ALLOIMMUNIZATION IN PREGNANCY DIAGNOSIS & MANAGEMENT

FLAME LECTURE: 108B

NEPOMUCENO / BURNS 3.2.20

OBJECTIVES

- Describe the pathophysiology and diagnosis of alloimmunization
- Discuss the use of immunoglobulin prophylaxis during pregnancy for the prevention of alloimmunization
- Discuss the management of a patient with Rh-D sensitization in pregnancy
- Prerequisites:
  - FLAME LECTURE 108A: Alloimunization Introduction

SCREENING & DIAGNOSIS

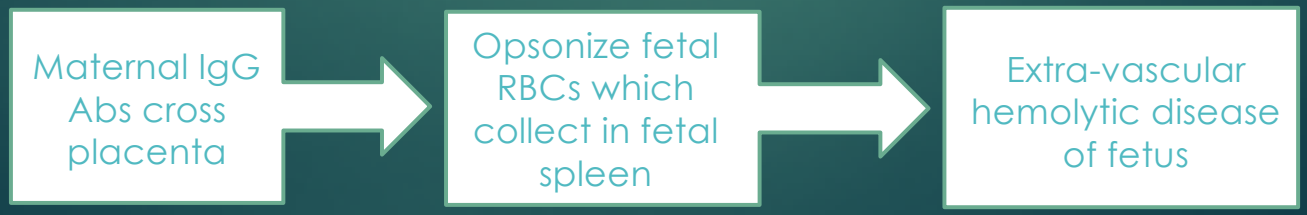
- All women receive a **blood type** and **antibody screen** during their first prenatal visit to assess Rh(D) status and antibody presence
- However, the reality is that we often do not have record of the FOB's blood type
  - *And there is always the risk of false paternity (~10%)*
- Thus, in absence of knowing FOB's blood type, **Rh- / Ab-** women are given Rhogam to prevent alloimmunization from occurring
- **Rh- / Ab+** women have already been alloimmunized

RHOGAM

- Rho(D) immune globulin can prevent a Rh- mother from creating antibodies to Rh+ antigens from the fetus
- It is not useful once a mom is already "Rh-sensitized" or has antibodies to the Rh antigen
- It is often given universally to Rh- / Ab- women around 28 weeks gestation
  - It can also be given earlier if there is any concern for maternal/fetal blood mixing (trauma, bleeding, procedures)
- Rhogam is again administered within 72 of delivery if the fetus is Rh+
- Rhogam is given at 28 wks because it's effective for ~12 weeks
  - Thus if delivery doesn't occur within 12 weeks of this first prophylactic doses, consider a second dose though this evidence is limited

PATHOPHYSIOLOGY REMINDER

- Once a Rh- mother is alloimmunized, the following scenarios are possible during pregnancy:
  - FOB is Rh- → child must be Rh- → no concern for fetal anemia because mother and fetus are both Rh-
  - FOB is Rh+ → child can be Rh- → no concern for fetal anemia
  - FOB is Rh+ → child can be Rh+ → risk of fetal anemia



ASSESSING FETAL SUSCEPTIBILITY

- A mother with a positive antibody screen should reflexively have Rh antibody titers assessed
  - Ab titers of 1:2, 1:4, 1:8 can usually be monitored with q4w titers
    - Note that in Rh- women who receive Rhogam, Ab screen may be transiently positive from the circulating Rhogam Abs but this does not indicate alloimmunization
  - Titers ≥1:16 (though specific thresholds vary by lab) warrant fetal health surveillance (next slide)
- Also consider assessment of paternal blood type
  - If father is heterozygous or unknown, then fetal blood type can also be assessed
    - Amniocentesis or CVS (CVS has higher hemorrhage risk)
    - Cell-free DNA testing

