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Original Review

Is It Time to Rethink Cord Management When Resuscitation Is Needed?

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A newborn who receives a placental transfusion at birth, either from cord milking or delayed cord clamping, obtains about 30% more blood volume than the newborn whose cord is cut immediately. Receiving an adequate blood volume from placental transfusion at birth may be protective for the distressed neonate as it prevents hypovolemia and can support optimal perfusion to all organs. New research shows that ventilating before clamping the umbilical cord can reduce large swings in cardiovascular function and help to stabilize the newborn. Hypovolemia, often associated with nuchal cord or shoulder dystocia, may lead to an inflammatory cascade and subsequent ischemic injury. A sudden unexpected neonatal asystole at birth may occur from severe hypovolemia. The restoration of blood volume is an important action to protect the hearts and brains of these neonates. Current protocols for resuscitation imply immediate cord clamping and the care of the newborn away from the mother's bedside. We suggest that an intrapartum care provider can achieve placental transfusion for the distressed neonate by milking the cord several times or resuscitating the neonate at the perineum with an intact cord. Milking the cord can be done quickly within the current Neonatal Resuscitation Program guidelines. Cord blood gases can be collected with delayed cord clamping. Bringing the resuscitation to the mother's bedside is a novel concept and supports an intact cord. Adopting a policy for resuscitation with an intact cord in a hospital setting will take concentrated effort and team work by obstetrics, pediatrics, midwifery, and nursing.
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INTRODUCTION

Delayed umbilical cord clamping (DCC) or umbilical cord milking offers a newborn approximately 30% more blood volume at birth.[1] This transfusion results in higher ferritin levels and iron stores in full-term neonates aged from birth to 4 to 6 months.[2,3] The most recent meta-analysis informs us that preterm neonates who receive a placental transfusion at birth, either from DCC or umbilical cord milking, are less likely to need a transfusion in the early weeks of life and are offered some protection against intraventricular hemorrhage.[4] In 2012, the American College of Obstetricians and Gynecologists published a statement recommending DCC for preterm neonates and for full-term neonates in low-resource areas.[5] This statement was endorsed by the American Academy of Pediatrics in 2013.[6] A recent review offers background information on the mechanisms, benefits, risks, and techniques for delaying umbilical cord clamping at birth.[7]

But what about the newborn who needs resuscitation? Most are limp, pale, and without muscle tone, suggesting that hypovolemia plays a role in their condition. This article presents a coherent set of ideas and evidence from physiologic studies, clinical trials, and clinical practice showing how placental transfusion at birth allows the newborn to receive more protective blood volume. For the newborn needing resuscitation, the blood volume gained from DCC or umbilical cord milking has the potential to stabilize the cardiovascular system, reduce the severity of an inflammatory response, reduce or prevent damage from hypoxia/ischemia, and help keep the newborn from harm. A discussion of the role of blood volume in neonatal transition and the effects of hypovolemia on the newborn are reviewed. An explanation is offered for the causes of low heart rate or cardiac asystole immediately after birth. The process of inflammation and a possible etiology of seizures are described, along with techniques to achieve a placental transfusion when the newborn needs resuscitation. Our hypothesis is that an adequate blood volume, supported by DCC, plays a major and positive role in the neonatal transition.[8]

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THE EFFECT OF PLACENTAL TRANSFUSION IN FETAL-TO-NEONATAL TRANSITION

Blood volume cannot be measured in human neonates without invasive procedures[9]; therefore, the figures most frequently quoted are from the 1960s, when neonates' blood volume was studied with radioactive tracers. The inability to quantitatively measure blood volume has hampered current study concerning how DCC and blood volume may affect neonatal transition. However, results from an innovative study on neonatal transition using a lamb model support the idea that cardiovascular changes are smoother in fetal-to-neonatal transition with DCC.[10] We offer a brief review of transitional physiology to help explain how DCC can benefit a neonate who needs resuscitation at birth. Additional information about this is available in recent review articles.[7,11]

The Physiology of Fetal-to-Neonatal Circulation

Throughout pregnancy, the fetal blood volume is approximately 115 mL/kg.[12] In a preterm fetus, about one-half of the blood is circulating in the placenta at any point in

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Quick Points

- ✦ Placental transfusion at birth results in approximately 30% more blood volume for most newborns, improving perfusion to all organs.
- ✦ Newborns who require resuscitation need a placental transfusion as much or more than healthy newborns.
- ✦ Hypovolemia can cause low heart rate, asystole, inflammation, and hypoxia/ischemia in the newborn.
- ✦ Umbilical cord milking can be performed quickly by the intrapartum care provider within the current recommended resuscitation timeline before clamping the umbilical cord.
- ✦ Resuscitation with an intact umbilical cord, although routine in out-of-hospital settings, will take a concentrated effort and teamwork in a hospital setting.

time. At full term, approximately two-thirds of the blood is circulating in the fetus, and at any point in time, one-third of the blood is circulating in the placenta.[1]

In fetal circulation, approximately 10% of the fetal cardiac output goes to the lungs, and 30% to 50% goes to the placenta, where gas exchange takes place. In order to change from placental gas exchange to lung air exchange at birth, 50% of the newborn cardiac output must rapidly go to the lungs.

Three anatomic shunts allow fetal circulation: the ductus venosus, the foramen ovale, and the ductus arteriosus. Deoxygenated blood travels to the placenta via the umbilical arteries, and oxygenated blood returns to the fetus via the umbilical vein. Approximately 60% of the oxygenated blood bypasses the liver via the ductus venosus and travels to the right atrium via the inferior vena cava. In the right atrium, the oxygenated blood streams preferentially across the atrium through the foramen ovale and into the left atrium where it is pumped into the left ventricle and into the ascending aorta. The majority of this more oxygenated blood is delivered to the heart and brain. Desaturated blood also arrives at the right atrium from the superior and inferior venae cavae. This blood travels with the oxygenated blood, but in the right atrium it is streamed toward the right ventricle instead of through the foramen ovale. The right ventricle empties into the pulmonary artery; however, due to high pulmonary vascular resistance in the fetus, only 10% of the blood that goes to the pulmonary artery flows into the lungs.[13,14] The remaining 90% of this blood flows through the ductus arteriosus and into the descending aorta.

