



## Chapter 154 – Cocaine and Other Sympathomimetics

### Episode Overview

- Rapid sedation with an IV benzodiazepine is the key for most symptoms from cocaine and other stimulants.
- Hyperthermia is a high-risk event, and body temperature must be reduced rapidly.
- Short-acting antihypertensive agents (such as, phentolamine, nitroglycerin, nicardipine, or clevidipine) are recommended for cocaine-induced hypertension, including in the presence of chest pain.
- Wide-complex rhythms secondary to cocaine may respond to IV sodium bicarbonate therapy.
- Cocaine body packers who develop symptoms of acute cocaine toxicity need emergent surgical intervention.
- Amphetamine symptoms and effects last longer than those produced by cocaine.
- Hyponatremia should be rapidly identified in patients with an altered mental status after use of illicit stimulants, most specifically MDMA.
- Synthetic cathinones or “bath salts” may be ingested, inhaled, or injected and can result in severe agitation, sympathomimetic effects, hyperthermia, and rhabdomyolysis. Fatalities have been reported.

### Core Questions

1. Describe the mechanism of action of cocaine
2. List clinical manifestations of cocaine toxicity
3. What are the mechanisms (routes) of cocaine exposure?
4. List 15 DDX of agitated delirium
5. Describe the management goals and pharmacologic interventions for severe cocaine intoxication
6. What is the differential diagnosis for a patient presenting with chest pain following cocaine use?
7. Describe the management approach to cocaine-related chest pain
8. List 3 pathophysiologic effects of cocaine-induced MI
9. What is the approach to ACS management in patients using cocaine?
10. Name five sympathomimetic drugs other than cocaine
11. List the 8 severe complications of sympathomimetics
12. Compare body packers to body stuffers
13. What are the primary risks with MDMA and Methamphetamines?

### Wisecracks

1. List 9 toxicologic causes of agitation and hyperthermia
2. What is speedballing?
3. List diagnostic and management priorities of stimulant-induced hyperthermia
4. List the complications of levamisole



## Rosen's In Perspective

Cocaine, amphetamines, and amphetamine derivatives are sympathomimetics. These agents cause central nervous system (CNS) stimulation and a cascade of adrenergic physiologic effects.

Cocaine is a plant-derived alkaloid that accounts for 40% of drug misuse-related deaths and up to 40% of United States emergency department (ED) visits for illicit drug use.

**NOTE:** Some sympathomimetic agents may also cause hallucinogenic effects as well

### [1] Describe the mechanism of action of cocaine

**Mechanism of Action:** cocaine causes release of dopamine, epinephrine, norepinephrine, and serotonin. This, in turn, causes the following:

- Vascular smooth muscle activation (alpha-1 receptor activation)
- Increases myocardial contractility and heart rate through stimulation of (beta-1 adrenergic receptors)
- Conduction abnormalities (sodium channel blockade)
- Serotonergic and dopaminergic effects

### [2] List clinical manifestations of cocaine toxicity

**Please refer to Box 149.1 in Rosen's 9<sup>th</sup> Edition for a comprehensive table of the clinical manifestations of cocaine toxicity.**

The clinical manifestations of cocaine toxicity include:

- CNS excitation
- Diaphoresis
- Hypertension
- Hyperthermia
- Increased motor tone
- Mydriasis
- Tachycardia

To remember all of these symptoms, just think about a massive sympathetic nervous system activation. Alpha- and beta-adrenergic receptors are activated, resulting in a patient presenting with a classic sympathomimetic toxidrome.

**NOTE:** More severely toxic patients may be agitated, combative, and hyperthermic. Additionally, patients may present with focal acute pain syndromes, circulatory abnormalities, delirium, or seizures. Clonus does not occur with acute cocaine toxicity.

**NOTE:** Typically, end organ damage is rare. However, if there is end-organ damage, it is manifested as an acute hypertensive emergency.



### [3] What are the mechanisms (routes) of cocaine exposure?

Please refer to Table 149.1 in Rosen’s 9<sup>th</sup> Edition for a comprehensive table outlining the various mechanisms by which cocaine is consumed.

Route	Formula	Onset of Action	Peak Effect	Duration
Inhalation	“Crack”	8 seconds	2-5 minutes	10-20 minutes
Intranasal	Cocaine HCl	2-5 minutes	5-10 minutes	30 minutes
Intravenous	Cocaine HCl	Seconds	10-20 minutes	60-90 minutes
Oral	Cocaine HCl	30-60 minutes	60-90 minutes	Unknown
Skin Popping (Subcutaneous or Intradermal Injection)	Cocaine HCl	Unknown	Unknown	Unknown

#### Crack Cocaine

**Route of Administration:** Inhalation

**Description:** The crystalline freebase form of cocaine. It is inhaled using a crack pipe designed to withstand high temperature required to volatilize the substance. Crack cocaine is highly lipid soluble, thus contributing to crack’s rapid onset of action.

