Review article

Impact of Cannabinoids on Blood Product Safety: Risks and Challenges in Transfusion Medicine

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As cannabis use continues to rise, particularly involving tetrahydrocannabinol (THC) and cannabidiol (CBD), new concerns are emerging in transfusion medicine. Legalization in many U.S. states has significantly increased both recreational and medical cannabinoid use. Research suggests that cannabinoids may alter blood function, posing potential risks for transfusion-dependent patients with sickle cell disease (SCD) and cancer. These patients are frequently prescribed cannabinoids for pain and often receive blood transfusions, raising concerns about additional risk from exposure to cannabinoids present in transfused products. Despite improvements in donor screening for infectious diseases, no protocols exist to detect cannabinoid use in blood donors. This represents a critical gap in transfusion safety.

THC may contribute to red cell hemolysis, enhance platelet aggregation, and increase thrombotic risk, while CBD may inhibit platelet function and disrupt coagulation. These pharmacologic effects may compromise transfusion safety in high-risk groups. Although the long-term impact of cannabinoid exposure in transfusion medicine remains unknown, evidence supports the need for immediate investigation. With no existing guidance from the Food and Drug Administration (FDA), interdisciplinary collaboration is essential to assess risks and develop appropriate screening measures to ensure blood product safety.

Keywords: Cannabinoid exposure; Transfusion Medicine; Hematologic Complications

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Introduction

Blood transfusion is fundamental to modern healthcare, supporting the treatment of anemia, hematologic disorders, trauma, and malignancies. The effectiveness of transfusion medicine relies on rigorous donor screening, comprehensive infectious disease testing, and meticulous blood product handling.[1] These measures have significantly enhanced patient outcomes; however, emerging challenges, particularly the increasing prevalence of cannabinoid use, are raising concerns about blood product safety at both national and state levels.[2,3,4] Historically, cannabis was restricted due to its classification as a Schedule I substance;[5] however, legislative shifts have led to increasing medical prescriptions and recreational legalization in multiple states, necessitating an evaluation of its implications for transfusion medicine.[6,7,8]

For transfusion-dependent patients, including those with sickle cell disease (SCD) and cancer, minor coagulation imbalances can have serious clinical consequences.[7,9] In patients with SCD, tetrahydrocannabinol (THC)-induced red blood cell (RBC) membrane instability may impair oxygen transport, potentially worsening vaso-occlusive crises (VOCs), a painful complication common in SCD.[7,10,11] Similarly, in cancer patients receiving anticoagulant therapy, cannabinoid-induced changes in platelet function and clotting factor activity may elevate thrombotic or hemorrhagic risks.[9,12] Recent clinical findings associate cannabis use in SCD patients with increased VOC-related hospitalizations, suggesting worsening disease severity rather than symptom relief.[11,13] Furthermore, cannabis users in transfusion-dependent populations exhibit higher polypharmacy rates compounding transfusion safety concerns due to drug interactions affecting platelet function and coagulation.[9,12]

The legalization of cannabis in multiple states has led to a rise in both medical prescriptions and recreational use, influencing various sectors of healthcare, including transfusion medicine.[14,15] Given the increasing medical and recreational use of cannabis, its presence in the blood donor pool raises critical concerns regarding transfusion safety.[15] Cannabinoids such as THC and cannabidiol (CBD) have gained prominence due to evolving legal frameworks and shifting public perceptions.[4] As more individuals use cannabis-based therapies or recreational products, an increasing number of blood donors present with detectable levels of these compounds. Recent data suggest that up to 13.8% of blood donors may have used cannabis within 72 hours before donation, revealing a critical gap in screening protocols that primarily focus on infectious agents and immunologic compatibility rather than drug-induced hematologic alterations.[3,4]

Unlike rapidly metabolized compounds, cannabinoids accumulate in adipose tissue, allowing THC and CBD to persist in circulation for days or even weeks after use.[16] This prolonged release into the bloodstream raises concerns that transfused blood products may contain residual cannabinoid metabolites, which could contribute to hematologic instability in recipients, particularly those with preexisting coagulation disorders.[16] This prolonged exposure raises concerns that residual cannabinoid metabolites could persist in stored blood products and, upon transfusion, interact with recipient physiology, particularly in individuals with preexisting hematologic disorders.[16,17]

Recent research highlights growing evidence that cannabinoids influence blood components.[3,7,13] THC disrupts RBC membrane integrity, making cells more fragile and prone to hemolysis.[3,13] Additionally, THC induces platelet hyperreactivity, increasing the risk of thrombosis.[3,17] In contrast, CBD inhibits platelet aggregation, which may elevate bleeding risks.[18,19]

Beyond cellular effects, cannabinoids influence coagulation pathways.[17,18] THC exposure has been associated with increased thrombin generation, whereas CBD inhibits fibrin clot formation by altering clotting factor synthesis and activity.[18,19] These disruptions to

coagulation homeostasis raise concerns about transfusion recipients, particularly those using cannabinoids for symptom management, facing increased clotting or bleeding risks.[18,19]

Despite growing evidence of these risks, transfusion protocols lack standardized screening measures for cannabinoid exposure.[15] Additionally, limited longitudinal data on cannabinoid persistence in stored blood products create gaps in understanding post-transfusion effects.[20] Mechanistic studies indicate that cannabinoids induce oxidative stress, alter membrane integrity, and impact coagulation, yet few clinical trials have systematically assessed these findings in transfusion-dependent populations.[21] Implementing mass spectrometry-based detection methods could enhance screening precision by quantifying THC and CBD metabolites in donor blood, ensuring transfusion safety.[20,21,22]

