Update CPR guidelines for poisoned patients

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Conflicts of Interest Disclosure:
No Conflicts of Interest to declare

This lecture for health education only
Part 12.7: Cardiac Arrest Associated With Toxic Ingestions

- With few exceptions, no unique antidotes or toxin-specific interventions recommended during resuscitation from cardiac arrest
- Once RoSC, urgent consultation with a toxicologist or poison center
- Cardiac arrest or severe cardiovascular instability

Cyanide:

Patients in cardiac arrest or those presenting with cardiovascular instability caused by known or suspected cyanide poisoning should receive cyanide-antidote therapy with a cyanide scavenger (either IV hydroxocobalamin or a nitrate such as IV sodium nitrite and/or inhaled amyl nitrite), followed as soon as possible by IV sodium thiosulfate.
- Benzodiazepines: no data of antidote use in cardiac arrest

- Beta-Blockers: no data of antidote use in cardiac arrest
  - refractory hemodynamic instability
  - glucagon, high-dose insulin, IV calcium salts

- Calcium Channel Blockers: no data of antidote use in cardiac arrest
  - refractory hemodynamic instability
  - high-dose insulin, or IV calcium salts

- Digoxin and Related Cardiac Glycosides: no data of antidote use in cardiac arrest
  - Antidigoxin Fab antibodies in severe life-threatening
- **Cocaine:** no data of specific interventions in cardiac arrest
  - acute coronary syndrome, wide-complex tachycardia

- **Cyclic Antidepressants:** Administration of [sodium bicarbonate](https://en.wikipedia.org/wiki/Sodium_bicarbonate) for cardiac arrest due to overdose may be considered (Class IIb, LOE C)

- **Carbon Monoxide:** no data of specific interventions in cardiac arrest
  - routine transfer to HBO facility following resuscitation should be carefully considered, weighing the risk against the possible improvement
Part 10: Special Circumstances of Resuscitation

Part 10.3: Cardiac or Respiratory Arrest Associated With Opioid Overdose

Part 10.4: Role of Intravenous Lipid Emulsion Therapy in Management of Cardiac Arrest Due to Poisoning
Part 10: Special Circumstances of Resuscitation

Table 1. Groups That May Benefit From Opioid Overdose Response Education and/or Naloxone Distribution and Training

- Persons who abuse prescription opioids or heroin
- Patients who have required emergency care for opioid overdose
- Patients enrolled in opioid dependence treatment programs, including methadone and buprenorphine maintenance programs, particularly at high-risk periods, such as induction or discharge
- Persons with a history of opioid abuse or dependence who are being released from prison
- Patients receiving prescription opioid therapy with risk factors for adverse effects
  - Coprescriptions of benzodiazepines or other sedatives
  - Ongoing alcohol use
  - High-dose prescription opioid therapy
- Persons living with or in frequent contact with those listed above

2015 AHA Guidelines Update for CPR and Emergency Cardiovascular Care
ACLS Modification: Administration of Naloxone

Respiratory Arrest
ACLS providers should support ventilation and administer naloxone to patients with a perfusing cardiac rhythm and opioid-associated respiratory arrest or severe respiratory depression. Bag-mask ventilation should be maintained until spontaneous breathing returns, and standard ACLS measures should continue if return of spontaneous breathing does not occur (Class I, LOE C-LD).

Cardiac Arrest
We can make no recommendation regarding the administration of naloxone in confirmed opioid-associated cardiac arrest. Patients with opioid-associated cardiac arrest are managed in accordance with standard ACLS practices.
After ROSC or return of spontaneous breathing, patients should be observed in a healthcare setting until the risk of recurrent opioid toxicity is low and the patient’s level of consciousness and vital signs have normalized (Class I, LOE C-LD).

If recurrent opioid toxicity develops, repeated small doses or an infusion of naloxone can be beneficial in healthcare settings (Class IIa, LOE C-LD).

Naloxone administration in post–cardiac arrest care may be considered in order to achieve the specific therapeutic goals of reversing the effects of long-acting opioids (Class IIb, LOE C-EO).
• ILE creates a lipid compartment in the serum, reducing by sequestration the concentration of lipophilic medications in the tissues + also increases cardiac inotropy by other mechanisms

• A 20% emulsion of long-chain TG, initial bolus of 1.5 mL/kg followed by an infusion of 0.25 mL/kg per minute for 30-60 minutes. The bolus can be repeated once or twice as needed; the suggested maximum total dose is 10 mL/kg over the 1st hour

2015 Guidelines Update: Part 10 Recommendations, Continued

<table>
<thead>
<tr>
<th>Year Last Reviewed</th>
<th>Topic</th>
<th>Recommendation</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Role of Intravenous Lipid Emulsion Therapy in Management of Cardiac Arrest Due to Poisoning</td>
<td>It may be reasonable to administer ILE, concomitant with standard resuscitative care, to patients with local anesthetic systemic toxicity and particularly to patients who have premonitory neurotoxicity or cardiac arrest due to bupivacaine toxicity (Class IIb, LOE C-E0).</td>
<td>updated for 2015</td>
</tr>
<tr>
<td>2015</td>
<td>Role of Intravenous Lipid Emulsion Therapy in Management of Cardiac Arrest Due to Poisoning</td>
<td>It may be reasonable to administer ILE to patients with other forms of drug toxicity who are failing standard resuscitative measures (Class IIb, LOE C-E0).</td>
<td>new for 2015</td>
</tr>
</tbody>
</table>
Avoid mouth-to-mouth breathing in the presence of chemicals such as cyanide, corrosives and organophosphates

Measure the patient’s temperature because hypo- or hyperthermia may occur after drug overdose

Consult regional or national poisons centres for information on treatment of the poisoned patient
There are no data on the use of any additional therapies beyond standard ALS guidelines in opioid-induced cardiac arrest.

