

Guidelines for the Management of Isoimmunization in Pregnancy

Background

- Hemolytic Disease of the Fetus and Newborn (HDFN) occurs when fetal red blood cells are destroyed. Most common cause is rhesus (Rh) incompatibility → Rh-negative mother's plasma cells are stimulated by the RhD antigen on fetal erythrocytes and rapidly proliferate immunoglobulin G antibodies (IgG Ab) → IgG Ab cross the placenta, attach to, and destroy RhD-positive 'foreign' fetal erythrocytes → Fetal Anemia.
- Isoimmunization occurs when the maternal immune response produces anti-D antibodies to fetal red blood cells in the maternal circulation (antibodies are recognized 5-15 weeks after sensitizing fetomaternal hemorrhage event such as birth, invasive procedure, termination, miscarriage, or placental abruption).
- Kell isoimmunization is less predictable and results in more severe anemia than other erythrocyte antigens and managed differently than Rh-isoimmunization
- anti-c, anti-D, anti-E, and anti-K(Kell) antibodies are responsible for the majority of cases of HDFN
- Isoimmunization immediately after current pregnancy is 1% and can occur after exposure to <0.1mL of Rh-positive blood. The incidence can be decreased to 0.2% after anti-D administration at 28 weeks or in 12 week intervals.
- Brand names of Rh immune globulin: RhoGAM and MICRhoGam (Johnson and Johnson), Rhophylac (CSL), BayRHO-D, Gamulin Rh, HypRho-D Mini-Dose, Mini-Gamulin Rh, WinRho SDF (Cangene), Partobulin SDF (Baxter) and Rhesonativ (Octapharma). RhesuGam (NBI)

RhD Clinical Management

- Depends on obstetric history and whether the patient has had a previously affected pregnancy.

Prior Affected Pregnancy is defined as:

- Prior fetal loss from HDFN
- Prior pregnancy requiring percutaneous umbilical blood sampling (PUBS)/intrauterine transfusion (IUT)
- Prior RhD+ infant requiring an exchange transfusion
- Prior RhD+ infant born with anemia without other cause
- Prior RhD+ infant treated for hyperbilirubinemia in the setting of positive maternal antibody titers

Special Circumstances:

- ❖ Fetomaternal hemorrhage:
 - Kleihauer-Betke stain to determine quantitative assessment.
 - $\text{Fetal blood cells (\%)} * 50 = \text{volume of fetomaternal hemorrhage}$
 - $\text{Fetomaternal hemorrhage volume}/30 = \text{number of vials Rh immune globulin to administer}$
- ❖ KELL SENSITIZATION:
 - Causes severe fetal anemia due to 2 mechanisms: fetal splenic sequestration of sensitized red cells and suppression of the fetal erythropoiesis.
 - The critical titer is NOT applicable for Kell and there is no need to follow antibody titers as values are not predictive of fetal anemia.
 - MCA PSV >1.5 MoM is reliable in predicting fetal anemia from Anti-Kell antibodies (89% sensitivity and specificity)
 - *Follow Algorithm of "RhD 2nd affected Pregnancy" for management of KELL sensitization.*
- ❖ Minor red blood cell antibodies (See Table 1)