The implications of cannabinoid exposure extend beyond donor eligibility, affecting blood product integrity and recipient safety.[2,13] As medically prescribed THC and CBD use continues to rise, transfusion-dependent patients—particularly those relying on cannabinoids for symptom management —may face increased transfusion-related risks.[2,11,17] The persistence of cannabinoid metabolites in donor blood introduces potential hematologic alterations, which could compromise transfusion efficacy, particularly in vulnerable populations with coagulation imbalances and oxygen transport deficiencies.[10,11,13]

Addressing the risks of cannabinoid exposure in transfusion medicine requires immediate updates to donor screening protocols and transfusion safety policies.[15,23] As the use of cannabinoids increases due to shifting legal and medical landscapes, the potential impact on blood products must be critically evaluated. Future research must prioritize the development of standardized cannabinoid screening measures and risk mitigation strategies to prevent transfusion-related complications and ensure the safety of blood products for all recipients. Cannabinoids alter hematological parameters, necessitating transfusion protocol updates to ensure blood product safety.[3,13,15,23]

Background

The medical practice of blood transfusion provides essential support for treating patients who face blood loss conditions alongside anemia and malignancies and other forms of hematological disorders.[24,25,26] Transfusion therapy has three main purposes: it advances oxygen delivery while providing immune system support along with maintaining blood clotting function primarily for surgeries, traumatic injuries and people who live with SCD or have cancer that requires long-term transfusions.[26] The safety of transfusions remains constant through extensive donor screening combined with blood collection practices alongside laboratory work and donor-receiver compatibility testing under regulatory institutions which minimize both infection transmission during transfusion and adverse reactions.[27]

The advancement of transfusion medicine occurred through both the discovery of scientific knowledge and solutions to newly emerging public health threats. Research into ABO/RH blood group identification methods eliminate life-threatening immune reactions against transfused blood.[1,24] The combination of plastic blood storage bags with anticoagulants and refrigeration technology permits prolonged blood product storage time.[24,28] Pathogen reduction technologies and nucleic acid testing became necessary after human immunodeficiency virus and acquired immunedeficiency syndrome (HIV/AIDS) appeared in the 1980s and the hepatitis C epidemic appeared in the 1990s.[29] Safety failures from the past demonstrates the requirement for strong safety measures and constant oversight of blood collection techniques as well as transfusion administration procedures.[28,30]

Donor screening operates as the core element in transfusion safety because it ensures that only individuals who meet eligibility criteria are permitted to donate blood.[23] The eligibility assessment for becoming a donor

includes standards for age within 18–65 years and body weight greater than 50 kg (110 lb.) and either female or male donor requirements for hemoglobin amounts set at 12.5 g/dL for females and 13.0 g/dL for males.[23] Physical assessments together with health questionnaires evaluate individual medical conditions that would be detrimental to the donor and prevent disease transmission to a recipient during transfusion processes. A review of patients' travel activities helps detect relevant infections like malaria or Zika virus postponing the donation process temporarily.[28,31] Modern nucleic acid testing (NAT) has become the standard procedure for discovering infectious agents including HIV, hepatitis B and C, syphilis, Zika virus, and West Nile virus.[36] Testing and handling protocols have evolved to such an extent that developed countries estimate HIV and hepatitis transmission occurs in only one case out of multiple million transfused products.[24,28] Donating blood is not possible for pregnant individuals and the exclusion extends to six weeks after childbirth.[28]

Blood donation policies receive regular updates through new scientific findings and epidemiological pattern changes.[32] The blood donation policies include permanent exclusion criteria for those with chronic health issues and transfusion-transmissible infections including HIV along with hepatitis B and C, syphilis, and human T-cell lymphotropic virus (HTLV).[33] More recently, the focus has expanded to include pharmacological contaminants, particularly cannabinoids, due to concerns about the potential impact on transfusion safety.[3,13] Unlike alcohol and opioids, which are routinely screened for because of the known effects on coagulation and RBC viability, cannabinoids are not yet addressed through standardized detection protocols in donated blood, despite similar concerns about the physiological effects.[3,13,34]

Blood donation happens through whole blood collection processes or the separation methods of apheresis for different blood supply requirements.[24,28] Whole blood donations are fractionated into red blood cells, platelets, and plasma through separation processes, whereas apheresis selectively collects a specific component such as platelets or plasma while returning the remaining elements to the donor.[24,28] An established set of sterility and safety guidelines for blood donation operates under the oversight of the World Health Organization (WHO) and U.S. Food and Drug Administration (FDA) policies and American Association of Blood Banks (AABB) protocols which comply with national and international standards.[1,24,28,35]

Transfusion-related adverse reactions happen occasionally even after applying strict screening methods alongside safety standards.[24] Three major adverse effects of transfusion are febrile non-hemolytic reactions along with allergic responses and immune-mediated hemolysis that destroys donor red cells. Serious transfusion complications such as transfusion-related acute lung injury (TRALI) and transfusion-associated circulatory overload (TACO) can be fatal to patients.[1,24,28] To control these, standard transfusion practice includes pre-transfusion compatibility testing and the use of irradiated leukoreduction blood products for immunocompromised and close post-transfusion monitoring.[1,24,28]

