5.2 Adverse events relating to anti-D immunoglobulin (Ig) (n=77)

Seventy-seven events were related to anti-D immunoglobulin administration and are summarised in table 18 below.

The cases of most concern were those in which administration of anti-D Ig following delivery was delayed or omitted, and those where misunderstanding of antenatal serology resulted in failure to monitor the antibody level appropriately during pregnancy (e.g. case 24 below).

The use of routine antenatal anti-D prophylaxis (RAADP) is increasing as the recommendations of the National Institute for Clinical Excellence (NICE) are being adopted[17]. There is therefore an increase in the number of antenatal samples with low levels of anti-D, presenting laboratories with the problem of determining whether this is passively acquired or immune. The BCSH guidelines for blood grouping and antibody testing in pregnancy provide guidance on appropriate follow-up and further investigation[18].

It should also be noted that administration of anti-D prior to taking the second blood sample at 28 weeks gestation (as recommended by NICE) carries the risk of inappropriate administration if the D group determination at booking was incorrect or a weak D unresolved. Implementation of routine fetal genotyping will mitigate these risks.

Table 18
Cases involving anti-D Ig administration with the site(s) of contributing errors
77 cases, 79 errors

Type of event	Number
Omission or late administration of anti-D Ig *Laboratory errors* *Midwife/nurse errors*	26 7 19
Anti-D Ig given to D pos patient *Laboratory errors (including 8 weak D groups)* *Midwife/nurse errors*	19 12 7
Anti-D Ig given to patient with immune anti-D *Laboratory errors* *Midwife errors*	13 6 8
Anti-D Ig given to mother of D neg infant *Midwife error (anti-D given before cord group done)* *Laboratory error (4 wrong D group determinations, 2 wrong result manually entered onto computer, 2 infants grouped as D neg but anti-D issued in error)*	9 1 8
Anti-D given to wrong patient (all were midwife/nurse errors)	4
Wrong dose given (1 lab error, 1 doctor error)	2
Anti-D Ig expired or out of temperature control *Laboratory error* *Also midwife error* *Clinical error in community*	2 1 1 1
Other (laboratory errors)	2
Total cases ***Total errors***	**77** ***79***

Omission or late administration of anti-D

This was a heterogeneous group of cases. Seven resulted from laboratory errors, including incorrect transcription of the D group of an infant, selection of an incorrect 'standard comment', failure to issue anti-D, failure to recognise the requirement for anti-D in a patient at 19/40 gestation admitted with an antepartum haemorrhage, and 1 difficult case in which the D group was determined as weak D and the patient treated as D positive, including transfusion of D positive blood, but subsequently developed anti-C+D.

In 19 cases the primary error was by a midwife or nurse, 7 occurred in the community and 12 in a hospital setting. In many cases the reason for late or non-administration was not clear. Lack of communication and poor documentation were common features.

These cases highlighted the need for clear protocols and definition of responsibilities within care pathways.

Anti-D Ig given to D positive patients

These cases resulted from errors in D group determination, documentation or communication, or reflected misunderstanding of the laboratory report. Ten involved patients with weak D antigen, and, as commented in previous reports, may be unavoidable, as technologies differ in their sensitivity.

Eight cases of weak D were reported as laboratory errors, but in 2, a change of D status was recorded in the notes but not noticed by the midwife.

In 4 cases, the D group was incorrectly determined by the laboratory as D negative, with 2 being due to problems with laboratory analysers.

Five patients documented as D positive were given anti-D in error, 2 by a community midwife without checking the group, 2 by hospital midwives (in 1 case the wrong patient's grouping result was stuck in the notes), and 1 by a theatre staff nurse following evacuation of retained products of conception.

Anti-D Ig given to patients with immune anti-D

These 13 cases revealed a worrying inability of laboratory staff and midwives, to interpret the finding of anti-D in routine antenatal serological testing. They are of major concern, as misinterpretation can result (as in case 24) in failure to monitor the antibody level during pregnancy, with the risk of missing the development of haemolytic disease of the fetus and newborn. In a further case, classified as 'other', an anti-D found at 28 weeks was assumed to be passively acquired and no further investigation was done.

Laboratory errors

Laboratory errors accounted for 37 (47%) of the reported errors in this section. In total there were 10 D typing errors, of which 2 involved manual tube tests that were incorrectly performed, 3 were errors in manual recording of results from automated / semi-automated analysers and 5 errors were reported due to analyser problems. Three of these cases were from one site that had a software problem on an automated analyser. Such failures should be reported to the manufacturer and to MHRA Medical Devices division so that all users are alerted.

Four laboratory errors, in particular, raise issues of appropriate staffing levels and experience: in 1 case an MLA was responsible for issuing anti-D to a woman who had immune anti-D. Another report stated that there were insufficient experienced staff to interpret a Kleihauer film, hence the Kleihauer was not reported within 72 hours and anti-D administration was delayed. In 2 cases, misinterpretation of antibody identification results by BMS staff meant that appropriate fetal monitoring was not carried out, with possible dire consequences, as discussed above.

Case 24 – misinterpretation of an antibody panel had serious consequences

A D negative pregnant woman suffered an antepartum haemorrhage at 16 weeks gestation and received anti-D Ig. At 28 weeks a strongly positive antibody screen was misinterpreted by the laboratory as being due to prophylactic anti-D, quantification was not done and she received a further prophylactic dose. She went into spontaneous labour at 33 weeks. A full antibody identification panel revealed anti-C+D, with a level of anti-D of 75.4iu/mL. The infant required phototherapy for 5/52 and 3 top-up transfusions. Investigation in the laboratory found that there was no SOP for laboratory testing following administration of prophylactic anti-D, and the laboratory report at 28 weeks had been inappropriately authorised.

Case 25 – anti-D Ig given unnecessarily

A D negative patient known to have alloimmune anti-D since 2003 delivered a D positive infant and was given 500iu of anti-D Ig. This was given by the midwife from stock held on the delivery ward, on receipt of the cord blood group result and without checking the patient's notes. An identical incident involving the same patient had occurred 2 years previously.

It appeared that the standard practice on the unit was to give anti-D Ig to all D negative mothers following delivery of a D positive infant, unless advised to the contrary by the laboratory. This policy has now been changed; stocks of anti-D Ig were withdrawn from all postnatal wards and are now issued from the transfusion laboratory for individual patients, after interrogation of electronic records to ascertain suitability.

Midwife education was also carried out.

Learning points

- 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[18].
- Laboratory reports should provide clear and unambiguous advice on the need for repeat testing and prophylactic anti-D administration.
- Senior, experienced laboratory staff should take responsibility for interpretation of results and issue of anti-D.
- The introduction of RAADP should be supported by education of doctors and midwives (in hospital and primary care) regarding the significance of antenatal antibodies.
- Agreed protocols, compliant with current legislation, should be implemented for the issue and prescription of anti-D Ig.
- Problems with reagents or laboratory equipment should be reported to the manufacturer and to MHRA Medical Devices division so that other users may be alerted. www.mhra.gov.org.