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SEMINARS IN PERINATOLOGY

Reducing Intrapartum-Related Neonatal Deaths in Low- and Middle-Income Countries—What Works?

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Each year, 814,000 neonatal deaths and 1.02 million stillbirths result from intrapartum-related causes, such as intrauterine hypoxia. Almost all of these deaths are in low- and middle-income countries, where women frequently lack access to quality perinatal care and may delay care-seeking. Approximately 60 million annual births occur outside of health facilities, and most of these childbirths are without a skilled birth attendant. Conditions that increase the risk of intrauterine hypoxia—such as pre-eclampsia/eclampsia, obstructed labor, and low birth weight—are often more prevalent in low resource settings. Intrapartum-related neonatal deaths can be averted by a range of interventions that prevent intrapartum complications (eg, prevention and management of pre-eclampsia), detect and manage intrapartum problems (eg, monitoring progress of labor with access to emergency obstetrical care), and identify and assist the nonbreathing newborn (eg, stimulation and bag-mask ventilation). Simple, affordable, and effective approaches are available for low-resource settings, including community-based strategies to increase skilled birth attendance, partograph use by frontline health workers linked to emergency obstetrical care services, task shifting to increase access to Cesarean delivery, and simplified neonatal resuscitation training (Helping Babies Breathe[SM]). Coverage of effective interventions is low, however, and many opportunities are missed to provide quality care within existing health systems. In sub-Saharan Africa, recent health services assessments found only 15% of hospitals equipped to provide basic neonatal resuscitation. In the short term, intrapartum-related neonatal deaths can be substantially reduced by improving the quality of services for all childbirths that occur in health facilities, identifying and addressing the missed opportunities to provide effective interventions to those who seek facility-based care. For example, providing neonatal resuscitation for 90% of deliveries currently taking place in health facilities would save more than 93,000 newborn lives each year. Longer-term strategies must address the gaps in coverage of institutional delivery, skilled birth attendance, and quality by strengthening health systems, increasing demand for care, and improving community-based services. Both short- and long-term strategies to reduce intrapartum-related mortality should focus on reducing inequities in coverage and quality of obstetrical and perinatal care.

Semin Perinatol 34:395-407

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0146-0005/10/$-see front matter
doi:10.1053/j.semperi.2010.09.009

KEYWORDS neonatal mortality, intrapartum, birth asphyxia, developing countries, stillbirths, emergency obstetrical care, neonatal resuscitation

Birth poses significant risks to the fetus and newborn, largely as the result of intrapartum hypoxia (ie, "birth asphyxia"), and is also the period of greatest risk of maternal mortality and morbidity. Every year, childbirth complications result in an estimated 814,000 neonatal deaths,[1] 1.02 million stillbirths,[2] in addition to a substantial fraction of the global maternal deaths (342,900 to 358,000 estimated in 2008[3,4]) and near-miss maternal events.[5,6] Child deaths resulting from labor and delivery outnumber those caused by malaria and HIV; however, there is considerably less attention and funding for these intrapartum-related deaths.[7]

The burden of intrapartum-related deaths occur almost entirely in low- and middle-income countries, yet coverage of skilled birth attendance, considered a marker of health system access and capacity, is lowest in countries with the greatest neonatal mortality rates, maternal mortality ratios, and stillbirth rates.[7,8,9] To achieve Millennium Development Goals 4 and 5, there is an urgent need to reduce intrapartum-related deaths by increasing coverage of skilled birth attendance, particularly for the 60 million home births each year, and to improve the quality of obstetrical and perinatal care, especially in first level and first-referral facilities (eg, district hospitals).[7] In this work, we summarize key findings from a recent comprehensive review of the evidence for strategies to reduce intrapartum-related deaths published in the *International Journal of Obstetrics and Gynecology*,[7,10-15] and prioritize points for action and future research.

Definitions and Terminology

The word "asphyxia" is derived from the Greek word (*asphuxia*) meaning "stopping of the pulse" and is defined as the clinical syndrome of hypoxia and metabolic acidosis resulting from hypoventilation.[16] However, the use of the term "birth asphyxia" (or "perinatal hypoxia") is imprecise, and the terminology used to describe the process of intrapartum-related hypoxia has shifted during past decades.[2] In 1997, the World Health Organization (WHO) broadly defined "birth asphyxia" as the condition in which a newborn "fails to initiate or maintain regular breathing at birth."[17] However, postnatal clinical condition, and other symptom-based clinical markers used to define "birth asphyxia" (such as Apgar scores or fetal distress), lack specificity, have low positive predictive value for long-term outcomes, and are no longer recommended.[18-20] Three consensus statements released by the American Academy of Pediatrics, American College of Obstetrics and Gynecology, and International Cerebral Palsy Task Force recommend against the use of the term "birth asphyxia" unless there is clear evidence of intrapartum-related causation.[21-23] In this work we will use the more precise terms intrapartum-related neonatal death, intrapartum stillbirth, neonatal encephalopathy, and "non-breathing baby" as defined in Table 1.

Table 1 Terms and Definitions—Shifting from "Birth Asphyxia" to Intrapartum Stillbirths and Intrapartum-Related Neonatal Deaths

Mortality outcomes

- **Intrapartum-related stillbirth: A stillborn baby (shows no signs of life at delivery and weighs more than 500 g or is >22-weeks gestation) with intact skin and no signs of disintegration in utero. The death is assumed to have occurred in the 12 h before delivery and was most likely because of an intrapartum hypoxic event. Infants with severe congenital abnormalities are not included (based on Wigglesworth's classification).[2]**
- **Intrapartum-related neonatal deaths (previously called "birth asphyxia" deaths): neonatal deaths of term infants with neonatal encephalopathy (see below) or who cannot be resuscitated (or for whom resuscitation is not available). Where possible, other causes should be excluded, such as lethal congenital malformations and preterm birth complications (less than 34 completed weeks' gestation or birth weight <2000 g).**

Also includes a smaller group of infants who die from birth injury without hypoxic brain injury—for example, organ rupture.[2,99,100]

