RESEARCH PAPER

Transfusion Transmission of Pathogens from Asymptomatic Donors: A Review

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ABSTRACT

Background: Ensuring the safety of blood transfusion has improved significantly over the years due to better donor screening and advanced testing methods. Techniques such as serological testing and nucleic acid amplification testing (NAT) have greatly reduced the risk of transmitting infections like HIV, hepatitis B, and hepatitis C. However, the risk has not been completely eliminated. One of the major concerns is the presence of infections during the "window period," when the pathogen is present in the blood but not yet detectable. Additionally, some donors may carry infections without showing any symptoms, making detection even more challenging. The emergence of new and re-emerging infectious diseases further complicates blood safety, especially in developing regions.

Methods: This review is based on a systematic analysis of research articles published over the last 20 years, sourced from databases such as PubMed, Scopus, and Web of Science. Relevant studies focusing on transfusion-transmitted infections, asymptomatic carriers, and advancements in screening technologies were selected. Information was carefully analyzed to understand patterns of infection, diagnostic challenges, and the effectiveness of current preventive strategies.

Results: The findings show that a wide range of pathogens can be transmitted through blood from donors who do not show symptoms. These include well-known viruses like HIV, HBV, and HCV, as well as emerging infections such as dengue and Zika virus. Although modern testing methods have improved early detection, they still have limitations, especially during the early stages of infection. Moreover, many emerging pathogens are not routinely screened in blood banks. Factors like globalization, climate change, and increased travel contribute to the spread of new infections. New approaches such as pathogen reduction technologies and advanced genetic testing methods offer promising solutions but are not yet widely used.

Conclusion: The risk of infection from asymptomatic donors remains a critical challenge in transfusion medicine. Continuous improvement in screening technologies, better surveillance of emerging diseases, and global cooperation are essential to ensure blood safety. Adopting innovative technologies and flexible strategies will play a key role in reducing future risks.

Keywords: Transfusion-transmitted infections, asymptomatic donors, blood safety, emerging infections, nucleic acid testing, pathogen reduction, window period.

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Introduction

Blood transfusions, critical medical interventions, transmit infectious agents from donors to recipients, termed transfusion-transmitted infections (TTIs) [(1)]. This constitutes an inherent risk. Asymptomatic blood donors harboring pathogens persistently challenge transfusion safety. This necessitates continuous vigilance and enhanced detection techniques despite stringent screening measures [(2)]. Despite advanced donor screening and blood processing, novel

pathogens and detection limitations threaten the global blood supply. This threat is particularly acute during the infection phase prior to seroconversion or symptom manifestation [(2)]. This review examines TTI mechanisms, obstacles, and countermeasures originating from asymptomatic donors. It covers both traditional and novel infectious agents. Specifically, it explores pathogen identification challenges during asymptomatic or pre-symptomatic stages. This includes the critical window period, during which standard tests fail to detect infected donors [(3)]. The review also investigates implicated pathogens, their asymptomatic dissemination processes, and advancing screening and mitigation approaches. These include pathogen inactivation methods [(2)]. Additionally, it highlights specific infection risks: SARS-CoV-2, dengue, Zika, and mpox. Asymptomatic viremia precedes symptoms for these agents, thereby heightening transfusion transmission potential [(4)]. The paper further considers global and Indian viewpoints on TTI monitoring and risk control. This highlights regional differences and efforts to bolster blood safety. It then discusses prospective strategies to reduce residual TTI risks. These include cutting-edge diagnostics, refined donor criteria, and unified 'One Health' surveillance models. This involves tackling emerging infections lacking routine screening, which can spread undetected and enable accidental transmission [(4)]. Blood-borne pathogen adaptability and novel agent emergence necessitate persistent surveillance and screening enhancements to safeguard the blood supply [(5)]. Transfusion medicine evolution integrates emerging science and technologies to protect public health [(6)]. Understanding donor TTI seroprevalence is vital for effective screening and risk reduction. This is critical for asymptomatic carriers and during infection window periods [(7)]. Nucleic acid amplification technology (NAT) has lowered risks for established agents—HIV, HCV, and HBV—to <1:10^6 units in high-resource nations. Conversely, vector-borne threats (e.g., West Nile Virus, Chikungunya virus) require swift screening or deferral adjustments during outbreaks [(8)],[(9)]. Globalization accelerates novel pathogen spread, necessitating coordinated global surveillance and responses. This shift mandates a forward-looking, cross-disciplinary 'One Health' framework. The framework links human, animal, and environmental monitoring to preempt blood supply risks [(10)]. It recognizes interconnectedness as a driver of disease emergence, requiring interdisciplinary collaboration for transfusion safety [(11)]. Combining serological virus antibody/antigen tests with NAT for HIV, HCV, and HBV has substantially improved global blood product viral safety. This has slashed classic pathogen transmission risks [(12)]. Conversely, resource-limited areas face higher TTI burdens. This highlights the need for flexible, robust screening [(13)]. For instance, Ghanaian research reports a 21.0% overall TTI rate. This rate varies by pathogen (e.g., HBV, HCV, HIV, syphilis), stressing the critical need for blood safety improvements in high-prevalence contexts [(14)].

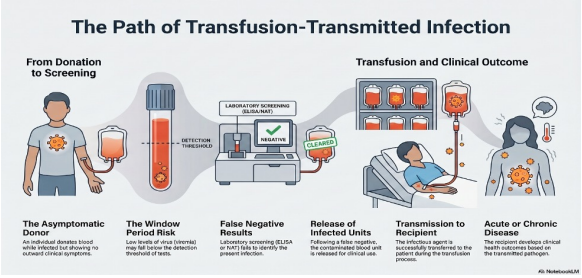

Figure 1: Flowchart illustrating the mechanism of transfusion-transmitted infections from asymptomatic donors. Despite routine screening, infections may escape detection during the window period or due to low-level viremia, leading to transmission in recipients.

Methods

This section delineates the systematic methodology underpinning this comprehensive review, detailing the search strategy, selection criteria for relevant literature, and the analytical framework used to synthesize the findings. The methodology encompassed a comprehensive search of peer-reviewed articles and relevant guidelines from reputable scientific databases, focusing on publications from 2018 to 2024 to ensure currency and relevance. Specific databases interrogated encompassed PubMed, Scopus, Web of Science, and Google Scholar, using a combination of keywords such as "transfusion-transmitted infection (TTI)," "asymptomatic donors," "blood safety," "emerging infectious diseases," "screening strategies," "window period," and specific pathogen names (e.g., "SARS-CoV-2," "Zika," "Dengue," "Hepatitis E," "Mpox"). The initial search yielded a substantial number of articles, whereupon subsequent systematic screening was conducted based on their titles and abstracts to identify studies directly pertinent to the transfusion transmission of pathogens from asymptomatic donors. Full-text articles, including original research, review articles, and systematic reviews, which met the defined inclusion criteria and focused on human blood transfusion safety and pathogen transmission, were

subsequently retrieved and subjected to critical appraisal for methodological rigor and relevance to the review's objectives. Data extraction focused on identifying common and emerging transfusion-transmissible infections, screening methodologies, challenges posed by the window period, risk mitigation strategies, and global epidemiological trends, with a particular emphasis on recent outbreaks and their impact on blood safety. This synthesis of extracted information facilitated a comparative analysis of screening efficacy, the identification of persistent gaps in blood safety protocols, and the delineation of future research directions. This structured approach ensured a thorough and evidence-based examination of the complex interplay between asymptomatic donors and TTI (TTI) risks, providing a robust foundation for the subsequent sections of this review. A medical librarian experienced in systematic review retrieval provided search strategy assistance [(15)].

Types of Pathogens Transmitted Through Transfusion

Blood transfusion-transmissible pathogens include established viral, bacterial, and parasitic agents. Emerging zoonotic infectious diseases increasingly contribute to this pathogen spectrum. These transfusion-transmissible infections cause substantial morbidity and mortality in recipients, necessitating rigorous donor screening and blood product testing protocols [(16)]. Historically, pathogens such as HBV, HCV, HIV, and *Treponema pallidum* (syphilis) have been major concerns, prompting development of sensitive serological and nucleic acid amplification tests (NATs) [(17,18)]. Despite these advancements, numerous bloodborne agents beyond routinely screened pathogens persist as concerns [(18,19)]. The evolving infectious disease landscape, coupled with global travel and climate change, introduces new or re-emerging pathogens into the blood supply. This poses ongoing challenges for blood safety agencies worldwide [(18,20)]. These agents include bacterial, viral, parasitic, and prion entities. Each presents unique detection and prevention challenges for transfusion transmission [(21),(19),(17,22)]. Prioritized pathogens include HIV, HBV, HCV, and *Treponema pallidum* (syphilis). These pathogens, despite advanced screening methodologies, present a substantial, albeit attenuated, risk. This risk is attributable to nascent infection's asymptomatic presentation and dynamic pathogen evolution [(23),(24),(25)].

