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TRANSFUSION

REVIEW ARTICLE

TRANSFUSION MEDICINE

Current advances 2024: A critical review of selected topics by the Association for the Advancement of Blood and Biotherapies (AABB) Clinical Transfusion Medicine Committee

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1 | INTRODUCTION

The Association for the Advancement of Blood and Biotherapies (AABB) Clinical Transfusion Medicine Committee (CTMC) includes experts from various backgrounds in clinical transfusion medicine (TM). This committee conducts yearly assessments of significant developments in TM for the AABB Board of Directors. Beginning in 2018, these assessments have been summarized and published in the journal *Transfusion*, establishing an educational resource for practitioners in TM. What follows is a synopsis of key advancements derived from publications in calendar year 2024.

2 | MATERIALS AND METHODS

CTMC members selected notable English-language publications relevant to TM from calendar year 2024. While all attempts were made to be comprehensive, our approach was not a systematic review with structured search methodology, nor did we formally evaluate evidence certainty. Specialists (2–3 CTMC members per topic) summarized key publications within their respective areas of interest, occasionally including contextual references. Each summary underwent independent review and editing by at least two CTMC members. The first and senior authors compiled these summaries and edited them for length and content to assemble the final manuscript.

3 | BLOOD COMPONENT THERAPY

3.1 | Key points

- Active surveillance of transfusion-related acute lung injury (TRALI) identified more cases than passive surveillance.
- Riboflavin and UV light-treated platelets failed to demonstrate noninferiority when compared to conventional apheresis platelets.
- Cold stored platelets (CSP) did not differ significantly from conventional platelets in the primary safety outcome of 24-h mortality in trauma patients.

3.2 | TRALI surveillance methods

A meta-analysis of 80 studies covering 176 million transfusions found higher estimates of TRALI with active surveillance compared to passive surveillance.[1] Pooled TRALI estimates among the active surveillance studies were 0.17/10,000 (95% confidence intervals [CI]: 0.03–0.43) s (RBCs), 0.31/10,000 (95%CI: 0.22–0.42) for platelets, and 3.19/10,000 (95%CI: 0.09–10.66) for plasma. Studies using passive surveillance estimates reported TRALI rates an order of magnitude lower, 0.02–0.10/10,000, depending on the component. Passive surveillance methods underreport TRALI, but the benefits of large-scale active surveillance must be weighed against potential costs.

3.3 | Platelet trials

MiPLATE, a prospective, multicenter, randomized noninferiority trial of riboflavin and UV-light treated apheresis platelets (MIRASOL®, Terumo Blood and Cell Technologies, Lakewood, CO) versus conventional apheresis platelets in plasma showed increased days with World Health Organization (WHO) grade ≥2 bleeding in the MIRASOL® arm (1.7 vs. 0.6 days in the conventional arm, relative risk [RR] 2.79, 95% CI 1.67–4.67).[2] This failed to meet the prespecified noninferiority margin of 1.6, and the trial was stopped for futility. Patients in the MIRASOL® arm required more platelet transfusions (RR = 1.22, 95% CI 1.05–1.41) and had a greater risk of platelet refractoriness.

CRISP-HS, a prospective, phase 2, randomized, open-label trial evaluated CSP in 200 traumatically injured, non-pregnant patients at risk of bleeding and requiring large-volume transfusion.[3] Participants were randomized to receive either a single CSP unit stored up to 14 days or usual care. The principal clinical outcome of 24-h

mortality was seen in 6 patients in the CSP arm and 10 patients in the usual-care arm (difference −4.3%, 95% CI −12.8% to 3.5%). Only 47 (48%) participants in the usual-care arm received a platelet transfusion, at a median of 56 min after the average CSP transfusion. The possible prolonged storage time and safety of CSPs warrant further investigation; several trials are ongoing.

4 | INFECTIOUS DISEASES, BLOOD DONOR SCREENING, AND COLLECTIONS

4.1 | Key points

- The FDA licensed a new ribosomal RNA (rRNA) based nucleic acid test (NAT) to screen whole blood donations for malaria parasites.
- The FDA issued a Draft Guidance with strategies to mitigate the risk of transfusion-transmitted malaria while minimizing unnecessary donor deferral.
- NAT tests for malaria screening of donors are now available outside the United States (US).

A test targeting rRNA and DNA for the major causative agents of malaria (*Plasmodium falciparum, Plasmodium knowlesi*, *Plasmodium malariae, Plasmodium ovale*, and *Plasmodium vivax*) is the first NAT licensed by the FDA for screening whole blood donations.[4] The test is highly sensitive (100% sensitivity at 3-5-fold the limit of detection) and specific (100% with 95% CI 99.982%–100%).[4] While pathogen reduction technology (PRT) is considered effective for *P. falciparum* mitigation, it is not yet available for RBC components. Current screening is limited to the donor history questionnaire, which identifies donors with a history of malaria or those who have visited or lived in malaria-endemic areas. This current strategy defers 50,000 to 160,000 donors/year, but still fails to capture all asymptomatically infected donors, which has resulted in 13 transfusion-transmitted malaria cases from 2000 to 2021.[5]

In January 2025, the FDA issued Draft Guidance to indicate testing strategies for *Plasmodium* species; testing each donation is not necessary.[6] Blood establishments may instead implement either:

- A selective testing strategy using an FDA-licensed donor screening NAT for *Plasmodium* species to test (1) donors who have had malaria (each donation) or resided in (test once) or traveled to a malaria-endemic country (all donations occurring within 1 year of return), and (2) donations collected in US regions with local, mosquito-borne malaria transmission; or
- PRT for platelet and plasma donations using an FDA-approved device indicated for use against *P. falciparum*.

