# Local anesthetic toxicity and lipid resuscitation in pregnancy

Sarah Bern[a] and Guy Weinberg[a,b]

[a]Department of Anesthesiology, University of Illinois at Chicago, UIC Medical Center and [b]Jesse Brown VA Medical Center, Chicago, Illinois, USA

Correspondence to Professor Guy Weinberg, MD, Department of Anesthesiology, University of Illinois at Chicago, UIC Medical Center, 1740 West Taylor Street, Suite 3200W, MC 515, Chicago, IL 60612, USA
Tel: +1 312 996 4020; fax: +1 312 996 4019; e-mail: guyw@uic.edu

**Current Opinion in Anesthesiology** 2011, 24:262–267

**Purpose of review**

Lipid emulsion has emerged as an effective treatment of local anesthetic-induced cardiac arrest, but its therapeutic application for the obstetric patient requires definition at present. This review discusses clinical reports, relevant laboratory studies, and future directions for the development of an optimal protocol for lipid resuscitation in pregnancy.

**Recent findings**

Several mechanisms have been postulated to account for the apparent enhanced sensitivity to local anesthetic systemic toxicity during pregnancy. One case report of lipid resuscitation in the pregnant patient demonstrates favorable outcomes and supports the safety of lipid therapy. Current guidelines and case reports propose that a large bolus of lipid at the earliest signs of toxicity may prevent cardiovascular collapse.

**Summary**

As the obstetric demographic becomes older and more obese, new technologies and strategies can assist in controlling maternal death and major morbidity secondary to anesthesia complications. Lipid resuscitation appears to be an effective treatment for toxicity induced by lipophilic medications and may be useful in treating systemic toxicity in the pregnant patient. Obstetric care providers should be aware of lipid resuscitation and consider its use as described by American Society of Regional Anesthesia and Pain Medicine guidelines.

**Keywords**

intravenous lipid emulsion, lipid, local anesthetics, pregnancy, resuscitation

Curr Opin Anesthesiol 24:262–267

0952-7907

## Introduction

Intravenous lipid emulsion (ILE) has emerged over the past decade as a promising antidote to local anesthetic systemic toxicity (LAST), a potentially fatal complication of regional anesthesia occurring in up to 1/500 peripheral nerve blocks [1–3]. A growing number of case reports have documented instances of severe LAST in which the use of ILE appeared to facilitate recovery. Infusion at the earliest signs of systemic toxicity is believed to have reduced fatalities associated with lipophilic local anesthetics, because several reports indicate that ILE resulted in return of spontaneous circulation after standard resuscitative measures had failed. The apparent efficacy of ILE is particularly encouraging in the context of LAST that is related to the lipophilic local anesthetics (e.g., bupivacaine, ropivacaine), which are known to produce intransigent cardiac toxicity [4–7]. Moreover, these successes have led the Association of Anaesthetists of Great Britain and Ireland (AAGBI), the American Society of Regional Anesthesia and Pain Medicine (ASRA) and other professional organizations to adopt recommendations for treatment of LAST that include ILE. Widespread acceptance of this technique has led many facilities to store lipid emulsion in close proximity to operating rooms and labor suites.

Pregnancy represents one of several clinical settings in which LAST can be potentiated [8–10,11••,12]. LAST has been recognized for decades as an important potential cause of maternal mortality, and more so now that obstetric care providers face increasingly severe and complex cases due to rising maternal age, obesity, and other comorbidities [13]. Local anesthetic toxicity in pregnancy remains a critical issue, and the clinical success of ILE suggests that the parturient and anesthesiologist may both benefit from clinical translation of this new treatment modality. However, many questions remain unanswered in regards to the distinct considerations, risks, and optimal protocols for lipid resuscitation in the pregnant patient.

## Systemic toxicity in the parturient

LAST is caused by a high circulating plasma concentration of local anesthetic, generally occurring as a result of either intravenous entrainment of local anesthetic or delayed absorption from the anesthetic depot at the

injection site. A 1979 editorial by Albright [14] signaled the first alarm raising serious concern about the clinical dangers of toxicity secondary to long-acting, lipophilic local anesthetics (especially bupivacaine and etidocaine). This raised general awareness of the problem among the community of anesthesiologists and served as a stimulus for study of the underlying mechanisms and potential treatments for LAST. Notably, several of the original anecdotal reports of LAST-related fatal cardiac arrests involved pregnant women [15]. It has since been established that pregnancy increases the risk for LAST, and subsequent guidelines preclude use of 0.75% bupivacaine in late gestation because this concentration was involved in instances of fatal toxicity in parturients [8].

