Australian Journal of Basic and Applied Sciences

2024; 18(5): pages 1-7
https://doi.org/10.22587/ajbas.2024.18.5.1

ORIGINAL ARTICLE AENSI Publications

An Updated Assessment of Safety Strategies for Platelet Blood Concentrates (PCs): A Short Review Article

Ali Hadadi[1], Sulaiman Alatawi[1], Munirah Almulhim[1], Maryam M. Almousa[1], Adel K. Alkhathami[1], Jawaher Alnahyan[1], Safia I. Aljabr[1], Maryam K. Almuhaysh[1], Abdullah Alanazi[2], Amani M. Marawan*[3]

[1]Medical Technologist II, King Abdulaziz Hospital, Al-Ahsa Ministry of National Guard Health Affairs, Saudia Arabia
[2] Medical Technologist II, Prince Mohammed Bin Abdullaziz Hospital, AL Madinah Ministry of National Guard Health Affairs, Saudia Arabia;
[3] Lecturer of Microbiology, Medical Laboratory Technology department, Faculty of Applied Medical Sciences, Jazan University, Saudia Arabia.

Correspondence Author:: Amani M. Marawan, Lecturer of Microbiology, Jazan University, Medical Laboratory Technology department, Faculty of Applied Medical Sciences, Saudia Arabia, e-mail: amanymarwan110@gmail.com; ORCID: https://orcid.org/0000-0001-6343-2669

Received date: 10 **September 2024, Accepted date: 6 October 2024**

ABSTRACT: Background: Platelet concentrates (PCs) are one of the most used blood components in blood banks due to their essential role in treating thrombocytopenia, and while viral transmission has been largely addressed, bacterial contamination of platelet concentrates (PCs) are still regarded as a crucial safety concern. Objective: This short review aimed to consolidate current knowledge on the strategies followed in blood banks to maximize the quality and shelf life of platelet concentrates (PCs). Different methods of each strategy were considered, focusing on outcomes related to approved and effective outcomes. Methods: The current study is based on PubMed, Wiley, and Web of Science databases to assess donor selection, bacterial screening, and pathogen reduction technologies utilized for PCs quality. All articles were collected until April 2024. Studies utilizing approved interventions and relevant hospital outcomes were inclusive. However, repetitive data and unapproved methods were among the exclusive criteria. Collected published manuscripts were reviewed. Results: The studies reviewed and referenced in this article consensus that pathogen reduction technologies (PRTs) utilizing Ultraviolet rays (UV) was found to be effective in eliminating various bacterial contamination. Furthermore, the need for donor and bacterial screening is still essential and could not be overlooked. Pathogen reduction technologies (PRTs) remain important and valid despite studies suggesting the reduced platelet concentrates (PCs) quality and the need for frequent transmission of PCs. Some studies even foresee pathogen reduction technologies (PRTs) as replacing the cultural bacterial detection methods. Conclusion:We conclude that preventing bacterial contamination in platelet concentrates (PCs) requires a multifaceted approach. However, future research should focus on optimizing these strategies while minimizing their potential adverse effects on platelet function and safety.

Keywords: *Platelet concentrates, Bacterial contamination, Blood transfusion, Pathogen reduction technology, Ultraviolet radiation.*

INTRODUCTION

Blood transfusions are a common medical procedure, with platelet concentrates (PCs) being a vital component for treating patients with platelet disorders. However, bacterial contamination of PCs rather than viral contamination, remains a serious health concern due to their storage conditions and the potential for life-threatening infections (Levy et al., 2018; Lozano & Cid, 2016). Researchers have explored various strategies to reduce bacterial contamination in PCs, starting with careful donor selection, and various bacterial screening methods up to pathogen reduction technologies (PRTs).

In their recent study, (Yamket et al., 2023) stated that PRTs, such as those utilizing ultraviolet (UV) radiation, can extend the shelf life of PCs, reduce bacterial contamination, and provide an extra layer of protection against blood-borne diseases. While PRTs offer several advantages, their impact on the function and quality of PCs is still under investigation. (Esmaili et al., 2017) showed that

the choice of PRTs depends on factors like cost, effectiveness, and potential side effects. The ongoing search for effective methods to prevent bacterial contamination in PCs is crucial to guarantee safer blood transfusions and improving patient outcomes.

Standard platelet concentrates (PCs) are optimally stored at about: 22 degrees Celsius/ 72 degrees Fahrenheit (room temperature) with continuous shaking, but their shelf life is limited to up to 120 hours; estimated as 5 days. (Montag, 2008) early proved that these conditions are conductive to bacterial growth, increasing the risk of contamination and potentially leading to life-threatening infections in transfused patients. To enhance PCs safety, researchers have explored various strategies.

