

# Circulation

JOURNAL OF THE AMERICAN HEART ASSOCIATION



## Part 7: Neonatal Resuscitation

*Circulation* 2005;112;III-91-III-99

DOI: 10.1161/CIRCULATIONAHA.105.166477

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 72514

Copyright © 2005 American Heart Association. All rights reserved. Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:

[http://circ.ahajournals.org/cgi/content/full/112/22\\_suppl/III-91](http://circ.ahajournals.org/cgi/content/full/112/22_suppl/III-91)

Data Supplement (unedited) at:

[http://circ.ahajournals.org/cgi/content/full/112/22\\_suppl/III-91/DC1](http://circ.ahajournals.org/cgi/content/full/112/22_suppl/III-91/DC1)

Subscriptions: Information about subscribing to *Circulation* is online at  
<http://circ.ahajournals.org/subscriptions/>

Permissions: Permissions & Rights Desk, Lippincott Williams & Wilkins, a division of Wolters Kluwer Health, 351 West Camden Street, Baltimore, MD 21202-2436. Phone: 410-528-4050. Fax: 410-528-8550. E-mail:  
[journalpermissions@lww.com](mailto:journalpermissions@lww.com)

Reprints: Information about reprints can be found online at  
<http://www.lww.com/reprints>

## Part 7: Neonatal Resuscitation

Approximately 10% of newborns require some assistance to begin breathing at birth, and about 1% require extensive resuscitation. Although the vast majority of newborn infants do not require intervention to make the transition from intrauterine to extrauterine life, the large number of births worldwide means that many infants require some resuscitation. Newborn infants who are born at term, had clear amniotic fluid, and are breathing or crying and have good tone must be dried and kept warm but do not require resuscitation.

All others need to be assessed for the need to receive one or more of the following actions in sequence:

- A. Initial steps in stabilization (clearing the airway, positioning, stimulating)
- B. Ventilation
- C. Chest compressions
- D. Medications or volume expansion

Progression to the next step is based on simultaneous assessment of 3 vital signs: respirations, heart rate, and color. Progression occurs only after successful completion of the preceding step. Approximately 30 seconds is allotted to complete one step successfully, reevaluate, and decide whether to progress to the next (Figure).

Since publication of the last International Liaison Committee on Resuscitation (ILCOR) document,<sup>1</sup> several controversial neonatal resuscitation issues have been identified. The literature was researched and a consensus was reached on the role of supplementary oxygen, peripartum management of meconium, ventilation strategies, devices to confirm placement of an advanced airway (eg, tracheal tube or laryngeal mask airway [LMA]), medications, maintenance of body temperature, postresuscitation management, and considerations for withholding and discontinuing resuscitation.

### Initial Resuscitation

#### Supplementary Oxygen

##### *Supplementary Oxygen Versus Room Air*<sup>W202A, W202B</sup>

There is growing evidence from both animal and human studies that air is as effective as 100% oxygen for the resuscitation of most infants at birth. There are concerns about potential adverse effects of 100% oxygen on breathing physiology, cerebral circulation, and potential tissue damage from oxygen free radicals.

##### *Consensus on Science*

Studies examining blood pressure, cerebral perfusion, and biochemical indicators of cell damage in asphyxiated animals

resuscitated with 100% versus 21% oxygen show conflicting results (LOE 6).<sup>2-6</sup> One study of preterm infants (<33 weeks of gestation) exposed to 80% oxygen found lower cerebral blood flow when compared with those stabilized with 21% oxygen (LOE 2).<sup>7</sup> Some animal data indicates the opposite effect, ie, reduced blood pressure and cerebral perfusion with air versus 100% oxygen (LOE 6).<sup>2</sup>

Meta-analysis of 4 human studies showed a reduction in mortality and no evidence of harm in infants resuscitated with air compared with those resuscitated with 100% oxygen (LOE 1).<sup>8,9</sup> The 2 largest newborn human studies of room air versus oxygen resuscitation were not blinded. In those studies, if there was no response after 90 seconds, those resuscitated with air were switched to supplementary oxygen; a similar proportion who failed to respond while receiving oxygen were not crossed over to room air.<sup>10,11</sup> These results require careful interpretation because of significant methodological concerns (regarding patient selection, lack of blinding, randomization methods, and follow-up).

Trials have not examined in sufficient detail infants with a birth weight of <1000 g, those with known congenital pulmonary or cyanotic heart disease, and those without discernible signs of life at birth.<sup>10-13</sup> Continuous oximetry studies show that term healthy newborns may take >10 minutes to achieve a preductal oxygen saturation >95% and nearly 1 hour to achieve this postductally (LOE 5).<sup>14-16</sup>

##### *Treatment Recommendation*

There is currently insufficient evidence to specify the concentration of oxygen to be used at initiation of resuscitation. After initial steps at birth, if respiratory efforts are absent or inadequate, lung inflation/ventilation should be the priority. Once adequate ventilation is established, if the heart rate remains low, there is no evidence to support or refute a change in the oxygen concentration that was initiated. Rather the priority should be to support cardiac output with chest compressions and coordinated ventilations. Supplementary oxygen should be considered for babies with persistent central cyanosis. Some have advocated adjusting the oxygen supply according to pulse oximetry measurements to avoid hyperoxia, but there is insufficient evidence to determine the appropriate oximetry goal because observations are confounded by the gradual increase in oxyhemoglobin saturation that normally occurs following birth. Excessive tissue oxygen may cause oxidant injury and should be avoided, especially in the premature infant.

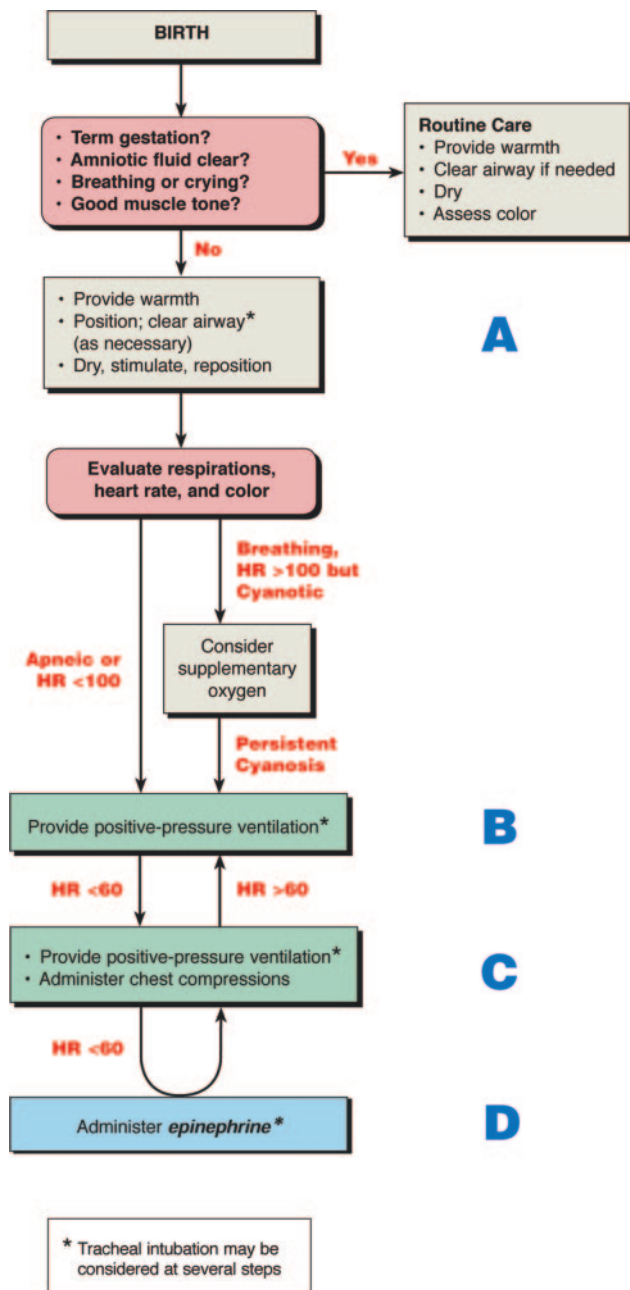
From the 2005 International Consensus Conference on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science With Treatment Recommendations, hosted by the American Heart Association in Dallas, Texas, January 23-30, 2005.

