Review Promoting physiologic transition at birth: Re-examining resuscitation and the timing of cord clamping

Susan Niermeyer a, *, Sithembiso Velaphi b

a Section of Neonatology, University of Colorado School of Medicine, 13121 E. 17th Avenue, B8402, Aurora, CO 80045, USA
b Faculty of Health Sciences, University of the Witwatersrand, Department of Paediatrics, Chris Hani Baragwanath Academic Hospital, Soweto, Johannesburg, South Africa

Keywords: Asphyxia neonatorum
Blood transfusion
Blood volume
Newborn infant
Resuscitation
Umbilical cord clamping

SUMMARY

Delayed clamping of the umbilical cord is recommended for term and preterm infants who do not require resuscitation. However, the approach to the newly born infant with signs of fetal compromise, prematurity and extremely low birthweight, or prolonged apnea is less clear. Human and experimental animal data show that delaying the clamping of the umbilical cord until after the onset of respirations promotes cardiovascular stability in the minutes immediately after birth. Rather than regarding delayed cord clamping as a fixed time period before resuscitation begins, a more physiologic concept of transition at birth should encompass the relative timing of onset of respirations and cord occlusion. Further research to explore the potential benefits of resuscitation with the cord intact is needed.

1. Introduction

1.1. Case scenario

A 29-week infant is delivered by cesarean section with epidural anesthesia for progressive cervical dilation despite tocolysis and breech presentation. The amniotic fluid is clear at intraoperative rupture of membranes. At birth the infant appears consistent with estimated gestation, her arms are flexed, but she does not cry. The obstetrician places the infant on a warm towel, covers her body with a second towel, and holds the head straight in a sniffing position. The infant takes a breath between 10 and 15 s. The obstetrician provides gentle tactile stimulation but does not clear the airway, as no secretions are visible. Occasional spontaneous respirations continue, and by 45 s the infant has sustained respirations. The cord is clamped at 60 s. The baby is breathing and moving actively on arrival at the warmer. Continuous positive airways pressure (CPAP) is applied with 30% oxygen. The heart rate is > 100 bpm.

1.2. Repeat case scenario

The same 29-week infant is delivered by cesarean section. At birth the infant appears consistent with estimated gestation, her arms are flexed, but she does not cry. The obstetrician immediately clamps and cuts the cord. The baby is apneic and motionless on arrival at the warmer. CPAP is applied with 30% oxygen. The heart rate by cord palpation is 70 bpm. Positive-pressure ventilation is begun with T-piece. Saturations fail to meet time-specific targets and oxygen is increased to 60%. At 3 min the baby begins to breathe spontaneously and heart rate is consistently >100 bpm.

Current neonatal resuscitation guidelines recommend a rapid assessment at the moment of birth to gauge the likelihood of need for further resuscitation. The three rapid assessment questions include: Is the baby term? Is the baby breathing? Is there good muscle tone? If the answer to any question is ‘no’, the infant is carefully evaluated and provided the initial steps of resuscitation: warmth, drying, clearing the airway as necessary and stimulation to breathe. Breathing and heart rate are evaluated next and cycles of re-evaluation (breathing, heart rate, saturation) guide progress through the resuscitation algorithm [1]. The 2010 International Liaison Committee on Resuscitation (ILCOR) Consensus on Science also states that ‘Cord clamping should be delayed for at least 1 min in babies who do not require resuscitation.... Evidence is insufficient to recommend a time for clamping in those who require resuscitation [2].’

Analyzing the first case scenario according to the rapid assessment questions highlights that this preterm baby who is not breathing, but has good muscle tone, needs ongoing evaluation and the initial steps of warmth, clearing the airway as necessary, and stimulation to breathe. When the initial steps are provided with the umbilical
circulation intact, the infant establishes regular spontaneous respirations and needs only CPAP and a low concentration of supplemental oxygen. When the umbilical cord is clamped immediately to move the newly born infant to an open warmer for the initial steps, the baby remains apneic and has a low heart rate, prompting positive-pressure ventilation. Higher oxygen concentrations are needed to achieve time-specific saturation targets, and regular spontaneous breathing and normal heart rate are achieved only after a few minutes of positive-pressure ventilation.