Morbidity outcomes

- **Neonatal encephalopathy (NE): "A disturbance of neurological function in the earliest days of life in the term infant manifested by difficulty initiating and maintaining respiration, depression of tone and reflexes, abnormal level of consciousness, and often by seizures,[101,102] which may follow an intrapartum hypoxic insult or be the result of another cause. Neonatal encephalopathy is usually separated into 3 grades (mild, moderate, severe) by clinical findings during the first week of life. Virtually all infants with mild NE who are normal at the end of the first week of life will be free of long-term neurological damage. The majority of infants with severe NE will die or manifest severe neurological impairment**
- **Hypoxic ischemic encephalopthy: A syndrome of abnormal neurological behavior in the neonate, which is frequently associated with multisystem dysfunction and follows severe injury before or during delivery. There are several systems for categorizing hypoxic ischemic encephalopthy (most commonly into mild, moderate, severe). Most authorities now prefer the term neonatal encephalopathy and then specifying if the encephalopathy is associated with intrapartum injury.**

Need for resuscitation

- **"Nonbreathing Baby": infant with perinatal respiratory depression after birth that may be due to any of a multitude of causes, including but not restricted to intrapartum hypoxia, respiratory distress syndrome-preterm birth, infection, general anesthesia during labor, meconium, intracranial disease, and neuromuscular disease. Some clinicians use the term depressed baby or "perinatal depression."**

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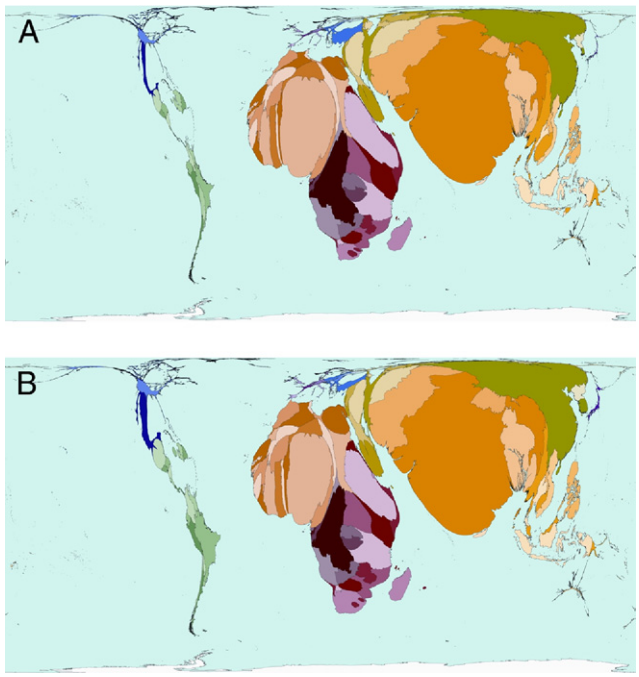

Figure 1 The Global Burden of Intrapartum-related Neonatal Deaths (A), and Stillbirths (B). (Reprinted with permission granted by FIGO from Lawn et al.[7] © Copyright SASI Group [University of Sheffield] and Mark Newman [University of Michigan].) (Color version of figure is available online.)

Epidemiology

There were 814,000 (95% confidence interval (CI): 0.563-0.997 million) intrapartum-related neonatal deaths in 2008, the most recent year with global estimates available, accounting for 23% of the world's 3.6 annual neonatal deaths.[1] Stillbirths occurring during labor ("fresh" stillbirths) were last estimated at1.02 million (95% CI: 0.66-1.48) annually in the year 2000,[24] accounting for 32% of the 3.2 million stillbirths in that year. Furthermore, the burden of impairment resulting from intrapartum events is substantial. The WHO World Health Report 2005 estimated that as many as 1 million survivors of "birth asphyxia" may develop cerebral palsy, learning difficulties, or other disabilities each year,[24] whereas the Global Burden of Disease assessment for the year 2004 estimated 41,683,855 disability-adjusted life years due to "birth asphyxia."[25]

Almost all (99%) intrapartum-related deaths occur in low-middle income countries, where 60 million births occur each year outside of health facilities and up to one-half without a skilled birth attendant. The maps shown in Figure 1A, B strikingly depict the global burden of intrapartum-related neonatal deaths and stillbirths, which are most highly concentrated in South Asia and sub-Saharan Africa.[16] Inequities between low- and high-income settings are substantial, both between and within countries, and the gaps are widening. For example, rates of intrapartum-related neonatal mortality and stillbirth are more than 20-fold greater in the poorest versus richest countries (eg, the intrapartum stillbirth rate is 14/1000 births in Cote d'Ivorie vs 0.4/1000 in Canada).[15] The regions with the greatest burden of intrapartum-related mortality are also those suffering from the lowest access to skilled birth care—with this inverse care law graphically depicted by the shortage of skilled births attendants shown in the first paper in the series on epidemiology in this Seminars supplement.[2,7]

Pathophysiology

Etiology

The fetus may experience hypoxia during the antepartum, intrapartum, or postpartum periods. Some obstetrical conditions leading to hypoxia are chronic and predate labor with their influence on the pregnancy often suggested by fetal growth restriction. Pre-eclampsia is a prime example of this type of condition. Obstetrical conditions that lead to intrapartum hypoxia include those that (1) primarily impact blood flow through the placenta, such as pre-eclampsia/eclampsia; (2) separate the placenta from the maternal circulation, such as a placental abruption; (3) compress the umbilical cord, impeding blood flow; (4) are associated with prolonged labor because contractions themselves decrease fetal oxygenation; and (5) lead to fetal entrapment during delivery, such as a breech presentation or shoulder dystocia. Postpartum hypoxia results from the failure of the newborn to initiate ventilation after birth.

