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Address for correspondence: N. Sarita Shah, Department of Medicine, Division of General Internal Medicine, Albert Einstein College of Medicine, 111 E. 210 St, Bronx, NY 10467, USA; email: sshah@montefiore.org

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研究報告の概要

○アフェレーシス血小板の細菌スクリーニング及び輸血による敗血症の残存リスク：米国赤十字の経験（2004～2006年）
背景：米国赤十字は2004年3月にすべてのアフェレーシス血小板（PLT）の細菌検査を開始したが、それでもなお、検査済み製剤による輸血後敗血症の報告がある。
試験デザイン及び方法：前方視的品質管理テスト(QC) 及び細菌検査陰性のアフェレーシスPLTにより生じた敗血症の報告の調査から確認された敗血症とアフェレーシスPLTの細菌汚染率を、採取方法ごとに解析した。
結果：2004年3月1日～2006年5月31日の期間に、1,004,206本の供血血液に細菌培養テストが行われた。そのうち186(1:5,399)本に陽性の培養結果が確認された。293製剤のうち1件を除くすべての輸血が回避された。両腕法を用いて採取した製剤では、片腕法と比較して、確認された陽性細菌培養の割合が有意に高かった（105供血当り22.7vs.11.9; オッズ比[OR], 1.9; 95%信頼区間[CI], 1.4-2.7)。この期間中に、死亡3名（死亡/供血数1:498,711供血）を含む20例の敗血症が報告され、これはスクリーニング結果陰性のアフェレーシスPLTに関係したものであった。両腕法(1:41,173; 95% CI, 1:25,000-1:66,667)を用いて採取した場合の敗血症性副作用の頻度は、片腕法（1:193,305; 95% CI, 1:52,632-1:500,000; OR, 4.7; 95% CI, 1.2-18.4)と比較して4.7倍高かった。ほとんどの敗血症性副作用(16/20)は、*Staphylococcus spp.* を起炎菌とし、採血後5日目（13/ 20)に発現した。
結論：当該試験期間中においてQC培養による検出をすり抜けたPLTの細菌汚染（特に古いPLTや、両腕法で採取された血液成分中の皮膚常在菌など）は、いまだに輸血の重大な残存リスクである。

使用上の注意記載状況・その他参考事項等

合成血「日赤」
照射合成血「日赤」
合成血-LR「日赤」
照射合成血-LR「日赤」

血液を介するウイルス、細菌、原虫等の感染
vCJD等の伝播のリスク

報告企業の意見	今後の対応
2004年3月1日～2006年5月31日の期間に、細菌培養で陽性となったアフェレーシス血小板293製剤のうち1件を除くすべての輸血が回避されたが、スクリーニング陰性の製剤に関係した敗血症が20例（うち死亡3例）報告された。両腕法を用いて採取した場合の敗血症性副作用の頻度は、片腕法と比較して4.7倍高かったとの報告である。	日本赤十字社では、輸血情報リーフレット等により、細菌感染やウイルス感染について医療機関へ情報提供し注意喚起している。また、「血液製剤等に係る遡及調査ガイドライン」（平成17年3月10日付薬食発第0310009号）における「本ガイドライン対象以外の病原体の取扱い イ．細菌」に準じ細菌感染が疑われる場合の対応を医療機関に周知する。 今後も細菌感染に関する情報の収集に努める。

Bacterial screening of apheresis platelets and the residual risk of septic transfusion reactions: the American Red Cross experience (2004-2006)

Anne F. Eder, Jean M. Kennedy, Beth A. Dy, Edward P. Notari, John W. Weiss, Chyang T. Fang, Stephen Wagner, Roger Y. Dodd, Richard J. Benjamin, and the American Red Cross Regional Blood Centers

BACKGROUND: The American Red Cross initiated systemwide bacterial testing of all apheresis platelet (PLT) collections in March 2004, yet continues to receive reports of septic reactions after transfusion of screened components.

STUDY DESIGN AND METHODS: The rates of confirmed bacterial contamination of apheresis PLT collections detected by prospective quality control (QC) testing, and by surveillance of reported septic reactions to screened-negative apheresis PLTs, were analyzed according to the technology utilized for collection.

