An international survey on the use of low titer group O whole blood for the resuscitation of civilian trauma patients in 2020

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There is increasing military and civilian evidence demonstrating that early intervention with blood products in patients with traumatic bleeding saves lives.[1–4] One component that provides balanced resuscitation is whole blood (WB). When it is provided to a recipient whose ABO group is unknown, such as in the pre-hospital phase of resuscitation or early in the patient's in-hospital course, it must be group O to avoid immediate hemolytic reactions, and the plasma must contain levels anti-A and -B that are below the institute's maximum titer threshold.[5] Units fulfilling these criteria are known as low titer group O WB (LTOWB), and its use is increasing. A survey conducted in 2018 revealed 15 hospital systems in the USA and a hospital in Norway that were using LTOWB, primarily for the resuscitation of trauma patients.[6] The survey was repeated in 2019 and the number of respondents from the USA increased to 24.[7] The 2019 iteration of the survey included two international air ambulance services that transfuse LTOWB in the pre-hospital setting in Israel and the United Kingdom. To appreciate the number of hospitals and emergency providers that are currently using LTOWB, and the scope of their practice vis-à-vis LTOWB, the THOR (Trauma, Hemostasis & Oxygenation Research network)/AABB working party conducted another survey of the known American and international services that are either currently using LTOWB or are in the advanced planning stages of implementing an LTOWB program as a guide for other hospitals that are considering implementing a similar program (Table 1).

Amongst the 37 respondents (Table 2), there were nine hospitals that did not have a limit on the number of LTOWB units that could be administered to traumatically injured patients, although at four of these hospitals there was a requirement for the blood bank physician to communicate with the trauma team about the patient's ongoing blood needs at some point during the resuscitation. Seven of these nine centers provided the number of LTOWB units in their hospital's inventory, and the average was 17 with a standard deviation (SD) of 7 units. Note that the 31st edition of the AABB Standards, Standard 5.27.1.1, requires each transfusing center to have a policy that dictates the maximum number of LTOWB units that a patient can receive; an institute's policy of having no maximum number of units would satisfy this Standard as long as the policy is codified in writing. At the remaining 28 sites that have a limit on the number of LTOWB units per patient, the average number of units that could be administered per patient was 4 units with an SD of 2 and a range of 2-8 units. The maximum number of LTOWB units at the pre-hospital providers in this survey (Magen David Adom in Israel, and Barts Health NHS Trust/London air ambulance; two and four units, respectively) were not included in this average as it is expected that the number of LTOWB units transported in a rescue vehicle would be fewer than those available in a hospital.

Interestingly, 8 out of 37 (22%) of the respondents indicated that LTOWB could be administered to both trauma and non-trauma patients who are massively bleeding, while 2 out of 37 (5%) respondents indicated that LTOWB could be used for both trauma and selected non-trauma massive bleeding patients whose bleeding etiologies included bleeding in the operating room. The remaining 27 out of 37 (73%) respondents indicated that LTOWB was only administered to trauma patients.

Consistent with previous surveys, more than half of the respondents (23 out of 37, 62%) use leukoreduced LTOWB. The most common definition of low titer anti-A and -B continued to be <200 followed by <50. The hospital in Norway uses two requirements to qualify a low titer unit: IgM titer <250 and IgG titer <500 (listed as "Other" for Question 6 in Table 1). Of the 29 respondents who indicated the method by which the anti-A and -B titers were performed on their LTOWB units, the majority (22 out of 29, 76%) used the saline tube without anti-human globulin (AHG) technique;

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TABLE 1. Demographic information on the LTOWB programs at 16 hospital respondents to the THOR/AABB survey

