6. Adverse Events Relating to Anti-D Immunoglobulin

Definition

An adverse event relating to anti-D administration may be defined as any reaction due to anti-D when administered, or any serious adverse event relating to the prescription or administration of anti-D which has the potential to cause harm to the mother or foetus immediately or in the future.

DATA SUMMARY

Total number of cases	**63**

Implicated Components	
Red cells	**0**
FFP	**0**
Platelets	**0**
Anti-D	**63**

Mortality / morbidity	
Deaths due to transfusion	**0**
Deaths in which reaction was contributory	**0**
Major morbidity	**24**

Gender	
Male	**0**
Female	**63**

Age	
<16 years	**2**
<1 year	**0**
<4 weeks	**0**

Emergency vs. routine Core hours vs. out of core hours	
Emergency	
Routine	
Not known	**63**
In core hours	**0**
Out of core hours *	**2**
Not known	**61**

Where transfusion took place	
A & E	**0**
Theatre	**1**
ITU/HDU/recovery	**0**
Wards (clinics)	**58**
Community	**4**
Other	**0**
Not known	**0**

Information technology and appropriateness of transfusion (in the opinion of the SHOT reviewer)		
In how many cases was failure or absence of IT a factor?	**6**	
In how many cases was a transfusion possibly unnecessary or inappropriate?	**35**	

* 2 were possibly out of core hours but it was not possible to tell definitively from the questionnaire.