RESULTS: Between March 1, 2004, and May 31, 2006, bacterial culture testing was performed on 1,004,206 donations; of these, 186 (1:5,399) had confirmed-positive culture results. Transfusion of all but 1 of the associated 293 components was prevented. A significantly higher rate of confirmed-positive bacterial cultures was seen with products collected utilizing two-arm collection procedures compared to one-arm procedures (22.7 vs. 11.9 per 10^5 donations; odds ratio [OR], 1.9; 95% confidence interval [CI], 1.4-2.7). During this period, 20 septic transfusion reactions were reported, including 3 fatalities (1:498,711 fatalities per distributed component), which implicated screened-negative apheresis PLT products. The frequency of septic reactions was 4.7-fold higher for collections utilizing two-arm procedures (1:41,173; 95% CI, 1:25,000-1:66,667) compared to collections from one-arm procedures (1:193,305; 95% CI, 1:52,632-1:500,000; OR, 4.7; 95% CI, 1.2-18.4); most septic reactions (16 of 20) were due to *Staphylococcus* spp. and occurred on Day 5 (13 of 20) after collection.

CONCLUSION: PLT contamination with bacteria that evade detection by QC culture remains a significant residual transfusion risk, in particular for older PLTs and skin-commensal bacteria in components collected by two-arm apheresis procedures during the study period.

Bacterial contamination of platelet (PLT) components remains a significant infectious risk to transfusion recipients, despite the implementation of preventive measures.[1-3] Contamination occurs from the introduction of low concentrations of skin bacteria at the time of phlebotomy; less commonly, from asymptomatic donor bacteremia; or rarely, during blood processing.[4] The low initial bacterial inoculum may lead to gross contamination during the 5-day storage period allowed for PLTs.[5,6] Septic transfusion reactions to PLT transfusion were estimated to occur with approximately 1:25,000 (range, 1:13,000-1:100,000) transfusions before 2004.[7-9] Actual contamination rates were measured to be substantially higher at 1:2,000 to 1:3,000 transfused PLT products.[3,10] The difference may be explained by low-level contamination that did not evoke a clinical response or the difficulty in recognizing septic transfusion reactions in patients with neutropenia or concomitant fever or on antibiotic therapy.

In 2004, professional standards were introduced by AABB that required measures to limit and detect bacterial contamination in all PLT components.[11] In response, blood centers and transfusion services implemented a variety of different preventive measures and bacterial

From Biomedical Services, Medical Office, National Headquarters, American Red Cross, Washington, DC; the Jerome H. Holland Laboratory, Rockville, Maryland; and the Badger Hawkeye Region, American Red Cross, Madison, Wisconsin.

Address reprint requests to: Dr Anne Eder, MD, PhD, Biomedical Services, National Headquarters, American Red Cross, 2025 E Street NW, Washington, DC 20006; e-mail: EderA@usa.redcross.org.

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detection strategies. In March 2004, the American Red Cross began routine in-process quality control (QC) testing for bacterial contamination in all apheresis PLTs with an automated microbial detection system (BacT/ALERT 3D, bioMérieux, Durham, NC).[12,13] Despite these efforts, septic reactions and rare fatalities linked to bacterially contaminated apheresis PLTs still occur, suggesting a substantial rate of false-negative bacterial culture results. We performed a retrospective analysis of our QC bacterial testing results and clinical reports of septic transfusion reactions to identify risk factors for bacterial contamination and transfusion-associated sepsis associated with apheresis PLTs.

MATERIALS AND METHODS

Collection of apheresis PLTs

Between March 1, 2004, and May 31, 2006, apheresis PLTs were collected utilizing standard protocols, from volunteer donors at 35 regional blood centers of the American Red Cross with one of three apheresis devices (Amicus, Baxter Healthcare, Round Lake, IL; Spectra, Gambro BCT, Lakewood, CO; or Trima, Gambro BCT), as previously described.[12] The Amicus and the Spectra devices have two configurations for collection, a continuous-separation protocol that requires an intravenous (IV) line in both arms for blood withdrawal (inlet line) or venous return (two-arm procedure; Amicus collection set, 4R2310; Spectra collection set, 777-003-015) and a discontinuous protocol that intermittently withdraws and returns blood through a single IV access line (one-arm procedure; Amicus collection set, 4R2312; Spectra collection set, 777-003-215). The Trima device utilizes a discontinuous protocol with single IV line access (Trima collection sets 777800100 and 777800400). All collection sets divert the initial 40 to 50 mL of whole blood drawn into a secondary collection container or tubes for viral marker and immunohematology testing. For two-arm procedures performed on the Amicus and Spectra technologies included in this report, the sample was collected from the first line placed during operation, which was the venous return line, not the inlet draw line.

