Optimal Timing of Umbilical Cord Clamping:
Is the Debate Settled? Part 1 of 2: History, Rationale, Influencing Factors, and Concerns

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Educational Gaps
1. Clinicians may not fully understand the history of how early cord clamping became a practice standard.
2. Clinicians should understand the factors that contribute to the amount of placental transfusion and concerns that have postponed the adoption of delayed cord clamping into standard practice.

Abstract
In the middle of the 20th century, practices regarding the timing of umbilical cord clamping changed from delaying cord clamping to clamping the umbilical cord soon after delivery of the infant. In the last several years, interest in reviving delayed cord clamping has led to an abundance of literature on the subject. On the basis of recent research, many professional organizations in the fields of obstetrics, midwifery, and pediatrics have started to recommend the use of delayed cord clamping for at least a subset of infants. In part 1 of this 2 part review, we present the history of the delayed cord clamping debate, discuss the rationale behind the use of delayed cord clamping from a physiologic standpoint, detail the factors that affect transfusion volume during a delay in cord clamping, and examine the concerns that exist regarding the use of delayed cord clamping. In part 2, we present the evidence surrounding timing of cord clamping for the preterm and term infant and maternal outcomes. Finally, we discuss alternatives to delayed cord clamping and present a summary of unanswered questions on the subject.

Objectives  After completing this article, readers should be able to:
1. Understand the reasons why early cord clamping was adopted into standard practice.
2. Describe the role cord clamping has in normal fetal-to-newborn transition.
3. Identify factors that contribute to the amount of placental transfusion.
4. Understand concerns that exist regarding implementation of routine delayed cord clamping.

The History of the Debate
"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 part of the blood being left in the placenta which ought to have been in the child and at the same time the placenta does not so naturally collapse, and withdraw itself from the sides of the uterus, and is not therefore removed with so much safety and certainty."—Erasmus Darwin (1731-1802) (1)

For centuries, this quotation represented the opinion of the medical community. Even Aristotle (384–322 BC) believed that it was harmful to tie and cut the umbilical cord too soon after birth. (2) Timing of cord clamping was studied early by the likes of Pierre Budin, who in his 1875 article entitled “When Should We Clamp the Umbilical Cord?” reported that the volume of blood retained in the placenta after early cord clamping (ECC) (and therefore denied to the infant) was 92 cm³. (3)(4) In 1899, the first surgical cord clamp was introduced to replace a tie with the objective of reducing infections; instructions were to apply the clamp after cord pulsation ceased. (2)(4) In these times, ECC occurred approximately...
1 minute after birth, whereas late clamping was considered as occurring more than 5 minutes after birth. (5)

In the middle of the 20th century, practices rapidly changed and cord clamping began to occur much earlier after birth. In retrospect, the reasons for this shift in practice are hard to determine, and we are left with only theories. Contributory factors likely included the following: (1) improvements in obstetric care with more women delivering in hospitals, (2) more obstetricians conducting deliveries, (3) an increasing number of surgical deliveries, and (4) increasing expertise and availability of neonatal resuscitation. (4)(5)(6) In fact, Virginia Apgar’s seminal 1953 article only included infants whose cords had been clamped early because the 60-second scores were determined after cord clamping. (4) Perhaps most important, in the 1960s, the package known as active management of the third stage of labor (AMTSL) was introduced with the overall goal of preventing maternal postpartum hemorrhage (PPH), a major cause of maternal mortality. (6) The AMTSL package included the following: (1) administration of a prophylactic uterotonic agent, (2) clamping and cutting the umbilical cord shortly after birth, and (3) controlled cord traction of the umbilical cord. (7) Although ECC was initially described as an option in AMTSL, ECC evolved into an unintended standard component of AMTSL that had no physiologic rationale. (6)(8) More recently, the components of AMTSL have been subject to renewed scrutiny; studies have confirmed that prophylactic uterotonics are beneficial in preventing PPH, while finding that controlled cord traction has little benefit and ECC has no benefit in preventing PPH. (8) Finally, a series of blood volume measurements performed in healthy term infants in the 1960s revealed that more than 90% of blood volume was transferred from placenta to child within the first several breaths after birth. Conclusions from these studies led to the redefinition of early vs late cord clamping, with ECC occurring within 15 seconds of birth and late clamping occurring at approximately 1 minute. (5)(9) Thus, over a period of several years and with relatively minimal scientific evidence of benefit, ECC became the norm, and delayed cord clamping (DCC) was “discarded from mainstream practice without careful study or regard to the physiologic processes at work.” (10)

