HDFN- Hemolytic Disease of the Fetus and Newborn

HDFN REVIEW AND CASE STUDIES

Objectives

At the end of this presentation the learner will be able to:

- List and briefly describe the 3 categories of HDFN
- Name the indications for Rh Immunoglobulin
- Recall when and who marketed the first Rh Immunoglobulin
- State why most cases of HDFN due to anti-D are in white females
- List the main causes of fetomaternal bleeds

Objectives

- State why an ABO incompatibility will decrease the chances of an Rh negative mother of an Rh positive baby making an anti-D
- Describe the two forms of RhIg
- State the two doses of Rhogam
- Explain why you may not be able to perform antigen typing with a positive DAT
- List the Blood Bank tests needed when testing for HDFN

Hemolytic Disease of the Fetus and Newborn

HDFN occurs when the fetal cells are coated with IgG alloantibodies from the mother.

These antibodies are directed towards the antigens inherited from the father.

There are 3 categories of HDFN:

- D hemolytic disease
  - caused by anti-D
- "Other" hemolytic disease
  - caused by antibodies to the Rh system (other than D) or other blood group systems
    - Anti-c, -e, -C, -E and -Kell most common
- ABO HDFN
  - caused by anti-A,B in group O mothers

D Hemolytic Disease

- HDFN due to Anti-D is the most common and most severe.
- The D antigen is very antigenic; requires very little to stimulate antibodies
- <0.1mL of fetal blood needed to immunize

Anti-D

- The first antibody discovered to cause HDFN was Anti-D.

- Before the advent of Rh Immune Globulin 98% of all HDFN cases were due to Anti-D; approx. 1 in 180 of all newborn white infants

Anti-D

- Most cases of HDFN due to Anti-D occur in white females because:

  12-18% of white women are D-

  2-5% of black women are D-

  1.7% of Asian women are D-

Anti-D

- The probability of immunization occurring in an untreated D- mother with a D+ baby is about 16%.
- 9% will occur with the first pregnancy and 7% with the second pregnancy.

Immunization of mother

- Immunization occurs due to exposure to the baby's red cells by a fetomaternal hemorrhage:
  - Delivery is the most common cause
  - Amniocentesis
  - Spontaneous or induced abortion
  - Chorionic villus sampling
  - Cordocentesis
  - Rupture of an ectopic pregnancy
  - Blunt trauma to the abdomen

Immunization of mother

- Decrease in immunization to D if baby is ABO incompatible
- Chance decreases from 16% to 2%
- Anti-A and/or Anti-B destroys cells before immune system can formulate Anti-D

Immunization of mother

- Immunization can also occur due to a transfusion of a product containing Rh+cells.

- It is very important to give only **Rh-** products to **Rh-** women of childbearing age.

Immunization of mother

- If it is necessary to give Rh+ products (like platelets) a prophylaxis dose of Rh Immunoglobulin should be considered.

- RhIg given now could prevent the development of an Anti-D that could potentially cause HDFN in future pregnancies.

Rh Immune Globulin

- 1968: Ortho marketed the first Rh Immune Globulin product: RhoGAM.
- After 1968 the rate of HDFN due to Anti-D decreased dramatically.
- When Rh IG is given at 28 weeks antipartum and postpartum the incidence of Anti-D drops to 0.1%.

Severity of HDFN

- Severity of the disease can vary depending on level of destruction of IgG coated cells
- Severity can range from no symptoms at all to intrauterine death.

Severity of HDFN

- Red cell destruction can lead to many levels of severity:
  - hyperbilirubinemia
    - slight jaundice
    - kernicterus (bilirubin neurotoxicity)
  - Erythroblastosis fetalis
  - Hydrops fetalis

Erythroblastosis fetalis

- ↑ RBC destruction = ↑ RBC production = ↑reticulocytes =“erythroblastosis fetalis”

- “Hydrops fetalis” (generalized massive edema) can occur in severe cases.

Anti-D

- When Anti-D is the cause of HDFN the severe anemia can cause cardiovascular failure, tissue hypoxia and death in utero.

- Intrauterine transfusion can save the baby's life in these cases.

