Can be very sneaky!!

Passive Aggressive!

WHEN COMPATIBILITY ISSUES AREN'T AS STRAIGHT FORWARD AS YOU THINK!!!

Saint Luke's Hospital of Kansas City
SAINT LUKE'S HEALTH SYSTEM
saintlukeshealthsystem.org

Beth Jones, MT(ASCP)BB
Saint Luke's Hospital, KC, MO

BEFORE THINGS GOT COMPLICATED…

- In 2005, a 60 year old,"very pleasant" male, presented to us with mild anemia and low B12 levels.
- He had been receiving B12
- His hgb was 7.9 g/dl
- Order was to give 1 unit of packed red cells
- He typed as A positive with a negative antibody screen
- *Life was easy in the Blood Bank!!*

SCROLL FORWARD TO OCTOBER, 2012

- Where has he been the last 7 years???
- What about treatment/transfusion histories???
- His lab report from the doctor's office chart (April 2012) showed:

  Hgb 11.0 g/dL, Folate was normal
- However, over last few months he has been very tired, dyspneic with exertion, and unable to perform usual cardiac exercises

Lab Results from early October

- Hgb *7 g/dL* (13-17)
- MCV *124 fl* (80-99)
- WBC *3.4 th/uL* (4-11)
- Plt *73 th/uL* (140-400)
- Bilirubin *6 mg/dL* (0.3-1.4)
- BNP *3290 pg/mL* (0-100)
- Total protein, transaminases, albumin and TSH normal
- Trace hgb in urine
- Ferritin: *192*, folate *>20*, retic count *219,000* = appropriate response to anemia

Laboratory indices of hemolytic anemia and ultrasonographic evidence of mild to moderate hepatosplenomegaly

PHYSICAL EXAMINATION, OCT. 2012

- Exertional Dyspnea
- Dizziness
- Loss of balance
- Slight Fever
- Severely Icteric
- Dryness on Face
- Rash on palms
- 3+ pedal edema

ACTION PLAN….

Diagnosis:

- Hemolytic anemia-likely autoimmune
- "Check Coombs"
- No evidence of TTP
- AIHA idiopathic in nature *or* associated with lymphoproliferative malignancies
- Order Bone Marrow Biopsy
- CT neck through pelvic regions
- Elevated BNP & edema consistent with hyperdynamic heart failure; anemia

Treatment:

- Steroids, possibly chemotherapy
- "Transfusion may be required"

10/10: ORDER FOR 2 RBC'S TO BE TRANSFUSED

Blood Bank Results:

- *A pos*
- *Positive Screen (SCII) 2+*
- *Anti-E identified*
- *Negative DAT (polyspec)*
- *Crossmatched 2 units :*

  A positive, E negative blood
- *No big deal…*

Life is still relatively easy in the Blood Bank!

THAT'S WHAT WE THOUGHT ANYWAY….

From patient's chart, 10-21-12:

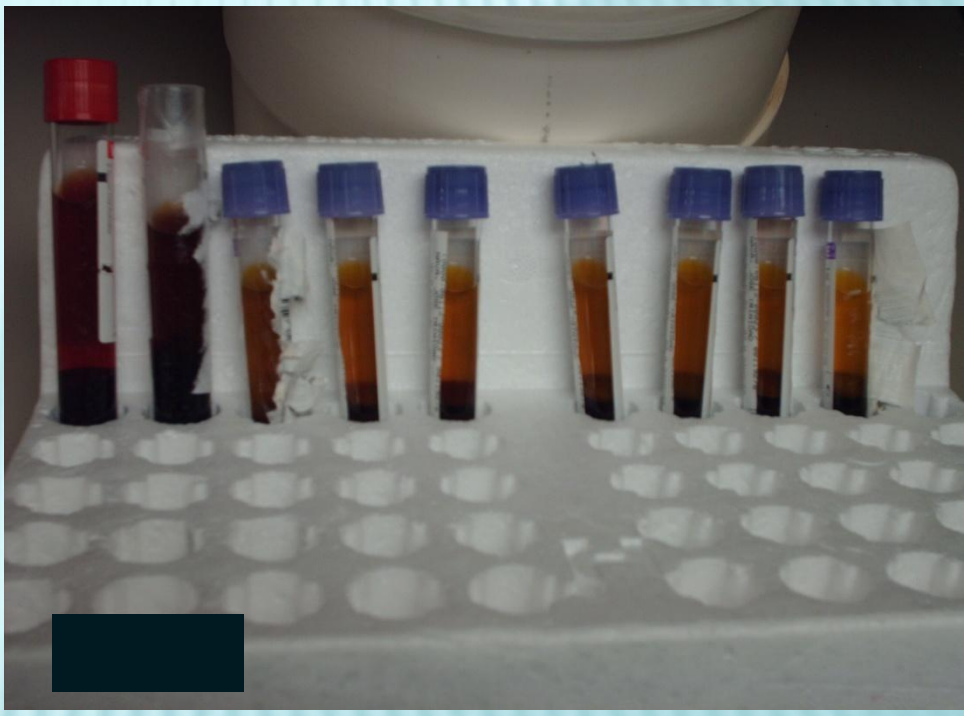
" The patient's dyspnea has been stable until the last week when he has been getting more and more short of breath. He did receive a blood transfusion a little over a week ago that was supposed to improve his dyspnea, however he states it did not. He has been very weak over the last few days and it was tonight that his wife was finally able to talk him into presenting to the ER. When the patient arrived, it was found that he had a ***hgb of 4.4*** and was hypotensive with a systolic blood pressure in the 80s. He was transferred to ICU and to be seen by hematology. At this time the patient is very jaundiced. The patient is mildly confused, and his wife said he has been confused over the last couple of days"

Life in the Blood Bank may be getting a little harder!

IT JUST GOT HARDER!

- Order was placed for 2 units RBC's to be transfused ASAP, and 2 units to be placed on hold
- Specimen arrived and was

very icteric !



- Patient typed as A positive, positive Ab Screen
- Now *both* screening cells positive (SCI 2+, SCII 3+)
- Panel results: following slide, note positive auto control… dang it!

plasma

Ortho Clinical Diagnostics

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1001 US Highway 202, Raritan, NJ 08869 USA

PATIENT NAME: _____

PATIENT ID: _____

DATE: 10-21-12 TECH: _____

CONCLUSION: anti-E, anti-Jkb

Lot No. VRA174 Exp. Date 2012 CCYY

Panel A

Reagent Red Blood Cells
0.8% Resolve® Panel A
Antigram® Antigen Profile

			Rh-hr								KELL						DUFFY		KIDD		Sex Linked	LEWIS		MNS				P	LUTHERAN		Special Antigen Typing		Test
Cell#	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub		Cell#	
1	R1wR1	307142	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	+	0	+		1	2+
2	R1R1	108285	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+		2	0
3	R2R2	306725	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+		3	3+
4	Ror	306607	+	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	0	0	+	+	0	+		4	0
5	r'r	304034	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	0	+	+	@	5	0
6	r''r	304019	0	0	+	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	0	+	@	6	3+
7	rr	104477	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	0	+	@	7	2+
8	rr	304486	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	+	0	+	+	+	+	0	+	+	@	8	3+
9	rr	303097	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	0	0	0	0	+	0	+	+	0	+		9	0
10	rr	308638	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	+	0	+		10	2+
11	R1R1	103180	+	+	0	0	+	0	0	0	+	+	0	+	0	+	0	+	0	+	0	0	+	0	+	0	+	+	0	+		11	3+
	Patient Cells																																AC=W
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold				Var.					

Shaded columns indicate those antigens which are destroyed or depressed by enzyme treatment.
* f antigen status may have been determined presumptively based on Rh-hr phenotype.