2. Background: The circular argument

Did the infant in the second case scenario need resuscitation or did that infant suffer from an interruption of physiologic transition at birth? For this infant, and likely for many others, interruption of physiologic transition at birth by immediate cord clamping can result in the vital sign indicators that call for neonatal resuscitation interventions. Barcroft [3] reported that bradycardia occurs in the fetus in response to umbilical cord occlusion. In the newly born infant who has not yet taken the first breath, the response to cord occlusion (or clamping and cutting) is essentially the same and results in neonatal bradycardia. Dawes et al. [4,5], performed an experiment in Rhesus monkeys that is often cited as the model for fetal asphyxia and neonatal resuscitation. Primate fetuses were delivered by cesarean section and prevented from breathing by occluding the mouth and nose. Tying of the cord produced a sudden and profound bradycardia followed by a period of irregular, gasping respirations. A period of complete apnea followed. If the blood pressure remained above a critical threshold, however, rapid restoration of normal heart rate could be achieved by providing positive-pressure ventilation. Improvement in blood pressure and onset of spontaneous respirations followed [4].

Even without deliberate airway occlusion, conditions very similar to those in Dawes’ experiment exist with immediate cord clamping before onset of respirations. True to the model, the newly born infant who is bradycardic and apneic or breathing ineffectually usually does respond to positive-pressure ventilation alone. In some cases, though, chest compressions may be necessary to increase coronary perfusion pressure above the critical threshold. Especially in extremely preterm infants, in whom much of the fetoplacental blood volume normally remains in the placenta [6], the critical threshold for blood pressure may not be reached and chest compressions plus volume expansion may be given before adequate heart rate is restored. For these extremely preterm infants, effective expansion of the lung with bag and mask may also be difficult and intubation may be necessary to achieve effective lung inflation and restore heart rate.

This review summarizes the evidence that supports a delay in cord clamping as part of facilitating physiologic transition at birth. For many infants who have not experienced severe in-utero compromise, such an approach has the possibility to decrease the extent of resuscitative intervention needed in the delivery room setting. The discussion outlines options for management of those infants who have experienced significant fetal asphyxia and highlights areas in which further research is needed.

3. Synopsis of the physiology of placental transfusion

During fetal life the fetoplacental blood volume distribution changes with increasing gestation; early in development, a larger proportion of the blood volume resides in the placenta, but as gestation advances, more circulating volume is present in the fetus [6]. In the minutes after birth, transfer of blood continues from placenta to the newly born infant through the patent umbilical vein. This transfer occurs most rapidly in the first minute, but continues until constriction of the umbilical arteries occurs and cord pulsations cease. The volume of blood transfused often ranged between 25 and 40 ml/kg and is dependent not just on timing, but also on a series of modifying factors, including gestation, onset of respirations, uterine contractions, and relative position of infant and placenta [7–9]. Delayed clamping of the cord has been shown to have immediate, short-term, and long-term benefits. Immediate benefits are related to its effects on cardiopulmonary adaptation. Short-term benefits include reduction in need for blood transfusion, incidence of intraventricular hemorrhage and necrotizing enterocolitis in preterm infants [10]. Term infants exhibit improved hematocrit at birth, better iron status and reduced anemia of infancy [11].

4. The condition of immediate cord clamping before onset of respirations

Several historical studies illuminate the condition of immediate cord clamping before the onset of respirations. Lind, Peltonen, and colleagues presented cineradiographs of the aeration of the lung at birth during the Second Scandinavian Summer Meeting of Biochemistry, Medical Chemistry, Pharmacology and Physiology in Turku, Sweden in 1859.

Among early clamped infants, those clamped prior to the first breath can be distinguished as a separate group. If the umbilical cord is tied prior to the first breath, the result is a decrease in the size of the heart during the first three or four cardiac cycles. Then the heart again increases in size, almost to that of the fetal heart. This change should be interpreted as due to the filling of the opened vascular system of the lungs in connection with aeration, which requires a considerable amount of blood. If the umbilical circulation is closed, the flow from the caval vein through the via sinistra to the left heart will hardly suffice and for a moment the left heart will not have enough blood. Usually, however, this condition improves when adequate amounts of blood flow through the lungs to the left atrium [12].

Tiisala et al. [13] quantitated similar observations in 1966, by calculating cardiac volume on the basis of antero-posterior and lateral chest radiographs. Among 15 term infants with immediate cord clamping and an equal number of infants with delayed cord clamping, cardiac volume normalized for birthweight was significantly smaller among the early clamped group at 5 and 15 min and 4 and 24 h after birth. Brady and James [14] observed that whether or not an infant had established spontaneous respirations before cord clamping was more important than the actual interval between birth and cord occlusion. They monitored fetal/neonatal heart rate during delivery with tococardiography followed by application of electrodes with presentation of the shoulders. Immediate clamping of the umbilical cord before onset of respirations resulted in a rapid and profound bradycardia. Even those infants whose cords were clamped at 30 s maintained a heart rate >100 bpm if they breathed spontaneously before that time.

