In This Issue

Lesson 13 Cocaine-Associated Chest Pain ........................................... Page 2
The LLSA Literature Review ......................................................... Page 9
Lesson 14 Metabolic and Infectious Emergencies in Cancer Patients ....... Page 10
The Critical ECG ................................................................. Page 16
The Critical Image ............................................................... Page 17
CME Questions ................................................................. Page 18
The Drug Box ................................................................. Page 20

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Contributor Disclosures

In accordance with ACCME Standards and ACEP policy, contributors to Critical Decisions in Emergency Medicine must disclose the existence of significant financial interests in or relationships with manufacturers of commercial products that might have a direct interest in the subject matter. Authors and editors of these Critical Decisions lessons reported no such interests or relationships.

Method of Participation

This educational activity consists of two lessons with a posttest and should take approximately 5 hours to complete. To complete this educational activity as designed, the participant should, in order, review the learning objectives, read the lessons, and complete the online posttest. Release date March 1, 2010. Expiration date February 28, 2013.

Accreditation Statement

The American College of Emergency Physicians (ACEP) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians. ACEP designates this educational activity for a maximum of 5 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. Approved by ACEP for 5 Category I credits. Approved by the American Osteopathic Association for 5 hours of AOA Category 2-B credit (requires passing grade of 70% or better).

Target Audience

This educational activity has been developed for emergency physicians.
Objectives

On completion of this lesson, you should be able to:

1. Discuss the pathogenesis of cocaine-induced myocardial injury.
2. Discuss the cardiovascular morbidity and mortality associated with cocaine use.
3. List other diagnostic possibilities to consider in the setting of cocaine-associated chest pain.
4. Compare and contrast the strengths and weaknesses of the various diagnostic tools available in the evaluation of cocaine-associated chest pain.
5. Discuss the various treatment options for cocaine-associated myocardial injury and dysrhythmias.
6. Discuss the prognosis of cocaine-induced myocardial injury.
7. Create an appropriate disposition plan for patients who present to the emergency department with cocaine-associated chest pain.

From the EM Model

17.0 Toxicologic Disorders
17.1 Drug and Chemical Classes (Cocaine)

Since the first reported case of cocaine-associated myocardial infarction in 1982, the cardiovascular complications of cocaine have been increasingly recognized. Drug Abuse Warning Network (DAWN) data from 2005 report that there were nearly 450,000 cocaine-related emergency department visits. This was an increase of 17% from 2004. During the first hour after cocaine is used, the risk of myocardial infarction is 24 times the baseline risk. Cocaine accounts for up to 25% of acute myocardial infarctions in patients 18 to 45 years of age. Unfortunately up to 60% of these patients continue to use cocaine, and 75% will have recurrent chest pain. Knowledge of the pharmacology of cocaine, the differential diagnosis of cocaine-associated chest pain, the diagnostic tools and therapeutic options in the care of these patients, and a practical disposition plan are all essential for the care of these patients.

Case Presentations

Case One

A 47-year-old man presents to the emergency department with a 2-hour history of severe (10/10), constant, substernal chest pain. He admits to crack cocaine use 4 hours prior to arrival. His past medical history is pertinent for poorly-controlled hypertension for which he takes hydrochlorothiazide and lisinopril. He smokes 1 pack of cigarettes per day.

The patient appears uncomfortable. Vital signs are blood pressure 166/102, heart rate 82 (sinus rhythm on the monitor), respiratory rate 18, temperature 37°C (98.6°F), and oxygen saturation 94% on room air. Examination demonstrates a clear sensorium, normal heart tones, scattered rhonchi, and no peripheral edema; the neurologic examination findings are normal.

An ECG is obtained (Figure 1).

Case Two

A 32-year-old man presents to the emergency department with a 3-hour history of sharp, intermittent chest pain accompanied by mild shortness of breath. He acknowledges the use of crack cocaine over the past 12 hours. He describes the pain as severe (8/10), left-sided, sharp, and nonradiating.

On physical examination the patient appears anxious and slightly diaphoretic and continues to complain of chest pain. Vital signs are blood pressure 148/95, heart rate 115 (monitor shows a sinus tachycardia), respiratory rate 22, temperature 37°C (98.6°F), and oxygen saturation 97% on room air. The physical examination reveals a normal mental status, supple neck, clear lungs, normal heart tones, a soft abdomen, equal peripheral pulses, and a nonfocal neurologic examination.

An ECG (Figure 2) and chest radiograph are obtained.
**Critical Decisions**

- What other diagnostic possibilities should be considered in patients with cocaine-associated chest pain?
- What complications should the clinician anticipate in patients who present with cocaine-induced chest pain?
- Which diagnostic tests are useful when evaluating cocaine-associated chest pain?
- Which therapeutic strategies are most effective for cocaine-induced myocardial damage?
- Can any of these patients be safely discharged?

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**The Pathogenesis of Cocaine’s Cardiovascular Effects**

Crack cocaine, alone among the forms of cocaine, produces symptoms and effects in a matter of seconds. This almost instantaneous high contributes to its potency and high rate of addiction. Cocaine is a local anesthetic of the ester type. This leads to myocardial depression of depolarization and the slowing of the conduction velocity. The ECG can manifest prolongation of the QRS, QT, and PR intervals similar to effects produced by Class 1 antiarrhythmics.

The systemic effects of cocaine are secondary to its inhibition of the re-uptake pumps in the presynaptic cleft for norepinephrine, epinephrine, dopamine, and serotonin. This leads to prolongation of their respective actions. Peripheral manifestations (both α and β) will include hypertension, tachycardia, diaphoresis, tremors, and mydriasis. The central effects are numerous and depend on the specific neurotransmitter. This produces a sympathomimetic toxidrome familiar to emergency physicians.

The pathogenesis of cocaine-induced myocardial ischemia is multifactorial and is compounded by the traditional cardiovascular risk factors. The pathophysiology of cocaine-associated myocardial ischemia can best be explained in terms of the timeframe of cocaine’s actions on the cardiovascular system. The immediate effects are due to vasoconstriction, which can be enhanced at sites of atherogenesis. This vasoconstriction is thought to be mainly α-mediated, but serotonin could also be involved. In addition, increased myocardial oxygen demand results from the tachycardia and hypertension that accompany this sympathomimetic toxidrome. The intermediate mechanisms center on increased thrombogenicity. A direct platelet effect leads to enhanced aggregation, thromboxane production is increased, and tissue plasmin activator inhibition is increased. Together, these provide a rich environment for thrombus formation. Although thrombus formation is more common with underlying coronary artery disease, this can occur in coronary arteries without disease. The long-term consequences of cocaine use include accelerated atherogenesis and the development of left ventricular hypertrophy, as well as a dilated cardiomyopathy.

**Figure 1.** Inferior acute myocardial infarction

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**Critical Decision**

What other diagnostic possibilities should be considered in patients with cocaine-associated chest pain?

Just as for other patients who present with chest pain, a working differential diagnosis should be developed (Table 1). Myocardial ischemia is a primary consideration, but because of the way cocaine can be used (insufflation, inhalation, and injection) other specific conditions must be entertained such as pneumothorax, pneumomediastinum, and pneumopericardium. In addition, aortic dissection secondary to cocaine use has been described in the literature. Endocarditis, pericarditis, and pulmonary embolus must be considered along with pneumonia, musculoskeletal chest pain, and crack lung (an acute pulmonary syndrome manifesting as fever, hypoxia, hemoptysis, respiratory failure, and diffuse alveolar infiltrates on chest radiograph). The differential diagnosis is broad for this clinical presentation,
and it is incumbent on physicians to keep these entities in mind. If not considered and promptly recognized, many of these can have significant clinical consequences.

