Carter BloodCare

Hospital Forum Minutes
"*Texas Proud*"
July 19, 2019

Attendees:

Guests: Krista Roberts, Texas Health Arlington Memorial Hospital; Tanya Robohm, Texas Health Dallas; Serelia Ball, Cook Children's Medical Center; Kristin Resch, Cook Children's Medical Center; Rick Melman, BSW All Saints Medical Center; Michael Martin, BSW All Saints Medical Center; Julia Blackburn, Texas Health HEB; Jessica Gandy, Texas Health Southwest; Tess Attard, Texas Health Clearfork; Ryan Phillips, Methodist Charlton Medical Center; Sarah Fluitt, BSW Sunnyvale; Simeonette Ballesteros, Methodist Dallas Medical Center; James Burner, MD, UTSW; Erin Portillo, Parkland; Jennifer Packard, Children's Health Dallas; Callie Carson, Lake Granbury Medical Center; Lesley Lee, BSW Heart Plano; Liang Shen, THR Fort Worth; Catrina Donnelly, THR Fort Worth; Cindy Yarborough, THR Fort Worth; Barbara McComas; BSW Carrollton; Annie Tabor, Methodist Mansfield Medical Center, Frances Compton, MD, Clements University Hospital; Dani Grant, BSW Heart Plano; Salma Thobani, BSW Irving; Vaishali Patel, UTSW; Caitlin Miller, BSW Heart Plano; Kevin Reynolds, CareFlite; Julie Jackson, Medical City Weatherford; Roberta Murfin, Children's Health Dallas; Laura Gilbert, Providence Health; Theresa Aguillard, Providence Health; Monica Phillips Bryant, Goodall Witcher HealthCare;

Carter BloodCare: Dr. Merlyn Sayers, Nancy Perez, Pam Boyd, Judy Thornburg, Dr. Todd Nishimoto, Sandy Wortman, Josey Keep, Marla Boren, B.J. Smith, Dr. Laurie Sutor, Dr. Geeta Paranjape, Rose Ongaro, Clint McCoy, Mike Newhouse, Marie Becerra, Andrea Sign, Dr. William Crews, Karen Himes, Veronica Moore

Pre-hospital Administration of Blood Products, Kevin Reynolds, Vice President & Chief Operating Officer, CareFlite

- ✓ Presentation handouts attached, review for comprehensive information shared.
  - Blood transfusion is a relatively new endeavor for CareFlite. It has been very rewarding, challenging and informative experience thus far.

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- This is our 40th year of service. We are the 8th air medical program in the Nation and the second in Texas. We hope to be around for another 40 years.
- Helicopter EMS: The Vietnam War era was really the launching point for civilian air EMS in the US. There was a definitive need to transport injured people from rural areas to the few locations where they could get the care they needed.
- 1970s to 1992: primarily not for private, consortium, of university and /or hospital based.
- In 2002, payment reform happened and it became more advantageous to enter the market. In the 17 years from 2002-2019, we have seen a 150% increase in the number of helicopters. The number of helicopters went roughly from 400 – 1000; 73% are owned by 2 of the largest private equity companies. Prior to 2002, the Air Medical program was seen as a cost center of the hospital. Industry is facing many challenges; news stories about outrageous air ambulance bills and charges? We anticipate that there is legislation that will make significant changes.
- CareFlite started with one helicopter, and it was primarily used by two hospitals, THHMFW and Methodist Dallas Medical Center; rotated monthly at each hospital.
- In 2016, equipped with 6 helicopters and 1 backup. The circles on the map indicate a 20 minute radius. The helicopters have a 150 mile range; they can travel to Abilene, Tyler and Palestine. They have had to travel to Houston, Oklahoma, and Austin, but only a rare occasion.
- From 2002- 2019, there has been a 387% increase (8-39 air helicopters) in the number of air medical helicopters in Texas. To put this into perspective, in that same time frame the Texas population has grown 37%. The capacity has outpaced the demand.
- Historical practice of trauma
  - Infuse large volumes of normal saline and other IV fluids to everyone
  - Use of anti-shock trousers
  - Ad-hoc blood products
  - Typically would take 30-45 minutes to get patients to the hospital
- Post PAMPer Study
  - Showed approximately a 10% decrease in 30 day mortality
  - EMS article (PAMPer study finding) published in NEJM
- Current protocol and practice launched December 2018
  - 2 units of liquid plasma and 2 units of PRBCs
  - All four units can be transfused in about 12-13 minutes
  - Average transport time to hospital is 12 minutes
- Challenges to conquer

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        - We live in the “about” world; blood bankers live in the “exact” world.
        - There is very little guidance for pediatric transfusions; must get the receiving facility physician to place the order.
    - We work together…
        - Sacred trust
        - 100% convinced that pre-hospital transfusions have a huge impact on patients.

Attendee questions/comments

- Q1: Associated cost?
    - Average air medical bill is $27,000.
    - Bill by mileage only.
- Q2: Does insurance cover the cost?
    - Yes and no
    - We are contracted with 2 of the big 4.
- Q3: Do you notify the receiving facility of the transfusion?
    - Yes. We make direct radio contact to the receiving facility as well as provide the traditional blood administration paper form.
- Q4: How do you deal with recalls? Who is responsible for any product recalls?
    - CareFlite is responsible to work with the hospital.
- Q5: Do you still have agreements at hospitals that provide ad-hoc blood products?
    - No. I am sure that it used to create significant stress to the blood bank staff.
    - Our goal (benchmark) is to be off the ground in six minutes. If we try to get ad-hoc blood products from the hospital blood bank, it can delay getting off the ground by 10-15 minutes; therefore, we do not practice getting ad-hoc products any longer.
- Q6: How does CareFlite know there is a patient need?
    - The EMS accrediting body CAAS has very clear definitions of who can activate:
        - Law Enforcement
        - Hospital
        - Fire/EMS
    - In the 1980s, we had “private listing”. This was where patients had chronic conditions and needed medical attention and we picked up the patient(s) in unsecured locations. This is no longer offered because of the danger involved in landing at unsecured locations.