Despite the paucity of data, patients with both cardiovascular collapse and cardiac arrest attributable to local anaesthetic toxicity may benefit from treatment with intravenous 20% lipid emulsion in addition to standard ALS.

Patients with severe cardiovascular toxicity (cardiac arrest, cardiovascular instability, metabolic acidosis, or altered mental status) caused by known or suspected cyanide poisoning should receive cyanide antidote therapy in addition to standard resuscitation.
Part 3: Adult Basic and Advanced Life Support

TOP 10 TAKE-HOME MESSAGES FOR ADULT CARDIOVASCULAR LIFE SUPPORT

5. Recognition that all cardiac arrest events are not identical is critical for optimal patient outcome, and specialized management is necessary for many conditions (eg, electrolyte abnormalities, pregnancy, after cardiac surgery).

6. The opioid epidemic has resulted in an increase in opioid-associated out-of-hospital cardiac arrest, with the mainstay of care remaining the activation of the emergency response systems and performance of high-quality CPR.

7. Post–cardiac arrest care is a critical component of the Chain of Survival and demands a comprehensive, structured, multidisciplinary system that requires consistent implementation for optimal patient outcomes.

Activate ERS + CPR
<table>
<thead>
<tr>
<th>CLASS (STRENGTH) OF RECOMMENDATION</th>
<th>Benefit &gt;&gt; Risk</th>
<th>Benefit ≥ Risk</th>
<th>Benefit = Risk</th>
<th>Risk &gt; Benefit</th>
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</thead>
<tbody>
<tr>
<td><strong>CLASS 1 (STRONG)</strong></td>
<td>Benefit &gt;&gt; Risk</td>
<td><strong>CLASS 2b (WEAK)</strong></td>
<td>Benefit ≥ Risk</td>
<td><strong>CLASS 3: No Benefit (MODERATE)</strong></td>
</tr>
<tr>
<td>Suggested phrases for writing recommendations:</td>
<td>• Is recommended</td>
<td>• May/might be reasonable</td>
<td>• Is not recommended</td>
<td>• May/might be considered</td>
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<td></td>
<td>• Is indicated/useful/effective/beneficial</td>
<td>• Usefulness/effectiveness is unknown/unclear/uncertain or not well-established</td>
<td>• Is not indicated/useful/effective/beneficial</td>
<td>• Should be performed/administered/other</td>
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<td>• Should be performed/administered/other</td>
<td>• Should be performed/administered/other</td>
<td>• Should not be performed/administered/other</td>
<td>• Should not be performed/administered/other</td>
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<td></td>
<td>• Comparative-Effectiveness Phrases†:</td>
<td>• Suggested phrases for writing recommendations:</td>
<td>• Class: Harm (STRONG)</td>
<td>• Suggested phrases for writing recommendations:</td>
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<td>− Treatment/strategy A is recommended/indicated in preference to</td>
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<td>• Potentially harmful</td>
<td>• Potentially harmful</td>
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<td></td>
<td>treatment B</td>
<td>• Is not indicated/useful/effective/beneficial</td>
<td>• Causes harm</td>
<td>• Causes harm</td>
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<td>− Treatment A should be chosen over treatment B</td>
<td>• Should not be performed/administered/other</td>
<td>• Associated with excess morbidity/mortality</td>
<td>• Associated with excess morbidity/mortality</td>
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### Class of Recommendation and Level of Evidence

As with all AHA guidelines, each 2020 recommendation is assigned a Class of Recommendation (COR) based on the strength and consistency of the evidence, alternative treatment options, and the impact on patients and society (Table 1). The Level of Evidence (LOE) is based on the quality, quantity, relevance, and consistency of the available evidence. For each recommendation, the writing group discussed and approved specific recommendation wording and the COR and LOE assignments. In determining the COR, the writing group considered the LOE and other factors, including systems issues.

