15 Adverse Events Related to Anti-D Immunoglobulin

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Definition:

An adverse event relating to anti-D Ig is defined as relating 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.

DATA SUMMARY Total number of cases: 313							
Implicated components				**Mortality/morbidity**			
Red cells			0	Deaths due to transfusion			0
FFP			0	Deaths probably/likely due to transfusion			0
Platelets			0	Deaths possibly due to transfusion			0
Cryoprecipitate			0	Major morbidity			4
Granulocytes			0	Potential for major morbidity (Anti-D or K only)			200
Anti-D Ig			313				
Multiple components			0				
Unknown			0				
Gender		**Age**		**Emergency vs. routine and core hours vs. out of core hours**		**Where anti-D Ig administration took place**	
Male	1	≥18 years	305	Emergency	0	Emergency Department	0
Female	312	16 years to <18 years	7	Urgent	9	Theatre	0
Not known	0	1 year to <16 years	1	Routine	304	ITU/NNU/HDU/Recovery	0
		>28 days to <1 year	0	Not known	0	Wards	259
		Birth to ≤28 days	0			Delivery Ward	0
		Not known	0	In core hours	304	Postnatal	0
				Out of core hours	9	Medical Assessment Unit	0
				Not known/Not applicable	0	Community	54
						Outpatient/day unit	0
						Hospice	0
						Antenatal Clinic	0
						Unknown	0

This section describes the main findings from 301 completed questionnaires. Three questionnaires in the 'Handling and Storage Error' category and one in the 'administration to a RhD positive woman' category refer to 16 separate events, so the total number of cases analysed is actually 313.

This continues the upward trend in reporting since SHOT reporting commenced in 1996 (Figure 15.1), and is probably a reflection of an increasing awareness of the need to report rather than a decline in standards of practice.

In addition 26 reports were withdrawn as they did not meet the reporting criteria. Nine reports were moved to the Near Miss chapter (Chapter 6), and 1 report to the Right Blood Right Patient chapter (Chapter 13). Nineteen reports were added from 'near miss', and 2 from 'incorrect blood component transfused'.

The reports are broken down into the reporting categories shown in Table 15.1.

Under current legislation[65], adverse events related to the prescription and administration of anti-D Ig are reportable as 'SHOT-only'. Clinical reactions to anti-D Ig are reportable via the Medicines and Healthcare products Regulatory Agency (MHRA) 'Yellow Card' scheme (www.yellowcard.mhra.gov.uk).

