14 Adverse Events Related to Anti-D Immunoglobulin (Ig) n=426

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Definition:

An adverse event related to anti-D immunoglobulin (Ig) is defined as related to the prescription, requesting, administration or omission of anti-D Ig which has the potential to cause harm to the mother or fetus immediately or in the future.

Key SHOT messages

- A total of 426 reports related to errors involving anti-D immunoglobulin (Ig) were reviewed in 2017, of which 327/426 (76.8%) related to omission or late administration of anti-D Ig. This is a continuing and worrying trend that is resulting in many women being put at risk of sensitisation to the D antigen
- This year, in addition to poor knowledge about indications and delivery of anti-D Ig, there is also evidence of a lack of knowledge of basic blood group theory. This was demonstrated by the interpretation of cell-free fetal deoxyribonucleic acid (cffDNA) results and the requirements for anti-D Ig based on these results
- It is important that D-negative women understand the importance of reporting potentially sensitising events (PSE) to their midwife or maternity provider, so that they receive appropriate anti-D Ig cover in a timely manner

Recommendations

- All staff involved in the requesting, issuing or administration of anti-D immunoglobulin (Ig) should have received appropriate training and education in relation to anti-D Ig, such as completion of the anti-D Ig module in the Learn Blood Transfusion (LBT) e-learning package (www.learnbloodtransfusion.org.uk)

Action: Hospital Transfusion Laboratories, Hospital Transfusion Committees, Trust/Health Board Chief Executive Officers (CEO), Obstetric Departments, Community Midwifery Teams

- Maternity services should have systems in place to ensure that women who are D-negative are made aware of their results and the importance of attending their midwife for anti-D Ig prophylaxis in the event of having a potentially sensitising event (PSE) from 12/40 onwards
- D-negative women should be educated about what constitutes a PSE so that they are aware of when anti-D Ig may be required

Action: Royal College of Obstetricians and Gynaecologists, Royal College of Midwives

- All healthcare professionals, including laboratory staff, are responsible for ensuring that women who are found to have become sensitised to the D antigen in pregnancy are reported to SHOT with an accurate and complete dataset

Action: Hospital Transfusion Laboratories, Hospital Transfusion Committees, Trust/Health Board Chief Executive Officers (CEOs), Obstetric Departments, Community Midwifery Teams

Good practice point

- Hospital blood transfusion laboratories should have systems in place to identify any anti-D Ig that has been issued for a woman but not collected from the laboratory. The system should include a mechanism to escalate the urgency of the anti-D Ig administration to ensure that it is administered before the 72-hour time limit has elapsed. Although this is a suggested time limit, there is some evidence* that giving anti-D Ig after these limits may offer some protection

**Note: Experimental evidence is quoted (in Klein and Anstee 2005) 'there is evidence that in a proportion of subjects the response to D can be suppressed by giving antibody [anti-D Ig] as late as 2 weeks'. The experimental evidence was from a study by Samson and Mollison following development of anti-D in volunteer male blood donors injected intravenously with 1mL D-positive red cells (Samson and Mollison 1975)*

Learning points

- Hospitals should ensure that there are robust systems in place for the administration of anti-D immunoglobulin (Ig) in a timely manner in response to a potentially sensitising event (PSE). This is particularly important when other departments may be involved in the care of the woman but not directly administer the anti-D Ig (i.e. emergency departments)
- Hospitals should have clear processes developed for the checking of historical blood group records prior to the requesting of anti-D Ig by clinical staff or issue of anti-D Ig by laboratory staff to prevent inappropriate requests and administration
- Where cell-free fetal deoxyribonucleic acid (cffDNA) testing is performed there should be robust systems in place for checking of the results to prevent inappropriate requesting and administration of anti-D Ig when the fetus is predicted to be D-negative

In 2017 two new categories have been introduced to the report for errors related to anti-D Ig

- **Right product right patient**; where women have received anti-D Ig prophylaxis appropriately, with the correct dose at the correct time but where an error related to the issue of anti-D Ig from the blood transfusion laboratory has been noted subsequently, e.g. the transfusion sample tested in the laboratory was inadequately labelled but this error was only noticed following testing of the sample and release of the product
- **Unnecessary administration of anti-D Ig**; where a woman has received a dose of anti-D Ig that was not clinically required as they have not experienced a PSE

Commentary

The 2017 Annual SHOT Report highlights some recurring issues about provision of anti-D Ig. A lack of knowledge and understanding particularly among clinical staff continue to result in women being put at risk of sensitisation.

