Antenatal and Postnatal Administration of Anti-D Immunoglobulin for the Prevention of RhD Alloimmunisation – Guideline

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1. Scope and Purpose

1.1. Scope of the guideline

This guideline applies to nurses, midwives and medical staff working in maternity and gynaecology. It is applicable to all pregnant women who are Rh (D) negative.

1.2. Aim of the guideline

This guideline outlines antenatal screening for Rh antibodies (and other blood group antibodies), indications for, and the actual administration of, anti-D both prophylactically during pregnancy and following a sensitising event.

1.3. Guideline objectives

This guideline aims to offer a plan of care for women who are Rh (D) negative that will reduce their individual risk of developing antibodies.

2. Introduction

The prevention of haemolytic disease of the newborn is an essential cornerstone of modern obstetrics. This is achieved by close monitoring of women potentially at risk of developing antibodies and the careful use of anti-D after clinical events when sensitising may occur. Following NICE guidelines (NICE 2008), antenatal prophylaxis is recommended in an attempt to reduce the number of RhD negative women who become sensitised each year. Studies have shown that routine antenatal prophylaxis can reduce the sensitisation rate from 1.5% to 0.2% or less.

This guideline outlines antenatal screening for Rh antibodies (and other blood group antibodies), indications for, and the actual administration of, anti-D both prophylactically during pregnancy and following a sensitising event.

This guideline aims to offer a plan of care for women who are RhD negative that will reduce their individual risk of developing antibodies.

3. Screening for blood group antibiotics

All women should be screened for the presence of blood group antibodies (including RhD, Rhc, RhE, Kell, etc) during pregnancy.

- **Antenatal antibody screening.** All women should be offered screening using a blood group and antibody check at booking, ideally by 12 weeks. (1x 7ml sample, taken into EDTA bottle (purple top) and labelled at time of taking blood).

- **RhD negative non-sensitised women.**

- Women who are RhD negative should be offered the option of fetal blood grouping using free fetal DNA. This requires a further blood test to be performed at 16 weeks of pregnancy.

- If the fetus is shown to be RhD negative, no anti-D is required during the pregnancy or after the birth (See flowchart in associated UHS Guideline 'Use of cffDNA to determine fetal RhD status during pregnancy'. 2017)

- Further antibody check at 28 weeks to check for other blood group antibodies

- If the fetus is shown to be RhD positive, or the woman declines the offer of cffDNA testing, further antibody check at 28 weeks prior to administration of prophylactic anti-D at 30 weeks

RhD positive women should be offered a further antibody check at 28 weeks to check for other blood group antibodies

If any antibodies are detected at any gestation, discussion should take place with the fetal medicine team who may suggest referral to a Consultant Obstetrician.

4. Administration of anti-D for antenatal prophylaxis

- It is recommended that routine antenatal anti-D prophylaxis is offered to all non-sensitised pregnant women who are RhD negative and whose baby is known to be RhD positive or the fetal group is unknown

- The health professional responsible for the antenatal care of such a woman should discuss antenatal prophylaxis and the options available with her so she can make an informed choice about treatment. Accurate documentation of this discussion should be entered into the woman's hand held notes.

- Circumstances where antenatal prophylaxis may be unnecessary include where the woman:

    - has opted to be sterilised after the birth of the baby
    - Has chosen to have cell free fetal DNA testing and the fetus has been shown to be RhD negative.
    - is certain she will not have another child after the current pregnancy

- A woman's use of antenatal anti-D prophylaxis should NOT be affected by whether she has already had anti-D for a sensitising event in pregnancy. Similarly administration of

anti-D following a sensitising event or delivery should NOT be affected by whether the woman has had antenatal anti-D prophylaxis.

- RhD negative women and health professionals should be offered high-quality information regarding anti-D prophylaxis, and information leaflets are available in different languages.