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Cold Stored Platelets, Laurie J. Sutor, M.D., Vice President of Medical and Technical Services, Carter BloodCare

- ✓ Presentation handouts attached, review for comprehensive information shared.

Attendee Questions/Comments

- Blood bank may need to have dual inventory – room temperature stored and cold stored platelets to manage multiple patient needs.
- One facility indicated that they may choose to include in their MTP packs since all the products would be refrigerated.
- In patients with marrow suppression there may be increased usage of platelets.
- Group shared that physician education would be necessary prior to accepting this product. Suggestions included:
  - Present at hospital trauma/transfusion committee
  - Present at next Children's Transfusion Medicine Conference
  - Q1: Are the cold stored platelets apheresis?
    - Yes.
  - Q2: Will these platelets be priced lower than the regular apheresis platelet?
    - Good question, possibly.
  - Q3: Would they still be collected in the same bag?
    - Yes.
  - Q4: Will there be different ISBT product codes?
    - Yes.
  - Q5: How would aliquots be handled? Can you assume the same expiration as red cells?
    - Good questions, have not yet explored that.
  - Q6: How soon after collection would the platelets need to be cooled?
    - There is a defined time when the platelets should be cooled to reach 1-10°C following collection; approximately one hour after collection.

Thank the Donor™, Andrea Sign, Manager of Client Relations, Carter BloodCare

- ✓ Presentation handouts attached, review for comprehensive information shared

Attendee Questions/Comments

- Q1: Would you be willing to help train and educate on-site?
  - Yes, most definitely.
- Q2: Does access to the website require a username?
  - No. You can access now if you wanted to.
- Q3: Can you share examples of the tag and pamphlet?

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- Yes.

Open Discussion

✓ Presentation handouts attached, review for comprehensive information shared.

Attendee Questions/Comments:

Low – Yield Platelets

- We have not been asked to take low –yield platelets
  - Several hospitals indicated that they would be willing to accept these products.
- Should I get approval to use?
  - Recommend getting approval from the Transfusion committee, rather than at each event
- Can you bill for a low yield platelet?
  - Yes.

Advanced Diagnostic Laboratory Tests

- Do you have any thoughts on what volume of testing ordered for molecular and/or HLA typing is requested on outpatients?
  - Assume it would be a small percentage; approximately 5%.

A most sincere thank you to the presenters – this program exists because of your generosity to share your knowledge and experiences with the group.

And of course, thank you to all the attendees!

Pre-Hospital Administration of Blood Products

CareFlite is a 501(c)3 Not For Profit Air and Ground Ambulance Service Sponsored by:

Baylor Scott & White Health | IPS Health Network | Methodist Health System | Parkland | Texas Health Resources

The Symbol for Help & Hope In North Central Texas Since 1979

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Our Mission

To provide help and hope to all who need medical transportation in the communities we serve

Our Vision

CareFlite will be recognized for the safety and quality of its medical, aviation and ground services.

Our Core Values

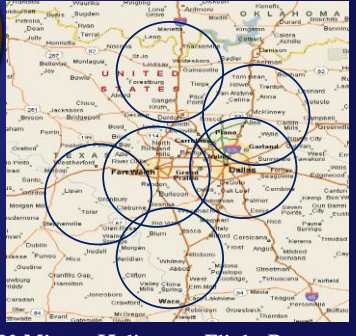
Safety ♥ Customer Service ♥ Quality
Urgency ♥ Fiscal Responsibility ♥ Teamwork

Helicopter EMS

Photo Courtesy of Sheldon Cohen

Oldest Joint Use Air Medical Program
(8th Oldest Air Medical Program)
in the United States

Helicopter Fleet
Replacement
Completed 2016
7 New Bell
Helicopters
$35 Million



20 Minute Helicopter Flight Response

CareFlite's Journey to Pre-hospital Blood Product Transfusion

- Historical Practice
- Evolution and the PAMPer Study Experience
- What Today Looks Like

Past EMS Practices

IV Fluids

PASG (MAST)

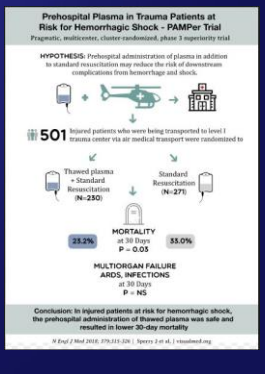
Ad hoc Blood Products

PAMPer Study

May 2014 – July 2017
First Collaboration with CBC
65 Eligible Enrollments

Study Results Drove Protocol

Launched Protocol December 2018



Current Protocol and Practice

Indications for Use

Controlled or Suspected Hemorrhage in the presence of SBP < 90 AND HR > 110
OR
Modified Shock Index (MAP/HR) of > 1.3

ACUTE **TRAUMATIC** Hemorrhage
OR
Hemodynamic Instability

TRAUMATIC BRAIN Injury (epidural, subdural, SAH)
OR
Spontaneous Intracerebral Hemorrhage

Each Helicopter Carries:

Liquid Plasma | O+ PRBC | Liquid Plasma | O+ PRBC

Current Protocol and Practice

- Pelican Credo ProMed Coolers
- Units are stored on the helicopter at all times

- HypothermX LG warmer
- Blood products are warmed to 38 ± 3 ° C
- 50-100 ml/min flow rate

