2. Scott EP. The safety of blood donation—is it what it should be? (editorial). Transfusion 1995;35:717-8.
3. Boynton MH, Taylor ES. Complications arising in donors in a mass blood procurement project. Am J Med Sci 1945;209:421-36.

The above letter was sent to Dr. Popovsky and coworkers, who offered the following reply.

Dr. Schmidt's comments about possible overrepresentation of autologous blood donors in the VSO group in our study are well taken. We noted in the article that elderly donors, both autologous and allogeneic, could have been sent to the hospital more readily because of blood collection staffers' assumptions or concerns about the donors' underlying disease and potential predisposition to morbidity. With regard to Dr. Schmidt's statement about the decision for hospitalization being "administratively easy," our study did not address this issue, but from our record review, it appeared that the decision to hospitalize was in the hands of emergency room physicians, not the physician who requested the autologous blood donation.

Although the perception of autologous donors as "sicker" may account for some of the difference in their incidence of VSOs in comparison to that incidence in the allogeneic blood donor population, we doubt that it negates the overall conclusion of the paper, that older autologous blood donors are at increased risk for the more severe complications of donation.

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Reference

1. Popovsky MA, Whitaker B, Arnold NL. Severe outcomes of allogeneic and autologous blood donation: frequency and characterization. Transfusion 1995;35:734-7.

Multi-gallon blood donors

To the Editor:

The recent **TRANSFUSION** article entitled "Multi-gallon blood donors: who are they?" by Royse and Doochin[1] was of interest to me, as a multi-gallon blood donor. I fit nicely into the stereotype of a white, male, college-educated individual with feelings of "responsibility to the community." One conclusion that could be drawn from the results of Royse and Doochin's research was that donor recruitment efforts could best be targeted at groups in which community-minded individuals congregate (e.g., Rotary and other service clubs, school parent–teacher organizations, and active religious groups). Parent–teacher organizations have a large number of female members, and blood banks might preferentially target that subset of the population. In addition, approaches to minority churches might improve minority representation in the donor pool. To me, the conclusions reached by Royse and Doochin suggest that changes are needed in how and where we recruit our donors.

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Reference

1. Royse D, Doochin KE. Multi-gallon blood donors: who are they? Transfusion 1995;35:826-31.

The above letter was sent to Dr. Royse, who offered the following reply.

Dr. Parker's suggestion that donor recruitment efforts be aimed at community-minded individuals who congregate in group activities and service organizations is well taken. At the same time, it is reasonable to expect that many of these individuals might already be blood donors. I believe that most blood banks do appeal to Rotary clubs and other service clubs. Targeting parent–teacher organizations is likewise a good approach to finding more female donors, but these groups tend to have a much more limited focus, and it can be difficult to get on their agenda.

Recruiting from minority churches presents a different problem. Many African Americans appear to be reluctant to donate blood or sign up for bone marrow or organ registries. The vestiges of racism that still exist in our society make it easy for some African Americans to believe that these donations are of more benefit to whites. It is not uncommon for recruiters in our community to hear from African Americans the concern that their blood or marrow might be given to whites and not to African Americans. Prottas[1] has noted these concerns with regard to African American families and organ donation. Callender[2] found that African American patients awaiting renal transplant in a network covering the District of Columbia and parts of Maryland and Virginia received proportionately fewer transplants than whites, although there were more African Americans with end-stage renal disease.

While on the one hand it is easy to say that special educational programs should target African Americans, I wonder whether these programs can be successful as long as major racial inequalities continue in our society. In the meantime, communities may find it beneficial to give greater publicity to their multi-gallon donors who are African American.

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References

1. Prottas JM. Encouraging altruism: public attitudes and the marketing of organ donation. Milbank Mem Fund Q/Health Soc 1983;61:278-306.
2. Callender CO. Organ donation in the black population: where do we go from here? Transplant Proc 1987;19:36-40.

Questions to be answered about umbilical cord blood

To the Editor:

The recent **TRANSFUSION** article by Broxmeyer[1] and the accompanying editorial by Wagner[2] did not deal with the most pressing issues in cord blood banking: the ethical, medical, and legal aspects of the collection of umbilical cord blood. In his editorial, Wagner stated, "...the collection of umbilical cord blood poses no risk to the donor...." The collection of cord blood, however, is the deliberate taking from an infant of blood that historically has gone to the infant.[3]

There are many references in the literature to the technique of *immediate* clamping of the cord at delivery. In addition, Broxmeyer and colleagues, in a cord blood patent application,[4]

wrote, in the section Vaginal Delivery of the Term Infant (5.1.1.2.2.), "In the most preferred embodiment, *immediate* cord clamping after delivery is carried out, in order to achieve collection of the greatest possible volume of cord blood." In the same patent application, under the heading for Premature Births (5.1.1.2.3.1), they state, "[The c]ollection procedure should be the same as for term births." In a recent letter, Bertolini et al.[5] declared that the drop in hemoglobin following the clamping of the cord within 30 seconds of delivery should not be considered harmful.

