



## Cocaine Toxicity in Emergency Medicine: Rapid Assessment, Stabilization, and Evidence-Based Management

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### Abstract

**Background:** Cocaine toxicity is a critical global health issue, frequently encountered in emergency departments due to its rapid progression from sympathetic overdrive to life-threatening cardiovascular and neurologic complications.

**Aim:** To review the pathophysiology, clinical presentation, diagnostic strategies, and evidence-based management of acute cocaine toxicity in emergency medicine.

**Methods:** This narrative review synthesizes current literature on cocaine's toxicodynamics, epidemiology, and emergency care protocols, emphasizing rapid assessment, stabilization, and multidisciplinary management.

**Results:** Cocaine toxicity manifests through catecholamine excess, vasoconstriction, and sodium-channel blockade, leading to tachydysrhythmias, hypertensive crises, myocardial ischemia, stroke, seizures, and hyperthermia. Evaluation requires comprehensive laboratory testing (electrolytes, troponin, creatine kinase), ECG monitoring, and targeted imaging for complications such as intracranial hemorrhage or body-packer syndrome. First-line treatment includes benzodiazepines for agitation and cardiovascular stabilization, with adjunctive use of calcium channel blockers, vasodilators, and labetalol for refractory hypertension and tachycardia. Hyperthermia management through external cooling and aggressive sedation is critical. Prognosis depends on early intervention, with severe cases complicated by excited delirium, rhabdomyolysis, and multi-organ failure.

**Conclusion:** Effective management of cocaine toxicity requires rapid recognition, physiologic stabilization, and integrated team-based care. Benzodiazepines remain cornerstone therapy, while adjunctive pharmacologic strategies and aggressive temperature control improve outcomes. Long-term success hinges on harm-reduction counseling and linkage to addiction services.

**Keywords:** Cocaine toxicity, emergency medicine, sympathomimetic toxidrome, hyperthermia, benzodiazepines, cardiovascular complications, multidisciplinary care.

### Introduction

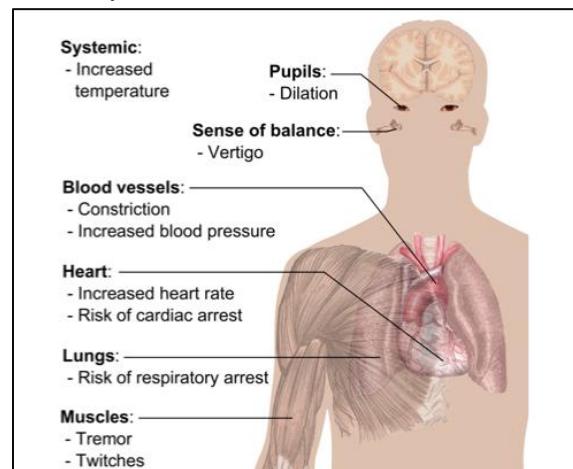
Cocaine misuse remains a substantial global public health concern, contributing to significant morbidity and mortality across diverse populations and healthcare systems. In the emergency department (ED), acute cocaine toxicity is encountered as a time-sensitive clinical syndrome because it can rapidly progress from agitation and sympathetic overdrive to life-threatening cardiovascular and neurologic events. Patients may present with a spectrum of manifestations, ranging from anxiety, tremor,

diaphoresis, and hyperthermia to severe tachycardia, malignant dysrhythmias, hypertensive emergencies, and coronary vasospasm. These acute physiologic disturbances can precipitate catastrophic sequelae, including acute coronary syndrome, ischemic or hemorrhagic stroke, seizures, and sudden death.[1][2][3] The emergency clinician's role is therefore defined by rapid recognition of a toxidrome, early stabilization of airway, breathing, and circulation, and prompt initiation of therapies that address both the underlying sympathomimetic state

and its end-organ consequences. Cocaine's acute toxicity is best understood through its potent stimulation of the sympathetic nervous system and its direct effects on cardiac conduction and vascular tone. By increasing catecholaminergic activity, cocaine can produce marked increases in heart rate and blood pressure, raising myocardial oxygen demand at the very moment that coronary blood flow may be compromised by vasoconstriction and vasospasm. This mismatch between oxygen demand and supply provides a mechanistic basis for cocaine-associated chest pain and myocardial ischemia, even in patients without traditional atherosclerotic risk factors. In addition, cocaine's proarrhythmic potential—stemming from altered ion channel activity and heightened adrenergic stimulation—creates a clinically dangerous substrate for dysrhythmias that may deteriorate into cardiac arrest. The ED must also remain vigilant for concurrent hyperthermia, rhabdomyolysis, and metabolic derangements, especially in patients with severe agitation or prolonged physical restraint, because these factors can further destabilize cardiovascular function and worsen outcomes.

A complicating feature of modern ED presentations is the evolving pattern of cocaine exposure and associated risks. Over recent decades, emergency clinicians have increasingly managed “body packers” and “body stuffers,” individuals who conceal cocaine in the gastrointestinal tract for transport or to evade law enforcement. In body packers, rupture of concealed packets can lead to abrupt, massive systemic absorption of cocaine, producing fulminant toxicity that can progress quickly to seizures, refractory dysrhythmias, and cardiovascular collapse. These cases require a heightened index of suspicion, careful risk stratification, and coordinated multidisciplinary management due to the potentially explosive onset and severity of symptoms. Furthermore, many patients present after polysubstance use, which complicates diagnosis and treatment. Co-ingestion with alcohol is particularly relevant because it can alter cocaine's metabolism and clinical effects, and additional substances—such as opioids, benzodiazepines, or other stimulants—may mask or amplify key signs, making toxicome recognition more challenging and increasing the risk of adverse outcomes. Although cocaine can adversely affect nearly every organ system, the most lethal consequences are typically cardiovascular. This reality shapes ED priorities: rapid control of

sympathetic excess, early evaluation of chest pain and neurologic symptoms, and continuous monitoring for evolving dysrhythmias and hemodynamic instability. In this setting, effective emergency care depends not only on immediate stabilization but also on anticipating downstream complications, recognizing high-risk presentations such as suspected packet rupture, and managing patients within protocols that support safe monitoring and timely escalation of care.[1][2][3]



**Fig. 1:** Cocaine Toxicity.

#### Etiology

Cocaine use originates from the long-standing cultural and botanical history of the coca plant, *Erythroxylon coca*, whose leaves have been utilized as a stimulant in parts of South America for more than four millennia. Traditionally, coca leaf use was embedded in social and ritual contexts, valued for perceived benefits such as increased endurance and reduced fatigue at high altitude. The modern etiologic pathway to cocaine toxicity, however, is primarily linked to the extraction, refinement, and commercialization of cocaine alkaloids, processes that transformed a naturally occurring plant product into a highly potent psychoactive substance with substantial abuse liability. Cocaine was first isolated from coca leaves in the mid-nineteenth century, a development that coincided with a broader period of rapid expansion in pharmacologic experimentation and consumer “patent medicine” markets. In that era, cocaine was widely viewed as safe and was incorporated into an array of commercial preparations, including remedies marketed for toothache, gastrointestinal symptoms such as nausea, and general “energy tonics.” Its presence in early formulations of the “Coca-Cola” beverage reflects the historical normalization of cocaine-containing products before systematic regulatory frameworks,

controlled trial data, and modern pharmacovigilance standards were established. This early medical and commercial enthusiasm contributed to wider exposure and familiarity, which, in turn, set the stage for later patterns of misuse once the drug's addictive potential and harm profile became more clearly recognized [3][4].

