9. Adverse Events Relating to Anti-D Immunoglobulin

Definition

An adverse event relating to anti-D Ig is defined as an event relating to the prescription, administration or omission of anti-D Ig that has the potential to cause harm to the mother or foetus immediately or in the future.

DATA SUMMARY

Total number of cases	**137**	*Implicated Components*		*Mortality / morbidity*	
		Red cells	**0**	Deaths due to transfusion	**0**
		FFP	**0**	Deaths in which reaction was implicated	**0**
		Platelets	**0**	Potential for major morbidity	**58**
		Other (anti-D Ig)	**137**		
		Unknown	**0**		

Gender		*Age*		*Emergency vs. routine and core hours vs. out of core hours*		*Where transfusion took place*	
Male	**0**	< 18 years	**4**	Emergency		ED	
Female	**137**	< 16 years	**0**	Routine		Theatre	
Unknown	**0**	< 1 year	**0**	Not known	**137**	ITU/NNU/HDU/Recovery	
		< 4 weeks	**0**			Wards	**118**
		unknown		In core hours	**25**	Community	**19**
		Total	**4**	Out of core hours	**7**	Other	
				Not known/applicable	**105**	Not known	

This section describes the main findings from 137 completed questionnaires. The reports are broken down into the reporting categories shown in Table 41. Under current legislation,[1] adverse events related to anti-D immunoglobulin are reportable as 'SHOT only'.

Table 41
Reporting Categories

Category of adverse event	Number of cases
Omission or late administration of anti-D immunoglobulin	58
Inappropriate administration of anti-D immunoglobulin	63
to a D positive patient	*38*
to a patient with immune anti-D	*14*
to a mother of a D negative infant	*6*
given to the wrong patient	*5*
Wrong dose of anti-D immunoglobulin given according to local policy	10
Administration of expired or out of temperature control anti-D Ig	3
Additional laboratory errors	3
administration of a different product instead of anti-D Ig	*1*
clerical error recording batch of anti-D Ig issued	*2*
TOTAL	**137**

Mortality *n* = 0

There was no known foetal mortality following the omission or delay in administration of anti-D, but these data have not been systematically reported or collected.

Major morbidity *n* = 58

In 58 of the 137 cases anti-D was administered late or omitted altogether, resulting in the potential for sensitisation of the patient to the D antigen. This satisfies the current SHOT definition of major morbidity.

In 1 case, sensitisation to the D antigen occurred following failure to administer anti-D (see Case 1 below). A recommendation in the 2007 SHOT report regarded the follow up of potentially sensitised patients, stating that the outcome should be reported to SHOT. This is not yet taking place, and at the present time there is no mechanism for active follow up by the SHOT office of these cases. It is anticipated that this will become possible in future using SHOT's new web-based data collection system.

Clinical versus laboratory errors

For the reporting year 2008, 137 events relating to anti-D immunoglobulin administration are summarised in Table 42 below, with a breakdown of the proportion of clinical and laboratory errors that were primarily responsible.

Table 42
Adverse incidents involving anti-D Ig administration, with site of primary error

Type of event	Cases	Number of Primary Errors		
		Midwife	Laboratory	Doctor
Omission or late administration of anti-D Ig	**58**	50	8	-
Anti-D Ig given to D positive patient	**38**	19	18	1
Anti-D Ig given to patient with immune anti-D	**14**	7	7	-
Anti-D Ig given to mother of D negative infant	**6**	1	5	-
Anti-D given to wrong patient	**5**	5	-	-
Wrong dose of anti-D given	**10**	4	6	-
Anti-D Ig expired or out of temperature control	**3**	3	-	-
Other handling errors – 1 x wrong product given and 2 x clerical error recording batch number issued	**3**	-	3	-
TOTALS	**137**	**89**	**47**	**1**

Of most concern were 58 cases in which administration of anti-D Ig following potentially sensitising events was delayed or omitted, placing the patient at risk of developing an immune anti-D. In 63 cases anti-D was inappropriately administered, resulting in unnecessary exposure to a human blood product.