Fetal/Newborn Response to Hypoxia

The healthy fetus exists in a state of physiological hypoxia relative to the newborn, which permits unimpeded oxidative metabolism and regulates fetal circulation; however, tolerance to further reduction of fetal P_{O_2} is limited.[26] In the experimental animal, the response to acute fetal hypoxia includes 3 phases.[27] First, a redistribution of blood flow directs a greater fraction of cardiac output to the heart and central nervous system without creating metabolic acidosis.[28] More profound hypoxia results in metabolic acidosis as the oxygen supply becomes inadequate to the skeletal muscles and some viscera with increasing diversion of cardiac output to the heart and brain. The final stage of fetal hypoxia corresponds to an inadequate oxygen supply to all organs, including the heart and brain.

The fetus and the newly born infant both respond initially to acute hypoxia with shallow breathing followed by cessation of respirations, termed primary apnea. After the period of primary apnea, gasping—deep, irregular respirations—develops, then respirations gradually become weaker until the onset of secondary or terminal apnea when all respiratory effort ceases. Heart rate decreases from baseline during primary apnea, decreases even lower during gasping, and eventually ceases after several minutes of secondary apnea. Blood pressure initially increases during primary apnea and gasping, but then rapidly decreases during secondary apnea.

Primary and secondary apnea are indistinguishable at the moment of birth—both present as a newly born infant who is not breathing and whose heart rate is slow. Appropriate tactile stimulation during primary apnea can restore spontaneous respirations. Secondary apnea requires assisted ventilation to restore

Table 2 Antepartum, intrapartum, and Infant Risk Factors for "Birth Asphyxia"

Antepartum risk factors
Primiparity[103,104]
Febrile illness (presumed malaria)[105]
Pregnancy induced hypertension,[103-106]
Severe pre-eclampsia/eclampsia[105]
Antepartum hemorrhage[103,105]
Anemia[105]
Intrapartum risk factors
Malpresentation[29,105,106]
Prolonged labor[106,107]
Maternal fever[105]
Meconium-stained amniotic fluid[29,103,105]
Premature rupture of membranes[105]
Oxytocin augmentation of labor[105]
Umbilical cord prolapsed[29,106]
Infant/postnatal factors
Prematurity[108]
Low birth weight[100,105]
Intrauterine growth restriction[106,109]

spontaneous breathing. A low heart rate almost always returns to normal with the timely provision of appropriate tactile stimulation and assisted ventilation. Any delay in initiating resuscitation becomes magnified in slower recovery. For every minute of delay in initiating assisted ventilation, approximately a 2-minute delay occurs in the time to first gasp and a 4-minute delay in time to regular spontaneous breathing.[29]

Risk Factors for "Asphyxia"

Certain obstetrical conditions detected in the antepartum and intrapartum periods are associated with chronic or acute fetal hypoxia, resulting in perinatal respiratory depression. Furthermore, certain conditions of the infant are also related to failure to initiate or maintain regular breathing at birth (Table 2). Circumstances common in developing countries increase the prevalence and severity of intrapartum-related hypoxic events—such as delays in problem-recognition/care seeking, inadequate antenatal and intrapartum care, and poor access to health facilities. Prevention and treatment require an integrated approach that focuses on obstetrical and neonatal interventions, but extends throughout the life cycle with strategies, such as optimizing growth and nutrition of young girls and women.[15]

Unique features of epidemiology (eg, an elevated incidence of pre-eclampsia) or pathophysiology (eg, high-altitude hypoxia compounding maternal anemia or hemorrhage) may have importance in a geographic region or population group.[30,31] Economic and social factors (eg, poverty, large family size, illegitimate birth, cultural beliefs) underlie access to care and care-seeking behaviors. Finally, infanticide by deliberate asphyxiation at birth (via active smothering, withholding of resuscitation, or lack of care seeking for intrapartum-related injury) is not uncommon in some countries and cultures, especially for female infants in South Asia, but is notably under-reported.[31-33]

Interventions to Reduce Intrapartum-Related Neonatal Deaths

Linking Mothers-Newborns to Skilled Birth Care

In an obstetrical emergency, every moment of delay in seeking and receiving emergency obstetrical and neonatal care may result in worsening hypoxic injury to the newborn. Delays in accessing care for women with obstetrical emergencies, have been described as the "three delays"[7,34]: (1) delays in the decision to seek care (recognition of problems in pregnancy/labor, cultural beliefs, family decision-making), (2) delays to reach a health facility (distance, transportation, road infrastructure), and (3) delays in receiving quality care (inadequate staffing, training, equipment, clinical algorithms). Strategies to link the 60 million women who give birth at home to skilled obstetrical-newborn care may involve: increasing community demand for skilled birth care, bringing pregnant women closer to the formal health system, or bringing skilled care to the community.[12,13] Examples of these interventions include community mobilization, financial strategies (ie, conditional cash transfers, voucher schemes, loan funds, elimination of user fees), community referral and transport schemes, maternity waiting homes, and task shifting. These strategies are addressed in a recent review on intrapartum-related deaths in the *International Journal of Obstetrics and Gynecology*.[12]

Obstetrical Interventions

A comprehensive review of the evidence for specific obstetrical interventions to reduce intrapartum-related hypoxic injury in the context of low resource settings was recently published in the *International Journal of Obstetrics and Gynecology*.[10] Here we review the aforementioned obstetrical interventions related to the pathophysiology of fetal and neonatal hypoxia and identify those interventions that are likely effective and feasible for implementation in low-resource countries.