At birth, the 3 shunts must close quickly so that the lungs can assume the function of oxygenation and receive the blood that was previously going to the placenta. In order to initiate respiration and for these shunts to close, a dramatic fall in pulmonary vascular resistance and an 8- to 10-fold increase in pulmonary blood flow must occur.

When the umbilical cord is clamped immediately at birth, there is cessation of flow to the umbilical vein leading to the ductus venosus. This abrupt halt in the umbilical circulation causes a dramatic, albeit transient, drop in heart rate and more than a 50% fall in right ventricular output.[10] Bhatt et al randomized 12 preterm lambs to either clamp first, followed by ventilation or to vent first, followed by umbilical cord clamping. Ventilation was controlled so that it could be manipulated to occur before or after clamping. Upon umbilical cord clamping, lambs in the clamp-first group experienced a large drop in heart rate and right ventricular output as well as a rise in carotid artery pressure and flow and higher pulmonary artery pressures (Figure 1). Lambs in the vent-first group did not experience the large swings in heart rate, pressures, and flows. They instead had higher pulmonary blood-flow levels and right ventricular output up to 30 minutes after birth, representing higher blood volume circulating through their lungs and body. These results show improved cardiovascular function and stability during neonatal transition when ventilation (or respiration) occurs before umbilical cord clamping. This study suggests that delaying umbilical

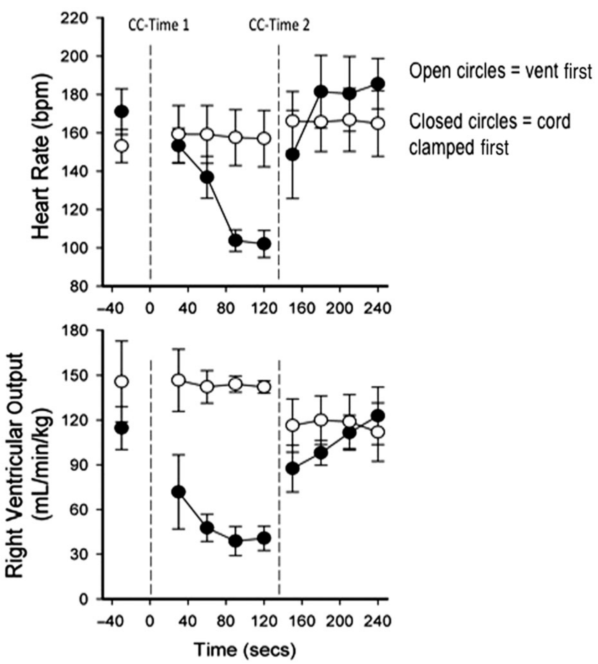

Figure 1. Ventilation Before Cord Clamping Stabilizes the Cardiovascular Transition at Birth
Lambs ventilated after cords were clamped (CC: Time 1 and closed circles) had a drop in pulse and RVO of more than 50%. Lambs ventilated before the cords were clamped (CC: Time 2 and open circles) had stable pulse and RVO.

Abbreviation: CC, cord clamped; RVO, right ventricular output.
Adapted with permission from Bhatt.[10]

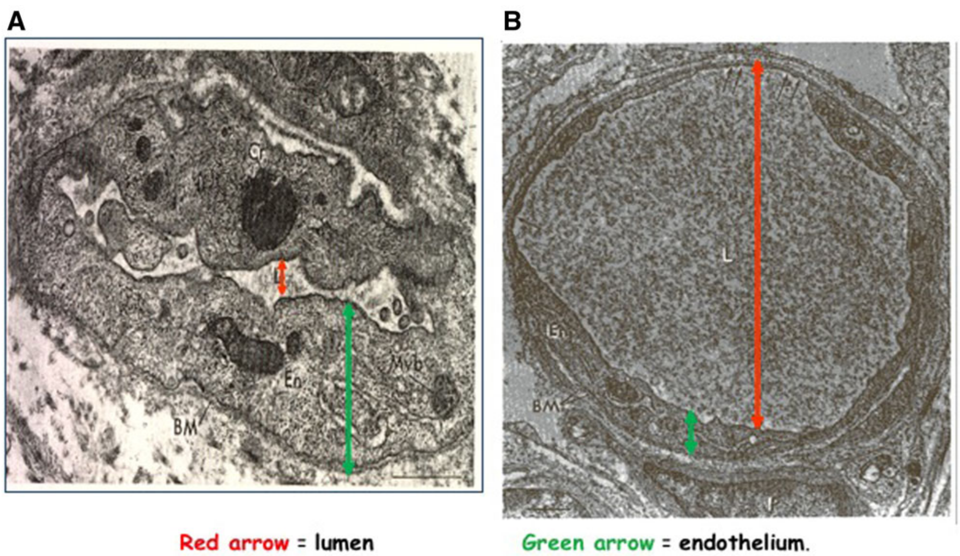

Figure 2. **Heel Capillaries from Newborns with Early and Late Cord Clamping**
Capillaries shown are the width of one red blood cell. Capillary A shows a thick endothelium with a collapsed lumen. Capillary B shows a thin endothelium and a full lumen. Small fenestrations can be seen at the top of the capillary, which would allow for the rapid transfer of nutrients and waste products.

Adapted with permission from Pietra.[18]

cord clamping until after ventilation could have beneficial effects for newborns requiring respiratory assistance.

In summary, new evidence shows us that ventilation (or respiration) before umbilical cord clamping results in a smoother, more stable cardiovascular transition for the newborn and also results in higher blood flow in the heart and lungs. Placental transfusion allows for increased blood in the circulatory beds in the lung as it changes from an organ of fluid excretion to an organ of gas exchange.

Neonatal Perfusion Following Placental Transfusion

Classic physiologic studies completed over the past 60 years document that placental transfusion results in improved perfusion in the neonate's hematologic, urinary, gastrointestinal, neurological, and respiratory systems, as shown in Table 1.[15–17] This improved perfusion was demonstrated in an earlier study by Petra et al.[18] Heel capillaries were biopsied at 2 to 5 hours after birth from 12 neonates who had either immediate cord clamping (ICC) or DCC (when pulsations ceased). As seen in Figure 2, the capillaries are about the width of one red blood cell. In capillary A, the lumen is very small and irregular, whereas the endothelium is thick. In capillary B, the lumen is large and full, whereas the endothelium is thin, allowing for maximal exchange of nutrients and waste products. There were significantly more capillaries found resembling capillary A in the neonates who received ICC and more resembling capillary B in the neonates who experienced DCC, suggesting better blood volume and perfusion with DCC. The heels are usually the last area of the body to be well perfused, so it can be assumed that other more vital areas such as the brain and heart are also better perfused when the neonate receives a placental transfusion.

