Routine Administration of Anti D

Anti D Timing – Prophylactic & Sensitising Doses are Completely INDEPENDENT of each other (Diagram 3)

| 28 weeks* Prophylactic Dose (or when woman presents, if later) | • Test Blood Group Antibodies before giving Rh D Immunoglobulin
  o < 1% will have developed antibodies if negative at booking
  o if previously received Rh D Immunoglobulin for a sensitising event, the date of this must be included on the request form
  • Give prophylactic 625 IU Rh D Immunoglobulin (Anti D) – even if recently received a dose for a sensitising event |

| 34 weeks Prophylactic Dose (or when woman presents, if later) | • Give prophylactic 625 IU Rh D Immunoglobulin (Anti D) – even if recently received a dose for a sensitising event
  • Do NOT test blood group antibodies as antibodies often persist from the 28-week Rh D Immunoglobulin injection → confusion |

| Birth and other Sensitising Events after first trimester | • Test FMHQ (test because ‘sensitising event’, not prophylactic dose) before giving Rh D Immunoglobulin, to calculate how many vials of Rh D Immunoglobulin are indicated (usually only 1 vial)
  o Time elapse of 30 – 45 minutes between sensitising event and FMHQ is sufficient to allow dispersal of fetal RBCs around the mother’s circulation (BCSH 2014)
  • Immediately give 625 IU Rh D Immunoglobulin (Anti D)
  o Give this dose without waiting for FMHQ result
  • If FMHQ indicates additional Rh D Immunoglobulin is needed
    o Give required additional Rh D Immunoglobulin.
    o 48 – 72 hours later, test both FMHQ (negative result is good) and Blood Group Antibodies (residual Anti D in circulation is good) while liaising closely with blood bank |

*If presents after 28 weeks give as soon as possible. Then give next dose 6 weeks later.

- Prophylactic doses at 28 and 34 weeks are protective for about 6 weeks (see later for how duration of protection may be much shorter in the situation of fetomaternal haemorrhage)
- An uncomplicated pregnancy proceeding to 42 weeks does not need a further dose of Rh D Immunoglobulin as the level of antibody detected 8 weeks post injection is unlikely to be much different from 6 weeks in an uncomplicated pregnancy. Any significant FMH event occurring after 40 weeks would likely precipitate labour or lead to intervention to deliver the baby and this would then be shortly followed by postnatal Rh D Immunoglobulin.

- Routine Rh D Immunoglobulin administration at 28 weeks, 34 weeks and after birth is completely independent of administration for sensitising events during pregnancy
  o The routine administration of Anti D at 28 & 34 weeks and postpartum must occur even if Rh D Immunoglobulin was recently given for a sensitising event.
  o Likewise, potential sensitising events soon after prophylactic 28- or 34-week doses should be managed with collection of FMHQ (to determine dose needed) and then immediate administration of Rh D Immunoglobulin 625 IU without awaiting the FMHQ result or testing for presence of residual Anti D from previous dose (NSW Health 2015 - see Education Notes for more information)

Refs: NSW Health 2015, ARCBS NBA 2015, RANZCOG 2015, BCSH 2014
Anti D Dosage

- 100 IU of Anti D neutralises 1 mL of fetal RBC (2 mL of fetal blood, haematocrit 50%)
- Standard Dosages
  - **250 IU** is the standard dose up to and including 12 weeks (except multiple pregnancy when 625 IU/L is administered)
    - It is sufficient to neutralise 2.5 mL of fetal red blood cells (5 mL of fetal blood)
    - This is more than adequate for first trimester losses → FMHQ not required
  - **625 IU** is the standard dose after 12 weeks
    - It is sufficient to neutralise 6 mL of fetal red blood cells (12 mL of fetal blood)
    - Typical size of FMH after the first trimester:
      - 99% involve < 5 mL of fetal red blood cells / 10 mL fetal blood
      - 50% involve < 0.05 mL fetal red blood cells (very tiny amounts)
      - 0.6% may be greater than 30 mL fetal red blood cells (very large amounts)
    - Therefore, 625 IU is adequate for over 99% of routine postnatal administration and for most sensitising events – however, FMHQ is assessed in these situations to detect the just under 1% requiring additional Anti D vials.
      - An FMH of 50 mL fetal cells (100 mL fetal blood) requires 8 - 9 x 625 IU vials of Anti D – usually rounded up to 9 vials to avoid under-dosing (see Management of Large FMH).
      - Laboratories reporting the size of any FMH, must do so in a way that facilitates easy calculation of the required RhD Immunoglobulin dose.
      - Clinicians must be in close consultation with Blood Bank.
    - The risk of needing more than 1 vial is increased with:
      - Abruption
      - Manual removal of placenta (including at caesarean - strongly discouraged)
      - In-utero needling of the umbilical cord

(NSW Health 2015, ARCBS NBA 2015)

Diagram 4

<table>
<thead>
<tr>
<th>Estimated FMH (mL)</th>
<th>Rh (D) Immunoglobulin vials (625IU/mL) required</th>
</tr>
</thead>
<tbody>
<tr>
<td>3mL</td>
<td>1</td>
</tr>
<tr>
<td>6mL</td>
<td>1</td>
</tr>
<tr>
<td>12mL</td>
<td>2</td>
</tr>
<tr>
<td>18mL</td>
<td>3</td>
</tr>
<tr>
<td>24mL</td>
<td>4</td>
</tr>
</tbody>
</table>