Several mechanisms have been postulated to account for the apparent enhanced sensitivity to LAST during pregnancy. Epidural vein distention makes entrainment of local anesthetic and catheter migration more likely. Increased cardiac output can presumably alter uptake of local anesthetic from the epidural space and distribution to potential target sites. Pregnancy-related decreases in protein binding may also alter local anesthetic dynamics by increasing the availability of free drug in the vascular compartment [16,17], although this effect has been challenged to some extent [18]. The hormonal effects of estradiol [10] and progesterone [9] appear to alter cardiomyocyte electrophysiology sufficiently to increase the risk of arrhythmias specifically and cardiotoxicity in general. Increased neuronal susceptibility to anesthetics may also occur during pregnancy [8], reducing the threshold to local anesthetic induced seizure.

A Mayo clinic report estimates that 54% of cardiac arrests during spinal anesthesia are directly attributable to an anesthesia complication [19]. Cardiac arrest secondary to LAST remains a serious potential problem during delivery, despite the use of low concentration anesthetics and increased awareness of toxicity [20,21]. Today, with modern neuraxial labor analgesia (which uses very low concentration of local anesthetic solutions) the 'therapeutic dose' corresponds to the 'test dose' and the accidental intravenous or intrathecal injection will not cause harmful signs of systemic toxicity but may produce respectively the absence of analgesic effects or a faster onset of analgesia or even anesthesia and some motor block, depending on the dose given. Specifically, a recent British survey by Regan and O'Sullivan [22] suggests that the conversion of epidural analgesia during labor to surgical anesthesia for Caesarean section can have important medical implications and that the incidence of life-threatening complications due to local anesthetic toxicity were strongly associated with the epidural extension. The pregnant woman in cardiac arrest, although younger than the average out-of-hospital cardiac arrest patient, might actually have a poorer survival rate, currently estimated at 6.9% [23•]. Attempted resuscitation of the pregnant woman is complicated by physiological changes during pregnancy, including aortocaval compression by the gravid uterus that reduces venous return and cardiac output, causing hypotension and aggravating the pathophysiology of the arrest state [12]. A logical plan for the prevention and treatment of maternal anesthesia-related complications is crucial for the safety of both mother and fetus. Lipid resuscitation should represent a step forward in parturient safety by facilitating a reduction in morbidity and mortality associated with LAST in pregnancy.

**Key points**

- ILE has emerged over the past decade as a promising antidote to LAST.
- Pregnancy represents one of several clinical settings in which LAST can be potentiated.
- At present, the 'lipid sink' effect remains the dominant mechanistic theory for the efficacy of ILE in LAST.
- Lipid resuscitation should represent a step forward in parturient safety by facilitating a reduction in morbidity and mortality associated with LAST in pregnancy.
- We emphasize the need for effective airway management, controlling for lean body mass in lipid dosing, and urgent cesarean delivery without compromised maternal resuscitation.

## Lipid resuscitation: mechanism of action

Despite laboratory and clinical efficacy of lipid resuscitation, the exact mechanism has not been established. At present, the 'lipid sink' effect remains the dominant mechanistic theory for the efficacy of ILE in LAST. It is thought that the rapid addition of exogenous lipid into the vascular compartment can create a concentration gradient between tissue and blood that draws the anesthetic from the heart or brain (and other target areas of high concentration) into the aqueous plasma phase, where the bulk lipid phase provides an adequate reservoir (or sink) to harbor the offending drug from plasma and target tissues. We predict that lipid emulsion would operate in a similar manner in the parturient, providing a safe and effective alternate binding source for lipophilic local anesthetics. However, this has not been studied and it is possible that the lipid sink could demonstrate different characteristics due to pregnancy-related changes in blood volume, cardiac output, protein composition, or overall metabolism. Moreover, the possible effects of rapid lipid infusion on uteroplacental circulation and drug exchange are unknown. This is certainly an area ripe for basic laboratory investigation.

