Immune Anti-D in Pregnancy n=68

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Key findings:

- 68 cases were analysed by SHOT, 13 women or birthing people with no previous pregnancy (NPP) and 55 women or birthing people with previous pregnancies (PP)
- There were 94.1% live births and 43.8% of babies that required treatment for haemolytic disease of the fetus and newborn (HDFN)
- Data regarding multiple (>2) pregnancies and high body mass index (BMI) (>30) continue to be collected to assess their impact as contributory factors for D immunisation

Gaps identified:

- Omission or late administration of anti-D immunoglobulin (Ig) following potentially sensitising events (PSE) continues to be an identifiable risk factor for D immunisation
- Anti-D Ig may be less effective in preventing D immunisation in gestations beyond 40 weeks
- Lack of awareness or knowledge gaps resulting in missed reporting when two SHOT submissions are required: one report for D immunisation and one report for anti-D Ig administration error

Good practice:

- Correct management of pregnancy was identified in 55.9% cases reported to SHOT
- There was an increase of D immunisation cases reported to SHOT in 2024 compared to 2023, potentially suggesting a better awareness of the reporting requirements

Next steps:

- Cases of alloimmune anti-D found for the first time in pregnancy should be reported to SHOT, aiming to provide a complete data set after delivery
- Hospital transfusion teams and women's services to check the advice in guidelines, policies and reflex pathways regarding women or birthing people typed D variant is to assign a D-negative treatment pathway
- Systems should be in place to support women or birthing people with complex social situations who are less likely to report PSE resulting in inequitable care
- The British Society for Haematology (BSH) and the National Institute for Health and Care Excellence (NICE) should update their respective guidelines to address discrepancies to facilitate consistent practice and optimise safety

For all abbreviations and references used, please see the **Glossary** and **Reference list** at the end of the full Annual SHOT Report. Please see the supplementary information on the SHOT website (https://www.shotuk.org/shot-reports/annual-shot-report-2024/).

Definition:

Cases of D-negative pregnant women and birthing people who become sensitised and are found to have developed immune anti-D, which is detected during pregnancy, either at booking or later in the index pregnancy

Introduction

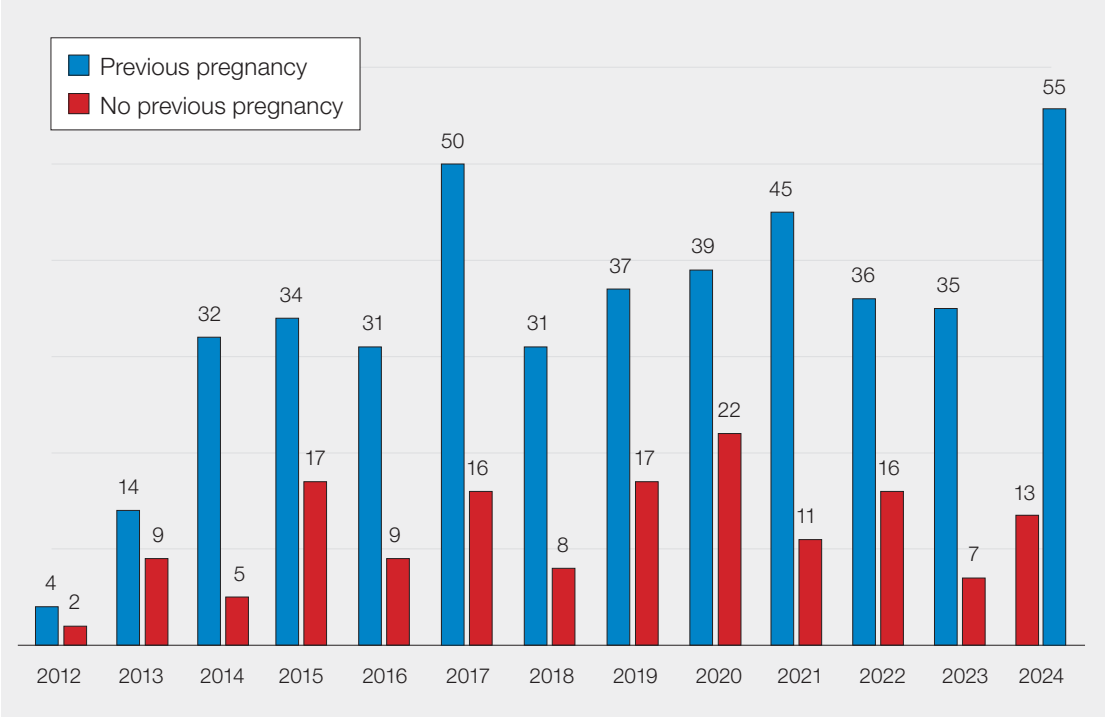
Since 2012, SHOT has been collecting and analysing cases of D immunisation where the antibody is first detected during pregnancy. This category includes cases where the management of pregnancy was suboptimal e.g., errors in anti-D Ig administration, but also cases where immunisation occurred despite ideal management of pregnancy. The information collected in this category aims to improve understanding of the causes of continuing D immunisation. For example, BMI/weight and birth beyond 40 weeks are two factors that have been analysed to understand their impact in D immunisation as mentioned in other studies (Davies, et al., 2011; Sørensen, et al., 2022; Ngan, et al., 2024). NICE has estimated that there are 65,000 D-positive births in the United Kingdom (UK) per year where the mother is D-negative (NICE, 2008). As 68 cases of D immunisation were reported in 2024, this represents an estimated ratio of 0.1% cases of D-negative women or birthing people who have been immunised. Of these 68 cases, immune anti-D was identified in 25 cases at booking. In 39 cases immune anti-D was identified during pregnancy, and in 2 after birth. In 64/68 (94.1%) cases, the index pregnancy resulted in live births. However, in 28/64 (43.8%) cases, the baby required treatment for HDFN. Treatments included phototherapy, intravenous immunoglobulin (IVIg), intrauterine transfusion (IUT), top-up transfusions and exchange transfusions.

