Blood Transfusion Safety: Pathogen Inactivation Reduces Transfusion-Transmitted Infections

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> The administration of blood products carries inherent risks, primarily transfusion-transmitted infections (TTIs), which historically posed a significant threat to patient safety. Contemporary strategies, particularly the implementation of pathogen inactivation technologies, have substantially mitigated these risks, making blood transfusions considerably safer.

KEY TAKEAWAYS

- The Pivot: Pathogen inactivation technologies have been adopted to reduce residual risk of TTIs.
- The Data: The risk of HIV transmission via transfusion has decreased from 1 in 2,500 units in 1985 to approximately 1 in 2.3 million units today.
- The Action: Clinicians should continue to adhere to established transfusion guidelines, recognising the enhanced safety profile of modern blood products.

Historically, blood transfusions were associated with substantial risks of transmitting infectious agents, including hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV). The recognition of these risks prompted a series of advancements in blood screening and processing to enhance safety. Early efforts focused on donor selection criteria, excluding individuals at high risk for infectious diseases. This was followed by the development and implementation of serological testing for specific viral markers. For instance, testing for hepatitis B surface antigen (HBsAg) became routine in the 1970s, significantly reducing HBV transmission. The emergence of HIV in the 1980s spurred rapid development of HIV antibody testing, introduced in 1985, which dramatically decreased the risk of HIV transmission via transfusion from an estimated 1 in 2,500 units to less than 1 in 100,000 units by the early 1990s. Nucleic acid testing (NAT) for HIV and HCV, introduced in the late 1990s, further reduced the window period for detection, lowering the risk of HIV transmission to approximately 1 in 2.3 million units and HCV to 1 in 1.5 million units.

Advancements in Blood Processing and Pathog en Inactivation

Beyond donor screening and serological/NAT testing, significant strides have been made in blood product processing. Leukoreduction, the removal of white blood cells from blood components, was implemented to reduce the risk of transfusion-related acute lung injury (TRALI), febrile non-hemolytic transfusion reactions, and cytomegalovirus (CMV) transmission. While not directly targeting bacterial or viral pathogens in plasma, leukoreduction improved overall transfusion safety. The most recent major advancement has been the introduction of pathogen inactivation technologies. These methods aim to inactivate a broad spectrum of viruses, bacteria, parasites, and leukocytes that may be present in blood components, particularly plasma and platelets, without compromising the therapeutic efficacy of the blood product.

Technologies such as psoralen-based systems (e.g., INTERCEPT Blood System) involve the addition of a photoactive compound (e.g., amotosalen) to the blood product, followed by ultraviolet A (UVA) light illumination. The photoactive compound intercalates into the nucleic acids (DNA and RNA) of pathogens and leukocytes, and upon UVA activation, forms covalent bonds, irreversibly blocking replication. This process effectively inactivates a wide range of enveloped and non-enveloped viruses, gram-positive and gram-negative bacteria, and protozoa, including those for which routine screening tests are not available or are in early stages of infection (e.g., West Nile virus, dengue virus, Zika virus, chikungunya virus, and emerging pathogens).

Another pathogen inactivation method involves the use of riboflavin and UV light (e.g., Mirasol PRT System). Riboflavin, a naturally occurring vitamin B2, binds to nucleic acids and, when exposed to UV light, generates reactive oxygen species that damage the nucleic acids of pathogens, preventing their replication. This method has demonstrated efficacy against a similar spectrum of pathogens as psoralen-based systems. The implementation of pathogen inactivation for plasma and platelets has provided an additional layer of safety, particularly for regions with endemic emerging infectious diseases or for pathogens with prolonged asymptomatic phases that evade standard donor screening. While these technologies are primarily applied to plasma and platelets, research continues into their application for red blood cell concentrates, which present unique challenges due to the high concentration of hemoglobin and its potential interference with inactivation processes.

The clinical impact of pathogen inactivation is particularly relevant for immunocompromised patients, such as those undergoing chemotherapy, organ transplantation, or with hematological malignancies, who are at increased risk for severe outcomes from transfusion-transmitted infections. For these vulnerable populations, the reduction in residual risk from known and emerging pathogens offers a significant safety advantage. Furthermore, pathogen inactivation mitigates the risk of bacterial contamination in platelet concentrates, which, despite stringent donor screening and collection practices, remains a leading cause of transfusion-related septic reactions due to the storage of platelets at room temperature. The broad-spectrum efficacy of these systems addresses pathogens that may not be routinely screened for, such as bacterial species that can proliferate in stored blood components, or rare parasitic infections.

While pathogen inactivation significantly enhances transfusion safety, it is important to acknowledge certain limitations. These technologies do not inactivate non-enveloped viruses as effectively as enveloped viruses, and some viruses, such as parvovirus B19, exhibit resistance to inactivation. Additionally, the cost of implementing pathogen inactivation technologies can be substantial, influencing their widespread adoption, particularly in resource-limited settings. Ongoing research aims to refine existing methods and develop new approaches to overcome these limitations, further enhancing the safety profile of all transfused blood components.

CLINICAL IMPLICATIONS

The evolution of blood transfusion safety represents a triumph of public health and scientific innovation. The current risk profile for transfusion-transmitted infections is remarkably low, a testament to decades of rigorous screening, testing, and processing advancements. Clinicians should convey this enhanced safety to patients, particularly those with anxieties rooted in historical perceptions of transfusion risks. The residual risk, while minimal, underscores the importance of continued vigilance in donor selection and adherence to strict transfusion guidelines, ensuring that transfusions are administered only when clinically indicated.

The integration of pathogen inactivation technologies into routine blood banking practices, especially for platelets and plasma, provides a robust additional safeguard. This is particularly pertinent in an era of global travel and emerging infectious diseases, where conventional serological and nucleic acid testing may not always capture novel or rapidly evolving threats. Blood services and regulatory bodies must continue to evaluate and adopt such technologies, balancing cost-effectiveness with the imperative of patient safety. The industry's investment in these advanced processing methods reflects a commitment to continuous improvement, even as the baseline safety is already high.

For patients, the current landscape means that the benefits of a necessary blood transfusion overwhelmingly outweigh the risks of infection. While no medical procedure is entirely without risk, the collective efforts of the medical community have transformed blood transfusion from a potentially hazardous intervention into a routine, life-saving therapy with an exceptionally low incidence of infectious complications. This allows clinicians to focus on other transfusion-related complications, such as immune reactions, with greater confidence in the infectious safety of the product.

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