The many reports of late administration of anti-D Ig illustrate the lack of awareness of the importance of administering anti-D Ig within 72 hours of a PSE by both D-negative women and the clinical staff that manage their care. This requirement should be emphasised to all staff involved in the care of pregnant women and the women identified as being D-negative. There have been cases reported this year where a woman has presented with a PSE and a subsequent appointment for her to receive anti-D Ig has been made for more than 72 hours later.

Figure 14.1: Distribution of anti-D Ig-related error reports

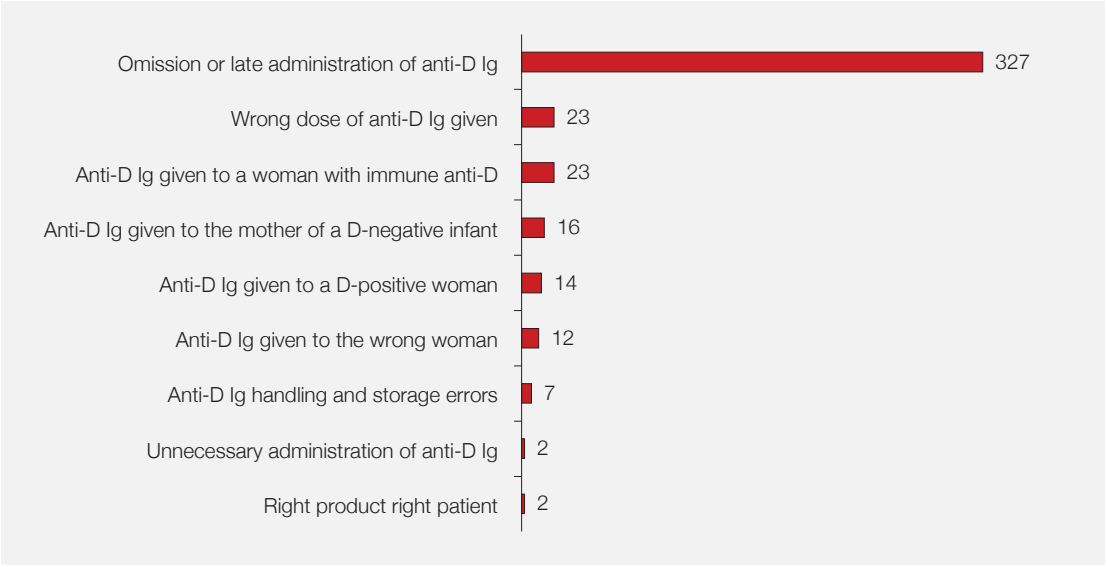
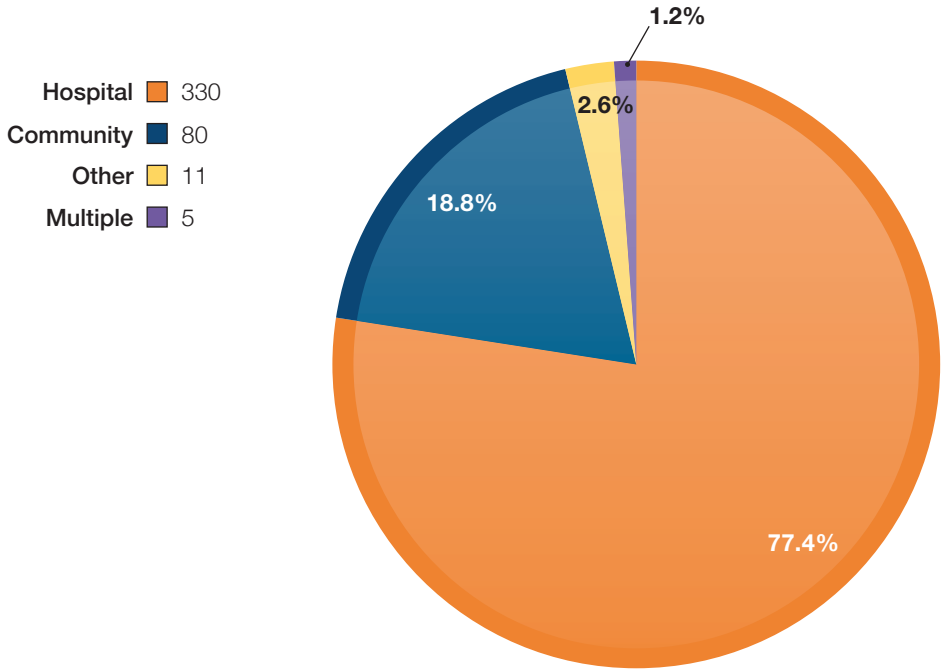


