New York State Trauma Advisory Committee

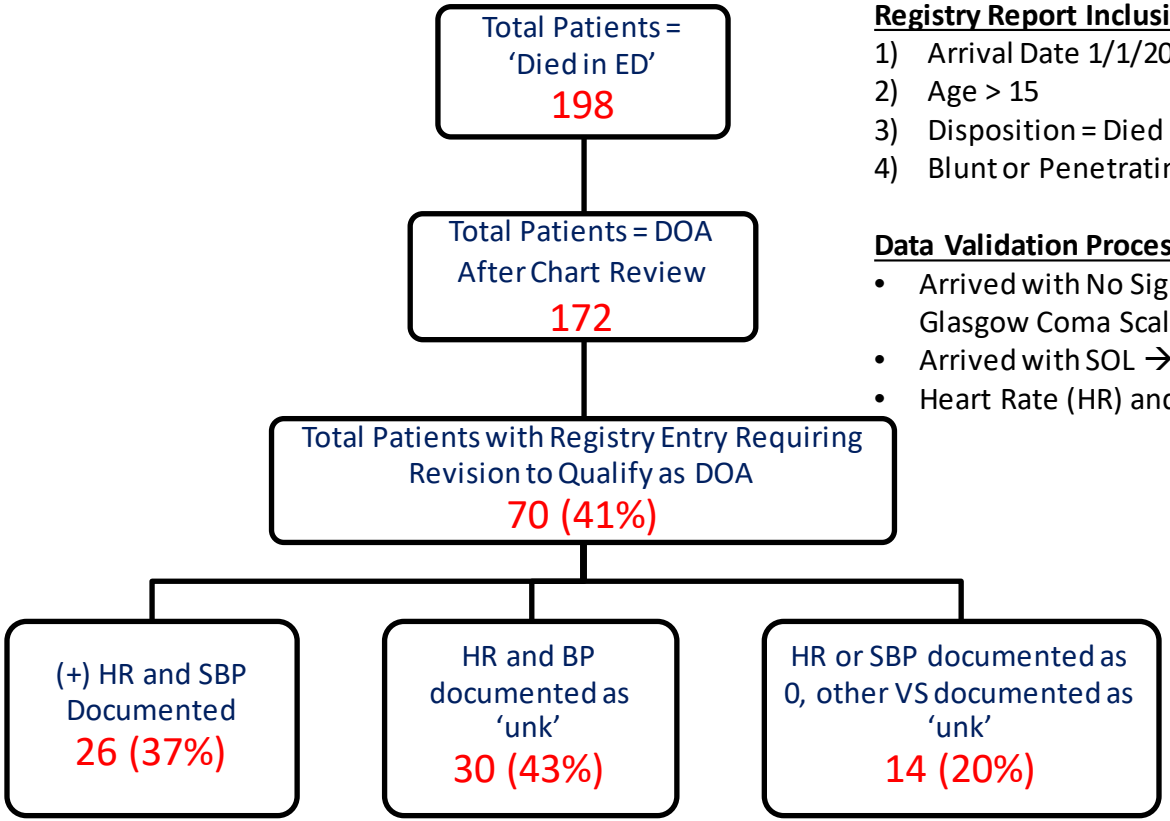
Performance Improvement Subcommittee

October 30, 2024

Agenda

- Select mortality review
  - Michael Vella, MD; Kate Dellonte, RN, BSN; Eric Klein, MD; Maggie Ewen, MS, PA-C
- *Back to the future for Mass Transfusion Protocols (MTP's)*
  - Eric Senaldi, MD
- Open discussion re: autopsy reports (time permitting)

‘Died In Emergency Department’ Data Validation



Registry Report Inclusion Criteria

1) Arrival Date 1/1/2018-8/15/2024
2) Age > 15
3) Disposition = Died in Emergency Department
4) Blunt or Penetrating Injury

Data Validation Process

- Arrived with No Signs of life (SOL) Heart Rate (HR) & Systolic BP (SBP) = 0, Glasgow Coma Scale Motor = 1) → No further review
- Arrived with SOL → Chart review to confirm
- Heart Rate (HR) and/or Systolic BP (SBP) = Unk → Chart review

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Blunt/Penetrating Trauma, Died in ED, Arrival 1/1/2018-8/15/2024

	DOA Case Review Data			DOA Registry Entry Data		
	Total Pts DOA (HR = 0, SBP = 0) *After Chart Review*	Total Registry Entry Req. Revision to Qualify as DOA	% Total DOA with Registry Entry	(+) HR **and** SBP	HR **and** BP = Unk	HR or SBP = 0, Other VS = Unk
2018	19	5	26%	2	2	1
2019	24	13	54%	2	7	4
2020	27	9	33%	2	5	2
2021	38	19	50%	9	7	3
2022	32	12	38%	5	3	4
2023	21	10	48%	4	6	0
2024	11	2	18%	2	0	0
Total	172	70	41%	26	30	14
Column Definition	*Total # of DOA following chart reviews*	*Total # of pts w/ registry data req. revision following chart reviews*	*# in Column 2/# in Column 1*	*Total # of pts who were documented incorrectly as having + vital signs despite being DOA*	*Total # of pts with both HR and SBP = unk in registry despite having documentable VS*	*Total # of pts with inconsistent documentation*

Trauma Quality Improvement Program Penetrating Mortality Deep Dive

Spring 2023

Total Patients = 9

- Registry entry req. revision = 7
  - HR = 1
  - SBP = 1
  - SBP and GCS M= 1
  - SBP and Additional Comorbids = 1
  - Additional Comorbids= 3

Total excluded from Trauma Quality Improvement Program report after review = 1

Spring 2024

Total Patients = 6

- Registry entry req. revision = 5
  - GCS M = 3
  - HR and SBP = 2

Total excluded from Trauma Quality Improvement report after review = 2

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Injury Characterization

>>Current chart documentation:

	AIS Description
1. BLE extremity deformities	*not specific enough to code an injury
2. open fx to LUE - the forearm is circled on the body diagram in the note	forearm fx- open
3. bilateral chest tubes placed- no further documentation	*not specific enough to code an injury

TOTAL ISS = 4

>>Examples of slightly more detailed chart documentation:

	AIS Description
1. bilateral femur deformities	femur fx- NFS
2. open fx to LUE - the forearm is circled on the body diagram in the note	forearm fx- open
3. bilateral chest tubes placed- rush of air noted	pneumothorax- NFS

TOTAL ISS = 13

Injury Characterization

	AIS Description
1. bilateral femur deformities	femur fx- NFS
2. open fx to LUE - the forearm is circled on the body diagram in the note	forearm fx- open
3. bilateral chest tubes placed- rush of air noted, with 500mL blood out	hemopneumothorax- NFS

