

Prevention of Rh D Alloimmunization

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Nomenclature

- The RBC membrane contains many anchored surface proteins.
- A blood group system consists of one or more antigens controlled at a single locus, or by two or more closely linked homologous genes with no recombination.
- 30 human blood group system genes have been identified and sequenced
- Many terminologies have been used to denote human blood groups.
- Most common groups: ABO and Rh

Nomenclature

- Different types of Rh types include: D, C, c, E, and e
- Women who carry Rh D Antigen are considered Rh (D) positive.
- Frequency of Rh D negative phenotype is:
 - European and North American descent (~15%)
 - African and India (3-8%)
 - Asia (0.1-0.3%)

Nomenclature

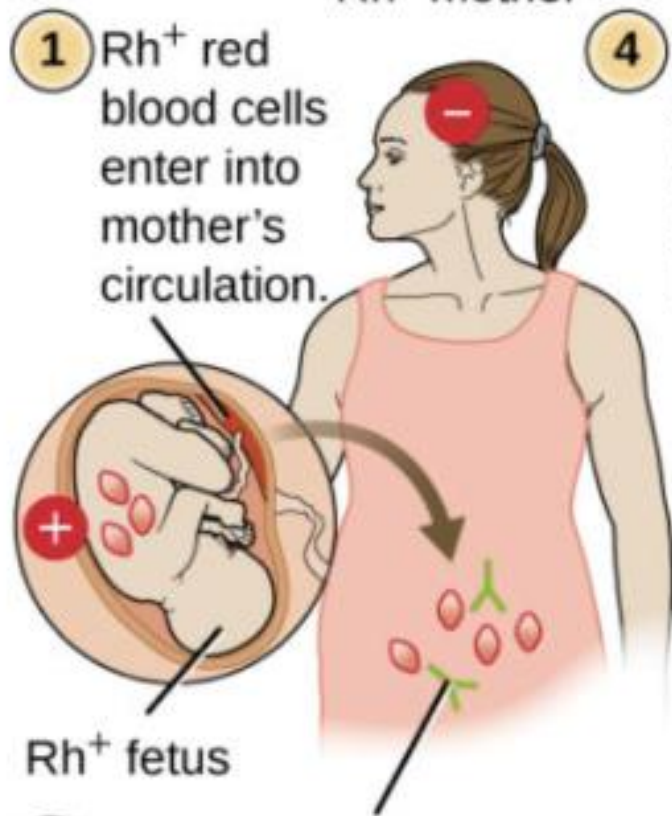
- Alloimmunization- immunologic reaction against foreign antigens that are distinct from antigens on an individual's cells.
- The most commonly discussed type of alloimmunization refers to Rh D alloimmunization.
 - This refers to the maternal formation of antibodies against fetal Rh D.
- Rhogam- Rh D immunoglobulin or anti-D immune globulin- immune globulin used specifically to bind to Rh D antigen

Causes of Rh D Allo- immunization

- Occurs when a Rh D negative woman is exposed to RBCs expressing Rh D antigen
- This can occur when there is antenatal mixing of maternal and fetal blood, even in asymptomatic individuals.