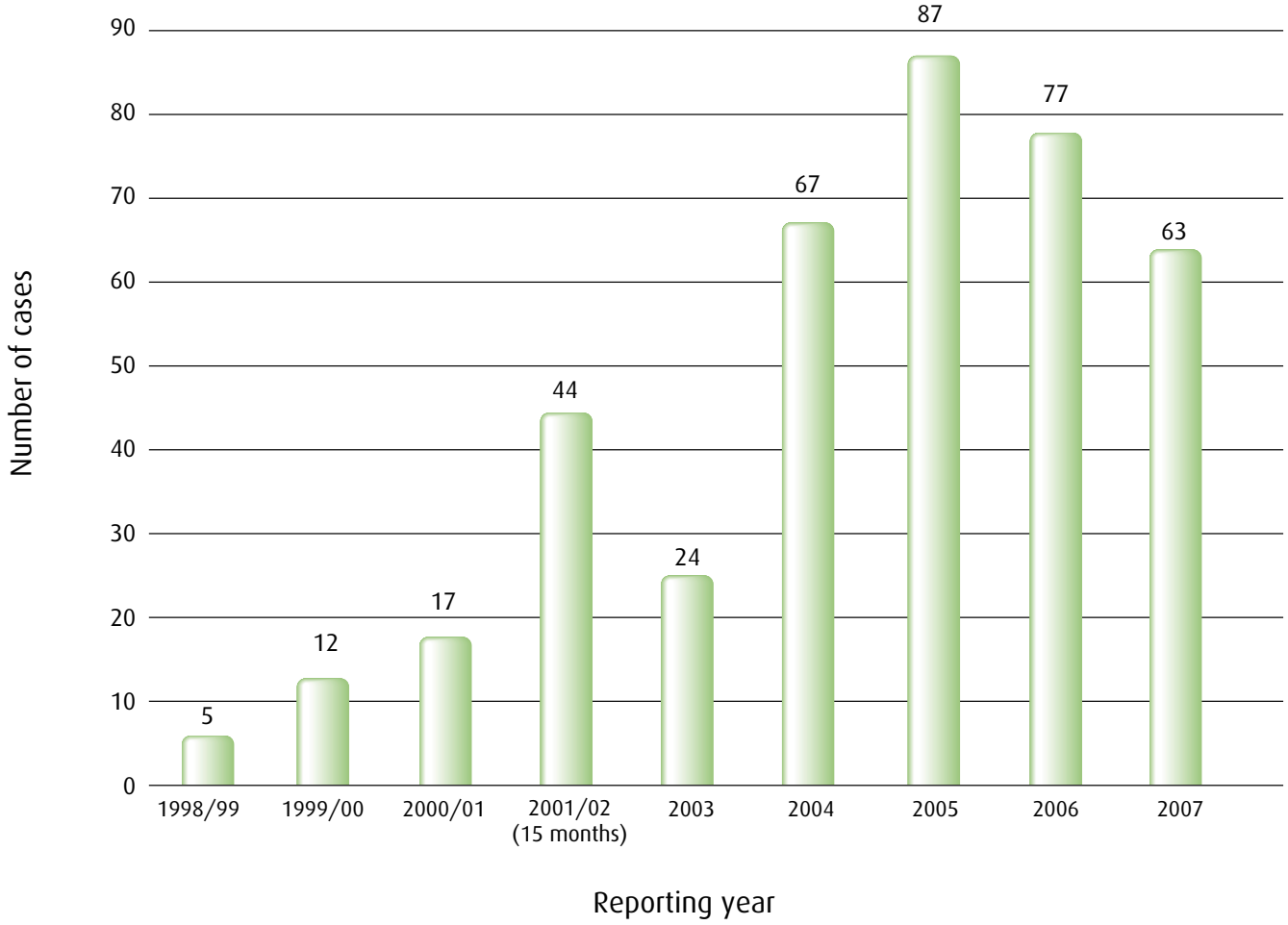
Reporting categories

- Omission or late administration of anti-D immunoglobulin
- Inappropriate administration of anti-D immunoglobulin to:
  - a D positive patient
  - a patient who already has immune anti-D
  - a mother of a D negative infant
  - a different patient from the patient for whom it was issued
- An incorrect dose of anti-D immunoglobulin according to local policy
- Administration of expired, or otherwise out of temperature control, anti-D immunoglobulin

Mortality and morbidity

There are no data in the reports this year to indicate any mortality or degree of morbidity resulting from errors relating to anti-D immunoglobulin although, in 24 cases where anti-D was administered late or omitted altogether, there is the potential for sensitisation of the patient to the D antigen, which satisfies the current SHOT definition of major morbidity.

Figure 5
Anti-D cases 1998 to 2007



In the reporting year 2007, 63 events relating to anti-D immunoglobulin administration occurred. These are summarised in Table 20 below.

Of most concern were 24 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, and 35 cases where anti-D was inappropriately administered, resulting in unnecessary exposure to a human blood product.

Table 20
Errors in cases involving anti-D Ig administration

Type of event	Cases	Primary *(All)* Errors		
		Midwife / Nurse	Laboratory	Doctor
Omission or late administration of anti-D Ig	**24**	22 *(24)*	2	-
Anti-D Ig given to D positive patient	**17**	3 *(5)*	11	3
Anti-D Ig given to patient with immune anti-D *(In 4 reported cases, there was no actual error involved)*	**6**	*(1)*	2	-
Anti-D Ig given to mother of D negative infant	**6**	-	6	-
Anti-D given to wrong patient	**6**	5 *(5)*	-	1
Wrong dose of anti-D given	**2**	*(2)*	2	-
Anti-D Ig expired or out of temperature control	**1**	*(1)*	1	-
Other *(anti-D Ig administered instead of anti-tetanus globulin)*	**1**	-	-	1
Total cases	**63**	30 *(38)*	24 *(24)*	5 *(5)*
Total errors: Primary / *(All)*		59 *(67)*		

Omission or late administration of anti-D n = 24

In 22/24 cases the primary error was by a midwife or nurse. Three cases occurred in the community (including one in which the midwife went to the wrong hospital to collect the anti-D) and 21 in a hospital setting. Lack of communication and poor documentation were common features – failure of the maternity discharge checklist was noted in 10 cases. In 1 case the laboratory did not telephone results to the ward, which was compounded by the clinical area not chasing the result, and in 4 cases there was significant delay because the original samples had been inadequately labelled.

In 1 case, anti-D was not administered in response to a sensitising event because the patient was due to receive routine antenatal anti-D prophylaxis (RAADP) a week later. The anti-D had been correctly issued in response to the sensitising event by the laboratory, but was returned unused by the ward. This case highlights the real need for targeted education around RAADP, where the principle is to administer anti-D in response to sensitising events regardless of recent or planned administration of prophylactic anti-D in the third trimester.

These cases, as in last year's report, emphasise the need for clear protocols and delineation of responsibilities within care pathways.

Anti-D Ig given to D positive patients n = 17

These cases resulted from variation in D group determination, poor documentation or communication, or misunderstanding of the laboratory report. Variation in D-typing of patients with weak D antigen, as commented in previous reports, may be unavoidable, as technologies differ in their sensitivity, but it is important that D type is determined by the most robust routine method available.

