Anti-D failures: Information from SHOT reports

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With thanks to:

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Declarations

- *No affiliations to declare*
- *Assume audience has basic understanding of pathophysiology of haemolytic disease of fetus and newborn (HDFN)*

Anti-D prophylaxis in pregnancy

- Passive (prophylactic) anti-D, if given in **correct dose at correct time**, can prevent active sensitisation to D antigen and thus prevent haemolytic disease of fetus and newborn (HDFN)
- Mechanism of action of prophylactic anti-D is unclear
- ***Correct dose*** depends on stage of pregnancy and size of feto-maternal haemorrhage (FMH)
- ***Correct time*** requires recognition of potentially sensitising events and administering anti-D within 72 hours

REF. BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn H. Qureshi et al *Transfusion Medicine*, 2014, **24**, 8–20 or www.bcshguidelines.com

Anti-D prophylaxis-when

- **Post-delivery**
  Began in UK in 1969**.** Deaths due to HDFN due to anti-D fell from 46/100 000 births before 1969 to 18.4/100 000 in 1977
- **Antepartum after sensitising events**
  Introduced in 1976. Deaths due to HDFN due to anti-D fell further to 1.6/100 000 births by 1990
- **Routine antenatal anti-D prophylaxis (RAADP)**
  Introduced in 2002 (NICE)

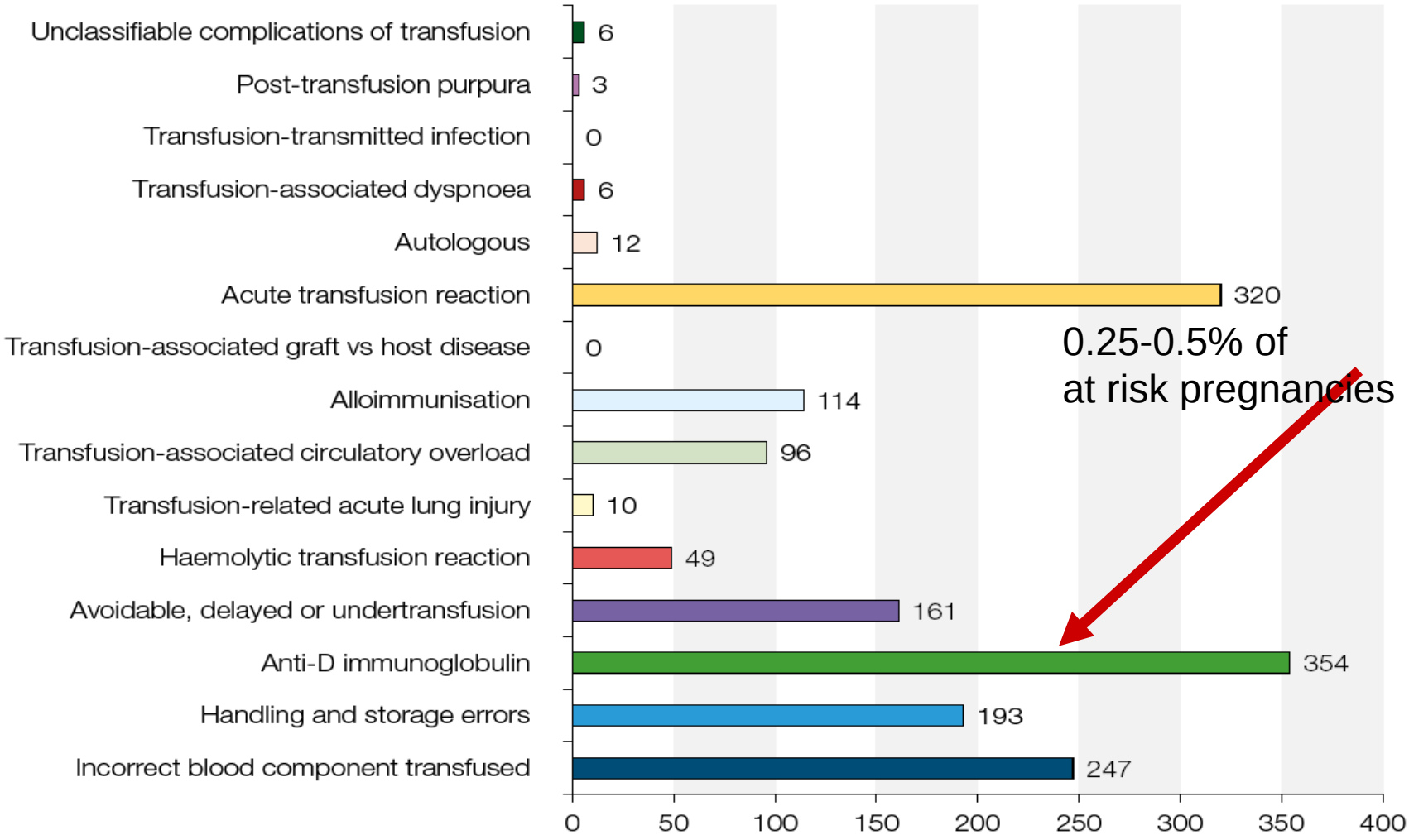
Points of potential failure of anti-D prophylaxis