As international legal and public health perspectives evolved, cocaine became progressively restricted. The International Single Convention on Narcotic Drugs (1961) was a pivotal policy milestone that criminalized non-medical, recreational cocaine use internationally, framing cocaine misuse as a transnational regulatory and enforcement concern. Despite these restrictions, cocaine experienced a well-documented resurgence in popularity during the 1970s, a period often associated with nightlife and club cultures, and again in the 1980s with the emergence and spread of crack cocaine. The development of crack cocaine—characterized by rapid onset of effect and high reinforcing potential—marked a significant etiologic shift, facilitating patterns of use associated with increased dependence risk, more frequent dosing cycles, and higher incidence of acute toxicity presentations. In the United States, cocaine is classified as a DEA Schedule II controlled substance, reflecting a dual reality: cocaine has recognized medical utility, but also a high potential for abuse and dependence.[4] Clinically, this classification aligns with the etiologic understanding that cocaine toxicity is driven predominantly by non-medical exposure—often through illicit supply chains, variable purity, and high-risk routes of administration—while also acknowledging that controlled medical use exists within tightly regulated contexts. Overall, the etiology of cocaine toxicity is best conceptualized as the intersection of historical cultivation and extraction, shifting sociocultural trends, regulatory milestones, and contemporary illicit drug markets that amplify exposure intensity and unpredictability.[4]

### Epidemiology

Cocaine abuse continues to pose a major public health challenge across the globe, affecting both developed and developing nations. According to the most recent United Nations World Drug Report, approximately 20 million individuals worldwide are estimated to use cocaine, marking it as one of the most prevalent illicit stimulants in circulation. Despite significant efforts to curb production and

distribution, global consumption patterns reveal persistent—and in some regions, resurgent—use. While North America historically represented the highest concentration of cocaine users, recent epidemiological trends demonstrate emerging usage in Europe, Latin America, and parts of Asia, reflecting the drug's expanding global footprint. In North America, after a period of gradual decline in regular cocaine use beginning in the mid-2000s, the last several years have shown a renewed increase, with an estimated 1% of the population reporting active cocaine use. This resurgence corresponds with increased availability and changes in trafficking routes, particularly involving synthetic cocaine derivatives and the mixing of cocaine with other substances such as fentanyl, which has compounded the mortality risk associated with use. In the United States, data from the Drug Enforcement Administration (DEA) highlight the ongoing prevalence of cocaine initiation and dependence. In 2012 alone, approximately 639,000 individuals aged 12 years or older reported using cocaine for the first time in the preceding 12 months, which equates to an alarming 1,800 new users per day. These numbers underscore the persistent appeal and accessibility of cocaine, especially among young adults in urban environments [4][5].

Cocaine use contributes significantly to healthcare utilization, particularly in emergency and critical care settings. The Substance Abuse and Mental Health Services Administration (SAMHSA) reported that in 2011, cocaine was the most frequent drug of abuse linked to emergency department (ED) visits in the United States, accounting for 505,224 cases, or 40.3% of all drug-related ED presentations. This translates to approximately 162 ED visits per 100,000 population. Many of these admissions are related to acute toxicity symptoms—such as chest pain, tachycardia, seizures, and hypertensive crises—or complications arising from polysubstance use, including concurrent alcohol or opioid ingestion. Epidemiologic data also reveal disproportionate effects across demographic and socioeconomic groups. Cocaine abuse tends to be more common among males, individuals aged 18 to 35, and those residing in urban areas. Moreover, disparities in access to addiction treatment and preventive healthcare contribute to sustained cycles of relapse and readmission. On a global scale, the trafficking and production of cocaine remain concentrated in regions of South America, particularly Colombia,

Peru, and Bolivia, while consumption patterns remain highest in North America and Western Europe. In summary, cocaine abuse remains a global epidemic with rising prevalence and severe public health implications. Despite periodic declines in specific populations, the overall burden on emergency medical systems, the persistence of new users, and the expanding geographic distribution of cocaine use underscore the need for continued surveillance, prevention, and treatment efforts at both national and international levels.[5][6]

### **Pathophysiology**

Cocaine toxicity is fundamentally a disorder of extreme sympathetic activation combined with direct cardiotoxic and neurotoxic effects that can destabilize multiple organ systems within minutes to hours. Patients who abuse cocaine are therefore at risk for a broad range of acute, life-threatening consequences, including tachydysrhythmias, severe hypertension, acute coronary syndrome, stroke, acute myocardial and renal failure, seizures, hyperthermia, cocaine-induced rhabdomyolysis, and significant fetal and maternal morbidity and mortality.[7] The clinical heterogeneity of presentations reflects both dose-related toxicity and variability in route of exposure, co-ingestions, baseline cardiovascular reserve, and the presence of underlying structural disease. From an emergency medicine perspective, the pathophysiologic mechanisms are clinically important because they explain why symptoms can escalate rapidly and why management must address both the sympathetic toxicodrome and the downstream end-organ injuries it provokes. At the neurochemical level, cocaine exerts its most consequential acute effects by inhibiting presynaptic reuptake of catecholamines—particularly norepinephrine and dopamine—at sympathetic nerve endings. By blocking these transporters, cocaine increases synaptic concentrations of catecholamines and prolongs receptor stimulation, leading to marked adrenergic excess. The resulting sympathomimetic surge manifests as tachycardia, hypertension, vasoconstriction, diaphoresis, psychomotor agitation, and hyperthermia, and it creates a physiologic environment in which myocardial oxygen demand rises sharply while vascular tone becomes dysregulated. This catecholamine-driven state is central to the cardiovascular lethality of cocaine because it simultaneously increases the heart's workload and promotes vasospasm, thereby producing supply–demand mismatch in coronary

perfusion that can culminate in ischemia or infarction [7].

Cocaine's adverse cardiac effects are not solely mediated by catecholamines; the drug also possesses local anesthetic properties that impair myocardial impulse conduction. By interfering with ion channel function in cardiac tissue, cocaine can slow conduction velocity and facilitate re-entrant electrical circuits. When combined with heightened catecholaminergic stimulation—which increases automaticity and irritability—this conduction impairment creates an ideal substrate for life-threatening ventricular arrhythmias. Clinically, this explains why patients may develop tachydysrhythmias that are disproportionate to their apparent intoxication and why arrhythmias can occur even in the absence of pre-existing heart disease. In the acute setting, severe hypertension also contributes to afterload stress, increased myocardial wall tension, and potential plaque rupture in patients with coronary atherosclerosis, further increasing the likelihood of acute coronary syndrome. Long-term cocaine exposure adds an additional layer of risk by inducing structural and histologic cardiac changes. Chronic use has been associated with myocardial fibrosis, myocarditis, and contraction band necrosis, reflecting repeated catecholamine surges, microvascular ischemia, and direct cellular injury. These changes may reduce cardiac compliance and reserve, increasing susceptibility to arrhythmias, heart failure, and ischemic events during subsequent intoxication episodes. Importantly, cocaine significantly increases myocardial oxygen requirements by elevating heart rate and cardiac output; when even mild coronary disease is present, these hemodynamic changes—combined with cocaine's vasoconstrictive capacity—can trigger acute coronary syndrome through both demand ischemia and impaired coronary blood flow. This pathophysiologic convergence is why cocaine-associated chest pain is treated as potentially ischemic until proven otherwise and why the ED approach emphasizes rapid risk stratification and continuous monitoring. Beyond the myocardium, cocaine exerts potent cerebrovascular effects. It increases the risk of ischemic stroke through mechanisms that include acute hypertension, vasoconstriction, endothelial dysfunction, and potentially prothrombotic changes. Severe blood pressure elevations can compromise cerebral autoregulation, while vasospasm can reduce regional cerebral perfusion, creating conditions conducive to ischemia. Cocaine also lowers the seizure threshold,

making seizures a recognized manifestation of toxicity. This may occur via enhanced excitatory neurotransmission and catecholamine excess, as well as through secondary contributors such as hyperthermia, hypoxia, or metabolic derangements. In chronic exposure, neuroadaptation can occur: long-term cocaine use can reduce dopamine receptor density, a change associated with extrapyramidal features such as dystonia, bradykinesia, akinesia, and akathisia. While these chronic neurologic sequelae are not the typical focus of emergent care, they underscore the drug's capacity to produce enduring neurobiologic injury in addition to acute toxicity [6][7][8].