The phlebotomy site is prepared by a standard, FDA-recommended, skin disinfection protocol utilizing povidone-iodine scrubs (or chlorhexidine gluconate in 70% isopropyl alcohol scrubs in donors allergic to iodine) in all Red Cross regional blood centers.[14,15]

The total number of apheresis PLT donations collected and the number of components manufactured was derived from the Red Cross centralized database. The proportion of procedures performed with different collection sets was calculated based on the purchased volume of collection sets for the system during the 3-year study period.

Detection of bacterial contamination

An automated microbial detection system was used for aerobic cultures according to manufacturer's instructions, as previously described.[12] The Red Cross, like the majority (85%) of licensed blood centers in North America, inoculated only an aerobic bottle, although an additional anaerobic bottle was recommended, but not required, by the manufacturer. This decision was based on our assessment of the data supporting the practice.[16,17] PLT components were sampled at least 24 hours after collection, divided into two cocomponents if PLT yield was greater than 6.5×10^{11} PLTs and released into inventory for distribution 12 hours after initiation of culture, if cultures were negative. Cultures were continued for the 5-day shelf life of the PLT components. All components associated with positive initial culture results were quarantined or retrieved if already distributed to transfusion services. A second 4- to 5-mL sample was taken from these initially positive components or cocomponents and inoculated into a new aerobic bottle for confirmatory culture. The initial and subsequent positive culture bottles were sent to independent microbiology laboratories for bacterial isolation and identification. A confirmed-positive result is defined as the growth of the same organism in the initial and confirmatory sample; a false-positive result is defined as a positive bottle signal but a negative result on subsequent culture, which was further characterized as either possible sampling contamination or instrument error.[12] If PLT components were not available for confirmatory culture, because they were transfused or destroyed during the manufacturing process, the initial positive signal could not be resolved and the results were classified as "indeterminate."

Septic transfusion reactions

All transfusion reactions reported to American Red Cross blood centers were investigated by regional physicians and compiled in a centralized database. Clinical criteria for a possible septic transfusion reaction to apheresis PLTs were any of the following symptoms within 4 hours of transfusion: fever of greater than 39°C or a change of greater than 2°C from pretransfusion value, rigors, tachycardia greater than 120 bpm or a change of more than 40 bpm from pretransfusion value, or an increase or decrease of more than 30 mmHg in blood pressure.[8] A definite septic transfusion reaction was defined by clinical criteria associated with a culture-positive residual component and a culture-positive recipient demonstrating the same bacteria as determined by antibiotic sensitivity and/or pulsed-field gel electrophoresis or by clinical criteria in both recipients of proven culture-positive cocomponents. A probable septic transfusion reaction was defined by clinical criteria and a positive culture on the residual component without matching positive culture results in the

recipient or clinical criteria and matching culture results in two different recipients of each cocomponent that was not cultured. For the risk analysis, the probable and definite septic reactions were combined and the generic term "septic reactions" denotes the sum of these reports. Possible septic reactions that did not meet the criteria of probable or definite reactions were excluded.

Statistical analysis

Rates of culture-positive reactions were compared with chi-square statistics with Yates correction and adjustment for multiple comparisons (5 × 2 table, degrees of freedom [df] = 4).[18] Odds ratios (ORs) and 95 percent confidence intervals (CIs) were computed to compare the odds of contamination with collections performed utilizing one-arm versus two-arm procedures.[19] A p value of less than 0.05 was considered significant.

The American Red Cross Institutional Review Board reviewed and approved this study.

RESULTS

Characterization of positive results from the bacterial detection system

From March 1, 2004, to May 31, 2006, the American Red Cross performed routine QC testing for bacterial detection on 1,004,206 apheresis PLT donations from approximately 150,000 donors, which yielded 1,496,134 components for distribution for transfusion. Culture results of 186 donations were confirmed positive for bacterial contamination with 188 organisms (2 cultures contained 2 species each). The overall rate for confirmed-positive cultures was 18.5 in 10^5 donations (1:5,399); false-positive cultures, 34.7 in 10^5 donations (1:2,886); and indeterminate, 7.8 in 10^5 donations (1:12,874) (Table 1). Of the total donations, 61 percent were collected by a two-arm procedure (46%, Amicus; 15%, Spectra) and 39 percent by a one-arm procedure (12%, Amicus; 7%, Spectra; 20%, Trima) (Table 2). A significant difference was noted in the rates of confirmed-positive cultures (confirmed-positive cultures, df = 4, χ^2 = 16.6; p = 0.002; Fig. 1), but not false-positive cultures (false-positive cultures, df = 4, χ^2 = 7.1; p = 0.1) among the five collection