In the antepartum period, fetal hypoxia from reduced placental blood flow, such as pre-eclampsia, can be detected by several methods (such as fetal movement counting, contraction stress or non-stressed fetal heart rate monitoring, ultrasound biophysical profile, and umbilical artery Doppler blood flow), reducing intrapartum hypoxic injury, and death if linked to timely Cesarean section.[35,36] However, the evidence supporting antenatal detection methods in the reduction of intrapartum-related mortality is limited.[10]

Many obstetrical conditions associated with intrapartum hypoxia are not easily predicted during antenatal care, including placental abruption, fetal distress, umbilical cord complications, and malposition.[35,37] These conditions are usually detected during the intrapartum period by clinical signs, such as maternal bleeding and abdominal pain, abnormal fetal heart rate patterns, and obstructed-prolonged labor. Prompt detection of fetal compromise, and rapid delivery, usually by Cesarean section, may be life saving for the new-

born and the mother.[38,39] Carefully monitoring the fetal heart rate pattern can provide information about fetal condition during labor. Although continuous electronic fetal heart rate monitors are in general use in developed countries today, much of the historical reduction in fetal deaths occurred with intermittent auscultation with fetoscopes. There is little evidence that complex, continuous fetal monitoring improves intrapartum-related outcomes.[40-43] In low-resource settings, a well trained nurse using a fetoscope, or innovative tools, such as a hand-held Doptone device, may be effective, yet simple and affordable, although this requires further research.[44]

Monitoring the progress of labor is essential to identify obstructed labor, and the need for instrumental delivery and/or Cesarean section.[40] The partograph was designed to monitor the progress of labor and alert the attendant about prolonged labors in settings where intrapartum surveillance is limited.[36,45-47] A Cochrane review found partograph use associated with a nonsignificant reduction in risk of Cesarean delivery, but this included higher income as well as low income settings.[48] A large WHO prospective study found that partograph use in South-East Asia was associated with a reduction in prolonged labor, need for augmentation, emergency Cesarean, and stillbirth.[49]

For many, or even most, of these conditions, preventing intrapartum fetal hypoxic injury requires the ability to perform a timely Cesarean delivery.[7,38,50] For example, planned Cesarean delivery for breech presentation is associated with significant reductions in perinatal or neonatal mortality or serious morbidity (relative risk [RR]: 0.33%, 95% confidence interval [CI]: 0.10-0.5).[40] However, access to Cesarean delivery in low-income settings is often limited by lack of qualified physicians, and there is growing evidence from Mozambique and Malawi that nonphysician providers can be trained to safely perform Cesarean deliveries.[51,52] This task shifting may be a feasible and effective strategy to provide access to emergency obstetrical care in low resource settings.

Finally, improving quality of emergency obstetrical care is an essential element of improving intrapartum-related birth outcomes in developing countries. Training courses in emergency obstetrical care in the UK have been shown to reduce the incidence of neonatal encephalopathy (RR: 0.51%, 95% CI: 0.35-0.74) and low 5-minute Apgar scores (RR: 0.50%, 95% CI: 0.26-0.9).[53] The impact may be arguably higher in low-middle income settings with lower baseline standards of care. The use of obstetrical drills, checklists and perinatal audits are promising methods to improve obstetrical care quality.[10,14]

The major reductions in fetal and neonatal mortality in developed countries occurred before 1980 before the routine use of ultrasound, Doppler, magnesium sulfate, and the very high Cesarean delivery rates. Reducing cases of intrapartum stillbirth and neonatal deaths requires a functioning system of obstetrical and neonatal care in which the mother and fetus are regularly monitored for signs and conditions associated with fetal compromise, both prenatally and in labor, and provided access to basic and comprehensive emergency obstetrical and neonatal care.[36,38]

Neonatal Resuscitation

Perinatal respiratory depression, while due to multiple etiologies as well as intrapartum hypoxia (eg, preterm birth), is a useful clinical indicator of the global need for neonatal resuscitation. Approximately 5% to 10% of all infants born in facilities require some degree of resuscitation, such as tactile stimulation or airway clearing (Fig. 2).[54-56] This proportion is likely greater in community-based, low-resource settings, where mothers may not have access to obstetrical care.[56] Thus, each year an estimated 10 million infants require some level of assistance to initiate breathing. Approximately

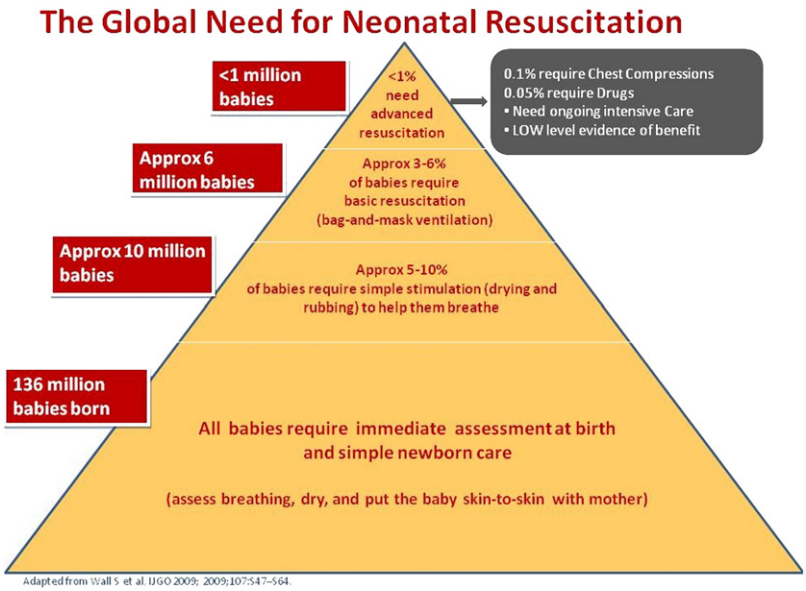

Figure 2 The Global Need for Neonatal Resuscitation. (Reprinted with permission granted by FIGO from Wall et al.[11]) (Color version of figure is available online.)

3%-6% of all newborns (~6 million babies/year) require basic neonatal resuscitation consisting of stimulation at birth plus assisted ventilation.[17,57] Very few (~0.1% of all babies born) require advanced resuscitation, such as endotracheal intubation and medications.[57] Hence, most lives that could be saved would be saved through basic resuscitation, and reaching high coverage of basic resuscitation should be the priority.