- Woman books at correct time
- Blood group & antibody screen performed and reported correctly (weak D types, anti-G)
- Routine antenatal anti-D prophylaxis (RAADP) administered correctly-dose/route/time
- Potentially sensitising events in pregnancy managed correctly both clinically and in laboratory
- Post partum anti-D administered in correct dose by correct route, at correct time

National Comparative audit of anti-D immunoglobulin prophylaxis 2013

- 99% of eligible women received RAADP
  - Single dose regimen - 89.9% received right dose at right time
  - Two dose regimen -58.6% received right dose at right time
- 98.5% received post delivery anti-D
  - 91.6% received right dose at right time
- 95.7% compliance post sensitising events
  - 79% received required dose within 72 hrs

Cases reviewed by SHOT in 2013



Types of error

- ***Errors of omission:*** *failing to do something that has the potential to prevent an undesirable outcome (not doing something that should be done)*

  Omission /late administration of anti-D 277 cases (20)

- ***Errors of execution:*** *doing something that should be done, but doing it incorrectly*

  Wrong dose of anti-D 9 cases (4)

  Handling and storage errors 9 cases (2)

- ***Errors of commission:*** *doing something that has the potential to result in an undesirable outcome (doing something that shouldn't be done)*

  Inappropriate administration of anti-D 59 cases (29)

Anti-D Cases from the 2013 SHOT Annual Report

Thanks to Tony Davies

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Omission/late administration

Transcription errors when recording results

- The laboratory telephoned results to the clinical area, advising that anti-D Ig was required for a woman who had delivered an RhD positive baby.
- The post-natal ward staff entered the maternal blood group into the results section for the baby, and the woman was discharged without receiving any anti-D Ig.
- On follow-up by the laboratory as to why the anti-D Ig had not been collected, the error was realised and it was eventually administered 5 days post delivery.

System failure in the laboratory results in late administration of anti-D Ig

- Mother and cord samples were sent in a timely manner post delivery.
- However, the laboratory was reportedly severely understaffed and also had no robust system in place to identify outstanding work, so the tests were not performed until the 72 hour window for administration had passed.

System failure in testing and recording maternal blood group

- Antenatal booking bloods were rejected by the laboratory because of a labelling error, but the woman was never recalled to have repeat samples taken.
- It was noted at delivery that she was RhD negative and had received no anti-D Ig prophylaxis during her pregnancy.

Changing a reference laboratory report

from anti-C+D to anti-G

results in missed administration of anti-D Ig

- Blood Service reference laboratory reported anti-C+D in booking sample, so the woman was not offered anti-D Ig prophylaxis when she underwent an amniocentesis.
- The report was subsequently updated to state that the woman had anti-G rather than anti-C+D, so should have received anti-D Ig prophylaxis for the invasive procedure.
- Where anti-C+D is suspected in antenatal sample, laboratories must perform differential adsorption studies to confirm specificity BEFORE issuing a report.

