

# Early Versus Delayed Cord Clamping in Term and Preterm Births: A Review

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## Abstract

The optimal timing for cord clamping, early versus delayed, in the third stage of labour is a controversial subject. Issues surrounding the timing of cord clamping include gestational age and maternal and neonatal considerations. Delayed cord clamping (DCC) has been shown to increase placental transfusion, leading to an increase in neonatal blood volume at birth of approximately 30%. In the term infant, although this may result in an increase in iron stores, thereby decreasing the risk of anemia, it may adversely increase the risk of jaundice and the need for phototherapy. In the preterm infant, DCC (or even milking of the cord) decreases the need for blood transfusions for anemia, the number of such transfusions, and the risks of intraventricular hemorrhage and late-onset sepsis. Advantages of DCC also include a reduction in alloimmunization in Rh-negative women, although this advantage is theoretical and unproven.

We searched multiple databases including PubMed Clinical Queries, Trip Database, Cochrane Systematic Reviews, and UpToDate, as well as published guidelines from the Society of Obstetricians and Gynaecologists of Canada, the American Congress of Obstetricians and Gynecologists, and the Royal College of Obstetricians and Gynaecologists. We preferentially selected systematic reviews and randomized controlled trials for this literature review.

Overall, the available evidence appears to suggest that DCC is likely to result in better neonatal outcomes in both term and preterm infants, even in areas where neonatal iron deficiency anemia is rare. However, there is insufficient evidence to date to support a recommendation to delay cord clamping in non-vigorous infants requiring resuscitation.

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## Résumé

La détermination du moment optimal pour procéder au clampage du cordon (précoce ou différé) au cours du troisième stade du travail constitue un sujet controversé. Parmi les facteurs entourant la détermination du moment optimal pour procéder au clampage du cordon, on trouve l'âge gestationnel et des considérations maternelles et néonatales. Il a été démontré que le clampage différé du cordon (CDC) entraînait une hausse de la transfusion placentaire, menant ainsi à une hausse de la volémie néonatale à la naissance d'environ 30 %. Chez l'enfant né à terme, bien que cela puisse donner lieu à une augmentation des réserves de fer (atténuant ainsi le risque d'anémie), le risque d'ictère et la nécessité de procéder à une photothérapie pourraient également s'en trouver augmentés. Chez l'enfant préterme, le CDC (ou même la compression du cordon en vue d'en extraire le sang) atténue la nécessité de procéder à des transfusions sanguines en raison d'une anémie, réduit le nombre de telles transfusions et entraîne une baisse des risques d'hémorragie intraventriculaire et de septicémie d'apparition tardive. Parmi les avantages du CDC, on trouve également une baisse du taux d'allo-immunisation chez les femmes séronégatives pour le facteur Rh, bien que cet avantage demeure théorique et non prouvé.

Nous avons mené des recherches dans de multiples bases de données, dont *PubMed Clinical Queries*, *Trip Database*, *Cochrane Systematic Reviews* et *UpToDate*, ainsi que dans les directives cliniques publiées par la Société des obstétriciens et gynécologues du Canada, le *American Congress of Obstetricians and Gynecologists* et le *Royal College of Obstetricians and Gynaecologists*. Au fin de cette analyse documentaire, nous avons accordé une préférence aux analyses systématiques et aux essais comparatifs randomisés.

De façon générale, les données disponibles semblent indiquer que le CDC est susceptible de donner lieu à de meilleures issues néonatales tant chez les enfants nés à terme que chez les enfants prétermes, même dans les régions où l'anémie ferriprive néonatale est rare. Toutefois, nous ne disposons pas à ce jour de données suffisantes pour recommander de différer le clampage du cordon chez les nouveau-nés non vigoureux qui nécessitent une réanimation.

## INTRODUCTION

The third stage of labour is defined as the period of time between the birth of an infant and the complete expulsion of the placenta. The timing for umbilical cord clamping (more specifically, early cord clamping versus

delayed cord clamping) remains a controversial issue and a subject of continuing debate. Possible advantages of ECC include permitting prompt resuscitation and treatment of the newborn,<sup>1</sup> harvesting of stem cells for public blood banking,<sup>1,2</sup> and prevention of potential postpartum hemorrhage,<sup>1,3</sup> although the latter is not viewed as an advantage in the most recent Canadian guidelines.<sup>3</sup> Delayed cord clamping, on the other hand, has been associated with increased placenta-to-neonate transfusion, leading to an increase in neonatal blood volume at birth. This increases iron stores and decreases the risk of anemia, although it may also increase the risk of hyperbilirubinemia and lead to jaundice requiring phototherapy. The objective of this review was to assess the evidence regarding the optimal timing for umbilical cord clamping, outlining maternal and neonatal outcomes in both term and preterm infants.

