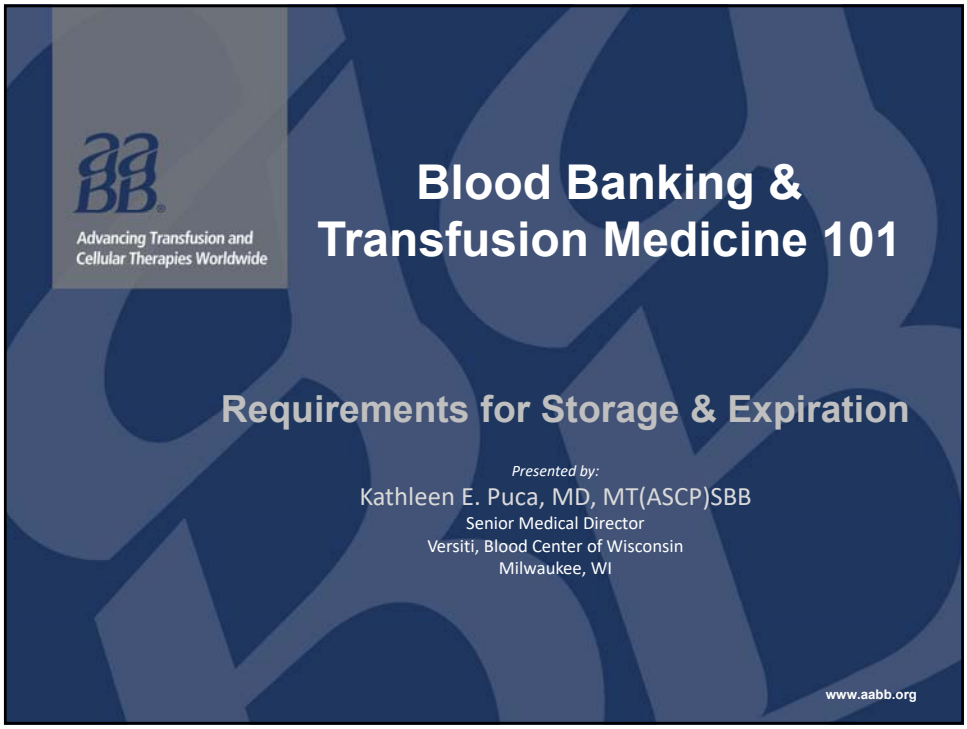

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Learning Objectives

After participating in this program you should be able to….

- Describe the rationale for different storage requirements, by blood product.
- List shelf-life limits for commonly available blood products.

2

Primary Goals of Blood Component Preparation and Storage

- Maximum viability and function of cells (or clotting factors)
- Prevent physical changes that would be detrimental to the viability or function
- Minimize bacterial proliferation
- For best inventory management, longest duration while maintaining cell viability and function

3

Factors that can determine or affect storage conditions

1. Type of cell or constituent to be stored/transfused
2. Changes to the cell during storage → *Storage Lesion*
3. Storage solutions and composition used
4. Storage temperature

4

Factors that determine or affect storage conditions

5. "Open" vs "closed" system

	"Open" System	"Closed" System
	Hermetic seal broken; loss of sterility	Hermetic seal not broken
Expiration:	Stored at 1-6C →24 hr Stored at RT → 4 hr	No change

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5

Guidelines for Storage Requirements

Regulatory

- FDA (Food and Drug Administration)
- AABB (Standards for Blood Banks and Transfusion Services)

Based on outcomes from research and various studies

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6

Evaluation of WB/RBC Storage Solutions

FDA requirements

- Survival: >75% of RBCs still detectable in circulation 24 hours post transfusion
- Integrity of RBCs: Free hemoglobin must be <1% at end of shelf-life

Dumont LJ, AuBuchon JP. Transfusion 2008;48:1053-60.

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7

Measurement of Viability and Function of Stored Platelets

In-vitro:

- Swirling phenomenon (light-scattering ability of discoid platelets may correlate with platelet viability)
- Maintenance of pH >6.2

In-vivo:

- Measuring pre- and post-transfusion platelet counts

Shrivastava M. The platelet storage lesion. Transfus and Apheresis Science 2009:41:105-113.

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8

Storage Solutions and Requirements by Blood Component

RBCs
Platelets
Plasma
Cryoprecipitate

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9

What happens to red cells stored in the refrigerator?

