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## CORRESPONDENCE

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### COLLECTION OF UMBILICAL CORD BLOOD FOR TRANSPLANTATION

To the Editor:

The article by Wagner et al<sup>1</sup> was very encouraging on the potential use of human umbilical cord blood. On page 1879, 1st column 2nd paragraph, there appears a sentence that raises considerable legal, ethical, and medical<sup>2</sup> questions, similar to what occurred in our studies approximately 25 years ago.<sup>3,4</sup> The statement, which read, "However, recent alterations in the technique of cord blood collection (eg, earlier clamping of the cord) routinely yield twofold to fourfold larger harvest (ie, 150 to 300 mL)," raises considerable concern.

During the period of 1965 through 1975, the obstetricians associated with our group collected cord blood from 253 deliveries. Rarely did the volume go over 125 mL and was usually much less. This volume was in accordance with existing literature.<sup>5</sup> More recent publications give similar volumes.<sup>6,7</sup> However, to quote from one of the obstetricians involved, "we made absolutely sure that no blood was still going into the baby."

Currently, umbilical cord blood is considered a waste product,

but to deny any amount of blood, even a small amount, to the newborn would raise both ethical and, possibly, legal issues. Please note the necessary clearance needed for fetal tissue in the earlier article in the same issue by Kyoizumi et al.<sup>8</sup> The deliberate early clamping of the cord could remove umbilical cord blood from a "waste" product<sup>9</sup> into a highly controversial and legal area.

In a specific case, such as that reported by Wagner et al,<sup>1</sup> wherein blood was given to a sibling, umbilical cord blood collection so described by the authors could probably be justified. Sibling aiding sibling goes back into history. However, as a routine procedure, "earlier clamping" and a volume of "300 mL" could raise serious issues.

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#### REFERENCES

1. Wagner JE, Broxmeyer HE, Byrd RL, Zehnauer B, Schneck-peper B, Shah N, Griffin C, Emanuel PD, Zuckerman KS, Cooper S, Carow C, Bias W, Santos GW: Transplantation of umbilical cord blood after myeloablative therapy: Analysis of engraftment. *Blood* 79:1874, 1992
2. Moss AJ, Monset-Couchard M: Placental transfusion: Early versus late, clamping of the umbilical cord. *Pediatrics* 40:109, 1967
3. Ende M: Lymphangiosarcoma. *Pac Med Surg* 74:80, 1966
4. Ende M, Ende N: Hematopoietic transplantation by means of fetal (cord) blood. A new method. *Virginia Med Monthly* 99:276, 1972
5. Smith CA: *Physiology of the Newborn*. Springfield, IL, Thomas, 1959, p 122
6. Iffy L, Kaminetzky HA: *Principle and Practice of Obstetrics and Perinatology: Neonatology*. New York, NY, Wiley, 1981, p 1623
7. Iffy L, Kaminetzky HA: Principles and practice of obstetrics and perinatology, in Philipp E, Savage JP (eds.): *The Placenta and its Membranes*. New York, NY, Wiley, 1981, p 181
8. Kyoizumi S, Baum CM, Kaneshima H, McCune JM, Yee EJ, Namikawa R: Implantation and maintenance of functional human bone marrow in SCID-hu mice. *Blood* 79:1704, 1992
9. Federal Register #16, vol 46, paragraph 46.110, January 26, 1981

To the Editor:

We were the obstetricians that participated in the collection of cord blood used in the studies performed by Drs Milton and Norman Ende et al in 1962. We usually obtained less than 100 mL in more than 252 specimens. The most obtained was 125 mL. We made very certain that the cord was not clamped until it stopped pulsating and that no blood was going from the placenta to the baby. But several factors, including the length of the cord and the efficiency of the placenta, enter into the amount of blood obtained. Work performed by other physicians at that time showed that the blood in the placenta and cord was 125 mL and the volume in the

baby 300 mL.<sup>1</sup> In the article by Wagner et al concerning cord blood the statement is made that early clamping of the cord routinely yield twofold to fourfold larger harvests (ie, 150 to 300 mL).<sup>2</sup> Because the total volume of placenta, cord, and baby is 425 mL, we wonder about the 300 mL obtained by early clamping. It was shown many years ago that early clamping could deprive the baby of blood.<sup>1</sup>

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#### REFERENCES

1. Smith CA: *The Physiology of the Newborn Infant* (ed 3). 1959, p 122
2. Wagner JE, Broxmeyer HE, Byrd RL, Zehnauer B, Schneck-peper B, Shah N, Griffin C, Emanuel PD, Zuckerman KS, Cooper S, Carow C, Bias W, Santos GW: Transplantation of umbilical cord blood after myeloablative therapy: Analysis of engraftment. *Blood* 79:1874, 1992