Results

In 2024, a total of 68 D immunisation cases were reported to SHOT, 13 with women or birthing people with NPP, and 55 in women or birthing people with PP. Since reporting in this category began in 2012, SHOT has collected data on 152 NPP cases and 443 PP cases. Reporting has been fairly consistent as per Figure 28.1; however, data suggests that cases of D immunisations remain under-reported (Narayan, et al., 2019).

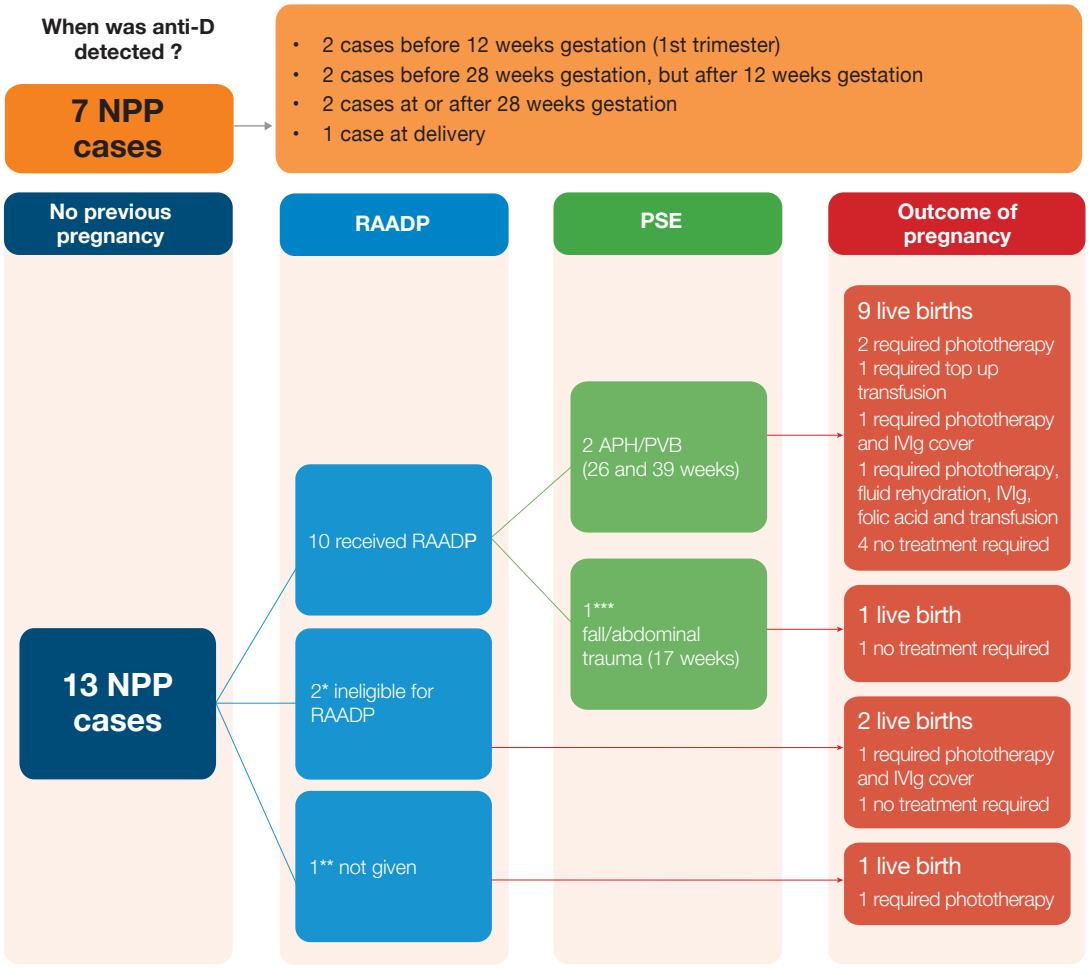
Information regarding multiple (>2) pregnancies and high body mass index (BMI) (>30) continues to be collected to assess their impact as contributory factors for D immunisation. In 2024, there were 21/68 (30.9%) cases of multiple pregnancies and 15/68 (22.1%) cases with a high BMI.