Current Protocol and Practice

- TempTale dataloggers in all coolers and blood refrigerators
- Chemical indicators on each unit for immediate verification

Transfusion Statistics

- 33 transfusions since 12.27.2018
- 0 complications, transfusion reactions
- Loss due to temperature excursion = 0.5%

- 55% received (1) plasma
- 33% received (1) plasma and (1) PRBC
- No patient has received all (4) units

- Average Age: 50, 19 M – 14 F

- Scene Response: 64%
- Interfacility Response: 36%

- Trauma Related to MVC: 39%
- Auto-Pedestrian: 12%
- GI Bleed: 12%
- GSW, TBI, AAA, Stabbing: 37%

Outcomes and Quality Improvement

- Each transfusion case is evaluated by CQI Team, Chief Flight Nurse, and the Medical Director within 24 hours.
- Tracking 30 data points on each transfusion.
- Follow up with Trauma Services and Hospital CQI Committees to compile outcome data.

Remembering the Why

- Most compelling outcome to date is a pediatric auto-ped victim struck by a car travelling 60 mph. SBP 48, HR 164, MSI 3.9.
- CareFlite Flight Crew began rapid transport and initiated IV access, intubated, administered 1 plasma, 1 PRBC enroute to tertiary care center
- At transfer of care, SBP 100, HR 120, MSI 2.3.
- DX: Grade V splenic laceration (shattered spleen), Grade II L kidney laceration, Grade II liver laceration, multiple FX (pelvis, rib x 4, femur, clavicle, SAH, and 2 cerebral contusions.
- Disposition: IR and OR, ICU x 10 days, discharged to neuro-rehab and expected to make a full recovery.

Challenges to Conquer

- Blood Bank to EMS: Lost in Translation
- Road Trip!
- Intake from Blood Product Partner
- Storage vs Transport
- Flow Rates
- Pediatric Scenes

We work together…

as a team with each other and ground EMS in the best interest of each patient entrusted to us.

Questions?

Kevin Reynolds
kreynolds@careflite.org
972-339-4245

Cold Stored Platelets

Laurie J. Sutor, M.D.
Vice President of Medical and Technical Services
Carter BloodCare

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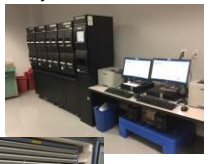
The Problems With Our Current Platelets

- **Stored at room temperature (20-24ºC) – risk of bacterial growth**
  - Short shelf life (5-7 days)
  - Need for bacterial testing or pathogen reduction
  - FDA is about to impose more bacterial testing rules
- **Constant agitation needed**



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Sepsis Attributed to Bacterial Contamination of Platelets Associated with a Potential Common Source — Multiple States, 2018

4 apheresis platelets in different states, 2018

Caused septic transfusion reactions

Acinetobacter* and *Staph saprophyticus

Despite bacterial testing, Verax, PR

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On The Horizon: Cold-Stored Platelets

- Stored at refrigerator temperature (1-6ºC)
- Potentially longer shelf life (14-17 days)
- No need for bacterial testing
- No need for agitation
- May have improved immediate hemostatic function because of platelet activation
- Cleared from circulation more quickly – not good for prophylactic transfusion

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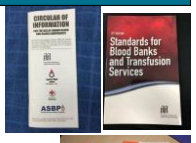
Why Haven't We Done Cold Platelets Before?



- Not AABB allowed
- Not in Circular of Information
- Not FDA approved as described
- FDA does allow 1-6º storage (21 CFR 640.24)
- FDA approved for limited indications – trauma only
- FDA approved for limited shelf life – 3 days

- The military is expecting an FDA variance for 14 day cold stored platelets for bleeding patients
- This should allow others to apply for the same variance without repeating the research

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Draft AABB Standards, 32nd Edition

5.19.7 Specially Selected Platelets

The BB/TS shall have a policy regarding indications for specially selected platelet requirements where applicable. Including but not limited to:

2) The use of cold stored platelets

Effective April 1, 2020 if approved as written.

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How Will Cold Platelets Help Us?

- **Improved platelet inventory flexibility**
- **We have already reduced platelet outdates to <3%**
  - Use of 6 day extended shelf life with retesting for bacteria
  - Use of aggressive inventory management with incentives
- **But we will have increased need for platelets in the coming months**
  - Increasing numbers of hematopoietic stem cell transplants
  - Maternal level of care designation in state of Texas

Of note: we will not be able to go to 100% cold platelets

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References

Cold platelets for trauma-associated bleeding: regulatory approval, accreditation approval, and practice implementation – just the "tip of the iceberg". JR Stubbs, SA Tran, RL Emery et al. Transfusion 2017; 57:2836-2844 (Mayo Clinic implementation).

Cold stored platelets in treatment of bleeding. TO Apelseth, AP Cap, PC Spinella et al. ISBT Science Series 2017; 12:488-495. (Review)

Studies of platelet concentrates stored at 22 C and 4 C. GA Becker, M Tuccelli, T Kunicki et al. Transfusion 1973; 13: 61-68. (classic article)

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Open Discussion

Listserv

- A Listserv is a method of communicating with a group of people via email. You send one email message to the "reflector" email address, and the software sends the email to all of the group's subscribers.
- Third party software
- Yes or No?