Omission or late administration of anti-D *n* = 58

In 50/58 cases the primary error was made by a midwife. Five cases occurred in the community, and 53 in a hospital setting. A recurring theme in the review of these incidents is the need for more robust procedures and documentation of anti-D administration as recommended by the Health Service Circular 'Better Blood Transfusion',[10] together with clearer lines of communication and strict adherence to existing protocols.

In 8 cases the primary error was in the transfusion laboratory.

Overall, where anti-D was given late 3 cases occurred in the antenatal setting and 36 postnatally, while in reports where anti-D was omitted altogether 11 were antenatal cases and 8 postnatal.

Clinical error examples *n* = 50

In 1 case, anti-D was never issued because the relevant samples took 12 days to reach the laboratory and the clinical area did not follow up on the requirement for prophylaxis.

In 7 cases, anti-D was correctly issued by the laboratory and collected by the clinical area, but subsequently found in a ward refrigerator up to 10 days after the patient had been discharged.

Laboratory error examples *n* = 8

In 1 case, anti-D was correctly issued to the mother, but the cord results were telephoned to the ward from the laboratory as D negative, and the resulting confusion led to a significant delay in administering the immunoglobulin.

A lone worker BMS omitted issuing anti-D for a postnatal patient owing to pressure of work, and then forgot to tell other staff at shift handover. The outstanding work was picked up 48 hours later, and the anti-D was eventually given outside the 72 hour window.

Case 1

Manual transcription error in the laboratory results in omission of anti-D and D sensitisation

A pregnant patient had bloods taken at booking clinic. The BMS performing ABO and D grouping manually recorded the result as D positive instead of D negative. Consequently routine antenatal anti-D prophylaxis was not administered, nor would anti-D have been considered for any potentially sensitising event the patient may have suffered. This patient was found later in pregnancy to have developed an immune anti-D.

Case 2

Baby with weak D recorded as D negative, resulting in omission of anti-D for the mother

A BMS altered a baby's blood group on the LIMS from 'weak D' to D negative in order to facilitate a request for blood made by the clinical area for the baby. Because the baby's group was now ostensibly D negative, the mother never received anti-D Ig.

Inappropriate administration of anti-D *n* = 63

This group is further subdivided into four categories (see Table 41).

Anti-D Ig given to D positive patients *n* = 38

There were 28/38 cases in the antenatal setting, and 10/38 in postnatal patients.

Overall 20 errors were clinical, 19 made by midwives and 1 by a doctor, and 18 primary errors arose in the laboratory.

Clinical error examples n = 20

In 19/38 of these cases the primary error was made by a midwife, with 15 originating in the community and the other 4 in hospital.

It is striking that all these cases involved issue of anti-D from a remote stock held in the clinical area, or at a GP surgery. A number of the case reviews offered by reporters highlighted the intention to issue anti-D on a named patient basis only following the discovery of the errors, in line with recommendations made in HSC 'Better Blood Transfusion'.[10]

Case 3

Lack of knowledge of when it is appropriate to issue anti-D

Two midwives separately checked the hospital computer system, which clearly showed the patient as D positive, but still proceeded to issue anti-D Ig to the patient from a stock held in the clinical area.

In 2 further cases, anti-D was administered by midwives on the basis of a 'D negative' warning sticker incorrectly affixed to the front of a D positive patient's notes, and in 2 cases anti-D was administered on the basis of an incorrectly transcribed verbal grouping report.

Case 4

Junior doctor gives anti-D without knowledge of patient's blood group

Following a day case gynaecological procedure, a FY2 grade doctor prescribed and administered anti-D immunoglobulin from a clinical stock to a patient, without a blood grouping report being available in the clinical area, and without checking to see what the blood group was. The patient was subsequently reported to be D positive.