- Two patients had been tested as D negative at booking and received anti-D, but were confirmed as weak D positive later in the pregnancy.
- Two patients received anti-D for sensitising events on the basis of testing performed at other hospitals, but were subsequently found to be D positive.
- One patient was clearly flagged as a weak D on the LIMS, but this hazard flag was ignored by a BMS, who issued anti-D on request.
- A patient was on record as D positive, but this result was ignored by a BMS who had been asked to perform a Kleihauer test because the patient was known to have anti-C^w, and who then issued anti-D on request.
- In 1 case a midwife had recorded the D type incorrectly, and then insisted on anti-D being issued even though the patient's record on the LIMS clearly showed she was D positive.

One patient was mistyped as D negative by a Blood Service reference laboratory, and there were 2 further errors in hospital laboratories involving 'emergency' manual techniques which were later contradicted by routine automated testing. There was no comment made by reporters as to whether the non-routine processing of post-natal samples was appropriate in these cases.

In 1 case a patient testing as D negative at booking was confirmed as weak D by a reference laboratory after administration of the 28-week RAADP anti-D. However, the final laboratory report failed to give advice as to future treatment, so the 34-week RAADP dose was administered as well, from stock held in the maternity department. This case again highlights the need for education around the subject of anti-D, including interpretation of results, and also the need for a review of standard comments issued by reference laboratories to make them more relevant to the end-user.

In 6 cases, and also in 1 separate case where anti-D was administered instead of anti-tetanus immunoglobulin, the anti-D was stored in a batch either in the maternity department or at a GP surgery. In 2 of these cases, the patients informed the clinician that they were D negative on the basis of remembering they had received 'injections' in previous pregnancies. In all 6 cases no check was made on the D type of the patient prior to injection of anti-D (Case 1).

Better Blood Transfusion 3[11] requires anti-D to be subject to the same rigorous patient identification, recording and traceability requirements as all other blood components and products, and remote batch issue cannot come close to compliance with this.

Case 1

Anti-D administered with no blood group check

Having been told by the patient's husband that his wife was D negative, the consultant ordered anti-D from the pharmacy rather than blood bank, and proceeded to administer it without any grouping checks being made. The patient was in fact D positive.

Anti-D Ig given to patients with immune anti-D n = 6

There was 1 case in which anti-D was issued to a patient who was on record as already having anti-c+D. The mother and cord request made no mention of the antibodies, and the BMS did not check the LIMS prior to issue of the immunoglobulin.

In 1 case anti-D was issued on the basis of a historical group and screen result. When the current sample was tested, the patient was found to already have a strong immune anti-D.

In 4 cases women who had been tested at booking and found to have no antibodies, and who had no subsequent record of receiving prophylactic anti-D, were found to have immune anti-D at 28 weeks in the group and screen sample taken immediately before RAADP was administered.

These are not errors, as National Institute for Clinical Excellence (NICE) recommendations were clearly being followed to the letter (see commentary below), but it is interesting that hospitals have reported what appear to be genuine sensitisations prior to 28 weeks gestation as adverse events. One hospital has felt it necessary to alter its procedure by taking the second group and save sample a full week before planned administration of the anti-D, resulting in extra clinic commitment for both patients and midwives. However, it should be noted that in 1 of these cases the positive antibody screen was reported by the laboratory as 'post-injection of anti-D', even though there was no evidence that the patient had received prophylactic anti-D prior to the current sample.

There were no clinical sequelae reported in any of the babies following late development of anti-D in the mothers during the pregnancy. Data on subsequent pregnancies would be of interest.

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

These 6 cases were exclusively laboratory errors, 3 involving errors in transcription of cord D typing results, 2 involving testing errors where the laboratory SOP was not followed, and 1 where the anti-D was issued in error by a BMS not normally working in transfusion.

Case 2

Transcription error results in unnecessary administration of Anti-D

Mother and cord samples were correctly tested, both as D negative. The BMS then incorrectly transcribed the maternal result onto the request card as D positive. When the ward telephoned the laboratory to ask for the results, a second BMS assumed that the D positive result belonged to the cord, and issued anti-D on that basis.

Anti-D given to the wrong patient n = 6

These were exclusively clinical errors due to misidentification of the patient prior to administration of anti-D. The implication is that 6 patients who *should* have received anti-D did not, though none of the reports state whether or not the correct patients were eventually administered their immunoglobulin, and whether it was within the appropriate time frame.

Case 3

Anti-D given to wrong patient owing to lack of ID check

Anti-D was issued by the laboratory for a named patient scheduled to attend antenatal clinic. The ampoule of anti-D was clipped to the wrong patient's notes by a midwife in clinic and was administered by a second midwife, along with other medication, without any further checks being made.

