IRISH ASSOCIATION FOR EMERGENCY MEDICINE

IAEM Clinical Guideline

The use of anti-D immunoglobulin for the prevention of haemolytic disease of the foetus and newborn secondary to trauma in pregnancy

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Revision History

Date	Version	Section	Summary of changes	Author
01/11/2024	1	All	Final version	ROS, DP

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GLOSSARY OF TERMS

Anti-D Ig	Anti-D Immunoglobulin
BCSH	British Committee for Standards in Haematology
cfDNA	Cell Free Deoxyribonucleic Acid
EDTA	Ethylenediaminetetraacetic Acid
EM	Emergency Medicine
FMH	Foetal Maternal Haemorrhage
HDFN	Haemolytic Disease of the Foetus and Newborn
IM	Intramuscular
IU	International unit
IV	Intravenous
NICE	The National Institute for Health and Care Excellence
RAADP	Routine Antenatal Anti-D Prophylaxis
RBCs	Red Blood Cells
RCOG	Royal College of Obstetricians and Gynaecologists
RhD	Rhesus D

The use of anti-D immunoglobulin for the prevention of haemolytic disease of the foetus and newborn secondary to trauma in pregnancy

INTRODUCTION

The purpose of this guideline is to provide Emergency Medicine (EM) physicians in Ireland with a practical guidance on the use of anti-D Immunoglobulin (Ig) to prevent sensitisation to the Rhesus D (RhD) antigen due to trauma in pregnancy, and in turn, for the prevention of haemolytic disease of the foetus and newborn (HDFN).

This guideline is based on the most recent evidence available. It incorporates the recommendations for trauma patients made by the British Committee for Standards in Haematology (BCSH) guideline which was published in 2013.[1] The BCSH guidelines have replaced the Royal College of Obstetricians and Gynaecologists (RCOG) Green-Top guidelines (2011), National Institute for Health and Care Excellence (NICE) guideline (2008) and Irish Institute of Obstetricians and Gynaecologists Clinical Practice Guidelines (2012).[4-6]

RhD-negative pregnant patients who are exposed to RhD-positive red blood cells (RBCs) from a foetus or neonate are at risk of developing anti-D antibodies (RhD alloimmunisation).[2] Trauma is considered a “sensitising event” and can result in such exposure. When transplacental transfer of maternal antibody occurs, the RhD-positive foetus/neonate is at risk of developing HDFN, which can be associated with serious morbidity and mortality. Outcomes can include hydrops fetalis, thrombocytopenia and neutropenia affecting the newborn.[2]

RhD alloimmunisation can be prevented by the administration of anti-D Ig to females within 72 hours of a sensitising event.[1-3] Once alloimmunisation has occurred, anti -D Ig is no longer effective for preventing or reducing the severity of HDFN in current or future pregnancies.[2] This is why it is imperative to ensure all eligible pregnant patients who are at risk of

sensitisation due to trauma receive anti-D at the appropriate dose and within the appropriate time frame.[1,2]

In addition, women over 20 weeks gestation who require anti-D treatment will also require a foetomaternal haemorrhage (FMH) test (Kleihauer test) to determine the size of FMH and, in turn, to ensure adequate dosing of anti-D.[1,2] If the FMH (Kleihauer) test is positive, early consultation with the obstetric team is imperative. The dose recommended for this group (i.e. women > 20 weeks gestation) is 500 IU of anti-D which will treat up to 4ml of FMH. If >4ml of FMH is detected further anti-D Ig will likely be required to prevent RhD alloimmunisation.[1-3]

Anti-D will be required for other potential sensitising events during pregnancy such as miscarriage, ectopic pregnancy, delivery etc. These potentially sensitising events are outside the scope of this guideline. A comprehensive list of sensitising events is available from the BCSH guidelines.[1] In all cases of potentially sensitising events, we recommend referral to the local obstetric team for further patient management.

PARAMETERS

Target audience:	This guideline is intended for use by EM clinicians managing trauma in pregnant patients.
Patient population:	All pregnant RhD-negative pregnant patients who sustain trauma.
Exclusion criteria:	All pregnant RhD-positive patients. All pregnant RhD-negative patients who sustain trauma less than 12 weeks gestation. All pregnant RhD-negative patients who sustain injury remote from the uterus, for example, isolated distal extremity injury. -Confirmed RhD-negative foetus as deemed using foetal cell free DNA (cfDNA).
Contraindications:	Previous severe hypersensitivity to anti-D administration.