Low yield apheresis platelets

- Per regulatory standards, platelet yield (platelet count x volume) : $\geq 3.0 \times 10^{11}$
- Low yield platelets distributed by CBC (3/week)
- $2.8 - 2.9 \times 10^{11}$
- Appropriate usage of a low-yield platelet
- ISBT product codes (E4643, E4644, E4645, E5656; E4639, E4640, E4641, E4642)
- Reference Material: Example SOP and Letter to MD

Low titer O whole blood

- Not currently available
- Non-returnable
- Leukoreduced or non-leukoreduced

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Laboratory Date of Service :Advanced Diagnostic Laboratory Tests

In the CY 2018 Hospital Outpatient Prospective Payment System (OPPS)/Ambulatory Surgical Center (ASC) final rule published December 14, 2017, CMS established another exception to laboratory DOS policy for Advanced Diagnostic Laboratory Tests (ADLTs) and molecular pathology tests excluded from OPPS packaging policy so that the DOS is the date the test was performed, if certain conditions are met. This new exception to the laboratory DOS policy is effective beginning on January 1, 2018. Specifically, in the case of a molecular pathology test or an ADLT that meets the criteria of section 1834A(d)(5)(A) of the Social Security Act, the date of service must be the date the test was performed only if the following conditions are met:

The test is performed following a hospital outpatient's discharge from the hospital outpatient department;

The specimen was collected from a hospital outpatient during an encounter (as both are defined 42 CFR 410.2);

It was medically appropriate to have collected the sample from the hospital outpatient during the hospital outpatient encounter;

The results of the test do not guide treatment provided during the hospital outpatient encounter; and

The test was reasonable and medically necessary for the treatment of an illness.

If all of the requirements are met, the DOS of the test must be the date the test was performed, which effectively separates the laboratory test from the hospital outpatient encounter. As a result, the laboratory performing the test must bill Medicare directly for the test, instead of seeking payment from the hospital outpatient department.

https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/ClinicalLabFeeSched/Clinical-Lab-DOS-Policy.html

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Laboratory Date of Service: Advanced Diagnostic Laboratory Test

- August – October 2019
- Request if the patient encounter is an Outpatient
- Physician information
- New form on iweBB may be forthcoming for molecular and HLA requests

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Enrichment Lab 2019

- September 13, 2019
- 7am-4pm
- Texas Star Conference
- 6 hours of PACE® continuing education credit
- REGISTER Early - $50 registration fee
- http://www.cbcspecialtyservices.org/enrichmentlab/

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AABB Association Bulletin #19-02

- Recommendations on the Use of Group O Red Blood Cells

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Trivia

Question 1

What is the volume of the LRBC? I know it is less than 500 ml. Is it approximately 400 ml?

I have a question about volume of the red blood cells on the ISBT label of the unit. Most of the units have 500 ml on the ISBT labels but some of them have actual volume on the label, even though those are not the low volume units. I know because of different additives added to the units but can you explain me in detail.

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Trivia

Question 2

What is the turn-around-time for STAT/ASAP/Routine orders?

What is the turn-around-time for delivery of aliquotted blood in pediatric packs?

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Thank the Donor

What is Thank-The-Donor™?

Thank-The-Donor™ is an online, patient and donor relationship management tool that enables patients who have received a blood transfusion to send a special message to their blood donor(s) in an anonymous, user-friendly format.

How will this Program Work?

Step 1 – Products delivered with hearts on them

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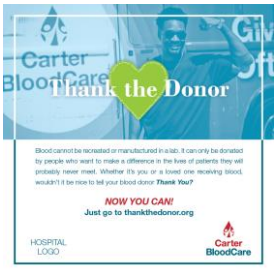
Step 2 – Recipient education

Front



Back

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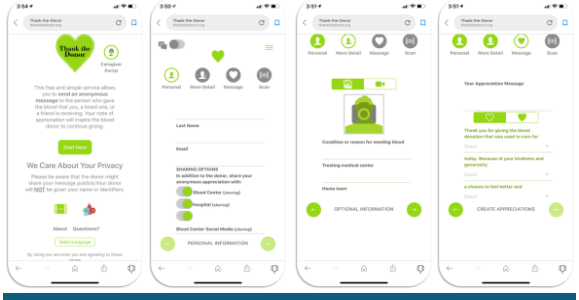
Step 3 - Creation



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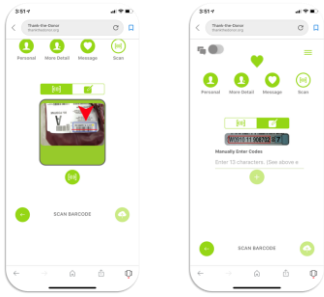
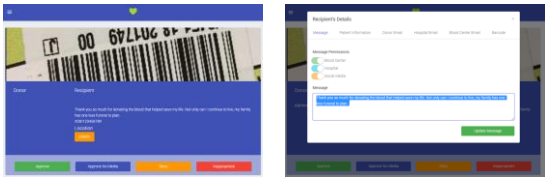
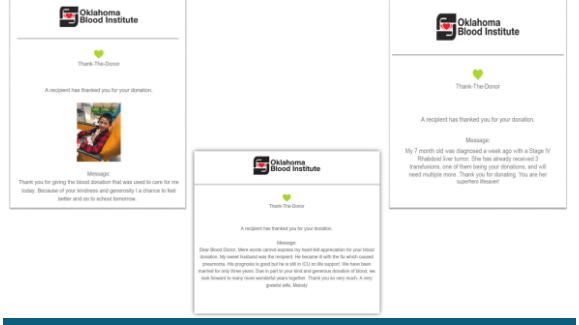
Step 4 - Submission



Step 5 –Approval



Step 6 – Message sent



Why Participate?

