mistaken for eclampsia (a pregnancy specific disorder) at presentation; consequently routine laboratory studies (liver and kidney function tests) may be the key differential between the two disorders.⁴⁴

The differential diagnosis is usually aided by maternal urine toxicology screening. Unfortunately, many of the currently available toxicology screening tests are performed in the hospital laboratory and the results may not be available for several days. A rapid latex agglutination test detecting cocaine metabolites in urine within a few minutes has been developed (Ontrak TesTcup™, Roche Diagnostic Systems, Branchburg,

NJ, USA).^{45,46} This test has been utilized by many specialties in emergency situations and can be performed easily at bedside in labour and delivery.⁴⁶ In most instances an anesthesiologist without any special training in toxicology testing is able to complete the test in less than five minutes, with results identical to those reported by the hospital laboratory. The cost of each TesTcup™ is approximately 20.00 US dollars.⁴⁶

The bio-metabolites of cocaine may be detected in maternal urine for 24–60 hr after administration of the drug, depending on the cholinesterase activity.⁴⁷ Analysis of fetal urine may also serve as a marker of cocaine abuse in pregnancy. Metabolites of cocaine can be found in fetal urine 72–96 hr after maternal drug ingestion. Other methods for detection of suspected cocaine abuse in pregnancy include maternal hair and fetal meconium analysis.^{48–50}

5. Impact on pregnancy

Pregnancy enhances the cardiovascular toxicity of cocaine.^{41,42} This may result from the effects of progesterone, which increases the metabolism of cocaine to norcocaine (a biologically active metabolite), or the increasing sensitivity of alpha-adrenergic receptors associated with pregnancy.⁵¹ Plessinger *et al.* demonstrated that pregnancy increases the cardiovascular toxicity of cocaine in gravid ewes.⁵² Cardiovascular complications resulting from cocaine-related myocardial ischemia or infarction are significantly greater in pregnancy in the face of increased oxygen demand and limited or decreased supply. Cocaine induces an increase in the three major determinants of the myocardial oxygen demand: the heart rate, the systemic arterial pressure and the left ventricular contractility.^{51,52} It has been reported that even small recreational drug ingestions may cause vasoconstriction of the epicardial coronary arteries.^{51,52}

For the fetus, maternal cocaine intake is particularly hazardous.¹⁸ The low molecular weight of cocaine and its breakdown products combined with the high water and lipid solubility are primarily responsible for the rapid transplacental diffusion and high fetal blood and tissue cocaine levels.⁵² It has been reported that bolus injections of cocaine, 0.5 to 1.0 mg·kg⁻¹ in pregnant animal models (ewe) resulted in maternal and fetal tachycardia as well as maternal and fetal hypertension. Maternal plasma concentrations of norepinephrine were elevated by approximately 200%, and there was a dose-related decrease in uterine blood flow leading to fetal hypoxemia in 40% of studied subjects.⁵³ Maternal complications of cocaine ingestion include premature onset of labour, placental abruption, uterine rupture, cardiac dysrhythmias, hepatic

rupture, cerebral ischemia/infarction, and death.^{54–60} Cocaine is rapidly transferred across the placenta to the fetus by simple diffusion.⁶¹ It may cause significant vasoconstriction by directly affecting fetal blood vessels. Indirect fetal effects of cocaine result from maternal vasoconstriction. Since uterine blood flow is not autoregulated, decreased uteroplacental blood flow may lead to uteroplacental insufficiency, acidosis, hypoxia and fetal distress.⁵³

Depending on timing and duration of the exposure, fetal implications of maternal cocaine abuse in pregnancy can be divided into acute and chronic. Acute effects of cocaine intake in pregnancy include fetal distress, premature rupture of membranes, preterm delivery, placental abruption, fetal tachycardia, hypertension and intra-uterine fetal death.⁵¹ A fourfold increase in fetal distress syndrome leading to abdominal delivery has been reported in patients abusing cocaine in the third trimester of pregnancy. The risk of preterm delivery is also increased fourfold in these parturients.