## **METHODS**

We searched multiple databases including PubMed Clinical Queries, Trip Database, Cochrane Systematic Reviews, and UpToDate, as well as published guidelines from the Society of Obstetricians and Gynaecologists of Canada, the American Congress of Obstetricians and Gynecologists, and the Royal College of Obstetricians and Gynaecologists. We preferentially selected systematic reviews and randomized controlled trials for this literature review. MeSH terms used were “cord clamping,” “timing of cord clamping,” “delayed vs. early cord clamping,” “placental transfusion,” “umbilical cord blood banking,” and “pH cord clamping.”

## **PHYSIOLOGICAL RATIONALE**

Placental transfusion is defined as the amount of blood that flows from the placenta to the infant at birth.<sup>4</sup> A 2011 study weighing babies with the cord intact showed that the maximal mean volume of placental transfusion is between 24 and 32 mL/kg of body weight or an additional 30% to 40% of blood volume.<sup>4</sup> This is in keeping with a study conducted in the late 1960s which showed a placental transfusion of 22.5 mL/kg, or an additional 32% of blood volume after three minutes.<sup>5</sup> Moreover, net placental flow appears to stop at two minutes.<sup>4</sup> The quantity of blood transferred to the infant is thought to be influenced by

several factors: the timing of umbilical cord clamping, gravity, the administration of a uterotonic agent (such as oxytocin), and the milking of the cord.

### **Timing of Clamping**

The definition of ECC and DCC in terms of timing of clamping varies widely and differs between term and preterm births. In term babies, ECC is most often defined as the clamping of the umbilical cord between delivery and one minute after delivery,<sup>6-8</sup> while DCC is defined as clamping anywhere between 30 seconds after delivery and one minute after delivery or after complete cessation of cord pulsations.<sup>6-8</sup> In preterm births, the definitions are more homogenous, with most studies defining ECC as the clamping of the umbilical cord immediately after delivery (within 15 to 30 seconds), while DCC is usually any time beyond 30 seconds after delivery.<sup>7,9,10</sup> DCC can provide the term infant with approximately 30% more blood volume than ECC.<sup>5,8,11</sup> Placental transfusion in preterm infants is much less understood because there is less information available, but the reduction of blood volume following ECC in this population may be greater than in term infants as more blood is sequestered in the placenta,<sup>12</sup> although this may be a proportional increase. One study found that a delay of 30 to 45 seconds in cord clamping in preterm infants resulted in a blood volume of 8.0 to 19.3 mL/kg higher than ECC,<sup>13</sup> whereas another study showed a difference in blood volumes of 11.7 mL/kg with a 30 to 90 second delay in clamping.<sup>14</sup>

### **Effect of Gravity**

Gravity may also play a role in placental transfusion. A study conducted in 1969 showed that lowering the baby at least 10 cm below the level of the introitus decreased the time needed for complete placental transfusion. For term vaginal deliveries, lowering the baby by 40 cm led to complete transfusion within 30 seconds.<sup>5,15</sup> However, a more recent Cochrane review found no reliable studies illustrating the effect of gravity on placental transfusion.<sup>16</sup>

### **Effect of Uterotonic Agents**

How giving uterotonic agents may interact with gravity and placental transfusion is not known. Many studies do not specify the use or timing of a uterotonic agent, thus making it difficult to reach any conclusion regarding their influence on placental transfusion.<sup>7,8</sup> The use of intravenous ergot alkaloids does increase placental transfusion<sup>17</sup>; however, these agents have been replaced by slower acting uterotonics, specifically oxytocin. Farrar et al. showed that the conventional use of oxytocin does not have a substantial effect on the amount of placental transfusion, although this was a small study.<sup>4</sup> This is logical, since intramuscular oxytocin takes three to five minutes to stimulate a uterine contraction, and placental transfusion is usually complete within two minutes.<sup>18</sup>

## **ABBREVIATIONS**

DCC	delayed cord clamping
ECC	early cord clamping
Hb	hemoglobin
PPH	postpartum hemorrhage

## Milking of the Cord

Milking of the umbilical cord four times within 10 to 12 seconds seems to be as effective in terms of placental transfusion as delaying cord clamping.<sup>19</sup> However, this observation is based on one randomized controlled trial in the preterm population only. More research is needed to justify its use in practice.

