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REVIEW

Platelet concentrates: reducing the risk of transfusion-transmitted bacterial infections

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Dirk de Korte[1]
Jan H Marcelis[2]

[1]Department of Product and Process Development, Sanquin Blood Bank, Amsterdam, [2]Department of Microbiology, St Elisabeth Hospital, Tilburg, the Netherlands

Abstract: The introduction of a combination of interventions during collection of whole-blood or platelet concentrates has been successful in lowering the degree of bacterial contamination in the final product, the platelet concentrate, by 50%–75%. These interventions were improved donor questionnaires, best-practice skin disinfection, and diversion of first blood volume. These interventions have reduced the number of bacteria present in the platelet concentrates. In combination with screening for bacterial contamination of platelet concentrates with a culture method, the degree of transfusion-transmitted bacterial infection has been reduced significantly. Due to the very low initial bacteria counts upon collection of the products, the need for improved sensitivity of early screenings tests or highly selective point-of-issue tests remains. The latter should be rapid and easy to perform. An alternative approach might be the implementation of pathogen-inactivation methods for cellular blood products to reduce the amount of pathogens. However, these methods are costly, and so far not proved to be cost-effective, especially in countries with an already-low incidence of transfusion-transmitted infections by viruses, parasites, or bacteria.

Keywords: blood products, bacterial contamination, screening, point of issue, pathogen inactivation

Introduction

Transfusion-transmitted bacterial infection (TTBI) has been a serious complication of transfusion since the start of blood banking at the beginning of the twentieth century. By introduction of donor-arm disinfection and by sterilization of materials and reagents, significant improvement was achieved. The introduction of closed systems for blood collection, component preparation, and storage was a further step in reducing the frequency of TTBI. During the 1970s, the focus moved from TTBI to viral transmissions, especially as a result of the acquired immunodeficiency-syndrome epidemic, caused by human immunodeficiency virus (HIV). In the last decade of the twentieth century, there were huge efforts in screening of blood products by serological methods and the introduction of nucleic acid testing. This was combined with improved donor selection for cellular products and the introduction of pathogen-reduction techniques for plasma-derived products. Altogether, this resulted in a drastic fall in the estimated frequency of infectious donations entering the blood supply. For hepatitis B, this was brought down to 1.66 per million, for hepatitis C to 0.80 per million, and for HIV to only 0.14 per million, as reported for the UK over the period 1996–2003.[1] At the same time, people started to realize that the risk of TTBI was still high, with up to 10% of blood transfusion-associated deaths caused by TTBI, as reported by Sazama.[2] Therefore,

Correspondence: Dirk de Korte
Department of Product and Process Development, Sanquin Blood Bank, 125 Plesmanlaan, Amsterdam 1066 CX, the Netherlands
Tel +31 20 512 3578
Fax +31 20 617 8080
Email d.dekorte@sanquin.nl

more attention was given to bacterial contamination as the major adverse effect of transfusion. Twenty years later, the risk of TTBI is now much lower than it was before, but still TTBI is responsible for about one fatality and multiple severe complications per 1–2 million platelet transfusions. This review describes the interventions that have led to the rapid decrease of TTBI to the current level, and the remaining risk for TTBI.

Donor bacteremia

The major source of bacterial contamination in blood products is the donor arm,[3,4] and to a much lesser extent donor bacteremia,[5] contaminated collection equipment,[6] contamination of the blood (product) during processing,[7,8] and finally procedures around transfusion in the hospital.