The integrity of blood transfusion is maintained and must continue to be evaluated in donor screening protocols, laboratory test methods, and storage technologies. While widespread use of screening has greatly decreased the risk of transfusion transmitted infection, usage of cannabinoids poses a new potential safety concern.[21] THC and CBD are both lipophilic compounds that remain in circulation in the blood and may be retained in blood components.[7,9,10,37] For that matter, their presence in donor blood remains uncertain in terms of their potential impact on coagulation and oxygen transport, especially in patients with preexisting hematologic disease.[7,10] The prevalence of individuals using cannabinoids for medical and recreational purposes has increased significantly, which

demands transfusion medicine to develop procedures and policies to implement new cannabinoid-specific screening protocols and mitigation strategies to safeguard the blood products.[4,14,15]

Cannabinoid metabolism

The metabolism of both THC and CBD starts in the liver where it is handled by complex enzymatic processes that determine absorption and systemic circulation.[38] In oxidative metabolism, the cytochrome P450 (CYP450) enzyme system is particularly important with isoforms CYP2C9 and CYP3A4 being of prime significance in the conversion of THC to active metabolites 11-hydroxy-THC (11-OH-THC) and THC-COOH.[16,38] These are lipophilic (fat soluble) metabolites that remain in the circulation because they bind to adipose tissue where they accumulate and slowly are released over time.[38]

CBD metabolizes more slowly than alcohol and opioids and therefore has a longer half-life in the human body.[20,38,39] This persistence is because of the interaction with the cytochrome P450 enzymes.[38] Cannabinoids are present longer in circulation and this raises concern for the accumulation in stored blood products.[20,38] Because cannabinoids are lipid soluble, there may be potential for binding to cellular components in blood and possibly alter structural or functional properties in transfused products.[3,13,20] In addition, temperature fluctuations during storage can affect cannabinoid stability and lead to quality issues in blood product transfusion medicine.[20]

Cannabinoids have pleiotropic effects on blood cell components and coagulation factors beyond pharmacokinetics.[3,12,13,16] The functional integrity of blood elements is essential for achieving favorable transfusion results. The flexible membranes along with the stable structure of red blood cells (RBCs) enable the cells to move throughout microvascular systems for the purpose of oxygen delivery and tissue perfusion.[40] Disruption of RBC membrane lipids by THC reduces cellular deformability and promotes early disaggregateion.[3,10,13] The contribution of this membrane disruption to eryptosis, a form of early programed RBC death, may limit the post transfusion lifespan of donor RBCs. Oxidative stress induced by CBD may cause abnormal RBC morphologies, echinocytosis (spiked cells) and acanthocytosis (irregularly shaped cells), and may interfere with microcirculatory flow and decrease oxygen carrying capacity in transfusion dependent patients.[3,10,13,41]

Expanding the discussion from RBC integrity to platelet function, the hemostatic process begins with platelets that initiates a sequence of adhesion and activation followed by aggregation which results in clot stability.[17,18,19,42] When THC activates the cannabinoid receptor type 1 (CB1), it leads to increased production of thromboxane A_2 (TXA_2), which functions as an aggressive platelet aggregator while causing vasoconstriction.[18,19,42] The drug interaction results in incorrectly aggregated platelets that raise patients' susceptibility to blood clot formation.[9,18,43] The anticoagulant properties of CBD stem from its ability to block the triggering of glycoprotein IIb/IIIa receptors that keep platelets from binding to fibrinogen and forming stable clots.[9,18,19,43] The anticoagulant effects of THC enhance bleeding risks especially among thrombocytopenic patients receiving platelet transfusions.[9,12,17,43]

Blood coagulation proceeds from two pathways intrinsic and extrinsic through thrombin generation and fibrin clot formation until it achieves stable hemostasis.[17] The administration of THC causes elevated levels of clotting factors VII and X in transfusion recipients which leads to increased thrombotic activity.[17,35,38] CBD works to reduce fibrinogen synthesis levels thereby extending coagulation parameters including international normalized ratio (INR), prothrombin time (PT), and partial thromboplastin time (PTT).[12,17,35] Transfusion management becomes more complex for patients with cannabinoid-associated coagulopathies, as these alterations may affect the

efficacy and safety of transfused blood products.[17] This includes patients with thrombocytopenia due to cancer and those with inherited bleeding issues.[35,38]

As a result of these interactions, cannabinoids change blood elements while controlling immune responses resulting in potential negative effects on blood product safety and blood cross-matching. Alloimmunization formation of antibodies against non-self-antigens on transfused cells remains a crucial safety concern in transfusion medicine by activating T-cells while releasing pro-inflammatory cytokines.[44] CBD administration leads to decreased T-cell activation, which might make individuals more prone to graft-versus-host disease (GVHD), mainly affecting immune-compromised patients.[39,44,45] The pro-inflammatory cytokines interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), and interferon-gamma (IFN-γ) are affected by THC, which may impair the recipient's ability to respond appropriately to transfused blood products.[45,46] The immunomodulatory characteristics of cannabinoids create issues that might compromise transfusion results in patients with weakened immune systems.[44,47]

The immunomodulatory capabilities of cannabinoids present distinct challenges for transfusion-dependent populations, particularly individuals with SCD and malignant disorders.[44] These patient populations, due to the chronic need for frequent blood product transfusion, will guarantee the development of alloantibodies that will further complicate the challenge of finding compatible blood products and heighten the likelihood of hemolytic transfusion reactions.[11,44,45] Transfusion-transmitted infections combined with reduced treatment efficacy become more likely for immunocompromised individuals who receive chemotherapy or organ transplantation.[39,47] Further research is necessary to analyze cannabinoid impacts on immune regulation, alloimmune reactions, and transfusion safety in high-risk populations, particularly as the use of prescribed and recreational cannabinoids continues to rise within these vulnerable groups.[35,39,44]