Bacterial Pathogens

Routine screening for *Treponema pallidum* is standard. Other bacterial pathogens lack routine screening in blood donations. These agents clearly present a substantial risk, particularly considering evolving demographics and increased global mobility [(26)]. Bacterial contamination, though infrequent, may constitute a primary etiology of transfusion-associated sepsis, often originating from donor bacteremia or suboptimal venipuncture site preparation[(27),(28),(29)]. This can result in significant morbidity and mortality, especially in immunocompromised recipients[(27,30)]. Principal bacterial contaminants frequently implicated in septic transfusion reactions encompass *Staphylococcus aureus*, coagulase-negative staphylococci, *Bacillus cereus*, and *Yersinia enterocolitica*, with cold-storing pathogens like *Yersinia* clearly present specific challenges for refrigerated blood products[(31),(32)]. The implementation of bacterial culture and rapid detection assays, alongside enhanced donor screening questionnaires and improved collection procedures, has been crucial in mitigating this risk [(33,34)]. The emergence of multidrug-resistant bacteria poses an additional threat to transfusion safety. This necessitates continuous surveillance and the development of rapid detection technologies[(35)].

Viral Pathogens

Viral pathogens comprise a diverse, continuously evolving agent class. This class significantly impacts transfusion safety, encompassing characterized viruses and novel strains [(36)]. Historically, the most critical viral agents appear to encompass human immunodeficiency virus (HIV), hepatitis C virus (HCV), and hepatitis B virus (HBV), These three viruses drove substantial advancements in donor screening and blood product testing protocols[(37,38)]. Nonetheless, despite stringent testing protocols, residual risk of transfusion-transmitted viral infections (TTVIs) persists. This risk demonstrably stems from: the "window period" phenomenon, false-negative test results, and novel viral threats unaddressed by routine screening panels[(39,40)]. Additionally, certain viral pathogens may not cause severe acute symptoms in donors. However, they establish persistent infections or significant disease in immunocompromised recipients. This complicates risk assessment and mitigation strategies.[(30,41)].

Parasitic Pathogens

Transfusion-transmitted parasitic infections (TTPIs) represent a critical concern in endemic regions. Global travel and migration patterns increase this risk, despite

lower incidence in developed countries [42], [43]. TTPIs exhibit prolonged asymptomatic carriage in donors. This presents unique diagnostic challenges, stemming from parasitic life cycle diversity and the absence of universal screening assays for all relevant parasites [42]. Malaria, Chagas disease (*Trypanosoma cruzi*), and babesiosis (*Babesia microti*) constitute significant parasitic threats. These necessitate specific donor deferral criteria or targeted testing strategies in high-prevalence areas [42], [43]. Toxoplasmosis and leishmaniasis also pose transfusion risks. This is due to varying geographical pathogen distribution and current broad-spectrum screening methodology limitations [44], [45]. Protozoan parasites (*Plasmodium* species, *Trypanosoma cruzi*) present specific challenges. Their long-term persistence in asymptomatic carriers facilitates inadvertent transmission via blood transfusions [42]. These cryptic infections frequently circumvent conventional donor screening. This is particularly true in non-endemic regions with low clinical suspicion [42]. The low incidence of TTPIs compared to bacterial and viral contamination masks their severe illness potential. These infections significantly impact immunocompromised recipients [43].

Prion Diseases

Prion diseases, including variant Creutzfeldt-Jakob disease (vCJD), present a distinct challenge to transfusion safety. This is primarily due to prolonged asymptomatic incubation periods, absence of reliable ante-mortem diagnostic tests, and resistance to conventional pathogen inactivation methods [46]. The potential for transfusion-transmitted vCJD, despite its low documented incidence, prompted extensive precautionary measures. These include donor deferral policies and leukoreduction to minimize theoretical risks [47], [48].

Mechanisms of Asymptomatic Transmission

The asymptomatic nature of certain infections in blood donors constitutes a central tenet for transfusion transmission risk assessment: infected individuals carry pathogens without overt clinical symptoms, thus eluding standard health assessments[49]. This phenomenon spans a wide pathogen spectrum: viruses, bacteria, and parasites. Each employs distinct silent carriage mechanisms[50]. These mechanisms include pathogen immune evasion, host genetic factors influencing disease presentation, or dynamic equilibrium between pathogen replication and immune control, preventing overt disease expression in donors [51],[52]. Consequently, infected asymptomatic donors present an insidious challenge to blood safety. This necessitates advanced detection strategies beyond symptomatic presentation[53],[49]. Pathogen establishment of latent or chronic infections, coupled with host immune response variability, contributes significantly to the asymptomatic carrier state, complicating detection [51]. Moreover, the "window period" following initial infection further complicates early detection. During this period, a donor is infectious, but standard serological tests remain negative, expanding the asymptomatic carrier pool[54].

Window Period Infections

The window period (WP) represents the interval between infection and detectability of pathogen-specific markers (antibodies, antigens, or nucleic acids) by routine screening assays [25]. This WP constitutes a critical vulnerability within the blood supply chain [55]). During this phase, infected donors can transmit pathogens through transfusion even when conventional serological or nucleic acid tests (NAT) yield negative results. This phenomenon presents significant challenges for emerging infections and those with highly variable incubation periods. Seroconversion dynamics frequently do not align with established testing protocols, facilitating the ingress of infectious donations into the blood supply. WP duration and characteristics vary significantly among disparate pathogens. These factors directly influence the residual risk of transfusion transmission [25]. For example, dengue virus-infected individuals present asymptomatic states for extended periods. Their blood may test negative via conventional methods, yet transmission occurs [56]. Similarly, HIV and HCV infections exhibit high viral loads during the pre-seroconversion phase. This necessitates NAT implementation for transmission risk mitigation during this critical interval [57],[58].

Latent Infections

Latent infections involve pathogen persistence in a quiescent state within the host, without active replication or overt disease. This poses a significant challenge to transfusion safety.

Classical Transfusion-Transmitted Infections (TTIs)

Hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) are historically prevalent pathogens. They necessitate rigorous monitoring due to established asymptomatic carriage and profound clinical transmission implications (59). Despite nucleic acid testing (NAT) implementation and stringent donor selection, residual risks persist. These risks originate particularly from donations made during infection window periods (60),(61). These

classical transfusion-transmitted infections (TTIs) drive diagnostic innovation in sensitivity and specificity. Robust surveillance and adaptable screening protocols are thus required to maintain blood product safety (61). Historically, serological testing for TTIs served as a blood safety cornerstone. However, it often fails to detect early window period infections; only NAT identifies low-level viremia or early infection stages (60). However, novel and re-emerging infectious agents necessitate continuous re-evaluation of existing screening paradigms. This requires the development of assays with high sensitivity and specificity for broader pathogen detection. This clearly demonstrates the continuous challenge of achieving zero risk. False negatives and transmissions, even if rare, demonstrably occur with advanced technologies like nucleic acid amplification tests (NATs) (62).

Human Immunodeficiency Virus (HIV)

The introduction of highly sensitive nucleic acid testing for human immunodeficiency virus (HIV) significantly curtailed the window period, reducing the risk of transmission to approximately 11 days post-exposure, thereby, the substantial enhancement of blood safety(63). Consequently, this advancement has clearly decreased the residual risk of transfusion-associated HIV, thereby transforming it from a significant concern to an extremely rare event in regions with advanced screening infrastructure. Model-based estimates clearly establish the residual risk of HIV transmission via transfusion at approximately one in 1,800,000 to one in 2,000,000 donations (64),(63). This reduction results from antigen and antibody testing combined with NAT. This combination significantly shortens the diagnostic window period (65). Despite these improvements, ongoing surveillance and the development of even more sensitive assays remain crucial. This necessity stems from viral strain evolution and variations in diagnostic performance across diverse donor populations.

Hepatitis B Virus (HBV)

Hepatitis B virus (HBV) exhibits persistent global prevalence. This necessitates stringent, evolving screening protocols due to its chronic infection capacity and its long, often asymptomatic incubation period. The implementation of highly sensitive HBsAg assays and HBV DNA NAT has been pivotal. These assays reduce HBV transfusion-transmission risk by detecting occult and acute infections prior to seroconversion (66). Despite these advances, challenges persist: HBV's occult infection phase (HBsAg undetectable, HBV DNA present) and mutations in the 'a' determinant region impacting HBsAg detection. These necessitate vigilant monitoring and exploration of new diagnostic strategies. Moreover, the potential for immune escape mutants complicate diagnostic efforts. This underscores the necessity for multi-target NAT and improved serological assays capable of detecting diverse viral variants. The residual risk of HBV transmission, even with advanced testing, persists due to the prolonged, often asymptomatic window period, estimated at approximately 11.6 days when tested individually (67).

Hepatitis C Virus (HCV)

Rigorous screening for Hepatitis C Virus (HCV) has also demonstrably enhanced transfusion safety. This was achieved via anti-HCV antibody testing and Nucleic Acid Testing (NAT) for HCV RNA, which critically reduced both the window period and the residual risk of transfusion-transmitted HCV (68). These implemented methods effectively reduced the residual HCV transmission risk to 1 in 0.83 million donations (69). Challenges persist. These include detection of low viral loads in immunocompromised donors or during early seroconversion. Furthermore, novel HCV genotypes or variants may evade current detection methods. Historically, post-transfusion hepatitis, specifically HBV and HCV infections, presented substantial challenges in blood safety. HBV exhibited a higher residual transmission risk than HCV or HIV due to its prolonged serologically negative window period (70).