If FMH is > 15mL always consult with Haematology and consider intravenous administration of Rh (D) Immunoglobulin (RHOPHYLAC®)

Source: NSW Health GL2015_011
Anti D Route

- Rh (D) Immunoglobulin-VF is brought to room temperature (store at 2 – 8 °C, do not freeze) and then administered as a deep intramuscular (IM) injection, not a subcutaneous injection.
- The ideal injection site is:
  - The deltoid muscle or anterolateral thigh.
  - Not the dorso-gluteal area (upper outer buttock) as the fat in this area often renders the injection inadvertently subcutaneous (SC) rather than IM, resulting in unpredictable and delayed absorption and reduced effectiveness.
- High BMI women
  - To avoid inadvertent subcutaneous rather than deep IM injection in women with high BMI, care needs to be taken regarding:
    - Site of injection
    - Accessibility of the underlying muscle
    - Length of the needle used
- IV administration (note: with an *alternative product) may be required if the woman
  - Has a bleeding disorder (cannot have IM injection)
  - Needs multiple IM injections (for example, for FMHQ > 15 mL fetal RBCs)
  - Is obese such that inadvertent subcutaneous rather than IM injection may occur
- If IV administration is required, an *alternative product (see Appendix 1) must be sourced from Blood Bank for use because Rh (D) Immunoglobulin-VF can only be given IM and must not be given IV due to risk of anaphylaxis. For general approach to management of anaphylaxis see https://www.allergy.org.au/hp/papers/acute-management-of-anaphylaxis-guidelines (NSW Health 2015, ARCBS NBA 2015, RANZCOG 2015, BCSH 2014, CSL 2014, ASCIA 2019)

Duration of Anti D Effect

- Anti D has a half-life of approximately 3 – 4 weeks and can still be detected in a patient’s serum 6 weeks after administration and sometimes longer.
- It is therefore generally accepted that a dose of 625 IU provides coverage for a period of 6 weeks.
- However, if there are ongoing large or recurrent fetomaternal haemorrhages occurring during pregnancy, Anti D will be removed from the circulation and the half-life and duration of effect will be considerably shortened. (ARCBS NBA 2015)

How should ‘Weak D’ Blood Type be interpreted?

- Weak D (formerly known as Du) blood type occurs in a small number of people. Some express reduced numbers of normal Rh D antigens while others express partial or abnormal Rh D antigens. It is possible for such people to develop antibodies to the part of the Rh D antigen that they are missing.
- A reasonable rule of thumb for such patients is that they be considered
  - Rh Negative as blood recipients (and therefore should receive Anti D in pregnancy)
  - Rh Positive as blood donors (ACOG 2017)
**Distinguishing Pre-formed from Administered Anti-D Antibodies**

- Anti D should not be given to women with Anti-D antibodies detected on testing except where such antibodies are due to the antenatal administration of RhD Immunoglobulin.
  - Unfortunately, the laboratory cannot distinguish immune pre-formed antibodies (made by the woman) from passive antibodies (from the injection)
  - Therefore, the history is of critical importance
  - If it is unclear whether the antibody in the woman's blood is passive or pre-formed / immune, the treating clinician should be consulted for a decision. If there is continuing doubt, Anti D should be administered (ARCBS NBA 2015, NSW Health 2015)

**Threatened Miscarriage (where the pregnancy continues)**

- With cases of threatened miscarriage, Rh D immunoglobulin is currently not generally advised as there is insufficient evidence of benefit (RANZCOG 2015, NSW Health 2015)
- However, if the bleeding is particularly heavy or associated with a visible subchorionic haematoma, some authorities advise Anti D should be given (ARCBS NBA 2015)

**Multiple Pregnancy after the first trimester**

- For both singleton and multiple pregnancies
  - The routine prophylactic dose at 28 and 34 weeks is 625 IU
  - The dose after sensitising events is determined by the FMHQ – always giving the standard 625 IU dose while awaiting FMHQ result

**Simultaneous Maternal Postnatal Anti-D and MMR Vaccine**

- This guideline advises that the Anti D injection can be given at the same time as the measles mumps rubella (MMR) vaccination although into a different injection site and via a separate syringe
- This is in accord with the current (February 2019) online Australian Government advice that no time interval need separate the two injections (Australian Immunisation Handbook 2018). Note that this is at variance with ARCBS and the official CSL product information which advise that the MMR should be deferred for 3 months after Anti D in case the presence of passive antibody inhibits the body’s response to the vaccine (Australian Immunisation Handbook 2018, ARCBS NBS 2015; CSL 2014).

**Management when well newborn is ‘DAT positive’**

- The baby of an Rh negative mother may be found to be direct antiglobulin test positive (DAT positive, Coombs positive) at routine blood group & DAT testing after birth
- The neonatology team will review the baby - vigilance for anaemia & jaundice is needed. However, in the baby at low risk of HFDN, this result is usually due to passively administered maternal Anti D which has passed across to the fetus and is of no consequence. (BCSH 2014)