NHS Greater Glasgow and Clyde

CLINICAL GUIDELINE

Anti-D Immunoglobulin Administration Following Potentially Sensitising Events and Routine Antenatal Anti-D Prophylaxis in RhD Negative Women

A guideline is intended to assist healthcare professionals in the choice of disease-specific treatments.

Clinical judgement should be exercised on the applicability of any guideline, influenced by individual patient characteristics. Clinicians should be mindful of the potential for harmful polypharmacy and increased susceptibility to adverse drug reactions in patients with multiple morbidities or frailty.

If, after discussion with the patient or carer, there are good reasons for not following a guideline, it is good practice to record these and communicate them to others involved in the care of the patient.

Version Number:	6
Does this version include changes to clinical advice:	Yes
Date Approved:	2nd September 2025
Date of Next Review:	31st July 2030
Lead Author:	Julie Murphy
Approval Group:	Maternity Clinical Governance Group

Important Note:

The online version of this document is the only version that is maintained.
Any printed copies should therefore be viewed as 'Uncontrolled' and as such, may not necessarily contain the latest updates and amendments.

Greater Glasgow & Clyde Obstetric Guideline - anti-D Immunoglobulin Administration Following Potentially Sensitising Events in D Negative Women

The following guideline refers to non-sensitised D negative women in pregnancy. Women who are confirmed to have immune (allo) do not require anti-D.

Adequate prophylaxis is effective in reducing the incidence of sensitisation.

Consent should be obtained before anti-D administration in all events.

Patient information document and green card should be given to patient following a D negative result at booking.

Indications for administration – Potentially Sensitising Events (PSEs)

Anti-D Ig 1500 IU should be given after the following:

1) Vaginal bleeding with associated severe pain

2) Evacuation of retained products of conception/molar pregnancy

3) Invasive prenatal diagnostic procedures e.g. amniocentesis, CVS

4) Other invasive procedures e.g. embryo reduction, insertion of shunts, intrauterine transfusion, laser therapy for TTTS, transabdominal cerclage

5) Antepartum haemorrhage

6) Abdominal trauma – sharp/blunt, open/closed

7) External cephalic version

8) Therapeutic termination of pregnancy

- Anti-D Ig 1500 IU is required for women having a medical or surgical TOP on or after 12+0 weeks' gestation.
- Anti-D Ig is **NOT** required for women having a medical or surgical TOP up to 12+0 weeks' gestation.

9) Spontaneous miscarriage, threatened miscarriage ≥12+0weeks (if the gestational age is different to the size of the fetal pole on ultrasound, the ultrasound measurements should be used)

- **Complete spontaneous miscarriage**
  - Prior to 12+0 weeks – anti-D Ig not required.
  - ≥ 12+0 weeks - anti-D Ig 1500 IU is required.
- **Medical management of miscarriage**
  - Anti-D Ig is not required for solely medical management of miscarriage prior to 12+0 weeks.
  - Anti-D Ig 1500 IU should be given to all women receiving medical management of miscarriage ≥12+0 weeks.
- **Surgical management of miscarriage/Manual Vacuum Aspiration (MVA)**
  - Anti-D Ig 1500 IU should be given to women undergoing a surgical procedure for management of miscarriage or MVA. This is also the case for women undergoing evacuation of uterus for molar pregnancy.

- **Threatened miscarriage**
    - Anti-D Ig 1500 IU should only be considered in women with threatened miscarriage and a viable fetus prior to 12+0 weeks if PV bleeding is recurrent, heavy and/or associated with significant abdominal pain.
    - Anti-D Ig 1500 IU should be given to women with a threatened miscarriage after 12+0 weeks gestation.

10) Ectopic pregnancy

- Anti-D Ig 1500 IU should be given to women who have surgical management of an ectopic pregnancy.
- Anti-D Ig is not required for women who have solely medical management of ectopic pregnancy or a pregnancy of unknown location (PUL).

11) Intrauterine death (IUD)

- Diagnosis and birth of an IUD at ≥20+0 weeks should be considered as **2 separate PSEs.**
- Therefore, anti-D Ig 1500 IU should be given to women **at the time of diagnosis** of IUD, unless the patient presents in advanced labour.
- At diagnosis of IUD ≥20+0 weeks, maternal bloods for Group & Save and Kleihauer should be taken.
- At the point of diagnosis of IUD ≥20+0 weeks, Blood Bank would aim to process the request for anti-D in an urgent manner following a telephone call. There should be minimal delay for the patient. Ensure relevant details on the request form.
- Please ensure Group & Save is repeated every 72hours until delivery.
- Following birth, maternal Group & Save and Kleihauer samples should be obtained and sent to Blood Bank. Bloods should be obtained 30-45 minutes following delivery.
- Administration of anti-D Ig 1500IU should be **repeated** as soon as possible and always within 72 hours of delivery.