Figure 28.1: Number of SHOT reports of D immunisation by year, 2012-2024



No previous pregnancy n=13

Figure 28.2: Summary of the 2024 NPP data (n=13)



APH=antepartum haemorrhage; IVIg=intravenous immunoglobulin; NPP=no previous pregnancy; PSE=potentially sensitising event; PVB=per vaginal bleeding; RAADP=routine antenatal anti-D Ig prophylaxis

**Immune anti-D detected before 28 weeks gestation (at 12^{+4}- and 27-weeks' gestation)*

***Woman concealed pregnancy until 37 weeks gestation*

****PSE at 17^{+5} weeks, anti-D Ig given beyond 72 hours post PSE. Anti-D and anti-C detected at birth.*

Case 28.1: Anti-D Ig administered in error for a case with known immune anti-D

Immune anti-D was identified while testing the first group and screen sample at 37 weeks due to a concealed pregnancy. The sample was insufficient to complete investigations. Further samples were received 4 days later and sent to the referral laboratory for quantification. A verbal report was provided by the reference laboratory which confirmed the presence of immune anti-D (result level: 1.5IU/mL). The birth was at 38 weeks gestation, but the presence of immune anti-D was not checked resulting in anti-D Ig being issued and administered unnecessarily. The baby's group was O D-positive, and no treatment was required for HDFN.

In this case, the suboptimal management of pregnancy could not be avoided as the pregnancy was concealed. As such, RAADP was not given in a timely manner and if any PSE occurred, they were not reported or managed. Despite the immune anti-D identified and confirmed by the reference laboratory, the healthcare record was not updated. This led to unnecessary administration of anti-D Ig post birth. This highlights the importance of interoperability between the different laboratory and clinical information technology (IT) systems.

Case 28.2: Confirmation of D immunisation potentially masked by large fetomaternal haemorrhage (FMH)

A woman gave birth to a D-positive baby at 40 weeks gestation. No evidence of the presence of immune anti-D in the antenatal testing. The FMH volume post birth was calculated to be 101.5mL and 17,000IU anti-D Ig was administered. In the follow-up sample, a bleed of 17mL was identified and a further 3,000IU anti-D Ig was administered. The second follow-up sample showed a volume of <1mL bleed and a further 500IU anti-D Ig was administered. The baby needed a top-up transfusion to treat HDFN post birth. Two weeks after birth, a maternal sample was taken where anti-D, anti-C and an autoantibody were identified. The sample was not referred for quantification or further investigation. One year later, the antibodies remained detectable.

This case highlights the complexity of immune anti-D in pregnancy. The nature of the anti-D, if immune or passive, cannot be differentiated by standard laboratory testing. The quantification of the antibody is proved to be the most useful technique available to understand if anti-D is immune or prophylactic even though this technique does not always provide a definite conclusion. As mentioned in the 2023 Annual SHOT Report, it is important to consider a long-term follow-up e.g., 3 to 6 months for women or birthing people who have had a large FMH bleed at birth (Narayan et al., 2024). This follow-up will help to identify cases where D immunisation have occurred even despite recommended practice.

