EVERYTHING YOU NEEDED TO KNOW ABOUT HDN IN ONE CASE STUDY
or, The Couple That Just Wouldn't Give Up
Case Study by Jim Perkins, M.D. (©2009)

Pregnancy #1

JP, a 24 year old woman was found to be group A, Rh negative with a negative antibody screen on initial prenatal testing. She was given Rh immune globulin (RhIG) at 28 weeks gestation, after similar results on a repeat "type-and-screen". She went into labor at 42 weeks gestation, was found to have a breech presentation, and delivered by cesarean section. The infant was Rh positive and RhIG was administered.

Pregnancy #2

Two years later, during pregnancy #2, JP was again shown to be group A, Rh negative with a negative antibody screen on her first visit and at 28 weeks. Antenatal RhIG was administered. A repeat cesarean section was performed at 36 weeks after demonstration of a non-reactive non-stress test and decreased fetal growth rate. Cord blood RBCs were Rh negative, and no postnatal RhIG was given.

Pregnancy #3

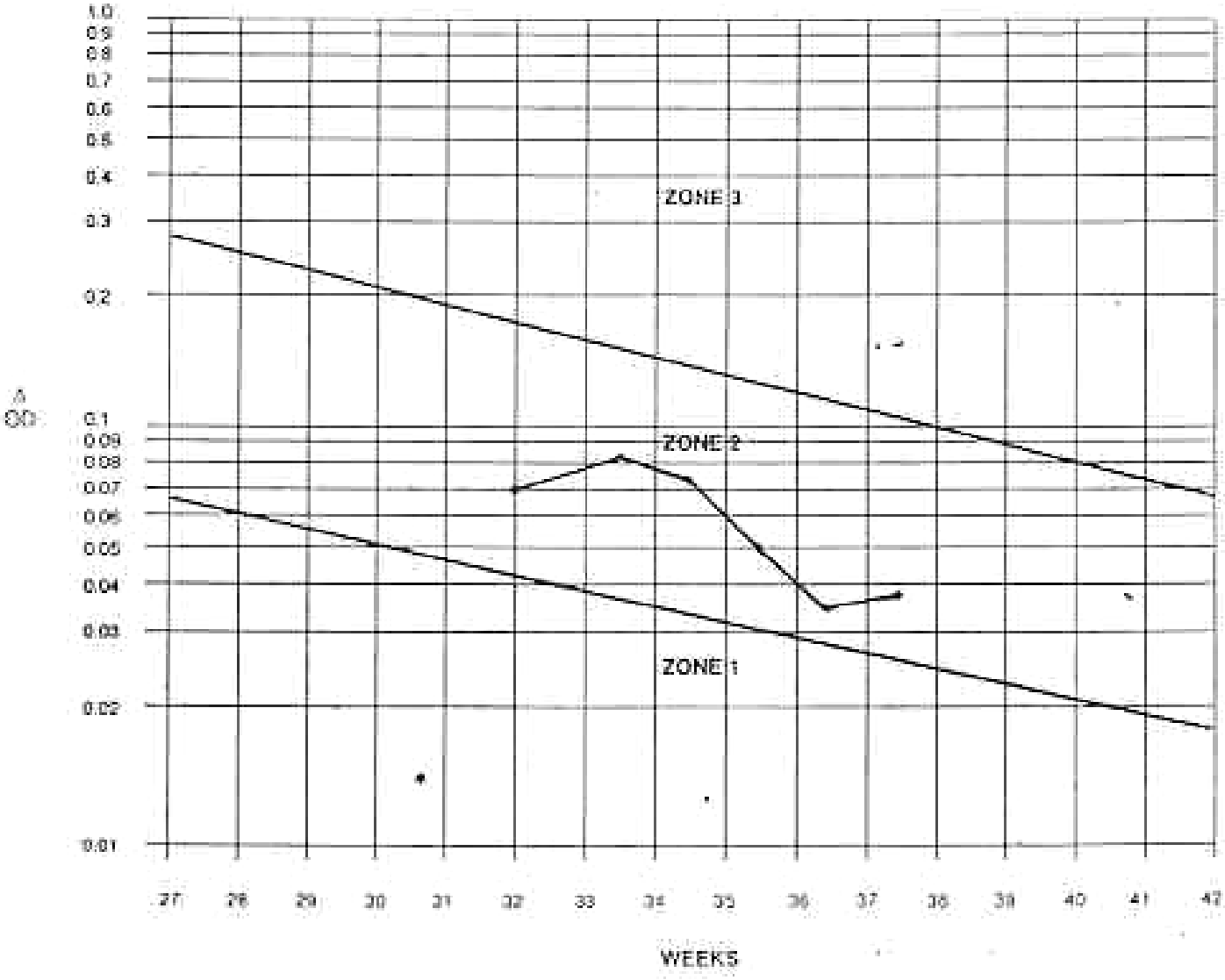
During pregnancy #3, JP, now 27 years old, had a negative antibody screen initially and at 28 weeks when she received RhIG. On admission for repeat cesarean section the antibody screen was positive and anti-D was demonstrated at a titer of 8. RhIg was administered. The baby went home without complications.