12) Birth of D positive baby or baby of unknown Blood Group

- Following birth, maternal Group & Save and Kleihauer samples should be obtained and sent to Blood Bank. The Kleihauer sample should be taken when sufficient time has elapsed to allow fetal cells to be distributed within the maternal circulation following birth, or manual removal of placenta. A period of 30-45 minutes is considered adequate.
- Cord bloods should also be obtained from baby to determine baby's ABO and D type.
- If cord samples cannot be obtained, document on maternal request form and the neonatologist must be contacted to obtain a newborn group sample from the baby. Every effort should be made to obtain cord blood to avoid unnecessary invasive sampling of baby. If the baby requires blood samples for any other reason eg sepsis or blood sugars, please obtain newborn group sample at the same time to avoid unnecessary sampling of the newborn.
- If baby confirmed to be D positive, give anti-D Ig 1500 IU as soon as possible and always within 72 hours of birth.
- If for any reason a sample from baby cannot be obtained, the baby should be assumed to be D positive for the purposes of anti-D Ig administration.
- If the Kleihauer test indicates a FMH >12ml then further anti-D Ig will be required. The dose advised will be dependent on the estimated volume of FMH. A further repeat Kleihauer should then be taken 72 hours after administration of the additional anti-D Ig if given IM and 48hours if given IV to ensure clearance of fetal cells.

- Any postnatal D negative patients leaving the hospital without receiving anti-D Ig should be discussed with an obstetric consultant.

13) Intra-operative cell salvage Intraoperative Blood Cell Salvage, Obstetrics (555) | Right Decisions

- When intra-operative cell salvage is used during a Caesarean birth, reinfused blood may contain fetal red cells.
- The volume of fetal red cells in reinfused blood can vary from 1-20ml.
- It is therefore recommended that a minimum dose of **1500 IU** anti-D Ig is administered after reinfusion of salvaged cells if baby group is confirmed as D positive (or blood group unknown).
- Maternal samples for estimation of FMH should be taken 30 – 45 mins after reinfusion of salvaged red cells. Depending on the Kleihauer result, an additional dose of anti-D should be administered if necessary and additional follow up Kleihauer sent as appropriate if there is a FMH >12ml.
- It is important that clinicians inform Blood Bank if intra-operative cell salvage is being used to ensure that the correct dose of anti-D Ig is issued. This information should be added to the pre-operative maternal request for Group & Save/Crossmatch.

Timing of Administration

Anti-D should be given as soon as possible and always within 72 hours of a sensitising event. If, however, this does not happen some protection may be provided even if anti-D Ig is given up to 10 days later. Women who are known to already be sensitised should not be given anti-D Ig.

Dose of Anti-D

The standard dose is 1500 IU intramuscularly. A 1500 IU dose of anti-D is capable of suppressing immunisation of up to 12 mls of D positive fetal red cells. Intramuscular anti-D Ig is best given into the deltoid muscle.

Doses of 1500 IU of anti-D Ig are administered for RAADP.

Doses of 1500 IU of anti-D Ig are administered following the use of cell salvage.

In women with severe thrombocytopenia (platelet count ≤30 × 10^9/L) or a history of a bleeding disorder such as severe Von Willebrand disease, anti-D Ig should be administered IV. Women with significant bleeding disorders such as Von Willebrand disease should be managed jointly with a haemophilia centre.

Recurrent/ongoing bleeding

<12+0 weeks

See 'Threatened miscarriage' section above.

12+0 – 19+6 weeks

- If discrete episodes of recurrent PV bleeding occur, each new PSE should be managed separately with a further dose of anti-D Ig 1500 IU, regardless of the timing or dose of anti-D Ig given for previous events.
- However, in the event of **ongoing** PV bleeding which is clinically judged to be as a result of the **same** potentially sensitising event (i.e. not suggestive of a new presentation or of significant change in the volume or pattern of the bleeding), anti-D Ig 1500 IU should be given at a

minimum of 6 weekly intervals. A plan for this should be documented in the notes by the patient's obstetric consultant.

≥20+0 weeks

- Follow guidance for 12+0-19+6 weeks above.
- In addition to giving anti D Ig 1500 IU at a minimum of 6 weekly intervals, Kleihauer testing should be performed after each bleed, or every two weeks if the bleeding is ongoing.
- If the bleed is > 12mls, a further dose of anti-D is administered as advised by Blood Bank. All Kleihauer results > 12mls should be repeated 72 hours after the additional dose of IM anti-D and 48 hours after any additional dose given IV, and if still positive, should be discussed with the on-call haematologist.