## CURRENT GUIDELINES

In 2007, the World Health Organization recommended that “the cord should not be clamped earlier than necessary,”<sup>8</sup> but stopped short of specifying what was meant by this statement. In 2008, a Cochrane review showing the effect of the timing of clamping the umbilical cord on maternal and neonatal outcomes in term infants was published.<sup>8</sup> In response to this review, the American Congress of Obstetricians and Gynecologists deemed that “the evidence doesn’t seem sufficiently strong for a change in policy, but it does encourage a relaxed approach to the timing of cord clamping.” In 2009, the Society of Obstetricians and Gynaecologists of Canada published a clinical practice guideline on the management of the third stage of labour, which stated that “whenever possible, delaying cord clamping by at least 60 seconds is preferred to clamping earlier in premature newborns (< 37 weeks’ gestation) since there is less intraventricular hemorrhage and less need for transfusion in those with late clamping (I-A).”<sup>22</sup> “For term newborns, the possible increased risk of neonatal jaundice requiring phototherapy must be weighed against the physiological benefit of greater hemoglobin and iron levels up to 6 months of age conferred by delayed cord clamping (I-C).”<sup>23</sup> They further suggested that ECC is recommended in the case of cord blood banking in order to improve recovery volume.<sup>2</sup>

## MATERNAL OUTCOMES

Primary PPH is defined clinically by the SOGC as any blood loss occurring in the first 24 hours after a delivery that has the potential to cause hemodynamic instability.<sup>2</sup> It occurs in 5% of all deliveries<sup>20</sup> and is the leading cause of maternal death worldwide, with an estimated mortality rate of one maternal death every four minutes or 140 000 per year.<sup>21</sup> However, the mortality rates have significantly decreased in the developed world, due in part to the implementation of active management of the third stage of labour. Many active management protocols include early clamping of the cord,<sup>22</sup> leading some to imply that DCC may increase the chances of PPH. However, immediate versus delayed cord clamping is not universally accepted as part of the management of this stage of labour, with many studies showing no benefit of ECC for the prevention of PPH. Similarly, two recent systematic reviews found no significant difference in the risk of PPH when delayed cord clamping was practised

after delivery of the term infant<sup>7,8</sup> (Table 1). Concern that DCC may increase the risk of PPH may stem from the belief that DCC prolongs the third stage of labour. In fact, placental transfusion may actually decrease the duration of the third stage of labour, since drainage of the placental bed may encourage earlier placental separation and facilitate its delivery.<sup>16</sup> This has yet to be proven, because no significant difference in the duration of the third stage of labour has been shown between ECC and DCC (Table 1).<sup>8</sup>

An additional advantage of DCC is that it decreases the risk of hemolytic disease of the fetus and newborn secondary to Rh(D) alloimmunization.<sup>8,23</sup> The mechanism by which DCC may do this is by promoting more placental transfusion, resulting in less blood remaining in the placenta. Therefore, clamping the cord earlier may be problematic in Rh(D)-negative women because of the increased risk of alloimmunization arising from the higher quantity of fetal blood sequestered in the placenta. This can be important when anti-Rh(D) is unavailable, but because immunoprophylaxis is now given routinely to all Rh-negative women at 28 weeks’ gestation and postpartum, the risk of alloimmunization in general is almost non-existent.<sup>24,25</sup>

## EFFECTS OF DCC IN TERM INFANTS

A number of systematic reviews have examined the risks and benefits of DCC in healthy term infants. These have found an increase in hemoglobin concentration and improved iron status up to six months after birth, thus decreasing the risk of early neonatal anemia and iron deficiency without anemia, even in the developed world.<sup>6-8,26</sup> Iron deficiency has been associated with an increased risk of infection, impaired feeding, and impaired neurodevelopment.<sup>27-29</sup> However, potential implications of reduced iron status in early childhood have not been sufficiently investigated in the context of DCC versus ECC. Whether an increase in iron stores at birth affects a child’s long-term health and development is speculative, and long-term studies are lacking.<sup>27-30</sup> It remains uncertain whether or not there is a true causal link between iron deficiency and poor developmental outcome.<sup>27,31</sup>

The increase in neonatal blood volume seen with DCC has the potential both to increase iron stores and hemoglobin concentrations and to overload the newborn’s system, leading to jaundice. In a recent Cochrane review, the difference in risk between ECC and DCC for the development of jaundice requiring phototherapy was significantly higher in the DCC group, the equivalent of a reduction in risk ratio of 0.59.<sup>8</sup> Conversely, two separate systematic reviews and the most recent RCT found no significant difference in mean serum bilirubin, development of neonatal jaundice, or requirement for phototherapy between these groups.<sup>6,7,26</sup> The review by Hutton and Hassan<sup>6</sup> included non-randomized clinical trials

