

Inspiring and facilitating best transfusion practices in Ontario.

The Elephant in the Transfusionist's Skill Set: Understanding Compatibility for Transfusion Safety

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Speaker Disclosure

- No commercial product conflicts of interest to declare
- Transfusion Transmitted Injuries Surveillance System, member Education Committee
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- Canadian Society of Transfusion Medicine, member Standards Committee

Pre Transfusion Knowledge Question 1

Paramedics arrive in ED with Emma, a 21-year-old female trauma patient. She is unresponsive, being intubated, unstable & bleeding. Lab tests are pending. Blood, 4 units RBC & 4 units plasma (FP), is ordered.

The safest blood for this patient, Emma is:

- a) Group O, Rh positive RBC and group O FP.
- b) Group O, Rh negative RBC and group O FP.
- c) Group O, Rh positive RBC and group AB FP.
- d) Group O, Rh negative RBC and group AB FP.

Pre Transfusion Knowledge Question 2

An RBC unit crossmatched, compatible is safe for transfusion when:

- a) The ABO antigens on the red blood cells in the unit of blood will not be hemolysed by ABO antibodies in the patient's plasma.
- b) The ABO antigens on the red blood cells in that unit of blood will be hemolysed by ABO antibodies in the patient's plasma.
- c) The ABO antibodies on the red blood cells in the unit of blood will not be hemolysed by ABO antigens in the patient's plasma.
- d) The ABO antibodies on the red blood cells in the unit of blood will be hemolysed by ABO antigens in the patient's plasma.

The Elephant in the Transfusionist's Skill Set: Understanding Compatibility for Transfusion Safety

Objectives:

- To recognize and understand the antigens & antibodies in the ABO & Rh(D) blood groups, the clinically significant antibodies, and the potential for incompatibility (patient/component).
- To increase confidence in this knowledge by evaluating patient cases.

Outline:

- Blood Compatibility
- ABO Blood Group System
- Rh(D) Antigen, Rh Blood Group System
- Clinically Significant Antibodies
- Patient Cases with Blood Compatibility Check Visual Aid
- Take Home Messages/Summary

Blood Compatibility (1)

- Transfusionist: responsibility & accountability for confirming blood compatibility.
- Refers to the ability of one individual's blood to be transfused safely (without an adverse reaction) into another individual's body.
- An incompatible transfusion can lead to hemolysis.
- Hemolysis is the destruction of red blood cells & subsequent leakage (hemoglobin) into intravascular (circulation, main blood vessels) or extravascular (reticuloendothelial system) space.
- Both immune (antigen-antibody mismatch) and non-immune (thermal, osmotic, or mechanical injury to blood products) mediated hemolytic transfusion reactions can occur.
- Most hemolytic transfusion reactions are benign, however lifethreatening anemia, coagulopathy & renal failure can ensue.

Blood Compatibility (2)

- An antigen is a substance that can cause an immune system reaction.
 It is a marker or identifier (*name badge*) that indicates if a substance is foreign or not foreign (does not belongs or belongs) in your body.
- An **antibody** is a protein that the immune system produces to attack & fight foreign antigens (*protector*).
- Determined by the presence or absence of antigens & antibodies (in the blood to be transfused & the patient's blood).
- Blood group antigens are categorized into blood group systems (July 2023, 45 blood group systems are known) based on genetic origins.



Antigen: on exterior surface of red blood cell



Antibody: in the plasma

 For transfusion, ABO blood group system is most significant, with Rh blood group system, Rh(D) antigen second in importance.

ABO Blood Group System (1)



ABO Antibodies

• are naturally acquired, starting at 4 months of age.

If, the <u>antigen is present</u> on the surface of the red blood cells, then the <u>corresponding antibody will NOT</u> be in the plasma.

If, the <u>antigen is NOT present</u> on the surface of the red blood cells, then the <u>corresponding antibody will</u> be in the plasma.

Learning Review 1

For blood group O, no ABO antigens are on the exterior surface of red blood cells. What antibody(ies) will be in the plasma?



- a) Anti-A antibody.
- b) Anti-B antibody.
- c) Both anti-A and anti-B antibodies.
- d) No antibodies.

