Is there any value in transfusing prestorage leukoreduce blood products through a bedside leukoreduction filter?

A member of the e-Network Forum has indicated that some hematologists at his institution are insisting on **transfusing pre-storage leukoreduced RBC's through a bedside leukoreduction filter (double leukocyte reduction)**. This member wants to know if other institutions are also being 'encouraged' to perform double leukocyte reduction. Furthermore, the Editor has a question: Even if double leukocyte reduction (pre-storage plus bedside) causes fewer WBC's to be transfused, are there data to substantiate that the transfusion of doubly leukocyte-reduced red cells offers a better outcome for the patient than the transfusion of red cells that have only been leukoreduced at a blood center?

This question was **previewed by two experts** in transfusion medicine, who had this to say:

1. "Personally, if I were going to spend another 20-30 dollars, it would be on plasma supernatant depletion (References: Transfusion Medicine 11: 45, 2001 and The Lancet, June 23rd edition, 2001)."
2. "There are no data to suggest that a second filter reduces the white cell burden by a significant amount, but it does reduce the red cell dose by another few percent."

Please share your experience, opinions, or sound scientific evidence to support or refute the above mentioned practice of using double leukocyte reduced red blood cell transfusions.

The following responses have been received.

ADDENDUM June 30, 2001

1. **A European member** of the e-network forum shared the opinion that the main purpose of leukocyte filtration is to reduce the leukocyte burden to avoid primary alloimmunization within the HLA system! Such alloimmunization may cause platelet transfusion refractoriness. However, even adequate leukocyte reduction of blood products will not 'prevent' alloimmunization to HLA altogether, especially among **adult women**, in whom the rate of alloimmunization is about 20%, probably due to previous pregnancies. In a recent series reported by Kurz et al in Transfusion, June 2001, about 40% of patients were found to have HLA antibodies. De novo alloimmunization, nevertheless, can be substantially reduced with prestorage filtration with an appropriate filter. The responding member thinks that perhaps 1-2% of patients may benefit from a second round of filtration. However, he admits that there are no studies to prove that there is a benefit from a second round of filtration. He also points out that the only appropriate way to perform leukocyte filtration is to do it before storage! He doubts that anyone, other than a filter company, would fund such a study.

2. A **second member** commented that bedside leukoreduction is known to be less efficacious than prestorage leukoreduction. This member was not aware of any data that says filtering twice in the reported manner yields any benefit, and she would not do it. Furthermore, at her hospital, double leukocyte filtation does NOT occur. The main reason that double leukocyte filtration does not occur is because all RBC units either arrive prestorage leukodepleted or the filtering is done in the Transfusion Service. Leukoreduction filters are no longer supplied to nursing units, so the nurses do not have them to use, even in error (or under duress).

3. A third reply was received from a **transfusion specialist** who says that a single leukocyte reduction reduces HLA alloimmunization by 50%, but that leaves many frequently transfused hematology patients still developing HLA antibodies. If this occurs before a transplant, the transplant's outcome can be threatened by rejection. Thus this specialist believes **we still need to do something to prevent HLA alloimmunization** due to receiving RBCs and platelets pre-transplant. Selecting pedigree donors is one approach, but lately this specialist has been thinking about double filtration and he is going to study if double leukocyte reduction removes the final 2 million WBC from the bag or not. If it does, he will study the benefit in patients.

ADDENDUM July 1, 2001

4. Another blood banker wrote that this **seems to be a strange practice**. She has not heard of this request in her hospital. To avoid such a transfusion from occurring, they **attach another label** on the blood bags, informing the transfusionists **not** to use a bed-side leukodepletion filter for the transfusion of the pre-storage leukodepleted pheresis/red cells. They do not want the transfusionists to "waste" a more costly bed-side leukodepletion filter.

ADDENDUM Feb. 23, 2003

5. The following response is from a **transplant surgeon in Southern California**. According to this colleague, what strikes him about this discussion is that the comments are not from transplant professionals who (verbatim)" see the devastating effect an HLA immunization has on a patient who needs a transplant". He adds (verbatim) "I have seen that several times in my own practice. For transplant purposes, **a small reduction in the red cells transfused would be a small price to pay if the result is a reduction in the number of patients prevented from receiving a transplant**. What we need to see is **a comparison of the immunizing effect of single versus double filtered blood**. I would also be curious to know what the white cell count is after the second filtration compared to the first pass. Until we can have more factual evidence, I would rather **err on the side of double filtration**. I greatly appreciate your input and I will keep an open mind on this topic."

ADDENDUM Feb. 23, 2003

6. **A colleague in Saudi Arabia** reports that EU standards require there be less than 1 million WBC remain in leukoreduced RBC units. If additional leukoreduction is felt to be of value, studies should concentrate on a second filtration in the **blood bank** and not at the bedside, since according to the responding colleague "bedside filtration is difficult if not impossible to QC with many filters failing and many different hands handling the process."

ADDENDUM Mar. 11, 2003

7. **A colleague from Los Angeles offers a cautionary note** that in the FDA/CBER DRAFT Guidance for Industry on Pre-Storage Leukocyte Reduction of Whole Blood and Blood Components Intended for Transfusion, January 2001 it states "The effect of repeated filtration, including bedside filtration, on the safety and efficacy of blood components has not been established." This is included in the section on "Unexpected results and actions"

ADDENDUM Mar. 13, 2003

8. **A colleague in Spain** does NOT see the benefit of 'filtering the blood twice' for leukoreduction, and there are disadvantages. When they started universal leukoreduction at his institution in Spain, they had some accidents and blood was actually filtered twice, without consequence other than losing some red cells. The Spanish colleague reports that there still is controversy about the potential immune benefit of leukoreduction, and there is no objective evidence of the "maximal tolerable" amount of leukocytes in a blood product.

   The Spanish colleague adds that the standard for residual WBC in a leukocyte-reduced product differ in Europe from those in the USA ($5x10^6$ in USA, $1X10^6$ in Europe), adding another incongruency. If one is already achieving the European Standard, is there really additional room for improvement from a clinical outcomes standpoint?

   Further, the Spanish colleague adds that using the component preparation and leukocyte reduction technology employed in Spain, they are currently achieving leukocyte numbers well below $5x10^5$, especially in red cell concentrates, which often contain no detectable white cells. It would be very hard to lower those numbers.

   Finally, the Spanish colleague concludes that bedside filtration is a poorer technique than in-laboratory filtration; patients benefit more when filtration is done in the laboratory under controlled conditions.

Please submit comments to the e-Network Forum.

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