- Further creates a positive hospital experience
- Positive public relations opportunities
- Increase satisfaction survey scores
- Cobranding of program collateral
- Share stories internally with staff for a morale boost
- Inspire future donations to help provide a stable blood supply for patients
- Limited impact on hospital resources

How Soon Can We Get Started?

- Pilot
  Andrea Sign
  asign@carterbloodcare.org
  817-412-5825
- Across all customers

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Date: July 2019

To: Transfusion Service Medical Director

From: Carter BloodCare Medical Directors

Subject: Use of low-yield platelet units in time of shortage

We would like your help in utilizing low-yield platelet unit in times when apheresis platelets are in short supply and you have a patient that needs transfusion urgently. We are always working to maintain an adequate platelet inventory, but occasionally, especially around holiday times, temporary shortages may occur.

We sometimes have apheresis platelet units that do not quite meet the regulatory standard of 3×10^{11} platelets per bag. Often these lower-yield bags just barely missed the cut-off and have a count of 2.9 or 2.8×10^{11}. If we haven't told you over the phone what the exact bag count is, please feel free to ask. We do give you a substantial price discount on these units, so the clinical impact should be minimal, it is a platelet that is available in a time of need, and it is a financial win too. We should not be offering you any platelets with counts below 2.8×10^{11}.

If this practice is acceptable to you and your hospital, to help your blood bank staff take advantage of these units with minimal hurdles in the future, we suggest putting in place a standing order (or something similar) that gives them the ability to accept these units without calling for approval each and every time this situation might arise.

If you have any questions or concerns you would like to discuss, please feel free to contact Dr. Laurie Sutor at 817-412-5601 or Lsutor@carterbloodcare.org

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Example of Standing Policy

The blood bank technologists shall be empowered to accept into inventory apheresis platelets with a bag count between 2.8 X 10^{11} and 3 X 10^{11} when patients are in need of transfusion and no other platelets are available for transfusion. These platelets shall only be used if other platelets are not available, but may be issued to patients who urgently need transfusion.

Signed by Blood Bank Medical Director (or Transfusion Committee)

Advancing Transfusion and Cellular Therapies Worldwide

Association Bulletin #19-02

Date: June 26, 2019

To: AABB Members

From: Michael Murphy, MD, FRCP, FRCPath, FFPath - President
Debra BenAvram - Chief Executive Officer

Re: Recommendations on the Use of Group O Red Blood Cells

Association Bulletins provide a mechanism for publication of documents that have been approved by the Board of Directors for distribution to individual and institutional members, such as:

- Standards that were adopted after publication of the most recent edition of *Standards*.
- Statements of AABB policy intended for distribution to members.
- Guidance, recommendations, and reports that have been developed by AABB Committees or National Office staff for distribution to members.

This Association Bulletin contains information and makes recommendations intended to decrease the over-reliance on group O Rh(D)-negative Red Blood Cells (RBCs). The recommendations provided are based on a review of current practice patterns, and the relative safety and feasibility of reducing group O Rh(D)-negative RBC use in specific patient populations. Hospitals and blood centers should work together to optimize the use of this precious resource; possible models for these collaborations are proposed. Although several important points are made in each section of this bulletin, the key recommendations are listed below.

Key Recommendations for Transfusion Services

1. Group O Rh(D)-negative RBCs should be reserved for three cohorts of females of childbearing potential: those who are group O Rh(D)-negative, those who are Rh(D)-negative requiring transfusion when type-specific blood is unavailable, and those of unknown blood type who require RBCs before the completion of pretransfusion testing.
2. Hospital transfusion services should closely monitor utilization of group O, Rh(D)-negative inventory, particularly during bleeding emergencies and during group O Rh(D)-negative shortages. Policies should be developed that describe when patients should be switched to Rh(D)-positive RBCs to avoid depletion of the group O Rh(D)-negative supply.
3. Hospitals should have protocols to expedite sample collection to quickly switch patients to type-specific blood upon completion of pretransfusion testing.

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Key Recommendations for Blood Centers

1. Collection facilities should work with hospital clients to develop reasonable targets for group O usage.
2. Collection facilities can work with hospital clients to develop ways to encourage optimal use of group O Rh(D)-negative RBCs.

Background on Use of Group O RBCs

Group O Rh(D)-negative RBCs may be safely transfused to recipients of any ABO Rh(D) type, which has led to a high demand for this limited resource. Utilization rates of group O Rh(D)-negative RBCs vary dramatically by practice setting. Factors that influence utilization rates include local availability of group O Rh(D)-negative units, available hospital and blood bank immunohematology testing services, and the variety and type of patient populations, among others.

Rural and/or smaller hospitals may stock only group A and O Rh(D)-negative RBCs to simplify inventory and decrease wastage, as these units are compatible with the majority of patient blood types.[1] This leads to a practice of transfusing more group O RBCs to non-group-O patients, as well as using group O Rh(D)-negative RBCs for non-group-O Rh(D)-negative patients.[2] Rural hospitals may also maintain proportionally larger group O Rh(D)-negative RBC inventories to avoid shortages during a bleeding emergency.[1,3]

Large hospitals commonly located in urban areas often require sizable inventories of group O RBCs to accommodate complex patient populations, including: neonates; stem cell transplant recipients; and patients requiring antigen-negative blood (i.e., sickle cell anemia and other commonly alloimmunized populations). Urban hospitals also use a proportionately large number of group O RBCs to care for trauma patients requiring emergent transfusion prior to blood group determination. Finally, larger hospitals may use proportionally more group O RBCs if they accept short dated units to avoid wastage due to expiration.[1]

In the United States approximately 6.9% of donors are group O Rh(D)-negative, yet the proportion of group O (Rh)D-negative RBCs transfused is higher, rising from 9.7% in 2013 to 10.8% in 2015.[4] The Choosing Wisely campaign[5] recommended that group O Rh(D)-negative RBCs should be reserved for group O Rh(D)-negative patients and females of childbearing potential. However, a recent study estimated that 44.5% of group O Rh(D)-negative RBC units used could have been replaced by group O Rh(D)-positive RBC units if age and gender factors were considered.[6] This overuse of group O Rh(D)-negative could lead to critical shortages, limiting the supply for patients who need them most.