AIMS

To provide an evidence-based guideline on the appropriate use of anti-D Ig in pregnant patients who sustain trauma. This guideline does not cover the appropriate use of anti-D Ig outside the context of trauma.

KEY RECOMMENDATIONS

- **Early consultation**
    - In all circumstances, we recommend early consultation with and/or referral to the local obstetric team for safe management of all patients who sustain trauma during pregnancy.

- **Sensitising events in context of trauma**
    - These include any trauma where abdominal injury was sustained. This includes blunt or sharp, and open or closed injuries to the abdomen or pelvis.
    - Patients who have sustained injuries remote from the uterus only (e.g. isolated distal limb injury) do not need to be considered for anti-D administration.
    - Any injury where a mother may have “banged the bump” should be considered a potentially sensitising event.

- **Blood tests**
    - A maternal blood group and antibody screen should be performed to determine or confirm the RhD group and check for the presence of immune anti-D for all pregnant women regardless of gestational age.
    - An FMH test is required in RhD-negative patients > 20 weeks gestation and should be performed prior to administration of anti-D Ig.

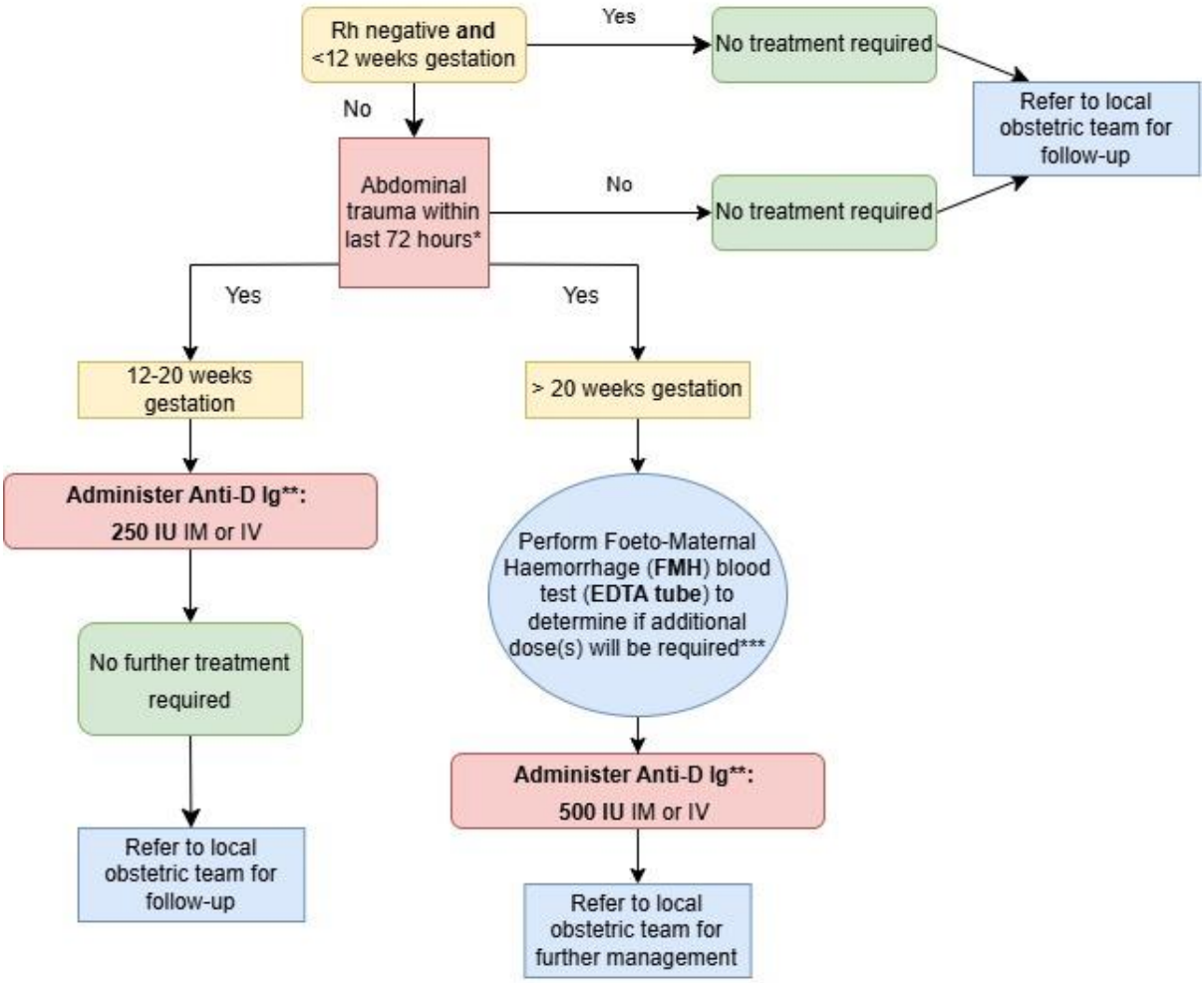
- **Timing of anti-D Ig administration**
    - When indicated, anti-D Ig should be administered as soon as possible and always within 72 hours of the event.
    - Some protection may be offered if anti-D Ig is given up to 10 days after the sensitising event and it is worth considering for all women who present within 10 days of injury.