† Indicates those antigens whose presence or absence may have been determined using a single example of a specific anti
^ Results are from historical testing. "/" represents "Not Tested" for new donors.

	Additional Cells		Rh-hr								KELL						DUFFY		KIDD		Sex Linked	LEWIS		MNS				P	LUTHERAN		Special Antigen Typing		Test
Cell#	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub		Cell#	

eluate

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1001 US Highway 202, Raritan, NJ 08869 USA

PATIENT NAME _____

PATIENT ID: _____

DATE: 10/21/12 TECH: _____

CONCLUSION: _____

Lot No. VRA174 Exp. Date 2012-1 (CCYY-M)

Panel A

Reagent Red Blood Cells
0.8% Resolve® Panel A
Antigram® Antigen Profile

JK1, E?

Cell #	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing
1	R1wR1	307142	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	+	+	0	+	
2	R1R1	108285	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	0	+	
3	R2R2	306725	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	
4	Ror	306607	+	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	0	0	+	+	0	+	0	+	
5	r'r	304034	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	+	@
6	r''r	304019	0	0	+	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	0	+	@
7	rr	104477	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	0	+	@
8	rr	304486	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	+	0	+	+	+	+	+	0	+	@
9	rr	303097	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	0	0	0	0	+	0	+	+	+	0	+	
10	rr	308638	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	+	+	0	+	
11	R1R1	103180	+	+	0	0	+	0	0	0	+	+	0	+	0	+	0	+	0	+	0	0	+	0	+	0	+	+	+	0	+	
	Patient Cells																														
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold				Var.			

Cell #	Test P
1	3+
2	0
3	3+
4	0
5	0
6	3+
7	3+
8	3+
9	0
10	2+
11	2+

Shaded columns indicate those antigens which are destroyed or depressed by enzyme treatment.
* f antigen status may have been determined presumptively based on Rh-hr phenotype.

† Indicates those antigens whose presence or absence may have been determined using a single example of a specific antibo
^ Results are from historical testing. "/" represents "Not Tested" for new donors.

Cell #	Additional Cells	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing

Cell #	Test R

(*elution*)

Ortho Clinical Diagnostics

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1001 US Highway 202, Raritan, NJ 08869 USA

PATIENT NAME: _____

PATIENT ID: _____

DATE: 10-22-12 TECH: _____

CONCLUSION: rule out - E

Lot No. VRB172 Exp. Date 2012-1
CCYY-M

Panel B

Reagent Red Blood Cells
0.8% Resolve® Panel B
Antigram® Antigen Profile

Cell #	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing
			Rh-hr								KELL						DUFFY		KIDD		Sex Linked	LEWIS		MNS				P	LUTHERAN		
12	rr	310901	0	0	0	+	+	+	0	0	0	+	0	+	/	+	+	0	+	0	0	0	+	0	+	+	+	+	0	+	
13	rr	310785	0	0	0	+	+	+	0	0	0	+	0	+	/	+	0	+	0	+	+	0	+	+	0	+	+	0	0	+	*
14	rr	304263	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	+	0	0	+	+	+	+	0	+	*
15	R2R2	306438	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	+	+	+	0	+	
16	R2R2	310591	+	0	+	+	0	0	0	0	0	+	0	+	/	+	+	+	+	0	+	+	0	+	+	+	0	0	0	+	*
17	R2R2	310886	+	0	+	+	0	0	0	0	0	+	0	+	/	+	+	0	+	+	+	0	+	0	+	0	+	+	0	+	
18	R1R1	310895	+	+	0	0	+	0	0	0	0	+	0	+	/	+	0	+	+	+	+	+	0	+	+	+	0	+	0	+	
19	R1R1	309200	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	0	+	0	+	+	+	
20	RzR1	309814	+	+	+	0	+	0	0	0	0	+	0	+	/	+	+	0	+	0	0	0	+	0	+	+	+	+	0	+	
21	r''r	305485	0	0	+	+	+	+	0	0	+	+	0	+	0	+	+	+	+	+	+	0	+	0	+	+	+	+	0	+	
22	R1R2	310540	+	+	+	+	+	0	0	0	+	0	0	+	/	+	+	+	+	+	+	0	+	0	+	+	+	+	0	+	
	Patient Cells																														
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold				Var.			