Testing Results

+DAT due to:	DAT results:
Anti-D	2+
Anti-A,B	m+

HDFN Case Study #1

PUBS

- **P**ercutaneous
- **U**mbilical
- **B**lood
- **S**ampling

Case Study

Unborn Baby A
PUBS sample

Anti-A	0
Anti-B	0
Anti-D	0
D control	0
DAT	4+
ABSCR	Positive

Baby A types

O negative

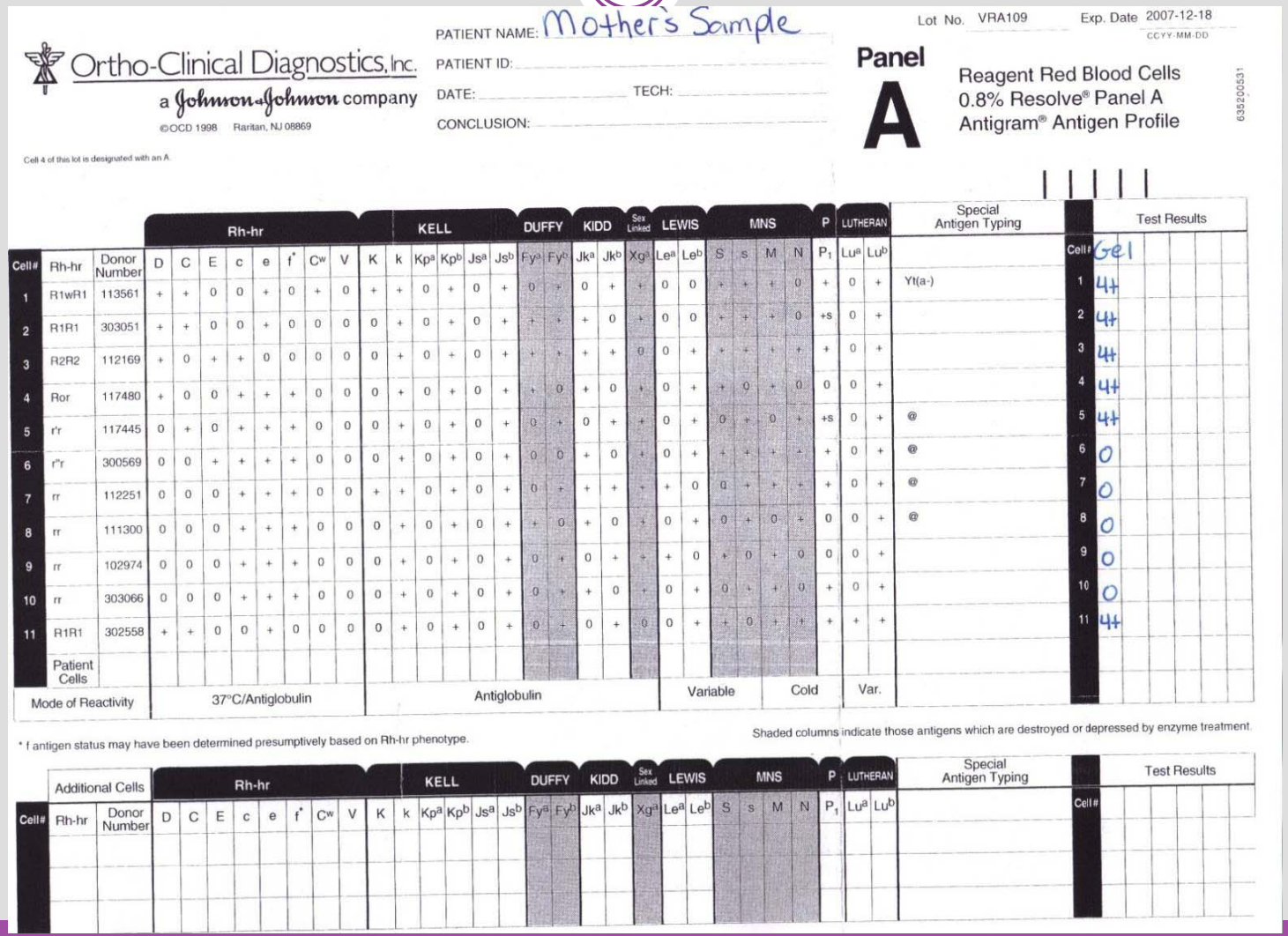
Unborn Baby B
PUBS sample

Anti-A	0
Anti-B	0
Anti-D	0
D control	0
DAT	Neg

Baby B types

O negative

Mother's Antibody ID



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a Johnson & Johnson company
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PATIENT NAME: Mother's Sample
PATIENT ID:
DATE: TECH:
CONCLUSION:

Lot No. VRA109 Exp. Date 2007-12-18 (CCYY-MM-DD)

Panel A

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

635200531

Cell 4 of this lot is designated with an A.

