Questions in a case of suspected HDFN with maternal anti-Vel reported

Karen Rubio MT(ASCP)SBB^{cm}
Children's Mercy Hospital
Transfusion Services Laboratory
Lead Technologist

Children's Mercy KANSAS CITY

© The Children's Mercy Hospital 2017

UMKC School of Medicine

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 10 SPECIALTIES 2016-17

MAGNET RECOGNIZED AMERICAN NURSES CREDENTIALING CENTER

Objectives

- Review Vel | Cellano | ISBT definitions
- Review of data for this case and discuss the problems
- A surprise conversation

Children's Mercy KANSAS CITY

The “not so” usual admission

- The call to evening shift
- The outside Bombshell maternal results.
- Pathologist on-call notified
- Our results???

Children's Mercy KANSAS CITY

Outside lab results

Mom is R_2r, O pos with anti-Vel identified in her plasma. Her phenotype at an outside facility was C-, E+, c+, e+; K+, k-; Fy(a+b+); Jk(a+-b+); M+, N-, S+, s+; Vel-

Mom had a positive antibody screen with anti-Vel identified. Titers performed indicated an increase from 16 to 64 prior to delivery.

Children's Mercy KANSAS CITY

Outside lab results

- Baby born at 39 weeks and weighed 2.96 Kg.

- Meconium stained fluid noted. Apneic and floppy with agars of 2,4,7 with poor respiratory effort | Large abdomen noted with absent bowel sounds | Bronze pale skin | Thrombocytopenic | Possible sepsis with bandemia of 26% | HDFN | Hyperbilirubinemia and elevated liver enzymes | CHD | Persistent pulmonary hypertension | Generalized edema | Anemic with birth Hgb of 7 g/dL | Excessive umbilical bleeding during line insertion | CRP increasing from 0.37 to 2.32

    - Cord Blood results – O pos with a negative DAT test
    - Transfusions – 3 syringes of Red Cells all from the same donor unit
      3 syringes of platelets all from the same donor unit
      2 syringes of plasma, both from the same donor unit

Children's Mercy KANSAS CITY

Extreme blood banking results

Results from specialists at the CBC IRL; ARC in California & Wichita

ARC Mom Prenatal

RBCs:

ABO Group	Most Probable Rh Genotype	D	C	E	c	e	Other Blood Groups	Direct Antiglobulin Test
O	R_2r	+	neg	+	+	+	S+s+ K+k− Fy(a+b+) Jk(a+b+) Vel−	Negative

SERUM: The patient's serum contained alloanti-Vel reactive at RT, 37C, and by LISS, PEG, and ficin AGT.

COMMENTS: The patient's serum reacted strongly with all RBCs of common phenotype at RT, 37C, and by LISS, PEG, and ficin indirect antiglobulin test. The patient's serum was non-reactive with 7 of 7 examples of rare Vel− RBCs by LISS and PEG indirect antiglobulin test. All other common alloantibodies were excluded.

Anti-Vel in the sera of prenatal patients is potentially clinically significant, depending on the antigen status of the neonate. These antibodies are generally IgG and will cross the placenta. This patient should be monitored carefully during her pregnancy. Additional testing could include typing the father of the child for the Vel antigen.

Anti-Vel defines an antigen of high frequency in the Vel blood group collection. The antigen is found on nearly 100% of all donor RBCs. Anti-Vel has been reported to be associated with none to severe hemolytic transfusion reaction, and none to severe HDFN, even though Vel antigen expression on cord RBCs is weak, as compared to adult RBCs.

TRANSFUSION RECOMMENDATIONS: Units for transfusion may be found by crossmatching Vel− donors of the appropriate ABO and Rh groups and selecting those units which are non-reactive with the patient's serum.

Because Vel− blood is so rare, this patient should consider autologous blood donation in anticipation of future blood needs and should become registered with the American Rare Donor Program. Family members, especially siblings should be screened as possible sources of additional rare Vel− blood. If we may be of assistance in these matters please let us know.

CBC Mom postpartum

ABO Group	Rh Type	Other Antigen Types	Polyspecific	IgG Specific	Complement
O	Pos	C-, E+, c+, e+; K+, k-; Fy(a+b+); Jk(a+b+); M+, N-, S+, s+; Vel-	Negative	NA	NA

Antibody Identification

Previous Serologic Findings			Current Serologic Findings		
Source	Antibody	Clinical Significance	Source	Antibody	Clinical Significance
	See Below		Plasma	Anti-Vel	Significant
			Plasma	No new alloantibodies	

Anti-Vel is clinically significant and is associated with hemolytic disease of the fetus/newborn (HDFN).

The incidence of Vel-negative donors is <1%. We recommend that the patient donate units to be frozen

Children's Mercy KANSAS CITY

Baby result per the experts

Red Blood Cell			Direct Antiglobulin Test		
ABO Group	Rh Type	Other Antigen Types	Polyspecific	IgG Specific	Complement
O	Pos		Positive	Negative	Positive

Current Serologic Findings		
Source	Antibody	Clinical Significance
Plasma & Eluate	No alloantibodies detected	See Below

The patient's mother has a history of anti-Vel. Anti-Vel is clinically significant and is associated with hemolytic disease of the fetus/newborn (HDFN).