Shaded columns indicate those antigens which are destroyed or depressed by enzyme treatment.
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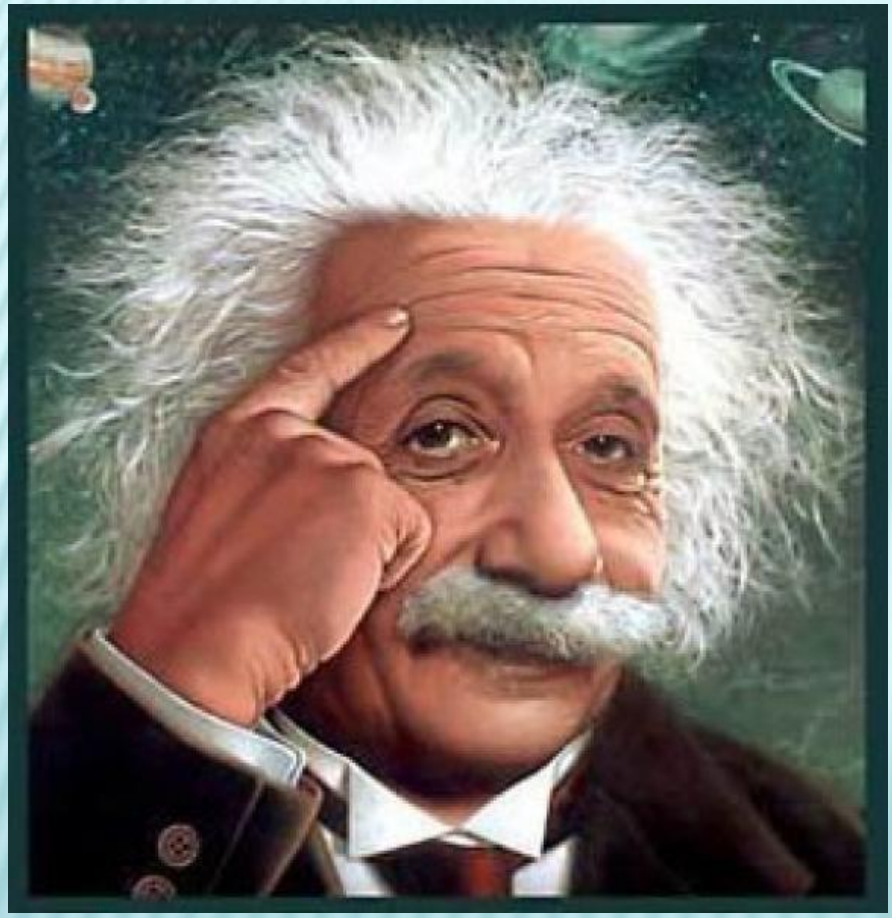
Additional Cells	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing
			Rh-hr								KELL						DUFFY		KIDD		Sex Linked	LEWIS		MNS				P	LUTHERAN		

Test Re

Cell #	Test Re
12	pryHB
13	3+
14	3+
15	
16	0
17	
18	
19	
20	
21	
22	

IN OUR INFINITE WISDOM, WE CONCLUDED…



What we have here is a delayed transfusion reaction going on!

- The patient's plasma demonstrated a previously identified *anti-E* and a newly formed *anti-Jkb*!
- The patient's DAT was positive with polyspecific and -IgG Coombs reagent and negative with -C3 reagent.
- The patient's eluate demonstrated anti-Jkb only
- We crossmatched 2 E -, Jkb – units of blood!