**CRITICAL DECISION**

What complications should the clinician anticipate in patients who present with cocaine-induced chest pain?

Several emergency medicine-based studies have attempted to determine the potential complications and the associated morbidity and mortality rates of patients with cocaine-associated chest pain. The first study was a prospective, cohort multicenter study that evaluated 246 patients. The incidence of myocardial infarction was 5.7%, congestive heart failure (CHF) developed in 4 patients, 10 patients sustained arrhythmias, and 2 patients suffered a cardiac arrest (both prehospital). Once patients were in the emergency department, no life-threatening complications occurred. The second study was a retrospective, multicenter study of 250 patients admitted to the hospital with cocaine-associated chest pain. Complications were again uncommon, and the “rule in” rate for acute myocardial infarction (AMI) was 6%. Of note, no complications developed more than 12 hours after emergency department presentation. The third study, a cohort, retrospective, multicenter design, went one step further and evaluated 130 patients with 136 documented AMIs secondary to cocaine. The mortality rate was 0% (CI 0% to 2%) with cardiovascular complications occurring in 36%. Approximately 90% of these complications occurred within the first 12 hours, and all episodes of ventricular fibrillation and ventricular tachycardia developed prior to emergency department arrival. All patients with complications were identified by one of the following: a 12-hour period of observation, an initial positive ECG, or an elevated creatine kinase-MB (CK-MB) within the first 12 hours. The authors went on to calculate that 1.6 of every 1,000 patients presenting to the emergency department with cocaine-associated chest pain might be expected to develop cardiovascular complications not identified by the three referenced factors. Of interest, 52 of these patients underwent cardiac catheterization, and two thirds were found to have at least single-vessel disease (>50% narrowing).

Several conclusions can be drawn regarding the emergency department clinical course of these patients: the rate of myocardial infarction approaches 6%; the mortality rate for those with myocardial infarction is very low (almost 0); and almost all complications will occur within the first 12 hours of presentation.

**CRITICAL DECISION**

Which diagnostic tests are useful when evaluating cocaine-associated chest pain?

The first diagnostic tool the clinician relies on is a focused history of the presenting clinical scenario. Not surprisingly, a patient’s presentation to the emergency department for cocaine-associated chest pain can be delayed, and the history of cocaine use may not be forthcoming. One study found that up to 25% of patients who later admitted to it initially denied the use of cocaine in relation to their presentation with chest pain. Traditionally, the clinical characteristics of the chest pain can aid clinicians in determining a pretest probability of coronary artery disease, but for cocaine-associated chest pain this is not the case. Neither the location, duration, or quality of the chest pain, nor the associated symptoms have been shown to be predictive of myocardial ischemia in this patient population.

The ECG is a time-honored tool to aid in evaluating patients with chest pain. Several studies have evaluated
the performance of the ECG in the clinical setting of cocaine-associated chest pain. A cross-sectional study compared ECGs in patients with cocaine-associated chest pain against matched controls.\textsuperscript{16} Benign early repolarization was found in 35\% of the cocaine group and in 30\% of the controls. Normal or nonspecific changes were found in 46\% of each group. The authors found no difference between the mean frequencies of ECG diagnoses between the two groups and concluded that “normal” variations account for many of the “abnormal” ECGs observed in these young patients with cocaine-associated chest pain. Hollander et al calculated a sensitivity of 35.7\% and a specificity of 89.9\% for the ECG in this clinical setting.\textsuperscript{12} In other words, the ECG had a high false-negative rate.

Clinicians rely heavily on the results of cardiac markers to make management and disposition decisions for this patient population. It has been postulated that the CK and the CK-MB may frequently be elevated in this patient population secondary to agitation and rhabdomyolysis.\textsuperscript{17} Cardiac troponin I is thought to have no cross-reactivity with human skeletal muscle troponin I. Hollander et al evaluated 97 chest pain patients with potential myocardial ischemia, 19 (20\%) of whom had recently used cocaine.\textsuperscript{18} Myoglobin, CK-MB, and troponin I were drawn at presentation, then every 8 hours. Specificity, assessing the incidence of false positives, was compared for each marker with and without cocaine use. The results of specificity with and without cocaine use were: myoglobin 50\% with and 82\% without; CK-MB 75\% with and 88\% without; and troponin I 94\% both with and without. The authors concluded that the specificity of troponin I was not affected by recent cocaine use. Kontos et al studied the utility of troponin I in patients with cocaine-associated chest pain.\textsuperscript{19} Of 246 admitted patients (out of 526 patients presenting to the emergency department with cocaine-associated chest pain), 14% met CK-MB criteria for AMI, and 16% had troponin I elevations. The authors concluded that troponin I appeared to have an equivalent diagnostic accuracy compared to CK-MB for diagnosing myocardial necrosis in this patient population. From these two studies, it is reasonable to conclude that troponin I has at least the same diagnostic accuracy as CK-MB, if not better.

Other diagnostic tests to obtain include a chest radiograph to evaluate for noncardiac causes of chest pain. Significant cocaine intoxication can lead to hyperglycemia and hypokalemia. Severe intoxication can also induce acid-base disorders. Thus, routine blood tests to complement cardiac marker determination are of value. The urine drug screen can detect the cocaine metabolite benzoylecgonine for 48 to 72 hours after last use (longer in chronic users). Although this may be of interest, its impact on the initial patient management is minimal.

**Table 2.**

<table>
<thead>
<tr>
<th>Treatment of cocaine-associated myocardial damage</th>
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<tbody>
<tr>
<td>Aspirin</td>
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<tr>
<td>Benzodiazepines</td>
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<tr>
<td>Heparin</td>
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<tr>
<td>Nitrates</td>
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<tr>
<td>PCI if patient has STEMI</td>
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</table>

**Avoid:**

- β-Blockers
- Class 1A antiarrhythmics (quinidine, procainamide, disopyramide)

**CRITICAL DECISION**

**Which therapeutic strategies are most effective for cocaine-associated myocardial damage?**

Unfortunately, there have been very few well-designed randomized, prospective trials that have compared the various treatment strategies for cocaine-associated acute coronary syndromes. Recommendations to date are based on well-controlled animal studies, observational series, case series and reports, clinical experience, and a few small clinical trials (Table 2). The American Heart Association (AHA) acknowledges in their 2008 guidelines for the management of cocaine-associated chest pain the paucity of good evidence.\textsuperscript{20}

The central nervous system has a major role in the development of many of the sympathomimetic manifestations of cocaine toxicity. It is believed and has been clinically demonstrated that benzodiazepines blunt this sympathomimetic response. Benzodiazepines have anxiolytic properties and attenuate the rise in blood pressure and pulse secondary to cocaine use. This leads to a reduction in myocardial oxygen consumption. The 2008 AHA guidelines recommend benzodiazepines as primary therapy.\textsuperscript{20} Decades of clinical experience confirm this efficacy.

