



Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive



INSTITUTE OF OBSTETRICIANS
& GYNAECOLOGISTS
ROYAL COLLEGE OF PHYSICIANS OF IRELAND

CLINICAL PRACTICE GUIDELINE

**THE USE OF ANTI-D IMMUNOGLOBIN FOR THE
PREVENTION OF RHD HAEMOLYTIC DISEASE OF THE
NEWBORN**

The Irish Haematology Society,
Institute of Obstetricians and Gynaecologists,
Royal College of Physicians of Ireland
And
Obstetrics and Gynaecology Programme
HSE Directorate for Quality and Clinical Strategy

Version 2.0
Guideline No. 13

Date of publication: June 2012
Revision date: June 2014

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Key Recommendations

1. The RhD negative status of all RhD negative women presenting in pregnancy should be clearly identified in her maternity record and the requirement for Anti-D Ig administration included in her pregnancy care plan.
2. Consideration should be given to the provision of hand-held cards (RhD neg cards) to the woman at booking once identified as being RhD negative.
3. Each hospital where anti-D Ig is used should have an up-to-date standard operating procedure for anti-D administration. This procedure should cover the indications and criteria for anti-D Ig, checking of laboratory results before administration, details of dose and administration, patient consent, verification checks before administration and documentation of anti-D Ig.
4. There should be regular multiprofessional education updates on the use of anti-D Ig for RhD prophylaxis. Documentation accompanying the issue of Anti-D Ig injection should include the following details:
 - a. Identity of the women to include surname, forename, date of birth and hospital medical record number with the date the injection is to be given.
 - b. Identity and address of the antenatal clinic/ ward/ GP surgery / administering the injection.
 - c. Details of the injection will include batch number and strength of dose and route of administration.
5. Verbal or written informed consent should be obtained prior to administration of Anti-D Ig. The woman should be given information on the risks and benefits of anti-D Ig. Information sheets are available from the manufacturer or a hospital may produce their own leaflet based on the template provided (Appendix). If verbal consent is obtained then this should be documented in the woman's file. If the woman declines, this should also be recorded.
6. Before administration of anti-D Ig, two members of staff should verify that the identification details match those on the documentation provided with the injection.
7. The details of the administration of anti-D must be recorded in the antenatal record. It is also important that these details are centrally recorded in the hospital blood bank computer so that this information is readily available should pre-transfusion testing be required.
8. Intramuscular injections are best given into the deltoid muscle to optimise absorption, but can also be given into the gluteus muscle if required.
9. The woman should remain in the hospital for approximately 20 minutes after the administration, in case of an anaphylactic reaction.
10. Regular audits of practice against the current guidelines should be performed in each maternity unit.

1. Purpose and Scope

The purpose of this guideline is to improve the management of women during and after pregnancy whose blood group is Rhesus negative. These guidelines are intended for healthcare professionals, particularly those in training, who are working in HSE-funded obstetric and gynaecological services. They are designed to guide clinical judgement but not replace it. In individual cases a healthcare professional may, after careful consideration, decide not to follow a guideline if it is deemed to be in the best interests of the woman.

2. Background and Introduction

Prior to 1970, haemolytic disease of the newborn (HDN) was a significant cause of perinatal mortality and morbidity due to the development of anti-D antibodies secondary to feto-maternal haemorrhage (FMH) occurring in RhD negative women carrying an RhD positive fetus. The introduction of post-natal immunoprophylaxis and prophylaxis for other sensitising events with anti-D Ig (immunoglobulin) has significantly reduced the deaths due to RhD alloimmunisation and significantly reduced the incidence of seroconversion with anti-D antibodies among RhD negative women (Chown et al, 1996; Tovey and Wagstaff, 1981). Despite these successes, maternal alloimmunisation still occurs in a small proportion of RhD negative women for a number of reasons, including, silent antepartum immunisation, failure to administer or administration of inadequate amounts of anti D following sensitising events (Bowman and Pollock, 1987).

