



# Behave Jr<sup>a</sup>: When an HTLA isn't an HTLA

Mary Madden, MLS(ASCP)SBB<sup>CM</sup>

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# Patient Profile



- 25 y.o. female
- Currently pregnant
  - Second pregnancy
- No history of transfusions
- History of an unidentified HTLA



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# Patient Testing

- ABO/Rh: B Pos
- DAT: Negative with Polyspecific AHG
- Initial Screen:

Cell	IS	PEG IAT	Gel IgG
SC I	O	1+	1+
SC II	O	1+	1+
SC III	O	1+	1+



CELL	D	C	c	E	e	f	V	C	K	k	K p a	K p b	J s a	J s b	F y a	F y b	J k a	J k b	L e a	L e b	P 1	M	N	S s	L u a	L u b	X g a		Patient's Results IS 37	LISS IgG		
1	+	+	0	+	+	0	0	0	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	0	+	+	1	0	0	w+		
2	+	+	0	0	+	0	0	+	+	+	0	+	0	+	0	+	+	+	0	+	+	0	+	0	+	0	+	0	2	0	0	1+
3	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	0	+	+	3	0	0	1+		
4	+	0	+	0	+	+	0	0	0	+	0	+	0	0	+	0	0	+	0	+	0	0	0	0	+	+	4	0	0	w+		
5	0	+	+	0	+	+	0	0	+	+	0	+	0	+	+	0	0	+	+	0	+	0	0	+	+	5	0	0	1+			
6	0	0	+	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	+	6	0	0	w+			
7	0	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	0	+	0	0	+	0	+	0	7	0	0	w+		
8	0	0	+	0	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	+	+	+	0	+	0	8	0	0	w+			
9	0	0	+	0	+	+	0	0	0	+	0	+	0	+	0	0	+	+	0	+	0	0	+	+	9	0	0	w+				
10	+	+	+	+	+	+	0	0	0	0	+	0	+	0	+	+	0	+	0	+	+	+	+	0	0	+	+	10	0	0	1+	
11	+	w	+	+	w	0	0	0	0	+	0	+	0	+	0	0	+	0	0	+	+	0	0	+	+	11	0	0	1+			
PC	+	+	0	0	+			0					+	0	+	+		0	0	0	+	+	+	+		P C	0	0	0✓			



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# Titer Results

Dil 30' 37 IgG	1:1	1:2	1:4	1:8	1:16	1:32	1:64	1:128	1:256
Result	w+	w+	w+	w+	w+	w+	+ <sup>m</sup>	+ <sup>m</sup>	o✓



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# HTLA-like Antibodies

## “High Titer, Low Avidity”

- Reactivity remains after serial dilutions
  - Titrations are usually greater than 32
- Weak reacting (“avidity”)
  - $\leq 1+$  reactivity
  - Not enhanced by potentiators, but may be affected by enzymes and chemical treatments
- HTLA does *not* refer to a system
  - Includes anti-Ch, -Rg, -Cs<sup>a</sup>, -Yk<sup>a</sup>, -Kn<sup>a</sup>, -McC<sup>a</sup>, -JMH, -Yt<sup>a</sup>, etc.

# Selected Cells...

Cell phenotype	Reactivity (patient serum)
McC(a+) Sl(a-)	w+
Kn(a-) McC(a-)	w+
Yk(a-)	w+



# Helpful Potentiators and Chemical and Enzyme Treatments

- Polybrene (short incubation phase)
  - Abolishes HTLA reactivity
- DTT/AET (cleaves disulfide bonds)
  - Destroys Yt<sup>a</sup>, JMH, McC<sup>a</sup>, Yk<sup>a</sup>, Kn<sup>a</sup>, etc.
- Trypsin (cleaves GPA/removes sialic acid)
  - Destroys KN, DO, JMH, etc.
- Papain/Ficin (cleaves GPA & GPB/removes sialic acid)
  - Destroys Ch, Rg, JMH, etc.

Note: Resistance to some of these treatments may help to place the antibody as well. Example: Cs<sup>a</sup> is resistant to DTT/AET, Trypsin, and Papain/Ficin.

# Treated Panels

<u>CELL</u>	D	C	c	E	e	f	V	C	K	k	K	K	J	J	F	F	J	J	L	L	P	M	N	S	s	L	L	X	g		Patient's Results Ficin 15' 37 IgG
-------------	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	---	--	--

1	+	+	0	0	+	0	0	0	+	+	0	+	0	+	0	+	+	+	0	0	0	0	0	0	+	0	+	/	<sup>1</sup>	W+
2	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	0	+	+	0	+	+	+	0	+	0	+	/	<sup>2</sup>	W+
3	0	0	+	0	+	+	0	0	+	+	0	+	0	+	+	0	+	+	0	+	+	0	+	+	0	+	+	/	<sup>3</sup>	W+
4	0	0	+	0	+	+	0	0	0	+	0	+	0	+	+	0	+	0	0	+	0	+	0	+	+	0	+	/	<sup>4</sup>	W+

<u>CELL</u>	D	C	c	E	e	f	V	C	K	k	K	K	J	J	F	F	J	J	L	L	P	M	N	S	s	L	L	X	g		Patient's Results DTT 15' 37 IgG
1	0	0	+	0	+	+	0	0	0	+	0	+	0	+	0	+	+	+	0	0	0	0	0	0	+	0	+	+	<sup>1</sup>	W+	
2	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	+	+	0	+	+	0	0	+	0	+	0	/	<sup>2</sup>	W+	
3	0	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+	<sup>3</sup>	W+		
4	0	0	+	0	+	+	0	0	0	+	0	+	0	+	+	0	+	0	0	+	0	+	+	+	0	+	+	<sup>4</sup>	W+		