Emerging evidence also suggests that cannabinoids have the capacity to affect RBC integrity, platelet function, coagulation pathways, and immune responses, all of which can significantly affect transfusion outcomes.[3,13,44,48] These findings highlight the need to evaluate the risks associated with cannabinoid use in transfusion medicine with well-designed clinical research. To improve transfusion safety, it is essential to implement standardized donor screening protocols and conduct long-term studies that assess the effects of cannabinoids on blood components and recipient responses.[21,23] Supporting the development of safe, effective, and evidence-based transfusion strategies for high-risk patient populations requires a comprehensive understanding of cannabinoid metabolism, blood product hematological alterations, and recipient physiology.[3,13,23]

Clinical implications

Blood transfusions act as a crucial therapeutic approach to manage complications affecting patients who have SCD, cancer, or different chronic hematologic conditions.[28] Patient health stabilization depends on improved oxygen delivery through transfusion along with immune and hemostatic system support.[26] As the use of medical and recreational cannabis increases, clinicians are encouraged to assess the reduction of benefits from using blood products that are contaminated with cannabinoids. Blood product safety is compromised when collected from individuals who use cannabis. THC and CBD, the two primary cannabinoids in medical cannabis, have demonstrated effects on RBC morphology, platelet aggregation, and coagulation pathways.[3,9,13] The unknown health risks that blood transfusion-dependent patients, who are highly reliant on safe and functional blood components, are a concern that needs further investigation.

Regular blood transfusions form a critical therapeutic approach for SCD management for

the treatment of chronic anemia as well as lowering the risk of stroke while decreasing the frequency of VOCs.[49] SCD patients have naturally high RBC turnover rates as well as fragile membranes which means any additional harm to the cells becomes a major clinical concern.[50] Exposure to THC has been shown to compromise erythrocyte membrane stability, promoting hemolysis, and decreasing the ability of transfused red blood cells capacity to carry oxygen.[3,10,13] These adverse effects may exacerbate anemia and hinder the overall efficacy of transfusion therapy in SCD patients, further complicating clinical outcomes.

Cannabinoid compounds that influence RBC deformability characteristics, as well as viscosity levels, can potentially worsen blood vessel blockages and lead to elevated frequency of VOCs among SCD patients.[7,11,41] Sickled RBCs that obstruct small blood vessels trigger both tissue damage from reduced blood flow and local tissue inflammation which define these crises.[7,11,41] When THC impairs the membrane flexibility of transfused erythrocytes, it increases cellular rigidity and the likelihood of vascular occlusion.[7,11,41] This risk is further compounded in patients who are exposed to cannabinoids from two routes: their own personal cannabis usage and transfusions involving blood products from cannabinoid-positive donors.[3,11,13]

Alloimmunization, which leads to the development of antibodies against non-self-antigens on transfused red blood cells, creates a major difficulty in managing SCD patients who are frequently in need of blood transfusion therapy.[11,44] The presence of alloantibodies complicates the process of finding compatible blood units while making patients susceptible to delayed hemolytic transfusion reactions (DHTRs).[28] Cannabinoids exert immunomodulatory effects that may alter global immune function by suppressing T-cell activity and disrupting cytokine signaling pathways.[39,44] The immunomodulatory properties have dual effects on alloantibody production by preventing the formation or simultaneously impairing the immune system's ability to recognize or respond to hemolytic reactions following transfusion.[44]

Patients who have cancer share the same high-risk status for transfusion-related complications that SCD patients experience.[8] Thrombocytopenia caused by chemotherapy creates a high-risk state for patients because it leads to spontaneous bleeding and inadequate clot formation.[3,8,13,19,26] Physicians order platelet transfusions for cancer patients to help them maintain adequate platelet count levels to support hemostasis.[28] The biological effects of cannabinoids complicate transfusion safety and efficacy in this population.[3,13,19] THC has been associated with platelet hyperactivity, potentially increasing the risk of thrombosis, while CBD shows anticoagulant properties that inhibit platelet aggregation and elevate bleeding risk.[9,13,17,19,43] Platelet transfusions administered to patients under cannabinoid exposure may display unpredictable efficacy, complicating the clinical management of both hemorrhagic and thrombotic disorders.[9,13,19]

SCDs and cancer patients are not the only transfusion-dependent groups who face potential risks from cannabinoid exposure, individuals with hemophilia represent another patient population.[17,35] Hemophilia requires frequent administration of clotting factor replacement therapy, often delivered through transfusions, to prevent or control bleeding episodes.[12,17,51] THC and CBD may influence coagulation factor activity, but the impact on bleeding duration depends on the direct involvement in blood clotting processes.[17,44] Furthermore, cannabis may enhance the sensitivity of immune systems toward transfused blood components, particularly in immunocompromised individuals.[52] Cannabinoids immunosuppressive properties, especially the inhibition of T-cell function, may elevate the risk of graft-versus-host disease (GVHD) and impair immune responses following transfusion in vulnerable groups, including transplant recipients and patients with autoimmune disorders.[39,44]

Cannabinoid physiology affects clinical outcomes of transfusion-dependent patients

who suffer from SCD as well as those diagnosed with cancer or hemophilia or autoimmune diseases and individuals undergoing immunosuppressive therapy following organ transplantation.[39,44] Blood transfused products alter safety and effective performance because THC and CBD make an impact on the dynamics of coagulation along with red cell integrity and immune system response .[3,13,44] The effects of cannabinoids result in prolonged bleeding time, increased thrombotic potential, and degraded immunological product compatibility between donor and recipient.[17,43] The health complications from THC and CBD therapy can work against treatment objectives and boost transfusion-associated medical issues for patients with health problems. The development of safe blood product transfusion practice mandates the identification of cannabinoid-related risks. There is an urgent need to update blood donor questionnaires to include cannabinoid consumption, as well as to promote temporary cessation of prescribed cannabinoid therapy in transfusion-dependent patients.

