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Part 7: Neonatal resuscitation

International Liaison Committee on 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, have 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 stabilisation (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 three vital signs: respirations, heart rate, and colour. Progression occurs only after successful completion of the preceding step. Approximately 30 s is allotted to complete one step successfully, re-evaluate, and decide whether to progress to the next (Figure 7.1).

Since publication of the last International Liaison Committee on Resuscitation (ILCOR) document,[1] 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 (e.g. 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
W202A,W202B

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).[2—6] One study of preterm infants (<33 weeks of gestation) exposed to 80% oxygen found lower cerebral blood flow when compared with those stabilised with 21% oxygen (LOE 2).[7] Some animal data indicate the opposite effect, i.e. reduced blood pressure and cerebral perfusion with air versus 100% oxygen (LOE 6).[2]

Meta-analysis of four human studies showed a reduction in mortality and no evidence of harm in infants resuscitated with air compared with those

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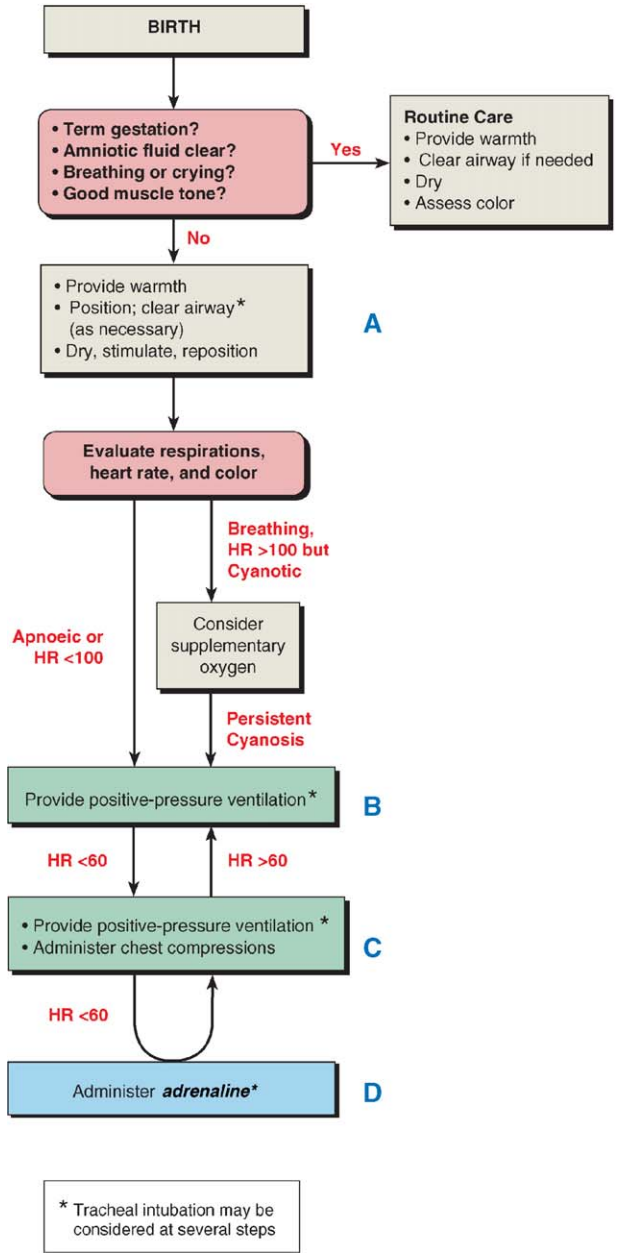

Figure 7.1 ILCOR neonatal flow algorithm.

resuscitated with 100% oxygen (LOE 1).[8,9] The two largest newborn human studies of room air versus oxygen resuscitation were not blinded. In those studies, if there was no response after 90 s, 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.[10,11] These results require careful interpretation because of significant methodological concerns (regarding patient selection, lack of blinding, randomisation 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.[10–13] Continuous oximetry studies show that term healthy newborns may take >10 min to achieve a preductal oxygen saturation >95% and nearly 1 h to achieve this postductally (LOE 5).[14–16]

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 oxyhaemoglobin saturation that normally occurs following birth. Excessive tissue oxygen may cause oxidant injury and should be avoided, especially in the premature infant.

Peripartum management of meconium

Management of meconium was examined from two 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
W206

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[17]; LOE 4[18,19]). A recent large multicenter randomised trial found that intrapartum suctioning of meconium does not reduce the incidence of meconium aspiration syndrome (LOE 1).[20]

Treatment recommendation. Routine intrapartum oropharyngeal and nasopharyngeal suctioning

for infants born with meconium-stained amniotic fluid is no longer recommended.