In the majority of cases, bacteremic donors will be too sick to attend for donation and will not show up. However, bacteremia can be asymptomatic during the incubation period of an infection and in low-grade chronic infections or can be transient, eg, after dental procedures.[9,10]

Yersinia enterocolitica is one of the most important microorganisms in asymptomatic donors as the result of a low-grade gastrointestinal infection. Indeed, it was reported by Tipple et al[11] that half of the *Yersinia* cases reported were asymptomatic. Transfusion of red cells contaminated with *Y. enterocolitica* after long storage is most risky, as this microorganism is one of the few human pathogens that can grow at 4°C (psychrophilic). Stenhouse and Milner[12] demonstrated that upon inoculation of low numbers of *Y. enterocolitica* into a fresh unit of whole blood, counts of 5×10^6/mL were achieved after 21 days of incubation at 4°C. After an initial 4-day lag phase, growth proceeded briskly throughout the duration of storage at 4°C. A recent review by Guinet et al[13] found 55 reported cases of *Yersinia* over the period 1975–2007, with an overall fatality of 55%. Important to note is that *Yersinia* is a siderophilic (iron-loving) strain of bacteria. From a review of transfusion-associated cases with *Yersinia*, only non-siderophore-producing serogroups have been recovered from transfused and recipient blood.[14] These results suggest that upon lysis of aged erythrocytes, iron stores are liberated, which enhance *Y. enterocolitica* growth. For platelet concentrates, contamination with *Y. enterocolitica* does not seem to be a problem, with only one case reported in contrast to 54 cases related to erythrocyte transfusions. This might be related to the siderophilic character of *Yersinia*. After a peak in the mid-1990s,[15,16] the incidence of transfusion-associated *Yersinia* infections seems diminished, probably related to the increased use of leukocyte-depleted blood products.[13] Leukocyte removal is thought to remove *Yersinia* internalized but not yet killed by phagocytes, before disintegration of these phagocytes and subsequent release of viable *Yersinia* in the blood product during further storage.

Many other microorganisms have been described to be involved in asymptomatic bacteremia. Among them, Gram-negative bacteria usually elicit the most severe septic reactions in the recipient. This is due to the presence of lipopolysaccharides or endotoxin, a major cell-wall component in all Gram-negative bacteria that retains its toxicity even in killed bacteria.[17] A well-known case of a *Salmonella enterica*-transfusion transmission to two patients (one of whom died) was due to asymptomatic infection of the donor with this organism from his pet boa constrictor.[18]

It is believed that predonation questionnaires scrutinized by skilled personnel can reveal hidden donor bacteremia, eg, to ask adequate follow-up questions if the donor reports some minor health problems. However, there are no publications to support this assumption, except for some cases with syphilis or after dental procedures.[9] A case of *Staphylococcus aureus* contamination of platelets may have been due to bacteremia in the donor, who had undergone a tooth repair 2 hours prior to donation.[7] Also the use of electric toothbrushes has been shown to significantly increase the rate of bacteremia in comparison with manual brushing,[9,19] but this effect is only transient for a couple of hours.

In sum, a well-defined predonation questionnaire will help to prevent some donors with hidden bacteremia from donating. However, based on current literature data, it is not expected that changes in predonation questionnaires will add significantly to this prevention.

Disinfection methods

Commensal (resident) skin flora, mainly composed of coagulase-negative staphylococci, corynebacteria, and propionibacteria, are the most commonly detected organisms on the donor's arm.[20] Incidentally, a wide spectrum of pathogenic bacteria, such as Bacilli species and Enterobacteriaceae, temporarily present on the skin (transient flora), has been detected in blood products, as reported in screening studies.[21–23] In total, skin-derived organisms (resident and transient) account for over 90% of reported platelet concentrate- and 70% of reported erythrocyte concentrate-associated bacterial transmissions.[24–26]

Therefore, effective disinfection of the skin will result in reduction of bioburden during skin penetration upon venipuncture. Several factors affect the efficacy of skin disinfection,

including the type and concentration of antiseptic used, the mode of application (scrub, swab, applicator, or ampoule), whether a single- or two-step method is used, the time that the antiseptic is in contact with the skin, and the training of the personnel applying the disinfectant. Formerly, optimal skin disinfection was associated with the use of multiple antiseptic agents in a two-step protocol that involved a sponge scrub to clean followed by fluid from an ampoule to kill remaining organisms.[27] In 1999, an initial study on the effectiveness of donor arm-disinfection techniques was undertaken by the National Health Service Blood and Transplant in the UK to find a best practice. McDonald et al[28] compared six methods, and found a two-stage process with an initial application of isopropyl alcohol followed by tincture of iodine to produce the best arm disinfection.