The cause of the patient's positive direct antiglobulin test (DAT) is not known. Increased reactivity of the DAT or unexplained failure of transfused or autologous red cells to survive may warrant further evaluation.

Children's Mercy KANSAS CITY

Our Labs “?”

3/2 – 3/3

Order	Date	Pe...	St...	ID	Procedure	C	Result
Type and Screen	03/02/2016 18:50	P...	Ve...		Received		Yes
ABO/Rh Neo	03/02/2016 18:50	P...	Ve...		History Check		Reviewed
ABO/Rh Neo	03/02/2016 18:50	P...	Ve...		Anti-A		0
ABO/Rh Neo	03/02/2016 18:50	P...	Ve...		Anti-B		0
ABO/Rh Neo	03/02/2016 18:50	P...	Ve...		Anti-D		3+
ABO/Rh Neo	03/02/2016 18:50	P...	Ve...		ABO/Rh Neonatal Inte...		O POS
ABS Gel	03/02/2016 18:50	P...	Ve...		History Check		Reviewed
ABS Gel	03/02/2016 18:50	P...	Ve...		Blood Bank ID		R12471
ABS Gel	03/02/2016 19:59	P...	Ve...		SC1 GEL		0
ABS Gel	03/02/2016 19:59	P...	Ve...		SC2 GEL		0
ABS Gel	03/02/2016 19:59	P...	Ve...		SC3 GEL		0
ABS Gel	03/02/2016 19:59	P...	Ve...		Antibody Screen Interp		Negative
Direct Antiglobulin Test Neonatal	03/02/2016 18:50	P...	Ve...		IgG GEL		0
Direct Antiglobulin Test Neonatal	03/02/2016 18:50	P...	Ve...		DAT Neonatal Interp		Negative
Confirm ABO					History Check		
Confirm ABO					Anti-A		
Confirm ABO					Anti-B		
Confirm ABO					Anti-D		
Xmatch Comp	03/02/2016 23:02	P...	Ve...		Blood Bank ID		R12471
Xmatch Comp	03/02/2016 23:02	P...	Ve...		History Check		Reviewed
Xmatch Comp	03/02/2016 23:02	P...	Ve...	W0450160146...	XM GEL		0
Xmatch Comp	03/02/2016 23:02	P...	Ve...	W0450160146...	XM Interp		Compatible
Xmatch Comp	03/02/2016 23:02	P...	Ve...	W0450160174...	XM GEL		0
Xmatch Comp	03/02/2016 23:02	P...	Ve...	W0450160174...	XM Interp		Compatible
Xmatch Comp	03/03/2016 08:51	Wi...	Ve...	W0450160235...	XM GEL		0
Xmatch Comp	03/03/2016 08:51	Wi...	Ve...	W0450160235...	XM Interp		Compatible
DAT	03/03/2016 08:55	P...	Ve...		Poly		0
DAT	03/03/2016 08:55	P...	Ve...		Poly 5 min		1+
DAT	03/03/2016 08:55	P...	Ve...		IS Complement		0
DAT	03/03/2016 08:55	P...	Ve...		Complement 5min		1+
DAT	03/03/2016 08:55	P...	Ve...		IgG GEL		0
DAT	03/03/2016 08:55	P...	Ve...		DAT Interp		IgG Neg/Complement Pos
BB Hold	03/03/2016 11:03	Gr...	Ve...		BBK HOLD		NP
BB Hold	03/03/2016 11:03	Gr...	Ve...		Blood Bank ID		R12471
ABID REF	03/04/2016 14:49	B...	Ve...		Antibody Result	f	Other
T-Activation	03/07/2016 14:48	M...	C...		T - Activation		The patient's cells were nonreactive when tested against six

3/7

Order	Date	S	ID	Procedure	C	Result
Type and Scre...	03/07/2016 10:25	V		Received		Yes
DAT	03/07/2016 10:37	V		Poly		0
DAT	03/07/2016 10:37	V		Poly 5 min		0
DAT	03/07/2016 10:37	V		Poly CC		2+
DAT	03/07/2016 10:37	V		DAT Interp		Negative
ABO/Rh Neo	03/07/2016 10:25	V		History Check		Reviewed
ABO/Rh Neo	03/07/2016 10:25	V		Anti-A		0
ABO/Rh Neo	03/07/2016 10:25	V		Anti-B		0
ABO/Rh Neo	03/07/2016 10:25	V		Anti-D	f	1+
ABO/Rh Neo	03/07/2016 10:25	V		ABO/Rh Neonatal Int...		O POS
ABS Gel	03/07/2016 10:25	V		History Check		Reviewed
ABS Gel	03/07/2016 10:25	V		Blood Bank ID		R12377
ABS Gel	03/07/2016 10:44	V		SC1 GEL		0
ABS Gel	03/07/2016 10:44	V		SC2 GEL		0
ABS Gel	03/07/2016 10:44	V		SC3 GEL		0
ABS Gel	03/07/2016 10:44	V		Antibody Screen Interp		Negative
Xmatch Comp	03/07/2016 10:37	V		Blood Bank ID		R12377
Xmatch Comp	03/07/2016 10:37	V		History Check		Reviewed
Xmatch Comp	03/07/2016 10:45	V	W045016024982	XM Interp		Compatible
Xmatch Comp	03/07/2016 11:45	V	W045016020130	XM GEL		0
Xmatch Comp	03/07/2016 11:45	V	W045016020130	XM Interp		Compatible
Xmatch Comp	03/07/2016 11:45	V	W045016020155	XM GEL		0
Xmatch Comp	03/07/2016 11:45	V	W045016020155	XM Interp		Compatible
Xmatch Comp	03/09/2016 06:54	V	W045016014297	XM GEL		0
Xmatch Comp	03/09/2016 06:54	V	W045016014297	XM Interp		Compatible
Xmatch Comp	03/10/2016 19:04	V	W045016027425	XM GEL		0
Xmatch Comp	03/10/2016 19:04	V	W045016027425	XM Interp		Compatible