October 20, 2020  S367

<table>
<thead>
<tr>
<th>LEVEL (QUALITY) OF EVIDENCE‡</th>
<th>LEVEL A</th>
<th>LEVEL B-R</th>
<th>LEVEL B-NR</th>
<th>LEVEL C-LD</th>
<th>LEVEL C-EO</th>
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<tr>
<td><strong>High-quality evidence‡ from more than 1 RCT</strong></td>
<td>(Limited Data)</td>
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<td><strong>Meta-analyses of high-quality RCTs</strong></td>
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<td><strong>One or more RCTs corroborated by high-quality registry studies</strong></td>
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<td>(Randomized)</td>
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<td><strong>Moderate-quality evidence‡ from 1 or more RCTs</strong></td>
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<td><strong>Meta-analyses of moderate-quality RCTs</strong></td>
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<tr>
<td><strong>Moderate-quality evidence‡ from 1 or more well-designed, well-executed nonrandomized studies, observational studies, or registry studies</strong></td>
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<td><strong>Meta-analyses of such studies</strong></td>
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<tr>
<td><strong>Randomized or nonrandomized observational or registry studies with limitations of design or execution</strong></td>
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<td><strong>Meta-analyses of such studies</strong></td>
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<td><strong>Physiological or mechanistic studies in human subjects</strong></td>
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<td><strong>Consensus of expert opinion based on clinical experience</strong></td>
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经济因素、伦理因素等如公平性、可接受性、可行性的证据评估方法，包括特定标准的使用来确定COR和LOE。更详细的内容可以参见“第二部分：证据评估和指南发展”。成人和高级生命支持编写组成员有最终决定权并正式批准这些推荐意见。
Opioid Overdose

» The ongoing opioid epidemic
» Increase in opioid-associated OHCA
» Approximately 115 deaths/day in US, predominantly patients 25-65 years old
» Isolated opioid toxicity: CNS + respiratory depression, progresses to respiratory arrest followed by cardiac arrest
» Opioid-associated resuscitative emergencies: defined by the presence of cardiac arrest, respiratory arrest, or severe life threatening instability suspected to be due to opioid toxicity

» The mainstay of care: early recognition of an emergency followed by activation of the emergency response systems

» Opioid overdoses deteriorate to cardiopulmonary arrest because of loss of airway patency and lack of breathing; addressing airway and ventilation in a periarrest patient is of the highest priority
Naloxone can be administered along with standard ACLS care if it does not delay components of high-quality CPR.
Recommendation-Specific Supportive Text

» Initial management should focus on support of airway and breathing

» No studies demonstrating improvement in patient outcomes from administration of naloxone during cardiac arrest, provision of CPR should be the focus of initial care

» Naloxone can be administered along with standard ACLS care if it does not delay components of high-quality CPR
» Early activation of the emergency response system: critical for patients with suspected opioid overdose

» Twelve studies examined the use of naloxone in respiratory arrest: report that **naloxone is safe and effective** in treatment of opioid-induced respiratory depression, that complications are rare and dose related
**Opioid-Associated Emergency for Lay Responders Algorithm**

1. **Suspected opioid poisoning**
   - Check for responsiveness.
   - Shout for nearby help.
   - Activate the emergency response system.
   - Get naloxone and an AED if available.

2. **Is the person breathing normally?**
   - Yes: **Prevent deterioration**
     - Tap and shout.
     - Reposition.
     - Consider naloxone.
     - Continue to observe until EMS arrives.
   - No: **Start CPR**
     - Give naloxone.
     - Use an AED.
     - Resume CPR until EMS arrives.

3. **Ongoing assessment of responsiveness and breathing**
   - Go to 1.

*For adult and adolescent victims, responders should perform compressions and rescue breaths for opioid-associated emergencies if they are trained and perform Hands-Only CPR if not trained to perform rescue breaths. For infants and children, CPR should include compressions with rescue breaths.*

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Opioid:
- standard resuscitative measures
- high-quality CPR
- activate EMS
- naloxone IV
Opioid Overdose

2015 (Old): Empiric administration of intramuscular or intranasal naloxone to all unresponsive opioid-associated life-threatening emergency patients may be reasonable as an adjunct to standard first aid and non-healthcare provider BLS protocols.

2015 (Old): ACLS providers should support ventilation and administer naloxone to patients with a perfusing cardiac rhythm and opioid-associated respiratory arrest or severe respiratory depression. Bag-mask ventilation should be maintained until spontaneous breathing returns, and standard ACLS measures should continue if return of spontaneous breathing does not occur.

2015 (Old): We can make no recommendation regarding the administration of naloxone in confirmed opioid-associated cardiac arrest.

2020 (Updated): For patients in respiratory arrest, rescue breathing or bag-mask ventilation should be maintained until spontaneous breathing returns, and standard PBLS or PALS measures should continue if return of spontaneous breathing does not occur.

2020 (Updated): For a patient with suspected opioid overdose who has a definite pulse but no normal breathing or only gasping (ie, a respiratory arrest), in addition to providing standard PBLS or PALS, it is reasonable for responders to administer intramuscular or intranasal naloxone.

2020 (Updated): For patients known or suspected to be in cardiac arrest, in the absence of a proven benefit from the use of naloxone, standard resuscitative measures should take priority over naloxone administration, with a focus on high-quality CPR (compressions plus ventilation).
Why: The opioid epidemic has not spared children. In the United States in 2018, opioid overdose caused 65 deaths in children younger than 15 years and 3618 deaths in people 15 to 24 years old, and many more children required resuscitation. The 2020 Guidelines contain new recommendations for managing children with respiratory arrest or cardiac arrest from opioid overdose.

These recommendations are identical for adults and children, except that compression-ventilation CPR is recommended for all pediatric victims of suspected cardiac arrest. Naloxone can be administered by trained providers, laypersons with focused training, and untrained laypersons. Separate treatment algorithms are provided for managing opioid-associated resuscitation emergencies by laypersons, who cannot reliably check for a pulse (Figure 5), and by trained rescuers (Figure 6). Opioid-associated OHCA is the subject of a 2020 AHA scientific statement.