ABO Blood Group System (1)



ABO Antibodies

• are naturally acquired, starting at 4 months of age.

If, the <u>antigen is present</u> on the surface of the red blood cells, then the <u>corresponding antibody will NOT</u> be in the plasma. If, the <u>antigen is NOT present</u> on the surface of the red blood cells, then the <u>corresponding antibody will</u> be in the plasma.

Learning Review 2

For blood group AB, antigens A and B are on the exterior surface of red blood cells. What antibody(ies) will be in the plasma?



- a) Anti-A antibody.
- b) Anti-B antibody.
- c) Both anti-A and anti-B antibodies.
- d) No antibodies.

ABO Blood Group System (1)



ABO Antibodies

• are naturally acquired, starting at 4 months of age.

If, the <u>antigen is present</u> on the surface of the red blood cells, then the <u>corresponding antibody will NOT</u> be in the plasma. If, the <u>antigen is NOT present</u> on the surface of the red blood cells, then the <u>corresponding antibody will</u> be in the plasma.

• cause immediate intravascular red blood cell destruction, may lead to severe/fatal hemolysis.



ABO Blood Group System (2)

Compatibility is determined by the presence or absence of antigens & antibodies (in the blood to be transfused & the patient's blood).



Red blood cells: Antigen(s)



Plasma: Antibody(ies)

- **Transfusing RBC**: ensure the patient's plasma antibodies will not hemolyze the transfused RBC (the RBC unit's red blood cells do not have corresponding antigen on their surface).
- **Transfusing FP:** ensure the antibodies in the FP will not hemolyse the patient's red blood cells (patient's red blood cells do not have the corresponding antigen on their surface).
- Transfused platelets: should be ABO compatible with patient's red blood cells (platelets are suspended in donor plasma & also contain a few red blood cells).
 If platelets are in short supply, TML policy re: blood group substitution.

ABO Blood Group System (3)

RBC unit Group A transfused to patient Group A (microscope, schematic)



RBC unit Group B transfused to patient Group A (microscope, schematic)



Rh(D) Antigen, Rh Blood Group System (1)

Rh(D) is clinically the most important of the 54 antigens in the Rh blood group system.



Rh(D) Antigen, Rh Blood Group System (2)

Anti-D Antibody

- Anti-D antibody is **NOT** naturally occurring and is **NOT** in the plasma of:
 - Rh(D) positive patients
 - Rh(D) negative patients <u>UNLESS</u> exposed to the D antigen, and then anti-D antibody may be produced.
- Rh(D) negative individuals can be exposed to the D antigen (and then may produce anti-D antibody) through:
 - Transfusion of Rh(D) positive RBC
 - Transfusion of Rh(D) positive platelets (platelets contain small amounts of red blood cells)
 - Pregnancy/delivery of an Rh(D) positive fetus
- Anti-D antibody can cause severe immediate or delayed hemolysis.
- Rh(D) positive blood should not be transfused to a patient with anti-D.
- Anti-D: most common cause of severe Hemolytic Disease of the Fetus & Newborn (HDFN). Rh immune globulin (RhIG) prophylaxis, used since late1960's.



Rh(D) Antigen, Rh Blood Group System (3)

- <u>Rh(D) positive patients:</u>
 can be transfused blood that is Rh(D) positive or Rh(D) negative.
- <u>Rh(D) negative patients:</u> ideally should be transfused blood that is Rh(D) negative to avoid producing the anti-D antibody.
- <u>Rh(D) negative females of child-bearing age/potential</u> (to avoid producing the anti-D antibody and risk of HDFN) :
 - should be transfused blood that is Rh(D) negative.
 - if Rh(D) positive platelets are transfused (re: platelet supply), Rh immunoglobulin (RhIG) is required.
- For FP transfusion:

Rh(D) blood group is not relevant (plasma has no red blood cells, i.e., no antigens)



Clinically Significant Antibodies (1)

- In addition to antigens A, B, and D human red blood cells have many other antigens on their surface.
- If exposed to "foreign" red blood cell antigens via pregnancy or transfusion, antibodies against these antigens may be produced.



Clinically Significant Antibodies: If a patient forms these antibodies, then hemolysis of transfused RBC unit that has the corresponding antigen on the red blood cells can occur.