However, in the first minute after birth, up to 20 percent of an infant's blood volume is contributed by the placenta.[6] In 1988, an article published from South Africa indicated that immediate clamping of the umbilical cord could produce brain hemorrhage in premature infants as a result of the sudden increase in pressure in the vascular system.[7] The 1994 Code of Medical Ethics from the Council on Ethical and Judicial Affairs of the American Medical Association states:

> The use of umbilical cord blood raises three main ethical problems. First, the exact timing of the clamping has a significant impact on the neonate. Studies indicate that early clamping may cause an abrupt surge in arterial pressure, resulting in intraventricular hemorrhage (particularly in premature infants). Second, the parents of the infant may not realize the implications of the protocol and the potential risks involved.... To avoid health risks, normal clamping protocol should be followed and not altered in such a way that might endanger the infant. To ensure appropriate informed consent, parents of the infant must be fully informed of the risks of the donation and written consent should be obtained from them.[8(p30)]

Neurologic defects are known to be difficult to detect in newborns. Unless the authors who recommend and practice *immediate* clamping of the cord are willing for the infant donors to undergo careful long-term neurologic evaluations, Wagner's statement that it "poses no risk to the donor" cannot be considered valid. The obvious ethical, medical, and legal issues for the practicing physician, where informed consent is mandated, should be self-evident.

Readers of **TRANSFUSION** may be interested to know that in 1972 I co-authored what may have been the first article on the use of cord blood as a method of bone marrow transplantation.[9] My belief is that the obstetricians of that era were very cognizant of the medical ethics of collecting blood from the newborns.

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References

1. Broxmeyer HE. Questions to be answered regarding umbilical cord blood hematopoietic stem and progenitor cells and their use in transplantation. Transfusion 1995;35:694-702.
2. Wagner JE. Umbilical cord blood transplantation (editorial). Transfusion 1995;35:619-21.
3. Grizzard WS, Payne FR. Collection of umbilical cord blood for transplantation. Blood 1992;80:163.
4. Boyse EA, Broxmeyer HE, Douglas GW, inventors; Biocyte Corp., assignee. Preservation of fetal and neonatal hematopoietic stem and progenitor cells of the blood. US patent 5,004,681. 1991 April 2. Int Cl[2] A01N 1/02; A61K 35/14.
5. Bertolini F, Battaglia M, DeIulio C, et al. Placental blood collection: effects on newborns (letter). Blood 1995;85:3361-2.
6. Yao AC, Moinian M, Lind J. Distribution of blood between infant and placenta after birth. Lancet 1969;2:871-3.
7. Hoffmeyer GJ, Bolton KD, Bowen DC, et al. Periventricular/intraventricular haemorrhage and umbilical cord clamping. S Afr Med J 1988;73:104-6.
8. Code of medical ethics. Council on Ethical and Judicial Affairs. Chicago: American Medical Association, 1994.
9. Ende M, Ende N. Hematopoietic transplantation by means of fetal (cord) blood—a new method. VA Med Mon 1972;99:276-80.

The above letter was sent to Drs. Wagner and Broxmeyer, who offered the following response.

As Dr. Ende suggests, the collection, storage, and use of umbilical cord and placental blood have opened up a plethora of intriguing ethical and legal issues that are beginning and will continue to be addressed by experts in these areas. Our review[1] and accompanying editorial[2] were purposely focused on the biologic and clinical aspects of umbilical cord stem and progenitor cells; discussion of the ethical and legal questions raised by such a procedure is beyond our expertise. Certainly, others will address issues such as 1) categorization of cord blood as an organ or as discarded tissue, 2) consent and ownership, 3) commercialization, and 4) deliberate conception and embryonal cloning.

Ende cited several publications pointing to the fact that early clamping of the umbilical cord might increase the yield of blood collection. Certainly no one would recommend a practice that is harmful to the newborn infant. We have taken a conservative approach regarding umbilical cord blood collection—that is, allowing the obstetricians to determine a standard of practice for this. Therefore, we offer no advice or direction as to the timing of umbilical cord blood clamping. Moreover, there does not seem to be a consensus on this matter, as illustrated by a review of various textbooks of obstetrical medicine and conversations with well-respected obstetricians. Directions in print on the collection of umbilical cord blood appear limited to the procedure that occurs after the infant has been removed from the surgical field. In this context, we find the implication in the last sentence of Dr. Ende's letter to be an uncalled-for slight of present-day obstetricians. In summary, because there is no standard practice for the collection of cord blood, we feel that it is best left to obstetricians to determine the optimal timing of umbilical cord clamping. We do still feel strongly, however, that umbilical cord blood collection poses no risk to the donor.

