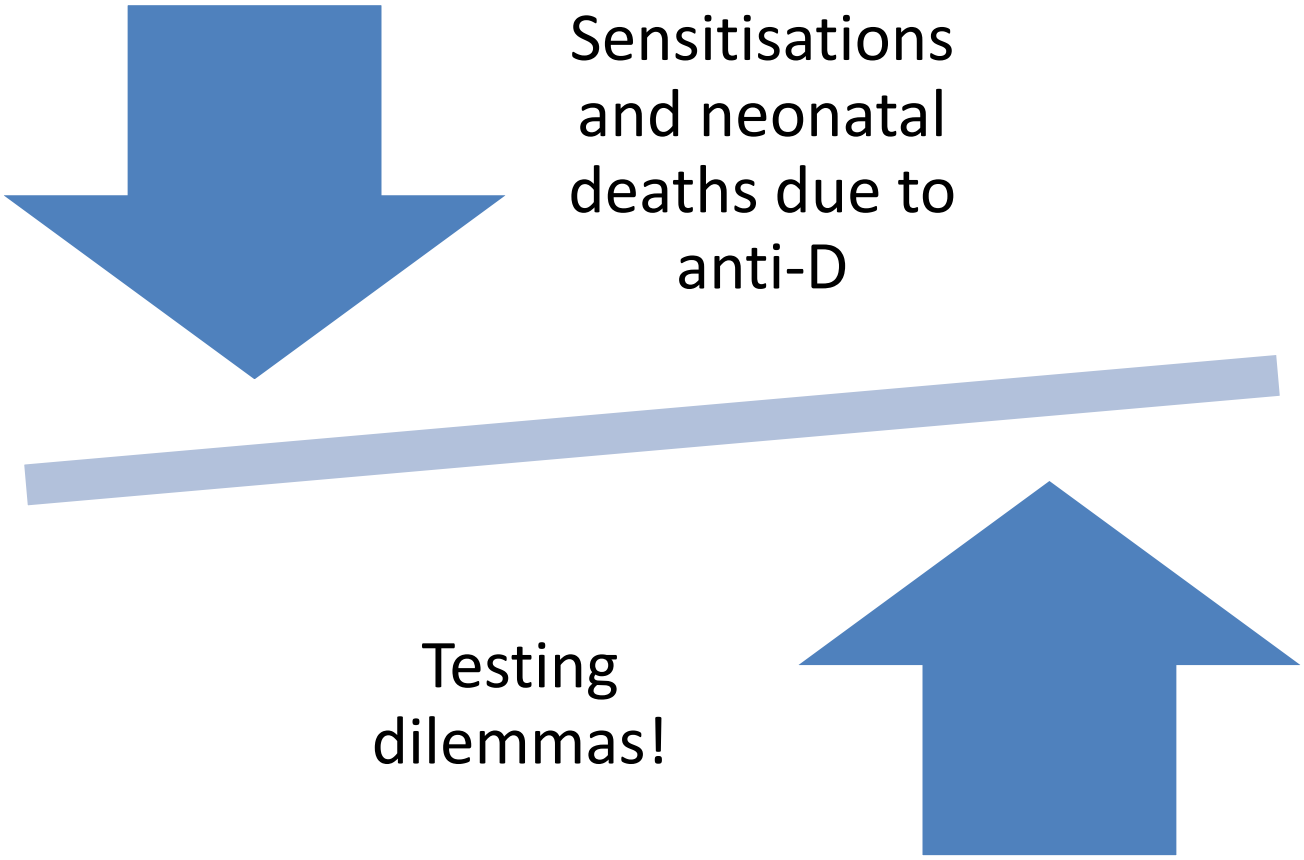
Immune or prophylactic anti-D – what do the new BCSH antenatal guidelines say?

Jenny White
Deputy Scheme Manager
UK NEQAS (BTLP)

RAADP at 28 (+/- 34 weeks)



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Effect of anti-D Ig on transfusion testing in pregnancy

- Antibody screening
  - Panel of D negative cells covering clin. sig. antigens
  - Not suitable for EI if blood required
    - Positive antibody screen
- Where anti-D identified - ?immune or passive

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Anti-D kinetics

- Immune anti-D detectable approx. 4 weeks after exposure to D+ cells, and reaches a peak concentration at 6-8 weeks

- Anti-D Ig peak concentration post i.m. at 3-7 days
- Pharmacokinetic study in pregnant women 1500IU anti-D Ig
  - iv was equivalent to 0.4IU/mL
  - im equivalent to 0.2 IU/mL
- Half-life of anti-D Ig is approx. 3 weeks
- Anti-D Ig rarely > 0.4 IU/mL unless >1500 IU given
- Detectable for 12 weeks & in *exceptional cases* several months

Anti-D Ig product and dose

NHS Blood and Transplant

What *product* is used for anti-D Ig prophylaxis?