2020 (New): It is reasonable for lay rescuers to receive training in responding to opioid overdose, including provision of naloxone.

Why: Deaths from opioid overdose in the United States have more than doubled in the past decade. Multiple studies have found that targeted resuscitation training for opioid users and their families and friends is associated with higher rates of naloxone administration in witnessed overdoses.
• Wide variation in recommended naloxone doses

Mental status depression + modest respiratory depression

Starting dose
• 0.04 mg IV in opioid-dependent patients
• 0.4 milligram IV in non–opioid-dependent patients

Subsequent doses
• 0.04-0.4 mg IV every 2-3 minutes until desired effect is reached
• Incremental dosing mitigates the precipitation of acute opioid withdrawal

Apnea or near-apnea and cyanosis

Starting dose
• 2 milligrams IV regardless of drug use history
• Repeated doses of 2 mg IV every 3 minutes until a maximum of 10 milligrams

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**TABLE 186-3 Naloxone**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Route</th>
<th>Initial Dose*</th>
<th>Onset of Action</th>
<th>Duration of Action*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naloxone</td>
<td>IV</td>
<td>0.04 milligrams if breathing spontaneously and suspected of chronic opioid use</td>
<td>1–2 min</td>
<td>20–90 min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0.4 milligrams if breathing spontaneously and opioid naive</td>
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<td></td>
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<tr>
<td></td>
<td></td>
<td>2 milligrams if apneic or cyanotic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IM or SC</td>
<td></td>
<td>2 milligrams</td>
<td>5–6 min</td>
<td></td>
</tr>
<tr>
<td>Intranasal</td>
<td></td>
<td>2 milligrams (1 milligram in each nostril)</td>
<td>6–8 min</td>
<td></td>
</tr>
<tr>
<td>Nebulized</td>
<td></td>
<td>2 milligrams in 3 mL normal saline</td>
<td>5 min</td>
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</tbody>
</table>

*See text regarding subsequent dosing.

*Duration dependent on amount of opioid agonist present.
The goal: not necessarily complete restoration of normal consciousness; rather, reinstitution of adequate spontaneous ventilation.

- Most patients respond to 0.04 IV.
- Requirement for ventilatory assistance: often slightly prolonged because the onset will be slower than with larger doses.
- Recommend repeating this dose for several doses at 3-minute intervals, with escalation up to 0.4-mg and 2-mg doses.
- If presumption of opioid overdose persists, repetitive bolus doses of 2 mg up to a total of 10 mg is indicated.

Goldfrank 11th ed
Management of Opioid Analgesic Overdose

Edward W. Boyer, M.D., Ph.D.

OPIOID ANALGESIC OVERDOSE IS A PREVENTABLE AND POTENTIALLY LETHAL CONDITION THAT RESULTS FROM PRESCRIBING PRACTICES, INADEQUATE UNDERSTANDING ON THE PATIENT'S PART OF THE RISKS OF MEDICATION MISUSE, ERRORS IN DRUG ADMINISTRATION, AND PHARMACEUTICAL ABUSE. Three features are key to an understanding of opioid analgesic toxicity. First, opioid analgesic overdose can have life-threatening toxic effects in multiple organ systems. Second, normal pharmacokinetic properties are often disrupted during an overdose and can prolong intoxication dramatically. Third, the duration of action varies among opioid formulations, and failure to recognize such variations can lead to inappropriate treatment decisions, sometimes with lethal results.

EPIDEMIOLOGY OF OVERDOSE
» Initial 0.4 - 2 mg IV

» Repeated doses of 0.04, 0.4, 2 mg IV every 3 min (until a maximum of 10 mg IV or respiratory depression reversed)

» 0.04 (or 0.05 mg) IV recommended in opioid-dependent patients

» Goal: reinstitution of adequate spontaneous ventilation
Toxicity: Benzodiazepines

» Flumazenil: a specific benzodiazepine antagonist
» Significant side effects: seizures and arrhythmia

Toxicity: Benzodiazepines

<table>
<thead>
<tr>
<th>Recommendation for Benzodiazepine Overdose</th>
<th>COR</th>
<th>LOE</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>3: Harm</td>
<td>B-R</td>
<td></td>
<td>1. The administration of flumazenil to patients with undifferentiated coma confers risk and is not recommended.</td>
</tr>
</tbody>
</table>

Benzodiazepines

There are no data to support the use of specific antidotes in the setting of cardiac arrest due to benzodiazepine overdose. Resuscitation from cardiac arrest should follow standard BLS and ACLS algorithms.

Flumazenil is a potent antagonist of the binding of benzodiazepines to their central nervous system receptors. Administration of flumazenil can reverse central nervous system and respiratory depression caused by benzodiazepine overdose. Flumazenil has a role in the management of cardiac arrest.

