# Adverse Events Related to Anti-D Immunoglobulin (Ig) n=425

# 9

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## Definition:

**Events relating to the requesting and administration of anti-D immunoglobulin (Ig) to women of childbearing potential and events relating to the administration of anti-D Ig following transfusion of D-mismatched platelets.**

## Abbreviations used in this chapter

| | | | |
|---|---|---|---|
| **BSH** | British Society for Haematology | **NICE** | National Institute for Health and Care Excellence |
| **cffDNA** | Cell-free fetal deoxyribonucleic acid | **NIPT** | Non-invasive prenatal testing |
| **FMH** | Fetomaternal haemorrhage | **PSE** | Potentially sensitising event |
| **IBGRL** | International Blood Group Reference Laboratory | **RAADP** | Routine antenatal anti-D Ig prophylaxis |
| **Ig** | Immunoglobulin | **SOP** | Standard operating procedure |
| **IT** | Information technology | **SOT** | Solid organ transplant |
| **LIMS** | Laboratory information management system | | |

## Key SHOT messages

- High numbers of anti-D Ig errors continue to be reported. Delays and omissions in administration of anti-D Ig (following PSE and RAADP) account for the majority of errors. Previous SHOT recommendations remain relevant to reduce risk of these errors
- NIPT using cffDNA can predict the D-type of the fetus supporting targeted use of anti-D Ig/ RAADP. Challenges remain with access to results, misinterpretation of results and false-positive/ negative results

## Recommendations

- Interoperability between LIMS, including reference laboratory, and maternity systems reduces risk of transcription errors and should be implemented
- Organisations should review current processes to identify gaps where improvements could be implemented to support safe practice
- Processes should be in place that support recognition of the need for anti-D Ig in non-gynaecology and maternity settings

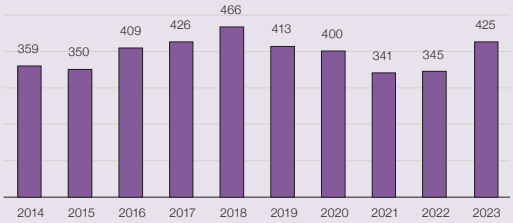
**Action: Laboratory management, IT departments, maternity services, reference laboratories**


SHOT
Serious Hazards of Transfusion

### Headline data 2023

Number of reports n=425
Deaths n=0
Major morbidity n=1

### Anti-D Ig reports by year




### Demographic data

Male n=0
Female n=425
Adults n=412
Paediatric n=1
Unknown n=12

### Potential for major morbidity n=284

Late/omitted RAADP n=98
Late/omitted anti-D Ig following a PSE (including delivery) n=186

## Introduction

Guidelines for safe and appropriate administration of anti-D Ig post sensitising events and RAADP have now been in place for many years (Qureshi, et al., 2014; NICE, 2008; NICE, 2019; NICE, 2023). It is essential that these guidelines are reflected in local policies and systems are in place that support compliance in all healthcare settings. Anti-D Ig is also important in reducing the risk of developing immune anti-D in D-negative patients with childbearing potential (including paediatric patients) following transfusion of D-positive blood components and D-mismatch SOT (Qureshi, et al., 2014). In this chapter, 425 cases have been analysed, mainly related to anti-D Ig management during pregnancy. In addition, 41 near miss cases were reported.

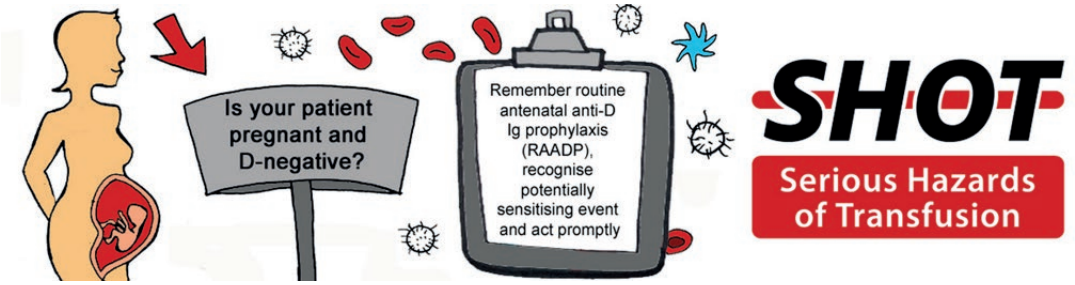
SHOT data continue to demonstrate that errors in anti-D Ig and RAADP management occur in both clinical and laboratory settings. The management of patients requiring anti-D Ig and RAADP is multifaceted, errors can occur at all stages of the process.