Children's Mercy KANSAS CITY

Anti-Vel?

- Isn’t that really rare?
- Doesn’t everybody have Vel?
- Why are baby’s labs negative?
- Mom is Cellano negative as well?
- Possible ECMO ?!?!?!?!?!?

Children’s Mercy KANSAS CITY

To review:

- Vel? Series, Collection or System
- Cellano?
- Bilirubin pathway?

Children's Mercy KANSAS CITY

ISBT definitions isbtweb.org

- Nomenclature: Systems; Collections; Lows and Highs
- ***Systems*** consist of one or more antigens controlled at a single gene locus, or by two or more very closely linked homologous genes with little or no observable recombination between them.
  - ABO, MNS, P, Rh, Lutheran, Kell, Lewis, Duffy, Kidd, Diego, Yt, Xg, Scianna, Dombrock, Colton, Landsteiner-Wiener, Chido,Rodgers, Hh, Kx, Gerbich, Cromer, Knops, Indian, Ok, Raph

Children's Mercy KANSAS CITY

ISBT definitions isbtweb.org

- ***Collections*** *(200 series)* consist of serologically, biochemically, or genetically related antigens, which do not fit the criteria required for system status

  These antigens appear to be unique unto themselves

  Cost, Ii, Er, GLOB, MN CHO

Children's Mercy KANSAS CITY

ISBT definitions isbtweb.org

All are inherited and none is eligible to join a system

Lows- 700 series

- *Antigens that occur in less than 1% of most populations studies and don't appear to belong to a system*
  - *TM 18th edition : By, Chr^a, Bi, Bx^a, To^a, Pt^a, Re^a, Je^a, Li^a, Milne, RASM, JFV, Kg, JONES, HJK, HOFM, SARA, and REIT*

Highs -901 series

- *Antigens that occur in more than 90% of the populations and are not known to be long to a system. In Transfusion April 2000*
  - *Vel+, Lan+, At(a+), Jr(a+) [901:1,2,3,5]*
- *Vel became a collection in 2008 with ABTI*

Children's Mercy KANSAS CITY

5/30/2013 “Transfusion news” Vel is classified as a new blood group system

- Isbtweb.org **Responsible Committee Member**

034	Vel	Jill Storry

ABTI is serologically related to Vel. However is has been excluded from SM1M1 by sequencing analysis and thus remains in a collection.

Children's Mercy KANSAS CITY

OK so it's a system; what is it and what does it do?

- Dr. Storry and colleagues identified a common deletion across 20 Vel-negative individuals on chromosome 1, and identified SMIM1 as the erythroid gene encoding a conserved transmembrane protein.
- Vel-negative blood group phenotype was first identified in 1952, after Ms. Vel had an acute hemolytic transfusion reaction. She had a history of 3 pregnancies and colon cancer requiring transfusions.

Children's Mercy KANSAS CITY

Vel System

- This newly discovered protein's function on the RBC surface is currently unknown
- Antigen expression is generally weak on cord RBCs and differs substantially from one individual to another. Patterns of expression are consequence ob both zygosity for the 17-base pair deletion and a SNP in a GATA-1 transcription factor site in intron 2.
- Serological expression is not affected by protease treatment although sensitivity to reducing agents such as 0.2M DTT is variable.
- Antibody is IgM and IgG and readily activate complement and have been implicated in mild to severe HTRs although HDFN is rare.

