

## Part 10: Special Circumstances of Resuscitation

Web-based Integrated 2010 & 2015 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care

Key Words: cardiac arrest    defibrillation    emergency

### 1 Highlights & Introduction

#### 1.1 Highlights

##### Summary of Key Issues and Major Changes

- Experience with treatment of patients with known or suspected opioid overdose has demonstrated that naloxone can be administered with apparent safety and effectiveness in the first aid and BLS settings. For this reason, naloxone administration by lay rescuers and HCPs is now recommended, and simplified training is being offered. In addition, a new algorithm for management of unresponsive victims with suspected opioid overdose is provided.
- Intravenous lipid emulsion (ILE) may be considered for treatment of local anesthetic systemic toxicity. In addition, a new recommendation is provided, supporting a possible role for ILE in patients who have cardiac arrest and are failing standard resuscitative measures as the result of drug toxicity other than local anesthetic systemic toxicity.
- The importance of high-quality CPR during any cardiac arrest has led to a reassessment of the recommendations about relief of aortic compression during cardiac arrest in pregnancy. This reassessment has resulted in refined recommendations about strategies for uterine displacement.

##### Opioid Overdose Education and Naloxone Training and Distribution

**2015 (New):** It is reasonable to provide opioid overdose response education, either alone or coupled with naloxone distribution and training, to persons at risk for opioid overdose (or those living with or in frequent contact with such persons). It is reasonable to base this training on first aid and non-HCP BLS recommendations rather than on more advanced practices intended for HCPs.

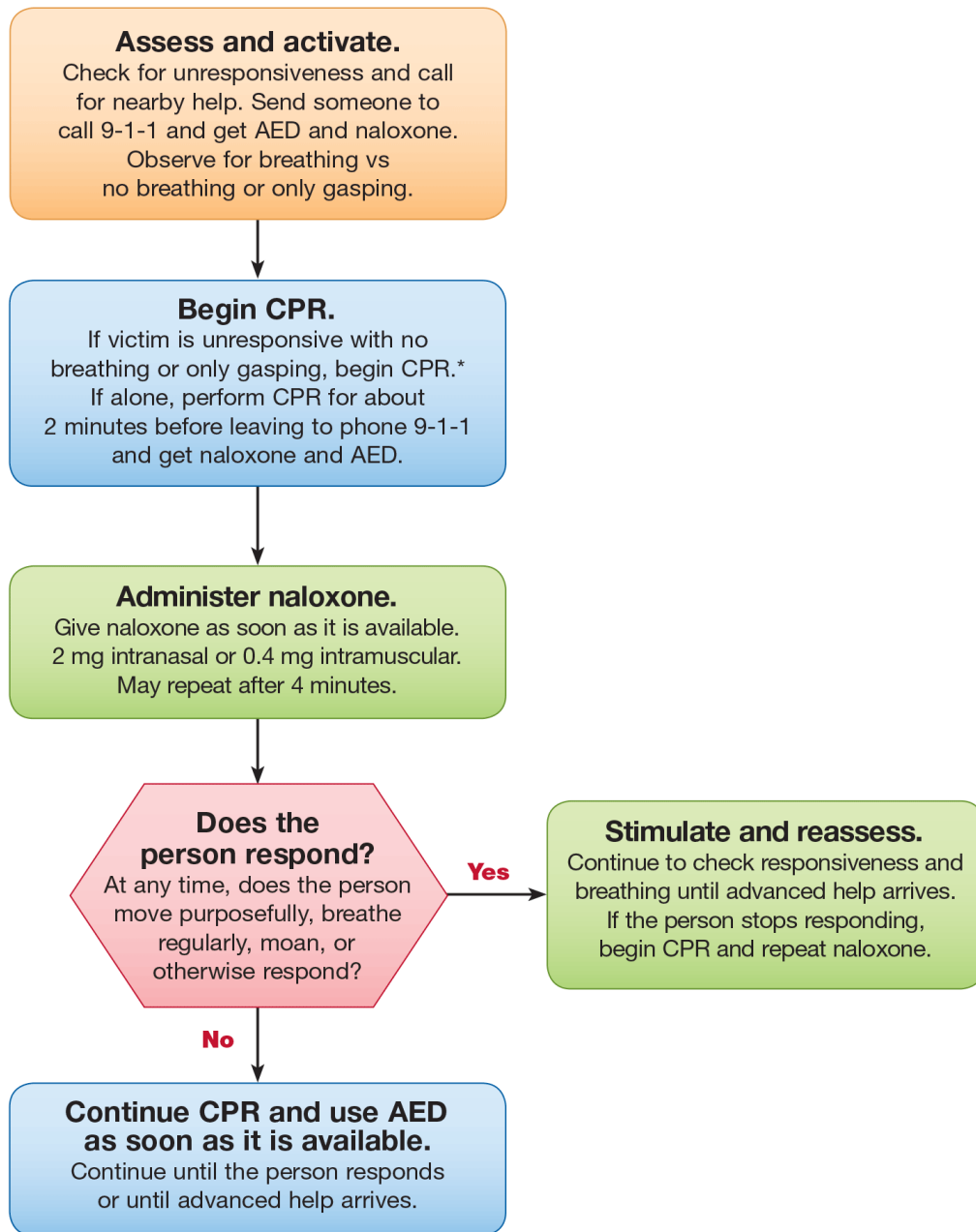
##### Opioid Overdose Treatment

**2015 (New):** Empiric administration of IM or IN naloxone to all unresponsive victims of possible opioid-associated life-threatening emergency may be reasonable as an adjunct to standard first aid and non-HCP BLS protocols. For patients with known or suspected opioid overdose who have a definite pulse but no normal breathing or only gasping (ie, a respiratory arrest), in addition to providing standard care, it is reasonable for appropriately trained rescuers to administer IM or IN naloxone to patients with an opioid-associated respiratory emergency (Figure 1). Responders should not delay access to more advanced medical services while awaiting the patient's response to naloxone or other interventions.

Empiric administration of IM or IN naloxone to all unresponsive opioid-associated resuscitative emergency patients may be reasonable as an adjunct to standard first aid and non-HCP BLS protocols. Standard resuscitation procedures, including EMS activation, should not be delayed for naloxone administration.

Figure 1: Opioid-Associated Life-Threatening Emergency (Adult) Algorithm

### Opioid-Associated Life-Threatening Emergency (Adult) Algorithm—New 2015



\*CPR technique based on rescuer's level of training.

© 2015 American Heart Association

### Cardiac Arrest in Patients With Known or Suspected Opioid Overdose

**2015 (New):** Patients with no definite pulse may be in cardiac arrest or may have an undetected weak or slow pulse. These patients should be managed as cardiac arrest patients. Standard resuscitative measures should take priority over naloxone administration, with a focus on high-quality CPR (compressions plus ventilation). It may be reasonable to administer IM or IN naloxone based on the possibility that the patient is in respiratory arrest, not in cardiac arrest. Responders should not delay access to more-advanced medical services while awaiting the patient's response to naloxone or other interventions.

**Why:** Naloxone administration has not previously been recommended for first aid providers, non-HCPs, or BLS providers. However, naloxone administration devices intended for use by lay rescuers are now approved and available for use in the United States, and the successful implementation of lay rescuer naloxone programs has been highlighted by the Centers for Disease Control. While it is not expected that naloxone is beneficial in cardiac arrest, whether or not the cause is opioid overdose, it is recognized that it may be difficult to distinguish cardiac arrest from severe respiratory depression in victims of opioid overdose. While there is no evidence that administration of naloxone will help a patient in cardiac arrest, the provision of naloxone may help an unresponsive patient with severe respiratory depression who only appears to be in cardiac arrest (ie, it is difficult to determine if a pulse is present).

### Intravenous Lipid Emulsion

**2015 (Updated):** It may be reasonable to administer ILE, concomitant with standard resuscitative care, to patients who have premonitory neurotoxicity or cardiac arrest due to local anesthetic toxicity. It may be reasonable to administer ILE to patients with other forms of drug toxicity who are failing standard resuscitative measures.

**2010 (Old):** It may be reasonable to consider ILE for local anesthetic toxicity.

**Why:** Since 2010, published animal studies and human case reports have examined the use of ILE for patients with drug toxicity that is not the result of local anesthetic infusion. Although the results of these studies and reports are mixed, there may be clinical improvement after ILE administration. As the prognosis of patients who are failing standard resuscitative measures is very poor, empiric administration of ILE in this situation may be reasonable despite the very weak and conflicting evidence.

### Cardiac Arrest in Pregnancy: Provision of CPR

**2015 (Updated):** Priorities for the pregnant woman in cardiac arrest are provision of high-quality CPR and relief of aortocaval compression. If the fundus height is at or above the level of the umbilicus, manual left uterine displacement can be beneficial in relieving aortocaval compression during chest compressions.

**2010 (Old):** To relieve aortocaval compression during chest compressions and optimize the quality of CPR, it is reasonable to perform manual left uterine displacement in the supine position first. If this technique is unsuccessful, and an appropriate wedge is readily available, then providers may consider placing the patient in a left lateral tilt of 27° to 30°, using a firm wedge to support the pelvis and thorax.

**Why:** Recognition of the critical importance of high-quality CPR and the incompatibility of the lateral tilt with high-quality CPR has prompted the elimination of the recommendation for using the lateral tilt and the strengthening of the recommendation for lateral uterine displacement.

### Cardiac Arrest in Pregnancy: Emergency Cesarean Delivery

**2015 (Updated):** In situations such as nonsurvivable maternal trauma or prolonged maternal pulselessness, in which maternal resuscitative efforts are obviously futile, there is no reason to delay performing perimortem cesarean delivery (PMCD). PMCD should be considered at 4 minutes after onset of maternal cardiac arrest or resuscitative efforts (for the unwitnessed arrest) if there is no maternal ROSC. The clinical decision to perform a PMCD—and its timing with respect to maternal cardiac arrest—is complex because of the variability in level of practitioner and team training, patient factors (eg, etiology of arrest, gestational age of the fetus), and system resources.

**2010 (Old):** Emergency cesarean delivery may be considered at 4 minutes after onset of maternal cardiac arrest if there is no ROSC.

**Why:** PMCD provides the opportunity for separate resuscitation of the potentially viable fetus and the ultimate

relief of aortocaval compression, which may improve maternal resuscitation outcomes. The clinical scenario and circumstances of the arrest should inform the ultimate decision around the timing of emergency cesarean delivery.

## 1.2 Introduction - Updated

These Web-based Integrated Guidelines incorporate the relevant recommendations from 2010 and the new or updated recommendations from 2015.

Part 10 of the *2015 American Heart Association (AHA) Guidelines Update for Cardiopulmonary Resuscitation (CPR) and Emergency Cardiovascular Care (ECC)* addresses cardiac arrest in situations that require special treatments or procedures other than those provided during basic life support (BLS) and advanced cardiovascular life support (ACLS).

This Part summarizes recommendations for the management of resuscitation in several critical situations, including cardiac arrest associated with pregnancy (Part 10.1), pulmonary embolism (PE) (10.2), and opioid-associated resuscitative emergencies, with or without cardiac arrest (10.3). Part 10.4 provides recommendations on intravenous lipid emulsion (ILE) therapy, an emerging therapy for cardiac arrest due to drug intoxication. Finally, updated guidance for the management of cardiac arrest during percutaneous coronary intervention (PCI) is presented in Part 10.5. A table of all recommendations made in this 2015 Guidelines Update as well as those made in the 2010 Guidelines is contained in the Appendix.

The special situations of resuscitation section (Part 12) of the *2010 AHA Guidelines for CPR and ECC*<sup>1</sup> covered 15 distinct topic areas. The following topics were last updated in 2010, and are included in this Web-based integrated Guidelines document:

- Management of cardiac arrest associated with asthma (Part 12.1)
- Anaphylaxis (12.2)
- Morbid obesity (12.4)
- Electrolyte imbalance (12.6)
- Trauma (12.8)
- Accidental hypothermia (12.9)
- Avalanche (12.10)
- ACLS treatment of cardiac arrest due to drowning (12.11)
- Electric shock or lightning strikes (12.12)
- Cardiac tamponade (12.14)
- Cardiac surgery (12.15)
- Toxic effects of benzodiazepines,  $\beta$ -blockers, calcium channel blockers, digoxin, cocaine, cyclic antidepressants, carbon monoxide, and cyanide (12.7)

Additional information about drowning is presented in Part 5, "[Adult Basic Life Support and Cardiopulmonary Resuscitation Quality](#)."

The recommendations in the 2015 Guidelines Update are based on an extensive evidence review process that was begun by the International Liaison Committee on Resuscitation (ILCOR) with the publication of the ILCOR *2010 International Consensus on CPR and ECC Science With Treatment Recommendations (CoSTR)*<sup>2</sup> and was completed with the preparation of the 2015 CoSTR publication.<sup>3,4</sup>

In the in-depth international evidence review process, the ILCOR task forces examined topics and then generated prioritized lists of questions for systematic review. The process by which topics were prioritized for review are described in the CoSTR publication.<sup>5,6</sup> Questions were first formulated in PICO (population,

intervention, comparator, outcome) format,<sup>7</sup> the search strategy and inclusion and exclusion criteria were defined, and then a search for relevant articles was performed. The evidence was evaluated by using the standardized methodological approach proposed by the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group.<sup>8</sup>

The quality of the evidence was categorized based on the study methodologies and the 5 core GRADE domains of risk of bias, inconsistency, indirectness, imprecision, and other considerations (including publication bias). Then, where possible, consensus-based treatment recommendations were created. Further information about this international evidence evaluation process can be found in the 2015 CoSTR, "[Part 2: Evidence Evaluation and Management of Conflicts of Interest](#)."<sup>9,10</sup>

To create the 2015 Guidelines Update, the AHA formed 15 writing groups, with careful attention to avoid or manage conflicts of interest, to assess the ILCOR treatment recommendations and to write AHA treatment recommendations by using the AHA Class of Recommendation and Level of Evidence (LOE) system. The recommendations made in the 2015 Guidelines Update are informed by the ILCOR recommendations and GRADE classification of the systematic reviews in the context of the delivery of medical care in North America. In the online version of this publication, live links are provided so the reader can connect directly to those systematic reviews on the ILCOR Scientific Evidence Evaluation and Review System (SEERS) website. These links are indicated by a combination of letters and numbers (eg, ALS 436). We encourage readers to use the links and review the evidence and appendixes, such as the GRADE tables. Further information about this evidence evaluation process can be found in "[Part 2: Evidence Evaluation and Management of Conflicts of Interest](#)" of this 2015 Guidelines Update.

Contemporaneous with the ILCOR evidence-review process, the AHA ECC Committee; Council on Cardiopulmonary, Critical Care, Perioperative, and Resuscitation; Council on Cardiovascular Diseases in the Young; and Council on Clinical Cardiology have developed an AHA Scientific Statement on cardiac arrest in pregnancy.<sup>11</sup> While this document provides treatment recommendations for the intra-arrest management of pregnant patients, a full discussion of preparation, prevention, resuscitation, emergency delivery, and postresuscitation care are beyond the scope of this article. Readers are directed to the full Scientific Statement for more complete recommendations.

## 2 Cardiac Arrest Associated With Pregnancy - Updated [ALS 436](#)

Cardiac arrest associated with pregnancy is rare in high-income countries. Maternal cardiac arrest occurs in approximately 1:12 000 admissions for delivery in the United States.<sup>12</sup> Maternal cardiac arrest rates appear to be increasing in the United States, from 7.2 deaths per 100 000 live births in 1987 to 17.8 deaths per 100 000 live births in 2009.<sup>13</sup> Maternal mortality rates are lower in Canada, where maternal mortality is reported as 6.1 deaths per 100 000 deliveries, with a decreasing trend from 2001 until 2011.<sup>14,15</sup>

The best outcomes for both mother and fetus are likely to be achieved by successful maternal resuscitation. The most common causes of maternal cardiac arrest are hemorrhage, cardiovascular diseases (including myocardial infarction, aortic dissection, and myocarditis), amniotic fluid embolism, sepsis, aspiration pneumonia, PE, and eclampsia.<sup>12,16</sup> Important iatrogenic causes of maternal cardiac arrest include hypermagnesemia from magnesium sulfate administration and anesthetic complications.

The 2015 ILCOR systematic review addressed the questions of patient positioning during CPR and the role of perimortem cesarean delivery (PMCD) in the management of pregnant women in cardiac arrest during the second half of pregnancy.

### 2.1 2015 Evidence Summary

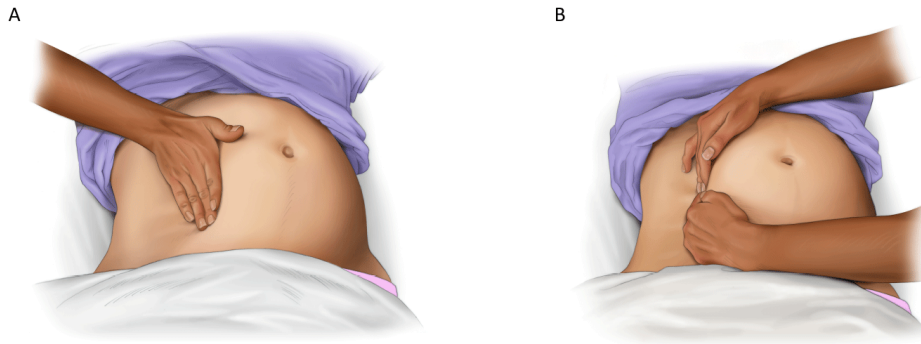
The evidence regarding advanced treatment strategies for cardiac arrest in pregnancy is largely observational. As a result, the recommendations are based on application of physiologic principles and on close examination of observational studies that are susceptible to bias. The lack of high-quality studies examining treatment of cardiac arrest in late pregnancy represents a major scientific gap.

#### 2.1.1 Patient Positioning During CPR - Updated

Patient position has emerged as an important strategy to improve the quality of CPR and resultant compression

force and cardiac output. The gravid uterus can compress the inferior vena cava, impeding venous return, thereby reducing stroke volume and cardiac output. In general, aortocaval compression can occur for singleton pregnancies at approximately 20 weeks of gestational age,<sup>17</sup> at about the time when the fundus is at or above the umbilicus. Although chest compressions in the left lateral tilt position are feasible in a manikin study,<sup>18</sup> they result in decreased CPR quality (less forceful chest compressions) than is possible in the supine position.<sup>19</sup> Manual left lateral uterine displacement (LUD) effectively relieves aortocaval pressure in patients with hypotension<sup>20</sup> (Figure 2). No cardiac arrest outcome studies have been published examining the effect of LUD or other strategies to relieve aortocaval compression during resuscitation.

**Figure 2: A, Manual LUD, performed with one-handed technique. B, Two-handed technique during resuscitation**



A, Manual LUD, performed with one-handed technique. B, Two-handed technique during resuscitation.

### 2.1.1.1 Emergency Cesarean Delivery in Cardiac Arrest - Updated

Evacuation of the gravid uterus relieves aortocaval compression and may improve resuscitative efforts.<sup>21-25</sup> In the latter half of pregnancy, PMCD may be considered part of maternal resuscitation, regardless of fetal viability.<sup>26</sup> In a case series, 12 of 20 women for whom maternal outcome was recorded who underwent PMCD during resuscitation had return of spontaneous circulation (ROSC) immediately after delivery, and no cases of worsening maternal status were reported.<sup>27</sup> A systematic review of the literature evaluated all case reports of cardiac arrest in pregnancy, but the wide range of case heterogeneity and reporting bias does not allow for any conclusions regarding the timing of PMCD.<sup>28</sup> Survival of the mother has been reported up to 15 minutes after the onset of maternal cardiac arrest.<sup>21,29-31</sup> Neonatal survival has been documented with PMCD performed up to 30 minutes after the onset of maternal cardiac arrest.<sup>21</sup>

## 2.2 2015 Recommendations—New and Updated

### 2.2.1 BLS Modification: Relief of Aortocaval Compression - Updated

***Priorities for the pregnant woman in cardiac arrest are provision of high-quality CPR and relief of aortocaval compression. (Class I, LOE C-LD)***

***If the fundus height is at or above the level of the umbilicus, manual LUD can be beneficial in relieving aortocaval compression during chest compressions. (Class IIa, LOE C-LD)***

### 2.2.2 ALS Modification: Emergency Cesarean Delivery in Cardiac Arrest - Updated

***Because immediate ROSC cannot always be achieved, local resources for a PMCD should be summoned as soon as cardiac arrest is recognized in a woman in the second half of pregnancy. (Class I, LOE C-LD)***

Systematic preparation and training are the keys to a successful response to such rare and complex events.

***Care teams that may be called upon to manage these situations should develop and practice standard institutional responses to allow for smooth delivery of resuscitative care. (Class I, LOE C-EO)***

***During cardiac arrest, if the pregnant woman with a fundus height at or above the umbilicus has not achieved ROSC with usual resuscitation measures plus manual LUD, it is advisable to prepare to evacuate the uterus while resuscitation continues. (Class I, LOE C-LD)***

***In situations such as nonsurvivable maternal trauma or prolonged pulselessness, in which maternal resuscitative efforts are obviously futile, there is no reason to delay performing PMCD. (Class I, LOE C-LD)***

***PMCD should be considered at 4 minutes after onset of maternal cardiac arrest or resuscitative efforts (for the unwitnessed arrest) if there is no ROSC. (Class IIa, LOE C-EO)***

The clinical decision to perform a PMCD and its timing with respect to maternal cardiac arrest is complex because of the variability in level of practitioner and team training, patient factors (eg, etiology of arrest, gestational age), and system resources.

### **3 Cardiac Arrest Associated With Pulmonary Embolism - Updated ALS 435** ALS 435

PE is a potentially reversible cause of shock and cardiac arrest. Acute increase in right ventricular pressure due to pulmonary artery obstruction and liberation of vasoactive mediators produces cardiogenic shock that may rapidly progress to cardiovascular collapse. Management of acute PE is determined by disease severity.<sup>32</sup> Fulminant PE, characterized by cardiac arrest or severe hemodynamic instability, defines the subset of massive PE that is the focus of these recommendations.<sup>33</sup>

Less than 5% of patients with acute PE progress to cardiac arrest. Disease of this severity is associated with mortality of 65% to 90%.<sup>34-36</sup> PE-related cardiac arrests may occur within hours of symptom onset. Between 5% and 13% of unexplained cardiac arrests are associated with fulminant PE.<sup>37,38</sup>

Because establishing the diagnosis of acute PE in cardiac arrest situations is often difficult, separate systematic reviews were performed for management of patients with suspected and confirmed PE. Although clinical markers specific to fulminant PE are limited, acute symptoms frequently prompt medical attention before cardiac arrest. Conventional thromboembolism risk factors, prodromal dyspnea or respiratory distress, and witnessed arrest are features associated with cardiac arrest due to PE.<sup>37,39</sup> Pulseless electrical activity is the presenting rhythm in 36% to 53% of PE-related cardiac arrests, while primary shockable rhythms are uncommon.<sup>37,40,41</sup> Specific recommendations about the use of diagnostic ultrasonography during resuscitation can be found in “[Part 7: Adult Advanced Cardiovascular Life Support](#)” in this 2015 Guidelines Update.

Prompt systemic anticoagulation is generally indicated for patients with massive and submassive PE to prevent clot propagation and support endogenous clot dissolution over weeks.<sup>42</sup> Anticoagulation alone is inadequate for patients with fulminant PE. Pharmacologic and mechanical therapies to rapidly reverse pulmonary artery occlusion and restore adequate pulmonary and systemic circulation have emerged as primary therapies for massive PE, including fulminant PE.<sup>32,43</sup> Current advanced treatment options include systemic thrombolysis, surgical or percutaneous mechanical embolectomy, and extracorporeal cardiopulmonary resuscitation (ECPR).

The 2015 ILCOR systematic review addressed the treatment of PE as the known or suspected cause of cardiac arrest. The role of thrombolytic medications in the management of undifferentiated cardiac arrest was last reviewed in the 2010 Guidelines and is not reviewed again here.<sup>44</sup>

#### **3.1 2015 Evidence Summary**

The evidence regarding advanced treatment strategies for fulminant PE is largely observational. The lack of high-quality studies examining treatment of cardiac arrest due to PE represents a major scientific gap.

##### **3.1.1 Confirmed Pulmonary Embolism - Updated**

Systemic thrombolysis is associated with ROSC and short-term survival in PE-related cardiac arrest in nonrandomized observational studies.<sup>37,45-54</sup>



There is no consensus on the ideal dose of thrombolytic therapy in PE-associated cardiac arrest. Contemporary examples of accelerated emergency thrombolysis dosing regimens for fulminant PE include alteplase 50 mg intravenous (IV) bolus with an option for repeat bolus in 15 minutes, or single-dose weight-based tenecteplase; thrombolytics are administered with or followed by systemic anticoagulation.<sup>55-57</sup> Early administration of systemic thrombolysis is associated with improved resuscitation outcomes compared with use after failure of conventional ACLS.<sup>46</sup>

Successful surgical and percutaneous mechanical embolectomy in cases of PE-related cardiac arrest have been reported in limited series.<sup>58-60</sup> Many of these patients developed cardiac arrest before or during embolectomy. The feasibility of embolectomy under uncontrolled CPR conditions is not known.

### 3.1.2 Suspected Pulmonary Embolism - Updated

No evidence is available to support or refute the effectiveness of empiric thrombolysis in suspected but unconfirmed PE.

## 3.2 2015 Recommendations—New and Updated

### 3.2.1 ALS Modification: Confirmed Pulmonary Embolism - Updated

***In patients with confirmed PE as the precipitant of cardiac arrest, thrombolysis, surgical embolectomy, and mechanical embolectomy are reasonable emergency treatment options. (Class IIa, LOE C-LD)***

Comparative data are not available to recommend one strategy over another. Patient location, local intervention options, and patient factors (including thrombolysis contraindications) are recognized elements to be considered.

***Thrombolysis can be beneficial even when chest compressions have been provided. (Class IIa, LOE C-LD)***

Given the poor outcomes associated with fulminant PE in the absence of clot-directed therapy, standard contraindications to thrombolysis may be superseded by the need for potentially lifesaving intervention.

***In patients with cardiac arrest and without known PE, routine fibrinolytic treatment given during CPR shows no benefit<sup>61, 62</sup> and is not recommended. (Class III, LOE A)***

### 3.2.2 ALS Modifications: Suspected Pulmonary Embolism - Updated

***Thrombolysis may be considered when cardiac arrest is suspected to be caused by PE. (Class IIb, LOE C-LD)***

There is no consensus on inclusion criteria (eg, risk factors, signs, or symptoms that constitute suspected PE), thrombolytic timing, drug, or dose in this situation. There are insufficient data on surgical and mechanical embolectomy to evaluate these therapies for cardiac arrest associated with suspected but unconfirmed PE.

## 4 Cardiac or Respiratory Arrest Associated With Opioid Overdose - Updated ALS 441 BLS 811 BLS 891

In the United States in 2013, 16 235 people died of prescription opioid toxicity, and an additional 8257 died of heroin overdose.<sup>63,64</sup> In the United States in 2012, opioid overdose became the leading cause of unintentional injurious death in people aged 25 to 60 years, accounting for more deaths than motor vehicle collisions.<sup>65</sup> A majority of these deaths are associated with prescription opioids. Statistics are similar in Canada.<sup>66</sup>

Isolated opioid toxicity is associated with central nervous system (CNS) and respiratory depression that can progress to respiratory and cardiac arrest. Most opioid deaths involve the co-ingestion of multiple drugs or medical and mental health comorbidities.<sup>67-70</sup> In addition, methadone and propoxyphene can cause torsades de pointes, and cardiotoxicity has been reported with other opioids.<sup>71-77</sup> Except in specific clinical settings (eg,

unintended opioid overdose during a medical procedure), rescuers cannot be certain that the patient's clinical condition is due to opioid-induced CNS and respiratory depression toxicity alone, and might therefore misidentify opioid-associated cardiac arrest as unconsciousness or vice versa. This is particularly true in the first aid and BLS contexts, where determination of the presence or absence of a pulse is unreliable.<sup>78,79</sup> Any treatment recommendations intended for use in the first aid or BLS settings must therefore have benefit that exceeds harm when applied to a mixed patient population that may include people with severe CNS and respiratory depression, respiratory arrest, and cardiac arrest.

In creating the 2015 Guidelines Update, the writing group considered the difficulty in accurately differentiating opioid-associated resuscitative emergencies from other causes of cardiac and respiratory arrest. Opioid-associated resuscitative emergencies are defined by the presence of cardiac arrest; respiratory arrest; or severe life-threatening instability (such as severe CNS or respiratory depression, hypotension, or cardiac arrhythmia) that is suspected to be due to opioid toxicity. The term "opioid-associated life-threatening emergency" is used for first aid and non-healthcare providers.

Naloxone is a potent opioid receptor antagonist in the brain, spinal cord, and gastrointestinal system. Naloxone has an excellent safety profile and can rapidly reverse CNS and respiratory depression in a patient with an opioid-associated resuscitative emergency. Based on the rescuer's training and clinical circumstance, naloxone can be administered intravenously,<sup>80-83</sup> intramuscularly,<sup>80,81,84</sup> intranasally,<sup>82,84-88</sup> or subcutaneously<sup>89</sup>; nebulized for inhalation<sup>90,91</sup>; or instilled into the bronchial tree via endotracheal tube.<sup>92</sup> Appropriate dose and concentrations differ by route.

There are no known harms or major clinical effects associated with the administration of naloxone in typical doses to patients who are not opioid-intoxicated or dependent.<sup>93,94</sup> Naloxone administration may precipitate acute withdrawal syndrome in patients with opioid dependency, with signs and symptoms including hypertension, tachycardia, piloerection, vomiting, agitation, and drug cravings. These signs and symptoms are rarely life-threatening, and they may be minimized by using the lowest effective dose of naloxone.<sup>95</sup> Pulmonary edema has been reported with naloxone administration, but it also may be caused primarily by opioid toxicity.<sup>95</sup>

The ideal dose of naloxone is not known. In the 2010 Guidelines, an empiric starting dose of 0.04 to 0.4 mg IV or intramuscular (IM) was recommended to avoid provoking severe opioid withdrawal in patients with opioid dependency and to allow for consideration of a range of doses, depending on the clinical scenario.<sup>1</sup> Repeat doses or dose escalation to 2 mg IV or IM was recommended if the initial response was inadequate. Few comparative data exist about the appropriate dose of intranasal (IN) naloxone; most studies used a fixed dose of 2 mg, repeated in 3 to 5 minutes if necessary.<sup>82,84-88,96</sup> Nebulized naloxone has been studied and well-tolerated in opioid-intoxicated patients at a dose of 2 mg diluted in 3 mL normal saline.<sup>90,91</sup> Regardless of the care setting and route of administration, the initial goal of therapy is to restore and maintain patent airway and ventilation, preventing respiratory and cardiac arrest, without provoking severe opioid withdrawal.

The 2015 ILCOR systematic review addressed the questions of whether opioid overdose response education (with or without naloxone distribution) improves outcomes related to opioid overdose and whether naloxone administration or any other therapy improves outcomes in the patients with opioid-associated cardio/respiratory arrest in the first aid, BLS, or ACLS settings.

## 4.1 2015 Evidence Summary

### 4.1.1 Opioid Overdose Response Education and Naloxone Training and Distribution - Updated

Several studies have shown that community-based opioid overdose response education and naloxone distribution programs are feasible and that naloxone administration occurs frequently by persons trained by these programs.<sup>97</sup> Because patients who have CNS and respiratory depression from opioid overdose cannot self-administer naloxone, naloxone is typically administered in the first aid setting by friends, family, or bystanders.<sup>98,99</sup>

In 2014, the US Food and Drug Administration approved of the use of a naloxone autoinjector by lay rescuers<sup>100</sup> as well as healthcare providers. Both the IM and IN<sup>97</sup> routes of administration have been successfully used in first aid settings, with commercially available devices or kits containing a naloxone vial or prefilled syringe and a nasal atomizer or other administration device. IM, IN, and nebulized routes of administration have also been used to treat opioid-associated resuscitative emergencies in the BLS and ACLS settings.<sup>81,82,90,101</sup> Recent recommendations by an international working group called for uniform training standards based on simplified (first aid) resuscitation principles for community-based naloxone distribution programs.<sup>102</sup>

#### 4.1.2 Administration of Naloxone in Opioid-Associated Resuscitation Emergencies - Updated

##### 4.1.2.1 Respiratory Arrest - Updated

Two clinical trials and 12 observational studies examined outcomes after naloxone treatment for opioid-induced respiratory arrest or severe CNS and respiratory depression. Of these, 5 studies compared routes of naloxone administration,<sup>82,84,85,89,103</sup> and 9 assessed the safety of naloxone use or were observational studies of naloxone use alone.<sup>81,104-111</sup> All studies reported improvement in level of consciousness and spontaneous breathing after naloxone administration in the majority of patients treated, and complication rates were low. No study compared resuscitation outcomes achieved with naloxone with those achieved through standard therapy alone (eg, manual or mechanical ventilation).

##### 4.1.2.2 Cardiac Arrest - Updated

One small observational study noted an improvement in cardiac rhythm in some patients after naloxone administration, but it did not compare outcomes in patients managed with and without naloxone administration.<sup>112</sup>

#### 4.2 2015 Recommendations—New

##### 4.2.1 Opioid Overdose Response Education and Naloxone Training and Distribution - Updated

***It is reasonable to provide opioid overdose response education, either alone or coupled with naloxone distribution and training, to persons at risk for opioid overdose. (Class IIa, LOE C-LD)***

Some populations that may benefit from opioid overdose response interventions are listed in Table 1.

***It is reasonable to base this training on first aid and non-healthcare provider BLS recommendations rather than on more advanced practices intended for healthcare providers. (Class IIa, LOE C-EO)***

**Table 1: 2015 - Groups That May Benefit From Opioid Overdose Response Education and/or Naloxone Distribution and Training (100,111–119)**

Open table in a [new window](#)

Groups That May Benefit From Opioid Overdose Response Education and/or Naloxone Distribution and Training [reference id="1798" range="" /][reference id="1809,1810,1811,1812,1813,1814,1815,1816,1817" range="9" /]

- 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

#### **4.2.2 First Aid and Non–Healthcare Provider BLS Modification: Administration of Naloxone - Updated**

Although naloxone has no clear role in the management of confirmed cardiac arrest, first aid and other non-healthcare providers are not instructed to attempt to determine whether an unresponsive person is pulseless.

