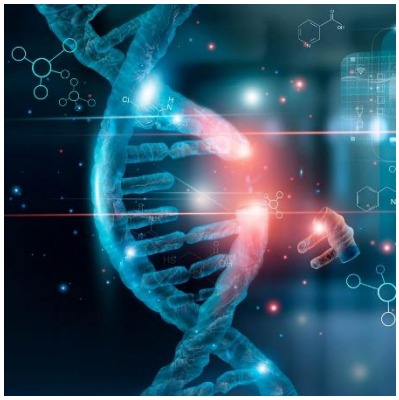
Spring 2022 PLUS Articles



How to Investigate those Pesky Serologic Weak D Samples

When typing a patient for the RhD antigen, hospitals have been forced to convert a non-binary result into a positive or negative for purposes of entry into the electronic health record as well as for selection of blood products including Rh immune globulin (RhIG). RhD is not unique amongst blood group antigens in demonstrating a property by which, in some individuals, the antigen phenotype is weakly positive. It may also type positive with one reagent or methodology used for antigen typing while typing negative with another. Since alloimmunization to RhD is clinically significant, both in the context of pregnancy and transfusion, it is critical to manage patients with serologic weak D or RhD typing discrepancies appropriately.

It has been known for more than 30 years that the RHD gene is the source of much genetic variation that leads to variant antigens. The RhD antigen is complex and is comprised of many epitopes, the portions of the antigen that are bound by antibodies. Panels of monoclonal anti-D reagents can be used to show epitope loss. These antigens are typically categorized as weak, partial or DEL. The term “weak” when initially applied to RhD variants, was used to indicate that though the number of antigen copies present on the red blood cell surface was likely lower than normal; however, the epitopes that are detected with anti-D reagents were thought to be intact. The term ‘partial” when applied to RhD variants indicates that one or more of the epitopes has been destroyed or altered. The DEL phenotype describes red cells on which the RhD antigen (which may have been altered or lost epitopes), can only be detected by use of adsorption-elution techniques.

Since establishing this naming convention, some weak D types have been associated with allo-anti-D formation. Also, the RhD antigen in DEL phenotypes may or may not have all epitopes intact. Addtionally, some RHD alleles discovered by molecular approaches with no available information about alloimmunization were classified as weak or partial based on the location of the amino acid changes and the predicted impact on epitopes. The use of the term **D variant** has been suggested to describe any RhD antigen different from that encoded by the reference RHD allele, without requirement to have structural or clinical data for classification.

Prior to 2015, a phenotype was considered “weak D” if testing yielded a negative result at immediate spin but a positive result with the indirect antiglobulin test (IAT). This phenotype had been referred to as D^U positive, but this term is no longer utilized. For the last 50 years or so, women who typed weakly positive with anti-D reagents were managed as RhD+. However, over the last 25 years, we have gained a better understanding of the genetic backgrounds of individuals in whom RhD type is not equivocal, as well as the clinical implications.
A survey of hospitals conducted in 2012 by the College of American Pathologists that generated responses from 3100 hospitals showed a lack of standardization for handling patients with serologic weak D.

In 2015, an interorganizational team representing AABB, CAP, ABC, ARC, ACOG published a commentary redefining a “serologic weak D” phenotype result with a strength of reactivity less than or equal to 2+, without specifying methodology or reagent type, or a subject with a discrepant type, which could involve current vs historic type.

This article summarized decades of research and laboratory findings and provided a workflow for when a hospital blood bank should consider using *RHD* genotyping to resolve a serologic weak D type. The approach is designed to precisely identify patients at risk of RhD alloimmunization and therefore candidates for Rh immunoprophylaxis or D negative red cell units for transfusion. A financial analysis indicated that this approach could be cost saving, though the greater benefit would arise from better portability of personal health information and/or a national electronic health record.