The FDA has not issued a final guidance.

Other recently developed tests include the new Brazilian NAT PLUS HIV/HBV/HCV/Malaria (Bio-Manguinhos/Fiocruz) kit, which can detect *Plasmodium* species in plasma samples and is sufficiently sensitive to detect subpatent infections.[7] In addition, a second highly sensitive and specific rRNA-based test for *Plasmodium* species received a CE mark but has not been implemented for routine blood donor screening and is not available in the United States.[8]

5 | PATIENT BLOOD MANAGEMENT (PBM)

5.1 | Key points

- Iron deficiency anemia treatment with intravenous (IV) iron compared to RBC transfusions improved outcomes.
- Hemoglobin-based RBC transfusion thresholds were evaluated in patients with acute neurologic injury.

5.2 | Iron deficiency anemia treatment

A propensity-matched retrospective cohort analysis of surgical patients with iron deficiency anemia from the TriNetX Research Network compared preoperative treatment with IV iron ($n = 77{,}179$) or with RBC transfusions ($n = 77{,}179$).[9] Preoperative iron was associated with lower postoperative mortality (RR, 0.63, 95% CI, 0.60–0.66), lower postoperative morbidity (RR, 0.76, 95% CI, 0.75–0.78), higher hemoglobin concentration (10.1 ± 1.8 g/dL vs. 9.4 ± 1.7 g/dL, $p = .001$), and fewer postoperative RBC transfusions (RR, 0.30, 95% CI, 0.29–0.31). The authors concluded that iron supplementation can improve patient outcomes, reduce blood utilization, and avoid the associated risks and costs of transfusion.

5.3 | RBC transfusion for acute neurologic injury

Three multicenter RCTs—HEMOTION, TRAIN, and SAHARA—evaluated liberal versus restrictive RBC transfusion strategies in neurocritically ill adults.[10–12] These studies varied in the hemoglobin thresholds defining liberal and restrictive strategies, type of neurologic injury, and primary neurologic outcome measure. In the

HEMOTION trial, which included 722 patients with traumatic brain injury (TBI), a liberal transfusion strategy (hemoglobin ≤10 g/dL) was compared with a restrictive one (hemoglobin ≤7 g/dL).[10] The liberal strategy did not significantly reduce the risk of unfavorable neurologic outcome at 6 months (overall RR, 0.93, 95% CI 0.83–1.04). Similarly, the SAHARA trial, involving 725 patients with aneurysmal subarachnoid hemorrhage (SAH), found no significant difference between a liberal transfusion strategy (hemoglobin ≤10 g/dL) versus a restrictive one (hemoglobin ≤8 g/dL) on the risk of unfavorable neurologic outcome at 12 months (risk ratio, 0.88; 95% CI, 0.72–1.09; $p = .22$).[12] However, the TRAIN trial, which included 820 patients with several forms of acute brain injury (59% with TBI, 23% with SAH, 18% with intracerebral hemorrhage [ICH]), did identify a benefit to the liberal transfusion strategy (hemoglobin <9 g/dL) compared with a restrictive one (hemoglobin <7 g/dL) on neurologic outcomes at 6 months (adjusted RR, 0.86 [95% CI, 0.79–0.94]; $p = .002$).[11] Although two trials showed no statistically significant difference, point estimates favored liberal strategies in all three trials. A future evidence synthesis could further inform transfusion strategy decisions for this patient group, if feasible.

6 | HEMOSTASIS

6.1 | Key points

- Tranexamic acid (TXA) did not benefit patients undergoing liver resection, those with ICH, or those with thrombocytopenia due to hematological malignancies.
- Andexanet alfa was associated with reduced ICH expansion but more thrombotic events than standard care in Xa inhibitor-associated ICH.