THE EFFECTS OF INDIVIDUAL COMPONENTS OF PLACENTAL TRANSFUSION

The 30% more blood volume that a newborn receives from a placental transfusion contains iron-rich red blood cells, stem cells, and plasma volume as well as other substances that play a role in the newborn's adaptation to life outside the womb. For a 3-kg newborn, this represents between 50 mL and 85 mL of fresh whole blood containing a large number of red

Table 1. **Characteristics of Neonates with Euvolemia Versus Hypovolemia**

Euvolemia (Placental Transfusion)	Hypovolemia (Immediate Clamping)
↑ Blood pressure[a,b]	↓ Blood pressure
↓ Vascular resistance[b]	↑ Vascular resistance
↑ RBC flow to brain (18%) and to gut (20%)[b]	↓ RBC flow to all organs
↑ Renal blood flow[c]	↓ Renal blood flow
↑ Urine output[c]	↓ Urine output
↓ Sodium excretion[c]	↑ Sodium excretion
↑ Pulmonary vasodilatation[a]	↓ Pulmonary vasodilatation
↑ RCV, Hct, Hb[a,b]	↓ RCV, Hct, Hb

Abbreviations: Hct, hematocrit; Hb, hemoglobin; RBC, red blood cell; RCV, red cell volume. The arrows signify increase and decrease.
[a]Source: Oh et al.[16]
[b]Source: Nelle et al.[15]
[c]Source: Oh et al.[17]

blood cells. These help prevent newborn anemia and may have a positive impact on brain development. Placental transfusion also delivers several million to 1 billion stem cells, resulting in an autologous stem cell transplant for the newborn.[19] Approximately 20 mL/kg to 30 mL/kg or 60 mL to 120 mL of plasma is available for volume expansion and circulatory support, respectively.[1] Other substances in cord blood such as hormones and cytokines are not discussed here.

Red Blood Cell Transfusion

The newborn who receives a placental transfusion obtains about 15 mL/kg of red blood cells—50% more than a newborn who has ICC. Because 80% of the iron in the human body resides in the red blood cells, this amount provides enough iron to meet the newborn's needs for 3 to 6 months.[2,20] Prior concerns that the increase in red blood cell volume made available by placental transfusion would lead to increased symptomatic polycythemia or jaundice have not been substantiated in any of the randomized trials conducted since 2000.[7]

Clamping the umbilical cord immediately can result in low red blood cell volume, potentially leading to iron deficiency in newborns.[2] Even if the hemoglobin level is within normal range, iron deficiency due to low iron stores can have negative effects.[21] Shafir et al found that, at one year of age, iron deficiency without anemia negatively influenced motor development.[22] Lozoff found that, even 20 years after infants received successful treatment for iron deficiency, the individuals scored lower in cognitive, motor, social-emotional, and neurophysiologic development.[23,24] Lozoff reported an average drop in intelligence quotient (IQ) of 25 points at age 19 years if the individual experienced the double burden of iron deficiency in infancy and low socioeconomic status.[23] To date, no studies have looked at developmental indices beyond 6 months in newborns with DCC versus those in newborns with ICC, although such a study is underway.[25]

The negative effect of iron deficiency on the developing brain may be related to iron's essential role in the maturation of oligodendrocytes; low iron availability may impede their development.[26] Oligodendrocytes are the brain cells that make myelin by forming sheaths around axons, thereby creating the brain's white matter. Myelination is essential for the development and proper functioning of the nervous system and forms an electrical insulation around the brain's axons, which allows for the rapid transmission of signals through the nerve cells. Hypomyelination is a noted feature found on the brain scans of children with autism and other developmental impairments, which is why this issue is a high priority.[27,28]

Stem Cell Transfusion

Placental transfusion offers an autologous stem cell transplant containing a high volume of stem cells.[19] Animal studies show that human umbilical-cord blood stem cells will selectively repair damaged areas in the body such as the heart and brain.[29] Cytokines (signaling proteins that are released from damaged tissues) summon stem cells to damaged areas for repair.[30] The role of these cells in vivo in human neonates is difficult to study and remains unclear. However, animal studies indicate that cerebral damage can be prevented by the infusion of human umbilical cord blood within 24 hours after induced brain injury in rats.[29] Preliminary studies are underway to examine the effect of stem cell infusions for human neonates with brain damage at birth.[31] Some scientists suggest that the stem cells received at birth from DCC or umbilical cord milking may play an important role throughout a person's lifetime.[19]

FACTORS AFFECTING THE AMOUNT AND SPEED OF PLACENTAL TRANSFUSION

Factors that affect the amount and speed of the placental transfusion include the timing of umbilical cord clamping, the level that the newborn is held in relation to the placenta, uterine contractions, and milking the umbilical cord.[32–34] Holding the newborn above the placenta slows transfusion, whereas lowering the newborn hastens transfusion.[1,32] Uterine contractions aid in emptying the placenta, as does the use of oxytocics. The umbilical cord can be milked in order to speed placental transfusion in situations when an intrapartum care provider feels that a wait is unwise (Table 2). When the umbilical cord is milked, newborns receive almost as much of their placental blood as when umbilical cord clamping is delayed.[35] Some intrapartum care providers are hesitant to milk the umbilical cord out of fear that it may be harmful. However, when milking is used in both full-term and preterm newborns, available literature shows the same early benefits as DCC and an absence of harm.[4,35–38]

HYPOVOLEMIA IN THE NEWBORN

The authors' interest in the subject of placental transfusion began with a newborn born with a double nuchal cord who was extremely pale and lifeless and who was resuscitated with an intact cord during a home birth. This case represents our first experience of resuscitation with an intact umbilical cord. A description of the case, along with other relevant case reports, can be found in a previously published article.[39]