Hitherto, there were no national guidelines for the use of anti-D Ig for RhD prophylaxis in pregnant women attending for antenatal care in the Republic of Ireland. In particular, there is no uniform policy on routine antenatal anti-D prophylaxis (RAADP). Policy documents for many European countries, Australia and North America, have described guidelines, which vary in relation to dosage, schedule of testing and administration of anti-D (Engelfriet et al 2003; RCOG 2012; Fung et al, 2003). The guidelines mainly followed within the Republic of Ireland are those produced by the Joint Working Group of the Royal College of Obstetricians and Gynaecologists and British Blood Transfusion Society and also the British Committee for Standards in Haematology (BCHS 2006; RCOG 2002) which can also be read in conjunction with this guidelines document. Recommendations for the implementation of the RAADP are based on the technological appraisal performed by the National Institute of Clinical Excellence (NICE) in the United Kingdom.

The purpose of this document is to outline a guideline indicative of best practice for the Republic of Ireland, which has been adopted by the Institute of Obstetricians and Gynaecologists and the Irish Haematology Society.

3. Methodology

Medline, EMBASE and Cochrane Database of Systematic Reviews were searched using terms relating to obesity, pregnancy and interventions. Searches were limited to humans and restricted to the titles of English language articles before September

2009. Relevant meta-analyses, systematic reviews, intervention and observational studies were reviewed.

Guideline developed by Dr Joan Fitzgerald, Dr Eibhlin Conneally, Professor John Morrison on behalf of the Irish Anti-D Ig Working Group. The guideline was peer-reviewed by the Institute of Obstetricians and Gynaecologists Clinical Advisory Group.

Abbreviations:

BSCH: British Committee for Standards in Haematology

HDN: Haemolytic Disease of the Newborn

RADDP: Routine Antenatal anti D Prophylaxis

FMH: Fetomaternal Haemorrhage

4. Anti-D Ig Preparations available in the Republic of Ireland

There are currently two Anti D products licensed by the Irish Medicines Board, Rhesonativ® (license issued 30 October 1998) and Rhophylac® (license issued 02 June 2006). Both products are prepared from human plasma obtained from hyper immune donors who have not resided in a country endemic for bovine spongiform encephalopathy (BSE).

Rhesonativ: is available as 625iu and 1250iu vials and is licensed for intramuscular injection only.

Rhophylac: is available as a 1500iu pre-filled syringe. It can be administered either intravenously or intramuscularly.

All anti-D Ig preparations carry a small risk of localised or generalised allergic reactions. Although blood donors are carefully screened for transmissible infections and the anti-D Ig preparations undergo a viral inactivation procedure there is a very low but residual risk of transfusion transmitted infection.

5. General Principles

Anti-D Ig should only be given to women who are not already sensitised or have immune anti-D in their serum. It cannot reverse the immune response once sensitisation has occurred.

Some women who have anti-D Ig administered earlier in the pregnancy for a sensitising event, may have anti-D identified in their serum when their blood is screened at a later date. As it is not possible to differentiate passive from immune anti-D when the antibody level is weak, a woman should be regarded as eligible for anti-D Ig where there is a history of anti-D Ig administration in the previous 8 weeks for a sensitising event or post delivery whatever the case may be.

Anti-D Ig should be given as soon as possible following the sensitising event and always within 72 hours to avoid sensitisation. If however the dose is missed then it

is still advised to give anti-D Ig up to 10 days following the event as there may be some protection afforded (Samson and Mollison, 1975)

RhD negative and women with known partial D variants (e.g. DVI) type are eligible for anti-D Ig. However women who have a weak expression of the RhD antigen 'weak D' positive are not eligible for prophylaxis as these women do not make anti-D on exposure to RhD positive blood.

If a woman confirms that her partner is the biological father and there is documented evidence (blood group report or donor card) that he is RhD negative then anti-D may be omitted.

6. Issue, administration and audit of anti-D immunoglobulin

The EU guide on good manufacturing practice recommends that records are kept to enable traceability of all blood products (including anti-D Ig) from donors to recipients and vice versa (European Commission 2000). Following the 2002 EU Directive on Blood Transfusion and its transposition into Irish Law, traceability systems have been implemented in all hospital blood banks for blood components.