A prompt fall in rate was consistently seen when the cord was clamped before the onset of respiration, while no such change was seen in vigorous infants who began breathing before cord occlusion. A fall in rate was also seen in mildly depressed infants who cried only occasionally and were not breathing when the cord was clamped. The rapidity of change suggests that the mechanism is reflex in nature.

Brady and James hypothesized that immediate cord clamping before lung expansion suddenly removed the low-resistance placental vascular bed and offered no alternative in the pulmonary vascular bed, where resistance remained high. Stimulation of the aortic baroreceptors resulted in reflex bradycardia.

Modern evidence in both human infants and experimental animals has amplified and supported the historical observations
around immediate cord clamping before onset of respirations. Dawson et al. [15] reported heart rate immediately after delivery in a cohort of 468 healthy preterm and term infants from three centers; none of the infants received supplemental oxygen or respiratory assistance in the delivery room. Reliable recordings of heart rate at 1 min after birth for 181 infants showed a median value of 96 bpm [interquartile range (IQR): 65–127]. Both term (median 99 bpm IQR: 66–132) and preterm (median: 96; IQR: 72–122) infants, whether born by vaginal or cesarean route, showed a similar pattern. In a subset of infants with reliable recordings at exactly 1, 2, and 3 min, the proportions of infants with heart rate < 100 were 61%, 21%, and 7% respectively. At 1 min, heart rate <60 bpm was present in 17%, but only 2% by 3 min. Heart rates rose more slowly and showed a broader range of initial values among preterm compared with term infants. Approximately half the cohort (52%) delivered vaginally. No information was collected on the timing of umbilical cord clamping relative to onset of respirations; however, immediate clamping was generally practised at the time of the observations (J. Dawson, personal communication).

Carefully controlled experiments in fetal lambs have elucidated the physiologic changes that accompany cord clamping before the onset of respirations. Bhatt et al. [16] studied preterm lambs (day 126 of 147-day gestation at term) prepared with carotid, left main pulmonary artery, and ductus arteriosus flow probes as well as carotid artery, jugular vein, and left pulmonary artery catheters. Fetuses were anesthetized, intubated, and randomized to either clamping of the umbilical cord first (Clamp 1st: immediate cord clamping and ventilation at 2 min) or ventilation before umbilical cord clamping (Vent 1st: ventilation until pulmonary blood flow increased, ~3–4 min, then cord clamping). Ventilation commenced with a sustained inflation of 20 s duration with peak inspiratory pressure of 35 cm H2O and continued with PEEP 5 cm H2O, oxygen concentrations, and rate to achieve target saturations (90–95%) and PCO2.

Clamping the umbilical cord before onset of respirations resulted in an immediate decrease in heart rate from mean values above 160 bpm to mean values around 100 bpm. Pulmonary blood flow remained unchanged at the low levels present during fetal life. Flow through the ductus arteriosus remained right to left, as in fetal life, and right ventricular output fell progressively during the first 90 s and remained low until ventilation began at 2 min. With cord clamping a sudden spike occurred in carotid arterial pressure, followed by equilibration of pressure; this was paralleled by a sharp increase in carotid arterial flow followed by a large fall, reflecting pressure-passive flow. Once ventilation was initiated at 2 min, heart rate rose quickly and surpassed baseline. Pulmonary blood flow increased, but remained low relative to the Vent 1st group. Carotid arterial pressure and flow rose back to high levels equivalent to those during the spike immediately after cord clamping. In summary, umbilical cord clamping before onset of respirations resulted in decreased right ventricular output and persistently low pulmonary blood flow, but provoked wide fluctuations in both carotid arterial pressure and flow.

5. The condition of cord clamping delayed until after onset of respirations

Many historical sources advocate for delayed clamping until after onset of respirations or until cord pulsation ceases. Erasmus Darwin, the British physician, philosopher, and grandfather of Charles Darwin, wrote in 1801,

Another thing very injurious to the child, is the tying and cutting of the navel string too soon; which should always be left till the child has not only repeatedly breathed but till all pulsation in the cord ceases. As otherwise the child is much weaker than it ought to be, a portion of the blood being left in the placenta, which ought to have been in the child [17].

