

Case Study
An Unusual Case of Anti-JK3
Alloantibody and Implications for
Pregnancy Management

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HAABB Meeting

September 21, 2016

Patient History

- 32 year old Caucasian woman from Mennonite community
- Recently moved to Columbia, MO from PA
- Presented to OB/GYN in Oct 2015 at approximately 21 weeks gestation
- 9 prior pregnancies with 4 1st trimester spontaneous abortions
- Known anti-Jk3, and anti-E from outside hospital record

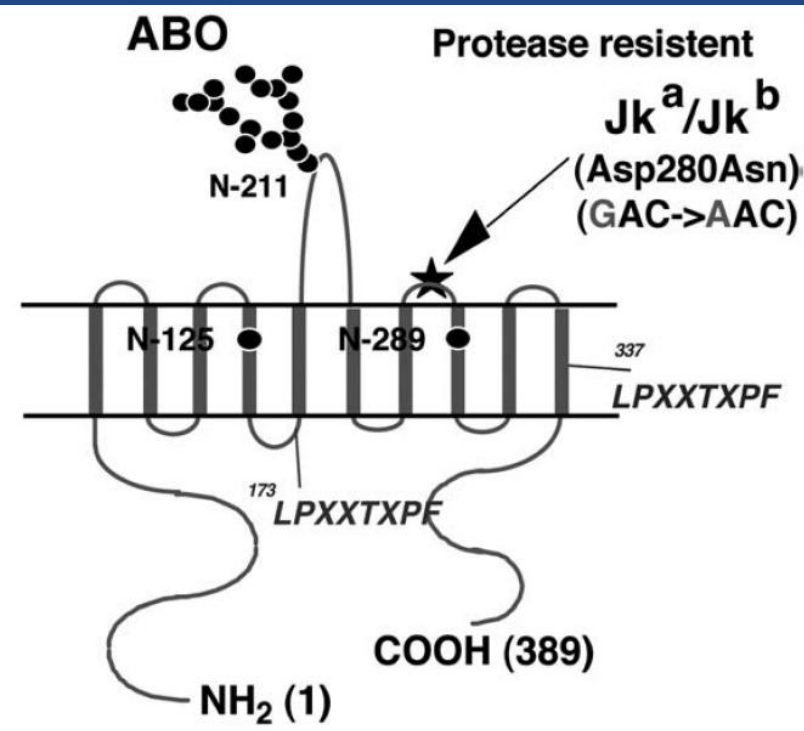
Jk (Kidd) Antigen

- Part of urea transporter on RBCs

- Human urea transporter 11 (HUT11)