Discussion

Cannabinoids present multiple safety risks to transfusion medicine; therefore, health organizations should establish specific guidelines to mitigate these risks. Both THC and CBD degrade blood product quality through hematological alterations, affecting the stability of RBCs, and interfering with platelet aggregation and coagulation mechanisms.[3,10,13,17,19] The changes in the composition and function of blood that result from cannabinoid consumption introduce substantial, measurable changes in health to transfusion-dependent patients, particularly those with SCD and cancer.[3,11,13,53] SCD patients using cannabinoids face increased hospital admissions due to worsening VOCs, demonstrating an immediate need to address transfusion risks from cannabinoids.[11,53]

Despite this growing concern, research evaluating the transfusion-specific consequences of cannabinoid exposure remains limited. While some *in vitro* research on cannabinoid exposure has produced reputable data on impaired blood products, there is not enough comprehensive research evaluating the potential risks associated with transfusing cannabinoid-exposed blood products.[13,20,35] As a result, there is no compelling data to support the transfusion management team in requesting special unique blood products that are cannabinoid-free to prevent adverse reactions for the most vulnerable patients. Research data lacks sufficient information about the prolonged preservation of cannabinoids and the metabolites in blood products and the ability to worsen blood system conditions through cumulative exposure.[54] Cannabinoid potential risks are primarily dependent on research that relies on *in vitro* and animal experiments, which often fail to replicate the outcomes that occur during human transfusion procedures.[13,16,19]

These limitations significantly hinder the ability to develop evidence-based transfusion guidelines. Developing clinically useful guidelines becomes more challenging because of the different routes used to consume cannabinoids, varying periods of exposure, and the absence of standardized dosage information.[43,54] The persistent presence of cannabinoids in blood products donated by cannabinoid users must be measured explicitly through clinical research to determine the impact on blood product safety.

The research gaps are mirrored by regulatory shortcomings in donor screening protocols. The lack of standard cannabinoid-specific donor screening impedes the creation of extensive transfusion safety regulations. Donor screening developed by the FDA along with the WHO focuses primarily on detecting infectious disease markers and does not address cannabinoid use.[23,32] The present gap is exacerbated by federal restrictions on medically prescribed THC and CBD, which create issues related to standardization and difficulties in clinical oversight.[55] Furthermore, the legalization of prescribed medical and recreational cannabis in 24 states in the US complicates legal procedures related to donor privacy and

informed consent.[56] The policies must align with regional laws, making it difficult to establish consistent national standards.[56,57] These factors contribute to inconsistent donor eligibility evaluations and may ultimately reduce the pool of acceptable donors.

To address the regulatory and clinical gaps, a multifaceted approach must be implemented. The medical community must implement evidence-based solutions to resolve problems from cannabinoid exposure in transfusion services. Implementing screening protocols designed to monitor both the recreational and medically prescribed cannabinoid consumption frequencies among donors and immunocompromised patients will assist in policy development by providing crucial data regarding prevalence.[15,22,58] Incorporating cannabinoid-specific questions into donor screening questionnaires will enable more accurate risk assessments of donors without reducing the available donor pool. Collaboration among healthcare professionals, laboratory scientists, bioethicists, and policymakers are essential for creating transfusion safety guidelines that address donor consent, cannabinoid use disclosure, and the associated legal, ethical, and privacy concerns.[55,56,57]

To further support these efforts, clinical practices must reflect the differential risks faced by vulnerable patient populations. Healthcare institutions need to modify transfusion protocols according to the unique risks within a specific population such as SCD, cancer or immunocompromised patients. The use of cannabinoids intensifies RBC deformity and increases RBC viscosity and elasticity, potentially affecting the ability to flow properly, leading to worsening anemia and more frequent VOCs in SCD patients.[3,11,13,35,53] However, transfusion guidelines continue to overlook this fact. Among patients with cancer undergoing chemotherapy treatments, cannabinoids cause changes to blood clotting factors, thereby increasing the risk for thrombocytopenia, and consequently raising the likelihood of potential bleeding.[12,13,17,19,26] The outcomes of blood transfusions for immune-compromised patients, as well as those at risk for allergic reactions and GVHD, become more complex when cannabinoid metabolites are present in donor blood, potentially influencing the immune response in the recipient and complicating the risk of allergic reactions or GVHD in susceptible individuals.[44,45,46,47,52] Cannabinoids' negative impacts on blood product safety support the need for medical facilities to perform pre-transfusion risk assessments, which include cannabinoid exposure among other risk factors.[8,13,17] Integrating cannabinoid screening into pre-transfusion protocols may improve transfusion outcomes and patient safety across high-risk populations, ensuring that evolving patterns of drug use do not compromise the integrity or efficacy of life-saving blood products.

However, translating clinical recommendations into standardized practice remains difficult without conclusive scientific data. Despite the urgency to revise transfusion protocols, significant limitations persist. The existing knowledge about how cannabinoids affect transfusion safety remains imperfect due to various inconsistencies and availability of unreliable, reproducible data.[16,35] The lack of comprehensive research is hindered by the scarcity of human clinical trials, the use of unstandardized dosing methods in studies, and limited knowledge regarding the persistence of cannabinoids in blood components.[20,22] Challenges in experimental design make it difficult for researchers to establish conclusive findings regarding the safety of blood products, especially concerning the persistence of cannabinoids and their effects.