However, upon use in the field, this best-practice procedure caused too much waiting time (2-minute procedure),[29] and thus the search continued. A single-step procedure of isopropyl alcohol with chlorhexidine was found to be a very efficacious disinfectant, but at first the volume needed was too high for comfortable use, as the donor arm remained wet too long. In a study with different volumes of 70% isopropyl alcohol/2% chlorhexidine, McDonald[30] showed that the volume could be reduced to 1.5 mL and still be equivalent in terms of disinfection efficiency. Their final method was ChloraPrep® (a one-step chlorhexidine and isopropyl alcohol kit, 1-minute procedure; CareFusion, San Diego, CA, USA); this was introduced as the national method of donor-arm disinfection in the UK in 2006.[31] The results from McDonald et al[31] were confirmed by studies from Ramirez-Arcos and Goldman[32] and Benjamin et al,[33] although Ramirez-Arcos and Goldman reported that isopropyl alcohol/chlorhexidine disinfectants were even superior to two-step isopropyl alcohol and iodine. Ramirez-Arcos and Goldman[32] reported no difference in efficacy between one-step and two-step procedures or between methods of application for the isopropyl alcohol/chlorhexidine disinfectants. Following this study, ChloraPrep was successfully implemented at the Canadian Blood Service (CBS) in 2009. Benjamin et al found a single-step 2% chlorhexidine swab disinfection technique superior to a two-step povidone-iodine,[33] followed by implementation of this technique as a method of disinfection for the American Red Cross (ARC).

Despite all efforts to use a "best-practice" disinfectant procedure, the result of the disinfection depends also on the quality of the skin. Dimpled skin or skin with scars or eczema will prevent proper disinfection of the surface. It has also to be kept in mind that surface disinfection will not reach microorganisms in the deeper layers of the skin or those present as biofilms. These microorganisms can only be reduced by removal of the first blood volume, as described in the next section.

Removal of first blood volume

During the 1980s, several studies were published about bacterial contamination in blood products. The results of these studies showed a broad range for the mean contamination rate of whole blood, with very wide confidence intervals due to the low numbers included in these studies. A study by de Korte et al[4] was the first with sufficient numbers to show that 0.35% (95% confidence interval 0.27%–0.44%) of whole-blood units contained enough bacteria to give a positive signal in a bacterial culture test (BacT/Alert®; BioMérieux, Marcy l'Etoile, France). In this study, it was confirmed that most of the microorganisms found were most probably derived from the skin of the donor, either resident or transient. Therefore, it was already suggested by Olthuis et al[34] to avoid use of the first volume of collected blood. This was based on the assumption that during venipuncture, a so-called skin plug containing bacteria was punched by the needle.[35,36] If the first volume of blood, containing this skin plug with bacteria, would be removed, this would reduce the bacterial load considerably. Several studies showed that this hypothesis could be true, starting with Olthuis et al,[34] reporting that if one collects two blood samples in a row, the degree of contamination in the first sample is significantly higher than in the second sample. This was confirmed by Bruneau et al.[37] Also, Wagner et al[38] showed in an in vitro model that removal of the first volume would reduce the degree of contamination in the subsequently collected volume. However, all these studies showed only that the first blood volume collected indeed contained the highest amount of bacteria, but did not show that the finally collected blood unit had a lower degree of bacterial contamination. The final proof that removal of the first collected volume resulted in a lower degree of bacterial contamination was published by de Korte et al.[39] In their study with culture of whole blood in the BacT/Alert, they showed that removal of the first 10 mL of the collected blood unit into a waste tube reduced the number of positive cultures by 40%. The difference was statistically significant ($P<0.05$) for the total contamination rate, and for staphylococcal species the reduction was most strikingly from 0.14 to 0.03% ($P<0.02$).

