

Troubleshooting transfusion needs in patients with sickle cell disease undergoing transformative treatment

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Disclosures

- **Board of Directors**

- Association for the Advancement of Blood and Biotherapies (AABB)

- **Speaker fees:**

- Terumo BCT
 - BEAM Therapeutics

Learning objectives

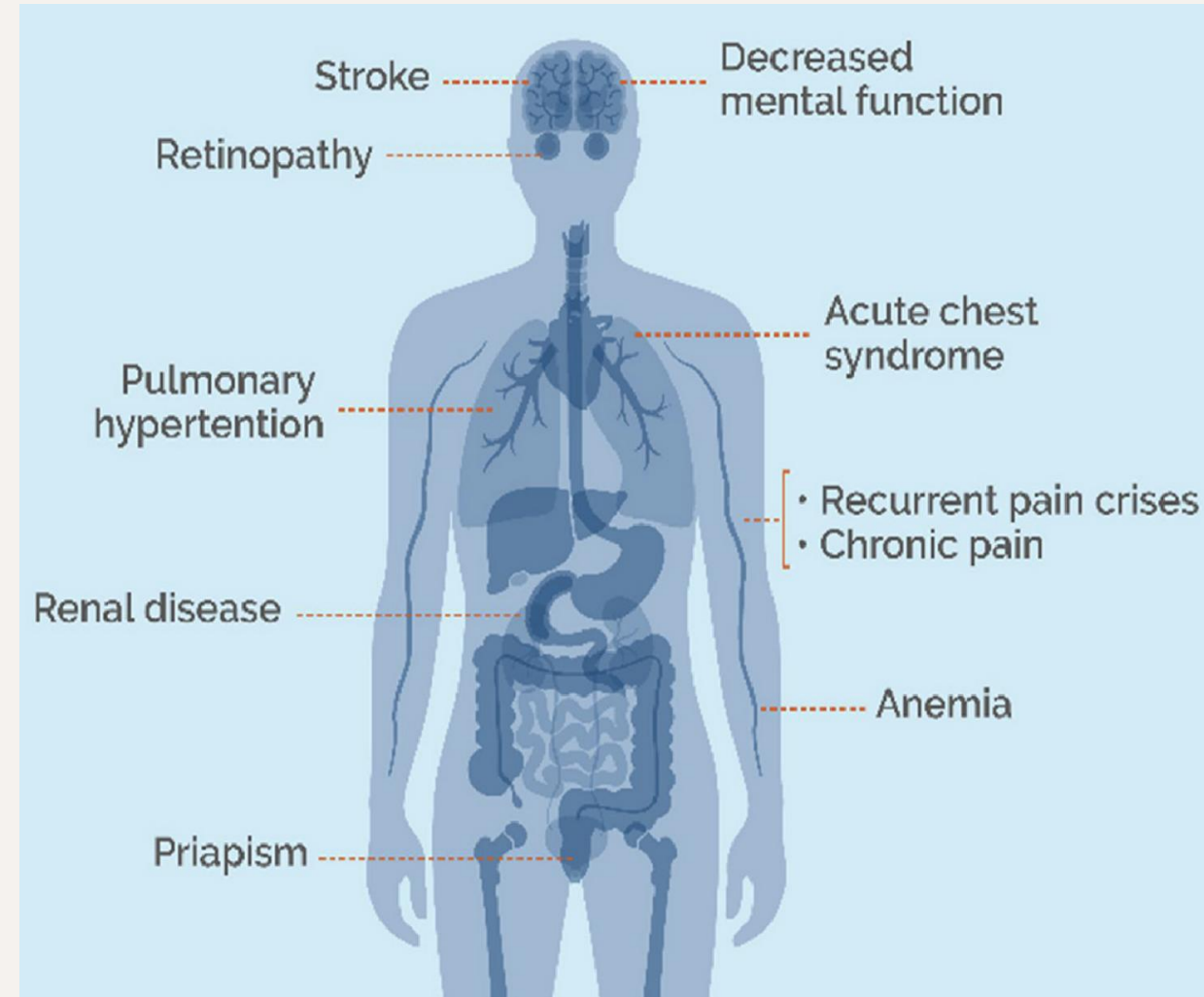
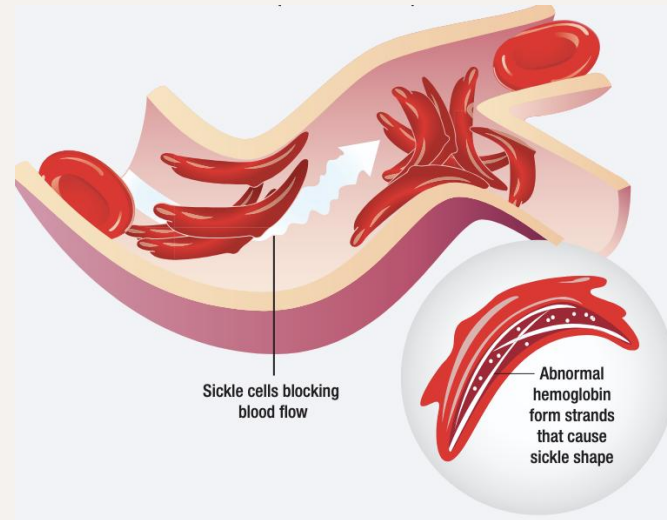
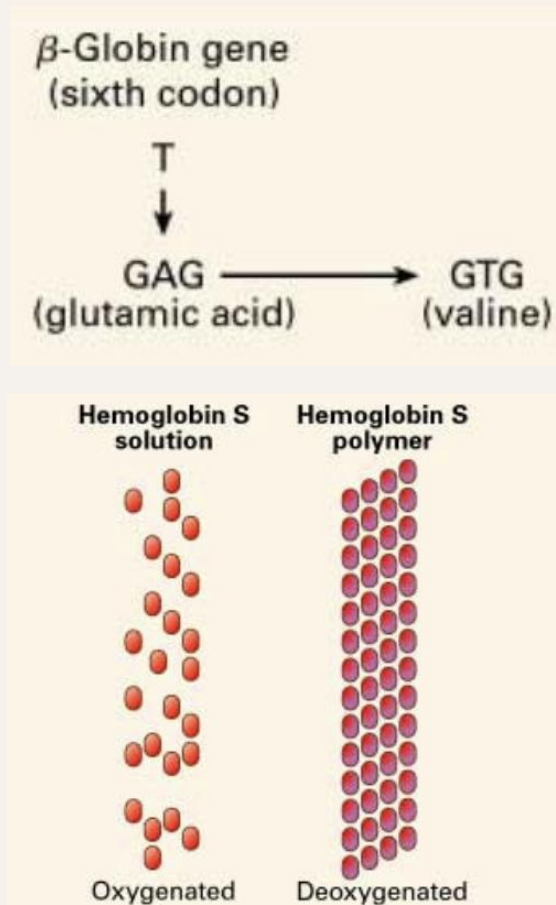
By the end of the presentation, audience members should be able to:

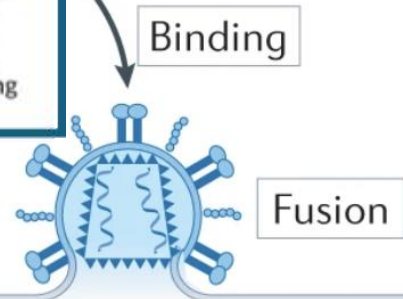
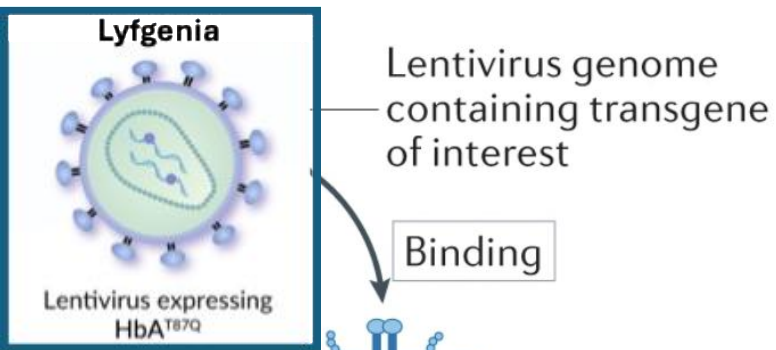
- 01 Recall potential clinical impact of evolving red blood cell alloimmunization.**
- 02 Describe interplay of blood needs for patients undergoing the process of autologous genetically modified hematopoietic stem cell transplantation.**