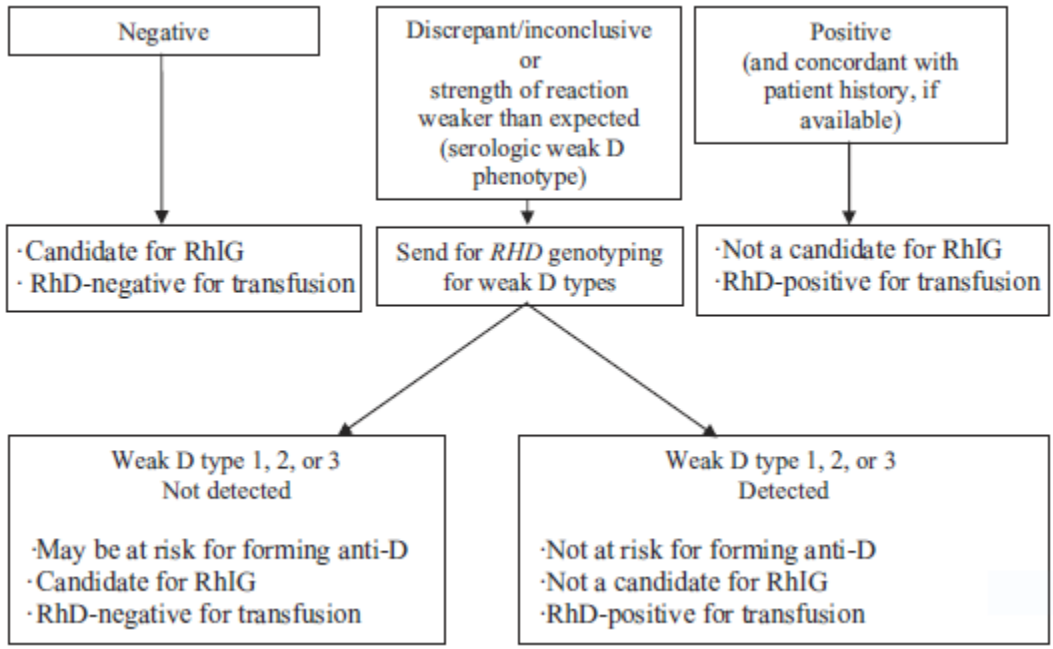


Figure 1. Algorithm for resolving serologic weak D phenotype test results by RHD genotyping to determine candidacy for RhIG and RhD type for transfusion

A joint statement by AABB, American Red Cross, ABC, CAP (https://www.cap.org/) later that year recommended implementation of the workflow in women of child-bearing age. Since then, many hospitals have been unsure of how to operationalize this recommendation. One large urban hospital evaluated three criteria and showed (in collaboration with the American Red

Cross National Molecular Laboratory (NML)) that two provided excellent specificity for identifying samples that express RhD variants. Another hospital recently published their approach (also in collaboration with the American Red Cross NML) focused on obstetrics patients. Both studies demonstrate that discordant results with two test methodologies or anti-D reagents can effectively identify patients expressing D variants and that RHD genotyping can differentiate these patients into those at risk and those not at risk for allo-anti-D formation.

These studies highlight two important findings. First, subjects who express partial D can present with a serologic weak D phenotype. This finding should give those managing hospital blood banks pause if their policy would classify patients who type weakly with anti-D reagents as RhD+ since some of these patients may be at risk of forming allo-anti-D. Second, automated antigen typing instruments can result partial D subjects as D+ such that their risk of alloimmunization may be undetected. This also should concern blood bankers, since this finding would suggest that some patients who may be at risk of allo-anti-D formation are going undetected. This is especially concerning for women of child-bearing age and especially in women of African descent, in whom the partial D phenotype is most common.
In 2020, the interorganizational team reconvened to recommend that blood banks consider a lab value of “serologic weak D” an incomplete result. They recommend that the sample be tested, typically at a molecular reference laboratory, to determine alloimmunization risk. Specifically, RHD genotyping is used determine if the subject expresses a D variant, and if so, the identification of the variant is used to make an assessment of alloimmunization risk that can aid the clinical team regarding transfusion and immunoprophylaxis candidacy.

Margaret Keller, PhD

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- It's Time to Phase Out" Serologic Weak D Phenotype" and Resolve D Types With RHD Genotyping Including Weak D Type 4 WA Flegel et al Transfusion 2020. 60 (4), 855-859

- Experience with RHD* weak D type 4.0 in the USA CM Westhoff et al Blood Transfusion 2019. 17 (2), 91

- Strategies to identify candidates for D variant genotyping X Luo et al Blood Transfusion 2018. 16 (3), 293

- Financial implications of *RHD* genotyping of pregnant women with a serologic weak D phenotype S Kacker et al Transfusion 2015. 55 (9), 2095-2103

- It’s time to phase-in RHD genotyping for patients with a serological weak D phenotype
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- How do I manage Rh typing in obstetric patients? Haspel RL & Westhoff CM. Transfusion 2015,55:470-4.