Figure 14.2: Location of errors associated with anti-D Ig n=426



Deaths n=0

No deaths were reported related to errors associated with anti-D Ig in 2017.

Major morbidity n=2

Two women developed immune anti-D. The first resulted from an error in clinical management. This woman delivered at 32/40, no post-delivery blood samples from mother or baby were received in the laboratory and post-delivery anti-D Ig was not issued by the laboratory. Mother and baby were both transferred to another hospital. Immune anti-D was detected in this woman's booking sample for a subsequent pregnancy in 2017.

The second case was not fully investigated in a timely manner therefore putting the baby at an increased risk of developing haemolytic disease of the fetus and newborn (HDFN). This woman had anti-D detected in her sample at 20/40, however this was not investigated by the transfusion laboratory at the time and there was no record of anti-D Ig having been administered to account for it. The woman's 28/40 sample was also found to contain anti-D which was then investigated. The quantification result was 17.1IU/mL, however routine antenatal anti-D prophylaxis (RAADP) had already been administered unnecessarily before this result was available.

Potential for major morbidity n=326

Altogether a total of 327/426 (76.8%) case reports related to the omission or late administration of anti-D Ig. In one of these cases a woman developed an immune anti-D (counted in major morbidity above), but the remainder of the omission or late administration incidents (326) have the potential for the woman to develop an immune anti-D. This is a worrying situation, putting a significant number of women at risk of potential sensitisation to the D antigen.

Overview of cases

Most errors 385/426 (90.4%) occurred during normal working hours. Clinical staff were responsible for 331/426 (77.7%) of the errors reported across all categories with 47/426 (11.0%) involving doctors, including consultants.

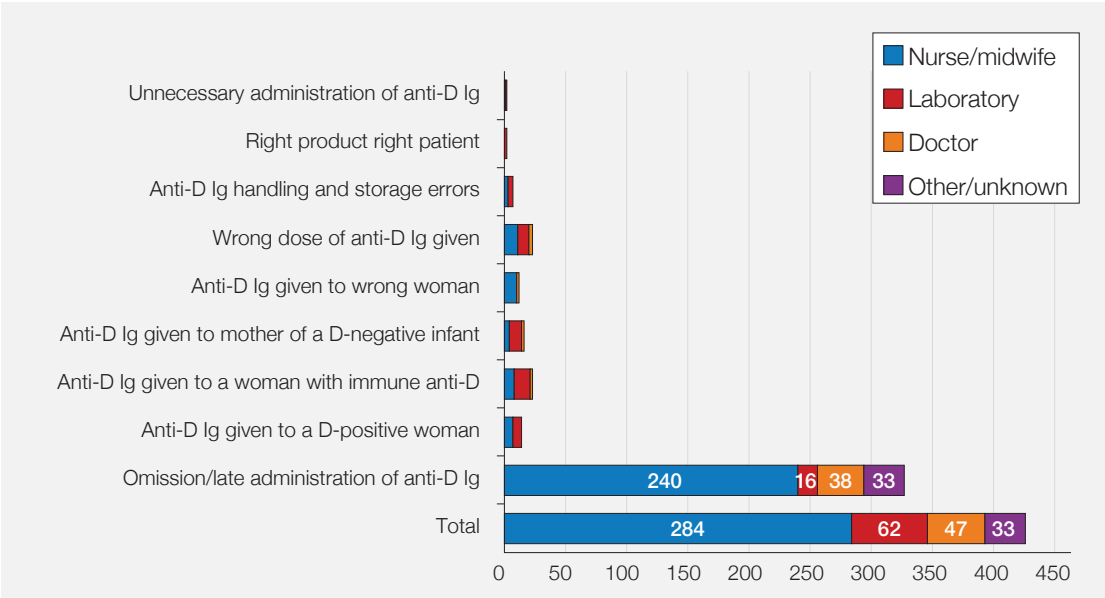


Figure 14.3: Staff group responsible for primary error associated with anti-D Ig by category