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# Treated Panels (cont'd)

<u>CELL</u>	D	C	c	E	e	f	V	C w	K	k	K p a	K p b	J s a	J s b	F y a	F y b	J k a	J k b	L e a	L e b	P 1	M	N	S	s	L u a	L u b	X g a		Patient's Results Trypsin 15' 37 IgG
<sup>1</sup>	O	O	+	O	+	+	O	O	O	+	O	+	O	+	O	+	+	+	O	O	O	O	+	O	+	O	++	W+		
<sup>2</sup>	+	O	+	+	O	O	O	O	O	+	O	+	O	+	O	+	+	+	O	+	+	O	O	+	O	+	O	W+		
<sup>3</sup>	O	O	+	O	+	+	O	O	+	+	O	+	O	+	O	+	O	+	O	+	O	O	+	O	+	O	++	W+		
<sup>4</sup>	O	O	+	O	+	+	O	O	O	+	O	+	O	+	O	+	O	+	O	O	O	+	O	+	O	++	W+			

<u>CELL</u>	D	C	c	E	e	f	V	C w	K	k	K p a	K p b	J s a	J s b	F y a	F y b	J k a	J k b	L e a	L e b	P 1	M	N	S	s	L u a	L u b	X g a		Patient's Results Polybrene IS IgG
<sup>1</sup>	O	O	+	O	+	+	O	O	O	+	O	+	O	+	O	+	+	+	O	O	O	O	+	O	+	O	++	O W+		
<sup>2</sup>	+	O	+	+	O	O	O	O	O	+	O	+	O	+	O	+	+	+	O	+	+	O	O	+	O	+	O	O W+		
<sup>3</sup>	O	O	+	O	+	+	O	O	+	+	O	+	O	+	O	+	O	+	O	+	O	O	+	O	+	O	O W+			
<sup>4</sup>	O	O	+	O	+	+	O	O	O	+	O	+	O	+	O	+	O	+	O	O	O	+	O	+	O	++	O W+			



# Power of Persistence...

- High prevalence?
  - Potentiators, chemical and enzyme treatments failed to abolish reactivity
  - High prevalence with “HTLA-like” behavior
    - Lu<sup>b</sup>, Vel, Kp<sup>b</sup>, At<sup>a</sup>, Jr<sup>a</sup>, etc.



# High Prevalence Negative Panel

<u>CELL</u>	D	C	c	E	e	f	V	C	K	k	K p a	K p b	J s a	J s b	F y a	F y b	J k a	J k b	L e a	L e b	P 1	M	N	S	s	L u a	L u b	X g a		Patient's Results LISS IgG
1	0	0	+	0	+	+	0	0	0	w	+	0	0	+	+	0	+	0	0	+	0	+	+	+	+	0	+	/	Kp(b-)	+m
2	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	/	Yk(a-) McC(a-)	1+
3	0	0	+	0	+	+	0	0	0	+	0	+	0	+	0	+	0	0	0	+	0	+	+	0	+	0	+	/	Rg- Yk(a-)	1+
4	+	0	+	+	+	+	/	/	0	/	/	/	/	+	+	+	0	+	0	+	/	+	+	0	+	0	+	/	Yt(a-)	w+
5	0	0	+	0	+	/	/	0	/	/	/	/	+	0	+	+	0	0	+	+	+	+	0	+	+	0	0	/	Lu(b-)	w+
6	+	+	0	0	+	0	0	+	0	+	0	+	0	+	0	+	+	+	0	+	+	0	+	0	+	0	+	/	Kn(a-)	w+
7	0	0	+	0	+	/	/	+	+	/	/	/	+	0	+	+	0	+	0	+	+	+	+	0	+	0	+	/	Vel-	1+
8	0	0	+	0	+	/	0	0	+	0	0	/	+	+	0	0	+	0	+	0	+	+	+	0	0	+	/	SC:-1	1+	

## Typing Patient for High Prevalence

Antisera	At <sup>a</sup>	JMH	Jr <sup>a</sup>	Jr <sup>a</sup>	Probable Anti-Jr <sup>a</sup> !
Patient	2+	1+	0✓	0✓	
Pos Cont	2+	1+	1+	1+	



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## Anti-Jr<sup>a</sup>

- Jr<sup>a</sup> originally classified as a Series 901 Antigen
  - Graduated to its own system in 2012
    - ABCG2 defined the Jr(a-) phenotype
      - Most often found in those of Asian heritage (Japanese)
    - Anti-Jr<sup>a</sup> may be stimulated by pregnancy
  - Patient's Anti-Jr<sup>a</sup> confirmed by molecular genotype



# Clinical Significance?

- Few cases of Anti-Jr<sup>a</sup>
  - Cr<sup>51</sup> Studies did show decreased survival of RBC
  - One fatal case of HDFN has been reported
- Consider MMA
  - Patient currently pregnant
  - Transfusion recommendations



# The MMA

- Monocyte Monolayer Assay
  - Simple test used to assess clinical significance
  - Sensitized red blood cells are introduced to phagocytic monocytes
  - Test is incubated for 2 hours then washed to remove unbound RBCs
    - Monocytes with phagocytosed RBCs are counted and a percentage is reported
      - >3% is considered positive
        - <5% incompatible blood may be transfused with little risk
        - 5-20% risk of reaction increased to 33%
        - >20% risk of reaction increased to 64%

# Transfusion Recommendations

- Anti-Jr<sup>a</sup> considered mildly, clinically significant
- Transfusion should be avoided
  - Jr(a-) blood should be provided if needed
  - No blood needed and a healthy baby was delivered!



# References

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Thank You!

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