- How I manage donors and patients with a weak D phenotype. Flegel, WA, Curr Opin Hematol 2006,13:476–483.

- Tentative model for the mapping of D epitopes on the RhD polypeptide J P Cartron et al. Transfus Clin Biol. 1996;3(6):497-503.

Margaret Keller, PhD

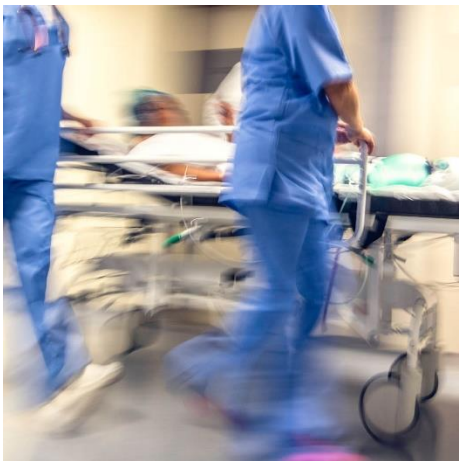
Additional Resources

- **AABB Joint Statement** on Phasing-In RHD Genotyping for Pregnant Women and Other Females of Childbearing Potential with a Serologic Weak D Phenotype: https://www.aabb.org/docs/default-source/default-document-library/positions/statement150722.pdf?sfvrsn=f4f44c30_6

- **American Red Cross Immunohematology Reference Lab Testing (IRL) Website**: https://www.redcrossblood.org/biomedical-services/blood-diagnostic-testing/immunohematology-reference-lab-testing.html

- **American Red Cross Molecular Testing Website**: https://www.redcrossblood.org/biomedical-services/blood-diagnostic-testing/molecular-testing.html

- **American Red Cross SUCCESS Webinar**: All Things Rh and The Rh Blood Group System, accessible at SuccessEducation.Redcross.org.



Low Titer Group O Whole Blood: Back to the Future

Traumatic injury claims over 5 million lives each year, making it the leading cause of mortality in people younger than 45 years of age. Treatment is extremely time sensitive as most deaths occur within two hours of injury. Blood is key for patient survival and typically type O blood is used since transfusion is often required before the patient's blood type is known. Type O positive red cells are the usual default for most patients, however females of childbearing potential (FCP) and children are most often given O negative blood. This measure is taken to prevent formation of anti-D which can potentially cause hemolytic disease of the fetus and newborn (HDFN) in future pregnancies.

Treatment has increasingly included low-titer group O whole blood (LTOWB) as an alternative to component therapy of red cells, plasma, and platelets. This practice is largely based on the military experience of lowered risk of death from bleeding with its use. The ease of transfusing one product rather than three lowers the number of donor exposures, increases the speed of availability, and simplifies product storage to a single repository site –all of which are benefits of LTOWB. Whole blood product is stored refrigerated to support red blood cell shelf-life needs. This has two beneficial effects: the growth of any bacteria present is slowed and platelet hemostatic function is enhanced.

Although large, randomized control trials comparing LTOWB to standard blood component therapy are limited, some observational studies have suggested the product is safe and is associated with equivalent clinical outcomes compared to standard component therapy. In one study the outcomes of 135 patients who received LTOWB (median 2 units) were compared to an equal number who received individual blood components. No significant differences were observed between the two groups in in-hospital mortality, 24-hour mortality, hospital and intensive care unit lengths of stay or number of RBCs transfused. Furthermore, the time to normalization of elevated plasma lactate levels tended to be shorter among the LTOWB recipients.

The overall number of blood transfusions has decreased in recent years, yet the demand for O negative blood continues to increase. One of the biggest challenges in providing whole blood to the than 70 trauma centers in the United States is the lack of sufficient blood donors. Whole

blood for this purpose must be from donors with type O negative blood. Considering that only 7% of the general population has this phenotype, along with the fact that less than10% of the estimated 38% eligible people donate, one can see how adequate inventories of O negative blood are hard to maintain.

Other requirements for making LTOWB further limit the number of possible donors. To lower the risk of Transfusion Related Acute Lung Injury (TRALI), the donor must be male or a never-pregnant female, which excludes an estimated 25% of available donors. They must have low-titer anti-A and anti-B antibodies [for the American Red Cross the titer must be less than 1:200], which removes another 2-5% of donors from consideration. Finally, donors must not have taken aspirin in the last 48 hours to preserve platelet function, another factor limiting the available blood donor pool for LTOWB collections.

