NHS
Blood and Transplant

HDN awareness

Reducing the impact of haemolytic disease of the (fetus and) newborn

Haemolytic Disease of the Fetus and Newborn (HDFN)

There have been significant medical advances in the prevention of Haemolytic Disease caused by immune anti-D (RhD HDN), together with changes in management which have resulted in improved survival of affected babies.

However, the Serious Hazards of Transfusion (SHOT) UK haemovigilance scheme has highlighted that there are areas where practice could still be improved, in particular around the use of anti-D immunoglobulin in prophylaxis.

This booklet has been produced in response to feedback from midwives wanting a readily accessible resource around this subject.

The series of posters reproduced in this booklet was originally designed as part of the Royal College of Pathologists National Pathology Week in November 2010, as an initiative aimed at raising awareness amongst patients, public and health care professionals around recent advances in prevention and treatment of RhD HDN.

Produced by the NHSBT Patient Blood Management Team, with acknowledgements to NHSBT Appropriate Use of Blood Working Group, who designed the original posters.

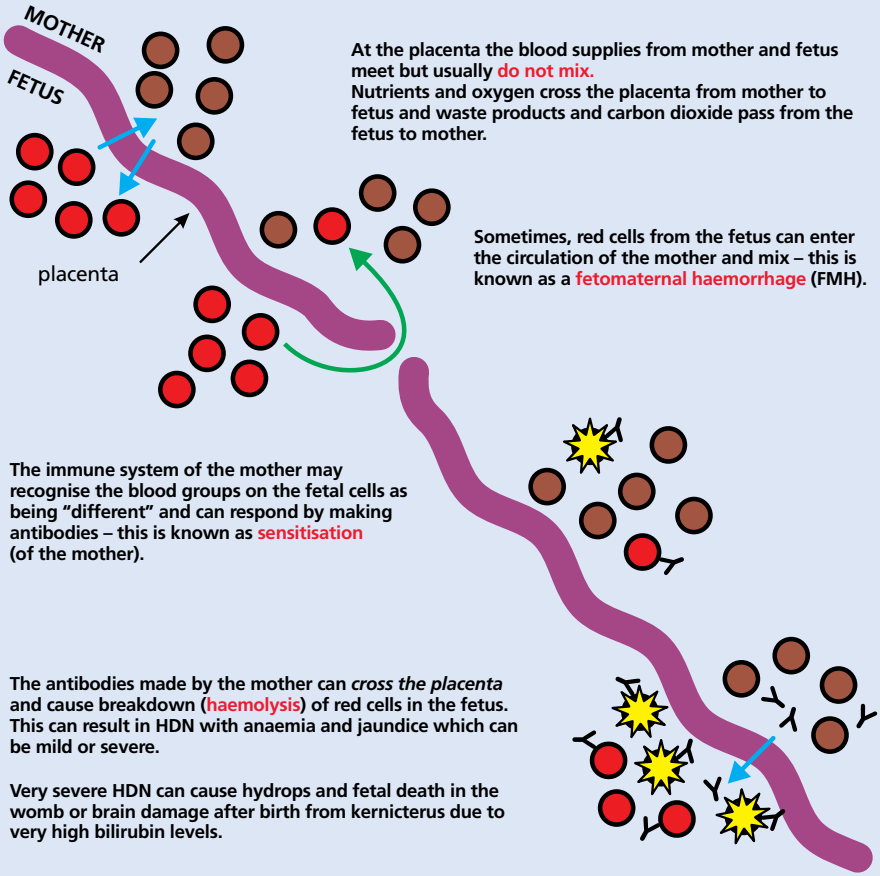
Contents

WHAT IS HDN?

Haemolytic Disease of the Newborn (HDN) occurs when antibodies made by the mother bring about the destruction of red cells in the fetus and/or neonate.

Different Blood Groups

There are lots of different blood groups on our red cells - half of them inherited from our father and half from our mother. Therefore a fetus will have some blood groups which are the same as the mother's and some (inherited from the father) which *could* be different.



