Anti-D

The 2013 Annual SHOT Report, and more.....

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Anti-D Ig Prophylaxis

- Post-delivery anti-D Ig prophylaxis for RhD negative women began in the UK in 1969
- The programme has been a huge success
- Deaths due to haemolytic disease:
  - **320 / 100,000** births in the 1940s
  - **46 / 100,000** births pre-1969
  - **18.4 / 100,000** births by 1977
  - **1.6 / 100,000** births by 1990

....but RhD alloimmunisation continues to occur

- Maternal anti-D level 10.5iu/ml
- Unmonitored pregnancy
- Bilirubin reached exchange trigger by end of day 1

Liumbruno et al Review of antenatal prophylaxis Blood Transfusion 2010; 8: 8-16

- Risk of sensitisation if Baby RhD pos and ABO-compatible – 16%
- Risk of sensitisation if baby RhD pos and ABO-incompatible – 2% (so ABO antibodies are protective)
- 92% women develop immune anti-D AFTER 28 weeks gestation

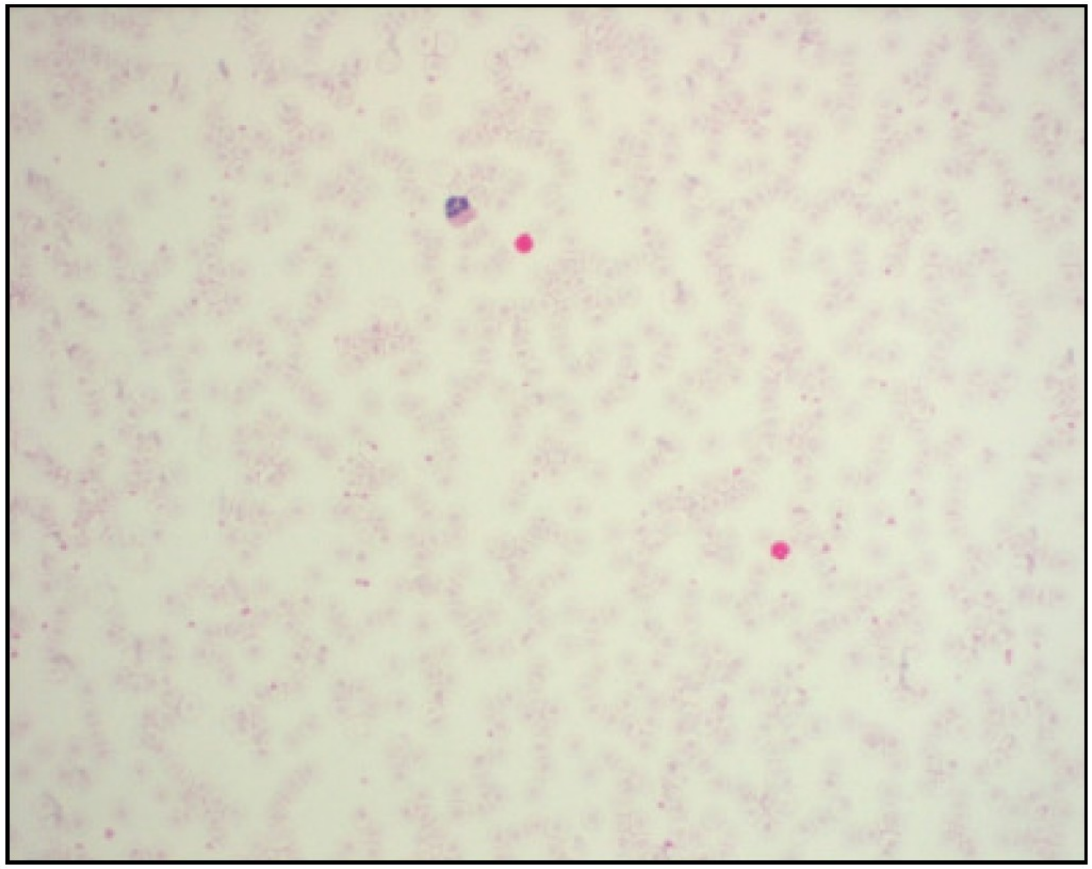
Liumbruno et al Review of antenatal prophylaxis Blood Transfusion 2010; 8: 8-16