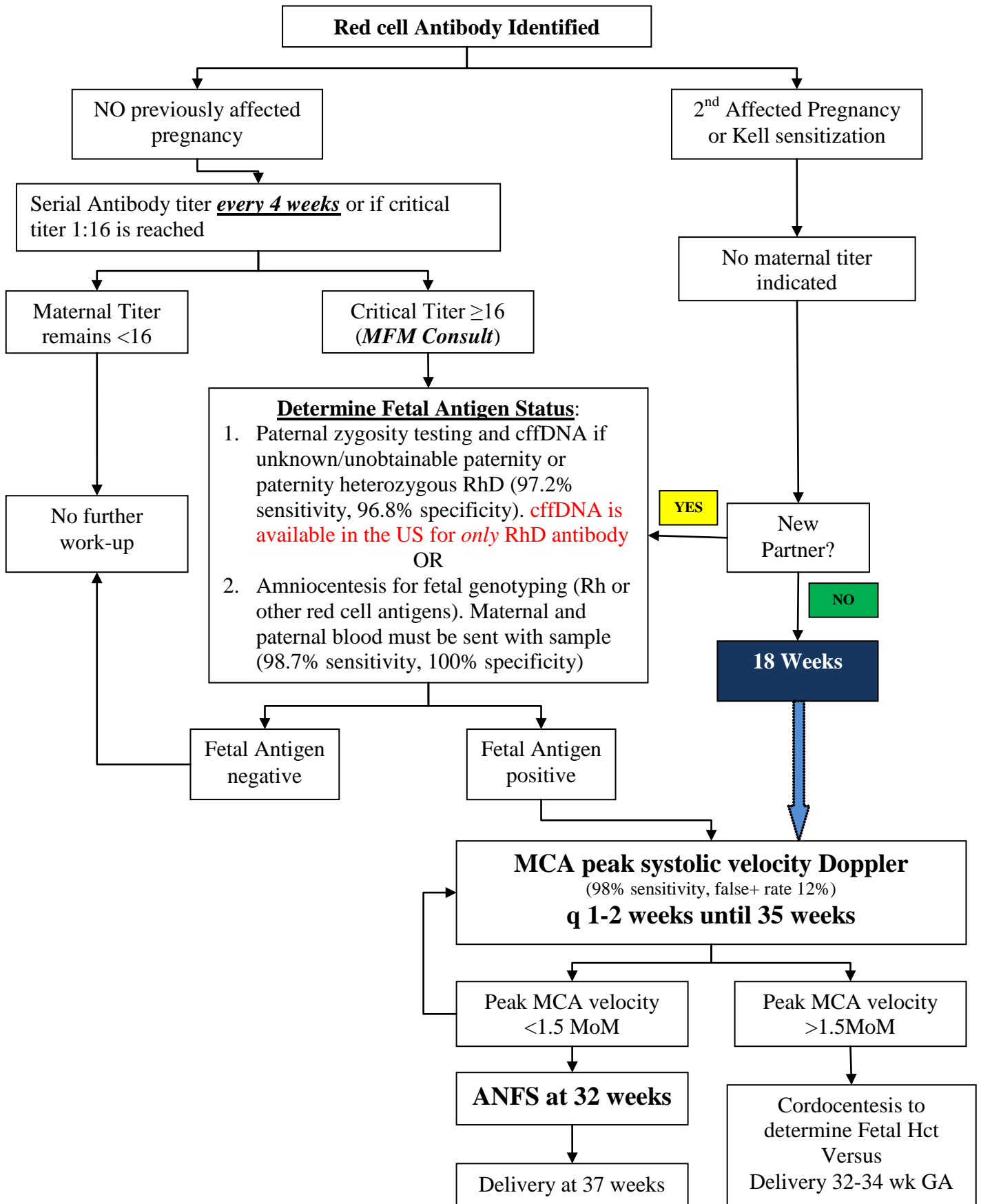


Figure 1 – RhD isoimmunization management algorithm.

<u>Antigen System</u>	<u>Specific Antigen</u>	<u>Management</u>
FREQUENTLY ASSOCIATED WITH SEVERE DISEASE		
Kell	-K (K1)	MCA Doppler studies (18wks)
Rhesus	-D -c	See Figure 1 Algorithm
INFREQUENTLY ASSOCIATED WITH SEVERE DISEASE		
Colton	-Co ^a -Co3	Check maternal antibody titers every 4 weeks.
Diego	-ELO -Di ^a -Di ^b -Wr ^a -Wr ^b	
Duffy	-Fy^a	
Kell	-Js ^a -Js ^b -k (K2) -Kp ^a -Kp ^b -K11 -K22 -Ku -Ul ^a	
Kidd	-Jk ^a	
MNS	-En ^a -Far -Hil -Hut -M -Mi ^a -Mit -Mt ^a -MUT -Mur -M ^v -s -s ^D -S -U -Vw	Rarely associated with HDFN if occurs alone but may have <i>additive effect</i> to anti-D. If found <u>alone</u> , maternal antibody titers every 4 weeks.
Rhesus	-Be ^a -C -Ce -C ^w -C ^x -ce -D ^w -E -E ^w -Evans -e -G -Go ^a -Hr -Hr _o -JAL -HOFM -LOCR -Riv -Rh29 -Rh32 -Rh42 -Rh46 -STEM -Tar	
Other antigens	-HJK -JFV -JONES -Kg -MAM -REIT -Rd	Check Maternal Antibody titer every 4 weeks
ASSOCIATED WITH MILD DISEASE		
Dombrock	-Do ^a -Gy ^a -Hy -Jo ^a	Check titers every 4 weeks
Duffy	-Fy ^b -Fy ³	
Gerbich	-Ge ² -Ge ³ -Ge ⁴ -Ls ^a	
Kidd	-Jk ^b -Jk ³	
Scianna	-Sc2	
Other	-Vel -Lan -At ^a -Jr ^a	

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