Setting the Stage

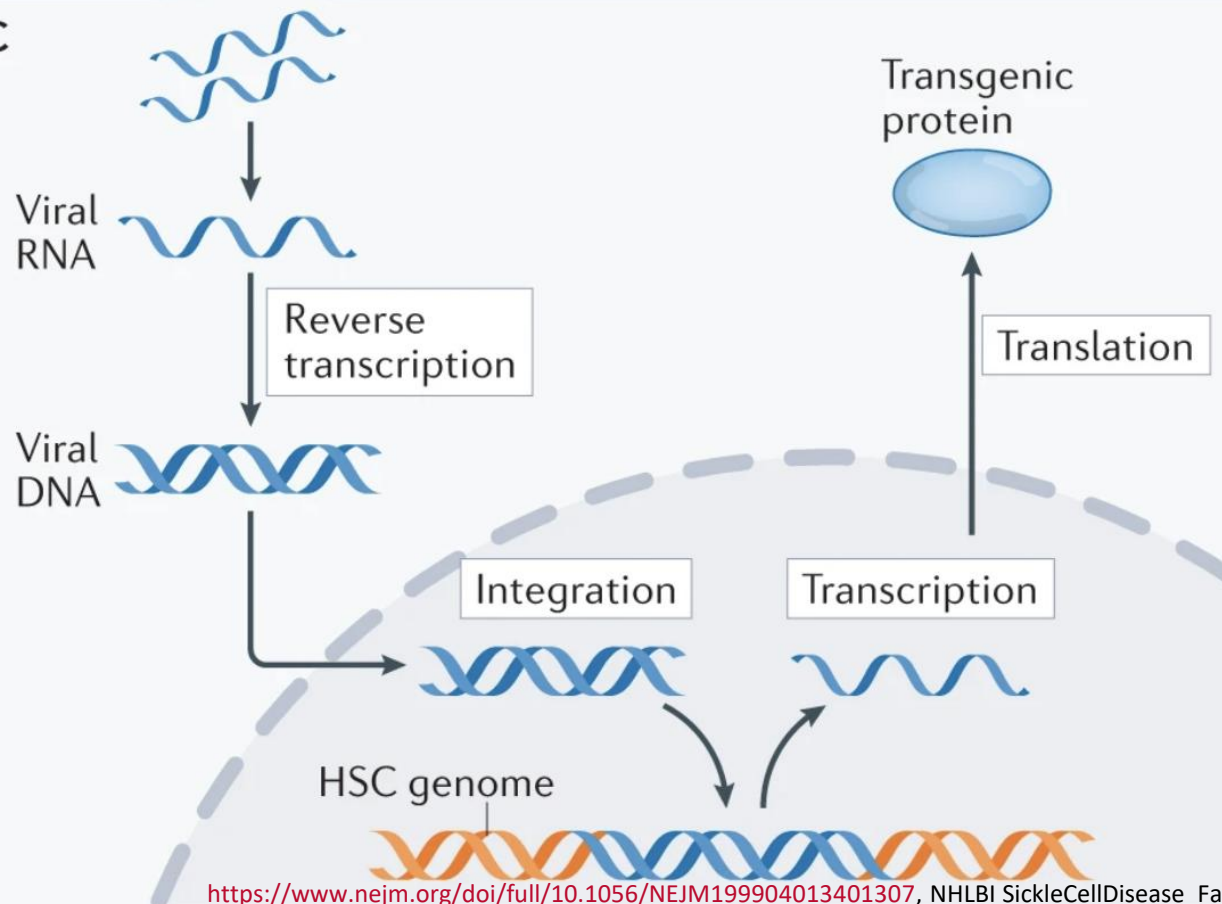
- 22-year-old patient with history of hemoglobin SS disease
 - History of silent cerebral infarcts
 - Splenic sequestration requiring splenectomy
- Transfusion history significant for:
 - Anti-HTLA-like antibody detected once in 2021 - That's it 😊
- Starting to prepare for transformative therapy for sickle cell disease
lovotibeglogene Autoemcel (Lyfgenia)

Sickle cell disease impacts quantity and quality of life

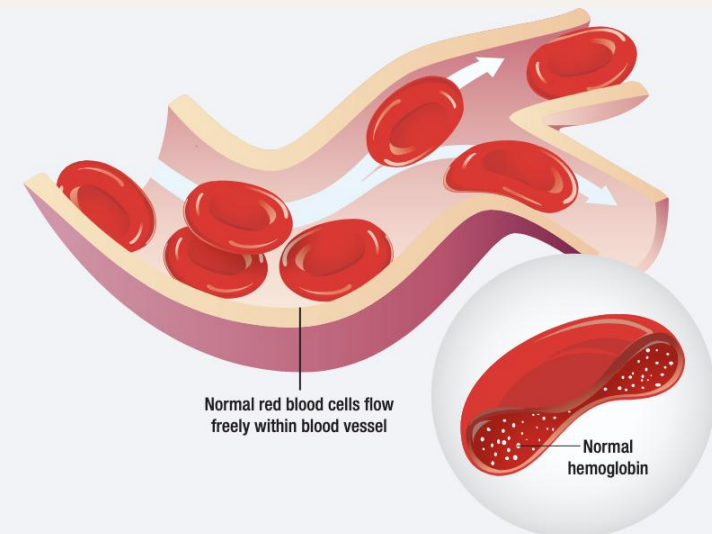
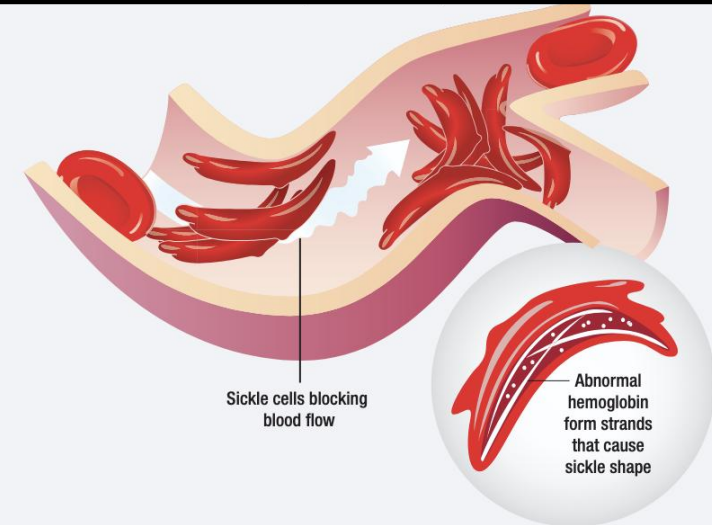




HSC



Lovo-cel (lovotibeglogene autotemcel) restores Hemoglobin A expression in red blood cells



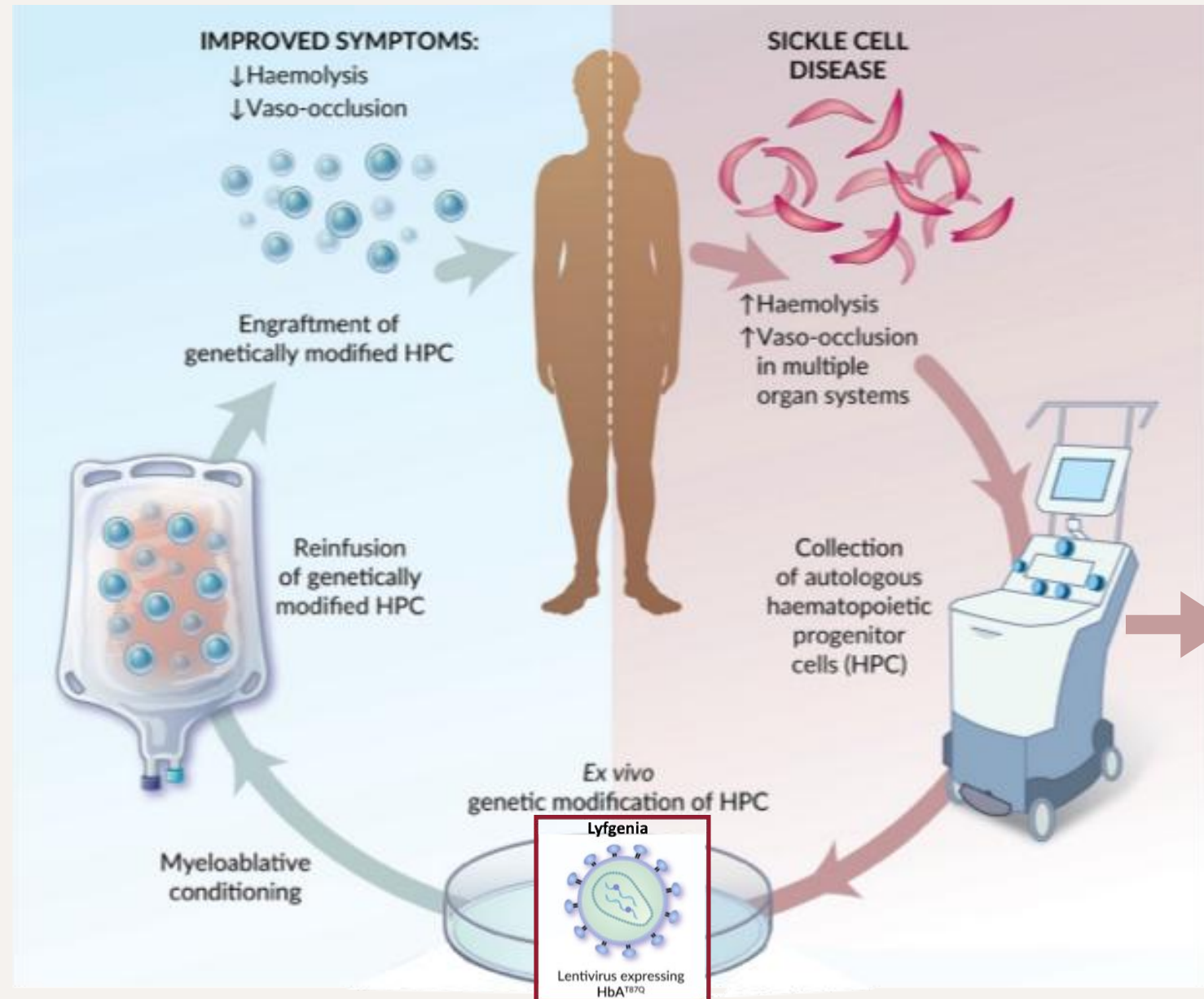
The process of receiving gene therapy has multiple steps