All recommendations advocate the use of aspirin in this clinical setting, with the premise that it will impede thrombus formation.\textsuperscript{20} There have been no clinical studies to assess this, but it intuitively makes sense based on the pathogenesis involved, safety profile, and the extensive investigation in patients with ischemic heart disease unrelated to cocaine. Like aspirin, heparin’s efficacy in this clinical setting has not been studied. Potential risks of the use of heparin in this specific patient population focus on an increased incidence of trauma and the concern for potential intracranial bleeding and aortic dissection. Both the AHA and Hahn support heparin use based on the pathophysiology involved as well as a favorable benefit/harm profile.\textsuperscript{20,21}

Nitrates are a mainstay in the treatment of myocardial ischemia, and this holds true for cocaine-induced myocardial ischemia. There is some evidence demonstrating relief of cocaine-induced vasoconstriction with nitrates.\textsuperscript{22-24}
β-Adrenergic blockade is standard treatment for patients with AMI. Traditionally, β-blockers have been avoided in the setting of cocaine-associated chest pain, because of concern that β-blockade would lead to unopposed α effects. This, in turn, would enhance cocaine-induced vasoconstriction, increase blood pressure, fail to control heart rate, increase the likelihood of seizures, and ultimately decrease survival. Labetalol might be an attractive alternative, but its β-blocking effects are much more potent than its α-blocking effects. No clinical research supports its role. One study evaluated intravenous labetalol in 15 patients undergoing cardiac catheterization who received intranasal cocaine. The cocaine-induced vasoconstriction was not decreased with labetalol. A recent study, however, has brought into question the longstanding avoidance of β-blockers in this setting. This retrospective, cohort study evaluated 363 admitted patients with a positive urine drug screen for cocaine. Findings included less AMI and death in those treated with β-blockers, which is in direct contrast to previous literature warning of the use of β-blockers in the setting of cocaine-associated AMI. On further scrutiny of the article, there was significant patient selection bias, other diseases besides AMI were included along with their associated treatment, and data on the actual time of cocaine use was not included. With these shortcomings in the study design, these results must be considered preliminary at best. Therefore, until more evidence is forthcoming, the use of β-blockers for the treatment of cocaine-associated myocardial ischemia should be avoided.

Calcium channel blockers are currently not recommended in the treatment of acute coronary syndromes. In the setting of cocaine-associated chest pain, there is some evidence that calcium channel blockers can provide some benefit. A study of 10 healthy volunteers demonstrated that verapamil relieved cocaine-induced coronary vasospasm. The 2008 AHA guidelines recommend calcium channel blockers as a second-line agent in this clinical setting.

Phentolamine, a pure α antagonist, is theoretically attractive in this setting. A case report documented its efficacy in a patient unresponsive to traditional treatments who then improved dramatically with its use. The 2008 AHA guidelines also list phentolamine as a second-line agent.

Definitive treatment for cocaine-associated ST-elevation myocardial infarction (STEMI) will depend on the individual resources of the treating institution. Thrombolysis is theoretically a good choice because of the pathophysiology of enhanced thrombogenesis associated with cocaine, but there are several concerns. There is an unclear benefit/harm assessment, some patients are ultimately found not to have thrombus, overall morbidity and mortality are low, and ECGs in this patient population have a high incidence of benign early repolarization which can be misinterpreted as an injury pattern, and there have been case reports of intracranial hemorrhage when using thrombolytics in this setting. Because of these concerns as well as demonstrated benefit, timely percutaneous coronary intervention (PCI) by experienced interventionalists in high-volume centers is the treatment of choice. Fibrinolytic therapy is recommended for that small subset of patients who are clearly experiencing a STEMI and for whom PCI is not available. No studies to date have compared these two interventions. One study evaluated 90 patients who underwent coronary angiography within 5 weeks of an emergency department evaluation for cocaine-associated chest pain and found that significant disease, defined as stenosis of 50% or more of a coronary artery or major branch or bypass graft, was present in 50% of patients. Significant disease was present in 77% of patients with AMI or troponin I elevations, and in only 35% of patients without myocardial necrosis. These findings add credence to the argument that PCI should be the primary treatment for cocaine-associated STEMI.

Many arrhythmias have been reported in the setting of acute cocaine toxicity (Table 3). Most atrial arrhythmias will respond to benzodiazepines and time. Suggested mechanisms for cocaine-induced ventricular arrhythmias include increased ventricular irritability, lower ventricular threshold, and prolonged QRS and QT intervals similar to the effect of class 1 antiarrhythmics (from sodium channel blockade). The treatment of ventricular arrhythmias depends on the time interval between cocaine use and arrhythmia onset. Ventricular arrhythmias occurring immediately after cocaine use are thought to be secondary to the sodium channel blockade effects of cocaine on the myocardium. Sodium bicarbonate administration is therefore suggested. For those arrhythmias that occur several hours later, myocardial ischemia is the more likely cause. Standard management would include addressing any metabolic derangements and using antiarrhythmics such as lidocaine. There is no literature reporting the efficacy of amiodarone for cocaine-induced ventricular tachycardia or ventricular fibrillation. It is suggested that class 1A agents (quinidine, lidocaine, corticotropin, and procainamide) are the most likely to be effective. It appears as if there is a strong scientific basis for the use of β-adrenergic blockers, but little evidence for the use of calcium channel blockers or sodium channel blockers. The potential role of α-adrenergic blockers (phentolamine and labetalol) remains to be further explored. The 2008 AHA guidelines list phentolamine as a second-line agent.

<table>
<thead>
<tr>
<th>Asystole</th>
<th>Atrial fibrillation</th>
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<tbody>
<tr>
<td>Bundle-branch block</td>
<td>Complete heart block</td>
</tr>
<tr>
<td>Sinus bradycardia (very early)</td>
<td>Sinus tachycardia</td>
</tr>
<tr>
<td>Supraventricular tachycardia</td>
<td>Torsade de pointes</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>Ventricular tachycardia</td>
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Table 3.
Potential arrhythmias secondary to cocaine
procaïnamide, and disopyramide) and β-blockers be avoided. There have been reports of torsade de pointes occurring in association with cocaine use. Magnesium would be the initial treatment choice.

**CRITICAL DECISION**

Can any of these patients be safely discharged?

There is a subset of these patients for whom the disposition is straightforward. Those with an acute coronary syndrome require admission and, as previously mentioned, those with a STEMI should quickly undergo PCI. Others will need admission to a monitored bed for ongoing evaluation and treatment. Patients experiencing CHF and significant arrhythmias will require admission. Noncardiac complications (seizures, stroke, and rhabdomyolysis) will also warrant admission. However, most of these patients have a nondiagnostic evaluation. The short- and long-term prognosis for this patient population has been studied. Hollander et al reported on 203 patients that were followed for a mean of 408 days after discharge from the emergency department or hospital for cocaine-associated chest pain. Mortality data were available for all patients. The study endpoints were death or AMI within 1 year of the initial presentation. The survival rate was 98%. There were six deaths—three from HIV; one from end-stage renal disease; one from CHF; and one from sepsis. There were two nonfatal AMIs; both these patients had continued to use cocaine. Approximately 60% of the patients continued to use cocaine, and 75% experienced recurrent chest pain. There were no deaths or myocardial infarctions in those claiming abstinence.