Content in Resource-Limited Settings

The evidence for individual components of neonatal resuscitation is reviewed by the International Liaison Committee on Resuscitation[58] and, further, in the context of low-income settings, by Newton and English.[59] Basic neonatal resuscitation is feasible and effective in resource-limited settings as well as middle- and high-income settings.[11,59,60] Stimulation and ventilation are the most important steps of resuscitation to reduce intrapartum-related deaths, whereas technically advanced procedures, such as chest compressions and intubation add relatively little mortality benefit. Current evidence indicates that resuscitation with air may be as effective as resuscitation with oxygen, and may even increase the chance for survival.[61] Suctioning of the airway has been recommended and practiced for years, but recent data from randomized trials indicate that oronasopharyngeal suction does not improve physiological measures of airway patency.[62] Oronasopharyngeal suctioning at birth also did not reduce the risk for respiratory disorders in a large randomized controlled trial.[63] Furthermore, meconium-stained vigorous infants do not benefit from endotracheal suctioning, although suctioning is still recommended for meconium stained infants with severe respiratory depression, before initiating assisted ventilation.[64]

Simple and affordable resuscitation devices are increasingly available in low resource settings. The standard resuscitation equipment in facility settings—a self-inflating bag and mask—has also been found to be feasible and effective when used by lower-skilled health workers in community settings.[56,65,66] Where bag and mask devices were not affordable, lower-cost tube and mask devices have been used, although development of operator fatigue is a concern with their use.[67] Use of these devices is not recommended by WHO, and they probably have no role as affordable bag and masks are now widely available.

The Helping Babies Breathe[SM] (HBB) program of the American Academy of Pediatrics is an example of a resuscitation training program aimed for global implementation in the resource limited setting. The Action Plan (Fig. 3) is a simple step-by-step algorithm that focuses on establishing breathing, either spontaneously or with bag-and-mask ventilation if needed, within the first Golden Minute[SM] after birth. Advanced procedures, such as chest compressions and medications are not included, while other aspects of essential newborn care are emphasized (hand-washing, thermoregulation, breastfeeding, care of the preterm or small baby, and recognition of danger signs).[68] The program has recently been piloted in 5 countries in sub-Saharan Africa and South Asia. Implementation and scale-up in United Republic of Tanzania is highlighted in Panel 1.

Effectiveness of Facility-Based Neonatal Resuscitation

Sixteen observational reports from primarily low- and middle-income countries have reported the effect of facility-based neonatal resuscitation training on perinatal-early neonatal mortality before versus after training (China, Bulgaria, Zambia, India, Macedonia, Uganda, Turkey, United Kingdome, Pakistan, Malaysia, Kenya, Ukraine).[67,69-83] These studies included settings with all deliveries attended by physicians as well as settings where all deliveries were attended by midwives and combinations of different types of birth attendants. Several of the reports included neonatal resuscitation training within a comprehensive package of perinatal care training and/or improvements of facility equipment for resuscitation. A systematic review and meta-analysis determined that neonatal resuscitation training at the facility level in middle- and low-income country settings may avert approximately 30% of intrapartum-related neonatal deaths.[11] On the basis of the limitations of the available data, this estimate should be used with caution. Furthermore, implementation research is needed to identify more effective and efficient training and implementation approaches, including new training equipment, supervision and refresher training, and audit feedback loops for quality improvement.

Effectiveness of Community-Based Neonatal Resuscitation

The effect of neonatal resuscitation has also been assessed in several community settings (India, Indonesia, Argentina, Democratic Republic of The Congo, Pakistan, Zambia), where births may be attended by skilled birth attendants (eg, physicians, midwives, nurses) as well as by traditional birth attendants and community health workers. Most of these studies have been performed as before-and-after comparisons or quasi-experimental studies.[65,66,84,85] These studies largely provided packages of interventions (essential newborn care [ENC] with or without community-based infection management) rather than resuscitation alone, but all had emphasis on resuscitation practice. Reduction in neonatal or perinatal mortality rates were in the range of 15%-40% and reduction in intrapartum-related neonatal mortality rate ranged from 42% to 70%.[11] Because these interventions were under study conditions, the effect sizes are probably larger than would be seen with routine program implementation. A recent multicentered trial, the First Breath study, found that the WHO ENC course, including basic neonatal resuscitation with bag-mask, reduced stillbirths and perinatal mortality in deliveries performed by birth attendants, including traditional birth attendants. The reduction in stillbirth was likely attributable to the improved recognition and intervention for severely depressed infants who would have otherwise been considered "stillborn."

While some of the reduction in "stillbirth" may have been the result of misclassification, there was no increase in early neonatal mortality. Although overall reduction in perinatal mortality did not reach statistical significance, births that