1. How many units of LTOWB can a patient receive?	
Average (SD) at the 28 sites with a limit on the number of LTOWB units	4 (2), range (2-8)
Number of sites without an upper limit of LTOWB units	5
Number of sites without an upper limit of LTOWB units, but the transfusion and trauma physicians must communicate about the patient's ongoing needs	4
2. What type(s) of patient(s) qualify(ies) to receive LTOWB?	
Trauma patients only	27 (73)
Trauma and all non-trauma massive bleeding recipients	8 (22)
Trauma and selected non-trauma massive bleeding patients	2 (5)
3. What is the RhD type of the LTOWB supplied to males?	
RhD+ only	17 (46)
RhD- only	8 (22)
RhD+ and RhD- are available	12 (32)
4. What is the RhD type of the LTOWB supplied to females?	
RhD+ only regardless of her age	10 (27)
RhD- only regardless of her age	7 (19)
RhD- if she is of reproductive age (defined locally), D+ if she is older	11 (30)*
RhD+ LTOWB is only provided to females older than reproductive age (defined locally)	6 (16)
LTOWB is not provided to females of any age	3 (8)
5. Is the LTOWB leukoreduced?	
Yes	23 (62)
No	14 (38)
6. What is the maximum titer of antibodies in LTOWB?	
<50	6 (16)
<100	5 (14)
<128	1 (3)
<200	20 (54)
<256	4 (11)
Other	1 (3)
7. By what method is the anti-A and -B titer determined?	
Saline tube without anti-human globulin (AHG)	22 (76)
Saline tube with anti-human globulin (AHG)	2 (7)
Automated instrument	4 (14)
Gel card with and without anti-human globulin (AHG)	1 (3)
8. What is the maximum storage length for LTOWB units for use in trauma patients?	
10 days	2 (5)
14 days	13 (35)
21 days	20 (54)
35 days	1 (3)
Other	1 (3)
9. If your center uses LTOWB in non-trauma patients, is the storage length the of the units the same as for trauma patients?	
Yes	8 (80)
No	2 (20)
If No to Question 9, please specify the maximum storage length of LTOWB units for use in non-trauma patients	35 days
10. What do you do with unused LTOWB units that exceed storage length for trauma patients?	
Discard it	21 (57)
Produce an RBC unit	13 (35)
Use it as LTOWB for non-trauma patients	2 (5)
Return it to blood supplier	1 (3)
11. Do you offer LTOWB for pediatric trauma or massive bleeding patients? (Do not include use in priming CPB pumps.)	
Yes	9 (24)
No	28 (76)
12. Please indicate if you monitor the following hemolysis parameters *specifically* in your LTOWB recipients. (Indicate all that apply.)	
Lactate Dehydrogenase (LDH)	15 (41)
Bilirubin (total, fractionated, unfractionated etc.)	17 (46)
Haptoglobin	14 (38)
Reticulocyte count	2 (5)
Urinalysis	4 (11)
Direct antiglobulin test (Coomb's test)	10 (27)
Creatinine or other kidney function tests	13 (35)
Other laboratory testing that is performed *specifically* on LTOWB recipients (please specify)	2 (5)
indentLevel="1"No laboratory monitoring for hemolysis is performed	12 (32)

(Continues)

TABLE 1. Continued

13. From where do you obtain LTOWB units?	
Collected in-hospital only	2 (5)
Purchased from blood supplier only	34 (92)
Blood collector responded to survey	1 (3)

* For Question 4: one hospital stocks both RhD+ and RhD- LTOWB and would transfuse RhD+ LTOWB to an RhD+ female of reproductive age once her RhD group becomes known.

one of these centers performs a 5-minute room temperature incubation before centrifugation.

Most of the respondents stored the LTOWB as such for either 21 days (20 out of 37, 54%) or 14 days (13 out of 37, 35%). In the 2018 survey, half (8 out of 16, 50%) of the hospitals discarded an unused LTOWB unit, while some (6 out of 16, 38%) produce an RBC unit once the LTOWB unit reaches its maximum storage length. These figures have remained stable at 21 out of 37 (57%) and 13 out of 37 (35%), respectively, in the current survey. Given that in the USA a special license is not required for a hospital to manufacture an RBC unit from an LTOWB unit as long as the RBC is transfused at that institution, it is surprising that more hospitals do not avail themselves of this waste mitigation strategy. One hospital keeps LTOWB units available in the pre-hospital setting for up to 14 days and if they are not used in that setting, they are added to the hospital blood bank's LTOWB inventory for trauma patients for up to 35 days. Another hospital uses LTOWB units for trauma patients for up to 21 days; after that time they can be used for up to 35 days for other bleeding patients such as those in the operating room (listed as "Other" for Question 8 in Table 1).