## Dosing and resuscitation guidelines

The 2010 ASRA practice advisory on the management of local anesthetic systemic toxicity suggests the following infusion of 20% lipid emulsion (values in parenthesis are for a 70-kg patient) as a therapeutic antidote [11••]:

(1) Bolus 1.5 ml/kg (lean body mass) intravenously over 1 min (~100 ml).
(2) Continuous infusion at 0.25 ml/kg per min (−18 ml/min, adjust by roller clamp).
(3) Repeat bolus once or twice for persistent cardiovascular collapse.
(4) Double the infusion rate to 0.5 ml/kg per min if blood pressure remains low.
(5) Continue infusion for at least 10 min after attaining circulatory stability.
(6) Recommended upper limit: approximately 10 ml/kg lipid emulsion over the first 30 min.

An initial intravenous bolus of 1.5 ml/kg (lean body mass) should be administered over 1–2 min and repeated after 5 min if there is no clinical improvement after the first bolus. The first bolus is generally followed by a continuous infusion at a rate of approximately 0.25 ml/kg per min (lean body mass) for 10 min after establishing stable vital signs. The current recommendations give a total dose limit recommendation of 10 ml/kg over the first 30 min. It is not known how this dose limit would be affected in pregnancy. Age of the patient, pre-existing conditions, site of the injection, and presence or absence of epinephrine are also variables that may influence the maximum total dose of lipid, as well as local anesthetic pharmacokinetics [24]. The goal in setting a dose limit is to provide sufficient lipid for resuscitation but avoid any adverse reactions due to patient overload of either volume or lipid.

Lipid therapy is not a substitute for Advanced Cardiac Life Support (ACLS) or standard resuscitation techniques. Early recognition of the problem, in addition to prompt and effective airway management, is the most important step in treating severe LAST. Successful ILE in the pulseless patient also requires high-quality Basic Life Support (BLS) to assure circulation of the lipid bulk to the coronary circulation. Inadequate resuscitation can result from poor airway management and secondary inadequate oxygenation and ventilation. The parturient may be especially vulnerable to hypoxia in the latter half of pregnancy, as a gravid uterus pushes the diaphragm more cephalic, reducing maternal functional residual capacity.

The specific exigencies of resuscitation during pregnancy are addressed at length in the American Heart Association/Advanced Cardiac Life Support (AHA/ACLS) guidelines for resuscitation in special situations (part 12.3) [25••]. Patient positioning for left uterine displacement is one important BLS modification that can reduce aortocaval compression syndrome, resulting in improved maternal hemodynamics and cardiopulmonary resuscitation quality. The recommended left-lateral tilt position may be accomplished manually or by placement of wedge support. As a result of the mother's elevated diaphragm, chest compressions should be performed higher on the parturient sternum and a reduction in ventilation volumes may be necessary. Bag-mask ventilation with 100% oxygen before intubation is emphasized because airway management of the parturient may be difficult due to pregnancy-related changes in airway mucosa, size, and significantly faster desaturation [26–29]. Resuscitation team leaders are encouraged to activate the protocol for emergency cesarean delivery as soon as cardiovascular instability is identified to ensure that delivery occurs within a 4–5-min window after the mother's heart stops. Expeditious perimortem cesarean delivery not only improves infant survival rate, but may also prove lifesaving to the mother – a benefit unappreciated by many clinicians [30]. Several cases [23•,31,32,33•,34] have reported spontaneous circulation and improved maternal hemodynamic status only after emptying the uterus, and there are no reports of worsened maternal status after cesarean section [34].

Concern over the difficulties and delays associated with parturient transport to the operating room for emergency cesarean delivery has sparked discussion as to whether maternal resuscitation should ever be intentionally delayed to expedite fetal delivery [35]. One letter in particular [36] addressed the merits of urgent cesarean delivery in nonoperating room locations. Although some obstetricians believe that perimortem delivery always merits transfer to the operating room, a crash cesarean delivery in the labor room may optimize maternal survival by allowing maternal resuscitation and fetal delivery to be accomplished simultaneously. Given the narrow 5-min window between maternal arrest and infant delivery, urgent cesarean delivery in nonoperating room locations is an alternative that must be re-emphasized.