The American Red Cross began making LTOWB in 2018 with a demand that has steadily increased since then.

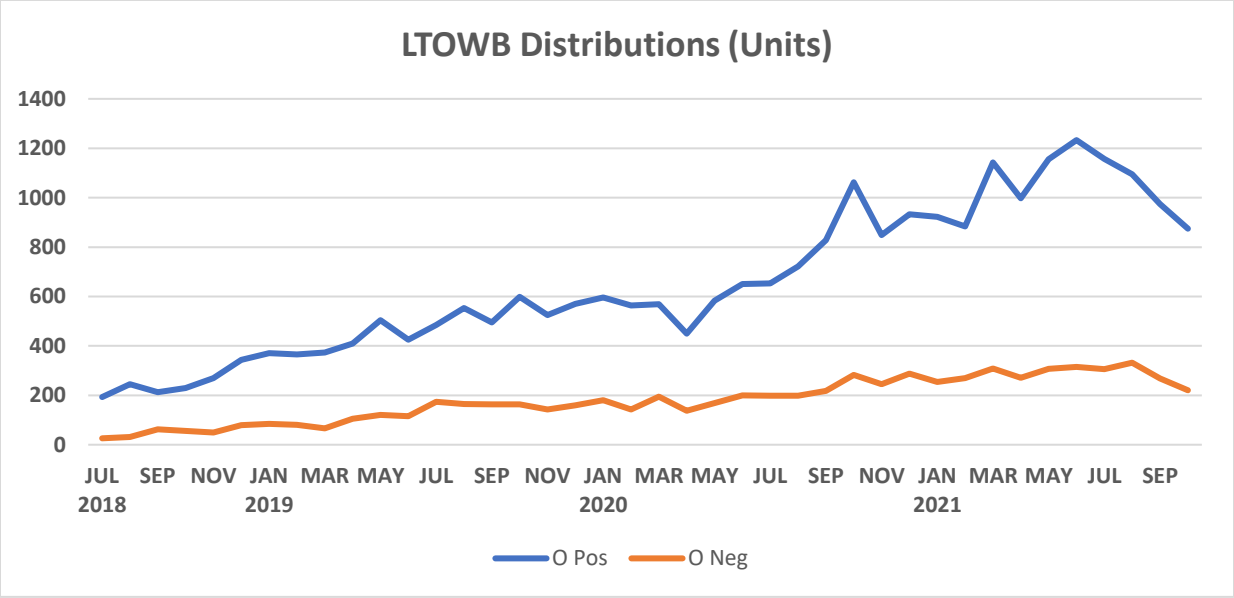


Figure I LTOWB Distributions July 2018 – September 2021

The average fraction of O negative packed red blood cells provided to hospitals is 12-13%, but the percent of O negative LTOWB is more than 23% of the LTOWB requested. Given the limited group O negative donor pool, this level of use will make it challenging to meet ongoing and increasing demands. Of the 17 largest hospital users of Red Cross LTOWB with transfusion protocols for FCP, about a third will transfuse O positive LTOWB; a third will only use O negative LTWOB; and the remaining third will only use O negative red cell components.

Several recent papers have suggested expanding the use of O positive blood for traumatic injury in females of childbearing age. This is based upon consideration of the high rate of death due to traumatic bleeding as contrasted with the low estimated long-term risk of the possible effects of anti-D on for pregnancy. The recent commentary by Dr. Marla Troughton and Dr.

Pampee Young in the June issue of *Transfusion* suggests that the following should be considered when weighing the use of O positive versus O negative LTOWB: immediate risk of dying versus the lower risk of anti-D to future pregnancy; overall risk of red cell antibody formation versus risk of dying; the fact that most trauma patients are male; and the need to manage the scarcity of O negative blood. The article concludes with a call to the transfusion medicine and trauma communities to work together to perform a consensus risk assessment and to develop standardized transfusion protocols for use of O positive LTOWB in the adult trauma population. The ultimate goal is to ensure all have access to this potentially superior LTOWB product, while maintaining sufficient supplies of O negative components for those who require this limited resource.