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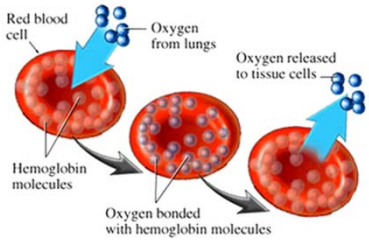
10

RBC Function and "Storage Lesion"



- Primary function of red blood cells is the delivery of O2 from the lungs to the tissues.
- Hemoglobin (Hgb) is the main carrier protein for O2
- Level of 2,3 DPG affects the release of O2 from Hgb
- As stored RBCs metabolize glucose to lactic acid, pH falls, and 2,3-DPG declines
- Around the 2nd week of storage, pH drops and 2,3 – DPG levels begin to fall

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11

RBC "Storage Lesion"

Metabolism continues and biochemical and structural changes occur…..

Biochemical

Plasma Hgb, Plasma K+

ATP, pH, 2,3-DPG, plasma Na+

Structural

Changes are correlated with loss of RBC viability

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12

Prevent or slow down the changes that occur….

- ***To maintain optimal viability….RBCs are stored at 1-6℃ for specific # of days as determined by the preservative solution used***
- ***Composition of the preservative solution for storing WB/RBCs***

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13

Anticoagulant-Preservatives Solutions

- Purpose:
  - Prevent clotting
  - Maintain the RBC (or platelet) viability and functionality during storage
- Basic Composition
  - Anticoagulant
  - Sugar or dextrose
  - Phosphate
  - Adenine (some types)

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14

Anticoagulant-Preservative Solutions – Basic Ingredients

Ingredient	Main Function
Sodium citrate	Anticoagulant- Citrate interferes with calcium-dependent steps of coagulation
Citric acid	Maintains anticoagulated state
Dextrose	Supports generation of ATP; provides nutrients for cell metabolism
Sodium phosphate	Serves as buffer to minimize effects of declining pH during storage
Adenine (some types)	Improves synthesis of ATP for cell metabolism

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15

Current FDA-Approved Anticoagulant-Preservative Solutions

	ACD-A	CPD	CP2D	CPDA-1
Trisodium Citrate	22.0 g/L	26.3 g/L	26.3 g/L	26.3 g/L
Citric acid	8.0 g/L	3.27 g/L	3.27 g/L	3.27 g/L
Dextrose	24.5 g/L	25.5 g/L	51.1 g/L	31.9 g/L
Monobasic Sodium Phosphate	0	2.22 g/L	2.22 g/L	2.22 g/L
Adenine	0	0	0	0.275 g/L
FDA-APPROVED SHELF-LIFE	**21 days**	**21 days**	**21 days**	**35 days**

Apheresis **Whole Blood**

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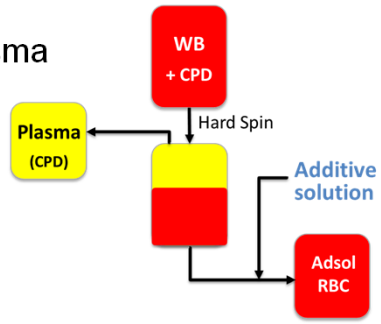
16

Additive Solutions (AS) - RBCs

- Added <u>after</u> removal of plasma

Advantages

- Extend the shelf-life to 42 days
- Harvest more plasma (and platelets) from WB unit
- Lowers viscosity of RBC product (Hct 60%); easier to infuse



Approved AS in US

- AS-1
- AS-2
- AS-5
- AS-7

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17

Common FDA-Approved Additive Solutions: Biochemical Changes

	AS-1 (Adsol)	AS-3 (Nutricel)	AS-5 (Optisol)
FDA approved Shelf-life	**42 days**	**42 days**	**42 days**
24–hour survival (%)*	83	85.1	80
Hemolysis (%)**	0.5	0.7	0.6
pH (measured at 37C)	6.6	6.5	6.5
AP (% of initial)	68	67	68.5
2,3-DPG (% of initial)	6	6	5

Per FDA requirements: *24-hr survival >75%; **Hemolysis <1%

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Modified from: Harmening DM, Brown MR. Red blood cell and platelet preservation: historical perspectives and current trends. Harmening DM (editor). Modern blood banking & transfusion practices. 7th Ed. FA Davis Co. 2019:1-23.