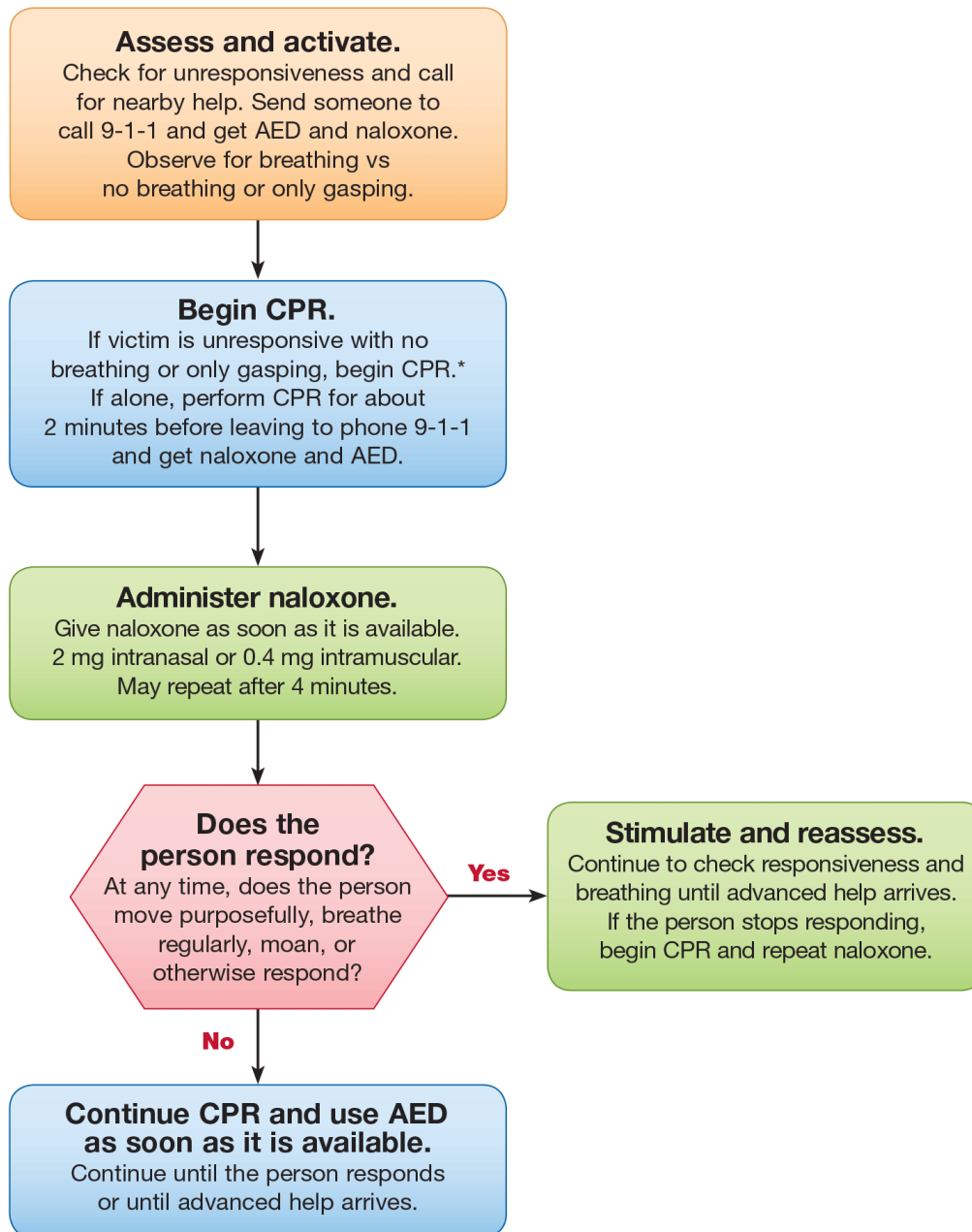
***Empiric administration of IM or IN naloxone to all unresponsive opioid-associated life-threatening emergency patients may be reasonable as an adjunct to standard first aid and non–healthcare provider BLS protocols. (Class IIb, LOE C-EO)***

Standard resuscitation, including activation of emergency medical services, should not be delayed for naloxone administration. However, family members and friends of those known to be addicted to opiates are likely to have naloxone available and ready to use if someone known or suspected to be addicted to opiates is found unresponsive and not breathing normally or only gasping (see sequence in Figure 1).

***Victims who respond to naloxone administration should access advanced healthcare services. (Class I, LOE C-EO)***

Figure 1: Opioid-Associated Life-Threatening Emergency (Adult) Algorithm

### Opioid-Associated Life-Threatening Emergency (Adult) Algorithm—New 2015



\*CPR technique based on rescuer's level of training.

© 2015 American Heart Association

#### 4.2.3 Healthcare Provider BLS Modification: Administration of Naloxone - Updated

##### 4.2.3.1 Respiratory Arrest - Updated

***For patients with known or suspected opioid overdose who have a definite pulse but no normal breathing or only gasping (ie, a respiratory arrest), in addition to providing standard BLS care, it is reasonable for appropriately trained BLS healthcare providers to administer IM or IN naloxone. (Class IIa, LOE C-LD)***

For further information, see “[Part 5: Adult Basic Life Support and Cardiopulmonary Resuscitation Quality](#).”

#### **4.2.3.2 Cardiac Arrest - Updated**

Patients with no definite pulse may be in cardiac arrest or may have an undetected weak or slow pulse. These patients should be managed as cardiac arrest patients.

***Standard resuscitative measures should take priority over naloxone administration, with a focus on high-quality CPR (compressions plus ventilation). (Class I, LOE C-EO)***

***It may be reasonable to administer IM or IN naloxone based on the possibility that the patient is not in cardiac arrest. (Class IIb, LOE C-EO)***

***Responders should not delay access to more-advanced medical services while awaiting the patient’s response to naloxone or other interventions. (Class I, LOE C-EO)***

***Unless the patient refuses further care, victims who respond to naloxone administration should access advanced healthcare services. (Class I, LOE C-EO)***

#### **4.2.4 ACLS Modification: Administration of Naloxone - Updated**

##### **4.2.4.1 Respiratory Arrest - Updated**

***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)***

##### **4.2.4.2 Cardiac Arrest - Updated**

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.

##### **4.2.4.3 Observation and Post-Resuscitation Care - Updated**

***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)***

Patients who respond to naloxone administration may develop recurrent CNS and/or respiratory depression. Although abbreviated observation periods may be adequate for patients with fentanyl, morphine, or heroin overdose,<sup>104,111,113-116</sup> longer periods of observation may be required to safely discharge a patient with life-

threatening overdose of a long-acting or sustained-release opioid.<sup>95,117,118</sup>

***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)***

## **5 Role of Intravenous Lipid Emulsion Therapy in Management of Cardiac Arrest Due to Poisoning - Updated** ALS 834

The use of ILE therapy was first developed as a treatment for cardiac arrest resulting from the local anesthetic bupivacaine.<sup>119-121</sup> Local anesthetics inhibit voltage at the cell membrane sodium channels, limiting action potential and the conduction of nerve signals. Local anesthetic systemic toxicity (LAST) can present with fulminant cardiovascular collapse that is refractory to standard resuscitative measures. A CNS toxicity phase (agitation evolving to frank seizures or CNS depression) may precede cardiovascular collapse. A recent review of peripheral nerve anesthetic blocks estimated the incidence of LAST equal to 0.87/1000 patients.<sup>122</sup> When a local anesthetic is administered, professional organizations recommend continuous neurologic and cardiovascular monitoring, dose fractionation, slow injection, concurrent use of an intravascular marker of systemic absorption (epinephrine 10 to 15 µg), and the use of ultrasound techniques.<sup>123</sup>

Administration of ILE creates a lipid compartment in the serum, reducing by sequestration the concentration of lipophilic medications in the tissues.<sup>124</sup> Administration of ILE also increases cardiac inotropy by other mechanisms.<sup>125-127</sup>

Over time, common use of this modality has been expanded to include poisoning by other local anesthetics and other medications.<sup>128-131</sup>

The 2015 ILCOR systematic review addressed the question of whether administration of lipid emulsion improves outcomes for patients who develop cardiac arrest due to drug toxicity, including that caused by local anesthetics and other drugs.

### **5.1 2015 Evidence Summary**

To date, we identified no human studies that compared outcomes of patients in cardiac arrest treated with ILE plus supportive care versus supportive care alone. A small controlled trial of adults with poisoning from drugs other than local anesthetics showed a more rapid improvement in level of consciousness in the group that received ILE, but all patients survived in both groups.<sup>132</sup> Patients with glyphosate-surfactant herbicide ingestion treated with ILE had less hypotension and fewer arrhythmias than historic controls, but there was no difference in survival outcomes.<sup>133</sup> Registry studies of patients receiving ILE are difficult to interpret because of a lack of comparison groups.<sup>134,135</sup>

Animal studies in rats consistently show a benefit of ILE in LAST caused by bupivacaine.<sup>130,136</sup> Studies are less consistently positive in porcine models of LAST and from poisoning by drugs other than local anesthetics.<sup>131</sup> In a recent systematic review of human case reports, the majority (81/103) reported clinical improvement, such as ROSC, relief of hypotension, resolution of dysrhythmia, improved mental status, or termination of status epilepticus, after ILE administration.<sup>131</sup> In this review, all 21 published cases of the use of ILE to treat LAST from bupivacaine demonstrated clinical improvement after ILE administration.

Comparative dose studies are not available. The most commonly reported strategy is to use a 20% emulsion of long-chain triglycerides, giving an initial bolus of 1.5 mL/kg lean body mass over 1 minute followed by an infusion of 0.25 mL/kg per minute for 30 to 60 minutes. The bolus can be repeated once or twice as needed for persistent cardiovascular collapse; the suggested maximum total dose is 10 mL/kg over the first hour.<sup>130,137-139</sup> The safety of prolonged infusions (beyond 1 hour) has not been established.<sup>140</sup>

The most common adverse effect of ILE therapy is interference with diagnostic laboratory testing<sup>141</sup>; rare cases of pancreatitis<sup>141</sup> and pulmonary changes similar to those observed with acute respiratory distress syndrome<sup>142</sup> have also been reported. There appear to be complex pharmacodynamic interactions between ILE and epinephrine given during resuscitation, and in some situations, treatment with ILE alters the effectiveness of epinephrine and vasopressin in animal resuscitation studies.<sup>143</sup> Although some organizations recommend modification of the pharmacologic treatment of cardiac arrest after ILE administration,<sup>144,145</sup> there are no human data to support a modification in ACLS recommendations. More recently, concern has been raised that ILE administration may increase the absorption of lipophilic medications from the gastrointestinal tract<sup>146</sup> and

interfere with the operation of venoarterial extracorporeal membrane oxygenation circuits.<sup>147</sup>

## 5.2 2015 Recommendations—New and Updated

### 5.2.1 ACLS Modifications - Updated

***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-EO)***

***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-EO)***

## 6 Cardiac Arrest Associated With Other Toxic Ingestions

Poisoning has been likened to trauma on the cellular level, destroying the natural workings of a victim's physiology.<sup>148</sup> Severe poisoning alters the function of a cellular receptor, ion channel, organelle, or chemical pathway to the extent that critical organ systems can no longer support life.

As with any patient in cardiac arrest, management of the patient with a toxic exposure begins with support of airway, breathing, and circulation. Cardiac arrest due to toxicity is managed in accordance with the current standards of BLS and ACLS. With few exceptions, there are no unique antidotes or toxin-specific interventions that are recommended during resuscitation from cardiac arrest.

Once return of spontaneous circulation is achieved, urgent consultation with a medical toxicologist or certified regional poison center is recommended, as the postarrest management of the critically poisoned patient may benefit from a thorough understanding of the toxic agent. Consultation is also recommended early in the management of a patient with potentially life-threatening poisoning, when appropriate interventions might prevent deterioration to cardiac arrest. In the United States a certified poison center can be reached by calling 1-800-222-1222; in Canada, call 1-800-268-9017.

It is extremely difficult to conduct clinical trials of acute life-threatening poisoning. Challenges include the infrequency with which most specific conditions occur, the heterogeneity of presentation, and ethical challenges related to withholding established care from patients who are unable to provide informed consent because the patient has an altered mental status, the patient is suicidal, or there is a lack of time to explain treatment alternatives.<sup>149</sup>

The majority of questions addressing cardiac arrest due to drug toxicity remain unanswered. Epidemiological studies are required to document the incidence rate of cardiac arrests secondary to drug toxicity and the safety and efficacy baseline rates for current therapeutic strategies. This section presents recommendations for the care of the patient with a toxicological problem causing cardiac arrest or severe cardiovascular instability (respiratory depression, hypotension, life-threatening alterations of cardiac conduction, etc). Some recommendations are evidence-based, but most research in this area consists of case reports, small case series, animal studies, and pharmacokinetic studies in healthy volunteers. Virtually no toxicology research involves human cardiac arrest. Thus, many of these recommendations are based on expert consensus, and further research is needed to validate them.

### 6.1 Initial Approach to the Critically Poisoned Patient

Management of the critically poisoned patient begins with airway protection, support of respiration and circulation, and rapid assessment. Patients may or may not be able to provide an accurate history of exposure to a toxic substance. Whenever possible, history gathering should include questioning of persons who accompany the patient, evaluation of containers, review of pharmacy records, and examination of the patient's prior medical record.<sup>150</sup> Many patients who ingest medications in a suicide attempt take more than 1 substance, and the number of substances ingested is greater in fatal than in nonfatal suicide attempts.<sup>151</sup> Comprehensive toxicology laboratory testing is virtually never available in a time frame that supports early resuscitation decisions.<sup>152</sup>

Poisoned patients may deteriorate rapidly. Care for all adult patients who are critically ill or under evaluation for possible toxin exposure or ingestion, particularly when the history is uncertain, should begin in a monitored treatment area where the development of central nervous system depression, hemodynamic instability, or



seizures can be rapidly recognized and addressed.<sup>153</sup>

Gastrointestinal decontamination, once a mainstay in the management of ingested toxins, has a less significant role in poisoning treatment today. With rare exceptions, gastric lavage, whole bowel irrigation, and administration of syrup of ipecac are no longer recommended.<sup>154-156</sup> Administration of single-dose activated charcoal to adsorb ingested toxins is generally recommended for the ingestion of life-threatening poisons for which no adequate antidotal therapy is available and when the charcoal can be administered within 1 hour of poisoning.<sup>157</sup> Multiple-dose activated charcoal should be considered for patients who have ingested a life-threatening amount of specific toxins (eg, carbamazepine, dapsone, phenobarbital, quinine, or theophylline) for which a benefit of this strategy has been established.<sup>158</sup> Charcoal should not be administered for ingestions of caustic substances, metals, or hydrocarbons.<sup>157</sup>

Charcoal should only be administered to patients with an intact or protected airway. In patients who are at risk for aspiration, endotracheal intubation and head-of-bed elevation should be performed before charcoal administration.<sup>158,159</sup> Because the decision to perform gastrointestinal decontamination is complex, multifactorial, and associated with risk, expert advice can be helpful.

## 6.2 Toxidromes

A “toxidrome” is a clinical syndrome—a constellation of signs, symptoms, and laboratory findings—suggestive of the effects of a specific toxin. By recognizing these presentations, the clinician can establish a working diagnosis that guides initial management. Some common toxidromes are presented in Table 2: Common Toxidromes. Practically every sign and symptom observed in poisoning can be produced by natural disease, and many clinical presentations associated with natural disease can be mimicked by some poison.<sup>160</sup> It is important to maintain a broad differential diagnosis, particularly when the history of toxic chemical exposure is unclear.

**Table 2: 2010 - Common Toxidromes**

Open table in a [new window](#)

Common Toxidromes*		
Cardiac Signs		
Tachycardia and/or Hypertension	Bradycardia and/or Hypotension	Cardiac Conduction Delays (Wide QRS)
Amphetamines	Beta blockers	Cocaine
Anticholinergic drugs	Calcium channel blockers	Cyclic antidepressants
Antihistamines	Clonidine	Local anesthetics
Cocaine	Digoxin and related glycosides	Propoxyphene
Theophylline/caffeine	Organophosphates and carbamates	Antiarrhythmics (e.g., quinidine, flecainide)
Withdrawal states		
CNS/Metabolic Signs		
Seizures	CNS and/or Respiratory Depression	Metabolic Acidosis

Cardiac Signs		
Cyclic antidepressants	Antidepressants (several classes)	Cyanide
Isoniazid	Benzodiazepines	Ethylene glycol
Selective and non-selective norepinephrine reuptake inhibitors (eg, bupropion)	Carbon monoxide	Metformin
Withdrawal states	Ethanol	Methanol
	Methanol	Salicylates
	Opioids	
	Oral hypoglycemics	

• [?](#)\* Differential diagnosis lists are partial.

### 6.3 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 no 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 has been associated with seizures, arrhythmia, and hypotension in patients with coingestion of certain medications, such as tricyclic antidepressants.<sup>161,162</sup> 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).<sup>163</sup>

### 6.4 ?-Blockers

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

?-Blocker medication overdose may cause such severe inhibition of ?-adrenergic receptors that high-dose vasopressors cannot effectively restore blood pressure, cardiac output, or perfusion. Therapeutic options in the treatment of refractory hemodynamic instability due to ?-blocker overdose include administration of glucagon, high-dose insulin, or IV calcium salts.

#### 6.4.1 Glucagon

Administration of glucagon may be helpful for severe cardiovascular instability associated with ?-blocker toxicity that is refractory to standard measures, including vasopressors.

***The recommended dose of glucagon is a bolus of 3 to 10 mg, administered slowly over 3 to 5 minutes, followed by an infusion of 3 to 5 mg/h (0.05 to 0.15 mg/kg followed by an infusion of 0.05 to 0.10 mg/kg per hour).<sup>164-176</sup> (Class IIb, LOE C)***

The infusion rate is titrated to achieve an adequate hemodynamic response (appropriate mean arterial pressure and evidence of good perfusion). Because the amount of glucagon required to sustain this therapy may exceed 100 mg in a 24-hour period, plans should be made early to ensure that an adequate supply of glucagon is available. Glucagon commonly causes vomiting. In patients with central nervous system depression, the airway must be protected before glucagon administration. Animal studies have suggested that the concomitant use of dopamine alone or in combination with isoproterenol and milrinone may decrease the effectiveness of glucagon.<sup>177-179</sup>

#### 6.4.2 Insulin

Animal studies suggest that high-dose IV insulin, accompanied by IV dextrose supplementation and electrolyte monitoring, may improve hemodynamic stability and survival in  $\beta$ -blocker overdose by improving myocardial energy utilization.<sup>180,181</sup> A single human case report<sup>182</sup> showed improved hemodynamic stability and survival to discharge following administration of high-dose insulin in refractory shock due to a massive overdose of metoprolol.

***Administration of high-dose insulin in patients with shock refractory to other measures may be considered. (Class IIb, LOE C)***

Although the ideal human dose has not been determined, a commonly used protocol calls for IV administration of 1 U/kg regular insulin as a bolus, accompanied by 0.5 g/kg dextrose, followed by continuous infusions of 0.5 to 1 U/kg per hour of insulin and 0.5 g/kg per hour of dextrose.<sup>183</sup> The insulin infusion is titrated as needed to achieve adequate hemodynamic response, whereas the dextrose infusion is titrated to maintain serum glucose concentrations of 100 to 250 mg/dL (5.5 to 14 mmol/L). Very frequent serum glucose monitoring (up to every 15 minutes) may be needed during the initial phase of dextrose titration. Sustained infusions of concentrated dextrose solutions (>10%) require central venous access. Insulin causes potassium to shift into the cells. Moderate hypokalemia is common during high-dose insulin-euglycemia therapy, and animals treated with aggressive potassium repletion developed asystole.<sup>180</sup> To avoid overly aggressive potassium repletion, 1 human protocol targets potassium levels of 2.5 to 2.8 mEq/L.<sup>183</sup>

#### 6.4.3 Calcium

***One human case report<sup>184</sup> and a large-animal study<sup>185</sup> suggest that calcium may be helpful in  $\beta$ -blocker overdose. Administration of calcium in patients with shock refractory to other measures may be considered. (Class IIb, LOE C)***

One approach is to administer 0.3 mEq/kg of calcium (0.6 mL/kg of 10% calcium gluconate solution or 0.2 mL/kg of 10% calcium chloride solution) IV over 5 to 10 minutes, followed by an infusion of 0.3 mEq/kg per hour.<sup>183</sup> The infusion rate is titrated to adequate hemodynamic response. Serum ionized calcium levels should be monitored, and severe hypercalcemia (ionized calcium levels greater than twice the upper limits of normal) should be avoided. Sustained infusions of IV calcium require central venous access.

#### 6.4.4 Other Therapies

Case reports have suggested that in patients who remain critically hypotensive despite maximal vasopressor therapy, specific interventions using intra-aortic balloon counterpulsation, ventricular assist devices, and extracorporeal membrane oxygenation or other extra corporeal life support (ECLS) devices may be lifesaving.<sup>186-188</sup> While evidence remains weak, at least two human case reports indicate a possible benefit from lipid emulsion infusion for overdose by  $\beta$ -blockers.<sup>189,190</sup> Animal studies are mixed.<sup>191-194</sup> Because this area of therapy is rapidly evolving,<sup>195-197</sup> prompt consultation with a medical toxicologist or other specialists with up-to-date knowledge is recommended when managing treatment-refractory hypotension from  $\beta$ -blocker overdosage.

#### 6.5 Calcium Channel Blockers

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

Calcium channel blocker overdose also may cause life-threatening hypotension and bradycardia that are refractory to standard agents. Treatment with high-dose insulin has been described in a number of clinical case reports<sup>198-209</sup> and animal studies.<sup>210-213</sup>

***High-dose insulin, in the doses listed in the  $\beta$ -blocker section above, may be effective for restoring hemodynamic stability and improving survival in the setting of severe cardiovascular toxicity associated with toxicity from a calcium channel blocker overdose. (Class IIb, LOE B)***

Limited evidence supports the use of calcium in the treatment of hemodynamically unstable calcium channel blocker overdose refractory to other treatments.<sup>199,200,203,204,206-208,211,214-217</sup>

***Administration of calcium in patients with shock refractory to other measures may be considered. (Class IIb, LOE C)***

There is insufficient and conflicting evidence to recommend the use of glucagon<sup>203,204,208,210,211,214,217-220</sup> in the treatment of hemodynamically unstable calcium channel blocker overdose.

## 6.6 Digoxin and Related Cardiac Glycosides

Digoxin poisoning can cause severe bradycardia and life-threatening arrhythmias, including ventricular tachycardia, ventricular fibrillation, and high degrees of AV nodal blockade. Other plant- and animal-derived cardiac glycosides may produce similar effects, including those found in oleander, lily-of-the-valley, toad skin, and some herbal medications. There are no data to support the use of specific antidotes in the setting of cardiac arrest due to digoxin overdose. Resuscitation from cardiac arrest should follow standard BLS and ACLS algorithms, with specific antidotes used in the post-cardiac arrest phase if severe cardiotoxicity is encountered.

***Antidigoxin Fab antibodies should be administered to patients with severe life-threatening cardiac glycoside toxicity.<sup>221-230</sup> (Class I, LOE B)***

One vial of antidigoxin Fab is standardized to neutralize 0.5 mg of digoxin. Although the ideal dose is unknown, a reasonable strategy is as follows:

If the ingested dose of digoxin is known, administer 2 vials of Fab for every milligram of digoxin ingested.

In cases of chronic digoxin toxicity or when the ingested dose is not known, calculate the number of vials to administer by using the following formula: serum digoxin concentration (ng/mL) × weight (kg) / 100.

In critical cases in which therapy is required before a serum digoxin level can be obtained or in cases of life-threatening toxicity due to cardiac glycosides, administer empirically 10 to 20 vials.

Hyperkalemia is a marker of severity in acute cardiac glycoside poisoning and is associated with poor prognosis.<sup>231</sup> Antidigoxin Fab may be administered empirically to patients with acute poisoning from digoxin or related cardiac glycosides whose serum potassium level exceeds 5.0 mEq/L.<sup>232</sup>

## 6.7 Cocaine

There are no data to support the use of cocaine-specific interventions in the setting of cardiac arrest due to cocaine overdose. Resuscitation from cardiac arrest should follow standard BLS and ACLS algorithms, with specific antidotes used in the postresuscitation phase if severe cardiotoxicity or neurotoxicity is encountered. A single case series demonstrated excellent overall and neurologically intact survival (55%) in patients with cardiac arrest associated with cocaine overdose who were treated with standard therapy.<sup>233</sup>

Cocaine-induced tachycardia and hypertension are predominantly caused by central nervous system stimulation. Treatment strategies are extrapolated from acute coronary syndrome studies, small case series, and experiments in cocaine-naïve human volunteers.

***It may be reasonable to try agents that have shown efficacy in the management of acute coronary syndrome in patients with severe cardiovascular toxicity.  $\beta$ -Blockers (phentolamine),<sup>234</sup> benzodiazepines (lorazepam, diazepam),<sup>235</sup> calcium channel blockers (verapamil),<sup>236</sup> morphine,<sup>237</sup> and sublingual nitroglycerin<sup>238, 239</sup> may be used as needed to control hypertension, tachycardia, and agitation. (Class IIb, LOE B)***

***The available data do not support the use of 1 agent over another in the treatment of cardiovascular toxicity due to cocaine. (Class IIb, LOE B)***

***There is clear evidence that cocaine can precipitate acute coronary syndromes.<sup>240</sup> For cocaine-induced hypertension or chest discomfort, benzodiazepines, nitroglycerin, and/or morphine can be beneficial.<sup>235, 238, 241</sup> (Class IIa, LOE B)***

Because the effects of cocaine and other stimulant medications are transient, drugs and doses should be chosen carefully to minimize the risk of producing hypotension after the offending agent has been metabolized. Catheterization laboratory studies demonstrate that cocaine administration leads to reduced coronary artery diameter. This effect is reversed by morphine,<sup>237</sup> nitroglycerin,<sup>239</sup> phentolamine,<sup>234</sup> and verapamil<sup>236</sup>; is not changed by labetalol<sup>242</sup>; and is exacerbated by propranolol.<sup>243</sup> Several studies suggest that administration of  $\beta$ -blockers may worsen cardiac perfusion and/or produce paradoxical hypertension when cocaine is present.<sup>243, 244</sup>

***Although contradictory evidence exists,<sup>245, 246</sup> current recommendations are that pure  $\beta$ -blocker medications in the setting of cocaine are not indicated.<sup>247</sup> (Class IIb, LOE C)***

In severe overdose, cocaine acts as a Vaughan-Williams class Ic antiarrhythmic, producing wide-complex tachycardia through several mechanisms, including blockade of cardiac sodium channels.<sup>248</sup> Although there is no human evidence in cocaine poisoning, extrapolation from evidence in the treatment of wide-complex tachycardia caused by other class Ic agents (flecainide) and tricyclic antidepressants suggests that administration of hypertonic sodium bicarbonate may be beneficial.<sup>249</sup> A typical treatment strategy used for these other sodium channel blockers involves administration of 1 mL/kg of sodium bicarbonate solution (8.4%, 1 mEq/mL) IV as a bolus, repeated as needed until hemodynamic stability is restored and QRS duration is  $\leq 120$  ms.<sup>250-257</sup> Current evidence neither supports nor refutes a role for lidocaine in the management of wide-complex tachycardia caused by cocaine.

## 6.8 Cyclic Antidepressants

Many drugs can prolong the QRS interval in overdose. These include Vaughan-Williams class Ia and Ic antiarrhythmics (eg, procainamide, quinidine, flecainide), cyclic antidepressants (eg, amitriptyline), and cocaine. Type Ia and Ic antiarrhythmics were not reviewed in 2010. Similar to the type Ia antiarrhythmics, cyclic antidepressants block cardiac sodium channels, leading to hypotension and wide-complex arrhythmia in overdose.

Cardiac arrest caused by cyclic antidepressant toxicity should be managed by current BLS and ACLS treatment guidelines. A small case series of cardiac arrest patients demonstrated improvement with sodium bicarbonate and epinephrine,<sup>258</sup> but the concomitant use of physostigmine in the prearrest period in this study reduces the ability to generalize this study.

**Administration of sodium bicarbonate for cardiac arrest due to cyclic antidepressant overdose may be considered. (Class IIb, LOE C)**

Therapeutic strategies for treatment of severe cyclic antidepressant cardiotoxicity include increasing serum sodium, increasing serum pH, or doing both simultaneously. The relative contributions of hypernatremia and alkalemia are controversial, but in practice most experience involves administration of hypertonic sodium bicarbonate solution (8.4% solution, 1 mEq/mL).

**Sodium bicarbonate boluses of 1 mL/kg may be administered as needed to achieve hemodynamic stability (adequate mean arterial blood pressure and perfusion) and QRS narrowing.<sup>250-257</sup>**  
**(Class IIb, LOE C)**

Serum sodium levels and pH should be monitored, and severe hypernatremia (sodium >155 mEq/L) and alkalemia (pH >7.55) should be avoided. A number of vasopressors and inotropes have been associated with improvement in the treatment of tricyclic-induced hypotension, ie, epinephrine,<sup>259,260,261</sup> norepinephrine,<sup>261-264</sup> dopamine,<sup>264-266</sup> and dobutamine.<sup>265</sup>

## 6.9 Carbon Monoxide

Apart from complications from deliberate drug abuse, carbon monoxide is the leading cause of unintentional poisoning death in the United States.<sup>267</sup> In addition to reducing the ability of hemoglobin to deliver oxygen, carbon monoxide causes direct cellular damage to the brain and myocardium.<sup>268</sup> Survivors of carbon monoxide poisoning are at risk for lasting neurological injury.<sup>268</sup>

Several studies have suggested that very few patients who develop cardiac arrest from carbon monoxide poisoning survive to hospital discharge, regardless of treatment administered following return of spontaneous circulation.<sup>269-271</sup> Routine care of patients in cardiac arrest and severe cardiotoxicity from carbon monoxide poisoning should comply with standard BLS and ACLS recommendations.

### 6.9.1 Hyperbaric Oxygen

Two studies suggest that neurological outcomes were improved in patients with carbon monoxide toxicity of all severity (excluding “moribund” patients)<sup>272</sup> and mild to moderate severity (excluding loss of consciousness and cardiac instability)<sup>273</sup> who received hyperbaric oxygen therapy for carbon monoxide poisoning. Other studies found no difference in neurologically intact survival.<sup>274,275</sup> A systematic review<sup>276,277</sup> and a recent evidence-based clinical policy review<sup>278</sup> concluded that, based on the available evidence, improvement in neurologically intact survival following treatment for carbon monoxide poisoning with hyperbaric oxygen is possible but unproven.

**Hyperbaric oxygen therapy is associated with a low incidence of severe side effects. Because hyperbaric oxygen therapy appears to confer little risk,<sup>278</sup> the available data suggest that hyperbaric oxygen therapy may be helpful in treatment of acute carbon monoxide poisoning in patients with severe toxicity.**  
**(Class IIb, LOE C)**

Patients with carbon monoxide poisoning who develop a cardiac injury have an increased risk of cardiovascular and all-cause mortality for at least 7 years after the event, even if hyperbaric oxygen is administered.<sup>279,280</sup> Although data about effective interventions in this population are lacking, it is reasonable to advise enhanced follow-up for these patients.

On the basis of this conflicting evidence, the routine transfer of patients to a hyperbaric treatment facility following resuscitation from severe cardiovascular toxicity should be carefully considered, weighing the risk of transport against the possible improvement in neurologically intact survival.

## 6.10 Cyanide

Cyanide is a surprisingly common chemical. In addition to industrial sources, cyanide can be found in jewelry cleaners, electroplating solutions, and as a metabolic product of the putative antitumor drug amygdalin (laetrile). Cyanide is a major component of fire smoke, and cyanide poisoning must be considered in victims of smoke

inhalation who have hypotension, central nervous system depression, metabolic acidosis, or soot in the nares or respiratory secretions.<sup>281</sup> Cyanide poisoning causes rapid cardiovascular collapse, which manifests as hypotension, lactic acidosis, central apnea, and seizures.

Patients in cardiac arrest<sup>281-283</sup> or those presenting with cardiovascular instability<sup>281-287</sup> 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.<sup>285,288,289</sup>

Both hydroxocobalamin<sup>281-287</sup> and sodium nitrite<sup>285,288,289</sup> serve to rapidly and effectively bind cyanide in the serum and reverse the effects of cyanide toxicity. Because nitrites induce methemoglobin formation<sup>288</sup> and can cause hypotension,<sup>290</sup> hydroxocobalamin has a safety advantage, particularly in children and victims of smoke inhalation who might also have carbon monoxide poisoning. A detailed comparison of these measures has been recently published.<sup>291</sup>

Sodium thiosulfate serves as a metabolic cofactor, enhancing the detoxification of cyanide to thiocyanate. Thiosulfate administration enhances the effectiveness of cyanide scavengers in animal experimentation<sup>292-295</sup> and has been used successfully in humans with both hydroxocobalamin<sup>281,287</sup> and sodium nitrite.<sup>285,288,289</sup> Sodium thiosulfate is associated with vomiting but has no other significant toxicity.<sup>296</sup>

***Therefore, based on the best evidence available, a treatment regimen of 100% oxygen and hydroxocobalamin, with or without sodium thiosulfate, is recommended (Class I, LOE B)***

## **7 Cardiac Arrest During Percutaneous Coronary Intervention - Updated** ALS 479

Cardiac arrest during PCI is rare, occurring in approximately 1.3% of catheterization procedures.<sup>297,298</sup> Although the risk of cardiac arrest during PCI is present in both elective and emergency procedures, the incidence is higher in emergency cases.<sup>299</sup>

In general, patients who develop cardiac arrest during PCI have superior outcomes to patients in cardiac arrest that occurs in other settings, including in-hospital units.<sup>300</sup> Many patients will respond to standard ACLS resuscitation, including high-quality CPR and rapid defibrillation. Rapid defibrillation (within 1 minute) is associated with survival to hospital discharge rates as high as 100% in this population.<sup>301</sup>

A subset of patients who develop cardiac arrest during PCI will require prolonged resuscitation efforts. Providing effective prolonged resuscitation in the catheterization laboratory has unique challenges, and a number of interventions and adjuncts for management of cardiac arrest during PCI have been described. Inconsistent availability and lack of comparative studies limit recommendations of one approach over another.