Advancing Transfusion and Cellular Therapies Worldwide

Recommendations for Appropriate Group O Use

Recommendation 1: **Group O Rh(D)-negative RBCs should be reserved for three cohorts of females of childbearing potential: those who are group O Rh(D)-negative, those who are Rh(D)-negative requiring transfusion when type-specific blood is unavailable, and those of unknown blood type who require RBCs before the completion of pretransfusion testing.**[5]

Significant efforts should be made to avoid transfusion of Rh(D)-positive RBCs to females of childbearing potential (unless there is no alternative), as alloimmunization may cause hemolytic disease of the fetus/newborn during future pregnancies.

In emergencies, males and postmenopausal females should be given group O Rh(D)-positive RBCs,[7] then switched to type-specific RBCs as soon as testing is completed. In addition, group O Rh(D)-positive RBCs should be given to group O Rh(D)-negative patients in cases of significant surgical or medical bleeding when group O Rh(D)-negative cells are not available or are in short supply.[7] Under non-emergent conditions group O Rh(D)-negative males and females of no childbearing potential can also receive group O Rh(D)-positive RBCs when inventory conditions dictate, unless they are known to be alloimmunized to Rh(D).

Using Rh(D)-positive RBCs in Rh(D)-negative patients is generally a safe practice. The risk of alloimmunization is 21-26% for hospitalized Rh(D)-negative patients who have received at least one Rh(D)-positive RBC product in the setting of hemorrhage.[7-11] This risk decreases to less than 10% for marrow and solid-organ transplant patients on immunosuppressive regimens,[12-14] and it is 3-6% for patients with an unknown blood type receiving Rh(D)-positive RBCs in the emergency room setting. [7] The risk of an acute hemolytic transfusion reaction after receipt of an RhD-incompatible RBC unit is less than 1% in emergency settings,[15] and it is usually mild. Unlike acute hemolytic transfusion reactions caused by isohemagglutinins, D antibodies cause extravascular hemolysis, which is usually not associated with severe complications. In addition, alloimmunization to Rh(D) will not be a clinical issue for the majority of patients who experience only a single lifetime transfusion episode.

Switching to Rh(D)-positive is discouraged for some Rh(D)-negative patient populations, as they are more heavily transfused. Patients who require chronic transfusion support, pediatric patients undergoing multiple surgical procedures, or patients destined for a stem cell transplant procedure should be maintained on Rh(D)-negative RBCs. Because most Rh(D)-negative patients in the United States are of the rr serotype (ce/ce), providing Rh(D)-negative RBCs will also mitigate the risk of alloimmunization to the C and E antigens, making it easier to find compatible units for future transfusions.

If a patient requires antigen-negative RBCs, the blood bank should try to provide ABO type-specific phenotyped RBCs. Even if group O antigen-negative RBCs are available, blood bank technologists should be trained to phenotype type-specific units instead. This may not always be

practical, especially in emergent settings or in patients with multiple alloantibodies. However, ensuring that blood bank technologists are using type-specific RBCs when possible will help reduce overall group O usage.

Hospitals supporting sickle cell patients generally try to match Rh (D, C, and E) and Kell (K) antigens prophylactically to prevent alloimmunization.[16] To avoid using Rh(D)-negative RBCs, hospitals should maintain an inventory of CEK-negative Rh(D)-positive RBCs for patients who require C-negative or E-negative RBCs. Approximately 17.6% of donors of European ancestry are Rh(D)-positive CEK-negative vs. 3% who are Rh(D)-negative CEK-negative, making this an obvious choice for inventory control. Some blood centers are providing Rh(D)-positive CEK-negative RBCs to hospitals at discounted rates to decrease Rh(D)-negative RBC use.

Recommendation 2: **Hospital transfusion services should closely monitor utilization of Rh(D)-negative inventory. Policies should be developed that describe when patients should be switched to Rh(D)-positive RBCs to avoid depletion of the group O Rh(D)-negative supply.**

Benchmark data are not widely available to guide hospitals in what is appropriate group O Rh(D)-negative usage. Therefore, hospitals should conduct periodic audits of group O blood use to better understand their utilization patterns and develop policies for appropriate usage.

Recommendation 3**: Hospitals should have protocols to expedite sample collection to quickly switch patients to type-specific blood upon completion of pretransfusion testing.[2]**

Group O RBCs should be used for group O patients and for emergent/initial transfusion support in patients of unknown blood group. Other situations for which use of group O RBCs may be justified for non-group-O patients include neonatal transfusions, solid-organ transplant patients with passenger lymphocyte syndrome, and during stem cell transplantation, as discussed below.