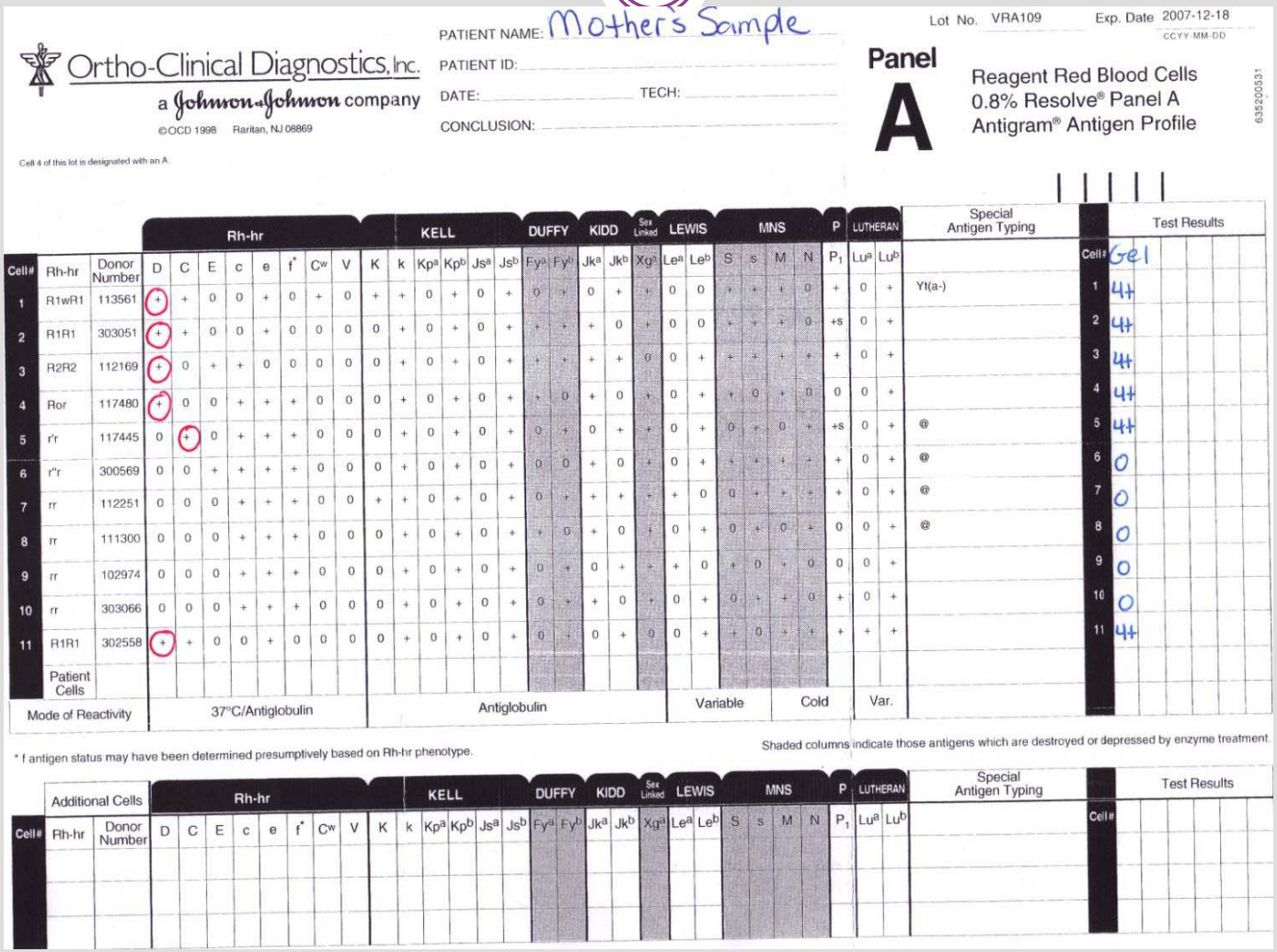
Cell #	Rh-hr	Donor Number	D	C	E	c	e	f*	Cw	V	K	k	Kpa	Kpb	Jsa	Jsb	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Special Antigen Typing	Test Results
1	R1wR1	113561	+	+	0	0	+	0	+	0	+	+	0	+	0	+	0	+	0	+	+	0	0	+	+	+	0	+	0	+	Yt(a-)	4+
2	R1R1	303051	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	+	0	+	0	0	+	+	+	0	+s	0	+		4+
3	R2R2	112169	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	+	+	0	+		4+
4	Ror	117480	+	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	0	0	+		4+
5	r'r	117445	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+s	0	+	@	4+
6	r"r	300569	0	0	+	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	+	+	+	+	+	+	0	+	@	0
7	rr	112251	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	0	+	@	0
8	rr	111300	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	0	+	0	+	0	+	0	+	0	0	+	@	0
9	rr	102974	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	+	0	+	0	+	0	0	0	+		0
10	rr	303066	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	0	+	+	0	+		0
11	R1R1	302558	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	0	+	0	0	+	+	0	+	+	+	+	+		4+
	Patient Cells																															
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold				Var.			