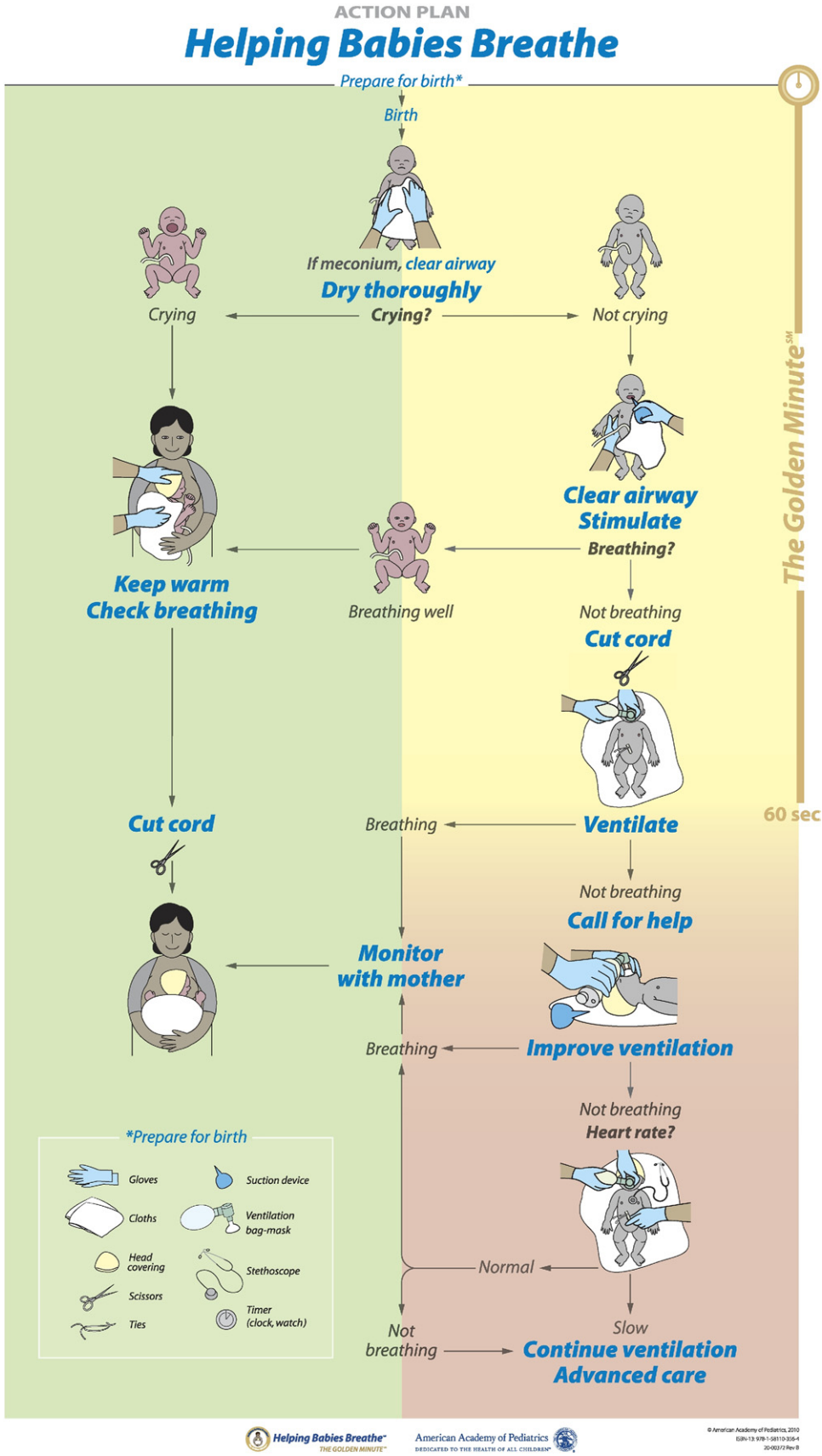

Figure 3 Action Plan for HBB for lower levels of the health system. (Reprinted with permission granted by the American Academy of Pediatrics.[68]) (Color version of figure is available online.)

Panel 1 Helping Babies Breathe in United Republic of Tanzania

United Republic of Tanzania has a population of approximately 42 million with 1.4 million annual deliveries, of which approximately 50% are born in facilities. The neonatal mortality rate approximates 35/1000 live births with 25% to 30% attributed to birth asphyxia. The incidence of intrapartum-related mortality has remained unchanged during the past 15 years despite efforts to intervene and meet Millennium Development Goal 4.[1,2] This finding in part reflects several factors, including: (1) the proportion of skilled providers present at delivery remains <50%, (2) a global lack of essential basic resuscitation equipment, (3) a failure to initiate resuscitation in a timely manner—interventions in a nonbreathing infant are often delayed beyond 5 minutes, and (4) the inability to administer effective basic resuscitation. In the 2006 Tanzanian national service provision assessment, only 12% of hospital providers had been trained in neonatal resuscitation in the prior 35 months, and only 78% of hospitals and 36% of health centers had delivery rooms equipped with Ambu-bags.

The Tanzanian Health Ministry has embraced the HBB program to reduce intrapartum-related mortality for several reasons. The teaching curriculum is clear and simple (Fig. 3), and the neonatal simulator is a novel low cost manikin with inflatable lungs designed for low-resource settings. The HBB curriculum stresses clinical assessment and intervention within the first minute following delivery in a nonbreathing infant (ie, the "Golden minute") by the use of simple basic steps, including drying, suctioning, stimulating and if necessary bag mask ventilation. The program is basic and easy to teach at the peripheral health facility level, particularly to less skilled health providers. Moreover, the government has committed to providing essential basic resuscitation equipment for scaling up throughout the country.

The United Republic of Tanzania is implementing the HBB program using a cascade method of dissemination to interdigitate with existing programs and systems. Structures that lend United Republic of Tanzania to being a successful HBB training site include a strong commitment by the Ministry of Health to train all birth attendants in the current health workforce; a stable decentralized health system with 3 functional levels: district, regional, and referral hospitals; the fact that 90% of the population lives within 10 km of a primary health facility; committed skilled birth attendants; the availability of collaborating institutions for conducting teaching and research and integration of HBB training within the health system; and starting from district level for sustainability

HBB implementation thus far has been achieved as follows: training of master trainers was initiated in late 2009, with the goal of training 1332 instructors and over 10,000 providers within the following 18 months. The training of providers will follow the 3 functional levels of the decentralized health system using a cascade model of dissemination throughout the country. Because midwives attend most deliveries, great emphasis will be placed on their training. Each facility with trained personnel will report all births and their outcome using the existing reporting format. A standardized reporting HBB form has been developed. There are 4 active research sites (Hospitals) with a corresponding collaborating institution where data are being collected in a standardized manner, entered into a database and sent to a central repository. The primary goal of the program at full-scale implementation is to reduce intrapartum-related neonatal mortality by 50% in 2015.

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were attended by an ENC trained attendant were associated with a significant, 19% lower perinatal mortality rate. Reductions in the proportions of births with a 5-minute Apgar score <4, and with an abnormal neurologic examination at 7 days were observed.[66] A subsequent cluster randomized controlled trial further evaluated the impact of additional training in neonatal resuscitation using a model adapted from the Neonatal Resuscitation Program (NRP) of the American Academy of Pediatrics. The study investigators found that this additional resuscitation training in NRP did not further reduce mortality beyond the positive effects observed for the WHO ENC care course that already included basic resuscitation. The randomized controlled trial intervention was limited to NRP training, an intervention that may singularly lack additional impact where an ENC package, including newborn resuscitation is already in place, or alternately, where an effective health delivery system is lacking.

Cost

Recent data on cost-effectiveness in facility births show that neonatal resuscitation training can be a very cost-effective intervention, with a cost of approximately US$208 per life saved and approximately US$5.24 per disability adjusted life year.[86] This cost indicates that neonatal resuscitation is among the most cost-effective perinatal care strategies available, and among the most cost-effective of all child health interventions.

