Akron Children's Hospital Clinical Pathways Disclaimer

Important Notice

Disclaimer

Akron Children's Hospital's clinical pathways are available for informational and guidance purposes only. Use of this site is subject to our Terms of Use, which are incorporated into this Disclaimer.

No Medical Advice

Clinical pathways contained on this website is for guidance purposes only and are not intended to be substitutes for professional medical advice, diagnosis, or treatment for any particular patient. Providers may need to adapt the pathways for a variety of reasons, including but not limited to, their professional judgment, unique patient clinical circumstances, and/or available resources. Patients should never rely on clinical pathways as a substitution for advice for your physician or other qualified health care provider, nor should you disregard professional medical advice or delay in seeking it because of something you have read on this website. This website does not recommend or endorse any specific tests, physicians, products, procedures, opinions, or other information that may be mentioned on the website. Reliance on any information provided by this website is solely at your own risk.

Emergency Situations

If you think you may have a medical emergency, call 911 immediately or proceed to the nearest emergency room.

Accuracy of Information

The clinical pathways are based on publicly available medical evidence and/or a consensus of medical practitioners at Akron Children's Hospital at the time of publication on our website. We do not make any guarantees about the information provided. The information and materials on this website are provided "as is" without any representations or warranties, express or implied.

No Liability

The materials on the Akron Children's site are provided, "AS IS" WITHOUT WARRANTY OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT.

IN NO EVENT SHALL AKRON CHILDREN'S HOSPITAL BE LIABLE FOR ANY DAMAGES WHATSOEVER, INCLUDING SPECIAL, INDIRECT, CONSEQUENTIAL OR INCIDENTAL DAMAGES OR DAMAGES FOR LOSS OF PROFITS, REVENUE, USE, OR DATA WHETHER BROUGHT IN CONTRACT OR TORT, ARISING OUT OF OR CONNECTED WITH ANY AKRON CHILDREN'S HOSPITAL SITE OR THE USE, RELIANCE UPON OR PERFORMANCE OF ANY MATERIAL CONTAINED IN OR ACCESSED FROM ANY AKRON CHILDREN'S HOSPITAL SITE.

Changes to the Disclaimer

We reserve the right to amend this disclaimer at any time. Any changes will be posted on this page, and your use of the website after such changes have been made will constitute your acceptance of the revised disclaimer.

Management of Alloimmunized Pregnancy

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 attached table)
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 Q 4 weeks until critical titer reached.
    c. Typically between 8 and 32, most commonly used 16.
    d. Exceptions
        i. Prior affected pregnancy
        ii. Kell antibody
        iii. 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)
        i. Homozygous = fetus inherited the antigen of interest
        ii. Heterozygous = 50% risk
        iii. Negative = not at risk
        iv. 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 HDFN or markedly elevated initial titers ($\geq$ 64 for Kell or $\geq$ 1024 for D). Consideration of IVIG +/- plasmapheresis typically by 12-13 weeks.
    c. Start at 18 weeks for Kell positive, prior affected pregnancy
    d. MCA Doppler with MCA > 1.5 MoM should be repeated within 24 hours and if elevated, needs scheduled for PUBS/IUT.
    e. MCA PSV may be lowered by 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 BPP to MCA Doppler at 32 weeks