18

18

In the US most RBC units are stored in additive solution (AS-1, AS-3, AS-5)…..

At 1-6°C

for up to 42 days

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19

Storage Solutions and Requirements by Blood Component

RBCs

Platelets

Plasma

Cryoprecipitate

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20

Platelets: 2 types

91% of All Platelets Distributed in US in 2017

Whole-blood derived

≥5.5 x 10^{10} platelets in 40-70 mL plasma

Single Donor Apheresis

≥3.0 x 10^{11} platelets

Jones JM, et al. Slowing decline in blood collection and transfusion in the United States – 2017. Transfusion March 2020.

21

Platelets: Anticoagulant-Preservatives

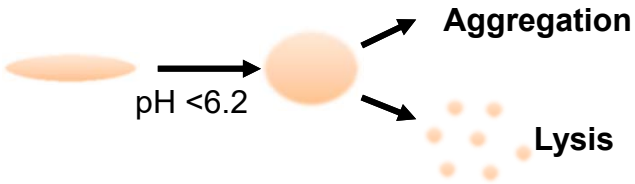
- Apheresis Platelets
  - Collected with ACD-A
- WB-derived platelet
  - Same anticoagulant as for WB collection (e.g. CPD)
- Contain citrate to prevent clotting and maintain proper pH; dextrose as an energy source
- Platelet storage bag: needs to be gas permeable

22

Platelet "Storage Lesion"

When O2 ↓↓…

- ↑ lactic acid, ↓ pH, ↓ ATP
- When pH <6.2 → irreversible shape change



- Lead to ↓ platelet viability and function

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23

Platelets - Unique Storage Conditions

- Stored in large flat bags (high surface to volume ratio for better gas exchange)
- Stored with **agitation** to facilitate O2-CO2 gas exchange*
- Shelf-life of platelets stored at RT (20-24C) is generally only 5 days

**FDA allows platelets to be stored without agitation for up to 24 hrs*

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24

- Platelets can be stored up to 7 days **IF**….
  - Use a container cleared or approved by the FDA for 7-day storage **AND**
  - Individual platelet units are subsequently tested for bacteria using a bacterial detection device cleared by FDA and labeled for use as a "safety measure".

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25

Quality Requirements for Platelet Collection and Storage

At time of collection:

- Actual platelet yield (platelet count x volume) → ≥3.0 x 10^{11} platelets
- Residual WBC count → 95% of units samples contain <5 x 10^{6}
- Bacterial detection testing (as specified by storage container manufacturer→ negative

At end of storage:

- Actual platelet yield (platelet count x volume) → 90% of samples contain ≥3.0 x 10^{11} platelets
- pH → 90% of units sampled ≥6.2

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26

Platelet Additive Solutions (PAS) for Platelet Storage

- Residual plasma reduced to 1/3 of its original volume
- Advantages:
  - Reduce plasma-associated transfusion reactions (e.g. allergic)
  - Mitigates any adverse event related to transfusion of ABO-incompatible platelets
  - Potentially reduces bacterial contamination/growth
  - Conserves plasma for other purposes
- Results related to improved platelet quality and in vivo survival are mixed

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Alhumaidan H, Sweeney J. Current status of additive solutions for platelets. J Clin Apheresis 2012;27:93-98.

27

27

Storage Solutions and Requirements by Blood Component

RBCs
Platelets
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Cryoprecipitate

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28

28

Frozen Plasma Products

Plasma	Frozen w/in:	Store at:	Exp. from Collection:
FFP	8 hrs @ 1-6C	-18C or colder	12 months
PF24	24 hrs @ 1-6C	-18C or colder	12 months
PF24RT24	24 hrs @ RT	-18C or colder	12 months

FFP = Fresh Frozen Plasma
PF24 = Plasma Frozen within 24 Hrs after phlebotomy
PF24RT24 = Plasma Frozen within 24 Hrs after Phlebotomy Held at Room Temperature up to 24 Hrs after Phlebotomy

Circular of Information for the Use of Human Blood and Blood Components, Revised October 2017

29

Plasma Products

WB-derived

- Same anticoagulant-preservative as used for WB collection
- Majority of anticoagulant-preservative solution from primary WB bag ends up in the plasma