The administration of flumazenil to patients with undifferentiated coma confers risk and is not recommended (Class III, LOE B). Flumazenil administration can precipitate seizures in benzodiazepine-dependent patients and increase risk of rechallenge with seizures, arrhythmia, and hypotension in patients with co-ingestion of certain medications, such as tricyclic antidepressants. However, flumazenil may be used safely to reverse excessive sedation known to be due to the use of benzodiazepines in a patient without known contraindications (eg, procedural sedation).
These risks: increased in patients with benzodiazepine dependence, with coingestion of cyclic antidepressant medications

T1/2 flumazenil: shorter than many benzodiazepines

A recent meta-analysis of 13 RCTs: adverse events and serious adverse events were more common in patients who were randomized to receive flumazenil than placebo (number needed to harm: 5.5 for all adverse events and 50 for serious adverse events)

» The most commonly adverse events: psychiatric (anxiety, agitation, aggressive behavior)

» Serious adverse events reported: tachycardia, supraventricular arrhythmia, PVC, seizures, hypotension

» Rare cases of death associated with flumazenil reported

Toxicity: β-Adrenergic Blockers and Calcium Channel Blockers

<table>
<thead>
<tr>
<th>Recommendations for β-Adrenergic Blocker Overdose</th>
<th>Recommendations for Calcium Channel Blocker Overdose</th>
</tr>
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<tbody>
<tr>
<td><strong>COR</strong></td>
<td><strong>LOE</strong></td>
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<td>2a</td>
<td>C-LD</td>
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<tr>
<td>2a</td>
<td>C-LD</td>
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<tr>
<td>2b</td>
<td>C-LD</td>
</tr>
<tr>
<td>2b</td>
<td>C-LD</td>
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</tbody>
</table>
Overdose: life-threatening hypotension and/or bradycardia that may be refractory to standard treatments e.g. vasopressor infusions

- A 2017 expert consensus statement recommended calcium as first-line treatment for catecholamine-refractory shock from CCB, acknowledging a very low certainty of evidence for this intervention.

Nonvasopressor Medications During Cardiac Arrest

<table>
<thead>
<tr>
<th>Recommendations for Nonvasopressor Medications</th>
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<tbody>
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<td>2b</td>
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<td>2b</td>
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<tr>
<td>3: No Benefit</td>
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<tr>
<td>3: No Benefit</td>
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<tr>
<td>3: No Benefit</td>
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Electrolyte Abnormalities

<table>
<thead>
<tr>
<th>Recommendations for Electrolyte Abnormalities in Cardiac Arrest</th>
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<tr>
<td><strong>COR</strong></td>
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<td>2b</td>
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<tr>
<td>3: Harm</td>
</tr>
</tbody>
</table>

15-30 mL of 10% calcium gluconate solution
CCBs

» Atropine, Calcium, Glucagon

» HDI therapy: treatment of choice for patients who a severely poisoned by CCBs

» ILE: should not be used as first-line therapy, reasonable for CCB induced severe cardiovascular toxicity that persists despite maximal treatment with standard resuscitative measures and ECMO and other ECLS are not available

BBs

» Glucagon Calcium, HDI, Catecholamines

» ILE: reasonable to administer in patients poisoned with lipid-soluble BBs who have cardiac arrest or circulatory failure that does not respond to usual therapy; especially if mechanical life support is not promptly available

» Phosphodiesterase Inhibitors, Ventricular Pacing, Extracorporeal Removal

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2010

- **Beta-Blockers**: no data of antidote use in cardiac arrest
  - refractory hemodynamic instability
  - glucagon, high-dose insulin, IV calcium salts

- **Calcium Channel Blockers**: no data of antidote use in cardiac arrest
  - refractory hemodynamic instability
  - high-dose insulin, or IV calcium salts
Toxicity: Cocaine

» Cocaine toxicity: adverse effects on the cardiovascular system, including dysrhythmia, hypertension, tachycardia, coronary artery vasospasm, cardiac conduction delays

» Also precipitate acute coronary syndrome, stroke

Toxicity: Cocaine

<table>
<thead>
<tr>
<th>Recommendations for Cocaine Toxicity</th>
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<td>COR</td>
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<td>2a</td>
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<td>2b</td>
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Contradictory data surround the use of β-adrenergic blockers.

A well-conducted human trial showed that administration of propranolol reduces coronary blood flow in patients with cocaine exposure.

Although recent systematic reviews suggest that β-adrenergic blocker use may not be harmful, safe alternatives are available.

Toxicity: Local Anesthetics

» Local anesthetic overdose (local anesthetic systemic toxicity, LAST): a life-threatening emergency, present with neurotoxicity or fulminant cardiovascular collapse.
A 20% emulsion of long-chain TG, initial bolus of 1.5 mL/kg followed by an infusion of 0.25 mL/kg per minute for 30-60 minutes. The bolus can be repeated once or twice as needed; the suggested maximum total dose is 10 mL/kg over the 1\textsuperscript{st} hour.
The most commonly reported agents associated with LAST: bupivacaine, lidocaine, and ropivacaine.