Laboratory error examples n = 18

- 3 cases where anti-D was issued incorrectly to a D positive patient by an MLA or a trainee BMS, and in 1 of these cases the incorrect issue was validated by a second BMS.
- 7 cases where the laboratory issued anti-D Ig even though the LIMS clearly showed the patient to be D positive, and in 1 case it was noted that the issue labels also clearly stated the patient was D positive.
- 1 case where anti-D was issued on the basis of an incorrect verbal grouping result from another hospital.
- 1 case where anti-D was issued on the basis of a D-negative result from another hospital, but the patient subsequently tested as weak D by a different methodology in the issuing laboratory.
- 1 case where a BMS incorrectly entered D-typing results onto the LIMS.
- 2 cases where anomalous results from automated testing systems were incorrectly interpreted and edited.
- 2 cases where anti-D was issued on the basis of previous, much older, D negative results, but where the patient tested as weak D using the current sample.
- 1 case where the laboratory made no check at all on grouping records before issuing anti-D by a manual process, assuming the clinical area must have checked the D-type before making the request.

Anti-D Ig given to patients with immune anti-D *n* = 14

Of these 14 reported cases, 7 resulted from a primary clinical error and 7 from a laboratory error; 6/14 cases occurred in the antenatal setting, with 8/14 being reported postnatally.

Clinical errors n = 7

In the 7 clinical cases the primary error was made by a midwife or nurse and in 5 of these cases anti-D was administered from stock held in the clinical area.

In 6/7 of these cases, there was a failure to take note of, or even read, laboratory reports that clearly indicated the patient either already had immune anti-D or required further investigation to resolve a positive antibody screen.

In the last case, the patient was admitted to the ED, where anti-D Ig was obtained from pharmacy and administered on the basis of a historical group on an old admission card, which did not have a record of her new antibody status.

Laboratory errors n = 7

5/7 of the laboratory errors involve IT to some degree.

- 1 case in which there was no hazard flag on the LIMS, even though the patient was known to have immune anti-D, and a locum BMS issued anti-D on request.
- 1 case where a hazard flag was ignored and anti-D issued by a manual method.
- 1 case where a hazard flag indicating immune anti-D was deliberately overridden by a BMS when issuing anti-D via the LIMS.
- 2 cases which involved not checking reports properly before issue. In both cases the laboratory reports clearly indicated that the patients had immune anti-D, but also contained comments from earlier (unsensitised) pregnancies advising issue of prophylactic anti-D in response to sensitising events. Midwives administered anti-D from stocks held in the clinical area.

Of the 2 further cases, 1 was due to failure of the laboratory to recognise a very strongly positive antibody screen in the maternal sample as immune anti-D rather than post-injection anti-D.

In the final case, anti-D was issued postnatally on the basis of the cord D type, but before the results of the maternal antibody screen were available. The patient had a strongly positive antibody screen, and appeared to have been sensitised against the D antigen even though RAADP had been administered correctly during the pregnancy.
It must of course be remembered that administration of unnecessary anti-D may be preferable, in terms of risk, to omission of necessary anti-D. The BCSH guidelines state that if there is any doubt as to the true D status of a patient, or whether anti-D detected in an antibody screen is of immune or prophylactic origin, and these questions can not be quickly resolved, then prophylactic anti-D should be administered rather than place the patient at risk by withholding it.[11]

Anti-D Ig given to mothers of D negative infants *n* = 6

Only 1 of these was a clinical error, where anti-D Ig was administered from a remote stock held in the maternity department despite there being a report that the infant was D negative.

The remaining 5 cases resulted from laboratory errors.