TOTAL ISS = 18

	AIS Description
1. bilateral femur deformities	femur fx- NFS
2. open fx to LUE - the forearm is circled on the body diagram in the note	forearm fx- open
3. bilateral chest tubes placed- rush of air noted, 1000mL blood out	hemopneumothorax - major; GT 20% blood loss

TOTAL ISS = 25

Summary of Findings & Action Items

Findings

- Inconsistent clinical documentation leading to higher GCS M scores being entered in registry.
- HR and SBP entered as 'unk' with documented asystole or Pulseless Electrical Activity (PEA).
- (+) HR and SBP entered with documented asystole or PEA.
- Asystole or PEA documented but no Vital Signs (VS) (HR = 0, BP = 0/0) entered on flowsheet.
- Vital signs entered as 'unk' if not taken prior to ED departure even if set of VS documented within 30 mins in OR/ICU/IR.
- Injury documentation during trauma bay resuscitation not detailed enough to code injuries which would increase AIS/ISS.
- Comorbid not being thoroughly captured due to delay in chart merges of patient's actual chart and trauma chart.

Action Items

- Education – faculty, residents, nursing, registrars
- Standardizing registry entry
- Audits
- Documentation changes - Trauma consult note, Attending attestations
- Morning report discussion

North Shore University Hospital

Blunt/Penetrating Trauma, Died in ED, Arrival 1/1/2018-8/15/2024

	DOA Case Review Data			DOA Registry Entry Data				
	Total Pts DOA (HR = 0, SBP = 0) *After Chart Review*	Total Registry Entry Req. Revision to Qualify as DOA	% Total DOA with Registry Entry	(+) HR **and** SBP	HR **and** BP = Unk	HR or SBP = 0, Other VS = Unk	(+) HR **but** SBP = 0	HR = 0 **but** (+) SBP
2018	5	2	40%	0	2	0	0	0
2019	11	1	9%	0	1	0	0	0
2020	10	2	20%	1	1	0	0	0
2021	4	1	25%	0	0	0	1	0
2022	4	0	0%	0	0	0	0	0
2023	13	2	15%	0	1	0	0	1
2024	2	0	0%	0	0	0	0	0
Total	49	8	16%	1	5	0	1	1

NYC Health & Hospital - Bellevue

Blunt/Penetrating Trauma, Died in ED, Arrival 1/1/2018-8/15/2024						
	DOA Case Review Data			DOA Registry Entry Data		
	Total Pts DOA (HR = 0, SBP = 0) *After Chart Review*	Total Registry Entry Req. Revision to Qualify as DOA*	% Total DOA with Registry Entry	(+) HR **and** SBP	HR **and** BP = Unk	HR or SBP = 0, Other VS = Unk
2018	0	0	0%	0	0	0
2019	6	0	0%	0	0	0
2020	11	1	9%	0	0	1
2021	10	0	0%	0	0	0
2022	32	3	10%	0	0	3
2023	34	2	6%	0	1	1
2024	20	1	5%	0	0	1
Total	113	7	6%	0	1	6

*None changed whether or not patient reported DOA to TQIP

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Return of Spontaneous Circulation (ROSC)

- Patient arrives with no signs of life, ROSC obtained, then patient expires. How is this documented?

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Back to the Future for MTPs

Am I back in the 60's???

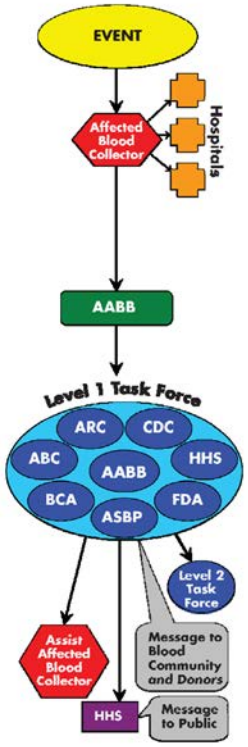
Eric Senaldi, MD

Deputy Chief Medical Officer, New York Blood Center

esenaldi@nybc.org 646-539-8988

Objectives

- Emergency Plans – National and Regional
- Does Rh matter for Red Blood Cells (RBCs)?
- Plasma – how much, what type, what temp?
- Titering to prevent hemolysis
- Whole blood – filtered, platelet sparing or not
- Platelets – cold or warm



RESPONSE PLAN FLOW CHART

Step 1. Affected Blood Collector (BC) Assesses Medical Need for Blood

- ✓ Contact local hospital customers and emergency services to determine impact of event, including:
  - Nature of emergency (e.g., disaster, terrorism)
  - Number of current and expected hospital admissions
  - Types of expected injuries
  - Potential effect on local donor base
- ✓ Gather information on local blood inventory levels from both BC and hospital customers.
- ✓ Calculate the medical need for blood for a nonbiological event based on three units of type O RBCs per current and expected hospital admissions resulting from the event (see Event Assessment Form).

Step 2. Affected BC Contacts AABB (ideally within 1 hour of event)

- ✓ Contact AABB (use redundant communication channels in order listed below):
  1. Land line: (800) 458-9388
  2. Cell phone: (240) 994-6700
  3. E-mail: nbe@aabb.org
  4. Text message: (240) 994-6700
  5. Satellite phone: (254) 377-3726
- ✓ Report medical need and local blood inventories.

Step 3. Interorganizational Task Force (TF) Conference Call

- ✓ AABB convenes a conference call with Level 1 TF members (Level 2 TF members included if necessary—see page 42 for a list of Level 1 and Level 2 TF member organizations).
- ✓ TF determines national strategy and coordination efforts, including:
  1. Message to blood community/donors
  2. Transportation and coordination of blood to affected BC
  3. Next steps until event is resolved
- ✓ AABB communicates decisions to Level 2 TF members.

Step 4. Implementation of Task Force Recommendations

- ✓ TF representatives communicate recommendations to their respective constituencies.
- ✓ TF distributes unified message to blood community and donors (e.g., joint press releases).
- ✓ TF coordinates message to the public with Department of Health and Human Services (HHS).