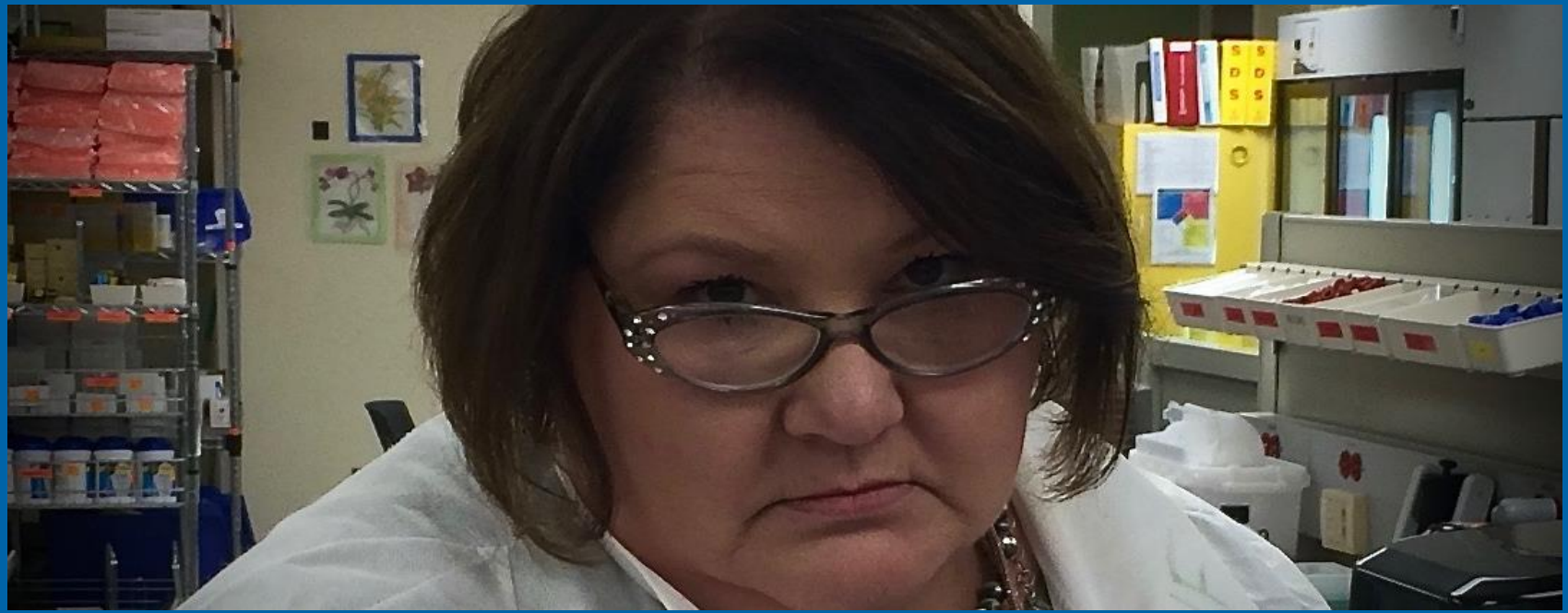
Children's Mercy KANSAS CITY

More on Vel

- Identifying the blood type's genetic basis will more easily screen patients.
- This mutation is a deletion of 17 nucleotides, causing the DNA sequence to be "frameshifted" -- a catastrophic mutation (from the gene's point of view) that destroys the integrity of the gene sequence. The Vel antigen is not produced by these individuals.
- Further analysis and experimentation revealed that *SMIM1* is linked to hemoglobin concentration, although its relevance in this function is unknown.
- http://www.realclearscience.com/blog/2013/04/the-mystery-of-the-vel-negative-blood-type.html **Vel Blood Group**