Future investigations must conduct extensive clinical research to determine how ongoing cannabinoid consumption, whether for recreational or medical purposes, can exacerbate hematological alterations in the blood system, thereby compromising the safety of blood products.[38,44] Research in this area requires standardized procedures for cannabinoid measurements combined with reliable analytical approaches to detect the presence of

these compounds and metabolites in stored blood products.[58,59] The development of evidence-based cannabinoid safety thresholds for blood components requires support from regulatory agencies through the facilitation of pilot screening programs. A multidisciplinary team, including transfusion specialists, clinical researchers, toxicologists, and bioethicists, should lead this effort to incorporate cannabinoid detection into donor evaluation protocols while ensuring that ethical considerations are upheld.[55,56]

Conclusion

The emerging threat of cannabinoid exposure in transfusion medicine lacks proper attention, even though it significantly affects the membrane integrity of RBCs, reduces platelet aggregation, and modulates blood coagulation.[3,9,10,13] The increasing number of cannabinoid users in society demands immediate changes to donor eligibility criteria and the creation of validated, reliable testing procedures for cannabinoid detection.[14] The evolution of transfusion medicine plays an integral role in healthcare; ensuring blood product safety is essential and requires multimethod longitudinal research to determine the complete risks associated with cannabinoids, combined with practical cost-effectiveness assessments and a mechanistic understanding.[16] A documented tenfold increase in cannabinoid consumption necessitates collaboration among healthcare professionals, laboratory personnel, and government agencies to establish a national healthcare policy impacting patient blood management, ensuring safety and informed decision-making.[55,60] Cannabinoid exposure threatens transfusion safety, demanding urgent action to prevent unpredictable hematologic risks to vulnerable patients.

References

1. Howard PR. Basic & applied concepts of blood banking and transfusion practices. 5th ed. Elsevier. 2021.
2. Troyer J, Tanco K. Review of the Use of Medicinal Cannabis Products in Palliative Care. Cancers (Basel). 2024;16(7):1412. Published 2024 Apr 4. doi:10.3390/cancers16071412
3. Lampron MC, Desbiens-Tremblay C, Loubaki L. In vitro exposure of whole blood to a cannabinoid mixture impairs the quality of red blood cells and platelets. Blood Transfus. 2023;21(3):240-250. doi:10.2450/2022.0100-22
4. Antunes M, Barroso M, Gallardo E. Analysis of Cannabinoids in Biological Specimens: An Update. Int J Environ Res Public Health. 2023;20(3):2312. Published 2023 Jan 28. doi:10.3390/ijerph20032312
5. Lopez MJ, Preuss CV, Tadi P. Drug Enforcement Administration Drug Scheduling. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated 2023 Jul 30. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557744/. Accessed 2025 Mar 5.
6. Cooper ZD, Abrams DI, Gust S, Salicrup A, Throckmorton DC. Challenges for Clinical Cannabis and Cannabinoid Research in the United States. J Natl Cancer Inst Monogr. 2021;2021(58):114-122. doi:10.1093/jncimonographs/lgab009
7. Gómez CT, Borda N, Moscovicz F, et al. In vitro effect of cannabidiol on red blood cells: implication in long-lasting pathology treatment. Curr Pharm Des. 2024;30(28):2222-2228. doi:10.2174/0113816128287272240529072040
8. Woerdenbag HJ, Olinga P, Kok EA, et al. Potential, Limitations and Risks of Cannabis-Derived Products in Cancer Treatment. Cancers (Basel). 2023;15(7):2119. Published 2023 Apr 1. doi:10.3390/cancers15072119
9. Greger J, Bates V, Mechtler L, Gengo F. A Review of Cannabis and Interactions With Anticoagulant and Antiplatelet Agents. J