In the experimental model of the fetal lamb, Bhatt et al [16], compared the previously described conditions of immediate cord clamping with those when ventilation was established first and cord clamping delayed until pulmonary blood flow increased to a stable baseline, indicating physical recruitment of the lung. Heart rate remained stable before and after clamping and pulmonary blood flow rose progressively through establishment of ventilation and further with the immediate functional closure of the ductus arteriosus that occurred with cord clamping. At 2 min after cord clamping, pulmonary blood flow in the Vent 1st group was twice that in the Clamp 1st group. Carotid arterial pressure drifted modestly lower during ventilation, then returned to baseline with clamping; carotid flow remained essentially stable before and after clamping. At 30 min, pulmonary blood flow and right ventricular output remained higher in the Vent 1st group compared with the Clamp 1st group. In summary, establishment of lung expansion prior to umbilical cord clamping results in stable heart rate, progressive rise in pulmonary blood flow, and stable carotid blood flow.

Only a few randomized controlled trials have focused on the impact of cord clamping on extremely premature infants and infants likely to require resuscitation, and scant data have been published on short-term physiologic outcomes such as heart rate, supplemental oxygen needs in the first minutes, and degree of respiratory support. However, quality improvement studies provide some additional clinical information regarding the impact of delayed cord clamping on the need for resuscitation. Kaempf et al. compared outcomes of 77 very-low-birthweight (VLBW) and 172 low-birthweight (LBW) infants <35 weeks in whom cord clamping was delayed 45 s with an equal number of historical controls born during the period immediately preceding the change in policy [18]. Infants born vaginally were held 10–20 cm below the introitus in a warm towel, gently dried, stimulated and suctioned as necessary. Infants born by cesarean section were placed between the mother’s legs on the operative field and received similar care. Six neonates (2%) did not receive delayed cord clamping because health care providers felt they needed immediate major resuscitation. One-minute Apgar score was higher in the VLBW infants who received delayed cord clamping (7 vs 5, P < 0.001) and fewer VLBW infants in the delayed clamping group required any delivery room resuscitative intervention (defined as supplemental oxygen, bag and mask ventilation, intubation, chest compressions, epinephrine). Notable decreases occurred in the number of infants who required supplemental oxygen and ventilation. Also of note, first temperature was equal in early- and late-clamped infants in both the VLBW and LBW groups.

A feasibility study of delayed cord clamping among infants <33 weeks compared eligible infants managed in compliance with delayed cord clamping (45 s) to those who were eligible but received non-compliant management [19]. The mean gestational age was just under 30 weeks and mean birthweight just under 1500 g. Among 236 late-clamped and 113 early-clamped infants, there was no observed difference in either 1 min or 5 min Apgar scores, nor was there any difference in the proportion of infants requiring intubation in the delivery room. The incidence of temperatures <36.3 °C was lower among infants who received delayed cord clamping, as was the incidence of necrotizing enterocolitis/intestinal perforation.

6. A refined paradigm: Delay of umbilical cord clamping until establishment of respirations

Promoting a more physiologic transition at birth by delaying umbilical cord clamping until respirations are established offers
numerous theoretical benefits for the premature or mildly depressed infant. Virtually every organ system is impacted by the placental transfusion (Box 1), and promoting physiologic transition could potentially reduce the acuity of care needed and the incidence of complications. In low- and middle-income countries, the value of bundling interventions such as antenatal steroids, delayed cord clamping, and use of low oxygen concentrations in resuscitation is life-saving and potentially reduces the burden on the health system; in the developed world, such management has cost-saving implications and holds promise for prevention of complications of prematurity.

Rapid assessment of the newly born infant and the initial steps of drying, providing warmth, clearing the airway, and providing specific stimulation to breathe can be carried out with the umbilical circulation intact. Data from observational studies in settings implementing the algorithm of Helping Babies Breathe show that the majority of infants will cry or breathe spontaneously during/after the initial steps when cord clamping is delayed for 1 min [20,21]. In the first seconds after birth, maintaining the umbilical circulation intact avoids triggering reflex bradycardia, which, as has been shown, may result in heart rate < 100 bpm, an indication for positive-pressure ventilation. Although the link between the bradycardia reported by Dawson et al. [15] and immediate cord clamping has not been directly established, the persistence of bradycardia for one to several minutes in these otherwise healthy, non-asphyxiated infants could have justified application of positive-pressure ventilation. Numerous studies of oxygen needs in the first minutes of birth after have shown a pattern of brief, increased oxygen requirement up to 50–70% in order to meet time-specific saturation targets [22–24]. After saturations begin to rise, oxygen generally is weaned rapidly, often to concentrations near 21% by admission to the neonatal intensive care unit (NICU). Improved right ventricular output and pulmonary blood flow would improve the contact of circulating blood with alveolar oxygen and perhaps decrease the concentration of supplemental oxygen needed. Avoiding the need for positive-pressure ventilation would be the ideal method to avoid volutrauma and barotrauma, but when positive-pressure ventilation is needed, experimental evidence suggests that lung aeration proceeds less traumatically with adequate pulmonary capillary filling [25].