Syphilis

Although less common than viral transfusion-transmissible infections (TTIs), bacterial infections like syphilis constitute a persistent risk, particularly due to the challenges inherent in the identification of asymptomatic donors with latent infections. Current syphilis screening utilizes serological assays for treponemal and non-treponemal antibodies. These methods exhibit detection limitations for early-stage or latent infections, where spirochetemia levels may be intermittent or below assay detection thresholds. Molecular diagnostics, such as PCR-based assays targeting specific treponemal DNA sequences, demonstrate augmented sensitivity for direct pathogen detection in early and latent syphilis. This clearly mitigates limitations of traditional serological screening (71) Integration of advanced molecular methods into routine screening reduces residual syphilis risk. These methods detect window-period and asymptomatic infections(72). Rapid multiplex assays for diverse bacterial pathogens—and adaptive screening, novel biomarkers, and pathogen-agnostic

detection—are essential for counteracting evolving strains and resistance. The development of broad-spectrum pathogen reduction technologies presents a promising avenue. These technologies inactivate a broad spectrum of bacterial contaminants, including syphilis-implicated pathogens, within blood products prior to transfusion. This approach provides an additional safety stratum beyond donor screening and testing. It addresses inherent limitations in identifying all asymptomatic bacterial carriers[73].

Malaria

Malaria, caused by Plasmodium, constitutes a notable transfusion-transmissible infection, particularly in endemic regions, thereby necessitating stringent donor screening attributable to its frequently asymptomatic parasitemia in semi-immune individuals. Malaria screening strategies in blood donations exhibit geographical variance. Non-endemic areas employ serological and molecular testing; endemic regions rely on donor deferral questionnaires and microscopy [74],[75]. Antigen and antibody detection tests are common. However, low parasitemia levels and Plasmodium species genetic diversity limit their sensitivity. Robust diagnostic modalities are imperative [76],[77]. Molecular diagnostic techniques, such as PCR, offer enhanced sensitivity for detecting low-level parasitemia and identifying different Plasmodium, thereby providing a more reliable method for mitigating transfusion-transmitted malaria[78].

Emerging Transfusion-Transmitted Infections (TTIs)

The landscape of transfusion-transmitted infections is continuously reshaped by the emergence of novel pathogens and the re-emergence of established infectious agents, Factors include globalization, climate change, and evolving human-animal interfaces [35]. This dynamic environment necessitates continuous vigilance and adaptable screening strategies to safeguard the blood supply against emerging threats [79]. The absence of established testing or mitigation interventions for certain diseases currently in widespread use poses a complex challenge for transfusion medicine. The implications of screening for these emerging transfusion-transmissible infections extend beyond direct pathogen detection, It encompasses resource allocation, test limitations, and donor deferral ethical dimensions [80]. New pathogen reduction technologies (PRTs) further mitigate these risks. PRTs inactivate a broad spectrum of infectious agents within blood products, thus enhancing overall transfusion safety [81],[82],[83].

Dengue Virus

Dengue virus constitutes a significant risk to blood safety, particularly in endemic regions, owing to its high prevalence and the frequently asymptomatic nature of infection during the viremic phase[11]. The challenge is further compounded by several factors: the absence of widespread licensed screening assays, the potential for occult viremia in afebrile donors, and the possibility of transfusion-associated dengue[84]. Nucleic acid testing (NAT) for dengue virus RNA functions as a crucial screening tool. NAT detects the virus during pre-symptomatic and early symptomatic phases. This effectively reduces transfusion-transmitted dengue (TTD) risk in high-incidence regions [85].

Zika Virus

Zika virus (ZIKV) emergence constitutes a significant public health concern. Its association with severe neurological complications necessitated rapid implementation of effective blood donation screening strategies [86]. Primary concern: prolonged viremic window in asymptomatic individuals and potential for sexual and congenital transmission. This necessitates comprehensive donor deferral policies and NAT screening in affected regions [87].

Chikungunya Virus

Chikungunya virus (CHIKV), a mosquito-transmitted arbovirus, poses a blood safety risk. This risk, similar to dengue and ZIKV, stems from asymptomatic viremia in infected donors, especially during outbreaks [88]. Given the rapid global spread of arboviruses and the high proportion of asymptomatic infections, A universal blood safety approach is imperative. This approach encompasses proactive surveillance and adaptable screening methodologies. Such methods mitigate the persistent threat posed by emergent infectious diseases to the blood supply [84],[89].

West Nile Virus

West Nile Virus (WNV) constitutes a significant transfusion-transmitted infection (TTI) in North America. Seasonal outbreaks mandate robust nucleic acid amplification test (NAT) screening of blood donations in affected regions [90]. Emergent and re-emergent arboviruses pose a persistent challenge. This necessitates continuous global surveillance and the development of highly sensitive, specific diagnostic platforms. These measures ensure transfusion safety [91].

SARS-CoV-2

The SARS-CoV-2 pandemic clearly demonstrated potential risks from respiratory viruses to blood safety, This instigated research into transfusion

transmissibility and donor screening protocols. Studies consistently indicate minimal transfusion risk, attributable to low, transient viremia. This redirects primary focus toward nosocomial prevention and supply continuity amidst prevailing restrictions. Future pandemics require ongoing variant monitoring, adaptable protocols, targeted screening, and pathogen inactivation. These efforts must mirror efficacious rapid response protocols for West Nile Virus (WNV), particularly regarding Nucleic Acid Testing (NAT) [(92)].

Hepatitis E Virus (HEV)

Hepatitis E Virus (HEV) demonstrates escalating recognition as a transfusion-transmissible pathogen. This is particularly true in highly endemic regions, where asymptomatic viremia contributes to chronic infections in immunocompromised recipients. Chronic HEV infection potential, particularly in vulnerable populations, necessitates robust screening strategies. Nucleic acid testing (NAT) detects viremic donations, especially in high-endemicity areas [(93)].

Mpox Virus

Mpox virus (MPXV), formerly monkeypox, emerged as a pathogen of concern for transfusion safety. Its potential for asymptomatic or oligosymptomatic presentation during prodromal and early eruptive phases could coincide with blood donation [(94)].

Trypanosoma cruzi (Chagas Disease)

Protozoan parasites cause babesiosis and Chagas disease. These organisms present significant, regionally specific transfusion transmission risks. Risk factors include prolonged asymptomatic parasitemia in infected donors and limitations in current routine blood center screening protocols[(42)]. The persistent asymptomatic carrier state in endemic areas necessitates the development and implementation of highly sensitive, specific diagnostic assays. These assays detect low-level parasitemia, preventing transfusion-associated infections. The varying geographical distribution of these parasitic infections necessitates a dynamic risk assessment framework. This framework enables the development of targeted screening strategies. These strategies account for donor travel history and epidemiological data.

Table 1: Comparison of Classical vs Emerging Transfusion-Transmitted Infections (TTIs)

Category	**Pathogen**	**Type**	**Primary Mode of Transmission**	**Risk from Asymptomatic Donors**	**Key Challenges**
Classical	HIV	Virus	Blood, sexual contact	High (long window period)	Early detection during window period
Classical	HBV	Virus	Blood, body fluids	Very high (occult infection possible)	Occult HBV infection, low viral load
Classical	HCV	Virus	Blood	Moderate to high	Asymptomatic chronic infection
Classical	*Treponema pallidum* (Syphilis)	Bacteria	Blood	Low to moderate	Reduced viability in stored blood
Emerging	Dengue virus	Virus	Vector-borne, transfusion	High (during viremic phase)	Seasonal outbreaks, asymptomatic donors
Emerging	Zika virus	Virus	Vector-borne, transfusion	High	Often asymptomatic, congenital risk
Emerging	Chikungunya virus	Virus	Vector-borne, transfusion	Moderate	Limited routine screening
Emerging	West Nile virus	Virus	Vector-borne, transfusion	High	Silent infections in donors

Category	Pathogen	Type	Primary Mode of Transmission	Risk from Asymptomatic Donors	Key Challenges
Emerging	Hepatitis E virus (HEV)	Virus	Feco-oral, transfusion	Moderate to high	Chronic infection in immunocompromised
Emerging	SARS-CoV-2	Virus	Respiratory (possible blood)	Low (uncertain)	Limited evidence, evolving data
Emerging	Mpox virus	Virus	Contact (potential blood)	Emerging risk	Insufficient transfusion data

A comparative overview of classical and emerging transfusion-transmitted infections is presented in Table 1.

Screening Strategies for Asymptomatic Donors

Many transfusion-transmissible infections exhibit silent incubation or chronic phases. Therefore, effective screening is essential for blood safety [(95)]. Comprehensive strategies implement donor questionnaires, serological tests, and nucleic acid testing (NAT) to detect asymptomatic cases. Deferrals based on geography, travel, and lifestyle risks confer a preliminary protective effect. However, questionnaires exhibit limitations. These limitations result from potential unawareness or non-disclosure of infectious status by asymptomatic carriers. Laboratory assays primarily afford objective detection.

Documentation of transfusion-associated Mpox virus (MPXV) cases is unrecorded. Asymptomatic viremia and outbreaks necessitate heightened vigilance [(96)]. The MPXV pandemic initiated significant deliberation concerning universal PCR testing, despite deferral guidelines for cases and contacts [(97)]. Implementation of sensitive assays is paramount. MPXV DNA is detectable in the bloodstream during viremia; however, elucidation of associated donor risks warrants further investigation [(98)].