During pregnancy, prolonged (chronic) cocaine intake can affect 5-HT and catecholamine systems in the developing fetus.¹⁴ Several studies have shown that prenatal exposure to cocaine produces permanent biochemical and functional changes in the offspring. Chronic maternal cocaine use may also lead to subtle molecular and anatomical effects on developing fetal brain structures. In postnatal life this may be manifested in decreased IQ scores and in learning deficiencies. The association between cocaine use and increased risk of congenital anomalies is still controversial.⁵¹ In general, the anomalies reported to occur more frequently among cocaine-exposed fetuses involve congenital urogenital tract abnormalities, cardiovascular and central nervous system defects as well as musculoskeletal deformities.⁵¹ These congenital defects have been reported primarily in neonates born to women who abuse cocaine in early pregnancy.⁶²

6. Obstetric considerations

Any woman giving a history of cocaine (or of any other drug) abuse in pregnancy or with a positive toxicology screening should be counselled regarding the risks to her and her fetus of continued cocaine (or other drug) use in pregnancy.¹⁹ The American College of Obstetricians and Gynecologists (ACOG) recognized the fact that cocaine use in pregnancy has become a major health concern in the United States, and published a Committee Opinion regarding the management of cocaine abusing parturients.⁶³ The following recommendations have been made: 1) a drug history should be taken on all patients; 2) a

TABLE II Feto-maternal and neonatal complications of maternal cocaine intake

<i>Feto-maternal complications</i>	Preterm labour
	Premature rupture of membranes
	Placental abruption
	Decreased uteroplacental perfusion
	Fetal distress
	Fetal tachycardia
	Fetal hypertension
<i>Neonatal complications</i>	Intra-uterine fetal demise
	Irritability
	Cocaine withdrawal syndrome
	Myocardial ischemia
	Myocardial infraction

woman acknowledging cocaine use should be counselled and offered support mechanisms to aid in her abstinence; 3) periodic urine testing should be considered to encourage abstinence; and 4) testing the mother and neonate may be useful in some clinical situations, such as unexplained fetal growth restriction, prematurity and placental abruption.⁶³

Obstetricians and obstetric anesthesiologists should review the laws requiring reporting of positive toxicology screening to authorities. Under some legislatures, women with positive urine toxicology at the time of delivery may not be allowed to take their newborn home and it is the physician's legal responsibility to report the situation.¹⁹

7. Anesthetic considerations

Anesthesiologists become involved in the care of cocaine abusing patients either in emergency situations, such as fetal distress, placental abruption or uterine rupture, or in more controlled situations, such as the request for labour analgesia.^{4,17} However, it is increasingly too common for the obstetric anesthesiologist to be faced with an acutely ill mother and a fetus in need for urgent obstetrical intervention following acute cocaine ingestion.^{18,19} Fortunately the clinical manifestations of acute cocaine intake are frequently self-limited and respond to supportive therapy,¹⁸ although, on occasion, they may lead to life-threatening complications and significantly impact the management of obstetric analgesia or/and anesthesia.¹⁷

It is a general belief (and in most obstetric settings), that vaginal delivery and regional anesthesia, are, respectively, the preferred obstetric and anesthetic management choices for cocaine-abusing patients.¹ However, after it has been determined that a parturient is using cocaine in pregnancy, the obstetrician and

the anesthesiologist must decide on an individual, case-to-case basis whether the obstetric patient is a candidate for vaginal delivery and regional anesthesia.¹⁷ Epidural labour analgesia is recommended; however, the hemodynamic consequences of cocaine use should be taken under consideration.^{32,64,65} Hypertension may occur as a result of vasoconstriction and hypotension may follow cardiac arrhythmias, myocardial dysfunction or hemorrhage.

Anesthesia of any kind (regional or general) in the cocaine abusing parturient may be associated with serious maternal and fetal complications.^{64,65} When regional anesthesia is selected combative behaviour, altered pain perception, cocaine-induced thrombocytopenia, and ephedrine-resistant hypotension may be encountered.⁶⁵ Low doses of phenylephrine titrated to effect usually restore blood pressure to normal. Pronounced abnormalities in endorphin levels and changes in both mu and kappa opioid receptor densities resulting from cocaine addiction may result in perception of pain despite adequate spinal/epidural anesthesia sensory levels.⁶⁶

Many theories have been proposed to explain the possibility of a cocaine-induced thrombocytopenia.⁶⁷ It has been speculated that elevated levels of plasma catecholamines, such as epinephrine and norepinephrine, will cause a direct arterial vasoconstriction. Alpha-adrenergic agonists bind to specific receptors and platelets. Occupancy of these receptors induces platelet activation. The combination of arterial vascular spasm and platelet activation theoretically increases the risk of thrombocytopenia to the cocaine abusing parturient.^{68,69} Other possible etiologies for thrombocytopenia include bone marrow suppression, an autoimmune response with the induction of platelet-specific antibodies, chronic hepatitis, hypersplenism, sepsis, and possible concurrent autoimmune deficiency syndrome.⁷⁰⁻⁷² In patients who chronically abuse opioids, increased platelet destruction and clearance by the reticuloendothelial system correlate to a specific immunoglobulin G antiplatelet antibody.⁷⁰ While these concerns seem interesting, Gershon *et al.* did not find an increased risk of thrombocytopenia in the studied group of cocaine-abusing parturients.⁶⁷ Subsequently, the authors concluded that requiring a platelet count from otherwise healthy suspected cocaine abusing parturients prior to initiation of regional anesthesia may not be necessary.