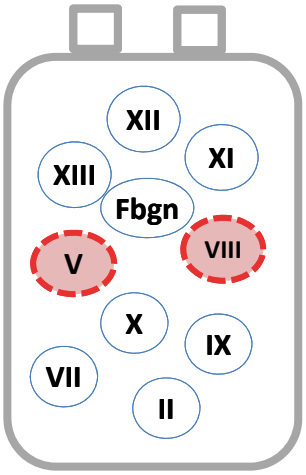
Apheresis

- Collected in ACD-A

30

Plasma Products

- Source of all clotting factors
- Limiting factor is the stability of certain clotting factors
  - Factor V and VIII are “labile factors”
- Plasma is frozen to -18C or colder within 24 hrs to preserve these factors at clinically effective level



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31

Plasma Products

- Temperature – primary storage condition
  - Store at -18C or colder to maintain clotting factor levels
  - Needs to be frozen within time limits based on type of plasma
  - Control of temperature is vital to maintain the shelf-life
- Stored frozen for 12 months from day of collection
- Published studies guide industry changes

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32

Preparing Plasma Products for Transfusion

- FFP/PF24/PF24RT24 products considered clinically equivalent
- At hospital: thawed at 30-37C
- Once thawed, 24 hr expiration when stored at 1-6°C

- **All can be converted to Thawed Plasma***:
  - Expiration is 5 days from date of thaw
  - Advantages: reduces wastage, more readily available for massively bleeding patients

*Collected in closed system

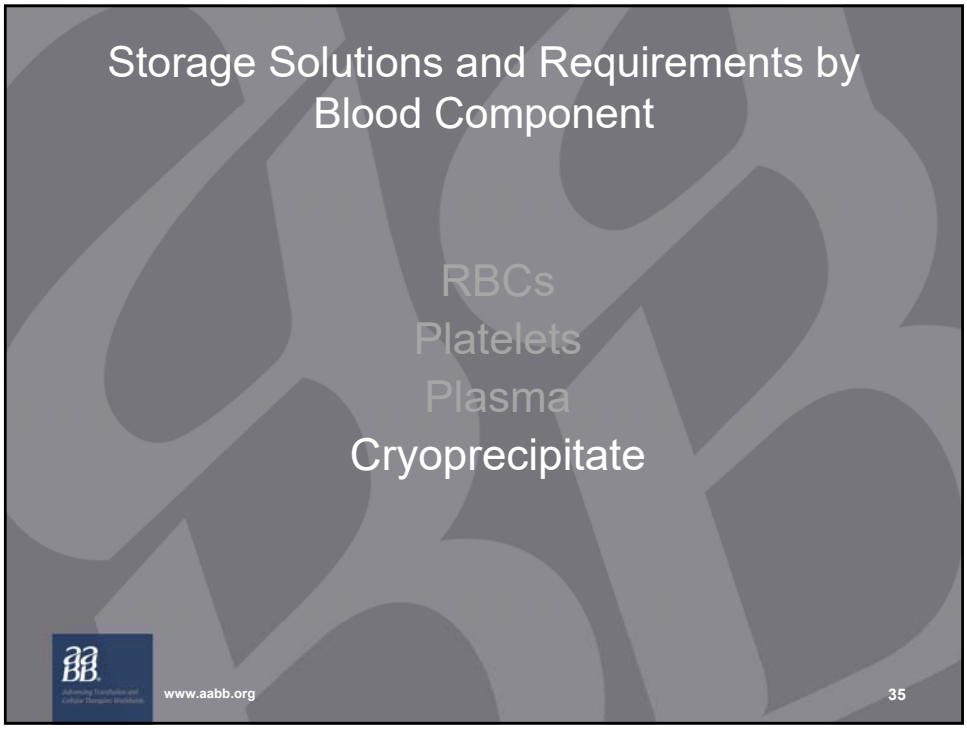
33

Liquid Plasma (*Never-frozen plasma*)

- Separated from whole blood and infused no later than 5 days after WB unit expires
  - CPD or CP2D: 21 + 5 = 26 days
  - CPDA-1: 35 + 5 = 40 days
- Stored at 1-6°C
- Indications: initial treatment of patients with life-threatening massive bleeding