Pathogen reduction technology (PRT) has emerged as a promising approach compared with traditional culture-based methods. PRTs can effectively eliminate a wide range of pathogens, including bacteria. By applying PRTs, blood centers can prolong the treated PCs shelf life an extra 2 days reaching a maximum of 7 days, alleviating shortages, and reducing the risk of bacterial contamination. Moreover, PRTs provide an added layer of protection against blood-borne infectious diseases (Escolar et al., 2022; Rezvany et al., 2024). While PRTs offer significant advantages, their impact on PC function, quality, and clinical efficacy is a subject of ongoing research. Several PRT technologies, including INTERCEPT, Mirasol, and THERAFLEX, utilize ultraviolet (UV) radiation to inactivate pathogens (Escolar et al., 2022). Each of these technologies has its own strengths and weaknesses, and their suitability for PC treatment depends on various factors (Esmaili et al., 2017).

As an objective, this study was designed as a walk through each strategy utilized in maximizing platelet concentrate quality and shelf life. This review contributes to equipping healthcare workers and medical technologist in blood bank units with an updated guidelines for PCs safety. Consequently, starting before donation (i.e: donor selection program and arm disinfection) up to storage (room temperature/cold storage and bacterial detection) and finally just before transfusion of PCs to the recipient (pathogen reduction technologies).

METHODS

We conducted a comprehensive search of articles using databases such as PubMed, Wiley, Scopus, and Web of Science. The search terms included “Platelet concentrate PCs,” “Bacterial screening,” “Pathogen reduction technologies,” and “review.” The search was originally limited to articles published in English from 2010 to April 2024, however more relevant data was found in older studies, so it was adjusted to articles published in English from 2006 to April 2024.
Studies were included if:

1. Studies conducted utilizing approved interventions.
2. Reported hospital outcomes in relevant timeframe.

Studies were excluded if they:

1- Duplicate studies and repetitive data.
2- Did not report relevant outcomes.
3- Discussed local unapproved methods.

Three reviewers were assigned independently to scan titles and abstracts for suitability. Articles meeting the inclusive criteria were retrieved and evaluated. A fourth reviewer was assigned to resolve any arising discrepancies. A narrative synthesis was conducted due to the heterogeneity of the included studies.

DISCUSSION

1. Platelet contamination (Bacterial):

Platelet concentrates (PCs) are essential for treating thrombocytopenia, especially chemotherapy-induced thrombocytopenia (George et al., 2023). However, bacterial contamination of PCs remains a significant concern, with *S. epidermidis* being the most isolated. Transfusion-transmitted bacterial infections (TTBIs) associated with contaminated platelets can lead to severe levels of morbidity & mortality (Esmaili et al. 2017; Hong et al., 2016). The first strategy to Preventing TTBIs involves a multi-faceted approach. Donor selection is a crucial component, with blood establishments implementing rigorous screening measures to decrease the risk of microbial transmission; (viral and bacterial). While the liability of viral transmission has been drastically reduced, variations in donor selection criteria and regional epidemiology can influence the risk of bacterial contamination across different countries (Lozano & Cid, 2016). Thorough donor screening involves completing a health questionnaire for assessing medical history, physical examination to identify signs of illness, and laboratory testing for infectious diseases. Additionally, it includes antibiotic usage to ascertain the safety of the donated platelets. (Levy et al., 2018) mentioned that by implementing these preventive measures, blood centers can help ensure the safety of transfusions as well as decrease the risk of TTBIs.

(De Korte & Marcelis, 2014) and (Hong et al., 2016) respectively, declared that bacterial sepsis remains a significant risk associated with platelet concentrate (PC) transfusions, despite efforts to prevent transmission through donor screening and blood testing. Asymptomatic bacteremia often goes undetected, leading to a discrepancy between confirmed positive contamination and actual septic reactions. Several factors contribute to this discrepancy. Many patients receiving contaminated PCs are already on antibiotics or have weakened immune systems (neutropenia), making them less susceptible to immediate signs of infection. Additionally, (Lozano & Cid, 2016) stated that approximately 60% of contaminated PCs do not cause any significant reactions. Almost every blood center has implemented a set of strategies to deal with and help decrease microbial (bacterial) contamination. (de Korte & Marcelis, 2014) blood donor proper selection and preceding screening, coupled with a diversion method that involves collecting a small sample of blood at the start of the donation process, was found to significantly decrease the liability of gram-positive bacteria