A particularly high-risk and clinically challenging manifestation of cocaine toxicity is delirium, including the syndrome often described as excited delirium. In this state, patients may exhibit aggression, hyperactivity, extreme paranoia, incoherent screaming, profound agitation, and apparent unusual strength. The pathophysiologic danger is that these individuals appear to be especially sensitive to elevated catecholamine levels, and the combination of agitation, hyperadrenergic physiology, and often hyperthermia can precipitate sudden cardiovascular collapse. Excited delirium is therefore associated with a heightened risk of sudden death, and it demands rapid de-escalation, sedation, temperature control, and careful monitoring to prevent progression to fatal dysrhythmias or multi-organ failure. Hyperthermia is another hallmark of severe cocaine toxicity and serves as a marker of poor prognosis. Temperatures may become extreme, reportedly reaching as high as 45 °C in severe cases. Hyperthermia reflects a convergence of catecholamine-driven heat production, intense psychomotor activity, impaired heat dissipation, and sometimes environmental factors. Clinically, severe hyperthermia is closely linked to skeletal muscle breakdown and rhabdomyolysis, which can lead to acute kidney injury through myoglobin-mediated tubular toxicity. Hyperthermia also contributes to hepatic injury, encephalopathy, and coagulopathy, including disseminated intravascular coagulation (DIC). As cellular injury accumulates, metabolic acidosis may develop, reflecting both hypoperfusion and lactic acid generation, further destabilizing cardiovascular and neurologic function. In this way, hyperthermia is not merely a symptom; it is an amplifier of systemic injury and a predictor of clinical deterioration. In summary, cocaine toxicity

represents a complex pathophysiologic syndrome driven by catecholamine excess, direct cardiotoxic conduction effects, vasoconstriction-induced ischemia, and neuroexcitatory mechanisms that lower seizure threshold and provoke delirium. Acute complications—arrhythmias, hypertensive crises, acute coronary syndrome, stroke, hyperthermia, and rhabdomyolysis—can occur rapidly and interact synergistically, producing multi-organ failure and sudden death.[7] Understanding these mechanisms is essential in emergency care because it informs rapid prioritization of sedation, cardiovascular stabilization, temperature management, and monitoring for evolving end-organ injury [7].

### Toxicokinetics

Cocaine toxicity is shaped by both the drug's route-dependent absorption and its rapid yet multifaceted pharmacologic actions on neurotransmitter systems and cardiovascular physiology. Clinically, cocaine may be administered through several routes—intranasal insufflation (snorting), oral ingestion (swallowing), intravenous injection, or inhalation (smoking). Each route produces a distinct onset and intensity of effect, which in turn influences the speed with which toxicity develops and the duration over which complications may unfold. Although cocaine is often described as a short-acting agent with an approximate half-life of about one hour, its toxic impact can persist well beyond the initial euphoric phase because active metabolites and downstream physiologic sequelae, such as vasoconstriction and thrombosis, may continue for hours after use.[7] For emergency clinicians, this means that an apparently improving patient may still be at risk for delayed ischemic events, dysrhythmias, or recurrent hypertension, particularly when co-ingestions or high-dose exposures are involved. At the core of cocaine's pharmacodynamics is its ability to bind and block monoamine reuptake transporters. Importantly, cocaine acts with relatively equal affinity at the dopamine, norepinephrine, and serotonin transporters, preventing reuptake and causing accumulation of these monoamines in the synaptic cleft. The net effect is enhanced and prolonged sympathetic stimulation, along with central nervous system excitation and mood-altering effects. In acute toxicity, the excess norepinephrine is especially consequential because it drives adrenergic receptor activation throughout the cardiovascular system and peripheral vasculature. This catecholaminergic state

explains the typical toxicodrome—tachycardia, hypertension, diaphoresis, agitation, and hyperthermia—and provides the physiologic substrate for life-threatening end-organ injury [7][8].

Cocaine's principal cardiovascular actions are mediated through alpha- and beta-1-adrenoceptor stimulation, which increases heart rate, systemic arterial pressure, and myocardial contractility. These changes are major determinants of myocardial oxygen demand; when demand rises abruptly, even modest limitations in coronary blood flow can precipitate ischemia. Simultaneously, cocaine can reduce oxygen supply by promoting arterial vasoconstriction—an effect that may persist for hours after consumption due to both cocaine and its metabolites.[7] Epicardial coronary arteries appear particularly vulnerable to this vasoconstrictive response, which can lead to clinically significant reductions in coronary perfusion and contribute to cocaine-associated chest pain, ischemia, and acute coronary syndrome. This mismatch between myocardial oxygen demand and oxygen delivery is a defining toxicodynamic feature of cocaine and is central to its lethality. In addition to vasospasm, cocaine promotes a prothrombotic milieu. Cocaine-induced platelet activation and thrombus formation occur through mechanisms that include alpha-adrenergic stimulation and adenosine diphosphate-mediated increases in platelet aggregation. Moreover, cocaine exposure is associated with increased levels of plasminogen activator inhibitor, which suppresses fibrinolysis and thereby further promotes thrombosis.[7] These effects are clinically significant because they can transform transient vasoconstriction into sustained vascular occlusion, increasing the risk of myocardial infarction and ischemic stroke, particularly when combined with severe hypertension and endothelial dysfunction. Cocaine also exhibits membrane-stabilizing, local anesthetic-like properties. Similar to lidocaine and related agents, cocaine blocks voltage-gated sodium channels and interferes with action potential propagation in excitable tissues. This mechanism corresponds to a Vaughan-Williams class IC-type effect and contributes to conduction disturbances and tachyarrhythmias, especially in the setting of heightened adrenergic tone. The combination of increased automaticity from catecholamine excess and slowed conduction from sodium-channel blockade creates conditions favorable for re-entry circuits and malignant ventricular dysrhythmias,

explaining why arrhythmias may occur abruptly and unpredictably in intoxicated patients [7].

Finally, cocaine's toxicologic profile is broadened by interactions with multiple receptor systems beyond monoamine transporters. The drug has been reported to affect muscarinic acetylcholine receptors, N-methyl-D-aspartate (NMDA) receptors, sigma receptors, and kappa-opioid receptors, adding complexity to its neurologic and autonomic manifestations.[8] These additional targets may contribute to altered perception, agitation, delirium, and neuroexcitation, and they help explain why presentations can be clinically heterogeneous, especially in patients with high-dose exposure or polysubstance use. Taken together, cocaine's toxicokinetics reflect a drug with rapid absorption and relatively short half-life but with prolonged and sometimes delayed cardiovascular and neurologic consequences driven by sustained vasoconstriction, prothrombotic changes, and multi-receptor interactions.[7][8]