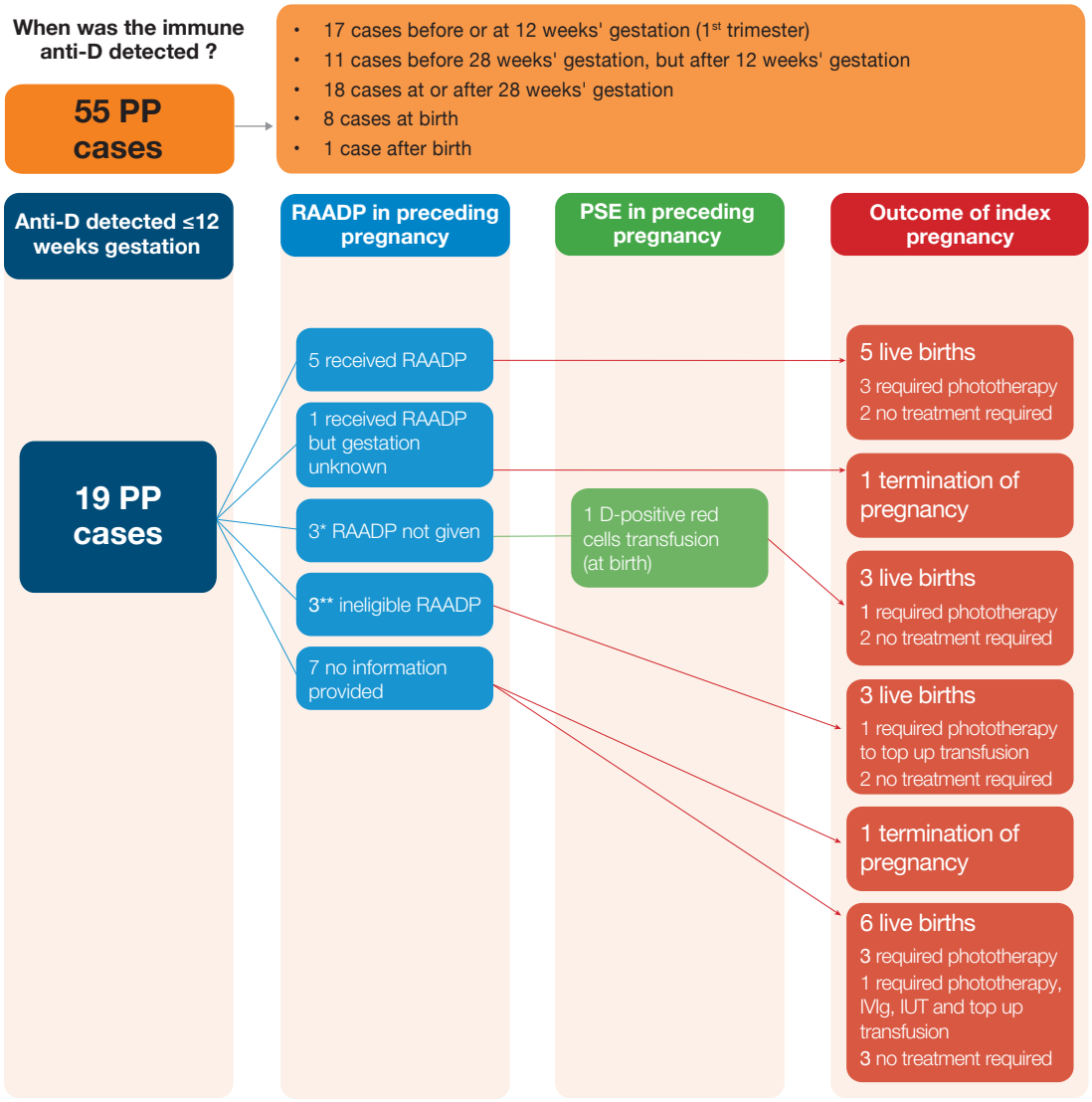
Learning points

- Confirmation of immune anti-D can be masked by the presence of prophylactic anti-D Ig administered as part of antenatal management. Referring samples for quantification should be part of the laboratory process to help confirm the nature of the antibodies
- The benefit of a long-term D immunisation follow-up should be considered on a case-by-case basis

No previous pregnancy n=55

The index pregnancy in these cases refers to the current pregnancy; the pregnancy in which alloimmune anti-D was first detected.

