Community Blood Center

# She's Having a Baby!
# Support for a Pregnant Patient With Rare Alloantibody

**Megan Dupont, MLS(ASCP)$^{CM}$SBB$^{CM}$**
Immunohematology Reference Laboratory Lead Technologist

innovation • experience • expertise



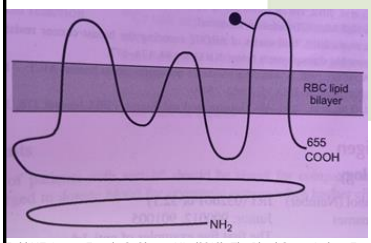
## Objectives

- Review the JR Blood Group System.
- Describe the case of Hemolytic Disease of the Fetus and Newborn in a patient with anti-Jr$^{a}$.
- Review strategies for obtaining uncommon or rare blood.

Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center

# JR Blood Group System

| Number of Antigens | History | Expression | Function | Gene |
|---|---|---|---|---|
| 1<br>$Jr^a$ | • First 7 examples of anti-$Jr^a$ reported in 1970<br>• Promoted from 901 Series to System in 2012 | • Highly expressed in placenta<br>• Low expression in many tissues & stem cells, erythroid precursors | • ATP-dependent transport protein involved in cellular detoxification<br>• Associated with drug resistance in cancer<br>• Role in folate & porphyrin homeostasis | *ABCG2*<br>Chromosome 4q22.1 |




Reid ME, Lomas-Francis C, Olsson, ML. (2012). *The Blood Group Antigen FactsBook*. 3rd ed. Elsevier Ltd

Modified from *The Blood Group Antigen FactsBook*

Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center

3

# $Jr^a$ Antigen

- ❑ **Obsolete name: Junior**
- ❑ **Named for first antibody maker, Rose Jacobs**
- ❑ **>99% occurrence in all populations**
  - Jr(a-) phenotype found mainly in Japanese as well as some European populations
- ❑ **Fully developed on cord blood red cells**

| Effect of Enzymes & Chemicals on $Jr^a$ antigen on intact RBCs | |
|---|---|
| Ficin/Papain | Resistant (enhanced) |
| Trypsin | Resistant |
| α-Chymotrypsin | Resistant |
| DTT | Resistant |
| Acid | Resistant |

Modified from *The Blood Group Antigen FactsBook*

Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center

# Alloanti-Jr$^a$

| *In vitro* Characteristics | |
|---|---|
| Immunoglobulin Class | IgG more common than IgM |
| Optimal Technique | IAT |
| Complement Binding | Some |
| Clinical Significance in Transfusion | • Variable<br>• Associated with reduced RBC survival & AHTR<br>• Documented success of transfusion of Jr(a+) RBCs |

Modified from *The Blood Group Antigen FactsBook*



# Impact of Alloanti-Jr$^a$ in Pregnancy

Anti-Jr$^a$ has been highly variable in pregnancy,
ranging from no clinical effect to severe anemia and fetal death.

Received: 19 August 2022 | Revised: 7 January 2023 | Accepted: 9 January 2023
DOI: 10.1111/trf.17265

CASE REPORT

TRANSFUSION

**Severe fetal anemia caused by anti-Jr$^a$: Burst forming unit-erythroid colony formation inhibition assay suggesting possible erythroid suppression mechanism**

Ann Tran[1] | Matthew T. S. Yan[1,2] | Donald R. Branch[2,3] | Megan Blacquiere[3] | Nicolas Pineault[2,4] | Roya Pasha[2] | Gwen Clarke[1,2]

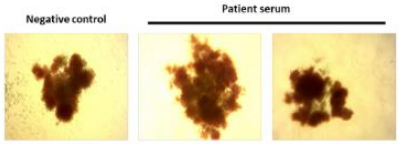



FIGURE 2 Representative burst forming unit-erythroid colonies produced in the presence of 5% patient serum showing similar hemoglobinization to the negative control.