### History and Physical

Patients with suspected cocaine toxicity often present to the emergency setting with a combination of neuropsychiatric activation and cardiopulmonary distress, and they may also arrive following blunt or penetrating trauma related to impaired judgment, violence, or high-risk behavior. Common presenting complaints include agitation, anxiety, chest pain, dyspnea, and psychotic features such as paranoia or hallucinations. Vital signs frequently demonstrate tachycardia and hypertension, reflecting a sympathomimetic toxicodrome. Importantly, many patients are unwilling to disclose cocaine use because of stigma, legal concerns, or altered mental status, which means clinicians must rely on objective findings, collateral history, and a structured differential diagnosis rather than disclosure alone. Early assessment should therefore proceed as it would for any undifferentiated unstable patient, prioritizing airway, breathing, circulation, and rapid identification of time-sensitive threats such as acute coronary syndrome, stroke, intracranial hemorrhage, hyperthermia, and seizure. History-taking should be purposeful and safety-oriented. A thorough substance use history is essential when possible, including route of use (snorted, smoked, injected, ingested), timing and amount of last exposure, and whether co-ingestants were used—particularly alcohol, opioids, sedatives, or other stimulants. Clinicians should seek prior admissions for intoxication, withdrawal, chest pain, seizures, rhabdomyolysis, or psychiatric crises,

as prior complications increase suspicion for recurrent severe toxicity. When the patient cannot provide reliable information, collateral history from family, emergency medical services, or accompanying persons can be valuable, while recognizing that such sources may be incomplete. Medication history is also important, because certain prescribed agents can mimic sympathomimetic features or worsen toxicity (for example, serotonergic medications in the presence of stimulant use). Clinicians must keep the differential broad during initial evaluation because multiple disorders can present with agitation, tachycardia, hypertension, and hyperthermia. Alternatives to consider include withdrawal syndromes, thyrotoxicosis, primary psychiatric illness with acute psychosis, sepsis, pheochromocytoma, anticholinergic toxicity, serotonin syndrome, neuroleptic malignant syndrome, and intracranial hemorrhage. The presence of focal neurologic deficits, severe headache, or altered consciousness should heighten concern for intracranial pathology even when stimulant use is suspected [8][9].

On physical examination, patients with cocaine toxicity may exhibit hypertension, altered mental status, seizures, chest pain, and dyspnea. Epistaxis may be present in intranasal users due to mucosal irritation and vasoconstriction. Headache and neurologic deficits can signal cerebrovascular complications, including ischemic or hemorrhagic stroke. Hyperthermia is a particularly concerning finding because it correlates with severe toxicity and may accompany profound diaphoresis, agitation, and metabolic derangements. Vascular spasm can manifest as cool extremities, diminished distal pulses, or signs of ischemia, underscoring cocaine's vasoconstrictive potential. Dermatologic findings may include extreme diaphoresis and, in some cases, pruritus. Ocular findings can occur, especially in those who handle cocaine or use it in ways that expose the eye; blurred vision, corneal ulceration, and even vision loss may be encountered and require urgent ophthalmic assessment. Gastrointestinal symptoms such as diarrhea, vomiting, and abdominal pain warrant careful attention because mesenteric ischemia is an important, potentially lethal diagnosis associated with vasospasm and thrombosis. Among the most alarming clinical syndromes is excited delirium, characterized by severe agitation, confusion, aggression, paranoia, hyperthermia, and often extraordinary physical strength; this state is

associated with sudden decompensation and demands rapid sedation and physiologic stabilization. Clinically, acute cocaine toxicity has been described in stages that reflect escalating neurologic and cardiopulmonary dysfunction. In early or stage 1 toxicity, patients may show central nervous system symptoms such as headache, nausea, mydriasis, vertigo, twitching, pseudohallucinations, and preconvulsive movements. Cardiovascular findings may include elevated blood pressure and ectopic beats, while pulmonary manifestations may involve tachypnea. Hyperthermia may begin to develop, and psychiatric features such as paranoia, euphoria, confusion, aggression, agitation, emotional lability, and restlessness are common. This stage is often the point at which early intervention—particularly sedation, cooling measures when indicated, and monitoring for ischemia—can prevent progression [8][9].

In stage 2 toxicity, clinical severity increases. Neurologic findings may evolve into encephalopathy, seizures, hyperreflexia with increased deep tendon reflexes, and incontinence. Cardiovascular instability may intensify, with persistent hypertension, arrhythmias, and signs such as peripheral cyanosis. Respiratory patterns may become abnormal, ranging from tachypnea and gasping to apnea or irregular breathing, reflecting both central dysregulation and metabolic stress. Hyperthermia may worsen, and the risk of rhabdomyolysis, acidosis, and multi-organ injury increases. Stage 3 represents critical, often terminal decompensation. Neurologically, patients may develop areflexia, coma, fixed and dilated pupils, and progressive loss of vital functions. Cardiovascular collapse may manifest as hypotension, ventricular fibrillation, and cardiac arrest. Pulmonary failure can present as apnea, respiratory failure, cyanosis, and agonal respirations. At this stage, resuscitation requires immediate advanced life support, aggressive treatment of hyperthermia and metabolic derangements, and rapid identification of reversible causes. Overall, the history and physical examination in suspected cocaine toxicity must balance broad diagnostic vigilance with rapid prioritization of immediate threats. Because presentations can be deceptive—particularly when patients deny use or have co-ingestions—clinicians should interpret tachycardia, hypertension, agitation, and hyperthermia in context, screen systematically for neurologic and cardiovascular complications, and

remain prepared to escalate care quickly when signs suggest progression from early toxicity to life-threatening instability [8][9].

### Evaluation

Evaluation of suspected cocaine toxicity in the emergency setting must be tailored to the patient's clinical presentation while maintaining a low threshold for identifying time-sensitive, high-mortality complications such as acute coronary syndrome, malignant dysrhythmias, stroke, intracranial hemorrhage, hyperthermia, rhabdomyolysis, and occult trauma. Because cocaine intoxication can mimic other medical and toxicologic syndromes—and because patients may deny use or present after polysubstance exposure—the diagnostic approach should combine focused laboratory testing, bedside monitoring, and targeted imaging to confirm organ involvement, rule out alternative diagnoses, and guide disposition. The clinician's overarching goal is not simply to "prove" cocaine exposure, but to quantify physiologic derangement, detect evolving end-organ injury, and identify conditions that require immediate intervention. Initial testing commonly includes a complete blood count and a comprehensive chemistry panel to assess for leukocytosis, anemia, electrolyte disturbances, renal dysfunction, and hepatic stress that may accompany severe agitation, dehydration, hyperthermia, or shock.[9][10] Electrolyte abnormalities—particularly potassium and bicarbonate derangements—are clinically important because they can predispose to dysrhythmias and reflect metabolic acidosis. Renal indices are essential when rhabdomyolysis is suspected or when hypotension, dehydration, or pigment nephropathy may be developing. In addition, serum glucose should be checked early, especially in patients with altered mental status or seizures, because hypoglycemia or hyperglycemia can be contributory or mimicking conditions.

Cardiac evaluation is central in many presentations, particularly when chest pain, dyspnea, hypoxia, or abnormal vital signs are present. Troponin testing is used to assess for myocardial injury and to help rule out myocardial infarction in patients with cocaine-associated chest pain.[9][10] Depending on institutional protocols and risk stratification, serial troponins may be required to capture evolving injury, particularly when symptoms began recently or when initial tests are nondiagnostic. B-type natriuretic peptide can be considered when pulmonary edema or heart failure physiology is suspected, as cocaine can precipitate myocardial

ischemia, cardiomyopathy, or hypertensive pulmonary edema.[9][10] An electrocardiogram (ECG) should be obtained in patients with chest pain, dyspnea, an irregular pulse, syncope, or hypoxia, because it provides rapid assessment for ischemic changes, conduction abnormalities, and dysrhythmias that may require immediate treatment.[9][10] Continuous cardiac monitoring is often warranted for symptomatic patients, those with abnormal ECG findings, or those with severe hypertension and tachycardia. Assessment for hyperthermia-related complications and muscle injury is also frequently indicated. Creatine kinase is particularly useful for detecting rhabdomyolysis in agitated, hyperthermic, or restrained patients, and rising levels may signal ongoing muscle breakdown and risk for acute kidney injury.[9][10] Urinalysis can complement this evaluation by identifying myoglobinuria, which may present as heme-positive urine with few red blood cells on microscopy. Early detection matters because aggressive hydration and supportive management can reduce renal complications. A urinalysis can also identify infection or other renal pathology that may contribute to altered mental status or systemic instability.