* f antigen status may have been determined presumptively based on Rh-hr phenotype.

Shaded columns indicate those antigens which are destroyed or depressed by enzyme treatment.

Additional Cells																																Test Results
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	Cell #

Mother's Antibody ID



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PATIENT NAME: Mothers Sample
PATIENT ID:
DATE: TECH:
CONCLUSION:

Lot No. VRA109 Exp. Date 2007-12-18 (CCYY-MM-DD)

Panel A

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Antigram® Antigen Profile

635200531

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2	R1R1	303051	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	+	+	0	+	0	0	+	+	+	0	+s	0	+		4+
3	R2R2	112169	+	0	+	+	0	0	0	0	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	+	+	0	+		4+
4	Ror	117480	+	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	0	0	+		4+
5	r'r	117445	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+s	0	+	@	4+
6	r"r	300569	0	0	+	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	+	+	+	+	+	+	0	+	@	0
7	rr	112251	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	+	+	+	0	+	@	0
8	rr	111300	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	+	0	+	0	+	0	+	0	+	0	0	+	@	0
9	rr	102974	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	+	0	+	0	+	0	0	0	+		0
10	rr	303066	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+	0	+	0	+		0
11	R1R1	302558	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	0	+	0	0	+	+	0	+	+	+	+	+		4+
	Patient Cells																															
Mode of Reactivity			37°C/Antiglobulin								Antiglobulin											Variable		Cold					Var.			

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Mother's Antibody ID

SELECTED CELL PANEL

REACTIONS

SOURCE & LOT #	CELL #	D	C	E	c	e	f	C^w	V	K	k	Kpa	Kpb	Js^a	Js^b	Fya	Fyb	Jka	Jkb	Xga	Lea	Leb	S	s	M	N	P1	Lua	Lub	Gel			
ortho VRA 111	5	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	0	+	0	+	0	+	0	+	+	+	+	0	+	4+			
ortho VRB 110	21	0	+	0	+	+	+	0	0	0	+	0	+	0	+	0	+	0	+	+	0	+	0	+	0	+	+s	0	+	4+			
ortho VRA 110	5	0	+	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	+	+	0	0	0	+	0	+	0	0	+	4+			

ANTIBODIES IDENTIFIED Anti-D + -C DC_____IGG_____IGG+_____C_____

PATIENT NAME Mother's Sample CPI/CI# _____

TECHNOLOGIST _____ DATE _____

Forsyth Medical Center 3333 Silas Creek Parkway Winston-Salem, NC 27103
I:\Shared\Blood Bank\WORKSHEET DISK\SELECTED CELL PANEL.doc

Case Study

- Why does baby have positive DAT?
- Mom has 2 antibodies: Anti-D and –C
- Need to antigen type Baby A
  - Baby types negative for C and D

Case Study

- How can baby type negative for D and C and still have a positive DAT?

Blocking Phenomenon!

Blocking phenomenon

- An over abundance of antibodies is coating the red cells
- The antibodies take up all antigen sites on the cell
- The antisera reagent has no antigen sites to attach to

Blocking phenomenon

- Will cause false negative reactions
- Anti-D is the most common in HDFN.
- Suspicious when baby has a strong DAT and types antigen negative for the antibody.