contamination. However, the storage conditions of PCs at room temperature (RT) are considered the optimal environment for bacteria to flourish. The FDA has recommended reducing the shelf-life of PCs from seven down to five days to mitigate this risk. Some studies have even suggested further shortening the shelf life to 3 days (Amano et al., 2022; Eder et al., 2017; Taha et al. 2017). According to (Jimenez-Marco et al., 2022) and (George et al., 2023) cold storage (CS) at 1-6°C offers a potential solution. While it can effectively reduce bacterial growth, maintain platelet function, and extend their lifespan, there are concerns about its potential negative impact on PC morphology and therapeutic effectiveness. In their studies, (Taha et al., 2017) and (Zhao & Devine, 2022) stated that further research is needed to determine whether Pathogen reduction technologies (PRTs) can be safely applied to cold-stored PCs without compromising their clinical efficacy. Thus, preventing bacterial contamination in PCs requires a multifaceted approach, including rigorous donor screening, diversion methods, careful storage practices, and ongoing research into innovative technologies like PRTs and cold storage.

2. Bacterial screening methods of platelet concentrates

Strategy number two in hampering the development of bacterial contamination is Bacterial Screening methods which play a crucial role in preventing Transfusion-Transmitted Bacterial Infections (TTBIs) accompanying with platelet concentrates (PCs). (Levy et al., 2018) declared that the underreporting of TTBIs due to factors like limited screening methods and inadequate quarantine practices remains a significant challenge. (Ramirez-Arcos et al., 2017) mentioned that culture-based bacterial screening are solid when it comes to detecting bacterial contamination in PCs. They involve culturing a sample of the platelet product to identify any bacterial growth. While effective, culture-based methods can be time-consuming, requiring incubation periods of over 24 hours.

Examples of culture-based methods are: “BacT / ALERT” and “e-BDS” systems, both of which have been FDA approved. However, (Rezvany et al., 2024) recommended the need for faster and more sensitive screening methods to address the limitations of current approaches. Non-culture-based screening methods, including both low & high-sensitivity techniques, offer potential alternatives. These methods can provide rapid results but may have lower sensitivity compared with culture-based methods. Effective bacterial screening of PCs is essential for preventing TTBIs. Both (Pietersz et al., 2014) and later (Amano et al., 2022) reported that a combination of both methods, along with improved quarantine practices, can help mitigate the risk of bacterial contamination, hence, ensure safety of platelet transfusions. (Hayashi et al., 2021) and (Amano et al., 2022) independently agreed that culture-based methods are highly sensitive in bacterial contamination detection in platelet concentrates (PCs), but their sensitivity can differ based on the age of the product and may not be powerful against biofilm-producing bacteria. However, the gold standard for quality control remains the culture-based methods despite of them being time-consuming and cannot guarantee complete prevention of sepsis (Störmer & Vollmer, 2014). Non-culture-based screening techniques offer a significant advantage in terms of speed and efficiency. These methods, such as polymerase-chain reaction; (PCR) and flow cytometry, have varying sensitivities and require smaller sample volumes compared with culture-based methods. However, implementing non-culture methods can be complex and costly (Satake et al., 2020; Schmidt et al., 2022).

Despite the challenges associated with early detection of bacterial contamination in PCs, the adoption of rapid screening methods, including both culture & non-culture-based approaches, is essential for ensuring the safety of blood transfusions (Störmer & Vollmer, 2014; Vollmer et al., 2013). Early on, (Yomtovian et al., 2006) stated that low-sensitivity techniques for bacterial contamination detection in platelet concentrates (PCs) namely included: “gram staining, pH measurement, glucose consumption, acridine orange, bio-responsive polymers, and pan-genera detection (PGD)”. While these methods can provide rapid results, they often have limitations such as high false positive rates, low sensitivity, and the need for specialized expertise. Among these methods, only PGD has been approved by the FDA. PGD can detect both gram-negative & gram-positive bacteria and can be used to extend the shelf life of PCs (Rezvany et al., 2024; Störmer & Vollmer, 2014).

Most recently, both (LaVerda et al., 2021; Mintz & Vallejo, 2021) concluded that The PGDprime assay offers a streamlined workflow and improved sensitivity, and specificity compared to its predecessor. Studies have demonstrated enhanced detection limits for *Pseudomonas aeruginosa*, *S. aureus*, and *S. epidermidis*. Additionally, the PGD-*prime* assay has shown a specificity of 99.9%–100% in various platelet concentrate components. To address the increasing prevalence of *Acinetobacter spp*. in transfusion reactions, a recent enhancement to the PGD-*prime* assay now includes recognition of this bacterium. On the other hand, non-culture-based methods in general are known for their higher false-positive rates and can be labor-intensive and costly (Gamerith et al., 2014).