Since the middle 20th century, when ECC became a standard practice, hints of the benefits of placental transfusion appear in the literature. One example of this is barker foal syndrome, described by 2 veterinarians in 1959 after their observations of births of thoroughbred foals. They noted that approximately 1% of foals born in captivity (under human supervision and with early umbilical cord clamping) developed a convulsive syndrome that was accompanied by a barking cough. (9)(11) At postmortem examination, the lungs of these foals were found to have hyaline membranes. Foals born in the wild, where umbilical cords commonly remained intact for up to 30 minutes, did not develop this syndrome. Residual placental blood volume in the foals born in captivity could be measured at up to 1,000 to 1,500 mL, whereas that in the foals born in the wild was usually as little as 50 mL. (11) The question was posed whether placental transfusion was of possible benefit.

During the past several years, interest in DCC has become reinvigorated. Ironically, those interested in reviving DCC as a practice are now burdened with presenting the rigorously gathered evidence of its benefit. The recent evidence has led to recommendations for the use of DCC by many professional organizations in the fields of obstetrics, midwifery, and pediatrics (Table). However, despite these recommendations, widespread adoption of these policies has been difficult. In this 2-part report, we present an updated review of the evidence and the recommendations. We also highlight possible future avenues of exploration. Changes in practice and implementation of policy are left to the discretion of the reader.

Back to Basics: The Physiology of Fetal-to-Newborn Transition

To truly understand the differences between DCC and ECC, we need to go back to the basics and review the physiology of transition from intrauterine to extrauterine life. The clamping and cutting of the umbilical cord are not necessities for this transition to occur; in fact, if we do not cut the umbilical cord, it will dry up and fall off within a few days after birth. (2) In other words, a physiologic closure of the umbilical vein and arteries occurs without the intervention of clamping the cord. The precise mechanism of closure of the umbilical vein and arteries is debated, but it is believed that the arteries constrict first, with arterial flow rapidly diminishing during the first 20 to 25 seconds after birth and becoming negligible by 40 to 45 seconds. This prevents the loss of blood from the infant back into the placenta. (19) The umbilical vein remains open, allowing flow for up to 3 minutes to facilitate transfusion of blood from placenta to the infant. (19)(20) After 3 minutes, flow is insignificant, and placental circulation absolutely ceases by 5 minutes in 95% of infants. (19)(21) Several definitions of ECC vs DCC exist. To simplify things, one could say that ECC is the application of a clamp across the umbilical cord while there is still a significant circulation occurring through the umbilical vessels, and DCC is sometime later, after physiologic closure has begun or has been completed. (2)
During fetal life, only approximately 10% of cardiac output is sent to the lungs, whereas more than 50% of cardiac output is sent to the placenta, the fetal organ of respiration. (10) After birth, the neonatal lungs need to take over as the organ of respiration. To facilitate this transition, a neonate must breathe. The initiation of pulmonary ventilation will stimulate a decrease in pulmonary vascular resistance and lead to the increase in pulmonary blood flow until approximately 50% of neonatal cardiac output is sent to the lungs. (5)(10) If the cord is not clamped and placental transfusion occurs during this transition, many experts believe that the transfused blood smoothly supplies the blood volume needed to fill the pulmonary vessels. (2)(5) Because most healthy infants are able to breathe at birth, increasing pulmonary blood flow and subsequently increasing pulmonary venous return, they are able to handle this transition despite early clamping of the cord. (6)

We do not tend to think of the consequences that early clamping of the cord could have because most healthy newborns tolerate ECC. Cord clamping blocks the umbilical arteries and vein simultaneously. Blocking of the umbilical arteries causes a marked increase in left ventricular afterload because of the removal of the low-resistance placental circulation; with this pressure increase, the foramen ovale is forced shut. (5) Equally important is the cessation of umbilical venous flow that had previously been supplying 50% of the right ventricular filling volume. This leads to a subsequent decrease in right ventricular output by 50% and a proportionate decrease in flow to the left heart via the foramen ovale. (5) Pulmonary ventilation is necessary for a smooth transition because the increased pulmonary blood flow will lead to increased pulmonary venous return and a continued supply of blood to the left side of the heart that will then be able to overcome its newly increased afterload.