First pregnancy with Rh⁺ fetus

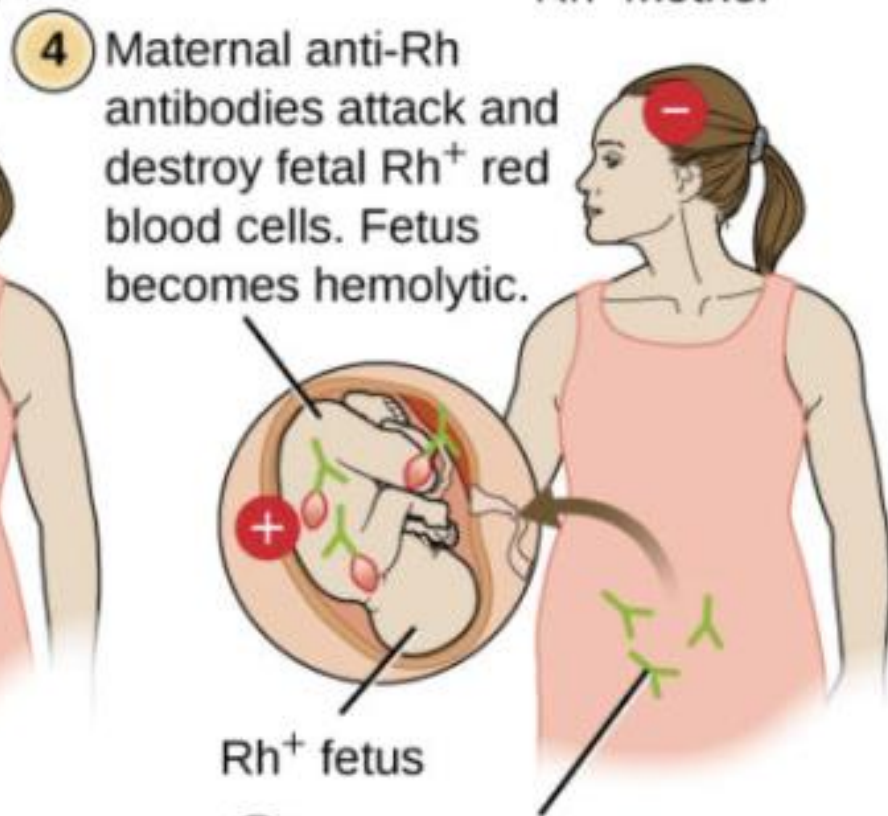
Rh⁻ mother



2 Anti-Rh antibodies are produced upon exposure to fetal Rh antigens.

Second pregnancy with Rh⁺ fetus

Rh⁻ mother

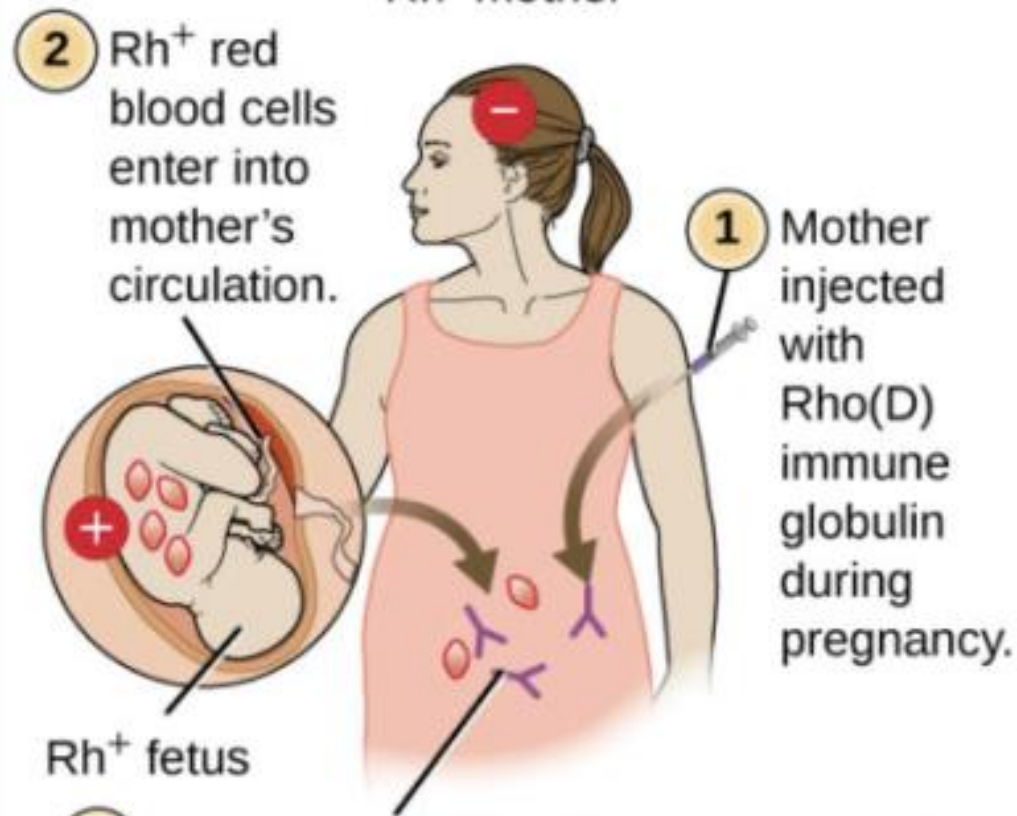


3 Anti-Rh antibodies remain in mother's circulation and cross placenta.

(a)

First pregnancy with Rh⁺ fetus and anti-Rh antibody treatment

Rh⁻ mother



(b)