This article has been copublished in *Resuscitation*.

(*Circulation*. 2005;112:III-91-III-99.)

© 2005 International Liaison Committee on Resuscitation, American Heart Association, and European Resuscitation Council.

This special supplement to *Circulation* is freely available at <http://www.circulationaha.org> DOI: 10.1161/CIRCULATIONAHA.105.166477



ILCOR Neonatal Flow Algorithm.

**Peripartum Management of Meconium**

Management of meconium was examined from 2 perspectives: (1) suctioning of the meconium from the infant’s airway after delivery of the head but before delivery of the shoulders (intrapartum suctioning) and (2) suctioning of the infant’s trachea immediately after birth (tracheal suctioning).

**Intrapartum Suctioning**<sup>W206</sup>

*Consensus on Science*

Previous studies have yielded conflicting results about the value of intrapartum oropharyngeal and nasopharyngeal suctioning of babies born with meconium-stained fluid (LOE 3<sup>17</sup>; LOE 4<sup>18,19</sup>). A recent large multicenter randomized trial found that intrapartum suctioning of meconium does not

reduce the incidence of meconium aspiration syndrome (LOE 1).<sup>20</sup>

*Treatment Recommendation*

Routine intrapartum oropharyngeal and nasopharyngeal suctioning for infants born with meconium-stained amniotic fluid is no longer recommended.

**Tracheal Suctioning**<sup>W206</sup>

*Consensus on Science*

A randomized controlled trial showed that tracheal intubation and suctioning of meconium-stained but vigorous infants at birth offers no benefit (LOE 1).<sup>17</sup> The benefit of tracheal suctioning in meconium-stained, depressed infants has not been systematically studied (LOE 5).<sup>21–23</sup>

*Treatment Recommendation*

Meconium-stained, depressed infants should receive tracheal suctioning immediately after birth and before stimulation, presuming the equipment and expertise is available. Tracheal suctioning is not necessary for babies with meconium-stained fluid who are vigorous.

**Ventilation Strategies**

Ventilation strategy was examined from 4 perspectives: (1) the characteristics of the initial assisted breaths, (2) devices to assist ventilation, (3) special considerations for babies born preterm, and the role of positive end-expiratory pressure (PEEP) or continuous positive air pressure (CPAP) during or following resuscitation.

**Initial Breaths**<sup>W203A,W203C</sup>

*Consensus on Science*

When performed properly, positive-pressure ventilation alone is effective for resuscitating almost all apneic or bradycardic newborn infants (LOE 5).<sup>24</sup> The primary measure of adequate initial ventilation is prompt improvement in heart rate (LOE 6).<sup>25–27</sup> The presence or absence of chest wall movement has been described but not assessed adequately (LOE 5).<sup>28</sup>

In term infants, initial inflations, either spontaneous or assisted, create a functional residual capacity (FRC) (LOE 5).<sup>28–33</sup> The optimum pressure, inflation time, and flow required to establish an effective FRC has not been determined. In case series reporting the physiological changes associated with initial ventilation of term human neonates, peak pressures used to initiate ventilation varied widely (18 to 60 cm H<sub>2</sub>O). Average initial peak inflating pressures of 30 to 40 cm H<sub>2</sub>O were used to successfully ventilate unresponsive term infants (LOE 5).<sup>31–35</sup> In a single small series a sustained inflation pressure of 30 cm H<sub>2</sub>O for 5 seconds for the first breath was effective in establishing lung volume in term infants requiring resuscitation (LOE 5)<sup>31</sup>; the risk and benefits of this practice have not been evaluated. Ventilation rates of 30 to 60 breaths per minute are commonly used, but the relative efficacy of various rates has not been investigated (LOE 8).

*Treatment Recommendation*

Establishing effective ventilation is the primary objective in the management of the apneic or bradycardic newborn infant

in the delivery room. In the bradycardic infant, prompt improvement in heart rate is the primary measure of adequate initial ventilation; chest wall movement should be assessed if heart rate does not improve. Initial peak inflating pressures necessary to achieve an increase in heart rate or movement of the chest are variable and unpredictable and should be individualized with each breath. If pressure is being monitored, an initial inflation pressure of 20 cm H<sub>2</sub>O may be effective, but a pressure  $\geq 30$  to 40 cm H<sub>2</sub>O may be necessary in some term babies. If pressure is not being monitored, the minimal inflation required to achieve an increase in heart rate should be used. There is insufficient evidence to recommend optimal initial or subsequent inflation times.

#### **Assisted Ventilation Devices**<sup>W203B</sup>

##### *Consensus on Science*

Studies on humans and manikins suggest that effective ventilation can be achieved with either a flow-inflating or self-inflating bag or with a T-piece mechanical device designed to regulate pressure (LOE 4<sup>36,37</sup>; LOE 5<sup>38</sup>). The pop-off valves of self-inflating bags are flow-dependent, and pressures generated during resuscitation may exceed the target values (LOE 6).<sup>39</sup> Target inflation pressures and long inspiratory times are achieved more consistently in mechanical models when using T-piece devices than when using bags (LOE 6),<sup>40</sup> although the clinical implications are not clear. To provide the desired pressure, healthcare providers need more training to use flow-inflating bags than they need to use self-inflating bags (LOE 6).<sup>41</sup>

##### *Treatment Recommendation*

A self-inflating bag, a flow-inflating bag, or a T-piece mechanical device designed to regulate pressure as needed can be used to provide bag-mask ventilation to a newborn.

#### **Laryngeal Mask Airway**<sup>W215A,W215B</sup>

##### *Consensus on Science*

Masks that fit over the laryngeal inlet are effective for ventilating newborn full-term infants (LOE 2<sup>42</sup>; LOE 5<sup>43</sup>). There is limited data on the use of these devices in small preterm infants (LOE 5).<sup>44,45</sup> There is currently no evidence directly comparing the laryngeal mask airway (LMA) with bag-mask ventilation during neonatal resuscitation. Data from 2 case series shows that use of the LMA can provide effective ventilation in a time frame consistent with current resuscitation guidelines (LOE 5).<sup>43,46</sup> A single randomized controlled trial found no significant difference between the LMA and tracheal intubation during resuscitation of babies by experienced providers after cesarean section (LOE 2).<sup>42</sup> Case reports suggest that when ventilation via a face mask has been unsuccessful and tracheal intubation is unsuccessful or not feasible, the LMA may provide effective ventilation (LOE 5).<sup>47,48</sup>

##### *Treatment Recommendation*

The LMA may enable effective ventilation during neonatal resuscitation if bag-mask ventilation is unsuccessful and tracheal intubation is unsuccessful or not feasible. There is insufficient evidence to recommend use of the LMA as the primary airway device during neonatal resuscitation or in the

settings of meconium-stained amniotic fluid, when chest compressions are required, or for the delivery of drugs into the trachea.