Kushman et al from the Cincinnati Chest Pain Center retrospectively studied 197 patients with cocaine-associated chest pain. The evaluation protocol consisted of an initial ECG, continuous ST-segment monitoring, and cardiac marker assays at 0, 3, 6, and 9 hours. They found that a provocative test, most commonly a stress treadmill, was not positive in any patient whose initial evaluation protocol results were negative.

Weber et al prospectively evaluated 344 patients with cocaine-associated chest pain. Of these, 42 (12%) were admitted to the hospital and 302 (88%) were evaluated in an emergency department chest pain observation unit. Along with continuous ST-segment monitoring, serial ECGs, and serial cardiac markers, the protocol initially included provocative testing in all patients, but because of the very low rate of positive tests, the protocol changed and stress testing prior to discharge ceased to be mandatory. Patients who had normal troponin I levels, were without new ischemic ECG changes, and had no cardiovascular complications (CHF, dysrhythmias) during the 9- to 12-hour observation period were discharged from the unit. During the 30-day followup period none of the patients died of a cardiovascular event and only 4 of the 256 patients for whom followup data were available had a nonfatal AMI. All AMIs occurred in patients who continued to use cocaine.

A very recent prospective, cohort study by Cunningham et al examined 1-year cardiac outcomes in 219 low- to intermediate-risk patients with cocaine-associated chest pain who completed an emergency department chest pain observation protocol. No patient experienced an AMI within the 1-year followup. These studies and others indicate that if the initial and ongoing cardiac evaluations are unremarkable, if the patient’s symptoms resolve, and if no other abnormalities are found, these patients can be safely discharged from the emergency department with appropriate followup arrangements. It is imperative for the practitioner to offer drug rehabilitation and tobacco cessation opportunities; these are important interventions to reduce the risk of subsequent adverse events for this patient population.

**Case Resolutions**

**Case One**

The patient was initially treated with aspirin, sublingual nitroglycerin, and lorazepam. The ECG was consistent with an acute inferior STEMI. The patient was started on a nitroglycerin infusion, administered a bolus of heparin, and given morphine sulfate for ongoing chest pain. Consultation with a cardiologist was obtained, and the patient was taken to the cardiac catheterization laboratory for coronary angiography.

**Pearls and Pitfalls**

- The pathogenesis of cocaine-associated myocardial injury is multifactorial.
- The differential diagnosis of cocaine-associated chest pain includes other life-threatening entities—aortic dissection, pulmonary embolus, pneumothorax, pericarditis, etc.
- Delayed (>12 hours) cardiovascular complications are unusual.
- The ECG finding of benign early repolarization is common in this patient population.
- Troponin I is a more specific cardiac marker than CK-MB in this patient population.
- Treatment of cocaine-associated acute coronary syndrome differs from the treatment of traditional acute coronary syndromes in several respects—use of benzodiazepines, avoidance of β-blockers, and possible use of calcium channel blockers and phentolamine.
- Primary coronary intervention (PCI) is the initial treatment choice for cocaine-associated STEMI.
- After a period of observation and testing, discharge home for certain low-risk patients is feasible.
for PCI. Results of this demonstrated total occlusion of the right coronary artery with underlying narrowing. A stent was placed.

**Case Two**

The patient was treated with aspirin, sublingual nitroglycerin, and lorazepam. The chest pain and his other symptoms resolved over the next 20 minutes. The chest radiograph was unremarkable. The presenting ECG was compared to a previous ECG and was thought to be consistent with benign early repolarization. The ECG at 8 hours was unchanged. The initial, 4-hour, and 8-hour cardiac markers were negative. The patient was discharged home and was provided primary care followup; he declined outpatient drug abuse counseling.

**Summary**

Cocaine-associated chest pain is a clinical entity that crosses all socioeconomic classes and will continue to be seen because of the widespread use of cocaine in the United States. Fortunately, this patient population has low morbidity and mortality rates, despite the fact that our current therapeutic interventions are poorly studied. Current knowledge does direct us toward those treatments that affect the pathophysiology of cocaine-associated chest pain and assures us that emergency department discharge after an appropriate negative evaluation is appropriate for most of these patients.

**References**

Appendicitis is the most common surgical etiology of abdominal pain. It occurs across all ages and is most common in the second decade of life. Although it is less common in children younger than 4 years old, the risk of perforation is greatest, between 80% and 100%, in this age group. In children younger than 12, the rate of missed diagnosis is between 28% and 57%. For these reasons, many studies have looked for reliable indices to diagnose appendicitis in children.

Bundy et al identified 42 articles that used primary data in children assessing signs and symptoms of disease. Those studies that were blinded and had more than 200 children in them were assigned a level 1. Level 2 studies were those with fewer than 200 patients. Level 3 studies included patients that were not consecutive and those who had suspected appendicitis.

Abdominal pain was universally present, but the presence of right lower quadrant (RLQ) pain had minimal impact on the likelihood of appendicitis. The absence of RLQ pain, however, decreased the likelihood of appendicitis. A history of periumbilical pain that migrated to the RLQ was more useful.

Other symptoms were found useful only in the level 1 study. Fever increased the likelihood of appendicitis threefold, while its absence lowered likelihood by two thirds. Both vomiting and diarrhea were useful in the level 1 study, but of inconsistent usefulness in the level 3 studies, confusing the picture.

Examination findings were mildly useful. Solely level 3 data was available for rebound, involuntary guarding, rectal tenderness, and a psoas sign. All were found to increase the chance of appendicitis, although their absence was minimally useful.

A white blood cell count of less than 10,000 lowered the likelihood ratio to 0.22, and an elevated WBC was only variably useful. The usefulness of C-reactive protein (CRP) was also inconsistent between studies.

Lastly, the authors examined whether clinical gestalt was useful. To do this, they examined the percentage of children who had appendicitis among those who were sent for an imaging study. They found that 31% to 50% of children who had either CT or ultrasonography looking for appendicitis had positive studies. This is compared to 10% of children who were diagnosed with appendicitis from the emergency department. Various algorithms such as the Alvarado/MANTRELS and Pediatric Appendicitis Score were no more useful than clinicians’ clinical gestalt.

**Highlights**

- Appendicitis remains a difficult diagnosis to make, especially in younger children. RLQ pain is a less useful sign in this population than it is in adults.
- A history of abdominal pain migrating to the RLQ and symptoms such as a fever are useful.
- Rebound, involuntary guarding, the psoas sign, and rectal tenderness are useful signs. Their absence is not useful.
- Both clinical gestalt and scoring systems are useful in predicting which children will have appendicitis.
- More research needs to be done to find more reliable signs, symptoms, and laboratory tests that can identify children with appendicitis.

Article 14

**Does This Child Have Appendicitis?**

Reviewed by Jane C. Preotle, MD, and J. Stephen Bohan, MD, MS, FACEP; Harvard Affiliated Emergency Medicine Residency; Brigham and Women’s Hospital

Metabolic and Infectious Emergencies in Cancer Patients

Jonathan M. Glauser, MD, MBA, FACEP

Objectives
On completion of this lesson, you should be able to:

1. Describe life-threatening metabolic and infectious entities in cancer patients.
2. Describe the evaluation of febrile patients with treatment-induced neutropenia.
3. Describe the signs and symptoms of the tumor lysis syndrome.
4. Discuss management of chemical and metabolic abnormalities specific to cancer and its therapy.
5. Detect and treat metabolic issues related to the syndrome of inappropriate antidiuretic hormone secretion.

