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Sporadic Leukocyte Reduction Filter Failure During RBC

Component Preparation:

Beware of Rapid Filtration

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Red cell leukoreduction filter (LRF) failure is relatively rare given the large number of leukoreduced red cell units produced each year.¹ With the current standards for quality control (QC) testing of leukoreduced products, 1% of production intervals,² sporadic isolated filter failures are not likely to be detected by routine QC testing. Abnormalities in the leukofiltration of red cells are well recognized in such conditions as sickle cell trait, often associated with slow filtration and filter occlusion,³ however features suggestive of general LRF failure are seldom otherwise described. We documented two isolated and independent instances of LRF dysfunction, occurring within a two and a half week span of time, discovered on visual inspection by astute laboratory personnel. An emphasis on simple yet effective observation measures as an integral part of laboratory standard operating procedures (SOPs) is advocated as additional means of safeguarding against undetected instances of isolated LRF failure.

During routine component preparation, a single unit of RBCs was noted to have completed passage through the inline LRF (Leukotrap RC System, CP2D/AS-3 with RCM1 filter, Pall Corporation, East Hills, NY) more rapidly than other units being similarly processed. Total filtration time was estimated to be less than 5 minutes, compared to the more typical 30-60 minutes seen in other units concurrently being prepared. Additionally noted was a large volume of air, approximately 4-5 inches, downstream of the LRF. The unit in question was quarantined and a sample was prepared and sent for determination of WBC count by flow cytometry.

The following day, a second RBC unit was noted to exhibit similarly aberrant filtration through the same type of inline LRF, with complete passage through the filter within 5 minutes, and accumulation of a large air pocket downstream of the LRF. Again the RBC component was quarantined and a sample prepared for flow cytometric measurement of the WBC count. Both samples from the suspect units and four additional routine QC samples were submitted as a single batch for flow analysis (LeucoCount assay, Becton Dickinson, San Jose, CA). Results obtained on both quarantined units revealed elevated leukocyte concentrations of greater than 0.35×10^9 WBC/L, which equated with total leukocyte counts per component exceeding the acceptable upper limit for a leukocyte reduced product (5×10^6 leukocytes per unit). The routine QC samples from four other leukoreduced RBC units with unremarkable component processing yielded WBC counts below detectable limits for the method (less than 0.001×10^9 WBC/L).

Subsequently, a third RBC component exhibited rapid flow through the inline LRF and abundant air collection in the distal tubing. We were concerned that additional failed units may have entered available inventory using the same collection bag lot number, at which point segments from all 226 RBC components in our facility's existing inventory were prepared for analysis. Given time considerations and the limitation of flow analysis used for enumeration of low-level residual leukocytes, which must be performed within 48 hours of collection, WBC measurements on the existing RBC inventory were performed with use of a cell counter as a

screening method (Cell-Dyn 4000, Abbott Diagnostics, Abbott Park, IL). For comparison, sample segments from the initial batch of two failed units along with the previously tested 4 QC samples were repeated with use of the Cell-Dyn cell counter method. The results for the two failed units ($>0.35 \times 10^9$ WBC/L by flow cytometry) were 9.60 and 7.77×10^9 WBC/L, respectively, while the results for the leukoreduced QC samples were all less than 0.05×10^9 WBC/L. Platelet counts for the failed units were 287 and 257×10^9 /L, respectively, compared to $<24 \times 10^9$ /L from the successfully leukoreduced units (Table 1). Notification of the manufacturer, Pall Corporation, initiated an inspection and evaluation of the implicated bag lot number (Leukotrap RC System, CP2D/AS-3 triple bag unit with in-line RCM1 filter and sample diversion pouch, Lot # 0700603).

Data collected on all inventoried units revealed only 2 of 226 existing RBC products to have elevated WBC counts (11.80 and 7.39×10^9 /L, respectively; platelet counts 259 and 99×10^9 /L, respectively; Cell-Dyn 4000). Both units were collected with the same collection set lot number as the initial two defective units (Leukotrap RC System, CP2D/AS-3 triple bag unit with in-line RCM1 filter and sample diversion pouch, Lot # 0700603). Immediate replacement of all collection bags of the implicated lot number was undertaken despite the manufacturer's investigation showing no detectable defects or aberrations of the filter media or assembly, and no evidence of air leak or compromise in the system. Verification of proper function and acceptable leukoreduction using the newly instituted collection kits (Leukotrap RC System, CP2D/AS-3 triple bag unit with in-line filter and Y sample site, Lot # 0700462) was performed on the first sixteen components processed, with all residual WBC counts below 0.001×10^9 WBC/L (below 5×10^6 total cells), as measured by flow cytometry.

Two weeks after institution of the replacement collection system, a single unit of RBCs was noted to have slightly atypical appearance upon completion of leukofiltration. A small amount of air accumulation was present distal to the LRF, although total filtration rate/time was within the expected range (30-60 minutes). Flow cytometric determination of the leukocyte count on the aberrant unit was found to be 2.8×10^7 total cells. Since then, no additional LRF defects were detected, and all quarantined units found to have elevated leukocyte content were discarded.

Prestorage leukoreduction of blood remains an effective and important means of reducing the incidence of several transfusion-related complications, such as CMV transmission, HLA alloimmunization, febrile nonhemolytic transfusion reactions, and transfusion-associated immune modulation.⁴⁻⁶ Our observed instances of unexpected LRF failure, identified in the course of routine component preparation, illustrate the importance of vigilance and awareness in the detection of sporadic LRF dysfunction. Our present experience highlights two features that can alert staff to possible defects in LRF function: an unusually rapid rate of flow through the LRF, and accumulation of air in the tubing downstream of the filter. While the manufacturer's package insert states, "If the filter housing (downstream side) and numbered tubing below the filter have drained (emptied) after filtration, it is recommended to perform QC on the unit," our current experience suggests that this event is associated with filter failure 100% of the time, and has not received the scrutiny accorded to the more typical types of LRF failure involving blockage or incomplete filtration, as seen in donors with sickle cell trait. The performance of simple visual checks during routine component preparation, with attention to signs of device failure, is advocated, and emphasizes the indispensable role of careful observation in maintaining quality control.

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Table 1

Residual leukocyte counts of two RBC components with unusual filtration characteristics (units 714689 and 714721) and four control units

Unit Number	WBC Counts Measured by Flow Cytometry		WBC and Platelet Counts Measured with an Automated Cell Counter (Cell Dyn 4000)	
	WBC events	WBC $\times 10^9/L$	WBC $\times 10^9/L$	Plts $\times 10^9/L$
714699	1	BDL	0.020	21.1
714696	3	BDL	0.030	17.6
714700	0	BDL	0.009	18.1
714701	0	BDL	0.012	23.7
714689	127,175	>0.35	9.600	287
714721	167,416	>0.35	7.770	257

BDL= below detectable limits