- **For potentially sensitising events before 12 weeks gestation**
    - Check maternal blood group and screen for antibodies.
    - No treatment with anti-D is required.
    - Refer these patients to the local obstetric service for follow-up and administration of prophylactic anti-D if required.

- **For potentially sensitising events between 12-20 weeks gestation**
    - Check maternal blood group and screen for antibodies .
    - If RhD-negative, a minimum dose of 250 IU should be administered within 72 hours of the event.
    - A test for FMH **is not** required.
    - Referral to the local obstetric service.

- **For potentially sensitising events after 20 weeks gestation**
    - Check maternal blood group and screen for antibodies.
    - If RhD-negative, a minimum anti-D Ig dose of 500 IU should be administered within 72 hours of the event.
    - A test for FMH **is** required **prior** to anti-D Ig administration. It can be requested using an ethylenediaminetetraacetic acid (EDTA) blood sample.
    - These patients should be referred to the local obstetric service for assessment, FMH testing and further anti-D Ig if required.
    - In these women, if FMH >4 mL is detected, follow-up samples are required at 48 hours following an intravenous (IV) dose of anti-D Ig or 72 hours following an intramuscular (IM) dose to check for clearance of foetal cells. This will determine if further anti-D should be administered.

- These key recommendations are also outlined in Figure 1 shown overleaf.



*There is potential for benefit from anti-D Ig if administered within 10 days of trauma and for cases presenting > 72 hours consult with local obstetric services for advice on anti-D administration.
**Consult pharmacy and haematology departments for information on anti-D Ig preparations available locally. Actual dose may vary and be more than clinically necessary.
*** The Foeto-Maternal Haemorrhage (FMH) or Kleihauer test can be sent in an EDTA blood bottle to the haematology lab.

Adapted from BCSH guideline, 2013.

Figure 1: Algorithm for use of anti-D Ig in RhD-negative pregnant patients who experience trauma

SPECIAL CONSIDERATIONS

Antenatal Prophylaxis

All RhD-negative pregnant women who are not sensitised are offered routine antenatal anti-D prophylaxis (RAADP). Patients with potentially sensitising events should be administered anti-D Ig regardless of whether the woman has already received RAADP.[1]

Side Effects

There is no evidence to suggest that anti-D Ig administered to women during pregnancy is harmful to the foetus.[1]

Allergic reactions are very rare but severe hypersensitivity including anaphylaxis may occur. Patients with known antibodies to IgA have a greater risk of developing anaphylaxis.[1] Adrenaline should be available for immediate treatment.

Anti-D Ig is prepared from pooled plasma and therefore there is a small risk of Hepatitis B, Hepatitis C, or HIV transmission. The theoretical risk of transmission of variant Creutzfeldt-Jakob disease is likely to be extremely small.[1]

Anti-D Ig dosing

The doses recommended in this guideline are based on the BCSH guidelines. The actual dose given will depend on the type and size of anti-D Ig preparations available in individual centres and thus may be higher than is clinically necessary. In all cases, discussion with local pharmacy and haematology teams should be sought for dose clarification.

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