- Transports urea across cell membranes in the hypertonic renal medulla

- Prevents cells from shrinking and swelling

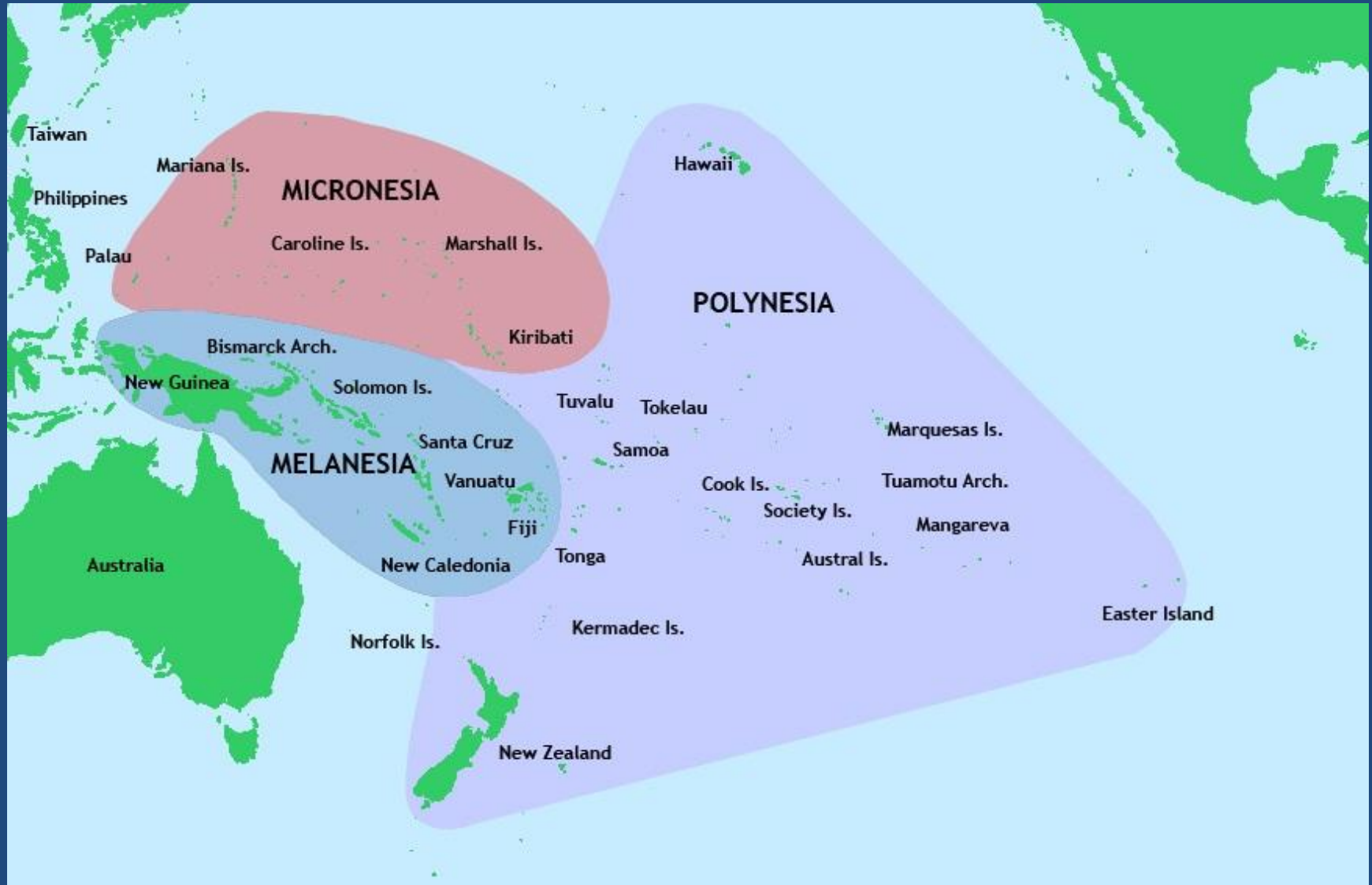


Prevalence

	Frequency (%)		
Phenotype	Whites	Blacks	Asians
Jk(a+b-)	26	52	23
Jk(a+b+)	50	40	50
Jk(a-b+)	24	8	27
Jk(a-b-)	>0.1	>0.1	>0.1

- Jk(a-b-) or null phenotype is rare
 - Discovered in 1959: antibody against both Jka and Jkb in a female patient
 - Called antibody anti-Jk3
 - Increased prevalence in Polynesians
 - 0.9% overall, 1.4% in Niueans
 - Increased prevalence in Finns
 - More rare than in Polynesians

Where is Polynesia?