NOTE: For females of child-bearing potential, providing Kell negative (K-) RBC decreases the incidence of K-immunized pregnancies (and potential HDFN). In Canada this is established practice, except in emergency transfusion scenarios.

Clinically Significant Antibodies (2)

Group & Screen Test - antibody screen (antibody detection test):

- TML tests the serum (plasma part of patient blood sample) to either rule out or identify the clinically significant antibodies.
- If all clinically significant antibodies are ruled out, the antibody screen is reported as negative.
- If clinically significant antibody(ies) are identified (red blood cell sensitization/alloimmunization), compatible RBC units for patient transfusion must be negative for the corresponding antigen(s).
 (e.g., anti-c and anti-FyA identified in the plasma of the patient's blood sample, then RBC units for transfusion must be antigens c- and FyA-).
- TML maintains meticulous transfusion history records; they are consistently checked.

Clinically Significant Antibodies (3)

Anamnestic/Recall Response:

- Clinically significant antibody levels in the patient's plasma will decrease over time and may become non-detectable.
- The anamnestic/recall response refers to when a second exposure to the same antigen occurs, the antibody response is typically faster, much more sustained & antibody levels are higher.
- Anti-JkA and anti-JkB (Kidd blood group system) are notable.
- If clinically significant antibody(ies) identified, patient should be counselled, provided "antibody card"; option medical alert bracelet.
- For RBC transfusion, when feasible, ask patients/their family (and follow up with TML as indicated).
 - Have they had previous transfusion?
 - If so, did they experience any side effects/reactions?

Summary: Blood Compatibility Checks

ABO Blood Groups (if antigen present, then antibody absent; if antigen absent then antibody present; ABO antibodies are naturally acquired, starting at 4 months of age).				
Blood Group	Population Frequency	ABO Antigen(s) - red blood cell surface	ABO Antibody(ies) - plasma	
0	45%	none	anti-A, anti-B	
А	40%	A	Anti-B	
В	11%	В	Anti-A	
AB	4%	AB	none	
Rh(D) Blood Group (antigen present or absent; Rh(D) antibody is NOT naturally occurring).				
Blood Group	Population Frequency	Rh(D) Antigen - red blood cell surface	Rh(D) Antibody(ies) - plasma	
Rh(D) positive	85%	D	none	
Rh(D) negative	15%	none	None; if exposed to Rh(D) antigen (transfusion or pregnancy), then anti-D may be produced.	
Clinically significant antibodies (antibody screen/detection test): anti-D, anti-C, anti-c, anti-E, anti-e,				

anti-K, anti-k, anti-JkA anti-JkB (Kidd), anti-FyA anti-FyB (Duffy), anti-S, anti-s.

Summary: Patient

Patient's group & screen test

RESULTS	2021/05/01 11:30	
Transfusion Medicine Lab		
Sample Outdate	2021/05/04	
Blood Group Confirmation	Blood group confirmed.	
ABO, Rh(D) Group	A POS	
Antibody Screen	# POSITIVE	
Antibody Identification	anti-K	
REVIEW Comment	REVIEW Comment	
Direct Antiglobulin Test	Negative	

Summary: RBC unit

Blood donor/blood unit {Canadian Blood Services (CBS)} group & screen test

Phenotype:

- Refers to which antigens are detectable on the red blood cells.
- Is noted on the CBS label if the donor is antigen negative (the red blood cells in that unit do not have that antigen on their surface and the unit would be compatible for a patient with that antibody).



Blood Compatibility Check Visual Aid RBC Transfusion

Blood Compatibility - RBC Transfusion		
RBC	 *Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential = Compatibility Check 	
•	RBC unit	Patient
ABO Blood Group		
ABO Antigen(s)	×	
ABO Antibody(ies)		
Rh(D) Blood Group		
Rh(D) Antigen **	*	
Rh(D) Antibody		
Clinically Significant Antibody(ies) Antigen(s) Negative **	-	
* Ensure the patient's plasma antibodies will not hemolyze the transfused RBC unit (the RBC unit red blood cells do not have corresponding antigen on their surface).		