The patient is supported with:

red blood cell exchange before cells are collected (at least 3)

red blood cell exchange before cells are infused

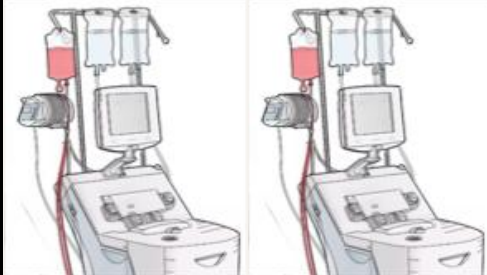
Transfusion after infusion until engraftment



RBC exchange



Cell Collection **Cell Collection**



Cell Collection



The process of receiving gene therapy is intense

Preparation



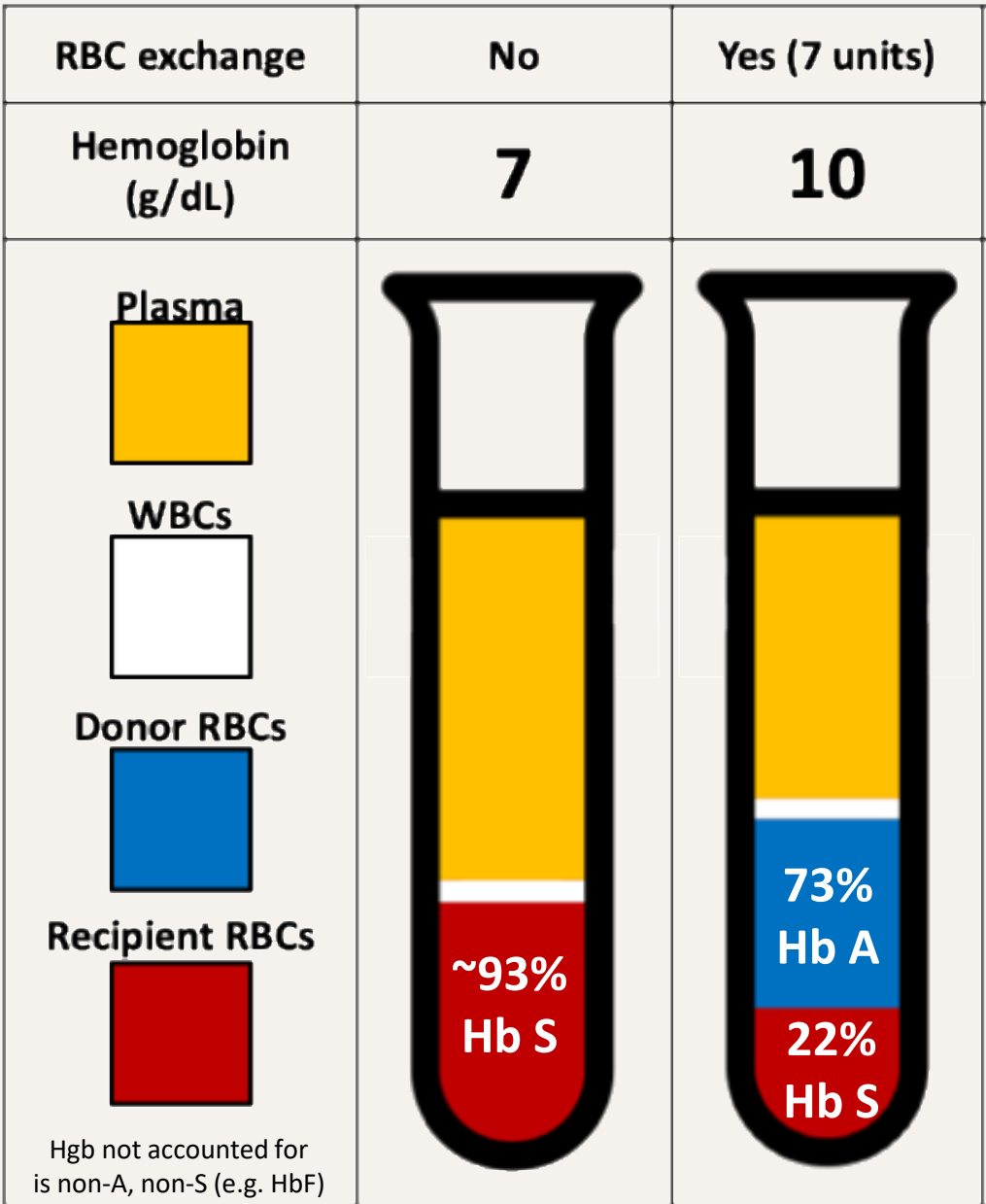
Collection



Therapy



Red blood exchange #1 was tolerated well



Twelve days later...