Omission or late administration of anti-D Ig n=327 (76.8%)

Most errors associated with the omission or late administration of anti-D Ig occurred in the hospital environment (237/327, 72.5%). However, there were still many errors occurring in the community including at general practitioner (GP) surgeries.

Common themes identified in this category include:

- Failure to administer anti-D Ig within 72 hours following a PSE
- Failure to follow up or check blood group results to determine the need for anti-D Ig
- Failure in the timely collection of anti-D Ig from the laboratory, in particular when women are discharged quickly post delivery
- Communication failures when women have shared care between hospital and community midwifery teams
- Failure to understand the results of cffDNA testing and the requirements for anti-D Ig

Additional case reports illustrating these themes are available in supplementary material on the SHOT website, www.shotuk.org.

Case 14.1: RAADP not given due to erroneous cffDNA testing result

The cffDNA testing predicted a fetus to be D-negative but at delivery the cord sample was shown to be D-positive. RAADP had not been administered during the pregnancy because of the cffDNA result. Further testing revealed that the likely cause of the discrepancy was very low levels of fetal DNA in the maternal plasma, below the limit of detection.

Handling and storage errors related to anti-D Ig n=7 (1.6%)

There were 3 clinical and 4 laboratory errors, all occurred in a hospital environment.

Doses of anti-D Ig should not be split in order to provide 250IU. It is safe to give a larger dose.

Case 14.2: Decanting of anti-D Ig to give a smaller dose than the one in the vial

A woman was due 250IU anti-D Ig, however no 250IU or 500IU vials were available in the laboratory, therefore 1500IU was issued. Clinical staff decanted the pre-filled syringe into a graduated syringe, and gave a third of the amount. This is against the manufacturer's recommendations.

Case 14.3: Decanting of half a vial of anti-D Ig to achieve the recommended dose

250IU anti-D Ig was prescribed following an ectopic pregnancy at less than 20/40 for a D-negative woman. The 250IU dose is no longer supplied by the manufacturer therefore the smallest dose available in the organisation was 500IU. The doctor overseeing the care of the woman noted that 250IU was the correct dose according to the departmental guidelines and the nurse was instructed to draw up half of a 500IU vial issued by the laboratory and administer it to the woman. The nurse did this despite objecting and informing the doctor of the smallest dose of anti-D Ig available.

Anti-D Ig given to D-positive women n=14 (3.3%)

There were 7 clinical staff and 7 laboratory staff errors; 10 in hospital and 4 in the community.

The main theme identified in this category was failure to check the woman's blood group on historical records prior to ordering or issuing anti-D Ig.

There were also 3 reports where the woman's blood group had been confirmed as 'Weak D-positive' however anti-D Ig was still issued by the laboratory.

Anti-D Ig given to a woman with a known immune anti-D n=23 (5.4%)

There were 10 clinical staff and 13 laboratory staff errors; 22 were in hospital and 1 in the community.

The main theme identified in this category was a failure to check historical records by both clinical and laboratory staff.

Case 14.4: Anti-D Ig issued from pharmacy for a woman with immune anti-D

RAADP was administered to a woman at 28/40. However, she was already alloimmunised with an anti-D level of 4.9IU/mL. In this organisation anti-D Ig is currently issued by pharmacy not the blood transfusion laboratory but plans are in place for the blood transfusion laboratory to take over the issue and distribution of anti-D Ig prophylaxis in the near future.