The 2015 ILCOR systematic review addressed the question of whether any special interventions or changes in care, compared with standard ACLS resuscitation alone, can improve outcomes in patients who develop cardiac arrest during PCI.

There are a number of mechanical devices available to provide hemodynamic support during cardiac catheterization in high-risk patients presenting with cardiogenic shock. The use of these devices in cardiogenic shock was not reviewed by ILCOR in 2015. Therefore, the *2015 AHA Guidelines Update for CPR and ECC* does not make recommendations on the use of mechanical support devices in patients presenting in cardiogenic shock who undergo PCI. Recent recommendations for the use of mechanical support devices in these situations can be found in the *2013 American College of Cardiology Foundation (ACCF)/AHA Guideline for the Management of ST-Elevation Myocardial Infarction*.<sup>302</sup>

### **7.1 2015 Evidence Summary**

The feasibility of using mechanical CPR devices during PCI has been demonstrated in both animal<sup>303</sup> and human<sup>304-307</sup> studies. No comparative studies have examined the use of mechanical CPR devices compared with manual chest compressions during PCI procedures. However, a number of case reports<sup>303,304,308</sup> and case series<sup>306,307</sup> have reported the use of mechanical CPR devices to facilitate prolonged resuscitation in patients who have a cardiac arrest during PCI. One study demonstrated that the use of a mechanical CPR device for cardiac arrest during PCI was feasible; however, no patients survived to hospital discharge.<sup>306</sup> Other studies have reported good patient outcomes, including ROSC, survival to discharge, and functional outcome at

hospital discharge, after use of mechanical devices in resuscitation from cardiac arrest during PCI.<sup>303,307</sup> Mechanical CPR devices may also allow the use of fluoroscopy during chest compressions without direct irradiation of personnel.

Patients in cardiogenic shock or with other high-risk features (eg, multivessel coronary disease) may be at increased risk for adverse outcomes during or after PCI. Ventricular assist devices, intraaortic balloon pumps (IABP), and ECPR are all rescue treatment options available to support circulation and permit completion of the PCI. Not all interventions are available or can be rapidly deployed in all centers.

Rapid initiation of ECPR or cardiopulmonary bypass is associated with good patient outcomes in patients with hemodynamic collapse and cardiac arrest in the catheterization lab.<sup>309-315</sup> The use of ECPR is also feasible and associated with good outcomes when used as a bridge to coronary artery bypass grafting.<sup>309,315-317</sup> The combination of ECPR and IABP has been associated with increased survival when compared with IABP alone for patients who present with cardiogenic shock, including those who have a cardiac arrest while undergoing PCI.<sup>310,314,318</sup> Available observational studies often implement ECPR 20 to 30 minutes after cardiac arrest.<sup>310,312</sup>

IABP counterpulsation increases coronary perfusion, decreases myocardial oxygen demand, and improves hemodynamics in cardiogenic shock states, but it is not associated with improved patient survival in cardiogenic shock.<sup>319-327</sup> The role of IABP in patients who have a cardiac arrest in the catheterization laboratory is not known.

Several case series have reported on the use of emergency coronary artery bypass graft surgery after failed PCI.<sup>328,329</sup> In patients with cardiogenic shock or cardiac arrest and failed PCI, mechanical CPR devices and/ or ECPR have been used as rescue bridges to coronary artery bypass graft. Although no comparison studies have examined the use of this therapy as an adjunct to PCI, survival to hospital discharge rates as high as 64% have been reported.<sup>309,310,315,317</sup>

## 7.2 2015 Recommendations—New and Updated

### 7.2.1 ACLS Modifications - Updated

***It may be reasonable to use mechanical CPR devices to provide chest compressions to patients in cardiac arrest during PCI. (Class IIb, LOE C-EO)***

***It may be reasonable to use ECPR as a rescue treatment when initial therapy is failing for cardiac arrest that occurs during PCI. (Class IIb, LOE C-LD)***

Because patients can remain on ECPR support for extended periods of time without possibility of recovery, practical and ethical considerations must be taken into account in determining which victims of cardiac arrest should receive ECPR support.

***Institutional guidelines should include the selection of appropriate candidates for use of mechanical support devices to ensure that these devices are used as a bridge to recovery, surgery or transplant, or other device. (Class I, LOE C-EO)***

Due to a lack of comparative studies, it is not possible to recommend one approach (manual CPR, mechanical CPR, or ECPR) over another when options exist.

## 8 Cardiac Arrest Associated With Asthma

Asthma is responsible for more than 2 million visits to the emergency department (ED) in the United States each year, with 1 in 4 patients requiring admission to a hospital.<sup>330</sup> Annually there are 5,000 to 6,000 asthma-related deaths in the United States, many occurring in the prehospital setting.<sup>331</sup> Severe asthma accounts for approximately 2% to 20% of admissions to intensive care units, with up to one third of these patients requiring intubation and mechanical ventilation.<sup>332</sup> This section focuses on the evaluation and treatment of patients with near-fatal asthma.



Several consensus groups have developed excellent guidelines for the management of asthma that are available on the World Wide Web:

<http://www.nhlbi.nih.gov/health-pro/guidelines/current/asthma-guidelines/full-report>

<http://www.ginasthma.com>

## 8.1 Pathophysiology

The pathophysiology of asthma consists of 3 key abnormalities:

- Bronchoconstriction
- Airway inflammation
- Mucous plugging

Complications of severe asthma, such as tension pneumothorax, lobar atelectasis, pneumonia, and pulmonary edema, can contribute to fatalities. Severe asthma exacerbations are commonly associated with hypercarbia and acidemia, hypotension due to decreased venous return, and depressed mental status, but the most common cause of death is asphyxia. Cardiac causes of death are less common.<sup>333</sup>

## 8.2 Clinical Aspects of Severe Asthma

Wheezing is a common physical finding, although the severity of wheezing does not correlate with the degree of airway obstruction. The absence of wheezing may indicate critical airway obstruction, whereas increased wheezing may indicate a positive response to bronchodilator therapy.

Oxygen saturation (SaO<sub>2</sub>) levels may not reflect progressive alveolar hypoventilation, particularly if oxygen is being administered. Note that SaO<sub>2</sub> may fall initially during therapy because  $\beta_2$ -agonists produce both bronchodilation and vasodilation and initially may increase intrapulmonary shunting.

Other causes of wheezing are pulmonary edema,<sup>334</sup> chronic obstructive pulmonary disease (COPD), pneumonia, anaphylaxis,<sup>335</sup> foreign bodies, PE, bronchiectasis, and subglottic mass.<sup>336</sup>

## 8.3 Initial Stabilization

Patients with severe life-threatening asthma require urgent and aggressive treatment with simultaneous administration of oxygen, bronchodilators, and steroids. Healthcare providers must monitor these patients closely for deterioration. Although the pathophysiology of life-threatening asthma consists of bronchoconstriction, inflammation, and mucous plugging, only bronchoconstriction and inflammation are amenable to drug treatment.

## 8.4 Primary Therapy

### 8.4.1 Oxygen

Oxygen should be provided to all patients with severe asthma, even those with normal oxygenation. As noted above, successful treatment with  $\beta_2$ -agonists may cause an initial decrease in oxygen saturation because the resultant bronchodilation can initially increase the ventilation-perfusion mismatch.

### 8.4.2 Inhaled $\beta_2$ -Agonists

Short-acting  $\beta_2$ -agonists provide rapid, dose-dependent bronchodilation with minimal side effects. Because the dose delivered depends on the patient's lung volume and inspiratory flow rate, the same dose can be used in most patients regardless of age or size. Studies have shown no difference in the effects of continuous versus intermittent administration of nebulized albuterol<sup>337,338</sup>; however, continuous administration was more effective in a subset of patients with severe exacerbations of asthma.<sup>337</sup> A Cochrane meta-analysis showed no overall difference between the effects of albuterol delivered by metered-dose inhaler spacer or nebulizer.<sup>339</sup> If prior use of a metered-dose inhaler has not been effective, use of a nebulizer is reasonable.

Although albuterol is sometimes administered intravenously (IV) in severe asthma, a systematic review of 15 clinical trials found that IV  $\beta_2$ -agonists, administered by either bolus or infusion, did not lead to significant improvements in any clinical outcome measure.<sup>338</sup>

Levalbuterol is the R-isomer of albuterol. Comparisons with albuterol have produced mixed results, with some studies showing a slightly improved bronchodilator effect in the treatment of acute asthma in the ED.<sup>340</sup>

There is no evidence that levalbuterol should be favored over albuterol.

One of the most common adjuncts used with  $\beta_2$ -agonist treatment, particularly in the first hours of treatment, include anticholinergic agents (see “Adjunctive Therapies” below for more detail). When combined with short-acting  $\beta_2$ -agonists, anticholinergic agents such as ipratropium can produce a clinically modest improvement in lung function compared with short-acting  $\beta_2$ -agonists alone.<sup>341,342</sup>

### 8.4.3 Corticosteroids

Systemic corticosteroids are the only treatment for the inflammatory component of asthma proven to be effective for acute asthma exacerbations. Because the antiinflammatory effects after administration may not be apparent for 6 to 12 hours, corticosteroids should be administered early. The early use of systemic steroids hastens the resolution of airflow obstruction and may reduce admission to the hospital.<sup>343</sup> Although there may be no difference in clinical effects between oral and IV formulations of corticosteroids,<sup>344,345</sup> the IV route is preferable in patients with severe asthma. In adults a typical initial dose of methylprednisolone is 125 mg (dose range: 40 mg to 250 mg); a typical dose of dexamethasone is 10 mg.

## 8.5 Adjunctive Therapies

### 8.5.1 Anticholinergics

Ipratropium bromide is an anticholinergic bronchodilator pharmacologically related to atropine. The nebulizer dose is 500 mcg.<sup>344,345</sup> Ipratropium bromide has a slow onset of action (approximately 20 minutes), with peak effectiveness at 60 to 90 minutes and no systemic side effects. The drug is typically given only once because of its prolonged onset of action, but some studies have shown that repeat doses of 250 mcg or 500 mcg every 20 minutes may be beneficial.<sup>346</sup> A recent meta-analysis indicated a reduced number of hospital admissions associated with treatment with ipratropium bromide, particularly in patients with severe exacerbations.<sup>347</sup>

### 8.5.2 Magnesium Sulfate

When combined with nebulized  $\beta_2$ -adrenergic agents and corticosteroids, IV magnesium sulfate can moderately improve pulmonary function in patients with asthma.<sup>348</sup> Magnesium causes relaxation of bronchial smooth muscle independent of serum magnesium level, with only minor side effects (flushing, lightheadedness). A Cochrane meta-analysis of 7 studies concluded that IV magnesium sulfate improves pulmonary function and reduces hospital admissions, particularly for patients with the most severe exacerbations of asthma.<sup>349</sup> The use of nebulized magnesium sulfate as an adjunct to nebulized  $\beta_2$ -adrenergic agents has been reported in a small case series to improve FEV1 and SpO<sub>2</sub>,<sup>350</sup> although a prior meta-analysis demonstrated only a trend toward improved pulmonary function with nebulized magnesium.<sup>351</sup> For those with severe refractory asthma, providers may consider IV magnesium at the standard adult dose of 2 g administered over 20 minutes.

### 8.5.3 Epinephrine or Terbutaline

Epinephrine and terbutaline are adrenergic agents that can be given subcutaneously to patients with acute severe asthma. The dose of subcutaneous epinephrine (concentration 1:1000) is 0.01 mg/kg, divided into 3 doses of approximately 0.3 mg administered at 20-minute intervals. Although the nonselective adrenergic properties of epinephrine may cause an increase in heart rate, myocardial irritability, and increased oxygen demand, its use is well-tolerated, even in patients >35 years of age.<sup>352</sup> Terbutaline is given in a subcutaneous dose of 0.25 mg, which can be repeated every 20 minutes for 3 doses. There is no evidence that subcutaneous epinephrine or terbutaline has advantages over inhaled  $\beta_2$ -agonists. Epinephrine has been administered IV (initiated at 0.25 mcg/min to 1 mcg/min continuous infusion) in severe asthma; however, 1 retrospective investigation indicated a 4% incidence of serious side effects. There is no evidence of improved outcomes with IV epinephrine compared with selective inhaled  $\beta_2$ -agonists.<sup>353</sup>

### 8.5.4 Ketamine

Ketamine is a parenteral, dissociative anesthetic with bronchodilatory properties that also can stimulate copious bronchial secretions. One case series<sup>354</sup> suggested substantial efficacy, whereas 2 published randomized trials in children<sup>355,356</sup> found no benefit of ketamine when compared with standard care. Ketamine has sedative and analgesic properties that may be useful if intubation is planned.

### 8.5.5 Heliox

Heliox is a mixture of helium and oxygen (usually a 70:30 helium to oxygen ratio mix) that is less viscous than ambient air. Heliox has been shown to improve the delivery and deposition of nebulized albuterol<sup>357</sup>

; however, a recent meta-analysis of clinical trials did not support its use as initial treatment for patients with acute asthma.<sup>358</sup> Because the heliox mixture requires at least 70% helium for effect, it cannot be used if the patient requires >30% oxygen.

### 8.5.6 Methylxanthines

Although once considered a mainstay in the treatment of acute asthma, methylxanthines are no longer recommended because of their erratic pharmacokinetics, known side effects, and lack of evidence of benefit.<sup>359</sup>

### 8.5.7 Leukotriene Antagonists

Leukotriene antagonists improve lung function and decrease the need for short-acting  $\beta_2$ -agonists for long-term asthma therapy, but their effectiveness during acute exacerbations of asthma is unproven.

### 8.5.8 Inhaled Anesthetics

Case reports in adults<sup>360</sup> and children<sup>361</sup> suggest a benefit of the potent inhalation anesthetics sevoflurane and isoflurane for patients with life-threatening asthma unresponsive to maximal conventional therapy. These agents may have direct bronchodilator effects. In addition, the anesthetic effect of these drugs increases the ease of mechanical ventilation and reduces oxygen demand and carbon dioxide production. This therapy requires expert consultation in an intensive care setting, and its effectiveness has not been evaluated in randomized clinical studies.

## 8.6 Assisted Ventilation

### 8.6.1 Noninvasive Positive-Pressure Ventilation

Noninvasive positive-pressure ventilation (NIPPV) may offer short-term support for patients with acute respiratory failure and may delay or eliminate the need for endotracheal intubation.<sup>362-364</sup> This therapy requires that the patient is alert and has adequate spontaneous respiratory effort. Bilevel positive airway pressure (BiPAP), the most common method of delivering NIPPV, allows for separate control of inspiratory and expiratory pressures.

### 8.6.2 Endotracheal Intubation With Mechanical Ventilation

Endotracheal intubation is indicated for patients who present with apnea, coma, persistent or increasing hypercapnia, exhaustion, severe distress, and depression of mental status. Clinical judgment is necessary to assess the need for immediate endotracheal intubation for these critically ill patients. Endotracheal intubation does not solve the problem of small airway constriction in patients with severe asthma; thus, therapy directed toward relief of bronchoconstriction should be continued. Mechanical ventilation in the asthmatic patient can be difficult and associated risks require careful management. Intubation and positive-pressure ventilation can trigger further bronchoconstriction and complications such as breath stacking that result from incomplete expiration, air trapping, and buildup of positive end-expiratory pressure (ie, intrinsic or auto-PEEP). This breath stacking can cause barotrauma. Decreasing tidal volume may avoid auto-PEEP and high peak airway pressures. Optimal ventilator management requires expert consultation and ongoing careful review of ventilation flow and pressure curves. Although endotracheal intubation introduces risks, it should be performed when necessary based on clinical condition.

Rapid sequence intubation is the technique of choice and should be performed by an expert in airway management. The provider should use the largest endotracheal tube available (usually 8 or 9 mm) to decrease airway resistance. Immediately after intubation, endotracheal tube placement should be confirmed by clinical examination and waveform capnography. A chest radiograph should then be performed.

## 8.7 Troubleshooting After Intubation

When severe bronchoconstriction is present, breath stacking (so-called auto-PEEP) can develop during positive-pressure ventilation, leading to complications such as hyperinflation, tension pneumothorax, and hypotension. During manual or mechanical ventilation, a slower respiratory rate should be used with smaller tidal volumes (eg, 6 to 8 mL/kg),<sup>365</sup> shorter inspiratory time (eg, adult inspiratory flow rate 80 to 100 L/min), and longer expiratory time (eg, inspiratory to expiratory ratio 1:4 or 1:5) than generally would be provided to patients without asthma.<sup>366</sup> Management of mechanical ventilation will vary based on patient-ventilation characteristics. Expert consultation should be obtained.

Mild hypoventilation (permissive hypercapnia) reduces the risk of barotrauma. Hypercapnia is typically well tolerated.<sup>367,368</sup> Sedation is often required to optimize ventilation, decrease ventilator dyssynchrony (and therefore auto-PEEP), and minimize barotrauma after intubation. Because delivery of inhaled medications may be inadequate before intubation, the provider should continue to administer inhaled albuterol treatments through the endotracheal tube.

Four common causes of acute deterioration in any intubated patient are recalled by the mnemonic **DOPE** (tube **D**isplacement, tube **O**bstruction, **P**neumothorax, **E**quipment failure). Auto-PEEP is another common cause of deterioration in patients with asthma. If the asthmatic patient's condition deteriorates or if it is difficult to ventilate the patient, check the ventilator for leaks or malfunction; verify endotracheal tube position; eliminate tube obstruction (eliminate any mucous plugs and kinks); evaluate for auto-PEEP; and rule out a pneumothorax.

High-end expiratory pressure can be reduced quickly by separating the patient from the ventilator circuit; this will allow PEEP to dissipate during passive exhalation. If auto-PEEP results in significant hypotension, assisting with exhalation by pressing on the chest wall after disconnection of the ventilator circuit will allow active exhalation and should lead to immediate resolution of hypotension. To minimize auto-PEEP, decrease the respiratory rate or tidal volume or both. If auto-PEEP persists and the patient displays ventilator dyssynchrony despite adequate sedation, paralytic agents may be considered.

In exceedingly rare circumstances, aggressive treatment for acute respiratory failure due to severe asthma will not provide adequate gas exchange. There are case reports that describe successful use of extracorporeal membrane oxygenation (ECMO) in adult and pediatric patients<sup>369-372</sup> with severe asthma after other aggressive measures have failed to reverse hypoxemia and hypercarbia.

## 8.8 BLS Modifications

BLS treatment of cardiac arrest in asthmatic patients is unchanged.

## 8.9 ACLS Modifications

When cardiac arrest occurs in the patient with acute asthma, standard ACLS guidelines should be followed.

Case series and case reports describe a novel technique of cardiopulmonary resuscitation (CPR) termed "lateral chest compressions"; however, there is insufficient evidence to recommend this technique over standard techniques.<sup>373-379</sup>

The adverse effect of auto-PEEP on coronary perfusion pressure and capacity for successful defibrillation has been described in patients in cardiac arrest without asthma.<sup>380,381</sup> Moreover, the adverse effect of auto-PEEP on hemodynamics in asthmatic patients who are not in cardiac arrest has also been well-described.<sup>382-385</sup>

***Therefore, since the effects of auto-PEEP in an asthmatic patient with cardiac arrest are likely quite severe, a ventilation strategy of low respiratory rate and tidal volume is reasonable. (Class IIa, LOE C)***

***During arrest a brief disconnection from the bag mask or ventilator may be considered, and compression of the chest wall to relieve air-trapping can be effective. (Class IIa, LOE C)***

***For all asthmatic patients with cardiac arrest, and especially for patients in whom ventilation is difficult, the possible diagnosis of a tension pneumothorax should be considered and treated. (Class I, LOE C)***

## 9 Cardiac Arrest Associated With Anaphylaxis

Anaphylaxis is an allergic reaction characterized by multisystem involvement, including skin, airway, vascular system, and gastrointestinal tract. Severe cases may result in complete obstruction of the airway and cardiovascular collapse from vasogenic shock. Anaphylaxis accounts for about 500 to 1000 deaths per year in the United States.<sup>386</sup>

The term *classic anaphylaxis* refers to hypersensitivity reactions mediated by the immunoglobulins IgE and IgG. Prior sensitization to an allergen produces antigen-specific immunoglobulins. Subsequent reexposure to the allergen provokes the anaphylactic reaction, although many anaphylactic reactions occur with no documented prior exposure. Pharmacological agents, latex, foods, and stinging insects are among the most common causes of anaphylaxis described.

### 9.1 Signs and Symptoms

The initial symptoms of anaphylaxis are often nonspecific and include tachycardia, faintness, cutaneous flushing, urticaria, diffuse or localized pruritus, and a sensation of impending doom. Urticaria is the most common physical finding. The patient may be agitated or anxious and may appear either flushed or pale.

A common early sign of respiratory involvement is rhinitis. As respiratory compromise becomes more severe, serious upper airway (laryngeal) edema may cause stridor and lower airway edema (asthma) may cause wheezing. Upper airway edema can also be a sign in angiotensin converting enzyme inhibitor-induced angioedema or C1 esterase inhibitor deficiency with spontaneous laryngeal edema.<sup>387-389</sup>

Cardiovascular collapse is common in severe anaphylaxis. If not promptly corrected, vasodilation and increased capillary permeability, causing decreased preload and relative hypovolemia of up to 37% of circulating blood volume, can rapidly lead to cardiac arrest.<sup>390,391</sup> Myocardial ischemia and acute myocardial infarction, malignant arrhythmias, and cardiovascular depression can also contribute to rapid hemodynamic deterioration and cardiac arrest.<sup>392</sup> Additionally, cardiac dysfunction may result from underlying disease or development of myocardial ischemia due to hypotension or following administration of epinephrine.<sup>393,394</sup>

There are no randomized controlled trials evaluating alternative treatment algorithms for cardiac arrest due to anaphylaxis. Evidence is limited to case reports and extrapolations from nonfatal cases, interpretation of pathophysiology, and consensus opinion. Providers must be aware that urgent support of airway, breathing, and circulation is essential in suspected anaphylactic reactions.

Because of limited evidence, the management of cardiac arrest secondary to anaphylaxis should be treated with standard BLS and ACLS. The following therapies are largely consensus-based but commonly used and widely accepted in the management of the patient with anaphylaxis who is not in cardiac arrest.

### 9.2 BLS Modifications

#### 9.2.1 Airway

Early and rapid advanced airway management is critical and should not be unnecessarily delayed.

***Given the potential for the rapid development of oropharyngeal or laryngeal edema,<sup>395</sup> immediate referral to a health professional with expertise in advanced airway placement is recommended. (Class I, LOE C)***

#### 9.2.2 Circulation

The intramuscular (IM) administration of epinephrine (epinephrine autoinjectors, eg, the EpiPen™) in the anterolateral aspect of the middle third of the thigh provides the highest peak blood levels.<sup>396</sup> Absorption and subsequent achievement of maximum plasma concentration after subcutaneous administration is slower than the IM route and may be significantly delayed with shock.<sup>396</sup>

***Epinephrine<sup>397</sup> should be administered early by IM injection to all patients with signs of a systemic allergic reaction, especially hypotension, airway swelling, or difficulty breathing. (Class I, LOE C)***

***The recommended dose is 0.2 to 0.5 mg (1:1000) IM to be repeated every 5 to 15 minutes in the absence of clinical improvement.<sup>398</sup> (Class I, LOE C)***

The adult epinephrine IM auto-injector will deliver 0.3 mg of epinephrine and the pediatric epinephrine IM auto-injector will deliver 0.15 mg of epinephrine.

***In both anaphylaxis and cardiac arrest the immediate use of an epinephrine autoinjector is recommended if available. (Class I, LOE C)***

### 9.3 ACLS Modifications

#### 9.3.1 Airway

Early recognition of the potential for a difficult airway in anaphylaxis is paramount in patients who develop hoarseness, lingual edema, stridor, or oropharyngeal swelling.

***Planning for advanced airway management, including a surgical airway,<sup>399</sup> is recommended. (Class I, LOE C)***

#### 9.3.2 Fluid Resuscitation

In a prospective evaluation of volume resuscitation after diagnostic sting challenge, repeated administration of 1000-mL bolus doses of isotonic crystalloid (eg, normal saline) titrated to systolic blood pressure above 90 mm Hg was used successfully in patients whose hypotension did not respond immediately to vasoactive drugs.<sup>390, 400</sup>

***Vasogenic shock from anaphylaxis may require aggressive fluid resuscitation. (Class IIa, LOE C)***

#### 9.3.3 Vasopressors

There are no human trials establishing the role of epinephrine or preferred route of administration in anaphylactic shock managed by ACLS providers.<sup>397</sup> In an animal study of profound anaphylactic shock, IV epinephrine restored blood pressure to baseline; however, the effect was limited to the first 15 minutes after shock, and no therapeutic effect was observed with the same dose of epinephrine administered IM or subcutaneously.<sup>401</sup>

***Therefore, when an IV line is in place, it is reasonable to consider the IV route as an alternative to IM administration of epinephrine in anaphylactic shock. (Class IIa, LOE C)***

For patients not in cardiac arrest, IV epinephrine 0.05 to 0.1 mg (5% to 10% of the epinephrine dose used routinely in cardiac arrest) has been used successfully in patients with anaphylactic shock.<sup>402</sup>

***Because fatal overdose of epinephrine has been reported,<sup>393, 400, 403, 404</sup> close hemodynamic monitoring***

***is recommended. (Class I, LOE B)***

In a study of animals sensitized by ragweed, a continuous IV infusion of epinephrine maintained a mean arterial pressure at 70% of preshock levels better than no treatment or bolus epinephrine treatment (IV, subcutaneous, or IM).<sup>405</sup> Furthermore, a recent human study suggests that careful titration of a continuous infusion of IV epinephrine (5 to 15 mcg/min), based on severity of reaction and in addition to crystalloid infusion, may be considered in treatment of anaphylactic shock.<sup>400</sup>

***Therefore, IV infusion of epinephrine is a reasonable alternative to IV boluses for treatment of anaphylaxis in patients not in cardiac arrest (Class IIa, LOE C) and may be considered in postarrest management. (Class IIb, LOE C)***

Recently vasopressin has been used successfully in patients with anaphylaxis (with or without cardiac arrest) who did not respond to standard therapy.<sup>406-408</sup> Other small case series described successful results with administration of alternative  $\alpha$ -agonists such as norepinephrine,<sup>409</sup> methoxamine,<sup>410,411</sup> and metaraminol.<sup>412-414</sup>

***Alternative vasoactive drugs (vasopressin, norepinephrine, methoxamine, and metaraminol) may be considered in cardiac arrest secondary to anaphylaxis that does not respond to epinephrine. (Class IIb, LOE C)***

No randomized controlled trials have evaluated epinephrine versus the use of alternative vasoactive drugs for cardiac arrest due to anaphylaxis.

#### 9.3.4 Other Interventions

There are no prospective randomized clinical studies evaluating the use of other therapeutic agents in anaphylactic shock or cardiac arrest.

***Adjuvant use of antihistamines (H1 and H2 antagonist),<sup>415,416</sup> inhaled  $\beta$ -adrenergic agents,<sup>417</sup> and IV corticosteroids<sup>418</sup> has been successful in management of the patient with anaphylaxis and may be considered in cardiac arrest due to anaphylaxis. (Class IIb, LOE C)***

#### 9.3.5 Extracorporeal Support of Circulation

Cardiopulmonary bypass has been successful in isolated case reports of anaphylaxis followed by cardiac arrest.<sup>419,420</sup>

***Use of these advanced techniques may be considered in clinical situations where the required professional skills and equipment are immediately available. (Class IIb, LOE C)***

### 10 Cardiac Arrest in the Morbidly Obese

Morbid obesity can provide challenges during the resuscitation attempt. Airway management may be more challenging, and changes to the thorax may make resuscitative efforts more demanding. Evidence from 2 case studies,<sup>421,422</sup> 1 case series,<sup>423</sup> and 1 related clinical study<sup>424</sup> indicated no differences in survival based on patient weight. However, one large case series demonstrated lower survival for morbidly obese children who required in-hospital pediatric CPR.<sup>425</sup>

#### 10.1 BLS and ACLS Modifications

No modifications to standard BLS or ACLS care have been proven efficacious, although techniques may need to be adjusted due to the physical attributes of individual patients.

### 11 Cardiac Arrest Associated With Life-Threatening Electrolyte Disturbances

Electrolyte abnormalities can be associated with cardiovascular emergencies and may cause or contribute to cardiac arrest, hinder resuscitative efforts, and affect hemodynamic recovery after cardiac arrest. An evidence-based review in 2010 focused on electrolyte abnormalities most often associated with cardiac arrest.

Early consideration may be given to using selective methods of therapeutic management in addition to standard ACLS protocols that can be provided rapidly and have been shown to be effective in patients with cardiovascular instability as outlined below. Current BLS and ACLS should be used to manage cardiac arrest associated with all electrolyte disturbances.

### 11.1 Potassium (K<sup>+</sup>)

Potassium is maintained mainly in the intracellular compartment through the action of the Na<sup>+</sup>/K<sup>+</sup> ATPase pump. The magnitude of the potassium gradient across cell membranes determines excitability of nerve and muscle cells, including the myocardium.

Potassium is tightly regulated. Under normal conditions potential differences across membranes, especially cardiac, are not affected by alterations in potassium level. Rapid or significant changes in serum concentrations of potassium result from the shifting of potassium from one space to another and may have life-threatening consequences.

### 11.2 Hyperkalemia

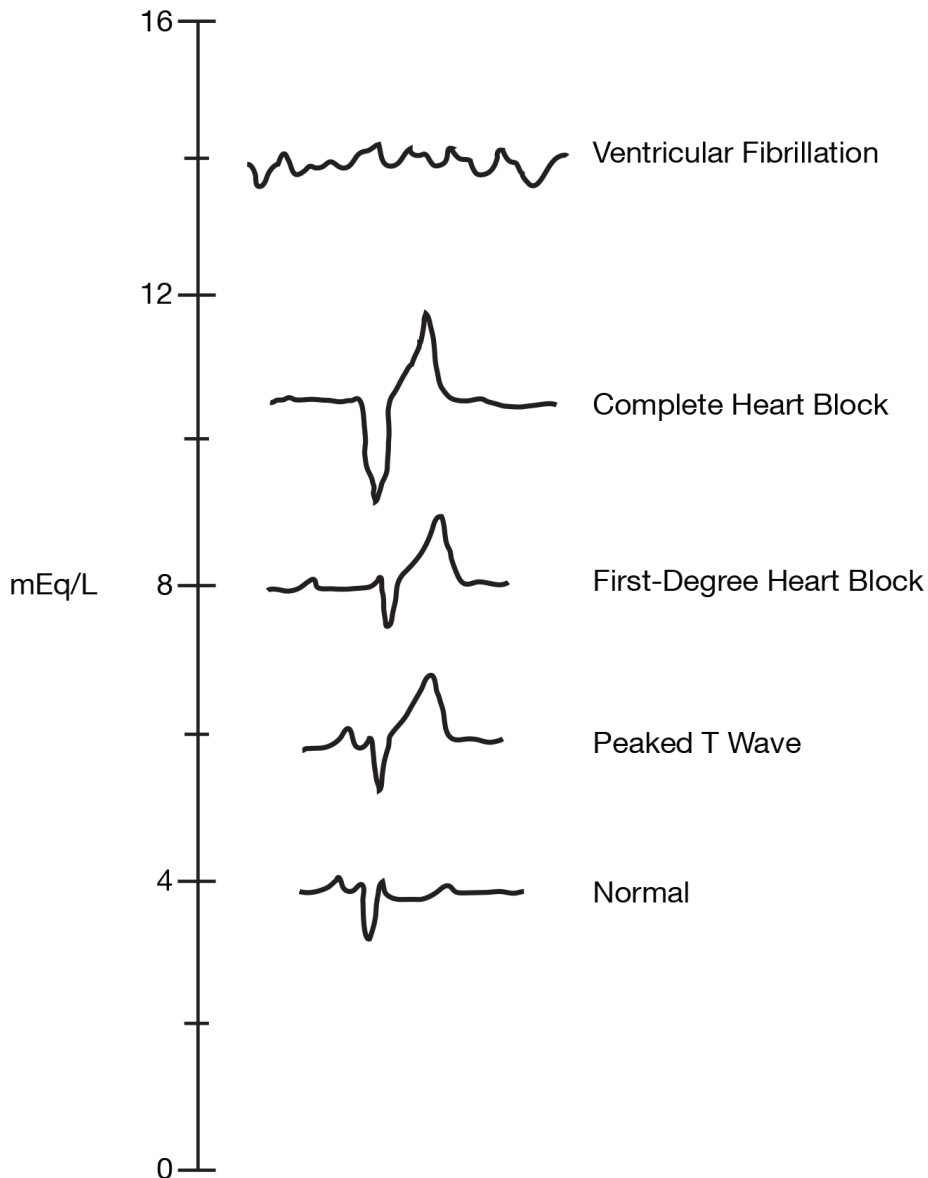
Hyperkalemia is one of the few potentially lethal electrolyte disturbances. Severe hyperkalemia (defined as a serum potassium concentration >6.5 mmol/L) occurs most commonly from renal failure or from release of potassium from cells and can cause cardiac arrhythmias and cardiac arrest. In 1 retrospective in-hospital study of 29 063 patients, hyperkalemia was found to be directly responsible for sudden cardiac arrest in 7 cases.<sup>426</sup> Acute kidney injury was present in all the arrest cases, accompanied by acute pancreatitis in 3 cases and acute hepatic failure in 2 cases. Overall renal failure and drug treatment were the most common causes of hyperkalemia, with the most severe cases occurring when excessive IV potassium was administered to a patient with renal insufficiency.