Cardiac arrhythmias, hypertension, and myocardial ischemia may be encountered under general anesthesia.⁷³ The pathogenesis of cocaine-related myocardial ischemia is multi-factorial and includes an increased myocardial oxygen demand in the face of a fixed or

limited supply caused by pronounced vasoconstriction of the coronary arteries and enhanced platelet aggregation and thrombus formation.⁶ Although thrombi are not the only cause of cocaine-induced myocardial infarction, thrombolytic therapy has been used successfully to dissolve intraluminal coronary thrombi in patients with acute infarction temporally related to cocaine use.³² Most patients with cocaine-induced myocardial ischemia have chest pain within an hour after they have used cocaine, when the blood cocaine level is highest.⁶ The electrocardiogram is reportedly abnormal in 43% of patients with cocaine-related chest pain without infarction.⁶

Given the high incidence of obstetric emergencies in cocaine-abusing parturients, it is not uncommon for an intoxicated patient to require emergency Cesarean delivery under general endotracheal anesthesia. Stimulation with the laryngoscope blade at the time of intubation may result in severe hypertension in the cocaine-intoxicated parturient. To limit the risk of this complication, pharmacological control of blood pressure prior to induction is recommended.¹⁷ However, the optimal regimen for blood pressure control remains controversial (Table III).¹⁷ Propranolol is contraindicated in cocaine-intoxicated patients because of the potential for unopposed alpha-adrenergic stimulation following beta blockade.⁶⁵ Although esmolol may provide effective control of tachycardia and hypertension, beta blockade has also been shown to enhance cocaine induced coronary vasoconstriction.⁶⁶ The short elimination half-life of esmolol may offer some advantage if beta blockade is deemed necessary.

Intravenous hydralazine has recently become a standard drug therapy for the treatment of hypertension in cocaine-addicted parturients.⁷³ The mechanism of action of this drug includes vasodilation and a decrease in systemic vascular resistance, leading to reflex tachycardia, which may not always be desirable in the patient who is already tachycardic from cocaine intake.⁷³ Labetalol, a combined non-selective beta and alpha-adrenergic blocker rapidly restores blood pressure without affecting heart rate or uterine blood flow and has been recommended by many in cocaine toxicity.^{74,75} Gay *et al.* reported the successful management of hypertensive cocaine crises with the administration of labetalol.⁷⁶ The authors concluded that labetalol offers the advantage of alpha and beta blockade in attenuating the hyperdynamic cardiovascular state resulting from acute cocaine intake.⁷⁶

Birnback has recommended the administration of labetalol with nitroglycerin prior to induction of general anesthesia as the most efficient treatment of severe cocaine-induced hypertension.³² However, Hollander

has suggested that labetalol should not be used to treat cocaine-induced hypertension because labetalol's antagonism of beta-adrenergic receptors is greater than its effect on alpha-adrenergic receptors.⁷⁷ The benefits of calcium channel blockers in drug abusing parturients remain unclear.⁷⁸ Many other drugs such as nitroglycerine and nitroprusside have been recommended, although the best drug intervention remains to be established.

Administration of the potent volatile anesthetic agents may produce cardiac arrhythmias and increase systemic vascular resistance in cocaine intoxicated parturients.⁷⁹ Halothane has been found to sensitize the myocardium to the effects of catecholamines and therefore should be avoided.^{65,80} When ketamine is used in cocaine abusing patients, caution is indicated, since ketamine may stimulate the central nervous system and potentiate the cardiac effects of cocaine by further increasing catecholamine levels.⁸¹ Nitroglycerin is safe and effective in the treatment of chest pain secondary to acute cocaine ingestion.⁸²

Cocaine has been reported to alter the metabolism of succinylcholine, possibly due to competing metabolism by plasma cholinesterases. Jatlow *et al.* reported prolonged block from succinylcholine in a cocaine-abusing patient, presumably secondary to a depletion of cholinesterase involved in cocaine metabolism.⁸³ However, Birnback has postulated that succinylcholine in standard doses can be used safely in cocaine-abusing parturients, should general anesthesia become necessary.⁸⁴