**Case Report Conclusions:**

- ❑ Anti-Jr$^a$ may impair erythropoiesis leading to clinically significant fetal/neonatal anemia (similar to anti-K, anti-Ge3, anti-M(rare))
- ❑ Referral to maternal fetal medicine for monitoring regardless of anti-Jr$^a$ titer

# Objectives

- Review the JR Blood Group System.
- Describe the case of Hemolytic Disease of the Fetus and Newborn in a patient with anti-Jr$^a$.
- Review strategies for obtaining uncommon or rare blood.



# Patient History


- ❑ 37 year old Caucasian pregnant female, 25 weeks gestation
- ❑ Group B, Rh Positive
- ❑ History of anti-Jr$^a$ and anti-P1
- ❑ Gravida 2, para 1
  - Paternal sample typed Group O, Rh Positive; Jr(a+)
  - Cord blood types Group B, Rh Negative; Jr(a+); DAT positive (IgG +C'). Eluate contained anti-Jr$^a$
- ❑ Patient received care/receiving care at multiple local hospitals
- ❑ History of donating autologous unit for surgery
- ❑ Hematology/Oncology physician request for antibody identification & titration as well as recommendation for rare blood procurement

## ABO/Rh & DAT

| | ABO Group | | | | Rh Type | |
|---|---|---|---|---|---|---|
| | Anti-A | Anti-B | $A_1$ Cells | B Cells | Anti-D | Control |
| IS | 0 | 4+ | 3+ | 0 | 4+ | 0 |

**Group B, Rh Pos**

| Direct Antiglobulin Test |
|---|
| Poly |
| (0) ✓ |

**DAT Negative**



## Initial Antibody Panel Results

- Anti-P1 detected at Room Temperature
  - All reagent cells 1+ PEG IAT
    - Negative autocontrol

| | | Rh | | | | | Kell | | | | | | Duffy | | Kidd | | MNSs | | | | Lutheran | | P | Lewis | | Plasma Results | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | K | k | $Kp^a$ | $Kp^b$ | $Js^a$ | $Js^b$ | $Fy^a$ | $Fy^b$ | $Jk^a$ | $Jk^b$ | M | N | S | s | $Lu^a$ | $Lu^b$ | $P_1$ | $Le^a$ | $Le^b$ | 5' RT | PEG IAT |
| 1 | $R_1R_1$ | + | + | 0 | 0 | + | + | + | 0 | + | 0 | + | 0 | + | 0 | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | 1+ |
| 2 | $R_2R_2$ | + | 0 | + | + | 0 | 0 | + | 0 | + | 0 | + | + | 0 | + | 0 | 0 | + | 0 | + | 0 | + | +w | 0 | + | r | 1+ |
| 3 | rr | 0 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | + | 0 | + | + | 0 | + | 0 | 0 | + | +s | 0 | + | r | 1+ |
| 4 | r'r | 0 | + | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | + | + | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | 1+ |
| 5 | rr | 0 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | + | +s | 0 | 0 | 1+ | 1+ |
| 6 | AC | | | | | | | | | | | | | | | | | | | | | | | | | 0 | (0) ✓ |

w = Weak
S = Strong
r = Rough

# Panel of Thawed Rare Cells

- Anti-P1 nonreactive with thawed rare cells
- Common clinically significant specificities not ruled out 2x using double-dose cells: Anti-E, -c, -K, -Jk$^a$, -S