Misuse of Kleihauer test results in failure to administer anti-D Ig for a sensitising event

- A woman presented with a vaginal bleed at 36/40 but was discharged without prophylactic anti-D Ig.
- Her midwife had recorded in the notes that as the woman had received RAADP at 28 weeks, and the Kleihauer test was ‘negative’, there was no need to administer further anti-D Ig.

Poor knowledge of prescribing doctor results in failure to administer anti-D Ig

- A woman suffered a faint and fall with abdominal trauma at 34 weeks.
- She was reviewed by a speciality trainee in obstetrics who incorrectly informed her that as she had received RAADP at 28 weeks, no further anti-D Ig was required until after delivery.

Inappropriate administration of anti-D

- Total 59 cases of which 29 (49%) attributed to laboratory
- No potential for sensitisation but unnecessary exposure to blood product
- Suggests poor laboratory practice

Merging of patient records leads to incorrect blood group being recorded

- During registration, it was noted that there were two women with identical names on the hospital system, and a merge was authorised.
- The merge overwrote the blood group as RhD negative in the patient record, though they were in fact two different women and one was RhD positive.
- She received anti-D Ig for a sensitising event before the discrepancy in paper grouping records was noticed.

Incorrect comment added to laboratory information management system (LIMS)

- A woman known to have immune anti-D had a number of quantitations on record during her pregnancy.
- A biomedical scientist added a comment '? Prophylaxis' in response to a positive antibody screen, and erroneously issued anti-D Ig for a potentially sensitising event.

Clinical pressure to issue anti-D Ig

- A woman had delivered a RhD negative baby, but persisted in asking the midwives where her anti-D injection was.
- They did not check results (which had been telephoned by the laboratory and recorded by the ward) but pressurised the duty biomedical scientist (BMS) on more than one occasion to issue anti-D Ig, which he eventually did without reference to the laboratory computer system.

Incorrect dose of anti-D

- Total 9 cases, of which 4 (44%) attributed to laboratory
- Potential for sensitisation if size of FMH/TPH underestimated

Overestimation of transplacental haemorrhage

- BMS interpreted a fetomaternal haemorrhage FMH (Kleihauer) test as showing a transplacental haemorrhage (TPH) of 15mL fetal cells, and the woman was administered 2000 international units (IU) anti-D Ig.
- On review by a senior BMS, the TPH was actually 0.3mL.

System Failures from SHOT cases (1)

- **Communication**
  - Lack of communication between hospital midwifery teams and those in the community – failure of RAADP in the community noted in 63 cases
- **Failing to take responsibility or ownership**
  - Lack of robust systems to identify outstanding work in the laboratory
  - Lack of robust systems for identifying women eligible for RAADP
  - Lack of robust systems for women booking late or transferring care
  - Assumptions that someone else is sorting out a particular issue

System Failures from SHOT cases (2)

- **Pressures of work / staffing issues**
  - Understaffing and availability of senior staff in both the laboratory and clinical area leading to pressurised and poor decision making
- **Poor practice / culture**
  - Manual transcription of blood grouping results onto notes, care plans and discharge sheets in the clinical area – repeatedly highlighted by SHOT but persists as poor practice
  - A culture of completing paperwork when the interventions have not actually been performed
  - Devolving responsibility to the pregnant/delivered woman to return at a later date for anti-D Ig administration, when they are obviously in a vulnerable and distressed state, instead of managing it at the presentation visit, be that in the ED, day unit or clinic