In hospital settings, this newborn would have been managed with ICC to accommodate resuscitation by neonatal staff at the warmer. The neonatal resuscitation program (NRP) guidelines presume ICC.[40] This case demonstrated the value of the placenta as a source of blood transfusion for a volume-depleted (hypovolemic) newborn. Immediate clamping of the umbilical cord may have inflicted harm by preventing the reperfusion of this pale, lifeless newborn. In an out-of-hospital setting, cutting the umbilical cord immediately might have resulted in an unsuccessful resuscitation. In a survey of American College of Nurse-Midwives members on umbilical cord clamping practices, midwives have described positive experiences with the resuscitation of a newborn with an intact umbilical cord in home birth and birth center settings.[41]

Nuchal Cord and Shoulder Dystocia

The literature demonstrates that cutting a tight nuchal cord before birth can result in hypovolemia and neonatal anemia. Cashore and Usher used radioactive tracers to measure blood volume in newborns with tight nuchal cords who were anemic, pale, hypotensive, tachycardiac, and had low Apgar scores at birth. They found significant reductions (20%) in

Table 2. Cord Management Procedures

Delayed Umbilical Cord Clamping
Vaginal birth
Newborn held below level of perineum
Hold the healthy, dried newborn below the level of the perineum or place on a clean, dry underpad on the bed.
Wait at least 2 minutes before clamping and cutting the umbilical cord.
Newborn held skin-to-skin
Place the healthy, dried newborn on the mother's bare abdomen and cover with a warm blanket.
Clamp and cut the umbilical cord after it is flat and lifeless (approximately 5 minutes).
Cesarean
Place the healthy, dried newborn on the sterile drape between the mother's thighs (below level of placenta).
Wait at least 2 minutes before clamping and cutting the umbilical cord.
Milking the Umbilical Cord
Vaginal birth
Hold the newborn below the level of the perineum or place on a clean, dry underpad on the bed.
Compress the umbilical cord between thumb and forefinger near the perineum.
While maintaining pressure, slide thumb and forefinger down toward the newborn's umbilicus.
Repeat 5 times and then clamp and cut the umbilical cord.
Cesarean
Place newborn on the sterile drape between the mother's thighs (below level of placenta).
Compress the umbilical cord between thumb and forefinger near the insertion site of the umbilical cord on the placenta.
While maintaining pressure, slide thumb and forefinger down toward the newborn's umbilicus.
Repeat 5 times and then clamp and cut the umbilical cord.

red blood cell volume.[42] In a large Canadian cohort study (more than 10,000, full-term liveborn newborns), neonates born with a nuchal cord cut before birth weighed approximately 67 g less than did neonates born without a nuchal cord (mean [SD] of 3481 [467] vs 3548 [475] g; $P < .001$). It is probable that more than an average of 60 mL of blood remained in the detached placenta due to prebirth umbilical cord clamping.[43]

A review of case reports shows that shoulder dystocia and the presence of a nuchal cord can be especially dangerous for a newborn. Of 9 case reports of shoulder dystocia in which the nuchal cord was cut before the birth, Iffy et al found that all newborns had poor Apgar scores and developed signs of hypoxic ischemic encephalopathy.[44,45] All births occurred within 3 to 7 minutes after birth of the head. Seven out of 9 newborns developed cerebral palsy. Iffy, an obstetrician, recommended that the nuchal cord not be cut before birth of the shoulders. In another case report of a shoulder dystocia, the obstetrician had almost cut the nuchal cord before receiving assurance of a vaginal birth.[46] The obstetrician was able to slip the umbilical cord over the head. However, the obstetrician could not deliver the shoulders. The Zavanelli maneuver was used, and Apgar scores after cesarean were 3,[1] 7,[5] and 9.[10] In summary, the practice of cutting the nuchal cord before birth of the shoulders is harmful because it puts the newborn at risk for hypoxic ischemic encephalopathy or death and also puts the intrapartum care provider at medical–legal risk.[47]

Clinical Picture of Newborns with Severe Hypovolemia

Newborns with severe hypovolemia present with a classic presentation. They have very pale, *drained* bodies (or mottled blue and white), lack muscle tone and reflexes, and have no respiratory effort. Usually the heart rate is above 100 bpm, but it may be lower. Experience as expert witnesses with several cases that involved newborns with hypoxic ischemic encephalopathy has led the authors to develop and publish the cardiac asystole theory.[47] This theory offers a hypothesis for why newborns with a good heart rate shortly before birth were born with no heart rate and developed hypoxic ischemic encephalopathy.

Cardiac Asystole Theory

The cardiac asystole theory suggests that, when the large fetus is squeezed tightly in the birth canal and the umbilical cord becomes constricted, blood is sequestered in the placenta—leading to a state of hypovolemia. The pressure on the fetus in the birth canal functions like an antishock garment and helps to maintain central perfusion, keeping a normal pulse and blood pressure even when the blood volume is low.[48] At birth, the sudden release of pressure acts like a fast removal of the antishock garment, and the central blood volume flows rapidly into the peripheral circulation. The newborn's heart stops due to a sudden and severe lack of central perfusion, which results in extreme hypovolemic shock. If the umbilical cord is cut immediately, the newborn can be left with a very low blood volume. The theory suggests that ICC in these cases can result in severe hypovolemic shock, leading to an inflammatory response. It is believed that the inflammatory response is what leads to seizures, hypoxic ischemic encephalopathy, brain damage, or death.[49]

Inflammation Can Be Caused by Blood Volume Loss Alone

Newborns who develop hypoxic ischemic encephalopathy invariably experience brain inflammation during the first week of life.[50] There is evidence that severe blood loss may lead to hypovolemic shock and subsequent ischemia and inflammation.[51] Rajnik (2002) demonstrated in an animal model that the loss of blood volume alone, without infection or reperfusion, can lead to cytokine gene expression—a precursor to inflammation.[51] Rajnik's work corroborates earlier studies showing that a severe reduction in blood volume can stimulate a cytokine cascade, leading to inflammation in a living organism.[49,52,53]