## Deaths related to transfusion n=0

There were no deaths reported in the cases analysed for 2023 related to anti-D Ig errors.

## Major morbidity n=1

A mother developed immune anti-D following omission of anti-D Ig during pregnancy, this is detailed in Chapter 27, Immune Anti-D in Pregnancy. Delays, omissions, under-dosing, and failures to perform follow up testing after an FMH of more than 4mL have the potential to result in development of immune anti-D and haemolytic disease of the fetus and newborn in future pregnancies. The impact of anti-D Ig and RAADP errors should not be underestimated.




## Overview of cases n=425

Omission or late administration of anti-D Ig/RAADP continue to account for the majority of errors, 284/425 (66.8%) (Table 9.1). These were mainly related to discharge prior to administration, 81/284 (28.5%), failure to order, 60/284 (21.1%), failure to check relevant results, 44/284 (15.5%) and incorrect decision to omit, 36/284 (12.7%). Where incorrect decisions resulted in omission, the majority were for PSE (30/36), notably where mothers were seen outside of maternity and gynaecology settings. Formal investigation following the error had been performed in 282/425 (66.4%) cases. Failures in team function, poor written or verbal communication, gaps in knowledge and mismatch between workload and staff provision were the most common contributory factors identified in errors.

| Anti-D Ig category | Number of reports |
|---|---|
| Omission or late administration of anti-D Ig | 284 |
| Anti-D Ig given to the mother of a D-negative infant | 59 |
| Wrong dose of anti-D Ig given | 16 |
| Anti-D Ig given to a woman with immune anti-D | 15 |
| Anti-D Ig handling and storage errors | 14 |
| Anti-D Ig given to a D-positive woman | 11 |
| Anti-D Ig given to the wrong woman | 10 |
| Right product right patient | 8 |
| Miscellaneous | 8 |
| **Total** | **425** |

**Table 9.1: Distribution of anti-D Ig related error reports in 2023 (n=425)**

### Case 9.1: Incorrect decision to omit anti-D Ig

*During a major haemorrhage protocol activation, an adult therapeutic dose of D-positive platelets was transfused to a D-negative mother. The baby's sample tested D-negative at delivery. The clinical team returned the anti-D Ig because the baby was D-negative, failing to recognise the need for anti-D Ig following the transfusion of D-positive platelets.*

It is important to remember that anti-D Ig may be required where D-positive blood components are given to D-negative patients of childbearing potential (Qureshi, et al., 2014). This can occur within, or outside the maternity setting and is unrelated to the infant D-type.

### Case 9.2: Incorrect dose of anti-D Ig following cell salvage

*A dose of 500IU anti-D Ig was given to a mother post delivery. The laboratory was not informed that cell salvage products had been re-infused and that a 1500IU dose should have been provided.*