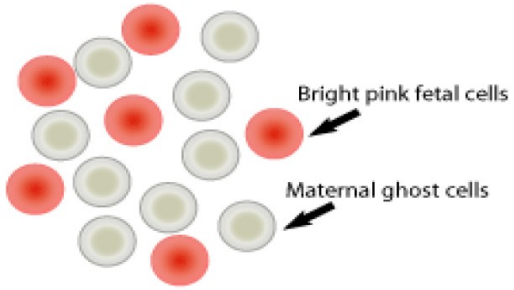
- Foetal red blood cells (typically <0.1mL) are found in;
  - 3% women in first trimester
  - 12% women in second trimester
  - 45% women in 3rd trimester
  - >50% women at delivery

Feto-Maternal Haemorrhages (FMH)

- **1st and 2nd Trimester:**
  - Miscarriage / Ectopic / TOP / CVS / Amnio
  - 0.05mL in 5% 0.5mL in 2%
- **After 20 weeks:**
  - APH / Abruption / Trauma / Amnio / ECV
  - <2mL in 98% >30mL in 0.03%
- **At Delivery:**
  - > 3mL in 1% >10mL in 0.03%
  - Increased by C-section, Cell Salvage or manual removal of placenta

The FMH (Kleihauer / Acid Elution) Test





Anti-D - What Guidelines are there ?

- **BCSH** Dec 2013
- **RCOG**
  - Green Top 22, 2011– Use of anti-D
  - Green Top 47, 2008/9 – Transfusion in Obstetrics
  - Green Top 38, 2010 – (molar pregnancies)
- **NICE**
  - Antenatal Care / Postnatal Care
  - Routine Antenatal Anti-D Prophylaxis
  - Early miscarriage & Ectopic pregnancy

What SHOULD we be doing.....

- **<12/13 weeks** gestation, give **at least 250iu** anti-D for surgical interventions (ectopic, molar, TOP) or persistent painful bleeding, within 72 hrs of the event

- **12/13 – 20 weeks**, give **at least 250iu** anti-D for PSEs such as bleeding, trauma etc

What SHOULD we be doing.....

- **>20 weeks** give **at least 500iu** anti-D for PSEs and perform Kleihauer test in case more is needed

- **28 – 34 weeks** Routine Antenatal Anti-D Prophylaxis RAADP,
  - **either** *at least* **500iu** at 28 and at 34 weeks
  - **OR 1 x 1500iu** at 28-30 weeks

- **At birth** (or stillbirth) If baby is RhD pos (or unknown) give **at least 500iu** anti-D and perform Kleihauer test in case more is needed

Cell Salvage in Obstetrics

An example of evolving practice, with increasing use of intra-operative cell salvage in the obstetric setting and the potential for relatively large volumes of foetal cells mixing with maternal circulation;

- Remember appropriate dosage of anti-D in RhD negative women – BCSH recommend *at least* 1500iu following cell salvage reinfusion, more if the Kleihauer indicates it

What Presentations of anti-D Ig are there ?

- **In the UK**:
  - CSL Behring: ‘Rhophylac’ 1500 IU pre-loaded syringe – IM/SC or IV
  - BPL: ‘D-Gam’
    - 250 IU – IM/SC only
    - 500 IU – IM/SC only
    - 1500 IU – IM/SC only
    - 2500 IU – IM/SC only
- **In Eire**;
  - Octapharma: ‘Rhesonativ’ 625 IU or 1250 IU vials
  - CSL Behring: ‘Rhophylac’ 1500 IU pre-loaded syringe