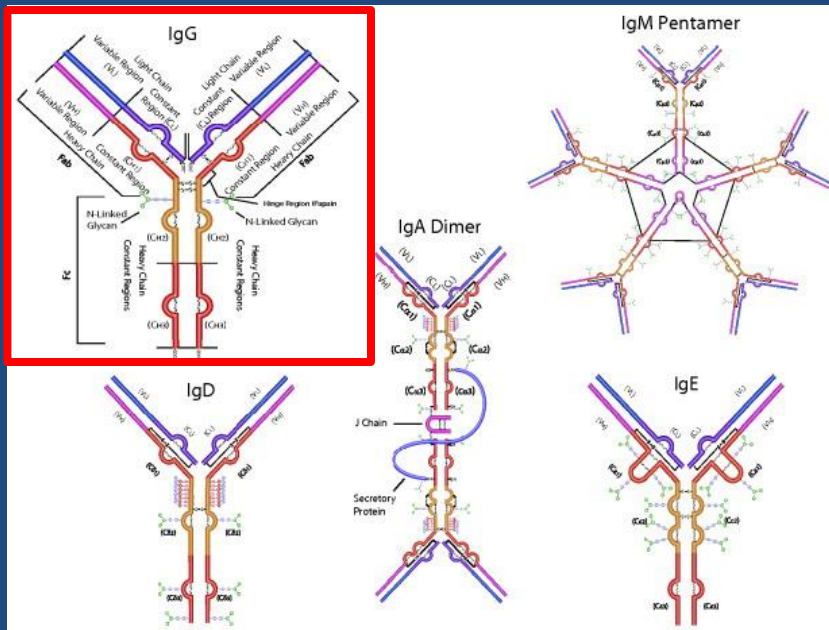


Where is Niue?



Anti-Kidd Antibodies

- Found in antibody mixtures
- Mostly IgG
- About half are able to fix complement → extravascular/intravascular hemolysis
- Transient and exhibit dosage
- Common cause of delayed HTRs
 - Likely due to transient nature on detection
- Rarely cause acute HTRs



Anti-Kidd and HDFN

- Rarely cause severe HDFN
- Anti-Jka first described in 1951; detection of antibodies against unknown RBC antigen in Mrs. Kidd during pregnancy
 - Led to fatal HDFN
- As of 2012 there were only 13 reported cases of Anti-Jk3 related HDFN
 - Most were mild, rarely fatal
 - Not previously described in a Mennonite community

Back to the Patient

- Original panel: plasma reacted with all test cells – negative auto-control
 - Kidd antigens are essentially ubiquitous
- Sample sent to ARC reference lab for antibody identification
 - Serum initially reacted with all test cells
 - No reaction with Jk3 negative cells



Red Cell Phenotypes

- Mother
 - Type: O +
 - C +
 - Fya +
 - K1 +
 - c (little) –
 - E –
 - Jka –
 - Jkb –
- Father
 - Type: unknown
 - C –
 - Fya +
 - K1 –
 - c (little) +
 - E +
 - Jka +
 - Jkb +

Implications

- 100% chance of having a Kidd antigen
- At least a 50% chance of having E
 - HDFN may occur from anti-E alone, but usually mild
- RBCs needed for mother, baby once born, and possibly before delivery for intrauterine transfusion (IUT)
 - In a similar case in 2014 there were only 2 Jk3 negative frozen units available

Autologous Units

- The patient had 3 autologous frozen units at a private institution in PA
- Couldn't ship frozen to us due to their use of a closed system for processing (APC 215)
- Good news: expiration date extended to 14 days from 24 hrs after thaw in closed system
- Bad news: 2-3 days for thawed units to arrive at our blood bank

Autologous Units



Request at ARC

- Request placed with ARC for O positive Jka/Jkb/E/c (little) negative units
- For possible IUTs we preferred O neg units
 - Very difficult to find O neg/c (little) neg units
 - We settled for units that were O positive

Fisher-Race Haplotype	Wiener Haplotype	Prevalence (%)		
		White	Black	Asian
Dce	R ₀	4	44	3
DCe	R ₁	42	17	70
DcE	R ₂	14	11	21
DCE	R ₂	<0.01	<0.01	1
ce	r	37	26	3
Ce	r'	2	2	2
cE	r''	1	<0.01	<0.01
CE	r ^y	<0.01	<0.01	<0.01

Frozen Units

- 1 frozen unit was found in Hawaii
 - Personal escort was denied and the unit was flown to our ARC facility in St. Louis (2 hour drive away)
 - Expiration in 24 hours after thaw begins and several hours to get to us



Directed Donation by Family

- Tested siblings were all blood type A
- One sister was pregnant and not tested
- Father type A
- Mother type O
- None went in for antigen testing



Rare Donor Registry



- ARC located one appropriate donor in CA willing to donate a fresh unit
 - This donor actually works for the ARC
- We planned to collect unit in January for February due date

Timing

Unit Location	Status	Time To Arrive	Shelf Life Post Thaw
3 autologous units in PA	Frozen	2-3 days	14 days
1 unit in St. Louis	Frozen	7 hours	24 hours
1 possible unit in CA	Fresh	1-2 days	42 days

- Fresh units (≤ 7 days old) preferred for fetal/neonate transfusions
 - When to collect?