- 1 case in which case D-typing was made more difficult because the cord had a weakly positive DAT. The BMS proceeded to issue anti-D Ig on the basis of a supposed D positive cord result, despite both the laboratory SOP and a senior BMS clearly stating repeat testing by a second BMS was necessary. Repeat testing on the same sample, and also a fresh sample, showed the cord to be D negative.
- 1 case where cord samples were 'swapped' in the laboratory prior to testing, and the incorrect result was reported.
- 1 case in which an MLA recorded the cord D-typing result incorrectly.
- 2 cases in which anti-D was issued when the results clearly showed the cord to be D negative. In 1 of these cases, the anti-D was issued by a locum BMS.

Anti-D Ig given to the wrong patient *n* = 5

These are exclusively clinical errors involving failure of basic identification checks at the bedside prior to administration.

There were 2/5 cases reported antenatally, and 3/5 cases involving postnatal patients.

In 2 cases, midwives checked the identification details on the anti-D against the laboratory issue form before administering it to the wrong patient.

In 2 cases, there appears to have been no formal identity check procedure undertaken at all.

The final case is below:

Case 5

Use of patient notes in an ID check, in place of the patient's wristband or verbal confirmation

A midwife collected anti-D Ig, and then took it to the wrong patient along with the intended patient's notes. She then proceeded to check identification details against the notes rather than with the patient and administered the anti-D.

Wrong dose of anti-D given *n* = 10

2/10 cases were in the antenatal setting and 8/10 were postnatal.

Laboratory errors n = 6

2 cases involved incorrect dose calculations cased on estimations of foeto-maternal haemorrhage (FMH) by hospital laboratories using Kleihauer Tests;

- in 1 case too much anti-D was issued (3750 iu instead of 1250 iu as indicated by FMH estimation)
- in 1 case too little anti-D was issued (500 iu instead of the required 1000 iu)

In 1 case a BMS issued 1500 iu anti-D in response to a sensitising event, for which 500 iu should have been issued, because the patient was due to receive RAADP in 3 days' time.

In 1 case the laboratory issued a second, unnecessary dose of anti-D, apparently not realising that the first dose had already been issued.

In 1 case a 2500 iu dose of anti-D was issued by the laboratory to replace stock 250 iu doses in the clinical area. This dose was subsequently administered by a midwife to a patient who required a 250 iu dose.

In 1 case a BMS issued 250 iu anti-D instead of the 1250 iu dose indicated by the clinical situation.

Clinical errors n = 4

In all 4 cases an incorrect dose of anti-D was selected for administration by clinical staff from remote stocks.

Anti-D expired or out of temperature control *n* = 3

These 3 cases were exclusively clinical errors in the antenatal setting, where expired anti-D Ig was selected and administered from remote stocks.

Other laboratory errors *n* = 3

In 2 cases there was a clerical error recording the batch number of anti-D Ig when issued by the laboratory.

In 1 case (below) the laboratory issued inappropriate products to replace remote clinical stock.

