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Alloimmunization References:

Moise K, Argoti P. Management and prevention of red cell alloimmunization in pregnancy. A systematic review. Obstet Gynecol 2012; 120: 1132-39. *Quantitative PCR can be used to more accurately determine the paternal RHD zyogosity. For unknown or a heterozygous paternal genotype, cell-free fetal DNA in maternal plasma can be used to diagnose fetal RHD type. This is only available for RHD at this time. MCA Doppler is the standard for detection of fetal anemia and can be used to determine the timing of the first (MCV PSV cut off 1.5 MoM) and second (using MCA PSV of 1.35 MoM) for the second transfusion. MCA not useful after the second transfusion.*

Moise K. Management of Rhesus Alloimmunization in Pregnancy. Obstet Gynecol 2008;112: 164-176. *In pregnancies with fetus at risk for HDN(homozygous paternal genotype/phenotype, antigen positive fetus by free fetal DNA or amniocentesis with antibody titer > 1:32 or 1:8 with Kell and no prior affected pregnancy), recommend start MCA Doppler PSV q 1-2 weeks at 24 weeks EGA. If antibody titers remain < critical titers, deliver at term. If there is a prior affected pregnancy, antibody titers are not used to determine fetal risk and recommend start MCV Doppler PSV q 1-2 weeks at 18 weeks EGA. In presence of mormal Dopplers through pregnancy, recommend weekly fetal testing with NST or BPP at 32 weeks and delivery at 38 weeks EGA. Elevated MCA PSV prior to 35 weeks EGA is an indication for fetal PUBS, after 35 weeks determine delivery planning based on FLM and ON450 at amniocentesis. Following intrauterine transfusion, recommend last transfusion at 35 weeks with delivery 2 weeks later.*

Opekes D, et al. Doppler ultrasonography versus amniocentesis to predict fetal anemia. N Engl J Med 2006; 355: 156-64. *Doppler measurement of the peak systolic velocity in the middle cerebellar artery can replace invasive testing in the management of Rh-alloimmunized pregnancies*.

Test	Sensitivity %	Specificity %	Accuracy %
MCV PSV > 1.5 MoM	88 (78.4-93.5)	82 (73.3-88.9)	85 (78.6-89.5)
AF ΔOD450 (Liley)	76 (64.8-84.0)	77 (67.3-84.0)	76 (69.3-82.2)

Mari G. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. N Engl J Med 2000; 342:9-14 Obstet. 1998; 63:195-202. *MCA PSV > 1.5 MoM for severe anemia (defined and Hgb < 0.55 x mean) demonstrated sensitivity of 100%, false positive rate of 12%, PPV = 65%, NPV = 100%.*

Prelove SJ, et al. Noninvasive methods of detecting fetal anemia: a systematic review and meta-analysis. BJOG 2009; 116:1558-1567. *Syst ematic review of 27 studies. Using the 1.5MoM cutoff for MCA PSV, the test parameters for fetal anemia, defined as hgb < 0.55MoM, for MCA PSV are: LR+ 4.3 (2.5-7.41); LR- 0.3 (0.13-0.69); sensitivity 75.5% (65.8-83.6) and specificity 90.8 (88.2-93.0).*

Trevett TN, et al. Antenatal maternal administration of phenobarbital for the prevention of exchange transfusion in neonates with hemolytic disease of the fetus and newborn. AJOG 2005;192, 478-82. *Following serial IUT, maternal phenobarbital 30 mg tid started at 35 weeks for 10 days was associated with a 67% reduction in the need for exchange transfusion (adjust RR: 0.23 95% CI 0.06-0.76).*

Scheier M, et al. Prediction of severe fetal anemia in red blood cell alloimmunization after previous intrauterine transfusion. AJOG 2006; 195, 1550-6. Using the definition of anemia as Hgb deficit of 6g/dl from gestational age mean, and MCV PSV > 1.5 MoM, to detect 95% of the cases of severe anemia, the false positive rate of severe anemia is 14%,

37%, and 90% prior to the first, second, and third transfusions respectively. MCA PSV is less useful after one transfusion and not useful after 2 prior transfusions.

Management of alloimmunization during pregnancy. ACOG practice bulletin No. 75. American College of Obstetricians and Gynecologists. Obstet Gynecol 2006; 108:457-64.

Table 1. Atypical Antibodies and Their Relationship to Fetal Hemolytic Disease

Blood Group System	Antigens Related to Hemolytic Disease	Hemolytic Disease Severity	Proposed Management
Lewis	a		
I	a		
Kell	K	Mild to severe[†]	Fetal assessment
	k	Mild	Routine obstetric care
	Ku	Mild	Routine obstetric care
	Kp^a	Mild	Routine obstetric care
	Kp^b	Mild	Routine obstetric care
	Js^a	Mild	Routine obstetric care
	Js^b	Mild	Routine obstetric care
Rh (non-D)	E	Mild to severe[†]	Fetal assessment
	C	Mild to severe[†]	Fetal assessment
	c	Mild to severe[†]	Fetal assessment
Duffy	Fy^a	Mild to severe[†]	Fetal assessment
	Fy^b	‡	Routine obstetric care
	By^a	Mild	Routine obstetric care
Kidd	Jk^a	Mild to severe	Fetal assessment
	Jk^b	Mild	Routine obstetric care
	Jk^3	Mild	Routine obstetric care
MNSs	M	Mild to severe	Fetal assessment
	N	Mild	Routine obstetric care
	S	Mild to severe	Fetal assessment
	s	Mild to severe	Fetal assessment
	U	Mild to severe	Fetal assessment
	M^g	Moderate	Fetal assessment
MNSs	Mi^a	Moderate	Fetal assessment
	Vw	Mild	Routine obstetric care
	Mur	Mild	Routine obstetric care
	Hil	Mild	Routine obstetric care
	Hut	Mild	Routine obstetric care
Lutheran	Lu^a	Mild	Routine obstetric care
	Lu^b	Mild	Routine obstetric care
Diego	Di^a	Mild to severe	Fetal assessment
	Di^b	Mild to severe	Fetal assessment
Xg	Xg^a	Mild	Routine obstetric care
P	$PP_{1}P^k$ (TP)	Mild to severe	Fetal assessment
Public antigens	Yt^a	Moderate to severe	Fetal assessment
	Yt^b	Mild	Routine obstetric care
	Lan	Mild	Routine obstetric care
	En^a	Moderate	Fetal assessment
	Ge	Mild	Routine obstetric care
	Jr^a	Mild	Routine obstetric care
	Co^a	Severe	Fetal assessment
	Co^{a-b-}	Mild	Routine obstetric care
Private antigens	Batty	Mild	Routine obstetric care
	Becker	Mild	Routine obstetric care
	Bowen	Mild	Routine obstetric care

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Notification to Users

These algorithms are designed to assist the primary care provider in the clinical management of a variety of problems that occur during pregnancy. They should not be interpreted as a standard of care, but instead represent guidelines for management. Variation in practices should take into account such factors as characteristics of the individual patient, health resources, and regional experience with diagnostic and therapeutic modalities.