Table 2: Screening Methods in Blood Transfusion – Advantages and Limitations

Screening Method	Principle	Advantages	Limitations
ELISA (Enzyme-Linked Immunosorbent Assay)	Detects antigen/antibody reaction	Cost-effective, widely used, high throughput	Cannot detect infections during window period
NAT (Nucleic Acid Testing)	Detects viral RNA/DNA directly	High sensitivity, early detection, reduces window period	Expensive, requires technical expertise
Rapid Diagnostic Tests (RDTs)	Immunochromatographic assays	Quick results, easy to perform, useful in remote areas	Lower sensitivity and specificity
Donor Health Questionnaire (DHQ)	Behavioral and medical risk assessment	Identifies high-risk donors, inexpensive	Depends on donor honesty, subjective
Chemiluminescence Immunoassay (CLIA)	Detects antigen/antibody using luminescence	Higher sensitivity than ELISA, automated	Costlier than ELISA

Table 2 summarizes commonly used screening methods along with their advantages and limitations.

Donor History Questionnaire

The questionnaire-based approach, while foundational, possesses inherent limitations. These include reliance on donor candor and exposure awareness, which is challenging for emerging or unrecognized infections. Furthermore, asymptomatic individuals cannot effectively self-defer due to absent overt clinical symptoms. This necessitates

complementary objective screening methodologies. Consequently, deployment of advanced laboratory testing, including Nucleic Acid Amplification Tests (NAATs), becomes indispensable. This enables infection identification during the pre-symptomatic or asymptomatic window period when conventional methods are insufficient [99].

Serological Testing

Serological testing detects infection-induced antibodies or specific antigens. This identifies past or ongoing infections, critical for pathogens with prolonged seroconversion windows or persistent humoral responses. Serological assays detect established infections. However, they may not detect acute infections during the pre-seroconversion window period. Molecular diagnostics integration is necessary for comprehensive donor screening[99]. Nucleic Acid Testing (NAT), a nucleic acid amplification technology, constitutes a cornerstone of modern blood safety protocols. NAT enables direct pathogen genetic material detection, significantly reducing the window period for numerous transfusion-transmissible infections[100]. This approach facilitates viremic donation identification prior to antibody development. It mitigates transmission risk for infections like HIV, HCV, and HBV during early, highly infectious stages[100]. This technological advancement demonstrates enhanced the safety of the blood supply, particularly for pathogens like West Nile Virus; NAT proves instrumental in transmission prevention[101].

Nucleic Acid Testing (NAT)

Nucleic Acid Testing (NAT) represents a pivotal advancement in transfusion safety. It offers the most sensitive, direct methodology for viral genetic material detection. This yields a significantly abbreviated infection-detectability window period compared to serological methods[102]. This mechanism facilitates infection identification prior to seroconversion. It addresses a critical vulnerability of traditional antibody-based screening[103]. The implementation of NAT demonstrates high efficacy in reducing the residual risk of transfusion-transmitted infections such as HIV, HCV, and HBV, resulting in per-unit risks less than 1:1,000,000 in high-income countries[104].

Pathogen Reduction Technologies

Pathogen reduction technologies constitute an additional stratum of safety through the inactivation of pathogens within donated blood components. This contributes to further residual risk reduction for transfusion-transmitted infections [105],[106].

Challenges in Detecting Pathogens During the Window Period

The "window period" defines the post-infection interval. Pathogens persist in the bloodstream before detectable antibody levels develop, despite negative diagnostic outcomes [107]. This interval impedes blood safety. Donors may unknowingly transmit pathogens, circumventing rigorous screening protocols. This demonstrates the persistent threat emergent infectious agents pose to blood supply integrity [107],[105]. This interval varies based on pathogen type and diagnostic assay sensitivity. The range typically spans several days to multiple weeks. For HIV, Nucleic Acid Testing (NAT) yields a window period of 7–11 days. This duration is significantly shorter than the 22-day interval for antibody-based tests [102],[104]. Despite this reduction, NAT presents a considerable challenge to blood product safety.

Limitations of Current Assays

Despite technological advancements, inherent limitations persist. These manifest in infections with low viral loads or in emergent pathogens where established diagnostic assays lack sufficient sensitivity or specificity [108]. Furthermore, pathogen genotype evolution facilitates detection evasion by assays calibrated for antecedent strains. This necessitates perpetual assay refinement and heightened surveillance protocols [5]. Consequently, the diagnostic window period remains a significant impediment in transfusion medicine. This mandates innovative strategy development for early pathogen detection in asymptomatic donors [109],[110]. For instance, heterogeneous immune responses influence antigen expression and antibody production rates. This complicates early detection and augments the residual risk of transfusion-transmitted infections [58].

Cost-Effectiveness of Advanced Screening

Highly sensitive, broad-spectrum screening methodologies present economic considerations. These include infrastructure investment, operational expenses, and increased donor deferral rates. A rigorous cost-benefit analysis is required. This analysis must balance enhanced safety with blood product sustainability and accessibility across diverse healthcare systems. Advanced screening methods, such as nucleic acid amplification testing (NAAT), significantly reduce the window period. However, they do not eliminate transmission risk from asymptomatic donors, especially for novel or evolving pathogens[108],[111].

Global and Indian Scenario of Transfusion-Transmitted Infections

Globally, transfusion-transmitted infection (TTI) prevalence and incidence demonstrate substantial

variation. This variation is due to disparate epidemiological landscapes, socioeconomic determinants, and blood screening protocol sophistication. Resource constraints in developing nations preclude advanced screening technology adoption, thus elevating TTI prevalence among blood donors [112]. Developed countries achieve substantial TTI incidence rate reduction via comprehensive screening. This includes nucleic acid testing (NAT), robust donor selection criteria, and stringent quality control measures. However, transmission risk persists during the window period or from emerging pathogens [113]. Specific challenges include hepatitis E virus genotype 3 in European regions and Babesia in USA regions; these highlight localized threats. Globally, continuous emergence of new infectious agents necessitates dynamic monitoring and adaptive safety measures [6]. In India, the existing scenario complicates TTI risk profiles [16]. Elevated TTI prevalence in India, primarily due to window-period donations, mandates comprehensive strategies. This includes mandatory NAT for enhanced blood safety within resource-constrained environments [114]. Furthermore, dependence on replacement donors in Indian blood banks introduces additional risks. These donors often do not undergo the rigorous screening protocols applied to voluntary, professional donors [7].

Future Perspectives and Research Directions

Further advancements in pathogen detection technologies, including multiplex PCR assays and next-generation sequencing, demonstrate capability in reducing the diagnostic window period and rapid identification of novel infectious agents[115]. Additionally, the development of pan-pathogen detection systems capable of identifying a broad spectrum of known and unknown infectious agents proves crucial for the proactive response to emerging threats[116]. Moreover, the integration of artificial intelligence and machine learning algorithms enhances predictive modeling for outbreak detection and risk assessment, This optimizes donor screening protocols.[117,118]. Ongoing research into pathogen reduction technologies also offers a pathway the neutralization of a diverse array of viruses, bacteria, and parasites in donated blood components. This provision provides an additional safety layer beyond donor screening [18].

Conclusion

Transfusion transmission of pathogens from asymptomatic donors continues to represent a significant challenge in ensuring the safety of the blood supply. Despite considerable advancements in donor screening and laboratory testing, the risk cannot be completely eliminated due to factors such as the diagnostic window period, occult infections, and the emergence of new pathogens. Both classical transfusion-transmitted infections and recently emerging infectious agents highlight the need for continuous vigilance and improvement in transfusion practices.

The integration of stringent donor selection criteria with advanced screening technologies, including nucleic acid testing and highly sensitive immunoassays, has substantially reduced the residual risk of infection. However, disparities in infrastructure and resource availability, particularly in developing regions, limit the universal implementation of these strategies. Therefore, strengthening hemovigilance systems, enhancing public awareness, and promoting voluntary blood donation remain essential components of a safe transfusion system.

Future efforts should focus on the adoption of innovative approaches such as pathogen reduction technologies and the incorporation of advanced diagnostic tools to address both known and emerging threats. A comprehensive and adaptable blood safety framework, supported by global collaboration and equitable resource distribution, is crucial to minimizing transfusion-related risks and ensuring safe and effective blood transfusion practices worldwide.