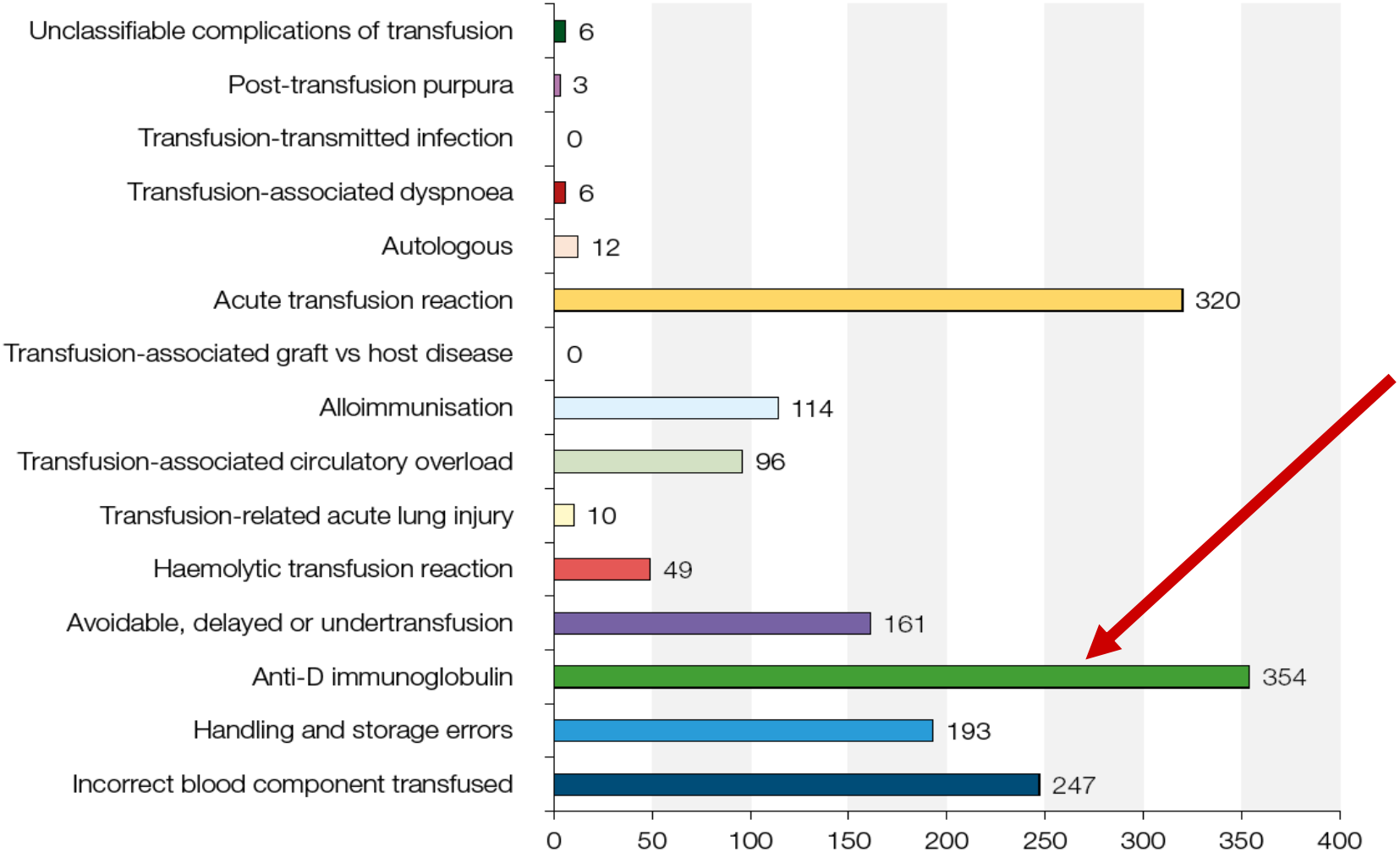
Should we give Rhophylac 1500IU IV in women with BMI >30 ?

- *Recent change in SmPC in Jan 2014 following concerns raised to the German licensing authority about POTENTIAL poor uptake following IM administration*
- *No clear evidence, no information about sites of injection etc etc*
- *Advise from BCSH, endorsed by RCOG members is to risk-assess process – very small risk of poor uptake balanced against training, calling women in to be cannulated, potential for error using BPL anti-D IV etc etc*