TABLE 2. Names of the participants in this survey

Advocate Christ Medical Center, Oak Lawn, Illinois.
Allegheny Health Network, Pittsburgh, PA
Barts Health NHS Trust/London air ambulance
Brooke Army Medical Center, San Antonio, TX
Cedars-Sinai Medical Center, Los Angeles, CA
Children's Hospital of Pittsburgh of UPMC, Pittsburgh, PA
Cincinnati University, Cincinnati, OH
Cooper University, Camden, NJ
Emory University, Atlanta, GA
Froedtert Hospital & the Medical College of Wisconsin, Milwaukee, WI
Haukeland University Hospital, Bergen, Norway
Hoxworth Blood Center & University Hospital, University of Cincinnati Academic Health Center, Cincinnati, OH
Intermountain Medical Center, Salt Lake City, Utah
Johns Hopkins University, Baltimore, MD
Los Angeles County Department of Health Services, California, USA
Massachusetts General Hospital, Boston, MA
Magen David Adom in Israel, Israel
Mayo Clinic, Rochester, MN
Miami Valley Hospital, Dayton, OH
Ohio State University, Columbus, OH
Penn Presbyterian Medical Center, Philadelphia, PA
Phoenix Children's Hospital, Phoenix, AZ
Scripps Memorial Hospital, La Jolla
St. Louis University hospital, St. Louis, IL
Tulane University, New Orleans, LA
UCHealth Memorial Hospital Central, Colorado Springs, CO
University of Alabama at Birmingham Medical Center
University of California Los Angeles, Los Angeles, CA
University of Minnesota Medical Center, M-Health
University of New Mexico, Albuquerque, NM
University of Oregon, Portland, OR
University of Pittsburgh Medical Center, Pittsburgh, PA
University of Pittsburgh Medical Center, Susquehanna, PA
University of Texas, Houston, TX
University of Texas, San Antonio, TX
University of Washington St Louis, St Louis, MO
Wake Forest University, Winston Salem, NC

Eight American hospitals and the Norwegian hospital offer LTOWB for use in traumatically injured children. One American hospital has changed their requirements for pediatric LTOWB eligibility in the interval between the 2018 and the current survey; previously pediatric patients at that institute had to be at least 3 years old and weigh at least 15 kg,[8] whereas the new requirement is only age ≥1 year old. This change was made to be able to provide LTOWB to more patients once the safety of transfusing LTOWB had been demonstrated at that institution. A second American health care system transfuses D+ LTOWB to traumatically injured children, both boys and girls, who are ≥5 years old in the pre-hospital setting only. Other eligibility criteria for administering LTOWB to children include weight >15, >20, >30 kg at three institutions, age ≥2 years old and weight ≥10 kg at an institution that transfuses only boys with LTOWB, age ≥1 in one of the air ambulance services, and a weight dependent dose (15-20 mL/kg) if the child weighs <35 kg at another American hospital. The Norwegian hospital does not have any requirements for qualifying pediatric recipients.

Finally, 12 out of 37 (32%) of the hospitals surveyed do not perform any degree of laboratory testing for hemolysis amongst the LTOWB recipients (Question 12 in Table 1).

This survey demonstrated the practice patterns for LTOWB in the USA and in several other countries. The practice remains quite variable in terms of how many units are available per patient, the definition of low titer anti-A and -B, and the storage length of the LTOWB units, and whether any testing for hemolysis occurs following LTOWB transfusion.

CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

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