- The process for antenatal anti-D prophylaxis is as follows;

    - Routine booking bloods tests should include both an antibody screen and determination of the maternal blood group. Cell-free fetal DNA testing at 16 weeks should be offered to women who are RhD negative
    - The health professional who has requested the blood tests is responsible for checking the results and identifying if a woman is RhD negative with a RhD positive fetus and suitable for anti-D prophylaxis
    - Women who are found to be RhD negative and have not been sensitised will also be identified by the HICSS system / results on Equest. An information leaflet for the woman is available. Verbal consent for administration of prophylactic anti-D should be taken at the next antenatal appointment and arrangements made for antenatal assessments at 28 (for repeat antibody screen) and 30 weeks (for anti-D administration). A record of the consent process and the woman's choice should be entered in the woman's notes (and recorded on the HICSS system if possible)
    - RhD negative non-sensitised women whose baby is RhD positive should have repeat antibody testing at 28 weeks PRIOR to the administration of 1500iu anti-D immunoglobulin at 30 weeks as described in the patient group directive
    - If repeat blood samples are taken for antibody testing following the administration of anti-D, the request form should clearly indicate when the anti-D was given

5. Administration of anti-D following sensitising event

5.1. Anti-D should be given to RhD negative non-sensitised women whose fetus is known to be RhD positive or the fetal group is unknown following any sensitising event in pregnancy. The following are potentially sensitising events:

- Vaginal bleeding:
    - In pregnancies less than 12 weeks, anti-D prophylaxis is only indicated following ectopic pregnancy, molar pregnancy, therapeutic termination of pregnancy, and in cases of uterine bleeding where this is repeated, heavy or associated with abdominal pain.
    - ≥12 weeks **any** bleeding

- Spontaneous miscarriage after 12 weeks gestation
- Surgical evacuation of retained products of conception (any gestation)

- Ectopic pregnancy
- Termination of pregnancy at any gestation (medical or surgical)
- Any invasive prenatal diagnosis procedures e.g. CVS, amniocentesis, cordocentesis
- Other intrauterine procedures such as insertion of shunts, embryo reduction
- External cephalic version
- Antepartum haemorrhage (any)
- Any blunt trauma to abdomen
- Birth
- Intrauterine death

5.2. Anti-D should be given to all such RhD negative non-sensitised women within 72 hours of sensitising events, preferably within 24 hours. It may have some protective value up to 9 – 10 days after a possible sensitising event and therefore later administration is still recommended.

5.3. Following a sensitising event anti-D should be given to all mothers who are RhD negative **unless**:

- They have been demonstrated to have an RhD negative fetus or baby.
- The woman is known to be sensitised and therefore already has anti-D antibodies present.
- The woman declines.

N.B. Women who have **recently been given anti-D** may have very low levels of antibody detectable in their blood. These women are probably not sensitised and are therefore likely to require anti-D with any subsequent sensitising event. It is strongly recommended that a Kleihauer result should be used as a guide in these cases. It is advisable if there is any uncertainty that anti-D should be given.

5.4. Dose following sensitising event:

- < 20 weeks - 1500 IU anti-D IM into the deltoid muscle (preferable to gluteal region to avoid delayed absorption)

- >20 weeks - 1500 IU anti-D IM into the deltoid muscle **after Kleihauer estimation** to establish size of feto-maternal haemorrhage (FMH). Additional anti-D will be required if the FMH is greater than 12ml of red cells and following discussion with the blood transfusion department (SGH ext 6464).

5.5. Recurrent antenatal bleeding

Where bleeding continues intermittently after 12 weeks gestation, anti-D should be given at 6 weekly intervals and a Kleihauer checked regularly after every new episode of bleeding (4 ml sample taken into EDTA (purple top) and labelled at time of taking blood).

6. Postnatal administration of anti-D

6.1. **If the fetus has been shown to be RhD negative** from antenatal testing, a confirmatory cord blood sample should be sent to exclude the small chance of a false negatve result.

