Rhesus Disease in Pregnancy and the Use of Anti D Immunoglobulin Prophylaxis Guideline

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2	Pending	Obstetric Written Documentation Review Group	12/02/2021	6/10/2021	12/02/2024

Brief Summary of Document:	Rhesus disease in pregnancy
Scope	For health professionals to identify and manage the need for and administration of anti-D immunoglobulins in pregnancy and the postnatal period
To be read in conjunction with:	Rhesus D Prophylaxis, The Use of Anti-D Immunoglobulin for (Green-top Guideline No. 22)Published: 27/04/2011 https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg22/ Routine antenatal anti-D prophylaxis for women w ho are rhesus D negative https://www.nice.org.uk/Guidance/TA156
Patient information	Your Blood Group and Pregnancy. hospital.blood.co.uk/media/29185/inf1665-bloodgroups-and-redcell-antibodies-inpregnancies.pdf Eich grŵp gwaed a beichiogrwyd: hospital.blood.co.uk/media/29185/inf1665-blood-groups-andred-cell-antibodies-inpregnancies.pdf

Owning group	Obstetric Written Documentation Review Group

Reviews and updates		
Version no:	Summary of Amendments:	Date Approved:
1	New guideline	14/9/2017
2	Updated guideline	12/02/21

Glossary of terms

Term	Definition
ADAU	Antenatal Day Assessment Unit
CMW	Community Midwife
HDN	Haemolytic Disease of the Newborn
Ig	Immunoglobulin
IM	Intra Muscular
IU	International Unit
FMH	Feto Maternal Haemorrhage
MLC	Midwife Led Care
Rh D	Rhesus Disease
PV	Per Vagina

Keywords	Rhesus disease pregnancy Anti D Immunoglobulin Prophylaxis

CONTENTS

1. **INTRODUCTION**

Rhesus disease is a cause of due to incompatibility between a rhesus negative parent and a rhesus positive baby. Severity can range from mild foetal anaemia to hydrops fetalis in utero, which can ultimately be fatal. Mortality from RhD sensitisation in the UK has declined significantly since the introduction of routine postnatal anti D prophylaxis in 1969. However there is still significant morbidity and mortality affecting the pregnancies of Rhesus negative women with around 20 to 30 babies dying each year from HDN in England and Wales. Sensitisation usually occurs due to small fetomaternal haemorrhages occurring during pregnancy which go undetected, but may also occur if insufficient anti D is given after delivery.

2. **PREVENTION OF ALLO IMMUNISATION**

- Anti D prophylaxis given to non-sensitised Rh-D negative people following any potentially sensitising event
- Routine Anti D prophylaxis is offered to all non-sensitised pregnant people who are Rh-D negative.
- Postnatal prophylaxis
- All pregnant people should have their blood grouping and antibody screening performed at booking (at 8 to 12 weeks) and once again at 28 weeks. If antibodies are detected, they should be identified and if necessary quantified to assess the likelihood of HDN.
- See table below for frequency of blood monitoring and titre levels

	HDN causing Antibodies	**Action**	**Plan**
ABO or Rhesus Group Antibodies	Anti-bodies present at booking (no past history of HDN)	Quantitate antibody	If anti-D quantitation < 4iu recheck monthly until 28 weeks, then 2 weekly thereafter
ABO or Rhesus Group Antibodies	Anti-bodies present at booking (plus history of HDN)	Quantitate antibody	Refer to specialist centre before 20 weeks or sooner if anti-D quantitation >4iu
ABO or Rhesus Group Antibodies	Antibodies present at 34 weeks	Quantitate antibody	If anti-D quantitation Remains < 4iu re-check 2 weekly
Kell or other non Rh HDN causing antibodies (see Appendix 1)	Any antibodies present	Discuss with Blood Bank and refer to fetal medicine unit UHW	Kell always need Fetal Blood Sampling

3. **ADMINISTRATION OF ANTI-D IMMUNOGLOBULIN**

For successful immunoprophylaxis, Anti-D should be given as soon as possible after **every** sensitising event but **always within 72 hours.** If it is not given within 72 hours, every effort should still be made to administer Anti-D as a dose given within 9 – 10 days may provide some protection.