At the placenta the blood supplies from mother and fetus meet but usually do not mix.
Nutrients and oxygen cross the placenta from mother to fetus and waste products and carbon dioxide pass from the fetus to mother.

Sometimes, red cells from the fetus can enter the circulation of the mother and mix – this is known as a fetomaternal haemorrhage (FMH).

The immune system of the mother may recognise the blood groups on the fetal cells as being "different" and can respond by making antibodies – this is known as sensitisation (of the mother).

The antibodies made by the mother can *cross the placenta* and cause breakdown (haemolysis) of red cells in the fetus. This can result in HDN with anaemia and jaundice which can be mild or severe.

Very severe HDN can cause hydrops and fetal death in the womb or brain damage after birth from kernicterus due to very high bilirubin levels.

WHICH ANTIBODIES ARE IMPORTANT IN CAUSING HDN?

There are many different blood group antigens on our red cells. Many of these (though not all) can cause HDN. If any fetal red cells (with their antigens) cross the placenta then the mother can form antibodies against an antigen that is different to her own.

RhD is the most important antigen causing HDN.
An RhD negative mother can form immune Anti-D antibodies if she is carrying an RhD positive baby.
She *might* also form antibodies if she receives a blood transfusion.
These immune antibodies can then cause HDN in future pregnancies.

Prevention of RhD HDN
Giving Anti-D to an RhD negative mother after a Potentially Sensitising Event (PSE), as part of Routine Antenatal Anti-D Prophylaxis (RAADP) and post delivery reduces the chances of her forming her own immune Anti-D antibodies (ie becoming sensitised).

Anti-c and Anti-K are also capable of causing severe HDN and must be monitored as carefully as Anti-D.

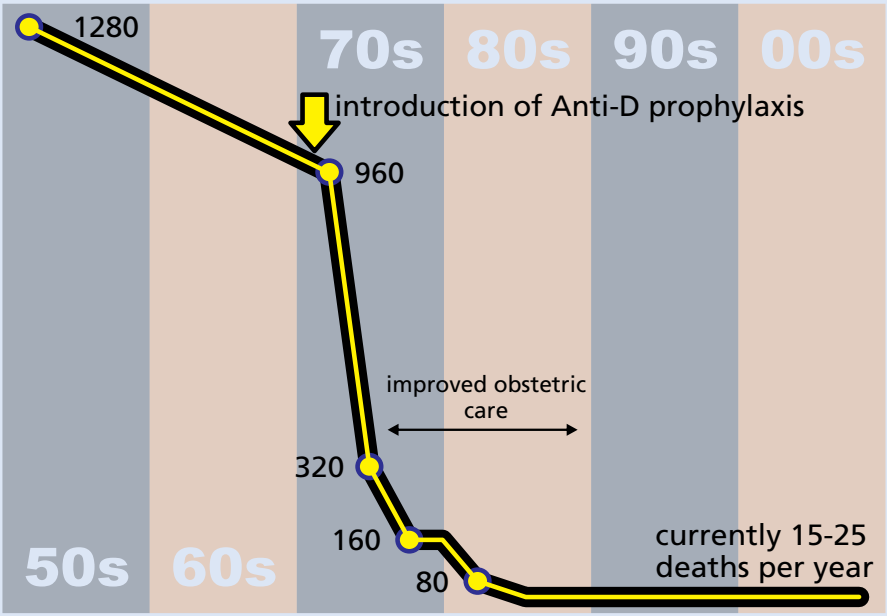
Many other antibodies can cause HDN.

All mothers with immune antibodies must be discussed with a consultant obstetrician and if at risk of HDN must be referred for expert management. Close collaboration is needed between obstetricians, midwives, neonatal teams, haematologists and the transfusion laboratory.

