Neonatal Resuscitation

Thomas E Wiswell MD

Ten million or more newborns worldwide each year need some type of resuscitation assistance. More than 1 million babies die annually from complications of birth asphyxia. Over the past 3 decades, neonatal resuscitation has evolved from disparate, word-of-mouth teaching methods to organized programs. The most widely-used curriculum is the Neonatal Resuscitation Program, which is supported by the American Academy of Pediatrics and the American Heart Association. To date more than 1.5 million individuals have been trained in the Neonatal Resuscitation Program. Resuscitation efforts are geared toward avoiding or mitigating the adverse sequelae of asphyxia neonatorum. Certain characteristics distinguish the preterm infant, including propensity to become hypothermic and higher potential for adverse neurologic and pulmonary complications from resuscitation efforts. In this era of evidence-based medicine the most recent Neonatal Resuscitation Program guidelines were developed to provide recommendations based on the best currently-available science. A number of major proposals received considerable scrutiny during the evaluation process. Many areas of neonatal resuscitation still need to be studied. *Key words: neonatal resuscitation, neonates, evidence-based medicine, EBM.* [Respir Care 2003;48(3):288–294.

Introduction

More than 100 million babies are born annually worldwide. They have to make the transition from a fluid-filled environment in which the placenta serves as the gas-exchange organ for the fetus, to an air-filled environment in which the baby's own cardiopulmonary system has to independently function within minutes of birth for survival. I am always amazed that at least 90% of neonates successfully make this transition without need of help. The remaining 10% of newborns require some assistance to begin breathing at birth, and 1% or more may require intensive resuscitative efforts.[1] Worldwide, approximately 19% of the 5 million neonatal deaths that occur annually are due to birth asphyxia. Successful neonatal resuscitation should prevent a large proportion of these deaths, as well as mitigate the outcomes of surviving asphyxiated infants.

There are many complications seen in infants following resuscitation. Obviously, death is the most severe. Brain injury may manifest as apnea, seizures, and hypoxic-isch-

Thomas E Wiswell MD is affiliated with the Department of Pediatrics, State University of New York at Stony Brook, Stony Brook, New York.

Thomas E Wiswell MD presented a version of this report at the 31st RESPIRATORY CARE Journal Conference, Current Trends in Neonatal and Pediatric Respiratory Care, August 16–18, 2002, in Keystone, Colorado.

Correspondence: Thomas E Wiswell MD, SUNY Stony Brook, Pediatrics, HSC-11–060, Stony Brook NY 11794-8111. E-mail: thomas.wiswell@stonybrook.edu.

emic encephalopathy. The most severely injured survivors may be afflicted with cerebral palsy and major cognitive impairment. Cardiovascular manifestations include hypotension and poor ventricular function. Acute tubular necrosis may be an indicator of kidney dysfunction. Persistent pulmonary hypertension of the newborn may be a symptom of pulmonary involvement. The hematopoietic system can also be affected, resulting in thrombocytopenia. Gastrointestinal effects include necrotizing enterocolitis and liver dysfunction. The latter is commonly characterized by elevations in liver enzymes (particularly aspartate aminotransferase [AST] and alanine aminotransferase [ALT]) and coagulation dysfunction. Systemic derangements commonly include hypoglycemia and hypocalcemia, as well as other electrolyte derangements.

What is the effect of a structured neonatal resuscitation program on the outcomes of depressed neonates requiring resuscitation? We have limited data. We need to know the effect on: (1) mortality; (2) short-term morbidity (eg, hypoxic-ischemic encephalopathy, seizures); and (3) long-term morbidity (eg, cerebral palsy, mental retardation). Although more than 1.5 million individuals worldwide have been trained under the Neonatal Resuscitation Program (NRP) of the American Academy of Pediatrics/American Heart Association, it is unclear what its demonstrable, measurable benefits may be. It would be unethical to perform randomized, controlled trials in which the therapy for the control group is no resuscitation.