Pregnancy #4

The patient became pregnant again at age 28. Serial anti-D titers were as follows:

Week of gestation	New Specimen	Last Specimen
10	16	
10½	32	
15	16	32
20	16	8
23	16	8
28	16	16
32	64	16

Serial amniocentesis was then started with the following results:



At 38 weeks gestation a 2520 gm boy was delivered by repeat cesarean section. Cord blood RBCs were group O positive with a 3+ DAT. Ultraviolet therapy ("bili lights") was started immediately. 2 aliquots of RBCs were administered during the hospitalization. His course is summarized in the following table:

Day of life	Time	Bili, T/D	Hgb/Hct	Retic
1	15:19	5.6/0.6	10.1/30.3	5.4
		Simple transfusion		
	21:39	7.6/1.0		
2	8:05	9.1/1.0	17.7/52.1	7.0
	20:50	10.1/1.4		
3	7:44	12.0/1.5	17.9/52.1	
4	7:24	14.3/1.2		
5	7:14	19.0/2.3		
	18:29	17.9/2.7		
6	9:16	14.2/2.0		
7	7:14	8.0/1.6		
	15:43		7.1/20.9	0.7
		Simple transfusion		
8	9:53	8.2/1.1		
		Discharged		
37			7.2/30	0.4
42			6.0/	1.2
52			8.3/23.4	9.0
58			5.3/14.8	20
	Admitted for anemia and chickenpox			
	17:00	4.1/0.2	3.9/11.3	11.5
59		Simple transfusion		
		3.9/1.3	11.9/35.1	

Pregnancy #5

Fourteen months after the previous delivery, JP became pregnant for the fifth time at age 30. Anti-D was present at a titer of 256 at week 8, and alternated between 256 and 512 for the remainder of the pregnancy. Percutaneous umbilical blood sampling (PUBS) was performed at week 22½.

Week	Pretransfusion hematocrit	Postransfusion hematocrit	Fetal anti-D titer
22½	28	48	32
24½	35	51	32
30	28	46	64
35 (Delivery)	32		64

A cesarean section delivery at 35 weeks gestation yielded a 2240 gm girl. Cord RBCs were group A positive with a 3+ DAT. A Kleihauer-Betke test on the infant's first venous blood sample revealed that approximately 50% of the circulating RBCs were of fetal origin, and 50% had adult hemoglobin. Other laboratory values are given in the table below. Phototherapy was started at birth.

Day of life	Time	Bili, T/D	Hgb/Hct	Retic
1	11:00	5.0/0.5	11.2/32.5	8.1%
	13:00	7.9/0.7		
	20:00	10.4/1.0		
2	01:32	11.4/1.1	13.4/39.0	
	06:45	11.4/1.0		
	17:05	13.8/1/1		
	23:52	15.7/1.3		
3	07:24	15.3/1.8		
	10:45	16.8/0.2		9.8
	16:01	18.0:1.5	10.5/29.6	
	20:48	16.8/1.4		
4	02:38	16.5/1.5		
	08:59	16.4/1.5		
	14:44	16.9/1.6		
	23:18	18.6/1.9		
5	09:28	20.9/2.0		
	11:48	21.4/2.9	8.3/23.7	5.6
	Double volume exchange transfusion			
	16:19	11.8/1.2	13.5/39.4	
	19:32	14.4/1.3		
6	01:19	13.5/8.4		
	07:55	12.0/1.6		
	20:19	11.7/1.2		
7	11:24	8.5/1.1		
32			8.1/23.3	

The baby did well with normal growth and development.

Pregnancy #6

JP became pregnant again at age 32 and was found to have twins. Vaginal bleeding began in her 9th week and continued with varying severity to the end of the pregnancy. At 19 weeks a combined amniocentesis/PUBS yielded black amniotic fluid characteristic of abruptio placenta. The PUBS samples showed one twin to be Rh positive and one to be negative. 24 hours after the procedure JP's membranes ruptured, and the Rh positive twin developed oligohydramnios which did not reaccumulate. At 22 weeks JP developed contractions and bleeding. Ultrasound demonstrated a 500 cc hematoma in the uterus, and delivery was induced for the mother's safety. Both twins were previable. The blood sample submitted for pretransfusion testing at the time of this delivery contained a new anti-Jk^b. Her husband was demonstrated to be Jk(a+b+).