| | | Rh | | | | | Kell | | | | | | Duffy | | Kidd | | MNSs | | | | Lutheran | | P | Lewis | | Plasma Results | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | D | C | E | c | e | K | k | Kp$^a$ | Kp$^b$ | Js$^a$ | Js$^b$ | Fy$^a$ | Fy$^b$ | Jk$^a$ | Jk$^b$ | M | N | S | s | Lu$^a$ | Lu$^b$ | P$_1$ | Le$^a$ | Le$^b$ | 5' RT | PEG IAT |
| | | ✖ | ✖ | | \ | ✖ | \ | ✖ | | ✖ | | ✖ | ✖ | ✖ | \ | ✖ | ✖ | | \ | ✖ | | ✖ | ✖ | ✖ | | | |
| 1 | Jr(a-) | + | + | 0 | 0 | + | 0 | + | 0 | + | 0 | + | + | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | (0) ✓ |
| 2 | Jr(a-) | + | + | 0 | 0 | + | 0 | + | 0 | + | 0 | + | 0 | + | + | 0 | + | + | 0 | + | 0 | + | + | 0 | + | 0 | (0) ✓ |
| 3 | Jr(a-) | + | + | + | + | + | 0 | + | 0 | + | 0 | + | 0 | + | + | + | + | 0 | 0 | + | 0 | + | 0 | 0 | + | 0 | (0) ✓ |
| 4 | Jr(a-) | + | + | 0 | 0 | + | 0 | + | 0 | + | 0 | + | + | 0 | + | + | + | 0 | 0 | + | 0 | + | + | 0 | 0 | 0 | (0) ✓ |
| 5 | Jr(a-) | + | + | + | + | + | 0 | + | 0 | + | 0 | + | + | 0 | + | + | + | + | 0 | + | 0 | + | + | 0 | + | 0 | (0) ✓ |
| 6 | Jr(a-) | + | + | 0 | 0 | + | 0 | + | 0 | + | 0 | + | + | + | 0 | + | + | + | 0 | + | 0 | + | 0 | + | 0 | 0 | (0) ✓ |
| 7 | Jr(a-) | 0 | 0 | 0 | + | + | 0 | + | 0 | + | 0 | + | + | + | 0 | + | + | + | + | 0 | 0 | + | + | 0 | 0 | 0 | (0) ✓ |
| 8 | Jr(a-) | 0 | + | 0 | + | + | + | 0 | 0 | 0 | 0 | + | + | + | + | + | + | + | + | + | 0 | + | 0 | 0 | + | 0 | (0) ✓ |
| 9 | Jr(a+) | + | + | + | + | + | 0 | + | 0 | + | 0 | + | + | + | 0 | + | + | + | + | + | 0 | + | + | 0 | + | 0 | 1+ |

Blood Bank of Delmarva · Community Blood Center · Connecticut Blood Center · Memorial Blood Centers · Nebraska Community Blood Bank · New York Blood Center · Rhode Island Blood Center

11

**Which common clinically significant specificities is the patient at risk to produce?**

| Patient Phenotype by Serology | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| E | c | C | e | K | Fy$^a$ | Fy$^b$ | Jk$^a$ | Jk$^b$ | M | N | S | s |
| + | + | 0 | + | 0 | + | + | + | + | + | 0 | + | + |

Common clinically significant specificities not ruled out 2x using double-dose cells: Anti-~~E~~, -~~c~~, -K, -Jk~~$^a$~~, -~~S~~

Recommend K-negative RBCs until presence of anti-K can be excluded.

Blood Bank of Delmarva · Community Blood Center · Connecticut Blood Center · Memorial Blood Centers · Nebraska Community Blood Bank · New York Blood Center · Rhode Island Blood Center

12

# Anti-Jr$^a$ Titer Results

| | Neat | 2 | 4 | 8 | 16 | 32 | 64 | 128 |
|---|---|---|---|---|---|---|---|---|
| 60' 37C → IAT<br>Jr(a+), P1- | 1+$^s$ | 1+$^s$ | 1+ | 1+ | 1+ | 1+$^w$ | 0 ✓ | 0 ✓ |