Laboratory errors n = 24

Laboratory errors accounted for 24 (36%) of the reported errors in this section.

In 2 errors anti-D was issued to mothers of D negative babies by laboratory staff who did not regularly work in transfusion. In 6 cases, historical results or hazard flags in the LIMS should have prevented the issue of anti-D, but these were ignored or overridden by the BMS on duty at the time of request.

There were 3 cases where the wrong dose, according to local policy, or an expired vial, of anti-D was issued, and these were compounded by failure to detect the error at the bedside prior to administration. In 1 of these cases, a 2500iu vial was issued instead of a 250iu dose, and in 1 case 500iu was issued instead of 250iu.

COMMENTARY

Many of the cases in this year's report involve failure to follow basic clinical protocols and laboratory SOPs, and these serve to highlight the need for targeted education to all groups of staff regarding the appropriate administration of anti-D immunoglobulin, related blood tests, and the significance of antenatal antibodies in general. This need is all the more pressing in the light of the proposed withdrawal of NHSBT from routine antenatal testing, meaning that some hospitals will have to formulate plans for taking it back 'in house', with all the implications of interpretation and advice which that entails.

The development of nationally agreed, robust laboratory SOPs and clinical care pathways, is essential for the safe administration of a blood product around which there is evidently still confusion and variation in practice, and where the laboratory is often the first port of call for advice to the clinical area.

The use of RAADP is increasing as the recommendations of NICE[12] are being adopted. The BCSH guidelines for blood grouping and antibody testing in pregnancy[13] provides guidance on appropriate follow-up and further investigation where low levels of anti-D are detected in these patients.

Current NICE guidance advises that anti-D be administered at 28 weeks gestation, immediately after the second group and screen sample is taken and before the results are available. This is to minimise the impact of the RAADP programme on patient and staff time and resources. It must be appreciated that this carries the risk of inappropriate administration if the D group determination at booking was incorrect or a weak D unresolved, or if the patient has developed an immune anti-D in the intervening weeks.

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 cannot be quickly resolved, then prophylactic anti-D should be administered rather than place the patient at risk by withholding it.

RECOMMENDATIONS

New recommendations from this report

- D-typing should be performed by the routine methodology available in the blood bank, not by emergency techniques which may not be as robust.

  Action: Trust CEOs, consultant haematologists with responsibility for transfusion, HTCs, HTTs

- Trusts should comply with the requirement in Better Blood Transfusion 3[11]: 'Ensure the use of anti-D immunoglobulin follows the same rigorous patient identification, recording and traceability requirements as all other blood products and components.'

  Action: Trust CEOs, consultant haematologists with responsibility for transfusion, HTCs, HTTs

- 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 ensure that all hospitals are able to develop local guidelines which reflect national consensus.

  Action: NBTC, NHS Blood and Transplants (NHSBT) Appropriate Use of Blood Group, BCSH, Royal Colleges of Midwives, Obstetricians and Gynaecologists, General Practitioners (GPs), HTCs and HTTs

- There should be clinical follow-up and retesting in 6 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.

  Action: Trust CEOs, consultant haematologists with responsibility for transfusion, HTCs, HTTs

Recommendations still active from previous years

Year first made	Recommendation (previously Learning Points)	Target	Progress
2005	Laboratories undertaking antenatal serological testing should have clear protocols based on BCSH Guidelines including algorithms for repeat testing in cases where there is uncertainty whether anti-D is passive or immune	**Trust CEOs consultant haematologists with responsibility for transfusion HTCs, HTTs**	Improving safety of anti-D prophylaxis has been highlighted as an area for action in BBT3 'SHOT in Obstetrics' (2008) downloadable from SHOT website Several educational symposia aimed at midwives and junior doctors have taken place A multidisciplinary working party formed under the NHSBT Appropriate Use of Blood group will examine issues around guidelines and training later in 2008
2005	Laboratory reports should provide clear and unambiguous advice on the need for repeat testing and prophylactic anti-D administration		
2005	Senior, experienced laboratory staff should take responsibility for interpretation of results and issue of anti-D		
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	**Royal Colleges of Midwives, Obstetricians and Gynaecologists, GPs, consultant haematologists with responsibility for transfusion, HTCs, HTTs**	
2005	Increase safety of routine anti-D prophylaxis.	**Royal Colleges of Midwives, Obstetricians and Gynaecologists, GPs, HTTs**	