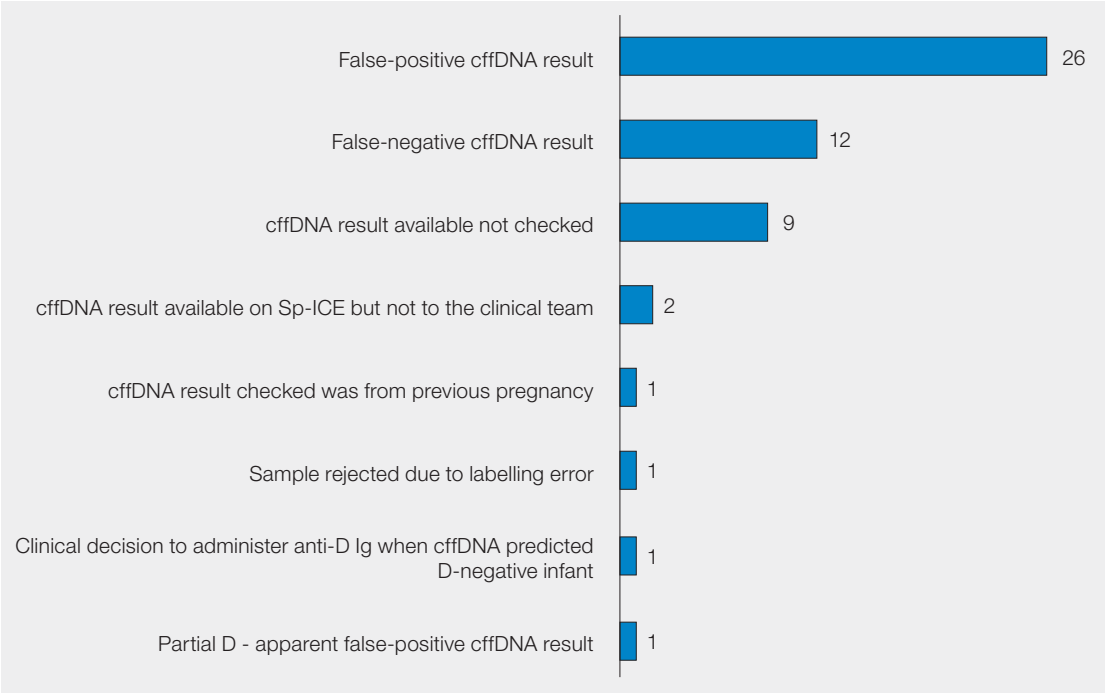
Where 500IU anti-D Ig is used for PSE and post delivery, effective communication with the laboratory where cell salvage has been re-infused helps ensure an appropriate dose (1500IU) is provided in accordance with BSH guidelines (Qureshi, et al., 2014).

## Non-invasive prenatal screening n=53

Since 2016, high-throughput NIPT for fetal *RHD* (cffDNA) screening has been available across the UK for non-immunised D-negative pregnant women (NICE, 2016). Prediction of the fetal D-type enables targeted administration of anti-D Ig. The assay has limitations, with sensitivity of 99.3% (95% CI 0.982-0.997) and specificity of 98.4% (95% CI 0.964-0.993) (Mackie, et al., 2017) leading to a small risk of false-positive or false-negative screening results. False-positive and false-negative results must be reported

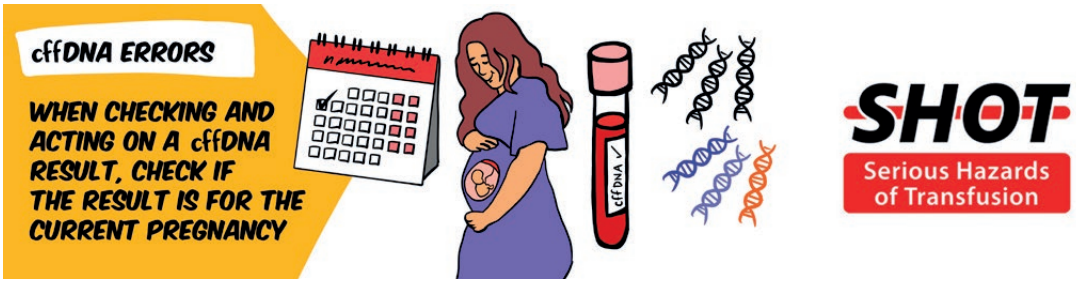
to SHOT and to the test provider. A checklist for investigation of discrepant results is available on the SHOT website and can be used for local investigation (see 'Recommended resources'). The screening assay should not be confused with the diagnostic assay for fetal D-typing, provided by IBGRL, which provides a higher level of specificity and sensitivity and is performed where the mother has immune anti-D. SHOT only collect data relating to errors with the screening assay.

**Figure 9.1: Number and breakdown of cases related to non-invasive prenatal screening for RHD (n=53)**




*cffDNA=cell free fetal deoxyribonucleic acid; Ig=immunoglobulin; Sp-ICE=Specialist Services Integrated Clinical Environment*

In total, 53 reports were analysed by SHOT in 2023. From those 26/53 were false-positive cffDNA results and 12/53 false-negative (Figure 9.1). Cases where cffDNA results were available to both laboratory and clinical areas but not checked prior to anti-D Ig issuing or administration accounted for 9/53 cases.




## Involvement of information technology n=68

IT was noted as being involved in errors in 68/425 (16.0%) of cases, the majority of these related to omission or delay, 26/68 (38.2%) and anti-D Ig administered to a mother with a D-negative infant, 20/68 (29.4%).