Preparation



Week 1



Week 4

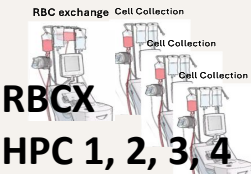


Week 8

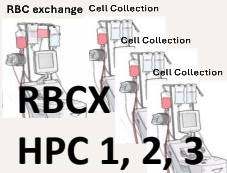


Week 12

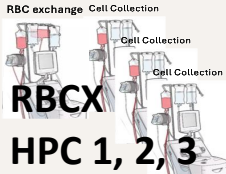
Collection



Week 1
Cycle 1



Week 4
Cycle 2



Week 8
Cycle 3



Week 12
maintain

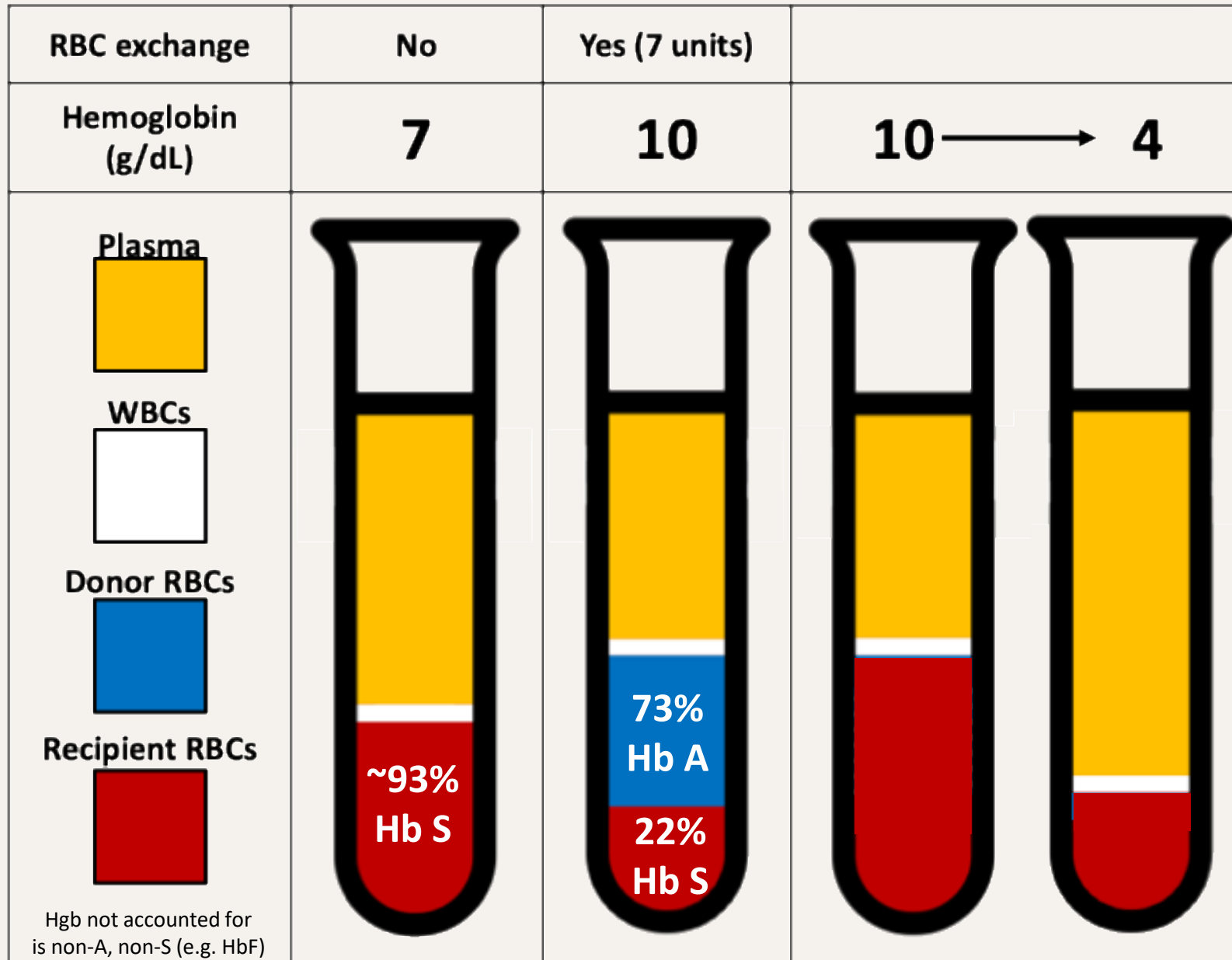
Therapy



RBCX, infusion of cells

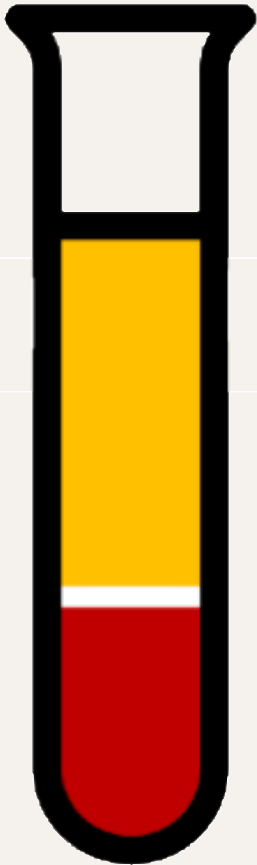
Week 1

Hemoglobin was much lower than before transfusion



Could this be hyperhemolysis?

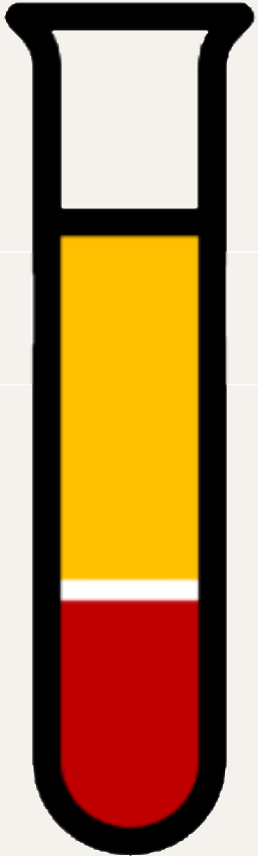
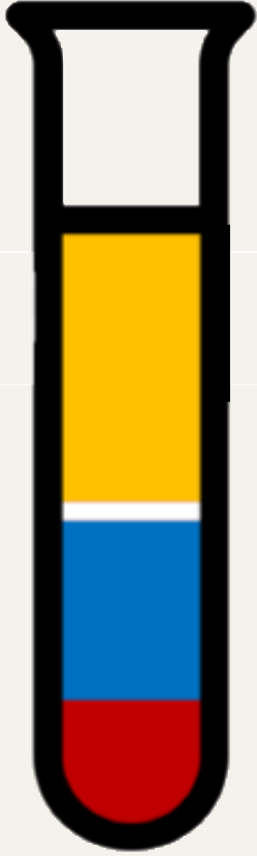
Hyperhemolysis involves “bystander hemolysis”

	Simple Transfusion		Transfusion reaction	
	No	Yes (2 units)	Delayed hemolysis	Hyperhemolysis
Hemoglobin (g/dL)	8	10		
Plasma WBCs Donor RBCs Recipient RBCs				

But this was not just a simple transfusion...

It was an automated red blood cell exchange!

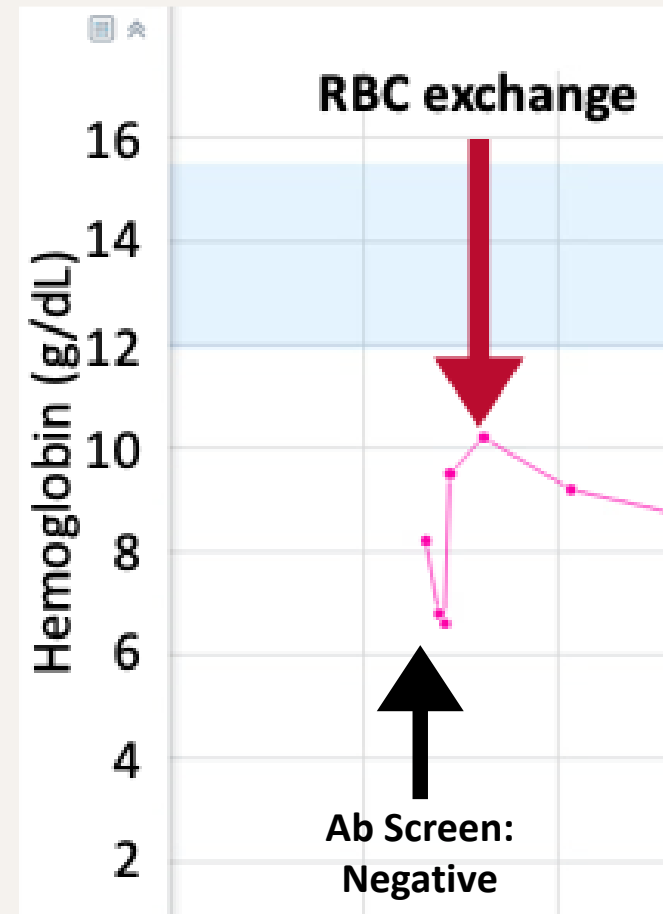
It can be difficult to distinguish delayed hemolysis and hyperhemolysis

	RBC exchange		Transfusion reaction	
	No	Yes (7 units)	Delayed hemolysis	Hyperhemolysis
Hemoglobin (g/dL)	8	10		
Plasma WBCs Donor RBCs Recipient RBCs				

There are some differences in presentation

	Delayed hemolytic transfusion reaction	Hyperhemolysis
Cells destroyed		
Hemoglobin drop		
Reticulocyte response		
Timing of development		
Antibody identification		
Future transfusion		

The patient presented with fatigue and pleuritic chest pain consistent with symptomatic anemia