Cocaine-induced vasoconstriction of the coronary arteries can be reversed with the administration of phentolamine, an alpha-adrenergic blocking agent.⁶ Conversely, administration of propranolol, a beta-adrenergic-blocking agent, exacerbates cocaine-induced vasoconstriction of the coronary arteries, and therefore should be avoided in parturients with cocaine-related chest pain.⁶ Since nitroglycerin and verapamil reverse cocaine-induced hypertension and vasoconstriction of the coronary arteries (which is clinically manifested as chest pain), they should be the agents of choice for patients, including parturients, with cocaine-associated chest pain. Aspirin has been recommended by some in patients with cocaine-induced myocardial ischemia to prevent platelet aggregation.⁶ Benzodiazepines may also be useful, because they reduce the heart rate and the systemic blood pressure. Thrombolytic therapy should only be considered after treatment with oxygen, nitrates, aspirin, and benzodiazepines has been unsuccessful, and when immediate coronary angiography and angioplasty are not available.⁶

TABLE III Suggested treatment of acute cocaine intake in pregnancy

<i>Clinical symptoms</i>	<i>Suggested treatment modality</i>
<i>Tachycardia/hypertension</i>	Hydralazine, nitroglycerin, labetalol, esmolol, benzodiazepines
<i>Seizures</i>	Benzodiazepines, airway control
<i>Myocardial ischemia</i>	Nitroglycerin, labetalol, aspirin, benzodiazepines
<i>Cardiac arrhythmias</i>	Lidocaine

The American Heart Association has recently revised its guidelines for emergency cardiovascular care and now recommends nitroglycerin and benzodiazepines as the first-line agents for patients with cocaine-related myocardial ischemia or infarction; phentolamine is indicated as a second-line agent, while propranolol is contraindicated.⁸⁵ Thrombolysis is not recommended unless evidence of myocardial infarction persists, despite medical therapy, and an occluded coronary artery is present on angiography.⁸⁵

Concerns have been raised regarding the use of lidocaine for the treatment of cocaine-induced arrhythmias in cocaine-abusing parturients. However, Shih *et al.* reported that the administration of lidocaine in patients with cocaine-associated ischemia does not appear to be associated with cardiovascular or central nervous system toxicity.⁸⁶

It has been well established that cocaine-abusing parturients are more likely to abuse other drugs and drug combinations may further increase hemodynamic and cardiovascular instability.^{87,88} Many patients with cocaine addiction are cigarette smokers, and admit to smoking while using cocaine. Cigarette smoking increases vasoconstriction of the coronary arteries through an alpha-adrenergic mechanism similar to that of cocaine.⁸⁹ Recent studies have demonstrated that concomitant cigarette smoking substantially exacerbates the deleterious effects of cocaine on myocardial oxygen supply and demand.⁶ Multi-drug interactions may additionally complicate anesthetic management of poly-substance-abusing pregnant patients.

Treatment of cocaine addiction with cocaine specific vaccines is currently under investigation. Binding of antibodies included in the vaccine to cocaine in plasma may prevent entry of the drug into the central nervous system.^{90,91} Despite promising initial results further investigations on the efficacy of cocaine vaccines in cocaine addiction are necessary.

8. Medicolegal considerations

In the United States the number of birth-related malpractice lawsuits has increased dramatically since 1980. Many legal settlements and judgements have involved brain-damaged newborns whose prenatal care was allegedly substandard for various reasons, including maternal substance addiction. While most of the cases have focused on the role of the obstetrician, anesthesiologists providing labour analgesia have not been immune from such litigations.⁹²

Medicolegal controversies regarding substance abuse in pregnancy and maternal rights and the status of the fetus are complex and vary among states.¹⁷ The ACOG has made multiple recommendations regarding management of patients with drug abuse during pregnancy.⁶³ Women who acknowledge use of illicit substance during pregnancy should be counselled and offered the necessary treatment. ACOG also acknowledged that some states consider intra-uterine fetal drug exposure to be a form of child neglect or abuse under the law.⁶³

Many public health organizations in the United States, including the American Medical Association and the ACOG, suggest that the imposition of criminal sanctions is inappropriate to the caregiver's role, which should rather focus on treatment and prevention.

At the University of California in San Diego, urine toxicology screening is performed (following the patient's consent) on all parturients considered at high-risk for drug abuse (including cocaine) in pregnancy. Any patient that refuses toxicology screening is considered positive.

In summary, maternal cocaine use in pregnancy continues to increase worldwide, despite preventive and rehabilitative efforts at local, national and international levels.^{4,17,93} A careful pre-anesthetic history and physical examination combined with a high index of suspicion, judgement free questioning for possible cocaine use are essential to determine the differential diagnosis of cocaine intoxication. Anesthetic management of these parturients should be tailored to individual needs and the urgency of obstetrical indications for either vaginal or abdominal delivery.⁹⁴

A complete knowledge of physiology of pregnancy, pathophysiology of pregnancy specific co-existing disease and anesthetic implications of cocaine use/abuse in pregnancy is essential to tailor a safe anesthetic plan for these patients.^{4,17}

References

- 1 Newman LM. The chemically dependent parturient. *Seminars in Anesthesia* 1992; 11: 66-75.
- 2 Stoelting RK, Dierdorf SF. Psychiatric illness and substance abuse. In: Stoelting RK, Dierdorf SF (Eds.).