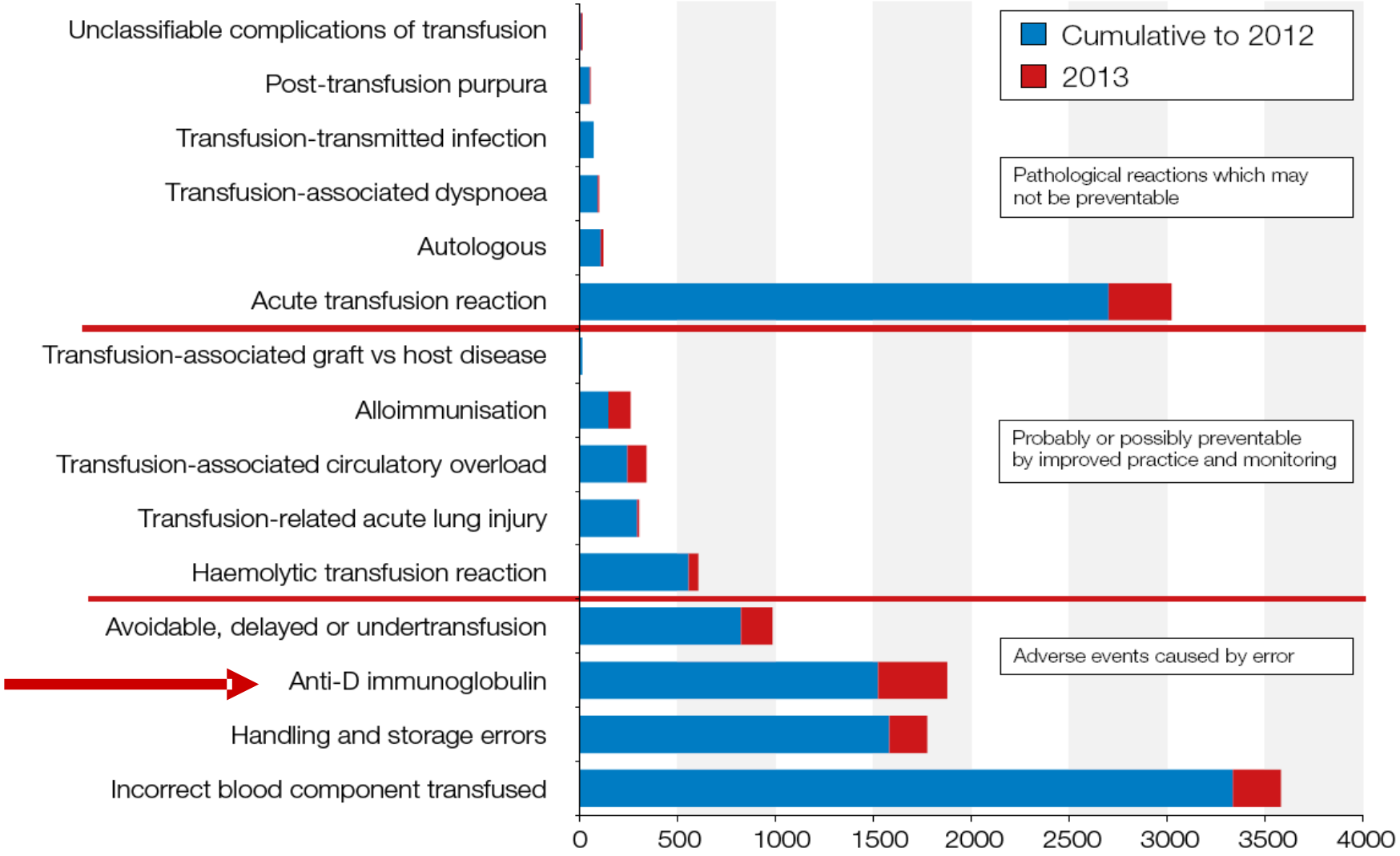
What Dose should we be using ?