References

1. Kim HJ, Ko D. Transfusion-transmitted infections. Blood Research [Internet]. 2024 Apr 12 [cited 2025 Sep];59(1). Available from: https://doi.org/10.1007/s44313-024-00014-w
2. Tsen SWD, Wu TC, Kiang JG, Tsen KT. Prospects for a novel ultrashort pulsed laser technology for pathogen inactivation. Journal of Biomedical Science [Internet]. 2012 Jan 1 [cited 2025 Oct];19(1):62. Available from: https://doi.org/10.1186/1423-0127-19-62
3. Pavia CS, Plummer MM. Transfusion-Associated Lyme Disease – Although Unlikely, It Is Still a Concern Worth Considering. Frontiers in Microbiology [Internet]. 2018 Sep 4 [cited 2025 Sep];9. Available from: https://doi.org/10.3389/fmicb.2018.02070
4. Dreier J, Juhl D. Emerging Pathogens: Novel and Well-Known Infectious Threats in Transfusion Medicine. Transfusion Medicine and Hemotherapy [Internet]. 2022 Jan 1

[cited 2025 Sep];49(4):189. Available from: https://doi.org/10.1159/000525327

5. Dreier J, Vollmer T. Inectious Screening of Blood Components: Is There Still a Need for Further Inventions? Transfusion Medicine and Hemotherapy [Internet]. 2019 Jan 1 [cited 2025 Jun];46(2):65. Available from: https://doi.org/10.1159/000499351
6. Zaaijer HL. Prevention of Transfusion-Transmitted Infections: Dilemmas. Frontiers in Medicine [Internet]. 2017 Dec 11 [cited 2025 Sep];4. Available from: https://doi.org/10.3389/fmed.2017.00221
7. Dobariya G, Raja K, Unagar CA, Pandya AN, Patel J, Jarag M, et al. Prevalence and trends of transfusion transmitted infections among blood donors of blood bank attached to government hospital of South Gujarat, India. International Journal of Research in Medical Sciences [Internet]. 2016 Jan 1 [cited 2025 Sep];4123. Available from: https://doi.org/10.18203/2320-6012.ijrms20162946
8. Prudent M, Tissot J, Fontana S, Niederhauser C. Editorial: Transfusion Medicine and Blood. Frontiers in Medicine [Internet]. 2019 Jan 8 [cited 2025 Oct];5. Available from: https://doi.org/10.3389/fmed.2018.00355
9. Kleinman S, King MR, Busch MP, Murphy EL, Glynn SA. The National Heart, Lung, and Blood Institute Retrovirus Epidemiology Donor Studies (Retrovirus Epidemiology Donor Study and Retrovirus Epidemiology Donor Study-II): Twenty Years of Research to Advance Blood Product Safety and Availability. Transfusion Medicine Reviews [Internet]. 2012 May 24 [cited 2026 Mar];26(4):281. Available from: https://doi.org/10.1016/j.tmrv.2012.04.004
10. Dengue Fever in a One Health Perspective - Latest Research and Recent Advances [Internet]. Infectious diseases. IntechOpen; 2023 [cited 2025 Oct]. Available from: https://doi.org/10.5772/intechopen.104140
11. Mulakoli F, Gachara G, Ndombi EM, Khamadi S. Dengue Virus Surveillance and Blood Safety: A One Health Perspective. In: Infectious diseases [Internet]. IntechOpen; 2023 [cited 2025 Oct]. Available from: https://doi.org/10.5772/intechopen.109413
12. Juhl D. Viral Safety of Blood Products: Beyond HBV, HCV, and HIV. Transfusion Medicine and Hemotherapy [Internet]. 2025 Dec 11 [cited 2026 Mar];53(1):1. Available from: https://doi.org/10.1159/000550012
13. Charwudzi A, Adela EM, Pereko KKA, Ampofo M, Fenuku A, Azumah D, et al. Prevalence and predictors of transfusion-transmitted infections among blood donor types at a teaching hospital in Ghana: Implications for haemovigilance. PLoS ONE [Internet]. 2025 Oct 31 [cited 2026 Mar];20(10). Available from: https://doi.org/10.1371/journal.pone.0335544
14. Hadfield PY, Vechey GA, Bansah E, Nyahe M, Khuzwayo N, Tarkang EE. Transfusion-Transmissible Infections Among Blood Donors in a Regional Hospital in Ghana: A 6-Year Trend Analysis (2017-2022). Journal of the International Association of Providers of AIDS Care (JIAPAC) [Internet]. 2024 Jan 1 [cited 2026 Mar];23. Available from: https://doi.org/10.1177/23259582241274305
15. Rohde JM, Dimcheff DE, Blumberg N, Saint S, Langa KM, Kuhn L, et al. Health Care–Associated Infection After Red Blood Cell Transfusion. JAMA [Internet]. American Medical Association; 2014 Apr 1 [cited 2025 Oct];311(13):1317. Available from: https://doi.org/10.1001/jama.2014.2726
16. Kaur P, Basu S. Transfusion-transmitted infections: existing and emerging pathogens. PubMed [Internet]. 2006 May 18 [cited 2025 Nov];51(2):146. Available from: https://pubmed.ncbi.nlm.nih.gov/16006714
17. Bianco C. Current concepts in transfusion transmitted diseases. ISBT Science Series [Internet]. 2011 May 13 [cited 2025 Nov];6(1):56. Available from: https://doi.org/10.1111/j.1751-2824.2011.01436.x
18. Busch MP, Kleinman S, Nemo GJ. Current and Emerging Infectious Risks of Blood Transfusions. JAMA [Internet]. 2003 Feb 26 [cited 2026 Jan];289(8):959. Available from: https://doi.org/10.1001/jama.289.8.959
19. Giorgi VD, Zhou H, Alter HJ, Allison RD. A microarray-based pathogen chip for simultaneous molecular detection of transfusion–transmitted infectious agents. Journal of Translational Medicine [Internet]. 2019 May 14 [cited 2025 Aug];17(1).

Available from: https://doi.org/10.1186/s12967-019-1905-4
20. Hussain MS, Qahtani SH, Alsubhi AAM, Alanazi AMH, Abdelbagi DE, Hattab KHA, et al. Overview on Blood Transfusion-Transmitted Diseases. Journal Of Advanced Zoology [Internet]. 2023 Nov 4 [cited 2026 Feb];44:1875. Available from: http://dx.doi.org/10.17762/jaz.v44is-5.1520
21. Mremi A, Yahaya JJ, Nyindo M, Mollel E. Transfusion-Transmitted Infections and associated risk factors at the Northern Zone Blood Transfusion Center in Tanzania: A study of blood donors between 2017 and 2019. PLoS ONE [Internet]. 2021 Mar 24 [cited 2025 Oct];16(3). Available from: https://doi.org/10.1371/journal.pone.0249061
22. Bloch EM, Vermeulen M, Murphy EL. Blood Transfusion Safety in Africa: A Literature Review of Infectious Disease and Organizational Challenges. Transfusion Medicine Reviews [Internet]. Elsevier BV; 2011 Aug 29 [cited 2025 Oct];26(2):164. Available from: https://doi.org/10.1016/j.tmrv.2011.07.006
23. Salah A, Abdulkader A, Gabr HY, Elhefnawy EM, Mohamed S, Abdulhady MY, et al. The transfusion-transmitted infections overview, Unveiling the novelist screening approaches. Microbes and Infectious Diseases /Microbes and Infectious Diseases [Internet]. 2024 Nov 9 [cited 2026 Jan];0. Available from: http://dx.doi.org/10.21608/mid.2024.331428.2317
24. Attaullah S, Khan S, Khan J. Trend of transfusion transmitted infections frequency in blood donors: provide a road map for its prevention and control. Journal of Translational Medicine [Internet]. 2012 Jan 31 [cited 2025 Sep];10(1). Available from: https://doi.org/10.1186/1479-5876-10-20
25. Niederhauser C, Tinguely C, Stolz M, Vock M, Dusouqui SAE, Gowland P. Evolution of Blood Safety in Switzerland over the Last 25 Years for HIV, HCV, HBV and Treponema pallidum. Viruses [Internet]. 2022 Nov 23 [cited 2025 Aug];14(12):2611. Available from: https://doi.org/10.3390/v14122611
26. Shulman IA, Appleman MD. Transmission of Parasitic and Bacterial Infections Through Blood Transfusion within the US. Critical Reviews in Clinical Laboratory Sciences [Internet]. 1991 Jan 1 [cited 2026 Jan];28:447. Available from: https://doi.org/10.3109/10408369109106873
27. Blajchman M. Incidence and significance of the bacterial contamination of blood components. PubMed [Internet]. 2002 Jan 1 [cited 2025 Nov];108:59. Available from: https://pubmed.ncbi.nlm.nih.gov/12220143
28. Bueno J. Skin disinfection and bacterial contamination of blood components: be simple [Internet]. Vol. 50, Transfusion. Wiley; 2009 [cited 2025 Nov]. p. 5. Available from: https://doi.org/10.1111/j.1537-2995.2009.02513.x
29. Arghittu A, Dettori M, Deriu GM, Soddu S, Manca PC, Carboni AA, et al. Controlling Infectious Risk in Transfusion: Assessing the Effectiveness of Skin Disinfection in Blood Donors. Healthcare [Internet]. 2022 May 5 [cited 2025 Nov];10(5):845. Available from: https://doi.org/10.3390/healthcare10050845
30. Udvardy M, Illés Á, Gergely L, Pinczés LI, Magyari F, Simon Z. Transfusion-Transmitted Disorders 2023 with Special Attention to Bone Marrow Transplant Patients. Pathogens [Internet]. 2023 Jul 1 [cited 2025 Dec];12(7):901. Available from: https://doi.org/10.3390/pathogens12070901
31. Brecher ME, Hay SN. Bacterial Contamination of Blood Components. Carolina Digital Repository (University of North Carolina at Chapel Hill) [Internet]. 2005 Jan 1 [cited 2025 Feb]; Available from: https://doi.org/10.17615/r4pg-na18
32. Frati P, Busardò FP, Stefano MD, Neri M, Sessa F, Fineschi V. A fatal case of post-transfusion sepsis caused by Yersinia enterocolitica after delivery. PubMed [Internet]. 2015 Jul 1 [cited 2025 Nov];13(3):528. Available from: https://pubmed.ncbi.nlm.nih.gov/25761326
33. Germain M, Goldman M. Blood Donor Selection and Screening: Strategies to Reduce Recipient Risk. American Journal of Therapeutics [Internet]. 2002 Sep 1 [cited 2026 Jan];9(5):406. Available from: https://doi.org/10.1097/00045391-200209000-00007
34. Lindholm PF, Annen K, Ramsey G. Approaches to Minimize Infection Risk in

