# Massive clotting in red cell concentrates during transfusion is caused by backflow of patient blood

B. Van Aelst, PhD[1], J. Coene, MD[1], H.B. Feys, PhD[2], M-P. Emonds, MD, PhD[3,4], K. Van Poucke, MD[5], J. Moerman, MD[6], E. Verhoye, Apr[7], V. Compernolle, MD, PhD[1-3,8]

## SUMMARY

We report three cases of massive *ex vivo* coagulation in a leukocyte depleted red cell concentrate during transfusion. Molecular blood typing indicated that patient blood was present in the filter housing of the infusion set and/or in the blood bag itself. Together with the history of events, this suggested that the observed clotting was caused by backflow of patient blood. Therefore, we recommend maintaining the blood bag above heart level during the entire transfusion procedure, until the infusion set is removed.

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## INTRODUCTION

During whole blood collection, slow blood flow or insufficient mixing with anticoagulant can cause *ex vivo* coagulation.[1] The resulting blood clots can then be found during component preparation. However, they are not expected in the fully processed and filtered red cell concentrates. Yet, several hospitals have reported cases of apparent blood clots in red cell concentrates during actual transfusion.

## CASE DESCRIPTION

Three cases of blocked transfusion of a leucocyte depleted red cell concentrate were reported by three different hospitals. Inspection of the blood bags by hospital staff revealed 'fibrin threads' to gross clots and all three bags were returned to the Blood Service. Large blood clots were found in these bags, as shown in *Figure 1*.

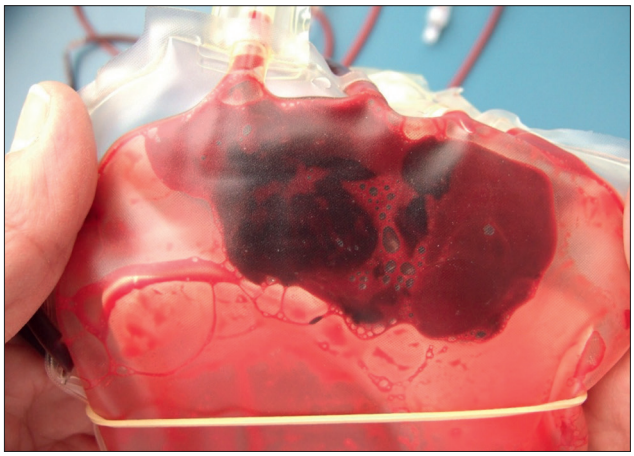

**FIGURE 1.** Massive blood clot in a red cell concentrate.

## INVESTIGATION

The entire track of events, from donation to blood component preparation to storage and transportation, was analysed for irregularities in the procedures or deviations of quality standards. No non-conformities were observed. There were no signs of bacterial contamination, nor could cold agglutinins be demonstrated. No drug or IV-solution had been added to the blood bag.

The events preceding the interruption of blood flow during transfusion were investigated. In two of the cases, the patient

[1]Blood Service, Belgian Red Cross, Mechelen, Belgium, [2]Transfusion Research Centre, Belgian Red Cross, Ghent, Belgium, [3]Laboratory for Histocompatibility and Immunogenetics (HILA), Belgian Red Cross, Mechelen, Belgium, [4]Department of Microbiology and Immunology, Catholic University of Leuven, Leuven, Belgium, [5]AZ Nikolaas, Sint-Niklaas, Belgium, [6]Imelda, Bonheiden, Belgium, [7]AZ Delta, Roeselare, Belgium, [8]Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium.

Please send all correspondence to: B. Van Aelst, PhD, Blood Service, Belgian Red Cross, Motstraat 40, 2800 Mechelen, Belgium, tel: +32 9 244 56 58, email: britt.vanaelst@rodekruis.be.