TABLE 1. All positive bacterial culture results from 1,004,206 apheresis PLT donations tested between March 1, 2004, and May 31, 2006

Result	Number (%)	Rate per 10^5 donations	Risk per donation
Confirmed-positive	186 (30.3)	18.5	1:5,399
False-positive			
Total	348 (57.0)	34.7	1:2,886
Sampling contamination	198 (32.4)	19.7	1:5,072
Instrument signal error	150 (24.5)	14.9	1:6,695
Indeterminate	78 (12.7)	7.8	1:12,874
Total number of positive donations	612	60.9	1:1,641

TABLE 2. Confirmed-positive bacterial cultures by donation type

	Two-arm procedure			One-arm procedure				
	Amicus	Spectra	Total	Amicus	Spectra	Trima	Total	OR (95% CI)*
Total number of collections	467,090	150,505	617,595	117,830	70,223	198,558	386,611	
Likely skin contaminants								
Coagulase-negative *Staphylococcus*†	70	16	86	3	2	10	15	
Staphylococcus aureus	2	1	3	2	0	3	5	
Streptococcus sp.‡	10	2	12	3	2	4	9	
Micrococcus sp.	1	0	1	0	0	0	0	
Bacillus sp.	2	2	4	0	0	1	1	
Total number of skin contaminants	85	21	106	8	4	18	30	
Rate per 10^5 cultures	18.2	14.0	17.2	6.8	5.7	9.1	7.8	2.2 (1.5-3.3)
Nonskin organisms								
Streptococcus sp.§	6	4	10	2	1	3	6	
Escherichia coli	5	3	8	0	1	3	4	
Klebsiella sp.	6	0	6	0	0	1	1	
Listeria sp.	1	1	2	2	0	0	2	
Serratia sp.	4	0	4	1	0	0	1	
Other‖	4	0	4	2	0	0	2	
Total nonskin organisms	26	8	34	7	2	7	16	
Rate per 10^5 cultures	5.6	5.3	5.5	5.9	2.8	3.5	4.1	1.3 (0.7-2.4)
All confirmed-positive cultures	111	29	140	15	6	25	46	
Rate per 10^5 cultures	23.8	19.3	22.7	12.7	8.5	12.6	11.9	1.9 (1.4-2.7)

* ORs compare the rates of positive cultures for total one-arm vs. total two-arm procedures.
† Coagulase-negative *Staphylococcus* including *S. epidermidis, S. capitis, S. hemolyticus, S. saprophyticus,* and *S. lugdunensis.*
‡ α-Hemolytic *Streptococcus, S. viridans* group, *S. mitis/oralis, S. sanguis,* and *S. salivarius.*
§ β-Hemolytic *Streptococcus, S. agalactiae, S. bovis,* and *S. pneumonia.*
‖ *Enterococcus avium, Granulicatella adiacens, Citrobacter* sp., *Lactobacillus* sp., and *Enterobacter aerogenes.*

procedures (Table 3). There was no significant difference in the rates of confirmed-positive cultures among the three collection devices for the one-arm procedures or between the two collection devices for two-arm procedures ($p > 0.05$), which were therefore analyzed as distinct groups for comparison (one-arm vs. two-arm procedures; Fig. 1). The rate of confirmed bacterial contamination of apheresis PLTs was 1.9-fold greater for two-arm procedures compared to one-arm procedures (OR, 1.9; 95% CI, 1.4-2.7; Fig. 1 and Table 2). There were no significant differences in the rates of false-positive culture results, due to either possible sampling contamination or instrument error, for two-arm procedures compared to one-arm procedures (OR, 1.1; 95% CI, 0.9-1.4; Table 3).