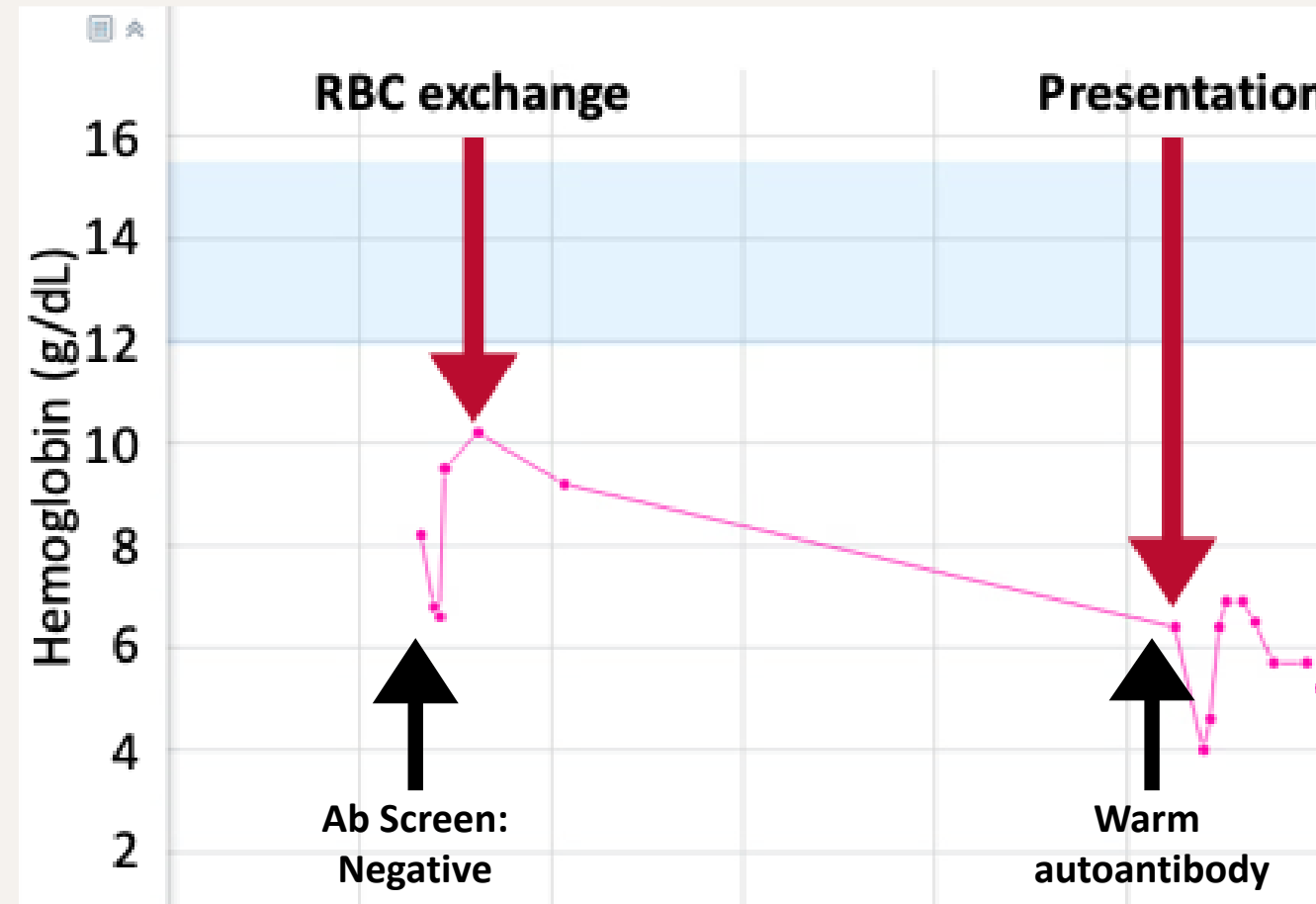


Blood bank workup findings were consistent with a warm autoantibody

			Rh-hr										KELL				DUFFY		KIDD	Sex Linked	LEWIS		MNS				P	LUTHERAN		Special Antigen Typing				
Cell#	Rh-hr	Donor Number	D	C	E	c	e	f	C ^w	V	K	k	Kp ^a	Kp ^b	Js ^a	Js ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	Xg ^a	Le ^a	Le ^b	S	s	M	N	P ₁	Lu ^a	Lu ^b			Cell#	
1	R1wR1	111364	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	+	+	+	0	+	+	+	+	+	+	+	0	+			1
2	R1R1	305296	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	0	0	+	0	0	+	0	+	+	+	+	+	0	+			2
3	R2R2	320411	+	0	+	+	0	0	0	0	0	+	0	+	/	+	0	0	0	+	+	0	0	0	+	+	+	+	+	0	+	HLA+		3
4	Ror	329575	+	0	0	+	+	+	0	+	0	+	0	+	/	+	0	0	+	+	0	0	0	0	+	0	+	+	+	0	+			4
5	r'r	330343	0	+	0	+	+	+	0	0	0	+	0	+	/	+	+	0	+	+	0	0	+	0	+	+	0	+	+	0	+	@		5
6	r''r	113145	0	0	+	+	+	+	0	0	0	+	0	+	0	+	+	+	+	+	+	+	0	0	+	0	+	+	+	0	+	@		6
7	rr	318917	0	0	0	+	+	+	0	0	+	+	0	+	/	+	0	+	0	+	+	0	+	0	+	0	+	+	+	0	+	@, HLA+		7
8	rr	323035	0	0	0	+	+	+	0	0	0	+	0	+	/	+	+	+	+	0	+	0	+	+	0	+	0	+	+	0	+	@		8
9	rr	306096	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	+	0	0	+	0	+	0	+	0	+	0	+			9
10	rr	329645	0	0	0	+	+	+	0	0	0	+	0	+	/	+	+	0	+	0	0	+	0	+	0	0	+	0	+	0	+			10
11	R1R1	303052	+	+	0	0	+	0	0	0	+	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	+	+	+	+	+			11
	Patient Cells																																AC	

AC 2+

Additional information



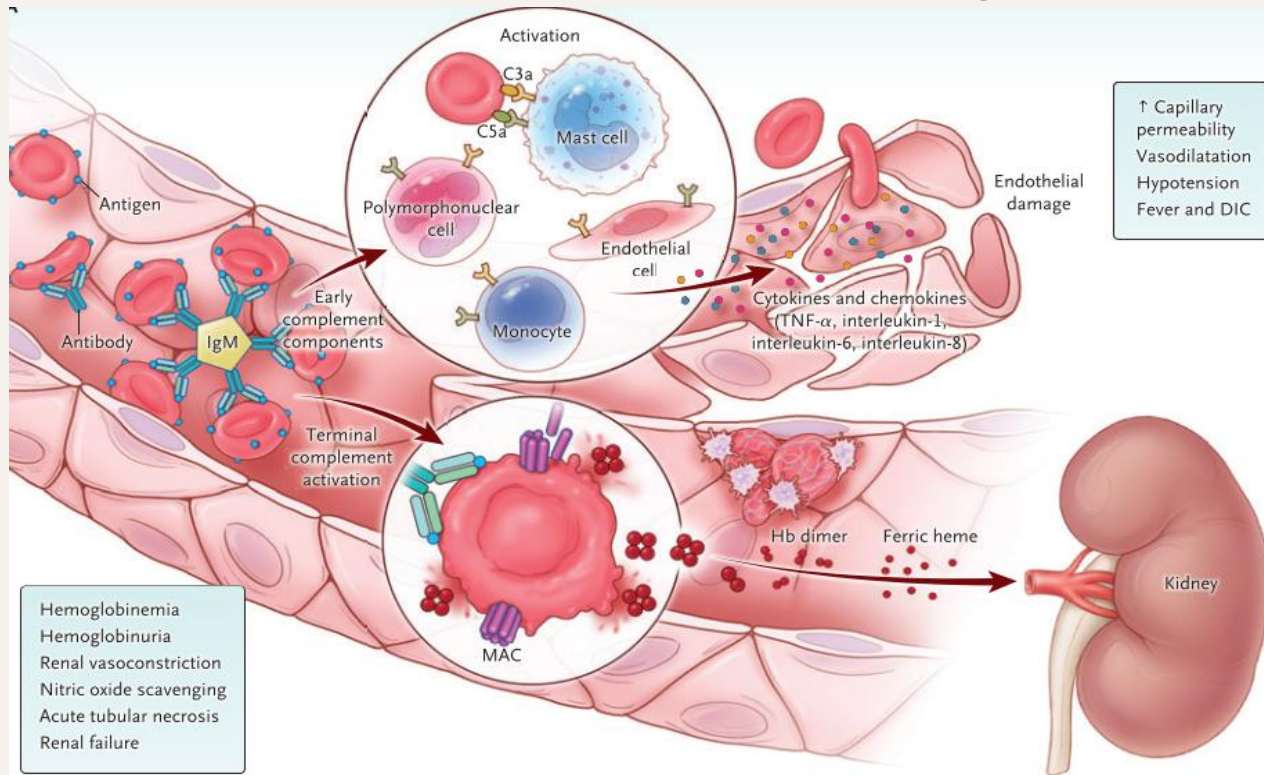
Blood bank workup findings were consistent with anti-Jk(b)