Nationwide Emergency Blood Plan

- Blood Center
  - Assess the need through local hospital and emergency services – type, number, effect on inventory and donors
  - Contact Association for the Advancement of Blood and Biotherapies (AABB)
  - AABB will create task force within the hour – government departments related to health, major blood collectors and membership organizations, military
  - Task force coordinates supplies & message
  - Hub and spokes system – major centers immediately ship to center in need, smaller centers backfill major shipping centers

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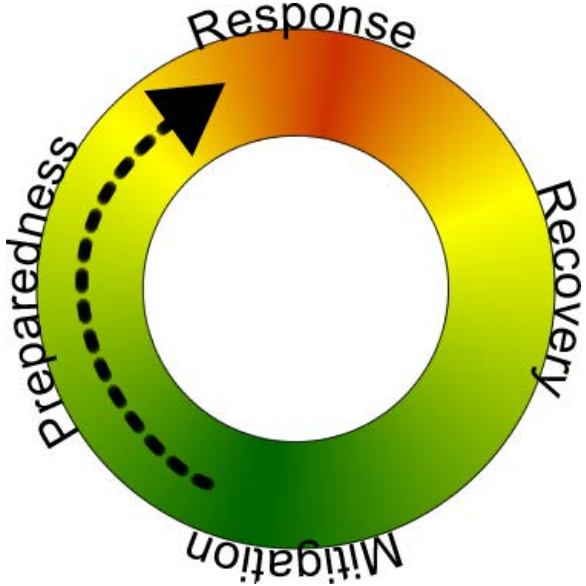
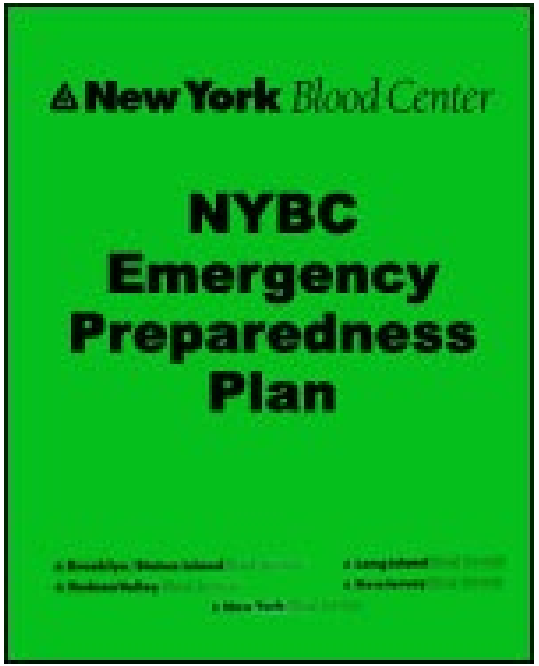
How Much Blood Do I Need per Estimated Casualty?

- AABB Disaster Operations Handbook recommends 3 units per casualty for planning purposes [A]
- More recent review of 32 articles involving mass casualty events using more than 50 rbcs [B]
  - Median trauma center use per patient, same event day 3.4 rbc, 2.4 plasma, 0.5 apheresis platelet
  - Next day use compared to original day 50% rbc, 28% plasma, 16% platelet
  - Planning purpose recommendation 6 rbc, 4 plasma, 0.5 apheresis

A. Vox Sang 2017; 112:648
B. Ramsey G. Vox Sang 2020; Jul;115(5) 358-366

Managing an Emergency – Four Phases





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On The Ground Preparedness

- Community Lifeline (hospitals, patients, donors)
- People (employees & families)
- Assets (property, equipment, inventory)
- Operation (mission critical services)
- Supply Chain (critical items, vendors)

9/11 Distribution

- Coming out of the summer with traditionally low inventory levels, and OR's at full blast post summer vacation
- Inventory 2500 O pos, 280 O neg
- Standing orders 2000 O pos, 325 O neg
- Planes hit the WTC
- Held standing orders
- Diverted 600 units to trauma centers
- Estimated trauma needs, plan for delays in testing and processing, ensure adequate supply
- Sourced 3000 O's in an hour with one phone call which arrived the next day
- Maintain communications with trauma centers

O+ vs O- RBCs

- Problem – not enough O negs, 6.5% in normal population
- vs. hospital usage of >10%
- Beth Israel Deaconess – Boston [A]
  - 268 patients in 10 year retrospective review of MTPs
  - 63% male, 23% female >50, 12%<50, 86% of all patients Rh +
  - 50% mortality male, 34% female in 7 days
  - 18 of 39 Rh neg received Rh + blood, median 10 u, avg 12.5 u
  - 8 of 18 lived > 7 days, antibody screens done, 1 of 8 had D ab
  - Rate of anti D formation, 12.5% of Rh neg getting Rh pos
  - Early papers showed Anti D formation 22% not in trauma pts [B,C]
- 88% of MTPs could get O+,
- Females Rh neg <50 were 1.5% of patients, received
- only 12% of O negs used
- Implemented O pos for all except Rh neg females < 50

A. Lynne Uhl Transfusion 2015 55:791-795
B. Yazer Transfusion 2007 47:2197-201
C. Frohn Transfusion 2003 43:893-8

Meta analysis of studies of anti-D in D neg patients transfused with D+ blood

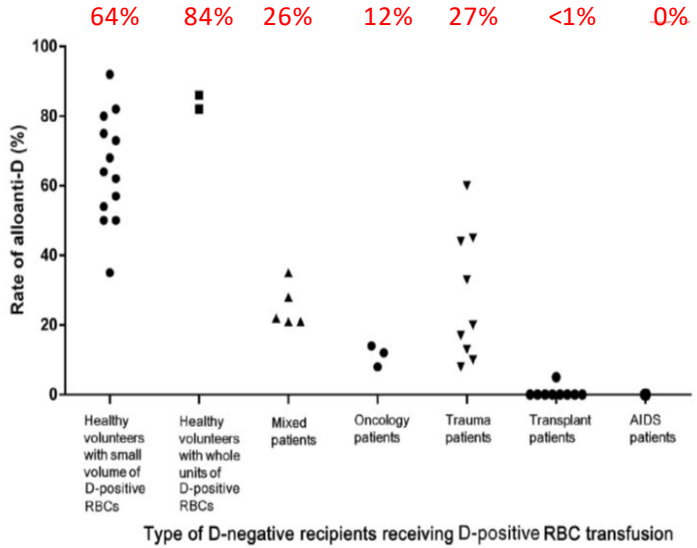

FIGURE 3 The diagram of incidence of anti-D immunization in D-negative recipients after D-positive RBC transfusion

- Antibody formation requires an intact immune system
- Trauma patients - more units does not increase % of pts who develop anti-D 43% in 3-5 units transfused, 18% in 11-20 units