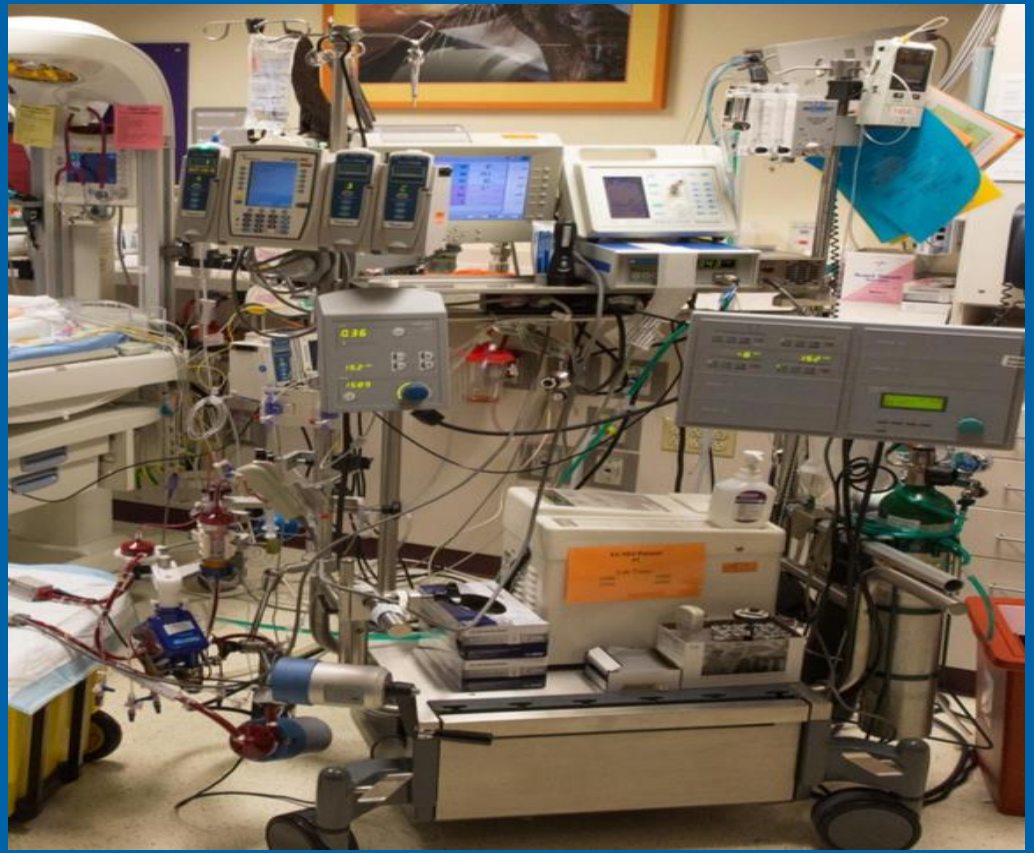
Children's Mercy KANSAS CITY

Wait…What…Weak on cord blood



Children's Mercy KANSAS CITY

ECMO initiated 3/2

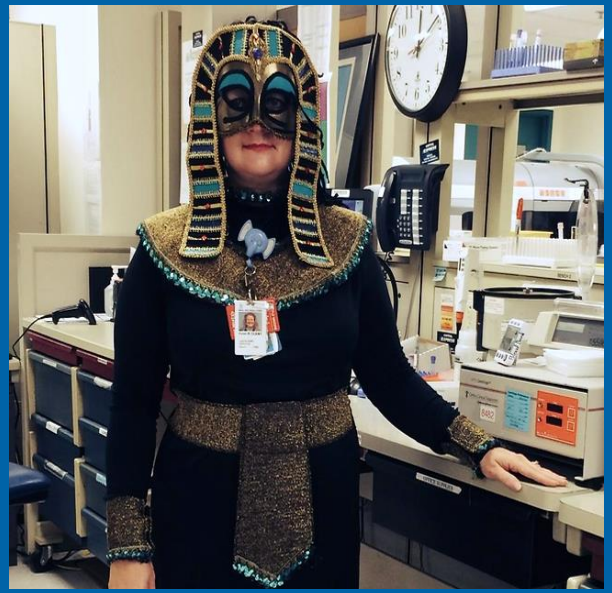


Children's Mercy KANSAS CITY

What about Cellano negative

Children's Mercy KANSAS CITY

What about these Labs



Children's Mercy KANSAS CITY

Prevalence of an antigen negative unit of RBCs (with a dash of Optimism)

- Blood type O [44%], k negative [99.8%], Vel negative [99.9%]
- >90% (optimistic if a known population of Swedes or Norwegians is known to donate in Kansas City) or 99.9% (realistically)

Take the antigen negative percentages:

- (44%)(0.2%)(0.1%) = .000088% or 9 in 10,000,000 or 1 in 1,136,364 (realistically)
- (44%)(0.2%)(~<10%) = .0088% or 1 in 11,364 (optimism for Scandinavia KC)