Anti-D Ig products	BPL D-Gam	CSL Rhophylac
RAADP	41%	56%
Post delivery	68%	31%
PSE <20 weeks	86%	14%
PSE >20 weeks	69%	31%

What *dose* is used for anti-D Ig prophylaxis?

Dose anti-D Ig	250 IU	500 IU	1500 IU	Other
RAADP	-	3%	95%	2%
Post delivery	-	66%	33%	1%
PSE <20 weeks	71%	14%	13%	2%
PSE >20 weeks	(1%)	66%	32%	1%

Organisational questionnaire, 147 sites

HIGHER ANTI-D Ig DOSES THAN THE 'MINIMUM REQUIREMENT'

29% of maternity units use >250 IU for PSEs less than 20 weeks

32% of maternity units use >500 IU for PSEs after 20 weeks

33% of maternity units use >500 IU post delivery

Slide from Megan Rowley

Bottom line...

- Potential for >1500IU anti-D
  - 2010 NCA 14% RAADP given i.v.

- Cannot differentiate immune and prophylactic anti-D serologically

Risks

- Immune anti-D, assumed to be passive
  - Pregnancy not monitored appropriately, and chance of early intervention to prevent or reduce HDFN missed
- Passive anti-D Ig, assumed to be immune
  - Anti-D prophylaxis may be withheld, risking sensitisation to the D antigen, and HDFN

SHOT data 2011

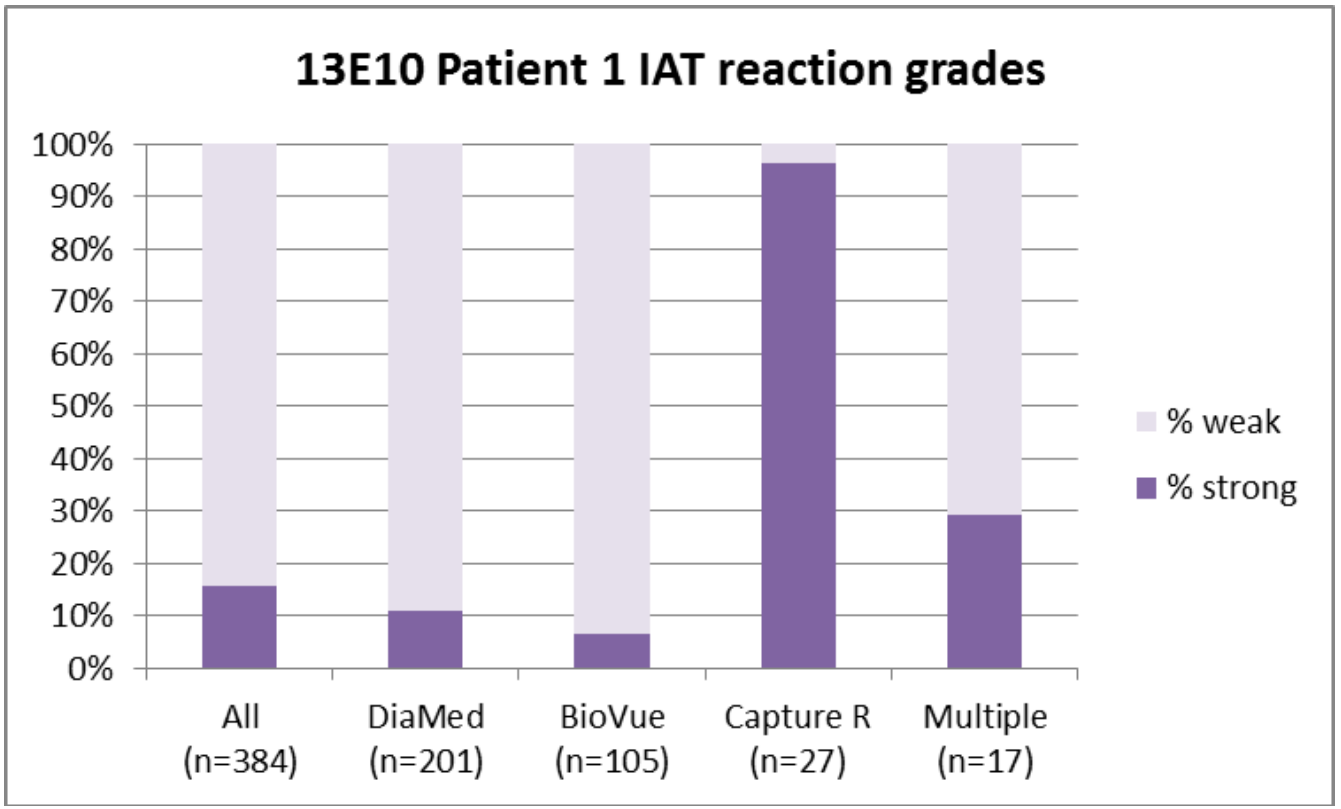
- 8 misinterpretations of immune anti-D as anti-D Ig
  - 1 weak antibody screen not followed up ? anti-D Ig
  - 7 cases no record of anti-D Ig having been administered
    - 1 a reference laboratory had already reported an immune anti-D