During stabilization in the several hours after birth, delayed cord clamping continues to be associated with increased physiologic stability and less need for intervention. In 1950 Landau et al. [26] reported infants born by cesarean section without labor who developed a clinical picture of shock from blood loss; he attributed the gradually developing picture of circulatory collapse and respiratory distress to the systemic steal of blood volume needed to perfuse the lungs after early clamping of the umbilical cord. Multiple studies have shown improved blood pressure in the first 4 h and less need for volume expansion (due to hypotension) or pres- tors with delayed cord clamping [10]. Several randomized controlled trials in premature infants have shown decreased intracranial hemorrhage among infants with delayed cord clamping [10]. Studies of superior vena cava (SVC) blood flow in human infants, which correlates with upper body perfusion, support improved SVC flow with delayed cord clamping [27,28], much as has been demonstrated with improved cerebral blood flow in experimental animal studies of delayed clamping delayed until after onset of respirations [16]. Studies which associate the origin of intracranial hemorrhage to cerebral blood flow dynamics in the first minutes and hours of life suggest the possible mechanistic link through which delayed cord clamping may exert a protective effect [27]. Two large series of preterm infants who were managed with delayed cord clamping showed stable or improved body temperature on admission [18,19]. Efforts were made to create a warm environment, using standard methods of increased room temperature, chemical warming mattresses, occlusive plastic wrap, and radiant warmers; however, studies also suggest that placental transfusion itself may improve peripheral skin temperatures [29].

Finally, long-term outcome of infants may be improved with delayed cord clamping because of improved iron stores and decreased anemia of infancy, as well as lesser need for transfusions. Among preterm infants, delayed cord clamping is associated with decreased need for and number of transfusions [10]. Term infants benefit most directly from improved iron status in infancy and decreased iron deficiency anemia [11]. Iron deficiency and iron deficiency anemia in infancy are associated with cognitive, motor, and behavioral deficits, as well as persistent neurophysiologic differences [30].

Delaying the clamping of the umbilical cord until onset of respirations has clear advantages for the infant who requires minimal support at birth, but what is the most appropriate management for the infant who has experienced severe acute or chronic fetal asphyxia resulting in fetal bradycardia and secondary apnea or gasping with profound acidosis? In 1967 Moss and Monset-Couchard questioned whether immediate clamping in the depressed infant might compound pre-existing compromise:

iatrogenic interruption of the placental circulation at birth has, in most cases, become an automatic procedure with little or no regard for the physiologic alterations evoked or for their subsequent effect upon the fetus.... In full-term, vigorous infants “early” versus “late” clamping is not a vital issue. In depressed full-term infants, the factor of time may be more significant since further insult may not be so well tolerated [31].

Virtually all studies of cord clamping in preterm and term in- fants have made the need for major resuscitative interventions an exclusion criterion. Consequently, few data exist on the resuscitation of severely compromised infants with the placental circulation intact. Although the experimental animal data would suggest that establishment of lung expansion and ventilation with positive pressure is effective in facilitating placental transfusion [16], the experimental model did not incorporate severe fetal metabolic acidosis, accompanying changes in fetal-placental blood distribution, and associated compromise of fetal cardiac, pulmonary, and

---

**Box 1**

Organ systems impacted by placental transfusion and timing of umbilical cord clamping.

<table>
<thead>
<tr>
<th>Cardiovascular</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate at birth</td>
<td></td>
</tr>
<tr>
<td>Cardiac output</td>
<td></td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulmonary</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulmonary blood flow</td>
<td></td>
</tr>
<tr>
<td>Lung injury — capillary erection, volutrauma, barotrauma, oxygen toxicity</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Central nervous system</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral blood flow</td>
<td></td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td></td>
</tr>
</tbody>
</table>

| Neurodevelopmental outcome (related to iron deficiency anemia) |  |
| Circulating blood volume |  |
| Anemia — acute and late (and need for transfusions) |  |

<table>
<thead>
<tr>
<th>Hematologic</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Peripheral blood flow</td>
<td></td>
</tr>
<tr>
<td>Temperature regulation</td>
<td></td>
</tr>
</tbody>
</table>

---

circular function. Finally, the physical arrangement to permit extensive resuscitation while maintaining the placental circulation intact is not a trivial obstacle to overcome.