Patient Case 1 Question

Wilma, an 80-year-old female post hip fracture surgery, is SOB when up with physio & Hb is 69 g/L. A 1-unit RBC transfusion is ordered. Wilma's group & screen test: group O, Rh positive, antibody screen negative.

TML issues RBC unit: group A, Rh positive, phenotype no information.

Patient Case 1 Compatibility Check

Wilma's group & screen test: group O, Rh positive, antibody screen negative. TML issues RBC unit: group A, Rh positive, phenotype no information.

Blood Compatibility - RBC Transfusion			
RBC	 *Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential = Compatibility Check 		
	RBC unit	Patient	
ABO Blood Group	Α	0	
ABO Antigen(s)	A 🔌		
ABO Antibody(ies)		Manti-A & anti-B	
Rh(D) Blood Group	Pos	Pos	
Rh(D) Antigen **	D 🗧	D	
Rh(D) Antibody		No	
Clinically Significant Antibody(ies) Antigen(s) Negative ** Neg			
* Ensure the patient's plasma antibodies will not hemolyze the transfused RBC unit (the RBC unit red blood cells do not have corresponding antigen on their surface).			

RBC

Select the most correct statement.

- a) This transfusion is compatible because Wilma has no antigens on her red blood cells (group O) and the RBC unit's red blood cells have A antigen (group A).
- b) This transfusion is compatiblebecause Wilma & the RBC unit are both Rh positive.
- c) This transfusion is incompatible because Wilma has both anti-A and anti-B antibodies in her plasma (group O) & the RBC unit's red blood cells have A antigen (group A)
 d) This transfusion is incompatible
 - This transfusion is incompatible because the RBC unit has no phenotype information.



Betty, a 32-year-old female, is admitted post successful endoscopy to treat a bleeding ulcer. Her Hb is 62 g/L. A 1-unit RBC transfusion is ordered. Betty's group & screen test: group B, Rh negative, antibody screen negative. TML issues RBC unit: group O, Rh negative, phenotype c-, FyA-.

Patient Case 2 Compatibility Check

Betty's group & screen test: group B, Rh negative, antibody screen negative. **TML issues RBC unit:** group O, Rh negative, phenotype c-, FyA-.

Blood Compatibility - RBC Transfusion			
RBC	 *Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential = Compatibility Check 		
•	RBC unit	Patient	
ABO Blood Group	0	В	
ABO Antigen(s)	none 🔍		
ABO Antibody(ies)		🔪 anti-A	
Rh(D) Blood Group	Neq	Neq	
Rh(D) Antigen **	none 🗧	none	
Rh(D) Antibody		No	
Clinically Significant Antibody(ies) Antigen(s) Negative ** C-, FyA-			
* Ensure the patient's plasma antibodies will not hemolyze the transfused RBC unit (the RBC unit red blood cells do not have corresponding antigen on their surface).			

Select the most correct statement.

- a) This transfusion is compatible
 because Betty has anti-A antibody
 in her plasma (group B) & the RBC
 unit's red blood cells have no
 antigens (group 0).
- b) This transfusion is compatible
 because Betty & the RBC unit are both Rh negative.
- c) This transfusion is compatible

because Betty has a negative antibody screen.

d)

This transfusion is not best practice for a non-urgent transfusion because the RBC unit's phenotype is not K- and Betty is of childbearing age/potential.



Fred, a 62-year-old male, is in the OR undergoing re-do aortic valve replacement surgery. His Hb is 70 g/L. A 1-unit RBC transfusion is ordered.

Fred's group & screen test: group AB, Rh positive, antibody screen positive: anti-K, anti-JkA antibodies.

TML issues RBC unit: group AB, Rh negative, phenotype no information.

Patient Case 3 Compatibility Check

Fred's group & screen test: group AB, Rh positive, antibody screen positive: anti-K, anti-JkA antibodies.

TML issues RBC unit: group AB, Rh negative, phenotype no information.

Blood Compatibility - RBC Transfusion			
RBC	*Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential = Compatibility Check		
*	RBC unit	Patient	
ABO Blood Group	AB	AB	
ABO Antigen(s)	A, B 🔨		
ABO Antibody(ies)	none		
Rh(D) Blood Group	Neg Pos		
Rh(D) Antigen **	none 🗧	D	
Rh(D) Antibody		No	
Clinically Significant Antibody(ies) Antigen(s) Negative ** NA Anti-JkA			
* Ensure the patient's plasma antibodies will not hemolyze the transfused RBC unit (the RBC unit red blood cells do not have corresponding antigen on their surface).			