**Table 1. Summary of outcomes among term pregnancies: delayed versus early cord clamping**

Outcome	Study	Number of studies/ number of patients	Results of DCC, compared with ECC (95% CI)
Postpartum hemorrhage	McDonald and Middleton, 2008 <sup>8</sup>	4/1878	RR 1.22 (0.96 to 1.55)
	Mathew, 2011 <sup>7</sup>	4/1878	RR 0.82 (0.65 to 1.04)
Duration of third stage of labour	McDonald and Middleton, 2008 <sup>8</sup>	1/963	RR 1.00 (0.29 to 3.41)
Neonatal serum ferritin at follow-up	McDonald and Middleton, 2008 <sup>8</sup> ; Hutton and Hassan, 2007 <sup>6</sup>	1/315	MD 11.80 µg/L (4.07 to 19.53)
	Mathew, 2011 <sup>7</sup>	4/857	MD 17.00 µg/L (12.15 to 21.85)
	Andersson et al., 2011 <sup>26</sup>	1/400	MD 45% (23 to 71) <i>P</i> < 0.001
Newborn hemoglobin concentration	McDonald and Middleton, 2008 <sup>8</sup>	3/671	MD 2.17 g/dL (0.28 to 4.06)
	Hutton and Hassan, 2007 <sup>6</sup>	1/354	MD 0.60 g/dL (0.11 to 1.09)
	Mathew, 2011 <sup>7</sup>	4/1059	MD 1.95 g/dL (0.81 to 3.10)
	Andersson et al., 2011 <sup>26</sup>	1/400	MD 1.35 g/dL (0.96 to 1.75)
Neonatal iron deficiency anemia in first 2–4 months	Hutton and Hassan, 2007 <sup>6</sup>	2/119	RR 0.53 (0.40 to 0.70)
	Mathew, 2011 <sup>7</sup>	3/402	RR 0.85 (0.54 to 1.35)
Neonatal iron deficiency	Andersson et al., 2011 <sup>26</sup>	1/400	RRR 0.90 (0.38 to 0.98)
Neonatal hyperbilirubinemia/ clinical jaundice	McDonald and Middleton, 2008 <sup>8</sup>	5/1828	RR 0.84 (0.66 to 1.07)
	Hutton and Hassan, 2007 <sup>6</sup>	2/163	MD 3.81 mmol/L (–17.55 to –25.18)
	Mathew, 2011 <sup>7</sup>	5/2210	RR 1.16 (0.92 to 1.45)
Neonatal jaundice requiring phototherapy	McDonald and Middleton, 2008 <sup>8</sup>	5/1762	RR* 1.69 (1.09 to 2.63)
	Hutton and Hassan, 2007 <sup>6</sup>	8/1009	RR 1.35 (1.00 to 1.81)
	Mathew, 2011 <sup>7</sup>	5/1974	RR 1.28 (0.48 to 3.42)
	Andersson et al., 2011 <sup>26</sup>	1/400	RRR 0.52 (–2.7 to 0.94) <i>P</i> = 0.62
Admission to NICU	McDonald and Middleton, 2008 <sup>8</sup>	3/1293	RR 1.03 (0.56 to 1.90)
	Hutton and Hassan, 2007 <sup>6</sup>	1/185	RR 2.02 (0.63 to 6.48)
	Mathew, 2011 <sup>7</sup>	2/1239	RR 0.96 (0.40 to 2.33)
Neonatal respiratory distress	McDonald and Middleton, 2008 <sup>8</sup>	4/1387	RR 1.01 (0.18 to 5.75)
	Hutton and Hassan, 2007 <sup>6</sup>	3/296	RR 2.48 (0.34 to 17.89)
	Mathew, 2011 <sup>7</sup>	2/1008	RR 0.99 (0.35 to 2.81)
Cord blood pH (arterial)	Wiberg, 2008 <sup>1</sup>	1/70	MD 0.03, <i>P</i> < 0.05

MD: mean difference; RR: relative risk; RRR: relative risk reduction

\*This study compared ECC with DCC, and the RR was adjusted to compare DCC with ECC

in the analysis, and the 2011 study by Mathew<sup>7</sup> did not clearly define the individual trials used in their analysis of outcomes, making it difficult to draw conclusions about the strength of either study. However, the conclusions of Andersson et al.,<sup>26</sup> the most recent and one of the largest studies evaluating neonatal outcomes after DCC, are promising and strengthen the belief that DCC does not increase the risk of hyperbilirubinemia. Aside from this negligible risk of jaundice and need for phototherapy, DCC has not been shown to affect other neonatal outcomes negatively in term infants. Specifically, there are no differences in Apgar scores < 7 at five minutes, rates of NICU admission, or rates of respiratory distress in comparisons of ECC and DCC in healthy term infants (Table 1).<sup>6–8,26</sup>

DCC presents a number of clinically relevant benefits, with minimal (if any) additive risks, even in healthy term

infants. These include decreasing neonatal anemia and iron deficiency, which may have an impact on development. These advantages are also present in populations in which iron deficiency has a relatively low prevalence.<sup>26,32</sup> Therefore, a universal approach to DCC in the term infant can be justified, given the currently available evidence.