From the EM Model
1.0 Signs, Symptoms, and Presentations

Case Presentations

Case One
A 73-year-old woman presents to the emergency department complaining of headache and dizziness. She has a history of recent weight loss and anorexia, and her family reports that she has seemed increasingly tired over the past week. She has been treated for multiple myeloma, which was initially diagnosed 2 years ago. The only abnormality in her vital signs is mild hypotension, with a blood pressure of 85/58. During her examination she has a brief generalized seizure. Serum chemistries, a coagulation profile, serum protein electrophoresis, and CBC with differential count are ordered. The hospital laboratory calls 30 minutes later to report that they are unable to perform the chemistry tests because their analyzer is jammed from the blood.

Case Two
A 57-year-old man with a history of squamous cell carcinoma of the lung is brought in by his wife and eldest daughter because he has become unresponsive. He has been increasingly fatigued over the past 2 weeks but is now stuporous. Apart from some abdominal pain last week, he seems to have been pain-free. His wife reports that he has been chronically constipated and has been essentially bed-confined for several days. On examination he does not answer questions and seems oriented to name only.

Case Three
A 23-year-old man is referred to the emergency department by his internist. He has been undergoing chemotherapy for acute leukemia, with his last chemotherapy session concluding 3 days prior. He has been vomiting for the past 2 days according to his mother, who is giving most of the history, as the patient seems lethargic. His initial laboratory values indicate a serum potassium of 6.2 mmol/L, a serum uric acid of 12.7 mg/dL, and a serum calcium of 6.3 mg/dL. His serum creatinine today is 2.3 mg/dL, and the physician notes that 1 week ago it was 1.5 mg/dL.
Fever in the Neutropenic Cancer Patient

Fever in the neutropenic patient is a medical emergency and a common problem. Historically, infections accounted for approximately 75% of the mortality related to cancer chemotherapy, and infection is still the leading cause of cancer death. Empiric antibiotics should be started on patients with drug-induced neutropenia. Fever is defined as a single temperature higher than 38.3°C (100.9°F), or a sustained temperature above 38°C (100.4°F) for more than 1 hour.2 Neutropenia is defined as an absolute neutrophil count (ANC) of less than 0.5 × 10^9/L or 500 cells/mm^3 or less than 1 × 10^9/L with an expected decline to less than 0.5 × 10^9/L within 24 hours.3 Most chemotherapy regimens result in a neutrophil trough 7 to 10 days after treatment, with an expected rise after 5 more days.4 Fever in these patients can have noninfectious causes such as inflammation, tumor necrosis, transfusions, and medication-related, to name a few. Factors that favor an infectious cause include prolonged duration of neutropenia, the presence of central and peripheral venous catheters, and a rapid decline in ANC.5,6

Signs of clinical deterioration can include hypothermia and hypotension. Alteration in mental status or agitation indicates the need for more urgent intervention. The risk of infection increases as the ANC diminishes. Chemotherapy itself can contribute to the problem by inducing mucositis throughout the gastrointestinal tract and causing seeding of endogenous flora. The use of rectal thermometers in these patients has been called into question because of the possibility of bacterial seeding from tearing the rectal mucosa.

Emergency physicians should be aware of infection patterns within their respective hospitals. Although gram-negative infections predominated in the 1970s, more recent data have shown that gram-positive infections have accounted for most infections in the 1990s, perhaps because of an increase in in-dwelling central venous catheters7,8 or quinolone prophylaxis.9 Fungal infections, especially with Candida species, are common, although immunocompromised patients could be infected with Histoplasma, Aspergillus, or other species. Candida is especially common from line infections. Aspergillus can manifest with skin ulcers, pneumonia, or sinusitis.10 Empiric antifungal therapy in persistently febrile neutropenic patients has become more palatable with the introduction of less toxic antifungal drugs. Viral pathogens that should be considered in cancer patients are herpes simplex, cytomegalovirus, and Epstein-Barr virus. Anaerobic bacteremia is unusual.9 An infectious source is identified in only approximately one-third of febrile neutropenic episodes.11

A broad range of diagnostic studies should be performed on cancer patients. A CBC with differential is crucial so that an ANC can be calculated. Blood chemistries, including transaminases and amylase and coagulation studies, should be obtained, as well as urine cultures and two sets of blood cultures. At least one set of cultures should be drawn from an indwelling venous line if one is present. A chest radiograph should be obtained, although an infiltrate might not be visible if the inflammatory response is minimal. Chest CT is more sensitive for detecting pneumonia and should be performed if pneumonia is clinically suspected because of persistent fever.12 Lumbar puncture should be considered if there is alteration of mental status or any suspicion of meningitis.

CRITICAL DECISION

What elements of the physical examination are particularly important for febrile cancer patients?

A full rather than focused physical examination should be performed on febrile cancer patients. The physical examination should include examination of the skin and mucous membranes for erythema, cellulitis, ulcers, paronychia, pilonidal abscess, and dental abscesses. All indwelling lines should be examined for fluctuance, exudates, and erythema. Ophthalmoscopic examination may show evidence of endophthalmitis. Indwelling feeding tubes may be causing sinusitis.

Antimicrobial Treatment

Treatment should be initiated with antimicrobial therapy as soon as possible after appropriate cultures have been obtained. The optimal regimen should be bactericidal, relatively nontoxic, and address a broad range of likely gram-positive and gram-negative pathogens. Vancomycin should be added if there is a suspicion of gram-positive infection such as from Staphylococcus epidermidis from an indwelling intravenous line. Vancomycin-resistant enterococcus infection may be managed with newer agents such as linezolid or dalfopristin.
constipation, polyuria, polydipsia, hypercalcemia can present with somnolence, to coma. Chronic paranoia, confusion, depression, personality changes such as lethargy, nervous system effects ranging from hypercalcemia presents with central levels as low as 12 mg/dL. Acute patients with acute hypercalcemia with levels of 15 mg/dL, while could be minimally symptomatic. Patients with chronic hypercalcemia appears minimally symptomatic. The rate of rise of serum calcium often determines symptoms and urgency of therapy. Patients with advanced malignancy; it has been reported in 10% to 30% of patients with cancer at some time during their disease. The rate of rise of serum calcium concentration as well as the degree of hypercalcemia often determines symptoms and urgency of therapy. Patients with chronic hypercalcemia could be minimally symptomatic with levels of 15 mg/dL, while patients with acute hypercalcemia might present with coma with levels as low as 12 mg/dL. Acute hypercalcemia presents with central nervous system effects ranging from personality changes such as lethargy, paranoia, confusion, depression, and somnolence, to coma. Chronic hypercalcemia can present with constipation, polyuria, polydipsia, anorexia, nausea, memory loss, or a shortened QT interval on ECG.

Multiple factors may cause hypercalcemia of malignancy: elaboration of a parathyroid-hormone-related protein; local bone destruction; and tumor-producing vitamin D-like substances.

The most common malignancies associated with hypercalcemia are multiple myeloma, lung cancer, and breast cancer. These patients may have other electrolyte abnormalities caused by hypokalemia or dehydration. Serum phosphorus, albumin, and alkaline phosphate should be measured as well. In patients with hypoalbuminemia, total serum calcium concentration can be normal while serum ionized calcium is elevated. The measured serum calcium should be added to 0.8 (4.0-albumin) to correct for hypoalbuminemia. A serum calcium level above 14 mg/dL generally constitutes a medical emergency requiring treatment even if the patient appears minimally symptomatic.