A urine toxicology screen is an important component of evaluation because polysubstance exposure is common and may change both risk assessment and management priorities.[9][10] While cocaine itself is often cleared from the body within approximately 24 hours, its metabolite benzoylecgonine can persist for much longer—sometimes weeks—depending on frequency of use, metabolism, and assay characteristics. This prolonged detectability makes it useful for confirming prior exposure even when acute intoxication is waning, although clinicians must interpret results in clinical context because a positive screen does not necessarily prove that current symptoms are solely attributable to cocaine. Benzoylecgonine has also been associated with neurotoxic effects, reinforcing the need for cautious monitoring when neurologic symptoms are prominent. Imaging is selected based on symptoms and suspected complications. A chest radiograph may be obtained to evaluate for pulmonary edema, pneumothorax, aspiration pneumonia, or other acute thoracic pathology that can accompany intoxication, seizures, or trauma.[9][10] In patients with abdominal pain, unexplained toxicity, or suspicion for body packing or body stuffing, abdominal radiography may reveal ingested packets.[9][10] However, plain radiographs can yield false-negative results;

therefore, contrast-enhanced studies or computed tomography are often recommended when suspicion remains high, because missed packets are dangerous and the risk of packet rupture increases with time. Prompt diagnosis is therefore a safety priority, as rupture can cause abrupt, massive absorption leading to fulminant toxicity.

Neurologic evaluation should be equally deliberate. Head computed tomography is recommended when altered mental status, focal neurologic deficits, severe headache, or seizures raise concern for intracranial hemorrhage or other structural pathology.[9][10] Although cocaine can directly precipitate seizures and stroke through hypertension and vasospasm, clinicians should not attribute neurologic findings to intoxication without excluding alternative causes, particularly because timely intervention for hemorrhage or ischemia can be outcome-determining. If meningitis is clinically suspected—based on fever, neck stiffness, immunocompromise, or other supportive findings—lumbar puncture should be pursued after appropriate imaging and stabilization, recognizing that cocaine toxicity does not exclude concurrent infection. Overall, evaluation of cocaine toxicity requires a dual focus: confirming exposure patterns and, more importantly, detecting end-organ injury and alternative diagnoses that can mimic or coexist with intoxication. By integrating laboratory studies (including troponin, creatine kinase, urinalysis, and toxicology), ECG monitoring, and targeted imaging (chest radiography, abdominal imaging for body packers, and head CT when neurologic compromise is present), clinicians can reduce missed high-risk complications and guide timely treatment and safe disposition decisions.[9][10]

### Treatment / Management

Management of acute cocaine toxicity in the emergency setting begins with immediate physiologic stabilization and a disciplined prioritization of life-threatening problems. Patients may arrive with severe agitation, hyperadrenergic cardiovascular instability, hyperthermia, seizures, chest pain, or altered mental status, and these features can evolve rapidly. Accordingly, clinicians should approach treatment using a structured resuscitation framework, with focused attention to airway, breathing, circulation, disability, and exposure (the ABCDE approach). Early airway assessment is essential because escalating agitation, recurrent seizures, or progressive hyperthermia can compromise ventilation and

oxygenation, while excessive sedation—sometimes required for behavioral control—may also precipitate hypoventilation. Simultaneously, circulation must be evaluated for hypertensive emergencies, dysrhythmias, ischemia, and shock, with continuous monitoring initiated as soon as possible. Disability assessment should include a rapid neurologic screen and bedside glucose measurement, since hypoglycemia can mimic or exacerbate neuropsychiatric symptoms and must be ruled out early as a reversible contributor. Temperature is a critical vital sign in suspected cocaine toxicity; fever or hyperthermia is not only a marker of severity but also an amplifier of end-organ injury risk, necessitating prompt temperature-directed interventions. In women of childbearing age, pregnancy testing should be obtained early because pregnancy influences both risk stratification and diagnostic imaging choices, and cocaine exposure is associated with fetal and maternal complications that may require tailored management. Across all stages of care, treatment should be symptom-driven and anchored in objective findings rather than solely on patient disclosure, as underreporting of cocaine exposure is common [9][10][11].

<ul style="list-style-type: none"> <li>- General supportive care includes stabilization, ABCs, and monitoring</li> <li>- Avoid succinylcholine if possible, especially in the setting of rhabdomyolysis, due to elevation of potassium</li> <li>- IV Lipid emulsion therapy a consideration for ongoing instability – consult Poison Control</li> </ul>	
Neuropsychiatric	<p>Benzodiazepines have been shown to lower mortality more than antipsychotics:</p> <ul style="list-style-type: none"> <li>- Diazepam IV 5-10 mg every 5 minutes PRN</li> <li>- Lorazepam IV 1-2 mg every 5 minutes PRN</li> <li>- Midazolam IV 1-2 mg every 5 minutes</li> <li>- Midazolam IM 5-10 mg every 10-20 minutes</li> </ul> <p>Ketamine, barbiturates, or propofol second line</p> <p>Haloperidol increases seizure risk so requires risk/benefit assessment</p>
Hypertension	<p>Start with benzodiazepines, but may also use phentolamine, nitroglycerin, and beta-blockers may be used despite risk of reflex hypotension and tachycardia.</p> <ul style="list-style-type: none"> <li>- Phentolamine IV 1 mg every 3 minutes with continuous blood pressure monitoring and if two doses fail to reduce MAP by at least one-third, then increase dose by 1 mg until 5 mg/dose until this goal is reached</li> <li>- Labetalol 0.25 mg/kg (20 mg) and then either 40-80 mg IV q 10 minutes or infusion 1- 2 mg/hour; total dose 300 mg</li> </ul>

**Fig. 2:** Emergency care of cocaine toxicity.

A central principle in treating cocaine toxicity is that the acute syndrome is often driven by excessive central sympathetic outflow, with downstream cardiovascular and behavioral consequences. For this reason, initial pharmacologic management prioritizes rapid reduction of adrenergic activation, control of agitation, and prevention of complications such as hyperthermia, rhabdomyolysis, and ischemia. Physical restraints should be avoided whenever possible, not because restraint is never necessary, but because struggling against restraints can intensify catecholamine release, worsen hyperthermia, increase lactic acidosis, and heighten the risk of rhabdomyolysis and sudden

decompensation. When immediate behavioral control is necessary to protect the patient and staff, rapid chemical sedation is generally preferred, with careful monitoring for respiratory compromise. Based on a large systematic review, benzodiazepines are considered first-line therapy for both agitation and cocaine-associated cardiovascular toxicity because they reduce central nervous system sympathetic outflow.[11] Clinically, this approach addresses the upstream driver of many manifestations—tachycardia, hypertension, anxiety, and psychomotor agitation—rather than treating each downstream effect in isolation. Benzodiazepines can decrease agitation, blunt catecholamine-mediated physiologic stress, and reduce the likelihood of escalating violence, hyperthermia, and metabolic deterioration. However, effective symptom control may require repeated dosing or higher cumulative doses, especially in severely agitated patients, and clinicians must recognize the attendant risk of over-sedation, hypoventilation, and respiratory depression when escalating benzodiazepine therapy. These risks underscore the need for continuous monitoring, readiness for airway support, and frequent reassessment of mental status and respiratory effort, particularly when benzodiazepines are combined with other sedating agents [11].