Hospital blood banks should consider taking over the storage and issue of anti-D Ig if they are not doing so already as they have the ability to comply with traceability recommendations and link the information on the provision of anti-D Ig prophylaxis to the woman's blood transfusion laboratory record. Irrespective of the local arrangements, it is essential that steps are taken to ensure traceability of anti-D Ig to recipients and that the hospital blood bank is informed.

Reports from the Irish National Haemovigilance Office and the UK Serious Hazards of Transfusion Scheme show that the most common errors in respect to anti-D Ig administration relate to: administering anti-D Ig to the wrong patient (e.g. RhD positive woman) or inappropriate administration (e.g. baby RhD negative) due to failure to perform the necessary pre administration checks of identity and prescription. Errors involving unnecessary Anti-D Ig administration to women with immune or preformed anti-D, occur due to failure to make the appropriate checks before prescribing anti-D Ig. Of significant concern are the delays or omissions of anti-D Ig which are associated with a lack of knowledge or understanding of the indications for anti-D Ig prophylaxis.

7. Antenatal Administration for Sensitising Events

The following guidance is based on the Royal College of Obstetricians guidelines on anti-D prophylaxis and also the updated BCSH 2006 guidelines. However as the 250iu and 500iu doses preparations of anti-D Ig are not available in Ireland, the dose ranges advised are based on the anti-D Ig preparations currently licensed in Ireland.

Anti-D Ig must be given to RhD negative women without anti-D antibodies as soon as possible following any of the events listed below. Before 20 weeks' gestation

625iu of anti-D is sufficient. After 20 weeks' gestation at least 1000iu anti-D Ig should be given and blood should be taken for the Kleihauer or other similar test to estimate the size of the FMH (see below). The events are as follows:

termination of pregnancy (medical or surgical)
evacuation of the uterus (medical or surgical)
ectopic pregnancy
threatened or complete miscarriage after 12 weeks
antepartum haemorrhage
invasive prenatal procedures, e.g.

- amniocentesis
- chorion villus sampling
- fetal blood sampling
- external version of the fetus
- closed abdominal injury
- intrauterine death
- stillbirth

8. Prophylaxis following fetal loss or threatened miscarriage

8.1 Spontaneous miscarriage

Anti-D is not required if a spontaneous miscarriage occurs before 12 weeks' gestation as long as medical or surgical methods have not been used to evacuate the products of conception. The risk of sensitisation in such circumstances is negligible.

Anti-D Ig should be given to all non-sensitised RhD negative women who have a spontaneous complete or incomplete abortion after 12 weeks of pregnancy. Anti-D Ig should be given to all non-sensitised RhD negative women who have a medical or surgical evacuation of the uterus regardless of gestational age.

8.2 Ectopic pregnancy

Anti-D Ig should be given to all non-sensitised RhD negative women who have a diagnosis of ectopic pregnancy.

8.3 Threatened miscarriage

Anti-D Ig is not routinely recommended for prophylaxis following a threatened miscarriage before 12 weeks of pregnancy. Evidence that women are sensitised after uterine bleeding in the first 12 weeks of pregnancy, where the fetus is alive and the pregnancy continues is scant, though there are rare examples. If, however, bleeding is heavy or repeated and there is associated abdominal pain then anti-D Ig should be given. The period of gestation should be confirmed by ultrasound.

Anti-D Ig should be given to all non-sensitised RhD negative women with a threatened miscarriage after 12 weeks of pregnancy. Where bleeding continues

intermittently after 12 weeks' gestation, anti-D Ig should be repeated at 6-weekly intervals.

8.4 Recurrent Uterine Bleeding after 12 weeks

RhD negative women should be given Anti-D Ig (625iu) at 6 weekly intervals if there is recurrent PV bleeding between 12 and 20 weeks.

Anti-D Ig 1000-1500iu should be given for vaginal bleeding after 20 weeks and repeated at 6 weekly intervals if bleeding is recurrent. A test for FMH must also be performed and repeated at 2 weekly intervals if recurrent bleeding. Additional anti-D Ig will be required if FMH exceeds the volume covered by the dose administered. (See FMH below)

9. Recommendations for Routine Antenatal Prophylaxis

The use of routine antenatal Anti-D prophylaxis (RAADP) is in addition to the administration of anti-D immunoglobulin following a potentially sensitised event. RAADP should be offered to all non-sensitized RhD negative women at 28 weeks gestation as a one-dose regimen. (1500iu). A one-dose regimen is selected, as there is evidence that compliance with the two-dose regimen is less than ideal and there is no data to suggest that the two-dose regimen is superior (Bowman et al 1978; Bowman and Pollock, 1978). The updated National Institute for Clinical Excellence (NICE) recommendations for RAADP in the UK advised that the most cost effective regimen for the treating facility should be adopted.