Vial No.	Manufacturer / Lot No.	Expiry Date	Donor Code	Rh - Hr							Kell					Duffy	Kidd	Lewis	P	MNS					Lutheran			Sex Link	Vial No.						
				D	C	c	E	e	f	V	C ^w	K	k	Kp ^a	Kp ^b	Js ^a	Js ^b	Fy ^a	Fy ^b	Jk ^a	Jk ^b	I ^a	I ^b	Le ^a	Le ^b	P ₁	M	N		S	s	Lu ^a	Lu ^b	Xg ^a	
	R1R1 x2																																		
3	IMM 15889	6-14-24	R2R2 C3265	+	0	+	+	0				0	+					+	+	+	+						+	+	+	+					OV
8	IMM 15889	6-14-24	R2R2 H9411	0	0	+	0	+				0	+					+	0	+	0						+	0	+	0					OV
	R2R2 x2																																		
2	IMM 16897	6-26-24	R2R2 B16715	+	+	0	0	+				+	+					+	+	0	+						+	+	+	+					mt
3	IMM 16897	6-26-24	R2R2 C3092	+	0	+	+	0				+	+					0	+	0	+						+	0	0	+					mt
5	IMM 15889	6-14-24	R2R2 E1001	0	+	+	0	+				0	+					0	+	+	0						+	0	+	+					OV
10	IMM 15889	6-14-24	R2R2 B1671	+	+	0	0	+				0	+					+	0	+	0						+	0	+	+					OV
	IMM 16903	6-26-24	R2R2 C1579	+	0	+	+	0				+	+					+	0	+	0						+	0	+	+					OV
	IMM 16903	6-26-24	R2R2 B1238	0	0	+	0	+				+	0					+	0	+	0						+	0	+	+					OV
	IMM 13879	5-31-24	R2R2 C6404	+	0	+	+	0				0	+					+	0	0	+						+	+	0	+					+
	R x2																																		
	6903	6-26-24	R2R2 C5673	+	0	+	+	0				0	+					0	+	+	+						0	+	0	+					OV

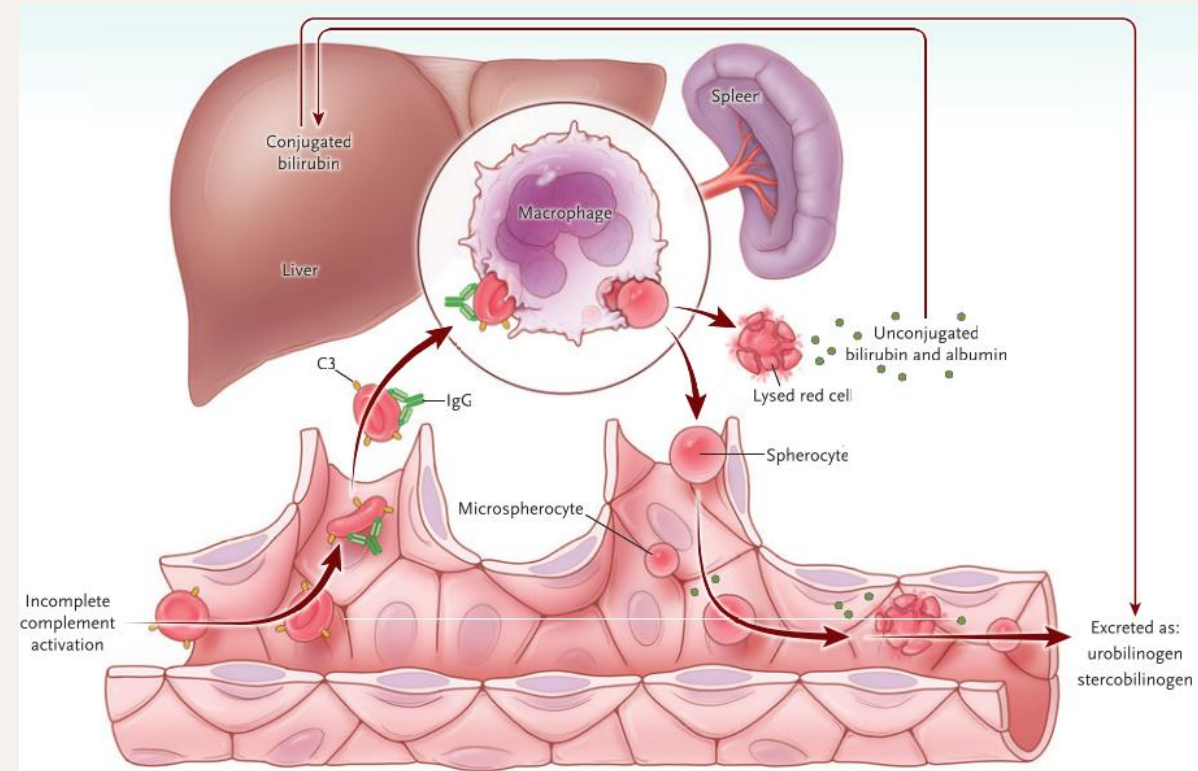
Ref R.6 Attachment A (01/29/24)

Kidd(s) can cause double the trouble!