The Uniqueness of the Preterm Infant

Premature infants (those of < 37 wk gestation) make up the largest proportion of neonates who require some degree of resuscitation, in particular those born at < 32 weeks' gestation and $< 1{,}500$ g birthweight. The latter group of infants make up approximately 1.4% of all children born in the United States each year. The majority of those born at ≤ 28 weeks gestation will require some form of resuscitation. Premature infants are commonly hypothermic because of their greater surface-area-to-body-weight ratio, minimal fat stores, and thinner dermis and epidermis. Additionally, this population has a high frequency of severe brain injury (intraventricular hemorrhage and periventricular leukomalacia) as well as long-term neurodevelopmental problems (eg, cerebral palsy, cognitive delays, learning disabilities). Hypocapnia among these infants has been associated with periventricular leukomalacia and chronic lung disease (bronchopulmonary dysplasia). The preterm infant often has electrolyte disturbances (hypo- and hypernatremia, hyperkalemia, and hypocalcemia), as well as hypoglycemia. Infants born at < 37 weeks gestation are more likely to develop necrotizing enterocolitis. Neonatal depression and true asphyxia may contribute to the development of these various disorders. Presumably, good resuscitation efforts should be of benefit under these circumstances. Unfortunately, however, in the past, several therapies used during resuscitation efforts may have played a role in the pathogenesis of several disorders. Rapid infusion of bicarbonate, epinephrine, and fluid boluses may have contributed to necrotizing enterocolitis and intraventricular hemorrhage.[1,2]

Ventilation in the Delivery Room

Ventilation is the key to neonatal resuscitation. Most depressed newborns will respond to ventilation alone, with no further therapies needed (eg, chest compressions, medications). Data from the 1970s and 1980s suggested that multiple sustained inflations immediately after birth would expand the lungs to functional residual capacity and result in a quicker response, with spontaneous respirations.[3] However, Björklund et al[4] demonstrated in premature lambs that as few as 5 sustained inflations (of 35–40 mL/kg) would lead to the release of pro-inflammatory cytokines and adverse lung histology. In addition, in the preterm population it has been shown that hypocapnia during the first days of life may play a role in the development of both periventricular leukomalacia and bronchopulmonary dysplasia.[5] One wonders if the pathogenesis of bronchopulmonary dysplasia begins during the first minutes of life, with overly aggressive ventilation causing hypocapnia and volutrauma. In the neonatal intensive care unit, nasal continuous positive airway pressure (CPAP) is frequently used as a noninvasive method of pulmonary support in newborns with respiratory disorders, particularly in premature infants with respiratory distress syndrome.[6] It is unclear what role either nasal CPAP or more gentle ventilation may play in the resuscitation of infants in the delivery room. No trials have been performed assessing either of these techniques in the delivery room.

Evidence-Based Medicine and Neonatal Resuscitation

Multiple organizations around the world have made recommendations or developed standards for resuscitation of neonates (Table 1). Unfortunately, much of what these

Table 1. International Organizations That Deal with Neonatal Resuscitation

- Neonatal Resuscitation Program of the American Academy of Pediatrics and the American Heart Association
- United Kingdom Resuscitation Council
- European Resuscitation Council
- Heart and Stroke Foundation of Canada
- Australian Resuscitation Council
- Resuscitation Council of Southern Africa
- Council of Latin America for Resuscitation

Table 2. Key Neonatal Resuscitation Issues That Were Considered During the 3-Year Process Leading to the Current Recommendations

- Is intratracheal suctioning of apparently vigorous, meconium-stained infants necessary?
- Should one use 100% oxygen or room air when ventilating infants during resuscitation?
- What are the appropriate solutions to use for volume expansion during resuscitation?
- Can guidelines be developed for withholding or withdrawing resuscitation of infants in the delivery room?
- Can heart rate thresholds for initiating and stopping cardiac compressions be simplified?
- Is cerebral hypothermia an effective therapy to prevent brain injury following resuscitation?
- Should the 1:3 ratio of ventilations to cardiac compressions during resuscitation be changed?
- What is the role of the laryngeal mask airway in delivery room resuscitation?
- Should end-tidal carbon dioxide detectors be routinely used to confirm endotracheal tube placement?
- Is high-dose intravascularly-administered epinephrine more effective than standard doses?
- Can one use the intraosseous route to administer fluids and medications in the delivery room?
- Is the "two-thumb, hands encircling the chest" method of chest compressions more effective than the "two-fingers perpendicular to the chest" technique?