- Appropriate monitoring did not take place
  - 1 required an emergency intrauterine transfusion (IUT)
  - 2 neonates required top up post-delivery
  - 3 born with symptoms of HDFN but no Tx required
  - 2 unaffected

BCSH Antenatal guidelines 2007

- If record of anti-D Ig in past 8 weeks and the antibody reaction is weak, test as for non-sensitised women i.e. no antibody testing after 28 weeks and Rh prophylaxis should continue.
- If no record of anti-D Ig or information re prophylaxis, the antibody should be monitored by both IAT and anti-D quantification as for immunised women.
  - If the anti-D becomes undetectable by IAT and the quantified level is falling it is probably passive. A rising or steady level indicates immune anti-D.
- If there is significant doubt re immune or passive refer for quantification.
- Anti-D prophylaxis should continue unless it is established beyond doubt that the anti-D is immune.

13E10 UK NEQAS ‘standard’ anti-D



- Includes labs testing by a single technology (once or more than once) where the group includes at least 12 laboratories.

12E6 UK NEQAS screening reactions recorded (UK and ROI)

- P2 and P4 same pool of anti-c
- 20/390 (5%) variable reaction strengths
- 18 x 1 strong and 1 weak
- 2 x 1 weak and 1 negative

UK NEQAS

TRANSFUSION MEDICINE
Official Journal of the British Blood Transfusion Society
Transfusion Medicine | GUIDELINES

BCSH guideline for the use of anti-D immunoglobulin for the prevention of haemolytic disease of the fetus and newborn (Quereshi *et al*)

Transfusion Medicine, 2014, **24**, 8–20

- Regardless of any prior administration of anti-D Ig, any anti-D detected at 28 weeks should be quantified and the results made available in the maternity notes
- Further history should be obtained and investigations undertaken to establish whether this is immune or passive
- If no clear conclusion can be reached as to the origin of anti-D, then prophylaxis should continue to be administered in accordance with guidelines for D negative women who have not formed immune anti-D

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Anti-D Ig for PSEs

NHS Blood and Transplant

Potentially sensitising event	Cases	Correct dose	Correct time
Antepartum haemorrhage	438	92%	79%
Miscarriage & Stillbirth	278	92%	77%
Fall/trauma	198	91%	83%
Amniocentesis	49	88%	65%
External cephalic version	47	100%	92%
Amniocentesis	49	88%	65%
In-utero procedure	11	82%	46%
Total	1052	92%	79%

Slide from Megan Rowley

2013 Anti-D Ig Prophylaxis Audit

BCSH antenatal guidelines (2014 *in draft*) **History**

- All efforts should be made to determine whether anti-D Ig has been given and why, i.e. as RAADP or following a PSE, by asking the woman & seeking written confirmation in the notes.

BCSH antenatal guidelines (2014 ***in draft***) **Testing**

- Prediction re immune / passive anti-D should not be made on reaction strength as this can be unreliable

- All anti-D detected in pregnancy should be quantified, or tested by a method that has been extensively validated against quantification, e.g. using a titration score [Bruce *et al* 2013]).
- *(one exception - where detected for the first time immediately prior to delivery)*

BCSH antenatal guidelines (2014 *in draft*) **Exception**

- Anti-D detected (1st time) immediately pre-delivery
  - **No** quantification required as results unlikely to influence clinical decisions at this stage
  - Baby monitored for signs of HDFN. Maternal anti-D quantification may be performed at a later stage if deemed necessary.

Draft BCSH antenatal guidance 2014

If ***all*** of the following apply, then testing should be as for non-sensitised women

- there is a written record of administration of anti-D Ig in the preceding 8 weeks
- the antibody screen was negative prior to the administration of anti-D Ig
- the concentration of anti-D is <0.2 IU/mL .