6.2 | Tranexamic use in multiple clinical settings

The HeLiX trial of 1245 participants with liver resection found no difference in RBC transfusion, intraoperative blood loss, or total estimated blood loss over 7 days; however, TXA was associated with more significant perioperative complications.[13] In the STOP-MSU trial with 201 participants, TXA within 2 h of ICH symptom onset did not reduce hematoma expansion compared with placebo.[14] In TREATT with 616 participants, TXA (IV or oral) did not reduce WHO grade ε2 bleeding or mortality in patients receiving chemotherapy or hematopoietic stem-cell transplantation for hematological malignancies.[15]

6.3 | Direct oral anticoagulant (DOAC) reversal

In an RCT of 530 patients with acute factor Xa inhibitor-associated ICH, andexanet alfa reduced ICH expansion on imaging, but had more arterial thrombotic events compared with standard of care.[16] Although the control group included non-standardized use of prothrombin complex concentrate (PCC), there were similar 30-day mortality and functional outcomes. Trials with standardized use of PCC and longer-term clinical outcomes are needed to compare andexanet alfa versus PCC.[17]

7 | IMMUNOHEMATOLOGY AND GENOMICS

7.1 | Key points

- Nipocalimab treatment delayed or prevented fetal anemia or intrauterine transfusions in pregnancies at high risk for early-onset severe HDFN.
- Variant *RHD* and *RHCE* alleles drive diverse alloimmunization rates in chronically transfused patients with sickle cell disease (SCD).
- Cell free fetal DNA analysis accurately predicts fetal RBC antigen status from 10 weeks' gestation.
- Blood donor sex, age, ABO group, and ethnicity influence anti-A and anti-B titers.

7.2 | Neonatal fc receptor blockade

UNITY was an international, open-label, phase 2 study of nipocalimab for hemolytic disease of the fetus and newborn (HDFN).[18] Nipocalimab blocks the neonatal Fc receptor, preventing transplacental IgG transfer. This study enrolled pregnant women with prior severe fetal anemia, stillbirth, or HDFN-related placental pathology who had a critical anti-D or anti-K titer, carried a D-positive or K-positive fetus, and had no current treatment with intravenous immunoglobulin or plasmapheresis. Participants received IV nipocalimab (30 or 45 mg/kg) from 14 to 35 weeks' gestation. Live births occurred in 12 of 13 pregnancies with a median gestational age of 36 weeks and 4 days. Of the 12 live-born infants, 1 required one exchange transfusion and one simple transfusion, and 5 infants required only simple transfusions. Maternal samples and cord blood showed decreased alloantibody titers and IgG levels. Nipocalimab shows early promise as an important treatment for HDFN, though larger studies are needed.

7.3 | *RH* genotypes and alloimmunization

A multisite study evaluated *RH* genotypes and RBC alloimmunization rates in 342 chronically transfused patients with SCD.[19] Despite serologic prophylactic antigen matching, RBC alloimmunization remained problematic and varied across sites (range 5%–41%). Genotyping using BeadChip arrays confirmed 33% with *RHD* and 57% with *RHCE* variant alleles in this cohort. No difference in anti-D, anti-C, or anti-E antibody formation was observed between individuals with variant versus conventional antigen expression. This study highlights the variability in alloimmunization rates in a population for which prophylactic Rh and K matching is widespread; a molecular approach might be necessary to further reduce alloimmunization rates in transfused SCD patients.

7.4 | Cell-free fetal DNA for RBC antigen genotyping

A multicenter prospective study evaluated next-generation sequencing-based quantitative cell-free fetal (cff) DNA for fetal antigen genotyping in alloimmunized pregnancies at 120 US sites.[20] The study included 156 pregnant patients (15.4% Hispanic, 9% non-Hispanic Black, 65.4% non-Hispanic White, 4.5% Asian, 1.3% more than one ethnicity, and 4.5% unknown ethnicity) mean gestational age of 16.4 weeks (range 10–37 weeks). Cell-free fetal DNA analysis was performed as part of prenatal care and validated with neonatal buccal swabs in a blinded laboratory. Concordance between cff DNA and neonatal genotype was determined for K, E, C, c, Fy^a, and D antigens. The investigators identified 145 instances in which the fetus was antigen positive and 320 instances in which the fetus was negative, with perfect concordance between prenatal cff DNA and neonatal genotyping. Cell-free fetal DNA testing is a promising technique for improved prenatal diagnosis and management of HDFN.

7.5 | Risk of high titers in donors

A study analyzing 6 million blood donations from the United Kingdom (UK) and Australia found significant risk factors for high anti-A or anti-B titers (defined as IgM titer ≥128 in this study, although high titer definitions can vary).[21] Female and group O donors were more likely to have high titers, whereas group B donors had the lowest proportion of high titer isoagglutinins. High titer positivity decreased with increasing donor age. Australian donors (37%) had higher rates of high titer versus the UK donors (9%). No obvious seasonal variation in titers was observed in either country. In the UK, donors identifying as Black, Asian, other, or mixed ethnicity were approximately twice as likely to have high titers compared to White donors after controlling for ABO group and sex. The authors conclude that age, sex, and self-reported ethnic background are strong predictors of high anti-A and anti-B titers.

8 | PEDIATRICS

8.1 | Key points

- RBC transfusions were not associated with higher risk of necrotizing enterocolitis (NEC) during 72-h posttransfusion periods in extremely low birth weight infants (ELBW).
- Platelet transfusion in infants born extremely preterm may be associated with an increased risk of death or severe neurodevelopmental impairment (NDI) at 2 years' corrected age.
- Transfusion practices for preterm infants vary widely across European neonatal intensive care units (NICUs).
- An international clinical practice guideline for RBC transfusion thresholds in very preterm neonates recommends a restrictive RBC transfusion strategy.