6.2. **If the fetus has been shown to be RhD positive** from antenatal testing, no further cord blood samples are required and anti- D can be given without delay.

Maternal blood should be taken after birth for FMH determination (Kleihauer test). Blood should be collected after sufficient time has elapsed for any FMH to be dispersed in the maternal circulation (30-60 minutes) but before 2 hours have elapsed (4 ml and 7ml sample taken into EDTA (purple top) and labelled at time of taking blood).

6.3. **If the fetal group has not been determined during pregnancy** cord blood should be taken at birth to determine the blood group of the baby (7 ml EDTA (purple top) bottle to be used and labelled at time of taking blood). Following the birth of a RhD positive baby at least 1500 iu anti-D IM should be given.

Maternal blood should be taken after birth for FMH determination (Kleihauer test and confirmation of blood group). Blood should be collected after sufficient time has elapsed for any FMH to be dispersed in the maternal circulation (30-60 minutes) but before 2 hours have elapsed (4 ml and 7ml sample taken into EDTA (purple top) and labelled at time of taking blood).

If cord blood is not taken at delivery options to be discussed with parents include:

- They may wish to have anti-D prophylactically rather than have blood taken from the baby.
- Arrange for paediatrician to take blood from the baby if parental verbal consent given.

6.4. Result of Kleihauer should be obtained within 48 hours of birth, not later than 72 hours. If feto-maternal haemorrhage >12mls, an increased dose of anti-D is required following discussion with the relevant consultant team and the transfusion laboratory. (SGH ext 6464)

7. Documentation and storage of anti-D immunoglobulin

Anti-D is only available on a named patient basis and should be ordered from the blood transfusion lab by fax (see appendix a) or phone call.

Timely ordering of anti-D, particularly when women are in established labour, will help reduce any delay in administration.

Once it has been ordered for a particular woman it may be stored in PAH in the `Blood Fridge` close to theatres on D level. It also may be stored in birthing centres/ peripheral units in fridges that are monitored to ensure strict temperature control.

Units that do not have access to suitable fridges should only order anti-D for a single days' use.

MRHA guidelines indicate that NHS Trusts should 'ensure the use of anti-D immunoglobulin follows the same rigorous patient identification, recording and traceability requirements as all other blood products ', hence anti-D is supplied with a black 'flimsy' and a red tag both of which identify the woman for whom the anti-D has been ordered. Part of the red tag and the flimsy should be returned to the blood transfusion laboratory once the dose of anti-D has been given. The peel off part of the red label should be applied to the woman's hand held notes and the administration of anti-D clearly documented

8. Consent

There is no evidence to suggest that antenatal prophylactic anti-D is associated with adverse events that are of consequence for the mother or baby, other than the possibility of blood-borne infection, and procedures are in place to minimise these risks.

However all women who are offered anti-D should be made aware that it is a blood product and verbal consent should be obtained before administering. This particularly concerns women who would prefer not to receive blood products (e.g. Jehovah Witnesses)

Any RhD neg women with a RhD positive fetus (or where the fetal group is unknown) who declines anti-D following a sensitising event and is therefore at risk of acquiring antibodies should be referred to a consultant obstetrician ideally within 72 hours.

Women who decline antenatal prophylactic anti-D at 30 weeks should be reminded of the NICE guidelines and a summary of the discussion documented in the woman's handheld notes.

9. Commercial production of anti-D

These notes below have been produced by the Blood Transfusion Department at UHS.

1. The process of producing anti-D is inherently safe. The method employed in the UK has not been implicated in the transmission of any viral disease.
2. The donors used in the production of anti-D are all accredited donors.
3. Each plasma donation undergoes screening tests to detect the presence of viral contamination.
4. The plasma used in the manufacture of anti-D is sourced from countries that do not have Bovine spongiform encephalopathy (BSE)
5. The final immunoglobulin product undergoes a treatment process to inactivate undetectable or unknown viruses.
6. Out of 5 million units of red cells collected in the UK there was only one incident of transmission of Hepatitis B by transfusion.