Case 6

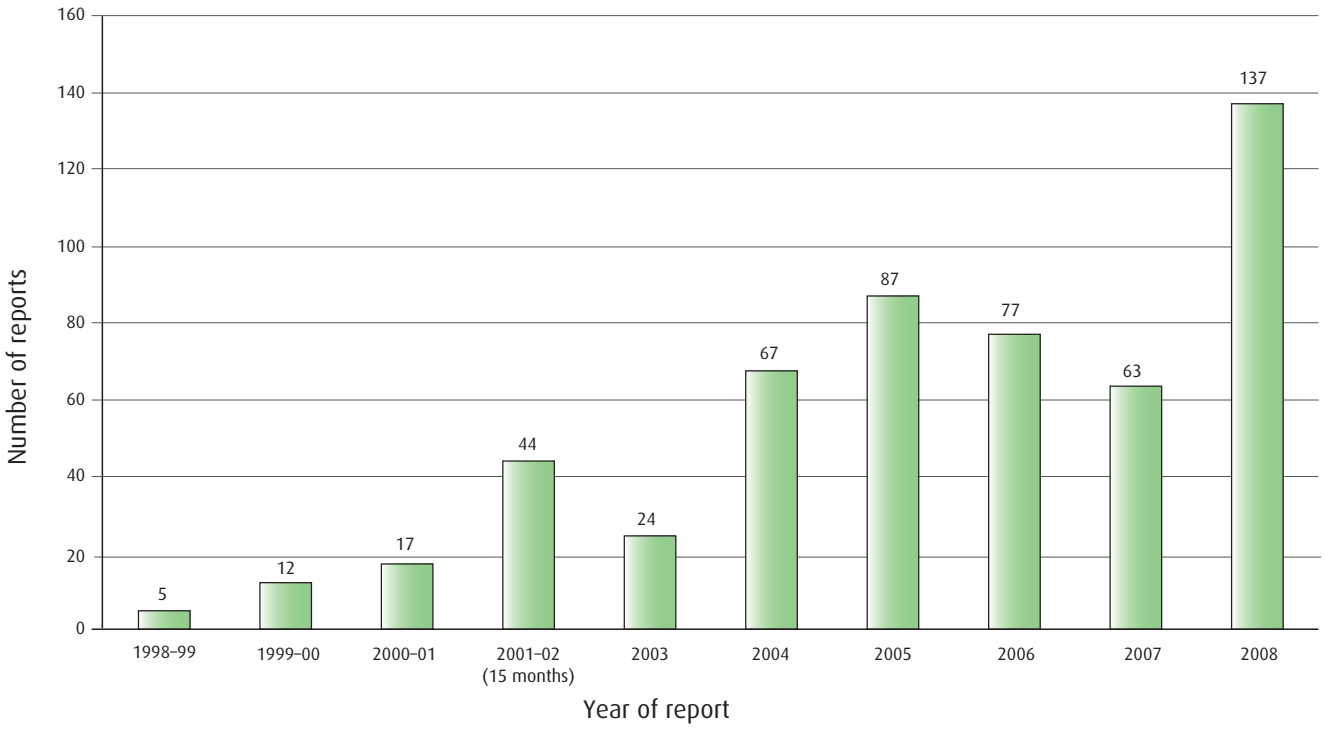
A totally different immunoglobulin given instead of anti-D

A vial of Herpes Varicella Zoster globulin was issued by the transfusion laboratory to the clinical area included in a supply of 250 iu anti-D bulk stock. The discrepancy was missed at the bedside checking stage, and a midwife administered the incorrect globulin in place of the indicated 250 iu anti-D Ig.

COMMENTARY

The number of cases reported to SHOT under the anti-D category has more than doubled in the reporting year 2008, presumably because of increased awareness of the need to report adverse events associated with the administration of this blood product. This represents the continuation of an upward trend in reporting since SHOT reporting commenced in 1996 (see Figure 8 below).

Figure 8
Anti-D cases 1998–2008



It is noted that many of the case reviews undertaken in the hospitals echo the recommendations in last year's SHOT report, of the need for robust protocols, for good communication, and for good record-keeping with regard to traceability of anti-D immunoglobulin.

It is perhaps surprising that the bulk of events (44/58), where anti-D Ig was given late or omitted altogether, occurred in the postnatal setting, where it has always been assumed that robust protocols already exist, rather than antenatally where there appears to be greater uncertainty regarding anti-D administration.

It is also instructive that many of the cases of inappropriate or incorrect administration involve the issue of anti-D from remote stocks held in the clinical area. In fact 21% of all anti-D cases reported in 2008 relate to anti-D issue from remote stocks or from pharmacy, and there appear to be insufficient checks in place to ensure the security of the process.

While it must be acknowledged that for reasons of geography and accessibility some maternity units will require their own stock of anti-D immunoglobulin, perhaps its release should be subject to laboratory control under the auspices of a robust agreed protocol. Trusts need to review and critically assess the need for anti-D Ig to be stored in and issued from clinical areas or pharmacy departments rather than from the transfusion laboratory.