Information (verbal and written) surrounding the advantages and potential adverse effects of this policy, should be provided to all RhD negative women at their antenatal booking visit. In some circumstances, women may choose not to accept RAADP. Cases when treatment may not be needed are:

- Women who are choosing to be sterilised following delivery.
- Where the father is known to be RhD-negative.
- The woman is sure she will not have another child.

However, it may be difficult for the woman to be certain about these factors and RAADP should be recommended. This should be documented in the hospital chart. The provision of RAADP should not be affected by previous anti-D administration for a sensitising event earlier in the pregnancy.

Anti-D prophylaxis must still be given for any subsequent sensitising events following the administration of RAADP, irrespective of the timing between the RAADP injection and the event. Similarly postpartum anti-D prophylaxis is administered in the event that the woman delivers a RhD positive infant irrespective of the RAADP. Women who miss their appointment for RAADP should be offered an alternative appointment as soon as is possible afterwards, and should the woman decline RAADP, this should be documented in her case notes.

10. Implications of RAADP for Antenatal Serological Testing

The following recommendations are based on the BSCH guidelines for blood grouping and antibody testing in pregnancy.

Routine blood testing for antibodies should be undertaken at booking, and again at 28 weeks gestation prior to RAADP administration.

It is not necessary to wait for the results of the 28 weeks antibody screen before administering the anti-D Ig. If however, the anti-D is detected in the sample, it should be referred for quantification and the woman followed up appropriately.

1. The blood transfusion laboratory must always be informed about the administration of anti-D Ig, to avoid confusion should the woman present at a later stage with anti-D detectable in her serum.
2. Further routine screening of the woman's serum for antibodies in pregnancy should not be performed if the result of the 28 week baseline sample is negative. This is because passive anti-D is detectable for up to 3 months in the maternal circulation following anti-D Ig administration and it is not possible to differentiate between passive and low levels of immune anti-D on testing.
3. If anti-D is detected in a sample referred for a compatibility testing after 28 weeks gestation and there was no anti-D detected in the 28 week sample then the woman should continue to be regarded as eligible for anti-D prophylaxis for any subsequent potentially sensitising antenatal events and postnatal administration.

11. Recommendations for Postnatal Prophylaxis

At delivery a cord blood sample should be taken from all non-sensitised RhD negative women to determine the ABO group and RhD type of the infant.

If the infant is RhD positive (in the absence of routine FMH testing) at least 1250iu of anti-D Ig should be given to every non-sensitised RhD negative woman as soon as possible and within 72 hours of delivery.

It may not be possible to obtain an RhD type of the fetus following an intrauterine death or in the event of delivery of a macerated fetus. In this instance Anti-D Ig should be given to the mother and a Kleihauer test should be performed to exclude a large spontaneous FMH.

Maternal blood should be taken for repeat ABO/D group prior to administration of anti-D Ig and if FMH testing is performed the sample should be taken after a gap of one hour following delivery to allow any FMH to be dispersed in the maternal circulation. A further antibody screen on the maternal sample at delivery is not advised, as it is not possible to identify if the anti-D detected is due to prophylactic administration or provoked immune response.

12. Role of Feto-Maternal Haemorrhage (FMH) Testing/Quantification

The need for testing for FMH is controversial and depends on the volume of FMH being in excess of the volume covered by the standard dose. Hence, the lower the standard post-natal dose of Anti-D administered, the greater the need to quantify FMH.

Practice and recommendations differ between North America, Australia, UK and continental Europe. In the UK and Australia where the recommended standard postnatal dose of anti-D is 500 and 600iu respectively, a test for FMH is recommended routinely. This dose is sufficient to cover up to 4mls of RhD positive fetal cells. If a larger haemorrhage is discovered by FMH testing, the woman is given supplementary anti-D Ig.