Circular of Information for Use of Human Blood and Blood Components, October 2017

34



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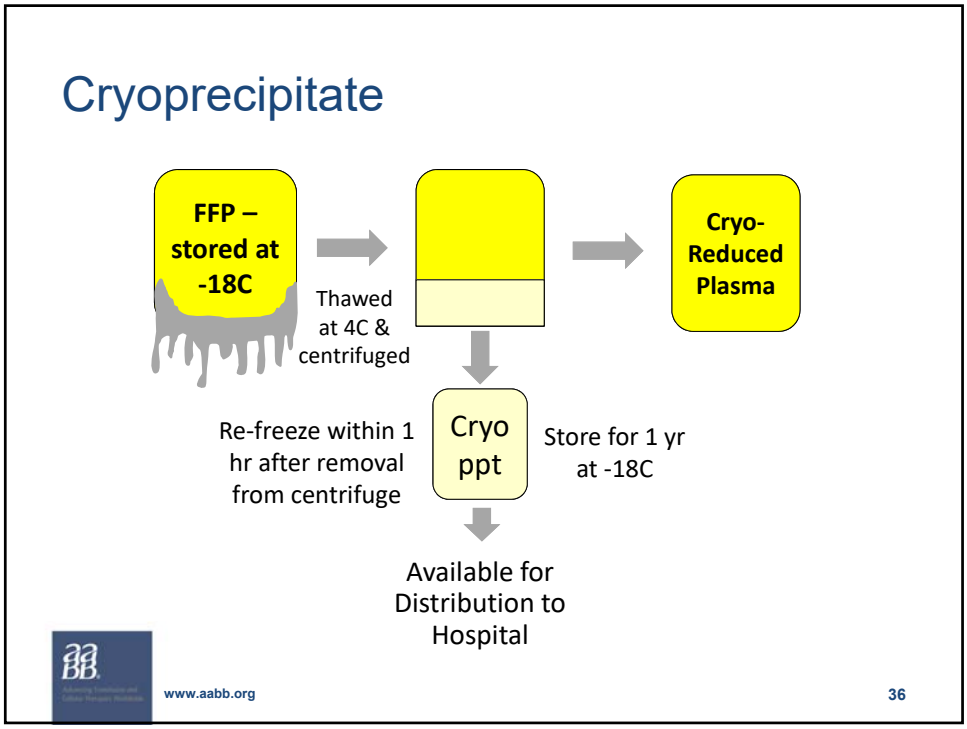
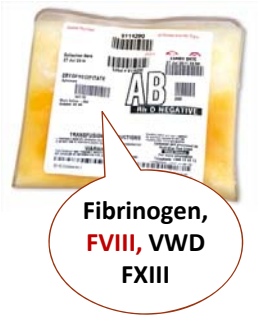


36

Cryoprecipitated AHF

- *Source of fibrinogen, FVIII, FXIII, vWF, fibronectin*
- At hospital: thawed at 30-37C
- Once thawed: store at RT
- Duration: 6 hrs if closed system (single or pooled); 4 hrs if open system (pooled)
  - FVIII is labile clotting factor & bacterial contamination risk
- Why RT once thawed?
  - If stored at 1-6C, may lead to formation of precipitate (clotting factors)



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37

Quality Control Requirements for Cryoprecipitate

- Per single unit
  - Minimum 80 IU Factor VIII
  - Minimum 150 mg Fibrinogen
- For pools (e.g. 5 pool)
  - Minimum 80 IU Factor VIII X # of units in pool (or 400 IU)
  - Minimum 150mg Fibrinogen X # of units in pool (or 750mg)
- Test each month 1% of products manufactured (or minimum of 4)

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38

Summary

- Proper storage conditions including optimal storage solutions and ideal temperature results in safe and efficacious products for the patient
- Regulatory requirements are defined for the storage of blood products
- Each “blood component” has unique requirements to provide safe and quality product

39

Summary Table

Component	Temperature	Duration
RBC	1-6°C	42 days
Platelets	20-24°C	5-7days
Plasma (frozen) Plasma (thawed)	-18°C 1-6°C	12 months 5 days
Cryo (frozen) Cryo (thawed)	-18°C 20-24°C	12 months 6 hrs*

*single unit or pooled closed system; if open system, 4 hrs

40

Questions?

Contact
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