Although severe hyperkalemia may cause flaccid paralysis, paresthesia, depressed deep tendon reflexes, or respiratory difficulties,<sup>427-429</sup> the first indicator of hyperkalemia may be the presence of peaked T waves (tenting) on the electrocardiogram (ECG). As serum potassium rises, the ECG may progressively develop flattened or absent P waves, a prolonged PR interval, widened QRS complex, deepened S waves, and merging of S and T waves (Figure 3). If hyperkalemia is left untreated, a sine-wave pattern, idioventricular rhythms, and asystolic cardiac arrest may develop.<sup>430,431</sup>



Figure 3: 2010 ECG Changes Hyperkalemia

### ECG changes in hyperkalemia



#### 11.2.1 ACLS Modifications in Management of Severe Cardiotoxicity or Cardiac Arrest Due to Hyperkalemia

Treatment of severe hyperkalemia aims at protecting the heart from the effects of hyperkalemia by antagonizing the effect of potassium on excitable cell membranes, forcing potassium into cells to remove it promptly from the circulation, and removing potassium from the body. Therapies that shift potassium will act rapidly but are temporary and thus may need to be repeated. In order of urgency, treatment includes the following:

- Stabilize myocardial cell membrane:
  - Calcium chloride (10%): 5 to 10 mL (500 to 1000 mg) IV over 2 to 5 minutes or calcium gluconate (10%): 15 to 30 mL IV over 2 to 5 minutes
- Shift potassium into cells:

- Sodium bicarbonate: 50 mEq IV over 5 minutes
- Glucose plus insulin: mix 25 g (50 mL of D50) glucose and 10 U regular insulin and give IV over 15 to 30 minutes
- Nebulized albuterol: 10 to 20 mg nebulized over 15 minutes
- Promote potassium excretion:
  - Diuresis: furosemide 40 to 80 mg IV
  - Kayexalate: 15 to 50 g plus sorbitol per oral or per rectum
- Dialysis

***When cardiac arrest occurs secondary to hyperkalemia, it may be reasonable to administer adjuvant IV therapy as outlined above for cardiotoxicity in addition to standard ACLS. (Class IIb, LOE C)***

### 11.2.2 ACLS Modifications in Management of Severe Cardiotoxicity Due to Hypokalemia

Life-threatening hypokalemia is uncommon but can occur in the setting of gastrointestinal and renal losses and is associated with hypomagnesemia. Severe hypokalemia will alter cardiac tissue excitability and conduction. Hypokalemia can produce ECG changes such as U waves, T-wave flattening, and arrhythmias (especially if the patient is taking digoxin), particularly ventricular arrhythmias,<sup>432,433</sup> which, if left untreated, deteriorate to PEA or asystole.

Several studies reported an association with hypokalemia and development of ventricular fibrillation,<sup>434-437</sup> whereas a single animal study reported that hypokalemia lowered the ventricular fibrillation threshold.<sup>438</sup> However, the management of hypokalemia in the setting of cardiotoxicity, specifically torsades de pointes, is largely based on historical case reports that report slow infusion of potassium over hours.<sup>439</sup>

***The effect of bolus administration of potassium for cardiac arrest suspected to be secondary to hypokalemia is unknown and ill advised. (Class III, LOE C)***

### 11.3 Sodium (Na<sup>+</sup>)

Sodium is the major intravascular ion that influences serum osmolality. Sodium abnormalities are unlikely to lead to cardiac arrest, and there are no specific recommendations for either checking or treating sodium during cardiac arrest. Disturbances in sodium level are unlikely to be the primary cause of severe cardiovascular instability.

### 11.4 Magnesium (Mg<sup>++</sup>)

Magnesium is an essential electrolyte and an important cofactor for multiple enzymes, including ATPase. Magnesium is necessary for the movement of sodium, potassium, and calcium into and out of cells and plays an important role in stabilizing excitable membranes. The presence of a low plasma magnesium concentration has been associated with poor prognosis in cardiac arrest patients.<sup>435,440-443</sup>

### 11.5 Hypermagnesemia

Hypermagnesemia is defined as a serum magnesium concentration >2.2 mEq/L (normal: 1.3 to 2.2 mEq/L). Neurological symptoms of hypermagnesemia include muscular weakness, paralysis, ataxia, drowsiness, and confusion. Hypermagnesemia can produce vasodilation and hypotension.<sup>444</sup> Extremely high serum magnesium levels may produce a depressed level of consciousness, bradycardia, cardiac arrhythmias, hypoventilation, and cardiorespiratory arrest.<sup>435,442,443</sup>

#### 11.5.1 ACLS Modifications in Management of Cardiac Arrest and Severe Cardiotoxicity Due to Hypermagnesemia

**Administration of calcium (calcium chloride [10%] 5 to 10 mL or calcium gluconate [10%] 15 to 30 mL IV over 2 to 5 minutes) may be considered during cardiac arrest associated with hypermagnesemia.**

**(Class IIb, LOE C)**

## 11.6 Hypomagnesemia

Hypomagnesemia, defined as a serum magnesium concentration <1.3 mEq/L, is far more common than hypermagnesemia. Hypomagnesemia usually results from decreased absorption or increased loss of magnesium from either the kidneys or intestines (diarrhea). Alterations in thyroid hormone function, certain medications (eg, pentamidine, diuretics, alcohol), and malnourishment can also induce hypomagnesemia.

### 11.6.1 ACLS Modifications in Management of Cardiac Arrest and Severe Cardiotoxicity Due to Hypomagnesemia

***Hypomagnesemia can be associated with polymorphic ventricular tachycardia, including torsades de pointes, a pulseless form (polymorphic) of ventricular tachycardia. For cardiotoxicity and cardiac arrest, IV magnesium 1 to 2 g of MgSO<sub>4</sub> bolus IV push is recommended. (Class I, LOE C)***

## 11.7 Calcium (Ca<sup>++</sup>)

Calcium abnormality as an etiology of cardiac arrest is rare. There are no studies evaluating the treatment of hypercalcemia or hypocalcemia during arrest.

***However, empirical use of calcium (calcium chloride [10%] 5 to 10 mL OR calcium gluconate [10%] 15 to 30 mL IV over 2 to 5 minutes) may be considered when hyperkalemia or hypermagnesemia is suspected as the cause of cardiac arrest. (Class IIb, LOE C)***

## 12 Cardiac Arrest Associated With Trauma

BLS and ACLS for the trauma patient are fundamentally the same as that for the patient with primary cardiac arrest, with focus on support of airway, breathing, and circulation. In addition, reversible causes of cardiac arrest need to be considered. While CPR in the pulseless trauma patient has overall been considered futile, several reversible causes of cardiac arrest in the context of trauma are correctible and their prompt treatment could be life-saving. These include hypoxia, hypovolemia, diminished cardiac output secondary to pneumothorax or pericardial tamponade, and hypothermia.

### 12.1 BLS Modifications

When multisystem trauma is present or trauma involves the head and neck, the cervical spine must be stabilized. A jaw thrust should be used instead of a head tilt–chin lift to establish a patent airway. If breathing is inadequate and the patient's face is bloody, ventilation should be provided with a barrier device, a pocket mask, or a bag-mask device while maintaining cervical spine stabilization. Stop any visible hemorrhage using direct compression and appropriate dressings. If the patient is completely unresponsive despite rescue breathing, provide standard CPR and defibrillation as indicated.

### 12.2 ACLS Modifications

After initiation of BLS care, if bag-mask ventilation is inadequate, an advanced airway should be inserted while maintaining cervical spine stabilization. If insertion of an advanced airway is not possible and ventilation remains inadequate, experienced providers should consider a cricothyrotomy.

A unilateral decrease in breath sounds during positive-pressure ventilation should prompt the rescuer to consider the possibility of pneumothorax, hemothorax, or rupture of the diaphragm.

When the airway, oxygenation, and ventilation are adequate, evaluate and support circulation. Control ongoing bleeding where possible and replace lost volume if the losses appear to have significantly compromised circulating blood volume. Cardiac arrest resuscitation will likely be ineffective in the presence of uncorrected severe hypovolemia.

Treatment of PEA requires identification and treatment of reversible causes, such as severe hypovolemia, hypothermia, cardiac tamponade, or tension pneumothorax.<sup>445</sup> Development of bradycardic rhythms often indicates the presence of severe hypovolemia, severe hypoxemia, or cardiorespiratory failure. Ventricular fibrillation (VF) and pulseless ventricular tachycardia (VT) are treated with CPR and defibrillation. For treatment recommendations regarding cardiac tamponade in traumatic cardiac arrest, see [“Cardiac Arrest Caused by Cardiac Tamponade.”](#)

Resuscitative thoracotomy may be indicated in selected patients. A review of the literature from 1966 to 1999, carried out by the American College of Surgeons Committee on Trauma, found a survival rate of 7.8% (11.2% for penetrating injuries and 1.6% for blunt lesions) in trauma victims who would otherwise have 100% mortality.<sup>446</sup> Practitioners should consult the guidelines for withholding or terminating resuscitation, which were developed for victims of traumatic cardiac arrest by a joint committee of the National Association of EMS Physicians and the American College of Surgeons Committee on Trauma.<sup>447,448</sup>

### 12.3 Commotio Cordis

Commotio cordis is VF triggered by a blow to the anterior chest during a cardiac repolarization.<sup>449,450</sup> Blunt cardiac injury may result in cardiac contusion with injured myocardium and risk of ECG changes and arrhythmias. Even a small blow to the anterior chest during a cardiac repolarization, such as that imparted by the strike of a baseball or hockey puck, may trigger VF, so-called commotio cordis.<sup>451</sup> Events causing commotio cordis are most commonly seen in young persons up to 18 years of age who are engaged in sports but may occur during daily activities. Prompt recognition that a precordial blow may cause VF is critical. Rapid defibrillation is often life-saving for these frequently young victims of cardiac arrest. Provision of immediate BLS care using an automated external defibrillator (AED) and ACLS for VF in this setting is appropriate.

## 13 Cardiac Arrest in Accidental Hypothermia

Unintentional or accidental hypothermia is a serious and preventable health problem. Severe hypothermia (body temperature <30°C [86°F]) is associated with marked depression of critical body functions, which may make the victim appear clinically dead during the initial assessment. Therefore, lifesaving procedures should be initiated unless the victim is obviously dead (eg, rigor mortis, decomposition, hemisection, decapitation). The victim should be transported as soon as possible to a center where aggressive rewarming during resuscitation is possible.

### 13.1 Initial Care for Victims of Accidental Hypothermia

When the victim is extremely cold but has maintained a perfusing rhythm, the rescuer should focus on interventions that prevent further loss of heat and begin to rewarm the victim immediately. Additional interventions include the following:

Prevent additional evaporative heat loss by removing wet garments and insulating the victim from further environmental exposures. Passive rewarming is generally adequate for patients with mild hypothermia (temperature >34°C [93.2°F]).

For patients with moderate (30°C to 34°C [86°F to 93.2°F]) hypothermia with a perfusing rhythm, external warming techniques are appropriate.<sup>452</sup> Passive rewarming alone will be inadequate for these patients.<sup>453</sup>

For patients with severe hypothermia (<30°C [86°F]) with a perfusing rhythm, core rewarming is often used, although some have reported successful rewarming with active external warming techniques.<sup>454,455</sup> Active external warming techniques include forced air or other efficient surface-warming devices.

Patients with severe hypothermia and cardiac arrest can be rewarmed most rapidly with cardiopulmonary bypass.<sup>452,456-461</sup> Alternative effective core rewarming techniques include warm-water lavage of the thoracic cavity<sup>459,462-466</sup> and extracorporeal blood warming with partial bypass.<sup>467-469</sup>

Adjunctive core rewarming techniques include warmed IV or intraosseous (IO) fluids and warm humidified oxygen.<sup>470</sup> Heat transfer with these measures is not rapid, and should be considered supplementary to active warming techniques.

Do not delay urgent procedures such as airway management and insertion of vascular catheters. Although these patients may exhibit cardiac irritability, this concern should not delay necessary interventions.

Beyond these critical initial steps, the treatment of severe hypothermia (temperature <30°C [86°F]) in the field remains controversial. Many providers do not have the time or equipment to assess core body temperature or to institute aggressive rewarming techniques, although these methods should be initiated when available.

### 13.1.1 BLS Modifications

When the victim is hypothermic, pulse and respiratory rates may be slow or difficult to detect,<sup>471,472</sup> and the ECG may even show asystole. If the hypothermic victim has no signs of life, begin CPR without delay. If the victim is not breathing, start rescue breathing immediately.

The temperature at which defibrillation should first be attempted in the severely hypothermic patient and the number of defibrillation attempts that should be made have not been established. There are case reports of refractory ventricular arrhythmias with severe hypothermia; however, in a recent animal model it was found that an animal with a temperature of as low as 30°C had a better response to defibrillation than did normothermic animals in arrest.<sup>473,474</sup>

If VT or VF is present, defibrillation should be attempted. If VT or VF persists after a single shock, the value of deferring subsequent defibrillations until a target temperature is achieved is uncertain.

***It may be reasonable to perform further defibrillation attempts according to the standard BLS algorithm concurrent with rewarming strategies. (Class IIb, LOE C)***

To prevent further loss of core heat, remove wet garments and protect the victim from additional environmental exposure. Insofar as possible, this should be done while providing initial BLS therapies. Rewarming should be attempted when feasible.

### 13.1.2 ACLS Modifications

For unresponsive patients or those in arrest, advanced airway insertion is appropriate as recommended in the standard ACLS guidelines. Advanced airway management enables effective ventilation with warm, humidified oxygen and reduces the likelihood of aspiration in patients in periarrest.

ACLS management of cardiac arrest due to hypothermia focuses on aggressive active core rewarming techniques as the primary therapeutic modality. Conventional wisdom indicates that the hypothermic heart may be unresponsive to cardiovascular drugs, pacemaker stimulation, and defibrillation; however, the data to support this are essentially theoretical.<sup>475</sup> In addition, drug metabolism may be reduced, and there is a theoretical concern that medications could accumulate to toxic levels in the peripheral circulation if given repeatedly to the severely hypothermic victim. For these reasons, previous guidelines suggest withholding IV drugs if the victim's core body temperature is <30°C (86°F).

In the last decade a number of animal investigations have been performed evaluating both vasopressors and antiarrhythmic medications that could challenge some of this conventional wisdom.<sup>476-481</sup> In a meta-analysis of these studies, Wira et al<sup>482</sup> found that vasopressor medications (ie, epinephrine or vasopressin) increased rates of return of spontaneous circulation (ROSC) when compared with placebo (62% versus 17%;  $P < 0.0001$ ,  $n = 77$ ). Coronary perfusion pressures were increased in groups that received vasopressors compared with placebo. But groups given antiarrhythmics showed no improvement in ROSC when compared with control groups, although sample sizes were relatively small ( $n = 34$  and  $n = 40$ , respectively).

One small-animal investigation suggested that the application of standard normothermic ACLS algorithms using both drugs (ie, epinephrine and amiodarone) and defibrillation improved ROSC compared with a placebo arm of defibrillation only (91% versus 30%;  $P<0.01$ ;  $n=21$ ). Human trials of medication use in accidental hypothermia do not exist, although case reports of survival with use of intra-arrest medication have been reported.<sup>460,464,483</sup>

Given the lack of human evidence and relatively small number of animal investigations, the recommendation for administration or withholding of medications is not clear.

***It may be reasonable to consider administration of a vasopressor during cardiac arrest according to the standard ACLS algorithm concurrent with rewarming strategies. (Class IIb, LOE C)***

### 13.1.3 After ROSC

After ROSC, patients should continue to be warmed to a goal temperature of approximately 32° to 34°C; this can be maintained according to standard postarrest guidelines for mild to moderate hypothermia in patients for whom induced hypothermia is appropriate. For those with contraindications to induced hypothermia, rewarming can continue to normal temperatures.

Because severe hypothermia is frequently preceded by other disorders (eg, drug overdose, alcohol use, or trauma), the clinician must look for and treat these underlying conditions while simultaneously treating hypothermia.

### 13.1.4 Withholding and Cessation of Resuscitative Efforts

Multiple case reports indicate survival from accidental hypothermia even with prolonged CPR and downtimes.<sup>456,468</sup> Thus, patients with severe accidental hypothermia and cardiac arrest may benefit from resuscitation even in cases of prolonged downtime and prolonged CPR. Low serum potassium may indicate hypothermia, and not hypoxemia, as the primary cause of the arrest.<sup>484</sup> Patients should not be considered dead before warming has been provided.

## 14 Cardiac Arrest in Avalanche Victims

Avalanche-related deaths are on the rise in North America due to winter recreational activities, including backcountry skiing and snowboarding, helicopter and snowcat skiing, snowmobiling, out-of-bounds skiing, ice climbing, mountaineering, and snowshoeing. The most common causes of avalanche-related death are asphyxia, trauma, and hypothermia, or combinations of the 3. Rescue and resuscitation strategies focus on management of asphyxia and hypothermia, because most field research has been done on these 2 conditions.

Avalanches occur in areas that are difficult to access by rescuers in a timely manner, and burials frequently involve multiple victims. The decision to initiate full resuscitative measures should be determined by the number of victims, resources available, and likelihood of survival. Studies of avalanche victims demonstrate a progressive nonlinear reduction in survival as the time of avalanche burial lengthens.<sup>485-488</sup> The likelihood of survival is minimal when avalanche victims are buried >35 minutes with an obstructed airway and in cardiac arrest on extrication<sup>486,487,489-495</sup> or are buried for any length of time and in cardiac arrest on extrication with an obstructed airway and an initial core temperature of <32°C.<sup>487-489,493,496</sup>

It may be difficult to know with any certainty how long an avalanche victim has been buried. The core temperature at time of extrication provides a proxy for duration of burial. A case series<sup>496</sup> of buried avalanche victims showed a maximum cooling rate of 8°C per hour, whereas a case report<sup>493</sup> described a maximum cooling rate of 9°C per hour. These cooling rates suggest that at 35 minutes of burial, the core temperature may drop as low as 32°C.

If information on the duration of burial or the state of the airway on extrication is not available to the receiving physician, a serum potassium level of <8 mmol/L on hospital admission is a prognostic marker for ROSC<sup>490</sup> and survival to hospital discharge.<sup>489,496</sup> High potassium values are associated with asphyxia,<sup>489,496-498</sup> and there is an inverse correlation between admission K<sup>+</sup> and survival to discharge in all-cause hypothermic patients.<sup>489,499-502</sup> In a series of 32 avalanche survivors the highest serum K<sup>+</sup> was 6.4 mmol/L,<sup>496</sup> but there is a single case report of a 31-month-old child with a K<sup>+</sup> of 11.8 mmol/L presenting with hypothermia from exposure unrelated to an avalanche who survived.<sup>503</sup> This suggests that the upper survivable limit of potassium is unknown for children who are hypothermic and victims of avalanche.

***Full resuscitative measures, including extracorporeal rewarming when available, are recommended for all avalanche victims without the characteristics outlined above that deem them unlikely to survive or with any obvious lethal traumatic injury. (Class I, LOE C)***

## 15 Cardiac Arrest Due to Drowning

Each year drowning is responsible for more than 500 000 deaths worldwide.<sup>504</sup> Drowning is a leading preventable cause of unintentional morbidity and mortality.<sup>505,506</sup>

***All victims of drowning who require any form of resuscitation (including rescue breathing alone) should be transported to the hospital for evaluation and monitoring, even if they appear to be alert and demonstrate effective cardiorespiratory function at the scene. (Class I, LOE C)***

A number of terms are used to describe drowning.<sup>507</sup> To aid in use of consistent terminology and uniform reporting of data, use of the Utstein definitions and style of data reporting specific to drowning is recommended.<sup>508,509</sup>

Although survival is uncommon in victims who have undergone prolonged submersion and require prolonged resuscitation,<sup>510,511</sup> successful resuscitation with full neurological recovery has occurred occasionally after prolonged submersion in icy water<sup>512-515</sup> and, in some instances, warm water.<sup>516,517</sup> For this reason, scene resuscitation should be initiated and the victim transported to the ED unless there is obvious death (eg, rigor mortis, decomposition, hemisection, decapitation, lividity).

### 15.1 BLS Modifications

The most important and detrimental consequence of submersion is hypoxia; therefore, oxygenation, ventilation, and perfusion should be restored as rapidly as possible. This will require immediate bystander CPR plus activation of the EMS system. With the *2010 AHA Guidelines for CPR and ECC*, CPR now begins with chest compressions in a C-A-B sequence. However, the guidelines recommend that healthcare providers tailor the sequence based upon the presumed etiology of the arrest. Healthcare provider CPR for drowning victims should use the traditional A-B-C approach in view of the hypoxic nature of the arrest. Victims with only respiratory arrest usually respond after a few artificial breaths are given.

### 15.2 Recovery From the Water

When attempting to rescue a drowning victim, the rescuer should get to the victim as quickly as possible. It is crucial, however, that the rescuer pays constant attention to his or her own personal safety during the rescue process.

The reported incidence of cervical spine injury in drowning victims is low (0.009%).<sup>518,519</sup> Unnecessary cervical spine immobilization can impede adequate opening of the airway and delay delivery of rescue breaths.

***Routine stabilization of the cervical spine in the absence of circumstances that suggest a spinal injury is not recommended.<sup>519,520</sup> (Class III, LOE B)***

### 15.3 Rescue Breathing

The first and most important treatment of the drowning victim is the immediate provision of ventilation. Prompt initiation of rescue breathing increases the victim's chance of survival.<sup>521</sup> Rescue breathing is usually performed once the unresponsive victim is in shallow water or out of the water. Mouth-to-nose ventilation may be used as

an alternative to mouth-to-mouth ventilation if it is difficult for the rescuer to pinch the victim's nose, support the head, and open the airway in the water.

Management of the drowning victim's airway and breathing is similar to that recommended for any victim of cardiopulmonary arrest. Some victims aspirate no water because they develop laryngospasm or breath-holding.<sup>511,522</sup> Even if water is aspirated, there is no need to clear the airway of aspirated water, because only a modest amount of water is aspirated by the majority of drowning victims, and aspirated water is rapidly absorbed into the central circulation.<sup>511,523</sup> Attempts to remove water from the breathing passages by any means other than suction (eg, abdominal thrusts or the Heimlich maneuver) are unnecessary and potentially dangerous.<sup>523</sup>

***The routine use of abdominal thrusts or the Heimlich maneuver for drowning victims is not recommended. (Class III, LOE C)***

## 15.4 Chest Compressions

As soon as the unresponsive victim is removed from the water, the rescuer should open the airway, check for breathing, and if there is no breathing, give 2 rescue breaths that make the chest rise (if this was not done previously in the water). After delivery of 2 effective breaths, if a pulse is not definitely felt, the healthcare provider should begin chest compressions and provide cycles of compressions and ventilations according to the BLS guidelines. Once the victim is out of the water, if he or she is unresponsive and not breathing after delivery of 2 rescue breaths and is pulseless, rescuers should attach an AED and attempt defibrillation if a shockable rhythm is identified. It is only necessary to dry the chest area before applying the defibrillation pads and using the AED. If hypothermia is present, follow the recommendations in "[Cardiac Arrest in Accidental Hypothermia](#)."

## 15.5 Vomiting by the Victim During Resuscitation

The victim may vomit when the rescuer performs chest compressions or rescue breathing. In fact, in a 10-year study in Australia, two thirds of victims who received rescue breathing and 86% of those who required compressions and ventilations vomited.<sup>524</sup> If vomiting occurs, turn the victim to the side and remove the vomitus using your finger, a cloth, or suction. If spinal cord injury is suspected, the victim should be logrolled so that the head, neck, and torso are turned as a unit to protect the cervical spine.

## 15.6 ACLS Modifications

Victims in cardiac arrest may present with asystole, PEA, or pulseless VT/VF. For treatment of these rhythms, follow the appropriate PALS or ACLS guidelines. Case reports of pediatric patients document the use of surfactant for fresh water-induced respiratory distress, but further research is needed.<sup>525-528</sup> The use of extracorporeal membrane oxygenation in patients with severe hypothermia after submersion has been documented in case reports.<sup>514,515,529</sup>

## 16 Cardiac Arrest Associated With Electric Shock and Lightning Strikes

Injuries from electric shock and lightning strike result from the direct effects of current on the heart and brain, cell membranes, and vascular smooth muscle. Additional injuries result from the conversion of electric energy into heat energy as current passes through body tissues.<sup>530</sup>

### 16.1 Electric Shock

Fatal electrocutions may occur with household current; however, high-tension current generally causes the most serious injuries.<sup>531</sup> Contact with alternating current (the type of current commonly present in most North American households and commercial settings) may cause tetanic skeletal muscle contractions, "locking" the victim to the source of the electricity and thereby leading to prolonged exposure. The frequency of alternating current increases the likelihood of current flow through the heart during the relative refractory period, which is the "vulnerable period" of the cardiac cycle. This exposure can precipitate VF, which is analogous to the R-on-T phenomenon that occurs in nonsynchronized cardioversion.<sup>532</sup>

### 16.2 Lightning Strike



The National Weather Service estimates that an average of 70 deaths and 630 injuries occur due to lightning strikes in the United States each year.<sup>533</sup> Lightning strike injuries can vary widely, even among groups of people struck at the same time. Symptoms are mild in some victims, whereas fatal injuries occur in others.<sup>534,535</sup>

The primary cause of death in victims of lightning strike is cardiac arrest, which may be associated with primary VF or asystole.<sup>534-537</sup> Lightning acts as an instantaneous, massive direct-current shock, simultaneously depolarizing the entire myocardium.<sup>535,538</sup> In many cases intrinsic cardiac automaticity may spontaneously restore organized cardiac activity and a perfusing rhythm. However, concomitant respiratory arrest due to thoracic muscle spasm and suppression of the respiratory center may continue after ROSC. Unless ventilation is supported, a secondary hypoxic (asphyxial) cardiac arrest will develop.<sup>539</sup>

Lightning also can have myriad effects on the cardiovascular system, producing extensive catecholamine release or autonomic stimulation. The victim may develop hypertension, tachycardia, nonspecific ECG changes (including prolongation of the QT interval and transient T-wave inversion), and myocardial necrosis with release of creatinine kinase-MB fraction.

Lightning can produce a wide spectrum of peripheral and central neurological injuries. The current can produce brain hemorrhages, edema, and small-vessel and neuronal injury. Hypoxic encephalopathy can result from cardiac arrest.

Victims are most likely to die of lightning injury if they experience immediate respiratory or cardiac arrest and no treatment is provided. Patients who do not suffer respiratory or cardiac arrest, and those who respond to immediate treatment, have an excellent chance of recovery. Therefore, when multiple victims are struck simultaneously by lightning, rescuers should give the highest priority to patients in respiratory or cardiac arrest.

For victims in cardiac arrest, treatment should be early, aggressive, and persistent. Victims with respiratory arrest may require only ventilation and oxygenation to avoid secondary hypoxic cardiac arrest. Resuscitation attempts may have high success rates and efforts may be effective even when the interval before the resuscitation attempt is prolonged.<sup>539</sup>

### 16.3 BLS Modifications

The rescuer must first be certain that rescue efforts will not put him or her in danger of electric shock. When the scene is safe (ie, the danger of shock has been removed), determine the victim's cardiorespiratory status. If spontaneous respiration or circulation is absent, immediately initiate standard BLS resuscitation care, including the use of an AED to identify and treat VT or VF.

Maintain spinal stabilization during extrication and treatment if there is a likelihood of head or neck trauma.<sup>540,541</sup> Both lightning and electric shock often cause multiple trauma, including injury to the spine,<sup>541</sup> muscular strains, internal injuries from being thrown, and fractures caused by the tetanic response of skeletal muscles.<sup>542</sup> Remove smoldering clothing, shoes, and belts to prevent further thermal damage.

### 16.4 ACLS Modifications

No modification of standard ACLS care is required for victims of electric injury or lightning strike, with the exception of paying attention to possible cervical spine injury. Establishing an airway may be difficult for patients with electric burns of the face, mouth, or anterior neck. Extensive soft-tissue swelling may develop rapidly, complicating airway control measures. Thus, early intubation should be performed for patients with evidence of extensive burns even if the patient has begun to breathe spontaneously.

For victims with significant tissue destruction and in whom a pulse is regained, rapid IV fluid administration is indicated to counteract distributive/hypovolemic shock and to correct ongoing fluid losses due to third spacing. Fluid administration should be adequate to maintain diuresis and facilitate excretion of myoglobin, potassium, and other byproducts of tissue destruction (this is particularly true for patients with electric injury).<sup>538</sup> Regardless of the extent of external injuries after electrothermal shock, the underlying tissue damage can be far more extensive.

## 17 Cardiac Arrest Caused by Cardiac Tamponade

Cardiac tamponade can be a life-threatening event. Increasing fluid and pressure in the pericardium reduces atrial and ventricular filling. As filling is reduced, stroke volume and cardiac output fall, with associated hypotension leading to cardiac arrest. Rapid diagnosis and drainage of the pericardial fluid are required to avoid cardiovascular collapse.

Pericardiocentesis guided by echocardiography is a safe and effective method of relieving tamponade in a nonarrest setting, especially when used in conjunction with a pericardial drain, and may obviate the need for subsequent operating room treatment.<sup>543-547</sup>

***In the arrest setting, in the absence of echocardiography, emergency pericardiocentesis without imaging guidance can be beneficial. (Class IIa, LOE C)***

***Emergency department thoracotomy may improve survival compared with pericardiocentesis in patients with pericardial tamponade secondary to trauma who are in cardiac arrest or who are prearrest,<sup>548-550</sup> especially if gross blood causes clotting that blocks a pericardiocentesis needle.<sup>551</sup> (Class IIb, LOE C)***

## 18 Cardiac Arrest Following Cardiac Surgery

The incidence of cardiac arrest following cardiac surgery is in the range of 1–3%. Causes include conditions that may be readily reversed such as ventricular fibrillation, hypovolemia, cardiac tamponade, or tension pneumothorax. Pacing wires, if present, may reverse symptomatic bradycardia or asystole. A recent review may be helpful for those seeking additional information.<sup>552</sup>

### 18.1 Resternotomy

Studies of patients with cardiac arrest after cardiac surgery who are treated with resternotomy and internal cardiac compression have reported improved outcome compared with a standard protocol<sup>553-563</sup> when patients are treated by experienced personnel in intensive care units. Findings of similar quality studies<sup>564-568</sup> reported no difference in outcomes when resternotomy was compared with standard management of cardiac arrest after cardiac surgery. Resternotomy performed outside an intensive care unit generally has a very poor outcome.<sup>553,560,567</sup>

***For patients with cardiac arrest following cardiac surgery, it is reasonable to perform resternotomy in an appropriately staffed and equipped intensive care unit. (Class IIa, LOE B)***

***Despite rare case reports describing damage to the heart possibly due to external chest compressions,<sup>569,570</sup> chest compressions should not be withheld if emergency resternotomy is not immediately available. (Class IIa, LOE C)***

### 18.2 Mechanical Circulatory Support

Nine case series have reported survival of some post–cardiac surgery patients during cardiac arrest refractory to standard resuscitation measures following the use of extracorporeal membrane oxygenation<sup>571-575</sup> and cardiopulmonary bypass.<sup>563,576-578</sup>

***In post-cardiac surgery patients who are refractory to standard resuscitation procedures, mechanical circulatory support (eg, extracorporeal membrane oxygenation and cardiopulmonary bypass) may be effective in improving outcome. (Class IIb, LOE B)***

### 18.3 Pharmacological Intervention

Rebound hypertension following administration of pressors during resuscitation has the potential to induce significant bleeding in this group of patients. Results from a single study of epinephrine<sup>579</sup> and another study evaluating the choice of antiarrhythmics<sup>580</sup>

in patients with cardiac arrest following cardiac surgery were neutral. There is insufficient evidence on epinephrine dose, antiarrhythmic use, and other routine pharmacological interventions to recommend deviating from standard resuscitation guidelines when cardiac arrest occurs after cardiac surgery.

## 19 Authorship and Disclosures

### 19.1 2015 Writing Team

Eric J. Lavonas, Chair; Ian R. Drennan; Andrea Gabrielli; Alan C. Heffner; Christopher O. Hoyte; Aaron M. Orkin; Kelly N. Sawyer; Michael W. Donnino

**Table 3: Part 10: Special Circumstances of Resuscitation: 2015 Guidelines Update Writing Group Disclosures**

Open table in a [new window](#)

Part 10: Special Circumstances of Resuscitation: 2015 Guidelines Update Writing Group Disclosures								
Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honora	Expert Witness	Ownership Interest	Consultant/Advis Board	Other
Eric J. Lavonas	Rocky Mountain Poison & Drug Center; Denver Health and Hospital Authority	None	None	None	None	None	None	BTG International, Inc. – relationship between Employer and BTG†
Ian R. Drennan	St. Michael's Hospital Rescu	None	None	None	None	None	None	None
Andrea Gabrielli	University of Florida College of Medicine	None	None	None	For intraoperative cardiac ischemia*	None	None	None
Alan C. Heffner	UNC School of Medicine	None	None	Edwards Lifesciences	Defense and plaintiff consultant and causation expert in cases focused on airway management and CPR*	None	None	None

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Expert Witness	Ownership Interest	Consultant/Advisory Board	Other
Christopher O. Hoyte	University of Colorado School of Medicine	None	None	None	None	None	None	None
Aaron M. Orkin	University of Toronto	Canadian Institutes of Health Research*	None	None	None	None	None	Remote Health Initiative*
Kelly N. Sawyer	William Beaumont Hospital	None	None	None	None	None	None	None
Consultants								
Michael W. Donnino	Beth Israel Deaconess Med Center	None	None	None	None	None	American Heart Association†	None

This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be "significant" if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be "modest" if it the preceding definition.\*Modest. †Significant.