Intramuscular Anti-D is best given into the deltoid muscle as injections into the gluteal region often only reach the subcutaneous tissues and absorption may be delayed.

Written consent must be obtained prior to administering Anti-D.

Record administration on drug chart, patient's notes and on blood bank administration form.

Dosage

Anti-D 500 iu < 20 weeks (usually given on the gynaecological ward)

Anti-D 500 iu > 20 weeks

Potential Sensitising Events

- Amniocentesis, Chorionic villus biopsy, and cordocentisis
- Antepartum haemorrhage/ Uterine bleeding in pregnancy
- External Cephalic Version.
- Abdominal Trauma (Sharp, blunt, open/closed)
- Ectopic pregnancy.
- Evacuation of Molar pregnancy
- Intrauterine death and stillbirth
- In-utero therapeutic interventions (transfusion, surgery, insertion of shunts, laser)
- Miscarriage, threatened miscarriage.
- Therapeutic termination of pregnancy
- Delivery: normal , instrumental or caesarean
- Intra-operative cell salvage

Kleihauer

To be offered following every sensitising event after 20 weeks gestation (if significant haemorrhage confirmed by kleihauer additional Anti-D to be given as required).

4. **ROUTINE ANTENATAL ANTI-D PROPHYLAXIS**

It is recommended that routine Anti-D prophylaxis is offered to all non-sensitised pregnant women who are Rh-D negative (NICE 2002). However parents can opt out if they:

- Are to be sterilised after childbirth
- In a stable relationship with the baby's parent and they are known to be RhD negative or
- Is certain not to have any further children
- All Rh-D negative people will receive verbal and written information to enable them to make an informed choice

If routine Anti-D is declined it must be documented in the women's pregnancy book.

Appointment sent by ADAU to attend routine Anti-D between 28 – 30 weeks of pregnancy.

Procedure:
Group and antibody screen sample **must be taken prior to** the injection at 28 weeks gestation. (If parent declines anti-D still take the group and antibody screen sample and send to the lab).

If anti-D is identified in the booking sample then further investigations should be undertaken to determine whether this is immune or passive (i.e. previous administration of Anti-D). If no clear conclusion as to the origin of the anti D detected then the parent should continue to be offered anti-D Ig prophylaxis and should continue to be monitored monthly until 28 weeks gestation and fortnightly thereafter.

Single dose 1500 IU (Rhophylac 300) given IM in the deltoid muscle. The parent should remain in ADAU for 20 minutes to ensure no adverse reaction.

Use of routine antenatal anti-D Ig prophylaxis should not be affected by previous anti-D Ig prophylaxis administered for a sensitising event earlier in the same pregnancy.

5. **SENSITISING EVENTS AFTER ROUTINE ANTI-D**

Anti-D must be given after **any event** even if routine prophylaxis has been given.
Kleihauer to be taken if over 20 weeks gestation.

Once Anti-D immunoglobulin has been administered during pregnancy it must be documented on the serology form – date Anti-D was given and documented in the hand held record.

6. **RECURRENT UTERINE BLEEDING**

Rh-D negative prent with recurrent PV bleeding between 12 – 20 weeks gestation should be given 500 iu Anti-D immunoglobulin at a minimum of 6 weekly intervals.

After 20 weeks gestation Anti-D 500 iu should be given at a minimum of 6 weekly intervals. Kleihauer to be carried out at 2 weekly intervals. If FMH > 4mls additional dose of Anti-D given as required.