Bacterial isolates that likely represent skin flora, including *Staphylococcus* spp., comprised the majority of confirmed-positive cultures (136 of 186 [73%]; Table 2), whereas the remainder (50 of 186 [27%]) were bacteria not typically found on skin surfaces that could reflect asymptomatic bacteremia in the donor.[20] Skin contaminants were more frequent in two-arm procedures (OR, 2.2; 95% CI, 1.5-3.3) compared to one-arm procedures, but there was no significant difference between procedure types for other bacteria (OR, 1.3; 95% CI, 0.7-2.4; Table 2).

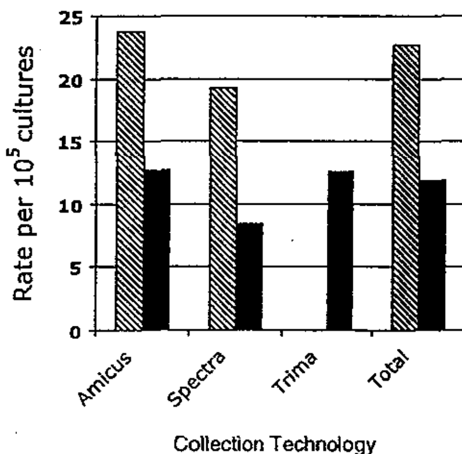

Fig. 1. The rate of confirmed-positive PLT cultures per 100,000 collections, analyzed by the technology utilized for collection, including the Baxter Amicus, Gambro Spectra, and Gambro Trima technologies and one-arm (■) and two-arm (▨) procedures.

Transfusion of culture-positive apheresis PLTs

Of the 612 donations that tested initially positive, 97 apheresis PLT components had been transfused at the time of the positive culture result, only one of which was associated with a confirmed-positive result (coagulase-negative *Staphylococcus*). The confirmed-positive component was transfused without reported recipient reaction on Day 2 after collection, and was detected 48 h after inoculation. No septic transfusion reactions were reported for the other recipients of apheresis components associated with false-positive or indeterminate results. The mean incubation time to a positive result for transfused components with false-positive or indeterminate culture results was 74 ± 30 hours. These data support the safety of the Red Cross protocol, which incorporated a 12-hour inventory hold period after inoculating the bacterial culture bottle. Operational constraints, including inventory release, distribution, and transport generally prevented transfusion of products within 24 hours of sample inoculation (data not shown).

Investigation of donors with confirmed-positive results

All donors with confirmed-positive bacterial culture results were investigated to evaluate a possible source of contamination. In one series of cases, *Listeria monocytogenes* was detected in three asymptomatic donors in different states during a 3-month time period. Investigation in collaboration with the Centers for Disease Control and Prevention revealed no common source. Donors of contaminated PLT products likely due to asymptomatic bacteremia were referred to their physician for further evaluation. One donor of a *Streptococcus bovis*–contaminated product was found to have an occult moderately differentiated adenocarcinoma, as previously reported[21] and another donor found with a positive

TABLE 3. False-positive cultures by donation type

	Two-arm procedure			One-arm procedure				
	Amicus	Spectra	Total	Amicus	Spectra	Trima	Total	OR (95% CI)*
Total number of collections	467,090	150,505	617,595	117,830	70,223	198,558	386,611	
False-positive (sampling contamination)	93	36	129	18	13	38	69	
Rate per 10^5 cultures	19.9	23.9	20.9	15.3	18.5	19.1	17.8	1.2 (0.9-1.6)
False-positive (instrument signal error)	77	19	96	7	11	36	54	
Rate per 10^5 cultures	16.5	12.6	15.5	5.9	15.7	18.1	14.0	1.1 (0.8-1.5)
All false-positive cultures	170	55	225	25	24	74	123	
Rate per 10^5 cultures	36.4	36.5	36.4	21.2	34.2	37.3	31.8	1.1 (0.9-1.4)

* ORs compare the rates of positive cultures for total one-arm vs. total two-arm procedures.

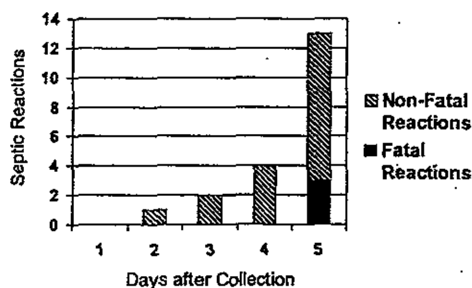

Fig. 2. Septic transfusion reactions analyzed by the interval between collection and transfusion. (■) Fatal reactions; (▨) nonfatal reactions.

culture for β-hemolytic *Streptococcus* G reported a diagnosis of colonic carcinoma 1 month after the involved collection. The donor investigation was unremarkable in most cases and the donors were allowed to continue to donate PLTs. No donor has been implicated in more than one episode of PLT contamination.