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**TABLE 1.** Blood typing results for the three cases.
Serological typing: donor samples. Molecular typing: patient samples and content of the blood infusion sets/bags. The discriminatory antigens are highlighted. In each case the typing found for the infusion set/bag corresponds with the patient and not with the donor.

| | Red Blood Cell Antigen | C | E | c | e | K | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | M | N | S | s |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Case 1 | Donor | + | – | + | + | – | + | + | + | + | – | + | – | + |
| | Patient | + | – | + | + | – | + | + | – | + | + | + | – | + |
| | Infusion set/bag | + | – | + | + | – | + | + | – | + | + | + | – | + |
| Case 2 | Donor | + | – | + | + | – | + | + | – | + | + | + | + | + |
| | Patient | + | – | - | + | – | + | + | + | + | + | – | – | + |
| | Infusion set/bag | + | – | - | + | – | + | + | + | + | + | – | – | + |
| Case 3 | Donor | – | – | + | + | – | – | + | + | + | + | – | - | + |
| | Patient | – | – | + | + | – | – | + | + | - | + | – | + | + |
| | Infusion set/bag | – | – | + | + | – | – | + | + | - | + | – | + | + |

took a walk during transfusion, carrying the blood bag in his hand. In the third case, the blood bag had fallen off the stand into the bed of the patient. In all three cases the blood bag had been displaced from the stand to below heart level for some time. We hypothesised backflow by simple gravity of patient blood into the infusion set and blood bag.

To investigate this hypothesis, DNA analysis for typing of red blood cell (RBC) antigens was performed on peripheral blood samples of the patient and on the content of the blood infusion set or the blood bag using the Lifecodes RBC Genotyping assay with Luminex's Xmap Technology or the Fluovista Verify kit by Innotrain.

## FINDINGS

The leukocyte-depleted red cell concentrate itself is virtually DNA-free, as was confirmed by the negative DNA-extraction on a sealed pilot sample of the blood bag. So, the mere presence of DNA found in the blood bag, suggests contamination with patient blood and more specifically patient white blood cells. This was also confirmed by the blood group antigen type found by analysis of the DNA in the blood bag, which was different from the type of the donor, but identical to the patient's blood type (*Table 1*). In case 1 the discriminatory blood group antigens were $Jk^a$ and M, in case 2 they were c, $Jk^a$, N and S and in case 3 they were $Jk^b$ and S.

In summary, the molecular blood group typing shows the presence of patient DNA high up in the infusion set or in the blood bag in all three cases, confirming the backflow of patient blood.

## CONCLUSION

During transfusion, blood of the patient can flow back into the blood bag when the latter is kept below heart level.[2] When the duration of this backflow is sufficiently long, the amount of free calcium ions entering the blood bag will exceed the chelating capacity of the anticoagulant. Consequently, the mix of patient blood and donor red cells are no longer anti-coagulated. Stasis and contact with non-biological substances (i.e. plastics) will initiate the contact pathway activation of the blood coagulation cascade, leading to massive coagulation and finally clogging in the infusion set filter, explaining the interrupted transfusion.

Blood clots formed in the blood bag will be stopped by the standard in-line blood filters (170-260 $\mu$m) of the infusion set. However, backflow of patient blood could also induce coagulation in the section of the infusion line between the filter and the patient arm. Blood clot (fragments) could then enter the patient's venous circulation. This may expose patients to an avoidable risk of venous embolisation. For this reason, instructions for red cell transfusion should include

## KEY MESSAGES FOR CLINICAL PRACTICE

1. During transfusion, keep the blood bag above the heart level at all times.
2. Backflow of patient blood into the infusion set might occur by gravity when the blood bag is kept below heart level.
3. Clinical personnel and patients should be instructed about the importance of a correctly positioned blood bag.

positioning the blood bag high above heart level during the entire transfusion procedure. Alternatively, the best possible position of the blood bag relative to the heart level should be investigated to obtain the pressure that is needed for the blood to naturally flow into the patient's circulation. Whenever the blood bag is moved to a lower position, the roller valve of the infusion set should be closed. Alternatively, an infusion set with a one-way valve could be used.

Until then, guidelines indicating that the blood bag should be positioned higher than heart level should be strictly adhered by the clinical personnel that initiate transfusion. The patient should be instructed that it is in his/her best interest to maintain the bag in the position set by the clinical staff during the entire transfusion.

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