## Intravenous lipid emulsion safety

A literature search revealed one documented instance of lipid resuscitation during pregnancy [37]. An 18-year-old primigravida presented at 38 weeks gestation for induction of labor when an inadvertent intravenous bupivacaine injection led to central nervous system toxicity. The patient became hypertensive, tachycardic, agitated, and subsequently unresponsive. Although the crash cart was being brought into the labor ward, the anesthesiologist elected to begin ILE therapy. Within 30 s the patient regained full consciousness and was transported

to the operating room. This case supports the merits of lipid resuscitation in the pregnant patient, but additional cases will be necessary to fully determine its effects.

The upper limit for lipid administration is unknown, but there has been concern that pulmonary or neurological complications could result from high volume infusions. A recent study by Hiller *et al.* [38] has preliminarily addressed the question of maximum dose in a rat model of lipid infusion. Results demonstrated normal tissue histology after administration of 20% lipid emulsion at volumes nearly one order of magnitude above typical doses reported in the literature (~4 ml/kg). The LD50 for a 30-min infusion was 67 ml/kg. It is not clear how to translate this value to a well tolerated maximum human dose, but these data suggest that there is a substantial margin of safety in ILE, particularly considering that it is generally used in settings where life (here, of both mother and child) are at stake. [11••].

Another key issue is whether adverse reactions may develop from the coadministration of lipid and other medications. A recent study addressed the effects of an epinephrine injection during concomitant lipid resuscitation in a rat model of bupivacaine overdose [39]. Interestingly, a threshold effect was observed. Doses of epinephrine above 10 μg/kg were found to impair lipid resuscitation from bupivacaine overdose, possibly by inducing acidosis and hyperlactatemia. There is a possibility that other medications could impair lipid resuscitation, but it should be noted that ILE does not produce adverse effects when administered with sodium bicarbonate, atropine, or calcium [40,41]. Nonetheless, drug interactions remain a consideration when administering lipid.

## Potential complications during pregnancy

It is important to consider the possible complications due to lipid administration for both mother and fetus. The only case of lipid resuscitation in the parturient supports its efficacious role and does not discuss any adverse effects from its use [37]. As randomized controlled trials are not feasible, we are forced to speculate about potential complications in light of previous studies. Pregnancy outcomes after administration of total parenteral nutrition to pregnant women may provide some insight into the effects of lipid infusion for the purpose of toxicity reversal. One study used ultrasonography to track fetal growth during a course of total parenteral nutrition in malnourished women [42]. Results indicate that total parenteral nutrition promoted fetal growth, in addition to reversing maternal malnourishment.

Another study looked at the effects of parenteral nutrition on the placenta [43]. Twenty cases of maternal hyperalimentation with lipid emulsions were described, with each woman having a normal placenta. However, in the case of a 31-year-old pregnant woman who had received total parenteral nutrition with daily lipid emulsions for 8 weeks, placental fat deposits were noted before intrauterine fetal death was diagnosed at 22 weeks gestation. This is the only reported case of placental fat deposition. Certainly, future laboratory studies are needed to gain insight into the potential impact of lipid administration on uteroplacental circulation.

The potential association between neonatal lipid infusion and the presence of pulmonary lipid emboli has been observed. Using a lung-staining technique on postmortem neonatal necropsy specimens, one study found lipid occlusion of small pulmonary capillaries in 15 of 30 infants who had received parenteral feeding, including intravenous lipid [44]. Another study assessed pulmonary lesions and parenteral nutrition in children admitted to the pediatric intensive care unit. These results indicated that lung injuries were significantly more frequent in children who had received total parenteral nutrition [45]. However, the authors state that it was impossible to conclude that the lipid infusion had a direct relationship with these injuries because there were many other significant cofactors.

These potential complications raise questions about the timing of lipid resuscitation in the parturient and whether the infant should be delivered, if possible, before administering lipid. Notably, AHA/ACLS guidelines support expeditious perimortem cesarean delivery to promote both fetal and maternal survival [25••,30]. Maternal resuscitation and cesarean delivery should occur simultaneously, so total fetal exposure to lipid would likely be very short, if at all. Anxiety over possible lipid deposits therefore seems unreasonable and should not preclude the use of lipid resuscitation as a means of treating LAST during pregnancy. In successful resuscitation of the parturient, it is important to remember that the best hope of fetal survival is maternal survival.