Clinical transfusion reactions to screened-negative apheresis components

From March 1, 2004, to May 31, 2006, a total of 20 definite or probable septic transfusion reactions, including 3 fatalities, were reported to the Red Cross, after transfusion of bacterially screened apheresis PLT components. More septic reactions occurred with older PLT units, and 13 of the 20 reactions including all 3 fatalities occurred after transfusion on Day 5 after collection (Fig. 2). During this period, a nationwide survey reported that the majority of apheresis PLT products were transfused on Day 3 or earlier (median, Day 3; mean, Day 3.08) after collection,[22] suggesting that the rate of septic reactions increases with PLT age. All of the implicated components had negative QC culture results after 5 days of culture indicating false-negative BacT/ALERT results. All collections were performed with the standard povidone-iodine–based skin preparation. Two-arm procedures were used for 15 implicated collections (17 septic transfusion reactions, including the 3 fatalities), and one-arm procedures for 2 implicated collections (3 septic transfusion reactions; Table 4). The risk of septic transfusion reactions after transfusion of screened-negative apheresis PLTs was 4.7-fold greater for two-arm collection procedures compared to one-arm procedures (OR, 4.7; 95% CI, 1.2-18.4). When analyzed by distributed components, PLTs from two-arm procedures tended to be 3.3-fold more likely to be involved in a reported septic reaction (OR, 3.3; 95% CI, 1.0-10.6). Components collected with two-arm procedures were implicated in the 11 definite septic transfusion reactions; 9 of the 11, including the 3 fatalities, were found with *Staphylococcus* spp. contamination.

One recipient fatality implicated *Staphylococcus lugdunensis* (coagulase-negative *Staphylococcus*) and has been described previously.[23] A second fatal case involved a 70-year-old woman with breast cancer who died shortly after receiving a PLT product stored for 5 days that was found to be contaminated with *Staphylococcus aureus.* The cocomponent had been transfused to a different patient on Day 3 of storage without reported reaction; however, subsequent chart review by the regional Red Cross physician revealed this patient developed fever 2 hours after transfusion with subsequent blood cultures demonstrating *S. aureus.* The bacterial isolates from both recipients and the residual apheresis PLT product implicated in the fatality had identical antibiotic sensitivity profiles and banding patterns on pulsed-field gel electrophoresis. The third fatal case involved a 68-year-old woman with multiple myeloma after autologous peripheral blood cell transplant and also implicated *S. aureus.* In contrast, eight of the donations implicated in septic reactions had an apheresis PLT cocomponent had been distributed and transfused without reported reaction in six cases or outdated in the hospital in two cases.

DISCUSSION

The rate of bacterial detection in apheresis PLT components in the American Red Cross was 1:5399 (18.5 per 10^5) donations after implementation of culture-based screening. Although this likely represents an important improvement in blood component safety, there remains an appreciable risk of transfusion-related sepsis or death after transfusion of screened-negative components. Utilizing data from passive surveillance of transfusion reactions reported to the Red Cross in the study period, this residual risk is estimated as at least 1:74,807 septic reactions and 1:498,711 fatalities per distributed component. Before the introduction of bacterial testing, comparable rates within the Red Cross system were estimated at approximately 1:40,000 and 1:240,000, respectively[12] (based on a 10-month period in 2003 when approximately 480,000 apheresis PLTs were distributed), an approximate 50 percent decrease in reported reactions and fatalities. The significance of this declining trend ($p = 0.11$) is unclear, given the likelihood of variable and incomplete reporting of cases in a passive surveillance system.