**19.2 2010 Writing Team**

Terry L. Vanden Hoek, Chair; Laurie J. Morrison; Michael Shuster; Michael Donnino; Elizabeth Sinz; Eric J. Lavonas; Farida M. Jeejeebhoy; Andrea Gabrielli

**Table 4: 2010 - Guidelines Part 12: Cardiac Arrest in Special Situations: Writing Group Disclosures**

Open table in a [new window](#)

2010 Guidelines Part 12: Cardiac Arrest in Special Situations: Writing Group Disclosures							
Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/Honoraria	Ownership Interest	Consultant/Advisory Board	Other
<b>Terry L. Vanden Hoek</b>	The University of Chicago-Associate Professor	*Vanden Hoek, Principal Investigator, Department of Defense, Office of Naval Research, "Proteomic					

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/ Advisory Board	Other
Laurie J. Morrison	St. Michaels Clinician scientist	None	None	None	None	None	None
Michael Shuster	Self-employed—emergency physician	None	None	None	None	None	None
Michael Donnino	Harvard Medical Faculty Physicians—Ph	† Corticosteroids in Post-arrest Shock (American Heart Association, Scientist Development Grant); Thiamine as a Metabolic Resuscitator in Septic Shock (NIH pending); * Statins in Sepsis (Eleanor Shore) Clinical Correlates to Influenza Genome (NIH); Thiamine Deficiency in Critically Ill (Harvard Medical School/NIH); Thiamine for Congestive Heart Failure (Baystate Incubator Fund-NON-industry, academic hospital funding)	None	None	None	None	None

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/ Advisory Board	Other
Elizabeth Sinz	Penn State Hershey Medical Center—Professor of Anesthesiology and Neurosurgery; AHA—Associate Science Editor	None	None	None	None	None	None

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/ Advisory Board	Other
Eric J. Lavonas	Rocky Mountain Poison & Drug Center; (RMPDC) Denver, Colo. Associate Director	<p>RMPDC performed research related to hydroxocobala prior to its licensure in the United States. This occurred prior to my arrival at RMPDC. RMPDC-DH performed work related to the development of hydroxocobala (CyanoKit, Dey LP) as a cyanide antidote. Various projects were completed in 2001, 2005, and 2006. Some of the sponsors of this research (EMD; Merck KGA) either no longer exist or no longer have an interest in hydroxocobala. I was not involved in this research, which was performed long before my arrival. RMPDC-DH does not have any current or pending hydroxocobala related projects. Neither I nor any other</p>	None	None	None	None	None

Writing Group Member	Employment	Research Grant	Other Research Support	Speakers' Bureau/ Honoraria	Ownership Interest	Consultant/ Advisory Board	Other
Farida M. Jeejeebhoy	Self employed cardiologist, affiliate with University Health Network/Mt Sinai and University of Toronto	None	None	None	None	None	None
Andrea Gabrielli	University of Florida—Professor of Anesthesiology and Surgery	†NIH-Biomarkers in Traumatic Brain Injury	None	None	None	None	None

- This table represents the relationships of writing group members that may be perceived as actual or reasonably perceived conflicts of interest as reported on the Disclosure Questionnaire, which all members of the writing group are required to complete and submit. A relationship is considered to be “significant” if (a) the person receives \$10 000 or more during any 12-month period, or 5% or more of the person's gross income; or (b) the person owns 5% or more of the voting stock or share of the entity, or owns \$10 000 or more of the fair market value of the entity. A relationship is considered to be “modest” if it is less than “significant” under the preceding definition.
- [?](#)\* Modest.
- [?](#)† Significant.

## 20 Footnotes

The American Heart Association requests that this document be cited as follows:

American Heart Association. Web-based Integrated Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care – [Part 10: Special Circumstances of Resuscitation](#). [ECCguidelines.heart.org](http://ECCguidelines.heart.org).

© Copyright 2015 American Heart Association, Inc.

## References

1. Wheeler E, Jones TS, Gilbert MK, Davidson PJ. Opioid overdose prevention programs providing naloxone to laypersons—United States, 2014. *MMWR Morb Mortal Wkly Rep*. 2015;64(23): 631-635.
2. Vanden Hoek TL, Morrison LJ, Shuster M, Donnino M, Sinz E, Lavonas EJ, Jeejeebhoy FM, Gabrielli A. Part 12: cardiac arrest in special situations: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(suppl 3):S829–S861. doi: 10.1161/ CIRCULATIONAHA.110.971069.
3. Deakin CD, Morrison LJ, Morley PT, Callaway CW, Kerber RE, Kronick SL, Lavonas EJ, Link MS, Neumar RW, Otto CW, Parr M, Shuster M, Sunde K, Peberdy MA, Tang W, Hoek TL, Böttiger BW, Drajer S, Lim SH, Nolan JP; Advanced Life Support Chapter Collaborators. Part 8: advanced life support: 2010 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2010;81 suppl 1:e93–e174. doi: 10.1016/j.resuscitation.2010.08.027.



4. Hazinski MF, Nolan JP, Aickin R, Bhanji F, Billi JE, Callaway CW, Castren M, de Caen AR, Ferrer JME, Finn JC, Gent LM, Griffin RE, Iverson S, Lang E, Lim SH, Maconochie IK, Montgomery WH, Morley PT, Nadkarni VM, Neumar RW, Nikolaou NI, Perkins GD, Perlman JM, Singletary EM, Soar J, Travers AH, Welsford M, Wyllie J, Zideman DA. Part 1: executive summary: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2015;132(suppl 1):S2–S39. doi: 10.1161/CIR.0000000000000270.
5. Nolan JP, Hazinski MF, Aickin R, Bhanji F, Billi JE, Callaway CW, Castren M, de Caen AR, Ferrer JME, Finn JC, Gent LM, Griffin RE, Iverson S, Lang E, Lim SH, Maconochie IK, Montgomery WH, Morley PT, Nadkarni VM, Neumar RW, Nikolaou NI, Perkins GD, Perlman JM, Singletary EM, Soar J, Travers AH, Welsford M, Wyllie J, Zideman DA. Part 1: executive summary: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2015. In press.
6. Callaway CW, Soar J, Aibiki M, Böttiger BW, Brooks SC, Deakin CD, Donnino MW, Drajer S, Kloeck W, Morley PT, Morrison LJ, Neumar RW, Nicholson TC, Nolan JP, Okada K, O'Neil BJ, Paiva EF, Parr MJ, Wang TL, Witt J; on behalf of the Advanced Life Support Chapter Collaborators. Part 4: advanced life support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2015;132(suppl 1):S84–S145. doi: 10.1161/CIR.0000000000000273.
7. Soar J, Callaway CW, Aibiki M, Böttiger BW, Brooks SC, Deakin CD, Donnino MW, Drajer S, Kloeck W, Morley PT, Morrison LJ, Neumar RW, Nicholson TC, Nolan JP, Okada K, O'Neil BJ, Paiva EF, Parr MJ, Wang TL, Witt J; on behalf of the Advanced Life Support Chapter Collaborators. Part 4: advanced life support: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2015. In press.
8. O'Connor D, Green S, Higgins J, eds. Chapter 5: defining the review questions and developing criteria for including studies. In: *The Cochrane Collaboration*. Higgins JPT, Green S, eds. *Cochrane Handbook for Systematic Reviews of Interventions*. Version 5.1.0. 2011. <http://hand-book.cochrane.org/>. Accessed May 6, 2015.
9. Schünemann H, Brozek J, Guyatt G, Oxman A. *GRADE Handbook*. 2013. <http://www.guidelinedevelopment.org/handbook/>. Accessed May 6, 2015.
10. Morley PT, Lang E, Aickin R, Billi JE, Eigel B, Ferrer JME, Finn JC, Gent LM, Griffin RE, Hazinski MF, Maconochie IK, Montgomery WH, Morrison LJ, Nadkarni VM, Nikolaou NI, Nolan JP, Perkins GD, Sayre MR, Travers AH, Wyllie J, Zideman DA. Part 2: evidence evaluation and management of conflicts of interest: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Circulation*. 2015;132(suppl 1): S40–S50. doi: 10.1161/CIR.0000000000000271.
11. Lang E, Morley PT, Aickin R, Billi JE, Eigel B, Ferrer JME, Finn JC, Gent LM, Griffin RE, Hazinski MF, Maconochie IK, Montgomery WH, Morrison LJ, Nadkarni VM, Nikolaou NI, Nolan JP, Perkins GD, Sayre MR, Travers AH, Wyllie J, Zideman DA. Part 2: evidence evaluation and management of conflicts of interest: 2015 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations. *Resuscitation*. 2015. In press.
12. Jeejeebhoy FM, Zelop CM, Lipman S, Carvalho B, Joglar J, Mhyre JM, Katz VL, Lapinsky SE, Einav S, Warnes CA, Page RL, Griffin RE, Jain A, Dainty KN, Arafeh J, Windrim R, Koren G, Callaway C; on behalf of the American Heart Association Emergency Cardiovascular Care Committee, Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation, Council on Cardiovascular Diseases in the Young, and Council on Clinical Cardiology. Cardiac arrest in pregnancy: a scientific statement from the American Heart Association. *Circulation*. 2015. In press. doi: 10.1161/CIR.0000000000000300.
13. Mhyre JM, Tsen LC, Einav S, Kuklina EV, Leffert LR, Bateman BT. Cardiac arrest during hospitalization for delivery in the United States, 1998-2011. *Anesthesiology*. 2014;120:810–818. doi: 10.1097/ALN.0000000000000159.
14. Centers for Disease Control and Prevention. Pregnancy mortality surveillance system <http://www.cdc.gov/reproductivehealth/maternalinfanthealth/pmss.html>. Accessed April 2, 2015.
15. Public Health Agency of Canada. Maternal mortality in Canada. [http://sogc.org/wp-content/uploads/2014/05/REVISED\\_Mortality-EN-Final-PDF.pdf](http://sogc.org/wp-content/uploads/2014/05/REVISED_Mortality-EN-Final-PDF.pdf). Accessed April 2, 2015.
16. Hogan MC, Foreman KJ, Naghavi M, Ahn SY, Wang M, Makela SM, Lopez AD, Lozano R, Murray CJL. Maternal mortality for 181 countries, 1980–2008: a systematic analysis of progress towards Millennium Development Goal 5. 2010. [http://cdrwww.who.int/pmnch/topics/maternal/20100402\\_ihmearticle.pdf](http://cdrwww.who.int/pmnch/topics/maternal/20100402_ihmearticle.pdf). Accessed April 2, 2015.
17. Creanga AA, Berg CJ, Ko JY, Farr SL, Tong VT, Bruce FC, Callaghan WM. Maternal mortality and morbidity in the United States: where are we now? *J Womens Health (Larchmt)*. 2014;23:3–9. doi: 10.1089/jwh.2013.4617.
18. Ueland K, Novy MJ, Peterson EN, Metcalfe J. Maternal cardiovascular dynamics. IV. The influence of gestational age on the maternal cardiovascular response to posture and exercise. *Am J Obstet Gynecol*. 1969;104:856–864.
19. Goodwin AP, Pearce AJ. The human wedge. A manoeuvre to relieve aortocaval compression during resuscitation in late pregnancy. *Anaesthesia*. 1992;47:433–434.
20. Rees GA, Willis BA. Resuscitation in late pregnancy. *Anaesthesia*. 1988;43:347–349.
- 21.

- Cyna AM, Andrew M, Emmett RS, Middleton P, Simmons SW. Techniques for preventing hypotension during spinal anaesthesia for caesarean section. *Cochrane Database Syst Rev.* 2006;CD002251.
22. Dijkman A, Huisman CM, Smit M, Schutte JM, Zwart JJ, van Roosmalen JJ, Oepkes D. Cardiac arrest in pregnancy: increasing use of perimortem caesarean section due to emergency skills training? *BJOG.* 2010;117:282–287. doi: 10.1111/j.1471-0528.2009.02461.x.
  23. Page-Rodriguez A, Gonzalez-Sanchez JA. Perimortem cesarean section of twin pregnancy: case report and review of the literature. *Acad Emerg Med.* 1999;6:1072–1074.
  24. Cardosi RJ, Porter KB. Cesarean delivery of twins during maternal cardio-pulmonary arrest. *Obstet Gynecol.* 1998;92(4 Pt 2):695–697.
  25. Rees SG, Thurlow JA, Gardner IC, Scrutton MJ, Kinsella SM. Maternal cardiovascular consequences of positioning after spinal anaesthesia for Caesarean section: left 15 degree table tilt vs. left lateral. *Anaesthesia.* 2002;57:15–20.
  26. Mendonca C, Griffiths J, Ateleanu B, Collis RE. Hypotension following combined spinal-epidural anaesthesia for Caesarean section. Left lateral position vs. tilted supine position. *Anaesthesia.* 2003;58:428–431.
  27. Svinos H. Towards evidence based emergency medicine: best BETs from the Manchester Royal Infirmary. BET 1. Emergency caesarean section in cardiac arrest before the third trimester. *Emerg Med J.* 2008;25:764–765. doi: 10.1136/emj.2008.066860.
  28. Katz V, Balderston K, DeFreest M. Perimortem cesarean delivery: were our assumptions correct? *Am J Obstet Gynecol.* 2005;192:1916–1920; discussion 1920. doi: 10.1016/j.ajog.2005.02.038.
  29. Einav S, Kaufman N, Sela HY. Maternal cardiac arrest and perimortem caesarean delivery: evidence or expert-based? *Resuscitation.* 2012;83:1191–1200. doi: 10.1016/j.resuscitation.2012.05.005.
  30. Kam CW. Perimortem caesarean sections (PMCS). *J Accid Emerg Med.* 1994;11:57–58.
  31. Kupas DF, Harter SC, Vosk A. Out-of-hospital perimortem cesarean section. *Prehosp Emerg Care.* 1998;2:206–208.
  32. Oates S, Williams GL, Rees GA. Cardiopulmonary resuscitation in late pregnancy. *BMJ.* 1988;297:404–405.
  33. Jaff MR, McMurtry MS, Archer SL, Cushman M, Goldenberg N, Goldhaber SZ, Jenkins JS, Kline JA, Michaels AD, Thistlethwaite P, Vedantham S, White RJ, Zierler BK; American Heart Association Council on Cardiopulmonary, Critical Care, Perioperative and Resuscitation; American Heart Association Council on Peripheral Vascular Disease; American Heart Association Council on Arteriosclerosis, Thrombosis and Vascular Biology. Management of massive and submassive pulmonary embolism, iliofemoral deep vein thrombosis, and chronic thromboembolic pulmonary hypertension: a scientific statement from the American Heart Association. *Circulation.* 2011;123:1788–1830. doi: 10.1161/CIR.0b013e318214914f.
  34. Schmid C, Zietlow S, Wagner TO, Laas J, Borst HG. Fulminant pulmonary embolism: symptoms, diagnostics, operative technique, and results. *Ann Thorac Surg.* 1991;52:1102–1105; discussion 1105.
  35. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Massive pulmonary embolism. *Circulation.* 2006;113:577–582. doi: 10.1161/CIRCULATIONAHA.105.592592.
  36. Kasper W, Konstantinides S, Geibel A, Olschewski M, Heinrich F, Grosser KD, Rauber K, Iversen S, Redecker M, Kienast J. Management strategies and determinants of outcome in acute major pulmonary embolism: results of a multicenter registry. *J Am Coll Cardiol.* 1997;30:1165–1171.
  37. Janata K. Managing pulmonary embolism. *BMJ.* 2003;326:1341–1342. doi: 10.1136/bmj.326.7403.1341.
  38. Kürkcıyan I, Meron G, Sterz F, Janata K, Domanovits H, Holzer M, Berzlanovich A, Bankl HC, Laggner AN. Pulmonary embolism as a cause of cardiac arrest: presentation and outcome. *Arch Intern Med.* 2000;160:1529–1535.
  39. Hess EP, Campbell RL, White RD. Epidemiology, trends, and outcome of out-of-hospital cardiac arrest of non-cardiac origin. *Resuscitation.* 2007;72:200–206. doi: 10.1016/j.resuscitation.2006.06.040.
  40. Courtney DM, Kline JA. Identification of prearrest clinical factors associated with outpatient fatal pulmonary embolism. *Acad Emerg Med.* 2001;8:1136–1142.
  41. Courtney DM, Kline JA. Prospective use of a clinical decision rule to identify pulmonary embolism as likely cause of outpatient cardiac arrest. *Resuscitation.* 2005;65:57–64. doi: 10.1016/j.resuscitation.2004.07.018.
  42. Comess KA, DeRook FA, Russell ML, Tognazzi-Evans TA, Beach KW. The incidence of pulmonary embolism in unexplained sudden cardiac arrest with pulseless electrical activity. *Am J Med.* 2000;109:351–356.
  43. Aghayev A, Furlan A, Patil A, Gumus S, Jeon KN, Park B, Bae KT. The rate of resolution of clot burden measured by pulmonary CT angiography in patients with acute pulmonary embolism. *AJR Am J Roentgenol.* 2013;200:791–797. doi: 10.2214/AJR.12.8624.
  44. Wood KE. Major pulmonary embolism: review of a pathophysiologic approach to the golden hour of hemodynamically significant pulmonary embolism. *Chest.* 2002;121:877–905.

45. Neumar RW, Otto CW, Link MS, Kronick SL, Shuster M, Callaway CW, Kudenchuk PJ, Ornato JP, McNally B, Silvers SM, Passman RS, White RD, Hess EP, Tang W, Davis D, Sinz E, Morrison LJ. Part 8: adult advanced cardiovascular life support: 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(suppl 3):S729–S767. doi: 10.1161/CIRCULATIONAHA.110.970988.
46. Böttiger BW, Böhrer H, Bach A, Motsch J, Martin E. Bolus injection of thrombolytic agents during cardiopulmonary resuscitation for massive pulmonary embolism. *Resuscitation*. 1994;28:45–54.
47. Er F, Nia AM, Gassanov N, Caglayan E, Erdmann E, Hoppe UC. Impact of rescue-thrombolysis during cardiopulmonary resuscitation in patients with pulmonary embolism. *PLoS One*. 2009;4:e8323. doi: 10.1371/journal.pone.0008323.
48. Lederer W, Lichtenberger C, Pechlaner C, Kroesen G, Baubin M. Recombinant tissue plasminogen activator during cardiopulmonary resuscitation in 108 patients with out-of-hospital cardiac arrest. *Resuscitation*. 2001;50:71–76.
49. Böttiger BW, Martin E. Thrombolytic therapy during cardiopulmonary resuscitation and the role of coagulation activation after cardiac arrest. *Curr Opin Crit Care*. 2001;7:176–183.
50. Ruiz-Bailén M, Aguayo-de-Hoyos E, Serrano-Córcoles MC, Díaz-Castellanos MA, Fierro-Rosón JL, Ramos-Cuadra JA, Rodríguez-Elvira M, Torres-Ruiz JM. Thrombolysis with recombinant tissue plasminogen activator during cardiopulmonary resuscitation in fulminant pulmonary embolism. A case series. *Resuscitation*. 2001;51:97–101.
51. Janata K, Holzer M, Kürkcayan I, Losert H, Riedmüller E, Pikula B, Laggner AN, Laczika K. Major bleeding complications in cardiopulmonary resuscitation: the place of thrombolytic therapy in cardiac arrest due to massive pulmonary embolism. *Resuscitation*. 2003;57:49–55.
52. Lederer W, Lichtenberger C, Pechlaner C, Kinzl J, Kroesen G, Baubin M. Long-term survival and neurological outcome of patients who received recombinant tissue plasminogen activator during out-of-hospital cardiac arrest. *Resuscitation*. 2004;61:123–129. doi: 10.1016/j.resuscitation.2003.12.016.
53. Stadlbauer KH, Krismer AC, Arntz HR, Mayr VD, Lienhart HG, Böttiger BW, Jahn B, Lindner KH, Wenzel V. Effects of thrombolysis during out-of-hospital cardiopulmonary resuscitation. *Am J Cardiol*. 2006;97:305–308. doi: 10.1016/j.amjcard.2005.08.045.
54. Renard A, Verret C, Jost D, Meynard JB, Tricheure J, Hersan O, Fontaine D, Briche F, Benner P, de Stabenrath O, Bartou C, Segal N, Domanski L. Impact of fibrinolysis on immediate prognosis of patients with out-of-hospital cardiac arrest. *J Thromb Thrombolysis*. 2011;32:405–409. doi: 10.1007/s11239-011-0619-0.
55. Dirican A, Ozkaya S, Atas AE, Ulu EK, Kitapci I, Ece F. Thrombolytic treatment (alteplase; rt-Pa) in acute massive pulmonary embolism and cardiopulmonary arrest. *Drug Des Devel Ther*. 2014;8:759–763. doi: 10.2147/DDDT.S61679.
56. Böttiger BW, Arntz HR, Chamberlain DA, Bluhmki E, Belmans A, Danays T, Carli PA, Adgey JA, Bode C, Wenzel V; TROICA Trial Investigators; European Resuscitation Council Study Group. Thrombolysis during resuscitation for out-of-hospital cardiac arrest. *N Engl J Med*. 2008;359:2651–2662. doi: 10.1056/NEJMoa070570.
57. Böttiger BW, Bode C, Kern S, Gries A, Gust R, Glätzer R, Bauer H, Motsch J, Martin E. Efficacy and safety of thrombolytic therapy after initially unsuccessful cardiopulmonary resuscitation: a prospective clinical trial. *Lancet*. 2001;357:1583–1585. doi: 10.1016/S0140-6736(00)04726-7.
58. Logan JK, Pantle H, Huiras P, Bessman E, Bright L. Evidence-based diagnosis and thrombolytic treatment of cardiac arrest or periarrest due to suspected pulmonary embolism. *Am J Emerg Med*. 2014;32:789–796. doi: 10.1016/j.ajem.2014.04.032.
59. Konstantinov IE, Saxena P, Koniuszko MD, Alvarez J, Newman MA. Acute massive pulmonary embolism with cardiopulmonary resuscitation: management and results. *Tex Heart Inst J*. 2007;34:41–45; discussion 45.
60. Doerge HC, Schoendube FA, Loeser H, Walter M, Messmer BJ. Pulmonary embolectomy: review of a 15-year experience and role in the age of thrombolytic therapy. *Eur J Cardiothorac Surg*. 1996;10:952–957.
61. Fava M, Loyola S, Bertoni H, Dougnac A. Massive pulmonary embolism: percutaneous mechanical thrombectomy during cardiopulmonary resuscitation. *J Vasc Interv Radiol*. 2005;16:119–123. doi: 10.1097/01.RVI.0000146173.85401.BA.
62. Böttiger BW, Arntz HR, Chamberlain DA, Bluhmki E, Belmans A, Danays T, Carli PA, Adgey JA, Bode C, Wenzel V. Thrombolysis during resuscitation for out-of-hospital cardiac arrest. *N Engl J Med*. 2008;359:2651–2662.
63. Abu-Laban RB, Christenson JM, Innes GD, van Beek CA, Wanger KP, McKnight RD, MacPhail IA, Puskaric J, Sadowski RP, Singer J, Schechter MT, Wood VM. Tissue plasminogen activator in cardiac arrest with pulseless electrical activity. *N Engl J Med*. 2002;346:1522–1528.
64. Centers for Disease Control and Prevention. Injury prevention and control: prescription drug overdose. <http://www.cdc.gov/drugoverdose/index.html>. Accessed March 17, 2015.
65. Hedegaard H, Chen LH, Warner M. Drug-poisoning deaths involving heroin: United States, 2000–2013. <http://www.cdc.gov/nchs/data/databriefs/db190.htm>. Accessed March 17, 2015.

66. Centers for Disease Control and Prevention. Fatal injury data. <http://www.cdc.gov/injury/wisqars/fatal.html>. Accessed April 4, 2015.
67. Carter CI, Graham B. Opioid overdose prevention and response in Canada. [http://drugpolicy.ca/wp-content/uploads/2014/07/CDPC\\_OverdosePreventionPolicy\\_Final\\_July2014.pdf](http://drugpolicy.ca/wp-content/uploads/2014/07/CDPC_OverdosePreventionPolicy_Final_July2014.pdf). Accessed March 17, 2015.
68. Jones CM, Paulozzi LJ, Mack KA; Centers for Disease Control and Prevention (CDC). Alcohol involvement in opioid pain reliever and benzodiazepine drug abuse-related emergency department visits and drug-related deaths - United States, 2010. *MMWR Morb Mortal Wkly Rep*. 2014;63:881–885.
69. Madadi P, Hildebrandt D, Lauwers AE, Koren G. Characteristics of opioid-users whose death was related to opioid-toxicity: a population-based study in Ontario, Canada. *PLoS One*. 2013;8:e60600. doi: 10.1371/journal.pone.0060600.
70. Webster LR, Cochella S, Dasgupta N, Fakata KL, Fine PG, Fishman SM, Grey T, Johnson EM, Lee LK, Passik SD, Peppin J, Porucznik CA, Ray A, Schnoll SH, Stieg RL, Wakeland W. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Med*. 2011;12 suppl 2:S26–S35. doi: 10.1111/j.1526-4637.2011.01134.x.
71. Paulozzi LJ, Logan JE, Hall AJ, McKinstry E, Kaplan JA, Crosby AE. A comparison of drug overdose deaths involving methadone and other opioid analgesics in West Virginia. *Addiction*. 2009;104:1541–1548. doi: 10.1111/j.1360-0443.2009.02650.x.
72. Krantz MJ, Kutinsky IB, Robertson AD, Mehler PS. Dose-related effects of methadone on QT prolongation in a series of patients with torsade de pointes. *Pharmacotherapy*. 2003;23:802–805.
73. Eap CB, Crettol S, Rougier JS, Schlöpfer J, Sintra Grilo L, Déglon JJ, Besson J, Croquette-Krokar M, Carrupt PA, Abriel H. Stereoselective block of hERG channel by (S)-methadone and QT interval prolongation in CYP2B6 slow metabolizers. *Clin Pharmacol Ther*. 2007;81:719–728. doi: 10.1038/sj.cpt.6100120.
74. Krantz MJ, Martin J, Stimmel B, Mehta D, Haigney MC. QTc interval screening in methadone treatment. *Ann Intern Med*. 2009;150:387–395.
75. Stallvik M, Nordstrand B, Kristensen Ø, Bathen J, Skogvoll E, Spigset O. Corrected QT interval during treatment with methadone and buprenorphine—relation to doses and serum concentrations. *Drug Alcohol Depend*. 2013;129:88–93. doi: 10.1016/j.drugalcdep.2012.09.016.
76. Chou R, Weimer MB, Dana T. Methadone overdose and cardiac arrhythmia potential: findings from a review of the evidence for an American Pain Society and College on Problems of Drug Dependence clinical practice guideline. *J Pain*. 2014;15:338–365. doi: 10.1016/j.jpain.2014.01.495.
77. Lipski J, Stimmel B, Donoso E. The effect of heroin and multiple drug abuse on the electrocardiogram. *Am Heart J*. 1973;86:663–668.
78. Labi M. Paroxysmal atrial fibrillation in heroin intoxication. *Ann Intern Med*. 1969;71:951–959.
79. Bahr J, Klingler H, Panzer W, Rode H, Kettler D. Skills of lay people in checking the carotid pulse. *Resuscitation*. 1997;35:23–26.
80. Eberle B, Dick WF, Schneider T, Wisser G, Doetsch S, Tzanova I. Checking the carotid pulse check: diagnostic accuracy of first responders in patients with and without a pulse. *Resuscitation*. 1996;33:107–116.
81. Leach M. Naloxone: a new therapeutic and diagnostic agent for emergency use. *JACEP*. 1973;2:21–23.
82. Sporer KA, Firestone J, Isaacs SM. Out-of-hospital treatment of opioid overdoses in an urban setting. *Acad Emerg Med*. 1996;3:660–667.
83. Robertson TM, Hendey GW, Stroh G, Shalit M. Intranasal naloxone is a viable alternative to intravenous naloxone for prehospital narcotic overdose. *Prehosp Emerg Care*. 2009;13:512–515. doi: 10.1080/10903120903144866.
84. Evans LE, Swainson CP, Roscoe P, Prescott LF. Treatment of drug overdosage with naloxone, a specific narcotic antagonist. *Lancet*. 1973;1:452–455.
85. Kelly AM, Kerr D, Dietze P, Patrick I, Walker T, Koutsogiannis Z. Randomised trial of intranasal versus intramuscular naloxone in prehospital treatment for suspected opioid overdose. *Med J Aust*. 2005;182:24–27.
86. Barton ED, Colwell CB, Wolfe T, Fosnocht D, Gravitz C, Bryan T, Dunn W, Benson J, Bailey J. Efficacy of intranasal naloxone as a needleless alternative for treatment of opioid overdose in the pre-hospital setting. *J Emerg Med*. 2005;29:265–271. doi: 10.1016/j.jemermed.2005.03.007.
87. Wolfe TR, Braude DA. Intranasal medication delivery for children: a brief review and update. *Pediatrics*. 2010;126:532–537. doi: 10.1542/peds.2010-0616.
88. Loimer N, Hofmann P, Chaudhry HR. Nasal administration of naloxone is as effective as the intravenous route in opiate addicts. *Int J Addict*. 1994;29:819–827.
- 89.

- Doe-Simkins M, Walley AY, Epstein A, Moyer P. Saved by the nose: bystander-administered intranasal naloxone hydrochloride for opioid overdose. *Am J Public Health*. 2009;99:788–791. doi: 10.2105/AJPH.2008.146647.
90. Wanger K, Brough L, Macmillan I, Goulding J, MacPhail I, Christenson JM. Intravenous vs subcutaneous naloxone for out-of-hospital management of presumed opioid overdose. *Acad Emerg Med*. 1998;5:293–299.
91. Baumann BM, Patterson RA, Parone DA, Jones MK, Glaspey LJ, Thompson NM, Stauss MP, Haroz R. Use and efficacy of nebulized naloxone in patients with suspected opioid intoxication. *Am J Emerg Med*. 2013;31:585–588. doi: 10.1016/j.ajem.2012.10.004.
92. Weber JM, Tataris KL, Hoffman JD, Aks SE, Mycyk MB. Can nebulized naloxone be used safely and effectively by emergency medical services for suspected opioid overdose? *Prehosp Emerg Care*. 2012;16:289–292. doi: 10.3109/10903127.2011.640763.
93. Greenberg MI, Roberts JR, Baskin SI. Endotracheal naloxone reversal of morphine-induced respiratory depression in rabbits. *Ann Emerg Med*. 1980;9:289–292.
94. Posner J, Burke CA. The effects of naloxone on opiate and placebo analgesia in healthy volunteers. *Psychopharmacology (Berl)*. 1985;87:468–472.
95. Borrás MC, Becerra L, Ploghaus A, Gostic JM, DaSilva A, Gonzalez RG, Borsook D. fMRI measurement of CNS responses to naloxone infusion and subsequent mild noxious thermal stimuli in healthy volunteers. *J Neurophysiol*. 2004;91:2723–2733. doi: 10.1152/jn.00249.2003.
96. Clarke SF, Dargan PI, Jones AL. Naloxone in opioid poisoning: walking the tightrope. *Emerg Med J*. 2005;22:612–616. doi: 10.1136/emj.2003.009613.
97. Walley AY, Doe-Simkins M, Quinn E, Pierce C, Xuan Z, Ozonoff A. Opioid overdose prevention with intranasal naloxone among people who take methadone. *J Subst Abuse Treat*. 2013;44:241–247. doi: 10.1016/j.jsat.2012.07.004.
98. Clark AK, Wilder CM, Winstanley EL. A systematic review of community opioid overdose prevention and naloxone distribution programs. *J Addict Med*. 2014;8:153–163. doi: 10.1097/ADM.0000000000000034.
99. Lagu T, Anderson BJ, Stein M. Overdoses among friends: drug users are willing to administer naloxone to others. *J Subst Abuse Treat*. 2006;30:129–133. doi: 10.1016/j.jsat.2005.05.010.
100. Tracy M, Piper TM, Ompad D, Bucciarelli A, Coffin PO, Vlahov D, Galea S. Circumstances of witnessed drug overdose in New York City: implications for intervention. *Drug Alcohol Depend*. 2005;79:181–190. doi: 10.1016/j.drugalcdep.2005.01.010.
101. US Food and Drug Administration. FDA News Release: FDA approves new hand-held auto-injector to reverse opioid overdose. 2015. <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm391465.htm>. Accessed May 11, 2015.
102. Tataris KL, Weber JM, Stein-Spencer L, Aks SE. The effect of prehospital nebulized naloxone on suspected heroin-induced bronchospasm. *Am J Emerg Med*. 2013;31:717–718. doi: 10.1016/j.ajem.2012.11.025.
103. Bingham K, Klaiman M, Leece P, Orkin A, Buick J. An agenda for naloxone distribution research and practice: Meeting report of the Surviving Opioid Overdose with Naloxone (SOON) International Working Group. *J Addict Res Ther*. 2015;6:212.
104. Kerr D, Kelly AM, Dietze P, Jolley D, Barger B. Randomized controlled trial comparing the effectiveness and safety of intranasal and intramuscular naloxone for the treatment of suspected heroin overdose. *Addiction*. 2009;104:2067–2074. doi: 10.1111/j.1360-0443.2009.02724.x.
105. Boyd JJ, Kuisma MJ, Alaspää AO, Vuori E, Repo JV, Randell TT. Recurrent opioid toxicity after pre-hospital care of presumed heroin overdose patients. *Acta Anaesthesiol Scand*. 2006;50:1266–1270. doi: 10.1111/j.1399-6576.2006.01172.x.
106. Buajordet I, Naess AC, Jacobsen D, Brørs O. Adverse events after naloxone treatment of episodes of suspected acute opioid overdose. *Eur J Emerg Med*. 2004;11:19–23.
107. Cantwell K, Dietze P, Flander L. The relationship between naloxone dose and key patient variables in the treatment of non-fatal heroin overdose in the prehospital setting. *Resuscitation*. 2005;65:315–319. doi: 10.1016/j.resuscitation.2004.12.012.
108. Cetrullo C, Di Nino GF, Melloni C, Pieri C, Zanoni A. [Naloxone antagonism toward opiate analgesic drugs. Clinical experimental study]. *Minerva Anesthesiol*. 1983;49:199–204.
109. Nielsen K, Nielsen SL, Siersma V, Rasmussen LS. Treatment of opioid overdose in a physician-based prehospital EMS: frequency and long-term prognosis. *Resuscitation*. 2011;82:1410–1413. doi: 10.1016/j.resuscitation.2011.05.027.
110. Osterwalder JJ. Naloxone—for intoxications with intravenous heroin and heroin mixtures—harmless or hazardous? A prospective clinical study. *J Toxicol Clin Toxicol*. 1996;34:409–416.
111. Stokland O, Hansen TB, Nilsen JE. [Prehospital treatment of heroin intoxication in Oslo in 1996]. *Tidsskr Nor Laegeforen*. 1998;118:3144–3146.
- 112.