8.2 | RBC transfusions and NEC

In a post-hoc secondary analysis of the Transfusion of Prematures (TOP) RCT, 1690 ELBW infants were included (mean [SD] gestational age, 26.0 [1.5] weeks; 899 infants [53.2%] were female).[22] After categorizing 4947 hazard periods (72 hours after transfusion) and 5813 control periods, 133 NEC cases were identified. Fifty-nine of these cases (44.4%) occurred during hazard periods. Baseline and clinical characteristics of infants with NEC during hazard periods did not differ from those of infants with NEC during control periods. The adjusted RR was 0.95 (95% CI, 0.68–1.32). The findings suggest that, among ELBW infants with the hemoglobin ranges occurring in the TOP trial, exposure to RBC transfusions was not temporally associated with a higher risk of NEC during 72-h posttransfusion periods.

8.3 | Platelet transfusion and death or NDI in extremely preterm neonates

An observational cohort study and secondary analysis of the Preterm Erythropoietin Neuroprotection Trial evaluated

819 infants (429 [52.4%] male; mean [SD] gestational age, 25.5 [1.1] weeks), 245 (30%) who received at least one platelet transfusion during initial hospitalization.[23] The primary outcome of death or severe NDI occurred in 46.5% (114 of 245) of infants transfused with platelets and 13.9% (80 of 574) of untransfused infants. After adjusting for propensity score, gestational age at birth, and trial treatment group, death or severe NDI was more common after platelet transfusion (adjusted odds ratio 2.43, 95% CI, 1.24–4.76). Platelet transfusion in extremely preterm infants may be associated with increased risk of death or severe NDI at 2 years' corrected age. The underlying mechanisms remain unknown.

8.4 | RBC transfusion in NICUs

An international prospective observational cohort study across 64 NICUs in 22 European countries examined RBC transfusion in 1143 preterm infants (<32 weeks' gestation).[24] Overall RBC transfusion prevalence rate during postnatal days 1–28 was 3.4 transfusion days per 100 admission days, with considerable variation across countries, only partly explained by patient mix. By day 28, 36.5% (95% CI, 31.6%–41.5%) of infants had received at least one transfusion. Most transfusions (82.8%) were given based on defined hemoglobin thresholds. Pretransfusion hemoglobin levels per study threshold were below the restrictive thresholds implemented in ETTNO in 324 of 729 transfusions (44.4%) and TOP in 265 of 729 (36.4%).[25,26] Conversely, they were between restrictive and liberal thresholds in 352 (48.3%) and 409 (56.1%) of transfusions, respectively.

8.5 | Clinical practice guideline for RBC transfusion in very preterm neonates

An international steering committee, parent representatives, and stakeholder organization member panel provide a clinical practice guideline recommending restrictive RBC transfusion strategy, with moderate certainty of evidence, for preterm neonates with less than 30 weeks' gestation.[27] The group reviewed evidence from a systematic review of 6 RCTs including 3483 participants to compare high versus low hemoglobin-based thresholds. The findings suggest lower hemoglobin thresholds likely result in little to no difference in key short-term and long-term outcomes. Consequently, the guideline recommends a restrictive transfusion strategy, with specific hemoglobin thresholds based on postnatal age and respiratory support requirements. For instance, during postnatal weeks 1, 2, and 3 or more, the recommended hemoglobin thresholds for neonates on respiratory support are 11, 10, and 9 g/dL, respectively; for those on minimal or no respiratory support, the thresholds are 10, 8.5, and 7 g/dL, respectively.

9 | APHERESIS

9.1 | Key points

- Therapeutic plasma exchanges (TPE) are the most performed apheresis procedure in the US and worldwide.
- Therapeutic cellular collections are increasing along with the demand for gene therapy and chimeric antigen receptor T-cell (CAR-T) treatments.
- Hematopoietic stem cell collections in patients with SCD present unique challenges.
- Extracorporeal photopheresis (ECP) remains a crucial therapy for steroid-refractory graft-versus-host disease (GVHD), though its role is evolving with the emergence of new pharmacological treatments.
- In a retrospective, observational study, caplacizumab, combined with immunosuppression, demonstrated efficacy in the management of immune thrombotic thrombocytopenic purpura (iTTP) without the need for TPE.

9.2 | Contemporary apheresis practices

A survey of 22 US apheresis centers found that TPE was the most common procedure, followed by hematopoietic progenitor cell collections and RBC exchanges.[28] CAR-T-cell collections were a consistent area of growth. The average nurse-to-patient ratio was 1.2, but the COVID-19 pandemic and increased cellular collections created staffing challenges for many programs due to the need for specialized staff.