(Adapted from References 2 and 9.)

organizations propose is based solely on the opinions of experienced clinicians or on less-than-optimal studies (eg, comparisons with historical cohorts). Such recommendations, although seemingly plausible, may be wrong. A good example is intrapartum oropharyngeal and nasopharyngeal suctioning of meconium-stained infants prior to delivery of the baby's shoulders. This widely-advocated procedure is based on a cohort trial published in 1976, in which suctioned infants were compared to historical controls.[7] Although there was a trend for suctioned infants to be less likely to develop meconium aspiration syndrome, the difference was not statistically significant. Nevertheless, virtually all resuscitation organizations advocated this therapy as being of benefit. Recently, however, a large randomized, controlled trial was finally performed (almost 2,500 enrolled patients) to assess the usefulness of intrapartum suctioning.[8] The results indicated there were absolutely no differences in outcomes between controls and the babies thus treated. Such findings emphasize the problem with relying on opinion rather than on the accepted standard of large, randomized, controlled trials.

Evidence-based medicine is an approach to health care practice in which clinicians are aware of the evidence and the strength of the evidence that supports their clinical practices. It is the conscientious, explicit, and judicious use of current best evidence in order to make clinical decisions. The Cochrane Collaboration (http://www.cochrane.org) is an example of an organization in which contributors perform systematic reviews concerning patient management in order to provide recommendations about specific therapies. Ideally, all medical practice should be evidence-based. The development of the most recent NRP guidelines were an attempt to implement evidence-based medicine concerning resuscitation.

Development of the New Neonatal Resuscitation Program Guidelines

The International Liaison Committee on Resuscitation was formed in 1992 to provide a forum for resuscitation organizations in the developed world.[9] During the subsequent decade, many international consensus conferences and publications have addressed many resuscitation issues. The Pediatric Working Group of the International Liaison Committee on Resuscitation, the Pediatric Resuscitation Subcommittee of the Emergency Cardiovascular Care Committee of the American Heart Association, and the NRP Steering Committee of the American Academy of Pediatrics worked together for 2 years in a systematic process of evidence evaluation and formulation of new recommendations for neonatal resuscitation.[2,9] Members of the participating organizations worked with resuscitation experts from various countries to assemble the most current scientific information relating to neonatal resuscitation. Multiple issues were considered, particularly those delineated in Table 2. The involved individuals defined existing guidelines and proposed changes (Table 3). They collected and analyzed data. The available evidence was classified at various levels (Table 4). Finally, recommendations were made, classified (Table 5), and published.[1,2]

The initial process, that of defining the hypothesis or potential changes in recommendations, was the result of the International Liaison Committee on Resuscitation, American Heart Association, and American Academy of

Table 3. The Process for Determining Final Recommendations

- Define existing and proposed guideline (eg, management of meconium in the delivery room, 100% oxygen versus room air)
- Collect the sources: literature, abstracts, textbooks, unpublished studies, etc.
- Critically review the quality of each source: research design, methods, statistical analysis, direction of results, etc.
- Summarize and classify the evidence
- Define a class of recommendation
- Debate and consensus
- Final endorsement of recommendations by participating organizations
- Publication of recommendations

Table 4. Classification of Sources by Level of Evidence

Classification	Type of Evidence
Level 1	Randomized, controlled trial with large effect
Level 2	Randomized, controlled trial with small effect
Level 3	Prospective, controlled, non-randomized study
Level 4	Historical, non-randomized cohort study
Level 5	Non-controlled case series
Level 6	Animal or mechanical model
Level 7	Extrapolation or theoretical analysis
Level 8	Rational conjecture or common practice

Table 5. Determination of the Class of Recommendation

Class	Recommendation
Class I	Definitely recommended; excellent evidence
Class IIa	Acceptable and useful; good evidence
Class IIb	Acceptable and useful; weaker evidence
Class III	Not acceptable, not useful; may be harmful
Indeterminate	No recommendation until further research

Pediatrics committees, as well as international resuscitation experts, defining questions and controversies that they believed were important and for which it was thought there may be substantial evidence. A standard worksheet served as a framework for uniform evaluation of the various topics. The next step was to gather the evidence. Articles published in peer-reviewed journals were collected, as well as other material (for instance, from electronic databases, abstracts, book chapters, and pre-publication material). Authors judged to be experts in certain resuscitation areas were queried as to the existence of other pertinent material. The evidence was collected and analyzed. Each piece of material was individually assessed for relevance to the hypothesis or recommendation change. Members of the reviewing group critically assessed the quality of each article and source for research design and methods. The reviewers assessed individual sources as to the direction of the results, statistics used, and whether the information supported, opposed, or was neutral regarding the guideline proposal. The strength of evidence was classified into 8 levels (see Table 4). The strongest level of evidence was a randomized, controlled trial with a large effect. The weakest level of evidence was rational conjecture or common practice.