Case 14.5: Historical records not available results in inappropriate administration of anti-D Ig

Anti-D Ig was administered to a patient at 28/40 without checking the historical record of her blood group as her notes were not available at the time. The midwife did not look for the notes, or access them via the electronic report browser. The woman had been provided with an appointment in the 28-week RAADP clinic for blood sampling to determine her known immune anti-D level at 28/40. The woman confirmed that her blood group was D-negative verbally with the midwife and anti-D Ig was given. When the midwife was placing the administration record in the woman's notes once they became available, they realised that the patient had immune anti-D (reported levels between 0.1IU/mL and 0.8IU/mL) and anti-D Ig was not indicated.

Case 14.6: Biomedical scientist (BMS) did not understand notes on the laboratory information management system (LIMS) related to the antibody result

An inexperienced BMS did not understand the significance of the notes against the woman's records on the LIMS. The woman had a complex antenatal history with anti-G being detected as well as anti-D. As a result, anti-D Ig was issued without the BMS seeking advice from a senior member of staff.

Anti-D Ig given to the mother of a D-negative infant n=16 (3.8%)

The majority, 10/16, resulted from BMS errors, 4 from midwife errors and 2 from doctor errors.

The laboratory errors resulted from issue of postnatal anti-D Ig before the infant blood group had been confirmed as D-positive or where the infant's blood group had been incorrectly recorded as D-positive.

For the first time this year there are also reports related to the misinterpretation of or failure to check cffDNA results by clinical staff.

Case 14.7: RAADP given at 29/40 because the midwife failed to check results of cffDNA

A D-negative woman with a predicted D-negative fetus based on cffDNA results was administered 1500IU RAADP anti-D Ig at 29/40 weeks gestation because the midwife failed to check the results of the cffDNA testing.

Case 14.8: Consultant administered anti-D Ig to a D-negative woman despite cffDNA results predicting fetus to be D-negative

Following external cephalic version (ECV) the midwife noted that the woman was D-negative and the fetus was predicted to be D-negative. The midwife informed the consultant obstetrician that there had been a previous case on the postnatal ward where the cffDNA results predicted a D-negative fetus but once born the baby typed as D-positive. Following this information, the consultant telephoned the haematology consultant and discussed the case and was advised 'to do what you think is clinically appropriate'. The consultant decided to give the anti-D Ig.

Anti-D Ig given to the wrong woman n=12 (2.8%)

There were 10 midwife/nurse errors and 2 doctor errors. 11 occurred in hospital and 1 in the community.

The themes identified in this category of reports were:

- Insufficient identification checks of the woman prior to administration of anti-D Ig
- Anti-D Ig administered that was labelled with the details of another woman

Wrong dose of anti-D Ig given n=23 (5.4%)

There were 14 errors by clinical staff, and 9 by laboratory staff.

In 10/23 cases women received less than the recommended dose of anti-D Ig which left them potentially susceptible to sensitisation.

Right product right patient n=2 (0.5%)

Both errors occurred in the laboratory. Anti-D Ig was issued and administered appropriately to women that needed it, however an error was subsequently identified related to inadequate labelling of the blood sample received in the laboratory. In one case the woman's date of birth (DOB) on the sample was incorrect and in the other case the sample had been labelled with the incorrect first name. Had these labelling errors been identified prior to testing, the samples would have been rejected and no blood products would have been issued until further samples had been received.

Unnecessary administration of anti-D Ig n=2 (0.5%)

This category has been introduced to include administration of anti-D Ig where the administration has not been deemed clinically necessary.