Blood Banking and Transfusion Practice. Infectious Disorders - Drug Targets [Internet]. 2011 Feb 1 [cited 2026 Jan];11(1):45. Available from: https://doi.org/10.2174/187152611794407746

35. Katz LM, Dodd RY, Saá P, Gorlin JB, Palmer KR, Hollinger FB, et al. Infectious disease agents and their potential threat to transfusion safety (an update to the 2009 Transfusion supplement). Transfusion [Internet]. 2024 Feb 1 [cited 2025 Dec];64. Available from: https://doi.org/10.1111/trf.17626
36. Dodd RY, Leiby DA. Emerging Infectious Threats to the Blood Supply. Annual Review of Medicine [Internet]. 2004 Jan 27 [cited 2025 Nov];55(1):191. Available from: https://doi.org/10.1146/annurev.med.55.091902.103831
37. Candotti D, Allain J. Molecular virology in transfusion medicine laboratory. PubMed [Internet]. 2013 Apr 1 [cited 2025 Nov];11(2):203. Available from: https://pubmed.ncbi.nlm.nih.gov/23356973
38. Gareayaghi N, Akkuş S, HAMZELİ N, Kocazeybek B. Six-year seroprevalence results for blood center mandatory donor screenings: single center experience. Journal of Health Sciences and Medicine [Internet]. 2022 Sep 25 [cited 2025 Aug];5(5):1246. Available from: https://doi.org/10.32322/jhsm.1136116
39. Busch MP, Bloch EM, Kleinman S. Prevention of transfusion-transmitted infections. Blood [Internet]. 2019 Feb 27 [cited 2026 Mar];133(17):1854. Available from: https://doi.org/10.1182/blood-2018-11-833996
40. Seltsam A. Pathogen Inactivation of Cellular Blood Products—An Additional Safety Layer in Transfusion Medicine. Frontiers in Medicine [Internet]. Frontiers Media; 2017 Dec 4 [cited 2025 Sep];4. Available from: https://doi.org/10.3389/fmed.2017.00219
41. Roback JD, Josephson CD. New insights for preventing transfusion-transmitted cytomegalovirus and other white blood cell–associated viral infections. Transfusion [Internet]. 2013 Oct 1 [cited 2025 Nov];53(10):2112. Available from: https://doi.org/10.1111/trf.12366
42. Leiby DA. Threats to blood safety posed by emerging protozoan pathogens. Vox Sanguinis [Internet]. 2004 Jun 22 [cited 2026 Jan];87:120. Available from: https://doi.org/10.1111/j.1741-6892.2004.00467.x
43. Smith L, Wright-Kanuth MS. Transfusion-transmitted parasites. PubMed [Internet]. 2003 Jan 1 [cited 2025 Nov];16(4):239. Available from: https://pubmed.ncbi.nlm.nih.gov/14626442
44. Karimi G, Mardani A, Zadsar M. Prevalence of Toxoplasma gondii among Iranian Blood Donors: A Narrative Review Article. PubMed [Internet]. 2016 Apr 20 [cited 2025 Nov];11(1):10. Available from: https://pubmed.ncbi.nlm.nih.gov/27095963
45. Pereira B, Nazareth C, Malcata L, Alves H, Fernández JR, Sargento C, et al. [Transfusion-transmitted protozoal infections: what is the risk in non-endemic countries?]. PubMed [Internet]. 2011 Dec 1 [cited 2025 Nov];897. Available from: https://pubmed.ncbi.nlm.nih.gov/22863498
46. Eglin R, Murphy WG. Beyond leukodepletion: removing infectious prions by filtration [Internet]. Vol. 45, Transfusion. Wiley; 2005 [cited 2025 Nov]. p. 1836. Available from: https://doi.org/10.1111/j.1537-2995.2005.00684.x
47. Dodd RY. Bovine spongiform encephalopathy, variant CJD, and blood transfusion: beefer madness? [Internet]. Vol. 44, Transfusion. Wiley; 2004 [cited 2025 Nov]. p. 628. Available from: https://doi.org/10.1111/j.0041-1132.2004.44501.x
48. Williamson LM. Leucocyte Depletion Of The Blood Supply – How Will Patients Benefit? British Journal of Haematology [Internet]. 2000 Aug 1 [cited 2026 Jan];110(2):256. Available from: https://doi.org/10.1046/j.1365-2141.2000.02062.x
49. Neslo R, Oei W, Janssen MP. Insight into “Calculated Risk”: An Application to the Prioritization of Emerging Infectious Diseases for Blood Transfusion Safety. Risk Analysis [Internet]. 2017 Feb 23 [cited 2025 Nov];37(9):1783. Available from: https://doi.org/10.1111/risa.12752

50. Potasman I. Asymptomatic Infections: The Hidden Epidemic. International Journal of Clinical Research & Trials [Internet]. 2017 Nov 22 [cited 2025 Sep];2(2). Available from: https://doi.org/10.15344/2456-8007/2017/118
51. Galatas B, Bassat Q, Mayor A. Malaria Parasites in the Asymptomatic: Looking for the Hay in the Haystack. Trends in Parasitology [Internet]. Elsevier BV; 2015 Dec 19 [cited 2025 Sep];32(4):296. Available from: https://doi.org/10.1016/j.pt.2015.11.015
52. Chen GY, Thorup NR, Miller AJ, Li Y, Ayres JS. Cooperation between physiological defenses and immune resistance produces asymptomatic carriage of a lethal bacterial pathogen. Science Advances [Internet]. 2023 Jun 23 [cited 2025 Nov];9(25). Available from: https://doi.org/10.1126/sciadv.adg8719
53. Kamaliddin C, Sutherland CJ, Houzé S, Cottrell G, Briand V, Castañeda-Mogollón D, et al. The Role of Ultrasensitive Molecular Methods for Detecting Malaria—The Broader Perspective. Clinical Infectious Diseases [Internet]. Oxford University Press; 2021 Mar 8 [cited 2025 Oct];73(6). Available from: https://doi.org/10.1093/cid/ciab221
54. Farshadpour F, Taherkhani R, Tajbakhsh S, Tangestani MG, Hajiani G, Sharifi N, et al. Prevalence and Trends of Transfusion-Transmissible Viral Infections among Blood Donors in South of Iran: An Eleven-Year Retrospective Study. PLoS ONE [Internet]. 2016 Jun 16 [cited 2025 Oct];11(6). Available from: https://doi.org/10.1371/journal.pone.0157615
55. Barbara JAJ. Transfusion Transmitted Infections. Tumori Journal [Internet]. 2001 Mar 1 [cited 2025 Nov];87(2):8. Available from: https://doi.org/10.1177/030089160108700218
56. Teo D, Ng LC, Lam S. Is dengue a threat to the blood supply? Transfusion Medicine [Internet]. Wiley; 2009 Apr 1 [cited 2025 Oct];19(2):66. Available from: https://doi.org/10.1111/j.1365-3148.2009.00916.x
57. Kolk DP, Dockter J, Linnen J, Ho-Sing-Loy M, Gillotte-Taylor K, McDonough SH, et al. Significant Closure of the Human Immunodeficiency Virus Type 1 and Hepatitis C Virus Preseroconversion Detection Windows with a Transcription-Mediated-Amplification-Driven Assay. Journal of Clinical Microbiology [Internet]. 2002 May 1 [cited 2025 Nov];40(5):1761. Available from: https://doi.org/10.1128/jcm.40.5.1761-1766.2002
58. Widell A, Busch MP. Exposed or not exposed—that is the question: evidence for resolving and abortive hepatitis C virus infections in blood donors [Internet]. Vol. 49, Transfusion. Wiley; 2009 [cited 2025 Nov]. p. 1277. Available from: https://doi.org/10.1111/j.1537-2995.2009.02266.x
59. Blejer JL, Vescio LAC, Salamone HJ. [Risk of transfusional-transmitted infections]. PubMed [Internet]. 2002 Jan 1 [cited 2025 Nov];62(3):259. Available from: https://pubmed.ncbi.nlm.nih.gov/12150011
60. Erhabor O, Akpotuzor JO, Afriyie EY, Okara GC, Erhabor T, Ofili DI, et al. Optimizing Blood Transfusion Service Delivery across the West African Sub-Region. In: IntechOpen eBooks [Internet]. IntechOpen; 2023 [cited 2025 Oct]. Available from: https://doi.org/10.5772/intechopen.108628
61. Pham TD, Galel SA. Testing for pathogens in donors [Internet]. 2016 [cited 2025 Nov]. p. 626. Available from: https://doi.org/10.1002/9781119013020.ch55
62. Dwyre DM, Fernando LP, Holland PV. Hepatitis B, hepatitis C and HIV transfusion-transmitted infections in the 21st century. Vox Sanguinis [Internet]. 2010 Dec 22 [cited 2026 Jan];100(1):92. Available from: https://doi.org/10.1111/j.1423-0410.2010.01426.x
63. Dellinger EP, Anaya DA. Infectious and immunologic consequences of blood transfusion. Critical Care [Internet]. BioMed Central; 2004 Jan 1 [cited 2025 Oct];8. Available from: https://doi.org/10.1186/cc2847
64. Stramer SL. Current Risks of Transfusion-Transmitted Agents: A Review. Archives of