The same group subsequently showed that by incorporating a small pouch with a Y-piece into the collection line of standard blood-collection systems, the diverted volume could be collected in a closed system and used for testing

purposes.[23] In this study, it was also shown that the frequency of bacterial contamination for platelet concentrates prepared from buffy coats could be reduced by more than 50% (from 0.85% to 0.37%) by the introduction of a blood-collection system with a diversion pouch. These results were confirmed by many other groups,[21,29,40,41] and since then the use of a diversion pouch in blood collection, either whole blood or apheresis, has become the standard procedure. An additional advantage of using an integrated diversion pouch is the fact that test material will always be available, although there is a very minimal risk caused by misuse of the collection system and dilution of the diverted volume with anticoagulant, for introducing false-negative test samples, as described by Nightingale et al.[42]

Taken together, the introduction and use of the integrated diversion pouch to remove the first blood volume from the donation has played a major role in risk reduction for TTBI, although this intervention has no effect on bacteria already in the bloodstream of the donor.

Screening for bacterial contamination

General

Of all blood products, platelet concentrates are most prone to be the source of TTBI, as these products are stored at room temperature, under aerated conditions with high concentrations of glucose and other nutrients for bacteria. Therefore, to reduce TTBI, screening of platelet concentrates for the presence of bacteria is most effective. For platelet concentrates derived from whole blood, this is indirectly also a screening of red blood cells, for those whole-blood units that are used to produce both products. In the Netherlands, in the case of a positive signal in a platelet-concentrate sample, related red blood cells are recalled and also tested. In the Netherlands, over the years it was found that for 97% of positive platelet concentrates, the related red blood cells were still in stock at the blood bank or hospital, and with very rare cases of already transfused red cells related to a positive platelet concentrate.[23] In about 30% of positive screening results for a platelet concentrate, one of the related red blood cell units was found positive, and in 90% the same microorganism was found in platelets and red cells.

Early testing

For early testing, culture methods are the most sensitive, and as such, the method of choice, despite the disadvantage of being time-consuming and sometimes yielding irreproducible positive results. The most frequently used culture method for blood products is the BacT/Alert culture system. Depending on the degree of standardization of the process of inoculation and sample placing in the BacT/Alert incubator, this system can have a relatively high degree of false-positive results, ie, no microorganism can be isolated from a positively flagged culture bottle. With a high degree of standardization and strict temperature control during sample placing in the incubator, these kinds of false positives can be reduced to a minimum (unpublished results, Sanquin Blood Bank). In the literature, false-positive units are often divided into two groups, one due to machine failure, in which no microorganism can be cultured from the positively flagged bottle, and one as so-called unconfirmed positives, in which the positive test could not be confirmed in a second culture from the platelet product and was considered as contaminated during inoculation. This number of unconfirmed positives, labeled as false positives, is very high in some studies, depending on the type of microorganism isolated. It is unlikely that the inoculation process, under aseptic conditions, results in such a high number of false positives.[4] Most probably, for most of these types of false positives, the microorganism detected in the screening did not survive in the platelet concentrate, resulting in a negative culture after second sampling. It is questionable whether these initially positive cultures that are not reproducible with repeated sampling should really be judged as false positives.

The time needed to detect bacteria is often mentioned as a disadvantage, as in early culture testing the moment of flagging positive is often after the investigated product has been transfused.[43] In the Netherlands, a look-back procedure is initiated for all products released as "negative to date" with a positive culture after the unit had already been transfused. Koopman et al[44] reported no cases of TTBI after such products were transfused for the period 2006–2007, a result that was confirmed in the following years (personal communication, Dr R Koopman, Sanquin Blood Bank). Similar results were obtained in Germany by Walther-Wenke et al,[3] who concluded that reported transfusion reactions upon transfusion of culture-positive units (after transfusion) were not attributed to the transfusion. Fortunately, for most of the bacteria related to bacterial transmissions with high clinical impact, like Gram-negative bacteria, *Bacillus cereus*, and *Staphylococcus aureus*, the cultures flag positive within the first 24–48 hours of culture.[23] Early culture testing resulted in a 50%–75% decrease in septic transfusion reactions (STRs), especially those due to Gram-negative bacterial contamination, which historically had accounted for approximately

two-thirds of transfusion fatalities associated with platelet units contaminated by bacteria.[30]