- Wampler DA, Molina DK, McManus J, Laws P, Manifold CA. No deaths associated with patient refusal of transport after naloxone-reversed opioid overdose. *Prehosp Emerg Care.* 2011;15:320–324. doi: 10.3109/10903127.2011.569854.
113. Saybolt MD, Alter SM, Dos Santos F, Calello DP, Rynn KO, Nelson DA, Merlin MA. Naloxone in cardiac arrest with suspected opioid overdoses. *Resuscitation.* 2010;81:42–46. doi: 10.1016/j.resuscitation.2009.09.016.
114. Vilke GM, Sloane C, Smith AM, Chan TC. Assessment for deaths in out-of-hospital heroin overdose patients treated with naloxone who refuse transport. *Acad Emerg Med.* 2003;10:893–896.
115. Rudolph SS, Jehu G, Nielsen SL, Nielsen K, Siersma V, Rasmussen LS. Prehospital treatment of opioid overdose in Copenhagen—is it safe to discharge on-scene? *Resuscitation.* 2011;82:1414–1418. doi: 10.1016/j.resuscitation.2011.06.027.
116. Moss ST, Chan TC, Buchanan J, Dunford JV, Vilke GM. Outcome study of prehospital patients signed out against medical advice by field paramedics. *Ann Emerg Med.* 1998;31:247–250.
117. Christenson J, Etherington J, Grafstein E, Innes G, Pennington S, Wanger K, Fernandes C, Spinelli JJ, Gao M. Early discharge of patients with presumed opioid overdose: development of a clinical prediction rule. *Acad Emerg Med.* 2000;7:1110–1118.
118. Etherington J, Christenson J, Innes G, Grafstein E, Pennington S, Spinelli JJ, Gao M, Lahiffe B, Wanger K, Fernandes C. Is early discharge safe after naloxone reversal of presumed opioid overdose? *CJEM.* 2000;2:156–162.
119. Zuckerman M, Weisberg SN, Boyer EW. Pitfalls of intranasal naloxone. *Prehosp Emerg Care.* 2014;18:550–554. doi: 10.3109/10903127.2014.896961.
120. Weinberg GL, VadeBoncouer T, Ramaraju GA, Garcia-Amaro MF, Cwik MJ. Pretreatment or resuscitation with a lipid infusion shifts the dose-response to bupivacaine-induced asystole in rats. *Anesthesiology.* 1998;88:1071–1075.
121. Weinberg G, Ripper R, Feinstein DL, Hoffman W. Lipid emulsion infusion rescues dogs from bupivacaine-induced cardiac toxicity. *Reg Anesth Pain Med.* 2003;28:198–202. doi: 10.1053/rapm.2003.50041.
122. Rosenblatt MA, Abel M, Fischer GW, Itzkovich CJ, Eisenkraft JB. Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. *Anesthesiology.* 2006;105:217–218.
123. Barrington MJ, Kluger R. Ultrasound guidance reduces the risk of local anesthetic systemic toxicity following peripheral nerve blockade. *Reg Anesth Pain Med.* 2013;38:289–297. doi: 10.1097/AAP.0b013e318292669b.
124. Neal JM, Mulroy MF, Weinberg GL; American Society of Regional Anesthesia and Pain Medicine. American Society of Regional Anesthesia and Pain Medicine checklist for managing local anesthetic systemic toxicity: 2012 version. *Reg Anesth Pain Med.* 2012;37:16–18. doi: 10.1097/AAP.0b013e31822e0d8a.
125. Weinberg G, Lin B, Zheng S, Di Gregorio G, Hiller D, Ripper R, Edelman L, Kelly K, Feinstein D. Partitioning effect in lipid resuscitation: further evidence for the lipid sink. *Crit Care Med.* 2010;38:2268–2269. doi: 10.1097/CCM.0b013e3181f17d85.
126. Weinberg GL, Palmer JW, VadeBoncouer TR, Zuechner MB, Edelman G, Hoppel CL. Bupivacaine inhibits acylcarnitine exchange in cardiac mitochondria. *Anesthesiology.* 2000;92:523–528.
127. Fettiplace MR, Akpa BS, Ripper R, Zider B, Lang J, Rubinstein I, Weinberg G. Resuscitation with lipid emulsion: dose-dependent recovery from cardiac pharmacotoxicity requires a cardiotoxic effect. *Anesthesiology.* 2014;120:915–925. doi: 10.1097/ALN.0000000000000142.
128. Harvey M, Cave G. Lipid rescue: does the sink hold water? And other controversies. *Br J Anaesth.* 2014;112:622–625. doi: 10.1093/bja/aeu010.
129. Turner-Lawrence DE, Kerns li W. Intravenous fat emulsion: a potential novel antidote. *J Med Toxicol.* 2008;4:109–114.
130. Jamaty C, Bailey B, Larocque A, Notebaert E, Sanogo K, Chauny JM. Lipid emulsions in the treatment of acute poisoning: a systematic review of human and animal studies. *Clin Toxicol (Phila).* 2010;48:1–27. doi: 10.3109/15563650903544124.
131. Weinberg GL. Lipid emulsion infusion: resuscitation for local anesthetic and other drug overdose. *Anesthesiology.* 2012;117:180–187. doi: 10.1097/ALN.0b013e31825ad8de.
132. Cao H, Zhou X, Zhang J, Huang X, Zhai Y, Zhang X, Chu L. Hydrogen sulfide protects against bleomycin-induced pulmonary fibrosis in rats by inhibiting NF- $\kappa$ B expression and regulating Th1/Th2 balance. *Toxicol Lett.* 2014;224:387–394. doi: 10.1016/j.toxlet.2013.11.008.
133. Taftachi F, Sanaei-Zadeh H, Sepehrian B, Zamani N. Lipid emulsion improves Glasgow coma scale and decreases blood glucose level in the setting of acute non-local anesthetic drug poisoning—a randomized controlled trial. *Eur Rev Med Pharmacol Sci.* 2012;16 suppl 1:38–42.
134. Gil HW, Park JS, Park SH, Hong SY. Effect of intravenous lipid emulsion in patients with acute glyphosate intoxication. *Clin Toxicol (Phila).* 2013;51:767–771. doi: 10.3109/15563650.2013.821129.
- 135.

- Cave G, Harvey M, Willers J, Uncles D, Meek T, Picard J, Weinberg G. LIPAEMIC report: results of clinical use of intravenous lipid emulsion in drug toxicity reported to an online lipid registry. *J Med Toxicol*. 2014;10:133–142. doi: 10.1007/s13181-013-0375-y.
136. Downes MA, Calver LA, Isbister GK. Intralipid therapy does not improve level of consciousness in overdoses with sedating drugs: a case series. *Emerg Med Australas*. 2014;26:286–290. doi: 10.1111/1742-6723.12237.
137. Weinberg GL, Di Gregorio G, Ripper R, Kelly K, Massad M, Edelman L, Schwartz D, Shah N, Zheng S, Feinstein DL. Resuscitation with lipid versus epinephrine in a rat model of bupivacaine overdose. *Anesthesiology*. 2008;108:907–913. doi: 10.1097/ALN.0b013e31816d91d2.
138. Weinberg G. LipidRescue resuscitation for drug toxicity. <http://www.lipidrescue.org/>. Accessed March 19, 2015.
139. American Society of Regional Anesthesia and Pain Medicine. Checklist for treatment of local anesthetic systemic toxicity. <https://www.asra.com/advisory-guidelines/article/3/checklist-for-treatment-of-local-anesthetic-systemic-toxicity>. Accessed March 19, 2015.
140. American College of Medical Toxicology. ACMT position statement: interim guidance for the use of lipid resuscitation therapy. *J Med Toxicol*. 2011;7:81–82.
141. Fettiplace MR, Akpa BS, Rubinstein I, Weinberg G. Confusion about infusion: rational volume limits for intravenous lipid emulsion during treatment of oral overdoses. *Ann Emerg Med*. 2015;66:185–188. doi: 10.1016/j.annemergmed.2015.01.020.
142. Levine M, Skolnik AB, Ruha AM, Bosak A, Menke N, Pizon AF. Complications following antidotal use of intravenous lipid emulsion therapy. *J Med Toxicol*. 2014;10:10–14. doi: 10.1007/s13181-013-0356-1.
143. Carreiro S, Blum J, Jay G, Hack JB. Intravenous lipid emulsion alters the hemodynamic response to epinephrine in a rat model. *J Med Toxicol*. 2013;9:220–225. doi: 10.1007/s13181-013-0291-1.
144. Harvey M, Cave G, Prince G, Lahner D. Epinephrine injection in lipid-based resuscitation from bupivacaine-induced cardiac arrest: transient circulatory return in rabbits. *Anesth Analg*. 2010;111:791–796. doi: 10.1213/ANE.0b013e3181e66050.
145. Neal JM, Bernardis CM, Butterworth JF 4th, Di Gregorio G, Drasner K, Hejtmanek MR, Mulroy MF, Rosenquist RW, Weinberg GL. ASRA practice advisory on local anesthetic systemic toxicity. *Reg Anesth Pain Med*. 2010;35:152–161. doi: 10.1097/AAP.0b013e3181d22fcd.
146. American Society of Regional Anesthesia and Pain Medicine. Checklist for Treatment of Local Anesthetic Systemic Toxicity. 2011. <https://www.asra.com/content/documents/checklist-for-local-anesthetic-toxicity-treatment-1-18-12.pdf>. Accessed May 11, 2015.
147. Cole JB, Stellpflug SJ, Engebretsen KM. Asystole immediately following intravenous fat emulsion for overdose. *J Med Toxicol*. 2014;10:307–310. doi: 10.1007/s13181-014-0382-7.
148. Lee HM, Archer JR, Dargan PI, Wood DM. What are the adverse effects associated with the combined use of intravenous lipid emulsion and extracorporeal membrane oxygenation in the poisoned patient? *Clin Toxicol (Phila)*. 2015;53:145–150. doi: 10.3109/15563650.2015.1004582.
149. Trestrail JH. *Criminal Poisoning: Investigational Guide for Law Enforcement, Toxicologists, Forensic Scientists, and Attorneys*. 2nd ed. Totowa, NJ: Humana; 2007.
150. Courtney DM, Neumar RW, Venkatesh AK, Kaji AH, Cairns CB, Lavonas E, Richardson LD. Unique characteristics of emergency care research: scope, populations, and infrastructure. *Acad Emerg Med*. 2009;16:990–994.
151. Matsika MD, Tournier M, Lagnaoui R, Pehourcq F, Molimard M, Begaud B, Verdoux H, Moore N. Comparison of patient questionnaires and plasma assays in intentional drug overdoses. *Basic Clin Pharmacol Toxicol*. 2004;95:31–37.
152. Neeleman J, Wessely S. Drugs taken in fatal and non-fatal self-poisoning: a study in south London. *Acta Psychiatr Scand*. 1997;95:283–287.
153. Wu AH, McKay C, Broussard LA, Hoffman RS, Kwong TC, Moyer TP, Otten EM, Welch SL, Wax P. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: recommendations for the use of laboratory tests to support poisoned patients who present to the emergency department. *Clin Chem*. 2003;49:357–379.
154. Shannon MW. A general approach to poisoning. In: Shannon MW, Borron SW, Burns MJ eds. *Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose*. 4th ed. Philadelphia, Pa: Saunders/Elsevier; 2007:13–30.
155. Position paper: ipecac syrup. *J Toxicol Clin Toxicol*. 2004;42:133–143.
156. Vale JA, Kulig K; American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: gastric lavage. *J Toxicol Clin Toxicol*. 2004;42:933–943.
157. Position paper: whole bowel irrigation. *J Toxicol Clin Toxicol*. 2004;42:843–854.
- 158.

- Chyka PA, Seger D, Krenzelok EP, Vale JA; American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position paper: single-dose activated charcoal. *Clin Toxicol (Phila)*. 2005;43:61–87.
159. American Academy of Clinical Toxicology; European Association of Poisons Centres and Clinical Toxicologists. Position statement and practice guidelines on the use of multi-dose activated charcoal in the treatment of acute poisoning. *J Toxicol Clin Toxicol*. 1999;37:731–751.
160. Metheny NA. Preventing respiratory complications of tube feedings: evidence-based practice. *Am J Crit Care*. 2006;15:360–369.
161. Adelson L. Poison and the pathologist. *JAMA*. 1964;187:918–920.
162. The Flumazenil in Benzodiazepine Intoxication Multicenter Study Group. Treatment of benzodiazepine overdose with flumazenil. *Clin Ther*. 1992;14:978–995.
163. Lheureux P, Vranckx M, Leduc D, Askenasi R. Flumazenil in mixed benzodiazepine/tricyclic antidepressant overdose: a placebo-controlled study in the dog. *Am J Emerg Med*. 1992;10:184–188.
164. Pitetti RD, Singh S, Pierce MC. Safe and efficacious use of procedural sedation and analgesia by nonanesthesiologists in a pediatric emergency department. *Arch Pediatr Adolesc Med*. 2003;157:1090–1096.
165. Fahed S, Grum DF, Papadimos TJ. Labetalol infusion for refractory hypertension causing severe hypotension and bradycardia: an issue of patient safety. *Patient Saf Surg*. 2008;2:13.
166. Fernandes CM, Daya MR. Sotalol-induced bradycardia reversed by glucagon. *Can Fam Physician*. 1995;41:659–660, 663–665.
167. Frishman W, Jacob H, Eisenberg E, Ribner H. Clinical pharmacology of the new beta-adrenergic blocking drugs, part 8: self-poisoning with beta-adrenoceptor blocking agents: recognition and management. *Am Heart J*. 1979;98:798–811.
168. Gabry AL, Pourriat JL, Hoang TD, Lapandry C. Cardiogenic shock caused by metoprolol poisoning: reversibility with high doses of glucagon and isoproterenol [in French]. *Presse Med*. 1985;14:229.
169. Hazouard E, Ferrandiere M, Lesire V, Joye F, Perrotin D, de Toffol B. Peduncular hallucinosis related to propranolol self-poisoning: efficacy of intravenous glucagon. *Intensive Care Med*. 1999;25:336–337.
170. Khan MI, Miller MT. Beta-blocker toxicity: the role of glucagon: report of 2 cases. *S Afr Med J*. 1985;67:1062–1063.
171. Moller BH. Massive intoxication with metoprolol. *BMJ*. 1976;1:222. Letter.
172. O'Mahony D, O'Leary P, Molloy MG. Severe oxprenolol poisoning: the importance of glucagon infusion. *Hum Exp Toxicol*. 1990;9:101–103.
173. Wallin CJ, Hulting J. Massive metoprolol poisoning treated with prenalterol. *Acta Med Scand*. 1983;214:253–255.
174. Weinstein RS. Recognition and management of poisoning with beta-adrenergic blocking agents. *Ann Emerg Med*. 1984;13:1123–1131.
175. Alderfliegel F, Leeman M, Demaeyer P, Kahn RJ. Sotalol poisoning associated with asystole. *Intensive Care Med*. 1993;19:57–58.
176. Kenyon CJ, Aldinger GE, Joshipura P, Zaid GJ. Successful resuscitation using external cardiac pacing in beta adrenergic antagonist-induced bradycardiac arrest. *Ann Emerg Med*. 1988;17:711–713.
177. Freestone S, Thomas HM, Bhamra RK, Dyson EH. Severe atenolol poisoning: treatment with prenalterol. *Hum Toxicol*. 1986;5:343–345.
178. Toet AE, Wemer J, Vleeming W, te Biesebeek JD, Meulenbelt J, de Wildt DJ. Experimental study of the detrimental effect of dopamine/glucagon combination in d,l-propranolol intoxication. *Hum Exp Toxicol*. 1996;15:411–421.
179. Toet AE, te Biesebeek JD, Vleeming W, Wemer J, Meulenbelt J, de Wildt DJ. Reduced survival after isoprenaline/dopamine in d,l-propranolol intoxicated rats. *Hum Exp Toxicol*. 1996;15:120–128.
180. Sato S, Tsuji MH, Okubo N, Nishimoto C, Naito H. Combined use of glucagon and milrinone may not be preferable for severe propranolol poisoning in the canine model. *J Toxicol Clin Toxicol*. 1995;33:337–342.
181. Kerns W II., Schroeder D, Williams C, Tomaszewski C, Raymond R. Insulin improves survival in a canine model of acute beta-blocker toxicity. *Ann Emerg Med*. 1997;29:748–757.
182. Holger JS, Engebretsen KM, Fritzlar SJ, Patten LC, Harris CR, Flottemesch TJ. Insulin versus vasopressin and epinephrine to treat beta-blocker toxicity. *Clin Toxicol (Phila)*. 2007;45:396–401.
183. Page C, Hackett LP, Isbister GK. The use of high-dose insulin-glucose euglycemia in beta-blocker overdose: a case report. *J Med Toxicol*. 2009;5:139–143.



184. Kerns W II.. Management of beta-adrenergic blocker and calcium channel antagonist toxicity. *Emerg Med Clin North Am.* 2007;25:309–331.
185. Pertoldi F, D'Orlando L, Mercante WP. Electromechanical dissociation 48 hours after atenolol overdose: usefulness of calcium chloride. *Ann Emerg Med.* 1998;31:777–781.
186. Love JN, Hanfling D, Howell JM. Hemodynamic effects of calcium chloride in a canine model of acute propranolol intoxication. *Ann Emerg Med.* 1996;28:1–6.
187. McVey FK, Corke CF. Extracorporeal circulation in the management of massive propranolol overdose. *Anaesthesia.* 1991;46:744–746.
188. Lane AS, Woodward AC, Goldman MR. Massive propranolol overdose poorly responsive to pharmacologic therapy: use of the intra-aortic balloon pump. *Ann Emerg Med.* 1987;16:1381–1383.
189. Rooney M, Massey KL, Jamali F, Rosin M, Thomson D, Johnson DH. Acebutolol overdose treated with hemodialysis and extracorporeal membrane oxygenation. *J Clin Pharmacol.* 1996;36:760–763.
190. Stellpflug SJ, Harris CR, Engebretsen KM, Cole JB, Holger JS. Intentional overdose with cardiac arrest treated with intravenous fat emulsion and high-dose insulin. *Clin Toxicol.* 2010;48:227–229.
191. Zimmer BW, Marcus RJ, Sawyer K, Harchelroad F. Salicylate intoxication as a cause of pseudohyperchloremia. *Am J Kidney Dis.* 2008;51():346–347.
192. Cave G, Harvey M. Lipid emulsion may augment early blood pressure recovery in a rabbit model of atenolol toxicity. *J Med Toxicol.* 2009;5:50–51.
193. Cave G, Harvey MG, Castle CD. The role of fat emulsion therapy in a rodent model of propranolol toxicity: a preliminary study. *J Med Toxicol.* 2006;2():4–7.
194. Harvey MG, Cave GR. Intralipid infusion ameliorates propranolol-induced hypotension in rabbits. *J Med Toxicol.* 2008;4:71–76.
195. Browne A, Harvey M, Cave G. Intravenous lipid emulsion does not augment blood pressure recovery in a rabbit model of metoprolol toxicity. *J Med Toxicol.* 2010:ePub.
196. Turner-Lawrence DE, Kerns li W. Intravenous fat emulsion: a potential novel antidote. *J Med Toxicol.* 2008;4:109–114.
197. Cave G, Harvey M. Intravenous lipid emulsion as antidote beyond local anesthetic toxicity: a systematic review. *Acad Emerg Med.* 2009;16:815–824.
198. Jamaty C, Bailey B, Larocque A, Notebaert E, Sanogo K, Chauny JM. Lipid emulsions in the treatment of acute poisoning: a systematic review of human and animal studies. *Clin Toxicol.* 2010;48:1–27.
199. Boyer EW, Duic PA, Evans A. Hyperinsulinemia/euglycemia therapy for calcium channel blocker poisoning. *Pediatr Emerg Care.* 2002;18:36–37.
200. Cohen E, Du D, Joyce D, Kapernick EA, Volovik Y, Kelly JW, Dillin A. Temporal requirements of insulin/IGF-1 signaling for proteotoxicity protection. *Aging Cell.* 2010;9:126–134.
201. Greene SL, Gawarammana I, Wood DM, Jones AL, Dargan PI. Relative safety of hyperinsulinaemia/euglycaemia therapy in the management of calcium channel blocker overdose: a prospective observational study. *Intensive Care Med.* 2007;33:2019–2024.
202. Harris NS. Case records of the Massachusetts General Hospital: case 24–2006: a 40-year-old woman with hypotension after an overdose of amlodipine. *N Engl J Med.* 2006;355:602–611.
203. Johansen KK, Belhage B. A 48-year-old woman's survival from a massive verapamil overdose [in Danish]. *Ugeskr Laeger.* 2007;169:4074–4075.
204. Kanagarajan K, Marraffa JM, Bouchard NC, Krishnan P, Hoffman RS, Stork CM. The use of vasopressin in the setting of recalcitrant hypotension due to calcium channel blocker overdose. *Clin Toxicol (Phila).* 2007;45:56–59.
205. Marques M, Gomes E, de Oliveira J. Treatment of calcium channel blocker intoxication with insulin infusion: case report and literature review. *Resuscitation.* 2003;57:211–213.
206. Ortiz-Munoz L, Rodriguez-Ospina LF, Figueroa-Gonzalez M. Hyperinsulinemic-euglycemic therapy for intoxication with calcium channel blockers. *Bol Asoc Med P R.* 2005;97():182–189.
207. Patel NP, Pugh ME, Goldberg S, Eiger G. Hyperinsulinemic euglycemia therapy for verapamil poisoning: case report. *Am J Crit Care.* 2007;16:518–529.
208. Rasmussen L, Husted SE, Johnsen SP. Severe intoxication after an intentional overdose of amlodipine. *Acta Anaesthesiol Scand.* 2003;47:1038–1040.

209. Smith SW, Ferguson KL, Hoffman RS, Nelson LS, Greller HA. Prolonged severe hypotension following combined amlodipine and valsartan ingestion. *Clin Toxicol (Phila)*. 2008;46:470–474.
210. Yuan TH, Kerns WPI, Tomaszewski CA, Ford MD, Kline JA. Insulin-glucose as adjunctive therapy for severe calcium channel antagonist poisoning. *J Toxicol Clin Toxicol*. 1999;37:463–474.
211. Kline JA, Tomaszewski CA, Schroeder JD, Raymond RM. Insulin is a superior antidote for cardiovascular toxicity induced by verapamil in the anesthetized canine. *J Pharmacol Exp Ther*. 1993;267:744–750.
212. Kline JA, Leonova E, Raymond RM. Beneficial myocardial metabolic effects of insulin during verapamil toxicity in the anesthetized canine. *Crit Care Med*. 1995;23:1251–1263.
213. Kline JA, Leonova E, Williams TC, Schroeder JD, Watts JA. Myocardial metabolism during graded intraportal verapamil infusion in awake dogs. *J Cardiovasc Pharmacol*. 1996;27:719–726.
214. Kline JA, Raymond RM, Schroeder JD, Watts JA. The diabetogenic effects of acute verapamil poisoning. *Toxicol Appl Pharmacol*. 1997;145:357–362.
215. Durward A, Guerguerian AM, Lefebvre M, Shemie SD. Massive diltiazem overdose treated with extracorporeal membrane oxygenation. *Pediatr Crit Care Med*. 2003;4:372–376.
216. Fiszer M, Kolacinski Z, Rechcinski T. The application of 4-aminopyridine in calcium channel inhibitors acute poisoning [in Polish]. *Przegl Lek*. 2007;64:293–297.
217. Pfaender M, Casetti PG, Azzolini M, Baldi ML, Valli A. Successful treatment of a massive atenolol and nifedipine overdose with CVVHDF. *Minerva Anestesiol*. 2008;74:97–100.
218. Sabatier J, Pouyet T, Shelvey G, Cavero I. Antagonistic effects of epinephrine, glucagon and methylatropine but not calcium chloride against atrio-ventricular conduction disturbances produced by high doses of diltiazem, in conscious dogs. *Fundam Clin Pharmacol*. 1991;5:93–106.
219. Stone CK, May WA, Carroll R. Treatment of verapamil overdose with glucagon in dogs. *Ann Emerg Med*. 1995;25:369–374.
220. Stone CK, Thomas SH. Cardiopulmonary resuscitation (CPR) performance. *Prehosp Disaster Med*. 1996;11:120.
221. Tuncok Y, Apaydin S, Kalkan S, Ates M, Guven H. The effects of amrinone and glucagon on verapamil-induced cardiovascular toxicity in anaesthetized rats. *Int J Exp Pathol*. 1996;77:207–212.
222. Eddleston M, Rajapakse S, Rajakanthan, Jayalath S, Sjoström L, Santharaj W, Thenabadu PN, Sheriff MH, Warrell DA. Anti-digoxin Fab fragments in cardiotoxicity induced by ingestion of yellow oleander: a randomised controlled trial. *Lancet*. 2000;355:967–972.
223. Smith TW, Butler VP Jr., Haber E, Fozzard H, Marcus FI, Bremner WF, Schulman IC, Phillips A. Treatment of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments: experience in 26 cases. *N Engl J Med*. 1982;307:1357–1362.
224. Wenger TL, Butler VPJ, Haber E, Smith TW. Treatment of 63 severely digitalis-toxic patients with digoxin-specific antibody fragments. *J Am Coll Cardiol*. 1985;5(suppl):118A–123A.
225. Antman EM, Wenger TL, Butler VP Jr., Haber E, Smith TW. Treatment of 150 cases of life-threatening digitalis intoxication with digoxin-specific Fab antibody fragments: final report of a multicenter study. *Circulation*. 1990;81:1744–1752.
226. Woolf AD, Wenger T, Smith TW, Lovejoy FHJ. The use of digoxin-specific Fab fragments for severe digitalis intoxication in children. *N Engl J Med*. 1992;326:1739–1744.
227. Hickey AR, Wenger TL, Carpenter VP, Tilson HH, Hlatky MA, Furberg CD, Kirkpatrick CH, Strauss HC, Smith TW. Digoxin immune Fab therapy in the management of digitalis intoxication: safety and efficacy results of an observational surveillance study. *J Am Coll Cardiol*. 1991;17:590–598.
228. Wenger TL. Experience with digoxin immune Fab (ovine) in patients with renal impairment. *Am J Emerg Med*. 1991;9(suppl 1):21–23.
229. Woolf AD, Wenger TL, Smith TW, Lovejoy FHJ. Results of multicenter studies of digoxin-specific antibody fragments in managing digitalis intoxication in the pediatric population. *Am J Emerg Med*. 1991;9(suppl 1):16–20.
230. Taboulet P, Baud FJ, Bismuth C, Vicaud E. Acute digitalis intoxication: is pacing still appropriate? *J Toxicol Clin Toxicol*. 1993;31:261–273.
231. Lapostolle F, Borron SW, Verdier C, Taboulet P, Guerrier G, Adnet F, Clemessy JL, Bismuth C, Baud FJ. Digoxin-specific Fab fragments as single first-line therapy in digitalis poisoning. *Crit Care Med*. 2008;36:3014–3018.
232. Bismuth C, Gaultier M, Conso F, Efthymiou ML. Hyperkalemia in acute digitalis poisoning: prognostic significance and therapeutic implications. *Clin Toxicol*. 1973;6:153–162.
- 233.

- Lapostolle F, Borron SW. Digitalis. In: Shannon MW, Borron SW, Burns MJ eds. Haddad and Winchester's Clinical Management of Poisoning and Drug Overdose. Philadelphia, Pa: Saunders/Elsevier; 2007:949–962.
234. Hsue PY, McManus D, Selby V, Ren X, Pillutla P, Younes N, Goldschlager N, Waters DD. Cardiac arrest in patients who smoke crack cocaine. *Am J Cardiol.* 2007;99:822–824.
235. Lange RA, Cigarroa RG, Yancy CW Jr., Willard JE, Popma JJ, Sills MN, McBride W, Kim AS, Hillis LD. Cocaine-induced coronary-artery vasoconstriction. *N Engl J Med.* 1989;321:1557–1562.
236. Baumann BM, Perrone J, Hornig SE, Shofer FS, Hollander JE. Randomized, double-blind, placebo-controlled trial of diazepam, nitroglycerin, or both for treatment of patients with potential cocaine-associated acute coronary syndromes. *Acad Emerg Med.* 2000;7:878–885.
237. Negus BH, Willard JE, Hillis LD, Glamann DB, Landau C, Snyder RW, Lange RA. Alleviation of cocaine-induced coronary vasoconstriction with intravenous verapamil. *Am J Cardiol.* 1994;73:510–513.
238. Saland KE, Hillis LD, Lange RA, Cigarroa JE. Influence of morphine sulfate on cocaine-induced coronary vasoconstriction. *Am J Cardiol.* 2002;90:810–811.
239. Hollander JE, Hoffman RS, Gennis P, Fairweather P, DiSano MJ, Schumb DA, Feldman JA, Fish SS, Dyer S, Wax P, Whelan C, Schwarzwald E. Nitroglycerin in the treatment of cocaine associated chest pain: clinical safety and efficacy. *J Toxicol Clin Toxicol.* 1994;32:243–256.
240. Brogan WCI, Lange RA, Kim AS, Moliterno DJ, Hillis LD. Alleviation of cocaine-induced coronary vasoconstriction by nitroglycerin. *J Am Coll Cardiol.* 1991;18:581–586.
241. Mittleman MA, Mintzer D, Maclure M, Tofler GH, Sherwood JB, Muller JE. Triggering of myocardial infarction by cocaine. *Circulation.* 1999;99:2737–2741.
242. Honderick T, Williams D, Seaberg D, Wears R. A prospective, randomized, controlled trial of benzodiazepines and nitroglycerine or nitroglycerine alone in the treatment of cocaine-associated acute coronary syndromes. *Am J Emerg Med.* 2003;21:39–42.
243. Boehrer JD, Moliterno DJ, Willard JE, Hillis LD, Lange RA. Influence of labetalol on cocaine-induced coronary vasoconstriction in humans. *Am J Med.* 1993;94:608–610.
244. Lange RA, Cigarroa RG, Flores ED, McBride W, Kim AS, Wells PJ, Bedotto JB, Danziger RS, Hillis LD. Potentiation of cocaine-induced coronary vasoconstriction by beta-adrenergic blockade. *Ann Intern Med.* 1990;112:897–903.
245. Sand IC, Brody SL, Wrenn KD, Slovis CM. Experience with esmolol for the treatment of cocaine-associated cardiovascular complications. *Am J Emerg Med.* 1991;9:161–163.
246. Dattilo PB, Hailpern SM, Fearon K, Sohal D, Nordin C. Beta-blockers are associated with reduced risk of myocardial infarction after cocaine use. *Ann Emerg Med.* 2008;51:117–125.
247. Vongpatanasin W, Mansour Y, Chavoshan B, Arbique D, Victor RG. Cocaine stimulates the human cardiovascular system via a central mechanism of action. *Circulation.* 1999;100:497–502.
248. McCord J, Jneid H, Hollander JE, de Lemos JA, Cercek B, Hsue P, Gibler WB, Ohman EM, Drew B, Philippides G, Newby LK. Management of cocaine-associated chest pain and myocardial infarction: a scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology. *Circulation.* 2008;117:1897–1907.
249. Ellington C, Katz VL, Watson WJ, Spielman FJ. The effect of lateral tilt on maternal and fetal hemodynamic variables. *Obstet Gynecol.* 1991;77:201–203.
250. Wood DM, Dargan PI, Hoffman RS. Management of cocaine-induced cardiac arrhythmias due to cardiac ion channel dysfunction. *Clin Toxicol (Phila).* 2009;47:14–23.
251. Hoffman JR, Votey SR, Bayer M, Silver L. Effect of hypertonic sodium bicarbonate in the treatment of moderate-to-severe cyclic antidepressant overdose. *Am J Emerg Med.* 1993;11:336–341.
252. Koppel C, Wiegrefe A, Tenczer J. Clinical course, therapy, outcome and analytical data in amitriptyline and combined amitriptyline/chlordiazepoxide overdose. *Hum Exp Toxicol.* 1992;11:458–465.
253. Brown TC. Tricyclic antidepressant overdosage: experimental studies on the management of circulatory complications. *Clin Toxicol.* 1976;9:255–272.
254. Hedges JR, Baker PB, Tasset JJ, Otten EJ, Dalsey WC, Syverud SA. Bicarbonate therapy for the cardiovascular toxicity of amitriptyline in an animal model. *J Emerg Med.* 1985;3:253–260.
255. Knudsen K, Abrahamsson J. Epinephrine and sodium bicarbonate independently and additively increase survival in experimental amitriptyline poisoning. *Crit Care Med.* 1997;25:669–674.

256. Nattel S, Mittleman M. Treatment of ventricular tachyarrhythmias resulting from amitriptyline toxicity in dogs. *J Pharmacol Exp Ther.* 1984;231:430–435.
257. Pentel P, Benowitz N. Efficacy and mechanism of action of sodium bicarbonate in the treatment of desipramine toxicity in rats. *J Pharmacol Exp Ther.* 1984;230:12–19.
258. Sasyniuk BI, Jhamandas V, Valois M. Experimental amitriptyline intoxication: treatment of cardiac toxicity with sodium bicarbonate. *Ann Emerg Med.* 1986;15:1052–1059.
259. Pentel P, Peterson CD. Asystole complicating physostigmine treatment of tricyclic antidepressant overdose. *Ann Emerg Med.* 1980;9:588–590.
260. Clarke SF, Dargan PI, Jones AL. Naloxone in opioid poisoning: walking the tightrope. *Emerg Med J.* 2005;22:612–616.
261. Knudsen K, Abrahamsson J. Effects of epinephrine and norepinephrine on hemodynamic parameters and arrhythmias during a continuous infusion of amitriptyline in rats. *J Toxicol Clin Toxicol.* 1993;31:461–471.
262. Knudsen K, Abrahamsson J. Effects of epinephrine, norepinephrine, magnesium sulfate, and milrinone on survival and the occurrence of arrhythmias in amitriptyline poisoning in the rat. *Crit Care Med.* 1994;22:1851–1855.
263. Tran TP, Panacek EA, Rhee KJ, Foulke GE. Response to dopamine vs norepinephrine in tricyclic antidepressant-induced hypotension. *Acad Emerg Med.* 1997;4:864–868.
264. Tobis JM, Aronow WS. Effect of amitriptyline antidotes on repetitive extrasystole threshold. *Clin Pharmacol Ther.* 1980;27:602–606.
265. Vernon DD, Banner W Jr., Garrett JS, Dean JM. Efficacy of dopamine and norepinephrine for treatment of hemodynamic compromise in amitriptyline intoxication. *Crit Care Med.* 1991;19:544–549.
266. Follmer CH, Lum BK. Protective action of diazepam and of sympathomimetic amines against amitriptyline-induced toxicity. *J Pharmacol Exp Ther.* 1982;222:424–429.
267. Sangster B, de Groot G, Borst C, de Wildt D. Dopamine and isoproterenol in imipramine intoxication in the dog. *J Toxicol Clin Toxicol.* 1985;23:407–420.
268. Centers for Disease Control and Prevention. Unintentional poisoning deaths: United States, 1999–2004. *MMWR Morb Mortal Wkly Rep.* 2007;56:93–96.
269. Weaver LK. Clinical practice: carbon monoxide poisoning. *N Engl J Med.* 2009;360:1217–1225.
270. Hampson NB, Zmaeff JL. Outcome of patients experiencing cardiac arrest with carbon monoxide poisoning treated with hyperbaric oxygen. *Ann Emerg Med.* 2001;38:36–41.
271. Sloan EP, Murphy DG, Hart R, Cooper MA, Turnbull T, Barreca RS, Ellerson B. Complications and protocol considerations in carbon monoxide-poisoned patients who require hyperbaric oxygen therapy: report from a ten-year experience. *Ann Emerg Med.* 1989;18:629–634.
272. Chou KJ, Fisher JL, Silver EJ. Characteristics and outcome of children with carbon monoxide poisoning with and without smoke exposure referred for hyperbaric oxygen therapy. *Pediatr Emerg Care.* 2000;16:151–155.
273. Weaver LK, Hopkins RO, Chan KJ, Churchill S, Elliott CG, Clemmer TP, Orme JF Jr., Thomas FO, Morris AH. Hyperbaric oxygen for acute carbon monoxide poisoning. *N Engl J Med.* 2002;347:1057–1067.
274. Thom SR, Taber RL, Mendiguren II, Clark JM, Hardy KR, Fisher AB. Delayed neuropsychologic sequelae after carbon monoxide poisoning: prevention by treatment with hyperbaric oxygen. *Ann Emerg Med.* 1995;25:474–480.
275. Scheinkestel CD, Bailey M, Myles PS, Jones K, Cooper DJ, Millar IL, Tuxen DV. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. *Med J Aust.* 1999;170:203–210.
276. Raphael JC, Elkharrat D, Jars-Guinestre MC, Chastang C, Chasles V, Vercken JB, Gajdos P. Trial of normobaric and hyperbaric oxygen for acute carbon monoxide intoxication. *Lancet.* 1989;2:414–419.
277. Juurlink DN, Buckley NA, Stanbrook MB, Isbister GK, Bennett M, McGuigan MA. Hyperbaric oxygen for carbon monoxide poisoning. *Cochrane Database Syst Rev.* 2005;No. 1:CD002041.
278. Buckley NA, Isbister GK, Stokes B, Juurlink DN. Hyperbaric oxygen for carbon monoxide poisoning: a systematic review and critical analysis of the evidence. *Toxicol Rev.* 2005;24:75–92.
279. Wolf SJ, Lavonas EJ, Sloan EP, Jagoda AS. Clinical policy: critical issues in the management of adult patients presenting to the emergency department with acute carbon monoxide poisoning. *Ann Emerg Med.* 2008;51:138–152.
- 280.