Gene therapy treatments, particularly for SCD, have further increased demand for cellular collections.[29–31] Sufficient mobilization of hematopoietic stem cells (HSC) for patients with SCD is complicated by impaired bone marrow microenvironment, myelosuppressive effect of hydroxyurea (HU), and contraindication to granulocyte colony-stimulating factor (G-CSF). Response to plerixafor alone may be limited, necessitating multiple collection days to achieve the desired CD34 yield. In some cases, multiple stimulation/collection cycles, separated by at least 2–4 weeks, are necessary. Past trials have shown that HU discontinuation and pre-mobilization RBC exchange (an additional apheresis need) are beneficial.[32] Nevertheless, during gene therapy clinical trials, 5–10% of participants could not be treated due to insufficient HSC yields.[29,30]

9.3 | Evolving treatment of GVHD

ECP remains a treatment option for acute and chronic GVHD following allogeneic HSC transplantation;[33] however, JAK inhibitors have changed treatment priorities. For acute GVHD, ruxolitinib is now the preferred second-line therapy for acute GVHD with ECP used in cases of severe disease or in combination with ruxolitinib.[35] For chronic GVHD, ECP is still valuable in refractory cases, particularly for steroid-sparing benefits, though newer agents, like belumosudil and axatilimab, are expanding treatment alternatives.[34,35]

9.4 | Caplacizumab without TPE in iTTP

A retrospective study compared 42 iTTP episodes treated with caplacizumab and immunosuppression alone versus standard therapy (TPE, corticosteroids, rituximab).[36] There were no significant differences in time to platelet count normalization (median: 3 vs. 4 days), clinical response, or iTTP-related mortality. The TPE-free approach reduced hospital stays and intensive care unit admissions. Despite these findings, certain patients did require subsequent TPE, possibly due to concomitant disease such as infection. These findings suggest the potential for a paradigm shift in iTTP management.

10 | HEMOGLOBINOPATHIES

10.1 | Key point

- Autologous genetically modified hematopoietic stem cell therapy, exa-cel, increased transfusion independence in β-thalassemia and reduced vaso-occlusive crises in SCD.

10.2 | Clinical trials with exagamglogene autotemcel (exa-cel)

Two phase 3, single-group, open-label studies were reported of exagamglogene autotemcel (exa-cel, Vertex Pharmaceuticals Incorporated), a nonviral genetically modified hematopoietic stem cell therapy that reactivates fetal hemoglobin synthesis.[37,38] In a study of 44 patients with SCD with recurrent severe vaso-occlusive crises, 29 of 30 patients with sufficient follow-up (97%) were free from vaso-occlusive crises and all 30 (100%) did not require hospitalizations for vaso-occlusive crises for at least 12 consecutive months.[37] In a parallel study, 52 patients with transfusion-dependent β-thalassemia, transfusion independence occurred in 32 of 35 patients (91%) with sufficient follow-up with a mean total hemoglobin level of 13.1 g/dL.[38] Another FDA-approved gene therapy approach, lovotibeglogene autotemcel (lovo-cel, Bluebird Bio Inc.), employs a lentiviral vector-based system to genetically modify autologous hematopoietic stems, enabling the production of a modified hemoglobin A (HbA^{T87Q}) in patients with SCD.[39]

11 | BIOTHERAPIES

11.1 | Key points

- CAR-T therapy, while highly effective, warrants vigilance for oncogenic transformation risks.
- Lentiviral gene therapy may provide an alternative to frequent Factor VIII infusions in hemophilia A.
- Significant advances occurred with CRISPR-based interventions in hereditary angioedema, β-thalassemia, and SCD.
- The FDA granted approval of the first tumor-infiltrating lymphocyte (TIL) therapy.

11.2 | CAR T-cell therapy oncogenesis

Malignant T-cell transformation following CAR-T therapy remains a rare but serious concern. A recent case report describes a patient with multiple myeloma who developed CD4+ T-cell lymphoma following B-cell maturation antigen (BCMA)-directed CAR-T therapy.[40] Molecular analysis revealed that the CAR vector had integrated into the *TP53* tumor suppressor gene, potentially driving oncogenesis. While CAR-T therapies have demonstrated high efficacy, this case underscores the need for long-term genomic surveillance and improved vector design to prevent insertional mutagenesis.

11.3 | Lentiviral gene therapy for hemophilia a

A study evaluating lentiviral gene therapy for severe hemophilia A demonstrated promising results.[41] Five participants received autologous CD34+ HSCs transduced with the CD68-ET3-LV lentiviral vector. Patients who received transduction enhancers exhibited significantly higher Factor VIII activity (median: 37.1 IU/dL) compared with those without enhancers. All participants remained free from spontaneous bleeding events over a median follow-up of 14 months. These findings highlight the potential of lentiviral-based HSC therapy as a durable

treatment for hemophilia A, offering an alternative to frequent Factor VIII infusions.

11.4 | CRISPR-Cas9-based therapy

The application of CRISPR-Cas9 gene editing in therapeutic settings has seen major advances:

1. *Hereditary angioedema*: In a phase 2 randomized trial, NTLA-2002, an in vivo CRISPR-based therapy targeting kallikrein B1 (*KLKB1*) significantly reduced angioedema attacks.[42] A single dose resulted in a 75%–77% decrease in attack frequency, with sustained kallikrein suppression observed for up to 16 weeks, supporting continued investigation in a larger phase 3 trial.
2. *β-thalassemia*: See "Hemoglobinopathies" section.
3. *Sickle cell disease*: See "Hemoglobinopathies" section.

