CORRESPONDENCE

Cord Blood Collection: Effects on Newborns (Medical-Legal)

To the Editor:

The letter by Bertolini et al[1] is primarily addressed to three references. The first two references were two letters written to *BLOOD* in 1992 by myself and my colleagues.[2,3] These letters written in 1992 were not written to draw attention to the loss of hemoglobin, but to draw attention to ethical, medical, and legal issues revolving around the deliberate taking of blood from a newborn.[2,3] Some of these issues are as follows.

1. Can someone deliberately take from a newborn (even 5 mL) that which for millennia has been the infant's own blood? This advocacy of immediate clamping to obtain cord blood is only a relatively recent event.[4-7] Prior investigators have all taken a middle ground, with none advocating immediate clamping or prolonged delays.[8-10]

2. Immediate clamping has been reported to produce brain hemorrhage in premature infants.[11] These investigators postulated that the hemorrhage resulted from the sudden increase in arterial pressure caused by immediate clamping.[12] Unless the doctors of Bertolini's group or others who have practiced immediate clamping of the umbilical cord have had careful neurologic follow-up for a considerable period of time and can reassure the mother there is absolutely no increased risk of brain damage, then this is obviously a most significant, ethical, medical, and definite legal issue in which informed consent is practiced.[13] It should be noted that neurologic deficits at birth are particularly difficult to detect. Type I and type II periventricular hemorrhage have few clinical symptoms.[14]

3. What is the long-term effect of deliberately removing 20% of the circulating stem cells?[15] Do these children have a greater tendency for leukemia or autoimmune disease? Are there any published studies on this matter?

Our concern covers the first few moments of life, primarily the first 60 seconds of life outside of the womb, during which time the bulk of the blood returns to the child from the placenta.[16] The decrease and later recovery of the Hb as reported by the investigators would be expected. The rate of return is so great during this short period of time that the variability of the decrease in hemoglobin described in Bertolini et al's letter could be readily explained by the return of blood to the infant over a 30-second period.

Their conclusion, which "supports the safety of procedures for the collection of adequate numbers of hematopoietic progenitors," is totally unwarranted both ethically and legally.[13]

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Response

In his comment to our letter reporting hemoglobin and bilirubin values after placental blood (PB) collection,[1] Dr Ende indicates that, despite intense investigation in past and recent years, controversies still exist about the more appropriate time of umbilical cord clamping at birth. We reviewed 6 recent manuals of neonatology and obstetrics[2-7] and found investigators issuing "no indications about time of cord clamping because of lack of consensus"[2,3] or indications to clamp "as soon as possible"[4] or "within 30-45 seconds".[5-7] Although in our study none of newborns who had PB collected was reported to suffer from complications such as periventricular/intraventricular hemorrhage, weight loss, fatigue while feeding, tachypnoea and tachycardia, hypoxia, or cardiac, or pulmonary disease with reduced arterial oxygen saturation, Dr Ende has raised concern about risks for newborns who had their PB collected as he did in another 1992 letter.[8] The manuscript mentioned by Dr Ende to support his concern, reporting periventricular/intraventricular hemor-

rhage after immediate cord clamping, was published in 1988 in the *South African Medical Journal*[9] and is related to a small study in immature newborns who were never candidates for PB collection and never underwent PB collection in our PB banking program. Moreover, it must be noted that the same South African group reported in 1993 data about a larger randomized controlled clinical study in immature newborns and concluded that "the trial did not confirm previous observations that early clamping may contribute to the initiation of periventricular/intraventricular hemorrhage."[10] We can hardly understand Dr Ende's concern about early cord clamping (ie, 20 to 30 seconds after delivery) because he reports at the end of his letter that "the rate of [blood] return is so great [during the first few moments of life] that the variability of the decrease in hemoglobin described . . . could be readily explained by the return of blood to the infant over a 30-second period." On the other hand, as already pointed out by Wagner and Broxmeyer[11] in their response to the 1992 letter from Dr Ende, "delayed clamping of the umbilical cord is not beneficial to the neonate and in some instances may be harmful."[12]

Our study indicates that the time of umbilical cord clamping has an influence over the volume of PB collections. This is not surprising, because in our, as in most, obstetrical settings the newly delivered infant is kept below the uterine level, and the relationship between clamping time and PB volume has been already described.[13] In this context, we would like to point out that PB collection was obtained after informed consent and that we did not and will not ask the obstetrical staff involved in the unrelated PB bank program to fasten or modify their umbilical cord clamping procedures to increase the volume of PB collection. This is supported by a larger group of infants in our series who had the cord clamped after 35 to 180 seconds (n = 72) compared with the group of infants who had the cord clamped at 20 to 30 seconds (n = 59) and by the fact that, in the control group of 75 newborns who did not undergo PB collection, the umbilical cord was clamped 20 to 180 seconds after delivery.

Finally, Dr Ende's concern about the removal of 20% of circulating stem cells derives from an overestimate of the volume of PB collectable by early versus delayed clamping (about 75 *v* 40 mL, ie, a 35 mL difference, resulting in approximately 10% of 300 to 400 mL of blood circulating between the neonate and the placenta) and should be considered while keeping in mind that fetal-neonatal hematopoiesis is known to occur in the bone marrow and not in the peripheral blood, that more recent evaluations of the total number of multipotent hematopoietic stem cells indicate that this number is apparently enough for almost 2 lifespans,[14] and that tendency to develop leukemia or autoimmune disease has not been reported in bone marrow and/or peripheral blood stem cell donors of any age.[15]

Based on the facts reported above, we still believe that our data support the safety of procedures for the collection of adequate numbers of hematopoietic progenitors both ethically and legally.[16]

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