Regarding the issue raised by Dr. Ende in connection with a 1972 article,[3] in which multiple, non-HLA-typed cord bloods were transfused to a patient with malignancy who was not given myeloablative therapy, it seems clear that, at best, only transient detection of mature donor cells was demonstrated. Such a procedure without myeloablative therapy would not have been expected to demonstrate the existence in umbilical cord blood of long-term marrow-repopulating pluripotential hematopoietic stem cells. Our response to the quoted 1972[3] article is thus similar to that of Gale[4] in response to a letter to the editor of another journal.[5] To the best of our knowledge, rigorous proof of the existence of engrafting and marrow-repopulating stem cells in cord blood did not occur until October 1988, when Gluckman et al.[6] performed the first true cord blood transplant demonstrating long-term donor-derived hematopoiesis. It was only after the report of that procedure that others throughout the world started using cord blood for transplantation purposes.[7]

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References

1. Broxmeyer HE. Questions to be answered regarding umbilical cord blood hematopoietic stem and progenitor cells and their use in transplantation. Transfusion 1995;35:694-702.
2. Wagner JE. Umbilical cord blood transplantation (editorial). Transfusion 1995;35:619-21.
3. Ende M, Ende N. Hematopoietic transplantation by means of fetal (cord) blood—a new method. VA Med Mon 1972;99:276-80.
4. Gale PR. Transplantation of cord blood cells. (reply to letter). N Engl J Med 1995;333:68-9.
5. Ende M, Ende FI. Transplantation of cord blood (letter). N Engl J Med 1995;333:68.
6. Gluckman E, Broxmeyer HE, Auerbach AD, et al. Hematopoietic reconstitution in a patient with Fanconi's anemia by means of umbilical cord blood from an HLA-identical sibling. N Engl J Med 1989;321:1174-8.
7. Wagner JE, Kernan NA, Steinbuch M, et al. Allogeneic sibling umbilical cord blood transplantation in forty-four children with malignant and non-malignant diseases. Lancet 1995;346:214-9.

The hemostatic effect of adequate red cell transfusion in patients with anemia and thrombocytopenia

To the Editor:

The hemostatic effect of platelets has been well known since it was first reported by Duke in 1910.[1] The possible role of red cells in hemostasis was also suggested in that article, and, since that time, red cell transfusions have been used to stop uremic bleeding.[2-6] However, red cell transfusions have not often been used to prevent or stop bleeding in patients with thrombocytopenia as well as anemia. We found this to be a successful alternative to the use of platelets, and we report an example. A 68-year-old man was admitted to our hospital with aplastic anemia and intractable epistaxis. Laboratory data included: hemoglobin, 64 g per L; hematocrit, 20.3 percent; and platelet count, 18×10^9 per L. Epistaxis persisted despite treatment with tranexamic acid, nasal compression, and red cell transfusions to increase the hemoglobin to 81 g per L. Platelet transfusions were also given, but because of multiple previous exposures, the patient was refractory, and the platelet count never rose above 20×10^9 per L. After 2 weeks of this conventional treatment, daily transfusions with packed red cells were given to keep the hemoglobin above 120 g per L. Epistaxis improved gradually and stopped completely 4 days later when the hemoglobin reached 128 g per L. Nasal packing was carefully removed and no more bleeding was noted. The patient was discharged 1 week later.

Platelet transfusions are the conventional way to control bleeding in patients with thrombocytopenia due to marrow failure. However, platelet refractoriness is common. In such patients, red cell production is also impaired. Although most physicians usually transfuse red cells to raise the hemoglobin concentration to only 80 g per L, large-volume red cell transfusions to raise the hemoglobin to normal levels are also a good alternative for controlling life-threatening bleeding. Recently, Blajchman et al.[7] reported that anemic rabbits had significantly longer bleeding times than nonanemic animals with a similar degree of thrombocytopenia, and that red cell transfusions were capable of shortening the bleeding time in thrombocytopenic anemic animals. Their results were quite similar to our clinical result. In our experience, the hemostatic effect of red cell transfusion is longer-lasting than that of platelets (up to 2 weeks), and the procedure can be repeated as needed. From the above case, we conclude that red cell transfusion offers a hemostatic effect in patients with thrombocytopenia as well as anemia and may be an effective method of controlling bleeding when other methods have been applied without success.

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References

1. Duke WW. The relation of blood platelets to hemorrhagic disease. JAMA 1910;60:1185-92.
2. Livio M, Gotti E, Marchesi D, et al. Uraemic bleeding: Role of anaemia and beneficial effect of red cell transfusions. Lancet 1982;2:1013-5.
3. Vigano G, Benigni A, Mendogni D, et al. Recombinant human erythropoietin to correct uremic bleeding. Am J Kid Dis 1991;18:44-9.
4. Turitto VT, Weiss HJ. Red blood cells; their dual role in thrombus formation. Science 1980;207:541-3.
5. Fernandez F, Goudable C, Sie P, et al. Low haematocrit and prolonged bleeding time in uraemic patients: effect of red cell transfusions. Br J Haemotol 1985;50:139-48.
6. Boneu B, Fernandez F. The role of the hematocrit in bleeding. Transfus Med Rev 1987;1:182-5.
7. Blajchman MA, Bordin JO, Bardossy L, Heddle NM. The contribution of the haematocrit to thrombocytopenic bleeding in experimental animals. Br J Haematol 1994;86:347-50.