#### **Ventilation Strategies for Preterm Infants**<sup>W203A,W203C</sup>

##### *Consensus on Science*

There has been little research evaluating initial ventilation strategies in the resuscitation of preterm infants. Animal studies indicate that preterm lungs are more easily injured by large-volume inflations immediately after birth (LOE 6).<sup>49</sup> Additional studies in animals indicate that when positive-pressure ventilation is applied immediately after birth, the application of end-expiratory pressure protects against lung injury and improves lung compliance and gas exchange (LOE 6).<sup>50,51</sup> Case series in infants indicate that most apneic preterm infants can be ventilated with an initial inflation pressure of 20 to 25 cm H<sub>2</sub>O, although some infants who do not respond require a higher pressure (LOE 5).<sup>52,53</sup>

##### *Treatment Recommendation*

Providers should avoid creation of excessive chest wall movement during ventilation of preterm infants immediately after birth. Although measured peak inflation pressure does not correlate well with volume delivered in the context of changing respiratory mechanics, monitoring of inflation pressure may help provide consistent inflations and avoid unnecessarily high pressures. If positive-pressure ventilation is required, an initial inflation pressure of 20 to 25 cm H<sub>2</sub>O is adequate for most preterm infants. If prompt improvement in heart rate or chest movement is not obtained, then higher pressures may be needed.

#### **Use of CPAP or PEEP**<sup>W204A,W204B</sup>

##### *Consensus on Science*

Spontaneously breathing newborns establish functional residual capacity more quickly and with lower transpulmonary pressures than sick neonates (LOE 5).<sup>32</sup> In the sick neonate CPAP helps stabilize and improve lung function (LOE 4).<sup>54</sup> Excessive CPAP, however, can overdistend the lung, increase the work of breathing, and reduce cardiac output and regional blood flow (LOE 6).<sup>55,56</sup> There are no prospective, randomized, controlled clinical trials of sufficient power to compare CPAP and positive-pressure ventilation (via bag-mask or bag-tracheal tube) during resuscitation of either the preterm or term neonate. When compared with historical controls, use of CPAP for extremely premature babies in the delivery room was associated with a decrease in requirement for intubation, days on mechanical ventilation, and use of postnatal steroids (LOE 4).<sup>53</sup> A small underpowered feasibility trial of delivery room CPAP/PEEP versus no CPAP/PEEP did not show a significant difference in immediate outcomes (LOE 2).<sup>57</sup>

##### *Treatment Recommendation*

There is insufficient data to support or refute the routine use of CPAP during or immediately after resuscitation in the delivery room.

**Exhaled CO<sub>2</sub> Detectors to Confirm Tracheal Tube Placement**<sup>W212A,W212B</sup>*Consensus on Science*

After tracheal intubation, adequate ventilation is associated with a prompt increase in heart rate (LOE 5).<sup>35</sup> Exhaled CO<sub>2</sub> detection is a reliable indicator of tracheal tube placement in infants (LOE 5).<sup>58–61</sup> A positive test (detection of exhaled CO<sub>2</sub>) confirms tracheal placement of the tube, whereas a negative test strongly suggests esophageal intubation (LOE 5).<sup>58,60,61</sup> Poor or absent pulmonary blood flow may give false-negative results, but tracheal tube placement is identified correctly in nearly all patients who are not in cardiac arrest (LOE 7).<sup>62</sup> In critically ill infants with poor cardiac output, a false-negative result may lead to unnecessary extubation.

Exhaled CO<sub>2</sub> detectors identify esophageal intubations faster than clinical assessments (LOE 5).<sup>58,61</sup> Clinical techniques for confirmation of correct tracheal tube placement (eg, evaluation of condensed humidified gas during exhalation, chest movement) have not been evaluated systematically in neonates.

*Treatment Recommendation*

Tracheal tube placement must be confirmed after intubation, especially in infants with a low heart rate that is not rising. Exhaled CO<sub>2</sub> detection is useful to confirm tracheal tube placement. During cardiac arrest, if exhaled CO<sub>2</sub> is not detected, tube placement should be confirmed with direct laryngoscopy.

**Medications**

The primary considerations about medications focused on which drugs should be used and the route by which they should be given. Medications are rarely needed in neonatal resuscitation. Those that may be used include epinephrine and fluids. Very rarely, a narcotic antagonist, sodium bicarbonate,<sup>W200</sup> or vasopressors may be useful after resuscitation.

**Epinephrine****Route and Dose of Epinephrine**<sup>W213A,W213B,W217,W220</sup>*Consensus on Science*

Despite the widespread use of epinephrine/adrenaline during resuscitation, no placebo-controlled studies have evaluated either the tracheal or intravenous (IV) administration of epinephrine at any stage during cardiac arrest in human neonates. A pediatric study (LOE 7)<sup>63</sup> and studies in newborn animals (LOE 6)<sup>64,65</sup> showed no benefit and a trend toward reduced survival rates and worse neurologic status after administration of high-dose IV epinephrine (100 μg/kg) during resuscitation. Animal and adult human studies show that when given tracheally, considerably higher doses of epinephrine than currently recommended are required to show a positive effect (LOE 6).<sup>66–68</sup>

One neonatal animal study using the currently recommended dose of tracheal epinephrine (10 μg/kg) showed no benefit (LOE 6).<sup>69</sup> One neonatal cohort study of 9 preterm babies requiring resuscitation showed that tracheal epineph-

rine was absorbed, but the study used 7 to 25 times the dose recommended currently (LOE 5).<sup>70</sup>

*Treatment Recommendation*

Despite the lack of human data, it is reasonable to continue to use epinephrine when adequate ventilation and chest compressions have failed to increase the heart rate to >60 beats per minute. Use the IV route for epinephrine as soon as venous access is established. The recommended IV dose is 0.01 to 0.03 mg/kg. If the tracheal route is used, give a higher dose (up to 0.1 mg/kg). The safety of these higher tracheal doses has not been studied. Do not give high doses of intravenous epinephrine.

**Volume Expansion****Crystalloids and Colloids**<sup>W208</sup>*Consensus on Science*

Three randomized controlled trials in neonates showed that isotonic crystalloid is as effective as albumin for the treatment of hypotension (LOE 7).<sup>71–73</sup> No studies have compared the relative effectiveness of crystalloid during resuscitation.

*Treatment Recommendation*

In consideration of cost and theoretical risks, an isotonic crystalloid solution rather than albumin should be the fluid of choice for volume expansion in neonatal resuscitation.