The involvement of IT was varied but the main themes included:

- IT in place but not used, used incorrectly or not working
- Lack of interoperability between different IT systems (reference laboratory, local laboratory, and clinical systems)
- Flags in laboratory IT systems not heeded
- HSE cases where anti-D Ig was stored in devices outside laboratory control and without electronic temperature excursion alerts

## Near miss cases n=41

There were 41 near miss cases analysed in 2023. Omission or late administration (8/41) and wrong dose (8/41) were the most common categories, followed by anti-D Ig issued but not administered to a woman carrying/delivering a D-negative infant (7/41) (Table 9.2). Laboratory errors accounted for over half of the total cases, 28/41 (68.3%) with 12 errors occurring during component selection where baby's blood group, mother antibody status or cffDNA results for current pregnancy were not checked prior to issue of anti-D Ig (8/12).

In most cases, 28/41, (68.3%) the NM occurred due to a failure to follow SOP or policy. This highlights the importance of ensuring that SOP and policies are clear and comprehensive to allow easy and unambiguous practice embedded within a system that supports safe practice.

Checks at pre-administration were the point of error detection in 16/41 cases, with a pre-administration checklist used in 10/16 cases. Other stages of detection included during testing, at authorisation of results, at collection and during routine equipment checking.

| Anti-D Ig category | Number of reports |
|---|---|
| Omission or late administration of anti-D Ig | 8 |
| Wrong dose of anti-D Ig given | 8 |
| Anti-D Ig given to the mother of a D-negative infant | 7 |
| Anti-D Ig handling and storage errors | 4 |
| Right product right patient | 4 |
| Anti-D Ig given to a D-positive woman | 3 |
| Anti-D Ig given to a woman with immune anti-D | 3 |
| Anti-D Ig given to the wrong woman | 2 |
| Miscellaneous | 2 |
| **Total** | **41** |

**Table 9.2: Distribution of anti-D Ig related near miss events in 2023 (n=41)**

A formal investigation was performed in 30/41 (73.2%) cases. The NM event was reviewed in 32/41 (78.0%) cases and in 6/32 changes were made to transfusion procedures or policy. These changes included implementation of checklists and additional checking steps. In 1 case, a distraction-free area in the blood transfusion laboratory was created where critical tasks are performed. Learning from NM events is acknowledged as a process to improve patient safety where patient harm has occurred (Woodier, et al., 2023; Jung, et al., 2021). It is important to recognise the valuable learning from NM and apply the same investigation tools to NM as for actual incidents. SHOT has been promoting the learning from NM as 'free lessons' and organisations should embed the NM investigation as part of their policies.

### Learning point

- Management of anti-D Ig requires laboratory and clinical involvement. There are multiple steps to safe and appropriate administration. Formal investigation of errors and review of systems enables identification of potential gaps in processes and effective preventive measures that can be implemented

## Conclusion

Safe and appropriate management of anti-D Ig requires a collaborative approach between the laboratory and other services, including maternity and gynaecology. Application of a systems-thinking approach, including consideration of human factors and ergonomics, enables implementation of barriers to error at each step in the process. It is encouraging to note that more organisations are looking to IT systems to support safe practice. IT systems, laboratory and clinical, can support safe practice but it is important to remember that these provide a safety net, they do not replace staff knowledge, and they need to be configured, maintained, and used correctly to optimise benefit. Staff training is a keystone in safe practice, induction training is critical as processes may be different across organisations. D-negative mothers, or their carers, should be provided with clear information about anti-D Ig, including the risks of missing routine appointments, and considered partners in antenatal care. Errors related to anti-D Ig consistently account for the highest proportion of errors reported to SHOT. Organisations where effective processes have been implemented, and where low error rates are seen, are encouraged to share their excellent practice via SHOT ACE reporting.

## Recommended resources

**Anti-D Immunoglobulin (Ig) Administration to avoid sensitisation in pregnancy - an aide memoire SHOT 2023**
**cffDNA discrepancy investigation form**
**IT supports anti-D Ig management in pregnancy**
https://www.shotuk.org/resources/current-resources/

**SHOT Bite No 2: Anti-D Ig Administration**
**SHOT Bite No 28: cffDNA screening errors**
https://www.shotuk.org/resources/current-resources/shot-bites/

**SHOT Videos Anti-D Immunoglobulin errors and immunisation in pregnancy: insights from SHOT (Part 1 and Part 2)**
https://www.shotuk.org/resources/current-resources/videos/

## References

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