Rh D negative women and pregnancy

Clinical Guideline Presentation v1
Objectives

• Understand the pathogenesis and outcomes when Rh D negative woman is alloimmunised

• Identify the antenatal and postnatal blood tests offered to recognise and manage Rh D negative women

• Identify when prophylactic Rh D Ig is recommended during pregnancy
Objectives

- Identify and understand the management of sensitising events
- Understand Rh D immunoglobulin products available and their use
- Understand the care of the baby born to an Rh D negative woman
# Abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>APH</td>
<td>Antepartum haemorrhage</td>
<td>HDFN</td>
<td>Haemolytic disease of the fetus and newborn</td>
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<td>CVS</td>
<td>Chorionic villus sampling</td>
<td>Ig</td>
<td>Immunoglobulin</td>
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<td>DAT</td>
<td>Direct antiglobulin test</td>
<td>IM</td>
<td>Intramuscular</td>
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<td>DCT</td>
<td>Direct Coombs test</td>
<td>IU</td>
<td>International units</td>
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<td>DNA</td>
<td>Deoxyribonucleic acid</td>
<td>IV</td>
<td>Intravenous</td>
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<td>ECV</td>
<td>External cephalic version</td>
<td>NIPA</td>
<td>Non-invasive prenatal analysis</td>
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<td>FMH</td>
<td>Feto-maternal haemorrhage</td>
<td>NIPT</td>
<td>Non-invasive prenatal test</td>
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<td>Hb</td>
<td>Haemoglobin</td>
<td>ToP</td>
<td>Termination of pregnancy</td>
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<td>&lt;</td>
<td>Less than</td>
<td>&gt;</td>
<td>Greater than</td>
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# Definitions

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<th><strong>Alloimmunisation</strong></th>
<th>Rh D negative woman’s immune system response to Rh D positive fetal red blood cells expressing the Rh D antigen</th>
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| **Anti-D antibody**  | Rh D antibodies  
  • Passive antibodies–come from an external source (e.g. Rh D immunoglobulin)  
  • Preformed antibodies–develop after sensitising event when Rh D negative woman exposed to Rh D positive red cells |
| **Rh D Ig**          | Product administered to Rh D negative woman who has no preformed antibodies |
| **Rh D positive person (previously known as Rhesus positive)** | Carries D antigen on their red cells |
| **RHD**              | Gene that encodes Rh D blood type  
  Refers to the genotype in the fetus |
What happens when Rh D immunoglobulin is administered?

Rh D negative woman with Rh D positive baby has sensitising event

Rh D immunoglobulin is administered

Rh D immunoglobulin for prophylaxis and after sensitising events neutralises the Rh D antigen and prevents antibodies developing

After pregnancy the woman does not have antibodies from Rh D positive baby

Red blood cells
Rh D antibody with Rh D immunoglobulin attached
What happens when Rh D immunoglobulin is not administered?

Rh D negative woman with Rh D positive baby has sensitising event

If Rh D immunoglobulin has not been given, the woman develops antibodies

After pregnancy the antibodies remain

Next pregnancy

In the next pregnancy, if the baby is Rh D positive, antibodies cross the placenta and damage the baby’s RBC

Baby may develop HDFN, hydrops fetalis, fetal thrombocytopenia and develop jaundice
Amira attends antenatal clinic for her booking-in appointment in her first pregnancy. She mentions she is a blood donor and her blood group is A negative.

What care is offered to an Rh D negative woman?

- History to identify Rh D alloimmunisation risk (previous baby known to have HDFN or blood transfusion)
- Information about being Rh D negative and fetal/neonatal risk
  - Provide QCG consumer information
What information do you give Amira about risk factors for alloimmunisation?

- These include:
  - Rh D negative woman has an Rh D positive fetus
  - Sensitising event during pregnancy and birth
  - Incompatible blood transfusion
- If preformed anti-D antibodies are present refer woman for specialist management
What are the neonatal risks from maternal alloimmunisation?