## Implementation and training

The first step to reducing the LAST-associated morbidity and mortality in the parturient is the education of obstetric care providers. Recent studies indicate that providers are unaware of the special considerations for resuscitation of the parturient [30,46]. Educational programming provides a valuable tool that may profit in improved patient safety. Advanced scenario simulation training may also facilitate prevention, detection, and management of LAST, according to a recent case report by Smith *et al.* [47]. Their description of the sequence of events following local anesthetic injection details events in a real patient shortly after the team had simulator training on LAST. The patient lost consciousness then

developed a generalized tonic–clonic seizure and asystolic cardiac arrest. The team quickly began cardiopulmonary resuscitation and ILE administration, with the patient soon converting to normal sinus rhythm and regaining consciousness. The authors attribute their early, successful management to the previous simulation training focused on preparing clinicians to recognize and treat potentially fatal toxicities with innovative treatments in the setting of supportive ACLS measures and coordinated team efforts.

## Conclusion

Lipid resuscitation has emerged as a promising solution to local anesthetic toxicity refractory to conventional modes of resuscitation. The 2010 ASRA practice advisory on the management of LAST [11••] endorses the therapeutic use of ILE and provides recommended dosing guidelines. The clinical success of ILE suggests that this treatment modality can assist in reducing the likelihood of maternal death and major morbidity secondary to LAST. Obstetric care providers should be aware of lipid resuscitation and consider its use in conjunction with current AHA/ACLS guidelines for resuscitation of the pregnant patient [25••]. We emphasize the need for effective airway management, controlling for lean body mass in lipid dosing, and urgent cesarean delivery without compromised maternal resuscitation.

Case reports and bench research together have guided our current treatment of local anesthetic toxicity and will continue to provide insights into the scope of its use. Physicians have the responsibility to document all cases of lipid resuscitation at the educational sites www.lipidrescue.org and www.lipidregistry.org so that retrospective and prospective data analyses may be possible. Future laboratory studies and the development of more comprehensive registries are also crucial for evaluating the efficacy and potential side-effects of lipid resuscitation in pregnancy. Specifically, the effects of ILE on uteroplacental circulation should be studied, as well as the mechanisms, dosing, and timing of ILE in the parturient.

Many operating rooms and labor suites have made lipid kits available. This case of rapid adoption and implementation of ILE suggests that national guidelines, editorials, and scientific articles may motivate its introduction [48]. We anticipate that future reports will shape the evolving recommendations for local anesthetic toxicity and support the development of clinical guidelines specific for lipid resuscitation during pregnancy to help reduce confusion among obstetric care providers, as well as provide a motivating force to make lipid kits available. Enhanced parturient sensitivity to LAST is a long-recognized and deadly challenge, but lipid resuscitation may be a life-saving tool to control anesthesia-related morbidity and mortality during pregnancy.

## Acknowledgements

Dr Weinberg was awarded United States patent 7 261 903 B1 'Lipid emulsion in the treatment of systemic poisoning'. The noncommercial website www.lipidregistry.org is intended for the purpose of case documentation. Neither salary nor support is derived from this website.

## References and recommended reading

Papers of particular interest, published within the annual period of review, have been highlighted as:

- • of special interest
- •• of outstanding interest

Additional references related to this topic can also be found in the Current World Literature section in this issue (p. 355).

**1** Groban L, Butterworth J. Lipid reversal of bupivacaine toxicity: has the silver bullet been identified? Reg Anesth Pain Med 2003; 28:167–169.

**2** 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.

**3** Weinberg GL. Lipid infusion therapy: translation to clinical practice. Anesth Analg 2008; 106:1340–1342.

**4** Litz RJ, Roessel T, Heller AR, Stehr SN. Reversal of central nervous system and cardiac toxicity after local anesthetic intoxication by lipid emulsion injection. Anesth Analg 2008; 106:1575–1577; table of contents.

**5** Rosenblatt MA, Abel M, Fischer GW, *et al.* Successful use of a 20% lipid emulsion to resuscitate a patient after a presumed bupivacaine-related cardiac arrest. Anesthesiology 2006; 105:217–218.

**6** Warren JA, Thoma RB, Georgescu A, Shah SJ. Intravenous lipid infusion in the successful resuscitation of local anesthetic-induced cardiovascular collapse after supraclavicular brachial plexus block. Anesth Analg 2008; 106:1578–1580; table of contents.

**7** Weinberg GL, Ripper R, Murphy P, *et al.* Lipid infusion accelerates removal of bupivacaine and recovery from bupivacaine toxicity in the isolated rat heart. Reg Anesth Pain Med 2006; 31:296–303.