In the absence of initiation of pulmonary ventilation or if insufficient blood is present to fill the pulmonary vasculature, ECC can lead to important dangerous consequences. Inadequate ventilation prevents the normal postnatal decrease in pulmonary vascular resistance, increase in pulmonary blood flow, and return of oxygenated blood to the left side of the heart. In this situation, ECC increases left ventricular afterload and stops the delivery of oxygenated blood from the placenta to both the right- and left-sided circulations. Altogether, this leads to a significant decrease in left ventricular output, which may manifest as shock. (2)(5)(6) If insufficient blood is present to supply cardiac output to the lungs, blood may be shunted from other important areas and lead to hypoperfusion injury to sites such as the brain and gut. (20) As a consequence of clinical signs of shock and hypoperfusion, interventions

### Table. Recommendations From Professional Organizations

<table>
<thead>
<tr>
<th>Organization</th>
<th>Recommendation</th>
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<tbody>
<tr>
<td>World Health Organization (2014)</td>
<td>Late cord clamping (approximately 1–3 minutes after birth) is recommended for all births; early cord clamping (&lt;1 minute after birth) is not recommended unless the neonate needs to be moved immediately for resuscitation. (12)</td>
</tr>
<tr>
<td>American College of Obstetricians and Gynecologists (2012)</td>
<td>Evidence supports delayed cord clamping of 30–60 seconds after birth in preterm infants; insufficient evidence exists to support or refute benefits of delayed cord clamping for term infants, particularly in resource-rich areas. (13)</td>
</tr>
<tr>
<td>International Liaison Committee on Resuscitation/Neonatal Resuscitation Program (2010)</td>
<td>Delay in umbilical cord clamping for at least 1 minute is recommended for newborn infants not requiring resuscitation; there is insufficient evidence to support or refute a recommendation to delay cord clamping in infants requiring resuscitation. (14)</td>
</tr>
<tr>
<td>Society of Obstetricians and Gynaecologists of Canada (2009)</td>
<td>When possible, delaying cord clamping by at least 60 seconds is preferred in preterm infants (&lt;27 weeks’ gestation). (16)</td>
</tr>
<tr>
<td>European Association of Perinatal Medicine (2010)</td>
<td>If possible, delay clamping of the umbilical cord for at least 30–45 seconds with the infant held below the mother. (17)</td>
</tr>
<tr>
<td>International Confederation of Midwives (2003)</td>
<td>Endorses waiting until pulsations cease before cord clamping in low-risk pregnancies. (18)</td>
</tr>
</tbody>
</table>

Adapted from Raju. (6)
such as administration of fluid boluses and rapid volume expansion may become necessary. These practices are best avoided in fragile populations, such as the extremely premature, and may be harmful.

Transfusion in DCC and Factors That Affect Transfusion
The total amount of whole blood in the fetal-placental circulation throughout gestation is estimated to be 110 to 115 mL/kg of fetal body weight, with approximately 30 mL/kg of this volume in the placenta at any one time. In the debate on the use of DCC vs ECC, the first question that needs to be answered is whether, through the use of DCC, the neonate actually receives a placental transfusion. Research on this subject goes back to the 1960s, in the work of Alice Yao and John Lind. In their 1969 study, blood volume of infants and placental residual blood volume was measured in 111 full-term infants at varying cord clamping times. They found infant and placental blood volume distributions of 67% and 33% at birth, 80% and 20% at 1 minute, and 87% and 13% at 3 minutes, respectively, providing evidence that placental transfusion occurs (Figure 1). A study of term infants in which placental transfusion was estimated by measuring infant weight gain in the first 5 minutes after birth while the cord was left intact found that the mean transfusion of blood was 81 mL, or 25 mL/kg, predicting that placental transfusion could account for 24% to 40% of the total potential blood volume at birth. Present in this additional blood volume are iron-rich red blood cells and stem cells.