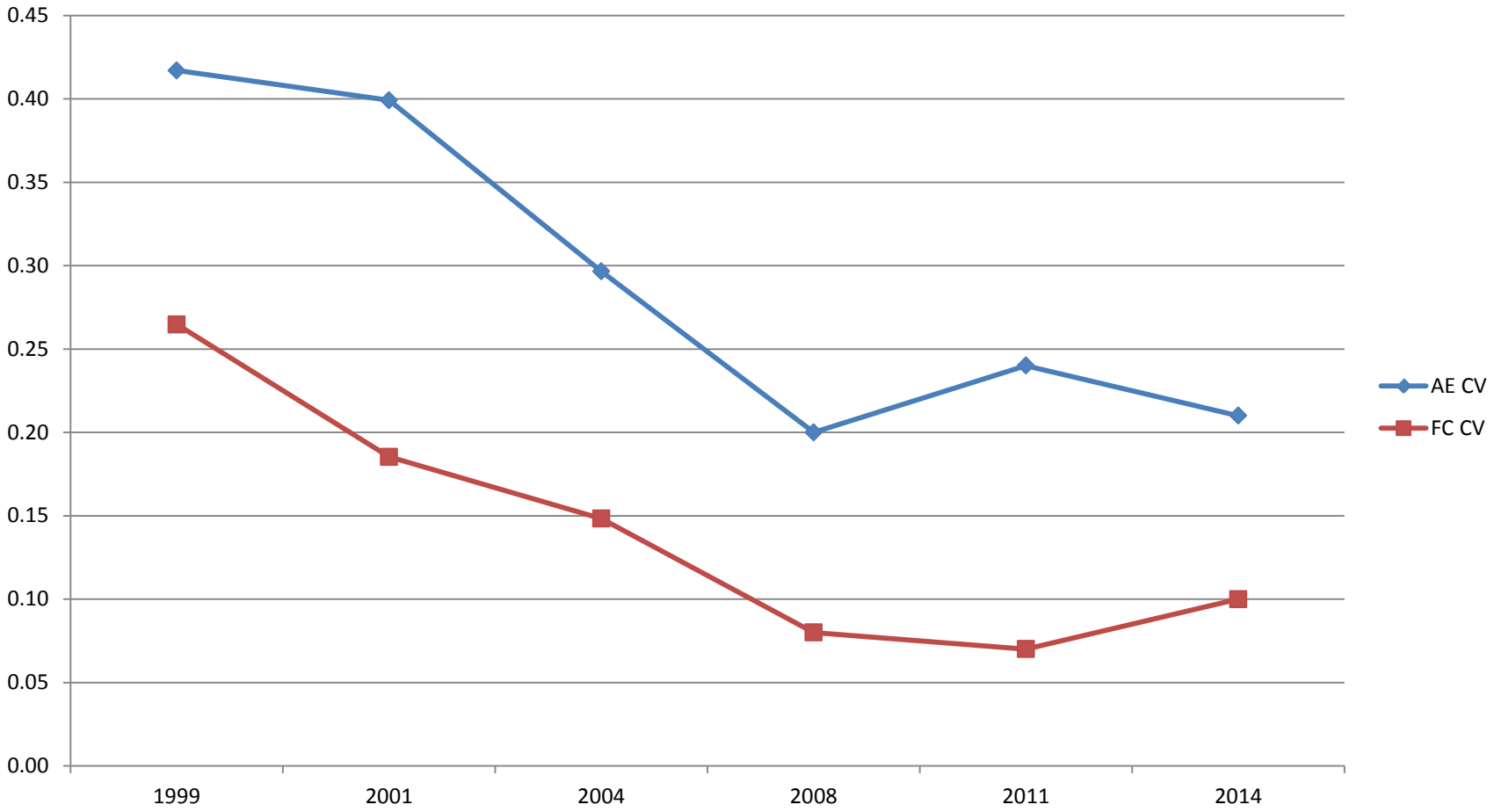
System Failures from SHOT cases (3)

- **Lack of understanding of the principles behind anti-D prophylaxis**
  - Increasing trend in poor advice being offered to women by (relatively senior) medical staff
  - Poor advice to clinical staff from laboratory
  - Decision making without reference to blood grouping results in both laboratory and clinical area
  - Misinterpretation of FMH (Kleihauer) tests in laboratories leading to dosing errors
  - Use of the Kleihauer test results by clinical staff to determine whether anti-D Ig should be given or not
  - Failure of laboratory staff to consider the need to issue anti-D Ig when giving RhD positive platelets to RhD negative patients of child-bearing potential