## RESPONSE

Recent successes with umbilical cord blood transplantation after myeloablative therapy<sup>1-4</sup> have resulted in considerable interest in the techniques of umbilical cord and placental blood collection. To optimize the volume of umbilical cord blood collected, we have offered the following recommendations.<sup>5</sup> The umbilical cord should be doubly clamped 3 to 5 cm above the umbilicus early after delivery. After the umbilical cord is transected and the baby is removed from the operative field, the exterior of the cord should be cleaned and then unclamped above the mouth of a sterile container that is below the level of the uterus. While flow of cord blood may be spontaneous, in many instances it may require gentle "milking." Most importantly, the blood collection should continue as long as there is a steady flow with or without continued "milking." Once the free flow has stopped, the umbilical cord should again be transected approximately 2 cm above the free end and "milked" until blood flow has stopped. Subsequently, the placental blood should be collected by gentle needle aspirations. The process should be continued until the placental vein remains collapsed.

Using the procedure described above, obstetricians nationwide have sent us umbilical cord blood for purposes of stem cell transplantation. The umbilical cord blood collection volumes have ranged from 42 to 240 mL, with a median volume of  $103 \pm 49$  mL, and the placental blood collection volumes have ranged from 8 to 85 mL, with a median volume of  $31 \pm 16$  mL. A more detailed description of the procedure as well as a more comprehensive summary of the results can be found elsewhere.<sup>5</sup>

There are several reasons that possibly account for the increase in the volume of cord blood collected: (1) early (versus delayed) clamping of the umbilical cord after delivery; (2) prolonged (ie,

more patient) collection attempts; and (3) better understanding of the placental blood volume.

Without question, the obstetricians' and pediatricians' first priority is the care of the mother and infant. However, there is no consensus as to the time the umbilical cord should be clamped. A variety of guidelines exist in the literature and have been published elsewhere.<sup>6-8</sup> The guidelines described in Pritchard et al<sup>6</sup> are "to clamp the cord after first thoroughly clearing the infant's airway, all of which takes upward of 30 seconds." Delayed clamping of the umbilical cord, however, is not beneficial to the neonate and in some instances may be harmful.<sup>8</sup>

The volume of blood that remains in the placenta after clamping the umbilical cord has often been grossly underestimated by obstetricians. For most, there is little experience with collection of umbilical cord blood other than for the purpose of diagnostic testing, which requires relatively small volumes. Such an underestimation of the placental blood volume might have influenced the duration of the collection process and the resultant lower yields.

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## REFERENCES

1. Gluckman E, Broxmeyer HE, Auerbach AD, Friedman H, Douglas GW, Devergie A, Esperou H, Thierry D, Socie G, Lehn P, Cooper S, English D, Kurtzberg J, Bard J, Boyse EA: Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical cord blood from an HLA-identical sibling. *N Engl J Med* 321:1174, 1989
2. Broxmeyer HE, Kurtzberg J, Gluckman E, Auerbach AD, Douglas G, Cooper S, Falkenberg JHF, Bard J, Boyse EA: Umbilical cord blood hematopoietic stem and repopulating cells in human clinical transplantation. *Blood Cells* 17:313, 1991
3. Wagner JE, Broxmeyer HE, Byrd RL, Zehnbauser B, Schmeckpeper B, Shah N, Griffin C, Emanuel PD, Zuckerman KS, Cooper S, Carow C, Bias W, Santos GW: Transplantation of umbilical cord blood after myeloablative therapy: Analysis of engraftment. *Blood* 79:1874, 1992
4. Vilmer E, Sterkers G, Rahimy C, Elion J, Broyart A, Lescoeur B, Gerota J, Blot P: HLA-mismatched cord blood transplantation in a patient with advanced leukemia. *Transplantation* 53:1155, 1992
5. Wagner JE, Broxmeyer HE, Cooper S: Umbilical cord and placental blood hematopoietic stem cells: Collection, cryopreservation and storage. *J Hematother* 1:167, 1992
6. Pritchard JA, MacDonald PC, Gant NF: Conduct of normal labor and delivery, in Pritchard JA, MacDonald PC, Gant NF (eds): *Williams Obstetrics* (ed 17). Norwalk, CT, Appleton-Century-Crofts, 1985, p 331
7. Yao AC, Moinian M, Lind J: Distribution of blood between infant and placenta after birth. *Lancet* 2:871, 1969
8. Oski FA: Normal blood values in the newborn period, in Oski FA, Naiman JL (eds): *Hematologic Problems in the Newborn*. Philadelphia, PA, Saunders, 1982, p 1