- Anesthesia and Co-Existing Disease. New York: Churchill Livingstone; 1993: 517–38.
- 3 Kuczkowski KM. Human immunodeficiency virus in pregnancy – anesthetic implications. *Progress in Anesthesiology* 2002; 26: 3–14.
 - 4 Kuczkowski KM, Benumof JL. Cesarean section in a parturient with HIV and recent cocaine and alcohol intake: anesthetic implications. *Int J Obstet Anesth* 2002; 11: 135–7.
 - 5 Kuczkowski KM, Benumof JL. Amphetamine abuse in pregnancy: anesthetic implications. *Acta Anaesthesiol Belg* 2003; 54:161–3.
 - 6 Lange RA, Hillis LD. Cardiovascular complications of cocaine use. *N Engl J Med* 2001; 345: 351–8.
 - 7 Fleming JA, Byck R, Barash PG. Pharmacology and therapeutic applications of cocaine. *Anesthesiology* 1990; 73: 518–31.
 - 8 Kleber HD. Cocaine abuses: historical, epidemiological, and psychological perspectives. *J Clin Psychiatry* 1988; 49(2 Suppl): 3–6.
 - 9 Van Dyke C, Byck R. Cocaine. *Sci Am* 1982; 246: 128–41.
 - 10 Fred S. On the general effects of cocaine. *Drug Depend* 1970; 5: 15–7.
 - 11 Cheng D. Perioperative care of the cocaine-abusing patient. *Can J Anaesth* 1994; 41: 883–7.
 - 12 Hatsukami DK, Fischman MW. Crack cocaine and cocaine hydrochloride. Are the differences myth or reality? *JAMA* 1996; 276: 1580–8.
 - 13 Jatlow PI. Drug of abuse profile: cocaine. *Clin Chem* 1987; 33: 66–71.
 - 14 Battaglia G, Napier TC. The effects of cocaine and the amphetamines on brain and behavior: a conference report. *Drug Alcohol Depend* 1998; 52: 41–8.
 - 15 Matera C, Warren WB, Moomjy M, Fink DJ, Fox HE. Prevalence of use of cocaine and other substances in an obstetric population. *Am J Obstet Gynecol* 1990; 63: 797–801.
 - 16 Bendersky M, Alessandri S, Gilbert P, Lewis M. Characteristics of pregnant substance abusers in two cities in the northeast. *Am J Drug Alcohol Abuse* 1996; 22: 349–62.
 - 17 Kuczkowski KM. Drug abuse in pregnancy – anesthetic implications. *Progress in Anesthesiology* 2001; 25: 355–72.
 - 18 Pedersen H, Santos AC, Finster M. Anesthesia in the high-risk patient. In: Reece EA, Hobbins JC, Mahoney MJ, Petrie RH (Eds.). *Medicine of the Fetus and Mother*. Philadelphia: JB Lippincott Company; 1992: 1482–93.
 - 19 Downey JJ, Whitaker AH. Important psychiatric problems during pregnancy and the postpartum period. In: Reece EA, Hobbins JC, Mahoney MJ, Petrie RH (Eds.). *Medicine of the Fetus and Mother*. Philadelphia: JB Lippincott Company; 1992: 1293–1307.
 - 20 Martinez Crespo JM, Antolin E, Comas C, et al. The prevalence of cocaine abuse during pregnancy in Barcelona. *Eur J Obstet Gynecol Reprod Biol* 1994; 56: 165–7.
 - 21 Smit BJ, Boer K, van Huis AM, Lie-A-Ling IS, Schmidt SC. Cocaine use in pregnancy in Amsterdam *Acta Paediatr Suppl* 1994; 404: 32–5.
 - 22 Davis RB. Drug and alcohol use in the former Soviet Union: selected factors and future considerations. *Int J Addict* 1994; 29: 303–23.
 - 23 Offidani C, Pomini F, Caruso A, Ferrazzani S, Chiarotti M, Fiori A. Cocaine during pregnancy: a critical review of the literature. *Minerva Ginecol* 1995; 47: 381–90.
 - 24 Spence MR, Williams R, DiGregorio GJ, Kirby-McDonnell A, Polansky M. The relationship between recent cocaine use and pregnancy outcome. *Obstet Gynecol* 1991; 78: 326–9.
 - 25 McCalla S, Minkoff HL, Feldman J, Glass L, Valencia G. Predictors of cocaine use in pregnancy. *Obstet Gynecol* 1992; 79: 641–4.
 - 26 Kuczkowski KM. Social drug use in pregnancy: anesthetic implications. *J Magh A Réa* 2002; 37: 170–3.
 - 27 Knisely JS, Spear ER, Green DJ, Christmas JT, Schnoll SH. Substance abuse patterns in pregnant women. *NIDA Res Monogr* 1991; 105: 280–1.
 - 28 Hughes SC, Dailey PA. Human immunodeficiency virus in the delivery suite. In: Hughes SC, Levinson G, Rosen MA (Eds.). *Shnider and Levinson's Anesthesia for Obstetrics*. Philadelphia: Lippincott Williams & Wilkins; 2002: 583–95.
 - 29 Gold MS, Washton AM, Dackis CA. Cocaine abuse: neurochemistry, phenomenology and treatment. *NIDA Res Monogr* 1985; 61: 130–50.
 - 30 Pitts DK, Marwah J. Autonomic actions of cocaine. *Can J Physiol Pharmacol* 1989; 67: 1168–76.
 - 31 Sprauve ME. Substance abuse and HIV in pregnancy. *Clin Obstet Gynecol* 1996; 39: 316–32.
 - 32 Birnback DJ. Substance abuse. In: Chestnut DH (Ed.). *Obstetric Anesthesia – Principles and Practice*. St. Louis: Mosby; 1999: 1027–40.
 - 33 Chiueh CC, Kopin IJ. Centrally mediated release by cocaine of endogenous epinephrine and norepinephrine from the sympathoadrenal medullary system of unanesthetized rats. *J Pharm Exp Ther* 1978; 205: 148–54.
 - 34 Kloner RA, Hale S, Alker K, Rezkalla S. The effects of acute and chronic cocaine use on the heart. *Circulation* 1992; 85: 407–19.
 - 35 Woods JR Jr, Plessinger MA. Pregnancy increases cardiovascular toxicity of cocaine. *Am J Obstet Gynecol*