The integration of evidence of multiple different levels and various quality occurred through consensus discussion among experts and formal presentation for debate at the Evidence Evaluation Conference of the American Heart Association in September 1999, in Dallas, Texas. This process led to the classification of recommendation for each proposed guideline,[2] based on the level of evidence and critical assessment of the quality of each study, the number of studies, the consistency of results, the outcomes measurements, and the magnitude of the potential benefit. The proposed guidelines, class of recommendation, and levels of evidence were ultimately debated at the Guidelines 2000 Conference in February 2000, in Dallas, Texas

A more extensive review of the evaluation process and a description of the final recommendations have been previously published.[2] These recommendations were the basis for the major changes in the NRP's *Neonatal Resuscitation Textbook*, which was published in 2000.[1] The major questions and recommendations are listed below.

Major Neonatal Resuscitation Program Recommendations

1. Which meconium-stained infants should have direct endotracheal intubation?

Only those who are not vigorous; that is, those who have poor tone, poor respiratory effort, or a heart rate $<$ 100 b/min on initial evaluation.

2. Is room air as effective as 100% oxygen in resuscitating newborns?

The evidence is insufficient to change the current recommendation of using 100% oxygen. If oxygen is not available, room air should be used.

3. What are the appropriate solutions for acute volume expansion for treatment of hypovolemia?

Normal saline or Ringer's lactate. O-negative blood may be used if a need for blood replacement is anticipated prior to birth. Albumin and other plasma substitutes carry a risk of infectious disease and higher mortality.

4. Is cerebral hypothermia an effective therapy following perinatal asphyxia?

Evidence is insufficient to change the current recommendation of isothermia. Hyperthermia should be avoided.

5. Are there appropriate guidelines for withholding resuscitation or stopping resuscitative efforts in the delivery room?

Noninitiation of resuscitation is appropriate in some conditions (anencephaly, known Trisomy 13 or 18, birthweight $<$ 400 g).

6. Can the heart rate thresholds for initiating chest compressions be simplified?

Yes. Chest compressions should be started whenever the heart rate is $<$ 60 b/min (after 30 s of assisted ventilation) and stopped when the heart rate is $>$ 60 b/min.

7. Should the 1:3 ratio of coordinating ventilation breaths with chest compressions be changed?

No.

8. Is there a role for the laryngeal mask airway in neonatal resuscitation?

Not generally. However, under certain circumstances (eg, failed intubation attempts), when the clinicians have

experience with the laryngeal mask airway, it may be appropriate.

9. Should carbon dioxide detectors be recommended as standard to confirm endotracheal intubation?

No. They are an option, but not standard of care.

10. Should high-dose epinephrine be removed as an option?

Yes.

11. Is the intraosseous route an appropriate alternative to the umbilical vein?

Yes, when the umbilical vein or other direct venous route is not accessible. Note that intraosseous access will probably be successful only in large, term-gestation neonates.

12. Is the 2-thumb/encircling hands technique preferable to the 2-finger technique for chest compressions?

Yes, when the size of the clinician's hands permits.

The individual evidence-evaluation worksheets for most of these recommendations are available at the NRP Web site (http://www.aap.org/profed/nrp/science.html).

Future Directions

Of note, only 2 of the above recommendations were Class 1 (highest level) recommendations. In this age of evidence-based medicine and clinical pathway guidelines, clearly many aspects of neonatal resuscitation need to be validated. Even the overall effectiveness of neonatal resuscitation and the NRP have not been verified. The NRP has recognized the necessity of assessing outcomes and is instituting a major drive to do so over the next several years. Additionally, there is a major need for randomized, controlled trials to assess new therapies, as well as those whose benefits are currently indeterminate. Both short-term and long-term outcomes should be measured in clinical trials. Moreover, there is a need for national and international databases to register infants who require resuscitation and the therapies that were provided. Such registries should provide a forum for short-term and long-term outcomes.