The potential mechanisms of action of IV lipid emulsion: active shuttling of drug away from the heart and brain, increased cardiac contractility, vasoconstriction, cardioprotective effects.
Toxicity: Sodium Channel Blockers, Including Tricyclic Antidepressants

» Overdose of sodium channel–blocking medications, e.g. TCAs and other drugs (eg, cocaine, flecainide, citalopram), can cause hypotension, dysrhythmia, death by blockade of cardiac sodium channels, among other mechanisms
No human controlled studies: found evaluating treatment of cardiac arrest due to TCA toxicity

An initial dose of 1-2 mEq/kg (1–2 mL/kg of 1 mEq/mL [8.4%]) sodium bicarbonate, repeated as needed to achieve clinical stability while avoiding extreme hypernatremia or alkalemia.
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Indication</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>GI decontamination</td>
<td>Activated charcoal 1 gram/kg PO</td>
<td>Within 1 h of ingestion as long as airway is stable and patient is awake</td>
<td>Do not give multidose charcoal; do not perform whole-bowel irrigation</td>
</tr>
<tr>
<td>Initial treatment of hypotension or dysrhythmias</td>
<td>Sodium bicarbonate; 1–2 mEq/kg IV bolus; repeat bolus or add 150 mEq to 1 L 1.5% dextrose in water at 2–3 mL/kg per hour</td>
<td>For dysrhythmias, conduction abnormalities (QRS &gt; 100 ms), or hypotension refractory to IV fluid</td>
<td>Keep blood pH 7.50–7.55</td>
</tr>
<tr>
<td>Hypokalemia</td>
<td>Replace potassium as needed</td>
<td>Serum potassium &lt; 3.5 mEq/L</td>
<td>Bicarbonate will decrease potassium level</td>
</tr>
<tr>
<td>Seizures or agitation</td>
<td>Benzodiazepines for seizures or agitation</td>
<td>Phenobarbital 10–15 milligrams/kg for seizures refractory to benzodiazepines; watch for hypotension; secure airway with intubation</td>
<td>Do not give physostigmine, flumazenil, or phenytoin</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Treat hypotension with normal saline, up to 30 mL/kg</td>
<td>Use norepinephrine or epinephrine if refractory to IV normal saline</td>
<td>Case reports suggest effectiveness of glucagon, 1 milligram IV bolus</td>
</tr>
<tr>
<td>Torsades de pointes and refractory dysrhythmias</td>
<td>Magnesium sulfate 2 grams IV; 3% saline 1–3 mL/kg IV over 10 min; overdrive pacing</td>
<td>Consider lipid emulsion for refractory dysrhythmias, but no convincing evidence of effectiveness</td>
<td>Do not give class I antiarrhythmics (i.e., procainamide, lidocaine, phenytoin, flecainide), β-blockers, calcium channel blockers, or class III antiarrhythmics (i.e., amiodarone, sotalol, ibutilide)</td>
</tr>
</tbody>
</table>

**TABLE 68-2** Treatment of Cyclic Antidepressant (CA) Toxicity

**Toxic Effect**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus rhythm with a QRS complex &gt; 100 ms</td>
<td>Sodium bicarbonate: 1–2 mEq/kg IV bolus at 3-5 min intervals to reverse the abnormality or to a target serum pH ≤ 7.55</td>
</tr>
<tr>
<td>Wide-complex tachycardia or ventricular tachycardia</td>
<td>Sodium bicarbonate: 1–2 mEq/kg IV bolus at 3-5 min intervals to reverse the abnormality or to a target serum pH ≤ 7.55</td>
</tr>
</tbody>
</table>

**Goldfrank 11th ed**

**Treatments for refractory dysrhythmias despite sodium bicarbonate administration:**

- Lidocaine for refractory dysrhythmias despite sodium bicarbonate administration: 1 mg/kg slow IV bolus followed by infusion of 20–50 mcg/kg/min
- Magnesium sulfate or Overdrive pacing (caution because of rate dependence of CA)
- 0.9% sodium chloride boluses (up to 30 mL/kg)
Toxicity: Carbon Monoxide, Digoxin, Cyanide

» Digoxin poisoning: severe bradycardia, AV nodal blockade, life-threatening ventricular arrhythmias

» Carbon monoxide poisoning: reduces ability of hemoglobin to deliver oxygen, causes direct cellular damage to the brain and myocardium, leading to death or long-term risk of neurological and myocardial injury

» The toxicity of cyanide: cessation of aerobic cell metabolism

» Cyanide: reversibly binds to ferric ion cytochrome oxidase in mitochondria, stops cellular respiration ATP production
Symptoms typically occur within minutes, findings may include arrhythmias, apnea, hypotension with bradycardia, seizures, cardiovascular collapse.

**Toxicity: Carbon Monoxide, Digoxin, and Cyanide**

| Recommendations for Carbon Monoxide, Digoxin, and Cyanide Poisoning |
|---|---|
| **COR** | **LOE** | **Recommendations** |
| 1 | B-R | 1. Antidigoxin Fab antibodies should be administered to patients with severe cardiac glycoside toxicity. |
| 2b | B-R | 2. Hyperbaric oxygen therapy may be helpful in the treatment of acute carbon monoxide poisoning in patients with severe toxicity. |
| 2a | C-LD | 3. Hydroxocobalamin and 100% oxygen, with or without sodium thiosulfate, can be beneficial for cyanide poisoning. |
» Antidigoxin Fab fragments: safe and effective for serious cardiac arrhythmias induced by digitalis, other cardiac glycoside overdose