### **EFFECTS OF DCC IN PRETERM INFANTS**

The issue of cord clamping in preterm infants is more controversial than in term infants because many clinicians fear that delaying cord clamping may interfere with resuscitation in this more vulnerable population. Many studies show that there are several advantages to delaying cord clamping by more than 30 seconds in preterm infants.<sup>7,9,10,33</sup> Importantly, doing so does not affect their

**Table 2. Summary of outcomes among preterm infants: delayed versus early cord clamping**

Outcome	Study	Number of studies/ number of patients	Results of DCC, compared with ECC (95% CI)
Serum ferritin at follow-up	Mathew, 2011 <sup>7</sup>	1/34	MD 19.00 (−60.93 to 98.93)
Newborn hematocrit	Mathew, 2011 <sup>7</sup>	9/457	MD 3.04 (2.58 to 3.51)
	Rabe et al., 2008 <sup>10</sup>	5/216	MD 3.05 (1.29 to 4.82) <i>P</i> < 0.001
Requirement for transfusions	Mathew, 2011 <sup>7</sup>	6/358	RR 0.72 (0.54 to 0.96)
	Rabe et al., 2004 <sup>9</sup> ; Rabe et al., 2008 <sup>10</sup>	3/111	RR* 0.50 (0.30 to 0.81) <i>P</i> = 0.005
Number of transfusions	Mathew, 2011 <sup>7</sup>	4/144	MD −0.92 (−1.78 to −0.05)
	Rabe et al., 2008 <sup>10</sup>	4/170	MD −1.16 (−1.80 to −0.52) <i>P</i> < 0.001
Jaundice requiring phototherapy	Mathew, 2011 <sup>7</sup>	3/180	RR 1.23 (0.94 to 1.60)
	Rabe et al., 2004 <sup>9</sup>	1/39	RR 0.95 (0.58 to 1.56)
Hyperbilirubinemia/clinical jaundice	Mathew, 2011 <sup>7</sup>	5/215	MD 0.91 mg/dL (0.21 to 1.60)
	Rabe et al., 2004 <sup>9</sup>	3/111	MD 21.49 mmol/L (4.94 to 38.04)
Apgar score (5 min)	Rabe et al., 2008 <sup>10</sup>	3/161	RR 1.17 (0.62 to 2.20) <i>P</i> = 0.64
Respiratory distress syndrome	Mathew, 2011 <sup>7</sup>	1/39	RR 1.84 (0.64 to 5.30)
	Rabe et al., 2004 <sup>9</sup>	2/75	RR 0.83 (0.59 to 1.15)
Intraventricular hemorrhage	Mathew, 2011 <sup>7</sup>	7/408	RR 0.49 (0.32 to 0.74)
	Rabe et al., 2008 <sup>10</sup>	7/329	RR* 0.53 (0.35 to 0.79) <i>P</i> = 0.002
	Rabe et al., 2004 <sup>9</sup>	5/225	RR* 0.57 (0.36 to 0.93)
	Mercer et al., 2006 <sup>33</sup>	1/72	OR* 0.29 (0.09 to 0.91)
Late-onset sepsis	Mercer et al., 2006 <sup>33</sup>	1/72	OR 0.10 (0.01 to 0.84)
Necrotizing enterocolitis	Mathew, 2011 <sup>7</sup>	3/137	RR 0.47 (0.13 to 1.69)
	Rabe et al., 2004 <sup>9</sup>	2/72	RR 2.08 (0.52 to 8.37)
Bronchopulmonary dysplasia	Mathew, 2011 <sup>7</sup>	1/72	RR 1.33 (0.51 to 3.46)
Neonatal mortality	Mathew, 2011 <sup>7</sup>	9/503	RR 0.55 (0.21 to 1.46)
	Rabe et al., 2008 <sup>10</sup>	8/382	RR 1.40 (0.59 to 3.32) <i>P</i> = 0.45
	Rabe et al., 2004 <sup>9</sup>	6/278	RR 1.05 (0.41 to 2.73)
Cord blood pH (unspecified)	Rabe et al., 2008 <sup>10</sup>	3/123	MD 0.01 (−0.03 to 0.05)