**Other Drugs****Naloxone**<sup>W214A,W214B</sup>*Consensus on Science*

There are no studies examining the use of naloxone in infants with severe respiratory depression from maternal opioids. Vigorous newborns whose mothers received opioids had brief improvement in alveolar ventilation with naloxone without affecting Apgar score, pH, PaCO<sub>2</sub>, or respiratory rate (LOE 7).<sup>74</sup> Compared with intramuscular naloxone, IV naloxone produces higher plasma concentrations but has a shorter half-life (LOE 5).<sup>75</sup> Tracheal or subcutaneous administration has not been examined in neonates, nor has the current recommended dose of 0.1 mg/kg been studied.

Naloxone may interfere with critical functions of endogenous opioids and exacerbate long-term neurohistologic injury of cerebral white matter in asphyxiated animals (LOE 6).<sup>76,77</sup> Cardiac arrhythmias, hypertension, and noncardiogenic pulmonary edema have been reported in adolescents and adults, especially when high doses have been used (LOE 7).<sup>78</sup> Naloxone given to a baby born to an opioid-addicted mother was associated with seizures.<sup>79</sup>

*Treatment Recommendation*

Naloxone is not recommended as part of the initial resuscitation of newborns with respiratory depression in the delivery room. Before naloxone is given, providers should restore heart rate and color by supporting ventilation. The preferred route should be IV or intramuscular. Tracheal administration is not recommended. There is no evidence to support or refute the current dose of 0.1 mg/kg.

## Supportive Therapy

### Temperature Control

#### *Maintenance of Body Temperature*<sup>W210A,W210B</sup>

##### *Consensus on Science*

Numerous observational studies showed an association between hypothermia and increased mortality in premature newborns. Premature infants continue to be at risk for hypothermia when treated according to current recommendations (dry the infant, remove wet linens, place the infant on a radiant warmer) (LOE 5).<sup>80</sup> Two randomized controlled trials (LOE 2)<sup>81,82</sup> and 3 observational studies (LOE 4<sup>83,84</sup>; LOE 5<sup>85</sup>) confirm the efficacy of plastic bags or plastic wrapping (food-grade, heat-resistant plastic) in addition to the customary radiant heat in significantly improving the admission temperature of premature babies of <28 weeks gestation when compared with standard care (LOE 2<sup>81,82</sup>; LOE 4<sup>83,84</sup>; LOE 5<sup>85</sup>). There is no direct evidence that this improves mortality or long-term outcomes. Temperature must be monitored closely because there is a small risk that this technique may produce hyperthermia (LOE 2).<sup>82</sup>

Other techniques have been used to maintain temperature in the delivery room during stabilization (drying and swaddling, warming pads, placing the newborn skin-to-skin with the mother and covering both, etc) but have not been compared with the plastic wrap technique for premature babies (LOE 8).<sup>86,87</sup>

##### *Treatment Recommendation*

Very low birth weight preterm babies remain at risk for hypothermia. Consider the use of plastic bags or plastic wrapping under radiant heat as well as standard techniques to maintain temperature. All initial resuscitation steps, including intubation, chest compression, and insertion of lines, can be performed with these temperature-controlling interventions in place.

## Postresuscitation Management

### Temperature

#### *Hyperthermia*<sup>W201</sup>

##### *Consensus on Science*

Babies born to febrile mothers (temperature >38°C) have an increased risk of death, perinatal respiratory depression, neonatal seizures, and cerebral palsy (LOE 4).<sup>88,89</sup> During the first 24 hours after adult stroke, fever is associated with a marked increase in neurologic morbidity and mortality (LOE 7).<sup>90,91</sup> Adult animal studies indicate that hyperthermia during or after ischemia is associated with a progression of cerebral injury (LOE 6).<sup>92,93</sup>

##### *Treatment Recommendation*

The goal is to achieve normothermia and to avoid iatrogenic hyperthermia in babies who require resuscitation.

#### *Therapeutic Hypothermia*<sup>W211A,W211B</sup>

##### *Consensus on Science*

A reduction of body temperature by 2°C to 3°C (modest hypothermia) following cerebral hypoxia-ischemia reduces

cerebral metabolic and biochemical abnormalities and cerebral injury and improves function in experimental neonatal models (LOE 6).<sup>94-96</sup> In adults, induced hypothermia (temperature of 32°C to 34°C) for 12 to 24 hours improves neurologic outcome after cardiac arrest due to ventricular arrhythmias but not after trauma or stroke (LOE 7).<sup>97</sup> In a multicenter trial involving newborns with suspected asphyxia (indicated by need for resuscitation at birth, metabolic acidosis, and early encephalopathy), selective head cooling to achieve a rectal temperature of 34°C to 35°C was associated with a nonsignificant reduction in the overall number of survivors with severe disability at 18 months but a significant benefit in the subgroup with moderate encephalopathy (LOE 2).<sup>98</sup>

Infants with severe electroencephalographic (EEG) suppression and seizures did not benefit from treatment with modest hypothermia (LOE 2).<sup>98</sup> A second small controlled pilot study in asphyxiated infants with early induced systemic hypothermia that achieved a rectal temperature of 33°C resulted in fewer deaths and disability at 12 months (LOE 2).<sup>99</sup>

Modest hypothermia is associated with bradycardia and elevated blood pressure that do not usually require treatment, but a rapid increase in body temperature may cause hypotension (LOE 5).<sup>100</sup> Profound hypothermia (core temperature <33°C) may cause arrhythmia, bleeding, thrombosis, and sepsis, but these complications have not been reported in infants treated with modest hypothermia (LOE 2).<sup>98,99,101,102</sup>

##### *Treatment Recommendation*

There is insufficient data to recommend the routine use of systemic or selective cerebral hypothermia after resuscitation of infants with suspected asphyxia. Further clinical trials are needed to confirm that treatment with cooling is beneficial, to identify infants who will benefit most, and to determine the most effective method and timing of cooling.

## General Supportive Care

#### *Glucose*<sup>W218A,W218B,W219A,W219B</sup>

##### *Consensus on Science*

Low blood glucose is associated with adverse neurologic outcomes in a neonatal animal model of asphyxia and resuscitation (LOE 6).<sup>103</sup> Hypoglycemia in animals at the time of an anoxic or hypoxic-ischemic insult resulted in larger areas of cerebral infarction and/or decreased survival rates when compared with controls (LOE 6).<sup>104,105</sup> One clinical study showed an association between hypoglycemia (blood glucose <40 mg/dL) measured shortly after resuscitation and poor neurologic outcome following perinatal asphyxia (LOE 4).<sup>106</sup>

Hyperglycemia induced in neonatal animal models of hypoxia-ischemia had conflicting effects on the extent of brain injury (LOE 6).<sup>107,108</sup> No clinical neonatal studies have investigated this topic.

##### *Treatment Recommendation*

Based on available evidence, the optimal range of blood glucose concentration to minimize brain injury following asphyxia and resuscitation cannot be defined. Infants requir-

ing resuscitation should be monitored and treated to maintain glucose in the normal range.

#### **Timing of Cord Clamping**<sup>W216A,W216B</sup>

##### *Consensus on Science*

Although delayed cord clamping (30 to 120 seconds after birth) in premature infants was associated with higher mean blood pressure and hematocrit and less intraventricular hemorrhage, most study subjects did not require resuscitation (LOE 1<sup>109</sup>; LOE 2<sup>110</sup>). Delayed cord clamping in term infants not requiring resuscitation resulted in no clinically significant improvement in stability over the first 4 to 6 hours after birth (LOE 3).<sup>111,112</sup>

##### *Treatment Recommendation*

No recommendation can be made about the timing of cord clamping when resuscitation is required.