» Clinical trials of HBO to prevent neurological injury from CO poisoning: conflicting results; patients with cardiac arrest excluded from all trials

» HBO: low incidence of side effects

» Several studies: patients with known or suspected cyanide toxicity presenting with cardiovascular instability or cardiac arrest who undergo prompt treatment with IV hydroxocobalamin, a cyanide scavenger can have reversal of life-threatening toxicity
- **Digoxin and Related Cardiac Glycosides:** no data of antidote use in cardiac arrest
  : Antidigoxin Fab antibodies in severe life-threatening
- **Carbon Monoxide:** no data of specific interventions in cardiac arrest
  : routine transfer to HBO facility following resuscitation should be carefully considered, weighing the risk against the possible improvement
- **Cyanide:**

  Patients in cardiac arrest or those presenting with cardiovascular instability caused by known or suspected cyanide poisoning should receive cyanide-antidote therapy with a cyanide scavenger (either IV hydroxocobalamin or a nitrate such as IV sodium nitrite and/or inhaled amyl nitrite), followed as soon as possible by IV sodium thiosulfate.
TABLE 193-2  Overview: Treatment of Digitalis Glycoside Poisoning

Asymptomatic patients
• Obtain accurate history.
• Secure IV access.
• Initiate continuous cardiac monitoring.
• GI decontamination: Activated charcoal, 1 gram/kg PO, can be considered in an awake, alert, cooperative patient who presents within 1 h of ingestion.
• Frequent reevaluation.

Symptomatic patients
• Obtain accurate history.
• Secure IV access.
• Initiate continuous cardiac monitoring.
• GI decontamination: Activated charcoal, 1 gram/kg PO, in an awake, alert, cooperative patient who presents within 1 h of ingestion.
• Bradycardia
  • Atropine: 0.5–1.0 milligram IV as a temporizing measure for bradycardia while awaiting digoxin-specific antibody fragments
  • Transcutaneous pacing while awaiting digoxin-specific antibody fragments for symptomatic bradycardia that does not respond to atropine
  • Digoxin-specific antibody fragments: IV infusion (see later discussion for dose)
• Cardiac arrest
  • CPR with current advanced cardiac life support protocols (prolonged CPR may be appropriate)
  • Digoxin-specific antibody fragments: IV bolus (10 vials if amount ingested is unknown)

TABLE 62-4  Indications for Administration of Digoxin-Specific Antibody Fragments

Any digoxin-related life-threatening dysrhythmias, regardless of SDC
—Includes ventricular tachycardia or ventricular fibrillation or progressive bradydysrhythmias such as atropine-resistant symptomatic sinus bradycardia or second or third-degree heart block

Potassium concentration >5 mEq/L in the setting of acute digoxin poisoning

Chronic elevation of SDC associated with dysrhythmias, significant GI symptoms, or altered mental status

SDC ≥15 ng/mL at any time or ≥10 ng/mL 6 h postingestion, regardless of clinical effects

Acute ingestion of 10 mg of digoxin in an adult

Acute ingestion of 4 mg of digoxin in a child

Poisoning with a nondigoxin cardioactive steroid

Tintinalli 9th ed  Goldfrank 11th ed
» Good supportive care with 100% oxygen along with crystalloids and vasopressors for hypotension is paramount

» The decision to administer a cyanide antidote is straightforward when faced with a critically ill patient with clear history of cyanide exposure

Tintinalli 9th ed

» Although either hydroxocobalamin or sodium nitrite and sodium thiosulfate combination should be administered as soon as CN poisoning is suspected, hydroxocobalamin is preferred

Goldfrank 11th ed
ACLS 2020

» **Opioid:** standard resuscitative measures, high-quality CPR, activate EMS, naloxone IV

» **Benzodiazepines:** flumazenil not recommended

» **CCB:** standard treatment -> refractory shock: calcium, HDI, glucagon, ECMO

» **β Blockers:** standard treatment -> refractory shock: HDI, glucagon, calcium, ECMO

» **Cocaine:** induced HT, tachycardia, agitation, chest discomfort - BZD, alpha blocker, CCB, NTG, +/-morphine, avoid pure β blocker
Local Anesthetics: IV lipid emulsion to LAST, particularly premonitory neurotoxicity or cardiac arrest due to bupivacaine toxicity

Sodium Channel Blockers + TCA: sodium bicarbonate for cardiac arrest or life-threatening cardiac conduction delays (ie, QRS > 120 ms), ECMO

Digoxin: digoxin-Fab - severe toxicity

CO: HBO - severe toxicity

Cyanide: Hydroxocobalamin + 100% oxygen, +/- sodium thiosulfate
### 2020 Adult Guidelines Critical Knowledge Gaps