Key factors that affect the volume of placental transfusion are time, gravity, uterine contractions, and onset of respirations. Studies have found that in an infant held at the level of the introitus, the beginning rate of placental transfusion is rapid and slows in a stepwise fashion; approximately 25% of the transfusion occurs in the first 15 to 30 seconds, 50% to 78% by 60 seconds, and the remaining amount by 3 minutes (Figure 2). As this finding suggests, the location of the infant during DCC affects the volume of blood transferred as well. It is known that gravity affects speed of placental transfusion but not the overall amount of placental transfusion; placement on the maternal abdomen will slow transfusion compared with being held well below the level of the placenta. If the infant is held higher than cord venous pressure, no blood will flow to the infant at all, and, in fact, there may be reverse flow if the infant is held high enough. Generally, it is thought that holding the infant within 10 cm above (on the maternal abdomen) to 10 cm below the placenta (near the level of the introitus) will lead to completion of placental transfusion within approximately 3 minutes (Figure 3). The presence of uterine contractions will speed up placental transfusion as well, and the administration of uterotonic medications is safe during DCC. As reported by Mercer and Erickson-Owens, in 1974 Yao found that the use of an intravenous uterotonic at birth increased the rate of placental transfusion without causing overtransfusion. In regard to onset of respiration, the size of the transfusion is reduced if cord clamping occurs before the onset of respiration, and transfusion is accelerated by the onset of breathing. (2)
Concerns About Using DCC

Despite an increasing body of research that seems to argue for the safety and efficacy of the use of DCC (detailed in part 2 of this review), the adoption of DCC as a standard practice has been sluggish. Concerns about excessive transfusion, polycythemia, and hyperbilirubinemia, particularly in the term infant, exist. These specific concerns are addressed in part 2 of this review. Others are concerned that a delay in cord clamping will lead to a subsequent delay in resuscitation and poorer outcomes in asphyxiated infants or those infants in cardiorespiratory failure. (6) The question of the effect of a delay in cord clamping on the results of cord blood gases has been investigated as cord gases have become a tool for quality control in addition to having medicolegal implications. (2)(23) Finally, with more mothers opting for cord blood banking, concerns exist that a delay in cord clamping will interfere with and leave insufficient amounts of blood for cord blood banking. (2)(6)

Neonatal Resuscitation and DCC

The delay in initiation of resuscitation as a concern has prompted many to come up with the following solution: if resuscitation is required, start resuscitation while the cord is still intact. As suggested by Mercer and Erickson-Owens, “it does not seem logical to cut the cord immediately and remove a non-breathing infant from his only source of respiratory support.” (10) One such situation in which an asphyxiated infant may certainly benefit from DCC is the infant with a tight nuchal cord. In this situation, selective intermittent occlusion of the thin-walled umbilical vein occurs, preventing oxygenated blood from the placenta from flowing to the infant. At the same time, the thicker-walled arteries stay somewhat patent, allowing blood to flow out of the infant and into the placenta. Therefore, clamping the umbilical cord directly after delivery without allowing for some unimpeded placental transfusion may actually reduce the amount of circulating blood volume and promote the development of shock in these infants. (6) A similar example is an infant with shoulder dystocia. (10) It seems that, in particular, asphyxiated infants or those infants in cardiorespiratory failure would benefit from the additional oxygenated blood volume from a placenta that continues to perform gas exchange. (5) In 1969, Philip et al (24) found that in asphyxiated infants who had their cords cut early, residual placental blood volume was lower than that of nonasphyxiated infants who had their cords cut early. This finding suggested that a physiologic in utero transfusion had occurred in these asphyxiated infants. These results were confirmed a few years later by Yao and Lind, who found that not only was residual placental blood volume lower in term asphyxiated infants but also the mean blood volumes in these infants were significantly greater than the mean blood volumes of normal term infants whose umbilical cords were clamped at comparable times after birth. In fact, the mean blood volumes in these asphyxiated infants were close to the values of mean blood volumes in term, nonasphyxiated, late clamped infants. (25)