Pathology & Laboratory Medicine [Internet]. 2007 May 1 [cited 2026 Feb];131(5):702. Available from: https://doi.org/10.5858/2007-131-702-crotaa

65. Soldan K, Davison K, Dow BC. Estimates of the frequency of HBV, HCV, and HIV infectious donations entering the blood supply in the United Kingdom, 1996 to 2003. Eurosurveillance [Internet]. 2005 Feb 1 [cited 2025 Nov];10(2):9. Available from: https://doi.org/10.2807/esm.10.02.00520-en
66. Stramer SL. Pooled hepatitis B virus DNA testing by nucleic acid amplification: implementation or not. Transfusion [Internet]. 2005 Jul 28 [cited 2025 Nov];45(8):1242. Available from: https://doi.org/10.1111/j.1537-2995.2005.00571.x
67. Grabarczyk P. Bezpieczeństwo krwi w aspekcie badań wirusologicznych. Acta Haematologica Polonica [Internet]. 2013 Jul 1 [cited 2025 Nov];44(3):294. Available from: https://doi.org/10.1016/j.achaem.2013.07.010
68. Epstein JS, Holmberg JA. Progress in monitoring blood safety [Internet]. Vol. 50, Transfusion. Wiley; 2010 [cited 2025 Nov]. p. 1408. Available from: https://doi.org/10.1111/j.1537-2995.2010.02728.x
69. Tashkovska M, Bojadjieva TM, Velkova E, Ilijevska VD, Petkovic E, Ristovska EC, et al. COMPARATIVE ANALYSIS OF SEROLOGICAL AND MOLECULAR TRANSFUSION TRANSMISSIBLE INFECTIONS SCREENING. Journal of Morphological Sciences [Internet]. 2025 Nov 25 [cited 2026 Jan];8(2):112. Available from: https://doi.org/10.55302/jms2582112t
70. Manzini P, Girotto M, Borsotti R, Giachino O, Guaschino R, Lanteri MC, et al. Italian blood donors with anti-HBc and occult hepatitis B virus infection. Haematologica [Internet]. 2007 Nov 30 [cited 2025 Oct];92(12):1664. Available from: https://doi.org/10.3324/haematol.11224
71. Setyarini W, Wiqoyah N, Ansori M. Molecular Diagnostic Tools for Treponema pallidum. Indonesian Journal of Tropical and Infectious Disease [Internet]. 2023 Dec 7 [cited 2025 Aug];11(3). Available from: https://doi.org/10.20473/ijtid.v11i3.44506
72. Shukalek C, Lee BE, Fathima S, Chú Á, Fonseca K, Somayaji R. Comparative Analysis of Molecular and Serologic Testing for Primary Syphilis: A Population-Based Cohort Study. Frontiers in Cellular and Infection Microbiology [Internet]. 2021 Apr 23 [cited 2025 Oct];11. Available from: https://doi.org/10.3389/fcimb.2021.579660
73. Liu H, Wang X. Pathogen reduction technology for blood component: A promising solution for prevention of emerging infectious disease and bacterial contamination in blood transfusion services. Journal of Photochemistry and Photobiology [Internet]. 2021 Oct 25 [cited 2026 Feb];8:100079. Available from: https://doi.org/10.1016/j.jpap.2021.100079
74. Niederhauser C, Galel SA. Transfusion-Transmitted Malaria and Mitigation Strategies in Nonendemic Regions. Transfusion Medicine and Hemotherapy [Internet]. Karger Publishers; 2022 Jan 1 [cited 2025 Sep];49(4):205. Available from: https://doi.org/10.1159/000525414
75. Louhenapessy N, Gantini RSE, Rahayu S, Lilipory E, Wibowo H, Soedarmono Y, et al. Evaluating laboratory screening tests for malaria on blood donors candidates to reduce the risk of transfusion-transmitted malaria in an endemic area of Indonesia. Medical Journal of Indonesia [Internet]. 2021 Oct 10 [cited 2025 Sep];30(3):191. Available from: https://doi.org/10.13181/mji.oa.215491
76. Mangano V, Perandin F, Tiberti N, Guerriero M, Migliaccio F, Prato M, et al. Risk of transfusion-transmitted malaria: evaluation of commercial ELISA kits for the detection of anti-Plasmodium antibodies in candidate blood donors. Malaria Journal [Internet]. 2019 Jan 22 [cited 2025 Oct];18(1). Available from: https://doi.org/10.1186/s12936-019-2650-0
77. Rodríguez-Morales AJ. Current Topics and Emerging Issues in Malaria Elimination [Internet]. Infectious diseases. IntechOpen; 2021 [cited 2025 Sep]. Available from: https://doi.org/10.5772/intechopen.87323
78. Martín-Díaz A, Rubio JM, Herrero-Martínez JM, Lizasoain M, Ruiz-Giardín JM, Aroca JJ, et al. Study of the diagnostic accuracy of

microbiological techniques in the diagnosis of malaria in the immigrant population in Madrid. Malaria Journal [Internet]. 2018 Aug 29 [cited 2025 Aug];17(1). Available from: https://doi.org/10.1186/s12936-018-2459-2

79. Dean CL, Wade J, Roback JD. Transfusion-Transmitted Infections: an Update on Product Screening, Diagnostic Techniques, and the Path Ahead. Journal of Clinical Microbiology [Internet]. 2018 Apr 19 [cited 2025 Nov];56(7). Available from: https://doi.org/10.1128/jcm.00352-18
80. Igbe MI, Adepoju EF, Amarachi BJ, Elujoba S, Adamu I, Musa MA. Implications of screening blood donors for selected transfusion-transmissible infections (TTIs): Compromise in blood safety? Sokoto Journal of Medical Laboratory Science [Internet]. 2024 Dec 6 [cited 2025 Dec];9(2):45. Available from: https://doi.org/10.4314/sokjmls.v9i2.6
81. McCullough J. Pathogen inactivation: a new paradigm for blood safety [Internet]. Vol. 47, Transfusion. Wiley; 2007 [cited 2025 Nov]. p. 2180. Available from: https://doi.org/10.1111/j.1537-2995.2007.01539.x
82. Jacquot C, Delaney M. Efforts Toward Elimination of Infectious Agents in Blood Products. Journal of Intensive Care Medicine [Internet]. 2018 Mar 21 [cited 2025 Nov];33(10):543. Available from: https://doi.org/10.1177/0885066618756589
83. Corash L. Inactivation of Viruses, Bacteria, Protozoa and Leukocytes in Platelet and Red Cell Concentrates. Vox Sanguinis [Internet]. 2000 Jul 1 [cited 2025 Dec];78:205. Available from: https://doi.org/10.1111/j.1423-0410.2000.tb00064.x
84. Lanteri MC, Busch MP. Dengue in the context of “safe blood” and global epidemiology: to screen or not to screen? Transfusion [Internet]. 2012 Aug 1 [cited 2025 Nov];52(8):1634. Available from: https://doi.org/10.1111/j.1537-2995.2012.03747.x
85. Arishi WA, Yaqinuddin A, Sajid MR. Molecular advances in transfusion medicine: a narrative review. Frontiers in Medicine [Internet]. Frontiers Media; 2025 Sep 29 [cited 2025 Sep];12. Available from: https://doi.org/10.3389/fmed.2025.1607340
86. Marks P, Petersen LR. Decision making in the face of uncertainty: the challenge of emerging infectious diseases. Transfusion [Internet]. 2017 Mar 1 [cited 2025 Nov];57:723. Available from: https://doi.org/10.1111/trf.14037
87. Kuehnert MJ, Epstein JS. Assuring blood safety and availability: Zika virus, the latest emerging infectious disease battlefront [Internet]. Vol. 56, Transfusion. Wiley; 2016 [cited 2025 Nov]. p. 1669. Available from: https://doi.org/10.1111/trf.13673
88. Bianco C. Dengue and Chikungunya viruses in blood donations: risks to the blood supply? [Internet]. Vol. 48, Transfusion. Wiley; 2008 [cited 2025 Nov]. p. 1279. Available from: https://doi.org/10.1111/j.1537-2995.2008.01806.x
89. Marks P, Epstein JS, Borio L. Maintaining a Safe Blood Supply in an Era of Emerging Pathogens. The Journal of Infectious Diseases [Internet]. 2016 Mar 8 [cited 2026 Jan];213(11):1676. Available from: https://doi.org/10.1093/infdis/jiw089
90. Mendoza C de, Altisent C, Aznar JA, Batlle J, Soriano V. Emerging viral infections--a potential threat for blood supply in the 21st century. PubMed [Internet]. 2013 Jun 25 [cited 2025 Nov];14(4):279. Available from: https://pubmed.ncbi.nlm.nih.gov/23258302
91. Petersen LR, Busch MP. Transfusion-transmitted arboviruses. Vox Sanguinis [Internet]. 2009 Nov 26 [cited 2026 Jan];98(4):495. Available from: https://doi.org/10.1111/j.1423-0410.2009.01286.x
92. LEBLANC J, Germain M, Delage G, O’Brien SF, Drews SJ, Lewin A. Risk of transmission of severe acute respiratory syndrome coronavirus 2 by transfusion: A literature review. Transfusion [Internet]. 2020 Aug 15 [cited 2025 Nov];60(12):3046. Available from: https://doi.org/10.1111/trf.16056
93. Cheung CKM, Wong SH, Law AWH, Law MF. Transfusion-transmitted hepatitis E: What we know so far? World Journal of Gastroenterology [Internet]. 2021 Dec 31 [cited 2026 Jan];28(1):47. Available from: https://doi.org/10.3748/wjg.v28.i1.47