Clin Pharmacol. 2020;60(4):432-438. doi:10.1002/jcph.1557
10. James TR, Watson CT, Pepple DJ. The effect of delta-9-tetrahydrocannabinol and cannabidiol on p50 of the oxygen haemoglobin dissociation curve. Fitoterapia. 2020;143:104539. doi:10.1016/j.fitote.2020.104539
11. Ballas SK. The Use of Cannabis by Patients with Sickle Cell Disease Increased the Frequency of Hospitalization due to Vaso-Occlusive Crises. Cannabis Cannabinoid Res. 2017;2(1):197-201. Published 2017 Jul 1. doi:10.1089/can.2017.0011
12. Thomas TF, Metaxas ES, Nguyen T, et al. Case report: Medical cannabis-warfarin drug-drug interaction. J Cannabis Res. 2022;4(1):6. Published 2022 Jan 10. doi:10.1186/s42238-021-00112-x
13. James TR, Richards AA, Lowe DA, Reid WA, Watson CT, Pepple DJ. The in vitro effect of delta-9-tetrahydrocannabinol and cannabidiol on whole blood viscosity, elasticity and membrane integrity. J Cannabis Res. 2022;4(1):15. Published 2022 Apr 5. doi:10.1186/s42238-022-00126-z
14. Farrelly KN, Wardell JD, Marsden E, et al. The Impact of Recreational Cannabis Legalization on Cannabis Use and Associated Outcomes: A Systematic Review. Subst Abuse. 2023;17:11782218231172054. Published 2023 May 9. doi:10.1177/11782218231172054
15. Annen K, DomBourian MG. Perceptions on acceptability and reported consumption of marijuana by blood donors prior to donation in the recreational use state of Colorado, USA. Vox Sang. 2022;117(2):177-184. doi:10.1111/vox.13183
16. Hansen JS, Boix F, Hasselstrøm JB, et al. Pharmacokinetics and pharmacodynamics of cannabis-based medicine in a patient population included in a randomized, placebo-controlled, clinical trial. Clin Transl Sci. 2024;17(1):e13685. doi:10.1111/cts.13685
17. Kelkar AH, Tarantino MD, Roberts JC. Synthetic Cannabinoid-Associated Coagulopathy. N Engl J Med. 2019;380(1):101-102. doi:10.1056/NEJMc1814118
18. Khayat W, Lehmann C. The Endocannabinoid System: A Potential Therapeutic Target for Coagulopathies. Metabolites. 2022;12(6):541. Published 2022 Jun 14. doi:10.3390/metabo12060541
19. De Angelis V, Koekman AC, Weeterings C. Endocannabinoids control platelet activation and limit aggregate formation under flow. PLoS One. 2014;9(9):e108282. doi:10.1371/journal.pone.0108282
20. Djilali E, Pappalardo L, Posadino AM, Giordo R, Pintus G. Effects of the Storage Conditions on the Stability of Natural and Synthetic Cannabis in Biological Matrices for Forensic Toxicology Analysis: An Update from the Literature. Metabolites. 2022;12(9):801. Published 2022 Aug 27. doi:10.3390/metabo12090801
21. Pagano C, Savarese B, Coppola L, et al. Cannabinoids in the Modulation of Oxidative Signaling. Int J Mol Sci. 2023;24(3):2513. Published 2023 Jan 28. doi:10.3390/ijms24032513
22. Couch AN, Lanza JM, Zall CM, Davidson JT. Differentiation of Δ9-THC and CBD Using Silver-Ligand Ion Complexation and Electrospray Ionization Tandem Mass Spectrometry (ESI-MS/MS). J Am Soc Mass Spectrom. 2024;35(7):1413-1421. doi:10.1021/jasms.3c00452
23. Marrero-Rivera G, García-Otálora MA, Gonzalez C, et al. Blood donor questionnaires and infectious disease screening in Latin American countries. Vox Sang. 2024;119(11):1201-1206. doi:10.1111/vox.13730
24. Cohn CS, Delaney M, Johnson ST, Katz LM. Technical Manual. 20th ed. AABB; 2020. Ngatuvai M, Zagales I, Sauder M, et al. Outcomes of Transfusion With Whole

Blood, Component Therapy, or Both in Adult Civilian Trauma Patients: A Systematic Review and Meta-Analysis. J Surg Res. 2023;287:193-201. doi:10.1016/j.jss.2023.02.010

25. Lotterman S, Sharma S. Blood Transfusion. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. Updated 2023 Jun 20. Available from: https://www.ncbi.nlm.nih.gov/books/NBK499824/. Accessed 2025 Mar 15.
26. Nayeri ND, Nadali J, Divani A, Hatefimoadab N. Ways To Enhance Blood Transfusion Safety: A Systematic Review. Florence Nightingale J Nurs. 2022;30(3):288-300. doi:10.5152/FNJN.2022.21214
27. Harmening DM. Modern Blood Banking & Transfusion Practices. 7th ed. F.A. Davis; 2019.
28. Roth WK. History and Future of Nucleic Acid Amplification Technology Blood Donor Testing. Transfus Med Hemother. 2019;46(2):67-75. doi:10.1159/000496749
29. Harris JC, Crookston KP. Blood Product Safety. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated 2023 Mar 27. Available from: https://www.ncbi.nlm.nih.gov/books/NBK539826/. Accessed 2025 Mar 15.
30. Zahidin MA, Saidin NIS, Ibrahim NA, et al. The Blood Donor Deferral Rate and the Reasons for Deferral at a Tertiary Care Teaching Institute in Northeastern Malaysia. Cureus. 2024;16(2):e54954. Published 2024 Feb 26. doi:10.7759/cureus.54954
31. Myers DJ, Collins RA. Blood Donation. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated 2024 Oct 7. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525967/. Accessed 2025 Mar 15.
32. Pierik R, Verweij M, van de Laar T, Zaaijer H. Facing difficult but unavoidable choices: Donor blood safety and the deferral of men who have sex with men. Bioethics. 2022;36(8):840-848. doi:10.1111/bioe.13063
33. Quraishi R, Kathiresan P, Verma K, Rao R, Jain R. Effect of chronic opioid use on the hematological and inflammatory markers: A retrospective study from North India. Indian J Psychiatry. 2022;64(3):252-256. doi:10.4103/indianjpsychiatry.indianjpsychiatry_751_21
34. Hatfield J, Suthar K, Meyer TA, Wong L. The use of cannabinoids in palliating cancer-related symptoms: a narrative review. Proc (Bayl Univ Med Cent). 2024;37(2):288-294. Published 2024 Feb 8. doi:10.1080/08998280.2023.2301241
35. Dean CL, Wade J, Roback JD. Transfusion-Transmitted Infections: an Update on Product Screening, Diagnostic Techniques, and the Path Ahead. J Clin Microbiol. 2018;56(7):e00352-18. Published 2018 Jun 25. doi:10.1128/JCM.00352-18
36. Stella N. THC and CBD: Similarities and differences between siblings. Neuron. 2023;111(3):302-327. doi:10.1016/j.neuron.2022.12.022
37. Neary JP, Singh J, Alcorn J, et al. Pharmacological and physiological effects of cannabidiol: a dose escalation, placebo washout study protocol. BMC Neurol. 2024;24(1):340. Published 2024 Sep 12. doi:10.1186/s12883-024-03847-1
38. Koyama S, Etkins J, Jun J, et al. Utilization of Cannabidiol in Post-Organ-Transplant Care. Int J Mol Sci. 2025;26(2):699. Published 2025 Jan 15. doi:10.3390/ijms26020699
39. Zhang X, Lin Y, Xin J, et al. Red blood cells in biology and translational medicine: natural vehicle inspires new biomedical applications. Theranostics. 2024;14(1):220-248. Published 2024 Jan 1. doi:10.7150/thno.87425
40. Obeagu EI, Igwe MC, Obeagu GU. Oxidative stress's impact on red blood cells: Unveiling implications for health and disease. Medicine (Baltimore).