Despite the use of early testing, some platelet concentrates remain contaminated with bacteria and sometimes result in STRs in recipients. This is due to false-negative testing results, as the actual degree of contamination might be below the sensitivity of the culture system used. For most bacteria species, it was shown that 1–10 colony forming units (CFU)/mL (with 4 mL inoculation) resulted in a positive culture in the BacT/Alert.[45–47] By mathematical modeling, the real number of bacteria upon collection in contaminated units is thought to be between 5 and 62 CFU per unit,[48] or even lower, as recently reported by Benjamin et al.[49] During the rest period between collection and inoculation, this number will increase. By using a higher inoculation volume (about 8 mL in most studies) and/or two test bottles, sensitivity can be improved. However, because in studies in which two bottles were inoculated, the frequency of double positives was very low,[22,23] it is generally accepted that the average contamination is around the detection limit of the BacT/Alert culture system, making false negatives inevitable. For several bacterial species (*Staphylococcus epidermidis, Streptococcus pyogenes*, *Klebsiella pneumonia*, and *Escherichia coli*), Stormer et al[50] showed that with a spiking of ~10 CFU per unit of platelets (actually 0.01–0.23 CFU/mL), the bacteria were able to grow to very high levels in platelet concentrates during storage.

Rapid, late testing

An alternative to early testing might be to test just before issuing the products to the recipients, in the blood bank or even at the bedside. If bacteria are present in the product, these can grow from the expected low initial level to easily detectable levels during storage of platelet concentrates at room temperature. Late testing can also be allowed to be less sensitive, as the level of bacteria shown to be harmful to patients is around 10^3 CFU/mL or higher. However, this depends very much on the bacteria species and the condition of the patient receiving the transfusion. Jacobs et al[51] showed that platelet units with bacteria concentrations of $<10^5$ CFU/mL are much less likely to cause severe STRs than units with higher bacteria concentrations. However, units with a low bacteria concentration might still be responsible for STRs at a later moment, especially for patients with vascular implants. Bacteria can form biofilms on these devices, which are less accessible to antibiotic treatment.[52]

For rapid testing, two companies developed an immunoassay, and both assays are currently licensed in the US for secondary screening of platelets. These are the Pan Genera Detection (PGD) test from Verax Biomedical (Marlborough, MA, USA)[53] and the BacTx® from Immunetics Inc. (Boston, MA, USA).[54] A substantial number of bacteria-contaminated units was found when the Verax test was used as a secondary detection assay. In a large multisite study with this test[53] on the day of issue applied to apheresis units released as culture-negative, one in 3,000 units was found to be repeatedly positive and verified by confirmatory culture. Based on these results, Jacobs et al[53] claimed that the implementation of rapid screening at the point of issue for apheresis platelets that tested negative by early culturing could prevent over 300 STRs per year. It is unclear whether point-of-issue screening could replace early culture testing.

In a smaller study by Dunbar et al,[55] no confirmed positives were detected in 3,505 4-day-old apheresis platelet units with the Verax test. Sensitivity for Gram-positive organisms was about 10^4–10^5 CFU/mL for most Gram-positive species, but detection of some strains of Gram-negative organisms (eg, *E. coli* and *K. pneumoniae*) was less sensitive. Also significant interoperator variability was reported, especially in weak-positive reactions.[56] A serious problem with the use of the Verax test is the rather high false-positive rates, which range from 0.3%–0.5%. This is of particular concern with respect to the risk–benefit analysis of special platelet products, eg, human leukocyte antigen-matched platelets.[53,55] A second generation of the Verax test was recently introduced that should have a lower false-positive rate.