Marla Troughton, MD

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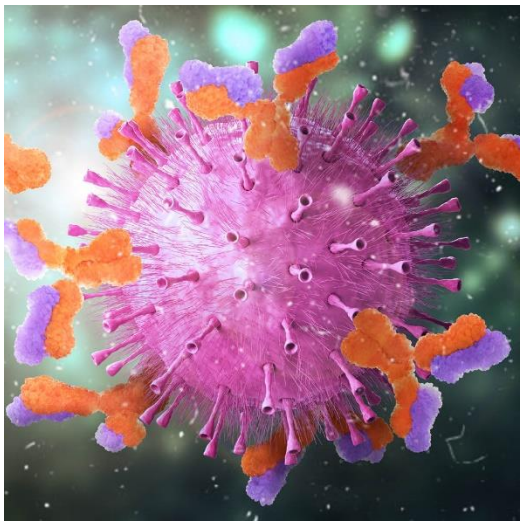
- It is time to reconsider the risks of transfusing RhD negative females of childbearing potential with RhD positive red blood cells in bleeding emergencies. Yazer MH et al Transfusion. 2019;59:3794–9.

Additional Resources

- **American Red Cross 'A Compendium of Transfusion Practice Guidelines' publication** – Chapter Low Titer Group O Whole Blood: https://www.redcrossblood.org/content/dam/redcrossblood/rcb/biomedical-services/components/compendium_v_4.0.pdf
- **American Red Cross Blood Product Offerings Websi**te: https://www.redcrossblood.org/biomedical-services/hospital-customers/blood-products-andservices.html
- A**merican Red Cross 'Hospital Partner Resource Guide' publication** – Blood Products for Transfusion listing: https://www.redcrossblood.org/content/dam/redcrossblood/hospital-page-documents/biomedproductsandservices_nov2020_rwv07_final.pdf
- **American Red Cross SUCCESS presentation**: **Whole Blood for Transfusion** Accessible at SuccessEducation.Redcross.org



The P1PK and GLOB blood group systems

This is an introductory review of the P1PK/(GLOB) blood group system, one of many carbohydrate-based blood antigen systems. The P1PK group consists of P_1, P^k, and NOR antigens. The GLOB group consists of P and PX2 antigens. The P1PK/GLOB blood group system is clinically important to transfusion and laboratory testing due to the significance of its antibodies, contributing to hemolytic transfusion reactions as well as hemolytic disease of the newborn (HDN).

The P1PK/GLOB blood group exists as glycosphingolipids. P, P^k, PX2 and LKE are high prevalence antigens expressed on the red cells of almost all individuals except in rare phenotypes (p, P_1^k, P_2^k). P1 and Pk are found on red cells, lymphocytes, granulocytes and monocytes.

Please refer to Figure 1 below to understand the relationships of the various antigens and how there is preferential production for certain antigens over others.

Phenotype	Antigens	Antibodies	Whites	Blacks
P_1	P_1, P, (P^k)	None	79%	94%
P_2	P, (P^k)	Anti-P_1	21%	6%
p	None	Anti- P, P_1, P^k	Rare	Rare
P_1^k	P_1, P^k	Anti-P	Very rare	Very rare
P_2^k	P^k	Anti-P, P_1	Very rare	Very rare

Table 1: Phenotypes with antigen and antibody frequency in Blacks and Whites.

The (P^k) antigen is written in parenthesis because when P antigen is present the P^k antigen is usually not detectable. The P blood group antigens are made by sequentially adding sugars to the precursors through the action of glycoslytransferases.

Lactosylceramide, also called ceramide dihexose (CDH, see Figure 1), is a glycolipid found in cellular membranes with many functions which include serving as a substrate for the generation of various other glycosphingolipids such as those listed in Figure 1.