**CRITICAL DECISION**

**What therapies are available in the emergency setting to treat hypercalcemia?**

Therapy usually is initiated with isotonic saline intravenously. This restores blood volume and increases urinary calcium excretion. The aim is to maintain urine output in adults at 100 to 150 mL/hour. If the patient is fluid overloaded initially, a loop diuretic such as furosemide, which inhibits passive resorption of sodium, may be given. Patients should be monitored for hypomagnesemia, hypokalemia, and hypovolemia if a loop diuretic is given. Medications such as thiazide diuretics, which increase serum calcium, should be avoided.

Bisphosphonates inhibit calcium release by interfering with osteoclast-mediated bone resorption. Their maximum effect occurs in 2 to 4 days, and they are usually given with saline as above and, possibly, calcitonin. Pamidronate, 60 to 90 mg IV over several hours, or zoledronic acid, 4 mg IV over at least 15 minutes, are recommended doses. These medications can cause impaired renal function, hypophosphatemia, and osteonecrosis of the jaw.

Calcitonin increases renal calcium excretion and decreases bone resorption. In intramuscular or subcutaneous doses of 4 IU/kg, salmon calcitonin works rapidly to lower serum calcium by 1 to 2 mg/dL within 4 to 6 hours. Glucocorticoids such as hydrocortisone, 100 mg IV every 6 hours, can be useful if the hypercalcemia is related to elevated levels of vitamin D, as in Hodgkin disease and some lymphomas. Treatment of the underlying malignancy can control the hypercalcemia. As treatments of last resort, hemodialysis and peritoneal dialysis are effective therapies for hypercalcemia.

**Hyperviscosity Syndrome**

Hyperviscosity syndrome is commonly seen in certain cancers and polycythemia vera. Elevated serum proteins elaborated by some cancers or elevated levels of leukocytes or erythrocytes can increase the viscosity of patients’ blood, with ensuing sludging and decreased perfusion at the microvascular level. When this occurs, multiple systems can be compromised. The most common causes of hyperviscosity syndrome are the dysproteinemias, IgG and IgA myelomas, IgM Waldenstrom macroglobulinemia, and certain leukemias. Hyperviscosity symptoms were present in 31% of patients with Waldenstrom macroglobulinemia in one report. The risk of developing this syndrome in patients with leukemias increases in those patients with granulocyte counts above 100,000 and lymphocyte counts greater than 750,000. The systems most at risk from vascular sludging are the visual, cardiopulmonary, and central nervous systems, in that order.
Critical Decision

What signs and symptoms should raise suspicion of hyperviscosity syndrome?

Classically, hyperviscosity syndrome presents with the triad of bleeding, visual disturbances, and neurologic symptoms. Hemorrhagic diathesis could manifest as epistaxis or gingival bleeding, hematuria, or rectal or vaginal bleeding. Visual disturbances can include visual loss, blurring, diplopia, nystagmus. Neurologic symptoms include headache, vertigo, ataxia, deafness, or seizures (jacksonian or generalized). More marked viscosity could result in confusion, dementia, stroke, or loss of consciousness. On physical examination, the patient might appear pale because of anemia from the underlying malignancy. Papilledema, retinal hemorrhages or exudates, or retinal detachment might be seen. Other manifestations apart from the typical triad are cardiac complications such as angina, myocardial infarction, and heart failure.

The diagnosis of hyperviscosity syndrome is largely a clinical one based on the presence of typical symptoms in a patient at risk. Laboratory testing in a patient with leukemia could increase suspicion if the WBC count is in the range above. Coagulation and renal profiles should be obtained, as well as serum and urine protein electrophoresis. Rouleaux formations can be noted on a peripheral smear. In patients with diseases that put them at risk of hyperviscosity syndrome, a serum viscosity level may be obtained, measured in centipoises (cP). A normal level is less than 1.8 cP, and most patients become symptomatic at levels over 6 cP. This number reflects the serum viscosity relative to water.

Management of hyperviscosity syndrome begins with recognition. Initial management includes careful hydration and diuresis. For a patient with an extreme elevation of the WBC count, leukopheresis may be initiated. If a dysproteinemia is the cause, plasmapheresis is indicated. If these interventions are not immediately available at an institution, phlebotomy should be performed with initial aliquots of 100 to 200 cc. The patient should then be transferred expeditiously to a center capable of plasmapheresis and leukopheresis.

Syndrome of Inappropriate Antidiuretic Hormone

In patients with cancer, the syndrome of inappropriate antidiuretic hormone (SIADH) is a paraneoplastic syndrome resulting from the secretion of arginine vasopressin (also known as antidiuretic hormone [ADH]). The increased production of ADH results in a characteristic constellation of chemical abnormalities including hypo-osmolality, hyponatremia, and an inappropriately elevated urine osmolality. Normovolemic hyponatremia such as diuretic therapy, preexisting renal disease, adrenal insufficiency, or hypothyroidism. The clinical findings of SIADH are primarily due to hyponatremia. In some cases, the patient will be asymptomatic. Patients could complain of fatigue, emesis, myalgias, and poor appetite. The extent of symptoms depends upon the rate of development of the hyponatremia and level of the serum sodium. As sodium levels falls below 100 mEq/L, patients can develop altered mental status, seizures, psychosis, lethargy, or coma.

Critical Decision

What are the treatment options for SIADH?

Treatment of SIADH depends on the severity of symptoms and the acuity of onset of the hyponatremia. Mild degrees of hyponatremia may not necessitate any immediate treatment. Mild fluid restriction until followup may be appropriate. The underlying malignancy should be treated. In cases unresponsive to fluid restriction, therapy with demeclocycline may be started to induce a reversible nephrogenic diabetes insipidus to counteract the influence of the excess vasopressin. If the SIADH is due to chemotherapeutic agents, the patient’s therapeutic regimen might need to be altered.

In those patients with more severe degrees of hyponatremia or those with significant central nervous system symptoms related to their hyponatremia, normal saline can be initiated, or for those with seizures and altered mental status, 3% hypertonic saline (300 to 500 mL at a time over 3 to 4 hours) may be administered followed by furosemide to control intravascular volume. It is desirable to control the rate of correction of serum sodium to no more than 0.5 to 1 mEq/L/hour in order to prevent central nervous system disorders such as central
pontine myelinolysis. These patients will require admission to an ICU.

**Tumor Lysis Syndrome**

Tumor lysis syndrome is an oncologic emergency caused by a massive destruction of cancer cells with ensuing release of nucleic acids, potassium, and phosphate into the circulation. Breakdown of the nucleic acids into uric acid leads to hyperuricemia. The precipitation of uric acid into the renal tubules can lead to renal failure. Tumor lysis syndrome most commonly occurs in cancer types with a high proliferative rate, large tumor burden, or those particularly sensitive to cytotoxic therapy. These include acute lymphoblastic leukemia and Burkitt or other non-Hodgkin lymphomas, but other tumor types have been implicated.