Intravascular hemolysis

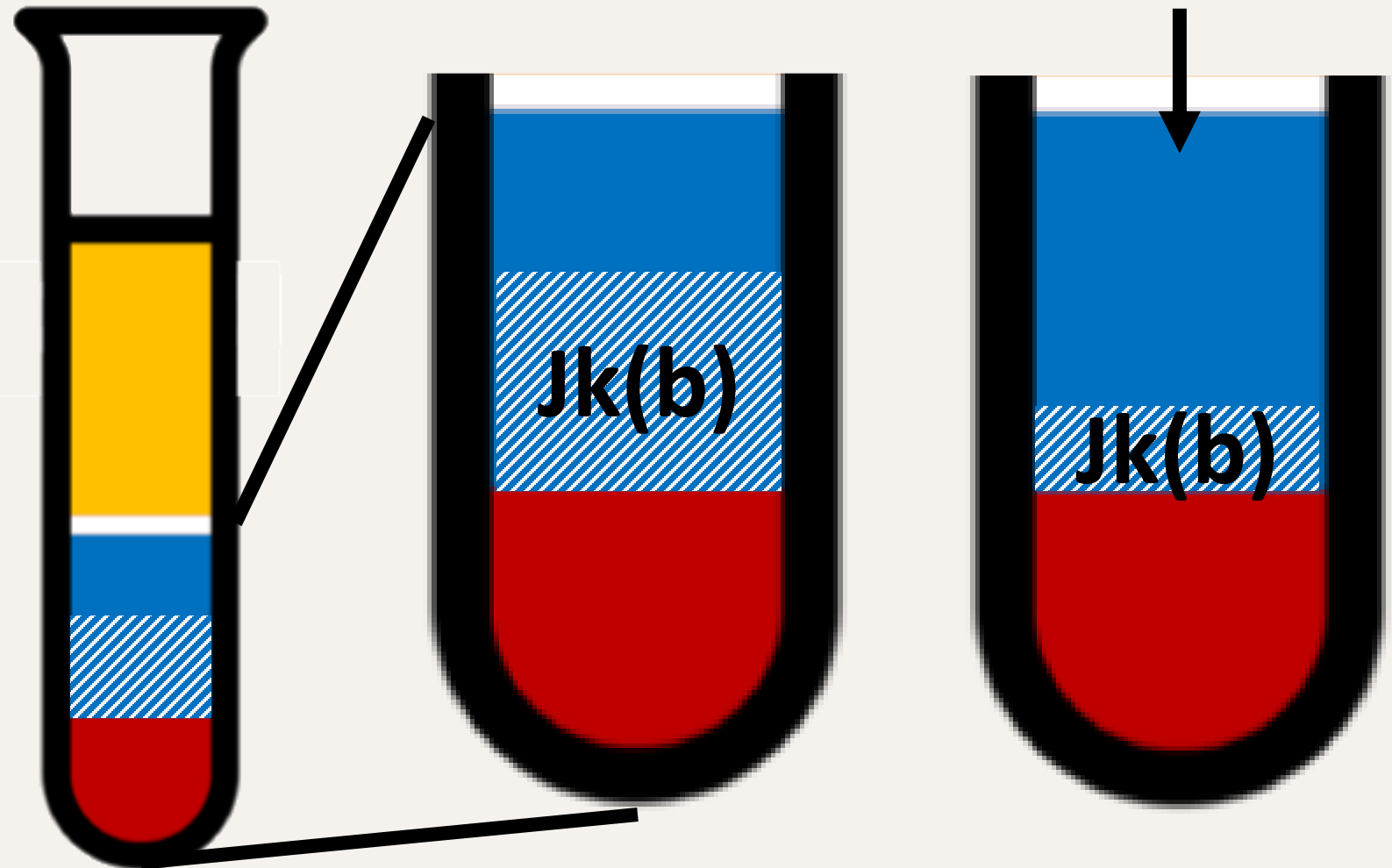


Extravascular hemolysis

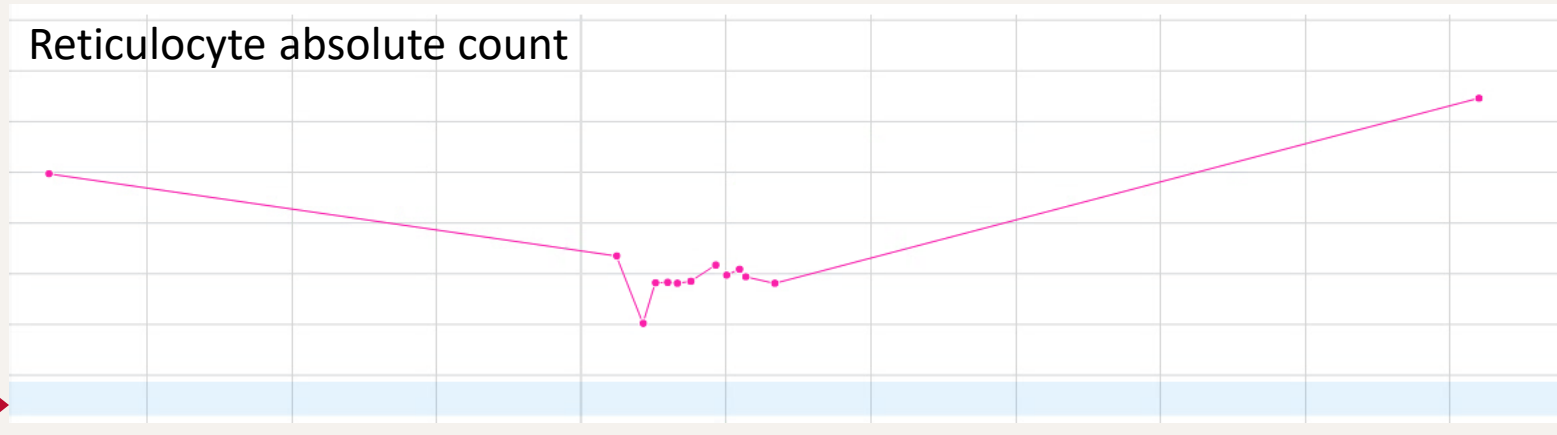
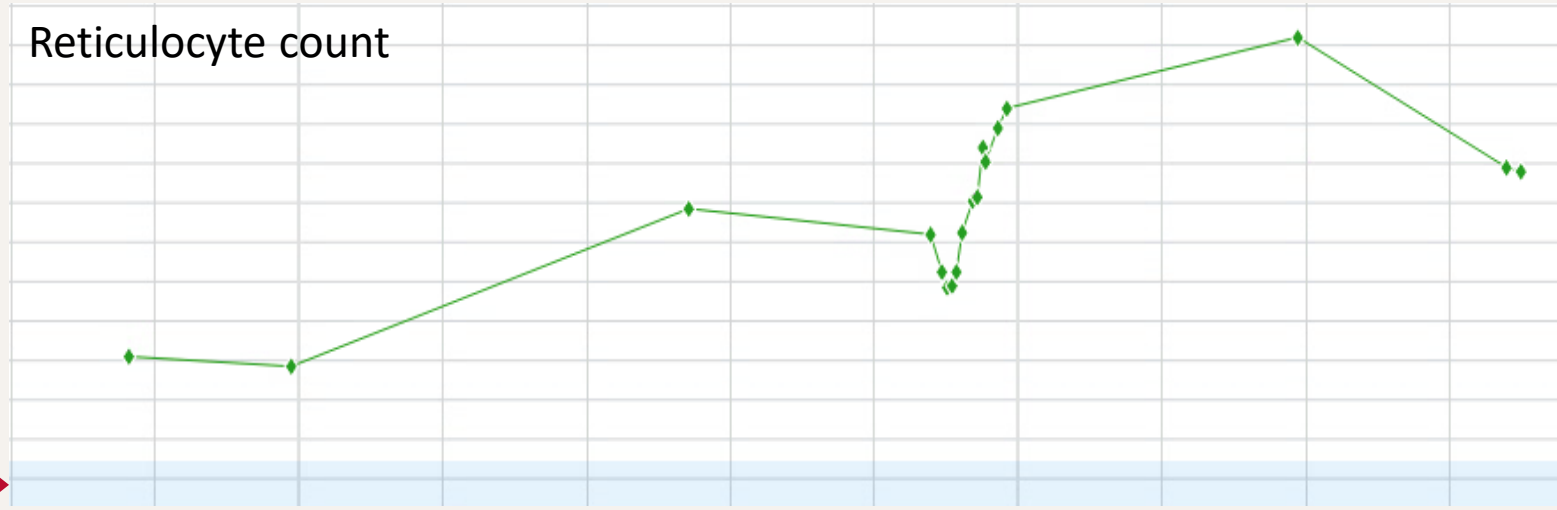


Transfused units were phenotyped...

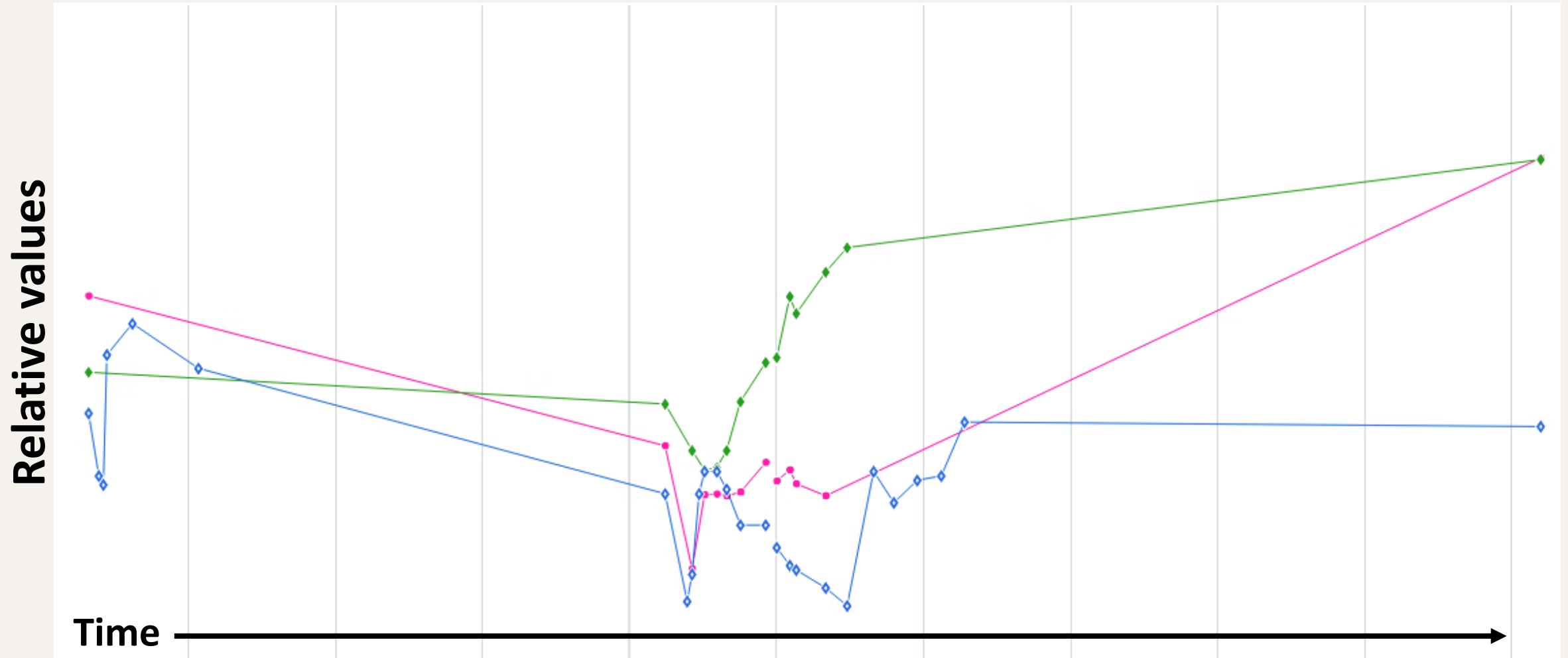
Patient/Unit #	Result
Transfused #1	
Transfused #2	
RBC exchange #1	
RBC exchange #2	
RBC exchange #3	
RBC exchange #4	
RBC exchange #5	
RBC exchange #6	
RBC exchange #7	