### **Withholding or Discontinuing Resuscitative Efforts**<sup>W209A,W209B</sup>

##### *Consensus on Science*

Mortality and morbidity for newborns varies according to region and availability of resources (LOE 5).<sup>113</sup> Social science studies indicate that parents would like a larger role in decisions to start resuscitation and continue life support of severely compromised newborns. Opinions among neonatal providers vary widely regarding the benefits and disadvantages of aggressive therapies in such newborns (LOE 5).<sup>114,115</sup>

Some data are available to help identify conditions associated with high mortality and poor outcome (LOE 5).<sup>80,116</sup> Such conditions may include extreme prematurity and infants with anomalies that predict extreme morbidity or early death. Data from infants without signs of life lasting at least 10 minutes or longer from birth despite continuous and adequate resuscitative efforts document either high mortality or severe neurodevelopmental disability (LOE 5).<sup>117,118</sup>

##### *Treatment Recommendation*

A consistent and coordinated approach to individual cases by obstetric and neonatal teams and parents is an important goal. Not starting resuscitation and discontinuation of life-sustaining treatment during or after resuscitation are ethically equivalent, and clinicians should not be hesitant to withdraw support when functional survival is highly unlikely. The following guidelines must be interpreted according to current regional outcomes and societal principles:

- When gestation, birth weight, or congenital anomalies are associated with almost certain early death and an unacceptably high morbidity is likely among the rare survivors, resuscitation is not indicated. Examples from the published literature from developed countries include
  - Extreme prematurity (gestational age <23 weeks or birth weight <400 g)
  - Anomalies such as anencephaly and confirmed trisomy 13 or 18
- In conditions associated with a high rate of survival and acceptable morbidity, resuscitation is nearly always indicated.

- In conditions associated with uncertain prognosis, when there is borderline survival and a relatively high rate of morbidity, and where the burden to the child is high, the parents' views on starting resuscitation should be supported.

If there are no signs of life after 10 minutes of continuous and adequate resuscitative efforts, it may be justifiable to stop resuscitation.

### **References**

1. American Heart Association in collaboration with International Liaison Committee on Resuscitation. Guidelines 2000 for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care: International Consensus on Science, Part 11: Neonatal Resuscitation. *Circulation*. 2000; 102(suppl 1):I343–I358.
2. Solas AB, Kutzsche S, Vinje M, Saugstad OD. Cerebral hypoxemia-ischemia and reoxygenation with 21% or 100% oxygen in newborn piglets: effects on extracellular levels of excitatory amino acids and microcirculation. *Pediatr Crit Care Med*. 2001;2:340–345.
3. Solas AB, Munkeby BH, Saugstad OD. Comparison of short- and long-duration oxygen treatment after cerebral asphyxia in newborn piglets. *Pediatr Res*. 2004;56:125–131.
4. Solas AB, Kalous P, Saugstad OD. Reoxygenation with 100 or 21% oxygen after cerebral hypoxemia-ischemia-hypercapnia in newborn piglets. *Biol Neonate*. 2004;85:105–111.
5. Huang CC, Yonetani M, Lajevardi N, Delivoria-Papadopoulos M, Wilson DF, Pastuszko A. Comparison of postasphyxial resuscitation with 100% and 21% oxygen on cortical oxygen pressure and striatal dopamine metabolism in newborn piglets. *J Neurochem*. 1995;64: 292–298.
6. Kutzsche S, Ilves P, Kirkeby OJ, Saugstad OD. Hydrogen peroxide production in leukocytes during cerebral hypoxia and reoxygenation with 100% or 21% oxygen in newborn piglets. *Pediatr Res*. 2001;49: 834–842.
7. Lundstrom KE, Pryds O, Greisen G. Oxygen at birth and prolonged cerebral vasoconstriction in preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 1995;73:F81–F86.
8. Tan A, Schulze A, O'Donnell CP, Davis PG. Air versus oxygen for resuscitation of infants at birth. *Cochrane Database Syst Rev*. 2004: CD002273.
9. Davis PG, Tan A, O'Donnell CP, Schulze A. Resuscitation of newborn infants with 100% oxygen or air: a systematic review and meta-analysis. *Lancet*. 2004;364:1329–1333.
10. Saugstad OD, Rootwelt T, Aalen O. Resuscitation of asphyxiated newborn infants with room air or oxygen: an international controlled trial: the Resair 2 study. *Pediatrics*. 1998;102:e1.
11. Ramji S, Rasaily R, Mishra PK, Narang A, Jayam S, Kapoor AN, Kambo I, Mathur A, Saxena BN. Resuscitation of asphyxiated newborns with room air or 100% oxygen at birth: a multicentric clinical trial. *Indian Pediatr*. 2003;40:510–517.
12. Ramji S, Ahuja S, Thirupuram S, Rootwelt T, Rooth G, Saugstad OD. Resuscitation of asphyxiated newborn infants with room air or 100% oxygen. *Pediatr Res*. 1993;34:809–812.
13. Vento M, Asensi M, Sastre J, Garcia-Sala F, Pallardo FV, Vina J. Resuscitation with room air instead of 100% oxygen prevents oxidative stress in moderately asphyxiated term neonates. *Pediatrics*. 2001;107: 642–647.
14. Harris AP, Sendak MJ, Donham RT. Changes in arterial oxygen saturation immediately after birth in the human neonate. *J Pediatr*. 1986; 109:117–119.
15. Reddy VK, Holzman IR, Wedgwood JF. Pulse oximetry saturations in the first 6 hours of life in normal term infants. *Clin Pediatr (Phila)*. 1999;38:87–92.
16. Toth B, Becker A, Seelbach-Gobel B. Oxygen saturation in healthy newborn infants immediately after birth measured by pulse oximetry. *Arch Gynecol Obstet*. 2002;266:105–107.
17. Wiswell TE, Gannon CM, Jacob J, Goldsmith L, Szyld E, Weiss K, Schutzman D, Cleary GM, Filipov P, Kurlat I, Caballero CL, Abassi S, Sprague D, Oltorf C, Padula M. Delivery room management of the apparently vigorous meconium-stained neonate: results of the multicenter, international collaborative trial. *Pediatrics*. 2000;105(pt 1):1–7.