REDUCING THE IMPACT OF HDN

Several advances in the investigation and treatment of HDN have greatly reduced the risk of death from this condition

Neonatal Deaths per Year in the UK



early 1950s exchange transfusion

Replacing baby's blood shortly after birth greatly reduced the risk of death from HDN and brain damage from kernicterus.

mid 1950s early delivery

Delivering babies up to eight weeks early can reduce the impact of haemolysis.

early 1960s amnio-centesis

Testing the amniotic fluid can measure the amount of red cell destruction so that appropriate action can be taken.

late 1960s intra-uterine transfusion

Transfusing the fetus in the womb reduces the impact of anaemia during pregnancy. This can be done from 20 weeks gestation onwards.

early 1970s Anti-D prophylaxis

The introduction of Anti-D prophylaxis greatly reduced maternal sensitisation and HDN in subsequent pregnancies.

POTENTIALLY SENSITISING EVENTS

A potentially sensitising event (PSE) is an event which can cause a fetomaternal haemorrhage (FMH) and can result in a pregnant woman becoming sensitised (making an antibody)

The following events are PSEs:

PV Bleeding; Abdominal Trauma; Miscarriage; Termination of Pregnancy; Diagnosis of Intrauterine Death; Stillbirth; Invasive Antenatal Procedures; Ectopic Pregnancy; External Cephalic Version (attempted & successful); Delivery of RhD Positive Baby

Management of PSE depends on gestation

IMPORTANT!
Different events and the stage of pregnancy when the event occurs has an effect on the dose of Anti-D required
CHECK YOUR PROTOCOLS
for the dose.

ALL births are considered to be potentially sensitising events

Events associated with large FMH:

Manual Removal of Placenta
Stillbirth
Intrauterine Death
Abdominal trauma

ANTI-D: WHEN AND HOW MUCH?

RAADP is given **in addition** to any prophylactic Anti-D given in response to a PSE

– 12 weeks –

– 20 weeks –

– 28 weeks –

– 34 weeks –

— Birth —

Potentially Sensitising Event (PSE) at less than 12 weeks
Anti-D is NOT indicated unless there has been therapeutic termination or a specific clinical request for continuous vaginal bleeding.
Give at least 250iu within 72 hours in these cases.

PSE between 12 and 20 weeks
Give at least 250iu within 72 hours of any sensitising event.

PSE between 20 weeks and delivery
Give at least 500iu Anti-D within 72 hours of a sensitising event. Request a Kleihauer Test in case more Anti-D is needed.

Routine Antenatal Anti-D Prophylaxis (RAADP)

RAADP must be offered to all RhD negative pregnant women.

Send sample for antibody screening and **then** give RAADP either:

*1500iu Anti-D single dose between 28 to 30 weeks or

*500iu Anti-D at 28 weeks and then again at 34 weeks.

IMPORTANT - DOCUMENTATION
It is essential to have a clear record of all mothers who receive Anti-D prophylaxis.

After delivery
Send mother and cord samples for testing.
Give at least 500iu Anti-D within 72 hours of birth where baby is RhD positive.
Give further Anti-D if needed based on the Kleihauer Test result.

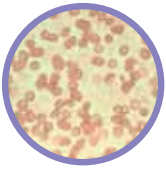
MEASURING FMH IN RhD NEGATIVE WOMEN

A Fetomaternal Haemorrhage (FMH) occurs when blood from the fetus crosses the placenta and enters the bloodstream of the mother.
Prophylactic Anti-D can be given to the mother to prevent her making her own Anti-D antibodies.
Standard doses of Anti-D must be given after a PSE/birth.
We need to measure the size of the FMH to determine if additional doses of Anti-D are required.

When do we need to measure an FMH?

- **Following any potentially sensitising event (PSE) at or after 20 weeks gestation.**
- **Following birth.**

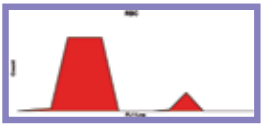
How is the size of a FMH measured?