Children's Mercy KANSAS CITY

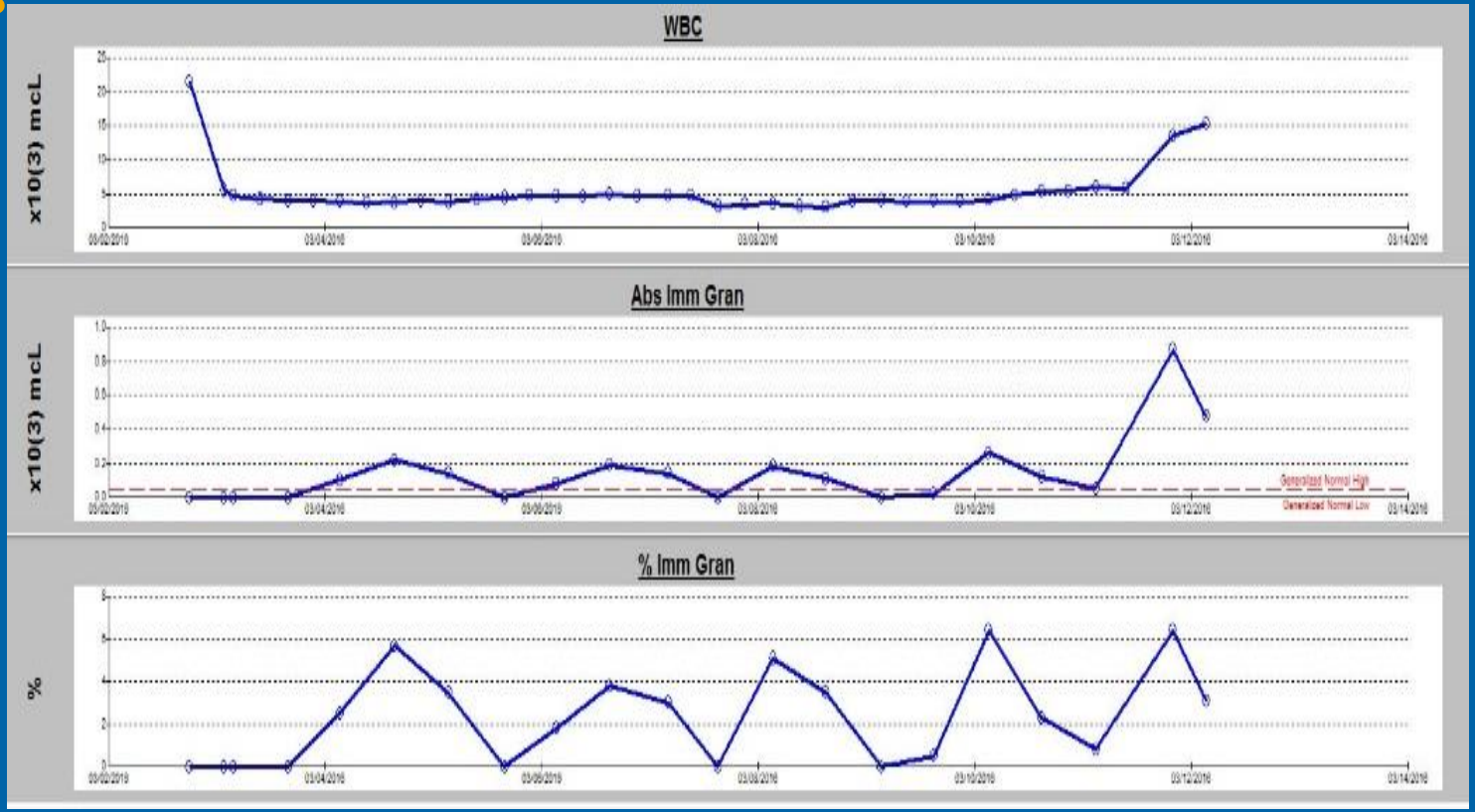
We are going to need more coffee…

Children's Mercy KANSAS CITY

Our Labs

Normal WBC:

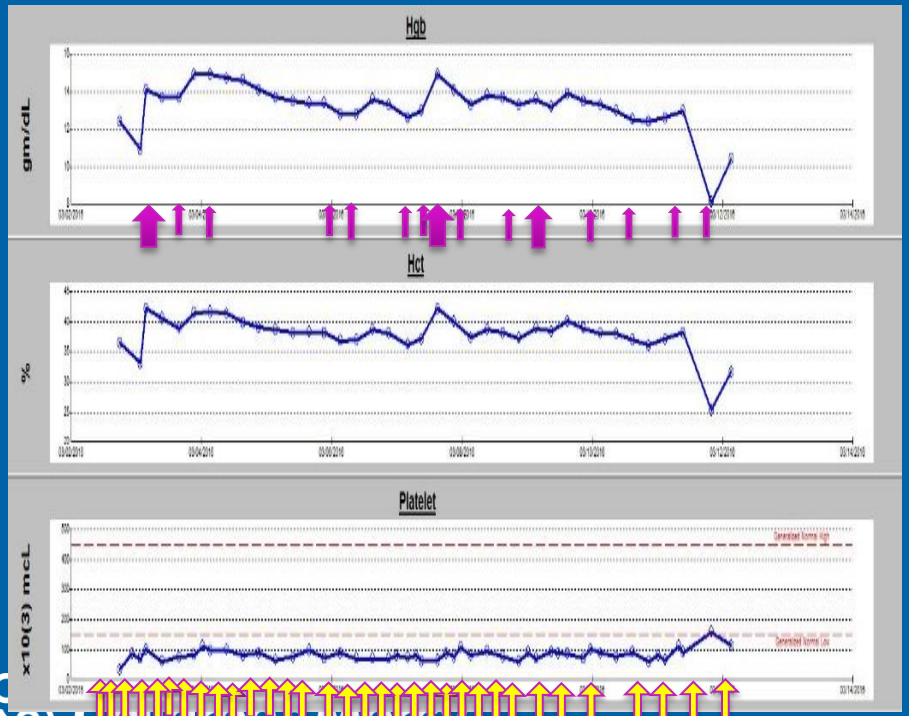
5 – 21

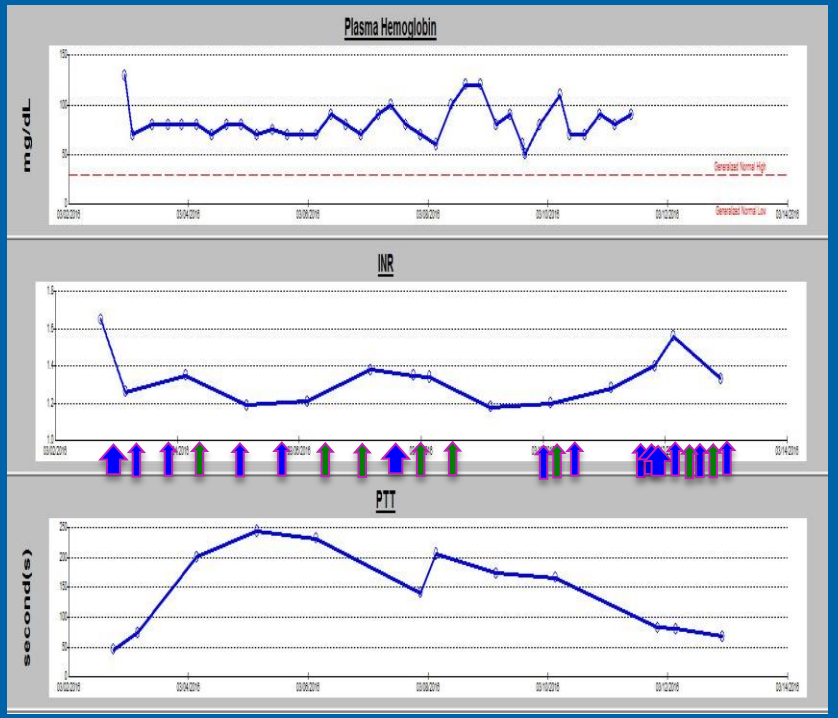


Children's Mercy KANSAS CITY

Our Labs

Cryo ↑ FFP ↑ plts ↑ RBCs ↑





Children's Mercy KANSAS CITY

More questions

- IgM v. IgG: Why so variable?
- Why is the indirect Bilirubin normal?
- What roll did the transfusions at birth play in the result we were getting?
- Why is there constant thrombocytopenia?

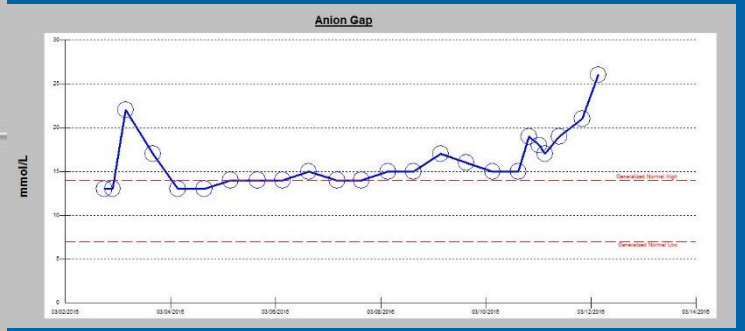
Children's Mercy KANSAS CITY

Underlying platelet AB?

			Date Tested:	3/9/2016
Immunohematology Platelet Antibody Testing				
Test Performed	**Results**	**Comments**	**Platelet Transfusion Recommendation**	
Antibody Screen	Negative		Selection of platelets by crossmatch is not necessary	