11.5 | Regulatory developments for TIL

In February 2024, the FDA granted accelerated approval to Lifileucel (Iovance Biotherapeutics), the first TIL therapy for unresectable or metastatic melanoma[43] based on a global, multicenter, multicohort, open-label, single-arm phase 2 clinical trial.[44] The study included 89 patients with unresectable or metastatic melanoma who had received at least one prior therapy. The objective response rate was 31.5% among 73 patients who received the recommended TIL dosage ($7.5–72 \times 10^9$ viable cells).[45]

12 | HEALTH CARE DISPARITIES

12.1 | Key points

- Reduced access to mobile blood drives might underlie disparities in blood donation.
- Innovative strategies should be considered to address blood deserts.

12.2 | Mobile blood collection disparities

Comparison of census data to mobile blood collection sites in Maricopa County, Arizona showed lower rates of blood collections in neighborhoods with a higher proportion of Hispanic/Latino residents (OR = 0.88, 95% CI 0.83–0.92, $p < .001$).[46] Easier access to blood donation locations may increase donations, improving the overall blood supply and donor diversity.[47]

12.3 | Strategies for blood deserts

A panel of international experts defined a blood desert as a "geographical region where essential clinical demand for blood components cannot be met in a timely and affordable manner, in at least 75% of cases" where transfusion is needed.[48] White papers on three potential strategies, civilian walking blood banks, intraoperative autotransfusion, and drone-based blood delivery highlight opportunities and challenges in addressing the urgent need for blood in these regions.

CONFLICT OF INTEREST STATEMENT

STC is a scientific advisor to Pfizer. EPC reports personal fees from Plas-Free Ltd. outside of submitted work. JJ and RM report serving as scientific advisors for Werfen. MS received research funding from Terumo BCT and Cerus Corp. The authors have no conflicts of interest to disclose.

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REFERENCES

1. White SK, Walker BS, Schmidt RL, Metcalf RA. The incidence of transfusion-related acute lung injury using active surveillance: a systematic review and meta-analysis. Transfusion. 2024;64(2):289–300.
2. Koepsell SA, Stolla M, Sedjo RL, Carson J, Knudson M, Cook R, et al. Results of clinical effectiveness of conventional versus Mirasol-treated apheresis platelets in patients with Hypoproliferative thrombocytopenia (MiPLATE) trial. Transfusion. 2024;64(3):457–65.