7. **POST-NATAL PROPHYLAXIS**

A maternal blood sample for Kleihauer to be taken within 2 hours post-delivery accompanied by a cord blood sample. If the baby is Rhesus positive, non-sensitised parent who are RhD

negative should be offered postnatal Anti-D immunoglobulin within 72 hours of delivery. (RCOG 2011).

Homebirths and early discharges from the postnatal ward:

- Delivery suites should review early discharge procedures to avoid omission or late administration of anti-D immunoglobulin
- In cases of early discharge , consideration should be given to administration of anti-D no later than day two of delivery in the community (SHOT 2020)

8. **MANAGEMENT OF BLOOD GROUP IMMUNISATIONS**

1. On detection of any abnormal blood antibodies refer to next Consultant Clinic

2. If partners' genotype unknown – blood sample to be obtained (currently not offered under All wales screening)

3. Paediatric referral form to be sent

4. USS to assess fetal wellbeing and evidence of hydrops

5. If any evidence of hydrops refer immediately to Cardiff

6. Give steroids if evidence of fetal compromise > 24/40 gestation

7. If low level of Anti D detected follow Anti D protocol for serial quantitative assay

8. Refer to UHW if rising titre

9. Non Rhesus D – refer to UHW for further assessment

9. **DECISION FOR DELIVERY OR WHEN IN LABOUR**

(in the presence of unusual/ High antibody titre levels)

Inform: -

1. SCBU
2. Paediatric Department
3. Blood Bank – cross match parent discuss exchange Transfusion

As much notice as possible needs to be given in order to ensure availability of blood for both parent and baby from Blood Transfusion Service.

10. **REFERENCES**

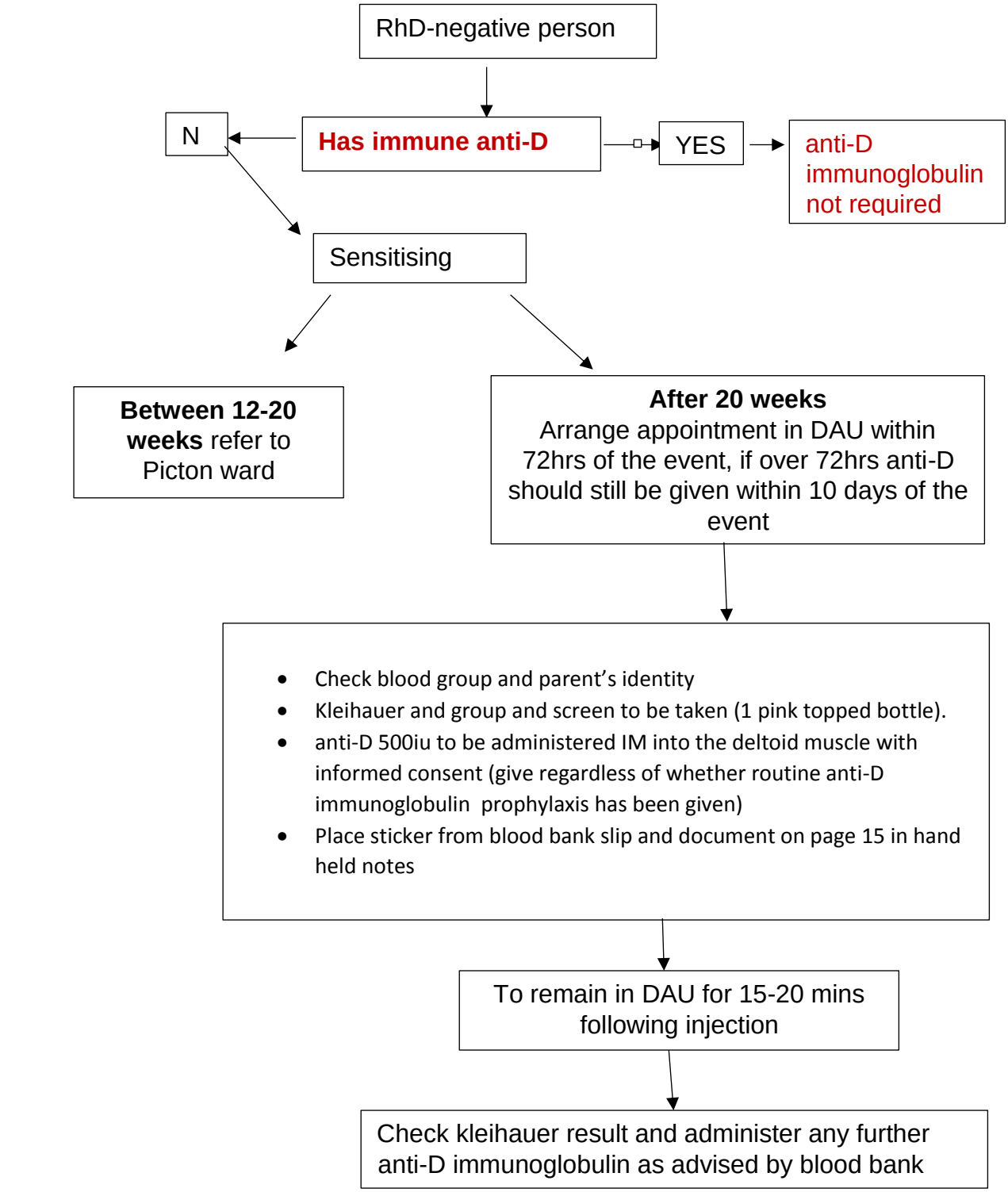
British Committee for Standards in Haematology (BCSH) (2011) guideline on anti-D administration in pregnancy. H Quereshi et al. 92014) BCSH guideline for the use of anti D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn. January 2014.