However, this differs from the standard doses used in Ireland and most other European countries, where 1250-1500iu is given to all women requiring postnatal anti-D prophylaxis; this approach would appear to make testing for larger episodes of FMH less necessary. The American Association of Blood Banks 1998 standard includes anti-D 1500iu and postpartum screening for FMH for all RhD negative women with RhD positive babies.

Studies have shown that approximately 0.3% of pregnancies are associated with an FMH in excess of 15 mls which would not be covered by 1500iu of anti-D Ig. (Sebrine and Polesky 1990). This means that up to 3 per 1000 RhD negative women could be alloimmunised as a result. However, not all women will mount an immune response to RhD positive blood particularly where there is ABO incompatibility between mother and baby and it is argued the actual rate of sensitisation is likely to be less than 0.07% of deliveries (Fung et al 2003). An alternative approach is to perform an FMH screen only where there is an associated risk factor for large FMH. However, up to 50% of large FMHs (>15mls fetal red cells) occur in women without identifying risk factors (Ness et al 1987). The associated risk factors for a large FMH are:

- Abdominal trauma during the third trimester
- Unexplained hydrops fetalis
- Placental abruption
- Cordocentesis
- External cephalic version
- multiple pregnancies (at delivery)
- stillbirths and intrauterine deaths
- instrumental deliveries and caesarean section
- Manual removal of the placenta

13. Recommendations for FMH Screening/Quantification

Where the standard postpartum dose of anti-D is less than 1250iu, a test for FMH should be employed routinely. Conversely, if FMH testing is routinely performed, the standard post-natal dose could be reduced to 625iu. FMH testing should always

be performed, irrespective of the anti-D Ig dose, where there are associated risk factors for large FMH present.

Where a quantitative test for FMH (see below) shows that the FMH volume exceeds that covered by the administered postnatal dose, then additional anti-D Ig must be given to cover the magnitude of the bleed (125 iu/ml fetal RhD positive cells as per BCSH guidelines or according to the manufacturer's instructions).

If the initial FMH quantitation, performed by a Kleihauer, showed a bleed greater than 2.5mls, the size of the bleed should be reassessed using flow cytometry, which is more accurate for the assessment of large bleeds. Following administration of supplemental Anti-D Ig, a repeat FMH test should be performed to confirm clearance of RhD positive cells from the maternal circulation. The follow-up sample should be performed 48-72 hours later depending on the mode of administration of the anti-D Ig and time required to obtain a result.

As the cost benefit of adopting routine postpartum FMH assessment and using a lesser standard Anti-D Ig dose has not been tested there is insufficient evidence to recommend implementation of routine FMH testing in hospitals where it is not in place.

14. Main tests used to assess the volume of FMH

The Kleihauer Acid Elution Test is the more widely used test, but relies on subjective interpretation. The principle involves the identification of haemoglobin F (HbF) containing cells. Problems with false positive results can occur due to the presence of inherited conditions resulting in elevated levels of HbF in the adult blood.

Although Kleihauer testing provides quantitative results precision is limited to small volumes of transplacental haemorrhage. It is open to interpretation by the laboratory staff performing the test and has resulted in a number of cases of inaccurate results. It is important that procedures for the performance of the Kleihauer should incorporate the published recommendations available to reduce the potential of error/ inaccurate results. For these reasons the Kleihauer is recommended only as a screen for a large FMH and an alternative method (flow cytometry) is advised for quantification of the volume of bleed (Lo et al, 1997).

Flow cytometry uses an antibody directed against RhD positive cells to estimate the size of the bleed. The major advantage of flow cytometry over the Kleihauer test, is that it is more accurate in estimating the size of a large bleed. However, this assay may not be available in all hospitals and would therefore necessitate referral of samples to external laboratories.

Until flow cytometry becomes more widely available the following recommendations must be ensured:

Laboratories undertaking quantitative assessment of FMH by any method must show acceptable performance in internal and external quality assurance schemes and use recommended test methods and optimal staff training programmes to ensure accuracy and reproducibility of results. Results of FMH should be reported in

a format that allows easy calculation of the supplemental dose of Anti-D Ig (expressed in mls of fetal cells).