Method 1: The Kleihauer Test (Acid Elution Test)

A blood film is made and treated so that red cells from the fetus appear deep pink while maternal red cells appear as "ghosts" (virtually colourless). The number of fetal and maternal cells are counted manually under a microscope to calculate the size of the FMH (expressed in ml).

Method 2: Flow Cytometry



If the Kleihauer Test shows an FMH of 2ml or greater, then a more accurate count is performed using Flow Cytometry.
A maternal blood sample is treated with reagents that label only RhD positive cells (fetal cells).
The Flow Cytometer takes a small volume of maternal sample and counts thousands of cells, identifying the labelled (fetal) and unlabelled (maternal) cells. The size of the FMH is then calculated.

Then what?

Following a standard dose of Anti-D after a PSE and delivery, FMH testing helps decide if an **additional** Anti-D dose is needed.
After the additional dose of Anti-D have been given, a further Kleihauer Test is again needed to see if this has been effective or if yet more Anti-D is required.

SENSITISED PREGNANCIES and RhD HDN - CURRENT MANAGEMENT

If the mother has been found to have immune red cell antibodies then she requires close monitoring and *must* be referred to a Consultant Obstetrician.

Close liaison is required between the obstetric, midwifery, neonatal and haematology teams, the hospital transfusion laboratory and specialist laboratory at the Blood Service.

Blood tests

The antibody level must be monitored at four-weekly intervals until 28 weeks and then two-weekly until birth. It is important to determine if the mother has had previous pregnancies affected by HDN.

The father's RhD type may help assess if the baby is at risk of HDN.

It may be possible to test the fetal RhD type using molecular techniques on free fetal DNA (ffDNA) present in a maternal sample.

Assessment and treatment during pregnancy

Invasive tests such as amniocentesis to assess severity of HDN have been replaced by non invasive tests such as Middle Cerebral Artery (MCA) doppler and ultrasound.

If the MCA doppler shows severe anaemia then fetal blood sampling is undertaken followed by an intrauterine blood transfusion if needed.

Assessment and treatment after delivery

Cord blood samples must be taken to check the baby's haemoglobin, bilirubin and Direct Antiglobulin Test (DAT) to check if the baby's red cells are coated with maternal Anti-D antibodies.

If mild HDN then the baby may need phototherapy only to reduce the level of bilirubin in the blood.

If severe HDN then the baby will need exchange transfusion which replaces the baby's blood with transfused blood, removing harmful bilirubin and Anti-D antibody, while at the same time treating the anaemia.

RED CELL ANTIBODIES IN PREGNANCY

Blood Group System	Antibody	Causes Transfusion Reaction?	Causes HDN?	% Blood Compatible
Rh	Anti-D	Probably	Commonly	15
Rh	Anti-c	Probably	Commonly	20
Kell	Anti-K	Probably	Probably	91
Rh	Anti-C	Probably	Possibly	32
Rh	Anti-C^w	Probably	Possibly	98
Rh	Anti-e	Probably	Possibly	2
Rh	Anti-E	Probably	Possibly	71
Kell	Anti-k (Cellano)	Probably	Possibly	0.2
Kell	Anti-Kp^a	Probably	Possibly	98
Duffy	Anti-Fy^a	Probably	Possibly	34
Duffy	Anti-Fy^b	Probably	Possibly	17
Kidd	Anti-Jk^a	Probably	Possibly	23
Kidd	Anti-Jk^b	Probably	Possibly	26
MNS	Anti-s	Probably	Possibly	11
MNS	Anti-S	Probably	Possibly	45
MNS	Anti-U	Probably	Possibly	<0.1
Lutheran	Anti-Lu^b	Probably	Possibly	<0.2
Lewis	Anti-Le^a	Rarely	Unlikely	78
Lewis	Anti-Le^b	Unlikely	Unlikely	28
MNS	Anti-M	Unlikely	Unlikely	22
MNS	Anti-N	Unlikely	Unlikely	28
P	Anti-P1	Unlikely	Unlikely	21
Lutheran	Anti-Lu^a	Unlikely	Unlikely	92

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.

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