The bacterial contamination rate associated with two-arm procedures (1:4,411) was almost twice that observed for one-arm procedures (1:8,405; OR, 1.9; 95% CI, 1.4-2.7). Similarly, more than a fourfold increase in reported septic transfusion reaction rates was observed between two-arm procedures (1:41,173 collections) compared to one-arm procedures (1:193,305 collections; OR, 4.7; 95% CI, 1.2-18.4). These observations may reflect the fact that during one-arm procedures, the initial volume of

TABLE 4. Septic transfusion reactions to bacterial screen–negative apheresis PLTs (false-negative cultures) by donation type

	Two-arm procedure			One-arm procedure				
	Amicus	Spectra	Total	Amicus	Spectra	Trima	Total	OR (95% CI)*
Total number of collections	467,090	150,505	617,595	117,830	70,223	198,558	386,611	
Total number of distributed components	725,105	218,233	943,338	182,918	101,823	268,054	552,796	
Definite								
Coagulase-negative *Staphylococcus*	5	0	5	0	0	0	0	
Staphylococcus lugdunensis†	1	0	1	0	0	0	0	
Staphylococcus aureus†	3‡	0	3	0	0	0	0	
Enterobacter aerogenes	2‡	0	2	0	0	0	0	
Probable								
Coagulase-negative *Staphylococcus*	3	1	4	0	0	1	1	
Staphylococcus intermedius	0	0	0	0	2‡	0	2	
Enterococcus fecalis	0	1	1	0	0	0	0	
Pseudomonas fluorescens	1	0	1	0	0	0	0	
Total number of septic reactions by collections‡	13	2	15	0	1	1	2	
Rate per 10^5 collections	2.8	1.3	2.4	0.0	1.4	0.5	0.5	4.7 (1.2-18.4)
Total number of septic reactions by components	15	2	17	0	2	1	3	
Rate per 10^5 components	2.1	0.9	1.8	0.0	2.0	0.4	0.5	3.3 (1.0-10.6)

* ORs compare the rates of septic reactions for total one-arm vs. total two-arm procedures.
† Organisms implicated in three recipient fatalities.
‡ In three cases, the components from a single PLT collection were implicated in two separate septic reactions.

blood that may be contaminated with skin organisms during phlebotomy is separately collected for viral marker testing and does not enter the apheresis product. In contrast, the configuration with the two-arm procedures performed during this study collected the sample for testing from the return line, not the inlet (draw) line, which may have allowed blood contaminated during inlet line phlebotomy to enter the collection set and PLT product. Removal of the initial 10 to 40 mL of blood after venipuncture before drawing donors' blood has been shown to reduce the bacterial load introduced into manufactured blood components by 40 to 90 percent.[24-28] The clinical importance of reducing the probability of contamination is supported by data from a hemovigilance program that showed a concomitant reduction in septic transfusion reactions, which were almost all associated with skin organisms, after implementation of a 40-mL diversion pouch for whole blood–derived PLTs.[29] The alternative explanation, that increased risk with two-arm procedures simply reflects an additional needle stick, is unlikely as blood from the return line in two-arm procedures does not generally enter the apheresis machine to contaminate the apheresis product.

Based on the current analysis and on recently published data, the American Red Cross has converted to Amicus two-arm procedures which utilize an inlet line diversion pouch system and will phase out the use of the Spectra system. Although the Spectra two-arm procedure was not associated with an increase in septic reactions in our data, the twofold increased rate of true-positive bacterial cultures with this technology raises concern. The volume of product cultured in the BacT/ALERT system will be doubled (from 4 to 8 mL), which is predicted to increase QC culture sensitivity by up to 25 percent.[30] This combination of interventions is predicted to reduce the rate of septic transfusion reactions described in this report by greater than 75 percent and efficacy will be monitored prospectively. Further strategies to reduce contamination may include additional modification of culture volume or conditions, improved skin decontamination procedures,[15,24,31] introduction of point-of-issue retesting of products, and prospective pathogen reduction of apheresis blood components,[32] although the latter two options are not yet available as FDA-approved technologies in the United States.

Our data raise the question as to why the BacT/ALERT culture system has a significant false-negative rate when used as a QC test for apheresis PLTs. This system was validated for testing apheresis PLTs by the manufacturer utilizing in vitro spiked products, on the assumption that the detectable concentration of bacteria was in the range of 1 to 10 colony-forming units (CFUs) per mL and that organisms enter a log phase of growth to reach these levels during the 24-hour hold period before sampling.[33,34] Bacterial contamination of apheresis products at collection, however, may be as low as 1 to 10 CFUs per bag (0.003-0.03 CFUs/mL). At these low concentrations, bacteria may behave in an idiosyncratic fashion such that the duration of the lag phase of growth is unpredictable. The BacT/ALERT system has not been validated to reliably detect bacteria in this clinically relevant range and a residual risk of contamination almost certainly remains, especially in