The term "negative" should be avoided when reporting FMH screens where less than 2mls of fetal cells are counted as it may be interpreted by the clinician that the standard post sensitising event dose of anti-D Ig is not required.

15. Management of anti-D Prophylaxis following the postnatal detection of a large fetomaternal bleed

Additional anti-D Ig should be administered as soon as possible and preferably within 72 hours of the delivery.

The dose administered for anti-D given by the intramuscular route recommended by the RCOG/BBTS and BCSH guideline groups is 125iu/ml of fetal cells counted rounded up to the nearest vial size taking into account the postnatal anti-D dose already given. However, the manufacturers of the intravenous product available in Ireland (Rhophylac) advise 100iu/ml of fetal cells.

Once the total dose exceeds the contents of two intramuscular injections (bleeds > 24ml) intravenous administration is advised.

The maximum dose given within a 24 hour period should be limited to 10000iu. We would also recommend that the maximum single intravenous dose be limited to 4500 iu with the remaining amount administered at 12 hourly intervals. This advice is based on the known risk of haemolysis associated with the high dose of intravenous anti-D Ig regimens used in RhD positive ITP patients.

It is good practice to advise checking the haemoglobin level of the baby. If a large FMH has been identified and the baby does not have the corresponding anaemia then the possibility that chronic FMH has been occurring should be entertained. In this case the women will need to be counselled that she may already have been sensitised antenatally.

16. Implications of Fetal RHD Genotyping

In 1998, Lo and co-workers demonstrated cell-free fetal DNA in plasma and serum from pregnant women (Lo et al 1997). This has led to the development of non-invasive real-time polymerase chain reaction (PCR) assays to determine the fetal RhD during pregnancy. Studies from the United Kingdom, France, The Netherlands and Belgium have reported their experience with these techniques in routine clinical practice (Lo et al 1998; Faas et al 1998; Finning et al, 2004; Rouillac-Le Sciellour et al, 2004; Gautier et al, 2005; Van Der Schoot et al, 2006; Minon et al, 2008). Currently large-scale studies are being conducted where routine antenatal Rh Ig prophylaxis is only offered to RhD negative women carrying an RhD positive infant (Daniels et al, 2006; Legler et al, 2002).

The feasibility of mass testing for the fetal RhD genotype in maternal plasma is highly desirable for ethical and economical reasons as it avoids unnecessary

administration of anti-D Ig to the 40% of RhD negative women bearing RhD negative fetuses. Moreover, these terms are evaluating automated approaches, which allow mass screening and also decrease the assay costs to below the price of anti-D Ig with a high accuracy of fetal RhD prediction. In the Dutch situation, the implementation of this strategy is cost-effective and has facilitated the extension of RAADP (Van der Schoot et al, 2006).

The Irish Anti-D Working Group strongly recommends the development of technology and assessment of the feasibility of mass testing antenatally for fetal blood group by analysis of circulating fetal DNA in maternal plasma in Ireland. If the fetal RhD type could be determined before 28 weeks gestation, RAADP would be necessary only for pregnancies where the fetus was RhD positive.

It is anticipated that such technology will be available in the UK for routine testing of RhD negative women in pregnancy in the future. Pending the development of similar technology in the Republic of Ireland, the possibility of referring samples of Irish RhD negative women to the appropriate laboratory in the UK should be explored.

17. Implementation Strategy

- Distribution of guideline to all members of the Institute and to all maternity units.
- Implementation through HSE Obstetrics and Gynaecology programme local implementation boards.
- Distribution to other interested parties and professional bodies.

18. Key Performance Indicators

To be developed

19. Qualifying Statement

These guidelines have been prepared to promote and facilitate standardisation and consistency of practice using a multidisciplinary approach. Clinical material offered in this guideline does not replace or remove clinical judgement or the professional care and duty necessary for each pregnant woman. Clinical care carried out in accordance with this guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion.
- Advising women of their choices and ensure informed consent is obtained.

- Meeting all legislative requirements and maintaining standards of professional conduct.
- Applying standard precautions and additional precautions, as necessary, when delivering care.
- Documenting all care in accordance with local and mandatory requirements.