#### Cocaine HCl

**Route of Administration:** Intranasal, IV, Oral, Skin Popping

**Description:** The water-soluble salts of cocaine are available as a white crystalline powder that is used intranasally or dissolved and injected intravenously. Typically, oral administration is rare (unless the patient is smuggling or concealing drugs).

**NOTE:** The use of ethanol with cocaine forms cocaethylene, a metabolite that may potentiate the drug’s stimulatory effects and lengthens the duration of effect. This form has a 3-5 times longer half life. Ingestion of this substance increases the risk of death 19-25 times.

### [4] List 15 DDx of agitated delirium

**NOTE:** Whenever you encounter a patient with delirium/altered level of consciousness, use the DIMES (drugs, infectious, metabolic, environmental, structural) approach to generate your list of differential diagnoses.

<b>Drugs</b>	Amphetamines, cocaine, caffeine, anticholinergics, lithium
<b>Infectious</b>	Meningitis, Encephalitis
<b>Metabolic</b>	Thyrotoxicosis, Hyperammonemia, Hypoglycemia, Hypoxia, Uremia
<b>Environmental</b>	Heat stroke
<b>Structural</b>	Hemorrhage, mass, stroke, trauma



Please refer to Box 149.2 in Rosen's 9<sup>th</sup> Edition for a comprehensive table outlining the differential diagnosis of agitated delirium.

### [5] Describe the management goals and pharmacologic interventions for severe cocaine intoxication

Please refer to Box 149.3 in Rosen's 9<sup>th</sup> Edition for a comprehensive table outlining the initial evaluation of patients with sympathetic stimulation.

#### Priorities:

- **SAFETY - patient and staff**
- **Chemical sedation**
  - IM benzo's (e.g. Midazolam 0.2 mg/kg IM = usually 10 mg)
- **Assessment**
  - Glucose, FULL set of vital signs
    - GET A CORE TEMPERATURE (rectal)
  - Full physical examination
  - IV access and oxygenation via NRB (doubles as a spit mask)
- **Chemical sedation**
  - Benzo's\*\* - Diazepam can be administered intravenously in increments of 5 to 10 mg every 5 minutes in adults until sedation is achieved.
  - PRN Haldol IM 2.5-5 mg [see note]
- **Investigations**
  - EKG
  - Urinalysis
  - Serum CK
- **Cooling**
  - AGGRESSIVELY cool if temp > 41°C (rectal temp)
- **IV fluids - repletion of salt and water depletion**
- **Consider need for paralysis and intubation**

**NOTE:** Antipsychotic agents such as haloperidol are rapidly effective and generally safe for drug-induced psychosis /agitation resulting from sympathomimetic agents.

**NOTE:** Although lorazepam also can be given intramuscularly, it may take 15 minutes to reach peak sedation; repeated doses given at more frequent intervals may accumulate, causing oversedation and respiratory depression.

**NOTE:** Safe antihypertensives to use in the patient with severe cocaine toxicity:

- Phentolamine
- Nitroglycerin
- Hydralazine



### Treatment of hyperthermia:

**NOTE:** Patients who sustain elevated core temperatures above 106°F (41°C) for more than 20 minutes are likely to subsequently have fatal multisystem organ failure, which is often heralded by disseminated intravascular coagulation.

- **It is crucial to reduce core temperature to 102°F (38.8°C) as soon as clinically possible, ideally within 20 minutes or less.**
  - Cooling blankets are insufficient. Ice water submersion in a portable tub is preferred when available; although some favor wet sheets with large fans.
  - These patients require continuous temperature monitoring and fluid resuscitation as judged by standard measures.
  - Invasive cooling techniques are often too delayed and inadequate against the vasoconstrictive effects of cocaine and other adrenergic agents.

### [6] What is the differential diagnosis for a patient presenting with chest pain following cocaine use?

- ACS /stent thrombosis
- PE
- Aortic Dissection
- Endocarditis
- Foreign Body Aspiration
- Pneumomediastinum / PTX / Pneumopericardium

### [7] Describe the management approach to cocaine-related chest pain

Same as patients with chest pain and NO COCAINE USE.

Check out this excerpt from Rosen's Emergency Medicine, 9<sup>th</sup> Edition:

*"Most patients presenting with troponin elevation and chest pain after cocaine use had angiographically proven obstructive coronary disease, often of a single vessel, but almost 20% have normal angiography.*

*Although the sensitivity and specificity of troponin cardiac markers are still being investigated for cocaine-related chest pain, we recommend that patients with cocaine use be evaluated for chest pain in a similar fashion to that for patients without cocaine use. Decisions regarding further investigation are based on the characteristics and course of the chest pain and results of serial troponin measurements and ECGs."*



**[8] List 3 pathophysiologic effects of cocaine-induced MI**

- Accelerated atherosclerosis
- Enhanced platelet aggregation
- Vasospasm
- Increased demand (increased HR and afterload)
- LVH with time