UK NEQAS

Draft BCSH antenatal guidance 2014

If ***any*** of the following apply, then monitor as for immunised women

- there is no written record of anti-D Ig administration
- anti-D was present before the administration of anti-D Ig
- the concentration of anti-D is …..
  - *? Dependent on dose of anti-D Ig, ?timing, ?route of admin*
  - *? Set value*

UKNEQAS

If in doubt – continue anti-D prophylaxis! (common to all guidance)

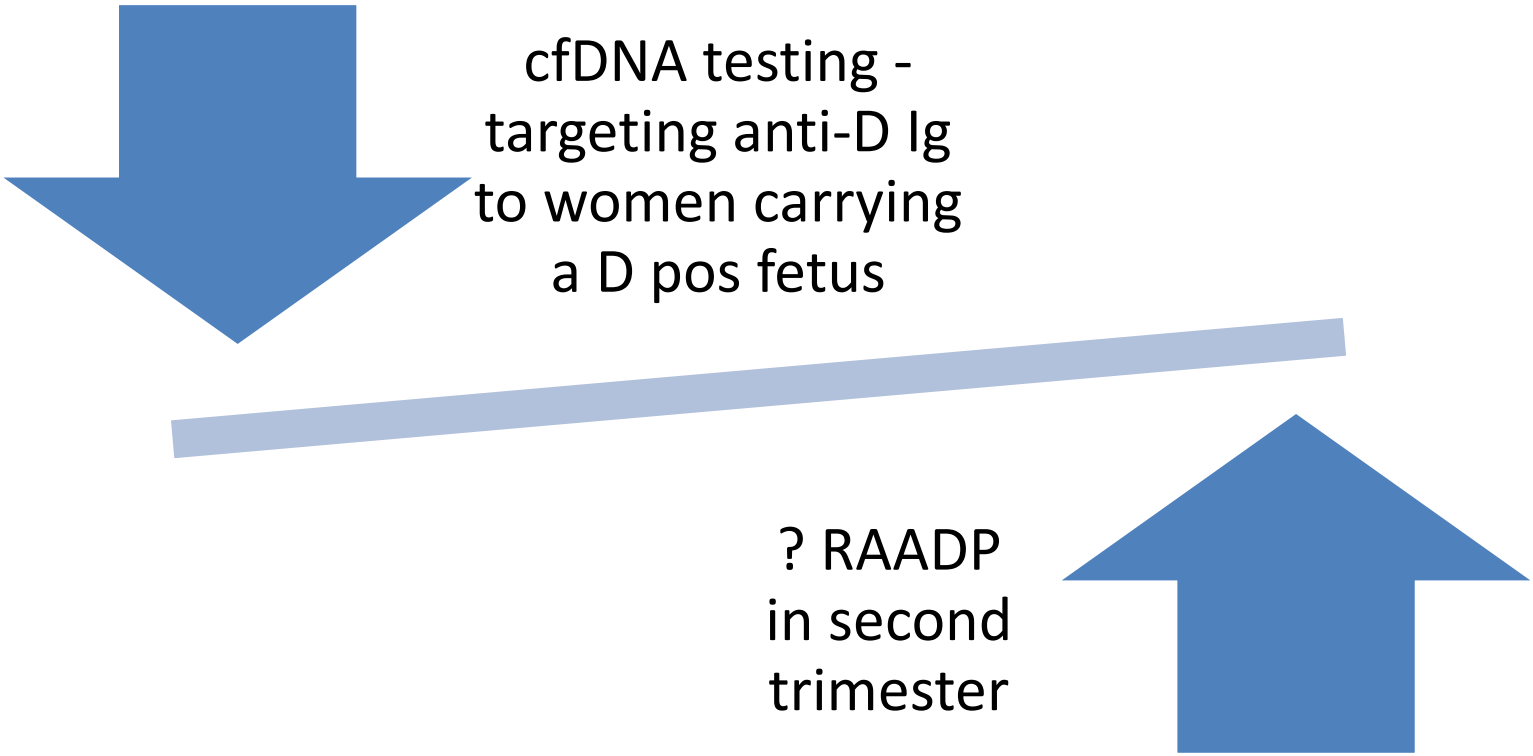
- Whilst the concentration of passive anti-D will fall with time, the concentration of immune anti-D will remain stable or rise if there is re-stimulation.

- Anti-D prophylaxis should continue to be offered as required for RAADP or PSEs, unless it is conclusively established that the anti-D is immune, in which case anti-D prophylaxis may be discontinued.

BCSH antenatal guidelines (2014 *in draft*) **Clinical context**

- The quantification results should be viewed in the context of the timing and dose of any anti-D Ig given previously, the reason for its administration, and the antibody status at the time of administration.
- The clinical history and knowledge of the results of previous laboratory testing are paramount in clinical decision making where anti-D is detected in pregnancy, and every effort should therefore be made to obtain this information.

Impact of future initiatives on immune or passive anti-D dilemma



Monoclonal anti-D Ig
? method developed to discriminate between this and immune anti-D

BCSH Antenatal guidelines

- To sounding board by end of Nov
- ? Published early 2015
- Writing group:
  - White J, Qureshi H, Massey E, Needs M, Byrne G, Daniels G, Allard S.