Kleihauer Testing

This is not necessary under 20 weeks gestation but should be performed following events on or after 20+0 weeks in order to assess the extent of any fetomaternal haemorrhage and ensure sufficient anti-D has been administered. When the Kleihauer indicates a bleed > 12mls, the appropriate additional dose of anti-D should be administered as soon as possible, as advised by Blood Bank. A further repeat Kleihauer should then be taken 72 hours after administration of the additional anti-D Ig if given IM and 48hours if given IV to ensure clearance of fetal cells.

Routine Antenatal Anti-D Prophylaxis (RAADP)

Consent should be obtained before Anti-D is administered

- Maternal Group & Save should be obtained **BEFORE** administering the RAADP. Do not wait for the results before giving a dose of anti-D Ig 1500 IU**.**
- The routine use of RAADP should not be affected by previous anti-D prophylaxis given for sensitising events earlier in the pregnancy.
- If the woman has had RAADP and has an antenatal sensitising event at any point in the pregnancy after this, then she should have a further dose of 1500 IU anti-D (or more if the Kleihauer is > 12ml).
- Administration of post-partum anti-D prophylaxis should not be affected by whether or not RAADP or AADP as a result of sensitising event have been given.

D variant red cells

Some individuals have weak expression of D and are known as D variants. These patients should be considered to be D negative and should receive anti-D for potentially sensitising events and RAADP while further testing is being carried out to confirm the D type. Once the D type has been confirmed, the lab will issue a report to state whether patient should be treated as D negative or positive and will issue anti-D as appropriate if D negative. It is important to note that such women may have been told previously that they are D positive if they are blood donors, this may give rise to confusion. If there is uncertainty about a patient's D type this should be discussed with Blood Bank or the haematologist on call.

Passive Anti-D

Passive anti-D may be detectable in the maternal circulation for many weeks or months after administration of anti-D. Its presence should not be a contraindication to giving further doses of

anti-D should the clinical situation arise. If there is any doubt in whether to administer a dose of anti-D then the case can be discussed with the obstetric team and Blood bank.

Allergic response to Anti-D

Allergic reactions are very rare but severe hypersensitivity including anaphylaxis may occur.

Symptoms of allergic or early signs of hypersensitivity reactions include generalised urticaria, tightness of the chest, wheezing, hypotension, and anaphylaxis.

Adrenaline should be available for immediate treatment of acute severe hypersensitivity reactions.

D Negative Women admitted with a Potentially Sensitising Event out with the maternity unit (for example A&E/Surgical dept/ HDU/ITU)

In the event of any D Negative women being admitted directly to a clinical area out with the maternity unit, the clinician admitting the patient must ensure that any requirement for Anti-D is identified and prescribed appropriately. Discussion with the obstetric or gynaecology team is advised if there is any uncertainty.

Clinical Risk Reporting

In the event of:

- An inappropriate dose of anti-D being administered
- A delay to anti-D being administered*
- Anti-D not being administered at all to a patient who is eligible and consenting*
- Anti-D being administered to a patient who is ineligible
- An adverse reaction to a dose of anti-D

A Datix should be completed by the member of staff aware of the incident and the event should be reported to the Serious Hazards of Transfusion (SHOT) Committee by the clinical risk team.

*In the event of a patient having a delayed or missed dose of anti-D, an appointment should be made for the patient at 6 weeks post birth with her obstetric consultant to discuss the event and a sample for Blood Group & Save should be obtained to check for the presence of immune anti-D. This should be repeated at 6 months post birth to ensure they have not been sensitised.

References

- Use of Anti-D Immunoglobin for the Prevention of Haemolytic Disease of the Fetus and Newborn. British Society for Haematology Jan2014, updated Nov 2023

- Ectopic pregnancy and miscarriage: diagnosis and initial management

  NICE guideline [NG126] Published date: 17 April 2019

- Abortion care

NICE guideline [NG140] Published date: 25 September 2019

- Abortion care [Q] Supporting document for the recommendations on anti-D prophylaxis NICE guideline NG140 May 2025

Title

Anti-D Immunoglobulin Administration following Potentially Sensitising Events in D Negative Women_Version 3

Implementation / Review Dates

Version 1: Implemented September 2011

Review date September 2013

Version 2: Implemented - on Staffnet 6.2015

Review date – 01/12/23

Version 3 Implemented 04/12/18

Version 4 Updated R McBride/A Marshall/C Watson/A Hanlon/J Murphy Mar 2021

Version 5 Updated A Marshall/C Watson/L Ellerker/J Murphy 2024

Version 6 Updated J Murphy/C Watson July 2025