Figure 28.3a: Summary of the 2024 PP data (n=55) where anti-D was detected ≤12 weeks gestation (n=19)



IUT=intrauterine transfusion; IVIg=intravenous immunoglobulin; PP=previous pregnancy; PSE=potentially sensitising event; RAADP=routine antenatal anti-D Ig prophylaxis
**1 case RAADP was not part of the policy, 1 case D-variant woman treated as D-positive*
***2 cases of miscarriage <12 weeks gestation and 1 case immune anti-D already present*

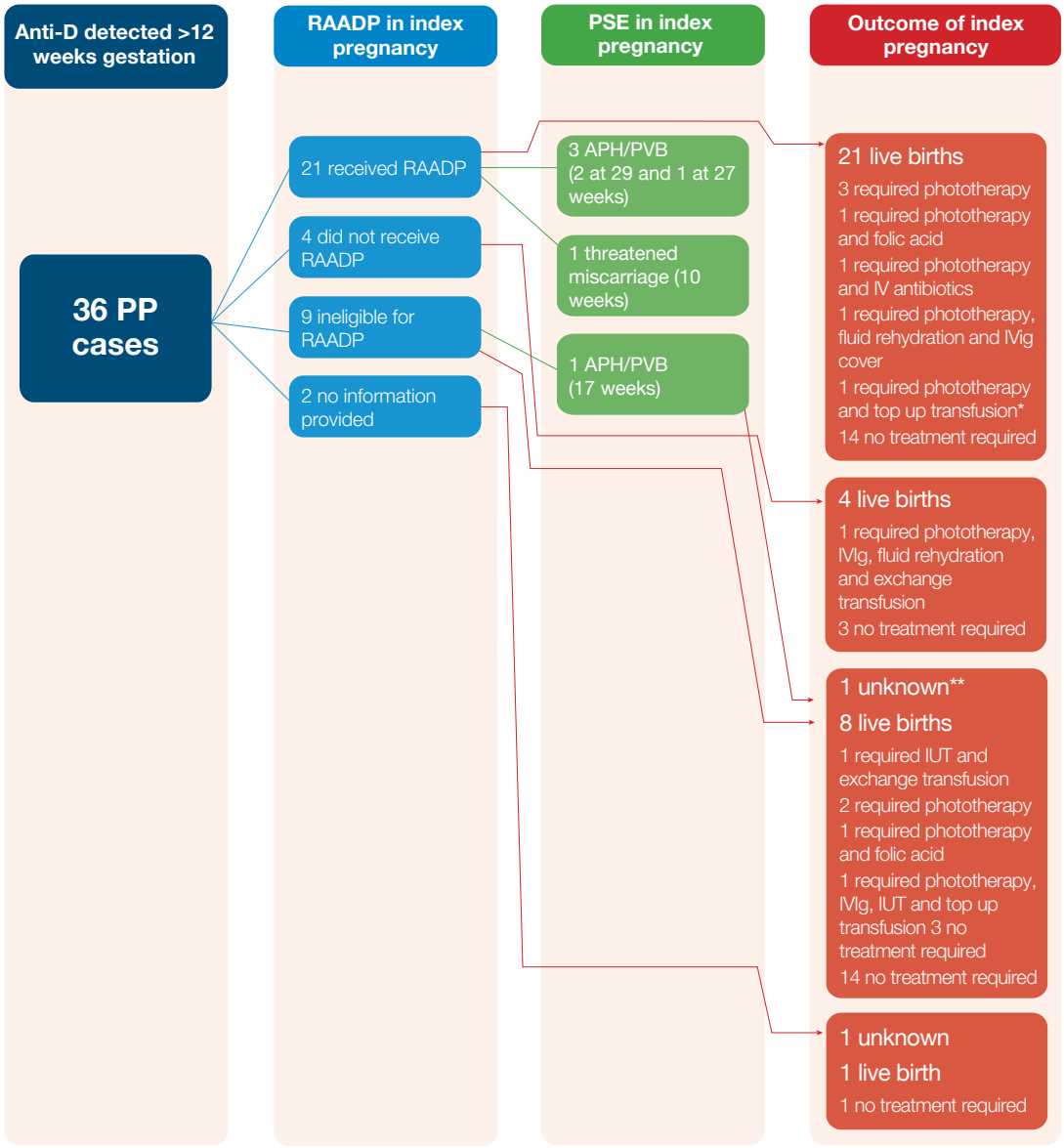
Case 28.3: D-variant identified by the presence of immune anti-D