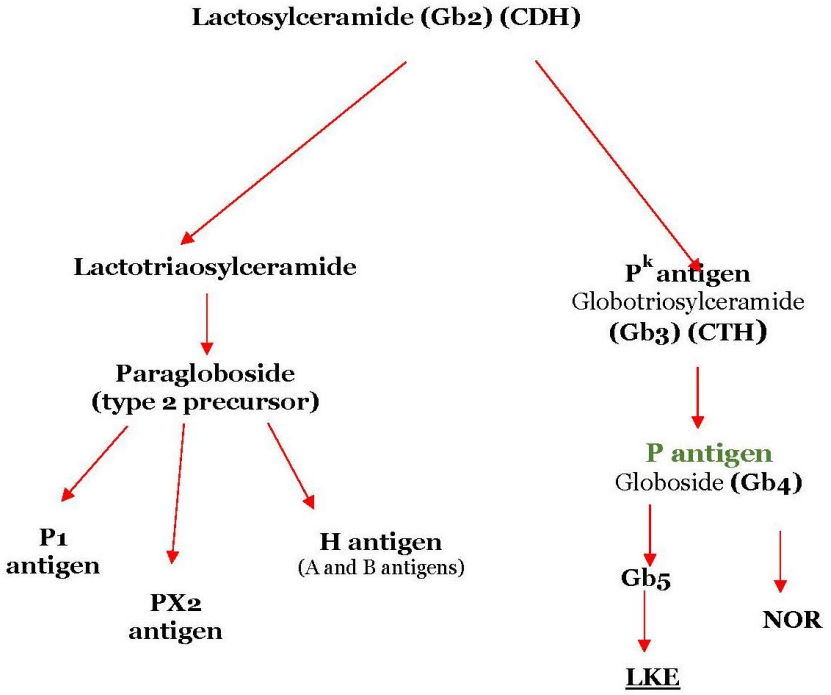


Figure 1. Biochemical overview of the P blood group system. The various added sugars and transferases required between each step are omitted for simplification.

The P_1 antigen is weakened with gestational age and is poorly developed at birth. For this reason, hemolytic disease of the fetus and newborn (HDFN) is not associated with anti-P1. It may take up to 7 years for full adult development. The Lutheran inhibitor In(Lu) reduces P_1 expression.

Anti-P_1 is common in P_1 negative persons and is usually IgM, and as such antibodies are generally not reactive at body temperature, anti-P_1 would not be considered clinically significant. Rarely there may be a case where anti-P_1 can react at 37^0C and bind complement. For antibody screening, one can prewarm the sample to prevent agglutination carryover. Antibody identification can be assisted by neutralization with certain substances, such as hydatid cyst fluid and pigeon egg white.

Anti-PP_1P^k is produced by all phenotype p (p null) individuals early in life, without the requirement of red cell sensitization, and reacts with all red cells except those of the p phenotype. Anti-PP_1P^k components are IgM and IgG. They react over a wide thermal range,

binding complement, and are potent hemolysins. Anti-PP_1P^k can cause severe hemolytic reactions and HDN. This antibody is associated with an increased incidence of spontaneous abortions in early pregnancy. When performing antibody identification, the anti-P, anti-P_1, and anti-P^k are separable through adsorption testing.

Anti-P is a component of anti-PP_1Pk in p phenotype individuals and is also found as a naturally occurring antibody in P^k individuals. Reactivity is similar to anti-PP_1P^k. Anti-P does not react with the P^k phenotype and although rarely seen is considered clinically significant. Anti-P has a correlation with spontaneous abortions as the placenta is rich in P antigen. Autologous anti-P is associated with paroxysmal cold hemoglobinuria. It is typically a transient condition secondary to viral infection in young children. Auto Anti-P is always IgG and a biphasic hemolysin, which requires a special test for detection.

Knowledge of the P/GLOB blood group systems enhances our understanding to identify the best blood matches for patients.

James Westra, MD

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Cold Stored Platelets: ‘CHIPS’ off the “Cold” Block?

Standard platelets are stored for up to 5 to 7 days at room temperature and are transfused for the treatment and prevention of bleeding. Room temperature storage presents a risk for bacteria to grow in platelet units, which limits the expiration date. The United States Food and Drug Administration (FDA) recently finalized guidance to reduce the risk of bacterial contamination in room temperature platelets which includes bacterial testing (e.g., large volume delayed sampling (LVDS)) and pathogen reduction mitigations (e.g., Cerus’s INTERCEPT technology).

Interest in cold storage (4°C) of platelets has been renewed because it may help to lower the risk of bacterial contamination and extend the shelf-life of platelets up to 14 days compared to room temperature (RT) storage. Cold stored platelets (CSP) have also been shown to reduce blood loss in actively bleeding patients; this is attributed to cold storage enhancing platelet clot properties (“Platelets stored at 4°C contribute to superior clot properties compared to current standard-of-care through fibrin-crosslinking. Room temperature platelets are still recommended for bleeding prevention because of their longer circulation in patients. In consideration of clinical circumstances, there are convincing data to justify the possibility of a dual inventory of cold-stored and room temperature-stored platelets.