Postresuscitation Care

Postresuscitation newborn care appropriate for low-resource settings has recently been summarized in the *International Journal of Gynecology and Obstetrics*.[11] Postresuscitation care may improve survival and long-term outcomes for newborns who have experienced intrapartum hypoxia and show signs of neonatal encephalopathy. Referral to a hospital neonatal unit for 12-24 hours of monitoring and essential and supportive newborn care is the first step in postresuscitation care. Referral-level hospitals should be prepared to support breathing, maintain adequate oxygenation, provide an appropriate thermal environment (ie, avoid hyperthermia), and ensure glucose and fluid balance.[11]

Panel 2 Key Messages

Complications of childbirth result in an estimated 814,000 neonatal deaths, 1.02 million stillbirths each year, and 1 million surviving infants with lifelong neurodevelopmental impairments.

Effective obstetrical interventions to reduce intrapartum-related mortality include intermittent fetal heart rate monitoring, monitoring the progress of labor with the partograph, and emergency obstetrical care. Task shifting to alternate cadres may increase coverage of emergency obstetrical care, while obstetrical drills and routine audit may improve quality of care.

Neonatal resuscitation is feasible and cost-effective in low resource settings; most babies can be resuscitated with basic resuscitation—stimulation, suction, and bag mask ventilation; advanced procedures are rarely needed, and are not promoted in recent resuscitation programs designed for low- and middle-income countries, such as Helping Babies Breath.

By addressing missed opportunities and providing full coverage of comprehensive emergency obstetrical care and neonatal resuscitation to births that already occur in facilities, an estimated 326,200 newborn lives could be saved each year.

By achieving full coverage of comprehensive emergency obstetrical care and neonatal resuscitation for all births, an estimated 686,200 newborn lives could be saved each year.

Newborns who have experienced hypoxia may have frequent apneic episodes and require mechanical ventilation or continuous positive airway pressure, if this is available. Postresuscitation hyperoxia is known to be harmful to the brain in animal models of hypoxia.[87,88] Because hypoglycemia can exacerbate brain injury after hypoxia, glucose should be monitored and maintained within normal parameters, avoiding hyperglycemia which is also potentially harmful.[89-91] Fluid and electrolyte balance should be closely monitored. Although there is no clear evidence that fluid restriction reduces adverse outcomes in infants who experience hypoxia, fluid overload should be avoided.[92] Anticonvulsants are commonly needed to treat seizures, which occur in approximately 50% of newborns with neonatal encephalopathy resulting from intrapartum hypoxia, but there is insufficient evidence to recommend the routine administration of anticonvulsants in nonseizing, encephalopathic infants.[11]

Thermal management should aim to protect from heat loss and cold stress, but hyperthermia should be avoided based on evidence that it increases central nervous system injury and apnea in the newborn exposed to intrapartum hypoxia.[93,94] Therapeutic hypothermia is a promising new intervention that seems to improve long-term outcomes in newborns with neonatal encephalopathy following hypoxia. There is emerging evidence that this intervention might be feasible and effective in low resource settings through simple approaches, such as using water bottles and servo-controlled fans, however, this requires further research.[95,96]

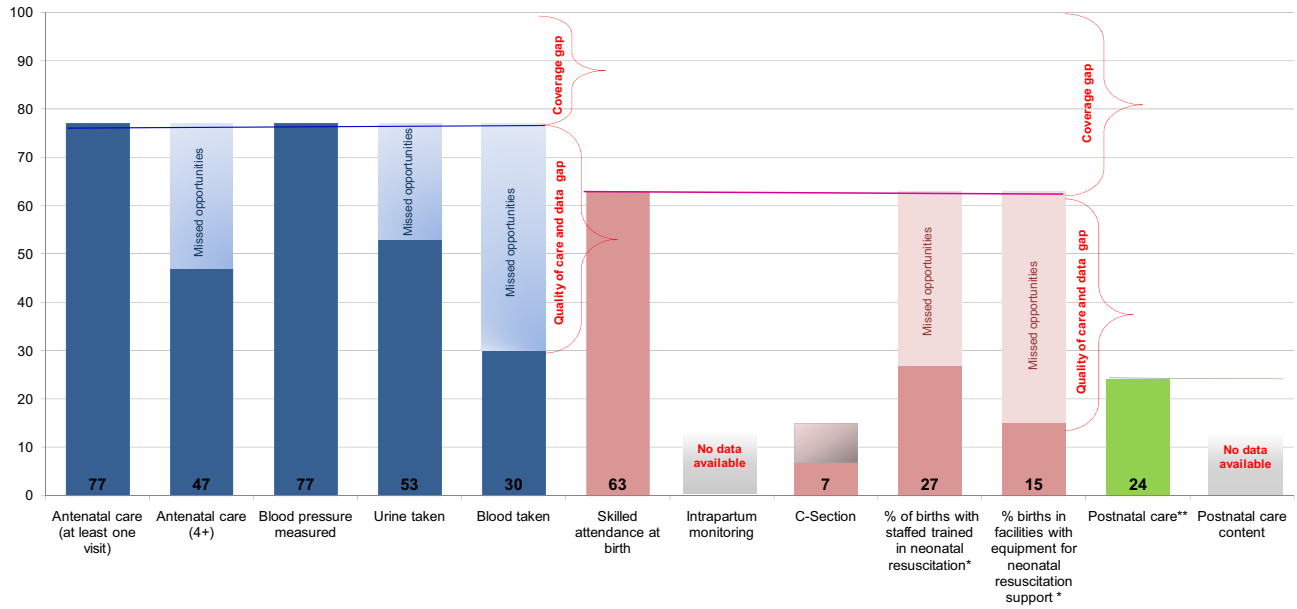
In most low- and middle-income countries, postresuscitation care may be provided at district and tertiary hospital level. At lower levels of the health system or in the community, emergency transport systems must be available and accessible, with basic supportive care to maintain appropriate temperature and glucose level during transport.