Tracheal suctioning
W206

Consensus on science. A randomised controlled trial showed that tracheal intubation and suctioning of meconium-stained but vigorous infants at birth offers no benefit (LOE 1).[17] The benefit of tracheal suctioning in meconium-stained, depressed infants has not been systematically studied (LOE 5).[21–23]

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 four 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
W203A,W203C

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

In term infants, initial inflations, either spontaneous or assisted, create a functional residual capacity (FRC) (LOE 5).[28–33] 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 (18–60 cm H_2O). Average initial peak inflating pressures of 30–40 cm H_2O were used to successfully ventilate unresponsive term infants (LOE 5).[31–35] In a single small series a sustained inflation pressure of 30 cm H_2O for 5 s for the first breath was effective in establishing lung volume in term infants requiring resuscitation (LOE 5)[31]; the risk and benefits of this practice have not been evaluated. Ventilation rates of 30–60 breaths min^{-1} 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 apnoeic 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 individualised with each breath. If pressure is being monitored, an initial inflation pressure of 20 cm H_2O may be effective, but a pressure $\geq$30–40 cm H_2O 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
W203B

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[36,37]; LOE 5[38]). The pop-off valves of self-inflating bags are flow-dependent, and pressures generated during resuscitation may exceed the target values (LOE 6).[39] 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),[40] 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).[41]

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-valve-mask ventilation to a newborn.

Laryngeal mask airway
W215A,W215B

Consensus on science. Masks that fit over the laryngeal inlet are effective for ventilating new-

born full-term infants (LOE 2[42]; LOE 5[43]). There are limited data on the use of these devices in small preterm infants (LOE 5).[44,45] There is currently no evidence directly comparing the laryngeal mask airway (LMA) with bag-valve-mask ventilation during neonatal resuscitation. Data from two case series show that use of the LMA can provide effective ventilation in a time frame consistent with current resuscitation guidelines (LOE 5).[43,46] A single randomised controlled trial found no significant difference between the LMA and tracheal intubation during resuscitation of babies by experienced providers after Caesarean section (LOE 2).[42] 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).[47,48]

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
W203A,W203C

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).[49] 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).[50,51] Case series in infants indicate that most apnoeic preterm infants can be ventilated with an initial inflation pressure of 20–25 cm H_2O, although some infants who do not respond require a higher pressure (LOE 5).[52,53]

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 20–25 cm H_2O 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
W204A,W204B

Consensus on science. Spontaneously breathing newborns establish functional residual capacity more quickly and with lower transpulmonary pressures than sick neonates (LOE 5).[32] In the sick neonate CPAP helps stabilise and improve lung function (LOE 4).[54] Excessive CPAP, however, can overdistend the lung, increase the work of breathing, and reduce cardiac output and regional blood flow (LOE 6).[55,56] There are no prospective, randomised, 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).[53] 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).[57]

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

Exhaled CO_2 detectors to confirm tracheal tube placement
W212A,W212B

Consensus on science. After tracheal intubation, adequate ventilation is associated with a prompt increase in heart rate (LOE 5).[35] Exhaled CO_2 detection is a reliable indicator of tracheal tube placement in infants (LOE 5).[58–61] A positive test (detection of exhaled CO_2) confirms tracheal placement of the tube, whereas a negative test strongly suggests oesophageal intubation (LOE 5).[58,60,61] 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).[62] In critically ill infants with poor cardiac output, a false-negative result may lead to unnecessary extubation.

Exhaled CO_2 detectors identify oesophageal intubations faster than clinical assessments (LOE 5).[58,61] Clinical techniques for confirmation of correct tracheal tube placement (e.g. 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_2 detection is useful to confirm tracheal tube placement. During cardiac arrest, if exhaled CO_2 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 adrenaline and fluids. Very rarely, a narcotic antagonist, sodium bicarbonate, [W200] or vasopressors may be useful after resuscitation.

Adrenaline

Route and dose of adrenaline
W213A,W213B,W217,W220

Consensus on science. Despite the widespread use of adrenaline/epinephrine 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 paediatric study (LOE 7)[63] and studies in newborn animals (LOE 6)[64,65] showed no benefit and a trend toward reduced survival rates and worse neurological status after administration of high-dose IV adrenaline ($100\,\mu g\,kg^{-1}$) during resuscitation. Animal and adult human studies show that when given tracheally, considerably higher doses of adrenaline than currently recommended are required to show a positive effect (LOE 6).[66–68]

One neonatal animal study using the currently recommended dose of tracheal adrenaline ($10\,\mu g\,kg^{-1}$) showed *no* benefit (LOE 6).[69] One neonatal cohort study of nine preterm babies requiring resuscitation showed that tracheal adrenaline was absorbed, but the study used 7–25 times the dose recommended currently (LOE 5).[70]

Treatment recommendation. Despite the lack of human data, it is reasonable to continue to use adrenaline when adequate ventilation and chest compressions have failed to increase the heart rate to >60 beats/min. Use the IV route for adrenaline as soon as venous access is established. The recommended IV dose is $0.01–0.03\,mg\,kg^{-1}$. If the tracheal route is used, give a higher dose (up to $0.1\,mg\,kg^{-1}$). The safety of these higher tracheal doses has not been studied. Do not give high doses of intravenous adrenaline.