MD: mean difference; RR: relative risk

\*These studies compared ECC with DCC, and the RR or OR was adjusted to compare DCC with ECC

Apgar scores significantly, nor does it increase the risk of other poor neonatal outcomes such as respiratory distress syndrome, jaundice requiring phototherapy, and mortality.<sup>7,9</sup> The benefits of DCC in this population include decreasing the need for and the number of blood transfusions for anemia by increasing blood volume and hemoglobin concentration at birth, decreasing the risk of intraventricular hemorrhage, and decreasing the risk of late-onset sepsis.<sup>7,9,10,33</sup> The proposed reason for the decreased incidence of late-onset sepsis after DCC is that cord blood contains a high concentration of hematopoietic progenitor cells. Thus, increasing neonatal blood volume with DCC leads to more of these cells in the neonatal circulation, resulting in less immunosuppression and consequently in less infection.<sup>33</sup> In addition, milking of the umbilical cord may be an appealing alternative strategy for increasing placental transfusion in the preterm baby. In a recent

study, milking the cord and DCC led to similar results in terms of hemoglobin concentration, need for transfusions, and other secondary outcomes such as intraventricular hemorrhage, sepsis, necrotizing enterocolitis, and death.<sup>19</sup> Further research is needed (Table 2). In light of the evidence regarding the advantages of DCC in preterm infants, we can state that this practice is beneficial and should be considered whenever possible. However, there is insufficient evidence to date to support a recommendation to delay cord clamping in non-vigorous infants requiring resuscitation.

## OTHER CONSIDERATIONS

### Cord Blood Banking

Umbilical cord blood is an excellent source of extremely proliferative stem cells, including hematopoietic stem cells that can be used as an alternative to bone marrow

transplantation.<sup>2,34</sup> Although blood banking for future autologous or familial use has limited utility, public storage of cord blood is encouraged.<sup>2</sup> Manoeuvres to optimize cord blood unit volume include placing the newborn on the mother's abdomen<sup>35</sup> and early clamping of the umbilical cord, within 30 seconds of delivery, if this does not compromise maternal or neonatal safety.<sup>2</sup> The SOGC guideline recommends ECC if umbilical cord blood banking is to be performed, in order to increase recovery volume.<sup>2</sup>

### **The Effect of Umbilical Cord Clamping on Cord Blood pH**

Although delaying cord clamping may theoretically affect umbilical cord arterial and venous blood gases, Rabe et al. found no significant difference in cord blood pH in the preterm infant after DCC, without specifying whether arterial or venous blood was analyzed.<sup>9,10</sup> A prospective observational study of vaginally delivered term newborn infants suggests a trend towards a mixed respiratory and metabolic acidosis when umbilical cord clamping is delayed.<sup>1</sup> The authors of this study found that there was a slight fall in arterial cord blood pH (by 0.03 units) in the DCC group.<sup>1</sup> Although this may be statistically significant, the clinical significance of this finding is uncertain; a more recent RCT analyzing the acid-base status of both arterial and venous cord blood showed no difference between the ECC and DCC groups.<sup>36</sup>

### **Optimal Timing of Cord Clamping at Caesarean Section**

Most of the published data on placental transfusion, especially for preterm infants, are derived from vaginal deliveries; data from cases of Caesarean section are limited.<sup>6,14</sup> Moreover, most of the time, outcome data for infants delivered by Caesarean section are not reported separately from those delivered vaginally, making it difficult to interpret the results and draw conclusions about the risks and benefits of DCC in infants born by this mode of delivery. A study published in 1975 suggests that there is actually no placental transfusion at the time of Caesarean section.<sup>37</sup> It has been speculated that this finding was due to the previous use of general anaesthesia instead of spinal anaesthesia for Caesarean section, the former having an important influence on uterine tone.<sup>4</sup> Farrar et al. found no statistically significant difference between term vaginal delivery and Caesarean section in the amount of placental transfusion, and they suggest that in general DCC provides an additional 30% to 40% of blood volume to the infant.<sup>4</sup>

An interesting finding in infants born by Caesarean section is that placental transfusion to the infant seems to increase until 40 seconds after delivery, but to decrease thereafter,

with a reversal of blood flow. This is possibly due to uterine atony, because active contraction of the uterine musculature is modified by surgical intervention and by the use of general anaesthesia.<sup>14,38</sup> Therefore, clamping the cord beyond 40 seconds may not be advantageous because it results in decreasing blood volume transfusion.<sup>14,38</sup> In more recent clinical studies, investigators showed a 6.4 mL/kg difference in blood volume between the ECC and DCC groups delivered by Caesarean section, but this difference was not statistically significant.<sup>14</sup> Similarly, in an RCT of 46 preterm infants born mainly by Caesarean section before 33 weeks' gestation, DCC did not appear to result in a significant difference in hemoglobin concentration or hematocrit.<sup>39</sup>

Overall, there is very limited information on the optimal timing for cord clamping at Caesarean section. The available data are equivocal and based on relatively small studies.<sup>4,14,37-39</sup> It remains uncertain that placental transfusion even occurs with DCC at the time of Caesarean section.