Anti-Jr$^a$ Titer = 16



## Workup Conclusion

| | |
|---|---|
| **ABO/Rh** | Group B, Rh Positive |
| **DAT** | Negative |
| **Plasma** | • Anti-P1<br>• Anti-Jr$^a$, titer = 16<br>• No new alloantibodies |
| **Transfusion Recommendation** | K-, Jr(a-) |
| **Additional Comments** | • Anti-P1 reactive at 22C only, generally not clinically significant in transfusion therapy and does not cause HDFN.<br>• Anti-Jr$^a$ is clinically significant in transfusion therapy.<br>• Anti-Jr$^a$ is not usually associated with HDFN, but one fatal case has been reported. Critical titers of anti-Jr$^a$ have not been established.<br>• Donor blood lacking Jr$^a$ is extremely rare (<1%) and often not readily available.<br>• Please contact the IRL to discuss options for procuring blood for transfusion for this patient!<br>• A letter was provided to the patient explaining the rarity of her blood type. |

## When Uncommon or Rare Blood is Needed


**IRL fresh and/or frozen inventory**


**Autologous**
**(If clinical situation allows)**


**Family Members**


**NYBCe Partners**


**American Rare Donor Program**

Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center

15

## Evaluation of Brother

| | |
|---|---|
| **ABO/Rh** | Group B, Rh Pos |
| **Antibody Screen** | Negative |
| **DAT** | Negative |

| Brother's Antigen Typing by Serology | |
|---|---|
| **P1** | **Jr$^a$** |
| 0 | 0 |


| | |
|---|---|
| Sequencing of *JR/ABCG2* | 2 null variants associated with Jr(a-) phenotype, at risk for alloanti-Jr$^a$ |

**Predicted Phenotype by DNA PreciseType HEA**

| E | c | C | e | V | VS | K | k | Kp$^a$ | Kp$^b$ | Js$^a$ | Js$^b$ | Fy$^a$ | Fy$^b$ | Jk$^a$ | Jk$^b$ | M | N | S | s | U | Lu$^a$ | Lu$^b$ | Di$^a$ | Di$^b$ | Co$^a$ | Co$^b$ | Do$^a$ | Do$^b$ | Hy | Jo$^a$ | Lw$^a$ | Lw$^b$ | Sc1 | Sc2 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 0 | + | + | + | 0 | 0 | 0 | + | 0 | + | 0 | + | + | + | + | + | + | + | 0 | + | + | 0 | + | 0 | + | + | 0 | + | + | + | + | + | 0 | + | 0 |

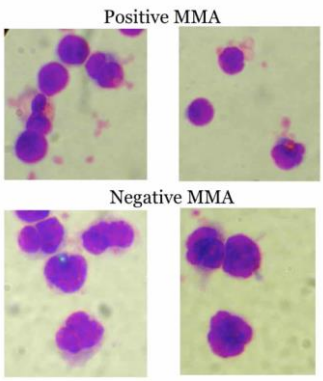
Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center

## Assessing the Clinical Significance of the Patient's Anti-Jr$^a$ Monocyte Monolayer Assay

| MI (percentage of RBCs adhered, ingested or both) |
|---|
| 16.25-29.25 |

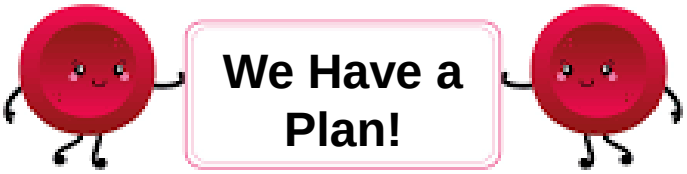
An MI of >20 indicates the antibody has clinical significance, which may range from abnormal RBC survival to clinically obvious reactions. The patient should not receive Jr(a+) units.