Testing Results

Two ways to treat DAT+ cells for antigen typing:

1) Choloroquin

2) Gentle heat elution
   - Best for blocking phenomenon cases

Case Study

Unborn Baby A
Choloroquin treated cells

Anti-C	0
Anti-D	2+
D control	0
DAT	negative

Baby A types
D positive and C negative

Case Study

- Unborn Baby A now types O positive and negative for C
- Unborn Baby A received an intrauterine transfusion of group O Rh negative, C negative blood

Case Study

- Babies born a few days later
- Baby B was ok
- Baby A had an increase in unconjugated bilirubin and a decrease in hemoglobin

Laboratory Results

NEWBORN BABY A							
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
T Bili	5.0	5.4	6.4	8.1	9.5	**13.4**	**13.6**
D Bili	0.3	0.3	0.3	0.2	0.3	**0.4**	**0.4**
Ind Bili	**4.7**	**5.1**	**6.1**	**7.9**	**9.2**	**13.0**	**13.2**
Hgb	13.0	13.6	**12.3**	**10.6**	**9.6**	**8.9**	**8.5**

Case Study

Newborn Baby A

Anti-A	0
Anti-B	0
Anti-D	0
D control	0
Weak D	1+
Wk D Cont	1+
DAT	4+

Baby A types

O, Rh?