The Inflammatory Cascade

Hypovolemia reduces perfusion to the various organs and creates subtle to overt hypoxia/ischemia. Hypoxia stresses living cells, which leads to an initiation of inflammatory processes. The damage begins in the endothelial cells that line the newborn's blood vessels and alters their normal microvascular function, leading to increased permeability of the vessels. With an ischemic insult such as hypovolemic shock, the injury begins immediately with a significant upregulation of proinflammatory cytokines. Cytokines, which were first mentioned earlier in this discussion, are signaling proteins produced by many different kinds of cells in distress. They send messages between cells, attach to cell walls, and cause cells to change behavior. The intracellular junctions in the endothelium move apart, allowing leakage between intravascular and interstitial tissues, which causes edema to form. Damaged endothelial cells lose their ability to regulate vascular perfusion, permeability, inflammation, and adhesion.[54] The microcirculatory injury continues, and within 24 to 48 hours there is loss of autoregulation.[55] Within 3 days, there is evidence of interstitial invasion of leukocytes, edema, hemorrhage, and fibrin.[56] Ischemic damage is progressive and can continue over several hours, days, and weeks.[57] Loss of these functions has a deleterious effect on the functioning of the target organ—whether it is the lung, liver, brain, or kidney—and can lead to dysfunction and organ failure. The resulting insult in the target organ is manifested by less blood flow, edema formation, vascular congestion, and infiltration of inflammatory cells.[54] Many newborns with hypoxic ischemic encephalopathy have multiple organ injury and/or failure. Hankins reported that 70% to 80% of newborns with hypoxic ischemic encephalopathy had overlapping organ system injury that included cardiac, renal, hepatic, and central nervous system damage.[58] No other mechanism—other than hypoperfusion and ischemia of these organs from blood loss—could cause such devastating damage so quickly. Evidence of long-term effects after resuscitation suggests that, even when a neonate is not ill during the newborn period, long-lasting subtle damage may occur.

Results from animal studies show that a transfusion with fresh whole blood ameliorates the inflammatory response and organ injury after hemorrhagic shock.[52] The authors developed the term *damage control resuscitation* to refer to the use of fresh whole blood after hemorrhagic shock. We suggest that DCC provides fresh whole blood to the newborn in distress. ICC, as used in traditional resuscitation practices, may put the newborn at a higher risk of damage due to reduced blood volume.

Outcomes of Children After Resuscitation

Odd et al (2009) conducted a cohort study (N = 5887) to determine whether newborns who were resuscitated at birth had a reduced IQ (less than 80) at 8 years of age.[59] There were 3 groups of newborns: newborns resuscitated at birth without symptoms of encephalopathy, newborns resuscitated at birth with symptoms of encephalopathy, and newborns not resuscitated at birth and without symptoms of encephalopathy. For newborns resuscitated at birth without symptoms of encephalopathy, the adjusted odds ratio (OR) was 1.65 (95% confidence interval [CI], 1.13-2.43) for a reduced IQ; and for those with symptoms of hypoxic ischemic encephalopathy, the adjusted OR was 6.22 (95% CI, 1.57-24.65), respectively, when compared to the control group of children who were not resuscitated. This study demonstrates that newborns who were resuscitated at birth had an increased risk of a low IQ score even if they were healthy in the neonatal period.[59]

Lindstrom et al (2008) investigated cognitive function and behavioral problems in adolescents (N = 684) who were born at full term in 1985 and who had Apgar scores lower than 7 at 5 minutes.[60] Of the total, 56 adolescents were identified who developed moderate neonatal encephalopathy and survived without cerebral palsy. When aged 15 to 19 years, 43 children whose parents gave permission were evaluated. Only 8 children were without impairments. In 71% of the participants, cognitive dysfunction was found, and 18% of the participants had hearing impairments. Children and parents reported that most of these dysfunctions interfered with daily life.

Both of these studies suggest that conditions leading to the need for neonatal resuscitation and the resuscitation itself may impact developmental outcomes. Currently, when resuscitation is needed, ICC at birth is the routine practice. It is theorized that the additional blood volume received with DCC with an intact umbilical cord or umbilical cord milking during resuscitation may improve long-term outcomes by reducing the severity of or preventing neonatal encephalopathy.

Lessons from Cardiopulmonary Resuscitation in Adults

Recent changes to the adult cardiopulmonary resuscitation (CPR) techniques support the hypothesis that adequate blood volume is a critical first step in human resuscitation. The recommended technique for adult CPR has recently changed to adopt cardiocerebral resuscitation, with emphasis on blood volume to maintain blood pressure and perfusion to the heart and brain.[61] Research using animal models has shown that cardiac arrest survival increased up to 80% when perfusion was supported by continuous chest compressions compared to 13% survival rates with standard CPR (chest compressions and interruptions for breathing).[62] The critical factor in improving survival is brain and heart perfusion secondary to stable blood flow. The new adult CPR guidelines for unwitnessed cardiac arrest support continuous chest compressions to circulate blood without interruption for ventilations.[61] In adults, the goal is to move the existing blood to the heart and brain. In newborns, adequate blood volume is also critical to perfuse and protect the heart and brain. Milking the umbilical cord of a newborn needing resuscitation or resuscitating a newborn with an intact umbilical cord allows the newborn access to at least 30% more blood volume—a step that may be essential for recovery.

CLINICAL PROCEDURES FOR ACHIEVING PLACENTAL TRANSFUSION

There are at least 2 ways to get placental transfusion to the newborn who needs resuscitation: umbilical cord milking or DCC. Refer to Table 2 for procedures. Umbilical cord milking is a simple technique that quickly can be instituted by any intrapartum care provider at any birth.[35] This technique supports the NRP guidelines because within 30 seconds after birth the umbilical cord can be milked and the newborn can be assessed. However, is milking *unnatural*? Yes, but it accelerates the transfer of blood into a pale, limp newborn, which is especially important in a hospital setting. No adverse events from umbilical cord milking have been reported.[4,35–37]

Delayed clamping of the umbilical cord is the standard of care in birth center and home birth settings.[41] If one is conducting the birth in a setting where there is no demand to *pass the newborn off quickly*, a full resuscitation can be conducted without severing the umbilical cord. If the umbilical cord is left intact or milked during resuscitation, reperfusion will occur while the blood remaining in the placenta returns to the newborn's body. If the heart rate is not above 100 bpm, vigorous drying (stimulation) and lowering the newborn below the level of the perineum or milking the umbilical cord can support resuscitative efforts by increasing blood volume. Bag-and-mask ventilation or even intubation can be performed at the perineum (on a clean, dry underpad) without clamping the umbilical cord. Once the newborn has regained muscle tone and color (reperfused) and breathing stabilizes, the newborn can be put skin-to-skin on the mother's abdomen.