- Satran D, Henry CR, Adkinson C, Nicholson CI, Bracha Y, Henry TD. Cardiovascular manifestations of moderate to severe carbon monoxide poisoning. *J Am Coll Cardiol.* 2005;45:1513–1516.
281. Henry CR, Satran D, Lindgren B, Adkinson C, Nicholson CI, Henry TD. Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. *JAMA.* 2006;295:398–402.
282. Baud FJ, Barriot P, Toffis V, Riou B, Vicaut E, Lecarpentier Y, Bourdon R, Astier A, Bismuth C. Elevated blood cyanide concentrations in victims of smoke inhalation. *N Engl J Med.* 1991;325:1761–1766.
283. Borron SW, Baud FJ, Barriot P, Imbert M, Bismuth C. Prospective study of hydroxocobalamin for acute cyanide poisoning in smoke inhalation. *Ann Emerg Med.* 2007;49:794–801, 801.e1–e2.
284. Fortin JL, Giocanti JP, Ruttimann M, Kowalski JJ. Prehospital administration of hydroxocobalamin for smoke inhalation-associated cyanide poisoning: 8 years of experience in the Paris Fire Brigade. *Clin Toxicol (Phila).* 2006;44(suppl 1):37–44.
285. Borron SW, Baud FJ, Megarbane B, Bismuth C. Hydroxocobalamin for severe acute cyanide poisoning by ingestion or inhalation. *Am J Emerg Med.* 2007;25:551–558.
286. Espinoza OB, Perez M, Ramirez MS. Bitter cassava poisoning in eight children: a case report. *Vet Hum Toxicol.* 1992;34:65.
287. Houeto P, Hoffman JR, Imbert M, Levillain P, Baud FJ. Relation of blood cyanide to plasma cyanocobalamin concentration after a fixed dose of hydroxocobalamin in cyanide poisoning. *Lancet.* 1995;346:605–608.
288. Pontal P, Bismuth C, Garnier R. Therapeutic attitude in cyanide poisoning: retrospective study of 24 non-lethal cases. *Vet Hum Toxicol.* 1982;24:286–287.
289. Kirk MA, Gerace R, Kulig KW. Cyanide and methemoglobin kinetics in smoke inhalation victims treated with the cyanide antidote kit. *Ann Emerg Med.* 1993;22:1413–1418.
290. Chen KK, Rose CL. Nitrite and thiosulfate therapy in cyanide poisoning. *JAMA.* 1952;149:113–119.
291. Kiese M, Weger N. Formation of ferrihaemoglobin with aminophenols in the human for the treatment of cyanide poisoning. *Eur J Pharmacol.* 1969;7:97–105.
292. Hall AH, Saiers J, Baud F. Which cyanide antidote? *Critical Reviews in Toxicology.* 2009;39:541–552.
293. Hobel M, Engeser P, Nemeth L, Pill J. The antidote effect of thiosulphate and hydroxocobalamin in formation of nitroprusside intoxication of rabbits. *Arch Toxicol.* 1980;46:207–213.
294. Mengel K, Kramer W, Isert B, Friedberg KD. Thiosulphate and hydroxocobalamin prophylaxis in progressive cyanide poisoning in guinea-pigs. *Toxicology.* 1989;54:335–342.
295. Friedberg KD, Shukla UR. The efficiency of aquocobalamine as an antidote in cyanide poisoning when given alone or combined with sodium thiosulfate. *Arch Toxicol.* 1975;33:103–113.
296. Hall AH, Rumack BH. Hydroxycobalamin/sodium thiosulfate as a cyanide antidote. *J Emerg Med.* 1987;5:115–121.
297. Forsyth JC, Mueller PD, Becker CE, Osterloh J, Benowitz NL, Rumack BH, Hall AH. Hydroxocobalamin as a cyanide antidote: safety, efficacy and pharmacokinetics in heavily smoking normal volunteers. *J Toxicol Clin Toxicol.* 1993;31:277–294.
298. Webb JG, Solankhi NK, Chugh SK, Amin H, Buller CE, Ricci DR, Humphries K, Penn IM, Carere R. Incidence, correlates, and outcome of cardiac arrest associated with percutaneous coronary intervention. *Am J Cardiol.* 2002;90:1252–1254.
299. Mehta RH, Harjai KJ, Grines L, Stone GW, Boura J, Cox D, O'Neill W, Grines CL; Primary Angioplasty in Myocardial Infarction (PAMI) Investigators. Sustained ventricular tachycardia or fibrillation in the cardiac catheterization laboratory among patients receiving primary percutaneous coronary intervention: incidence, predictors, and outcomes. *J Am Coll Cardiol.* 2004;43:1765–1772. doi: 10.1016/j.jacc.2003.09.072.
300. Martin-Yuste V, Alvarez-Contreras L, Brugaletta S, Ferreira-Gonzalez I, Cola C, Garcia-Picart J, Martí V, Sabate M. Emergent versus elective percutaneous stent implantation in the unprotected left main: long-term outcomes from a single-center registry. *J Invasive Cardiol.* 2011;23:392–397.
301. Sprung J, Ritter MJ, Rihal CS, Warner ME, Wilson GA, Williams BA, Stevens SR, Schroeder DR, Bourke DL, Warner DO. Outcomes of cardiopulmonary resuscitation and predictors of survival in patients undergoing coronary angiography including percutaneous coronary interventions. *Anesth Analg.* 2006;102:217–224. doi: 10.1213/01.ane.0000189082.54614.26.
302. Addala S, Kahn JK, Moccia TF, Harjai K, Pellizon G, Ochoa A, O'Neill WW. Outcome of ventricular fibrillation developing during percutaneous coronary interventions in 19 497 patients without cardiogenic shock. *Am J Cardiol.* 2005;96:764–765. doi: 10.1016/j.amjcard.2005.04.057.
- 303.

- O'Gara PT, Kushner FG, Ascheim DD, Casey DE Jr, Chung MK, de Lemos JA, Ettinger SM, Fang JC, Fesmire FM, Franklin BA, Granger CB, Krumholz HM, Linderbaum JA, Morrow DA, Newby LK, Ornato JP, Ou N, Radford MJ, Tamis-Holland JE, Tommaso CL, Tracy CM, Woo YJ, Zhao DX. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2013;127:e362–e425. doi: 10.1161/CIR.0b013e3182742cf6.
304. Groggaard HK, Wik L, Eriksen M, Brekke M, Sunde K. Continuous mechanical chest compressions during cardiac arrest to facilitate restoration of coronary circulation with percutaneous coronary intervention. *J Am Coll Cardiol*. 2007;50:1093–1094. doi: 10.1016/j.jacc.2007.05.028.
305. Agostoni P, Cornelis K, Vermeersch P. Successful percutaneous treatment of an intraprocedural left main stent thrombosis with the support of an automatic mechanical chest compression device. *Int J Cardiol*. 2008;124:e19–e21. doi: 10.1016/j.ijcard.2006.11.175.
306. Steen S, Sjöberg T, Olsson P, Young M. Treatment of out-of-hospital cardiac arrest with LUCAS, a new device for automatic mechanical compression and active decompression resuscitation. *Resuscitation*. 2005;67:25–30. doi: 10.1016/j.resuscitation.2005.05.013.
307. Larsen AI, Hjørnevik AS, Ellingsen CL, Nilsen DW. Cardiac arrest with continuous mechanical chest compression during percutaneous coronary intervention. A report on the use of the LUCAS device. *Resuscitation*. 2007;75:454–459. doi: 10.1016/j.resuscitation.2007.05.007.
308. Wagner H, Terkelsen CJ, Friberg H, Harnek J, Kern K, Lassen JF, Olivecrona GK. Cardiac arrest in the catheterisation laboratory: a 5-year experience of using mechanical chest compressions to facilitate PCI during prolonged resuscitation efforts. *Resuscitation*. 2010;81:383–387. doi: 10.1016/j.resuscitation.2009.11.006.
309. Linder R, Abdollahi P, Wennersten G. [Life-saving mechanical compression during percutaneous coronary intervention]. *Lakartidningen*. 2006;103:2390–2392.
310. Ladowski JS, Dillon TA, Deschner WP, DeRiso AJ 2nd, Peterson AC, Schatzlein MH. Durability of emergency coronary artery bypass for complications of failed angioplasty. *Cardiovasc Surg*. 1996;4:23–27.
311. Redle J, King B, Lemole G, Doorey AJ. Utility of rapid percutaneous cardiopulmonary bypass for refractory hemodynamic collapse in the cardiac catheterization laboratory. *Am J Cardiol*. 1994;73:899–900.
312. Overlie PA. Emergency use of portable cardiopulmonary bypass. *Cathet Cardiovasc Diagn*. 1990;20:27–31.
313. Shawl FA, Domanski MJ, Wish MH, Davis M, Punja S, Hernandez TJ. Emergency cardiopulmonary bypass support in patients with cardiac arrest in the catheterization laboratory. *Cathet Cardiovasc Diagn*. 1990;19:8–12.
314. Bagai J, Webb D, Kasasbeh E, Crenshaw M, Salloum J, Chen J, Zhao D. Efficacy and safety of percutaneous life support during high-risk percutaneous coronary intervention, refractory cardiogenic shock and in-laboratory cardiopulmonary arrest. *J Invasive Cardiol*. 2011;23:141–147.
315. SheuJJ, TsaiTH, LeeFY, FangHY, SunCK, LeuS, YangCH, ChenSM, Hang CL, Hsieh YK, Chen CJ, Wu CJ, Yip HK. Early extracorporeal membrane oxygenator-assisted primary percutaneous coronary intervention improved 30-day clinical outcomes in patients with ST-segment elevation myocardial infarction complicated with profound cardiogenic shock. *Crit Care Med*. 2010;38:1810–1817. doi: 10.1097/CCM.0b013e3181e8acf7.
316. Arit M, Philipp A, Voelkel S, Schopka S, Husser O, Hengstenberg C, Schmid C, Hilker M. Early experiences with miniaturized extracorporeal life-support in the catheterization laboratory. *Eur J Cardiothorac Surg*. 2012;42:858–863. doi: 10.1093/ejcts/ezs176.
317. Grambow DW, Deeb GM, Pavlides GS, Margulis A, O'Neill WW, Bates ER. Emergent percutaneous cardiopulmonary bypass in patients having cardiovascular collapse in the cardiac catheterization laboratory. *Am J Cardiol*. 1994;73:872–875.
318. Mooney MR, Arom KV, Joyce LD, Mooney JF, Goldenberg IF, Von Rueden TJ, Emery RW. Emergency cardiopulmonary bypass support in patients with cardiac arrest. *J Thorac Cardiovasc Surg*. 1991;101:450–454.
319. Tsao NW, Shih CM, Yeh JS, Kao YT, Hsieh MH, Ou KL, Chen JW, Shyu KG, Weng ZC, Chang NC, Lin FY, Huang CY. Extracorporeal membrane oxygenation-assisted primary percutaneous coronary intervention may improve survival of patients with acute myocardial infarction complicated by profound cardiogenic shock. *J Crit Care*. 2012;27:530. e1–530.11. doi: 10.1016/j.jcrc.2012.02.012.
320. Thiele H, Zeymer U, Neumann FJ, Ferenc M, Olbrich HG, Hausleiter J, de Waha A, Richardt G, Hennersdorf M, Empen K, Fuernau G, Desch S, Eitel I, Hambrecht R, Lauer B, Böhm M, Ebel H, Schneider S, Werdan K, Schuler G; Intra-aortic Balloon Pump in cardiogenic shock II (IABP-SHOCK II) trial investigators. Intra-aortic balloon counterpulsation in acute myocardial infarction complicated by cardiogenic shock (IABP-SHOCK II): final 12 month results of a randomised, open-label trial. *Lancet*. 2013;382:1638–1645. doi: 10.1016/S0140-6736(13)61783-3.
321. Ohman EM, George BS, White CJ, Kern MJ, Gurbel PA, Freedman RJ, Lundergan C, Hartmann JR, Talley JD, Frey MJ. Use of aortic counterpulsation to improve sustained coronary artery patency during acute myocardial infarction. Results of a randomized trial. The Randomized IABP Study Group. *Circulation*. 1994;90:792–799.

- Kaul U, Sahay S, Bahl VK, Sharma S, Wasir HS, Venugopal P. Coronary angioplasty in high risk patients: comparison of elective intraaortic balloon pump and percutaneous cardiopulmonary bypass support—a randomized study. *J Interv Cardiol.* 1995;8:199–205.
323. Stone GW, Marsalese D, Brodie BR, Griffin JJ, Donohue B, Costantini C, Balestrini C, Wharton T, Esente P, Spain M, Moses J, Nobuyoshi M, Ayres M, Jones D, Mason D, Grines L, O'Neill WW, Grines CL. A prospective, randomized evaluation of prophylactic intraaortic balloon counterpulsation in high risk patients with acute myocardial infarction treated with primary angioplasty. Second Primary Angioplasty in Myocardial Infarction (PAMI-II) Trial Investigators. *J Am Coll Cardiol.* 1997;29:1459–1467.
324. Ohman EM, Nanas J, Stomel RJ, Leeser MA, Nielsen DW, O'Dea D, Rogers FJ, Harber D, Hudson MP, Fraulo E, Shaw LK, Lee KL; TACTICS Trial. Thrombolysis and counterpulsation to improve survival in myocardial infarction complicated by hypotension and suspected cardiogenic shock or heart failure: results of the TACTICS Trial. *J Thromb Thrombolysis.* 2005;19:33–39. doi: 10.1007/s11239-005-0938-0.
325. Prondzinsky R, Lemm H, Swyter M, Wegener N, Unverzagt S, Carter JM, Russ M, Schlitt A, Buerke U, Christoph A, Schmidt H, Winkler M, Thiery J, Werdan K, Buerke M. Intra-aortic balloon counterpulsation in patients with acute myocardial infarction complicated by cardiogenic shock: the prospective, randomized IABP SHOCK Trial for attenuation of multiorgan dysfunction syndrome. *Crit Care Med.* 2010;38:152–160. doi: 10.1097/CCM.0b013e3181b78671.
326. Unverzagt S, Buerke M, de Waha A, Haerting J, Pietzner D, Seyfarth M, Thiele H, Werdan K, Zeymer U, Prondzinsky R. Intra-aortic balloon pump counterpulsation (IABP) for myocardial infarction complicated by cardiogenic shock. *Cochrane Database Syst Rev.* 2015;3:CD007398. doi: 10.1002/14651858.CD007398.pub3.
327. Sjauw KD, Engström AE, Vis MM, van der Schaaf RJ, Baan J Jr, Koch KT, de Winter RJ, Piek JJ, Tijssen JG, Henriques JP. A systematic review and meta-analysis of intra-aortic balloon pump therapy in ST-elevation myocardial infarction: should we change the guidelines? *Eur Heart J.* 2009;30:459–468. doi: 10.1093/eurheartj/ehh602.
328. Lee JM, Park J, Kang J, Jeon KH, Jung JH, Lee SE, Han JK, Kim HL, Yang HM, Park KW, Kang HJ, Koo BK, Kim SH, Kim HS. The efficacy and safety of mechanical hemodynamic support in patients undergoing high-risk percutaneous coronary intervention with or without cardiogenic shock: Bayesian approach network meta-analysis of 13 randomized controlled trials. *Int J Cardiol.* 2015;184:36–46. doi: 10.1016/j.ijcard.2015.01.081.
329. Reul GJ, Cooley DA, Hallman GL, Duncan JM, Livesay JJ, Frazier OH, Ott DA, Angelini P, Massumi A, Mathur VS. Coronary artery bypass for unsuccessful percutaneous transluminal coronary angioplasty. *J Thorac Cardiovasc Surg.* 1984;88(5 Pt 1):685–694.
330. Andreasen JJ, Mortensen PE, Andersen LI, Arendrup HC, Ilkjaer LB, Kjølner M, Thayssen P. Emergency coronary artery bypass surgery after failed percutaneous transluminal coronary angioplasty. *Scand Cardiovasc J.* 2000;34:242–246.
331. Kenyon N, Albertson TE. Status asthmaticus: from the emergency department to the intensive care unit. *Clin Rev Allergy Immunol.* 2001;20:271–292.
332. Division of Data Services. *New Asthma Estimates: Tracking Prevalence, Health Care, and Mortality.* Hyattsville, Md: National Center for Health Statistics; 2001.
333. McFadden ER Jr.. Acute severe asthma. *Am J Respir Crit Care Med.* 2003;168:740–759.
334. McFadden ER Jr., Warren EL. Observations on asthma mortality. *Ann Intern Med.* 1997;127:142–147.
335. Jorge S, Becquemin MH, Delerme S, Bennaceur M, Isnard R, Achkar R, Riou B, Boddaert J, Ray P. Cardiac asthma in elderly patients: incidence, clinical presentation and outcome. *BMC Cardiovasc Disord.* 2007;7:16.
336. Rainbow J, Browne GJ. Fatal asthma or anaphylaxis? *Emerg Med J.* 2002;19:415–417.
337. Kokturk N, Demir N, Kervan F, Dinc E, Koybasioglu A, Turktas H. A subglottic mass mimicking near-fatal asthma: a challenge of diagnosis. *J Emerg Med.* 2004;26:57–60.
338. Camargo CA Jr., Spooner CH, Rowe BH. Continuous versus intermittent beta-agonists in the treatment of acute asthma. *Cochrane Database Syst Rev.* 2003;No. 4:CD001115.
339. Travers A, Jones AP, Kelly K, Barker SJ, Camargo CA, Rowe BH. Intravenous beta2-agonists for acute asthma in the emergency department. *Cochrane Database Syst Rev.* 2001:CD002988.
340. Cates CJ, Crilly JA, Rowe BH. Holding chambers (spacers) versus nebulisers for beta-agonist treatment of acute asthma. *Cochrane Database Syst Rev.* 2006;No. 2:CD000052.
341. Kelly HW. Levalbuterol for asthma: a better treatment? *Curr Allergy Asthma Rep.* 2007;7:310–314.
342. Aaron SD. The use of ipratropium bromide for the management of acute asthma exacerbation in adults and children: a systematic review. *J Asthma.* 2001;38:521–530.
343. Rodrigo G, Rodrigo C, Burschtin O. A meta-analysis of the effects of ipratropium bromide in adults with acute asthma. *Am J Med.* 1999;107:363–370.

344. Edmonds ML, Camargo CA Jr., Pollack CV Jr., Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma. *Cochrane Database Syst Rev.* 2003;No. 3:CD002308.
345. Harrison BD, Stokes TC, Hart GJ, Vaughan DA, Ali NJ, Robinson AA. Need for intravenous hydrocortisone in addition to oral prednisolone in patients admitted to hospital with severe asthma without ventilatory failure. *Lancet.* 1986;1:181–184.
346. Ratto D, Alfaro C, Sipsley J, Glovsky MM, Sharma OP. Are intravenous corticosteroids required in status asthmaticus? *JAMA.* 1988;260:527–529.
347. Plotnick LH, Ducharme FM. Acute asthma in children and adolescents: should inhaled anticholinergics be added to beta(2)-agonists? *Am J Respir Med.* 2003;2:109–115.
348. Rodrigo GJ, Castro-Rodriguez JA. Anticholinergics in the treatment of children and adults with acute asthma: a systematic review with meta-analysis. *Thorax.* 2005;60:740–746.
349. Silverman RA, Osborn H, Runge J, Gallagher EJ, Chiang W, Feldman J, Gaeta T, Freeman K, Levin B, Mancherje N, Scharf S. IV magnesium sulfate in the treatment of acute severe asthma: a multicenter randomized controlled trial. *Chest.* 2002;122:489–497.
350. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr.. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department. *Cochrane Database Syst Rev.* 2000;No. 1:CD001490.
351. Gallegos-Solózanó MC, Pérez-Padilla R, Hernández-Zenteno RJ. “Usefulness of inhaled magnesium sulfate in the coadjuvant management of severe asthma crisis in an emergency department. *Pulm Pharmacol Ther.* 2010;23:432–437.
352. Blitz M, Blitz S, Hughes R, Diner B, Beasley R, Knopp J, Rowe BH. Aerosolized magnesium sulfate for acute asthma: a systematic review. *Chest.* 2005;128:337–344.
353. Cydulka R, Davison R, Grammer L, Parker M, Mathews JIV. The use of epinephrine in the treatment of older adult asthmatics. *Ann Emerg Med.* 1988;17:322–326.
354. Putland M, Kerr D, Kelly AM. Adverse events associated with the use of intravenous epinephrine in emergency department patients presenting with severe asthma. *Ann Emerg Med.* 2006;47:559–563.
355. Petrillo TM, Fortenberry JD, Linzer JF, Simon HK. Emergency department use of ketamine in pediatric status asthmaticus. *J Asthma.* 2001;38:657–664.
356. Howton JC, Rose J, Duffy S, Zoltanski T, Levitt MA. Randomized, double-blind, placebo-controlled trial of intravenous ketamine in acute asthma. *Ann Emerg Med.* 1996;27:170–175.
357. Allen JY, Macias CG. The efficacy of ketamine in pediatric emergency department patients who present with acute severe asthma. *Ann Emerg Med.* 2005;46:43–50.
358. Hess DR, Acosta FL, Ritz RH, Kacmarek RM, Camargo CA Jr.. The effect of heliox on nebulizer function using a beta-agonist bronchodilator. *Chest.* 1999;115:184–189.
359. Rodrigo G, Pollack C, Rodrigo C, Rowe BH. Heliox for nonintubated acute asthma patients. *Cochrane Database Syst Rev.* 2006;No. 4:CD002884.
360. Parameswaran K, Belda J, Rowe BH. Addition of intravenous aminophylline to  $\beta_2$ -agonists in adults with acute asthma. *Cochrane Database Syst Rev.* 2000;No. 4:CD002742.
361. Schultz TE. Sevoflurane administration in status asthmaticus: a case report. *AANA J.* 2005;73:35–36.
362. Wheeler DS, Clapp CR, Ponaman ML, Bsn HM, Poss WB. Isoflurane therapy for status asthmaticus in children: a case series and protocol. *Pediatr Crit Care Med.* 2000;1:55–59.
363. British Thoracic Society Standards of Care Committee. Non-invasive ventilation in acute respiratory failure. *Thorax.* 2002;57:192–211.
364. Soroksky A, Stav D, Shpirer I. A pilot prospective, randomized, placebo-controlled trial of bilevel positive airway pressure in acute asthmatic attack. *Chest.* 2003;123:1018–1025.
365. Ram FS, Wellington S, Rowe BH, Wedzicha JA. Non-invasive positive pressure ventilation for treatment of respiratory failure due to severe acute exacerbations of asthma. *Cochrane Database Syst Rev.* 2005;No. 3:CD004360.
366. Marik PE, Varon J, Fromm R Jr.. The management of acute severe asthma. *J Emerg Med.* 2002;23:257–268.
367. Brenner B, Corbridge T, Kazzi A. Intubation and mechanical ventilation of the asthmatic patient in respiratory failure. *Proc Am Thorac Soc.* 2009;6:371–379.
368. Darioli R, Perret C. Mechanical controlled hypoventilation in status asthmaticus. *Am Rev Respir Dis.* 1984;129:385–387.
- 369.



- Tuxen DV. Permissive hypercapnic ventilation. *Am J Respir Crit Care Med.* 1994;150:870–874.
370. Mikkelsen ME, Woo YJ, Sager JS, Fuchs BD, Christie JD. Outcomes using extracorporeal life support for adult respiratory failure due to status asthmaticus. *Asaio J.* 2009;55():47–52.
371. Leiba A, Bar-Yosef S, Bar-Dayana Y, Weiss Y, Segal E, Paret G, Vardi A. Early administration of extracorporeal life support for near fatal asthma. *Isr Med Assoc J.* 2003;5():600–602.
372. Conrad SA, Green R, Scott LK. Near-fatal pediatric asthma managed with pumpless arteriovenous carbon dioxide removal. *Crit Care Med.* 2007;35:2624–2629.
373. Elliot SC, Paramasivam K, Oram J, Bodenham AR, Howell SJ, Mallick A. Pumpless extracorporeal carbon dioxide removal for life-threatening asthma. *Crit Care Med.* 2007;35:945–948.
374. Barker P. Resuscitation in status asthmaticus. *Med J Aust.* 1985;142:238.
375. Diament RH, Sloan JP. Failed resuscitation in acute severe asthma: a medical indication for emergency thoracotomy? *Arch Emerg Med.* 1987;4:233–235.
376. Eason J, Tayler D, Cottam S, Edwards R, Beard C, Peachey T, Lanigan C, Knibb A, Dimond J. Manual chest compression for total bronchospasm. *Lancet.* 1991;337:366.
377. Fisher MM, Bowey CJ, Ladd-Hudson K. External chest compression in acute asthma: a preliminary study. *Crit Care Med.* 1989;17:686–687.
378. Fisher MM, Whaley AP, Pye RR. External chest compression in the management of acute severe asthma: a technique in search of evidence. *Prehosp Disaster Med.* 2001;16:124–127.
379. Mostert JW. Lung massage for total bronchospasm: a case report. *S Afr Med J.* 1960;34:703–704.
380. Smolnikoff VP. Total bronchospasm and lung massage. *Anaesthesia.* 1960;15:40–44.
381. Deakin CD, McLaren RM, Petley GW, Clewlow F, Dalrymple-Hay MJ. Effects of positive end-expiratory pressure on transthoracic impedance: implications for defibrillation. *Resuscitation.* 1998;37:9–12.
382. Voelckel WG, Lurie KG, Zielinski T, McKnite S, Plaisance P, Wenzel V, Lindner KH. The effects of positive end-expiratory pressure during active compression decompression cardiopulmonary resuscitation with the inspiratory threshold valve. *Anesth Analg.* 2001;92:967–974.
383. Tuxen DV. Detrimental effects of positive end-expiratory pressure during controlled mechanical ventilation of patients with severe airflow obstruction. *Am Rev Respir Dis.* 1989;140:5–9.
384. Myles PS, Madder H, Morgan EB. Intraoperative cardiac arrest after unrecognized dynamic hyperinflation. *Br J Anaesth.* 1995;74:340–342.
385. Mercer M. Cardiac arrest after unrecognized dynamic inflation. *Br J Anaesth.* 1995;75:252.
386. Rosengarten PL, Tuxen DV, Dziukas L, Scheinkestel C, Merrett K, Bowes G. Circulatory arrest induced by intermittent positive pressure ventilation in a patient with severe asthma. *Anaesth Intensive Care.* 1991;19:118–121.
387. Neugut AI, Ghatak AT, Miller RL. Anaphylaxis in the United States: an investigation into its epidemiology. *Arch Intern Med.* 2001;161:15–21.
388. Banerji A, Clark S, Blanda M, LoVecchio F, Snyder B, Camargo CA Jr. Multicenter study of patients with angiotensin-converting enzyme inhibitor-induced angioedema who present to the emergency department. *Ann Allergy Asthma Immunol.* 2008;100:327–332.
389. Agah R, Bandi V, Guntupalli KK. Angioedema: the role of ACE inhibitors and factors associated with poor clinical outcome. *Intensive Care Med.* 1997;23:793–796.
390. Bork K, Hardt J, Schicketanz KH, Ressel N. Clinical studies of sudden upper airway obstruction in patients with hereditary angioedema due to C1 esterase inhibitor deficiency. *Arch Intern Med.* 2003;163:1229–1235.
391. Fisher M. Blood volume replacement in acute anaphylactic cardiovascular collapse related to anaesthesia. *Br J Anaesth.* 1977;49:1023–1026.
392. Nicolas F, Villers D, Blanloeil Y. Hemodynamic pattern in anaphylactic shock with cardiac arrest. *Crit Care Med.* 1984;12:144–145.
393. Raper RF, Fisher MM. Profound reversible myocardial depression after anaphylaxis. *Lancet.* 1988;1:386–388.
394. Pumphrey RS. Lessons for management of anaphylaxis from a study of fatal reactions. *Clin Exp Allergy.* 2000;30:1144–1150.

395. Pumphrey RS. Fatal anaphylaxis in the UK, 1992–2001. *Novartis Found Symp.* 2004;257:116–128.
396. Yilmaz R, Yuksekbas O, Erkol Z, Bulut ER, Arslan MN. Postmortem findings after anaphylactic reactions to drugs in Turkey. *Am J Forensic Med Pathol.* 2009;30:346–349.
397. Simons FE, Gu X, Simons KJ. Epinephrine absorption in adults: intramuscular versus subcutaneous injection. *J Allergy Clin Immunol.* 2001;108:871–873.
398. Sheikh A, Shehata YA, Brown SG, Simons FE. Adrenaline (epinephrine) for the treatment of anaphylaxis with and without shock. *Cochrane Database Syst Rev.* 2008;No. 4:CD006312.
399. Korenblat P, Lundie MJ, Dankner RE, Day JH. A retrospective study of epinephrine administration for anaphylaxis: how many doses are needed? *Allergy Asthma Proc.* 1999;20:383–386.
400. Yunginger JW, Sweeney KG, Sturner WQ, Giannandrea LA, Teigland JD, Bray M, Benson PA, York JA, Biedrzycki L, Squillace DL, Helm RM. Fatal food-induced anaphylaxis. *JAMA.* 1988;260:1450–1452.
401. Brown SG, Blackman KE, Stenlake V, Heddle RJ. Insect sting anaphylaxis; prospective evaluation of treatment with intravenous adrenaline and volume resuscitation. *Emerg Med J.* 2004;21:149–154.
402. Bautista E, Simons FE, Simons KJ, Becker AB, Duke K, Tillett M, Kepron W, Mink SN. Epinephrine fails to hasten hemodynamic recovery in fully developed canine anaphylactic shock. *Int Arch Allergy Immunol.* 2002;128:151–164.
403. Bochner BS, Lichtenstein LM. Anaphylaxis. *N Engl J Med.* 1991;324:1785–1790.
404. Pumphrey R. Anaphylaxis: can we tell who is at risk of a fatal reaction? *Curr Opin Allergy Clin Immunol.* 2004;4:285–290.
405. Johnston SL, Unsworth J, Gompels MM. Adrenaline given outside the context of life threatening allergic reactions. *BMJ.* 2003;326:589–590.
406. Mink SN, Simons FE, Simons KJ, Becker AB, Duke K. Constant infusion of epinephrine, but not bolus treatment, improves haemodynamic recovery in anaphylactic shock in dogs. *Clin Exp Allergy.* 2004;34:1776–1783.
407. Kill C, Wranze E, Wulf H. Successful treatment of severe anaphylactic shock with vasopressin: two case reports. *Int Arch Allergy Immunol.* 2004;134:260–261.
408. Williams SR, Denault AY, Pellerin M, Martineau R. Vasopressin for treatment of shock following aprotinin administration. *Can J Anaesth.* 2004;51:169–172.
409. Schummer C, Wirsing M, Schummer W. The pivotal role of vasopressin in refractory anaphylactic shock. *Anesth Analg.* 2008;107:620–624.
410. Kluger MT. The Bispectral Index during an anaphylactic circulatory arrest. *Anaesth Intensive Care.* 2001;29:544–547.
411. McBrien ME, Breslin DS, Atkinson S, Johnston JR. Use of methoxamine in the resuscitation of epinephrine-resistant electromechanical dissociation. *Anaesthesia.* 2001;56:1085–1089.
412. Rocq N, Favier JC, Plancade D, Steiner T, Mertes PM. Successful use of terlipressin in post-cardiac arrest resuscitation after an epinephrine-resistant anaphylactic shock to suxamethonium. *Anesthesiology.* 2007;107:166–167.
413. Green R, Ball A. Alpha-agonists for the treatment of anaphylactic shock. *Anaesthesia.* 2005;60:621–622.
414. Heytman M, Rainbird A. Use of alpha-agonists for management of anaphylaxis occurring under anaesthesia: case studies and review. *Anaesthesia.* 2004;59:1210–1215.
415. Higgins DJ, Gayatri P. Methoxamine in the management of severe anaphylaxis. *Anaesthesia.* 1999;54:1126.
416. Simons FE. Advances in H1-antihistamines. *N Engl J Med.* 2004;351:2203–2217.
417. Sheikh A, Ten Broek V, Brown SG, Simons FE. H1-antihistamines for the treatment of anaphylaxis: Cochrane systematic review. *Allergy.* 2007;62:830–837.
418. Gibbs MW, Kuczkowski KM, Benumof JL. Complete recovery from prolonged cardio-pulmonary resuscitation following anaphylactic reaction to readministered intravenous cefazolin. *Acta Anaesthesiol Scand.* 2003;47:230–232.
419. Choo KJ, Simons FE, Sheikh A. Glucocorticoids for the treatment of anaphylaxis. *Cochrane Database Syst Rev.* 2010;3:CD007596.
420. Allen SJ, Gallagher A, Paxton LD. Anaphylaxis to rocuronium. *Anaesthesia.* 2000;55:1223–1224.
421. Laffogues E, Sleth JC, Pluskwa F, Saizy C. Successful extracorporeal resuscitation of a probable perioperative anaphylactic shock due to atracurium [in French]. *Ann Fr Anesth Reanim.* 2005;24:551–555.