We're on a roll…

WE HAD IT UNDER CONTROL.. OR SO WE THOUGHT!

We had transfused him with 2 units of "compatible" blood, so why was his hgb dropping ?

Transfused one unit on 10-22 and one unit on 10-23

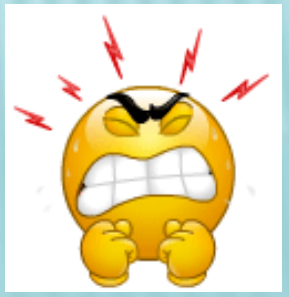
Date	Hgb	LDH
10/24	6.9	1720
10/25	6.7	1756
10/26	5.6	2700
10/27	5.3	2051
10/28	5.2	1805

NOT TO WORRY…. THE DOCTOR ORDERED 2 MORE UNITS OF BLOOD ASAP!

Oct. 27, 2012

- We received a new sample
- Performed a T&S
- Ordered 2 A+, E-, Jkb- units from Community Blood Center
- Crossmatched units using gel technology
- Units were 2+ incompatible!
- Repeated work-up, appeared no new antibodies had formed !

WHAT THE HECK!!! Time to send it on down the road to Community Blood Center



Ortho Clinical Diagnostics

PART OF THE Johnson & Johnson FAMILY OF COMPANIES

1001 US Highway 202, Raritan, NJ 08869 USA

BB 17318

hx of E, JKb

DATE: 10/28/12 TE

CONCLUSION: r/o

Lot No. VRA174 Exp. Date 2012 CCYY

Panel A

Reagent Red Blood Cell
0.8% Resolve® Panel A
Antigram® Antigen Profil

* E neg, JKb unit INCompat with pt CBC Consult (pos DAT+ Recent T
Sending Specimen to pt

Cell #	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing
1	R1wR1	307142	+	+	0	0	+	0	+	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	+	+	0	+	
2	R1R1	108285	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	0	+	
3	R2R2	306725	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	0	+	+	0	+	0	+	
4	Ror	306607	+	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	0	0	+	+	0	+	0	+	
5	r'r	304034	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	0	+	+	@
6	r''r	304019	0	0	+	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	+	0	+	+	+	+	+	0	+	@
7	rr	104477	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	0	+	@
8	rr	304486	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	+	0	+	+	+	+	0	+	+	@
9	rr	303097	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	0	0	0	0	+	0	+	+	0	+	
10	rr	308638	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	+	0	+	
11	R1R1	103180	+	+	0	0	+	0	0	0	+	+	0	+	0	+	0	+	0	+	0	0	+	0	+	0	+	+	0	+	
	Patient Cells																														
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold				Var.		

Shaded columns indicate those antigens which are destroyed or depressed by enzyme treatment.
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Cell #	Additional Cells Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa†	Jsb†	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing
21																														PIA DAT

WHAT DID OUR FRIENDS IN IRL SAY?

Tell us, wise Julie K. We know that you can figure it out!!