Immune anti-D was identified with a level of 0.8IU/mL at booking (11 weeks gestation) in the index pregnancy. This was the woman's third pregnancy, and all prior samples were grouped as D-positive. In the previous pregnancy, a sample had been referred to the reference laboratory for serological D-status investigation. This was reported as weak D and recommended the woman to be treated as D-positive. In the previous pregnancy, during birth, the woman received a unit of D-positive red cells in accordance with the reported D-status. In the index pregnancy, when anti-D was identified, samples were referred to the International Blood Group Reference Laboratory (IBGRL) for genotyping who confirmed that the woman was D-variant and had been immunised. The birth in the index pregnancy took place at 37 weeks gestation and the baby received phototherapy for treatment of HDFN.

This case highlights the complexities of the D antigen and the limitations of the standard serological techniques. In some D-variant types, as the case above, an accurate D-status is only likely to be identified after the woman or birthing person has been immunised. Due to the complexity of the D antigen and

its many polymorphisms, when anti-D is detected in individuals that have been previously grouped as D-positive (or weak D), samples should be referred for genotyping to confirm the true D-status and the recommended practice to follow.

Figure 28.3b: Summary of the 2024 PP data where anti-D was detected >12 weeks gestation (n=36)



APH=antepartum haemorrhage; IUT=intrauterine transfusion; IV=intravenous; IVIg=IV immunoglobulin; PP=previous pregnancy; PSE=potentially sensitising event; PVB=per vaginal bleeding; RAADP=routine antenatal anti-D Ig prophylaxis
**Twin pregnancy, one of the twins required transfusion as well as phototherapy*
*** 1 case pregnant woman moved abroad no information available including birth*

Case 28.4: Discrepancy between guidelines in early pregnancy results in D immunisation

A woman attended the early pregnancy unit at 10^{+4} weeks gestation reporting a PVB (no pain but bleed equivalent to a period and still ongoing). A group and screen sample was not taken, and anti-D Ig was not given. This was the recommended practice as per the NICE guidelines. The woman returned at 14^{+5} weeks gestation with another PVB episode where immune anti-D was identified during laboratory testing. The result of anti-D quantification was 0.3IU/mL, and although there were no records of the woman receiving anti-D Ig in this pregnancy, it was advised to continue prophylaxis. Immune anti-D was confirmed later during pregnancy. This case was reported to

highlight discrepancies between the BSH and NICE guidelines as according to BSH, anti-D Ig should have been given when the woman reported the first PSE at 10^{+4} weeks gestation. The antibody status of the booking sample tested before 10^{+4} weeks was negative.

It is recognised that discrepancies between guidelines increases the risk of errors impacting safety. SHOT has highlighted these issues through multiple routes so that appropriate actions can be taken.

Conclusion

The 2024 data demonstrates that issues continue to occur in the management of D-negative pregnant women and birthing people, which is reflected in this chapter and in Chapter 8, Adverse Events Related to Anti-D Ig. Errors resulting in D immunisation can have an impact on the outcome of pregnancy. These can be prevented if there is a plan for action to understand and minimise the contributory factors present in the system. Throughout this chapter, complexities inherent to biology and methodologies have also been discussed to increase awareness and share the learning.

Complex social situations can significantly impact reporting and care provided. Factors affecting these must be explored and addressed to ensure safe care is provided for all.

Detailed information about the cases and associated potential contributory factors for D immunisation will be available on the supplementary data on the SHOT website.

Recommended resources

SHOT Bite No 29 – Differences of reporting errors related to anti-D Ig and immune anti-D
https://www.shotuk.org/resources/shot-bite-no-29/

Anti-D immunoglobulin errors and immunisation in pregnancy: Insights from SHOT https://www.shotuk.org/resources/anti-d-immunoglobulin-errors-and-immunisation-in-pregnancy-insights-from-shot/

SHOT videos: Anti-D Immunoglobulin errors and immunisation in pregnancy: Insights from SHOT
https://www.shotuk.org/resources/anti-d-immunoglobulin-errors-and-immunisation-in-pregnancy-insights-from-shot/