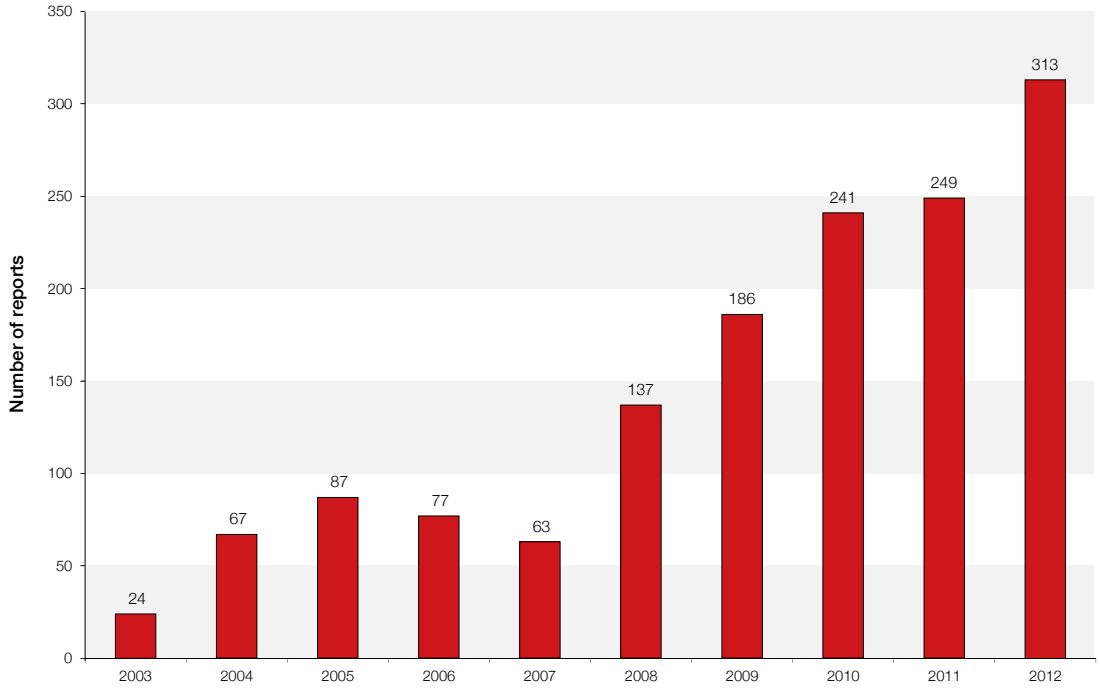

Figure 15.1: Cumulative data for anti-D events 2003-2012

Category of adverse event	Number of cases
Omission or late administration of anti-D immunoglobulin	204
Inappropriate administration of anti-D immunoglobulin	63
To a RhD positive woman	*28*
To a woman with immune anti-D	*20*
Erroneously to a mother of a RhD negative infant	*10*
Given to the wrong woman	*5*
Wrong dose of anti-D Ig given according to local policy	20
Handling and storage errors relating to anti-D Ig	26
Total	**313**

Table 15.1: Reporting categories

Deaths n=0

There was no reported fetal mortality following the omission or delay in administration of anti-D Ig.

Major morbidity n=4

There were 4 cases where a woman developed an immune anti-D following delay or omission in prophylaxis during the current or previous pregnancy.

Potential for major morbidity n=200

In a further 200 cases anti-D Ig was administered more than 72 hours following a potentially sensitising event, or omitted altogether, resulting in the potential for sensitisation of the woman to the D antigen. This satisfies the current SHOT definition of potential major morbidity.

Clinical versus laboratory errors

For the reporting year 2012, 313 events relating to anti-D Ig administration are summarised in Table 15.2 below, with a breakdown of the proportion of clinical and laboratory errors that were primarily responsible.

Table 15.2: Adverse incidents involving anti-D Ig administration, with site of primary error

Type of event	Cases	Number of primary errors		
		Nurse/ midwife	Laboratory	Doctor
Omission or late administration of anti-D Ig	**204**	177	20	7
Anti-D Ig given to RhD positive woman	**28**	16	11	1
Anti-D Ig given to woman with immune anti-D	**20**	6	14	0
Anti-D Ig given to mother of RhD negative infant	**10**	0	10	0
Anti-D given to wrong woman	**5**	5	0	0
Wrong dose of anti-D given	**20**	10	10	0
Anti-D Ig handling & storage errors	**26**	11	15	0
Totals	**313**	**225**	**80**	**8**

This year follows the pattern of 2009-2011 with clinical errors by midwives, nurses and doctors accounting for 233/313 (74.4%), and laboratory errors 80/313 (25.6%) of the total reports relating to prescription, requesting and administration of anti-D Ig.

Omission or late administration of anti-D Ig n=204

In 177/204 (86.8%) cases the primary error was made by a nurse or midwife, and in 7/204 (3.4%) cases by a doctor. In 20/204 (9.8%) cases, the errors originated from failures in the laboratory.

The location was in the community for 38 cases, and in a hospital setting for 166 cases. As in last year's report, there are multiple examples where anti-D Ig has been issued by the laboratory and not collected, or collected only to be found days or weeks later in maternity refrigerators. All 7 cases relating to medical staff involved poor decision making about the need for anti-D Ig which was not in line with national guidance.

Case 1: Poorly phrased communication from the laboratory

The laboratory telephoned results to the clinical area, advising that further anti-D Ig was not required to cover a transplacental haemorrhage of 1.2 mL fetal cells, not realising that the standard postnatal dose had not yet been administered from clinical stock. The message was recorded as 'no anti-D Ig required' and the woman was discharged without receiving any anti-D Ig.