National Institute for Clinical Excellence (2008) *National Institute for Clinical Excellence* Guidance on the use of Routine Antenatal Anti D Prophylaxis for Rh D Negative Women. August 2008

Serious Hazzards of transfusions 9SHOT) (2020) Summary of Recommendations. Annual report 2019.

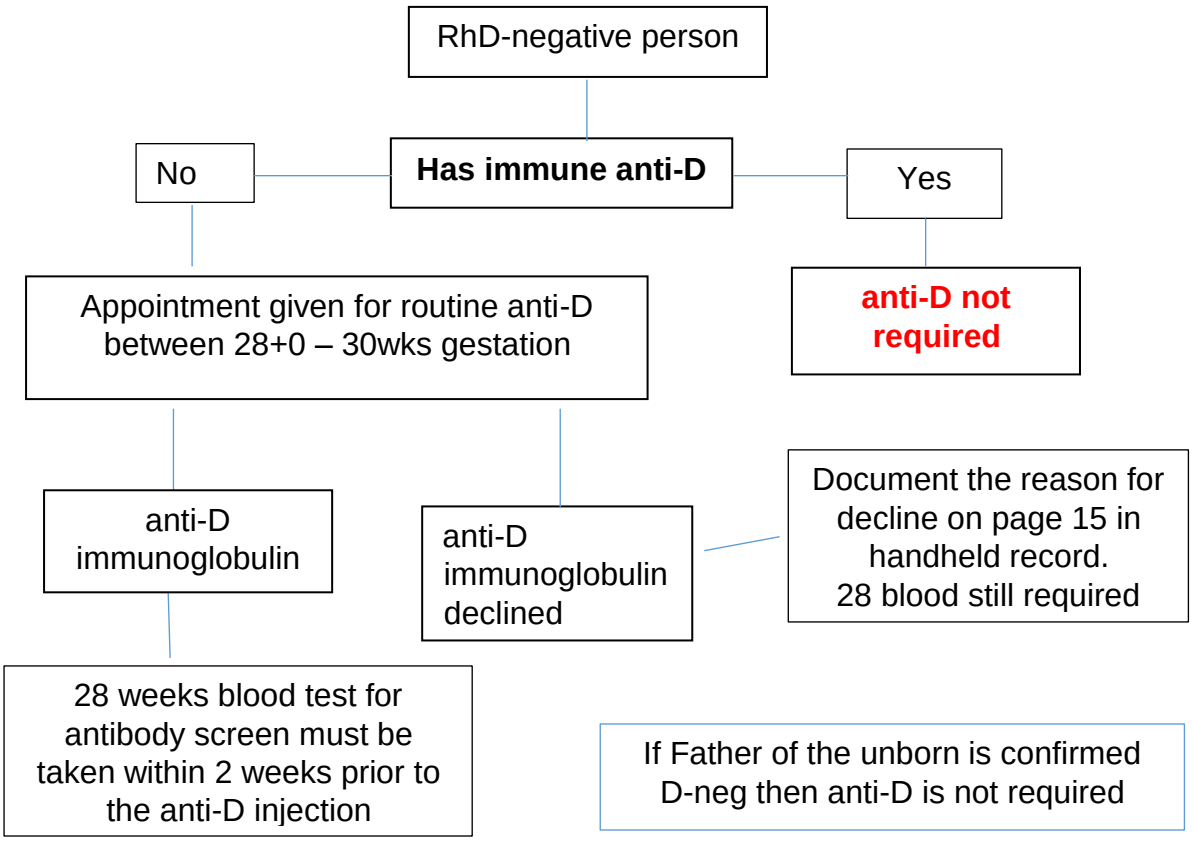
Royal College of Obstetricians and Gynaecology (2011) Royal College of Obstetricians and Gynaecology Green Top Guidelines Use of Anti-D Immunoglobulin for Rh Prophylaxis (22) available from https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg22/