Ji Y et al Vox Sang 2022;117:633-640

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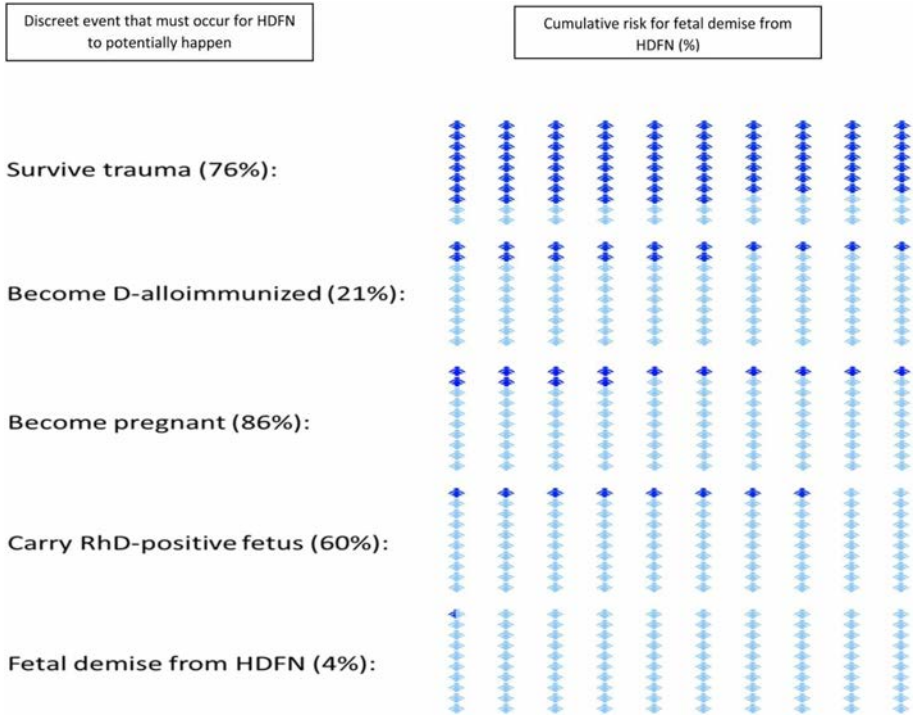
Modeling Risk for Women of Child Bearing Age when Using O+ RBC for resuscitation



- When using RH+ blood in women of child bearing age, fetal risk of death from HDFN is 0.3% which is counter-balanced against 24% risk of dying of hemorraghic shock.
- Risk declines as the age of the female when transfused increases.

Yazer et al. Hematology 2023 Dec;28(1):2161215. doi: 10.1080/16078454.2022.2161215.

Figure 1. Graphic representation of the risk of hemolytic disease of the fetus and newborn (HDFN) following the transfusion of RhD-positive RBCs to an injured RhD-negative female of childbearing age considering five critical events that must take place for HDFN to occur following trauma [Citation20]. The percentages in brackets are the risks of each discreet event occurring; the dark shaded icons represent the cumulative risk of each event occurring as a percentage. For example, 76% of injured adults survive the trauma and 21% become D-alloimmunized, therefore the cumulative risk of fetal death from HDFN at this stage is approximately 16%, assuming the three additional events also occur. The overall cumulative risk of fetal demise from HDFN was calculated to be 0.3%.

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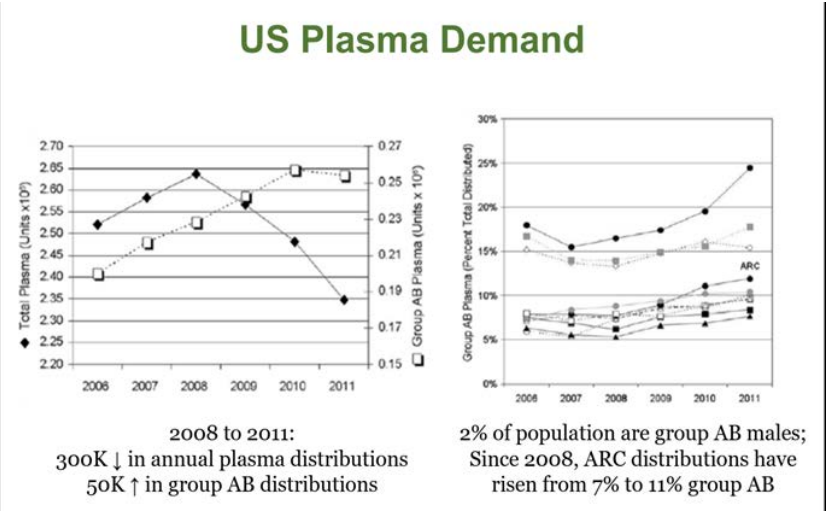
Plasma Ratios 1:1 vs 1:2 vs ?

- PROMMTT - RCT 1245 highest level trauma patients – 10 Level 1 trauma centers
- Real time data collection on infusions and interventions until resuscitation ended, also tracked in-hospital mortality, complications, subsequent treatments until death or discharge
- Increased plasma:rbc ratio associated with lower 6 hour mortality but not 24 hour or 30 day mortality
- Ratio less than 1:2 = 3-4 fold increase in risk of dying[36]
- 2nd analysis – time of transfusion vs ratio of plasma:rbc
- Early plasma transfusion <2.5 hours had half the mortality risk in 6hr, 24 hr and 30 day periods compared to no plasma or plasma >2.5 hours after admission
- Fewer rbc's used in early plasma transfusion group
- Speed to plasma transfusion more important than ratio of plasma:rbc[37]
- PROPPR – 1:1 more patients achieve hemostasis, reduced hemorrhagic mortality at 3 hours and fewer died by exsanguination at 24 hours vs 1:2 but no differences in complications or mortality at 24 hours or 30 days[38]
- 86% of 177 major trauma units in TQIP use 1:1:1
- Meta analysis plasma vs. crystalloid pre-hospital
  - No difference in 24 hour or 30 day mortality or multi-organ failure
  - Plasma – 24 hour rbc usage decreased with increased INR ratio on arrival at ER
  - No difference in plasma, platelet transfusions in 24 hours or in massive transfusion or vasopressor use in 24 hour period[A]

36. **Holcomb, JB et al.** 2, 2013, JAMA Surg, Vol. 148, pp. 127-36.
37. **del Junco, DJ et al.** 2013, J Trauma Acute Care Surg, Vol. 75, pp. s24-30.
38. Holcomb, JB et al. 2015 , JAMA Vol. 313, pp. 471-82
A. Abuelazm M et al. Eur Jour Trauma and Emer Surg doi.org/10.1007/s00068-024-02461-7