94. Youssouf A, Hnach N, Nabil M, Nada AA, Moumin Y, Khayar Y, et al. NEW EMERGING VIRUSES AND TRANSFUSION SAFETY. International Journal of Advanced Research [Internet]. 2025 Jan 31 [cited 2026 Jan];13(1):1194. Available from: https://doi.org/10.21474/ijar01/20310
95. Bihl F, Castelli D, Marincola F, Dodd RY, Brander C. Transfusion-transmitted infections. Journal of Translational Medicine [Internet]. BioMed Central; 2007 Jun 6 [cited 2025 Oct];5(1). Available from: https://doi.org/10.1186/1479-5876-5-25
96. Greninger AL, Alcorn K, Pagano MB, Hermelin D, Katz LN. Monkeypox and the safety of the blood supply. Transfusion [Internet]. 2022 Sep 10 [cited 2026 Feb];62(10):1933. Available from: https://doi.org/10.1111/trf.17100
97. Focosi D, Franchini M. What a Transfusion Physician Should Know about Monkeypox Virus: Barriers to and Risks for Transmission, and Possible Mitigation Strategies. Diagnostics [Internet]. 2022 Sep 11 [cited 2025 Nov];12(9):2200. Available from: https://doi.org/10.3390/diagnostics12092200
98. Meschi S, Colavita F, Carletti F, Mazzotta V, Matusali G, Specchiarello E, et al. MPXV DNA kinetics in bloodstream and other body fluids samples. Scientific Reports [Internet]. 2024 Jun 12 [cited 2025 Jul];14(1). Available from: https://doi.org/10.1038/s41598-024-63044-5
99. Eren C. An analysis on HBsAg, Anti-HCV, Anti-HIV½ and VDRL test results in blood donors according to gender, age range and years. PLoS ONE [Internet]. 2019 Sep 19 [cited 2025 Sep];14(9). Available from: https://doi.org/10.1371/journal.pone.0219709
100. Roth WK. History and Future of Nucleic Acid Amplification Technology Blood Donor Testing. Transfusion Medicine and Hemotherapy [Internet]. 2019 Jan 1 [cited 2026 Jan];46(2):67. Available from: https://doi.org/10.1159/000496749
101. Levi JE. Current concepts in molecular testing. ISBT Science Series [Internet]. 2011 May 13 [cited 2025 Nov];6(1):67. Available from: https://doi.org/10.1111/j.1751-2824.2011.01438.x
102. Vermeulen M, Lelie N, Reddy RS. Recent insights in testing for transfusion transmissible viral infections. ISBT Science Series [Internet]. 2011 May 13 [cited 2025 Nov];6(1):229. Available from: https://doi.org/10.1111/j.1751-2824.2011.01492.x
103. Cadena-Ullauri S, Gaviria A, Guevara-Ramírez P, Ruiz-Pozo VA, Tamayo-Trujillo R, Paz-Cruz E, et al. Nucleic acid amplification testing (NAT) impact on blood safety compared to Immunoassays in blood banks: A Review. Bionatura [Internet]. 2023 Dec 15 [cited 2025 Dec];8(4):1. Available from: https://doi.org/10.21931/rb/2023.08.04.33
104. Glynn SA. Blood supply safety: an NHLBI perspective [Internet]. Vol. 48, Transfusion. Wiley; 2008 [cited 2025 Nov]. p. 1541. Available from: https://doi.org/10.1111/j.1537-2995.2007.01754.x
105. Farrugia A. The mantra of blood safety: time for a new tune? Vox Sanguinis [Internet]. 2004 Jan 1 [cited 2026 Jan];86(1):1. Available from: https://doi.org/10.1111/j.0042-9007.2004.00386.x
106. Peliganga LB, Mello VM, Sousa PSF de, Horta MAP, Soares ÁD, Nunes JP, et al. Transfusion Transmissible Infections in Blood Donors in the Province of Bié, Angola, during a 15-Year Follow-Up, Imply the Need for Pathogen Reduction Technologies. Pathogens [Internet]. 2021 Dec 17 [cited 2025 Aug];10(12):1633. Available from: https://doi.org/10.3390/pathogens10121633
107. Chakrabarty P, Rudra S, Hoque MM. Update of pathogen reduction technology for therapeutic plasma. PubMed [Internet]. 2010 Apr 1 [cited 2025 Nov];19(2):308. Available from: https://pubmed.ncbi.nlm.nih.gov/20395932
108. Zakaria M, Hassan T, Sherief LM, Erhabor O, Bilgin M, Opeyemi AA, et al. Thalassemia Syndromes - New Insights and Transfusion Modalities [Internet]. IntechOpen eBooks. IntechOpen; 2023 [cited 2025 Oct]. Available from: https://doi.org/10.5772/intechopen.104338
109. Seifried E, Roth WK. Optimal blood donation screening. British Journal of

Haematology [Internet]. 2000 Jun 1 [cited 2026 Jan];109(4):694. Available from: https://doi.org/10.1046/j.1365-2141.2000.02100.x

110. Kourout M, Espich S, Fisher C, Tiper IV, Purkayastha A, Smith S, et al. Multiplex detection and identification of viral, bacterial, and protozoan pathogens in human blood and plasma using an expanded high-density resequencing microarray platform. Frontiers in Molecular Biosciences [Internet]. 2024 Jun 20 [cited 2025 Jul];11. Available from: https://doi.org/10.3389/fmolb.2024.1419213
111. Thivalapill N, Geng Z, Kumar N, Roy N, Bidanda B, Raykar N. The risk of transfusion transmissible infection in a civilian walking blood bank using rapid diagnostic tests: A modeling study. bioRxiv (Cold Spring Harbor Laboratory) [Internet]. 2025 Oct 23 [cited 2025 Oct]; Available from: https://doi.org/10.1101/2025.10.21.2533634 3
112. Das S. Blood Safety: New challenges & Opportunities in Developing Nation. Journal of Bacteriology & Mycology Open Access [Internet]. 2017 May 2 [cited 2025 Jan];4(5). Available from: https://doi.org/10.15406/jbmoa.2017.04.001 05
113. Mudgal S, Goel S, Varshney K, Khan MN. SEROPREVALANCE OF TRANSFUSION TRANSMITTED INFECTIONS AMONGST BLOOD DONORS IN TERTIARY CARE HOSPITAL IN U.P. PARIPEX-INDIAN JOURNAL OF RESEARCH [Internet]. 2022 Nov 15 [cited 2025 Aug];17. Available from: https://doi.org/10.36106/paripex/4100680
114. Shrivastava M, Mishra S. Nucleic Acid Amplification Testing (NAT): An Innovative Diagnostic Approach for Enhancing Blood Safety. SHILAP Revista de lepidopterología [Internet]. 2017 Apr 1 [cited 2026 Feb]; Available from: https://doaj.org/article/4e5d57f27032467b9e d4215e55b40d22
115. Carpenter RE. Advancing Clinical Microbiology: Applications and Future of Next-Generation Sequencing. SAR Journal of Pathology and Microbiology [Internet]. 2024 Jun 20 [cited 2025 Sep];5(3):107. Available from: https://doi.org/10.36346/sarjpm.2024.v05i03 .010
116. Metzgar D, Sampath R, Rounds MA, Ecker DJ. The value and validation of broad spectrum biosensors for diagnosis and biodefense. Virulence [Internet]. 2013 Oct 9 [cited 2026 Jan];4(8):752. Available from: https://doi.org/10.4161/viru.26652
117. Varghese A, Thilak K, Thomas SM. Technological advancements, digital transformation, and future trends in blood transfusion services. International Journal of Advances in Medicine [Internet]. 2024 Feb 22 [cited 2025 Oct];11(2):147. Available from: https://doi.org/10.18203/2349-3933.ijam20240368
118. Bajaj G, Davu G, Arti. Predictive modeling of infectious disease outbreaks: harnessing artificial intelligence for early detection and response. International Journal of Clinical Trials [Internet]. 2025 Oct 23 [cited 2026 Feb];12(4):270. Available from: https://doi.org/10.18203/2349-3259.ijct20253331
119. Qureshi Z, Handoo S, Sultan B, Reshi R, Bashir M. Transfusion Transmitted Infections (TTIs) among blood donors in the blood bank of a tertiary care hospital in India: A record-based study. SANAMED [Internet]. 2020 Jan 1 [cited 2025 Oct];15(3):279. Available from: https://doi.org/10.24125/sanamed.v15i3.445
120. Sundaramoorthy R, Arunagiri R, Ganesan V, Perumal S, Tiruvanamalai R, Charles J. Seroprevalence of transfusion transmissible infections among blood donors by chemiluminescent assay in a tertiary care centre. The Journal of Infection in Developing Countries [Internet]. 2018 Jan 31 [cited 2025 Oct];12(1):31. Available from: https://doi.org/10.3855/jidc.9430