12. FLOWCHART FOR ANTI –D ADMINISTRATION FOLLOWING A POTENTIALLY SENSITISING



Routine antenatal anti-D prophylaxis (RAADP) at 28 weeks must be administered regardless of anti-D that may have been given for potentially sensitising event

13 . FLOW CHART FOR ROUTINE ANTI D PPROPHYLAXISIS



- Check gestation correct
- Take group and screen blood test unless taken within the last 2 weeks (check blood result if taken within 2wks and document result on page 15)
- Check blood group
- Verbal consent obtained
- anti-D 1500iu to be administered IM into the deltoid muscle
- Place sticker from blood bank slip and document on page 15 in handheld notes
- Rhesus negative sticker on handheld notes
- Complete blood bank slip and return to blood bank

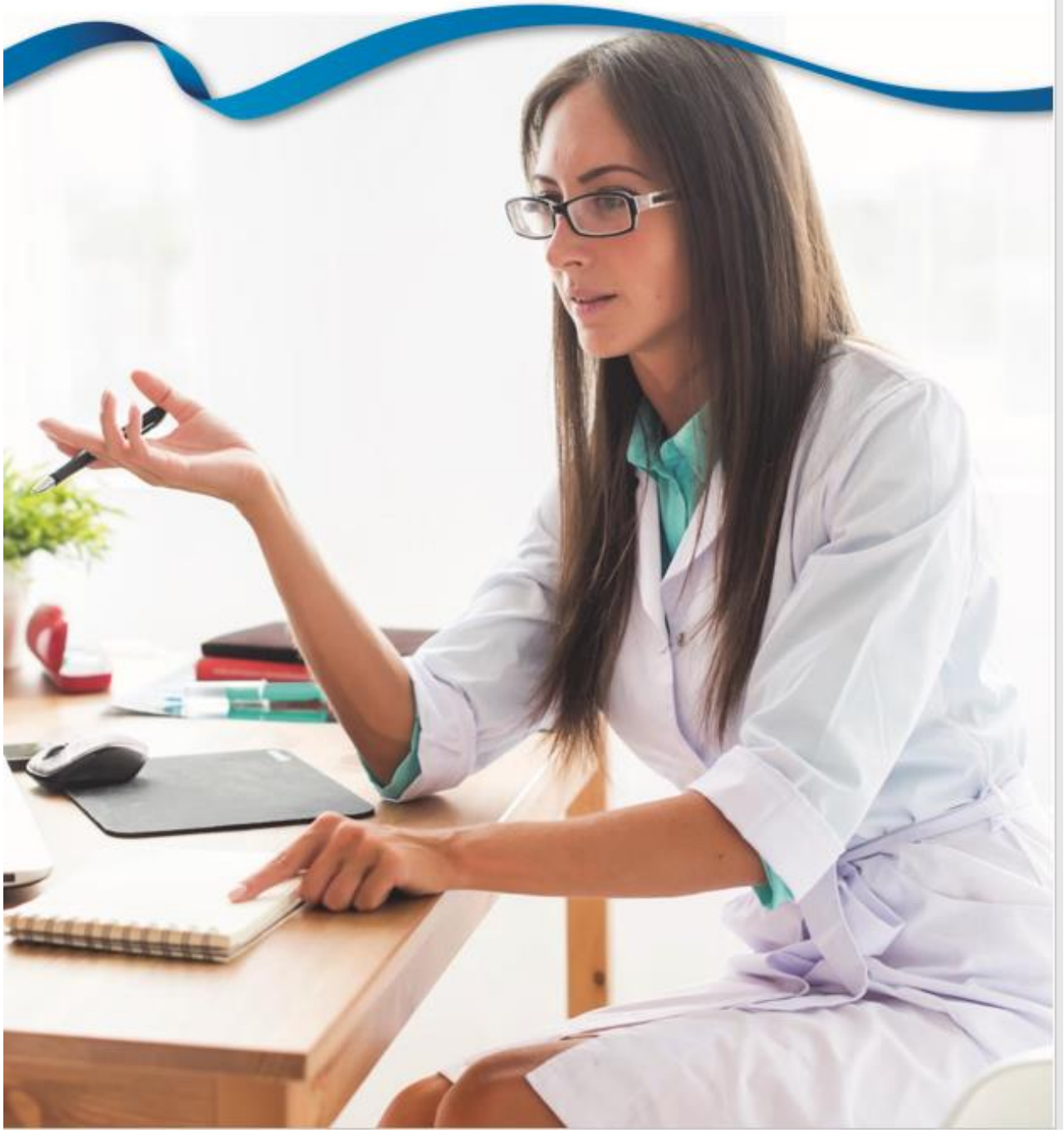
To remain in DAU for 15-20mins following injection
Observe for any reactions

Patient Information Leaflet

GIG CYMRU NHS WALES
Bwrdd Iechyd Hywel Dda Health Board

NHS Blood and Transplant

Protecting women and babies with anti-D Immunoglobulin



Blood Groups

Just as every human being is unique, so are the factors in your blood. People can belong to one of four blood groups, A, B, AB and O, which are substances carried on the red blood cells.

There is another important difference in people's blood called 'rhesus factor', or D-type, which is a substance found on the red blood cells. Blood group and D-type are inherited from both parents.

People who are 'rhesus' positive have what is known as the D antigen on the surface of their red blood cells – they are said to be D-positive.

People who are 'rhesus' negative do not have the D antigen on their blood cells – they are D-negative.

In Europe around 85% of people are D-positive and 15% D-negative.

Why is the 'Rhesus' D-type important in pregnancy?

Unborn babies inherit their blood type from BOTH parents. This is important because pregnant women with D-negative blood can carry babies who have D-positive blood, having inherited the factor from the father.

However it is important to realise that not ALL babies who have Dpositive fathers will have D-positive blood.

Inside the womb, the placenta usually acts as a barrier between the red blood cells of the mother and baby.

However, even in normal pregnancies small amounts of the baby's blood may cross over into the mother's blood stream.