### **LIMITATIONS OF STUDIES REVIEWED**

The definition of timing for ECC and DCC varies in the studies reviewed, especially with respect to the term infant. Most studies use 30 seconds to distinguish between ECC and DCC, but others define DCC as occurring more than one minute after delivery or after cord pulsations have ceased. The position of the baby at the time of cord clamping and the use of uterotonics are not described in many studies, making it difficult to assess their role in placental transfusion.

### **CONCLUSION**

Delayed cord clamping may not only be advantageous in term infants in areas where iron deficiency is endemic and associated with developmental problems, but in light of recent evidence it may also be beneficial in high income countries, where iron deficiency anemia is a relatively rare neonatal occurrence. The benefits of delaying cord clamping in the term baby seem to outweigh the risks of adverse outcomes, including neonatal jaundice requiring phototherapy. Similarly, the evidence regarding DCC in preterm infants clearly shows that delaying cord clamping by at least 30 seconds, or possibly even milking the cord in these babies, is beneficial and should be considered whenever possible. Thus, there is sufficient evidence to justify a change in practice in both populations. However, there is insufficient evidence to date to support a recommendation to delay cord clamping in non-vigorous infants requiring resuscitation.

## REFERENCES

1. Wiberg N, Kallen K, Olofsson P. Delayed umbilical cord clamping at birth has effects on arterial and venous blood gases and lactate concentrations. *BJOG* 2008;115(6):697–703.
2. Armson BA. Umbilical cord blood banking: implications for perinatal care providers. SOGC Clinical Practice Guidelines, No. 156, March 2005. *J Obstet Gynaecol Can* 2005;27:263–90.
3. Leduc D, Senikas V, Lalonde AB, Ballerman C, Biringer A, Delaney M, et al. Active management of the third stage of labour: prevention and treatment of postpartum hemorrhage. SOGC Clinical Practice Guideline no. 235, October 2009. *J Obstet Gynaecol Can* 2009;31:980–93.
4. 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;118:70–5.
5. Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. *Lancet* 1969;2(7626):871–3.
6. 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;297:1241–52.
7. Mathew JL. Timing of umbilical cord clamping in term and preterm deliveries and infant and maternal outcomes: a systematic review of randomized controlled trials. *Indian Pediatr* 2011;48:123–9.
8. McDonald SJ, Middleton P. Effect of timing of umbilical cord clamping of term infants on maternal and neonatal outcomes. *Cochrane Database Syst Rev* 2008;(2):CD004074.
9. Rabe H, Reynolds G, Diaz-Rossello J. Early versus delayed umbilical cord clamping in preterm infants. *Cochrane Database Syst Rev* 2004;(4):CD003248.
10. Rabe H, Reynolds G, Diaz-Rossello J. A systematic review and meta-analysis of a brief delay in clamping the umbilical cord of preterm infants. *Neonatology* 2008;93:138–44.
11. Usher R, Shephard M, Lind J. The blood volume of the newborn infant and placental transfusion. *Acta Paediatr* 1963;52:497–512.
12. Duley L, Weeks A.D. Clamping of the umbilical cord and placental transfusion. . RCOG Scientific Advisory Committee Opinion Paper 14. London: Royal College of Obstetricians and Gynecologists; June 26, 2009.
13. Narendra AB, Beckett C, Aitchison T, Kyle E, Coutts J, Turner T, et al. Is it possible to promote placental transfusion (PTFx) at preterm delivery? Abstract 213. *Pediatr Res* 1998;44:454.
14. Aladangady N, McHugh S, Aitchison TC, Wardrop CA, Holland BM. Infants' blood volume in a controlled trial of placental transfusion at preterm delivery. *Pediatrics* 2006;117:93–8.
15. Yao AC, Lind J. Effect of gravity on placental transfusion. *Lancet* 1969;2(7619):505–8.
16. Airey RJ, Farrar D, Duley L. Alternative positions for the baby at birth before clamping the umbilical cord. *Cochrane Database Syst Rev* 2010;(10):CD007555.