Priorities for Action

Urgent action is needed to reach mothers and newborns with effective interventions to prevent 814,000 intrapartum-related neonatal deaths and the closely linked 1.02 million intrapartum stillbirths occurring each year. Country strategies should prioritize high-impact interventions that are appropriate to the context. Appropriate priority setting decisions require use of local data on mortality, intervention coverage and quality, as well as feasibility to implement and scale-up interventions using existing delivery platforms. Emphasis should be given to interventions with highest mortality and morbidity impact that are feasible and affordable, and reduce inequities.[15,97]

A first action is to identify and address missed opportunities to provide effective interventions within existing programs. There are substantial gaps in both data and quality of care during established points of contact between mothers-newborns and the health system in the prenatal, intrapartum, and postnatal periods, particularly in low-resource settings. During every interaction of the mother-newborn with the health system, the effective application of available interventions must be ensured. Figure 4 depicts some of these missed opportunities for effective interventions. For example, whereas almost two-thirds of births occur with a skilled attendant, an unknown, but likely inadequate, proportion occur with intrapartum monitoring of the progress of labor or access to emergency obstetrical care. A survey in 6 African countries found that only 15% of facilities that provide care at birth had equipment for neonatal resuscitation.[11] In low-resource settings, addressing these missed opportunities is a key short-term strategy to reduce intrapartum-related mortality. This chapter has identified potential high-impact interventions that can be delivered within existing health systems now. Longer-term solutions require reducing the substantial gaps in coverage of prenatal and intrapartum care for the 60 million women a year who give birth outside of facilities; thus, more interactions of mothers-newborns with the health system are also needed.

The greatest-impact intervention and the top priority is to improve quality and coverage of intrapartum care. Key immediate actions include use of the partograph by birth attendants during labor, with improved fetal heart rate monitoring and access to emergency obstetrical care if needed. Sustained strategies are required to increase coverage of skilled birth attendance and access to emergency obstetrical care, with evidence using both supply- and demand-sided interventions. Typically, such strategies involve cross-sectoral policies of finance as well as health authorities and often rely on donor funding in low-resource settings. On the basis of the available evidence, such investment would reap substantial



Source: New analysis of data from Unicef State of the World's Children 2009. New York, Unicef, Bryce J, Daelmans B, Dwivedi A, et al. Countdown to 2015 for maternal, newborn, and child survival: the 2008 report on tracking coverage of interventions. Lancet 371:1247-58, 2008, DHS 2000-2007, and Service Provision Assessment Surveys (2003-2008).
* Data from Service Provision Assessment Surveys in.: Egypt, Ghana, Kenya, Rwanda, Tanzania, and Uganda
** Postnatal care is the median from 12 countries based on analysis for Bryce J, Requejo JH. Tracking progress in Maternal, Newborn and Child Survival: the 2008 Report. New York: Unicef, 2008

Figure 4 Coverage of maternal newborn care—quality and coverage gaps. (Reprinted with permission granted by FIGO from: Lawn et al.[15]) (Color version of figure is available online.)

dividends in newborn lives saved, and simultaneously reduce maternal deaths and intrapartum stillbirths. Providing 90% coverage of comprehensive emergency obstetrical care to women who already deliver in facilities would save an estimated 232,500 newborn lives, while achieving 90% coverage of comprehensive emergency care for all mothers would save 494,000 newborn lives each year.[15] Notably, the greatest impact would be expected in the highest mortality settings, where strategies, such as task-shifting for Cesarean delivery would provide life-saving interventions to women otherwise without access to emergency obstetrical care. This impact would likely be even greater than the aforementioned estimate because improved quality of care at facilities is associated with increased care seeking and use of facility-based services.[15]

Skilled birth attendants at all levels of facilities and at home should be competent and equipped to resuscitate infants who do not breathe. Increasing neonatal resuscitation coverage to 90% of all babies already being born in facilities would alone avert more than 93,000 neonatal deaths each year at minimal additional cost.[15] Furthermore, providing 90% of all infants born with access to newborn resuscitation would save 192,000 lives annually.[15] The newly developed HBB training curriculum provides a neonatal resuscitation program specifically designed for lower levels of the health system, settings that have typically lacked this intervention. The HBB algorithm and training guide, coupled with increasingly affordable basic resuscitation equipment (eg, self-inflating bag and mask) provide new opportunities for neonatal resuscitation in first-level and first-referral facilities where this intervention was previously unavailable.

Improving the link between mothers and newborns in the community with facility-based skilled obstetrical care is another important strategy, especially to reduce the coverage gap for the poor, and thereby reduce intrapartum-related neonatal deaths. A variety of approaches involving community mobilization, financial incentives, and use of community-based providers, may increase use of skilled birth attendance and make available life-saving emergency care for the 60 million babies born at home each year, along with their mothers.[12,13]

Priorities for Research

Although the actions needed to reduce intrapartum-related deaths are clear, a very strong implementation research agenda is also clear and critical. Many questions remain around improving coverage and quality of intrapartum care. Solutions often require health systems innovations, particularly around use of task shifting or whole system design. Research should test context-specific combinations of demand and supply approaches, with community health workers linked to trained and equipped staff in facilities, transport schemes, and financial incentives for seeking skilled care. A recent systematic research priority process has ranked the top questions for reducing intrapartum related neonatal deaths according to description (epidemiology), delivery, development and discovery categories.[98] This review identified the

need for further research on adaptation and use of the partograph, perhaps supplemented with hand-held equipment to assess fetal well-being, such as a Doptone device; and on the feasibility and effectiveness of therapeutic hypothermia in low- and middle-income settings.

Conclusions

In conclusion, increasing availability, quality, and demand for skilled care at birth will substantially reduce the more than 800,000 annual intrapartum-related neonatal deaths, and in addition will likely reduce intrapartum stillbirths and maternal mortality and morbidity. Achieving results requires addressing missed opportunities to improve quality of facility-based care, and reaching universal coverage of emergency obstetrical and immediate neonatal care, including neonatal resuscitation, and simple newborn care and care-seeking at the community level.

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