Early studies on the distribution of feto-placental blood volume suggested that fetal asphyxia resulted in intraterine shifts in blood volume from the placenta into the fetal circulation [32]; asphyxiated infants had a high blood volume in spite of early clamping, with values comparable to those in normal newborn infants with cords clamped late [7]. Observations by other investigators confirmed these findings in term neonates [33,34] through measurement of residual placentental blood volume and hematocrits. In a model of fetal hypoxia in the lamb, directly measured fetal blood volume increased from 86 to 109 and 102 ml/kg at 15 and 30 min of hypoxia, with the expected reciprocal decrease in placentental blood volume [35]. Blood volume changes persisted for 30–60 min following the termination of hypoxia. In the model of maternal hypoxia used to induce fetal hypoxia, placental vascular resistance increased, suggesting placental vasoconstriction as a possible mechanism for reduction of placentental blood volume and reciprocal increase in fetal blood volume. Linderkamp [36] cautioned that acute intrapartum asphyxia in the fetal lamb model resulted in a significant increase in umbilical blood flow and arterial blood pressure and decrease in placental vascular resistance during the first minutes of hypoxia, followed by a decrease in umbilical blood flow and blood pressure and an increase in placental vascular resistance when hypoxia is continued. The net shifts of blood volume may be variable during the evolution of intrapartum asphyxia, with some instances of blood loss into the placenta [37–39]. The midwifery literature reports numerous examples of ‘stunned or slow-to-start babies (who) revive with cord blood alone’ [40]. Lowering the infant below the placenta facilitates placental–infant transfusion and permits resuscitative intervention if needed.

Although blood volume shifts may occur prior to birth with asphyxia, the apneic depressed infant still must achieve physical expansion and perfusion of the pulmonary vascular bed. Pulmonary vascular resistance may be pathologically elevated and structural changes (vascular remodeling) may have occurred with more chronic asphyxia. Severe or chronic asphyxia or fetal infection may directly compromise myocardial contractility. There are limited data to describe the response of an asphyxiated neonatal myoccardium to sudden increase in afterload and reduction in preload as occurs with immediate cord clamping [41]. However, for the severely compromised infant, this sudden change in cardiac operating conditions may be more critical to survival than any change in the actual volume of blood transfused.

Overcoming the physical barriers to performing advanced resuscitation with the placental circulation intact requires reconfiguration of equipment and team members. While the initial steps of resuscitation can be performed on the mother’s abdomen or chest, such positioning makes positive-pressure ventilation difficult and raises concern over hydrostatic forces promoting blood flow back into the placenta. Experienced midwives advocate holding the asphyxiated infant below the level of the placenta while drying and providing stimulation. Positive-pressure ventilation can be performed on a flat surface adjacent to the mother while maintaining the umbilical cord intact. Whereas full resuscitation with the umbilical cord intact may be feasible at vaginal delivery, resuscitation with positive-pressure ventilation is more problematic at cesarean section because of the need for sterile equipment and neonatal care providers in full surgical attire. Specially designed resuscitation devices which provide a work surface immediately adjacent to the mother have been developed to permit resuscitation at either vaginal or cesarean birth while maintaining the umbilical circulation intact and keeping the newly born infant at the level of the placenta. Such arrangements offer the additional advantage that the mother and other family members can maintain visual contact with the newborn during resuscitation and be aware of the actions of the resuscitation team and the responses of the infant.

7. Umbilical cord milking or stripping as an alternative to delayed cord clamping

Despite the benefits of delayed cord clamping, there are some practical limitations associated with the delay itself. Delay in cutting of the cord might interfere with management of profuse bleeding in the mother and thus endanger the mother. Second, as previously noted, it may be difficult to institute effective resuscitation of the newborn when the baby is still at the perineum or on the operative field. Finally, VLBW infants might develop hypothermia because of difficulty with thermal protection using plastic wrap while the cord is still attached. To maintain the benefits of delayed cord clamping and respond to the above concerns, cord milking or stripping becomes an alternative.

Umbilical cord milking or stripping involves rapid transfer of blood from the placenta towards the infant. Milking or stripping of the cord actively moves blood from the cord and placenta to the baby, and therefore is more likely to achieve similar or better placental transfusion than delayed cutting of the cord, especially under conditions in which the baby is positioned above the placenta or uterine contractions are not present (e.g. cesarean section without labor). Milking or stripping also avoids the need for delay. The procedure of milking of the cord can be completed in an average time of 18 ± 5 s [42] much less than the 30–180 s recommended with delayed clamping of the cord. Therefore, stripping or milking of the umbilical cord might have technical advantage over delaying cutting of the cord especially when maternal bleeding demands immediate action or resuscitation is needed.