It would appear that despite the (presumed) presence of a clinical protocol for administration of anti-D and a patient group directive, there is still inadequate knowledge and understanding of the physiology and rationale behind RAADP among those making the decision to administer anti-D.

Laboratory errors continue to contribute to around one third of the cases reported, and it is of concern that errors similar to those previously reported are being made, despite the errors being publicised in previous SHOT reports.

Anti-D issues are still being manually processed outside the relative security of a laboratory computer system and, even where hazard flags are in place, they are being ignored or even purposely overridden in order to facilitate the easy option of issuing anti-D without considering whether or not it may be appropriate.

It is not appropriate to allow trainee BMS staff, MLAs or locum staff unfamiliar with local practice to issue anti-D immunoglobulin, and the recommendation from last year's SHOT report that only experienced BMS staff should interpret results and oversee the issue of anti-D bears repeating this year.

Robust protocols, drawn up in partnership by clinical and laboratory staff, are essential. Too often the laboratory is seen as the ultimate decision maker in whether or not a patient needs anti-D, when the request should clearly come from the clinicians (SHOT recommendation, 2005) based on both the clinical situation and a good understanding of the significance of the results produced by the laboratory.

It must also be remembered that anti-D Ig is a 'prescription only medicine'[12] and therefore must only be administered after individual prescription by a medical officer or independent prescriber or under the auspices of a patient group directive.

Trusts must ensure that there is representation from midwives and obstetricians on hospital transfusion committees, with the aim of drawing up straightforward local protocols for the request, issue and use of anti-D Ig based on well established national guidance.[11,13]

RECOMMENDATIONS

New recommendations from this report

- Trusts should ensure that robust systems under overall control of the hospital transfusion laboratory are in place for anti-D Ig to be issued on a named patient basis, to ensure both appropriate use and to meet traceability requirements.

  Action: HTCs

Recommendations still active from previous years

Year first made	Recommendation (Previously Learning Points)	Target	Progress
2007	D-typing should be performed by the routine methodology available in the blood bank, not by emergency techniques, which may not be as robust.	**Consultant haematologists with responsibility for transfusion, HTCs, HTTs**	
2007	Trusts should comply with the requirement in HSC 2007/001 Better Blood Transfusion, to: 'Ensure the use of anti-D immunoglobulin follows the same rigorous patient identification, recording and traceability requirements as all other blood products and components.'	**Consultant haematologists with responsibility for transfusion, HTCs, HTTs**	
2007	Obstetricians and midwives must be familiar with the national guidance for routine antenatal anti-D prophylaxis and the rationale behind it. National guidance regarding all anti-D prophylaxis should be standardised. There is a need for clear and unambiguous advice to enable all hospitals to develop local guidelines that reflect national consensus.	**NBTC, NHSBT Appropriate Use of Blood Group, IBMS, BBTS, BCSH, Royal Colleges of Midwives, O&G, GPs**	
2007	There should be clinical follow-up and retesting in six months of patients in whom anti-D administration has been delayed or omitted. The outcome should be reported to SHOT as well as internally within the Trust.	**Trust CEOs, consultant haematologists with responsibility for transfusion, HTCs, HTTs**	
2005	Laboratories undertaking antenatal serological testing should have clear protocols based on BCSH Guidelines (www.bcshguidelines.co.uk), including algorithms for repeat testing in cases where there is uncertainty whether anti-D is passive or immune.	**Trust CEOs**	
2005	The introduction of RAADP should be supported by education of doctors, midwives and laboratory staff regarding the appropriate administration of anti-D, related blood tests and the significance of antenatal antibodies. Current legislation does not permit issue of anti-D Ig from the laboratory without a clinical request.	**Royal Colleges of Midwives, O&G, GPs, consultant haematologists with responsibility for transfusion HTCs, HTTs**	Highlighted as an area for action in BBT3. 'SHOT in Obstetrics' document. Several educational symposia aimed at midwives and junior doctors have taken place.