Specific laboratory abnormalities have been proposed in 2004 to define tumor lysis syndrome. These are an elevated uric acid, above 8 mg/dL; a serum potassium of more than 6 mmol/L or a 25% increase from baseline; serum phosphate elevated above 6.5 mg/dL in children or above 4.5 mg/dL in adults; or a depressed serum calcium, lower than 7 mg/dL or a 25% decrease from baseline. Serum lactate dehydrogenase is typically elevated. Clinical tumor lysis syndrome includes increased serum creatinine, cardiac dysrhythmia or sudden death, or a seizure. Rapid lysis of tumor cells can be associated with a large tumor burden, with cytotoxic chemotherapy, or radiation therapy in the setting of a malignancy with a high proliferative rate.

Hyperuricemia is a result of the breakdown of purine nucleic acids and must be addressed. Historically, the xanthine oxidase inhibitor allopurinol has been employed to lower the peak uric acid level and to prevent uric acid nephropathy. Allopurinol treatment leads to the accumulation of hypoxanthine and xanthine. Since xanthine is less soluble than uric acid, it can precipitate in the renal tubules. Urinary alkalinization increases the solubility of uric acid but not of xanthine. This therapy for tumor lysis syndrome has the potential to form xanthine crystals resulting in obstruction of renal tubules.

Clinical manifestations of tumor lysis syndrome include nausea, vomiting, diarrhea, lethargy, anorexia, seizures, tetany, cramps, syncope, and possible sudden death. Urinalysis can show urate crystals. An ECG should be performed in patients with serious electrolyte abnormalities.

**CRITICAL DECISION**

**What is the appropriate treatment for tumor lysis syndrome?**

Treatment includes aggressive intravenous hydration at about 2 to 3 liters/m² per day to keep urine output at 80 to 100 mL/m² per hour. Potassium should be withheld from hydration fluids initially because of the risk of hyperkalemia; calcium should be withheld because of the risk of calcium phosphate precipitation. Urinary alkalinization could promote calcium phosphate deposition in the kidney and elsewhere.

The usual allopurinol dose in adults to address hyperuricemia is 100 mg/m² every 8 hours, initiated 24 to 48 hours before chemotherapy and continued for up to 1 week. An alternative to allopurinol is rasburicase, a recombinant urate oxidase, which catalyzes the degradation of uric acid and rapidly lowers serum uric acid levels. It is effective in preventing and treating hyperuricemia and in treating tumor lysis syndrome. It may be given at a dose of 0.15 to 0.2 mg/kg in 50 mL of isotonic saline infused over 30 minutes once daily for 5 to 7 days but is only FDA-approved for pediatric patients. Serum levels of calcium, phosphate, uric acid, potassium, creatinine, and lactate dehydrogenase should be monitored.

Hyperphosphatemia can be treated with aluminum hydroxide, a phosphate binder, and with restriction of phosphate intake. Dialysis can be necessary to treat persistent hyperphosphatemia, hypocalcemia, or low urine output. The best management is prevention via intravenous hydration and with hypouricemic agents.
Case Resolutions

Case One
The emergency physician suspected hypercalcemia syndrome in the 73-year-old woman because of her neurologic presentation, the history of myeloma, and the fact that the analyzer jammed with the patient’s blood. The patient’s hematologist was contacted, and emergency plasmapheresis was arranged. The emergency physician also hydrated the patient with simultaneous diuresis, because she had a documented mild cardiomyopathy with an ejection fraction of 40%. Her mentation improved, and she was discharged on the 4th hospital day.

Case Two
In the case of the 57-year-old man who was unresponsive, an intravenous line was established and normal saline solution was infused. Because of his fatigue and constipation in the face of known lung cancer, a diagnosis of hypercalcemia was suspected, and serum electrolytes were drawn. His serum calcium level was measured at 15.2 mg/dL (3.8 mmol/L), and isotonic saline was started at 250 mL/hour. He was treated with intravenous furosemide and, after consultation with the oncologist on call, he was given 4 mg of zoledronic acid intravenously, as well as salmon calcitonin, 4 IU/kg intramuscularly. Within 48 hours, his uric acid level was 7.8 mg/dL, and his potassium had normalized. He was discharged home on the 3rd hospital day.

Case Three
For the lethargic young man with acute leukemia, an intravenous line was started, and a Foley catheter was placed to monitor urine output. The emergency physician discussed further management with the oncology attending physician, and rasburicase was not on the formulary, allopurinol, 170 mg every 8 hours, was initiated, and the patient was admitted to a telemetry floor. Within 48 hours, his urine output was 1.45 liters/m² per day of hydration to keep his urine output at approximately 170 mL/hour. The emergency physician continued to monitor urine output.

Summary
Cancer remains the second leading cause of death in the United States. With an aging population, it is inevitable that the number of patients with acute illness and disability from malignancy will increase. The accurate diagnosis and treatment of metabolic and infectious emergencies in cancer patients can potentially forestall disability and enhance quality of life.

References
Atrial flutter with 2:1 atrioventricular conduction, rate 125, left bundle-branch block. The rhythm is wide-complex and regular, prompting consideration of ventricular tachycardia (VT), supraventricular tachycardia (SVT) with aberrant conduction, and sinus tachycardia (ST) with aberrant conduction. A less common entity should be considered as well – atrial flutter with aberrant conduction. Both ST and atrial flutter are characterized by regular distinct atrial complexes, whereas VT and SVT are less likely to demonstrate regular distinct atrial complexes. In this case, atrial complexes are clearly found in lead V1 and led to the misdiagnosis of ST. One can notice, however, an irregular appearance to the T wave in lead V1 – “a camel hump” appearance. This type of irregular appearance of the T wave should always prompt consideration of hypokalemia (T-U fusion complex) and “buried” P waves. In this case, the irregular T-wave appearance was caused by the latter; the first “hump of the camel” is a buried P wave, or flutter wave. Use of ECG calipers helps demonstrate the regularity of these flutter waves.
The Critical Image

A 39-year-old woman with no significant past medical history, presenting with 1 week of bilateral neck pain, shortness of breath with mild exertion, and lightheadedness. She noted enlarging of her neck veins a few days prior to her emergency department visit, and this was also noted on physical examination. A chest radiograph was ordered, followed by a chest CT.

The mediastinum and hilar region on frontal chest radiographs (A) should be routinely reviewed. A widened hilar and upper mediastinal region can indicate a mediastinal mass or adenopathy.

The lateral chest radiograph (B) can provide important information about soft tissue abnormalities of the upper mediastinum. The retrosternal region is normally quite lucent (black). In this case, it is occupied by a soft tissue density (white).

A CT with intravenous contrast (C) can identify mediastinal masses and associated vascular disorders. In this case, an anterior mediastinal mass with compression of the superior vena cava to a few millimeters width was revealed – superior vena cava syndrome – accounting for the patient’s jugular venous distension.

The patient underwent mediastinal biopsy showing a diffuse large B-cell lymphoma. This responded well to chemotherapy and radiation, and the patient was disease-free at 2-year followup.

Feature Editor: Joshua S. Broder, MD, FACEP
CME Questions

Qualified, paid subscribers to Critical Decisions in Emergency Medicine may receive CME certificates for up to 5 ACEP Category I credits, 5 AMA PRA Category I Credits™, and 5 AOA Category 2-B credits for answering the following questions. To receive your certificate, go to www.acep.org/criticaldecisiontesting and submit your answers online. You will immediately receive your score and printable CME certificate. You may submit the answers to these questions at any time within 3 years of the publication date. You will be given appropriate credit for all tests you complete and submit within this time. Answers to this month’s questions will be published in next month’s issue.