Complications

- Normally for IUT we wash units to increase HCT to 80%
 - We would not do this because then shelf life drops to 24 hours
- Irradiation
 - Required for units going to baby, but not mom
 - Shortens shelf life to 28 days
 - ARC irradiates units for us or emergency protocol in radiology
 - We chose to use our protocol when needed

More Problems

- In December, fetal ultrasounds became concerning for fetal anemia
- 12/18/15 fetal US PSV: 54.3 cm/s, 1.24 MoM
- 12/23/15 fetal US PSV: 65 cm/s, 1.43 MoM
- 12/30/15 fetal US PSV: 78.4 cm/s, 1.65 MoM
- On 12/23 we requested the fresh unit be collected to have on site for an emergency/possible urgent intrauterine transfusion

Birth

- OB/GYN elected for C-Section on 12/31 at 34 weeks due to more evidence of fetal anemia
- By then, we had 1 fresh unit on site
- Physician was uncomfortable with only 1 unit
 - We requested 1 autologous unit from PA 12/30
 - Arrived in 1 day, just before procedure
- Patient elected to have a tubal ligation

Outcome

- Procedure performed without transfusion
- Live male infant (2450 g, APGAR 6 at 1 min, 8 at 5 min) born with resuscitation performed by pediatrics
- Day of life 2, started on 2 banks of phototherapy (total bilirubin 7.9 mg/dL)
 - Discontinued 1 bank on DOL 5
 - Stopped on DOL 6 (total bilirubin 6.1)
- Autologous unit discarded
- Fresh unit released into general inventory
 - ARC informed us the fresh unit was frozen

Baby Screening



- Blood type: O positive
- DAT positive for IgG
- Pan-reactive eluate
- Cord blood cells type as E antigen positive
 - Presence/contribution to hemolytic anemia of anti-E undetermined due to pan-reactivity

Summary

- Very few reported cases of anti-Jk3 in pregnancy
- Most have been mild, requiring phototherapy
- This is another case supporting this trend
- Many facets of care to consider
 - Communication is key
 - With clinicians, patients, blood bank personnel, blood collection agency, etc.

Thank You!



References

- Dean, L. (2005). Blood Groups and Red Cell Antigens. *Bethesda (MD): National Center for Biotechnology Information (US)*. Ch 10. <http://www.ncbi.nlm.nih.gov/books/NBK2272/>
- Lin, Y., Pavenski, K., Saidenberg, E., Branch, D. (2009). Blood Group Antigens and Normal Red Blood Cell Physiology: A Canadian Blood Services Research and Development Symposium. *Transfusion Medicine Reviews*; vol 23, no 4.
- Ferrando, M., Martínez-Cañabate, S., Luna, I., de la Rubia, J., Carpio, N., Alfredo, P., Arriaga, F. (2008). Severe hemolytic disease of the fetus due to anti-Jkb. *Transfusion*. 48(2):402-4. <http://www.ncbi.nlm.nih.gov/pubmed/18230082>
- Velasco Rodríguez, D., Pérez-Segura, G., Jiménez-Ubieto, A., Rodríguez, M.A., Montejano, L. (2014). Hemolytic disease of the newborn due to anti-jkb: case report and review of the literature. *Indian J Hematol Blood Transfus*. 30(2):135-8. <http://www.ncbi.nlm.nih.gov/pubmed/24839369>
- Hamilton, J.R. (2015). Kidd blood group system: a review. *Immunohematology*. 31(1):29-35. <http://www.ncbi.nlm.nih.gov/pubmed/26308468>
- Fung, M.K., Grossman, B.J., Hillyer, C.D., Westhoff, C.M. (2014). Technical Manual, 18th ed. *AABB*. Ch 14, 351-352.