Some of the important questions that I believe need to be assessed in the near future include:

1. Is there any role at all for using sodium bicarbonate?

2. How common and harmful are the intracellular acidosis and decreased cardiac function that have been recognized following bicarbonate administration?

3. Does chest physiotherapy have any benefit in the delivery room, particularly for meconium-stained infants or those with abundant oral secretions?

4. Is albumin as effective or more effective than crystalloid solutions in volume replacement in the delivery room? Current recommendations are extrapolated from neonatal studies outside the delivery room or from investigations in older children and adults.

5. Will high-dose intratracheal epinephrine achieve responses equal to or better than standard intravascular or intratracheal doses?

6. Does low-tidal-volume ventilation achieve as good a response as current ventilation techniques?

7. What is the role of face-mask or nasal CPAP in the delivery room? Can either face-mask or nasal CPAP decrease the requirement for intubation or decrease lung injury?

8. Are there better ways to prevent hypothermia in preterm infants?

9. Does post-resuscitation head cooling or total body hypothermia mitigate brain injury in term-gestation neonates?

10. What is the role of room air versus 100% oxygen in resuscitating neonates?

The use of sodium bicarbonate as a medication during neonatal resuscitation has never been evaluated. Current recommendations[1,2] are to administer sodium bicarbonate if a child has undergone other resuscitation therapies (eg, ventilation, cardiac compressions) and fails to respond. It would be important to document substantial metabolic acidosis prior to administering sodium bicarbonate. Although there is a lack of data documenting its potential benefit, many clinicians use sodium bicarbonate early in resuscitation with the belief that it will "help" if there is metabolic acidosis. Bicarbonate is rapidly metabolized, producing carbon dioxide, which may contribute to respiratory acidosis, particularly in children having problems being ventilated. Moreover, as carbon dioxide easily crosses cell membranes, bicarbonate administration may contribute to a worsening intracellular acidosis.[10]

Chest physiotherapy is another therapy commonly provided to neonates in the delivery room, particularly those children born through meconium-stained amniotic fluid or those with abundant oral secretions, especially noted following cesarean section delivery. I have seen physicians, nurses, and respiratory therapists perform elaborate chest physiotherapy (eg, percussion, vibration, suctioning) in the delivery room, to the exclusion of the recommended sequence of resuscitation; for example, depressed, meconium-stained infants receiving chest physiotherapy without adequate ventilation. In the initial assessment of any infant, obvious nasal and oral secretions should be quickly suctioned. Intubation and suctioning are only recommended for infants who are meconium-stained and nonvigorous (defined as heart rate $<$ 100 b/min, poor respiratory effort, or poor muscle tone in the initial assessment within seconds of birth). The usefulness of other elements of chest physiotherapy in the delivery room (eg, percussion, vibration, instillation of saline) have no basis, and these should not be performed unless future investigations validate their benefit.

Are albumin or other colloid solutions of more benefit than crystalloid solutions in providing volume replacement in the delivery room? The current recommended solutions are normal saline and Ringer's lactate. Based on data extrapolated from neonatal intensive care unit studies of infants hours to days following birth, as well as extrapolations from the literature concerning adults and older children, it is currently believed that albumin or other plasma protein solutions are of no additional benefit and may in fact be harmful. I would comment, however, that delivery-room, randomized, controlled trials comparing colloid to crystalloid solutions have not yet been performed. Such studies should be done.

Would high-dose epinephrine be of more benefit via intratracheal administration than intravenously (which is currently recommended)? There are no data from newborn infants to assess higher doses of intratracheal epinephrine, which is not absorbed completely from the airways and may result in lower serum levels.

Low-tidal-volume ventilation in the delivery room could potentially avoid airway injury and adverse effects of hypocapnia in premature infants. Unquestionably, the key aspect of resuscitation is adequate ventilation. Most depressed neonates respond well to ventilation. My fear is that low-tidal-volume ventilation may not be adequate for newborns to respond (eg, with increased heart rate or spontaneous respirations). Moreover, there is no good way to measure tidal volume in the delivery room situation. Animal models need to be studied to evaluate the efficacy of this strategy before applying it to human infants.