When hypertension persists despite sedation or when cardiovascular toxicity is prominent, additional targeted therapies may be indicated. Non-dihydropyridine calcium channel blockers such as diltiazem and verapamil have been shown to reduce blood pressure reliably, although they may not resolve tachycardia.[11] Their utility is often considered in situations where hypertension remains clinically significant, or when coronary vasospasm is a concern, provided there are no contraindications. In contrast, dihydropyridine agents such as nifedipine should be avoided because reflex tachycardia may occur, potentially worsening myocardial oxygen demand in a patient already experiencing adrenergic excess.[11] The selective alpha-blocker phentolamine has been recommended in some contexts, but its role is limited: it primarily treats alpha-mediated hypertension without addressing tachycardia, and many clinicians are unfamiliar with its dosing, titration, and practical bedside use. Moreover, limited titratability and operational unfamiliarity can introduce delays or errors during high-acuity care, reducing its attractiveness as a routine option. Vasodilators such as nitroglycerin and nitroprusside can be effective for lowering blood pressure and may

be particularly useful when ischemic symptoms or suspected coronary vasospasm are present. Nevertheless, clinicians must anticipate reflex tachycardia as a potential consequence of potent vasodilation, especially in patients who remain catecholamine-driven. Reflex tachycardia can be clinically relevant because it increases myocardial oxygen demand and can exacerbate ischemia, so heart rate and symptoms must be monitored closely. In this context, a medication that can address both heart rate and blood pressure may be desirable. The mixed beta/alpha blocker labetalol has been shown to be safe and effective for treating concomitant cocaine-induced hypertension and tachycardia, with no “unopposed alpha-stimulation” adverse events recorded.[11] Importantly, the use of labetalol is approved by an AHA/ACC guideline for cocaine and methamphetamine patients with unstable angina/non-STEMI [12]. In practice, this supports labetalol as a reasonable option when combined tachycardia and hypertension threaten end-organ perfusion or when ischemic risk is elevated, while emphasizing that therapy should be individualized and carefully monitored [10][11][12].

Agitation control remains a parallel priority because uncontrolled psychomotor activity can worsen hyperthermia, precipitate rhabdomyolysis, increase catecholamine levels, and impair the ability to perform diagnostic evaluation safely. Benzodiazepines are typically the cornerstone of management for agitation, but antipsychotics such as haloperidol and olanzapine may also be useful, particularly when frank psychosis, severe paranoia, or persistent behavioral dysregulation complicates care.[13] Combination treatment with benzodiazepines and antipsychotics has been shown to be more efficacious than monotherapy, suggesting that dual-mechanism sedation can provide more reliable behavioral control in severe cases.[13] When antipsychotics are used, clinicians must remain attentive to potential adverse effects, including dystonia, akathisia, and QT-related risks, and should select agents and dosing strategies consistent with the patient’s clinical status and institutional protocols. Diphenhydramine is often added to enhance sedation and to provide prophylaxis against dystonia and akathisia. A commonly cited example is the “B-52,” which combines haloperidol (5 mg), diphenhydramine (50 mg), and lorazepam (2 mg), reflecting a pragmatic regimen used in many emergency departments for severe agitation requiring rapid control. While such combinations can be

effective, they also increase the cumulative sedative burden, reinforcing the need for respiratory monitoring and readiness for escalation of airway support if consciousness or ventilation deteriorates. In cases of serious ventricular tachydysrhythmia, treatment may require therapies beyond sedation and blood pressure control. Lidocaine and intravenous lipid emulsion have been used successfully for severe ventricular tachydysrhythmias in several case reports, reflecting the concept that cocaine's sodium-channel-blocking properties can contribute to conduction instability and malignant rhythms.[11] Although these interventions are not routine for all patients, they are clinically relevant when standard measures fail or when the dysrhythmia phenotype suggests significant membrane-stabilizing toxicity. Such scenarios require expert consultation when available and close adherence to advanced cardiac life support principles, while simultaneously correcting contributing factors such as hypoxia, acidosis, and hyperthermia [12][13].

Hyperthermia is one of the most dangerous manifestations of severe cocaine toxicity and should be treated aggressively because it correlates with poor prognosis and is tightly linked to rhabdomyolysis, metabolic acidosis, and multiorgan injury. External cooling measures are the preferred initial strategy for cocaine-related hyperthermia.[11] Among the most accessible and safe methods in both prehospital and emergency department environments is tepid water misting combined with convection cooling from a fan, which promotes evaporative heat loss without introducing the risks associated with overly cold immersion in unstable patients.[11] Cooling should be paired with rapid sedation to stop ongoing heat generation from agitation and muscle activity, while monitoring for complications such as electrolyte abnormalities, renal injury, and coagulopathy as clinically indicated. Overall, treatment of cocaine toxicity is best conceptualized as integrated supportive care that targets the hyperadrenergic state, prevents secondary injury, and addresses specific end-organ threats. Benzodiazepines remain first-line for both agitation and cardiovascular toxicity, with careful attention to respiratory safety.[11] Adjunctive agents—selected calcium channel blockers, vasodilators, and labetalol in appropriate contexts—may be used to manage refractory hypertension and tachycardia, particularly when ischemia is suspected.[11][12] Antipsychotics and combination sedation strategies can be useful for

severe agitation and psychosis, while recognizing cumulative sedation risks.[13] Finally, hyperthermia management through external cooling is essential to improving outcomes in severe presentations.[11]

#### Differential Diagnosis

Acute cocaine toxicity frequently presents with a sympathomimetic pattern—agitation, tachycardia, hypertension, hyperthermia, and neuropsychiatric disturbance—yet these findings are not specific to cocaine and may overlap with several medical, neurologic, psychiatric, and toxicologic emergencies. A careful differential diagnosis is therefore essential, particularly because patients may deny substance use, may present after polysubstance exposure, or may have an alternative primary pathology that demands different treatment. Hypoglycemia is a critical early consideration in any patient with altered mental status, diaphoresis, tremor, seizure, or behavioral changes, because it can mimic stimulant intoxication and is rapidly reversible. Bedside glucose measurement should be performed early, and persistent neuropsychiatric symptoms despite correction should prompt further evaluation. Anticholinergic toxicity is another key mimic, typically characterized by agitation, tachycardia, mydriasis, dry mucous membranes, urinary retention, decreased bowel sounds, and hyperthermia. While cocaine toxicity often produces diaphoresis, anticholinergic syndromes classically feature dry skin, though mixed presentations can occur with co-ingestants. Central nervous system hemorrhage must be considered when severe headache, focal deficits, seizures, or depressed consciousness are present, as cocaine can both mimic and precipitate intracranial hemorrhage through hypertensive surges and vascular injury. Neuroimaging is particularly important when neurologic findings are prominent or when the clinical course is atypical. Alcohol withdrawal syndromes, including delirium tremens, may closely resemble stimulant toxicity through agitation, tremor, tachycardia, hypertension, hallucinations, and hyperthermia; the presence of recent cessation, prior withdrawal history, or autonomic instability evolving over hours to days supports this diagnosis. Acute schizophrenia or other primary psychotic disorders may present with paranoia, hallucinations, disorganized behavior, and agitation; however, prominent autonomic instability, hyperthermia, or chest pain should prompt consideration of intoxication or medical illness rather than a purely

psychiatric etiology. Phencyclidine (PCP) toxicity is an important alternative diagnosis, often associated with severe agitation, analgesia, nystagmus, hypertension, and violent behavior; it may require similar sedation strategies but carries distinctive clinical features and risks. Neuroleptic malignant syndrome should be considered in patients taking dopamine antagonists who present with hyperthermia, rigidity, altered mental status, and autonomic dysfunction. Differentiating this entity from stimulant toxicity is clinically important because targeted therapies and supportive priorities may differ. Ultimately, the most reliable approach is syndromic: stabilize the patient, identify immediate threats, and use history, examination findings, labs, and imaging to narrow the diagnosis while remaining vigilant for coexisting conditions [13][14].