TABLE 3

Non–Rh (D) antibodies and associated hemolytic disease newborn and fetus

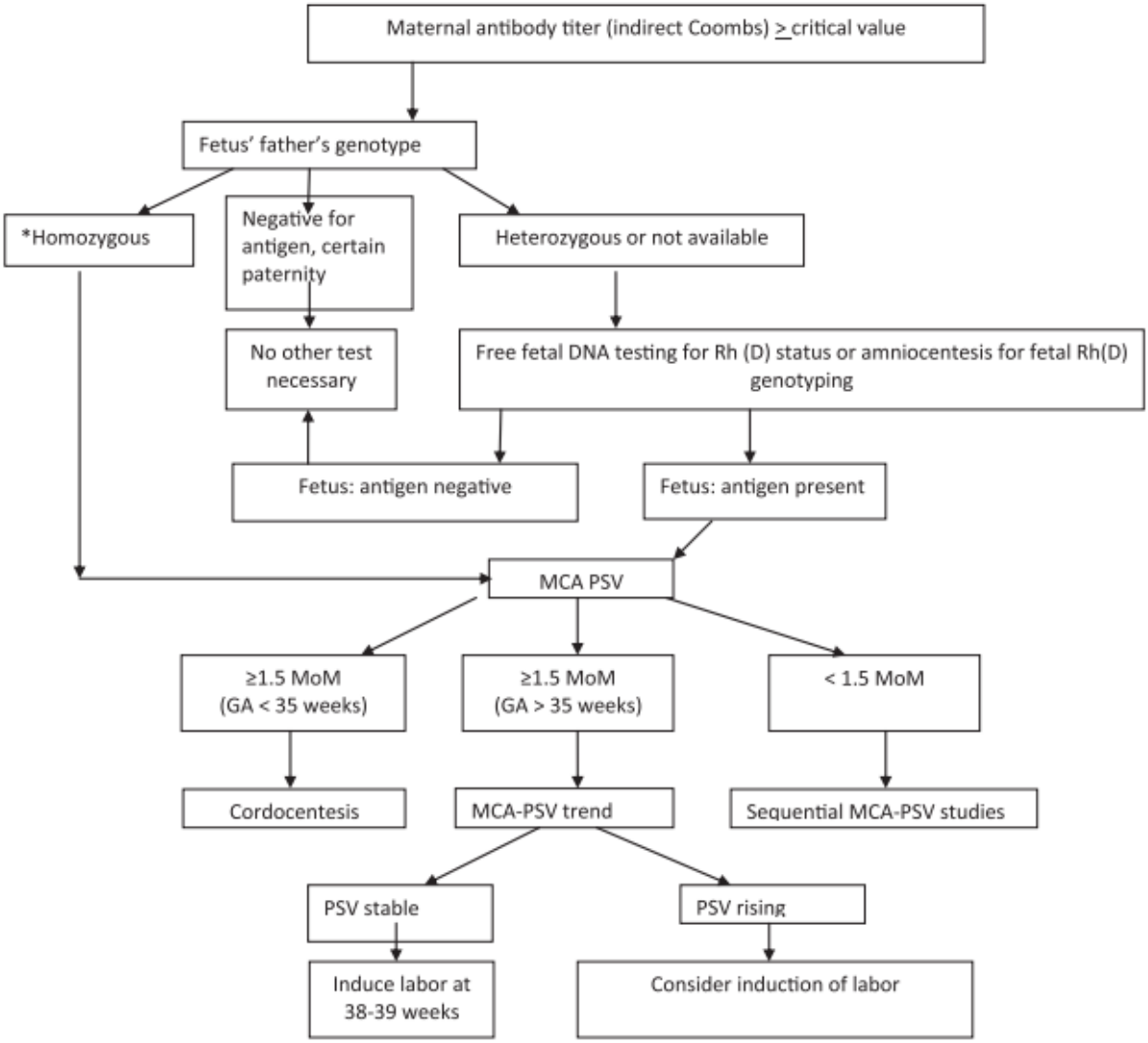
Antigen system	Specific antigen	Antigen system	Specific antigen	Antigen system	Specific antigen
Frequently associated with severe disease					
Kell	-K (K1)				
Rhesus-c					
Infrequently associated with severe disease					
Colton	-Coa	MNS	-Mta	Rhesus	-HOFM
	-Co3		-MUT		-LOCR
Diego	-ELO		-Mur		-Riv
	-Dia		-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		-JFV
	-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.[69]

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

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 Argoti.[77]

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

References:

American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 192: Management of alloimmunization during pregnancy. Obstet Gynecol. 2018 March;131(3):e82-e90. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 181: Prevention of Rh D Alloimmunization. Obstet Gynecol. 2017 Aug;130(2):e57-e70.

Moise KJ and Queenan J. Hemolytic disease of the fetus and newborn. Creasy and Resnik Maternal-fetal Medicine: Principles and Practice, Eighth Edition. 2019; Philadelphia, PA. Saunders Elsevier.

Moise KJ Jr, Argoti PS. Management and prevention of red cell alloimmunization in pregnancy: a systematic review. Obstet Gynecol. 2012 Nov;120(5):1132-9.

Alford B, Landry BP, Hou S, Bower X, Bueno AM, Chen D, Husic B, Cantonwine DE, McElrath TF, Carozza JA, Wynn J, Hoskovec J, Gray KJ. Validation of a non-invasive prenatal test for fetal RhD, C, c, E, K and Fy^{a} antigens. Sci Rep. 2023 Aug 7;13(1):12786. doi: 10.1038/s41598-023-39283-3.

Bombar AT et al. Fetal RHD genotype detection from circulating cell-free DNA in maternal plasma in non-sensitized RhD negative women. Prenat Diagn. 2011; 31: 802-8.

Mari G et al. Noninvasive diagnosis by Doppler ultrasonography of fetal anemia due to maternal red-cell alloimmunization. Collaborative Group for Doppler Assessment of the Blood Velocity in Anemic Fetuses. N Engl J Med 2000; 342:9-14.

Mayer B, Hinkson L, Hillebrand W, Henrich W, Salama A. Efficacy of Antenatal Intravenous Immunoglobulin Treatment in Pregnancies at High Risk due to Alloimmunization to Red Blood Cells. Transfus Med Hemother. 2018 Nov;45(6):429-436. doi: 10.1159/000490154. Epub 2018 Oct 31.