In their 20-years review, (Schmidt et al 2022) concluded that rapid detection methods enhance platelet concentration safety by detecting bacterial contamination. These methods are particularly effective for rapidly proliferating bacteria, which are more likely to cause septic transfusion reactions. However, their reduced sensitivity necessitates sample collection later in the storage period, ideally just before transfusion. The primary advantage of these approaches is that they are able to provide test results before platelet concentrates are released for transfusion or when used in conjunction with other early screening techniques.

Visual inspection remains a valuable tool for identifying bacterial contamination in PCs. Moreover, for non-culture-based methods, (Satake et al., 2020) stated that the sample collection should ideally occur within the last 2 days of PC storage or just before transfusion, due to their lower sensitivity. Yet, (Levy et al., 2018) pointed out that while low-sensitivity non-culture-based methods offer rapid results, they have limitations in terms of sensitivity, specificity, and the need for specialized expertise. The choice of screening method depends on factors such as the desired level of sensitivity, the available resources, and the specific requirements of the blood center (Schmidt et al., 2022).

3. Pathogen reduction technologies

The third and most effective strategy for pathogen reduction in blood products is the use of ultraviolet (UV) rays. Ultraviolet UV irradiation is a potent method for reducing pathogens in blood products. By inhibiting DNA and RNA replication, UV light effectively not only eliminating the contamination, but also mitigating the liability of transfusion-transmitted bacterial infections (TTBIs). Studies have demonstrated that UV's efficacy against a broad spectrum of pathogens, including viruses, bacteria, parasites, as well as leukocytes (Levy et al., 2018).

Pathogen reduction therapy (PRT) is designed to employ UV irradiation. (Escolar et al., 2022) found they offer a proactive approach to preventing contamination, extending the shelf life of platelet concentrates, and safeguarding against emerging blood-borne diseases. While PRT offers potential benefits, it is essential to weigh its risks, including the generation of pyrogenic compounds, limited efficacy against spore-forming and biofilm-producing microorganisms, treatment duration, and cost burden. (Fachini et al., 2021) conducted that a comprehensive evaluation of PRT's advantages is indispensable before implementation. The effectiveness of PRT is influenced by vast factors such as treatment time and the sort of bacteria. Delayed PRT can allow bacterial growth, and potentially overwhelm the system (Benjamin & Wagner, 2015). Postmanufacturing contamination remains a concern (Feys et al., 2019). Despite higher costs, PRT is of adequate value compared with other blood safety measures. Early application of PRT to platelet concentrates is crucial to prevent excessive bacterial growth (Lu et al., 2020). Research by (Prax et al., 2019) and another by (Schmidt et al., 2015) suggests that PRT has a negligible impact on platelet function throughout storage, particularly in the later stages. Nonetheless, many reviewed studies confirmed that PRT adheres to the required safety standards for patient transfusion. Studies by (Marschner & Goodrich, 2011; van der Meer et al., 2018; Infanti et al., 2022) recommended combining PRT with a rapid bacterial screening test could potentially alleviate the risk of bacterial transmission in incidence where PRT are not to be applied immediately after platelet preparation.

Three pathogen reduction therapy (PRT) technologies, INTERCEPT, Mirasol, and THERAFLEX, still currently available and utilized for reducing pathogen in platelet concentrates. While all three employ UV light (Feys et al., 2019; Levy et al., 2018), their mechanisms differ. (Fig.1)

INTERCEPT and Mirasol utilize photosensitive compounds prior to UV exposure, whereas THERAFLEX employs shortwave UV directly (Escolar et al., 2022). All three-systems damage bacterial DNA, hampering nucleic acid replication.