10. Roles and Responsibilities

This guideline applies to all clinical staff employed or contracted by University Hospital Southampton (UHS) Foundation Trust who provide care to women. Staff have a responsibility to ensure that they are aware of this guideline and its contents. They should clearly document their rationale if they have not complied with the recommendations detailed in this guideline. It is the responsibility of department managers, consultants, team leaders and education leaders to ensure staff are aware of this guideline.

Staff with specific responsibilities in offering Anti-D to women who are Rh (D) neg include:

- **Early pregnancy unit staff and Gynaecology nurses** are responsible for the care of women having early pregnancy problems including miscarriage
- **Midwives** are responsible for the day to day care of women during pregnancy and after birth.
- **Fetal medicine midwives** provide support for parents whose baby is found to have problems antenatally and who are undergoing invasive prenatal diagnosis

11. Related Trust Policies

'Use of cffDNAto determine fetal RhD status during pregnancy' UHS guideline 2017
Antenatal Booking Guideline UHS
Antenatal Framework Guideline UHS

12. Implementation

The guideline will be displayed on the Staffnet, and sent to the relevant Care Group clinical teams. The team leaders will be expected to cascade to all relevant staff groups. All medical, nursing and midwifery staff caring for women and newborns should have support and training in implementing the contents of the guideline. In addition, the guidelines will be included in local induction programmes for all new staff members.

13. Process for Monitoring Compliance/Effectiveness

The purpose of monitoring is to provide assurance that the agreed approach in the guidance is being followed to ensure we get things right for patients, use resources well and protect our reputation. Our monitoring will therefore be proportionate, achievable and deal with specifics that can be assessed or measured.

Audit results will be circulated and presented at the multidisciplinary audit meetings, identified in the monitoring table. Any areas of non compliance or gaps in assurance that

arise from the monitoring of this guideline will result in an action plan detailing recommendations and proposals to address areas of non compliance and/or embed learning. Monitoring of these plans will be coordinated by the group/committee identified in the monitoring table.

Those responsible for instigating the resulting actions will be identified in the audit meeting minutes and the action plans and results will also reviewed by *Maternity Services Group Meeting.*
The resulting actions will be reviewed or followed up at the subsequent multidisciplinary audit meeting(s).

Key aspects of the procedural document that will be monitored:

Element of Policy to be monitored	**Lead**	**Tool/Method (e.g. audit, review of minutes, records, training etc)**	**Frequency**	**Who will undertake**	**Where results will be reported** (e.g. which group/committee)
Appropriate administration of anti-D	Consultant Nurse in Prenatal Diagnosis	Ascertainment of all Rh (D) neg women within a one month period, and review of electronic and paper patient records	3 yearly, commencing 6 months after validation of the guideline. Last audited in August 2013	Consultant Nurse in Prenatal Diagnosis	W&N Multidisciplinary Audit meeting

(1) State post not person.

Where monitoring identifies deficiencies actions plans will be developed to address them.

14. Arrangements for Review of the Policy

Guideline to be reviewed after three years or sooner as a result of audit findings or as any changes to practice occurs.