Over the past decade, there has been a resurgence of interest in CPAP use with neonates.[6] This includes the possible use of CPAP in the delivery room. Some have suggested using nasal CPAP in spontaneously breathing babies with respiratory distress in the delivery room (Morley CJ, Royal Women's Hospital, University of Melbourne, Melbourne, Australia, 2002, personal communication). There are commercially available devices for providing mask CPAP in the delivery room (the NeoPuff, Fischer-Paykel, New Zealand). Additionally, one may adjust standard flow-inflating or self-inflating bags to provide CPAP. Nonetheless, to date there is no literature supporting CPAP use in the delivery room.

Hypothermia may result in adverse outcomes in babies, particularly those of preterm gestation. The latter population is at great risk for hypothermia, despite immediate drying and placing under a heat source in the delivery room. There are studies being performed in which premature infants are immediately wrapped in polyethylene in order to prevent heat loss.[11] Indeed, it is standard practice in some hospitals to immediately place extremely low birthweight infants in "zip-lock" bags of the type available in grocery stores. These various practices have to be adequately assessed to determine their potential value.

In contrast, among term infants with hypoxic-ischemic brain insults, it has been suggested that cooling the brain may prevent or mitigate injury.[12] The suggested methods include head-cooling and total body cooling. There are several ongoing or recently completed trials to assess the effects of these therapies. Core body temperatures in the range of 33.5–34.5° C are maintained for approximately 72 hours. I eagerly await the results of these investigations.

Over the past decade there has appeared considerable literature suggesting that resuscitation with room air is at least as efficacious as resuscitation with 100% oxygen.[13–15] The use of 100% oxygen may result in the generation of oxygen free radicals, which are markedly toxic to living tissues. Although the anecdotal data look promising, to date there have been no large, randomized, controlled trials evaluating the efficacy of room air versus 100% oxygen. Hopefully, such trials are on the horizon.

Summary

We have made remarkable strides in neonatal resuscitation over the past 3 decades. However, much work needs to be performed to validate its efficacy. There are many aspects and ideas that need to be explored. This branch of neonatology is constantly evolving, and I wholeheartedly support research in the various areas I have described.

REFERENCES

1. AHA/AAP Neonatal Resuscitation Program Steering Committee. Textbook of neonatal resuscitation, 4th ed. Elk Grove Village, Il: American Academy of Pediatrics; 2000.
2. Niermeyer S, Kattwinkel J, Van Reempts P, Nadkarni V, Phillips B, Zideman D, et al. International Guidelines for Neonatal Resuscitation: An excerpt from the Guidelines 2000 for cardiopulmonary resuscitation and emergency cardiovascular care: international consensus on science. Contributors and Reviewers for the Neonatal Resuscitation Guidelines. Pediatrics 2000 (Sept);106(3):e29.
3. Milner A. The importance of ventilation to effective resuscitation in the term and preterm infant. Semin Neonatol 2001;6(3):219–224.
4. Björklund LJ, Ingimarsson J, Curstedt T, John J, Robertson B, Werner O, Vilstrup CT. Manual ventilation with a few large breaths at birth compromises the therapeutic effects of subsequent surfactant replacement in immature lambs. Pediatr Res 1997;42(3):348–355.
5. Kraybill EN, Runyan DK, Bose CL, Khan JH. Risk factors for chronic lung disease in infants with birth weights of 751 to 1000 grams. J Pediatr 1989;115(1):115–120.
6. Wiswell TE, Srinivasan P. Continuous positive airway pressure (CPAP). In: Goldsmith J, Karotkin E, editors. Assisted ventilation of the neonate, 4th ed. Philadelphia: WB Saunders (2003, in press).
7. 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(6):712–715.
8. Vain N, Szyld E, Prudent L, Wiswell T, et al. Oro- and nasopharyngeal suction of meconium-stained neonates before delivery of their shoulders does not prevent meconium aspiration syndrome: results of the international, multicenter, randomized, controlled trial (RCT) (abstract). Pediatr Res 2002;51:379A.