3. Sperry JL, Guyette FX, Rosario-Rivera BL, Kutcher ME, Kornblith LZ, Cotton BA, et al. Early cold stored platelet transfusion following severe injury: a randomized clinical trial. Ann Surg. 2024;280(2):212–21.
4. Roche Molecular Systems. cobas® Malaria, Nucleic Acid Test for use on the cobas® 6800/8800 Systems [Internet]. Branchburg, NJ; 2024 Mar [cited 2025 Apr 14]. Report No.: 09618457001-01EN. Available from: https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/cobas-malaria
5. Center for Biologics Evaluation and Research, Food and Drug Administration. 125th Blood Products Advisory Committee (BPAC) Meeting [Internet]. 2024 [cited 2025 Apr 14]. Available from: https://www.fda.gov/advisory-committees/advisory-committee-calendar/blood-products-advisory-committee-may-9-2024-meeting-announcement-05092024
6. Recommendations to Reduce the Risk of Transfusion-Transmitted Malaria; Draft Guidance for Industry [Internet]. Food and Drug Administration Center for Biologics Evaluation and Research. 2025 [cited 2025 Apr 14]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommendations-reduce-risk-transfusion-transmitted-malaria-0
7. Costa E, Rocha D, Lopes JIF, Andrade E, Cardoso P, Ribeiro M, et al. Detection of plasmodium spp. in asymptomatic blood donors by the new Brazilian NAT PLUS HIV/HBV/HCV/malaria bio-Manguinhos kit. Transfusion. 2024;64(3):501–9.
8. Tonnetti L, Groves JA, Self D, Yadav M, Spencer BR, Livezey K, et al. A novel mitigation strategy for the prevention of transfusion-transmitted malaria. Transfusion. 2024;64(1):94–103.
9. Choi UE, Nicholson RC, Thomas AJ, Crowe EP, Ulatowski JA, Resar LMS, et al. A propensity-matched cohort study of intravenous Iron versus red cell transfusions for preoperative iron-deficiency anemia. Anesth Analg. 2024;139(5):969–77.
10. Turgeon AF, Fergusson DA, Clayton L, Patton MP, Neveu X, Walsh TS, et al. Liberal or restrictive transfusion strategy in patients with traumatic brain injury. N Engl J Med. 2024;391(8):722–35.
11. Taccone FS, Rynkowski Bittencourt C, Møller K, Lormans P, Quintana-Díaz M, Caricato A, et al. Restrictive vs Liberal transfusion strategy in patients with acute brain injury: the TRAIN randomized clinical trial. Jama. 2024;332(19):1623–33.
12. English SW, Delaney A, Fergusson DA, Chassé M, Turgeon AF, Lauzier F, et al. Liberal or restrictive transfusion strategy in aneurysmal subarachnoid hemorrhage. N Engl J Med. 2025;392(11):1079–88.
13. Karanicolas PJ, Lin Y, McCluskey SA, Tarshis J, Thorpe KE, Wei A, et al. Tranexamic acid in patients undergoing liver resection: the HeLiX randomized clinical trial. Jama. 2024;332(13):1080–9.
14. Yassi N, Zhao H, Churilov L, Wu TY, Ma H, Nguyen HT, et al. Tranexamic acid versus placebo in individuals with intracerebral haemorrhage treated within 2 h of symptom onset (STOP-MSU): an international, double-blind, randomised, phase 2 trial. Lancet Neurol. 2024;23(6):577–87.
15. TREATT Trial Investigators. Tranexamic acid versus placebo to prevent bleeding in patients with haematological malignancies and severe thrombocytopenia (TREATT): a randomised, double-blind, parallel, phase 3 superiority trial. Lancet Haematol. 2025;12(1):e14–22.
16. Connolly SJ, Sharma M, Cohen AT, Demchuk AM, Członkowska A, Lindgren AG, et al. Andexanet for factor Xa inhibitor-associated acute intracerebral hemorrhage. N Engl J Med. 2024;390(19):1745–55.
17. Levy JH, Shaw JR, Castellucci LA, Connors JM, Douketis J, Lindhoff-Last E, et al. Reversal of direct oral anticoagulants: guidance from the SSC of the ISTH. J Thromb Haemost. 2024;22(10):2889–99.
18. Moise KJ, Ling LE, Oepkes D, Tiblad E, Verweij EJTJ, Lopriore E, et al. Nipocalimab in early-onset severe hemolytic disease of the fetus and newborn. N Engl J Med. 2024;391(6):526–37.
19. Israelyan N, Vege S, Friedman DF, Zhang Z, Uter S, Fasano RM, et al. RH genotypes and red cell alloimmunization rates in chronically transfused patients with sickle cell disease: a multisite study in the USA. Transfusion. 2024;64(3):526–35.
20. Rego S, Ashimi Balogun O, Emanuel K, Overcash R, Gonzalez JM, Denomme GA, et al. Cell-free DNA analysis for the determination of fetal red blood cell antigen genotype in individuals with Alloimmunized pregnancies. Obstet Gynecol. 2024;144(4):436–43.
21. Robbins M, Huish S, Griffiths A, Powley T, Daly J, Cardigan R. Influence of donor age, sex and ethnicity on high-titre anti-a and -B: review of 6 million donations from two national blood providers. Vox Sang. 2024;119(9):987–95.
22. Salas AA, Gunn E, Carlo WA, Bell EF, Das A, Josephson CD, et al. Timing of red blood cell transfusions and occurrence of necrotizing enterocolitis: a secondary analysis of a randomized clinical trial. JAMA Netw Open. 2024;7(5):e249643.
23. Davenport PE, Wood TR, Heagerty PJ, Sola-Visner MC, Juul SE, Patel RM. Platelet transfusion and death or neurodevelopmental impairment in children born extremely preterm. JAMA Netw Open. 2024;7(1):e2352394.
24. Houben NAM, Fustolo-Gunnink S, Fijnvandraat K, Caram-Deelder C, Carrascosa MA, Beuchée A, et al. Red blood cell transfusion in European neonatal intensive care units, 2022 to 2023. JAMA Netw Open. 2024;7(9):e2434077.
25. Franz AR, Engel C, Bassler D, Rüdiger M, Thome UH, Maier RF, et al. Effects of Liberal vs restrictive transfusion thresholds on survival and neurocognitive outcomes in extremely low-birth-weight infants: the ETTNO randomized clinical trial. Jama. 2020;324(6):560–70.
26. Kirpalani H, Bell EF, Hintz SR, Tan S, Schmidt B, Chaudhary AS, et al. Higher or lower hemoglobin transfusion thresholds for preterm infants. N Engl J Med. 2020;383(27):2639–51.
27. Deschmann E, Dame C, Sola-Visner MC, Fustolo-Gunnink SF, Guyatt GH, Patel RM, et al. Clinical practice guideline for red blood cell transfusion thresholds in very preterm neonates. JAMA Netw Open. 2024;7(6):e2417431.
28. Yurtsever N, Jacobs JW, Booth GS, Schwartz J, Park YA, Woo JS, et al. A multi-institutional survey of apheresis services among institutions in the United States. J Clin Apher. 2024;39(4):e22138.
29. CASGEVY (exagamglogene autotemcel), suspension for intravenous infusion. Package Insert [Internet]. Vertex Pharmaceuticals Incorporated 2024 [cited 2025 Apr 16]. Available from: https://www.fda.gov/media/175481/download?attachment
30. LYFGENIA® (lovotibeglogene autotemcel) suspension for intravenous infusion. Package insert [Internet]. bluebird bio, Inc. 2023 [cited 2025 Apr 16]. Available from: https://www.fda.gov/media/174610/download