- **Anti-D Ig given IV**
  - **100 IU** will clear 1 ml of foetal red cells
  - is instantly available
- **Anti-D Ig given IM**
  - **125 IU** will clear 1 ml of foetal red cells
  - will take hours to get into bloodstream via muscle, much longer (if at all) via fat and will lose some on the way

Cases reviewed by SHOT in 2013



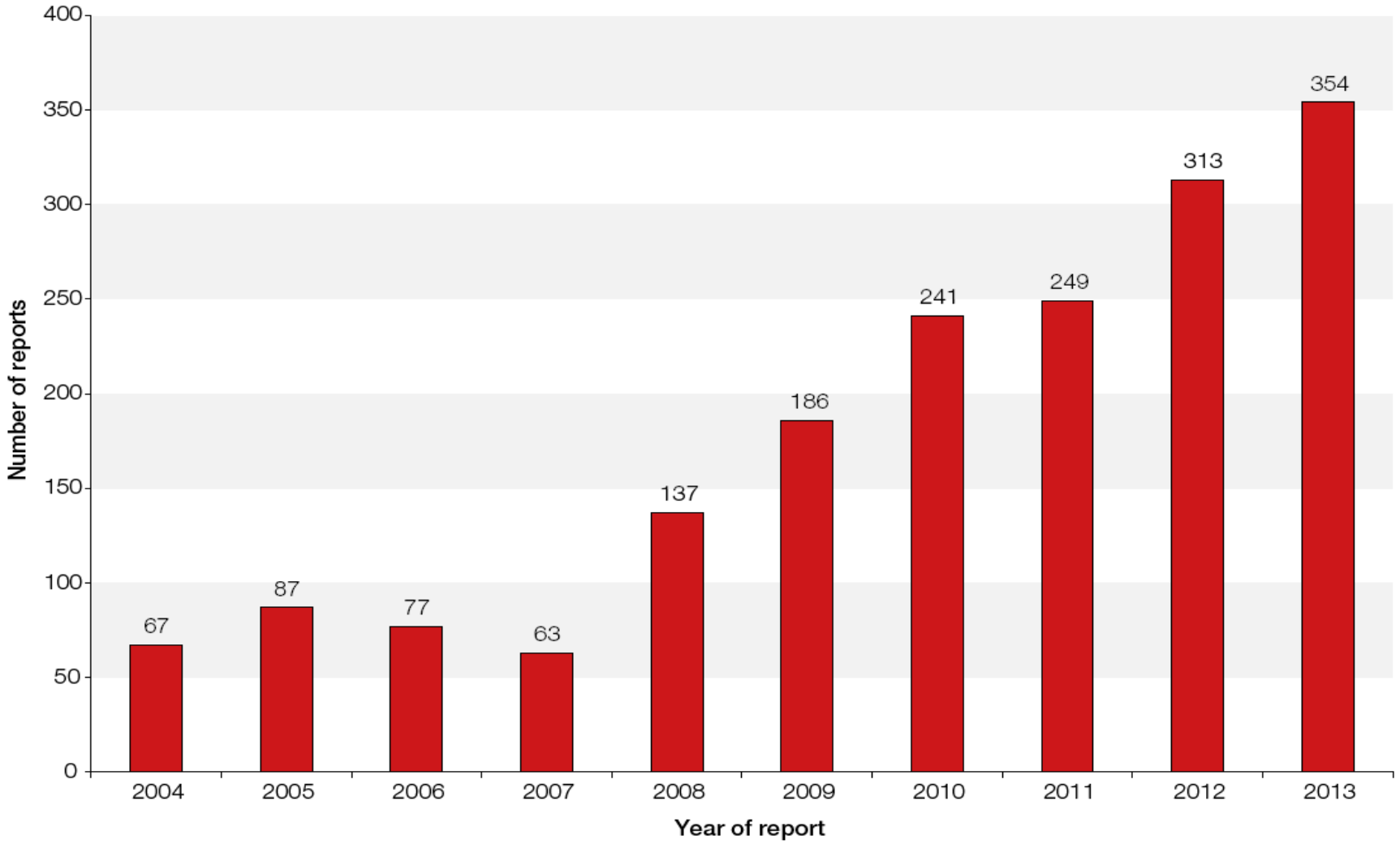
SHOT cumulative data 1996-2013



Anti-D Ig Reporting Categories

- Omission or late administration of anti-D immunoglobulin
- Inappropriate administration of anti-D immunoglobulin to:
  - a RhD positive woman
  - a woman who already has immune anti-D
  - a mother of a RhD negative infant (erroneously)
  - a different woman from the woman it was issued for
- Incorrect dose of anti-D Ig given
- Handling and storage errors
  - administration of expired, or otherwise out of temperature control, anti-D immunoglobulin

