



Management of Alloimmunized Pregnancy

May 2024

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Background

Maternal red blood cell antibodies may cross the placenta and cause hemolytic anemia and significant perinatal morbidity. The risk of this occurrence depends on several factors including the type of antibody, the amount of the antibody and if the fetus has the corresponding antigen.

Screening and Management

1. Is the maternal type and screen antibody positive? If yes, possible risk
2. Is the antibody capable of causing fetal anemia? (see table on page 3)
3. Is the antibody present in sufficient quantity to cause anemia?
 - a. Critical titer can vary by lab, use the same lab for serial titer
 - b. Titer every 4 weeks until critical titer reached
 - c. Typically, between 8 and 32, most commonly used 16
 - d. Exceptions
 - Prior affected pregnancy
 - Kell antibody
 - No need to follow serial antibody titers
4. Does the fetus have the antigen of interest?
 - a. Screen the father of the pregnancy for antigen phenotype (can also be offered for preconception counseling or prior to serial titers)
 - Homozygous = fetus inherited the antigen of interest
 - Heterozygous = 50% risk
 - Negative = not at risk
 - Limitations if paternity is incorrectly attributed (10%)
 - b. Cell free DNA screening available for RhD, C, c, E, Duffy (Fya), Kell
 - c. Amniocentesis is less optimal for determining fetal antigen status as it can worsen maternal antibody titers. If cell free testing is negative for the antigen of interest, can consider amniocentesis for confirmation.
5. Screening for fetal anemia with MCA Doppler
 - a. MCA Doppler every 1-2 weeks for the at-risk fetus
 - b. Can begin as early as 15 weeks for the high-risk patient (history of second trimester demise due to Hemolytic Disease of the Fetus and Newborn (HDFN) or markedly elevated initial titers (≥ 64 for Kell or ≥ 1024 for D). Consideration of IVIG +/- plasmapheresis typically by 12-13 weeks.
 - c. Start at 18 weeks for Kell positive, prior affected pregnancy

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- d. MCA Doppler with MCA greater than 1.5 MoM should be repeated within 24 hours and if elevated, needs scheduled for Percutaneous Umbilical Blood Sampling/ Intrauterine Transfusion (PUBS/IUT).
- e. Middle Cerebral Artery-Peak Systolic Velocity (MCA-PSV) may be lowered by betamethasone (BMZ) administration.
- f. MCA-PSV screening has a 12% false positive rate for at risk fetus
- g. If elevated MCA < 32 weeks, PUBS/IUT, 32-35 weeks individualize, > 35 weeks deliver

6. Antenatal fetal testing: add weekly biophysical profile (BPP) to MCA Doppler at 32 weeks

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TABLE 3
Non-Rh (D) antibodies and associated hemolytic disease newborn
and fetus

Antigen system	Specific antigen	Antigen system	Specific antigen	Antigen system	Specific antigen
Frequently associated with severe disease					
Kell	-K (K1)				
Infrequently associated with severe disease					
Colton	-Coa	MNS	-Mta	Rhesus	-HOFM
	-Co3		-MUT		-LOCR
Diego	-ELO		-Mur		-Riv
	-Dia		-Mv		-Rh29
	-Dib		-s		-Rh32
	-Wra		-sD		-Rh42
	-Wrb		-S		-Rh46
Duffy	-Fya		-U		-STEM
Kell	-Jsa		-Vw		-Tar
	-Jsb	Rhesus	-Bea	Other antigens	-HJK
	-k (K2)		-C		-JPV
	-Kpa		-Ce		-JONES
	-Kpb		-Cw		-Kg
	-K11		-Cx		-MAM
	-K22		-ce		-REIT
	-Ku		-Dw		-Rd
	-Ula		-E		
Kidd	-Jka		-Ew		
MNS	-Ena		-Evans		
	-Far		-e		
	-Hil		-G		
	-Hut		-Goa7		
	-M		-Hr		
	-Mia		-Hro		
	-Mit		-JAL		
Associated with mild disease					
Dombrock	-Doa	Gerbich	-Ge2	Scianna	-Sc2
	-Gya		-Ge3	Other	-Vel
	-Hy		-Ge4		-Lan
	-Joa		-Lsa		-Ata
Duffy	-Fyb	Kidd	-Jkb		-Jra
	-Fy3		-Jk3		

Reproduced, with permission, from Moise.²³

SMFM. The fetus at risk for anemia. *Am J Obstet Gynecol* 2015.