Learning point

- Messages from the laboratory regarding the need for anti-D Ig (or for further investigations) must be clear and unambiguous

Case 2: Student midwife relies on patient to confirm anti-D Ig administration

A student midwife asked a postnatal woman whether she had received her anti-D Ig and the woman confirmed that she had. The administration was confirmed on the electronic patient record and the woman was discharged. The anti-D Ig labelled for the woman was found some days later in the maternity refrigerator, and it transpired that the woman had in fact received an injection of Syntometrine (oxytocin with ergometrine). She was recalled and given her anti-D Ig injection a week late.

Case 3: Poor decision by obstetric registrar when further administration of anti-D Ig was required

A woman presented with a bleed at 34 weeks gestation. She was discharged by the obstetric registrar who told her that no anti-D Ig was required as she had received routine antenatal anti-D Ig prophylaxis (RAADP) at 28 weeks. The woman was concerned and contacted her midwife, who arranged administration of anti-D Ig 5 days post-event.

Case 4: Failure to issue anti-D Ig cover for RhD-incompatible platelets

A 4 year old female child with acute lymphoblastic leukaemia whose group is A RhD negative was issued with RhD positive platelets. The trainee biomedical scientist (BMS) did not issue anti-D Ig as cover, even though it was clearly stated in the laboratory standard operating procedure (SOP) and clinical protocols, thus putting this child at risk of sensitisation to the D antigen and therefore compromising her future childbearing potential.

Inappropriate administration of anti-D n=63

This group is further subdivided into four categories:

1. Anti-D Ig given to RhD positive women n=28

Overall 16/28 (57.1%) errors were made by a nurse or midwife, 1/28 (3.6%) by a doctor, and 11/28 (39.3%) primary errors arose in the laboratory.

- 25/28 (89.3%) errors were made in the hospital setting, with 3 in the community
- 6/17 of the clinical cases involved incorrect transcription of blood grouping results onto notes, care plans and discharge sheets in the clinical area
- 5/11 of the laboratory errors involved failures of manual D-typing
- 6/11 of the laboratory errors involved failure to consult historical information technology (IT) records prior to issue of anti-D Ig

Case 5: Grouping report misread by doctor

A doctor looked at the blood grouping report for a woman on the Early Pregnancy Unit, misread the negative antibody screen as the RhD status, and subsequently prescribed anti-D Ig for a RhD positive woman.

Case 6: Group change following merger of patient records

Two patient records with identical names were merged in the laboratory computer, although one patient was O RhD negative, and the other was B RhD positive. The merged record showed the patient as having blood group O RhD negative, on which basis anti-D Ig was issued. The current sample from the pregnant woman was erroneously rejected as a 'wrong blood in tube' by the laboratory as it grouped as B RhD positive and was discrepant with the blood group on record.

Case 7: Catalogue of errors leads to incorrect administration of anti-D Ig

A woman told her consultant that she was RhD negative, and anti-D Ig was requested on that basis. The biomedical scientist (BMS) issued anti-D Ig even though the laboratory information management system (LIMS) record clearly showed the woman to be RhD positive, and the midwife administered the anti-D Ig, knowing the woman was RhD positive, because the consultant had prescribed it.

2. Anti-D Ig given to women with immune anti-D n=20

Of these 20 cases 6/20 (30%) resulted from a primary clinical error and 14/20 (70%) from a laboratory error.

- The majority,17/20 cases, occurred in the hospital setting, with 3/20 in the community
- Three quarters,15/20 cases, involved failure to check laboratory records or take note of grouping reports before requesting or issuing anti-D Ig

- In 4/20 cases an assumption was made in the laboratory that positive antibody screens were due to residual prophylactic anti-D Ig, even though there was a computer record of the women having immune anti-D in 3 of those cases

Case 8: Erroneous advice from the laboratory to the ward

A woman known to have immune anti-D delivered a clinically unaffected baby. The presence of maternal anti-D was confirmed, and D-typing on the baby gave discrepant results due to a 4+ direct antiglobulin test (due to maternal antibody crossing the placenta). The laboratory sent a fax to the ward indicating that the baby was RhD positive and that the woman required anti-D Ig, which was subsequently administered.