**8** Santos AC, DeArmas PI. Systemic toxicity of levobupivacaine, bupivacaine, and ropivacaine during continuous intravenous infusion to nonpregnant and pregnant ewes. Anesthesiology 2001; 95:1256–1264.

**9** Moller RA, Datta S, Fox J, *et al.* Effects of progesterone on the cardiac electrophysiologic action of bupivacaine and lidocaine. Anesthesiology 1992; 76:604–608.

**10** Moller RA, Datta S, Strichartz GR. Beta-estradiol acutely potentiates the depression of cardiac excitability by lidocaine and bupivacaine. J Cardiovasc Pharmacol 1999; 34:718–727.

**11** •• Neal JM, Bernards CM, Butterworth JFt, *et al.* ASRA practice advisory on local anesthetic systemic toxicity. Reg Anesth Pain Med 2010; 35:152–161.
The American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Local Anesthetic Systemic Toxicity assimilates and summarizes current knowledge regarding the prevention, diagnosis, and treatment of this potentially fatal complication.

**12** Kasten GW, Martin ST. Resuscitation from bupivacaine-induced cardiovascular toxicity during partial inferior vena cava occlusion. Anesth Analg 1986; 65:341–344.

**13** Arendt KW, Segal S. Present and emerging strategies for reducing anesthesia-related maternal morbidity and mortality. Curr Opin Anesthesiol 2009; 22:330–335.

**14** Albright GA. Cardiac arrest following regional anesthesia with etidocaine or bupivacaine. Anesthesiology 1979; 51:285–287.

**15** Agarwal A, Kishore K. Complications and controversies of regional anaesthesia: a review. Indian J Anaesth 2009; 53:543–553.

**16** Santos AC, Pedersen H, Harmon TW, *et al.* Does pregnancy alter the systemic toxicity of local anesthetics? Anesthesiology 1989; 70:991–995.

**17** Tsen LC, Tarshis J, Denson DD, *et al.* Measurements of maternal protein binding of bupivacaine throughout pregnancy. Anesth Analg 1999; 89:965–968.

**18** Denson DD, Coyle DE, Thompson GA, *et al.* Bupivacaine protein binding in the term parturient: effects of lactic acidosis. Clin Pharmacol Ther 1984; 35:702–709.

**19** Kopp SL, Horlocker TT, Warner ME, *et al.* Cardiac arrest during neuraxial anesthesia: frequency and predisposing factors associated with survival. Anesth Analg 2005; 100:855–865; table of contents.

**20** Auroy Y, Narchi P, Messiah A, *et al.* Serious complications related to regional anesthesia: results of a prospective survey in France. Anesthesiology 1997; 87:479–486.

**21** Brown DL, Ransom DM, Hall JA, *et al.* Regional anesthesia and local anesthetic-induced systemic toxicity: seizure frequency and accompanying cardiovascular changes. Anesth Analg 1995; 81:321–328.

**22** Regan KJ, O'Sullivan G. The extension of epidural blockade for emergency Caesarean section: a survey of current UK practice. Anaesthesia 2008; 63:136–142.

**23** • Dijkman A, Huisman CM, Smit M, *et al.* Cardiac arrest in pregnancy: increasing use of perimortem caesarean section due to emergency skills training? BJOG 2010; 117:282–287.
Since implementing a course of Managing Obstetric Emergencies and Trauma (MOET) in the Netherlands, the use of perimortem Cesarean section has increased but the outcomes remain poor. This article points to the importance of the timely application of this life-saving procedure in order to improve maternal and neonate outcomes.

**24** Rosenberg PH, Veering BT, Urmey WF. Maximum recommended doses of local anesthetics: a multifactorial concept. Reg Anesth Pain Med 2004; 29:564–575; discussion 24.

**25** •• Vanden Hoek TL, Morrison LJ, Shuster M, *et al.* 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.
These are the most recent AHA guidelines for special situations. Part 12.3 discusses cardiac arrest associated with pregnancy and gives key interventions to prevent arrest. The importance of treating reversible causes of cardiac arrest is addressed, including local anesthetic toxicity.

**26** Elkus R, Popovich J Jr. Respiratory physiology in pregnancy. Clin Chest Med 1992; 13:555–565.

**27** Lapinsky SE, Kruczynski K, Slutsky AS. Critical care in the pregnant patient. Am J Respir Crit Care Med 1995; 152:427–455.