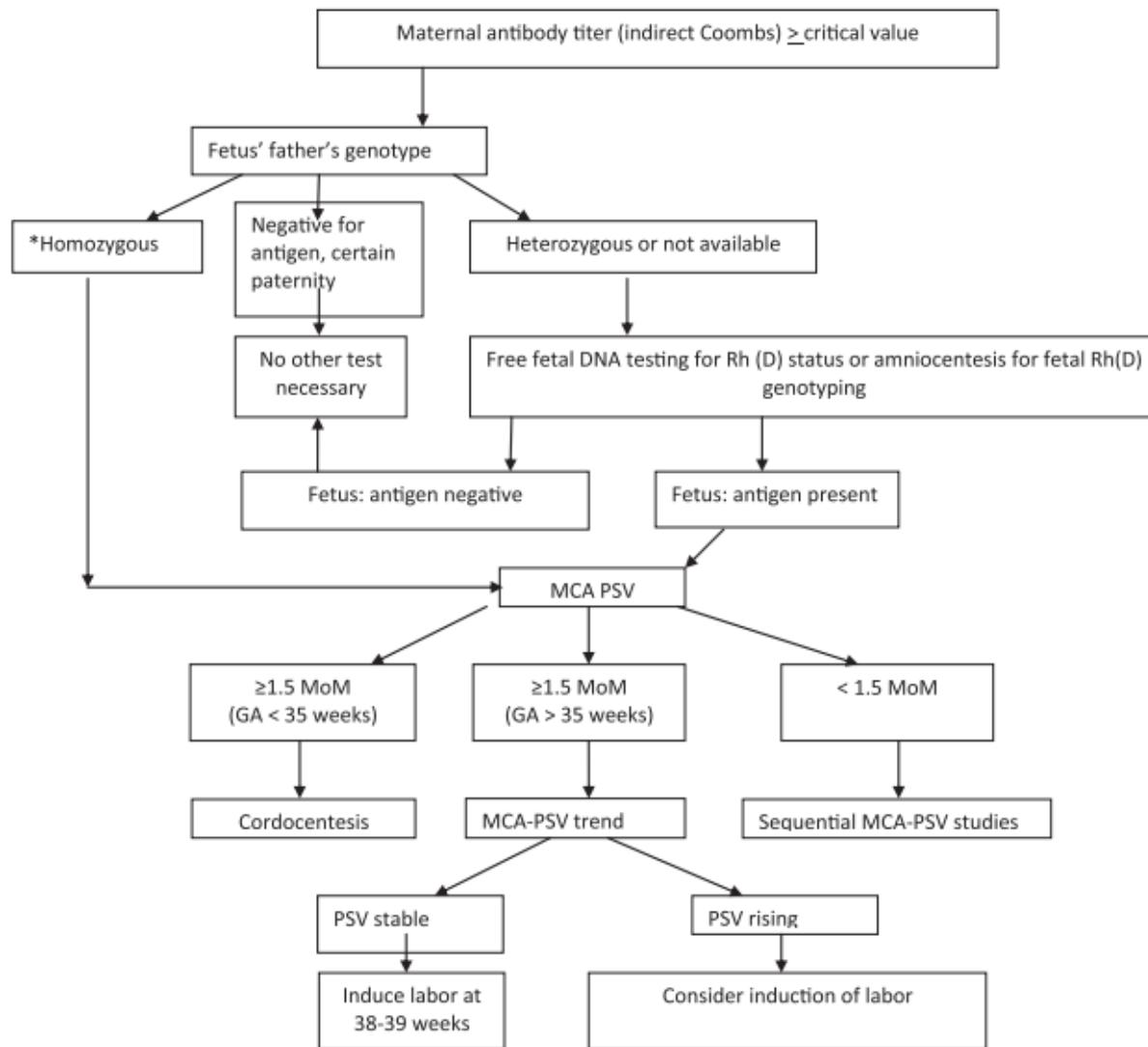
(SMFM, 2015)

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FIGURE 2

Algorithm for clinical management of the red cell alloimmunized pregnancy



GA, gestational age; MCA, middle cerebral artery; MoM, multiples of the median; PSV, peak systolic velocity.

Modified from Moise and Argot.⁷⁷

SMFM. *The fetus at risk for anemia*. Am J Obstet Gynecol 2015.

(SMFM, 2015)

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