### Prognosis

The prognosis of cocaine toxicity varies widely and is strongly determined by exposure magnitude, route of administration, co-ingestions, baseline cardiopulmonary reserve, and the presence or absence of early complications such as hyperthermia, seizures, dysrhythmias, acute coronary syndrome, or stroke. In severe cases, cocaine toxicity is associated with high mortality, particularly when patients present with excited delirium, profound hyperthermia, malignant ventricular dysrhythmias, or intracranial catastrophes. Prognostic risk is also heightened in individuals with delayed presentation or incomplete initial management, because the physiologic consequences of cocaine—vasospasm, thrombosis, and ongoing catecholaminergic stress—can persist after the perceived “high” has diminished. Injection drug use introduces additional prognostic hazards that extend beyond the acute toxicome. Intravenous cocaine exposure can be associated with pneumothorax, thrombosis, endocarditis, pseudoaneurysm formation involving central vessels, and the development of arteriovenous fistulas. These complications can result from traumatic vascular access, local vessel injury, and infection, and they may present subacutely, requiring ongoing clinical suspicion even after initial stabilization. The broader infectious and tissue sequelae of injection practices also worsen prognosis and can include cellulitis, HIV infection, thrombophlebitis, abscess formation, tetanus, and necrosis. These conditions may complicate hospitalization through sepsis risk, prolonged antibiotic requirements, surgical interventions, and long-term disability. Neurologic and psychiatric prognosis deserves particular

attention. Patients who develop neuropsychiatric symptoms—especially prolonged psychosis, delirium, or cognitive impairment—may experience extended recovery trajectories, and improvement may be incomplete. This is clinically relevant because discharge readiness cannot be judged solely by normalized vital signs; functional status, judgment, and safe follow-up must also be considered, particularly when suicidality, polysubstance dependence, or unstable housing is present. Prognosis is further worsened by concurrent use of alcohol or other substances, which can amplify cardiotoxicity, complicate sedation needs, and increase the risk of self-harm or unintentional overdose. Despite these risks, many patients recover fully from mild-to-moderate intoxication with timely supportive care, adequate sedation, and careful monitoring for evolving ischemia, rhabdomyolysis, and metabolic complications. Prognosis improves substantially when hyperthermia is corrected early, seizures are controlled promptly, and cardiovascular instability is treated before it progresses to end-organ injury. Long-term outcomes, however, are heavily influenced by relapse risk, access to substance-use treatment, and engagement with mental health services [14].

### Complications

Complications of cocaine toxicity include both acute physiologic derangements and secondary harms related to route of use, risk-taking behavior, and infectious exposures. Thrombophlebitis is a common complication in individuals who inject cocaine, reflecting vascular irritation, local endothelial injury, and infection risk from nonsterile injection practices. This may progress to deep venous thrombosis or septic thrombophlebitis, particularly when injections occur in high-risk sites such as the neck or groin. Pulmonary emboli can occur as a downstream consequence of thrombosis, presenting with dyspnea, pleuritic chest pain, hypoxemia, or hemodynamic collapse, and may be difficult to distinguish from cocaine-related cardiopulmonary symptoms without targeted evaluation. Infectious complications are prominent and clinically consequential. Cellulitis and soft tissue abscesses can develop at injection sites, sometimes complicated by necrosis or systemic spread. HIV and hepatitis are critical long-term complications related to injection drug use and shared equipment, and they carry significant morbidity, mortality, and public health implications. Endocarditis is another severe complication, particularly in injection users, and may

present with fever, embolic phenomena, new murmurs, or sepsis; it can require prolonged intravenous antibiotics and may necessitate surgical intervention depending on valvular involvement. The interplay between cocaine-induced vasoconstriction, tissue hypoperfusion, and infection can worsen healing and increase the likelihood of complicated soft tissue disease. Vascular injuries and structural complications can also occur, especially in those injecting into central vessels. Aneurysm formation and pseudoaneurysms may arise from repeated trauma to vessel walls, leading to rupture risk, compression of adjacent structures, or thrombotic obstruction. Arteriovenous fistulas can develop when simultaneous arterial and venous injury occurs, potentially causing high-output cardiac strain or limb ischemia depending on location. These complications may be underrecognized in early presentations because initial symptoms can overlap with intoxication, agitation, or trauma. Beyond these listed complications, clinicians must remain alert to systemic complications directly related to the toxicodynamic effects of cocaine, including acute coronary syndrome, stroke, seizures, hyperthermia, and rhabdomyolysis, each of which can precipitate multi-organ failure. Because complications often coexist—such as hyperthermia with rhabdomyolysis and renal injury, or vasospasm with thrombosis—the clinical course can deteriorate rapidly, underscoring the need for continuous monitoring and early intervention. Even after stabilization, complications may manifest later, so discharge planning should include explicit return precautions and linkage to follow-up care for infectious screening, vascular evaluation when indicated, and substance-use treatment referral [11][12][14].

#### Other Issues

A long-standing controversy in the management of cocaine-associated cardiovascular emergencies is the concept of “unopposed alpha-stimulation,” in which beta-blockade is theorized to worsen hypertension or coronary vasoconstriction by removing beta-2-mediated vasodilation while leaving alpha-adrenergic vasoconstriction unchecked. This theoretical concern has led some clinicians to argue that all beta-blockers—selective, non-selective, and mixed—should be absolutely contraindicated in cocaine-related chest pain or acute coronary syndrome. In contemporary practice, however, many clinicians do not adhere to this dogma and may administer beta-blockers when clinically indicated,

particularly when uncontrolled tachycardia is driving demand ischemia and worsening myocardial oxygen imbalance.[8] The key practical pearl is that treatment decisions should be guided by the patient’s hemodynamics, evidence of ischemia, and overall risk profile rather than by a simplified categorical prohibition. Evidence cited in the literature suggests that the feared phenomenon may be rare. In a systematic review encompassing 1,744 total patients, only seven adverse events were attributed to putative “unopposed alpha-stimulation,” associated with propranolol (n=3), esmolol (n=3), and metoprolol (n=1).[11] While any adverse event is clinically important, this small number relative to the total population challenges the assumption that beta-blocker administration commonly produces catastrophic vasoconstrictive consequences in cocaine-exposed patients. Adding nuance, the authors of the original reports from the 1980s that first raised the “unopposed alpha” concern later concluded in a 2017 review that the phenomenon might instead reflect the direct effects of cocaine itself, with or without concomitant beta-blocker use.[11] This interpretation matters because it reframes worsening hypertension or vasospasm as potentially part of the natural course of severe cocaine toxicity rather than a medication-induced complication.

A practical implication for emergency care is that clinicians should avoid rigid, one-size-fits-all rules and instead apply physiologic reasoning and evidence-informed judgment. When beta-blockers are considered, agent selection may matter; mixed alpha/beta blockers and careful titration in monitored settings can be preferred in some protocols, while nonselective beta-blockers may be avoided when vasospasm risk is high. Regardless of the strategy, continuous monitoring, readiness to treat vasospasm, and attention to sedation and anxiolysis remain foundational. Another crucial pearl is that co-ingestions, particularly alcohol and other stimulants, can change clinical trajectories and can confound medication response; therefore, clinicians should anticipate variability and reassess frequently. Ultimately, the “unopposed alpha” debate highlights a broader emergency medicine principle: cocaine toxicity management is dynamic, and therapies should be individualized, monitored, and adjusted as the physiologic picture evolves rather than determined solely by historical theoretical concerns.[8][11]