Case 9: Failure to check historical laboratory records and lack of understanding by the midwife

A biomedical scientist (BMS) was busy and failed to check computer records before issuing anti-D Ig for a woman known to have immune anti-D. The midwife assumed that because the laboratory had issued it, it should be given, citing a lack of understanding of the 'science' of anti-D. She also carried out a 'straw poll' of her midwifery colleagues that indicated every one of them would have administered the anti-D Ig because it had been issued by the laboratory.

Case 10: Failure to take heed of laboratory reports

A woman with immune anti-D was being regularly monitored, and the notes contained laboratory reports showing a steadily rising level of anti-D antibody. She presented with a bleed at 27/40 and was inappropriately administered anti-D Ig from stock held in the clinical area.

3. Anti-D Ig given erroneously to mothers of RhD negative infants n=10

All 10 of these errors originated in the laboratory in the hospital setting.

- 2/10 cases involved manual transposition of cord results before telephoning the ward
- 2/10 involved issue of anti-D Ig before cord D-typing was complete
- 3/10 involved issue of anti-D Ig without reference to cord grouping
- 3/10 involved issue of anti-D where the cord group was discrepant due to a positive direct antiglobulin test (DAT)

Case 11: Transposition of cord grouping results

A cord sample grouped as A RhD negative, but the result was transposed on the results sheet with another cord grouped as O RhD positive. Anti-D Ig was issued erroneously to the mother of the A RhD negative baby. The error was discovered in time to issue anti-D Ig within 72 hrs to the mother who had initially been told that she did not require any.

4. Anti-D Ig given to the wrong woman n=5

These were exclusively clinical errors, involving failure by nurses or midwives to identify the correct woman. Of these, 4/5 cases occurred in the hospital, and 1/5 in the community.

Case 12: Misidentification in the antenatal clinic

Routine antenatal anti-D Ig prophylaxis was administered to the wrong woman, when two women with similar 'eastern European-sounding' names were present in clinic at the same time.

Case 13: Misidentification at the GP surgery

Routine antenatal anti-D Ig prophylaxis was administered to the wrong woman, who had the same surname, and ABO group, and was at the same gestation as the intended recipient.

Wrong dose of anti-D given n=20

- 10/20 errors were made by nurses or midwives, and 10/20 errors occurred in the laboratory, 16/20 cases occurred in hospital and 3/20 in the community

- 1/20 involved an incorrect reporting of flow cytometry results as 0 mL by a Blood Service laboratory due to reagent failure

Case 14: Overestimation of transplacental haemorrhage (TPH)

A biomedical scientist (BMS) interpreted a fetomaternal haemorrhage (FMH) (Kleihauer) test as showing a TPH of 39 mL fetal cells, and the woman was administered 5000 IU anti-D Ig. On review by a senior BMS, the TPH was actually <2 mL.

Case 15: Overestimation of transplacental haemorrhage (TPH) due to high levels of haemoglobin F (HbF)

The laboratory reported a TPH of 37 mL fetal cells following a fetal death in utero (FDIU), and issued 6000 IU anti-D, which was administered. Confirmation by flow cytometry indicated a bleed of 0 mL. The woman was a beta thalassaemia carrier and had a raised level (5%) of HbF.

Learning point

- The previous two cases illustrate the difficulties in using the acid-elution (Kleihauer) test to determine transplacental haemorrhage, especially where the situation may be confused by staining of cells due to persistent HbF, and support the case for timely access to flow cytometry methodology

It may of course also be the case that the 37 mL fetal bleed reported in Case 15 represented cells from a RhD negative fetus and the count was accurate. In cases of FDIU, it is unusual to obtain a fetal blood group, and the established principle is to administer anti-D Ig regardless. However in Case 15 significantly more anti-D Ig was administered than was strictly necessary – 6000 IU was given, when a dose of 3700 IU given intravenously would have sufficed (more than covered by 3 x 1500 IU fixed-dose syringes of the IV preparation).