Alternative methods for rapid testing are flow cytometry-based methods, nucleic acid testing (polymerase chain reaction [PCR]),[57,58] and delayed sampling before culturing in BacT/Alert. Sireis et al[59] compared these different methods to select the best for extending the shelf life from 4 to 5 days. Standard flow cytometry did not meet the criteria for sensitivity, and although BacT/Alert was able to meet these criteria, the 12 hours needed for this method was thought to take too much time off from the additional day of shelf life that could be gained. The flow-cytometry method described by Vollmer et al,[60] called BactiFlow® (BioMérieux), was found to be sensitive enough and took about 2–3 hours. Also, 16S deoxyribonucleic acid testing with PCR was found to be sensitive enough for late testing.[59,61] Vollmer et al[62] showed also that BactiFlow and 21S RNA reverse-transcription PCR were sensitive enough to be used for late testing.

Remaining risk after introduction of screening

A large multicenter US study (PASSPORT [Post Approval Surveillance Study of Platelet Outcomes – Release Tested])

indicated that of 7-day-old platelets (outdated), one in 1,500 units was contaminated with bacteria that were not detected by early automated culturing.[63] Studies conducted in Ireland, Wales, and the Netherlands yielded similar results for outdated products (5–7 days) for either buffy coat-derived or apheresis products,[48,64,65] whereas Ramirez-Arcos et al published a frequency of one false negative in 4,000 outdated buffy coat-derived platelet concentrates.[66] Altogether, this would mean a relatively high chance for a false-negative result, but it has to be kept in mind that only a limited number of bacterially contaminated products will result in TTBI.[51,67]

Based on clinical data in the US, the STR rate following transfusion of whole blood-derived platelets screened for bacteria from 2007–2011 was estimated to be one in 100,000 by Harm et al.[68] Eder et al[41] reported one STR in 90,000 apheresis units, based on a large ARC database over the period 2006–2008 after the introduction of diversion, compared to one STR in 60,000 units before the introduction of diversion. All these clinical cases were due to false-negative results during initial screening, which is performed by the ARC with one BacT/Alert aerobic culture bottle per unit. Based on the period 2006–2011, the same group reported in 2014[49] this number to be one STR in 106,000 units (with one in 1,015,000 fatalities), showing further improvement. Compared with the initial rate of one STR in 40,000 units (with one in 240,000 fatalities) before the introduction of screening and diversion,[21] the overall improvement is significant, with a factor 2.5-fold reduction in STRs and a fourfold reduction in fatalities.

This improvement over the years is also reflected in the number of fatalities reported each fiscal year to the US Food and Drug Administration, as can be found on their website (http://www.fda.gov/biologicsbloodvaccines/safetyavailability/reportaproblem/transfusiondonationfatalities/default.htm), as well as in yearly published hemovigilance reports from Europe, eg, England (http://www.shotuk.org) and the Netherlands (http://www.tripnet.nl/pages/en). This improvement might be a combined result of increased awareness, implementation of improved disinfection methods (eg, ChloraPrep in the UK,[31] CBS,[32] and ARC[33]) and/or increased volume inoculated in BacT/Alert.[41] The majority of STRs in the US seem to be caused by aerobic Gram-positive species.[49,69]

Pathogen inactivation

A very effective measure to reduce viral load in plasma-derived products like albumin and factor VIII concentrates was the introduction of pathogen inactivation or removal steps in the production process. These techniques were mainly focused on viruses, either well-known viruses like HIV and hepatitis C or new viruses thought to threaten the blood supply. Well-known examples of the latter are chikungunya[70] and dengue virus,[71] but many other viruses, often without a disease caused by the virus, have been repeatedly mentioned in this respect.[72–74] Due to the nature of the methods in use for plasma products, like pasteurization,[75] solvent-detergent treatment,[70] freeze-drying[76] and nanofiltration,[77,78] these methods cannot be applied to cellular products.

It took some time before pathogen-inactivation methods to produce pathogen-reduced cellular products were developed. Although erythrocytes and platelets have the advantage that no nucleus is present, and thus nucleic acids can be the target for killing pathogens, the margin between doing harm to the viruses without damaging the blood cells is small. As a result of the current high level of safety with respect to viral transmission by blood products and major concerns about bacteria, especially in platelet concentrates, the focus for application of pathogen inactivation for cellular products has moved from viruses to bacteria. The risk for TTBI with severe morbidity and/or mortality is much higher than the risk for a transfusion-transmitted viral infection. This is still true after a fourfold reduction after the introduction of improved donor-arm disinfection, diversion of first collected blood volume, and screening for bacterial contamination.