Newborn Baby B

Anti-A	0
Anti-B	0
Anti-D	0
D control	0
Weak D	0
Wk D Cont	0
DAT	Neg

Baby B types

O negative

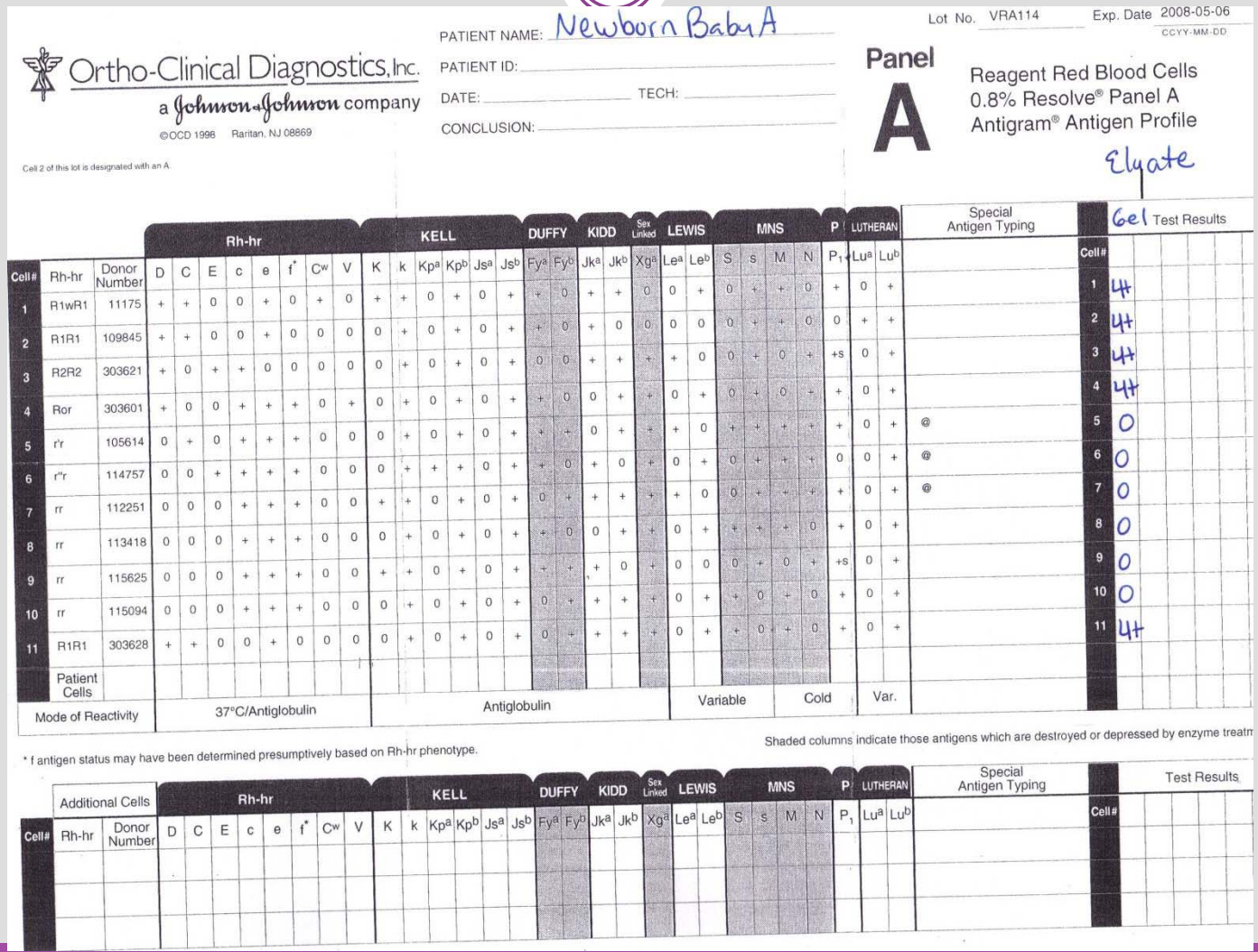
Case Study

Unborn Baby A
Choloroquin treated cells

Anti-C	0
Anti-D	2+
D control	0
DAT	negative

Baby A types
D positive and C negative

Elution Results



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PATIENT NAME: Newborn Baby A
PATIENT ID:
DATE: TECH:
CONCLUSION:

Lot No. VRA114 Exp. Date 2008-05-06 (CCYY-MM-DD)

Panel A

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

Elyate

Cell 2 of this lot is designated with an A.

Cell#	Rh-hr	Donor Number	Rh-hr: D	C	E	c	e	f*	Cw	V	KELL: K	k	Kpa	Kpb	Jsa	Jsb	DUFFY: Fya	Fyb	KIDD: Jka	Jkb	Sex Linked: Xga	LEWIS: Lea	Leb	MNS: S	s	M	N	P: P1	LUTHERAN: Lua	Lub	Special Antigen Typing	Test Results
1	R1wR1	11175	+	+	0	0	+	0	+	0	+	+	0	+	0	+	+	0	+	+	0	0	+	0	+	+	0	+	0	+		4+
2	R1R1	109845	+	+	0	0	+	0	0	0	0	+	0	+	0	+	+	0	+	0	0	0	0	0	+	+	0	0	+	+		4+
3	R2R2	303621	+	0	+	+	0	0	0	0	0	+	0	+	0	+	0	0	+	+	+	+	0	0	+	0	+	+s	0	+		4+
4	Ror	303601	+	0	0	+	+	+	0	+	0	+	0	+	0	+	+	0	0	+	+	0	+	0	+	0	+	+	0	+		4+
5	r'r	105614	0	+	0	+	+	+	0	0	0	+	0	+	0	+	+	+	0	+	+	+	0	+	+	+	+	+	0	+	@	0
6	r''r	114757	0	0	+	+	+	+	0	0	0	+	+	+	0	+	+	0	+	0	+	0	+	0	+	+	+	0	0	+	@	0
7	rr	112251	0	0	0	+	+	+	0	0	+	+	0	+	0	+	0	+	+	+	+	+	0	0	+	-	+	+	0	+	@	0
8	rr	113418	0	0	0	+	+	+	0	0	0	+	0	+	0	+	+	0	0	+	+	0	+	+	+	+	+	0	+	0	+		0
9	rr	115625	0	0	0	+	+	+	0	0	+	+	0	+	0	+	+	+	+	0	+	0	0	0	+	0	+	+s	0	+		0
10	rr	115094	0	0	0	+	+	+	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	+	0	+		0
11	R1R1	303628	+	+	0	0	+	0	0	0	0	+	0	+	0	+	0	+	+	+	+	0	+	+	0	+	0	+	0	+		4+
	Patient Cells																															
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Case Study

- Conclusion:

  Baby A has HDFN due to Anti-D

Treatment for HDFN

- Ultraviolet phototherapy
- Exchange transfusion
- Intrauterine transfusion

HDFN Case Study #2

ABO INCOMPATIBILITY

ABO HDFN

Mother's sample

Anti-A	0
Anti-B	0
A1 cells	4+
B cells	4+
Anti-D	4+
D control	0
Weak D	0
Wk D control	0

Antibody Scr	negative

Newborn Baby's sample

Anti-A	4+
Anti-B	0
Anti-D	4+
D control	0
DAT	MP

Total bili	4.4
Direct bili	0.4
Indirect bili	**4.0**

HDFN- Hemolytic Disease of the Fetus and Newborn

HDFN REVIEW AND CASE STUDIES