1. Which of the following is a potential mechanism for cocaine-induced myocardial injury?
   A. decreased atherogenesis
   B. decreased afterload
   C. decreased myocardial oxygen demand
   D. increased thrombogenicity
   E. vasodilation

2. According to the article by Hollander et al (Am Heart J. 1998), which of the following cardiac markers possesses the best specificity when used in the evaluation of cocaine-induced chest pain?
   A. CK-MB
   B. CK total
   C. C-reactive protein
   D. myoglobin
   E. troponin I

3. Which of the following has been associated with harm in the treatment of cocaine-associated myocardial infarction?
   A. aspirin
   B. β-blockers
   C. benzodiazepines
   D. heparin
   E. nitroglycerin

4. The vast majority of cardiovascular complications from cocaine will occur within what time frame?
   A. within 20 minutes
   B. within 1 hour
   C. within 12 hours
   D. within 48 hours
   E. within 72 hours

5. What nonacute ECG finding is commonly found in patients with cocaine-associated chest pain?
   A. benign early repolarization
   B. left bundle-branch block
   C. left ventricular hypertrophy
   D. QT prolongation
   E. acute right ventricular strain pattern

6. Which of the following is most accurate regarding the initial treatment choice for cocaine-associated STEMI?
   A. avoid thrombolitics
   B. the dose of aspirin should be tripled
   C. high-dose esmolol should be started
   D. heparin is contraindicated
   E. primary coronary intervention (PCI) is the initial intervention

7. What is the most appropriate agent to use for an acute cocaine-induced wide complex tachycardia?
   A. adenosine
   B. esmolol
   C. procainamide
   D. quinidine
   E. sodium bicarbonate

8. What is the most appropriate agent to treat the sympathomimetic toxidrome associated with cocaine?
   A. atropine
   B. diltiazem
   C. esmolol
   D. haloperidol
   E. lorazepam

9. According to the 2003 New England Journal of Medicine article by Weber on cocaine-associated chest pain, which of the following is routinely recommended for patients with cocaine-associated chest pain?
   A. admission to an ICU
   B. CT scan of chest, with contrast
   C. ECG
   D. empiric thrombolytics based on history alone
   E. stress testing for all patients

10. Which statement is correct regarding the complications seen with cocaine-associated chest pain?
    A. extended observation (24 to 48 hours) is necessary
    B. mortality rates for AMI approach 15%
    C. most lethal arrhythmias occur in the emergency department setting
    D. noncardiac complications must be considered
    E. rule-in rates for AMI approach 15%

11. How is neutropenia defined in cancer patients?
    A. an ANC less than 1.5 X 10⁹/L
    B. an ANC less than 500 cells/mm³
    C. any temperature greater than 38.3°C (100.9°F) in a patient who has received chemotherapy within the past 7 to 10 days
    D. total WBC count less than 5,000/mm³
    E. total WBC count less than 5,000/mm³ with an expected decline within 24 hours in a febrile patient
12. Which is true regarding a febrile patient on cancer chemotherapy?
A. empiric therapy should always be initiated in the emergency department with antifungal agents
B. an infectious source is detected in approximately 90% of febrile neutropenic patients
C. it is advisable to avoid measuring temperatures rectally
D. the neutrophil trough typically occurs 2 to 3 weeks after the last dose of chemotherapy
E. there has been an increased gram-negative predominance of infections since 1990

13. Which drug is suitable for monotherapy in the management of a febrile neutropenic patient?
A. ampicillin
B. doxycycline
C. piperacillin-tazobactam
D. trimethoprim/sulfamethoxazole
E. vancomycin

14. Which is true regarding a patient with malignancy and hypercalcemia?
A. if serum albumin is low, then the measured calcium will be falsely high
B. the most commonly associated primary tumors are from skin and bone
C. the rate of rise of serum calcium is much less important than the actual calcium level
D. a serum calcium level of greater than 11 mg/dL constitutes a medical emergency even if the patient is asymptomatic
E. this is reported as a complication in from 10% to 30% of patients with advanced malignancy

15. Which cancer is most likely to cause hyperviscosity syndrome?
A. breast
B. kidney
C. lung
D. melanoma
E. Waldenstrom macroglobulinemia

16. If hyperviscosity syndrome is suspected, what level of serum viscosity in centipoises (cP) would suggest the diagnosis?
A. 0.2 cP
B. 0.5 cP
C. 1 cP
D. 2 cP
E. 7 cP

17. In patients with SIADH, what is considered to be the most rapid correction of serum sodium with hypertonic saline deemed safe in order to prevent central pontine myelinolysis?
A. 0.5 to 1 mEq/hour
B. 3 mEq/hour
C. 5 mEq/L/hour
D. 10 mEq/hour
E. no specific number; in a symptomatic patient, correct it to normal as quickly as possible with 3% saline

18. In a patient with tumor lysis syndrome, which new agent shows promise in addressing hyperuricemia if there is concern that allopurinol might increase crystallization of xanthine in renal tubules?
A. furosemide
B. hypertonic saline
C. mannitol
D. rasburicase
E. vasopressin

19. Which of the following is first-line therapy for the acute management of most hypercalcemic cancer patients?
A. bisphosphonates
B. calcitonin
C. furosemide
D. gallium nitrate
E. hydration with normal saline

20. SIADH includes which chemical abnormality?
A. serum sodium of 140 mEq/L
B. serum sodium of 150 mEq/L
C. urine osmolality less than 50 mOsm/kg
D. urine sodium of 15 mEq/L
E. urine sodium of 50 mEq/L

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### The Drug Box: Lorazepam Use for Cocaine-Associated Chest Pain

By Allison M. Finley, MD; Summa Health System Emergency Medicine Residency

Between 1% and 6% of cocaine users whose chief complaint is chest pain will be found to be having an acute myocardial infarction (MI), and the risk of having an MI is 24 times greater in the first hour after cocaine is used. Initial evaluation with laboratory testing, ECG, etc., should be no different than for any other chest pain patient. In addition to treatment with oxygen, aspirin, and nitrates if appropriate, benzodiazepines, usually lorazepam, are now considered first-line therapy for cocaine-associated chest pain. In fact, symptoms may resolve with administration of lorazepam alone.

**Lorazepam (for Cocaine-Associated Chest Pain)**

| Mechanism of Action | Acts at the limbic, thalamic, and hypothalamic regions to produce varying degrees of CNS depression and relaxation. The effects are mediated by γ-aminobutyric acid (GABA), one of the inhibitory neurotransmitters. |
| Indications | First-line therapy for cocaine-associated chest pain; other uses include status epilepticus, sedation, and anxiety. |
| Dosing | 1 mg IV every 5 minutes, for 2 doses. May be repeated with caution until patient is pain free. |
| Side Effects | Respiratory depression and apnea, dizziness, nausea, drowsiness, confusion, and amnesia. |
| Estimated Cost to Hospital | $2 per 2-mg vial* |
| Contraindications/Precautions | Absolute contraindications include closed-angle glaucoma, sleep apnea, intra-arterial administration, and hypersensitivity to benzodiazepines. Precautions include breast feeding and pregnancy, patients under age 18, elderly patients, alcohol intoxication, dementia, and respiratory depression. |

*Cost data provided by Summa Health System Pharmacy

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