Keeping the Umbilical Cord Intact When There Is a Nuchal Cord

Many intrapartum care providers have been taught to double clamp and then immediately cut a tight nuchal cord. We recommend that intrapartum care providers learn to use the somersault maneuver to keep the umbilical cord intact.[63] It is used when a nuchal cord is not easily reducible over the head and is too tight to push down over the shoulders. During birth, the intrapartum care provider keeps the newborn's head close to the perineum (or thigh), "folding" the newborn up toward the symphysis. The umbilical cord is gently unwound from around the neck. If the newborn has poor muscle tone or is very pale, the newborn should be placed on the bed and dried and stimulated while receiving placental transfusion (via umbilical cord milking or DCC) until muscle tone returns and the newborn is breathing. Resuscitation can be performed at the perineum, as described previously.

Bringing the Resuscitation to the Newborn

In order to provide resuscitation with an intact cord, Hutchon et al devised a way to bring the resuscitation equipment to the newborn.[64] They have developed a small stand (trolley) that provides a stable, warmed platform for resuscitation of the newborn with an intact umbilical cord. This allows for additional support of the placental transfusion that is providing volume and red blood cells for improved oxygenation. The trolley is compact and allows for hands-free height adjustment. Suction, blender, and a continuous positive airway pressure (CPAP) device can all be easily mounted on the unit. A timer allows staff to keep track of the period after birth. Other equipment such as a pulse oximeter can be added to suit local practice. This trolley enables the newborn to have the support of the placenta and the available blood while resuscitation with the intact umbilical cord is underway. The trolley can be positioned very close to a labor bed or to an operating table. The layout ensures that access for the clinical team is not compromised and that the newborn's airway can be easily established.[65] The trolley is currently being tested at several sites in England (David Hutchon, MD, 2014, written communication). All steps of NRP can be followed when the umbilical cord still is attached to the placenta. There is no substitute for the newborn's own blood.

Blood Gas Sampling During Resuscitation

Umbilical cord gas collection often is required at the birth of a newborn needing resuscitation. Blood easily can be collected from the intact umbilical cord in the same manner used for detached umbilical cords. Andersson et al, in a recently published randomized controlled trial of 382 healthy full-term newborns, successfully collected umbilical cord blood gas samples from newborns with DCC of 180 seconds (n = 130) and from newborns newborns with ICC (n = 139).[66] In the DCC group, arterial and venous umbilical cord gas samples were collected within 30 seconds after birth. In the ICC group, similar samples were drawn from a segment of the umbilical cord by 10 minutes after birth. A 25- or 27-gauge needle was used, and leakage from the punctured umbilical cord was minimal. Each sample was analyzed within 20 minutes, and no significant differences between the 2 groups were reported with the exception of a lower arterial oxygen tension level that was noted in the ICC group.

MAKING CHANGES IN CLINICAL PRACTICE

Most midwives and other intrapartum care providers who practice within out-of-hospital settings already resuscitate newborns with an intact umbilical cord.[41] They believe that clamping or cutting the umbilical cord on a nonbreathing newborn is an unsafe practice. However, in most hospitals the policy is to immediately *cut the cord and run* to a warmer with a distressed newborn. Umbilical cord milking can be performed by any intrapartum care provider at any time; however, midwives and other intrapartum care providers cannot adopt DCC for newborns needing resuscitation without a major policy change because it requires the neonatal team to resuscitate at the bedside. Teamwork is essential; it is important that midwives and other health care providers start these discussions long before the need arises. Changing policy within a hospital setting is discussed at length in a recent review article by Mercer and Erickson-Owens.[7]

Currently, little research is being done on resuscitation with an intact umbilical cord. In California, a proposed study involving preterm neonates will have the attending neonatologist provide 2 sustained inflations and CPAP before the obstetrician clamps the umbilical cord (Anup Katheria, MD, written communication, 2013). According to the study protocol, the intrapartum care provider will hold the newborn, and the umbilical cord clamping will be delayed for 60 seconds. In England, Hutchon and colleagues are field testing use of the resuscitation trolley in a hospital setting.[64] More research on resuscitation with an intact umbilical cord is needed.

CONCLUSION

This article proposes that receiving an adequate blood volume from placental transfusion at birth is protective for the neonate, especially when distressed. We suggest that neonates who require resuscitation also need their placental transfusion as much or more than do healthy newborns. Placental transfusion plays a major role in neonatal transition by preventing hypovolemia and by providing better perfusion to all organs. Umbilical cord milking can be performed quickly by any intrapartum care provider within the NRP resuscitation guidelines. Adopting resuscitation with an intact umbilical cord in a hospital setting will take concentrated effort and teamwork by midwifery, obstetrics, pediatrics, and nursing.

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CONFLICT OF INTEREST

The authors have no conflict of interests to disclose.