<table>
<thead>
<tr>
<th>Issue</th>
<th>Question</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opioid overdose</td>
<td>What is the minimum safe observation period after reversal of respiratory depression from opioid overdose with naloxone? Does this vary based on the opioid involved?</td>
</tr>
<tr>
<td>Opioid overdose</td>
<td>Is there benefit to naloxone administration in patients with opioid-associated cardiac arrest who are receiving CPR with ventilation?</td>
</tr>
<tr>
<td>Opioid overdose</td>
<td>What is the ideal initial dose of naloxone in a setting where fentanyl and fentanyl analogues are responsible for a large proportion of opioid overdose?</td>
</tr>
<tr>
<td>Opioid overdose</td>
<td>In cases of suspected opioid overdose managed by a non–healthcare provider who is not capable of reliably checking a pulse, is initiation of CPR beneficial?</td>
</tr>
</tbody>
</table>

| Toxicty: β-adrenergic blockers and calcium channel blockers | What is the ideal sequencing of modalities (traditional vasopressors, calcium, glucagon, high-dose insulin) for refractory shock due to β-adrenergic blocker or calcium channel blocker overdose? |
| Toxicty: local anesthetics | What are the ideal dose and formulation of IV lipid emulsion therapy? |
| Toxicty: carbon monoxide, digoxin, and cyanide | Which patients with cyanide poisoning benefit from antidotal therapy? |
| Toxicty: carbon monoxide, digoxin, and cyanide | Does sodium thiosulfate provide additional benefit to patients with cyanide poisoning who are treated with hydroxocobalamin? |
Toxic agents

Prevention
- Poisoning rarely causes cardiac arrest.
- Manage hypertensive emergencies with benzodiazepines, vaso-dilators and pure alpha-antagonists.
- Drug induced hypotension usually responds to IV fluids.
- Use specific treatments where available in addition to the ALS management of arrhythmias.
- Provide early advanced airway management.
- Administer antidotes, where available, as soon as possible.

Cardiac arrest treatment
- Have a low threshold to ensure your personal safety.
- Consider using specific treatment measures as antidotes, decontamination and enhanced elimination.
- Do not use mouth-to-mouth ventilation in the presence of chemicals such as cyanide, hydrogen sulphide, corrosives and organophosphates.
- Exclude all reversible causes of cardiac arrest, including electrolyte abnormalities which can be indirectly caused by a toxic agent.
- Measure the patient's temperature because hypo- or hyperthermia may occur during drug overdose.
- Be prepared to continue resuscitation for a prolonged time. The toxin concentration may fall as it is metabolised or excreted during extended resuscitation measures.
- Consult regional or national poison centres for information on treatment of the poisoned patient.

European Resuscitation Council Guidelines 2021:
Executive summary


- Consider ECPR as a rescue therapy for selected patients with cardiac arrest when conventional CPR is failing in settings in which it can be implemented.
**RESUSCITATION**

» ABC, prolonged resuscitation: generally indicated

<table>
<thead>
<tr>
<th>TABLE 176-1</th>
<th>Potential Interventions in Toxin-Induced Cardiac Arrest[^11]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxin or Toxin/Drug Class</td>
<td>Intervention</td>
</tr>
<tr>
<td>Toxins with a specific antidote (examples)</td>
<td>Antidote</td>
</tr>
<tr>
<td>Digoxin</td>
<td>Digoxin Fab</td>
</tr>
<tr>
<td>Organophosphates</td>
<td>Atropine</td>
</tr>
<tr>
<td>Envenomation</td>
<td>Antivenom</td>
</tr>
<tr>
<td>Sodium channel blocker or wide-complex tachycardia</td>
<td>Sodium bicarbonate</td>
</tr>
<tr>
<td>Calcium channel blocker or beta-blocker</td>
<td>High-dose insulin infusion</td>
</tr>
<tr>
<td>Local anesthetic agents</td>
<td>IV lipid emulsion</td>
</tr>
<tr>
<td>Lipophilic cardiotoxins</td>
<td>Other Therapies to Consider</td>
</tr>
<tr>
<td>Cardiac pacing</td>
<td>Intra-aortic balloon pump</td>
</tr>
<tr>
<td>Extracorporeal membrane oxygenation</td>
<td></td>
</tr>
</tbody>
</table>

### ANTIDOTES

Stabilization of airway, breathing, and circulation allows further assessment of blood glucose concentration, temperature, and conscious state. Although the proper use of antidotes (Table 176-2) is important, only a few are indicated before cardiopulmonary stabilization (e.g., naloxone for opiate toxicity, cyanide antidotes for cyanide toxicity, and atropine for organophosphate poisoning).

[^11]: Tintinalli 9th ed
Summary:

» **Standard resuscitative measures, high-quality CPR, prolonged CPR**

» **Opioid**: high-quality CPR, activate ERS, naloxone IV

» **Benzodiazepines**: flumazenil not recommended

» **CCB**: standard treatment -> refractory shock: calcium, HDI, glucagon, ECMO

» **β Blockers**: standard treatment -> refractory shock: HDI, glucagon, calcium, ECMO
» **Cocaine:** BZD, alpha blocker, CCB, NTG, +/-morphine, avoid pure β blocker

» **Local Anesthetics:** IV lipid emulsion to LAST, particularly premonitory neurotoxicity or **cardiac arrest** due to bupivacaine toxicity

» **Sodium Channel Blockers + TCA:** sodium bicarbonate for **cardiac arrest** or life-threatening cardiac conduction delays (ie, QRS > 120 ms), ECMO

» **Digoxin:** digoxin-Fab - severe toxicity

» **CO:** HBO - severe toxicity

» **Cyanide:** Cyanide antidote – cyanide poisoning
Thank you for attention

Question?