Case 16: Incorrect route of administration results in an inadequate dose

A woman required a large dose of anti-D Ig following a reported transplacental haemorrhage (TPH) of 100 mL fetal cells. Seven 1500 IU vials of anti-D Ig were sourced from another hospital; the dose was calculated assuming they were to be given intravenously (100 IU/mL). Due to unfamiliarity with the particular formulation of anti-D Ig in the receiving hospital, all 7 vials were administered intramuscularly (IM). Not only was this extremely uncomfortable for the woman, but it also resulted in an underdosing by 2000 IU if calculated according to recommendations for IM route of administration (125 IU/mL).

Handling and storage errors related to anti-D n=26

Some errors, 11/26 (42.3%), occurred in the clinical area and 15/26 (57.7%) were laboratory errors. Most, 20 errors, occurred in hospital, and 6 in the community. Expired anti-D Ig was given in 7/26 cases from stock held in the clinical area. The laboratory issued anti-D Ig under the incorrect batch number in 11/26 cases (10 in one incident). Anti-D Ig was stored in a clinical refrigerator that had been out of temperature control for three days in 2/26 cases.

Case 17: Inappropriate administration of anti-D Ig to a male patient

An 84 year old O RhD negative male presented in the emergency department with a gastrointestinal bleed and was given a unit of O RhD positive red cells. The duty biomedical scientist (BMS) issued a dose of anti-D Ig 'in case the patient made immune anti-D'.

Case 18: Expired anti-D Ig administered in the community

Anti-D Ig that had expired two months earlier was administered in the community antenatal setting. On investigation, it transpired that the community clinic had 15 expired doses of anti-D Ig in stock still available for issue.

COMMENTARY

Recurring themes throughout the case reports include:

- Decision making, issuing and administration of anti-D Ig without reference to blood grouping results, in both the laboratory and clinical area
- Manual transcription of blood grouping results onto notes, care plans and discharge sheets in the clinical area
- A lack of understanding of the principles behind anti-D Ig prophylaxis, compounded by availability of uncontrolled anti-D Ig stocks held by clinics
- Failure of inventory management in both laboratory and clinical area, especially in the community setting
- Failure of the post-natal discharge checklist was mentioned in 58 cases this year and early discharge was cited as a reason in many of these
- Poor advice given to women and poor decision making by doctors regarding the need for anti-D Ig following sensitising events
- The misinterpretation of FMH (Kleihauer) tests in hospital laboratories leading to errors in dosing with anti-D Ig

This year's report again highlights a number of key issues in the provision of anti-D Ig, including poor knowledge and understanding in both the laboratory and the clinical area about the use of anti-D Ig, failure to utilise computer management systems (IT) to increase the security of the process, failure to refer to current grouping and antibody screening results, manual transcription of grouping results in the clinical area, and inadequate inventory management.

The use of checklists to improve processes has been described in many different areas of practice, including surgery[66], and to this end SHOT has produced both a flowchart and checklist covering key points in the process that may be used as an aide memoire, poster or as an audit tool, and these may be found at http://www.shotuk.org/resources/current-resources/. They are of necessity generic and hospitals wishing to adapt the resources to better fit their own practice should apply to the SHOT office staff who will arrange a bespoke version including the individual trust logo and version number.

Recommendations

- Current blood grouping and antibody screen results must be referred to when making decisions whether to issue or administer anti-D Ig
- SHOT recommends the use of a flowchart or checklist reflecting national guidance to aid decision making and ensure that an appropriate dose of anti-D Ig is issued and administered
- Cases where a new immune anti-D is discovered at booking, during pregnancy or at delivery should be reported to SHOT by contacting the office (further information in Chapter 3)

Action: Obstetric Departments, Community Midwifery Teams, Hospital Transfusion Teams (HTTs)

Repeated from last year

- Samples which in a FMH (Kleihauer) test suggests a TPH of >2 mL, or gives equivocal results, should be referred for flow cytometry at the earliest opportunity.
- Laboratories performing FMH (Kleihauer) tests must participate in an accredited EQA scheme such as the UK NEQAS FMH external quality assessment scheme

Action: Hospital Transfusion Laboratories, HTTs, Trust/Health Board Chief Executive Officers

Recommendations from previous years are available in the Annual SHOT Report 2012 Supplement located on the SHOT website, www.shotuk.org under SHOT Annual Reports and Summaries, Report, Summary and Supplement 2012.