15. References

'Use of cffDNAto determine fetal RhD status during pregnancy' UHS guideline 2017

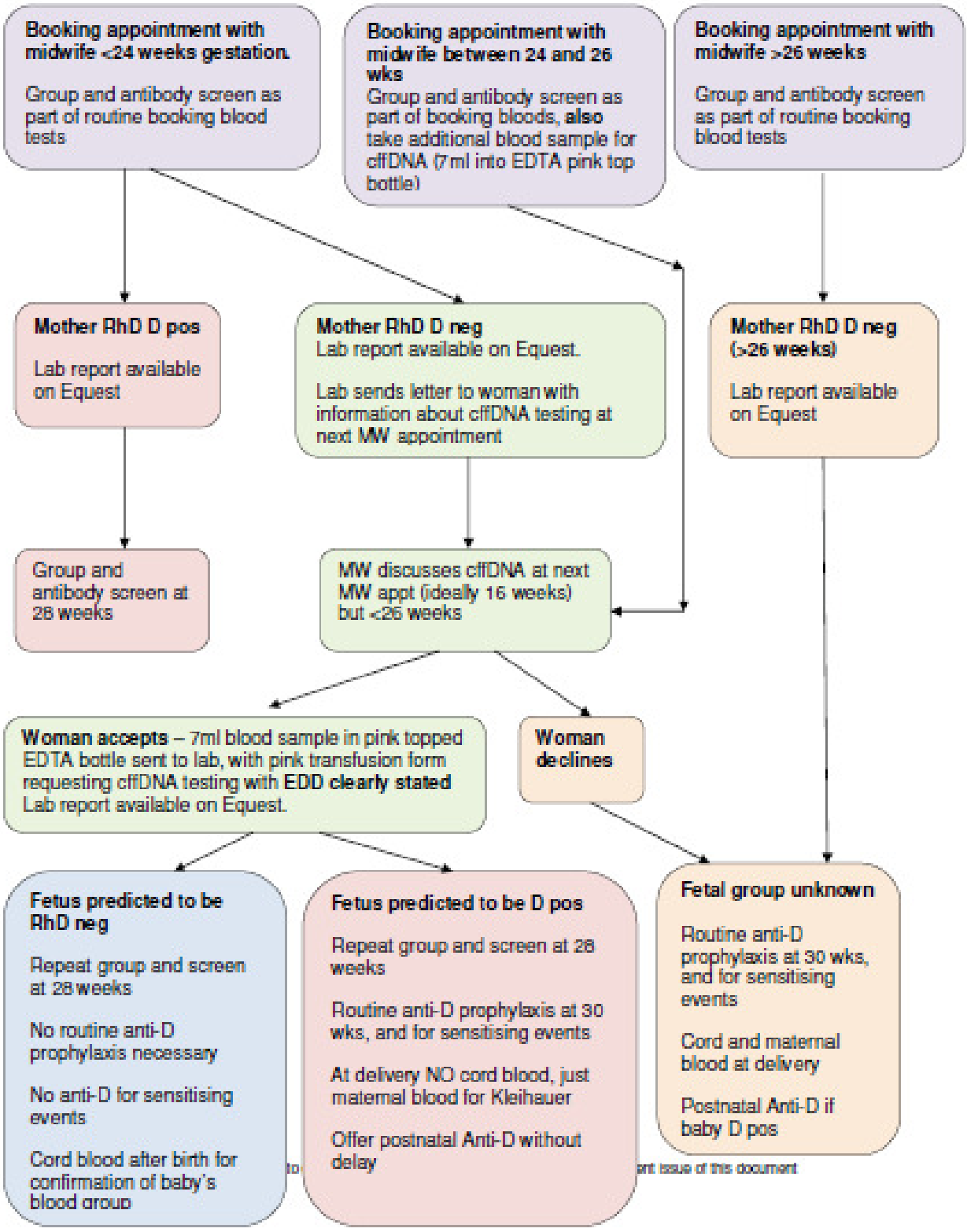
Routine antenatal anti-D prophylaxis for RhD negative women. National Institute for Clinical Excellence. August 2008.

Guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn, British Committee for Standards in Haematology 2013

UHSFT Patient Group Direction for anti-D administration 2012 (via staffnet)

NICE DG High throughput non-invasive prenatal testing for fetal RHD genotype 2016

Flowchart A for cffDNA pathway



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Name of responsible individual:	Peter Wilson – Divisional Clinical Director
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Should this document be made available on the public website?	No
Is this document to be published in any other format?	No

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