Select the most correct statement. This transfusion is compatible a) because Fred has no ABO antibodies in his plasma (group AB) & the RBC unit's red blood cells have antigens A and B (group AB). This transfusion is incompatible b) because Fred has anti-K, anti-JkA antibodies in his plasma & the RBC unit's phenotype is not K-, JkA-(the RBC unit's red blood cells may have K and JkA antigens). This transfusion is incompatible c) because Fred's red blood cells have the D antigen and the RBC unit's red blood cells do not have the D antigen. This transfusion is acceptable d) because the RBC unit group AB, Rh negative is rare, expires soon, & should not be wasted.

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Blood Compatibility Check Visual Aid FP Transfusion



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Barney, a 22-year-old male, is a trauma patient in the ED. Massive Hemorrhage Protocol has been ordered. Initially he received group O, Rh positive RBC, and group AB FP. His group & screen test is now completed. FP transfusion is requested. Barney's group & screen test: group A, Rh positive, antibody screen negative. TML issues FP units: group AB. Patient Case 4 Compatibility Check

Barney's group & screen test: group A, Rh positive, antibody screen negative. **TML issues FP units:** group AB.

Blood Compatibility - FP Transfusion			
PLASMA	*Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma		
	← → = Compatibility Check		
	FP unit	Patient	
ABO Blood Group	AB	Α	
ABO Antigen(s)	A		
ABO Antibody(ies)	none 🎽		
*Ensure the antibodies in the FP unit will not hemolyse the patient's red blood cells (patient's red blood cells do not have the corresponding antigen on their surface).			
** Rh(D) blood group is not relevant for FP (plasma has no red blood cells, i.e., no antigens).			

Select the most correct statement.

- a) Barney could be transfused group B
 FP (anti-A antibody) as he has A
 antigen on his red blood cells (group A).
- b) Barney could be transfused group A FP (anti-B antibody) as he has A antigen on his red blood cells (group
- c) Barney could be transfused group O
 FP (anti-A & anti-B antibodies) as he has A antigen on his red blood cells (group A).
- d) Barney must be transfused **only**
 - **group AB FP** (no ABO antibodies) as he has A antigen on his red blood cells (group A).

Blood Compatibility Check Visual Aid Platelet Transfusion

Blood Compatibility - Platelet Transfusion			
PLATELETS	 *Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential = Compatibility Check 		
0	Platelet	Patient	
ABO Blood Group			
ABO Antigen(s)		7	
ABO Antibody(ies)			
Rh(D) Blood Group			
Rh(D) Antigen **			
Rh(D) Antibody			
*Transfused platelets should be ABO compatible with patient's red blood cells (platelets are suspended in donor plasma). Platelet components also contain a few red blood cells. If platelets are in short supply, TML policy re: ABO group substitution.			
**For Rh(D) negative females of childbearing age/potential, if Rh(D) positive platelets are transfused (re: platelet supply), Rh immunoglobulin (RhIG) is required.			



Pebbles, a 33-year-old female, is undergoing induction chemotherapy for acute leukemia. Her clinical course is proceeding as anticipated. Today her platelet count is 8 $x10^{9}$ /L. A 1-dose platelet transfusion is ordered.

Pebbles' group & screen test: group A, Rh negative, antibody screen negative. **TML issues Platelet unit:** group A, Rh positive.

Patient Case 5 Compatibility Check

Pebbles' group & screen test: group A, Rh negative, antibody screen negative. **TML issues Platelet unit:** group A, Rh positive.

Blood Compati	bility - Platelet Transfusio	on	
PLATELETS	*Antigen(s) – on exterior surface of red blood cell *Antibody(ies) – in plasma ** Females of childbearing age/potential		
		Patient	
ABO Blood Group			
ABO Antigen(s)		A	
ABO Antibody(ies)	anti-B 🖌		
Rh(D) Blood Group	Pos	Neg	
Rh(D) Antigen **		none	
Rh(D) Antibody		No	
*Transfused platelets should be ABO are suspended in donor plasma). Plate If platelets are in short suppl	compatible with patient's re elet components also conta v. TML policy re: ABO grou	ed blood cells (platelets in a few red blood cells. p substitution.	
**For Rh(D) negative females of childb transfused (re: platelet supply	y), Rh immunoglobulin (Rh	(D) positive platelets are IG) is required.	