Community Blood Center Report

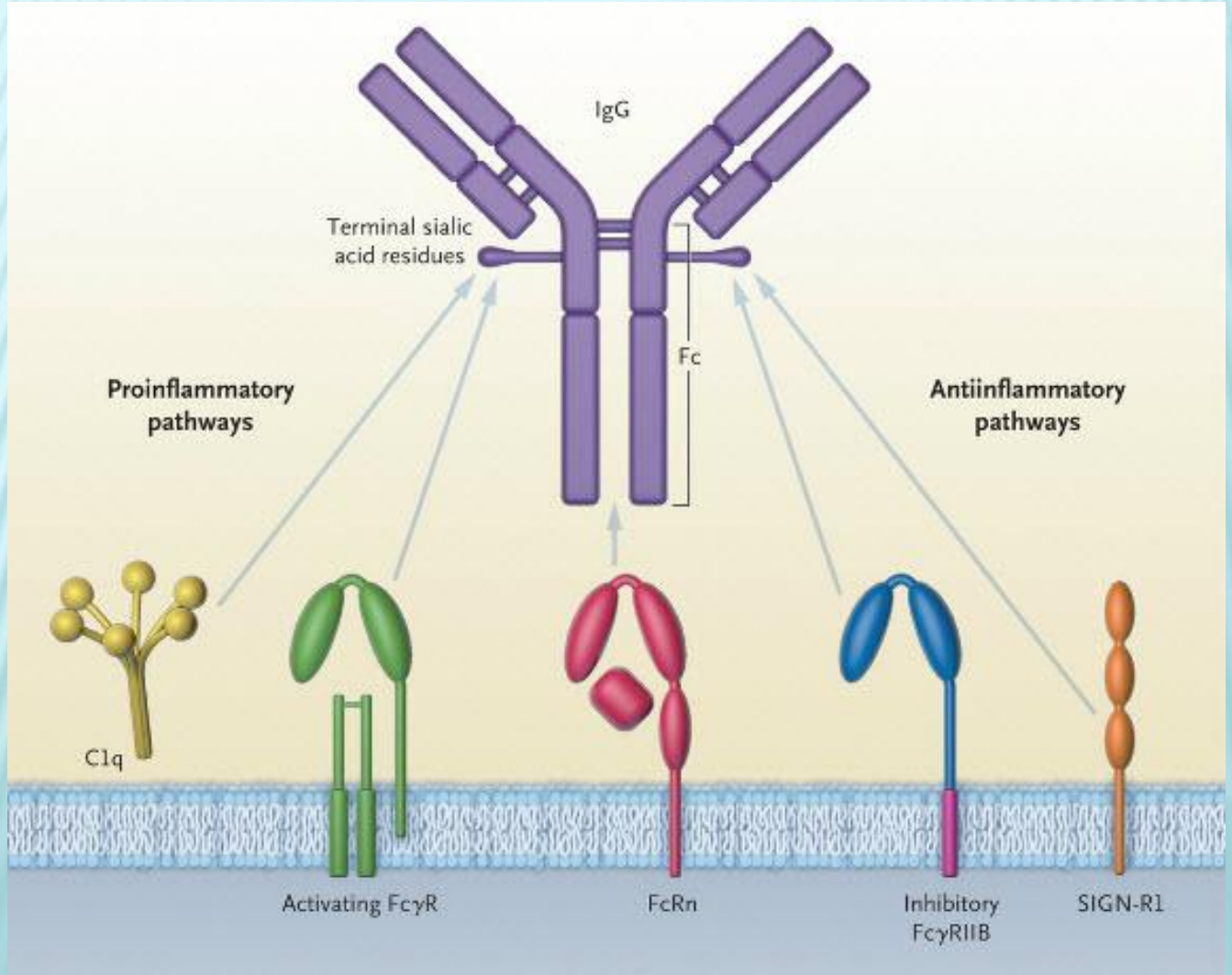
Oct. 28, 2012

- Patient's plasma contains the previously reported anti-E and anti- Jkb
- Patient's cells are weakly coated with IgG
- An eluate prepared from the patient's cells was reactive with one example of A1, A2 and B cells
- The plasma was also found to contain anti-A1
- *The –A1 and –B reactivity in the eluate and the –A1 in the patient's plasma is most likely due to passively acquired antibody from IVIg administration reported by the hospital! (10-26-12)*

WHAT IS IVIG?

- First used in 1952 to treat immunodeficiency
- Contains pooled immunoglobulin G (IgG-polyclonal) from thousands of donors
- Treated with physical and chemical viral inactivating regimens
- IVIg therapy has evolved over the past 60 years

IMMUNOMODULATING AGENT SEVERAL MECHANISMS



FYI….