THE CHIPS TRIAL (CHIlled Platelet Study)
The US (United States) military is funding a large clinical trial to evaluate the ability of cold stored platelets to prevent bleeding in adult and pediatric patients undergoing cardiac surgery compared to standard room temperature platelets. This study will also evaluate platelet efficacy after multiple storage durations (up to 21 days), the impact of pathogen reduction, and differences between platelet collection devices Trima and Amicus. The American Red Cross is one of three blood centers that will supply platelets for this research study over approximately the next three years. The goal of the trial is to determine whether platelets stored refrigerated (1-6°C) are non-inferior (or superior) in terms of hemostatic efficacy (prevention of bleeding) compared to standard room temperature (20°-24°C) stored platelets.

The study also aims to determine the maximum duration of cold storage that maintains non-inferiority; the trial will investigate increasing storage intervals up to 21 days with assessments done stepwise to evaluate platelet efficacy as each increasing storage time point is evaluated.

Dr. Phil Spinella of Washington University School of Medicine is the Primary Principal Investigator for this clinical trial. It is anticipated that the data generated in this trial with cardiac surgery patients will be generalizable to other patient populations with life-threatening hemorrhage to include traumatic injury, as well as gastrointestinal and obstetric bleeding. Should the trial support the transfusion of CSP these data could support FDA licensure of cold-stored platelets and contribute, through product shelf life, to enhancing the nation's platelet supply, particularly in rural areas.

Bethany Brown, PhD, MSCS

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- Exceptions and Alternative Procedures Approved Under 21 CFR 640.120a (https://www.fda.gov/media/86137/download)

Additional Resources

- American Red Cross Scientific Research Website: https://www.redcrossblood.org/biomedical-services/educational-resources/science.html
- American Red Cross SUCCESS Webinar: Cold Stored Platelets, accessible at SuccessEducation.Redcross.org
- Clinical Trials Website, Chilled Platelets Study: https://www.clinicaltrials.gov/ct2/show/NCT04834414

What It Means to Be Prepared

Diverse and complex disasters impact communities across our nation, which in turn affect blood providers and hospitals. Annually we have come to expect fires burning through neighborhoods, tornados ripping across the mid-west, and hurricanes plundering the coast. But despite the importance of preparedness, unexpected disasters prove to be a persistent challenge for responders.

The American Red Cross was put to the test on September 11, 2001 when modes of transport into the city of New York were shut down. Though the Red Cross was successful at moving over 10,000 units of blood in and around the city within 24 hours, the event evoked a shift in how to manage and prepare blood suppliers for emergencies across the nation, underscoring the importance of a safe and adequate supply of blood.

Since then, the Red Cross joined others to collaborate as members of the AABB Disaster Task Force and participated with other blood banking organizations, blood collector and hospital suppliers, and government agencies in the development of the AABB Disaster Handbook. Members are proactively engaged with FEMA and other state and federal agencies for disaster planning including developing scenarios for National Level Exercises and providing input on national emergency planning documents.

At an organizational level, the Red Cross has emergency readiness strategies to supply essential blood products and services around the clock, including during the need to respond to natural disasters and manmade events. These comprehensive plans manage both local and national disasters and include the coordination and communication of activities at the centralized Biomedical Service Operations Center (BSOC). The BSOC coordinates the organization's national network of blood regions to move aid to hospital customers where it is needed most. If the demand exceeds a local region supply, the BSOC directs other sites supply to fill a need. This can also involve transfer of operations from one site to another should a site be deemed inoperable.

In an emergency the Red Cross and other blood centers work together with Federal and State agencies, third-party contractors, Angel Flight, military airlift, State National Guard and law enforcement agencies.

At a community level, the Red Cross takes a proactive approach with hospital customers to collaborate on creating and testing disaster plans to ensure a more streamlined and effective response when the need arises. Additionally, educational opportunities are provided to our hospital partners through our SUCCESS program on leading industry practices, inventory management and recommendations for blood shortages that can be called upon during times of emergency.

As we continue to witness an unfortunate increase in man-made mass casualty events, there is a growing need for blood for trauma situations. It is the blood already on the shelves that saves in these types of events. To ensure we are ready to respond, the Red Cross must maintain active and ongoing recruitment efforts to be prepared for the unexpected.

Preparedness also requires innovation. Through product innovations, the blood supply can be enhanced. For example, Group O whole blood for transfusion, and other product advancements encourage sustainable practices necessary for a resilient blood supply to endure a disaster response.