- 1990; 162: 529–33.
- 36 *Chao CR*. Cardiovascular effects of cocaine during pregnancy. *Sem Perinatol* 1996; 20: 107–14.
- 37 *Liu SS, Forrester RM, Murphy GS, Chen K, Glassenberg R*. Anaesthetic management of a parturient with myocardial infarction related to cocaine use. *Can J Anaesth* 1992; 39: 858–61.
- 38 *Billman GE*. Mechanisms responsible for the cardiotoxic effects of cocaine. *FASEB J* 1990; 4: 2469–75.
- 39 *Nahas GG, Trouve R, Manger WM*. Cocaine, catecholamines and cardiac toxicity. *Acta Anaesthesiol Scand Suppl* 1990; 94: 77–81.
- 40 *Fraker TD Jr, Temeszy-Armos PN, Brewster PS, Wilkerson RD*. Mechanism of cocaine-induced myocardial depression in dogs. *Circulation* 1990; 81: 1012–6.
- 41 *Schindler CW, Tella SR, Erzouki HK, Goldberg SR*. Pharmacological mechanisms of cocaine's cardiovascular effects. *Drug Alcohol Depend* 1995; 37: 183–91.
- 42 *Rodriguez EM, Mofenson LM, Chang BH, et al*. Association of maternal drug use during pregnancy with maternal HIV culture positivity and perinatal HIV transmission. *AIDS* 1996; 10: 273–82.
- 43 *King JC*. Substance abuse in pregnancy. A bigger problem than you think. *Postgrad Med* 1997; 102: 135–50.
- 44 *Towers CV, Pircon RA, Nageotte MP, Porto M, Garite TJ*. Cocaine intoxication presenting as preeclampsia and eclampsia. *Obstet Gynecol* 1993; 81: 545–7.
- 45 *Birnbach DJ, Stein DJ, Grunebaum A, Danzer BI, Thys DM*. Cocaine screening of parturients without prenatal care: an evaluation of a rapid screening assay. *Anesth Analg* 1997; 84: 76–9.
- 46 *Birnbach DJ, Browne IM, Kim A, Stein DJ, Thys DM*. Identification of polysubstance abuse in the parturient. *Br J Anaesth* 2001; 87: 488–90.
- 47 *Kain ZN, Mayes LC, Ferris CA, Pakes J, Schottenfeld R*. Cocaine-abusing parturients undergoing cesarean section. A cohort study. *Anesthesiology* 1996; 85: 1028–35.
- 48 *Oyler J, Darwin WD, Preston KL, Suess P, Cone EJ*. Cocaine disposition in the meconium from newborns of cocaine-abusing mothers and urine of adult drug users. *J Anal Toxicol* 1996; 20: 453–62.
- 49 *Kline J, Ng SK, Schittini M, Levin B, Susser M*. Cocaine use during pregnancy: sensitive detection by hair assay. *Am J Public Health* 1997; 87: 352–8.
- 50 *Grant T, Brown Z, Callahan C, Barr H, Streissguth AP*. Cocaine exposure during pregnancy: improving assessment with radioimmunoassay of maternal hair. *Obstet Gynecol* 1994; 83: 524–31.
- 51 *Andres RL*. Social and illicit drug use in pregnancy. In: Resnik RR, Creasy R (Eds.). *Maternal-Fetal Medicine*. Philadelphia: WB Saunders Company; 1999: 145–64.