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REFERENCES

1. Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. *Lancet*. 1969;2(7626):871-873.
2. Hutton EK, Hassan ES. Late vs early clamping of the umbilical cord in full-term neonates: Systematic review and meta-analysis of controlled trials. *JAMA*. 2007;297(11):1241-1252.
3. McDonald S, Middleton P, Dowswell T, Morris P. Effect of timing of umbilical cord clamping of term in-fants on maternal and neonatal outcomes. *Cochrane Database Syst Rev*. 2013;7: CD004074. doi: 10.1002/14651858.CD004074.pub3.
4. Rabe H, Jewison A, Alvarez RF, Crook D, Stilton D, Bradley R, et al. Milking compared with delayed cord clamping to increase placental transfusion in preterm neonates: A randomized controlled trial. *Obstet Gynecol*. 2011;117(2 Pt 1):205-211.
5. ACOG. Committee Opinion No. 543: Timing of umbilical cord clamping after birth. *Obstet Gynecol*. 2012;120(6):1522-1526.
6. AAP. Timing of Umbilical Cord Clamping After Birth. 2013; 131(4):1323.
7. Mercer JS, Erickson-Owens DA. Rethinking placental transfusion and cord clamping issues. *J Perinat Neonatal Nurs*. 2012;26(3): 202-217.
8. Mercer J, Skovgaard R. Neonatal transitional physiology: A new paradigm. *J Perinat Neonatal Nurs*. 2002;15(4):56-75.
9. Nalbant D, Bhandary P, Matthews NI, Schmidt RL, Bogusiewicz A, Cress GA, et al. Comparison of multiple red cell volume methods performed concurrently in premature infants following allogeneic transfusion. *Pediatr Res*. 2013;74(5):592-600.
10. Bhatt S, Alison BJ, Wallace EM, Crossley KJ, Gill AW, Kluckow M, et al. Delaying cord clamping until ventilation onset improves cardiovascular function at birth in preterm lambs. *J Physiol*. 2013;591(8):2113-2126.
11. Graves BW, Haley MM. Newborn transition. *J Midwifery Womens Health*. 2013;58(6):662-670.
12. Linderkamp OL. Placental transfusion: Determinants and effects. *Clin Perinatol*. 1982;9:559-593.
13. Kiserud T, Ebbing C, Kessler J, Rasmussen S. Fetal cardiac output, distribution to the placenta and impact of placental compromise. *Ultrasound Obstet Gynecol*. 2006;28(2):126-136.
14. Mielke G, Benda N. Cardiac output and central distribution of blood flow in the human fetus. *Circulation*. 2001;103(12):1662-1668.
15. Nelle M, Zilow EP, Bastert G, Linderkamp O. Effect of Leboyer childbirth on cardiac output, cerebral and gastrointestinal blood flow velocities in full-term neonates. *Am J Perinatol*. 1995;12(3):212-216.
16. Oh W, Oh MA, Lind J. Renal function and blood volume in newborn infant related to placental transfusion. *Acta Paediatr Scand*. 1966;55:197-210.
17. Oh W, Wallgren G, Hanson JS, Lind J. The effects of placental transfusion on respiratory mechanics of normal term newborn infants. *Pediatrics*. 1967;40(1):6-12.
18. Pietra GG, D'Amodio MD, Leventhal MM, Oh W, Braudo JL. Electron microscopy of cutaneous capillaries of newborn infants: Effects of placental transfusion. *Pediatrics*. 1968;42(4):678-683.
19. Tolosa JN, Park DH, Eve DJ, Klasko SK, Borlongan CV, Sanberg PR. Mankind's first natural stem cell transplant. *J Cell Mol Med.* 2010;14(3):488-495.
20. Andersson O, Hellstrom-Westas L, Andersson D, Domellof M. Effect of delayed versus early umbilical cord clamping on neonatal outcomes and iron status at 4 months: A randomized controlled trial. *BMJ*. 2011;343:d7157.
21. Georgieff MK. Long-term brain and behavioral consequences of early iron deficiency. *Nutr Rev*. 2011;69(suppl 1):S43-48.