18. Carson BS, Losey RW, Bowes WA Jr, Simmons MA. Combined obstetric and pediatric approach to prevent meconium aspiration syndrome. *Am J Obstet Gynecol.* 1976;126:712-715.
19. Falciglia HS. Failure to prevent meconium aspiration syndrome. *Obstet Gynecol.* 1988;71:349-353.
20. Vain NE, Szyld EG, Prudent LM, Wiswell TE, Aguilar AM, Vivas NI. Oropharyngeal and nasopharyngeal suctioning of meconium-stained neonates before delivery of their shoulders: multicentre, randomised controlled trial. *Lancet.* 2004;364:597-602.
21. Gregory GA, Gooding CA, Phibbs RH, Tooley WH. Meconium aspiration in infants: a prospective study. *J Pediatr.* 1974;85:848-852.
22. Rossi EM, Philipson EH, Williams TG, Kalhan SC. Meconium aspiration syndrome: intrapartum and neonatal attributes. *Am J Obstet Gynecol.* 1989;161:1106-1110.
23. Davis RO, Philips JB 3rd, Harris BA Jr, Wilson ER, Huddleston JF. Fatal meconium aspiration syndrome occurring despite airway management considered appropriate. *Am J Obstet Gynecol.* 1985;151:731-736.
24. Perlman JM, Risser R. Cardiopulmonary resuscitation in the delivery room: associated clinical events. *Arch Pediatr Adolesc Med.* 1995;149:20-25.
25. Adamsons K Jr, Behrman R, Dawes GS, James LS, Koford C. Resuscitation by positive pressure ventilation and tris-hydroxymethylaminomethane of rhesus monkeys asphyxiated at birth. *J Pediatr.* 1964;65:807-818.
26. Campbell AM. A comparison of air and O<sub>2</sub> in a hyperbaric chamber or by positive pressure ventilation, in the resuscitation of newborn rabbits. *J Pediatr.* 1966;68:153-163.
27. Dawes GS, Jacobson HN, Mott JC, Shelley HJ, Stafford A. The treatment of asphyxiated, mature foetal lambs and rhesus monkeys with intravenous glucose and sodium carbonate. *J Physiol.* 1963;169:167-184.
28. Upton CJ, Milner AD. Endotracheal resuscitation of neonates using a rebreathing bag. *Arch Dis Child.* 1991;66:39-42.
29. Karlberg P, Koch G. Respiratory studies in newborn infants. III. Development of mechanics of breathing during the first week of life: a longitudinal study. *Acta Paediatr.* 1962;(Suppl 135):121-129.
30. Mortola JP, Fisher JT, Smith JB, Fox GS, Weeks S, Willis D. Onset of respiration in infants delivered by cesarean section. *J Appl Physiol.* 1982;52:716-724.
31. Vyas H, Milner AD, Hopkin IE, Boon AW. Physiologic responses to prolonged and slow-rise inflation in the resuscitation of the asphyxiated newborn infant. *J Pediatr.* 1981;99:635-639.
32. Boon AW, Milner AD, Hopkin IE. Lung expansion, tidal exchange, and formation of the functional residual capacity during resuscitation of asphyxiated neonates. *J Pediatr.* 1979;95:1031-1036.
33. Hull D. Lung expansion and ventilation during resuscitation of asphyxiated newborn infants. *J Pediatr.* 1969;75:47-58.
34. Milner AD, Vyas H, Hopkin IE. Efficacy of facemask resuscitation at birth. *Br Med J.* 1984;289:1563-1565.
35. Palme-Kilander C, Tunell R. Pulmonary gas exchange during facemask ventilation immediately after birth. *Arch Dis Child.* 1993;68:11-16.
36. Allwood AC, Madar RJ, Baumer JH, Readdy L, Wright D. Changes in resuscitation practice at birth. *Arch Dis Child Fetal Neonatal Ed.* 2003;88:F375-F379.
37. Hoskyns EW, Milner AD, Hopkin IE. A simple method of face mask resuscitation at birth. *Arch Dis Child.* 1987;62:376-378.
38. Cole AF, Rolbin SH, Hew EM, Pynn S. An improved ventilator system for delivery-room management of the newborn. *Anesthesiology.* 1979;51:356-358.
39. Ganga-Zandzou PS, Diependaele JF, Storme L, Riou Y, Klosowski S, Rakza T, Logier R, Lequien P. [Is Ambu ventilation of newborn infants a simple question of finger-touch?]. *Arch Pediatr.* 1996;3:1270-1272.
40. Finer NN, Rich W, Craft A, Henderson C. Comparison of methods of bag and mask ventilation for neonatal resuscitation. *Resuscitation.* 2001;49:299-305.
41. Kanter RK. Evaluation of mask-bag ventilation in resuscitation of infants. *Am J Dis Child.* 1987;141:761-763.
42. Esmail N, Saleh M, et al. Laryngeal mask airway versus endotracheal intubation for Apgar score improvement in neonatal resuscitation. *Egypt J Anaesth.* 2002;18:115-121.
43. Gandini D, Brimacombe JR. Neonatal resuscitation with the laryngeal mask airway in normal and low birth weight infants. *Anesth Analg.* 1999;89:642-643.
44. Lonnqvist PA. Successful use of laryngeal mask airway in low-weight expremature infants with bronchopulmonary dysplasia undergoing cryotherapy for retinopathy of the premature. *Anesthesiology.* 1995;83:422-424.
45. Brimacombe J, Gandini D. Airway rescue and drug delivery in an 800 g neonate with the laryngeal mask airway. *Paediatr Anaesth.* 1999;9:178.
46. Paterson SJ, Byrne PJ, Molesky MG, Seal RF, Finucane BT. Neonatal resuscitation using the laryngeal mask airway. *Anesthesiology.* 1994;80:1248-1253.
47. Hansen TG, Joensen H, Henneberg SW, Hole P. Laryngeal mask airway guided tracheal intubation in a neonate with the Pierre Robin syndrome. *Acta Anaesthesiol Scand.* 1995;39:129-131.
48. Osses H, Poblete M, Asenjo F. Laryngeal mask for difficult intubation in children. *Paediatr Anaesth.* 1999;9:399-401.
49. Ingimarsson J, Bjorklund LJ, Curstedt T, Gudmundsson S, Larsson A, Robertson B, Werner O. Incomplete protection by prophylactic surfactant against the adverse effects of large lung inflations at birth in immature lambs. *Intensive Care Med.* 2004;30:1446-1453.
50. Nilsson R, Grossmann G, Robertson B. Bronchiolar epithelial lesions induced in the premature rabbit neonate by short periods of artificial ventilation. *Acta Pathol Microbiol Scand [A].* 1980;88:359-367.
51. Probyn ME, Hooper SB, Dargaville PA, McCallion N, Crossley K, Harding R, Morley CJ. Positive end expiratory pressure during resuscitation of premature lambs rapidly improves blood gases without adversely affecting arterial pressure. *Pediatr Res.* 2004;56:198-204.
52. Hird MF, Greenough A, Gamsu HR. Inflating pressures for effective resuscitation of preterm infants. *Early Hum Dev.* 1991;26:69-72.
53. Lindner W, Vossbeck S, Hummler H, Pohlandt F. Delivery room management of extremely low birth weight infants: spontaneous breathing or intubation? *Pediatrics.* 1999;103:961-967.
54. Morley C. Continuous distending pressure. *Arch Dis Child Fetal Neonatal Ed.* 1999;81:F152-F156.
55. Heulitt MJ, Holt SJ, Wilson S, Hall RA. Effects of continuous positive airway pressure/positive end-expiratory pressure and pressure-support ventilation on work of breathing, using an animal model. *Respir Care.* 2003;48:689-696.
56. Furzan JA, Gabriele G, Wheeler JM, Fixler DE, Rosenfeld CR. Regional blood flows in newborn lambs during endotracheal continuous airway pressure and continuous negative pressure breathing. *Pediatr Res.* 1981;15:874-878.
57. Finer NN, Carlo WA, Duara S, Fanaroff AA, Donovan EF, Wright LL, Kandever S, Poole WK. Delivery room continuous positive airway pressure/positive end-expiratory pressure in extremely low birth weight infants: a feasibility trial. *Pediatrics.* 2004;114:651-657.
58. Aziz HF, Martin JB, Moore JJ. The pediatric disposable end-tidal carbon dioxide detector role in endotracheal intubation in newborns. *J Perinatol.* 1999;19:110-113.
59. Bhende MS, Thompson AE. Evaluation of an end-tidal CO<sub>2</sub> detector during pediatric cardiopulmonary resuscitation. *Pediatrics.* 1995;95:395-399.
60. Repetto JE, Donohue P-CP, Baker SF, Kelly L, Noguee LM. Use of capnography in the delivery room for assessment of endotracheal tube placement. *J Perinatol.* 2001;21:284-287.
61. Roberts WA, Maniscalco WM, Cohen AR, Litman RS, Chhibber A. The use of capnography for recognition of esophageal intubation in the neonatal intensive care unit. *Pediatr Pulmonol.* 1995;19:262-268.
62. Bhende MS, Karasic DG, Karasic RB. End-tidal carbon dioxide changes during cardiopulmonary resuscitation after experimental asphyxial cardiac arrest. *Am J Emerg Med.* 1996;14:349-350.
63. Perondi MB, Reis AG, Paiva EF, Nadkarni VM, Berg RA. A comparison of high-dose and standard-dose epinephrine in children with cardiac arrest. *N Engl J Med.* 2004;350:1722-1730.
64. Berg RA, Otto CW, Kern KB, Hilwig RW, Sanders AB, Henry CP, Ewy GA. A randomized, blinded trial of high-dose epinephrine versus standard-dose epinephrine in a swine model of pediatric asphyxial cardiac arrest. *Crit Care Med.* 1996;24:1695-1700.
65. Burchfield DJ, Preziosi MP, Lucas VW, Fan J. Effects of graded doses of epinephrine during asphxia-induced bradycardia in newborn lambs. *Resuscitation.* 1993;25:235-244.
66. Ralston SH, Voorhees WD, Babbs CF. Intrapulmonary epinephrine during prolonged cardiopulmonary resuscitation: improved regional blood flow and resuscitation in dogs. *Ann Emerg Med.* 1984;13:79-86.
67. Ralston SH, Tacker WA, Showen L, Carter A, Babbs CF. Endotracheal versus intravenous epinephrine during electromechanical dissociation with CPR in dogs. *Ann Emerg Med.* 1985;14:1044-1048.