Trend in Anti-D Ig reports



Anti-D Ig reports in 2013 (n = 354)

- **59** cases where anti-D Ig was inappropriately administered - *unnecessary exposure to a human medicinal blood product*
- **277** cases where anti-D Ig was delayed or omitted, putting patient at risk of sensitisation to the D antigen - *potential Major Morbidity*
- **9** cases where the wrong dose of anti-D Ig was administered (usually too little)
- **9** handling and storage errors

System Failures from SHOT cases (1)

- **Communication**
  - Lack of comms between hospital midwifery teams and those in the community – failure of RAADP in the community noted in 63 cases
- **Assumption / 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)

- **Lack of knowledge or training**
  - Failure of lab staff to consider the need to issue anti-D Ig when giving RhD positive platelets to RhD negative patients of child-bearing potential
  - A lack of understanding behind the principles of anti-D Ig prophylaxis, compounded by availability of uncontrolled stocks held by clinics
  - Increasing trend in poor advice being offered to women by (relatively senior) medical staff
  - Decision making without reference to blood grouping results in both lab and clinical area
  - Misinterpretation of FMH (Kleihauer) tests in labs leading to dosing errors
  - Failure of inventory management in lab and clinical area, especially in the community

System Failures from SHOT cases (3)

- **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
  - Use of the Kleihauer Test to determine whether anti-D Ig should be given in the first place

York Teaching Hospital NHS
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Anti-D Administration Flowchart

SERIOUS HAZARDS OF TRANSFUSION SHOT

Always confirm;
- the woman's identity
- that the woman is RhD Negative using the latest available laboratory report
- that the woman does not have immune anti-D using the latest available laboratory report
- that a blood sample has been taken to confirm group & antibody screen, (but do not wait for results before administration of anti-D Ig)
- that informed consent for administration of anti-D Ig is recorded in notes
- product / dose / expiry and patient ID pre-administration

Potentially Sensitising Events (PSEs) during pregnancy

Gestation up to 13 completed weeks • Surgical procedure to manage an ectopic pregnancy or miscarriage **Regardless of Gestation** • Amniocentesis, chorionic villus biopsy /cordocentesis • Antepartum haemorrhage / PV bleeding • External cephalic version • Fall or abdominal trauma (sharp / blunt, open or closed) • Intrauterine death (at diagnosis and delivery) • *In-utero* therapeutic interventions (transfusion, surgery, insertion of shunts, laser)	**Gestation up to 13 completed weeks** Administer at least **250 units** anti-D Ig within 72 hours of event. No need for a Kleihauer **Gestation 13 completed weeks to 20 weeks** Administer at least **250 units** anti-D Ig within 72 hours of event. No need for a Kleihauer under 20 weeks **Gestation 20 weeks to term** Request a Kleihauer and administer at least **500 units** anti-D Ig within 72 hours of event.

Administer anti-D Ig for a PSE irrespective of whether RAADP has already been given

Does the Kleihauer indicate that further anti-D Ig is required ?	Administer more anti-D Ig following discussion with laboratory

Recurrent bleeding should be clinically reviewed by an Obstetrician for further anti-D requirements

Size of FMH	Dose of anti-D required
Less than 2mL	500 units
2.1 – 12mL	1500 units
Greater than 12mL	Specialist advice required

Routine Antenatal Anti-D Prophylaxis (RAADP)

For Routine Antenatal Anti-D Prophylaxis (**Irrespective** of whether anti-D Ig already given for PSE)	Take 28 week blood sample to confirm group & check antibodies Administer **1500 units** anti-D Ig at **28 – 30** weeks

At Delivery (or at diagnosis of Intra Uterine Death more than 20 weeks and at delivery)

Is the baby's group confirmed as RhD positive ? Or are cord samples not available ?	Request a Kleihauer and administer at least **500 units** anti-D Ig within 72 hours of event
Transfusion Laboratory staff will advise if further anti-D Ig is required	Administer more anti-D following discussion with laboratory
Has Cell Salvage been used ? Is the baby's group confirmed as RhD positive or are cord samples not available ?	Request a Kleihauer after re-infusion of red cells, inform Transfusion staff that cell salvage has been used and administer at least **1500 Units** anti-D Ig within 72 hours of event

- Your Trust policy can be a mixture of NICE and BCSH guidance, but BE CONSISTENT
- DO NOT wait for the result of a Kleihauer test before giving a standard dose of anti-D Ig
- If in doubt – GIVE IT

NHS Blood and Transplant

Anti-D
When and How Much?