17. Yao AC, Hirvensalo M, Lind J. Placental transfusion-rate and uterine contraction. *Lancet* 1968;1(7539):380–3.
18. Lexicomp. Oxytocin: drug information. In: Basow D, ed. UpToDate. Waltham, MA: UpToDate; 2011. Available at: [http://www.uptodate.com/contents/oxytocin-drug-information?source=search\\_result&search=oxytocin&selectedTitle=1%7E109](http://www.uptodate.com/contents/oxytocin-drug-information?source=search_result&search=oxytocin&selectedTitle=1%7E109). Accessed October 20, 2011.
19. 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):205–11.
20. Reynders FC, Senten L, Tjalma W, Jacquemyn Y. Postpartum hemorrhage: practical approach to a life-threatening complication. *Clin Exp Obstet Gynecol* 2006;33:81–4.
21. AbouZahr C. Global burden of maternal death and disability. *Br Med Bull* 2003;67:1–11.
22. Smith JR, Brennan BG. Management of the third stage of labor 2012. Medscape Reference 2012. Available at: <http://emedicine.medscape.com/article/275304-overview#showall>. Accessed January 21, 2012.
23. Levy T, Blickstein I. Timing of cord clamping revisited. *J Perinat Med* 2006;34:293–7.
24. Fung Kee Fung K, Eason E, Crane J, Armson A, De La Ronde S, Farine D, et al. Prevention of Rh alloimmunization. SOGC Clinical Practice Guidelines, No. 133, September 2003. *J Obstet Gynaecol Can* 2003;25:765–73.
25. Urbaniak SJ. The scientific basis of antenatal prophylaxis. *Br J Obstet Gynaecol* 1998;105(Suppl 18):11–8.
26. 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 randomised controlled trial. *BMJ* 2011;343:d7157.
27. Grantham-McGregor S, Ani C. A review of studies on the effect of iron deficiency on cognitive development in children. *J Nutr* 2001;131(2S-2):649S-66S; discussion 66S–68S.
28. Harris RJ. Iron deficiency anaemia: does it really matter? *Paediatr Child Health* 2007;17(4):143–6.
29. Logan S, Martins S, Gilbert R. Iron therapy for improving psychomotor development and cognitive function in children under the age of three with iron deficiency anaemia. *Cochrane Database Syst Rev* 2001;(2):CD001444.
30. Mercer JS, Vohr BR, Erickson-Owens DA, Padbury JF, Oh W. Seven-month developmental outcomes of very low birth weight infants enrolled in a randomized controlled trial of delayed versus immediate cord clamping. *J Perinatol* 2010;30:11–6.
31. Lozoff B, Beard J, Connor J, Barbara F, Georgieff M, Schallert T. Long-lasting neural and behavioral effects of iron deficiency in infancy. *Nutr Rev* 2006;64(5 Pt 2):S34-S43; discussion S72–S91.
32. Idjradinata P, Pollitt E. Reversal of developmental delays in iron-deficient anaemic infants treated with iron. *Lancet* 1993;341(8836):1–4.
33. Mercer JS, Vohr BR, McGrath MM, Padbury JF, Wallach M, Oh W. Delayed cord clamping in very preterm infants reduces the incidence of intraventricular hemorrhage and late-onset sepsis: a randomized, controlled trial. *Pediatrics* 2006;117:1235–42.
34. Lubin BH, Shearer WT. Cord blood banking for potential future transplantation. *Pediatrics* 2007;119:165–70.
35. Grisar D, Deutsch V, Pick M, Fait G, Lessing JB, Dollberg S, et al. Placing the newborn on the maternal abdomen after delivery increases the volume and CD34 cell content in the umbilical cord blood collected: an old maneuver with new applications. *Am J Obstet Gynecol* 1999;180:1240–3.
36. De Paco C, Florido J, Garrido MC, Prados S, Navarrete L. Umbilical cord blood acid-base and gas analysis after early versus delayed cord clamping in neonates at term. *Arch Gynecol Obstet* 2011;283:1011–4.
37. Kleinberg F, Dong L, Phibbs RH. Cesarean section prevents placenta-to-infant transfusion despite delayed cord clamping. *Am J Obstet Gynecol* 1975;121:66–70.
38. Ogata ES, Kitterman JA, Kleinberg F, Dong L, Willis M, Mates J, et al. The effect of time of cord clamping and maternal blood pressure on placental transfusion with cesarean section. *Am J Obstet Gynecol* 1977;128:197–200.
39. McDonnell M, Henderson-Smart DJ. Delayed umbilical cord clamping in preterm infants: a feasibility study. *J Paediatr Child Health* 1997;33:308–10.