So far, the available methods for pathogen reduction, currently restricted to platelet concentrates and plasma, have been shown to be very effective in killing most bacteria species.[79] The bacteria species tested were selected from reports about clinical cases of TTBI and from screening results, and as such are representative for the type of microorganisms present in platelet concentrates. However, there are some limitations to these techniques.[80,81] Spores from bacteria like *Bacillus cereus* and *Clostridium perfringens* are not killed at all and will remain a risk. Also, as each pathogen reduction technique is a disinfecting technique with variable decimal reduction for distinct microorganisms, high numbers of bacteria cannot be removed completely. The current methods for pathogen inactivation have a negative effect on the quality of platelets, although this is not always reflected in clinical effectiveness.[82–86] In addition, introduction of these techniques is very costly, and for the Netherlands has been judged as not cost-effective.[87] It has to be kept in mind that this is partly influenced by the already-high level of safety with respect to pathogen transmission by transfusion in this and many other countries, and depending on the epidemiology

for various pathogens, the result of such exercises might differ by country.

Other aspects

Storage-time reduction

Fresher units have a lower risk for STRs than units stored for up to 5 days,[21] with a clear increase in risk from day 3 of storage and most fatalities related to units stored for 5 days. In Germany, 80% of fatalities after TTBI due to platelet transfusion were from units stored for 5 days.[61] Therefore, the authorities (Paul Ehrlich Institute) in Germany reduced storage time from 5 to 4 days. Only with additional bacterial screening on day 3 or 4, or after implementation of pathogen reduction, could shelf life be extended back to 5 days.[59] Although Jacobs et al[53] did not demonstrate definitive differences in the degree of bacterial contamination between day 3 and days 4–5, Harm et al[68] showed the median age of the individual whole blood-platelet units in the contaminated pools to be 5 days (range 3–5 days) versus 4 days (range 1–5 days) in false-positive whole blood-platelet pools (P=0.0012).

Therefore, an option to decrease STRs could be to screen platelets with an early culture method and to transfuse platelets as early as possible in their shelf life. For units stored longer than 4 days, a late and rapid testing should be implemented to reduce the risk that highly contaminated units would be transfused. This approach is currently used in Ireland[65] and Germany[59] (although in Germany without initial screening).

Difference between apheresis and pooled platelets

Before the introduction of diversion of first volume of blood, the risk of bacterial contamination for pooled buffy coat-derived platelet concentrates was clearly higher than that of apheresis products, as reported by de Korte et al.[23] After implementation of diversion for all collections, this difference disappeared.[23] Also, Schrezenmeier et al[88] demonstrated no significant differences in risk between pooled or apheresis platelets in the German situation. This was recently confirmed by Andreu et al for the French situation.[89] Lastly, a meta-analysis compared the occurrence of bacterial contamination of platelet-rich plasma (PRP)-derived and buffy coat-derived platelet concentrates versus the risk of apheresis platelet concentrates.[90] The risk was modeled assuming that both PRP- and buffy coat-derived concentrates were obtained from five donations, and indicated that PRP-derived platelet concentrates carried around a fivefold-higher risk of bacterial contamination than single-donor apheresis platelets, but that buffy coat-derived platelet concentrates showed no increased risk. Two of the three publications used as sources for the meta-analysis described leukoreduced PRP-derived platelet concentrates, rendering leukoreduction a less likely explanation for the observed difference. An alternative explanation might be that PRP-derived platelet concentrates are from whole blood held for at most 8 hours (as required in the US), while the publications cited for buffy coat-derived platelets all had an overnight holding time for the buffy coat (one publication) or for the whole blood (three publications). This longer holding time would allow leukocytes to phagocytose bacteria, which are subsequently removed together during the platelet concentrate preparation.

Disclosure

The authors report no conflicts of interest in this work.

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