Patients should be switched to type-specific RBCs as soon as pretransfusion testing is completed and compatible blood is available. Verification of the patient's ABO type requires either a second specimen drawn at the current visit or, if available, comparison of the current testing result with blood bank records. Alternatively, some institutions use electronic patient verification to eliminate the need to test a second separately drawn specimen to confirm the recipient blood type. This practice is permitted by AABB *Standards for Blood Banks and Transfusion Services*[17] (Standard 5.16.2.2, 31st ed.) and described in guidance from the Food and Drug Administration.[18]

Because a group O RBC unit with additive solution (AS) contains approximately 10-15 mL of plasma,[19] there is a small risk for hemolysis in non-group-O recipients due to the passive transfer of anti-A and anti-B isohemagglutinins. Although the plasma volume in a non-AS RBC unit (e.g., a CPDA unit) is greater than 10-15 mL, the risk of hemolysis remains small. Such plasma-

related hemolysis has been reported, but it is exceedingly rare.[20] Innate protective mechanisms include A and/or B antigen expression on the vascular endothelium; and A and/or B substance found in the plasma of secretors.[21] These additional antigens adsorb some of the isohemagglutinins and thus prevent hemolysis. As a result, switching to type-specific units should be safe, even after a patient has been massively transfused with group O RBCs.

The importance of early sample collection must be clearly communicated to those responsible for patient care. Transfusion services should work with their hospital transfusion committees and clinical champions to make sure this message is relayed to care teams. In addition, transfusion service staff should be fully engaged in minimizing group O Rh(D)-negative usage, as this can significantly improve inventory management.

Group O Use: Specific Patient Populations

Trauma and Mass Casualties

For safety reasons, group O RBCs are appropriately administered during the initial resuscitation of massively hemorrhaging patients of unknown ABO type.[22] Administering uncrossmatched RBCs in this setting is serologically safe, i.e., hemolysis is unlikely to occur even in recipients with RBC alloantibodies against antigens on the uncrossmatched RBCs.[23] As stated above, group O Rh(D)-positive should be given to males and females without childbearing potential in emergency settings. Switching to type-specific RBCs should be

accomplished once pretransfusion testing is complete; however, safety measures are essential when transfusing type-specific RBCs, especially in busy emergency departments with multiple trauma resuscitations.

The provision of uncrossmatched blood for transfusion in air and/or ground ambulances is an increasingly common aspect of planning for trauma care. The use of group O Rh(D)-positive RBCs should be considered for these settings as most patients in this setting are either males, or females of no childbearing potential.[24]

With regard to mass casualty events (MCEs) and disaster preparedness, the AABB Interorganizational Task Force on Domestic Disasters and Acts of Terrorism recommends an estimate of 3 units of group O RBCs per admission for transfusion needs.[25] When faced with a large number of patients simultaneously, transfusion services should prioritize uncrossmatched group O Rh(D)-negative RBCs for females presumed to be of childbearing potential. Identification of such patients in the format of the hospital emergency medical record numbering system has been suggested to facilitate allocation of group O Rh(D)-negative RBCs.[26] Event demographics may accentuate this concern: in the 2017 Manchester concert bombing, 69% of the

admissions were female and 39% were ≤21 years old.[27] As in other settings, rapid typing of MCE patients is very helpful, subject to check-typing requirements.

Neonatal and Pediatric Patients

Isohemagglutinins (anti-A, anti-B) present in neonates are passively acquired from the maternal circulation and usually disappear by two months of age,[28] therefore testing neonatal ABO forward type is all that is required. Further, these patients are thought to be at low risk of forming red cell alloantibodies. Therefore, type-specific RBCs may be issued but only after it is clearly shown that potential maternal isohemagglutinins will not be incompatible. According to AABB *Standards*, either the maternal ABO group must be compatible with the donor RBCs, or the neonatal serum or plasma must be tested for anti-A or anti-B at the antiglobulin phase to detect IgG isohemagglutinins.[17] Because both tests present logistical challenges, it is often easier to issue group O RBCs to neonates. In addition, using small aliquots from a single group O RBC unit can efficiently provide compatible RBCs for multiple patients. As a result of these safety considerations, routinely switching neonates to type-specific RBCs is unlikely to occur, and the small quantities used are unlikely to have a material impact on group O Rh(D)-negative RBC inventory.

Stem Cell Transplantation

Major, minor, or bidirectional ABO incompatibility is present in a large number of stem cell transplants.[29] Due to the potential effect of isohemagglutinins on engraftment and hemolysis, transfusion strategies focus on minimizing the use of RBCs that are incompatible with donor, recipient, and passively transfused isoagglutinins.[30] As a result, group O RBC usage is considerable in the transplant setting.

Preengraftment

Published recommendations for transfusion strategies have separated the pretransplant (Phase I), immediately postinduction/transplant (Phase II), and postengraftment (Phase III) periods.[31] Within this rubric, specific institutional transfusion recommendations may vary in practice. For example, transfused RBCs during Phase I may be compatible with both recipient and donor isohemagglutinins or simply compatible with the recipient.[32,33] Importantly, each institution should establish clear guidelines defining the beginning and end of each phase.

Postengraftment

It is generally recognized that a transplant recipient with complete RBC engraftment can be transitioned to a donor type-specific transfusion strategy (Phase III), but the timing of this switch currently varies among institutions.[29] Most agree that a recipient's forward and reverse typing

must show no evidence of recipient red cells or isohemagglutinins before switching to donor-compatible RBCs. Even in those cases, molecular chimerism assays may show evidence of incomplete marrow engraftment and the potential for graft failure.

Also, ongoing RBC transfusion requirements may be considered as evidence of potential graft failure in the future.[31] Transfusion services should create guidelines specific to their workflows and the risk of graft failure in their particular transplant populations.

Recommendations for Blood Collectors to Reduce Overuse of Group O RBCs

Blood collection facilities can benefit from continuing to work with hospital transfusion services to limit unnecessary group O Rh(D)-negative use. Enhanced demand translates into increased collections, causing a never-ending cycle of recruitment and donation for group O Rh(D)-negative donors. The nearly incessant recruitment causes a generalized weariness in these donors, while frequent donation may increase the risk of iron depletion. Blood collection facilities should develop a plan to reduce group O Rh(D)-negative usage that includes education, targets based on benchmarks, and formal surveillance of group O usage. Implementation of this plan will require clear communication of (bilateral) expectations between blood center and hospital.