“A” Plasma

- AB is universal plasma, problem is 4% of population is AB, not enough to keep thawed at all Level 1 trauma – cut in half as female plasma is not used due to TRALI mitigation
- ARC data – over 50% increase in % of AB distributed
- HABSWIN study – 73% of AB plasma transfused to non-AB patients[A]
- A plasma is the answer, compatible with 85% of people
- PROPPR trial[1]
  - 3 of 12 sites used type A thawed
  - 2 of 3 untitered, 1 titered 1:25
  - 141 A units transfused to AB or B patients – no evidence of hemolysis
  - 2 of 12 hospitals had 25% wastage of AB plasma
- Mayo Clinic Retrospective review [2]
  - 254 patients – 35 incompatible – 14%
  - No difference in clinical outcomes across wide variety of indicators – Safe to use Group A, they do not titer
  - Reduce AB plasma 96%



- U of Massachusetts – Four year retro review [B]
  - 385 patients, 85% compatible
  - 23 patients – incompatible, median use 2 units
  - 3 weak DAT+ 1+, no hemolysis seen
  - Used thawed plasma no titers done
  - No differences in morbidity or mortality

1.Holcomb, JB et al. 2015 , JAMA Vol. 313, pp. 471-82
A. Zeller MP, et al. Transfusion 2018Jan;58(1):151-157
2. Zielinski et al J Trauma Acute Care Surg 2013 74(1) 69-74
B. Chhibber et al Transfusion 2014 54:1751-55

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Mitigating Factors for Use of “A” Plasma

- You only need use it for as long as it takes to type the patient and thaw ABO identical plasma
- Early in resuscitation, most of the patient’s red blood cells will be the O rbcs you have transfused
- Group A donors have low anti-B titers
- Severe complications with Anti-B hemolysis are rare
- Group B & Group AB have soluble B antigens to adsorb “A” antibodies

Dartmouth Experience

- Dartmouth - rural trauma center – 100 miles to next Level 1 trauma center
- Four year retrospective review 38 MTPs with a focus on speed to transfusion of plasma
- 26 minutes longer to dispense plasma than rbcs
- Avg rbcs transfused before plasma – 8 units
- 1/3 patients had >=10 units rbc transfused before plasma
- Reason 17 minutes to thaw plus time to transport
- Wanted liquid plasma but not available from ARC
- Thawed group A may ensure rapid plasma availability, use <1:50 titer
- Only 2 of 81 units titered were > 1:50.

Mehr J Trauma Acute Care Surg 2013 74(6) 1425-31

Thawed vs. Liquid Never Frozen

- PROPPR trial [1] requirement, plasma at bedside within 10 minutes of admission.
  - 11 of 12 hospitals used thawed plasma
  - 1 hospital used liquid plasma
- Thawed plasma 5 day limit after thawing
- Liquid plasma – plasma which has been refrigerated but never frozen
- Liquid plasma expiration is 5 days after expiration of wb anticoagulant
  - cpd/additive – 26 days, cpda-1 - 40 days
- FDA licensed, available since 1940's
- Used in Sweden interchangeably for over 30 years, storage to 14 days only, roughly 1/3 liquid, 2/3 FFP
  - 10 yr observational study 90k pts, 350k units – no difference in clinical outcomes between FFP and liquid regardless of age of liquid even beyond 15 days [2]
- Liquid Plasma - more cost efficient for helicopter & out of hospital transfusion [3]
  - Less wastage as <8% of plasma used for trauma in the field
  - When returned to hospital, 58% thawed plasma transfused, 34% expired
  - Liquid plasma has extended shelf life compared to thawed plasma

1. Novak DJ et al Transfusion Volume 55, Issue 6, June 2015, Pages: 1331–1339
2. Norda et al J Trauma 2012 72(4) 954-961
3. Adams PW et al. Journal of Trauma and Acute Care Surgery doi:10.1097/TA.2406

Liquid Plasma Profile

TABLE 2. Mean (□ SD) values of screening tests (n = 12) for liquid-state plasma during refrigerated storage (all tests are measured for factor activity)

Analyte reference range (units)	Day 1	2	3	4	5	10	15	20	25	30
FBG 1.63-4.55 (g/L)	2.92 (□ 0.30)	2.87 (□ 0.27)	2.90 (□ 0.25)	2.83 (□ 0.32)	2.83 (□ 0.33)	2.82 (□ 0.29)	2.76* (□ 0.25)	2.78* (□ 0.24)	2.69*† (□ 0.26)	2.75*† (□ 0.24)
FII 0.70-1.20 (IU/mL)	0.92 (□ 0.15)	0.93 (□ 0.16)	0.90 (□ 0.12)	0.94 (□ 0.14)	0.91 (□ 0.14)	0.94 (□ 0.18)	0.91 (□ 0.18)	0.90 (□ 0.17)	0.91 (□ 0.13)	0.90 (□ 0.10)
FV 0.70-1.40 (IU/mL)	1.10 (□ 0.18)	1.10 (□ 0.30)	1.09 (□ 0.23)	1.11 (□ 0.25)	1.04 (□ 0.32)	1.04 (□ 0.27)	0.77*† (□ 0.24)	0.73*† (□ 0.17)	0.64*† (□ 0.17)	0.50*† (□ 0.12)
FVII 0.70-1.20 (IU/mL)	0.97 (□ 0.21)	0.91* (□ 0.19)	0.87* (□ 0.20)	0.84* (□ 0.17)	0.82* (□ 0.19)	0.78*† (□ 0.16)	0.78*† (□ 0.19)	0.93 (□ 0.46)	1.25 (□ 0.98)	1.08 (□ 0.73)
FVIII 0.50-1.50 (IU/mL)	0.72 (□ 0.18)	0.68 (□ 0.22)	0.67 (□ 0.18)	0.66 (□ 0.18)	0.64* (□ 0.17)	0.63* (□ 0.16)	0.56*† (□ 0.15)	0.56*† (□ 0.14)	0.51*† (□ 0.16)	0.50*† (□ 0.14)
F IX 0.50-1.50 (IU/mL)	0.86 (□ 0.16)	0.88 (□ 0.17)	0.90 (□ 0.17)	0.88 (□ 0.17)	0.87 (□ 0.17)	0.86 (□ 0.18)	0.84 (□ 0.15)	0.80*† (□ 0.14)	0.80*† (□ 0.13)	0.76*† (□ 0.13)
FX 0.7-1.2 (IU/mL)	1.10 (□ 0.18)	1.15* (□ 0.18)	1.08 (□ 0.18)	1.12 (□ 0.18)	1.11 (□ 0.20)	1.11 (□ 0.18)	1.11 (□ 0.21)	1.08 (□ 0.16)	1.15 (□ 0.27)	1.12 (□ 0.23)
FXI 0.65-1.50 (IU/mL)	0.93 (□ 0.07)	0.93 (□ 0.08)	0.93 (□ 0.10)	0.94 (□ 0.09)	0.94 (□ 0.09)	0.93 (□ 0.09)	0.91*† (□ 0.08)	0.91† (□ 0.09)	0.90*† (□ 0.08)	0.89* (□ 0.09)
FXII 0.65-1.50 (IU/mL)	0.89 (□ 0.16)	0.91 (□ 0.15)	0.91 (□ 0.16)	0.91 (□ 0.15)	0.90 (□ 0.15)	0.91 (□ 0.15)	0.94*† (□ 0.14)	0.92*† (□ 0.14)	0.94*† (□ 0.14)	1.05 (□ 0.32)
FXIII 0.70-1.40 (IU/mL)	1.13 (□ 0.23)	1.13 (□ 0.24)	1.13 (□ 0.24)	1.12 (□ 0.23)	1.11 (□ 0.23)	1.11 (□ 0.24)	1.12 (□ 0.22)	1.13 (□ 0.23)	1.11 (□ 0.22)	1.10 (□ 0.23)
VWF 0.50-1.50 (IU/mL)	0.73 (□ 0.17)	0.71 (□ 0.20)	0.71 (□ 0.19)	0.70 (□ 0.18)	0.70 (□ 0.19)	0.58*† (□ 0.17)	0.50*† (□ 0.17)	0.44*† (□ 0.17)	0.40*† (□ 0.17)	0.40*† (□ 0.18)