2024;103(9):e37360. doi:10.1097/MD.0000000000037360
41. Chaudhary PK, Kim S, Kim S. An Insight into Recent Advances on Platelet Function in Health and Disease. Int J Mol Sci. 2022;23(11):6022. Published 2022 May 27. doi:10.3390/ijms23116022
42. Smythe MA, Wu W, Garwood CL. Anticoagulant drug-drug interactions with cannabinoids: A systematic review. Pharmacotherapy. 2023;43(12):1327-1338. doi:10.1002/phar.2881
43. Aziz AI, Nguyen LC, Oumeslakht L, Bensussan A, Ben Mkaddem S. Cannabinoids as Immune System Modulators: Cannabidiol Potential Therapeutic Approaches and Limitations. Cannabis Cannabinoid Res. 2023;8(2):254-269. doi:10.1089/can.2022.0133
44. Sermet S, Li J, Bach A, et al. Cannabidiol selectively modulates interleukin-1β and IL-6 production in toll-like receptor activated human peripheral blood monocytes. Toxicology. 2021;464:153016. doi:10.1016/j.tox.2021.153016
45. Henshaw FR, Dewsbury LS, Lim CK, Steiner GZ. The Effects of Cannabinoids on Pro- and Anti-Inflammatory Cytokines: A Systematic Review of In Vivo Studies. Cannabis Cannabinoid Res. 2021;6(3):177-195. doi:10.1089/can.2020.0105
46. Nayak AP, Loblundo C, Bielory L. Immunomodulatory Actions of Cannabinoids: Clinical Correlates and Therapeutic Opportunities for Allergic Inflammation. J Allergy Clin Immunol Pract. 2023;11(2):449-457. doi:10.1016/j.jaip.2022.10.009
47. Reitsma SE, Lakshmanan HHS, Johnson J, et al. Chronic edible dosing of Δ9-tetrahydrocannabinol (THC) in nonhuman primates reduces systemic platelet activity and function. Am J Physiol Cell Physiol. 2022;322(3):C370-C381. doi:10.1152/ajpcell.00373.2021
48. Salinas Cisneros G, Thein SL. Recent Advances in the Treatment of Sickle Cell Disease. Front Physiol. 2020;11:435. Published 2020 May 20. doi:10.3389/fphys.2020.00435
49. Wang Q, Zennadi R. The Role of RBC Oxidative Stress in Sickle Cell Disease: From the Molecular Basis to Pathologic Implications. Antioxidants (Basel). 2021;10(10):1608. Published 2021 Oct 13. doi:10.3390/antiox10101608
50. Mannucci PM. Hemophilia therapy: the future has begun. Haematologica. 2020;105(3):545-553. doi:10.3324/haematol.2019.232132
51. Maggirwar SB, Khalsa JH. The Link between Cannabis Use, Immune System, and Viral Infections. Viruses. 2021;13(6):1099. Published 2021 Jun 9. doi:10.3390/v13061099
52. Roy AM, Konda M, Goel A, Sasapu A. Characteristics of marijuana usage in sickle cell patients: a nationwide analysis. Blood. 2019;134(Supplement_1):4848. doi:10.1182/blood-2019-131489
53. Kitdumrongthum S, Trachootham D. An Individuality of Response to Cannabinoids: Challenges in Safety and Efficacy of Cannabis Products. Molecules. 2023;28(6):2791. Published 2023 Mar 20. doi:10.3390/molecules28062791
54. Patel J, Marwaha R. Cannabis Use Disorder. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Updated 2024 Mar 20. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538131/. Accessed 2025 Mar 15.
55. Bhatia D. Editorial: Cannabis Legalization and Youth Cannabis Use: Findings From an Updated Systematic Review and Meta-Analysis. J Am Acad Child Adolesc Psychiatry. 2024;63(11):1075-1077. doi:10.1016/j.jaac.2024.05.005
56. Fink DS, Samples H, Malte CA, et al. Association of cannabis legalization with cannabis positive drug screening in US veterans. Preprint. medRxiv. Published 2023 Dec 9. doi:10.1101/2023.12.08.23299731. Accessed 2025 Mar 10.

57. Lo Faro AF, Venanzi B, Pilli G, et al. Ultra-high-performance liquid chromatography-tandem mass spectrometry assay for quantifying THC, CBD and their metabolites in hair. Application to patients treated with medical cannabis. J Pharm Biomed Anal. 2022;217:114841. doi:10.1016/j.jpba.2022.114841
58. Zancanaro F, Tedeschi G, Zamengo L, Frasson S, Frison G. Determination of cannabinoids in 50 µL whole blood samples by online extraction using turbulent flow chromatography and LC-HRAM-Orbitrap-MS: Application on driving under the influence of drugs cases. Drug Test Anal. 2024;16(2):210-220. doi:10.1002/dta.3532
59. Rhee TG, Rosenheck RA. Increasing Use of Cannabis for Medical Purposes Among U.S. Residents, 2013-2020. Am J Prev Med. 2023;65(3):528-533. doi:10.1016/j.amepre.2023.03.005