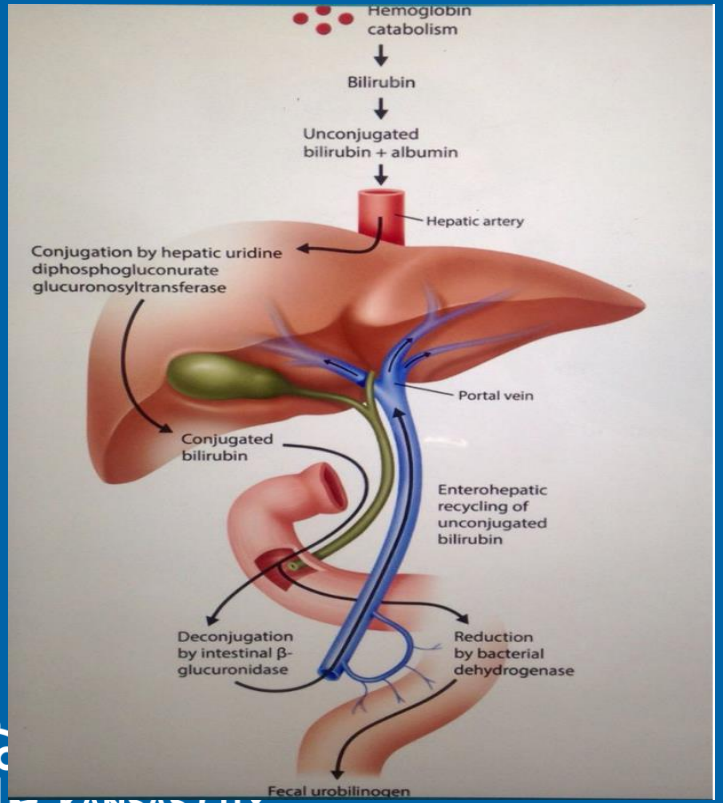
Children's Mercy KANSAS CITY

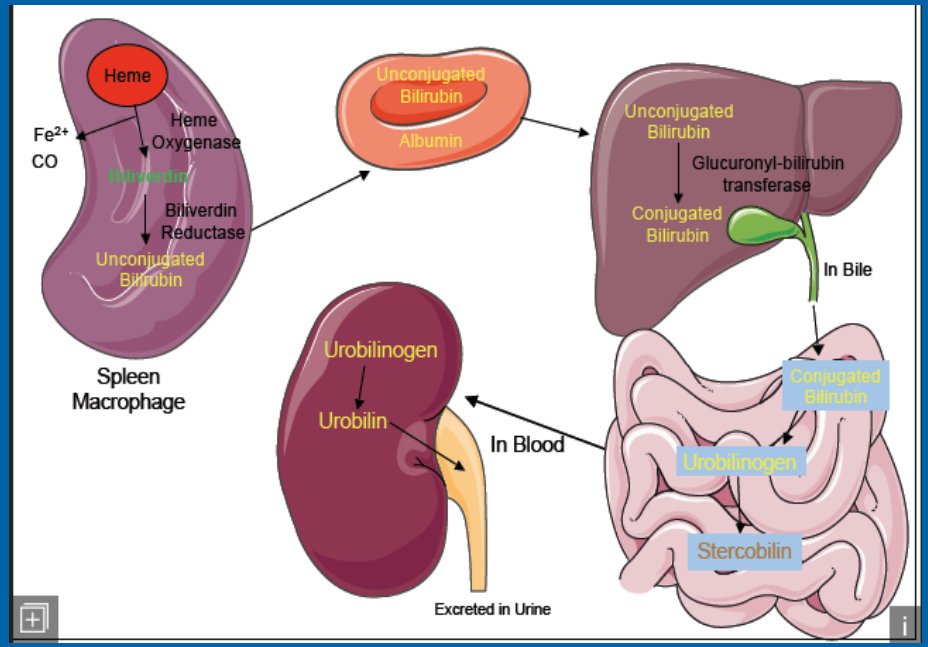
Our Labs



KANSAS CITY

Breakdown review





Possibilities

NEONATAL CHOLESTASIS

- Bile duct obstruction
  - Extrahepatic biliary atresia
- Neonatal infection
  - Cytomegalovirus
  - Bacterial sepsis
  - Urinary tract infection
  - Syphilis
- Toxic
  - Drugs
  - Parenteral nutrition
- Metabolic disease
  - Tyrosinemia
  - Niemann-Pick disease
  - Galactosemia
  - Defective bile acid synthetic pathways
  - α_1-Antitrypsin deficiency
  - Cystic fibrosis
- Miscellaneous
  - Shock/hypoperfusion
  - Indian childhood cirrhosis
  - Alagille syndrome (paucity of bile ducts)

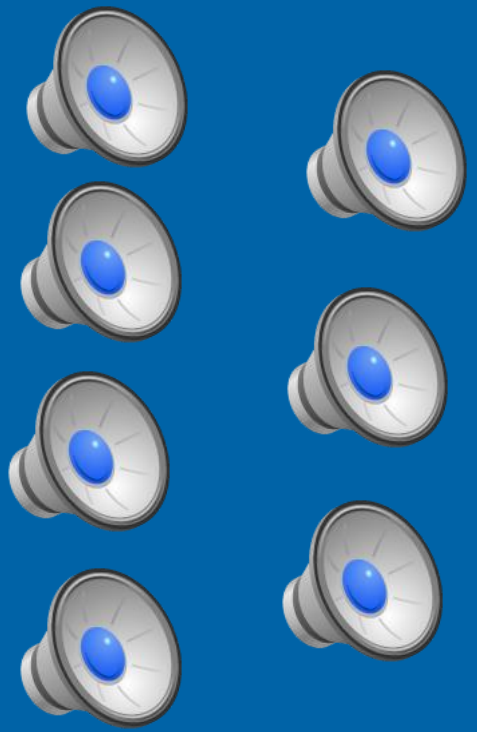
	HDFN	Sepsis	GALD	Metabolic | Other
Anemia	+	+	+	+
Dat	+	-	-	-
Plasma Hgb	+	+	-	+
Bilirubin	+	+	+	+

Children's Mercy KANSAS CITY

In mom's words

Hi Karen. This is [redacted] I received your call this afternoon pertaining to my daughter [redacted] I would more than happy to answer your questions. [redacted]

Children's Mercy KANSAS CITY

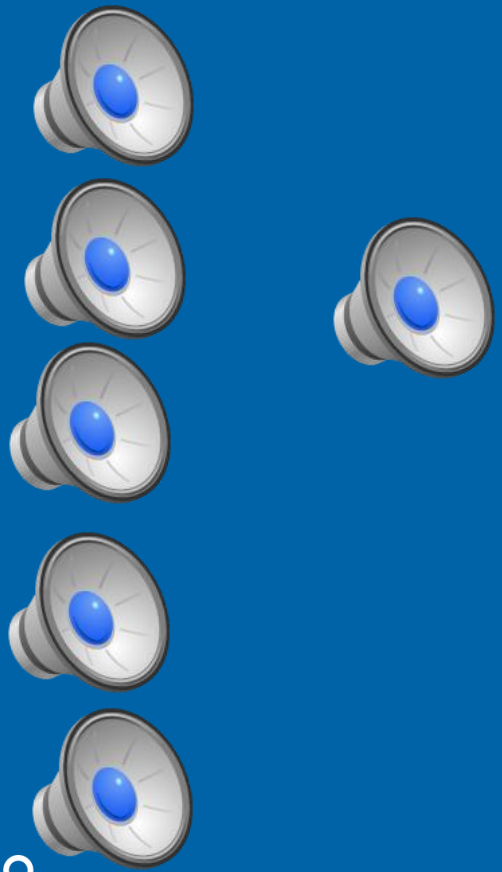


Problems?

- When did you know there was a problem?
- Did you know baby was sick?
- Titers?
- Siblings?
- Transfusions?
- Final Dx

Children's Mercy KANSAS CITY

Surprise



- Autologous donations
- Doppler/Protocol
- Houston specialist

Children's Mercy KANSAS CITY

Final thoughts

- As only someone in this situation can say

Children's Mercy KANSAS CITY

Thank you | Questions?

KANSAS CITY