Learn simply

Isoimmunization

Passion profession same

Routine screening for isoimmunization[1]

- **√ maternal blood type and antibody screen at first prenatal visit**

Blood type: / Antibody screen:	Rh(D)-positive Negative	Rh(D)-negative Negative	Rh(D)-negative Anti-Rh(D) positive
	Antepartum management • Routine prenatal care • √T&S in 3rd trimester (to exclude ABO isoimmunization[2]) • If fetal hydrops is noted on ultrasound, consider alternative diagnosis[3]	Antepartum management • √T&S in 3rd trimester (to exclude recent Rh(D)-isoimmunization) • √T&S of father of the baby[4] Prevention • **Anti-Rh(D) immunoglobulin** to prevent Rh(D)-isoimmunization after vaginal bleeding, empirically at 28 weeks, and after delivery, if indicated[5]	Rh(D)-isoimmunization[7] • **√T&S of father of the baby** [4] • *√serum anti-Rh(D) antibody titer* immediately and follow serial antibody titers q month • Serial ultrasound examinations for fetal growth and to exclude hydrops • No place for anti-Rh(D) immunoglobulin

Is hydrops present?

No

- Management depends on gestational age, severity, fetal wellbeing, and likely etiology
- Consider MFM, NICU consultation
- Antenatal steroids, if indicated
- Serial ultrasound examinations biweekly to evaluate fetal wellbeing, follow fetal growth, and **MCA Doppler velocimetry**[6]

Normal MCA Dopplers	Elevated MCA Dopplers
• Continue expectant management • **Serial MCA Doppler velocimetry measurements**	• **Consider delivery versus PUBS and IUT**[8] • **Serial MCA Doppler velocimetry measurements**

Yes

- Management depends on gestational age, severity, and likely etiology
- **Review management options with the couple** (including pregnancy termination if prior to viability)
- Consider MFM, NICU consultation
- **Antenatal steroids, if indicated**
- For moderate and severe hydrops, **consider immediate delivery regardless of gestational age vs PUBS and IUT**[8]
- Serial ultrasound examinations with MCA Doppler velocimetry

1. Isoimmunization occurs when fetal erythrocytes express a protein that is not present on maternal erythrocytes.
2. Since there is constant trafficking of fetal cells across the placenta into the maternal circulation, the maternal immune system can become sensitized and produce antibodies against these 'foreign' proteins.
3. Maternal IgG antibodies can cross the placenta and destroy fetal erythrocytes leading to fetal anemia and high-output cardiac failure, known as immune hydrops fetalis. Immune hydrops is associated with a fetal hematocrit <15% (normal, 50%).
4. The most antigenic protein on the surface of erythrocytes is D, also known as rhesus D or (Rh)D. Other antigens that can cause severe immune hydrops include Kell ("Kell kills"), Rh-E, Rh-c, and Duffy ("Duffy dies"). Antigens causing less severe hydrops include ABO, Rh-e, Rh-C, Fya, Ce, k, and s. Lewisa,b incompatibility can cause mild anemia but not hydrops ("Lewis lives") because they are primarily IgM antibodies, which do not cross the placenta.
5. Since the introduction of anti-(Rh)D immunoglobulin, 60% of immune hydrops is due to ABO incompatibility, which cannot be effectively prevented.

1. Hydrops fetalis (Latin for "edema of the fetus") is a radiologic diagnosis requiring the presence of an abnormal accumulation of fluid in more than one fetal extravascular compartment, including ascites, pericardial effusion, pleural effusion, and/or subcutaneous edema. Polyhydramnios is seen in 50–75% of cases.
2. Hydrops is a rare but very serious complication of pregnancy with a high perinatal mortality (>50%).

3. Of all cases of fetal hydrops, 90% are due to a non-immune cause and 10% have an immune etiology. Non-immune hydrops may be due to fetal cardiac abnormalities (20–35%), chromosomal anomalies such as Turner syndrome (15%), hematological aberrations such as α-thalassemia (10%), and other causes (infections such as CMV or parvovirus B19, twin-to-twin transfusion, vascular malformations, placental anomalies, congenital metabolic disorders); 50–60% have no clear explanation.
4. If the father of the baby is Rh(D)-negative, then the fetus must be Rh(D)-negative and Rh(D) sensitization will not occur.

5. However, because of the well-documented 10% likelihood of non-paternity in a clinic population, anti-(Rh)D immunoglobulin is often still recommended.
6. Fetal Rh(D) status can be confirmed by amniocentesis or, more recently, through the evaluation cell-free fetal DNA in the maternal circulation.

1. Exposure of Rh(D)-negative women to as little as 0.25 mL of Rh(D)-positive blood may induce an antibody response. Since the initial immune response is IgM (which does not cross the placenta), the index pregnancy is rarely affected.

2. However, immunization in subsequent pregnancies will trigger an IgG response that will cross the placenta and cause hemolysis. Risk factors for Rh(D) sensitization include mismatched blood transfusion (95% sensitization rate), pregnancy (16–18% sensitization rate following normal pregnancy without anti-Rh(D) IgG, 1.3% with anti-Rh(D) IgG at delivery, 0.13% with anti-Rh(D) IgG at delivery and empirically at 28 weeks), abortion (3–6%), CVS/amniocentesis (1–3%), and ectopic pregnancy (<1%). Passive immunization with anti-Rh(D) IgG can destroy fetal erythrocytes before they evoke a maternal immune response.

3. Anti-Rh(D) IgG should be given within 72 hours of potential exposure. 300 µg (U.S.) or 500 IU (U.K.) given intramuscularly will cover up to 30 mL of fetal whole blood or 15 mL of fetal red blood cells.

1. Immune-mediated fetal hemolysis results in release of bile pigment into amniotic fluid that can be measured as the change in optical density at wavelength 450 nm (ΔOD450).
2. Traditionally, the degree of hemolysis was measured by serial amniocentesis every 1–2 weeks starting in the mid 2nd trimester.
3. Amniotic fluid ΔOD450 measurements were then plotted against gestational age (Liley curve) in an attempt to predict fetal outcome. If the ΔOD450 rose into the upper 80% of zone 2 or into zone 3 of the Liley curve, prompt intervention was indicated. However, this test has been replaced almost entirely with non-invasive measurements of peak systolic velocity (PSV) in the middle cerebral artery (MCA) of the fetus using Doppler velocimetry. An elevated MCA PSV for gestational age has been shown to accurately identify fetuses with severe anemia requiring intervention.
4. Unlike ABO, the (Rh)D antigen is expressed only on primate erythrocytes. It is evident by 38 days of intrauterine life. Mutation in the D gene on chromosome 1 results in lack of expression of D antigen on circulating erythrocytes

1. Such individuals are regarded as Rh(D)-negative. This mutation arose first in the Basque region of Spain, and the difference in prevalence of Rh(D)-negative individuals between the races may reflect the amount of Spanish blood in their ancestry: Caucasians, 15%; African-Americans, 8%; African, 4%; Native American, 1%; and Asian, <<1%.
2. Percutaneous umbilical blood sampling (PUBS) involves ultrasound-guided aspiration of fetal blood from the umbilical cord.
3. Advantages include the ability to get a rapid fetal karyotype and to measure several hematological, immunological, and acid/base parameters in the fetus. Intrauterine fetal blood transfusions (IUT) can also be performed, but has a procedure-related fetal loss rate of 1–5% and is therefore rarely performed after 32 weeks.