- Severe anaemia resulting from haemolytic disease of the fetus and newborn (HDFN)
  - If anti-D level > 4 IU per mL and < 15 IU per mL– moderate risk of HDFN (unlikely to be severe)
  - If anti-D level > 15 IU per mL– risk of severe HDFN
- Hydrops fetalis
- Fetal thrombocytopenia
What blood tests are offered?

• Blood tests
  ◦ ABO Rh D group
  ◦ If Rh D negative, antibody screen for preformed anti-D antibodies
  ◦ Fetal RHD (NIPA/NIPT) if:
    ▪ Preformed anti-D antibodies
    ▪ Previous obstetric history (severe FMH, intra-uterine fetal death)
    ▪ Non-sensitised but relative contraindication to Rh D Ig (e.g. prior allergic reaction)
What do you discuss with Amira about sensitising events that occur in the first 12+6 weeks

- Miscarriage
- Surgical termination of pregnancy (ToP)
- Medical ToP after 10+0 weeks
- Ectopic pregnancy
- Molar pregnancy
- Chorionic villus sampling (CVS)
Sensitising events from 13 weeks

- Genetic studies—CVS, amniocentesis, cordocentesis
- Abdominal trauma
- Antepartum haemorrhage (APH)—revealed or concealed
- External cephalic version (ECV)—successful or attempted
- Miscarriage or ToP
- Birth of baby
Amira asks when she will receive Rh D Ig.

What information do you give Amira?

- Rh D Ig is administered:
  - Prophylactically at 28 and 34 weeks gestation— if no preformed antibodies and fetal RHD known to be Rh D positive or not known
  - Following sensitising event(s) including if antibody status not known
What type and doses of anti-D Ig are available? How are they administered?

- Rh (D) immunoglobulin VF
  - Routine prophylaxis and sensitising event(s)
  - If < 13 + 0 weeks: 250 IU IM injection
  - If ≥ 13 weeks: 625 IU IM injection
  - Deep, slow intramuscular (IM) injection in deltoid or anterolateral thigh
    - **Not** for IV administration (draw back on syringe)
  - Divided dose if > 5 mL volume (round up to nearest full vial)
Anti-D immunoglobulin

- Rhophylac®
  - Indicated for large FMH > 6 mL
  - Volume of Rh D immunoglobulin > 5 mL or there is a contraindication (e.g. previous allergic reaction to Rh (D) immunoglobulin VF)
  - Intravenous (IV) injection from prefilled syringe
Amira presents at 28 weeks for her first injection of Rh D Ig.

After providing information and education, and obtaining informed consent, how is Rh D Ig administered?

- Bring to room temperature just prior to administration
- Observe woman for 20 minutes after administration
- If BMI ≥ 30 kg/m²
  - No additional does required
  - Consider administration site and needle length (deltoid suggested)
Amira presents with some bleeding at 32 weeks gestation.

What management is recommended after a sensitising event?

- Check bloods–group (if required), and anti-D antibodies
- Quantify size of fetomaternal haemorrhage (FMH) from 20+1 weeks by flow cytometry or Kleihauer-Betke
- Administer Rh D Ig after blood sample as soon as possible (do not wait for test results)
Management of sensitising event

• If large FMH (≥ 6 mL), repeat quantitative test
  ◦ 48 hours after IV Rh D Ig
  ◦ 72 hours after IM Rh D Ig

• Postnatally
  ◦ If baby Rh D positive, maternal blood 45 minutes after birth and within 72 hours
  ◦ Collect maternal blood before Rh D Ig is administered
At 40+3 weeks gestation Amira gives birth to a well baby boy.

What neonatal care is recommended for Amira’s baby?

- Check Rh D group and direct antiglobulin test (DAT) from cord blood of all babies born to Rh D negative women
  - Regardless of immunoprophylaxis or alloimmunisation
  - Includes if non-invasive prenatal test (NIPT) predicted Rh D negative baby
Neonatal care

• If clinically significant antibodies in woman or increased risk of haemolysis
  ◦ Cord blood for haemoglobin (Hb) and bilirubin

• Usual newborn care

• If alloimmunised mother assessment of:
  ◦ Neurobehavioural state
  ◦ Jaundice
  ◦ Anaemia