Pregnancy #7

After the loss of her twins JP elected to have a tubal ligation. However, she subsequently had the ligation reversed and became pregnant again at age 34. Anti-D and anti-Jk^b were again demonstrated, now at titers of 256 and 8 respectively. At 22 weeks maternal blood (group A) was drawn for potential IUT and was washed, leukocyte filtered, and irradiated. The fetus proved to be anemic, and transfusion was started. However, for technical reasons the complete transfusion could not be delivered. Testing of the fetal RBCs demonstrated him to be group O, Rh positive and Jk^b positive, with a strongly positive DAT. The following immunohematologic and IUT data were obtained:

Week of gestation	Maternal titer		Fetal hct		Fetal K-B	Fetal Retic	Fetal DAT	Fetal titer	
	anti-D	anti-Jk^b	Pre-	Post-				anti-D	anti-Jk^b
21	256	8							
22			20.7	31.6		10.5%	3+	32	0
24	2560	32	23.0	46.6	30% A*	8.0%	3+	128	2
26	5120	64	25.2	40.8		2.2%	1+	512	8
30	5120	64	18.9	40.9	80% A	1.8%	vw+	512	16
33	5021	128	21.3	Deliv	80-90% A	1.0%	0	512	16

* (A)dult RBCs

All blood for IUT was drawn from the mother. It was predicted that the fetal hematocrit would again be in the range at which transfusion was needed at 33 weeks. Maternal blood was obtained for possible transfusion. Amniocentesis yielded fluid with an L/S ratio of 3:1 (no PG or PE present, lamellar body number density = 14,000/μL, consistent with an intermediate risk of RDS). Fetal heart monitoring yielded a sinusoidal tracing. A cesarean section was performed.

The 2005 gm male infant had Apgar scores of 7 and 9, but developed mild respiratory distress, and a simple transfusion with maternal blood was performed. He was intubated 5 hours after birth and was ventilated for approximately 36 hours. No anti-A was detected in the cord serum. The course of the infant's laboratory values is shown in the following table:

Day of life	Time	Bili, T/D	Hgb/Hct	Platelets
1	17:21		7.2/21.3	
	Simple transfusion, maternal RBCs			
2	10:19	11.5/	11.8/34.7	170,000
	18:32	12.5/1.5		
3	05:37	16.0/2.7	10.8/30.9	153,000
	10:33	17.2/3.0		
	12:57	15.9/2.0		
	Double volume exchange transfusion			
	13:57	12.3/1.5	13.5/39.2	43,000
	20:49	13.4/2.5		
4	05:06	12.4/2.3		
	13:48	10.9/2.2		
5	00:51	9.6/2.1		
	12:50	7.2/1.7	15.9/46.8	66,000
6	06:42	5.2/1.5		
7	07:08	5.2/1.6		

Before discharge from the hospital this infant failed a screening test for auditory brainstem evoked responses (ABER), and later proved to have a complex central hearing loss.

Questions, Pregnancies 1 & 2:

1. What immunohematologic tests are routinely performed at the first prenatal visit? What are their rationales?

2. What is RhIG? What is the goal of RhIG therapy? Why is RhIG delivered at 28 to 30 weeks gestation?

3. Why was RhIG not given after the second delivery? What tests are performed to determine RhIG candidacy at 28 to 30 weeks and after delivery?

4. Are there any other indications for RhIG?

Questions, Pregnancy 3:

1. Why did the patient have anti-D detected at delivery? Could it have been passively administered?

2. Why was postnatal RhIG given?

3. What are the known causes of failure of RhIG prophylaxis?

Questions, Pregnancy 4:

1. How are antibody titers used in monitoring alloimmunized pregnancies? Why is repeat testing of previous samples performed in parallel?

2. How does amniocentesis predict the risk of significant HDN in utero? How are the results interpreted?

3. What toxicity results from elevated bilirubin levels in the neonate? What levels of bilirubin are considered critical?

4. How does ultraviolet phototherapy ameliorate bilirubin toxicity?

5. Why did the infant need a transfusion at age 2 months?

Questions, Pregnancy 5

1. How is PUBS performed and interpreted?

2. How is blood selected and prepared for IUT?

3. How does exchange transfusion treat HDN? How is blood selected for exchange transfusion?

4. What are the indications for exchange transfusion?

Questions, Pregnancy 6

1. What are the risks of PUBS and amniocentesis?

Questions, Pregnancy 7

1. Discuss the use of maternal blood for IUT (including issue of the ABO type).

2. How does one determine fetal lung maturity?

3. What toxicity of bilirubin was present in this case?