**[9] What is the approach to ACS management in this patient?**

- DAPT
- Consider Cath lab
- Treat sympathetic storm with benzodiazepines

**[10] Name five sympathomimetic drugs other than cocaine**

- Amphetamines
- MDMA
- Methamphetamine
- Ephedrine
- Khat
- Bath Salts

**[11] List the 8 severe complications of sympathomimetics**

**NOTE:** The severe complications are listed near the top.

- **Hyperthermic storm**
- **Hypertensive emergencies**
  - Aortic dissection, pulmonary edema, myocardial ischemia and infarction, intracranial hemorrhage, stroke, and infarction in the distribution of the anterior spinal artery.
- **Vasospasm**
  - Compromised perfusion: intestinal infarctions and mesenteric ischemia can occur, particularly in body packers with large oral ingestions.
  - Retinal vasospasm, renal infarctions, and placental insufficiency and infarction in the gravid uterus.
- **Cardiac dysrhythmias**
  - Unstable atrial fibrillation
  - Unstable SVT
  - Wide-complex tachycardia
  - Torsades de pointe
  - Transient Brugada rhythm
- **Hyperkalemia** (from rhabdomyolysis)
- **Seizures**
- **Pneumothorax, pneumopericardium, and pneumomediastinum**



- **Others:**
  - Botulism
  - Endocarditis
  - Abscesses
  - Septicemia
  - Cocaine washout - cocaine withdrawal / drowsiness
  - Crack dance: a transient choreoathetoid movement disorder probably related to abnormalities in dopaminergic tone.
  - Paranoia, either drug-induced or from underlying psychiatric illness, may occur even after the acute effects of the drug subside.
  - Neuropsychiatric effects of cocaine can alter behavior and judgment, increasing the risk of violent injuries.
  - Fluid and electrolyte abnormalities; nutritional deficits
  - Nasopalatine necrosis
  - Agranulocytosis, vasculopathy with thrombosis, dermal ulcers, and purpura, often affecting the earlobes, occurred as a result of the unintentional exposure to levamisole.

## [12] Compare body packers to body stuffers

**Body Packers:** planned; ingested large (usually) amounts of illicit drugs in their body (usually GI tract)

**Body Stuffers** unplanned; ingest drugs without plan to avoid being caught (usually while being chased by police)

### Treatment:

- Cardiac Monitoring
- Whole bowel irrigation with pack count
- Immediate OR if signs of hemodynamic instability, obstruction or rupture

### Criteria for D/C:

- Three packet free stools
- Reliable packet count consistent with ingestion
- Normal contrast study

## [13] What are the primary risks with MDMA and Methamphetamines?

- Amphetamines are stimulants originally designed for use as decongestants and dietary aids that became popular as recreational drugs in the mid-20th century.
- Watch for :
  - Hypertensive crisis
  - Excited delirium
  - Serotonin syndrome



## Wisecracks:

### [1] What is speedballing?

**Answer:** Patients who are “speedballing” are using intravenous (IV) heroin and cocaine together. They may be initially sedated, and administration of naloxone may precipitously reveal the underlying cocaine toxicity.

### [2] List nine toxicologic causes of agitation and hyperthermia

- **Serotonin Syndrome**
- **Malignant Hyperthermia**
- **Sympathomimetic toxicity**
  - Amphetamine derivatives, phencyclidine (PCP), MDMA, cocaine
- **Anticholinergic toxicity**
- **Uncouplers of oxidative phosphorylation** (e.g. ASA overdose, 2,4-DNP overdose)
- **EtOH withdrawal**
- **Thyroxine overdose**
- **Neuroleptic Malignant Syndrome**
- **DRESS syndrome**

### [3] List diagnostic and management priorities of stimulant-induced hyperthermia

Please refer to Box 149.4 in Rosen’s 9<sup>th</sup> Edition for a comprehensive table outlining the initial treatment and evaluation of patients with stimulant-induced hyperthermia.

<b>Cooling</b>
<ul style="list-style-type: none"><li>• Early identification of elevated core temperature</li><li>• Large-bore IV access and rapid infusion of crystalloid</li><li>• Sedation and muscle relaxation with benzodiazepines</li><li>• Rapid cooling WITHIN 20 MINUTES (ideally in ice water bath)</li><li>• Paralysis and intubation if necessary</li></ul>
<b>Monitoring and Diagnostics</b>
<ul style="list-style-type: none"><li>• Urine output via Foley catheterization</li><li>• Laboratory investigations to quantify organ functioning:<ul style="list-style-type: none"><li>○ Serum chemistries</li><li>○ Creatinine</li><li>○ CK</li><li>○ Liver function</li><li>○ PT, PTT, fibrin split products</li><li>○ Bacterial cultures (consider LP in IVDU)</li><li>○ Urinalysis for myoglobinemia</li></ul></li><li>• Neuroimaging if aetiology unclear</li></ul>





**[4] List the complications of levamisole**

- Agranulocytosis
- Vasculitis