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 termination of pregnancy, or if something happens during the pregnancy such as having an amniocentesis, chorionic villus sampling, vaginal bleeding or after abdominal injury such as following a fall, a blow to the abdomen or trauma from a seat belt.

If any of the blood cells from a D-positive baby get into the blood of a D-negative woman, she recognises the D antigen in the baby's blood as a foreign substance and will produce antibodies to it.

This is called 'sensitisation', and anything that could cause the mother to produce antibodies against the D antigen is called a 'potentially sensitising event'.

As a general rule the first child that triggers this sensitisation does not suffer any adverse consequences, as it will already have been born by the time antibodies have developed.

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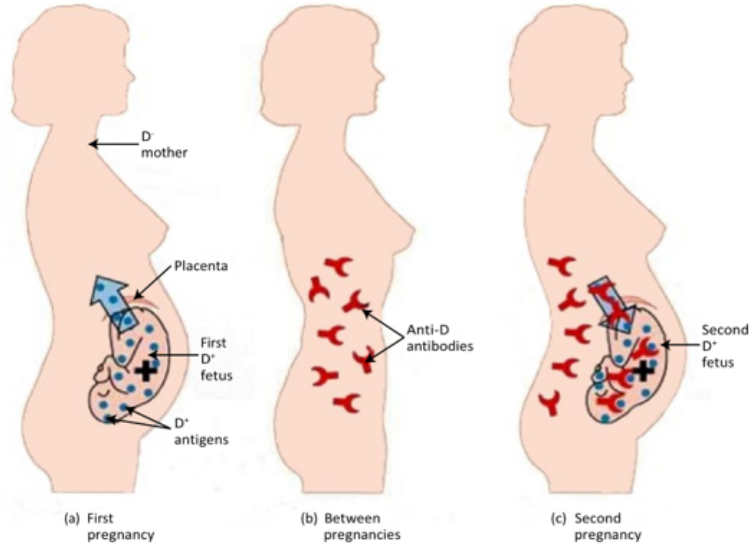
Bwrdd Iechyd Hywel Dda Health Board

However, if the woman becomes pregnant again with a D-positive baby, antibodies may cross into the baby's bloodstream and attack the baby's red blood cells.



This is called 'haemolytic disease of the fetus and newborn' or 'HDFN'.

HDFN can be mild, but if more severe can lead to anaemia, heart failure, jaundice, brain damage, or even to the death of the baby.

With further pregnancies and further D-positive babies the risk of earlier and more severe HDFN increases and the outcomes can be more serious. This is why a preventative measure such as the use of anti-D prophylaxis is so important.

There are about 65,000 births of D-positive babies to D-negative mothers in England and Wales each year and it is estimated that, without routine preventative treatment, there would be over 500 problem pregnancies each year, leading to the deaths of over 30 babies and more than 20 brain damaged children.

Prophylaxis with anti-D immunoglobulin

Prophylaxis means giving a medicine to prevent something happening. Anti-D prophylaxis means giving a medicine called anti-D immunoglobulin to prevent a D-negative woman producing antibodies against D-positive blood cells and so to prevent the development of HDFN in an unborn baby.

Thanks to prophylaxis with anti-D immunoglobulin, sensitisation during pregnancy and after childbirth can now largely be prevented.

Anti-D immunoglobulin is given as an injection, usually into the muscle of the upper arm (intramuscular injection) or sometimes into a blood vein (intravenous injection).

What exactly is anti-D immunoglobulin?

Anti-D immunoglobulin is made from the clear part of the blood, called plasma, and is sourced from countries outside of the UK. As with all blood products donors are screened very carefully and the plasma is treated during manufacture so that the chance of passing on any infection is very low.

Anti-D prophylaxis during pregnancy

a) Potentially Sensitising Events

In the event of potentially sensitising events such as the examples listed below, additional injections of anti-D immunoglobulin may be necessary.