Select all the correct statements.

- Pebbles could be transfused group A platelets (plasma has anti-B antibody) as she has A antigen on her red blood cells (group A).
- The platelets are Rh positive, and Pebbles is Rh negative, she should receive RhIG. This is to prevent Rebbles from producing anti-D antibody.
- Pebbles could be transfused group O platelets (plasma has anti-A & anti-B antibodies) as she has A antigen on her red blood cells (group A).
- Pebbles could be transfused group AB platelets (plasma has no ABO antibodies) as she has A antigen on her red blood cells (group A).

The Elephant in the Transfusionist's Skill Set: Understanding Compatibility for Transfusion Safety

Take Home Messages

- Transfusion safety is teamwork!
- Confirming compatibility is one aspect of transfusion safety.
- Confirming compatibility is a transfusionist responsibility & accountability.
- Compatibility starts with the group & screen blood sample.
- Antigens (name badge) are on red blood cells.
- Antibodies (protectors) are in the plasma.
- Clinically significant antibodies (troublemakers), especially anti-D and anti-K, must be assessed.
- Respect patient identification & blood labels.
- When in doubt, refer to the Compatibility Table or call TML.

Compatibility Table

Patient ABO/Rh(D)	Compatible Blood Group for Transfusion			
Blood Group	RBC	Platelets	Plasma	Cryoprecipitate
O Positive	O Rh(D) positive or negative	O preferred** Rh(D) positive or negative	O, A, B, AB	
O Negative	O Rh(D) negative*	O preferred** Rh(D) negative*	O, A, B, AB	
A Positive	A, O Rh(D) positive or negative	A preferred** Rh(D) positive or negative	A, AB	Any Group
A Negative	A, O Rh(D) negative*	A preferred** Rh(D) negative*	A, AB	Very infrequently used component
B Positive	B, O Rh(D) positive or negative	B preferred** Rh(D) positive or negative	B, AB	Cryoprecipitate is interchangeable with Fibrinogen Concentrate for fibrinogen replacement.
B Negative	B, O Rh(D) negative*	B preferred** Rh(D) negative*	B, AB	
AB Positive	AB, A, B, O Rh(D) positive or negative	AB preferred** Rh(D) positive or negative	AB	
AB Negative	AB, A, B, O Rh(D) negative*	AB preferred** Rh(D) negative*	AB	

* In urgent bleeding patient situations or during times of short supply, Rh(D) negative patients may need to receive Rh(D) positive RBC and platelets

** Platelets should be ABO compatible with patient's red blood cells (donor platelets are suspended in plasma). In urgent bleeding patient situations or during times of short supply, TML will follow established policies for ABO group substitution for platelets.

Post Transfusion Knowledge Question 1

Paramedics arrive in ED with Emma, a 21-year-old female trauma patient. She is unresponsive, being intubated, unstable & bleeding. Lab tests are pending. Blood, 4 units RBC & 4 units plasma (FP), is ordered.

The safest blood for this patient, Emma is:

- a) Group O, Rh positive RBC and group O FP.
- b) Group O, Rh negative RBC and group O FP.
- c) Group O, Rh positive RBC and group AB FP.
- d) Group O, Rh negative RBC and group AB FP.

Post Transfusion Knowledge Question 2

An RBC unit crossmatched, compatible is safe for transfusion when:

- a) The ABO antigens on the red blood cells in the unit of blood will not be hemolysed by ABO antibodies in the patient's plasma.
- b) The ABO antigens on the red blood cells in that unit of blood will be hemolysed by ABO antibodies in the patient's plasma.
- c) The ABO antibodies on the red blood cells in the unit of blood will not be hemolysed by ABO antigens in the patient's plasma.
- d) The ABO antibodies on the red blood cells in the unit of blood will be hemolysed by ABO antigens in the patient's plasma.

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