422. Bunch TJ, White RD, Lopez-Jimenez F, Thomas RJ. Association of body weight with total mortality and with ICD shocks among survivors of ventricular fibrillation in out-of-hospital cardiac arrest. *Resuscitation*. 2008;77:351–355.
423. White RD, Blackwell TH, Russell JK, Jorgenson DB. Body weight does not affect defibrillation, resuscitation, or survival in patients with out-of-hospital cardiac arrest treated with a nonescalating biphasic waveform defibrillator. *Crit Care Med*. 2004;32:S387–S392.
424. DeSilva RA, Lown B. Energy requirement for defibrillation of a markedly overweight patient. *Circulation*. 1978;57:827–830.
425. White RD, Blackwell TH, Russell JK, Snyder DE, Jorgenson DB. Transthoracic impedance does not affect defibrillation, resuscitation or survival in patients with out-of-hospital cardiac arrest treated with a non-escalating biphasic waveform defibrillator. *Resuscitation*. 2005;64:63–69.
426. Srinivasan V, Nadkarni VM, Helfaer MA, Carey SM, Berg RA. Childhood obesity and survival after in-hospital pediatric cardiopulmonary resuscitation. *Pediatrics*. 2010;125:e481–e488.
427. Paice B, Gray JM, McBride D, Donnelly T, Lawson DH. Hyperkalaemia in patients in hospital. *Br Med J (Clin Res Ed)*. 1983;286:1189–1192.
428. Weiner ID, Wingo CS. Hyperkalemia: a potential silent killer. *J Am Soc Nephrol*. 1998;9:1535–1543.
429. Weiner M, Epstein FH. Signs and symptoms of electrolyte disorders. *Yale J Biol Med*. 1970;43:76–109.
430. Rastegar A, Soleimani M. Hypokalaemia and hyperkalaemia. *Postgrad Med J*. 2001;77:759–764.
431. Mattu A, Brady WJ, Robinson DA. Electrocardiographic manifestations of hyperkalemia. *Am J Emerg Med*. 2000;18:721–729.
432. Frohnert PP, Giuliani ER, Friedberg M, Johnson WJ, Tauxe WN. Statistical investigation of correlations between serum potassium levels and electrocardiographic findings in patients on intermittent hemodialysis therapy. *Circulation*. 1970;41:667–676.
433. Gennari FJ. Hypokalemia. *N Engl J Med*. 1998;339:451–458.
434. Slovis C, Jenkins R. ABC of clinical electrocardiography: conditions not primarily affecting the heart [published corrections appear in *BMJ*. 2007;334(7603) doi: 10.1136/bmj.39219.615243.AE and *BMJ*. 2002;325:259]. *BMJ*. 2002;324:1320–1323.
435. Clausen TG, Brocks K, Ibsen H. Hypokalemia and ventricular arrhythmias in acute myocardial infarction. *Acta Med Scand*. 1988;224:531–537.
436. Higham PD, Adams PC, Murray A, Campbell RW. Plasma potassium, serum magnesium and ventricular fibrillation: a prospective study. *Q J Med*. 1993;86:609–617.
437. Nordrehaug JE. Malignant arrhythmia in relation to serum potassium in acute myocardial infarction. *Am J Cardiol*. 1985;56:20D–23D.
438. Nordrehaug JE, von der Lippe G. Hypokalaemia and ventricular fibrillation in acute myocardial infarction. *Br Heart J*. 1983;50:525–529.
439. Obeid AI, Verrier RL, Lown B. Influence of glucose, insulin, and potassium on vulnerability to ventricular fibrillation in the canine heart. *Circ Res*. 1978;43:601–608.
440. Curry P, Fitchett D, Stubbs W, Krikler D. Ventricular arrhythmias and hypokalaemia. *Lancet*. 1976;2:231–233.
441. Buylaert WA, Calle PA, Houbrechts HN. Serum electrolyte disturbances in the post-resuscitation period. *Resuscitation*. 1989;17(suppl):S189–S196.
442. Cannon LA, Heiselman DE, Dougherty JM, Jones J. Magnesium levels in cardiac arrest victims: relationship between magnesium levels and successful resuscitation. *Ann Emerg Med*. 1987;16:1195–1199.
443. McDonnell NJ, Muchatuta NA, Paech MJ. Acute magnesium toxicity in an obstetric patient undergoing general anaesthesia for caesarean delivery. *Int J Obstet Anesth*. 2010;19:226–231.
444. James MF. Cardiopulmonary arrest in pregnancy. *Br J Anaesth*. 2010;104:115.
445. Mordes JP, Swartz R, Arky RA. Extreme hypermagnesemia as a cause of refractory hypotension. *Ann Intern Med*. 1975;83:657–658.
446. Kloeck WG. A practical approach to the aetiology of pulseless electrical activity: a simple 10-step training mnemonic. *Resuscitation*. 1995;30:157–159.
447. Working Group, Ad Hoc Subcommittee on Outcomes, American College of Surgeons–Committee on Trauma. Practice management guidelines for emergency department thoracotomy. *J Am Coll Surg*. 2001;193:303–309.
448. Hopson LR, Hirsh E, Delgado J, Domeier RM, McSwain NE, Krohmer J. Guidelines for withholding or termination of resuscitation in prehospital traumatic cardiopulmonary arrest: joint position statement of the National Association of EMS Physicians and the American College of Surgeons Committee on Trauma. *J Am Coll Surg*. 2003;196:106–112.

449. Advanced Trauma Life Support for Doctors. 7th Ed. Chicago: American College of Surgeons; 2004.
450. Maron BJ, Estes NA III.. Commotio cordis. *N Engl J Med*. 2010;362:917–927.
451. Maron BJ, Doerer JJ, Haas TS, Estes NA, Hodges JS, Link MS. Commotio cordis and the epidemiology of sudden death in competitive lacrosse. *Pediatrics*. 2009;124:966–971.
452. Link MS, Maron BJ, Wang PJ, VanderBrink BA, Zhu W, Estes NA III.. Upper and lower limits of vulnerability to sudden arrhythmic death with chest-wall impact (commotio cordis). *J Am Coll Cardiol*. 2003;41:99–104.
453. Sheridan RL, Goldstein MA, Stoddard FJ Jr., Walker TG. Case records of the Massachusetts General Hospital: case 41–2009: a 16-year-old boy with hypothermia and frostbite. *N Engl J Med*. 2009;361:2654–2662.
454. Larach MG. Accidental hypothermia. *Lancet*. 1995;345:493–498.
455. Kornberger E, Schwarz B, Lindner KH, Mair P. Forced air surface rewarming in patients with severe accidental hypothermia. *Resuscitation*. 1999;41:105–111.
456. Roggla M, Frossard M, Wagner A, Holzer M, Bur A, Roggla G. Severe accidental hypothermia with or without hemodynamic instability: rewarming without the use of extracorporeal circulation. *Wien Klin Wochenschr*. 2002;114:315–320.
457. Gilbert M, Busund R, Skagseth A, Nilsen PÅ, Solb? JP. Resuscitation from accidental hypothermia of 13.7°C with circulatory arrest. *Lancet*. 2000;355:375–376.
458. Coleman E, Doddakula K, Meeke R, Marshall C, Jahangir S, Hinchion J. An atypical case of successful resuscitation of an accidental profound hypothermia patient, occurring in a temperate climate. *Perfusion*. 2010;25:103–106.
459. Walpoth BH, Walpoth-Aslan BN, Mattle HP, Radanov BP, Schroth G, Schaeffler L, Fischer AP, von Segesser L, Althaus U. Outcome of survivors of accidental deep hypothermia and circulatory arrest treated with extracorporeal blood warming. *N Engl J Med*. 1997;337:1500–1505.
460. Althaus U, Aeberhard P, Schubach P, Nachbur BH, Muhlemann W. Management of profound accidental hypothermia with cardiorespiratory arrest. *Ann Surg*. 1982;195:492–495.
461. Dobson JA, Burgess JJ. Resuscitation of severe hypothermia by extracorporeal rewarming in a child. *J Trauma*. 1996;40:483–485.
462. Farstad M, Andersen KS, Koller ME, Grong K, Segadal L, Husby P. Rewarming from accidental hypothermia by extracorporeal circulation: a retrospective study. *Eur J Cardiothorac Surg*. 2001;20:58–64.
463. Kangas E, Niemela H, Kojo N. Treatment of hypothermic circulatory arrest with thoracotomy and pleural lavage. *Ann Chir Gynaecol*. 1994;83:258–260.
464. Plaisier BR. Thoracic lavage in accidental hypothermia with cardiac arrest: report of a case and review of the literature. *Resuscitation*. 2005;66:99–104.
465. Winegard C. Successful treatment of severe hypothermia and prolonged cardiac arrest with closed thoracic cavity lavage. *J Emerg Med*. 1997;15:629–632.
466. Walters DT. Closed thoracic cavity lavage for hypothermia with cardiac arrest. *Ann Emerg Med*. 1991;20:439–440.
467. Hall KN, Syverud SA. Closed thoracic cavity lavage in the treatment of severe hypothermia in human beings. *Ann Emerg Med*. 1990;19:204–206.
468. Oberhammer R, Beikircher W, Hormann C, Lorenz I, Pycha R, Adler-Kastner L, Brugger H. Full recovery of an avalanche victim with profound hypothermia and prolonged cardiac arrest treated by extracorporeal re-warming. *Resuscitation*. 2008;76:474–480.
469. Tiruvoipati R, Balasubramanian SK, Khoshbin E, Hadjinikolaou L, Sosnowski AW, Firmin RK. Successful use of venovenous extracorporeal membrane oxygenation in accidental hypothermic cardiac arrest. *ASAIO J*. 2005;51:474–476.
470. Scaife ER, Connors RC, Morris SE, Nichol PF, Black RE, Matlak ME, Hansen K, Bolte RG. An established extracorporeal membrane oxygenation protocol promotes survival in extreme hypothermia. *J Pediatr Surg*. 2007;42:2012–2016.
471. Weinberg AD. The role of inhalation rewarming in the early management of hypothermia. *Resuscitation*. 1998;36:101–104.
472. Steinman AM. Cardiopulmonary resuscitation and hypothermia. *Circulation*. 1986;74():IV-29–IV-32.
473. Danzl DF, Pozos RS, Auerbach PS, Glazer S, Goetz W, Johnson E, Jui J, Lilja P, Marx JA, Miller J, Mills W Jr., Nowak R, Shields R, Vicario S, Wayne M. Multicenter hypothermia survey. *Ann Emerg Med*. 1987;16:1042–1055.
474. Incagnoli P, Bourgeois B, Teboul A, Laborie JM. Resuscitation from accidental hypothermia of 22 degrees C with circulatory arrest: importance of prehospital management [in French]. *Ann Fr Anesth Reanim*. 2006;25:535–538.

475. Boddicker KA, Zhang Y, Zimmerman MB, Davies LR, Kerber RE. Hypothermia improves defibrillation success and resuscitation outcomes from ventricular fibrillation. *Circulation*. 2005;111:3195–3201.
476. Reuler JB. Hypothermia: pathophysiology, clinical settings, and management. *Ann Intern Med*. 1978;89:519–527.
477. Elenbaas RM, Mattson K, Cole H, Steele M, Ryan J, Robinson W. Bretylium in hypothermia-induced ventricular fibrillation in dogs. *Ann Emerg Med*. 1984;13:994–999.
478. Kornberger E, Lindner KH, Mayr VD, Schwarz B, Rackwitz KS, Wenzel V, Krismer AC, Mair P. Effects of epinephrine in a pig model of hypothermic cardiac arrest and closed-chest cardiopulmonary resuscitation combined with active rewarming. *Resuscitation*. 2001;50:301–308.
479. Schwarz B, Mair P, Raedler C, Deckert D, Wenzel V, Lindner KH. Vasopressin improves survival in a pig model of hypothermic cardiopulmonary resuscitation. *Crit Care Med*. 2002;30:1311–1314.
480. Schwarz B, Mair P, Wagner-Berger H, Stadlbauer KH, Girg S, Wenzel V, Lindner KH. Neither vasopressin nor amiodarone improve CPR outcome in an animal model of hypothermic cardiac arrest. *Acta Anaesthesiol Scand*. 2003;47:1114–1118.
481. Stoner J, Martin G, O'Mara K, Ehlers J, Tomlanovich M. Amiodarone and bretylium in the treatment of hypothermic ventricular fibrillation in a canine model. *Acad Emerg Med*. 2003;10:187–191.
482. Wira C, Martin G, Stoner J, Margolis K, Donnino M. Application of normothermic cardiac arrest algorithms to hypothermic cardiac arrest in a canine model. *Resuscitation*. 2006;69:509–516.
483. Wira CR, Becker JU, Martin G, Donnino MW. Anti-arrhythmic and vasopressor medications for the treatment of ventricular fibrillation in severe hypothermia: a systematic review of the literature. *Resuscitation*. 2008;78:21–29.
484. Lienhart HG, John W, Wenzel V. Cardiopulmonary resuscitation of a near-drowned child with a combination of epinephrine and vasopressin. *Pediatr Crit Care Med*. 2005;6:486–488.
485. Kjaergaard B, Jakobsen LK, Nielsen C, Knudsen PJ, Kristensen SR, Larsson A. Low plasma potassium in deep hypothermic cardiac arrest indicates that cardiac arrest is secondary to hypothermia: a porcine study. *Eur J Emerg Med*. 2010;17:131–135.
486. Falk M, Brugger H, Adler-Kastner L. Avalanche survival chances. *Nature*. 1994;368:21.
487. Buser O, Etter HJ, Jaccard C. Probability of dying in an avalanche [in German]. *Z Unfallchir Versicherungsmed*. 1993;suppl 1:263–271.
488. Brugger H, Falk M. New perspectives of avalanche disasters: phase classification using pathophysiologic considerations [in German]. *Wien Klin Wochenschr*. 1992;104:167–173.
489. Brugger H, Durrer B, Adler-Kastner L, Falk M, Tschirky F. Field management of avalanche victims. *Resuscitation*. 2001;51:7–15.
490. Locher T, Walpoth B, Pfluger D, Althaus U. Accidental hypothermia in Switzerland (1980–1987): case reports and prognostic factors [in German]. *Schweiz Med Wochenschr*. 1991;121:1020–1028.
491. Mair P, Kornberger E, Furtwaengler W, Balogh D, Antretter H. Prognostic markers in patients with severe accidental hypothermia and cardiocirculatory arrest. *Resuscitation*. 1994;27:47–54.
492. Grosse AB, Grosse CA, Steinbach LS, Zimmermann H, Anderson S. Imaging findings of avalanche victims. *Skeletal Radiol*. 2007;36:515–521.
493. Stalsberg H, Albretsen C, Gilbert M, Kearney M, Moestue E, Nordrum I, Rostrup M, Orbo A. Mechanism of death in avalanche victims. *Virchows Arch A Pathol Anat Histopathol*. 1989;414:415–422.
494. Oberhammer R, Beikircher W, Hormann C, Lorenz I, Pycha R, Adler-Kastner L, Brugger H. Full recovery of an avalanche victim with profound hypothermia and prolonged cardiac arrest treated by extracorporeal re-warming. *Resuscitation*. 2008;76:474–480.
495. Radwin MI, Grissom CK. Technological advances in avalanche survival. *Wilderness Environ Med*. 2002;13:143–152.
496. Paal P, Ellerton J, Sumann G, Demetz F, Mair P, Brugger H. Basic life support ventilation in mountain rescue: official recommendations of the International Commission for Mountain Emergency Medicine (ICAR MEDCOM). *High Alt Med Biol*. 2007;8:147–154.
497. Locher T, Walpoth BH. Differential diagnosis of circulatory failure in hypothermic avalanche victims: retrospective analysis of 32 avalanche accidents [in German]. *Praxis (Bern 1994)*. 1996;85:1275–1282.
498. Farstad M, Andersen KS, Koller ME, Grong K, Segadal L, Husby P. Rewarming from accidental hypothermia by extracorporeal circulation: a retrospective study. *Eur J Cardiothorac Surg*. 2001;20:58–64.
499. Schaller MD, Fischer AP, Perret CH. Hyperkalemia: a prognostic factor during acute severe hypothermia. *JAMA*. 1990;264:1842–1845.
- 500.

- Danzl DF, Pozos RS, Auerbach PS, Glazer S, Goetz W, Johnson E, Jui J, Lilja P, Marx JA, Miller J, Mills W Jr., Nowak R, Shields R, Vicario S, Wayne M. Multicenter hypothermia survey. *Ann Emerg Med.* 1987;16:1042–1055.
501. Ruttman E, Weissenbacher A, Ulmer H, Muller L, Hofer D, Kilo J, Rabl W, Schwarz B, Laufer G, Antretter H, Mair P. Prolonged extracorporeal membrane oxygenation-assisted support provides improved survival in hypothermic patients with cardiocirculatory arrest. *J Thorac Cardiovasc Surg.* 2007;134:594–600.
502. Silfvast T, Pettila V. Outcome from severe accidental hypothermia in Southern Finland: a 10-year review. *Resuscitation.* 2003;59:285–290.
503. Hauty MG, Esrig BC, Hill JG, Long WB. Prognostic factors in severe accidental hypothermia: experience from the Mt. Hood tragedy. *J Trauma.* 1987;27:1107–1112.
504. Dobson JA, Burgess JJ. Resuscitation of severe hypothermia by extracorporeal rewarming in a child. *J Trauma.* 1996;40:483–485.
505. Peden MM, McGee K. The epidemiology of drowning worldwide. *Inj Control Saf Promot.* 2003;10:195–199.
506. Warner DS, Bierens JJ, Beerman SB, Katz LM. Drowning: a cry for help. *Anesthesiology.* 2009;110:1211–1213.
507. Joost JLM *Handbook on Drowning.* Berlin: Springer; 2004.
508. Papa L, Hoelle R, Idris A. Systematic review of definitions for drowning incidents. *Resuscitation.* 2005;65:255–264.
509. Idris AH, Berg RA, Bierens J, Bossaert L, Branche CM, Gabrielli A, Graves SA, Handley AJ, Hoelle R, Morley PT, Papa L, Pepe PE, Quan L, Szpilman D, Wigginton JG, Modell JH. Recommended guidelines for uniform reporting of data from drowning: the “Utstein style.” *Resuscitation.* 2003;59:45–57.
510. Youn CS, Choi SP, Yim HW, Park KN. Out-of-hospital cardiac arrest due to drowning: an Utstein Style report of 10 years of experience from St. Mary's Hospital. *Resuscitation.* 2009;80:778–783.
511. Quan L, Wentz KR, Gore EJ, Copass MK. Outcome and predictors of outcome in pediatric submersion victims receiving prehospital care in King County, Washington. *Pediatrics.* 1990;86:586–593.
512. Modell JH, Davis JH. Electrolyte changes in human drowning victims. *Anesthesiology.* 1969;30:414–420.
513. Southwick FS, Dalglish PH Jr.. Recovery after prolonged asystolic cardiac arrest in profound hypothermia: a case report and literature review. *JAMA.* 1980;243:1250–1253.
514. Siebke H, Rød T, Breivik H, Lind B. Survival after 40 minutes' submersion without cerebral sequelae. *Lancet.* 1975;1:1275–1277.
515. Bolte RG, Black PG, Bowers RS, Thorne JK, Corneli HM. The use of extracorporeal rewarming in a child submerged for 66 minutes. *JAMA.* 1988;260:377–379.
516. Gilbert M, Busund R, Skagseth A, Nilsen PÅ, Solb? JP. Resuscitation from accidental hypothermia of 13.7°C with circulatory arrest. *Lancet.* 2000;355:375–376.
517. Szpilman D, Soares M. In-water resuscitation: is it worthwhile? *Resuscitation.* 2004;63:25–31.
518. Allman FD, Nelson WB, Pacentine GA, McComb G. Outcome following cardiopulmonary resuscitation in severe pediatric near-drowning. *Am J Dis Child.* 1986;140:571–575.
519. Weinstein MD, Krieger BP. Near-drowning: epidemiology, pathophysiology, and initial treatment. *J Emerg Med.* 1996;14:461–467.
520. Watson RS, Cummings P, Quan L, Bratton S, Weiss NS. Cervical spine injuries among submersion victims. *J Trauma.* 2001;51:658–662.
521. Hwang V, Shofer FS, Durbin DR, Baren JM. Prevalence of traumatic injuries in drowning and near drowning in children and adolescents. *Arch Pediatr Adolesc Med.* 2003;157:50–53.
522. Kyriacou DN, Arcinue EL, Peek C, Kraus JF. Effect of immediate resuscitation on children with submersion injury. *Pediatrics.* 1994;94():137–142.
523. Modell JH. Drowning. *N Engl J Med.* 1993;328:253–256.
524. Rosen P, Stoto M, Harley J. The use of the Heimlich maneuver in near-drowning: Institute of Medicine report. *J Emerg Med.* 1995;13:397–405.
525. Manolios N, Mackie I. Drowning and near-drowning on Australian beaches patrolled by life-savers: a 10-year study, 1973–1983. *Med J Aust.* 1988;148:165–167, 170–171.
- 526.

- Onarheim H, Vik V. Porcine surfactant (Curosurf) for acute respiratory failure after near-drowning in 12 year old. *Acta Anaesthesiol Scand.* 2004;48:778–781.
527. Staudinger T, Bankier A, Strohmaier W, Weiss K, Locker GJ, Knapp S, Roggla M, Laczika K, Frass M. Exogenous surfactant therapy in a patient with adult respiratory distress syndrome after near drowning. *Resuscitation.* 1997;35:179–182.
528. Suzuki H, Ohta T, Iwata K, Yamaguchi K, Sato T. Surfactant therapy for respiratory failure due to near-drowning. *Eur J Pediatr.* 1996;155:383–384.
529. Cubattoli L, Franchi F, Coratti G. Surfactant therapy for acute respiratory failure after drowning: two children victim of cardiac arrest. *Resuscitation.* 2009;80:1088–1089.
530. Thalmann M, Trampitsch E, Haberkellner N, Eisendle E, Kraschl R, Kobinina G. Resuscitation in near drowning with extracorporeal membrane oxygenation. *Ann Thorac Surg.* 2001;72:607–608.
531. Fish RM, Geddes LA. Conduction of electrical current to and through the human body: a review. *Eplasty.* 2009;9:e44.
532. Budnick LD. Bathtub-related electrocutions in the United States, 1979 to 1982. *JAMA.* 1984;252:918–920.
533. Geddes LA, Bourland JD, Ford G. The mechanism underlying sudden death from electric shock. *Med Instrum.* 1986;20:303–315.
534. Medical aspects of lightning. National Weather Service Web site. Available at: [www.lightningsafety.noaa.gov/medical.html](http://www.lightningsafety.noaa.gov/medical.html). Accessed May 7, 2010.
535. Patten BM. Lightning and electrical injuries. *Neurol Clin.* 1992;10:1047–1058.
536. Browne BJ, Gaasch WR. Electrical injuries and lightning. *Emerg Med Clin North Am.* 1992;10:211–229.
537. Kleiner JP, Wilkin JH. Cardiac effects of lightning stroke. *JAMA.* 1978;240:2757–2759.
538. Lichtenberg R, Dries D, Ward K, Marshall W, Scanlon P. Cardiovascular effects of lightning strikes. *J Am Coll Cardiol.* 1993;21:531–536.
539. Cooper MA. Emergent care of lightning and electrical injuries. *Semin Neurol.* 1995;15:268–278.
540. Milzman DP, Moskowitz L, Hardel M. Lightning strikes at a mass gathering. *South Med J.* 1999;92:708–710.
541. Duclos PJ, Sanderson LM. An epidemiological description of lightning-related deaths in the United States. *Int J Epidemiol.* 1990;19:673–679.
542. Epperly TD, Stewart JR. The physical effects of lightning injury. *J Fam Pract.* 1989;29:267–272.
543. Whitcomb D, Martinez JA, Daberkow D. Lightning injuries. *South Med J.* 2002;95:1331–1334.
544. Maggolini S, Bozzano A, Russo P, Vitale G, Osculati G, Cantu E, Achilli F, Valagussa F. Echocardiography-guided pericardiocentesis with probe-mounted needle: report of 53 cases. *J Am Soc Echocardiogr.* 2001;14:821–824.
545. Salem K, Mulji A, Lonn E. Echocardiographically guided pericardiocentesis: the gold standard for the management of pericardial effusion and cardiac tamponade. *Can J Cardiol.* 1999;15:1251–1255.
546. Susini G, Pepi M, Sisillo E, Bortone F, Salvi L, Barbier P, Fiorentini C. Percutaneous pericardiocentesis versus subxiphoid pericardiotomy in cardiac tamponade due to postoperative pericardial effusion. *J Cardiothorac Vasc Anesth.* 1993;7:178–183.
547. Tsang TS, Barnes ME, Gersh BJ, Bailey KR, Seward JB. Outcomes of clinically significant idiopathic pericardial effusion requiring intervention. *Am J Cardiol.* 2003;91:704–707.
548. Tsang TS, Enriquez-Sarano M, Freeman WK, Barnes ME, Sinak LJ, Gersh BJ, Bailey KR, Seward JB. Consecutive 1127 therapeutic echocardiographically guided pericardiocenteses: clinical profile, practice patterns, and outcomes spanning 21 years. *Mayo Clin Proc.* 2002;77:429–436.
549. Coats TJ, Keogh S, Clark H, Neal M. Prehospital resuscitative thoracotomy for cardiac arrest after penetrating trauma: rationale and case series. *J Trauma.* 2001;50:670–673.
550. Powell DW, Moore EE, Cothren CC, Ciesla DJ, Burch JM, Moore JB, Johnson JL. Is emergency department resuscitative thoracotomy futile care for the critically injured patient requiring prehospital cardiopulmonary resuscitation? *J Am Coll Surg.* 2004;199:211–215.
551. Lewis G, Knottenbelt JD. Should emergency room thoracotomy be reserved for cases of cardiac tamponade? *Injury.* 1991;22:5–6.
552. Wang JC, Jiang P, Huang J, Qian GS. The protective effects and mechanisms of peroxisome proliferator-activated receptor-gamma agonist in rats with acute lung injury [in Chinese]. *Zhonghua Jie He He Hu Xi Za Zhi.* 2008;31:425–430.

553. Dunning J, Fabbri A, Kohl PH, Levine A, Lockowandt U, Mackay J, Pavie AJ, Strang T, Versteegh MI, Nashef SA EACTS Clinical Guidelines Committee. Guideline for resuscitation in cardiac arrest after cardiac surgery. *Eur J Cardiothorac Surg*. 2009;36:3–28.
554. Mackay JH, Powell SJ, Charman SC, Rozario C. Resuscitation after cardiac surgery: are we ageist? *Eur J Anaesthesiol*. 2004;21:66–71.
555. Raman J, Saldanha RF, Branch JM, Esmore DS, Spratt PM, Farnsworth AE, Harrison GA, Chang VP, Shanahan MX. Open cardiac compression in the postoperative cardiac intensive care unit. *Anaesth Intensive Care*. 1989;17:129–135.
556. Karhunen JP, Sihvo EI, Suojaranta-Ylinen RT, Ramo OJ, Salminen US. Predictive factors of hemodynamic collapse after coronary artery bypass grafting: a case-control study. *J Cardiothorac Vasc Anesth*. 2006;20:143–148.
557. Anthi A, Tzelepis GE, Alivizatos P, Michalis A, Palatianos GM, Geroulanos S. Unexpected cardiac arrest after cardiac surgery: incidence, predisposing causes, and outcome of open chest cardiopulmonary resuscitation. *Chest*. 1998;113:15–19.
558. Dimopoulou I, Anthi A, Michalis A, Tzelepis GE. Functional status and quality of life in long-term survivors of cardiac arrest after cardiac surgery. *Crit Care Med*. 2001;29:1408–1411.
559. el-Banayosy A, Brehm C, Kizner L, Hartmann D, Kortke H, Korner MM, Minami K, Reichelt W, Korfer R. Cardiopulmonary resuscitation after cardiac surgery: a two-year study. *J Cardiothorac Vasc Anesth*. 1998;12:390–392.
560. Fairman RM, Edmunds LH Jr.. Emergency thoracotomy in the surgical intensive care unit after open cardiac operation. *Ann Thorac Surg*. 1981;32:386–391.
561. Mackay JH, Powell SJ, Osgathorp J, Rozario CJ. Six-year prospective audit of chest reopening after cardiac arrest. *Eur J Cardiothorac Surg*. 2002;22:421–425.
562. Ngaage DL, Cowen ME. Survival of cardiorespiratory arrest after coronary artery bypass grafting or aortic valve surgery. *Ann Thorac Surg*. 2009;88:64–68.
563. Kriaras I, Anthi A, Michelopoulos A, Karakatsani A, Tzelepis G, Papadimitriou L, Geroulanos S. Antimicrobial protection in cardiac surgery patients undergoing open chest CPR. *Resuscitation*. 1996;31:10–11.
564. Rousou JA, Engelman RM, Flack JE III., Deaton DW, Owen SG. Emergency cardiopulmonary bypass in the cardiac surgical unit can be a lifesaving measure in postoperative cardiac arrest. *Circulation*. 1994;90():II-280–II-284.
565. Beyersdorf F, Kirsh M, Buckberg GD, Allen BS. Warm glutamate/aspartate-enriched blood cardioplegic solution for perioperative sudden death. *J Thorac Cardiovasc Surg*. 1992;104:1141–1147.
566. Feng WC, Bert AA, Browning RA, Singh AK. Open cardiac massage and periresuscitative cardiopulmonary bypass for cardiac arrest following cardiac surgery. *J Cardiovasc Surg*. 1995;36:319–321.
567. Wahba A, Gotz W, Birnbaum DE. Outcome of cardiopulmonary resuscitation following open heart surgery. *Scand Cardiovasc J*. 1997;31:147–149.
568. Pottle A, Bullock I, Thomas J, Scott L. Survival to discharge following open chest cardiac compression (OCCC): a 4-year retrospective audit in a cardiothoracic specialist centre: Royal Brompton and Harefield NHS Trust, United Kingdom. *Resuscitation*. 2002;52:269–272.
569. Kaiser GC, Naunheim KS, Fiore AC, Harris HH, McBride LR, Pennington DG, Barner HB, Willman VL. Reoperation in the intensive care unit. *Ann Thorac Surg*. 1990;49:903–907.
570. Bohrer H, Gust R, Bottiger BW. Cardiopulmonary resuscitation after cardiac surgery. *J Cardiothorac Vasc Anesth*. 1995;9:352.
571. Ricci M, Karamanoukian HL, D'Ancona G, Jajkowski MR, Bergsland J, Salerno TA. Avulsion of an H graft during closed-chest cardiopulmonary resuscitation after minimally invasive coronary artery bypass graft surgery. *J Cardiothorac Vasc Anesth*. 2000;14:586–587.
572. Chen YS, Chao A, Yu HY, Ko WJ, Wu IH, Chen RJ, Huang SC, Lin FY, Wang SS. Analysis and results of prolonged resuscitation in cardiac arrest patients rescued by extracorporeal membrane oxygenation. *J Am Coll Cardiol*. 2003;41:197–203.
573. Dalton HJ, Siewers RD, Fuhrman BP, Del Nido P, Thompson AE, Shaver MG, Dowhy M. Extracorporeal membrane oxygenation for cardiac rescue in children with severe myocardial dysfunction. *Crit Care Med*. 1993;21:1020–1028.
574. Ghez O, Feier H, Ughetto F, Fraisse A, Kreitmann B, Metras D. Postoperative extracorporeal life support in pediatric cardiac surgery: recent results. *ASAIO J*. 2005;51:513–516.
575. del Nido PJ, Dalton HJ, Thompson AE, Siewers RD. Extracorporeal membrane oxygenator rescue in children during cardiac arrest after cardiac surgery. *Circulation*. 1992;86(suppl):II-300–II-304.
- 576.



- Duncan BW, Ibrahim AE, Hraska V, del Nido PJ, Laussen PC, Wessel DL, Mayer JE Jr., Bower LK, Jonas RA. Use of rapid-deployment extracorporeal membrane oxygenation for the resuscitation of pediatric patients with heart disease after cardiac arrest. *J Thorac Cardiovasc Surg.* 1998;116:305–311.
577. Newsome LR, Ponganis P, Reichman R, Nakaji N, Jaski B, Hartley M. Portable percutaneous cardiopulmonary bypass: use in supported coronary angioplasty, aortic valvuloplasty, and cardiac arrest. *J Cardiothorac Vasc Anesth.* 1992;6:328–331.
578. Parra DA, Totapally BR, Zahn E, Jacobs J, Aldousany A, Burke RP, Chang AC. Outcome of cardiopulmonary resuscitation in a pediatric cardiac intensive care unit. *Crit Care Med.* 2000;28:3296–3300.
579. Overlie PA. Emergency use of cardiopulmonary bypass. *J Interv Cardiol.* 1995;8:239–247.
580. Cipolotti G, Paccagnella A, Simini G. Successful cardiopulmonary resuscitation using high doses of epinephrine. *Int J Cardiol.* 1991;33:430–431.
581. Kron IL, DiMarco JP, Harman PK, Crosby IK, Mentzer RM Jr., Nolan SP, Wellons HA Jr.. Unanticipated postoperative ventricular tachyarrhythmias. *Ann Thorac Surg.* 1984;38:317–322.