9. Kattwinkel J, Niermeyer S, Nadkarni V, Tibballs J, Phillips B, Zideman D, et al. ILCOR advisory statement: resuscitation of the newly born infant: an advisory statement from the pediatric working group of the International Liaison Committee on Resuscitation. Circulation 1999;99(14):1927–1938.
10. Burchfield DJ. Medication use in neonatal resuscitation. Clin Perinatol 1999;26(3):683–691.
11. 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(5):547–551.
12. Shankaran S, Laptook A, Wright LL, Ehrenkranz RA, Donovan EF, Fanaroff AA, et al. Whole-body hypothermia for neonatal encephalopathy: animal observations as a basis for a randomized, controlled pilot study in term infants. Pediatrics 2002;110(2 Pt 1):377–385.
13. 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(1):e1.
14. Saugstad OD. Resuscitation of newborn infants with room air or oxygen. Semin Natol 2001;6(3):233–239.
15. 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(4):642–647.

Discussion

Donn: I'd like to add one more to your list of ethical dilemmas. The whole concept of neonatal resuscitation is really an unproven experiment, if you think about it. I guess the issue is, can we ever really do a proper prospective, randomized, controlled trial? One: Do we have the equipoise to do that? Two: Would the ethicists believe that it's a doable experiment? And three: It dovetails into your comments about the need to get informed consent. I think it's really a black box, and I don't know what the answer is.

Wiswell: I agree with you, Steve. I think the best randomized, controlled trial would be to compare neonatal resuscitation (using whatever guidelines) to no resuscitation. But that's just not going to happen. Anecdotally, we can look at some of the regional stuff. In the state of Illinois a lot of hospitals are NRP qualified, and they have compared their outcomes to historical controls—not the best study design. The same thing's been done in India. We don't have that the optimal type of research, a randomized, controlled trial. So we *think* we're doing good things, but it may be something for which we'll never have the true answer.

Donn: Could you discuss the decision regarding 100% oxygen versus room air? There is some evidence that the outcomes are no different.

Wiswell: Most of the evidence we have comes from Ola Saugstad in Norway, who has done a masterful job of animal research and coordinating an early trial of using 100% oxygen versus room air in the delivery room. Clearly, 100% oxygen is going to generate oxygen radicals, and I think that's why people are concerned that 100% oxygen may cause some injury.

Ola Saugstad was the principal investigator of the Resair 2 trial,[1] which unfortunately was not a randomized, controlled trial. It was a trial in which approximately half the babies happened to get 100% oxygen and half the babies happened to get room air. The kids who were resuscitated on room air were quicker to cry, and there did not appear to be any kind of adverse effects by 28 days of age. There was not a lot of difference in mortality.

Other research that's helped includes some of the work by Max Vento, in Spain. Last year he published a randomized, controlled trial of room air versus 100% oxygen,[2] and he found elements of oxidative stress or injury (blood levels, as it were) 4 weeks after kids got 100% oxygen, which was intriguing. Max has also done a 6-year compilation of data from kids in his own unit in Spain who have gotten room air versus 100% oxygen.[3] The published data from that work makes it appear that morbidity and mortality may be a little bit better in the room air group. Again, however, it was not a randomized, controlled trial.

We're trying to get a good trial set up in term-gestation neonates. One upcoming trial with premature babies will compare 100% and 40% oxygen, because a lot of people were concerned about going to room air with premature babies. So I think room air resuscitation is an intriguing idea and the time has come to study it thoroughly.

REFERENCES

1. 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(1):e1.
2. 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(4):642–647.
3. Vento M, Asensi M, Sastre J, Garcia-Sala F, Vina J. Six years of experience with the use of room air for the resuscitation of asphyxiated newly born term infants. Biol Neonate 2001;79(3–4):261–267.

Davis: In regard to the ethical issues, how long should one resuscitate if there's asystole? And when do you *not* resuscitate? What do you tell your house staff, who are probably going to go out into rural communities and will have to do resuscitations?

Wiswell: I try to be wishy-washy. What I do is largely based on old but relevant data. A lot of it is a compilation of data from the Collaborative Perinatal Project that assessed outcomes of kids born in the early 1960s. From that project Karin Nelson[1] and others have demonstrated that if the Apgar score is ≤ 3 at 15 min or beyond, the vast majority of kids either die or have brain injury. Therefore, if a child has an Apgar score or either 0 or 1 (a point for a heart rate < 100), I personally do not resuscitate for longer

than 15–20 min. I have to be convinced, however, that I've done every resuscitative step and that I have done each one correctly and repetitively.