- 52 *Plessinger MA, Woods JR Jr*. Maternal, placental, and fetal pathophysiology of cocaine exposure during pregnancy. *Clin Obst Gynecol* 1993; 36: 267–78.
- 53 *Moore TR, Sorg J, Miller L, Key TC, Resnik R*. Hemodynamic effects of intravenous cocaine on the pregnant ewe and fetus. *Am J Obstet Gynecol* 1986; 155: 883–8.
- 54 *Dombrowski MP, Wolfe HM, Welch RA, Evans MI*. Cocaine abuse is associated with abruptio placentae and decreased birth weight, but not shorter labor. *Obstet Gynecol* 1991; 77: 139–41.
- 55 *MacGregor SN, Keith LG, Chasnoff IJ, et al*. Cocaine use during pregnancy: adverse perinatal outcome. *Am J Obstet Gynecol* 1987; 157: 686–90.
- 56 *Mishra A, Landzberg BR, Parente JT*. Uterine rupture in association with alkaloidal (“crack”) cocaine abuse. *Am J Obstet Gynecol* 1995; 173: 243–4.
- 57 *Buehler BA*. Cocaine: how dangerous is it during pregnancy? *Nebr Med J* 1995; 80: 116–7.
- 58 *Iriye BK, Bristow RE, Hsu CD, Bruni R, Johnson TR*. Uterine rupture associated with recent antepartum cocaine abuse. *Obstet Gynecol* 1994; 83: 840–1.
- 59 *Lamley EC, Williams S, Myers SA*. Cocaine-associated rhabdomyolysis causing renal failure in pregnancy. *Obstet Gynecol* 1996; 87(5 Pt 2): 804–6.
- 60 *Moen MD, Caliendo MJ, Marshall W, Uhler ML*. Hepatic rupture in pregnancy associated with cocaine use. *Obstet Gynecol* 1993; 82: 687–9.
- 61 *Krishna RB, Levitz M, Dancis J*. Transfer of cocaine by the perfused human placenta: the effect of binding to serum proteins. *Am J Obstet Gynecol* 1993; 169: 1418–23.
- 62 *Anonymous*. Urogenital anomalies in the offspring of women using cocaine during early pregnancy – Atlanta, 1968–1980. *MMKR Morb Mortal Wkly Rep* 1989; 38: 536, 541–2.
- 63 *Anonymous*. Cocaine in Pregnancy. ACOG Committee Opinion: Committee on Obstetrics: Maternal and Fetal Medicine number 114 - September 1992.
- 64 *Birnbach DJ, Stein DJ*. The substance-abusing parturient: implications for analgesia and anaesthesia management. *Baillieres Clin Obstet Gynaecol* 1998; 12: 443–60.
- 65 *Kuczkowski KM, Birnbach DJ, van Zundert A*. Drug abuse in the parturient. *Sem Anesthesiol Periop Med Pain* 2000; 19: 216–24.
- 66 *Kreek MJ*. Cocaine, dopamine and the endogenous opioid system. *J Addict Dis* 1996; 15: 73–96.
- 67 *Gershon RT, Fisher AJ, Graves WL*. The cocaine-abusing parturient is not an increased risk for thrombocytopenia. *Anesth Analg* 1996; 82: 865–6.
- 68 *Abramowicz JS, Sherer DM, Woods JR Jr*. Acute transient thrombocytopenia associated with cocaine abuse