31. Leonard A, Weiss MJ. Hematopoietic stem cell collection for sickle cell disease gene therapy. Curr Opin Hematol. 2024; 31(3):104–14.
32. Leonard A, Sharma A, Uchida N, Stroncek D, Panch SR, West K, et al. Disease severity impacts plerixafor-mobilized stem cell collection in patients with sickle cell disease. Blood Adv. 2021;5(9):2403–11.
33. Lozano M, Charry P, de Pablo-Miró M, Salas MQ, Martínez C, Suárez-Lledó M, et al. Role of extracorporeal photopheresis in the management of acute and chronic graft versus disease: current status. Bone Marrow Transplant. 2024;59(9):1209–14.
34. Inamoto Y, Kato K, Kawakita T, Onishi Y, Matsuoka K i, Shiratori S, et al. An open-label study of belumosudil, a selective ROCK2 inhibitor, as second or subsequent line of therapy for steroid-dependent/steroid-resistant chronic GVHD. Am J Hematol. 2024;99(10):1917–26.
35. Wolff D, Cutler C, Lee SJ, Pusic I, Bittencourt H, White J, et al. Axatilimab in recurrent or refractory chronic graft-versus-host disease. N Engl J Med. 2024;391(11):1002–14.
36. Kühne L, Knöbl P, Eller K, Thaler J, Sperr WR, Gleixner K, et al. Management of immune thrombotic thrombocytopenic purpura without therapeutic plasma exchange. Blood. 2024; 144(14):1486–95.
37. Frangoul H, Locatelli F, Sharma A, Bhatia M, Mapara M, Molinari L, et al. Exagamglogene Autotemcel for severe sickle cell disease. N Engl J Med. 2024;390(18):1649–62.
38. Locatelli F, Lang P, Wall D, Meisel R, Corbacioglu S, Li AM, et al. Exagamglogene Autotemcel for transfusion-dependent β-thalassemia. N Engl J Med. 2024;390(18):1663–76.
39. US Food & Drug Administration. Approves First Gene Therapies to Treat Patients with Sickle Cell Disease [Internet]. FDA. 2024 [cited 2025 Jun 7]. Available from: https://www.fda.gov/news-events/press-announcements/fda-approves-first-gene-therapies-treat-patients-sickle-cell-disease
40. Perica K, Jain N, Scordo M, Patel R, Eren OC, Patel U, et al. CD4+ T-cell lymphoma harboring a chimeric antigen receptor integration in TP53. N Engl J Med. 2025;392(6):577–83.
41. Srivastava A, Abraham A, Aboobacker F, Singh G, Geevar T, Kulkarni U, et al. Lentiviral gene therapy with CD34+ hematopoietic cells for hemophilia a. N Engl J Med. 2025;392(5):450–7.
42. Cohn DM, Gurugama P, Magerl M, Katelaris CH, Launay D, Bouillet L, et al. CRISPR-based therapy for hereditary angioedema. N Engl J Med. 2025;392(5):458–67.
43. Center for Drug Evaluation and Research. FDA grants accelerated approval to lifileucel for unresectable or metastatic melanoma [Internet]. FDA. FDA; 2024 [cited 2025 May 13]. Available from: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-lifileucel-unresectable-or-metastatic-melanoma
44. Sarnaik AA, Hamid O, Khushalani NI, Lewis KD, Medina T, Kluger HM, et al. Lifileucel, a tumor-infiltrating lymphocyte therapy, in metastatic melanoma. J Clin Oncol. 2021;39(24): 2656–66.
45. AMTAGVI (lifileucel) suspension for intravenous infusion. Package insert [Internet]. Iovance Biotherapeutics, Inc. 2024 [cited 2025 Apr 16]. Available from: https://www.fda.gov/media/176417/download?attachment
46. Ruiz JM, Hughes SD, Flores M, Custer B, Ingram M, Carvajal S, et al. Neighborhood ethnic density and disparities in proximal blood donation opportunities. Transfusion. 2024; 64(6):1008–15.
47. France CR, France JL, Ysidron DW, Martin CD, Duffy L, Kessler DA, et al. Blood donation motivators and barriers reported by young, first-time whole blood donors: examining the association of reported motivators and barriers with subsequent donation behavior and potential sex, race, and ethnic group differences. Transfusion. 2022;62(12):2539–54.
48. Raykar NP, Raguveer V, Abdella YE, Ali-Awadh A, Arora H, Asamoah-Akuoko L, et al. Innovative blood transfusion strategies to address global blood deserts: a consensus statement from the blood delivery via emerging strategies for emergency remote transfusion (blood DESERT) coalition. Lancet Glob Health. 2024;12(3):e522–9.

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