NEQAS schemes

- ABO and RhD grouping, including weak D
- Antibody screening
- Antibody identification
- Cross matching
- Feto-maternal haemorrhage

Estimation of FMH (NEQAS data on CV)

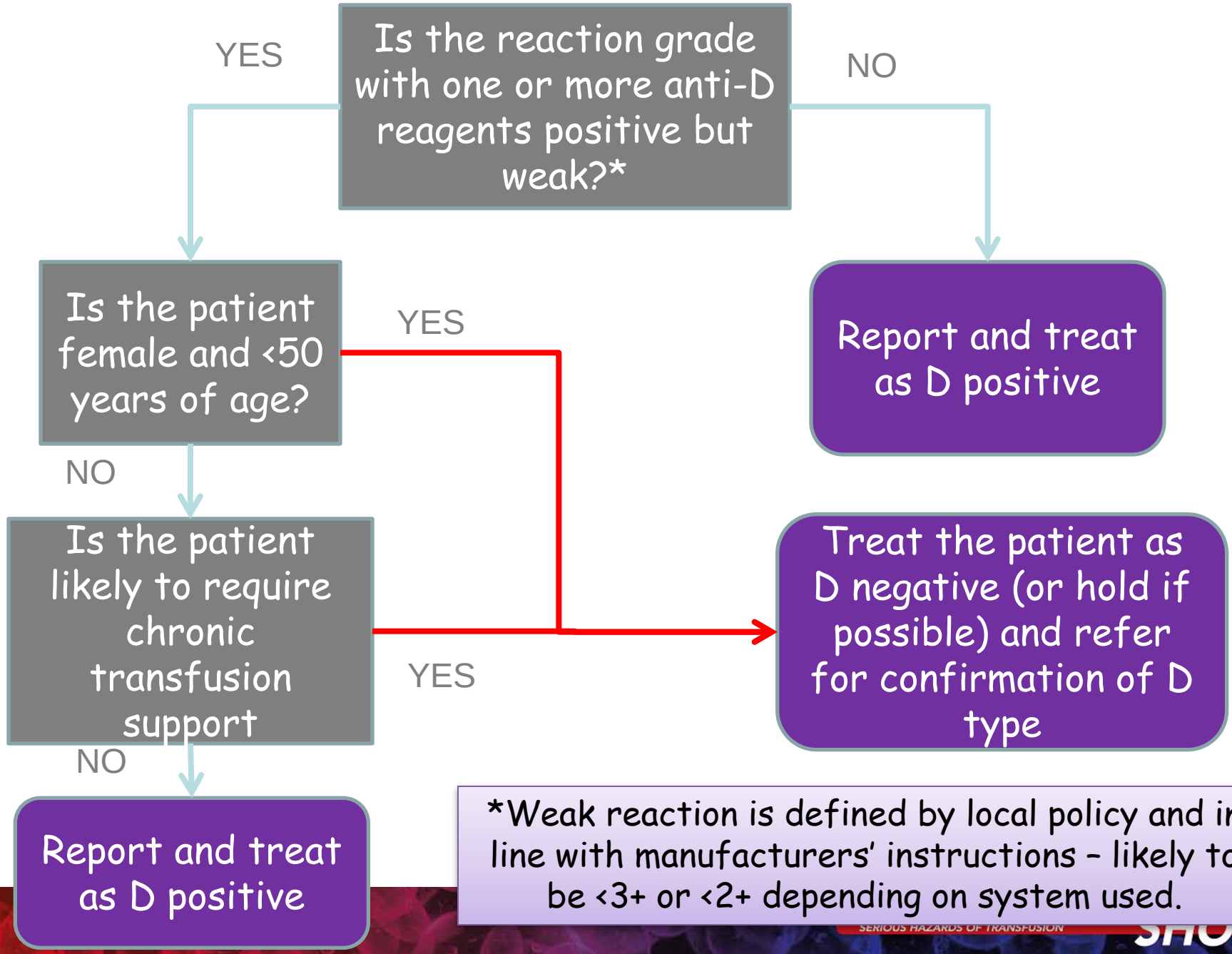


UKNEQAS for Feto-Maternal Haemorrhage 2011-12 (2 years' data)

- There were 19 episodes where participants **registered for quantification using acid elution**, potentially placed a woman at risk of sensitisation, as a consequence of an inadequate recommended dose of anti-D Ig coupled with no follow-up. This translates to an 'error' rate for UK NEQAS surveys of 0.55%.
- 45 participants were registered for **screening only.** There were five episodes where a woman was placed at risk of sensitisation, through quantification not being triggered and insufficient anti-D being prescribed. This translates into an 'error' rate of 0.75%.