LifeShare BLOOD CENTER




https://www.bbguy.org/2021/10/13/093/

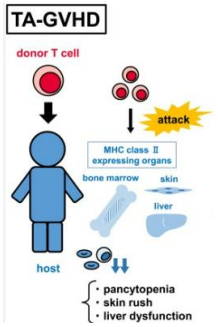





- ❑ Brother recruited as regular blood donor (units to be processed as rare)
- ❑ Brother donated double red cell donation on 5/6/2023
- ❑ Transfusion facility would request the units when patient admitted for delivery
- ❑ Irradiation required prior to transfusion
- ❑ Products would be returned to CBC to freeze if not needed

## Transfusion Associated-Graft Versus Host Disease (TA-GVHD)

Rare and usually fatal complication of blood transfusion in which lymphocytes from the transfused blood component attack the recipient's tissues, especially skin, bone marrow, and GI tract.

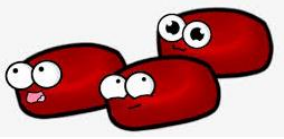



Technical Manual (21st Edition) and Circular of Information (December 2021):

- Fetal and neonatal recipients of intrauterine transfusions
- Selected immunocompromised recipients
- Recipients of cellular components known to be from a blood relative
- Recipients who have undergone marrow or peripheral blood progenitor cell transplantation
- Recipients of cellular components who donor is selected for HLA compatibility

https://www.sciencedirect.com/science/article/abs/pii/S1473050222000672





## A Change in Plans…

- ❑ On 5/10/2023, phone call received requesting 2 units that were collected from the brother…
- ❑ Patient had been admitted to a *different* hospital for delivery
- ❑ Transfusion service does not have irradiator
- ❑ Patient's Hgb 10.0 g/dL
- ❑ Ultrasound indicates signs of anemia in baby
- ❑ Plan is to deliver by C-section on Saturday
- ❑ Both units irradiated and sent to transfusion facility to have available for delivery

## Arrival of Baby Girl

- ❑ Baby girl born 5/13/2023
- ❑ Group O, Rh Negative
- ❑ 12.0 g/dL Hgb
- ❑ DAT results unknown

**Approximately 1 month later…**

- ❑ Antigen typing request on baby from Children's Hospital
- ❑ Hospital reports negative DAT & antibody screen
- ❑ No transfusions

| ABO/Rh | Group O, Rh Negative |
|---|---|
| DAT | Negative |
| Anti-Jra (2 unlicensed sources) | Jr(a+) |
| Sample submitted to Genomics Laboratory for HEA testing for full predicted phenotype | |



# Objectives

- Review the JR Blood Group System.
- Describe the case of Hemolytic Disease of the Fetus and Newborn in a patient with anti-Jr$^{a}$.
- Review strategies for obtaining uncommon or rare blood.

# References

AABB, American Red Cross, America's Blood Centers, Armed Services Blood Program. December 2021. Circular of Information for the Use of Human Blood and Blood Components. https://www.aabb.org/docs/default-source/default-document-library/resources/circular-of-information-watermark.pdf?sfvrsn=7f5d28ab_5

Chaffin, J. (Host) 10/13/2021. BBGuy Essentials 093: The Mighty MMA with Sandy Nance. Audio podcast episode. https://www.bbguy.org/2021/10/13/093/

Cohn CS, Delaney M, Johnson ST, Katz LM. Technical Manual. 20th ed. Bethesda, Maryland: AABB; 2020.

Issitt PD, Anstee DJ. Applied Blood Group Serology. 4th edition. Durham, North Carolina: Montgomery Scientific Publications 1998.

Reid ME, Lomas-Francis C, Olsson, ML. (2012). *The Blood Group Antigen FactsBook*. 3rd ed. Elsevier Ltd.

Tran A, Yan MTS, Branch DR, et al. Severe fetal anemia caused by anti-Jr$^{a}$: Burst forming unit-erythroid colony formation inhibition assay suggesting possible erythroid suppression mechanism. *Transfusion*. 2023;63: 877-882.



New York Blood Center Enterprises

innovation • experience • expertise

Blood Bank of Delmarva | Community Blood Center | Connecticut Blood Center | Memorial Blood Centers | Nebraska Community Blood Bank | New York Blood Center | Rhode Island Blood Center