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21. Appendix

Information Leaflet: Guidance on the use of routine antenatal anti-D prophylaxis for RhD negative women.

What does RhD negative mean?

The rhesus factor is found in the red blood cells. People who are rhesus positive have a substance known as D antigen on the surface of their red blood cells - they are said to be RhD positive. People who are rhesus negative do not have the D antigen on their blood cells - they are RhD negative. Whether a person is RhD positive or RhD negative is determined by their genes - that is, it is inherited from a parent.

Why does RhD status matter?

RhD status matters if a woman who is RhD negative becomes pregnant with a baby who is RhD positive. This can only happen if the baby's father is RhD positive - but not all children who have an RhD-positive father will be RhD-positive, because the father may have both RhD-positive and RhD- negative genes.

If any of the blood cells from an RhD-positive baby get into the blood of an RhD-negative woman, she will react to the D antigen in the baby's blood as though it is a foreign substance and will produce antibodies. This is not usually dangerous in a first pregnancy, but in later pregnancies the antibodies in the mother's blood can cross the placenta and attack the blood cells of an RhD-positive unborn baby. This can cause 'haemolytic disease of the newborn, which is also known as HDN. HDN can be very mild and only detectable by laboratory tests. But it can be more serious and cause the baby to be stillborn, severely disabled or to die after birth as a result of anaemia (lack of iron in the blood) and jaundice.

Each year in Ireland there are about 5000 births of RhD-positive babies to RhD-negative women. In Ireland about 50 babies develop HDN each year, and must be closely monitored. Each year between 2-5 babies die from HDN. A further 10 children each year will have developmental problems as a result of HDN.

The most common time for a baby's blood cells to get into the mother's blood is at the time of birth. But it can happen at other times, for example during a miscarriage or abortion, or if something happens during the pregnancy such as having an amniocentesis, chorionic villus sampling, vaginal bleeding or external cephalic version (turning the baby head down). An event that could cause the mother to produce antibodies against the D antigen is called a 'potentially sensitising event'.

What is anti-D prophylaxis?

Prophylaxis is the word given to a medicine that is used to prevent something happening. Anti-D prophylaxis means giving anti-D immunoglobulin to prevent a woman producing antibodies against RhD-positive blood cells and so to prevent the development of HDN in an unborn baby. Anti-D immunoglobulin is made from a part of the blood called plasma that is collected from donors. The production of anti-D immunoglobulin is very strictly controlled to ensure that the chance of a known virus being passed from the donor to the person receiving the anti-D immunoglobulin is very low - it has been estimated to be 1 in 10,000 billion doses.

Routine antenatal anti-D prophylaxis (RAADP) is given by injection to pregnant women who are RhD-negative usually at week 28 of their pregnancy. After the birth, a blood sample will be taken to test the baby's blood group. If the baby is RhD positive, a mother who is RhD negative will be given a further injection of anti-D immunoglobulin - this is known as **postnatal anti-D prophylaxis**. If an RhD-negative woman has a potentially sensitising event DURING THE pregnancy she will be offered anti-D prophylaxis at the time of the event: this is known as **antenatal anti-D prophylaxis** or **AADP**.

Occasionally anti-D prophylaxis causes allergic responses in the mother, but these are rare.

Recommendations for RAADP

If you are pregnant and are RhD negative you should be offered RAADP if you have not already been 'sensitised', this means that you have already have antibodies to the D antigen in your blood that can be detected by a blood test at the beginning of your pregnancy.

If you are pregnant and are RhD-negative, your midwife, obstetrician or GP (that is, whoever is responsible for your antenatal care) should discuss RAADP with you and explain the options available so that you can make an informed choice about treatment. The difference between RAADP and AADP should be clearly explained to you.

The healthcare professional should discuss the situations where anti-D prophylaxis would be neither necessary nor cost effective. Such situations might include those where a woman:

- has opted to be sterilised after the birth of the baby
 - is in a stable relationship with the father of the child, and it is certain that the father is RhD negative
 - is certain that she will not have another child after the current pregnancy.
- You should be offered RAADP even if you have already had AADP for a potentially sensitising event earlier in your pregnancy. You should be offered postnatal anti-D prophylaxis whether or not you have had AADP or RAADP.