### Enhancing Healthcare Team Outcomes

Improving outcomes in cocaine toxicity requires a coordinated, interprofessional approach that spans triage, acute stabilization, complication surveillance, and discharge planning with harm-reduction and mental health linkage. Epidemiologic trends underscore why system-level readiness matters. Over the past three decades, overdose rates involving cocaine have gradually increased, with deaths in the United States historically ranging from approximately 0.9 to 1.6 per 100,000 population, followed by more recent declines in the last five years to around 0.78 per 100,000 population. Although the direction of change may be encouraging, the absolute burden remains clinically significant, and emergency departments continue to encounter severe cases complicated by polysubstance exposure, medical comorbidity, and psychosocial instability.[14][15] These realities demand protocols that prioritize rapid recognition, de-escalation strategies that minimize harm, and early identification of high-risk trajectories such as hyperthermia, excited delirium, or evolving acute coronary syndrome. Injection-related practices create additional outcome risks that benefit from team-based vigilance. Individuals who inject cocaine into neck veins have been reported to develop pneumothorax, thrombophlebitis, hemothorax, and myositis, and intravenous injection has been associated with aneurysms that may rupture, obstruct, or form fistulas. These complications may not be apparent at triage and can be missed if the assessment focuses only on intoxication behaviors rather than on a full cardiopulmonary and vascular examination.[14][15] Polysubstance use further increases mortality risk, and the combination of cocaine and alcohol is associated with a markedly increased risk of suicide compared with either agent alone, with users often employing violent methods of self-harm. Cocaine use during pregnancy also correlates with adverse perinatal outcomes, adding another layer of urgency to early pregnancy screening and obstetric consultation when relevant.[14][15]

Within this complexity, delineated team roles improve safety. Emergency nurses are commonly responsible for triage and early monitoring; a high index of suspicion is essential to detect occult toxicity in patients presenting with trauma, psychosis, or nonspecific chest pain. Emergency physicians, urgent care clinicians, and nurse practitioners typically lead initial stabilization, sedation, and diagnostic evaluation, while

intensivists, cardiologists, and hospitalists may assume ongoing care for complications such as refractory hyperthermia, dysrhythmias, myocardial ischemia, renal injury, or stroke. Pharmacists add critical value by optimizing medication selection and dosing, anticipating drug–drug interactions, and identifying contraindications in high-acuity sedation and cardiovascular management. Specialty-trained nurses in emergency and critical care settings administer time-sensitive treatments, monitor for rapid changes in clinical status, and escalate concerns promptly, while also providing patient and family education tailored to literacy and readiness to change. Because there is currently no medication that prevents or cures cocaine addiction, improving long-term outcomes depends heavily on brief intervention and effective referral at the point of care. Patients should be counseled to seek substance-use treatment, offered resources for drug counseling, and provided clear harm-reduction guidance. Those presenting with suicidal intent or self-harm risk should receive mental health evaluation prior to discharge, with safety planning and follow-up arrangements. In sum, outcomes improve when emergency care extends beyond physiologic stabilization to include structured team communication, complication screening, and deliberate linkage to behavioral health and addiction services.[14][15]

### Conclusion:

Cocaine toxicity represents a complex, high-risk emergency that demands rapid, structured intervention. Its pathophysiology—marked by catecholamine excess, vasospasm, and sodium-channel blockade—creates a cascade of cardiovascular and neurologic threats, including malignant dysrhythmias, acute coronary syndrome, stroke, seizures, and hyperthermia. Prognosis is strongly influenced by the timeliness and adequacy of initial management. Benzodiazepines remain the cornerstone of therapy, effectively reducing sympathetic outflow and mitigating agitation, hypertension, and tachycardia. Adjunctive agents such as labetalol, calcium channel blockers, and vasodilators may be required for refractory cardiovascular instability, while aggressive external cooling is essential for hyperthermia control. Physical restraints should be minimized to prevent exacerbation of catecholamine surge and rhabdomyolysis. Beyond acute stabilization, clinicians must anticipate complications such as rhabdomyolysis, renal failure, and infectious sequelae in injection users. Discharge planning should

incorporate harm-reduction strategies, mental health evaluation, and referral to addiction treatment, as relapse risk and psychosocial instability remain significant determinants of long-term outcomes. Ultimately, successful management of cocaine toxicity hinges on a multidisciplinary approach that integrates emergency care, critical care, pharmacy, and behavioral health services to reduce morbidity and mortality.

#### References:

1. Hantson P, Mechanisms of toxic cardiomyopathy. *Clinical toxicology* (Philadelphia, Pa.). 2019 Jan
2. Mikhail A, Tanoli O, Légaré G, Dubé PA, Habel Y, Lesage A, Low NCP, Lamarre S, Singh S, Rahme E, Over-the-Counter Drugs and Other Substances Used in Attempted Suicide Presented to Emergency Departments in Montreal, Canada. *Crisis*. 2019 May
3. Narula N, Siddiqui F, Katyal N, Krishnan N, Chalhoub M, Cracking the Crack Dance: A Case Report on Cocaine-induced Choreaathetosis. *Cureus*. 2017 Dec 22
4. Mladěnka P, Applová L, Patočka J, Costa VM, Remiao F, Pourová J, Mladěnka A, Karlíčková J, Jahodář L, Vopršalová M, Varner KJ, Štěrba M, Comprehensive review of cardiovascular toxicity of drugs and related agents. *Medicinal research reviews*. 2018 Jul
5. Paulozzi LJ, Opioid analgesic involvement in drug abuse deaths in American metropolitan areas. *American journal of public health*. 2006 Oct
6. Turner C, Chandrakumar D, Rowe C, Santos GM, Riley ED, Coffin PO, Cross-sectional cause of death comparisons for stimulant and opioid mortality in San Francisco, 2005-2015. *Drug and alcohol dependence*. 2018 Apr 1
7. Zimmerman JL. Cocaine intoxication. *Critical care clinics*. 2012 Oct;28(4):517-26. doi: 10.1016/j.ccc.2012.07.003.
8. Richards JR, Hollander JE, Ramoska EA, Fareed FN, Sand IC, Izquierdo Gómez MM, Lange RA,  $\beta$ -Blockers, Cocaine, and the Unopposed  $\alpha$ -Stimulation Phenomenon. *Journal of cardiovascular pharmacology and therapeutics*. 2017 May
9. Agrawal PR, Scarabelli TM, Saravolatz L, Kini A, Jalota A, Chen-Scarabelli C, Fuster V, Halperin JL, Current strategies in the evaluation and management of cocaine-induced chest pain. *Cardiology in review*. 2015 Nov-Dec
10. Maraj S, Figueiredo VM, Lynn Morris D, Cocaine and the heart. *Clinical cardiology*. 2010
11. Richards JR, Garber D, Laurin EG, Albertson TE, Derlet RW, Amsterdam EA, Olson KR, Ramoska EA, Lange RA, Treatment of cocaine cardiovascular toxicity: a systematic review. *Clinical toxicology* (Philadelphia, Pa.). 2016 Jun
12. Anderson JL, Adams CD, Antman EM, Bridges CR, Califf RM, Casey DE Jr, Chavey WE 2nd, Fesmire FM, Hochman JS, Levin TN, Lincoff AM, Peterson ED, Theroux P, Wenger NK, Wright RS, Jneid H, Ettinger SM, Ganiats TG, Philippides GJ, Jacobs AK, Halperin JL, Albert NM, Creager MA, DeMets D, Guyton RA, Kushner FG, Ohman EM, Stevenson W, Yancy CW, 2012 ACCF/AHA focused update incorporated into the ACCF/AHA 2007 guidelines for the management of patients with unstable angina/non-ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Journal of the American College of Cardiology*. 2013 Jun 11;
13. Zun LS, Evidence-Based Review of Pharmacotherapy for Acute Agitation. Part 1: Onset of Efficacy. *The Journal of emergency medicine*.
14. Modisett KL, Walsh SJ, Heffner AC, Pearson DA, Kerns W 2nd, Outcomes in Cardiac Arrest Patients due to Toxic Exposure Treated with Therapeutic Hypothermia. *Journal of medical toxicology : official journal of the American College of Medical Toxicology*. 2016
15. Alfa-Wali M, Atinga A, Tanham M, Iqbal Q, Meng AY, Mohsen Y, Assessment of the management outcomes of body packers. *ANZ journal of surgery*. 2016 Oct