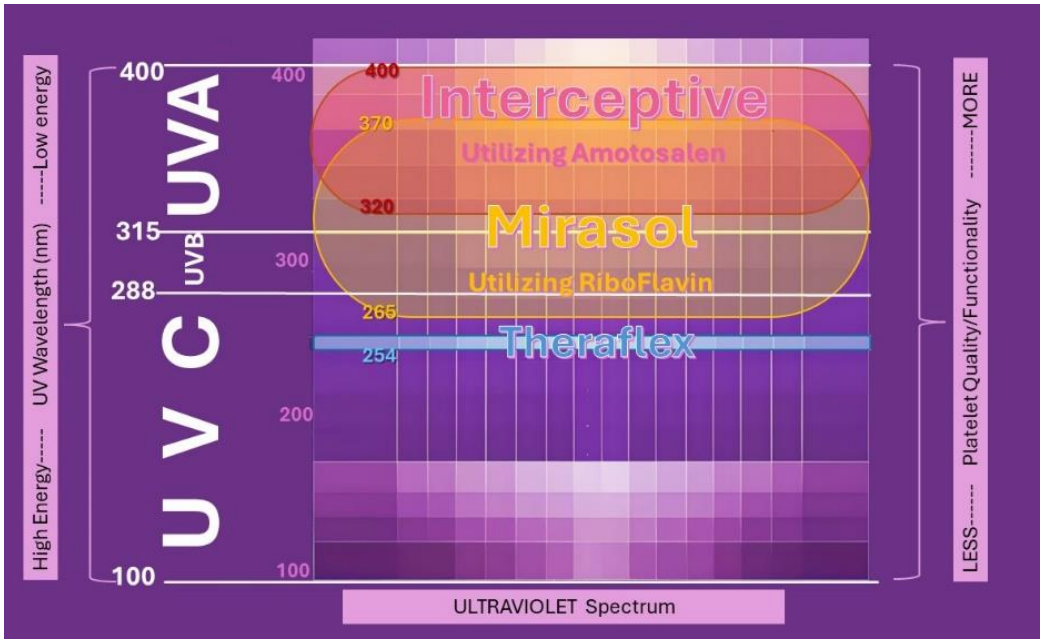

Fig.1: The three Pathogen reduction technologies displayed on the UV radiation Wavelength in nanometer (nm).

3.1 INTERCEPT technology:

The INTERCEPT System employs Amotosalen, a photosensitizing compound, in conjunction with UV A light to inactivate a wide range of pathogens (Irsch & Lin, 2011). Amotosalen is added to platelet components, exposed to UV A light, and subsequently removed by a compound adsorption device (Feys et al., 2019; Levy et al., 2018). Amotosalen intercalates into DNA and RNA and disrupts nucleic acid replication and repair (Irsch & Lin, 2011; Rezvany et al., 2024). Amotosalen is highly effective against various bacteria and viruses without adversely affecting platelet function (Hong et al., 2016). While Amotosalen can penetrate cellular membranes, it is able to preserve the normal functionality of blood components (Irsch & Lin, 2011). However, (Schmidt et al., 2015) noted that the INTERCEPT system may not be completely effective against high concentrations of specific pneumonia strains and/or spore-form *Bacillus cereus*. Additionally, (Ramirez-Arcos et al., 2017), stated that Amotosalen showed activity against residual leukocytes, potentially reducing the risk of graft-versus-host disease associated with transfusion and infections caused by

intracellular pathogens like Epstein-Barr virus. The use of INTERCEPT technology does not impair the biologic functionality of cryo-preserved platelets ensuring that clinical indications for INTERCEPT-treated platelets remain consistent with those for conventional platelet concentrates.

3.2 Mirasol technology:

The Mirasol technology utilizes a combination of riboflavin, a photosensitizer, and UVB light to decrease pathogen levels and inactivate residual leukocytes. It operates by generating reactive oxygen species through the oxidation of nucleic acids, specifically targeting guanine bases. The Mirasol system has obtained European conformity Class IIB and is used in over 20 countries (Alabdullatif et al., 2021; Feys et al., 2019; Levy et al., 2018). However, (Lu et al., 2020) mentioned it is undergoing a phase III clinical trial in the USA. Mirasol technology irreversibly damages DNA and RNA, preventing replication and repair. Studies have demonstrated its effectiveness against diverse bacterial, viral, and parasitic infections (Goodrich et al., 2009, 2010; Marschner & Goodrich, 2011). In their study, (Taha et al., 2017) found that while Mirasol technology can partially deactivate biofilm-producing species like Staphylococcus epidermidis, (Malvaux et al., 2022) found that INTERCEPT technology is more effective in preserving platelet quality in vitro, enabling storage for up to 7 days based on quality standards.

3.3 THERAFLEX technology:

Developed by Macopharma, France, was awarded Class IIB European Conformity in 2009 and remains under evaluation in a European phase III clinical trial. Unlike INTERCEPT and Mirasol, THERAFLEX does not require a photosensitizing agent. Instead, it uses short-wave UVC light for pathogen inactivation. THERAFLEX effectively inactivates various viral and bacterial species, including Staphylococcus aureus and Bacillus cereus (Hayashi et al., 2021). While UVC treatment has limited effects on platelet quality, proper pre-treatment with platelet inhibitors is essential to prevent biofilm formation, which can shield bacteria from UV inactivation (Taha et al., 2017). Although THERAFLEX shows promise, its development is less advanced compared with INTERCEPT and Mirasol (Lu et al., 2020).

CONCLUSION

While donor screening and blood testing have enhanced the safety of blood products transfusion, pathogen reduction technology (PRT) offers an additional layer of safety and extends the shelf life of platelet concentrates. However, these technologies may compromise platelet function. Future research is essential to optimize the safety and efficacy of these strategies while minimizing adverse effects on platelet survival post-transfusion.