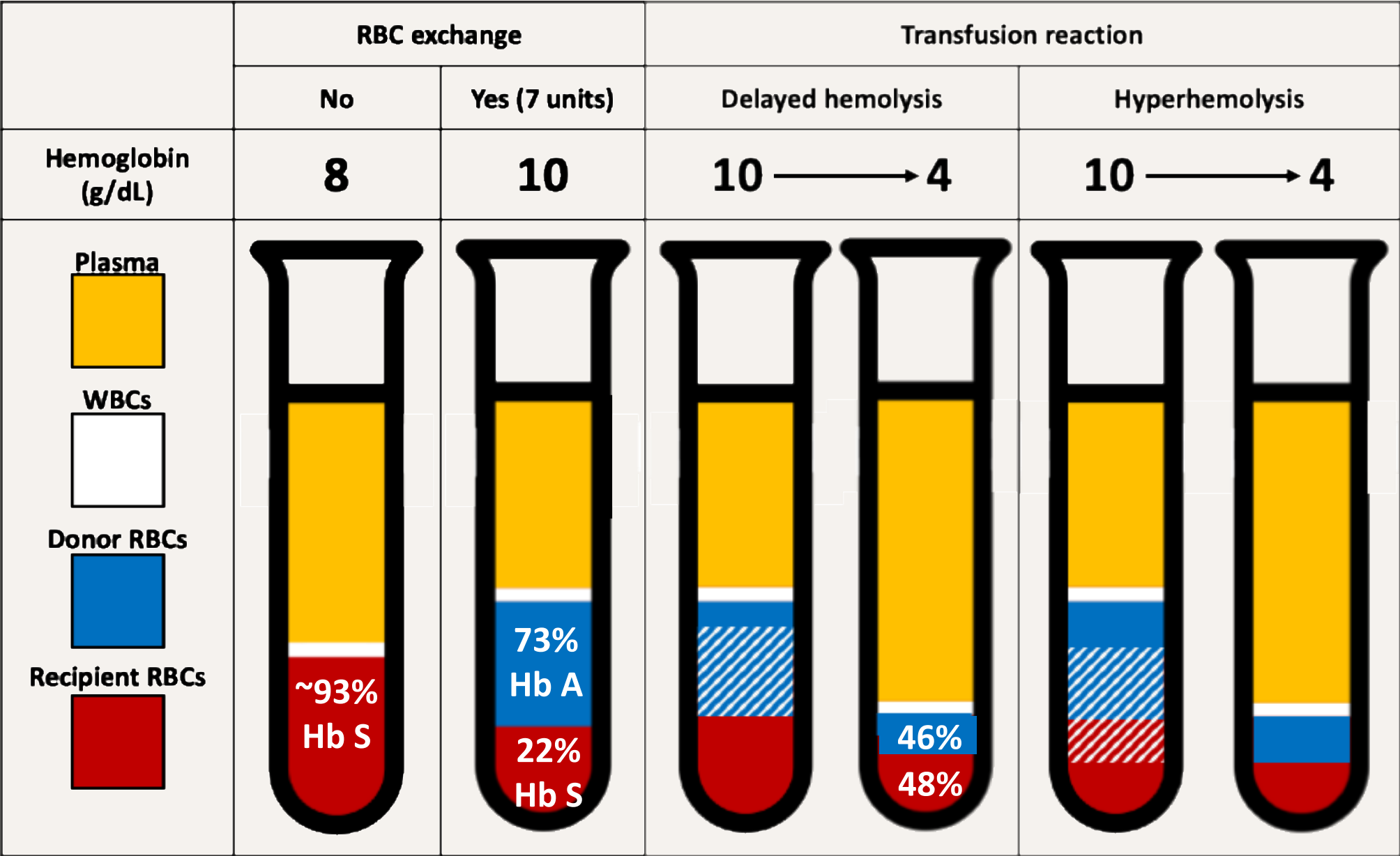
Reticulocyte response was very robust



Overall, information supported a delayed hemolytic transfusion reaction

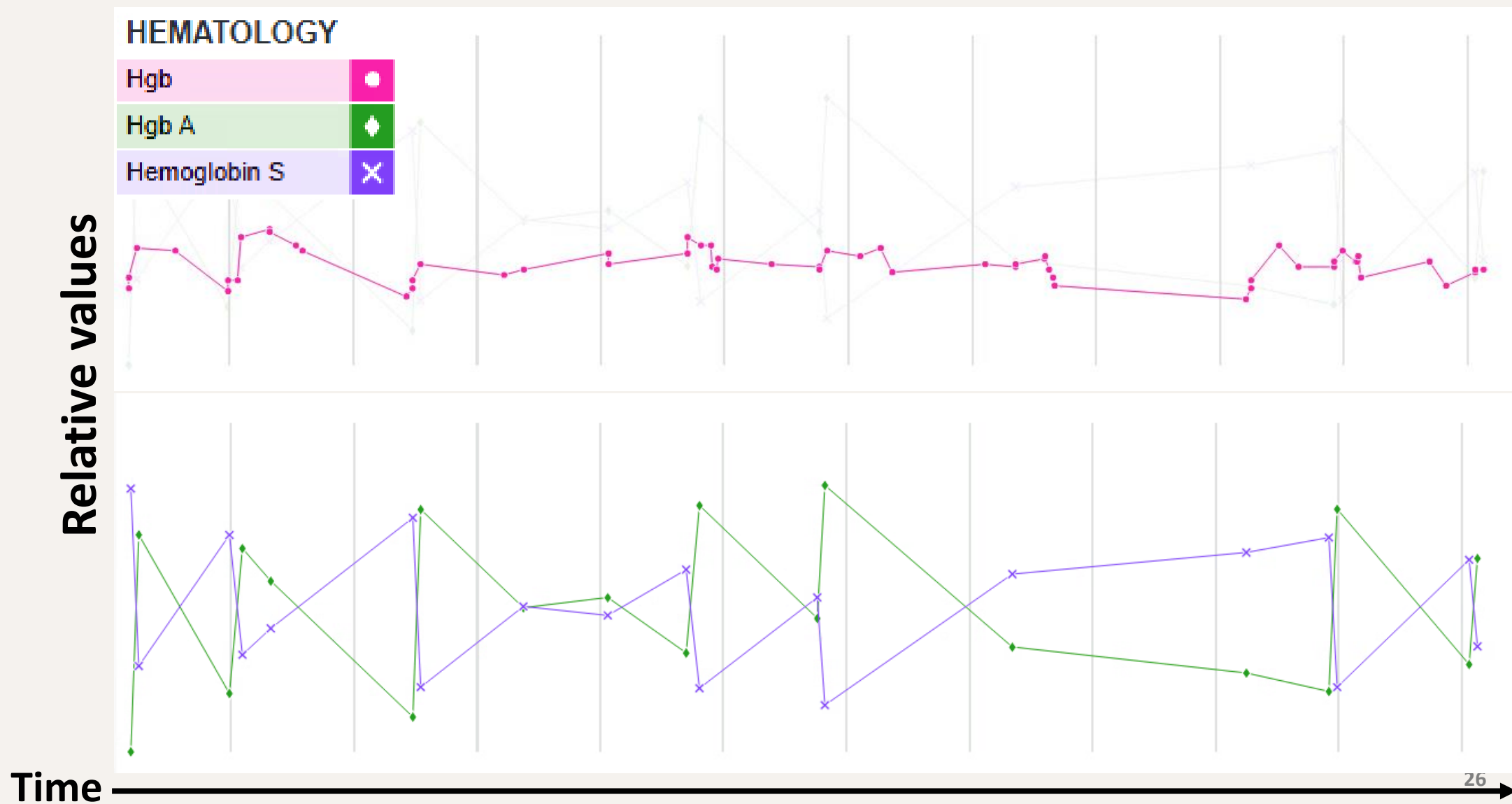


Information supported a delayed hemolytic transfusion reaction



Patient restarted automated RBC exchanges about 1 year later*

*anti-Js(b) developed in interim



Take 2...has been successful so far*

Preparation

RBC exchange



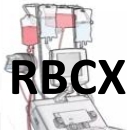
RBCX

RBC exchange



RBCX

RBC exchange



RBCX

RBC exchange



RBCX

Week 1

Blood search

Week 4

Blood search

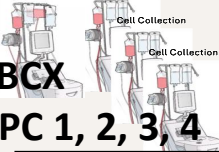
Week 8

Blood search

Week 12

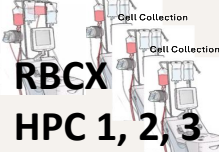
Collection

RBC exchange Cell Collection



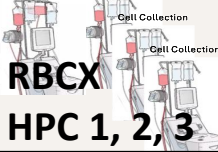
RBCX
HPC 1, 2, 3, 4

RBC exchange Cell Collection



RBCX
HPC 1, 2, 3

RBC exchange Cell Collection



RBCX
HPC 1, 2, 3

RBC exchange



RBCX

Week 1

Cycle 1

Blood search

Week 4

Cycle 2

Blood search

Week 8

Cycle 3

Blood search

Week 12

Maintain
every 4 weeks
Blood search

Therapy

RBC exchange



RBCX, infusion of cells

Week 1

Blood search

Conclusions and considerations

- **Evolving red blood cell alloimmunization can impact patient care.**
- **Severe delayed hemolytic transfusion reactions can mimic hyperhemolysis**
- **Anticipating ongoing blood needs for patients is critical throughout the process of autologous genetically modified hematopoietic stem cells**

Thank you!



WashU Medicine

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