Interpretation of weak D types in female patients of child-bearing potential – UK NEQAS (BTLP) exercise 2014

Results suggest that 27-30% of laboratories may not have the right testing algorithms or SOPs in place to prevent sensitisation to the D antigen in young female D variant patients


Is the reaction grade with one or more anti-D reagents positive but weak?*
YES
NO
Is the patient female and <50 years of age?
YES
Report and treat as D positive
NO
Is the patient likely to require chronic transfusion support
YES
Treat the patient as D negative (or hold if possible) and refer for confirmation of D type
NO
Report and treat as D positive
*Weak reaction is defined by local policy and in line with manufacturers' instructions – likely to be <3+ or <2+ depending on system used.

Do errors lead to sensitisation affecting future pregnancies?

We don’t know!!!

*No long term follow up of women who do not receive **optimal** care*

What is “optimal” care?

Questions being asked about current recommended practice

- Lack of detectable anti-D at delivery despite optimal RAADP (Clout 2008, Davies et al 2011)
- Sensitisation despite “perfect care” in 16% cases of immune anti-D (Amirthanayagam and Regan 2013)
- Concerns re dose and route of anti-D in obese women
- Concerns re pharmacokinetics of anti-D if >40 weeks gestation

Anti-D immunisation reporting to SHOT

- Aim is to gain a better understanding of the causes of continuing anti-D immunisations
- Report women who have produced immune anti-D that is detectable for the FIRST time in the current pregnancy, at any stage from booking to delivery
- For each case, there are supplementary questions about previous pregnancies, recorded sensitising events, anti-D prophylaxis adminstration, and pregnancy outcome

NO PREVIOUS PREGNANCIES (NPP)
n= 16

- **Gestation when anti-D first detected**- 10 at delivery, 5 at 28/40
- **Booking weight**- info in 12 cases, >68kg in 5 cases
- **RAADP details**- dose timing route
- **Sensitising events in 4 cases-** 3 received appropriate interventions, one not notified by woman
- **Peak anti-D 25.7**
- **Outcome of pregnancy-16 live births**

  6 babies (37.5%) required intervention

  1 baby had antenatal ultrasound for anaemia

  4 babies required phototherapy

  1 baby required exchange transfusion

PREVIOUS PREGNANCIES (PP)

n=41 (3 excluded)

Details of previous pregnancy

Booking weight, RAADP, sensitising events, mode of delivery, gestation at delivery, post partum prophylaxis

Index pregnancy

Date anti-D first detected, booking weight, RAADP, sensitising events, peak anti-D

Outcome data available for 14 cases

All live births

8 required no treatment

5 required phototherapy

1 required exchange transfusion and ivIg

CONCLUSIONS and RECOMMENDATIONS

- Marked progress in management of HDFN
- Process errors continue to occur and must be reported to SHOT
- Robust systems must be in place to identify woman eligible for anti-D prophylaxis and to communicate this information effectively to relevant care teams
- Anti-D must be readily available for administration to women presenting with potentially sensitising events
- Clinical and laboratory staff must maintain knowledge of pathophysiology of D sensitisation (use learnPro NHS LearnBlood Transfusion modules on anti-D)

New SHOT questionnaire on anti-D immunisations will provide data on reasons for continuing anti-D sensitisation including:

- Clinical significance and outcome of process errors

AND

- Improved understanding of the influence of maternal weight, length of gestation, dose, route and timing of anti-D prophylaxis

Desired outcome is to inform best practice and prevent anti-D immunisation

Thank You

Rhesus Macque