Author Contributions

A.H, A.A., and A.M.M constructed the idea for this review and draw the initial outlines. S.A and M.A, conducted the literature search and compiled the relevant studies. M.M.A and J.A reviewed and interpreted the data from the selected studies. A.K.A. and S.I.A. prepared the 1st draft of the manuscript. M.K.A and A.M.M provided a second revision and contributed to the final version of the manuscript. All authors have agreed to the final published version of the manuscript.

Funding Information

No financial support for this article's research, authorship, and/or publication was received by any authors.

Conflict of Interest:

The authors declare that they have no conflicts of interest.

Acknowledgment:

We would like to acknowledge the contributions of researchers whose work has been cited in this review. Their research has been instrumental in advancing our understanding of pathogen reduction technologies in platelet concentrates. We would also like to extend our thanks to Dr. Yasmine MH for their help in constructing Fig.1 and proofreading the article.

REFERENCES

Alabdullatif, M., Osman, I. E., Alrasheed, M., Ramirez-Arcos, S., Alyousef, M., Althawadi, S., & Alhumiadan, H. (2021). Evaluation of riboflavin and ultraviolet light treatment against Klebsiella pneumoniae in whole blood-derived platelets: A pilot study. Transfusion, 61(5), 1562–1569. https://doi.org/10.1111/trf.16347

Amano, M., Matsumoto, M., Sano, S., Oyama, M., Nagumo, H., Watanabe-Okochi, N., Tsuno, N. H., Nakajima, K., & Muroi, K. (2022). Characteristics of False-Positive Alarms in the BacT/Alert 3D System. Microbiology Spectrum, 10(3). https://doi.org/10.1128/spectrum.00055-22

Benjamin, R. J., & Wagner, S. J. (2015). Bacterial pathogen reduction requires validation under conditions of intended use. Transfusion, 55(9), 2060–2063. https://doi.org/10.1111/trf.13232

de Korte, D., & Marcelis, J. (2014). Platelet concentrates: reducing the risk of transfusiontransmitted bacterial infections. International Journal of Clinical Transfusion Medicine, 29. https://doi.org/10.2147/IJCTM.S40037

Eder, A. F., Dy, B. A., DeMerse, B., Wagner, S. J., Stramer, S. L., O'Neill, E. M., & Herron, R. M. (2017). Apheresis technology correlates with bacterial contamination of platelets and reported septic transfusion reactions. Transfusion, 57(12), 2969–2976. https://doi.org/10.1111/trf.14308

Escolar, G., Diaz-Ricart, M., & McCullough, J. (2022). Impact of different pathogen reduction technologies on the biochemistry, function, and clinical effectiveness of platelet concentrates: An updated view during a pandemic. Transfusion, 62(1), 227–246. https://doi.org/10.1111/trf.16747

Esmaili, M. A., Razjou, F., Nazel Khosroshahi, B., Amini, A., Namjoo, S., beigi, peyman, & Rezvani, M. R. (2017). Evaluations of Detection Methods of Bacterial Contamination in Platelet Components. International Journal of Medical Laboratory, 4(4), 232–245. https://ijml.ssu.ac.ir/article-1-197-en.html

Fachini, R., Fontão-Wendel, R., Achkar, R., Scuracchio, P., Brito, M., Amaral, M., & Wendel, S. (2021). The 4-Year Experience with Implementation and Routine Use of Pathogen Reduction in a Brazilian Hospital. Pathogens, 10(11), 1499. https://doi.org/10.3390/pathogens10111499

Feys, H. B., Van Aelst, B., & Compernolle, V. (2019). Biomolecular Consequences of Platelet Pathogen Inactivation Methods. Transfusion Medicine Reviews, 33(1), 29–34. https://doi.org/10.1016/j.tmrv.2018.06.002

Gamerith, C., Heinzle, A., Schneider, K. P., Hulla-Gumbsch, E., Gewessler, U., Ducoroy, L., Gehrer, M., Wagner, T., Sigl, E., & Guebitz, G. M. (2014). Bioresponsive polymers for the detection of bacterial contaminations in platelet concentrates. New Biotechnology, 31(2), 150–155. https://doi.org/10.1016/j.nbt.2013.11.001

George, C. E., Saunders, C. V., Morrison, A., Scorer, T., Jones, S., & Dempsey, N. C. (2023). Cold stored platelets in the management of bleeding: is it about bioenergetics? Platelets, 34(1). https://doi.org/10.1080/09537104.2023.2188969

Goodrich, R. P., Custer, B., Keil, S., & Busch, M. (2010). Defining "adequate" pathogen reduction performance for transfused blood components. Transfusion, 50(8), 1827–1837. https://doi.org/10.1111/j.1537-2995.2010.02635.x