**28** Izci B, Vennelle M, Liston WA, *et al.* Sleep-disordered breathing and upper airway size in pregnancy and postpartum. Eur Respir J 2006; 27:321–327.

**29** Cheun JK, Choi KT. Arterial oxygen desaturation rate following obstructive apnea in parturients. J Korean Med Sci 1992; 7:6–10.

**30** Cohen SE, Andes LC, Carvalho B. Assessment of knowledge regarding cardiopulmonary resuscitation of pregnant women. Int J Obstet Anesth 2008; 17:20–25.

**31** 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.

**32** Cardosi RJ, Porter KB. Cesarean delivery of twins during maternal cardiopulmonary arrest. Obstet Gynecol 1998; 92:695–697.

**33** • McDonnell NJ. Cardiopulmonary arrest in pregnancy: two case reports of successful outcomes in association with perimortem Caesarean delivery. Br J Anaesth 2009; 103:406–409.
The AHA recommends the commencement of a perimortem Caesarean delivery within 4 min of the onset of maternal arrest to improve survival in both mother and fetus. This short window presents significant logistical challenges to obstetric care providers and has been the source of major discussion. This report describes two cases of cardiac arrest in pregnancy in which a perimortem Caesarean was performed as part of the resuscitation process and resulted in excellent maternal and neonate outcomes.

**34** Katz V, Balderston K, DeFreest M. Perimortem cesarean delivery: were our assumptions correct? Am J Obstet Gynecol 2005; 192:1916–1920; discussion 1920–1921.

**35** Lofsky A. Doctors company reviews maternal arrests cases: APSF Newsletter. Summer 2007; 22:28–30.

**36** Carvalho B, Cohen SE. Resuscitation after maternal arrest clarified: APSF Newsletter. Winter 2007; 22:80.

**37** Spence AG. Lipid reversal of central nervous system symptoms of bupivacaine toxicity. Anesthesiology 2007; 107:516–517.

**38** Hiller DB, Di Gregorio G, Kelly K, *et al.* Safety of high volume lipid emulsion infusion: a first approximation of LD50 in rats. Reg Anesth Pain Med 2010; 35:140–144.

**39** Hiller DB, Gregorio GD, Ripper R, *et al.* Epinephrine impairs lipid resuscitation from bupivacaine overdose: a threshold effect. Anesthesiology 2009; 111:498–505.

**40** Bania TC, Chu J, Perez E, *et al.* Hemodynamic effects of intravenous fat emulsion in an animal model of severe verapamil toxicity resuscitated with atropine, calcium, and saline. Acad Emerg Med 2007; 14:105–111.

**41** Harvey M, Cave G. Intralipid outperforms sodium bicarbonate in a rabbit model of clomipramine toxicity. Ann Emerg Med 2007; 49:178–185; 185 e1–e4.

**42** Caruso A, De Carolis S, Ferrazzani S, *et al.* Pregnancy outcome and total parenteral nutrition in malnourished pregnant women. Fetal Diagn Ther 1998; 13:136–140.

**43** Jasnosz KM, Pickeral JJ, Graner S. Fat deposits in the placenta following maternal total parenteral nutrition with intravenous lipid emulsion. Arch Pathol Lab Med 1995; 119:555–557.

**44** Puntis JW, Rushton DI. Pulmonary intravascular lipid in neonatal necropsy specimens. Arch Dis Child 1991; 66:26–28.

**45** Ramos-Silva V, Castello JS, da Motta LL, *et al.* Pulmonary lesions and total parenteral nutrition in children admitted to a pediatric intensive care unit. J Pediatr (Rio J) 2005; 81:155–161.

**46** Einav S, Matot I, Berkenstadt H, *et al.* A survey of labour ward clinicians' knowledge of maternal cardiac arrest and resuscitation. Int J Obstet Anesth 2008; 17:238–242.

**47** Smith HM, Jacob AK, Segura LG, *et al.* Simulation education in anesthesia training: a case report of successful resuscitation of bupivacaine-induced cardiac arrest linked to recent simulation training. Anesth Analg 2008; 106:1581–1584; table of contents.

**48** Williamson RM, Haines J. Availability of lipid emulsion in obstetric anaesthesia in the UK: a national questionnaire survey. Anaesthesia 2008; 63:385–388.