Unfortunately, I think one of the major problems in our pediatric training programs is that pediatric residents are in the nursery and in the delivery room far less frequently during training than they used to be. Their clinical skills in the delivery room are as not as good as those who trained before the mid-1990s. It worries me to advise these individuals about when to start and stop resuscitation when I don't know that as clinicians they are as good as those who trained in an earlier era. The current group of trainees may not have as good resuscitation skills as most nurse practitioners or respiratory therapists, who have far more experience in the delivery room.

REFERENCE

1. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic neurologic disability. Pediatrics 1981;68(1):36–44.

Salyer: A recent report in *Anesthesia & Analgesia* was on the use of pulse oximetry in the delivery room to assess the efficacy of resuscitation.[1] What made the paper possible was the Masimo signal extraction technology. Are you familiar with that report?

REFERENCE

1. Kopotic RJ, Lindner W. Assessing high-risk infants in the delivery room with pulse oximetry. Anesth Analg 2002;94 (1 Suppl): S31-S36.

Wiswell: I'm familiar with it. Previous studies tried to use some form of oxygen saturation monitoring with a pulse oximeter in the delivery room, but oximetry didn't seem to work very well. The readings showed wide variations, and concomitant blood gas values from blood samples suggested that the oximetry values were inaccurate. One of the best things about the Masimo system is that it seemed to do away with a lot of the movement artifact. But I'm not yet convinced it's that accurate in the delivery room.

I'll throw a question back at you: What's a normal oxygen saturation in a baby in the delivery room? The normal saturation while the baby is inside the womb is typically between 40% and 70%. Seventy percent at maximum! So what saturation should we shoot for in the delivery room? Should we perhaps take longer to allow the baby's oxygen saturation to rise up more slowly? Or should we be aggressive? Am I going to cause oxygen toxicity by being aggressive and shooting for that magic 95%, 97%, or 100% saturation? I don't know. I'm intrigued by the improvement in oximetry equipment, but I'm not sure it's good enough yet, and even if it is, I don't know what saturation numbers are best. Do you have a comment, Steve?

Donn: Yes. I think the best thing about the pulse oximeter is that it shows a pulse!

Wiswell: And that's not a bad thing!

Rodriguez: There seems to be a recommendation for albumin use. In the United Kingdom, that's very common. In the United States, albumin is pretty much forbidden. The adult data and all the meta-analyses from the Cochrane group of albumin reviewers showed that it may be associated with higher mortality and morbidity,[1] but that's been questioned. There's still controversy on the whole issue of colloids versus crystalloids for volume expansion in newborns. How did you come up with your recommendation?

REFERENCE

1. The Albumin Reviewers (Alderson P, Bunn F, Lefebvre C, Li Wan Po A, Li L, Roberts I, Schierhout G). Human albumin solution for resuscitation and volume expansion in critically ill patients (Cochrane Review). In: The Cochrane Library, Issue 4 2002. Oxford: Update Software. Available at http://www.update-software.com/abstracts/titlelist.htm. Accessed Nov 14, 2002.

Wiswell: I think that in the evaluation, they were looking at the adult and pediatric trials and the very few neonatal trials. One excellent study, done in Hong Kong,[1] concerning normal saline versus albumin, was done in the neonatal ICU after the fact, not in the delivery room. It didn't show a significant difference in the blood pressure that was maintained. People believe that albumin could help because its oncotic pressure would hold fluid intravascularly, but to my knowledge, most studies show that it leaks out into the tissue pretty easily without holding fluid any better.[2] So until we have better data and, hopefully, delivery room studies or even animal studies to assess this better, I'm reluctant to use albumin, because the studies I'm familiar with show that you get as good an effect with crystalloid solutions.[3]

REFERENCES

1. 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(1):F43-F46.
2. Osborn DA, Evans N. Early volume expansion for prevention of morbidity and mortality in very preterm infants (Cochrane Review). In: The Cochrane Library, Issue 4 2002. Oxford: Update Software. Available at http://www.update-software.com/abstracts/titlelist.htm. Accessed Nov 14, 2002.
3. The Albumin Reviewers (Alderson P, Bunn F, Lefebvre C, Li Wan Po A, Li L, Roberts I, Schierhout G). Human albumin solution for resuscitation and volume expansion in critically ill patients (Cochrane Review). In: The Cochrane Library, Issue 4 2002. Oxford: Update Software. Available at http://www.update-software.com/abstracts/titlelist.htm. Accessed Nov 14, 2002.