8. Cord stripping/milking, and circulatory changes at birth

The effect of milking the cord at birth on blood volume was reported by Colozzi in 1954, where he stated

I have seen several infants with asphyxia pallida who were very pale and listless, with a rapid pulse and a very weak cry; with gentle, slow, methodical cord stripping, they were transformed within a few minutes to ruddy, lustily-crying infants [43].

The increase in blood volume to the lungs associated with cord stripping has also been documented with recording of electrocardiographic changes; infants who had cord stripping had a longer P-wave, PR and Q–Tc interval when compared with infants who had early clamping of the cord [44]. Preterm babies managed with milking of the cord have a higher mean arterial blood pressure on admission to the NICU, increased cerebral oxygenation, and improved left ventricular diastolic function from an increase in left ventricular load due to volume expansion [45]. They also have higher systolic and diastolic blood pressure within the first 12 h of life compared to infants with immediate clamping of the cord [46]. In term infants the effects of cord milking on blood pressure are maintained up to 48 h of life and include higher heart rate at 12 h of life compared to infants with immediate cord clamping [47].

Milking of the cord stabilizes blood pressure and heart rate at and soon after delivery.

Some studies have raised a concern about the volume of blood that can be transfused with milking of the cord. The average placental blood volume is estimated to be 75–125 ml [43,48]. Whipple et al. [49] reported that cord milking could increase blood volume of the newborn by up to 22% and red cell volume by 45%. He argued that though a normal infant could tolerate this, there may
be some element of danger if a newborn has congenital heart lesions, asphyxia with circulatory failure, or maternal–fetal blood group incompatibility. Walsh et al. [50] reported that after vigorous stripping of the cord 10 times for 5 min one of the infants became cyanotic and had to be transferred to the nursery. A number of contemporary studies that utilize a technique of milking a segment of cord rapidly 3–5 times have not reported any adverse events associated with milking of the cord [42,45,47,51,52].

9. Cord milking and haemoglobin or need for transfusion

Many studies have indirectly measured the effect of umbilical cord milking through looking at red blood cell mass, levels of haemoglobin and need for blood transfusion. They have compared it with early [42,43,45,47,49,51,53,54] and delayed [43,49,51,52] clamping of the cord in both preterm and term infants. Umbilical cord milking was associated with higher red blood cell mass and haemoglobin in both term [42,43,47,49,53,54] and preterm infants [45,51] compared with immediate cord clamping. Compared with delayed umbilical cord clamping, cord milking has variable results, with some studies in preterm infants reporting similar effects [55] and some reporting higher red cell mass and haemoglobin in term infants [43,49]. Umbilical cord milking has been associated with reduction in need for blood transfusion in preterm infants [51].

In summary, delaying clamping of the cord until the newborn has established respirations or is being ventilated improves the hemodynamic status soon after birth. In situations where delay clamping of the cord is not possible, umbilical cord milking may achieve similar results to delayed cord clamping. However, no studies to date have reported timing of cord clamping relative to time of onset of spontaneous respirations; clamping the cord immediately for later milking may reduce the hemodynamic benefits of ventilation before clamping, even though blood volume transfer is eventually accomplished.

10. Gaps in knowledge and areas for research

Physiologic data on the importance of the sequence of pulmonary expansion before clamping of the umbilical cord have changed the resuscitation paradigm from a simple time interval for delay in clamping to an ordered series of interventions. First, in order to accurately interpret neonatal stabilization and resuscitation, there is a need to note and record the time to onset of respirations and time to umbilical cord clamping in all deliveries, and especially in infants who will participate in neonatal research — whether that research is related to immediate stabilization/resuscitation, intermediate postnatal transition, or longer-term outcomes of intracranial hemorrhage (ICH), bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC), transfusions, or neurodevelopment. Data on short-term physiologic outcomes, such as heart rate, oxygen concentration/duration needed to achieve saturation targets, need for positive-pressure ventilation or intubation, chest compressions, or medications should be collected in studies of delayed cord clamping. Intermediate outcomes, such as need for volume expansion or pressors during stabilization, hematocrit/hemoglobin, need for transfusion and number of transfusions, occurrence of ICH, BPD, NEC remain important, especially with respect to sicker infants who require resuscitation. Finally, data are needed on long-term outcomes of mortality and neurodevelopmental abnormalities, including periventricular leukomalacia, cerebral palsy, and other behavioral and psychomotor conditions [56].