* Significant difference ($p < 0.05$) when compared to Day 1 results using a paired t test.
† Significant difference ($p < 0.05$) when compared to Day 5 results using a paired t test.

- 0-30 days factor activity, At least 50% or more activity in all factors at day 15
- Minimal changes in FII, FX, FXIII
- FBG, FIX, FXI – no change to day 5, significant reduction after day 20
- FXII – no change to day 5 then increase afterward similar pattern in FVII – cold activation
- vWF, FV, FVII, FVIII – no change to day 5, significant difference by day 15, 30% decline vs. day 1, still at 50% or better at day 15
- No change in AT, PLG, PC but significance drop in PS but remained at 53% level
- Increase in PT and aPTT by 2 sec, over 30 days, significance reached at day 15
- Recommendation – limit use to less than 15 days of age, use with FFP where feasible in MTP [A]
- Liquid plasma can be prepared from apheresis plasma or whole blood plasma with no differences in factors during storage [B]

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A. Gosselin Transfusion 2013 53(3) 579-590 B. Bostrom Transfusion 2007 47(3) 460-3

Liquid vs. Thawed

- Compare thrombin generation and clot kinetics liquid plasma and FFP at day 0 and storage limit
- Thrombogram at day 0 showed liquid plasma higher than thawed FFP in endogenous thrombin potential
- Higher performance continued until day 26 when liquid plasma equals thawed plasma on day 0
- Liquid retained 86% of day 0 potential at day 26
- TEG – Liquid had higher MA, G and TTG values at day 0 than thawed plasma
- At end of storage both were equal
- PT increased 2.2 seconds at day 26, aPTT increased 3.1 seconds at day 26 for liquid plasma
- All Factors on day 26 at 88% of day 0 except FV and FVIII, 39% and 60% resp.
- All inhibitors stable at day 26 except PS, 29%
- Initial hemostatic profile better in liquid than in thawed at day 0
- Residual platelet count 1.5x higher in liquid than thawed – better initial clot formation
- As platelets age, release vWf and microparticles, aiding thrombin formation
- Freezing plasma destroys platelets
- Explains why TEG and thrombin generation are better in liquid plasma
- Done by the trauma center in Houston which uses liquid plasma instead of thawed FFP
- What do you prefer, better coag factor percentages or better thrombin formation and clots?????

Matijevic J Trauma Acute Care Surg 74(1) 84-91

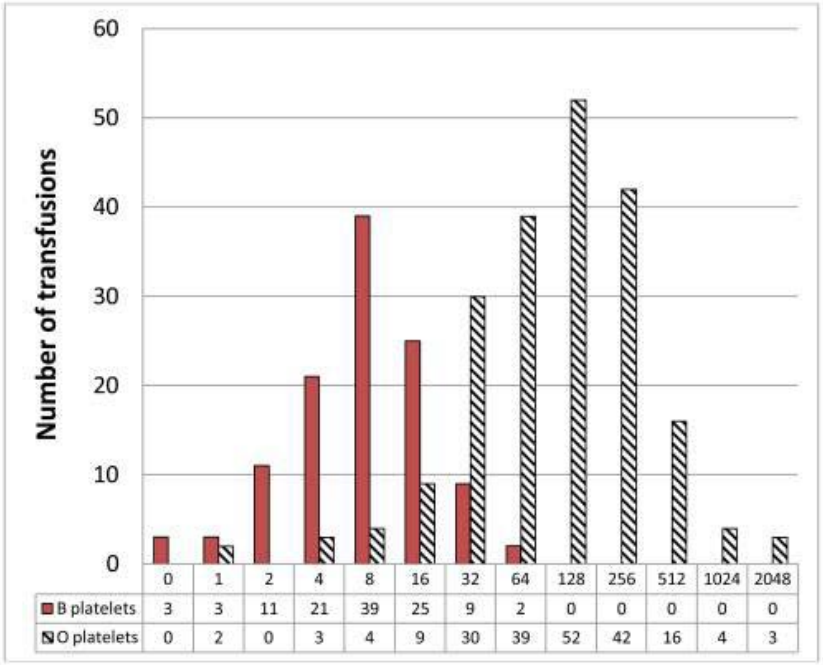
Titering

- Various methods but no universal technique for titering[E]
- Different methods give different results which is also dependent on ABO and antibody tested[G]
- Titers differ depending on sample, donor sample higher by 2 - 4 titers vs. segment, vs. bag sample[H]
- Transfused antibodies will complex with free A and B substance to form immune complexes and will also be diluted out[C]
- Swedish military – titers anti A and anti B in O donors – IgM – 100, IgG – 400[B]
- Hemolysis rare - 25 cases O apheresis to non-O patients, titers > 1000 - no consensus but general recommendation, anti-A and anti-B titers saline medium 100-200, IgG titer 250-400[D]
- Using saline titer at 200, approximately 5-30% donors could not be used as WB compatible[F]
- Use of immediate spin threshold of 50 defer 20% Group O WB and 14% Group A plasma
- In O donors, anti-A is generally in higher titers than anti-B though if anti-B is high so is anti-A [I]
- No seasonality to titer levels is seen [I]