68. Redding JS, Asuncion JS, Pearson JW. Effective routes of drug administration during cardiac arrest. *Anesth Analg*. 1967;46:253–258.
69. Kleinman ME, Oh W, Stonestreet BS. Comparison of intravenous and endotracheal epinephrine during cardiopulmonary resuscitation in newborn piglets. *Crit Care Med*. 1999;27:2748–2754.
70. Schwab KO, von Stockhausen HB. Plasma catecholamines after endotracheal administration of adrenaline during postnatal resuscitation. *Arch Dis Child Fetal Neonatal Ed*. 1994;70:F213–F217.
71. So KW, Fok TF, Ng PC, Wong WW, Cheung KL. Randomised controlled trial of colloid or crystalloid in hypotensive preterm infants. *Arch Dis Child Fetal Neonatal Ed*. 1997;76:F43–F46.
72. Oca MJ, Nelson M, Donn SM. Randomized trial of normal saline versus 5% albumin for the treatment of neonatal hypotension. *J Perinatol*. 2003;23:473–476.
73. Emery EF, Greenough A, Gamsu HR. Randomised controlled trial of colloid infusions in hypotensive preterm infants. *Arch Dis Child*. 1992; 67:1185–1188.
74. McGuire W, Fowlie PW. Naloxone for narcotic-exposed newborn infants. *Cochrane Database Syst Rev*. 2002;CD003483.
75. Moreland TA, Brice JE, Walker CH, Parija AC. Naloxone pharmacokinetics in the newborn. *Br J Clin Pharmacol*. 1980;9:609–612.
76. Laudenschach V, Calo G, Guerrini R, Lamboley G, Benoist JF, Evrard P, Gressens P. Nociceptin/orphanin FQ exacerbates excitotoxic white-matter lesions in the murine neonatal brain. *J Clin Invest*. 2001;107: 457–466.
77. de-Castro RM, Cabral-Filho JE, Costa JA, Costa FB, Gallindo MA, Hecksher CA. Neonatal treatment with naloxone causes permanent hyperalgesia in rats. *Braz J Med Biol Res*. 1993;26:747–751.
78. Hasan RA, Benko AS, Nolan BM, Campe J, Duff J, Zureikat GY. Cardiorespiratory effects of naloxone in children. *Ann Pharmacother*. 2003;37:1587–1592.
79. Gibbs J, Newson T, Williams J, Davidson DC. Naloxone hazard in infant of opioid abuser. *Lancet*. 1989;2:159–160.
80. Costeloe K, Hennessy E, Gibson AT, Marlow N, Wilkinson AR. The EPICure study: outcomes to discharge from hospital for infants born at the threshold of viability. *Pediatrics*. 2000;106:659–671.
81. Vohra S, Frent G, Campbell V, Abbott M, Whyte R. Effect of polyethylene occlusive skin wrapping on heat loss in very low birth weight infants at delivery: a randomized trial. *J Pediatr*. 1999;134:547–551.
82. Vohra S, Roberts RS, Zhang B, Janes M, Schmidt B. Heat Loss Prevention (HeLP) in the delivery room: a randomized controlled trial of polyethylene occlusive skin wrapping in very preterm infants. *J Pediatr*. 2004;145:750–753.
83. Lyon AJ, Stenson B. Cold comfort for babies. *Arch Dis Child Fetal Neonatal Ed*. 2004;89:F93–F94.
84. Lenclen R, Mazraani M, Jugie M, Couderc S, Hoenn E, Carbajal R, Blanc P, Paupe A. [Use of a polyethylene bag: a way to improve the thermal environment of the premature newborn at the delivery room]. *Arch Pediatr*. 2002;9:238–244.
85. Bjorklund LJ, Hellstrom-Westas L. Reducing heat loss at birth in very preterm infants. *J Pediatr*. 2000;137:739–740.
86. Baum JD, Scopes JW. The silver swaddler: device for preventing hypothermia in the newborn. *Lancet*. 1968;1:672–673.
87. Besch NJ, Perlstein PH, Edwards NK, Keenan WJ, Sutherland JM. The transparent baby bag: a shield against heat loss. *N Engl J Med*. 1971; 284:121–124.
88. Petrova A, Demissie K, Rhoads GG, Smulian JC, Marcella S, Ananth CV. Association of maternal fever during labor with neonatal and infant morbidity and mortality. *Obstet Gynecol*. 2001;98:20–27.
89. Lieberman E, Eichenwald E, Mathur G, Richardson D, Heffner L, Cohen A. Intrapartum fever and unexplained seizures in term infants. *Pediatrics*. 2000;106:983–988.
90. Hajat C, Hajat S, Sharma P. Effects of poststroke pyrexia on stroke outcome: a meta-analysis of studies in patients. *Stroke*. 2000;31: 410–414.
91. Azzimondi G, Bassein L, Nonino F, Fiorani L, Vignatelli L, Re G, D'Alessandro R. Fever in acute stroke worsens prognosis: a prospective study. *Stroke*. 1995;26:2040–2043.
92. Coimbra C, Boris-Moller F, Drake M, Wieloch T. Diminished neuronal damage in the rat brain by late treatment with the antipyretic drug dipyrrone or cooling following cerebral ischemia. *Acta Neuropathol (Berl)*. 1996;92:447–453.
93. Dietrich WD, Busto R, Halley M, Valdes I. The importance of brain temperature in alterations of the blood-brain barrier following cerebral ischemia. *J Neuropathol Exp Neurol*. 1990;49:486–497.
94. Gunn AJ, Gunn TR, de Haan HH, Williams CE, Gluckman PD. Dramatic neuronal rescue with prolonged selective head cooling after ischemia in fetal lambs. *J Clin Invest*. 1997;99:248–256.
95. Luptook AR, Corbett RJ, Sterett R, Burns DK, Garcia D, Tollefsbol G. Modest hypothermia provides partial neuroprotection when used for immediate resuscitation after brain ischemia. *Pediatr Res*. 1997;42: 17–23.
96. Thoresen M, Bagenholm R, Loberg EM, Apricena F, Kjellmer I. Post-hypoxic cooling of neonatal rats provides protection against brain injury. *Arch Dis Child Fetal Neonatal Ed*. 1996;74:F3–F9.
97. Bernard SA, Gray TW, Buist MD, Jones BM, Silvester W, Gutteridge G, Smith K. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. *N Engl J Med*. 2002;346:557–563.
98. Gluckman PD, Wyatt JS, Azzopardi D, Ballard R, Edwards AD, Ferriero DM, Polin RA, Robertson CM, Thoresen M, Whitelaw A, Gunn AJ. Selective head cooling with mild systemic hypothermia after neonatal encephalopathy: multicentre randomised trial. *Lancet*. 2005;365: 663–670.
99. Eicher DJ, Wagner CL, Katikaneni LP, Hulsey TC, Bass WT, Kaufman DA, Horgan MJ, Languani S, Bhatia JJ, Givelichian LM, Sankaran K, Yager JY. Moderate hypothermia in neonatal encephalopathy: efficacy outcomes. *Pediatr Neurol*. 2005;32:11–17.
100. Thoresen M, Whitelaw A. Cardiovascular changes during mild therapeutic hypothermia and rewarming in infants with hypoxic-ischemic encephalopathy. *Pediatrics*. 2000;106:92–99.
101. Shankaran S, Luptook A, Wright LL, Ehrenkranz RA, Donovan EF, Fanaroff AA, Stark AR, Tyson JE, Poole K, Carlo WA, Lemons JA, Oh W, Stoll BJ, Papile LA, Bauer CR, Stevenson DK, Korones SB, McDonald S. Whole-body hypothermia for neonatal encephalopathy: animal observations as a basis for a randomized, controlled pilot study in term infants. *Pediatrics*. 2002;110:377–385.
102. Eicher DJ, Wagner CL, Katikaneni LP, Hulsey TC, Bass WT, Kaufman DA, Horgan MJ, Languani S, Bhatia JJ, Givelichian LM, Sankaran K, Yager JY. Moderate hypothermia in neonatal encephalopathy: safety outcomes. *Pediatr Neurol*. 2005;32:18–24.
103. Brambrink AM, Ichord RN, Martin LJ, Koehler RC, Traustman RJ. Poor outcome after hypoxia-ischemia in newborns is associated with physiological abnormalities during early recovery: possible relevance to secondary brain injury after head trauma in infants. *Exp Toxicol Pathol*. 1999;51:151–162.
104. Vannucci RC, Vannucci SJ. Cerebral carbohydrate metabolism during hypoglycemia and anoxia in newborn rats. *Ann Neurol*. 1978;4:73–79.
105. Yager JY, Heitjan DF, Towfighi J, Vannucci RC. Effect of insulin-induced and fasting hypoglycemia on perinatal hypoxic-ischemic brain damage. *Pediatr Res*. 1992;31:138–142.
106. Salhab WA, Wyckoff MH, Luptook AR, Perlman JM. Initial hypoglycemia and neonatal brain injury in term infants with severe fetal acidemia. *Pediatrics*. 2004;114:361–366.
107. Hattori H, Wasterlain CG. Posthypoxic glucose supplement reduces hypoxic-ischemic brain damage in the neonatal rat. *Ann Neurol*. 1990; 28:122–128.
108. LeBlanc MH, Huang M, Patel D, Smith EE, Devidas M. Glucose given after hypoxic ischemia does not affect brain injury in piglets. *Stroke*. 1994;25:1443–1447; discussion 1448.
109. Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. *Cochrane Database Syst Rev*. 2004; CD003248.
110. Ibrahim HM, Krouskop RW, Lewis DF, Dhanireddy R. Placental transfusion: umbilical cord clamping and preterm infants. *J Perinatol*. 2000; 20:351–354.
111. Linderkamp O, Nelle M, Kraus M, Zilow EP. The effect of early and late cord-clamping on blood viscosity and other hemorheological parameters in full-term neonates. *Acta Paediatr*. 1992;81:745–750.
112. Nelle M, Zilow EP, Bastert G, Linderkamp O. Effect of Leboyer childbirth on cardiac output, cerebral and gastrointestinal blood flow velocities in full-term neonates. *Am J Perinatol*. 1995;12:212–216.
113. De Leeuw R, Cuttini M, Nadai M, Berbk I, Hansen G, Kuciskas A, Lenoir S, Levin A, Persson J, Rebagliato M, Reid M, Schroell M, de Vonderweid U. Treatment choices for extremely preterm infants: an international perspective. *J Pediatr*. 2000;137:608–616.
114. Sanders MR, Donohue PK, Oberdorf MA, Rosenkrantz TS, Allen MC. Perceptions of the limit of viability: neonatologists' attitudes toward extremely preterm infants. *J Perinatol*. 1995;15:494–502.
115. Kopelman LM, Irons TG, Kopelman AE. Neonatologists judge the "Baby Doe" regulations. *N Engl J Med*. 1988;318:677–683.

