

## CORRESPONDENCE

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## Plateletpheresis before Cardiopulmonary Bypass: II

*To the Editor:*—In a recent paper,<sup>1</sup> Ereth *et al.* report that “autologous platelet-rich plasma did not reduce perioperative bleeding or transfusion requirements in patients undergoing repeat valvular surgery.” Their findings prompted Horrow to question whether autologous platelet-rich plasma collection might be “following the same evolution as desmopressin, *i.e.*, initial enthusiasm followed by ultimate disappointment.” “We are concerned that what may yet prove to be an efficacious therapy in decreasing blood loss and transfusion requirements in cardiac surgery may be prematurely dismissed because of inadequate methodology rather than a true lack of efficacy.

Ereth *et al.* collected “platelet-rich plasma” using the Plasma Saver developed by Haemonetics (Braintree, MA). The median platelet yield was 2.7 units, with 75% of their patients having 3 or fewer units of platelets removed before cardiopulmonary bypass. Even if one accounts for the “freshness” of their harvested platelets *versus* blood bank products,<sup>2</sup> this platelet yield would likely be subtherapeutic. Furthermore, the authors note that their platelet-rich plasmapheresis “may not result in the collection of the very large and most potent platelets that remain in the packed erythrocyte layer during platelet-rich plasma separation.”<sup>3</sup>

The authors cite three studies<sup>4-6</sup> using a Haemonetics Plasma Saver system that reported beneficial effects of platelet-rich plasmapheresis. However, the participating clinicians were not blinded. Davies *et al.*,<sup>7</sup> using an Electromedics device (AT750, Englewood, CO), har-

vested a platelet-rich product with larger platelet yields ( $3.5 \times 10^{11}$ , or more than 6 units) and quite possibly a significant number of the large and potent platelets that are left behind in the packed erythrocyte layer during plasmapheresis with the Haemonetics Plasma Saver. The negative results of Ereth *et al.* may thus be a consequence of blinding or a result of the low platelet dose.

Although study design is no doubt potentially important in the examination of blood conservation therapies, one must not ignore the possibility of inadequate methodology in favor of concerns regarding experimental design. Specifically, one should question whether an available technique that yields an average of 6 units of platelets may simply be more efficacious than a technique that typically yields fewer than 3 units of platelets for transfusion after cardiopulmonary bypass. The beneficial effects of platelet-rich plasmapheresis found by Davies *et al.* might be attributable to a technique that yields a therapeutic *versus* subtherapeutic number of platelets, rather than to the study design or to the patient population selected.

It does not appear to be in the best interest of our patients to consider that the role of autologous platelet-rich plasmapheresis, even in repeat valvular surgery, is resolved. Patient care demands continued and careful examination of this potentially valuable technique; we believe that such investigations should use methods that yield a quantity of platelets that would be expected to provide a therapeutic hemostatic benefit to the patient.

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*In Reply:*—We agree with Davies *et al.* and Stover and Siegel that the clinical efficacy and appropriate application of autologous platelet-rich plasma in cardiac surgery is yet to be defined. We also agree that there are important differences in the techniques of platelet extraction and methodologies presented in the works by ourselves and others. We do, however, emphasize the importance of the introduction of blinding methods to the assessment of this particular blood conservation technique.

We acknowledge the concern about platelet yield and the limitations of the Haemonetics Plasma Saver (Braintree, MA). Yet, to our knowledge, the only two prospective, randomized, and blinded trials published to date have used the Haemonetics procedure in primary and repeat cardiac surgical cases and have shown no reduction in bleeding or transfusion requirements.<sup>1,2</sup> The variability of transfusion practice in cardiac surgery is well recognized and documented.<sup>3</sup> We believe that the blinding technique we introduced has enhanced experimental design in trying to limit the observational bias and subjective nature of transfusion practices.

With regard to the technical comments and calculations by Davies *et al.*, we did, in fact, alter the Haemonetics protocol to extend sampling 40 ml into the red cell layer. Our median platelet yield, as reported in our article, was 2.7 units, with a "unit" defined as  $5 \times 10^{10}$  platelets according to the American Association of Blood Banks standards for platelets from whole blood.<sup>4</sup> Accordingly, our median yield was  $1.5 \times 10^{11}$ , or 42% of the  $3.5 \times 10^{11}$  mean yield Davies *et al.* reported in their first article<sup>5</sup> to be efficacious and 50% of the American Association of Blood Banks standards for apheresis platelets. Apheresis platelets are stored for as many as 5 days, and the hypothesis that small amounts of fresh platelets might be as efficacious as twice their number of stored platelets is not unreasonable, based on the work of others.<sup>6</sup>

Techniques that provide higher yields of platelet-rich plasma may result in a more effective product. There may, in fact, be a critical level or volume of platelet-rich plasma that must be reached before a difference in transfusion requirements is demonstrated. However, we are unaware of any blinded trials of high-yield platelet-rich plasma procedures. We believe that the routine use of platelet-rich plasma

in cardiac surgery merits further consideration. Whether it is truly clinically efficacious and cost effective in cardiac surgical procedures is not known.

In summary, as we stated in our Discussion, "We cannot conclude that other groups of patients in other clinical situations may not benefit" from the use of platelet-rich plasma. We acknowledge that high-yield platelet-rich plasma techniques may be effective, but we believe that blinded methods must be used to evaluate further this procedure before it can be declared clinically efficacious for routine use in cardiac surgery. We appreciate the comments by the above groups and look forward to reviewing or conducting a prospective, randomized, and blinded trial of high-yield platelet-rich plasma.

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