A. Yazer M et al. Transfusion 2018;58:532-538 B. Spinella PC Transf Apher Sci 2012;46:113-7 C. Sikora J et al. Transfusion 2018;58;1006–1011
D. Berseus O Transfusion 2013;53:1145-1235 E. Belin TR J Trauma Acute Care Surg 2017;82(6)Supp1, S79-86 F. Garratty G. Am J Clin Path 1998;109(6):769-77
G. Kang SJ Ann Lab med 2014;34:300-306 H. Hill EA Transfusion 2014;54:1580-84 I. Harm SK et al. Transfusion 2019;59(2):762-767

ABO antibody levels

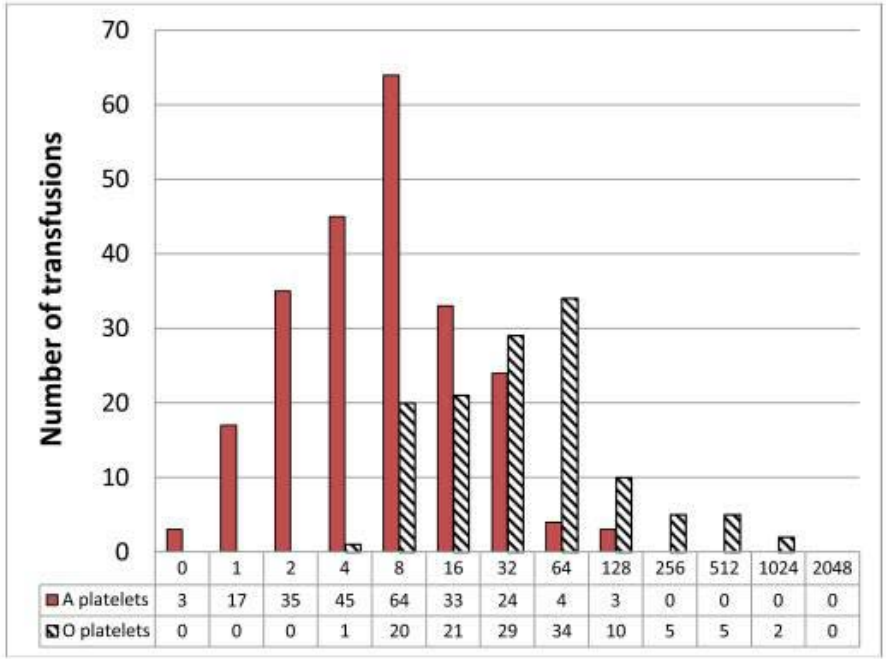
Anti-A antibodies



	0	1	2	4	8	16	32	64	128	256	512	1024	2048
B platelets	3	3	11	21	39	25	9	2	0	0	0	0	0
O platelets	0	2	0	3	4	9	30	39	52	42	16	4	3

B donor median 1:8, O donor median 1:128

Anti- B antibodies



	0	1	2	4	8	16	32	64	128	256	512	1024	2048
A platelets	3	17	35	45	64	33	24	4	3	0	0	0	0
O platelets	0	0	0	1	20	21	29	34	10	5	5	2	0

A donor median 1:8, O donor median 1:128

Karafin et al. Transfusion 2012 Oct;52(10):2087-93.

NEW YORK STATE Department of Health

Whole Blood(WB) Use

- Vietnam war - last massive use of whole blood
- Used titer of 1:100, risk of hemolysis, 1:10,000[C]
- Reconstituted WB has 180 ml of preservative [F] =
  - acidotic – ph<7 after 2 weeks 65% coagulation factor activity
  - anemic – 30% hct thrombocytopenic – 80,000
- Earlier is better – nonhospital use, WB in helicopter & ambulance
- Mortality rate increases 5% per minute in hemorrhagic shock[A]
- Less colloid and crystalloid to lessen risk of trauma coagulopathy
- Use in London – Used within 37 minutes of accident and 3 units average used[B]
- Use of WB in patients without brain injury may result in fewer transfusions compared to component therapy[D]
- Can use in pediatrics >3years old and >15kg, max dose 30ml/kg[E]
  - No difference in platelet number or function for pediatric trauma cases compared to room temperature platelets [G]

A. Meyer DE Journal Trauma Acute Care Surg 2017;83:19-24 B. Seghatchian J Transf Aph Sci 2015;53:412-22 C. Zielinski MD Surgery 2014;155:883-6D.
D. Cotton BA Ann Surg 2013;258:527-33 E. Yazer M et al. Transfusion 2018;58:532-538 F. Mays JA Blood Transf 2017;15:153-7
G. Leeper CM et al. J Trauma Acute Care Surg 2019;87(1);49-53

Whole Blood Use – Meta Analysis

- Meta- analysis civilian use WB odds ratio vs Component 0.72 for 24 hour mortality, 0.65 for early mortality <6 hour, no difference in late mortality 28 day, higher ratio of plt/rbc and plasma/rbc with wb use [H]
- Meta analysis 24 papers – 5,164 pts. LTO Whole Blood vs. Component therapy [A]
  - WB – Improved 24 hour survival adults, no difference in late survival
  - WB - Improved early and late survival children
- Meta analysis 21 papers LTO Whole Blood vs. Component therapy Adult only [B]
  - No differences in early mortality (3-6 hr), 24 hour, late mortality or overall in-hospital mortality
  - WB - Decreased 4 hour rbc and plasma transfusions
  - WB – Decreased 24 hour rbc transfusions but similar plasma transfusions
- Meta analysis 16 papers LTO Whole Blood vs. Component therapy Adult only [C]
  - WB – lower 24 hr mortality, similar 30 day mortality
  - WB –reduced rbc transfusion at 6 hour and 24 hour,
  - WB- no difference in plasma or platelet transfusion at 6 or 24 hour
  - WB – No difference in ICU length of stay

H. van der Horst RA et al. J Trauma Acute Care Surg 2023 Aug 1;95(2):256-266
A. Morgan KM et al. CCM July 2024 52;(7) e390-404 DOI:10.1097/CCM.0000000000006244
B. Meizoso JP et al. J Trauma Acute Care Surg2024;97(3):460-470
C. Ngatuvai, M et al. Jour of Surg Res July 2023;287; 193-201 DOI:10.1016/j.jss.2023.02.010

Whole Blood Product

- Use leukoreduced platelet sparing male WB to prevent TRALI
- Can be Rh+ or Rh- depending on mix of patients seen
- Can go to full Rh+ if need be
- Titer levels dependent on suppler can be 1:50 -1:256
- Procoag and anticoag maintain good levels to 11 days[A]
- Platelet concentration is about half expected in whole blood[B] – no rotator necessary, can lead to rbc hemolysis
- Platelets are activated with shortened clotting time, no effect on maximum clot firmness[D]
- Non platelet sparing filtration [E] –
  - Decreased maximum clot strength
  - Decreased rate of clot growth
  - Decreased maximum thrombin generation
- Limit use to 2-4 units[C]
- Monitor LDH, total bilirubin, haptoglobin, for 2 days post