- Dosage: 2 g/kg of body weight, over a period of 2-5 days on a monthly basis
- $48-$68/gram
- Single IVIg infusion:
  $3,000/child;
  $10,000/adult
- India: $25/gram
- Pakistan: $20/gram
- China: $17/gram
- Bangladesh: $10/gram

IVIG THERAPY

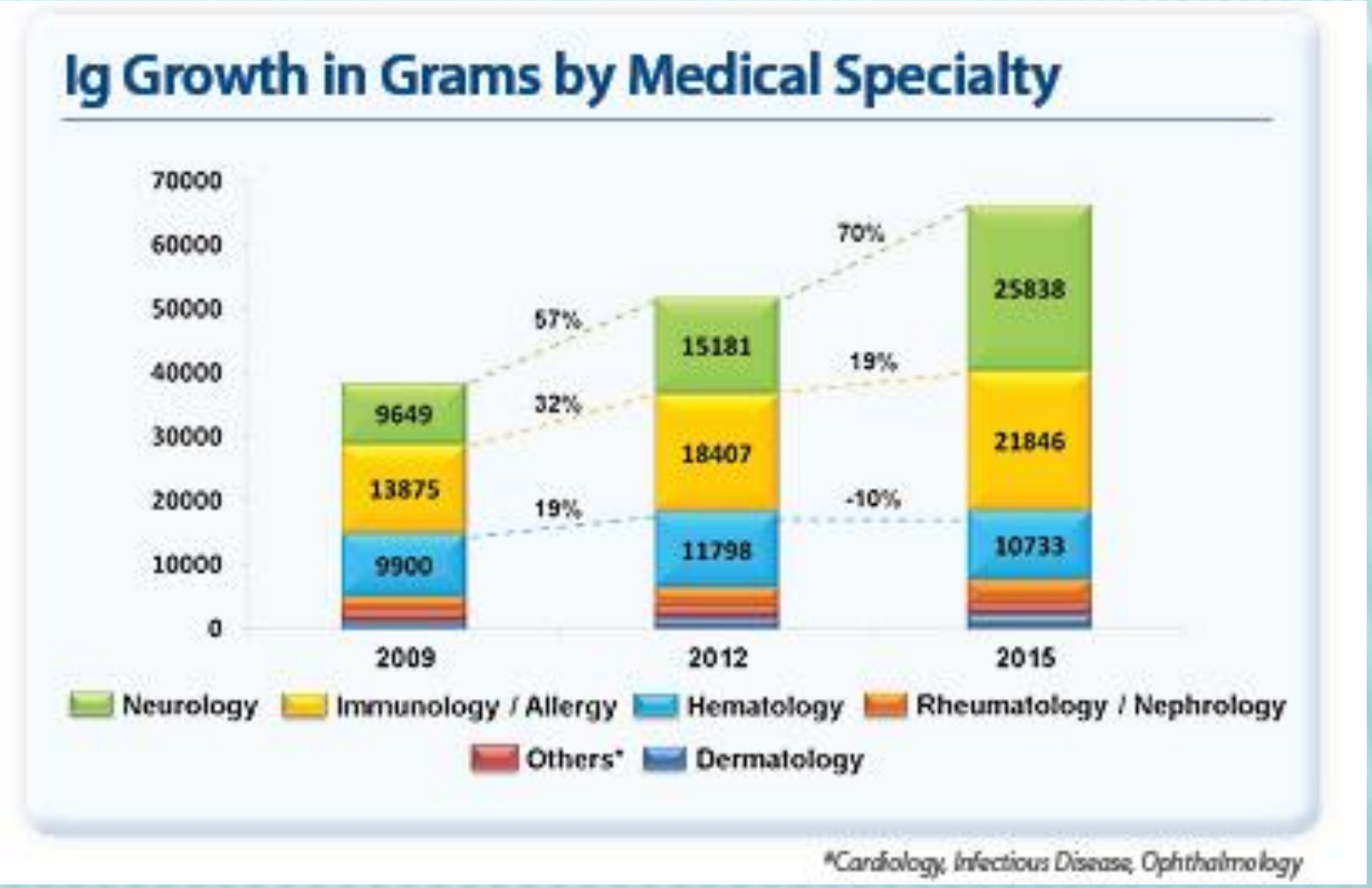
FDA approved:

- *Primary immunodeficiencies*
- *Immune-mediated thrombocytopenia*
- *Kawasaki disease*
- *Hematopoietic stem cell transplantation (>20 years)*
- *Chronic B-cell lymphocytic leukemia*
- *Pediatric HIV type 1 infection*

Off Label use: (growing…)

- *Aplastic Anemia*
- *HDFN*
- *Autoimmune Hemolytic Anemia*
- *Refractoriness to platelet trans.*
- *Multiple sclerosis*
- *Alzheimer's Disease*
- *Fibromyalgia*
- *Asthma*
- *Multiple myeloma*
- *Diabetes mellitus*
- *Chronic Fatigue Syndrome*
- *Hemolytic Transfusion Reaction*

PROJECTED USE OF IVIG



IMMUNE GLOBULIN INTRAVENOUS (HUMAN), 10% LIQUID PRIVIGEN™ US PACKAGE INSERT

5.7 Interference With Laboratory Tests

After infusion of IgG, the transitory rise of the various passively transferred antibodies in the patient's blood may yield positive serological testing results, with the potential for ***misleading interpretation***. Passive transmission of antibodies to erythrocyte antigens **(e.g., A, B, and D)** may cause a ***positive direct or indirect antiglobulin (Coombs') test.***

OUR PATIENT STILL NEEDS BLOOD!

- According to CBC, nothing "new" except the *passive anti- A* from the IVIg
- Transfused him with a total of 3 units:

  O positive, E- Jkb- units
- On Oct. 29th, hgb up to 8.4 g/dl
- Very positive outcome!

DISCHARGE NOTES

"… underwent a splenectomy on 10/30/12. His hemoglobin then stabilized and was about 9 g/dl at the time of discharge. The patient no longer had any symptoms. He was recovering well from his laparoscopic splenectomy, sitting up in a chair and ambulating freely. The patient was instructed to return to his primary care physician's office within one week to have a repeat CBC."

LESSONS LEARNED

"We're still working on it… We'll let you know when we have compatible blood available!"

- Look at the BIG picture
- Where did that –Jkb come from? Had he been transfused somewhere else recently?
- When we've identified the obvious offenders (-E,- Jkb) what else is going on (what is the blood type of the patient?)
- *Consider the drug history*
- If IVIg given, run eluate against A1 and B cells in addition to screening cells
- Switch over to "O" cells if indicated

TRANSFUSION, VOLUME 48, AUGUST 2008

"Hemolytic transfusion reactions after administration of intravenous immune (gamma) globulin"

Daw, Padmore, Neurath, Cober Tokessy, Desjardins, Olberg, Tinmouth and Giulivi

- Case series that summarized observations of hemolytic reactions after the administration of large amounts of IVIG.
- 16 cases were identified over a 2 ½ year period at the Ottawa Hospital of 1000 patients receiving IVIG (1.6%). Characteristics of the patients: Large dose of IVIG, female sex and non-O blood group.
- Conclusions: Significant hemolysis may occur after the administration of large doses of IVIG; (passive antibodies identified: -A and –B)
- 2 step mechanism of hemolysis proposed: sensitization by ABO isohemagglutinins followed by phagocytosis by activated macrophages.

THANK YOU!

Just when you think you're having a great day..

Here comes a positive antibody screen, "Great" you say!

You've run panels, DAT's and elutions to no avail

"I'm tired of working on this mess!" you start to wail

Check on the diagnosis and drug history- it's part of the game!

If IVIg is lurking around, a passive antibody may be to blame!

Remember your other options to help you out

You're friendly IRL is available- just give them a shout!

QUESTIONS????