- Impending or actual miscarriage.
- Ectopic pregnancy.
- Termination of pregnancy (abortion).

- Vaginal bleeding.
- Obstetric interventions such as chorionic villus sampling, amniocentesis, or external cephalic version (ECV) in a breech presentation.
- Abdominal injury e.g. after a fall, blow to the abdomen or a traffic accident.

In order to reduce the possible effects of a sensitising event, it is crucial to report any events such as vaginal bleeding or abdominal injury to your midwife or doctor as soon as possible.

b) Routine prophylaxis

Generally, all pregnant women who are D-negative and who have not already been sensitised (those who already have antibodies to the Dantigen) are advised to have prophylaxis with an anti-D immunoglobulin, regardless of whether they have already received anti-D for a sensitising event. This is known as 'routine antenatal antiD prophylaxis', or 'RAADP' and is achieved by:

- a single injection of 1500IU between the 28th and 30th week of pregnancy

Anti-D prophylaxis after childbirth

After birth, your baby's blood group will be tested. If your baby is found to be D-positive, you will receive a further injection of anti-D immunoglobulin, ideally within 3 days of delivery for it to be effective. This is known as 'postnatal prophylaxis'.

If baby's blood group has not been tested, or if there is any doubt as to the result, then you should receive anti-D.

Does every D-negative pregnant woman need prophylaxis? There are certain circumstances when this treatment may not be necessary:

- If you have opted for sterilisation after birth, though it may still be routinely offered.
- If you are certain that the father of the child is D-negative.
- If it is certain you will not have another child after the current pregnancy.
- If your antenatal clinic offers a screening test looking at baby's DNA in your blood that can show whether the baby is D-negative.

What should I do next?

If you are pregnant and have been informed that you are D-negative, the person responsible for delivering your antepartum care (midwife, obstetrician or GP) should discuss anti-D prophylaxis with you and explain the options available so that you can make an informed choice about treatment.

Anti-D prophylaxis following miscarriage, termination of pregnancy or stillbirth

The loss of any pregnancy, for whatever reason, is traumatic for all those involved and there are many competing concerns following such a difficult time.

However it is still important to receive anti-D immunoglobulin, to reduce the risk of sensitisation and problems in following pregnancies. This is the case even where it is not possible to determine the baby's blood group.

Your midwife, nurse or doctor should discuss anti-D prophylaxis with you so that you are able to make an informed choice as to your treatment.

Generally, anti-D prophylaxis is advised for:

- Any women undergoing expectant, surgical or medical management of miscarriage (including molar pregnancy).

- Any woman undergoing expectant, medical or surgical management of ectopic pregnancy.
- Any woman undergoing medical or surgical termination of pregnancy (abortion).
- At diagnosis of intrauterine death and again following delivery of the baby.

Remember – If in doubt, do not be afraid to ASK!

Appendix – Useful addresses and telephone numbers:

Midwife's name: .....

Telephone number: .....

Hospital doctor's name: .....

Telephone number: .....

GP's name: .....

Telephone number: .....

Blood Group: ..... **Antibody Screen:** .....

Date Tested: .....

Date of LMP: ..... **Date for RAADP:** .....

Patient Information Leaflet written by NHSBT Patient Blood Management Team, with acknowledgement to CSL Behring UK Ltd for kind permission to use text from their anti-D leaflet.

Further information may be accessed at: www.nhs.uk/conditions/Rhesus-disease/Pages/Introduction.aspx

NHS Blood and Transplant

NHS Blood and Transplant (NHSBT) saves and improves lives by providing a safe, reliable and efficient supply of blood and associated services to the NHS in England and North Wales. We are the organ donor organisation for the UK and are responsible for matching and allocating donated organs. We rely on thousands of members of the public who voluntarily donate their blood, organs, tissues and stem cells.

For more information Visit
nhsbt.nhs.uk Email
enquiries@nhsbt.nhs.uk Call 0300
123 23 23

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