- in pregnancy. *Obstet Gynecol* 1991; 78: 499–500.
- 69 *Burday MJ, Martin SE.* Cocaine-associated thrombocytopenia. *Am J Med* 1991; 91: 656–60.
 - 70 *Karpatkin S, Nardi MA.* Immunological thrombocytopenia purpura in human immunodeficiency virus - seropositive patients with hemophilia. Comparison with patients with classic autoimmune thrombocytopenic purpura, homosexuals with thrombocytopenia, and narcotic addicts with thrombocytopenia. *J Lab Clin Med* 1988; 111: 441–8.
 - 71 *Orser B.* Thrombocytopenia and cocaine abuse. *Anesthesiology* 1991; 74: 195–6.
 - 72 *Leissinger CA.* Severe thrombocytopenia associated with cocaine use. *Ann Intern Med* 1990; 112: 708–10.
 - 73 *Vertommen JD, Hughes SC, Rosen MA, et al.* Hydralazine does not restore uterine blood flow during cocaine-induced hypertension in the pregnant ewe. *Anesthesiology* 1992; 76: 580–7.
 - 74 *Birnback DJ.* Anesthesia and the drug-abusing parturient. *Anesthesiol Clin North Am* 1998; 16: 385–95.
 - 75 *Kuczkowski KM.* Infection and fever in pregnancy – anesthetic implications. *Progress in Anesthesiology* 2002; 26: 131–44.
 - 76 *Gay GR, Loper KA.* The use of labetalol in the management of cocaine crisis. *Ann Emerg Med* 1988; 17: 282–3.
 - 77 *Hollander JE.* The management of cocaine-associated myocardial ischemia. *N Engl J Med* 1995; 333: 1267–71.
 - 78 *Derlet RW, Tseng CC, Albertson TE.* Cocaine toxicity and the calcium channel blockers nifedipine and nimodipine in rats. *J Emerg Med* 1994; 12: 1–4.
 - 79 *Boylan JE, Cheng DC, Sandler AN, et al.* Cocaine toxicity and isoflurane anesthesia: hemodynamic, myocardial metabolic, and regional blood flow effects in swine. *J Cardiothorac Vasc Anesth* 1996; 10: 772–7.
 - 80 *Birnback DJ.* Cardiovascular disease in the pregnant patient. A new risk factor. *Cardiovascular Risk Fact* 1994; 4: 28–33.
 - 81 *Murphy JL Jr.* Hypertension and pulmonary oedema associated with ketamine administration in a patient with a history of substance abuse. *Can J Anaesth* 1993; 40: 160–4.
 - 82 *Hollander JE, Hoffman RS, Gennis P, et al.* Nitroglycerine in the treatment of cocaine associated chest pain – clinical safety and efficacy. *J Toxicol Clin Toxicol* 1994; 32: 243–56.
 - 83 *Jatlow P, Barash PG, Van Dyke C, Radding J, Byck R.* Cocaine and succinylcholine sensitivity: a new caution. *Anesth Analg* 1979; 58: 235–8.
 - 84 *Birnback DJ.* Anesthesia and maternal substance abuse. In: *Norris MC (Ed.). Obstetric Anesthesia*, 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1999: 491–9.
 - 85 *Anonymous.* Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. Part 8: advanced challenges in resuscitation: section 2: toxicology in ECC. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. *Circulation* 2000; 102(Suppl): I223–8.
 - 86 *Shih RD, Hollander JE, Burstein JL, et al.* Clinical safety of lidocaine in patients with cocaine-associated myocardial infarction. *Ann Emerg Med* 1995; 26: 702–6.
 - 87 *Hutchings DE.* The puzzle of cocaine's effects following maternal use during pregnancy: are there reconcilable differences? *Neurotoxicol Teratol* 1993; 15: 281–6.
 - 88 *Samuels J, Schwalbe SS, Marx GF.* Speedballs: a new cause of intraoperative tachycardia and hypertension. *Anesth Analg* 1991; 72: 397–8.
 - 89 *Winniford MD, Wheelan KR, Kremers MS, et al.* Smoking-induced coronary vasoconstriction in patients with atherosclerotic coronary artery disease: evidence for adrenergically mediated alterations in coronary artery tone. *Circulation* 1986; 73: 662–7.
 - 90 *Fox BS.* Development of a therapeutic vaccine for the treatment of cocaine addiction. *Drug Alcohol Depend* 1997; 48: 153–8.
 - 91 *Fox BS, Kantak KM, Edwards MA, et al.* Efficacy of a therapeutic cocaine vaccine in rodent models. *Nature Med* 1996; 2: 1129–32.
 - 92 *Dodge RE.* Obstetric anesthesia and lawsuits. In: *Hughes SC, Levinson G, Rosen MA (Eds.). Shnider and Levinson's Anesthesia for Obstetrics*, 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2002: 441–51.
 - 93 *Birnback DJ.* Interactions in anesthesia: anesthetic management of the drug abusing parturient. *Acta Anaesthesiol Belg* 2001; 52: 351–6.
 - 94 *Kuczkowski KM.* Cesarean section in a cocaine-intoxicated parturient: regional vs general anesthesia? *Anaesthesia* 2003; 58: 1042–3.