Goodrich, R. P., Gilmour, D., Hovenga, N., & Keil, S. D. (2009). A laboratory comparison of pathogen reduction technology treatment and culture of platelet products for addressing bacterial contamination concerns. Transfusion, 49(6), 1205–1216. https://doi.org/10.1111/j.1537- 2995.2009.02126.x

Hayashi, T., Oguma, K., Fujimura, Y., Furuta, R. A., Tanaka, M., Masaki, M., Shinbata, Y., Kimura, T., Tani, Y., Hirayama, F., Takihara, Y., & Takahashi, K. (2021). UV light-emitting diode (UV-LED) at 265 nm as a potential light source for disinfecting human platelet concentrates. PLOS ONE, 16(5), e0251650. https://doi.org/10.1371/journal.pone.0251650

Hong, H., Xiao, W., Lazarus, H. M., Good, C. E., Maitta, R. W., & Jacobs, M. R. (2016). Detection of septic transfusion reactions to platelet transfusions by active and passive surveillance. Blood, 127(4), 496–502. https://doi.org/10.1182/blood-2015-07-655944

Infanti, L., Pehlic, V., Mitrovic, S., Holbro, A., Andresen, S., Payrat, J., Lin, J., & Buser, A. (2022). Pathogen inactivation treatment of triple-dose apheresis platelets with amotosalen and ultraviolet a light. Transfusion Medicine, 32(6), 505–511. https://doi.org/10.1111/tme.12913

Irsch, J., & Lin, L. (2011). Pathogen Inactivation of Platelet and Plasma Blood Components for Transfusion Using the INTERCEPT Blood System^{TM} Transfusion Medicine and Hemotherapy, 38(1), 19–31. https://doi.org/10.1159/000323937

Jimenez-Marco, T., Castrillo, A., Hierro-Riu, F., Vicente, V., & Rivera, J. (2022). Frozen and coldstored platelets: reconsidered platelet products. Platelets, 33(1), 27–34. https://doi.org/10.1080/09537104.2021.1967917

Levy, J. H., Neal, M. D., & Herman, J. H. (2018). Bacterial contamination of platelets for transfusion: strategies for prevention. In Critical Care (Vol. 22, Issue 1). BioMed Central Ltd. https://doi.org/10.1186/s13054-018-2212-9

LaVerda, D., Shinefeld, L., Best, N., Lisitu, J., Tambolleo, G., & Vallejo, Y. R. (2021). Evaluation of an improved rapid bacterial assay with untreated and pathogen-reduced platelets: Detection of Acinetobacter strains. Transfusion, 61(9), 2710–2717. https://doi.org/10.1111/trf.16514

Lozano, M., & Cid, J. (2016). Platelet concentrates: Balancing between efficacy and safety? In Presse Medicale (Vol. 45, Issues 7–8, pp. e289–e298). Elsevier Masson SAS. https://doi.org/10.1016/j.lpm.2016.06.020

Lu, M., Dai, T., Hu, S., Zhang, Q., Bhayana, B., Wang, L., & Wu, M. X. (2020). Antimicrobial blue light for decontamination of platelets during storage. Journal of Biophotonics, 13 (1). https://doi.org/10.1002/jbio.201960021

Malvaux, N., Defraigne, F., Bartziali, S., Bellora, C., Mommaerts, K., Betsou, F., & Schuhmacher, A. (2022). In Vitro Comparative Study of Platelets Treated with Two Pathogen-Inactivation Methods to Extend Shelf Life to 7 Days. Pathogens, 11(3), 343. https://doi.org/10.3390/pathogens11030343

Marschner, S., & Goodrich, R. (2011). Pathogen Reduction Technology Treatment of Platelets, Plasma and Whole Blood Using Riboflavin and UV Light. Transfusion Medicine and Hemotherapy, 38(1), 8–18. https://doi.org/10.1159/000324160

Mintz, P. D., & Vallejo, R. P. (2021). The PGDprime immunoassay for detection of bacterial contamination in platelet concentrates: sensitivity and specificity. Annals of Blood, 6, 19–19. https://doi.org/10.21037/aob-2020-bcpc-01

Montag, T. (2008). Strategies of bacteria screening in cellular blood components. Clinical Chemistry and Laboratory Medicine, 46(7). https://doi.org/10.1515/CCLM.2008.176

Pietersz, R. N. I., Reesink, H. W., Panzer, S., Oknaian, S., Kuperman, S., Gabriel, C., Rapaille, A., Lambermont, M., Deneys, V., Sondag, D., Ramírez-Arcos, S., Goldman, M., Delage, G., Bernier, F., Germain, M., Vuk, T., Georgsen, J., Morel, P., Naegelen, C., … Jacobs, M. R. (2014). Bacterial contamination in platelet concentrates. Vox Sanguinis, 106(3), 256–283. https://doi.org/10.1111/vox.12098