This poster gives recommended dosages of anti-D immunoglobulin at different stages during pregnancy for women with an RhD negative blood type who do not already have immune anti-D antibodies.

At less than 12 weeks

- Anti-D is NOT usually indicated unless there has been therapeutic termination, molar or ectopic pregnancy, surgical intervention associated with miscarriage, or continued painful vaginal bleeding (request at least 250iu within 72 hours in these cases).

Between 12 and 20 weeks

- Administer at least 250iu anti-D Ig within 72 hours of a potentially sensitising event.

Between 20 weeks and delivery

- Administer at least 500iu anti-D Ig within 72 hours of a potentially sensitising event.
- Send a sample for a Kleihauer Test in case *additional* anti-D Ig is needed.
- *Anti-D Ig should be given for potentially sensitising events, even if RAADP has been given already.*

Routine Antenatal Anti-D Prophylaxis (RAADP) should be administered between 28 and 30 weeks

- Send a sample for blood group and antibody screen and then administer RAADP according to local policy, *even if anti-D Ig has been recently given for a sensitising event.*
- SINGLE DOSE: Administer 1,500iu anti-D Ig at 28-30 weeks.
- TWO-DOSE: Administer at least 500iu anti-D Ig at 28 and 34 weeks.

After delivery

- Send 'Mother & Cord' samples for testing.
- Where the baby is RhD positive, administer at least 500iu anti-D Ig within 72 hours of delivery.
- Administer further anti-D Ig on the advice of the laboratory if the Kleihauer shows a large fetomaternal haemorrhage.

For further information please refer to your local policy

British Committee for Standards in Haematology (BCSH) Guidelines for the use of prophylactic anti-D immunoglobulin 2006.

Royal College of Obstetricians and Gynaecologists (RCOG) Green Top Guideline No 22 The Use of Anti-D Immunoglobulin for Rhesus D Prophylaxis 2011.

BLC680.1 05/13

- If outside 72 hrs still give anti-D, as a dose up to 10 days may provide some protection

- Give RAADP **in addition** to prophylaxis for sensitising events, and *vice versa*

NHS
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ANTI-D QUICK FACTS

RAADP (Routine Antenatal Anti-D)

- Maternal blood sample for antibody check should always be taken at 28 weeks before giving Anti-D.
- If a woman has a PSE close to the date of her RAADP, both RAADP and Anti-D to treat the PSE should still be given.

Postnatal Care

- Only women who have an RhD positive baby will require Anti-D – Do not wait for the Kleihauer Test result before giving the standard dose.
- Some women may require more than one postnatal Anti-D injection.
- This depends on the results of the Kleihauer Test done on maternal samples taken at delivery.

Women who are already sensitised (have Anti-D antibodies)

- Women who have already made Anti-D or other antibodies must be referred to a Consultant Obstetrician as they may need specialised care.
- The Neonatal Team should be informed when any woman with Anti-D or other antibodies is admitted in labour.

IMPORTANT PATIENT INFORMATION

NHS
Blood and Transplant

Blood Groups and Red Cell Antibodies in Pregnancy

NHS
Blood and Transplant

HDN awareness

Reducing the impact of haemolytic disease of the (fetus and) newborn

Key Issues with Anti-D Ig

- Ignorance
- Failure to adhere to local protocol
- Failure to utilise IT systems properly / fully
- Late bookers
- Transfers of care
- Assumptions
- Failures of communication
- Failure to obtain valid consent for anti-D Ig

Anti-D Summary

- Effective anti-D prophylaxis is a *partnership* between the laboratory and the clinical area – *work together* to produce robust Trust guidelines, and follow them !

- Requests for anti-D should be driven by the clinicians, especially in early pregnancy

Thanks to;

- SHOT Team
- UK NEQAS
- Megan Rowley
- **YOU** for listening

www.shotuk.org