Collection facilities are an important source of information for community hospitals. Blood center representatives should provide guidance for improved group O Rh(D)-negative use in the form of live presentations, webinars and printed literature. Blood center representation on transfusion committees also helps with guidance and communication.

Reasonable targets for group O usage should be established. The inventory par levels for group O RBCs should be based on the best available evidence about the indications for their use and the specific circumstances of the hospital or system under consideration. Blood collection facilities and their customers should work together to define explicitly appropriate and inappropriate practices.

Blood centers can provide hospitals with information on the genotype or extended phenotype of RBC donors as part of an overall group O Rh(D)-negative reduction campaign. This will allow hospital blood banks to allocate type-specific RBCs quickly for alloimmunized patients, and also switch from Rh(D)-negative to Rh(D)-positive when it is feasible.

Collection facilities can also work with hospitals to establish surveillance programs to closely monitor and audit group O use. It may be useful to base any remediation program on such site-specific surveillance, and, in an iterative process, review the impacts of remedial interventions and modify them as needed over time. The consequences and “enforcement” procedures for nonadherence to predefined use guidelines will need to be determined prospectively, and bilaterally.

Education and surveillance are not likely to be adequate alone. Collection facilities can consider the use of both financial incentives and penalties to encourage optimal use of group O Rh(D)-negative RBCs to protect this critical clinical resource. Overuse should be defined and agreed upon. Many models may be acceptable including the following:

- Centers and hospitals should collaboratively establish inventory processes and procedures that reduce the risk that group O RBCs, near expiry, are transfused out-of-group solely to avoid outdate. This might, for example, involve structured stock rotation schedules to support optimal transfusion practices.
- Centers may wish to develop and implement financial strategies to help address group O RBC overuse. Issues to consider include the products' unique value, the need for conservation, and the marginal cost of finding, recruiting, and drawing the next group O donor.
- Clinically appropriate triage algorithms that assign specific decision-making responsibility and authority can be developed to control group O RBC use under both routine and shortage conditions (i.e., either short-term or extended shortfalls as might occur in the face of adverse local conditions, disasters or a pandemic, respectively).

General Recommendations from This Bulletin

A more extensive list of recommendations for transfusion services and blood centers is listed below.

Transfusion Services

- Patients should receive ABO type-specific blood for routine transfusion:
  - Switch patients receiving group O RBCs urgently to type-specific units as soon as possible, following completion of type and screen testing and verification of ABO group.
  - Implement an electronic patient verification system to eliminate the need for a second verification of the patient's blood type prior to providing type-specific blood (see Standard 5.16.2.2).[17]
- Group O Rh(D)-negative RBCs should be reserved for transfusion of group O Rh(D)-negative females of childbearing potential and in bleeding emergencies for females of childbearing potential with unknown blood group.
- A transfusion should never be withheld from a bleeding patient. If group O Rh(D)-negative units are not available for a female of childbearing potential then the benefit of an emergent Rh(D)-positive blood transfusion must be balanced against the risk of alloimmunization.
- Clinical conditions may dictate the need for a temporary switch to group O Rh(D)-negative RBCs for some patients. This remains within a medical director's purview.

- Hospital transfusion services should have policies describing when patients should be switched to Rh(D)-positive RBCs to avoid depletion of the group O Rh(D)-negative supply.
    - Group O Rh(D)-positive RBCs may be given to group O Rh(D)-negative patients for significant surgical or medical bleeding.
    - Group O Rh(D)-negative critical care patients over age 50 can be switched to group O Rh(D)-positive RBCs for routine transfusions.
    - Hospitals should have protocols in place to expedite sample collection during bleeding emergencies so that patients can promptly be switched to type-specific blood upon completion of pretransfusion testing.
- Hospitals should closely monitor utilization of group O Rh(D)-negative inventory during bleeding emergencies and perform periodic audits of group O blood use to better understand utilization patterns.
- Hospitals should develop reasonable goals for group O Rh(D)-negative usage and work together with blood collection facilities to design feasible plans that meet specific hospital needs.
- Provision of group O Rh(D)-positive RBCs should be considered for air and/or ground ambulance and/or emergency department transfusions because most patients in this setting are either males or females of no childbearing potential.

Blood Collection Facilities

- Blood center representatives should provide guidance to their client hospitals for better group O Rh(D)-negative use in the form of live presentations, webinars, and printed literature. AABB plans to develop materials to help with this effort.
- Collection facilities should work with hospital clients to develop reasonable targets for group O Rh(D)-negative usage.
- Collection facilities should provide genotype or extended phenotype information for RBC units of all blood types to encourage type-specific usage.
- Collection facilities should work with hospitals to establish surveillance programs to closely monitor and audit group O use.
- Collection facilities can work with hospital clients to develop ways to encourage optimal use of group O Rh(D)-negative RBCs.

Conclusion

Blood collection facilities have dealt with an overall reduction in the demand for RBCs, but the pressure to maintain sufficient group O Rh(D)-negative inventory continues to grow. Group O Rh(D)-negative volunteers make up 6.9% of the donor base but their RBCs are often used for patients of other ABO types simply because it is safe and convenient. Taking steps to implement some of the recommended changes in practice can reduce the collective dependence on group O

Rh(D)-negative use and avert potential shortages that could affect patient safety. Working together, collection facilities and hospital transfusion services can develop a mutually beneficial program that safely reduces group O usage.

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