116. Draper ES, Manktelow B, Field DJ, James D. Tables for predicting survival for preterm births are updated. *BMJ*. 2003;327:872.
117. Jain L, Ferre C, Vidyasagar D, Nath S, Sheftel D. Cardiopulmonary resuscitation of apparently stillborn infants: survival and long-term outcome. *J Pediatr*. 1991;118:778–782.
118. Haddad B, Mercer BM, Livingston JC, Talati A, Sibai BM. Outcome after successful resuscitation of babies born with Apgar scores of 0 at both 1 and 5 minutes. *Am J Obstet Gynecol*. 2000;182:1210–1214.

### Worksheets Cited

- W200. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC344>
- W201. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC345>
- W202A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC346>
- W202B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC347>
- W203A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC348>
- W203B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC349>
- W203C. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC350>
- W204A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC351>
- W204B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC352>
- W206. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC354>
- W208. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC357>
- W209A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC358>
- W209B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC359>
- W210A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC360>
- W210B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC361>
- W211A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC362>
- W211B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC363>
- W212A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC364>
- W212B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC365>
- W213A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC366>
- W213B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC367>
- W214A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC368>
- W214B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC369>
- W215A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC370>
- W215B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC371>
- W216A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC372>
- W216B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC373>
- W217. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC374>
- W218A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC375>
- W218B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC376>
- W219A. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC377>
- W219B. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC378>
- W220. <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.105.170522/DC379>