None of this would be possible without the support of volunteer blood donors. Our nation has witnessed time and time again the willingness of generous individuals to respond that is dependent on a donor base built through community partnership and trust, and collaboration at many local and government levels.

In summary, a layered and integrated approach to preparedness by which blood suppliers join health care providers and the donor community equips the Red Cross to be in an evolving state of readiness to support blood product needs during emergency events.

Nejela Almohanna, BA

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Additional Resources

- AABB Disaster Resources: accessible at https://www.aabb.org/about-aabb/organization/disaster-response#2
  "Emergency Preparedness: Continuity of Operations" Webinar available on SuccessEducation.R

Low Yield Platelets: The New Normal?

The need for platelets is increasing, and blood centers including Red Cross, are actively working to optimize supply. Platelet distributions have been building for years due in large part to a growing cohort of hematology-oncology patients. This is in turn driven by an aging population as well as improved diagnostic methodologies with earlier chemotherapy, further driving platelet need . The recent December 2020 FDA Guidance *Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion* further constrains platelet inventories[1]. With the advent of pathogen reduced platelets and ever-improving ways to move them across the country the ability for centers to serve patient need has never been better. However, recent supply challenges call for additional measures.

The minimum yield specification of a standard apheresis platelet in the United States is greater than or equal to $3.0x10^{11}$ platelets. However, testing requirements can result in products that don't meet this threshold. For example, large volume delayed sampling (LVDS) requires that each split unit be tested separately by bacterial culture. The larger sampling volume taken from each unit, can result in units with fewer platelets that don't meet the standard specification. As a result, every month, hundreds of 'low yield platelet' units collected by Red Cross fall short of this threshold.

The use of low yield platelets has demonstrated through numerous clinical observational studies to be effective to treat actively bleeding patient needs. For instance, the PLADO study for platelet transfusions to hematology-oncology patients demonstrated comparable efficacy in maintaining hemostasis whether it was a low, standard, or high dose platelet unit. Low yield platelets (LYP) can be used safely without an increase in bleeding events, although they did result in decreased intervals between platelet transfusions[2]. A more recent platelet transfusion practice study, published in the journal Transfusion, provided results of a US hospital survey that found of the 481 institutions that responded, 28.3% transfused platelet units with a dose of less than 3.0×10^{11} when inventory was low and 9.1% transfused them routinely[3].

In September 2021 (less than three months after the Red Cross submission) the FDA granted the American Red Cross licensure of LYP. It should also be noted that the US has a higher platelet count threshold for what constitutes a standard apheresis platelet than other countries, specifically: The European Directorate for the Quality of Medicines (roughly equivalent to the FDA) has established a count of $2.0x10^{11}$ or greater as acceptable and in 2017 Canadian Blood Services (CBS) successfully petitioned to set the standard apheresis platelet specification in Canada at a minimum of $2.4x10^{11}$.

The Red Cross Medical and Scientific Offices have determined that LYP can be used safely and effectively in massive transfusion protocols (MTPs) and other active bleeding scenarios[2]. During times of acute supply shortages, a low yield platelet is preferable to no platelet at all for any patient.

In light of these findings and to ensure more platelets can be provided to meet patient need, Red Cross now distributes low yield large volume delayed sampling (LVDS) and pathogen reduced (PR) platelets units containing 2.8 $x10^{11}$ to $2.9x10^{11}$ platelets.

It should be noted that the LYP Red Cross distributes have counts substantially higher than the minimum threshold that qualifies a platelet as low yield; 2.8 $x10^{11}$ is greater than that of other blood centers and indeed exceeds what Red Cross had previously distributed as low yield.

In conclusion the enhanced availability of low yield platelets increases the number of platelet units in inventory, helping to alleviate intermittent shortages thereby further benefiting patients.

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References

- Bacterial Risk Control Strategies for Blood Collection Establishments and Transfusion Services to Enhance the Safety and Availability of Platelets for Transfusion. December 2020. https://www.fda.gov/media/123448/download

- Dose of Prophylactic Platelet Transfusions and Prevention of Hemorrhage Slichter SJ *et al.*. *NEJM* 2010; 362:600-13.

- A survey of US hospitals on platelet inventory management, transfusion practice, and platelet availability. Pandey S et al. Transfusion 2021; 61: 2611-20.