Prax, M., Bekeredjian-Ding, I., & Krut, O. (2019). Microbiological Screening of Platelet Concentrates in Europe. Transfusion Medicine and Hemotherapy, 46(2), 76–86. https://doi.org/10.1159/000499349

Ramirez-Arcos, S., DiFranco, C., McIntyre, T., & Goldman, M. (2017). Residual risk of bacterial contamination of platelets: six years of experience with sterility testing. Transfusion, 57(9), 2174–2181. https://doi.org/10.1111/trf.14202

Rezvany, M. R., Moradi Hasan-Abad, A., Sobhani-Nasab, A., & Esmaili, M. A. (2024). Evaluation of bacterial safety approaches of platelet blood concentrates: bacterial screening and pathogen reduction. Frontiers in Medicine, 11. https://doi.org/10.3389/fmed.2024.1325602

Satake, M., Kozakai, M., Matsumoto, M., Matsubayashi, K., Taira, R., & Goto, N. (2020). Platelet safety strategies in Japan: impact of short shelf life on the incidence of septic reactions. Transfusion, 60(4), 731–738. https://doi.org/10.1111/trf.15733

Schmidt, M., Hourfar, M. K., Sireis, W., Pfeiffer, U., Göttig, S., Kempf, V. A. J., McDonald, C. P., & Seifried, E. (2015). Evaluation of the effectiveness of a pathogen inactivation technology against clinically relevant transfusion-transmitted bacterial strains. Transfusion, 55(9), 2104– 2112. https://doi.org/10.1111/trf.13171

Schmidt, M., Ramirez-Arcos, S., Stiller, L., & McDonald, C. (2022). Current status of rapid bacterial detection methods for platelet components: A 20-year review by the ISBT Transfusion-Transmitted Infectious Diseases Working Party Subgroup on Bacteria. Vox Sanguinis, 117(8), 983–988. https://doi.org/10.1111/vox.13283

Störmer, M., & Vollmer, T. (2014). Diagnostic Methods for Platelet Bacteria Screening: Current Status and Developments. Transfusion Medicine and Hemotherapy, 41(1), 19–27. https://doi.org/10.1159/000357651

Taha, M., Culibrk, B., Kalab, M., Schubert, P., Yi, Q. -L., Goodrich, R., & Ramirez-Arcos, S. (2017). Efficiency of riboflavin and ultraviolet light treatment against high levels of biofilm-derived Staphylococcus epidermidis in buffy coat platelet concentrates. Vox Sanguinis, 112(5), 408– 416. https://doi.org/10.1111/vox.12519

van der Meer, P. F., Ypma, P. F., van Geloven, N., van Hilten, J. A., van Wordragen-Vlaswinkel, R. J., Eissen, O., Zwaginga, J. J., Trus, M., Beckers, E. A. M., te Boekhorst, P., Tinmouth, A., Lin, Y., Hsia, C., Lee, D., Norris, P. J., Goodrich, R. P., Brand, A., Hervig, T., Heddle, N. M., … Kerkhoffs, J.-L. H. (2018). Hemostatic efficacy of pathogen-inactivated vs untreated platelets: a randomized controlled trial. Blood, 132(2), 223–231. https://doi.org/10.1182/blood-2018-02- 831289

Vollmer, T., Kleesiek, K., & Dreier, J. (2013). Detection of Bacterial Contamination in Platelet Concentrates Using Flow Cytometry and Real-Time PCR Methods (pp. 91–103). https://doi.org/10.1007/978-1-60327-353-4_5

Yamket, W., Sathianpitayakul, P., Santanirand, P., & Ratthawongjirakul, P. (2023). Implementation of helicase-dependent amplification with SYBR Green I for prompt naked-eye detection of bacterial contaminants in platelet products. Scientific Reports, 13(1), 3238. https://doi.org/10.1038/s41598-023-30410-8

Yomtovian, R. A., Palavecino, E. L., Dysktra, A. H., Downes, K. A., Morrissey, A. M., Bajaksouzian, S., Pokorny, M. A., Lazarus, H. M., & Jacobs, M. R. (2006). Evolution of surveillance methods for detection of bacterial contamination of platelets in a university hospital, 1991 through 2004. Transfusion, 46(5), 719–730. https://doi.org/10.1111/j.1537-2995.2006.00790.x

Zhao, H., & Devine, D. V. (2022). The Missing Pieces to the Cold-Stored Platelet Puzzle. International Journal of Molecular Sciences, 23(3), 1100. https://doi.org/10.3390/ijms23031100