Potential modifiers of placental transfusion should be studied for their contribution to blood transfer; such modifiers include relative position of placenta and infant, presence/intensity of uterine contractions, administration of uterotonic, maternal medical conditions such as diabetes or pre-eclampsia, intraperitoneal growth restriction, twin–twin transfusion syndrome, gestation at high altitude, and abnormal fetal heart rate tracings. Vain et al. [57] conducted a multicenter non-inferiority trial comparing weight change from immediately after birth to cord clamping at 2 min after birth among term, vaginally delivered infants positioned at the level of the introitus versus those placed on the maternal abdomen/ chest. Mean weight gain in the group positioned at the introitus was 56 ± 47 g (range: 50–63 g) compared with 53 ± 45 g (range: 46–59 g) for those infants positioned on the chest/abdomen. Infants were excluded if they received resuscitation, had a short cord or tight nuchal cord, or had birthweight <2500 g. Although mean difference in weight change was small between the two groups, the standard deviation was wide, likely related to whether the first weight was obtained before or after the first uterine contraction following expulsion and before or after the infant’s first breath [57]. Doppler and two-dimensional ultrasound also offers the possibility of real-time monitoring and study of factors modifying placental transfusion. Noori et al. [58] performed echocardiography in the first minutes after birth and documented marked increase in left ventricular output and left ventricular end-diastolic dimensions, likely representing increased preload from placental transfusion in the cohort vigorous term infants, all of whom cried before umbilical cord clamping. Similar techniques will be fundamental to the understanding of the hemodynamics of umbilical cord blood flow, both in experimental models with intrauterine asphyxia and perhaps eventually as monitoring to guide clinical resuscitation [59,60].

The approach to management of the VLBW infant and the infant who has high likelihood of needing resuscitation deserves further refinement. Watchful waiting during the minute(s) after birth, with drying (or occlusive wrapping for extremely low birthweight infants) and careful positioning of the airway represents the least interventionist approach. Performing the initial steps of resuscitation (drying, providing warmth, clearing the airway, giving specific stimulation to breathe) with the cord intact may hasten the onset of spontaneous respirations. The logistics and impact of initiating resuscitative interventions (positive-pressure ventilation, chest compressions, medications, volume expansion or cord milking) with the cord intact are yet to be fully defined.

Potential exclusion criteria preventing a delay in umbilical cord clamping should also be more fully explored, as should ways to mitigate their effects. Conditions that may prevent delay in cord clamping include placental abruption, placenta previa, and tight nuchal cord. However, the somersault maneuver can be used to facilitate delivery without cord division in the presence of tight nuchal cord. [61] Drainage of a long segment of cord by milking may also provide some additional blood volume when delay in clamping is not feasible. Some circumstances will inevitably remain exclusion criteria for delayed clamping, such as hemorrhage from vasa previa, velamentous cord insertion and cord avulsion.

Conflict of interest statement

None declared. Both Dr. Niermeyer and Dr. Velaphi are neonatal evidence evaluation reviewers for the International Liaison Committee on Resuscitation.

Funding sources

None.
Delay of umbilical cord clamping until after the onset of respirations promotes a smoother cardiopulmonary transition after birth.

Umbilical cord clamping before onset of respirations results in decreased cardiac output, bradycardia, and fluctuations in cerebral blood flow.

Time to onset of respirations and time to umbilical cord clamping should be recorded for all births, and should be considered important covariates in research on neonatal outcomes.

Cord milking may provide an alternative means to accomplish placental transfusion when delay is not feasible.

All research in term and preterm infants should control for timing of cord clamping relative to respirations and specifically consider the impact of delayed versus immediate clamping on immediate, short-term, and long-term outcomes.

Umbilical cord clamping in the term or preterm infant without evidence of fetal compromise should be examined with respect to immediate indicators of need for resuscitative intervention and respiratory support, subsequent neonatal morbidity, and long-term neurodevelopment.

Umbilical cord clamping in the term or preterm infant with evidence of fetal compromise should be examined with respect to immediate response to resuscitation, subsequent neonatal morbidity, and long-term neurodevelopment as well as the logistics of resuscitation with the cord intact.

Modifiers of placental transfusion (e.g. medical and obstetric conditions, relative position of placenta and infant) should be studied to define the dynamics and optimal management of the process.

Studies should specifically examine the equivalence of delayed cord clamping and cord milking.


guidelines and recommendations for training. Writing Group of the American Society of Echocardiography (ASE) in collaboration with the European Association of Echocardiography (EAE) and the Association for European Pediatric Cardiologists (AEPC). J Am Soc Echocardiogr 2011;24:1057–78.