Volume expansion

Crystalloids and colloids
W208

Consensus on science. Three randomised controlled trials in neonates showed that isotonic crystalloid is as effective as albumin for the treatment of hypotension (LOE 7).[71–73] 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
W214A,W214B

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, $PaCO_2$, or respiratory rate (LOE 7).[74] Compared with intramuscular naloxone, IV naloxone produces higher plasma concentrations but has a shorter half-life (LOE 5).[75] Tracheal or subcutaneous administration has not been examined in neonates, nor has the current recommended dose of $0.1\,mg\,kg^{-1}$ been studied.

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

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 colour 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^{-1}.

Supportive therapy

Temperature control

Maintenance of body temperature
W210A,W210B

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).[80] Two randomised controlled trials (LOE 2)[81,82] and three observational studies (LOE 4[83,84]; LOE 5[85]) 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[81,82]; LOE 4[83,84]; LOE 5[85]). 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).[82]

Other techniques have been used to maintain temperature in the delivery room during stabilisation (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).[86,87]

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
W201

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).[88,89] During the first 24 h after adult stroke, fever is associated with a marked increase in neurological morbidity and mortality (LOE 7).[90,91] Adult animal studies indicate that hyperthermia during or after ischaemia is associated with a progression of cerebral injury (LOE 6).[92,93]

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

Therapeutic hypothermia
W211A,W211B

Consensus on science. A reduction of body temperature by 2—3 °C (modest hypothermia) following cerebral hypoxia-ischaemia reduces cerebral metabolic and biochemical abnormalities and cerebral injury and improves function in experimental neonatal models (LOE 6).[94—96] In adults, induced hypothermia (temperature of 32—34 °C) for 12—24 h improves neurological outcome after cardiac arrest due to ventricular arrhythmias but not after trauma or stroke (LOE 7).[97] In a multicentre 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—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).[98]

Infants with severe electroencephalographic (EEG) suppression and seizures did not benefit from treatment with modest hypothermia (LOE 2).[98] 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).[99]

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).[100] 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).[98,99,101,102]

Treatment recommendation. There are 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
W218A,W218B,W219A,W219B

Consensus on science. Low blood glucose is associated with adverse neurological outcomes in a neonatal animal model of asphyxia and resuscitation (LOE 6).[103] Hypoglycaemia in animals at the time of an anoxic or hypoxic-ischaemic insult resulted in larger areas of cerebral infarction and/or decreased survival rates when compared with controls (LOE 6).[104,105] One clinical study showed an association between hypoglycaemia (blood glucose <40 mg dl^{-1}) measured shortly after resuscitation and poor neurological outcome following perinatal asphyxia (LOE 4).[106]

Hyperglycaemia induced in neonatal animal models of hypoxia-ischaemia had conflicting effects on the extent of brain injury (LOE 6).[107,108] No clinical neonatal studies have investigated this topic.

Treatment recommendation. Based on available evidence, the optimal range of blood glucose concentration to minimise brain injury following asphyxia and resuscitation cannot be defined. Infants requiring resuscitation should be monitored and treated to maintain glucose in the normal range.

Timing of cord clamping
W216A,W216B

Consensus on science. Although delayed cord clamping (30—120 s after birth) in premature infants was associated with higher mean blood pressure and haematocrit and less intraventricular haemorrhage, most study subjects did not require resuscitation (LOE 1[109] and LOE 2[110]). Delayed cord clamping in term infants not requiring resuscitation resulted in no clinically significant improvement in stability over the first 4—6 h after birth (LOE 3).[111,112]

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

Withholding or discontinuing resuscitative efforts
W209A,W209B

Consensus on science. Mortality and morbidity for newborns varies according to region and availability of resources (LOE 5).[113] Social science studies indicate that parents would like a greater 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).[114,115]

Some data are available to help identify conditions associated with high mortality and poor outcome (LOE 5).[80,116] In some settings with adequate resources, 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 min or longer from birth despite continuous and adequate resuscitation efforts document either high mortality or severe neurodevelopmental disability (LOE 5).[117,118]

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 rel-

atively 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 min of continuous and adequate resuscitative efforts, it may be justifiable to stop resuscitation.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.resuscitation.2005.09.014.

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