Box 1. Potential Sensitizing Events in Rh D-Negative Women in Pregnancy ↩

- Chorionic villus sampling, amniocentesis, cordocentesis
- Threatened miscarriage or miscarriage
- Ectopic pregnancy
- Evacuation of molar pregnancy
- Therapeutic termination of pregnancy
- Antepartum hemorrhage
- Abdominal trauma
- Intrauterine fetal death
- External cephalic version
- Delivery

Rates of feto-maternal hemorrhage

- 3-11% of women with threatened abortion (miscarriage) in first trimester
- 45% after third trimester delivery
- 1-2% after spontaneous abortion
- 4-5% after uterine instrumentation
- 14% after chorionic villus sampling
- 2-6% for amniocentesis or cordocentesis

Anti-D Immune Globulin to Prevent Allo- immunization

- Rhogam, or Anti-D immune globulin is extracted by cold alcohol fractionation from donated plasma.
- One prophylactic dose (300 mcg) of Rhogam can prevent Rh D alloimmunization after exposure to up to 30 mL of Rh D positive fetal whole blood.

Anti-D Immune Globulin to Prevent Allo- immunization

- All Rh D negative women at 28 weeks gestation should receive prophylactic Rhogam
- Rhogam should be given sooner if concern for fetomaternal hemorrhage
- After delivery, all neonates' blood type is tested.
 - If an Rh D negative woman gives birth to Rh D negative neonate, no Rhogam indicated.
 - If an Rh D negative woman gives birth to Rh D positive neonate, Rhogam work-up needs to be done and Rhogam needs to be given.

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- Rhogam should be given within 72 hours of delivery.

Screening for feto-maternal hemorrhage

Assessing need and dosing (if large maternal-fetal hemorrhage is suspected) , can be done using the Kleihauer-Betke and Rosette Test.

Rosette Test:

- Qualitative test
- Can detect minimum of 10 mL fetal blood in maternal circulation
- If negative, standard dose Rhogam sufficient
- If positive, use KB test

Kleihauer-Betke Test:

- Quantitative test
- Determines amt of fetal blood
- Fetal whole blood (mL)= % fetal cells x5000 mL of maternal blood

Failure to Prevent Rh D Allo-immunization

- Alloimmunization of Rh D negative woman may still occur.
- May be due to the following:
 - Failure to administer Rhogam altogether
 - Insufficient dosage
 - Untimely administration of Rhogam (>72 hours)
 - Unrecognized maternal-fetal hemorrhage during pregnancy
- Approximately 0.1-0.4% of women at risk become sensitized during pregnancy.
- Spontaneous immunization despite adherence can occur 0.1-0.2%. Thus prophylaxis is not 100% effective.

Is Rhogam
indicated in
sensitized
pregnancy?
-NO!

- All pregnant women should be tested for ABO blood group and Rh D type and presence of antibodies.
- If anti-D antibody is identified, further history should be obtained.
 - Ie. Did patient previously receive Rhogam, presence of another pregnancy that patient did not disclose.
- If patient is found to have anti D antibodies due to sensitization, Rhogam is not beneficial and should proceed in accordance with protocols in treating alloimmunization.

How should one deal with issue of paternity?

- If paternity is certain and the father is known to be Rh D negative, antenatal prophylaxis is not necessary.
 - BEWARE: MEAN NON-PATERNITY POPULATION RATE = 3%
- If the Rh type of the partner is not known, routine antenatal Rhogam prophylaxis is preferred.

How should weak D blood type be managed?

- An estimated 0.2 - 1% of Caucasian individuals inherit genes that code for serologic weak D phenotypes.
- Some individuals express reduced numbers of normal Rh D antigens whereas others express partial or abnormal Rh D antigens.
- Therefore, it is possible to develop antibodies against part of Rh D antigen that they are missing and if exposed to Rh D positive blood.
- Thus, Rhogam indicated in patients with weak Rh D blood type.

How long does the effect of Rhogam last?

- Median half-life is 23 days
- If delivery occurs within 3 weeks of previous Rhogam administration, post-natal dose may be withheld (if low suspicion for excessive maternal fetal hemorrhage)
 - Can assess with KB test

Should Rhogam be withheld from woman undergoing postpartum sterilization?

- NO! Rhogam should NOT be withheld for woman that are planning to undergo postpartum sterilization.
- Pregnancies occur despite sterilization (either naturally or via ART)
- Alloimmunization complicates crossmatching of blood products in the future.

What should be done if pt discharged home prior to Rhogam administration?

- Ideal time to administer Rhogam is 72 hours
- Some benefit seen for patients as late as 28 days

Questions?