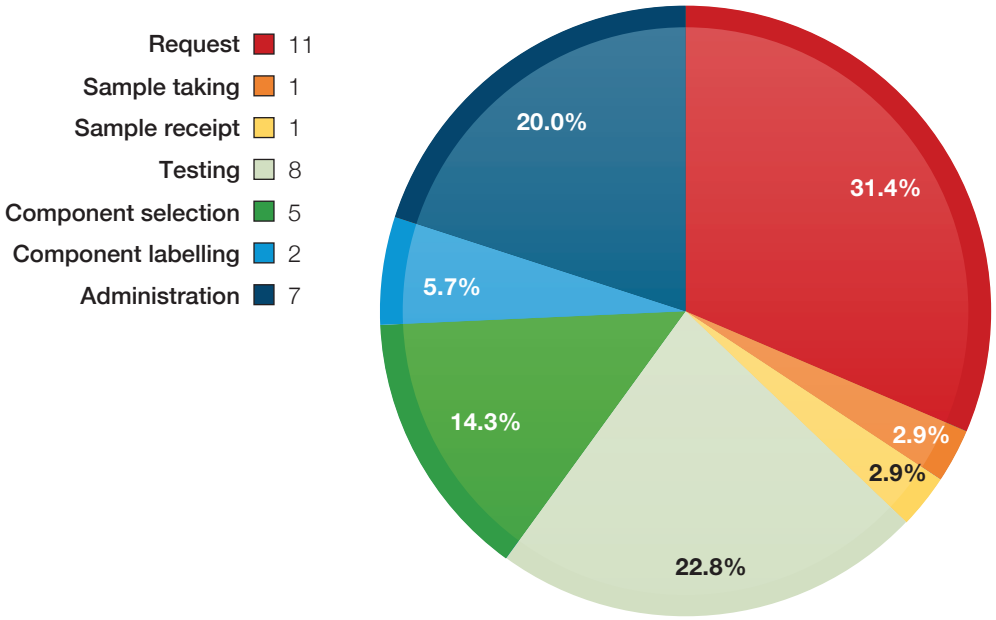
Case 14.9: Request, issue and administration of anti-D Ig unnecessarily

A woman was undergoing an appendectomy at 22/40. The clinical staff on the ward requested a Kleihauer test and the laboratory issued the anti-D Ig as the BMS incorrectly thought that an appendectomy was a PSE. The anti-D Ig was administered to the woman without there being a clinical need for it.

Near miss anti-D Ig cases n=35

The near miss incidents related to anti-D Ig errors show similar learning points to the full incidents.

Figure 14.4: Near misses that could have led to anti-D Ig errors n=35



It is important not to confuse fetal and maternal samples, either because they are wrongly labelled or because maternal blood has been obtained from the placenta. In 2017 there were 35 wrong blood in tube cases associated with maternal and cord/baby samples. The sample should be taken from the cord vessels (fetal blood) and not from the placenta which has maternal blood in the intervillous spaces.

Information technology (IT)-related anti-D Ig cases n=10

There are several examples where the use of IT systems failed to prevent women getting anti-D Ig unnecessarily and perhaps caused omissions or delays in anti-D Ig prophylaxis.

On 2 occasions anti-D Ig was given unnecessarily to a D-positive woman because the LIMS or analyser was not working, and back-up processes were not sufficiently robust.

There were 2 incorrect anti-D Ig administrations: 1 because the wrong DOB was input to the LIMS but not detected at the bedside and the other because a cord blood group report was interpreted incorrectly, manually authorised and transmitted.

There were 4 cases where a woman had an anomalous D group and there was some confusion in how to record the interim D group and then final D group on the LIMS, and to communicate this to the clinical team.

Case 14.10: A string of errors lead to a D-positive (variant) woman getting anti-D Ig

A pregnant woman with an anomalous D group was assigned a D-negative blood group pending reference testing. The reference report confirmed a D-variant and recommended that she should be managed as D-positive. This report was uploaded to her hospital LIMS record, which was in her maiden name. Subsequent tests were performed under her married name and the records were not merged or linked. A midwife used the report of the initial D-negative blood group in the maternity record and allocated the woman to an anti-D Ig prophylaxis regime as well as issuing the patient a D-negative card. Anti-D Ig was given without accessing the updated original record or the correct record in her married name.

Case 14.11: Delayed administration of anti-D Ig to a woman with an anomalous D group

A woman had a surgical termination of pregnancy and the D group was anomalous and referred for further testing. Although she was assigned a D-negative blood group, the laboratory staff were unable to issue anti-D Ig through the LIMS because the initial reference laboratory report stated that she was D-variant and should be treated as D-positive. Subsequently, after genotyping, she was found to have a D-variant associated with some D-sensitisations so the advice was to treat as D-negative for the purposes of anti-D Ig prophylaxis. Anti-D Ig was given but she had to return to hospital following discharge and administration was outside the 72-hour window.

Two women were given anti-D Ig despite having immune anti-D although the information was available on the LIMS and, if consulted, this unnecessary administration would have been prevented. On one occasion the LIMS was down but on the other occasion, the complex presentation of data on the screen was thought to have led to the BMS missing this important information.

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