If advanced resuscitation is indicated, several groups have found that interventions can be initiated with the cord still intact with some imagination and flexibility. In fact, providing ventilation to inflate the lungs may increase venous return to the heart, thereby promoting placental transfusion. Aladangady et al were able to initiate resuscitation, including intubation of 2 infants, while allowing for DCC. (26) Options for initiation of resuscitation with an intact cord include beginning resuscitation between a mother’s legs or use of a portable trolley that can be placed at the mother’s bedside. (2)(20) In this way, the neonatal clinicians may assess the newborn and begin positive pressure ventilation if indicated. (2)

Cord Blood Gases and DCC

De Paco et al compared umbilical cord arterial and venous blood gases in term infants randomized to 2 minutes of DCC or ECC and found that the only significant difference
between groups was a slightly higher $P_{O2}$ in the DCC group. (27) In a slightly different study design, Valero et al compared cord blood gases collected immediately after delivery to cord blood gases collected at the time that umbilical cord pulsation ceased in the same infants. (18) They found that cord gases collected after cessation of pulsation revealed significant decreases in pH, oxygen saturation, bicarbonate, and base excess, with an increase in lactate and $P_{CO2}$. (18) Therefore, to obtain cord gas values that will truly reflect fetal status at the time of delivery, there is a need for collection of cord blood gases immediately after delivery. Andersson et al attempted to address the concern that accurate and reliable early cord blood gases could be obtained while still practicing DCC. (23) They introduced a technique in which cord gas sampling from the unclamped pulsating cord is obtained, allowing for cord gas sampling and a delay in cord clamping. In an evaluation of 189 women who underwent ECC (cord gas sampling performed per standard double clamp technique) and 193 women who underwent DCC (cord gas sampling performed using the new technique within 30 seconds of delivery), they found that although the proportion of obtained paired arterial and venous blood gas samples was lower in the DCC group, there was no significant difference between the 2 groups in the proportion of valid paired samples that were obtained, pH, $P_{CO2}$, lactate, base deficit, or bicarbonate levels. The $P_{O2}$ was significantly higher in the DCC group. (23)

**Cord Blood Banking and DCC**

Private and public cord blood banking has become more popular among delivering mothers in the past several years because the use of stem cells from the cord blood can be used for treatment of certain medical diseases. Current methods of cord blood banking rely on the collection of a sufficient volume of residual placental blood to be successful. (2) The DCC results in much smaller residual placental blood volumes and, therefore, less available blood for banking. Farrar et al found that after a physiologic transition, only approximately $20 \pm 10$ mL of blood remains in the placenta, which is rarely a sufficient amount for cord blood banking. (21) For the future, current stem cell transfusion technology is beginning to combine cord blood donations to obtain an adequate amount for transfusion, which would support the collection of these smaller volumes. (10) Currently, the American Academy of Pediatrics does not support the practice of cord blood banking unless there is a clear medical need within the family, (28) and the American College of Obstetricians and Gynecologists states that collection of cord blood should not alter routine practice for the timing of umbilical cord clamping. (19)(29) Ultimately, this decision is left to the delivering mother and her provider, who need to determine the best use and ultimate recipient for the cord blood.

**Conclusions**

Immediate clamping of the umbilical cord after delivery evolved into standard care without sufficient evidence to support or refute its practice. As reviewed here, a significant transfusion from the placenta to the newborn occurs when clamping is delayed. This transfusion may have important implications for the newborn’s successful postnatal physiologic transition. In part 2 of this article, we review the evidence from trials of early vs delayed umbilical cord clamping in preterm and term infants and their mothers. We also present alternative methods of placental transfusion and a summary of unanswered questions.

**American Board of Pediatrics Neonatal–Perinatal Content Specifications**

- Know the role of the placenta in gas exchange and oxygenation of the fetus.
- Know the factors affecting and regulating the systemic circulation in the fetus (including umbilical vessels) and newborn infant during the transitional period.

**References**

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