22. Shafir T, Angulo-Barroso R, Jing Y, Angelilli ML, Jacobson SW, Lozoff B. Iron deficiency and infant motor development. *Early Hum Dev*. 2008;84(7):479-485.
23. Lozoff B, Jimenez E, Smith JB. Double burden of iron deficiency in infancy and low socioeconomic status: A longitudinal analysis of cognitive test scores to age 19 years. *Arch Pediatr Adolesc Med*. 2006;160(11):1108-1113.
24. Lozoff B, Smith JB, Clark KM, Perales CG, Rivera F, Castillo M. Home intervention improves cognitive and social-emotional scores in iron-deficient anemic infants. *Pediatrics*. 2010;126(4):e884-894.
25. Mercer J. *Infant Brain Study*. Bethesda, MD: 2014. http://clinicaltrials.gov/ct2/show/NCT01620008. Accessed February 13 2014.
26. Todorich B, Pasquini JM, Garcia CI, Paez PM, Connor JR. Oligodendrocytes and myelination: The role of iron. *Glia*. 2009;57(5): 467-78.
27. Connor JR, Menzies SL. Relationship of iron to oligodendrocytes and myelination. *Glia*. 1996;17(2):83-93.
28. Zikopoulos B, Barbas H. Changes in prefrontal axons may disrupt the network in autism. *J Neurosci*. 2010;30(44):14595-14609.
29. Meier C, Middelanis J, Wasielewski B, Neuhoff S, Roth-Haerer A, Gantert M, et al. Spastic paresis after perinatal brain damage in rats is reduced by human cord blood mononuclear cells. *Pediatr Res*. 2006;59(2):244-249.
30. Imitola J, Raddassi K, In Park K, Mueller F, Nieto M, Teng Y, et al. Directed migration of neural stem cells to sites of CNS injury by the stromal cell-derived factor 1a/CXC chemokine receptor 4 pathway. *Proc Natl Acad Sci U S A*. 2004;101(52):18117-18122.
31. Cotten M. Cord Blood- Neonatal Hypoxic Ischemic Encephalopathy. 2014. http://clinicaltrials.gov/ct2/show/NCT00593242 Accessed February 20, 2014.
32. Erickson-Owens DA. Placental Transfusion at birth in full-term infants. 6th Annual Normal Labour and Birth Conference. Grange-Over-Sands, England, United Kingdom; 2011.
33. Farrar D, Airey R, Law GR, Tuffnell D, Cattle B, Duley L. Measuring placental transfusion for term births: Weighing babies with cord intact. *BJOG*. 2011;118(1):70-75.
34. Yao AC, Hirvensalo M, Lind J. Placental transfusion-rate and uterine contraction. *Lancet*. 1968;1(7539):380-383.
35. Erickson-Owens DA, Mercer JS, Oh W. Umbilical cord milking in term infants delivered by cesarean section: A randomized controlled trial. *J Perinatol*. 2012;32:580-584.
36. Hosono S, Mugishima H, Fujita H, Hosono A, Minato M, Okada T, et al. Umbilical cord milking reduces the need for red cell transfusions and improves neonatal adaptation in infants born at less than 29 weeks' gestation: a randomised controlled trial. *Arch Dis Child Fetal Neonatal Ed*. 2008;93(1):F14-19.
37. March M, Hacker M, Parson A, Modest A, de Veciana M. The effects of umbilical cord milking in extremely preterm infants: A randomized controlled trial. *J Perinatol*. 2013;33:763-767.
38. Minami H. Cord milking reduces the need for blood transfusions and the incidence of severe intraventricular hemorrhage in infants born before 26 weeks of gestation. *PAS* 2008;Abstract 4450.
39. Mercer JS, Skovgaard R, Erickson-Owens DA. Fetal to neonatal transition: First do no harm. In: Downe S, ed. *Normal Childbirth Evidence and Debate*. 2nd ed. London, UK: Churchill Livingstone Elsevier; 2008.
40. Kattwinkel J. *Neonatal Resuscitation (NRP)*, 6th edition. Washington, DC:AAP and Am Heart Association; 2011.
41. Mercer JS, Nelson CC, Skovgaard RL. Umbilical cord clamping: beliefs and practices of American nurse-midwives. *J Midwifery Womens Health*. 2000;45(1):58-66.
42. Cashore WJ, Usher R. Hypovolemia resulting from a tight nuchal cord at birth. *Pediatr Res*. 1973;7:399.
43. Osak R, Webster KM, Bocking AD, Campbell MK, Richardson BS. Nuchal cord evident at birth impacts on fetal size relative to that of the placenta. *Early Hum Dev*. 1997;49(3):193-202.
44. Iffy L, Varadi V. Cerebral palsy following cutting of the nuchal cord before delivery. *Med Law*. 1994;13:323-330.
45. Iffy L, Varadi V, Papp E. Untoward neonatal sequelae deriving from cutting of the umbilical cord before delivery. *Med Law*. 2001;20(4):627-634.
46. Flamm BL. Tight nuchal cord and shoulder dystocia: A potentially catastrophic combination. *Obstet Gynecol*. 1999;94(5 Pt 2):853.
47. Mercer J, Erickson-Owens D, Skovgaard R. Cardiac asystole at birth: Is hypovolemic shock the cause? *Med Hypotheses*. 2009;72(4):458-463.
48. Miller S, Turan JM, Ojengbede A, Ojengbede O, Fathalla M, Morhason-Bello IO, et al. The pilot study of the non-pneumatic anti-shock garment (NASG) in women with severe obstetric hemorrhage: Combined results from Egypt and Nigeria. *Int J Gynaecol Obstet*. 2006;94(suppl 2):S154-156.
49. Pfeifer R, Litche P, Schreiber H, Sellei RM, Deinstknect T, Sadeghi C, et al. Models of Hemorrhagic Shock: Differences in the Physiological and Inflammatory Response. *Cytokine* 2013;61(2):585-590.
50. Cowan F, Rutherford M, Groenendaal F. Origin and timing of brain lesions in term infants with neonatal encephalopathy. *Lancet*. 2003;361:736-742.
51. Rajnik M, Salkowski CA, Thomas KE, Li YY, Rollwagen FM, Vogel SN. Induction of early inflammatory gene expression in a murine model of nonresuscitated, fixed-volume hemorrhage. *Shock*. 2002;17(4):322-328.
52. Makley AT, Goodman MD, Belizaire RM, Friend LAW, Johannigman JA, Dorlac WC, et al. Damage control resuscitation decreases systemic inflammation after hemorrhage. *J Surg Res*. 2012;175(2):e75-e82.
53. Makley AT, Goodman MD, Friend LAW, Deters JS, Johannigman JA, Dorlac WC, et al. Resuscitation with fresh whole blood ameliorates the inflammatory response after hemorrhagic shock. *J Trauma*. 2010;68(2):305-311.
54. Molitoris BA, Sutton TA. Endothelial injury and dysfunction: Role in the extension phase of acute renal failure. *Kidney Int*. 2004;66(2):496-499.
55. Conger JD, Robinette JB, Schrier RW. Smooth muscle calcium and endothelium-derived relaxing factor in the abnormal vascular responses of acute renal failure. *J Clin Invest*. 1988;82(2):532-537.
56. Leviton A, Dammann O. Coagulation, inflammation, and the risk of neonatal white matter damage. *Pediatr Res*. 2004;55(4):541-545.
57. Volpe JJ. *Neurology of the Newborn*, 4th ed. Philadelphia, PA: Saunders; 2001.
58. Hankins GD, Loen S, Fei AFea. Neonatal organ system injury in acute birth asphyxia sufficient to result in neonatal encephalopathy. *Obstet Gynecol*. 2000;99(5):668-691.
59. Odd D, Lewis G, Whitelaw A, Gunnel D. Resuscitation at birth and cognition at 8 years of age: A cohort study. *Lancet* 2009; 373(9675):1615-1622.
60. Lindstrom K, Hallberg B, Blennow M, Wolff K, Fernell E, Westgreen M. Moderate neonatal encephalopathy: Pre- and perinatal risk factors and long-term outcome. *Acta Obstet Gynecol Scand*. 2008;87(7):503-509.
61. Field JM, Hazinski MF, Sayre MR, Chameides L, Schexnayder SM, Hemphill R, et al. Part 1: Executive summary 2010 American Heart Association Guidelines for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2010;122(18 suppl 3):S640-S656.
62. Ewy GA, Kern KB. Recent advances in cardiopulmonary resuscitation: Cardiocerebral resuscitation. *J Am Coll Cardiol*. 2009;53(2):149-157.
63. Mercer JS, Skovgaard RL, Peareara-Eaves J, Bowman TA. Nuchal cord management and nurse-midwifery practice. *J Midwifery Womens Health*. 2005;50(5):373-379.

64. Hutchon D, Bewley S. Support transition by keeping the placental circulation intact–even in newborns apparently requiring resuscitation. *Arch Dis Child Fetal Neonatal Ed*. 2008;93 (3):F334-F336.
65. Inditherm plc. Neonatal Resuscitation (Life Start). www.inditherm.co.uk/medical/neonatal-resuscitation-lifestart/ Accessed October 3 2013.
66. Andersson O, Hellstrom-Westas L, Andersson D, Clausen J, Domellof M. Effects of delayed compared with early umbilical cord clamping on maternal postpartum hemorrhage and cord blood gas sampling: A randomized trial. *Acta Obstet Gynecol Scand*. 2012;92(5):567-574.

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