ASSESSING FETAL HEALTH

- Historical testing
  - Amniocentesis → amniotic fluid analysis (ΔOD450) which is a spectral analysis to measure fetal bilirubin
    - 450nm is the optical density at which bilirubin absorbs light so more bilirubin causes an increase in absorption at OD450
- Now, Doppler analysis of the fetal middle cerebral artery (MCA) is a non-invasive sonographic method of evaluating for fetal anemia
  - Increased peak systolic velocity in the fetal MCA reveals "brain-sparing" given fetal blood flow is compensatorily redistributed to this very important organ

MANAGEMENT
ALLOIMMUNIZED WITH TITERS ≥ 1:16

- Monitor fetal MCA Dopplers q1-2w starting at 16-18wks
  - If MCA PSV <1.5 MoMs, continue regular MCA Doppler scans
  - If MCA PSV >1.5 MoMs, there is significant concern for fetal anemia warranting fetal Hgb assessment via cordocentesis (aka percutaneous umbilical blood sample, PUBS)
    - If anemia confirmed, fetal transfusion is necessary; this can occur in the umbilical cord, in a fetal perihepatic vessel, or even into the fetal abdominal cavity (because it will be absorbed)
- If titers are >1:1028 or mom has previous baby with hydrops, can consider IVIG/plasmapheresis

MANAGEMENT
NON-ALLOIMMUNIZED MOTHER

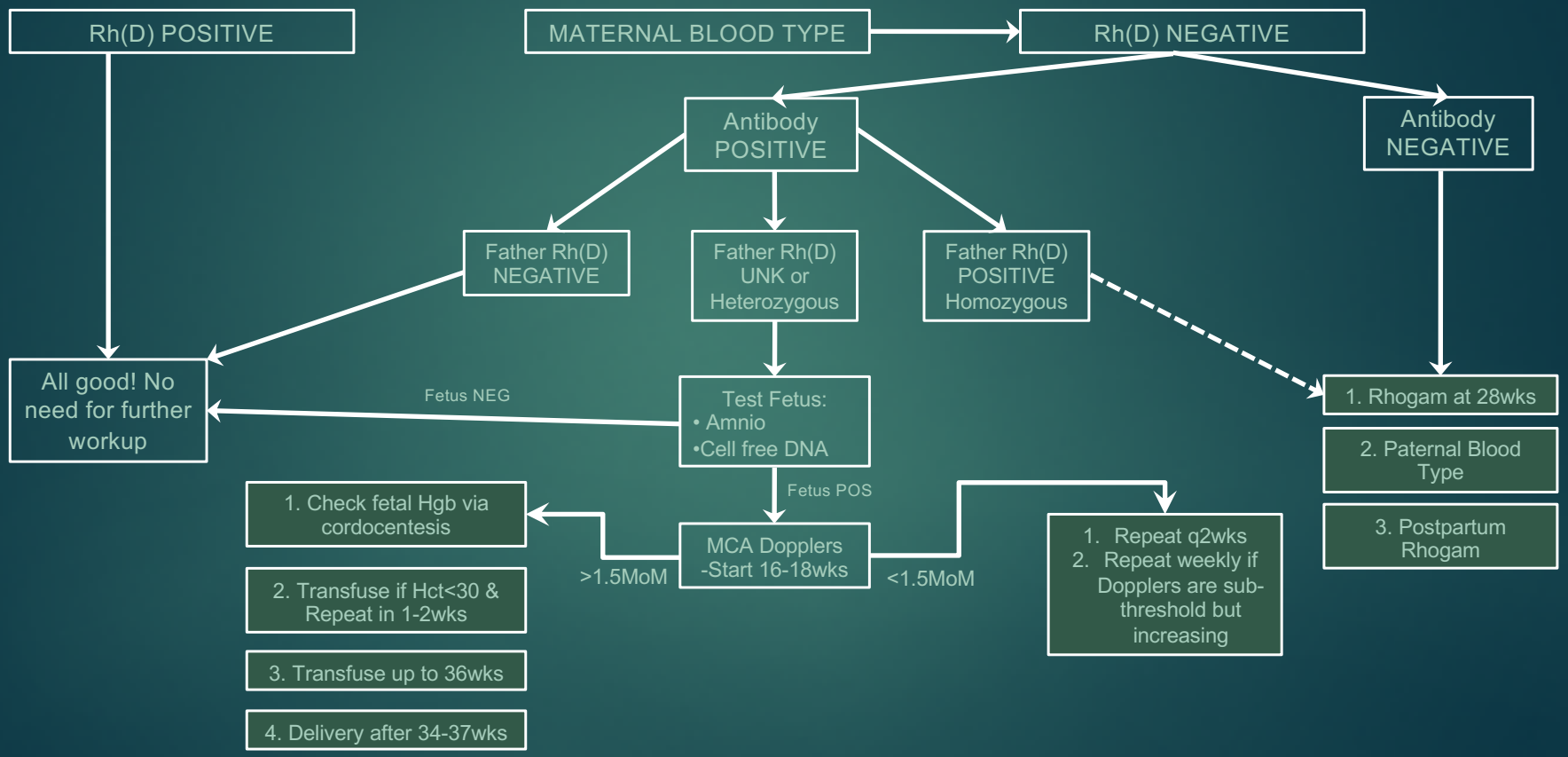
- Usual Rhogam dose is 300µg which covers 30mL of Rh(D)-positive blood
- Assessing need and dosing (if large maternal-fetal blood mixing is suspected) can be done using the Kleihauer-Betke Test and Rosette Test:

- **Rosette test is *qualitative***: determines if Maternal-Fetal hemorrhage occurred
  - Can detect a minimum of 10mL fetal blood in maternal circulation
  - If negative = 300µg dose of Rhogam is adequate
  - If positive = use KB test to quantify how much Rhogam needed

- **KB test is *quantitative*:** determines how much fetal blood has mixed
  - Reports % of circulating RBCs that are fetal origin
  - Maternal blood circulation is approximately 5000mL so to quantify hemorrhage:
  - Fetal whole blood (mL) = % Fetal Cells x 5000 mL of maternal blood

- Generally 1st trimester bleeding necessitates 50µg of Rhogam, 2nd/3rd tri bleeding needs 300µg (but perform KB test to confirm that this is the adequate dosing)
- College of American Pathologists Rhlg dose calculator takes into account variations in maternal blood volume

MANAGEMENT OVERVIEW



OTHER ANTIGENS

- Kell antigens are more rare but also concerning
  - Sensitization usually occurs through transfusion history
  - 90% of African Americans are Kell(-) thus particularly at risk in multiracial couples
  - Anemia is due to hemapoetic cell destruction rather than outright RBC destruction so there are less signs of hemolysis
    - Ab titers aren't reliable for risk prediction and can't determine severity, thus MCA dopplers most effective at determining fetal status
- Other rare antigens follow similar management strategies

SPECIAL CIRCUMSTANCES

- Molar pregnancies:
  - Partial: fetus will probably have Rh(D) antigens
  - Complete: there is no fetus, and thus no antigens, but may not know molar type until out of Rhogam window
  - If delivery occurs within 3 weeks of 28wk Rhogam, may not need to give a second dose
  - However KB test often performed to confirm no excessive amount of bleeding and need for higher dose

Summary of Recommendations

Rh-positive and negative status refers to the presence or absence of the D antigen found on red blood cells

All pregnant women should be screened for ABO and Rh blood groups at the first prenatal visit, as well as tested for the presence of alloantibodies.

300 micrograms IM RhIG can be administered at 28 weeks, post-partum, and with any episode of fetomaternal hemorrhage to prevent alloimmunization in RhD-negative women. Appropriate RhIG dosage can be estimated by calculating fetal blood volume in maternal circulation (Kb test)

The first step in management of an alloimmunized pregnant patient is to determine paternal Rh status.

Doppler measurement of peak systolic velocity in the fetal middle cerebral artery is an appropriate noninvasive method to monitor for fetal anemia.

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