A. Rahbar E Shock 2015;44(5):417-25
B. Yazer M Transfusion 2016;56:596-604
C. Yazer M Journ Trauma Acute Care Surg 2016;81:21-26
D. Wu X Br J Haem 2017;179:802-10
E. Siletz A Jour Trauma Acute Care Surg 83(3):420-26

Analysis of Filtered Whole Blood

- Filter successfully removed white blood cells while retaining platelet count and hemoglobin
- Platelet function, aggregation using collagen, shows greatest decline immediately after filtration and continues to worsen
- May be due to activation during filtration
- Clotting time was similar before and after filtration but increased over time and became abnormal on day 14
- Mean clot firmness remained in normal range but deteriorated by day 7 [A]
- Similar findings in another paper with significant reduction in aggregation and little effect on thrombin generation. [B]
- Do you need the platelets in whole blood for trauma???

A. Zielinski MD et al. J Thrombo Cir 2018, DOI:10.4172/2572-9462.1000124
B. Remy KE et al. J Trauma Acute Care Surg 2018;84(6Suppl1):S104-114

Whole Blood Filtration

- Platelet Sparing(PS) or No Platelet Sparing (nPS) [A]
- Testing
  - PS – had more platelets- 7.1x10e9 vs 1x10e9 for nPS
  - PS – normal TEG vs. grossly abnormal TEG for nPS with higher reaction times, lower alpha angles, and lower maximum amplitude
  - Platelet function testing – PFA-100 closure – more common with PS-72% than nPS-4%
- PT, PTT and factor activities – no difference in PS or nPS though Factor V and VIII were higher in nPS
- Thrombin generation higher in PS vs nPS
- PS - platelet count drops in two weeks but hemostasic function is maintained

A. Haddaway K et al. Transfusion 2019;59;1809-1817

Non-filtered Whole Blood

- Non-leuko red blood cells vs leukoreduced showed no difference in mortality in trauma patients [C,D]
- Reduced platelet count over time with decline in platelet aggregation
- May be due to aggregated masses composed of fibrin or fibrinogen which interacts with platelets
- None of this resulted in changes in thromboelastography findings
- Regardless of anticoagulant, CPD, CP2D, or CPDA-1 – all exhibited very little change beyond day 21 so theoretically these may be expanded to 35 days
- Fresh is better but old will work [E]

C. Phelan HA et al. J Surg Res 2007;138:32-36
D. Nathens AB et al. Shock 2006;26:342-347
E. Meledeo MA et al. Transfusion 2019;59:1549-1559

Cold Storage Platelets (CSP)Manufacturing and Storage Conditions

- Blood establishments should prepare CSP from apheresis platelets suspended in 100% plasma or an FDA-approved PAS.
- Blood establishments must place CSP that have not been treated with an FDA-approved pathogen reduction device at 1-6C no later than 4 hours from the end of collection to assure that the risk of bacterial contamination is adequately controlled (21 CFR 606.145(a)).
- Blood establishments should place pathogen-reduced apheresis CSP in cold storage at 1-6C no later than 4 hours after completion of the pathogen reduction process.
- Blood establishments must continuously store CSP at a temperature of 1-6C (21 CFR 640.24(d)(2)), must contain CSP at a temperature of 1-10C during shipment (21 CFR 600.15(a)), and should not return CSP placed in room-temperature conditions back into cold-stored inventory or relabel CSP as RTP.
- For CSP stored at a temperature of 1-6C for a period of up to 14 days, agitation is optional (21 CFR 640.25(a))

Alternative Procedures for the manufacture of Cold-Stored Platelets Intended for the Treatment of Active Bleeding when Conventional Platelets Are Not Available or Their Use Is Not Practical. FDA Guidance for Industry. June 2023. https://www.fda.gov/media/169714/download

Cold Platelets in Use

- As good or better hemostatic product as warm [A, A2]
  - Aggregation response, clot strength via thromboelastography, adhesion to collagen better with cold than room temperature
  - Agitation is not required for cold platelet storage
- Do not circulate as long as warm [B]
- Benefit may be better product, increased shelf life by decreasing risk of sepsis by inhibiting bacterial growth [G]
- Enhance endothelial barrier integrity and decrease endothelial cell permeability as well or better than warm [C]
- Decrease nonspecific adhesion to endothelial cells
- Enhanced aggregation to agonists – faster stronger, longer lasting clot with cold platelets
- Better clot retraction properties leading to better structural attributes = stronger more stable clots [E]
- RCT – 5 trauma centers, phase 2 cold stored vs. warm, mortality at 24 hours, 5.9% cold, 10.2% warm p=0.26, no difference in thromboembolism or adverse events [H]
- Variations in cold storage
  - Thermal cycling (1 hour RT every 11 hours cold) may increase recovery & survival over cold platelets but does not equal room temperature storage [D]
  - Cold storage extension and inventory management may be helped if room temperature platelets held for 4 days then refrigerated afterwards – these were equivalent to initial cold stored over 21 day period [F]
    - Platelet count, lactate production, glucose consumption, surface phosphatidylserine, aggregation all similar
    - pH higher in delayed cold platelets

A. Reddoch KM Shock 2014;41(Suppl 1):54-61
A2. Reddoch KM Shock 2016;45:220-27
B. Murphy S Transfusion 1976;16:2-3
C. Baimukova G et al. Transfusion 2016;56:S52-64
D. Vostal JG Transfusion 2018;58:25-33
E. Nair PM et al. Br J Haematol 2017 Jul;178(1):119-129
F. Wood B et al Vox Sang 2018;113;403-411
G. Ketter PM et al. Transfusion 2019;59;1479-89
H. Sperry JL et al. Ann Surg 2024 May 6 doi: 10.1097/SLA.0000000000006317

Decisions, Decisions

- Platelets
  - Room temp vs. cold storage
- Plasma
  - Liquid vs. thawed
  - Group A as universal or not
  - Titer - what level or no titer
- Whole Blood
  - Leukoreduce or not
  - Platelet sparing filter or not
  - Titer or not

- MTP is a relay race. O+ rbc, Group A plasma, liquid plasma, or Group O WB get you off to a fast start when time is blood lost, trauma coagulopathy, increased mortality.
- Pass the baton to ABO identical rbcs, fresh thawed FFP, apheresis platelets and cryoprecipitate as the finishers.